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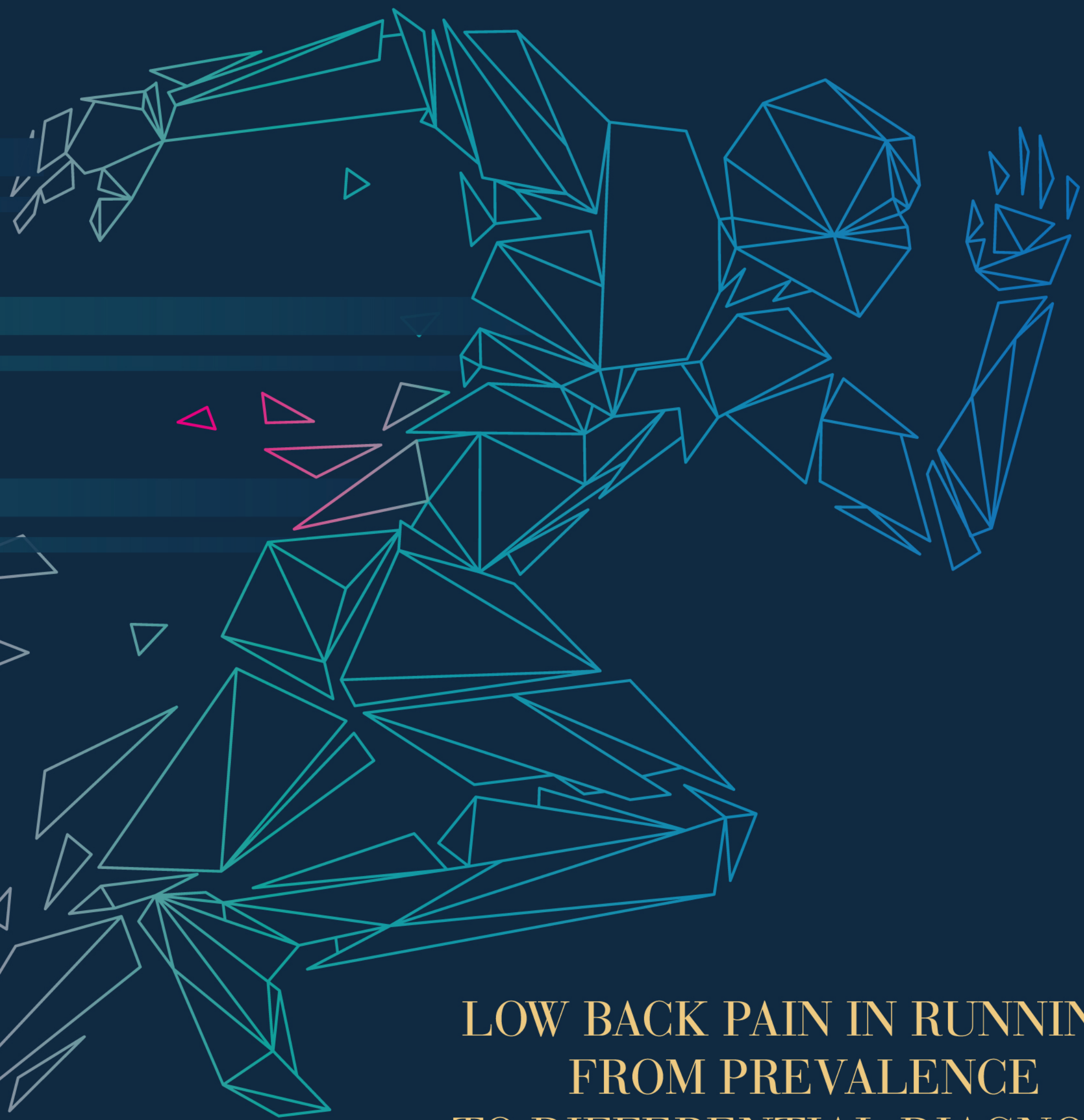

LOW BACK PAIN IN RUNNING: FROM PREVALENCE TO DIFFERENTIAL DIAGNOSIS

Filippo Maselli

Thesis submitted in fulfilment of the requirements for the
Doctoral Degree in Neuroscience

Curriculum: Motor and Sport Activity Sciences
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UNIVERSITY OF GENOVA

DEPARTMENT OF NEUROSCIENCE, REHABILITATION,

OPHTHALMOLOGY, GENETICS, MATERNAL AND CHILD HEALTH

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Promotor: DOTT. MARCO TESTA

Coordinator PhD: PROF. ANGELO SCHENONE

TO TAKE BIG STEPS, WE MUST NOT ONLY ACT,

BUT ALSO DREAM, NOT ONLY PLAN,

BUT ALSO BELIEVE.

(Anatole France, Paris, 1844 -1924)

To my Father

(3 Septmber 1943 – 3 June 2014)

Thanks to my family, my colleagues,

my best friends who sustained me during this PhD,

and to Patrizia who holds my hands showing me the best of life.

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CANDIDATE PROFILE

Filippo Maselli was born in Bari, Italy, February 5th, 1976.

He has a Bachelor's degree in Physiotherapy (2005), a Master's degree in Rehabilitation of Musculoskeletal Disorders (2007) and a Master's degree in Science Rehabilitation (2009).

He has been working as a physiotherapist since 2005 specializing in Rehabilitation of Musculoskeletal Disorders.

He is a lecturer of Methodology and Clinical Practice of the Thoracolumbar Spine in the Master's program of Rehabilitation of Musculoskeletal Disorders at Genova University and, he also lectures at Verona University: Bachelor's program of Manual Therapy in Physiotherapy.

His didactic, clinical and scientific interests concern the field of musculoskeletal rehabilitation, with special emphasis on:

- Running related injuries;
- lumbar spine disorders and its treatment (i.e spinal manipulation);
- differential diagnosis in physical therapy;
- development of student learning skills.

SCIENTIFIC ACTIVITIES: PHD (2016-2019)

Honours and Certifications

- **Elected** National President of the Gruppo di Terapia Manuale of Associazione Italiana Fisiotherapisti AIFI 2016-2019. The GTM is Italian Full Member of International of Orthopedic Manipulative Physical Therapy IFOMPT;
- **Re-Elected** National President of the Gruppo di Terapia Manuale of Associazione Italiana Fisiotherapisti AIFI 2019-2022. The GTM is Italian Full Member of International of Orthopedic Manipulative Physical Therapy IFOMPT;
- **Certification** in Vestibular Rehab Specialist by American Muscoloskeletal Institute (31/03/2019);
- **Peer Reviewer Certified** by Publons Academy (25/04/2018);
- **Certification** in Spinal Manipulative Therapy by Spinal Manipulation Institute (03/12/2017);
- **Diploma in Football Medicine** by The Fédération Internationale de Footbal Association FIFA (10/07/2017);

Articles

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- Pentassuglia D, Albertoni BD, **Maselli F,** Testa M "The Role Of Manual Therapy In The Lower And Upper Limb Lymphedema: Systematic Review. Poster Presentation At VII° Congresso Nazionale Sif: Linee Guida In Fisioterapia: Dalle Raccomandazioni Alla Pratica Clinica (20/10/2018 Milano);

Book Chapters

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Invited speaker: University Workshops

- L'utilizzo Della Manipolazione (Hvla) In Terapia Manuale: Dalle Migliori Evidenze Scientifiche Alla Sua Efficacia Clinica. (Università degli Studi di Brescia, 06/06/2017);
- La diagnosi differenziale in fisioterapia. (Università degli Studi di Brescia,

14/06/2018);

- Diagnosi differenziale in fisioterapia: una competenza core. (Università degli Studi di Salerno, 03/10/2018);
- Rehabilitation Advance in Shoulder Pain. (Università degli Studi di Salerno, 29/05/2019);

Invited speaker: Scientific Conferences

- La Diagnosi Differenziale in Fisioterapia. "Congresso Scientifico: La Diagnosi in Fisioterapia" AIFI Piemonte. (29/04/2017 Torino);
- Il Dolore Cronico in Riabilitazione. Congresso Regionale AIFI Puglia. (27/05/2017 Bari);
- Extremity manipulation: applications in sport. 2nd GISPT International Conference "Advances In Sport Rehabilitation: Clinical Reasoning And Practice". (17-18/06/ 2017 Roma);
- Recenti acquisizioni nella gestione dei disordini muscoloscheletrici del rachide. XV Congresso Nazionale GTM "Knowledge in Manual Therapy: Clinical practice meets the research". (23-24/09/2017 Brescia);
- Prevalence of Low Back Pain in Runners. "PTeX – Physical Therapy Excellence". (23/06/2018 Bologna);
- L'importanza della Diagnosi Differenziale attraverso i case report. "XVI Congresso Nazionale GTM – Differential Diagnosis in Physical Therapy: OMPT Core Competence ". (15/09/2018 Bari);
- Red Flag E Fratture Vertebrali: La Più Frequente Patologia Seria Nella Pratica Clinica Del Fisioterapista. 103° Congresso Nazionale SIOT Società Italiana Di Ortopedia E Traumatologia" – Section: Instabilità Articolare E

Fratture: Dall'intervento Riabilitativo Al Ritorno Alle Attività Sportive (9-12 Novembre 2018 Bari);

- La ricerca delle red flags nei disturbi dell'arto inferior. 55° Congresso Nazionale SIR Società Italiana Di Reumatologia " – La Ricerca Delle Red Flags Nei Disturbi Dell'arto Inferiore. SIR – Società Italiana Di Reumatologia. (23-24 Novembre 2018 Rimini);

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- Reviewer for Journal of Back and Musculoskeletal Rehabilitation;
- Reviewer for The Journal of Manual and Manipulative Therapy;
- Reviewer for The International Journal of Sports Medicine;
- Reviewer for The Journal of Sports Medicine and Physical Fitness;
- Reviewer for Journal of Orthopaedic and Sports Physical Therapy;
- Reviewer for BMJ Case Reports;
- Reviewer for Journal of Clinical Medicine;
- Reviewer for Journal of Patient Experience;
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FOREWORD

This PhD project represents the end point of my first 15-year journey in the world of physiotherapy. During the first fifteen of clinical practice I have always paid attention to the patients' care aimed at helping them to manage their ailments, their problems, their pains and their difficulties in performing out daily, working and sporting activities. This has led in recent years to bring me closer and deepen the world of back pain and such musculoskeletal disorder in sports and differential diagnosis, thus giving respects to those patients who presenting strange or dangerous symptoms and signs (e.g., alarm bells, red flags) which although rarely occurring, can have serious consequences for the patient, if not carefully evaluated.

The research conducted over the past three years has provided interesting insights into the beneficial relationship between running and the lumbar spine suggesting that it can be assumed to have a preventive role on the onset of back pain. In addition, the research offered understandings into the importance of the role of the physiotherapist in the management of low back pain among runners, and in the management of those suspicious cases that mimic only a non-specific musculoskeletal back pain. In fact, given the orientation of the new health systems, the freelance will be increasingly widespread in the national territory, with a progressive increase in patients who will turn to the physiotherapist, as a first contact health professional.

The research also helped improve my clinical reasoning and experience. The results of the project leave the door open to future studies and didactic activities concerning the correlation between lumbar spine, back pain and running and the ability of physiotherapists to develop increasingly advanced skills in differential diagnosis.

Heartfelt thanks to my mentor Marco Testa for helping and guiding me during the realization of this PhD project.

I'm grateful to my friend and colleague Dr. PhD Giacomo Rossettini for his support. His continuous inspiration to strive for excellence has been an example and source of motivation for my research and personal growth.

Special gratitude goes to my colleagues and friends Antonello Viceconti, Lorenzo Storari, Valerio Barbari, Tommaso Geri, Marco Minacci, Firas Mourad, Aldo Ciuro, Simone Cecchetto, Denis Pennella, Fabio Cataldi, Fabrizio Brindisino, Michael Palladino, Elisa Floriani, Silvia Gianola, Andrea Colombi, Mattia Bisconti, Mattia Salomon, Claudio Ceccarelli, Luigi Di Filippo, Diego Ristori, Graziano Mitaritonda and Andrea Turolla for their constructive feedback, which allowed me to compare and contrast my ideas with different viewpoints.

Finally, I would like to thank all the researchers and professor who have supported me during my PhD: Prof. Catherine C. Goodman, Prof. John Duane Heick.

CHAPTER I

GENERAL INTRODUCTION

A brief overview on running and its benefits

For many years it has been known how physical activity and fitness promote health and well-being among people of all ages [1-3]. A large number of evidences support the theories that physical activity produces several impacting health benefits [4]. The British Association of Sports and Exercise published, in 2010 [5], the evidence-based "ABC" recommendations defining the minimum amounts of associated physical activity leading to health and well-being effects [5].

"ABC" confirms that healthy adults aged 18 to 65 should perform at least 150 minutes of moderate intensity aerobic activity per week, or at least 75 minutes of higher intensity aerobic activity per week [5]. Moderate intensity activities are defined as those where heart rate and breathing increase, but it is still possible to speak quietly. The most intense activities are aerobic exercises in which the heart rate is even higher, breathing is heavier, but speaking fluently is much more difficult [5]. Although many sports provide the aerobic activity goals recommended in the ABC of the British Association of Sports and Exercise, running seems to be the best and more accessible: it can be done alone or in company, at any time of the day or year, it can be done everywhere and very expensive equipment is not required (i.e. only sports clothing and running shoes are sufficient) [5].

Running is one of the most practiced sports in the adult population worldwide, due to the sustainable cost of technical materials impacting significantly on health [6-14].

Indeed, more than 35 million people in the United States run for exercise or sport [15]. Running is also very popular in the Netherlands, in 2012, about 1,9 million Dutch citizens do run [16]. Moreover, Running is the third most common physical activity among Chilean population [17].

Although running has been very popular since the 1970s, only since 2000 the number of runners and running events have increased continuously [12,18,19].

This important growth seems to be related to an increase in female participation in running activities [12,20]. Another reason for this considerable growth is the increasing number of runners participating in specific events [21,22].

The benefits of running include weight control and prevention of chronic health disorders, such as the cardiovascular diseases, resulting in a general reduction of risk mortality [6-9]. The health benefits associated with running are well-documented, nevertheless the attention to lifestyle, diet, fitness and competitive athletics promoted by media in the last decade, led to a drastic increase of the levels of physical activity and interest in both competitive and recreational running, even in subjects without an appropriate knowledge on training methodology [8-11]. The evidence suggests, therefore, that running is one of the most effective ways to achieve a good state of health and fitness [12].

That is, running is very popular, the number of runners is still constantly growing, and runners run more and more often [16]. Since running is an ideal aerobic activity for health and well-being [4], it can be used for both prevention (e.g. heart disease and obesity [5]), and as a therapeutic intervention (e.g.

improvement of the metabolic control of subjects with established type-2 diabetes and reduction of blood pressure [4]).

Running-Related Injury

Although evidence suggests that running is one of the most effective ways to achieve a good state of health [12], recent studies show that a major drawback of running is the relatively high risk of associated injuries [13,14]. That is, Injury incidence rates has been reported between 20% and 79% [6]. The rate of prevalence of Running-Related Injuries (RRIs) among middle and long-distance runners has been reported to range between 19% and 92% [7,20-27]. Additionally, several studies reported that 11%-85% of recreational runners have at least one RRIs each year [13], resulting in a reduction or interruption of training in 30% to 90% of runners [14,28,29]. Notably, injuries increase costs because of medical treatments [16].

In a recent survey on sports injuries conducted in the Netherlands over a third of injured runners sought for medical treatment [16]. The majority of runners were managed by a physiotherapist, with a total number of 600 thousand treatments and an estimated expense of €21 million per year [16]. In few cases, runners went to the emergency department [16]. In total, 2100 runners visited an emergency department for an injury sustained during running [16].

The direct health costs per injured runner treated in the emergency department were estimated at €1300, with a total of €2.9 million [16]. The musculoskeletal injuries, on average, were considerably more expensive (€1100) than slight superficial injuries (€700) and sprains (€800) [16]. Moreover, in 2012, the cost of work absenteeism for runners who were treated for an RRI at an emergency department was on average €5400 per RRI, with a total of €5.4 million [16]. Therefore, the burden of running injuries on their costs for treatment and the absenteeism are high [16].

However, the discrepancies among studies limit the comparison of data due to the runners population, follow-up, study design, aetiology and RRIs definition heterogeneity [6,7,23-27,30-34].

In 2015, an international consensus [27] defined the RRIs as musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running, causing a total restriction or interruption of running for at least seven or more days and requiring medical/therapeutic assistance [27]. Although, RRIs encompass injuries affecting primarily the lower limb, pelvis and lumbar spine [25,34,35], a definition of RRIs is not fully shared because the difficulty in analysing the studies on RRIs [25].

Etiology of Running-Related Injury

Essentially, in runners can be classified into 2 major categories: acute injuries and overuse injuries [36,37]. Acute RRIs are rare, consisting mainly of muscle injuries, sprain, or skin lesions (e.g. blisters, abrasions) [36]. On the other hand, almost 80% of RRIs are due to overuse, are more insidious and usually develop over time resulting from an imbalance between the resistance capacity of connective tissue and the biomechanical load [36,37]. This imbalance occurs when a structure is exposed to repetitive forces, each of them below the lesion threshold of a structure that produce a cumulative fatigue effect over time that is beyond the loadability of the specific structure [37].

Running injuries have a multifactorial origin; according to the Comprehensive Model for Injury Causation [38] and the Conceptual Model for the Determinants of RRIs [39], the interplay between intrinsic or personal and extrinsic or running/training factors is responsible for the increased risk of running injuries. Intrinsic factors are hardly or not modifiable; they include gender, age, weight, BMI, history of previous injury, physical fitness; psychological factors also have been found to predispose runners to injury. Otherwise, extrinsic factors are modifiable, and comprise training volume, (e.g., weekly trainings frequency) running surface or other characteristics, as sport equipment and training environment, which increase runner's susceptibility to injury [29,30,40]. All these factors interacting with each other and their influence may also be mediated by cultural or social factors [41].

Due to the potentially high risk of being injured and its consequences on time-to-recovery and socio-economic costs, RRIs are an important public health issue. That is, RRIs prevention research approaches and strategies should be prioritized [33,42-46].

Therefore, in order to reduce the risk of injury, it is important to understand the causal factors and etiological mechanisms [47]. It is known that the nature of RRIs has a complex multifactorial origin [24,39]. Great efforts have been made by the sports medicine research community to shed light on the aetiology of RRIs [33,48]. The identification of risk factors for injuries could assist in identifying certain runners who may be at increased or decreased risk of developing an injury [49]. Furthermore, potentially effective injury prevention intervention strategies will have a greater chance to be effective if the identified etiologic factors are easily modifiable and consistent with a biologically plausible mechanism [47]. However, very few studies in the past 40 years examine the role of "effect-measure modification" on injury risk in order to analyse the association between a "participation-related exposure" and RRIs [50]. To facilitate future research, some authors, tried to build an evidence-informed conceptual framework outlining the multifactorial nature of RRIs aetiology [33]. The conceptual framework of running-related injury development consists of four parts [33]:

- (Part A) Structure-specific capacity when entering a running session;
- (Part B) structure-specific cumulative load per running session;
- (Part C) reduction in the structure-specific capacity during a running session;
- (Part D) exceeding the structure-specific capacity.

Therefore, RRIs occur from a combination of multiple risk factors and the aprtecipation in running-events under certain circumstances at a level where the loadability of the facility is exceeded [33].

Finally, the identification of risk factors may contribute to the development of injury prevention strategies and/or screening possibilities, especially when risk factors can be modified by adequate training, optimizing the training environment and using orthotics or modified footwear [12-14,33,47-49].

Low Back Pain as a Running-Related Injury: realty o myth?

In this paragraph the relationship between running and Low Back Pain (LBP) and their specific risk factors will be discussed.

As previously discussed, in 2015, an international consensus [27] defined the RRIs as musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running, causing a total restriction or interruption of running for at least seven or more days and requiring medical/therapeutic assistance [27]. RRIs therefore primarily affect joints of the lower limb, pelvis and lumbar spine [25,34,35], causing painful muscles, tendons and joints, often resulting in LBP [23-27,30-37].

Ninety% of the time LBP is defined as non-specific, because the patho-anatomical musculoskeletal causes are not clearly identifiable [51]. LBP is one of the most common worldwide health problems; that is, it is estimated that 80% of adults will experience LBP at some point in their life [52,53]. Although lots of literature has been published on the prevalence and incidence of LBP, there is still not a clear consensus regarding the actual epidemiologic impact in general population [54-57].

Similarly, a great number of athletes are affected by or experienced LBP [58]. Moreover, specific subgroups of sports such as ski, rowing, golf, volleyball, track and fields, swimming or gymnastics are at greater risk of LBP than non-athletes population [59-65].

Although several studies on the prevalence and incidence of LBP in general population and sports are available [52-57], it seems that this topic has not been clearly investigated in the runners.

Even though the lumbar spine was identified as the common sites for injury in runners [26,66], no conclusive data were published on the LBP among runners. Two studies reported that 10% of recreational distance runners experienced LBP during their first year of running [66,67]. Previous studies reported that variables such as gender, age, height, weight, BMI, leg-length discrepancy, hip flexion angles (female) and years of running experience may be risk factors for development of LBP [67-72]. Moreover, LBP in long distance runners may be a risk factor for future episodes of LBP [73]. That is, the risk of recurrent back injuries in athletes, including runners, with a previous history of LBP is increased by 3 to 6 times.

Few studies reported that runners between the ages of 30 and 50 years were at greater risk for LBP, compared to younger runners [74]. Other studies reported no difference in risk in runners between the ages of 20 and 27 and 50 and 57 years for LBP [75] The differences between the results of these studies could be due to the differences of other variables (e.g. demographic, gender, weight, physical/training, running speed, distance/week of running). Some researchers reported that increased body weight and Body Mass Index (BMI)>26 was a protective factor for running injuries including LBP [66]. Few evidences indicated that female runners with greater BMI were at greater risk for developing LBP [66,76].

In fact, in two recent studies reported that elevated BMI was associated with increased risk of running Injuries including LBP, in samples of 532 and 974 novice runners, respectively [77,78]. Previously studies suggested that runners with increased training volumes were at greater risk for RRIs including LBP [26,66,67,79]. In relation to height and mechanical stress, among the first studies that have measured stress on the lower back spine while running, Garbutt et al. [80], assumed that impacts absorbed by the back during running would affect the overall length of the spine [80]. The authors measured the height of the spine 3 times during running session of a marathon pace: after 15 minutes from the start, 30 minutes after, and post-workout session [80]. Although the study found a significant correlation between spinal height reduction, running speed and distance covered [80], the authors reported that LBP was independent from degree of spinal shrinkage [80]. These conclusions provide some evidence that the spine can bear the loads during running, even at high speeds [88]. Others authors suggested that running could have an anabolic effect on the intervertebral disc (IVD): such anabolic function could represent one of the multiple factors contributing to spinal pain in runners [81-83]. Belavý et al [83] reported that long-distance runners and joggers showed better hydration and glycosaminoglycan levels than the non-athletic individuals [83]. These finding reveal that in humans the IVD respond anabolically to certain types of loading, which may have some implications on spinal pain as well as IVD degeneration and herniation is one important contributing factor to spinal pain [84]. Although the data available on risk factors are not conclusive, they show that most of risk factors related to running were modifiable with specific treatments and training programs and they should be taken into account by physical therapists and/or trainer.

Risk factor for onset LBP on runners and differential diagnosis

The importance of considering and weighing each risk factor for onset LBP should be considered in the running population.

Previous studies reported that variables such as gender, age, height, weight, BMI, leg-length discrepancy, hip flexion angles (especially in women), years of running experience and being long distance runners may be risk factors for of LBP [67-73]. The data available on risk factors are weak and not conclusive, due to homogeneous definition of LBP was not adopted, populations investigated were different and risk factors for the onset of LBP are investigated by questionnaires that are exposed to recall bias. Furthermore there is a high risk of selection bias in the studies, in that persons with low back pain may not be able to run, increasing the rate of prevalence of LBP in general population. The scarcity and methodological weakness of the available studies invite to conduct further research about risk factors for LBP among runners.

Therefore this lack of studies on LBP as RRIs, is also reflected in the lack of studies that investigated physical therapists' point of view during the management of runners with LBP. Currently the management of runners with LBP does not seem very dissimilar to the management of non-runner with LBP [85-88]. For these reason, the research of my PhD also was oriented towards study of the important of differential diagnosis and screening for referral performed by physiotherapists when examine runners with unusual signs and symptoms that could mimic non-specific LBP. In that, clinicians have recently debated the reliance on the physical examination to determine the presence of a serious pathology. As most studies involving differential diagnosis are case reports, the evidence is lacking on a standardized screening approach to help physiotherapists during their clinical practice.

Finally, the researches were mainly focused on RRIs as a general concept but there are studies specifically addressing prevalence, incidence and risk factors for LBP in runners are lacking [14,25]. Moreover, no conclusive data were published on LBP specifically among the runners population.

That is, the current research showed that the following issues still remain unexplored:

- What is the real prevalence and incidence of LBP in running;
- How much really LBP impact Italian runners;

- What are the specific running-risk factors for the onset of LBP;

- Can LBP really be considered a RRI;

- Are there assumptions for defining LBP as a Running Related Disorder;

- How much Italian physiotherapists know about LBP in running;

- How much important is the differential diagnosis and screening for referral performed by physiotherapists when examine runners with unusual signs and symptoms that could mimic non-specific LBP.

General organization of the research project

The main goal of this PhD research project is to investigate the relevance of LBP in running, the specific risk factor for onset LBP on runners, the differential diagnosis in runners with LBP and the real impact of these data on therapeutic strategies to adopt in physiotherapy. Different studies were conducted during the 3-year period of PhD training (2016-2019).

The results, relative discussions and implications are reported in the following chapters of the present dissertation as follows:

- **Chapter I:** A brief overview on running and etiology of Running-Related Injury;
- **Chapter II:** Analysis of The Prevalence and The Incidence of Low Back Pain in running;
- **Chapter III:** The knowledge, attitude and behaviour of Italian physiotherapists specialized in manual therapy towards Low Back Pain as Related Running Injuries;
- **Chapter IV:** The prevalence, behaviours and risk factors of Low back pain about Italian runners;

- **Chapter V:** The Differential Diagnosis in Physical Therapy Practice, through two review:

  - The use of Red Flags in screening patients in physiotherapy. Narrative Review;

  - The diagnostic value of Red Flags in Thoracolumbar pain: A Systematic Review;

- **Chapter VI:** The study of Red Flags identification as an important step to Screening for Referral Process in runners with Low Back Pain through four Cases Reports;

- **Chapter VII:** General Discussion and Implication in physical therapy, and future research.

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CHAPTER II

PREVALENCE AND INCIDENCE OF LOW BACK PAIN AMONG RUNNERS: A SYSTEMATIC REVIEW

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Prevalence and incidence of low back pain among runners: A systematic review

Abstract

Background: Running is one of the most popular sports worldwide. Despite Low Back Pain (LBP) represents the most common musculoskeletal disorder in population and in sports, there is currently sparse evidence about prevalence, incidence and risk factors for LBP among runners. The aims of this systematic review were to investigate among runners: prevalence and incidence of LBP; and specific risk factors for the onset of LBP.

Methods: A systematic review has been conducted according to the guidelines of the PRISMA statement. The research was performed in PubMed, CINAHL, Google Scholar, Ovid, PsycINFO, PSYNDEX, Embase, SPORTDiscus, Scientific Electronic Library Online, Cochrane Library and Web of Science. The checklists of The Joanna Briggs Institute Critical Appraisal tools were used to investigate the risk of bias of the included studies.

Results: Nineteen papers were included and the interrater agreement was good (K=0.78; 0.61-0.80 IC 95%). Overall, low values of prevalence (ranging from 0,7% to 20,24%) and incidence (from 0.35% to 22%) of LBP among runners were reported. Most reported risk factors were: running for more than 6 years; body mass index>24; runner's height; not performing traditional aerobics activity weekly; restricted range of motion of hip flexion; difference between leg-length; poor hamstrings and back flexibility.

Conclusions: Prevalence and incidence of LBP among runners are low compared to the others Running Related Injuries and to general or athletes

population. View the low level of incidence and prevalence of LBP, running could be interpreted as a protective factor against the onset of LBP.

1. Background

Running is one of the most practiced sports in the adult population worldwide, due to the sustainable cost of technical materials and its great beneficial impacts on health [1-11]. The benefits of running include weight control and prevention of chronic health disorders, such as the cardiovascular diseases, resulting in a general reduction of mortality risk [1-6]. The health benefits associated with running are well-documented, nevertheless the attention to lifestyle, diet, fitness and competitive athletics promoted by media in the last decade, have led to a drastic increase of the levels of physical activity and interest in both competitive and recreational running, even in subjects without an appropriate knowledge on training methodology [3-8]. Although evidence suggests that running is one of the most effective ways to achieve a good state of health and fitness [9], recent studies indicate that it also involves a relatively high risk of associated injuries [10,11]. Several studies have reported that 11%-85% of recreational runners have at least one Running Related Injuries (RRIs) each year [10], resulting in a reduction or interruption of training in 30% to 90% of runners [11-13]. Acute RRIs are rare, almost 80% of RRIs are due to overuse, resulting from an imbalance between the resistance capacity of connective tissue and the biomechanical load of running [14,15]. The rate of prevalence of RRIs among middle and long-distance runners has been reported to range between 19% and 92% [2,16-20]. However, the discrepancies among studies limit the comparison of data due to the divergences in the type of runners studied, follow-up provided, study design, etiology and definition of RRIs [1,2,14-25]. In 2015, Yamato et al. [20] defined the RRIs as musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running, causing a total restriction or interruption of running for at least seven or more days and requiring therapeutic assistance [20]. Currently a definition of RRIs is not yet fully share, this is reflected in the difficulty of analyzing the studies about of RRIs [18]. RRIs therefore primarily affect joints of the lower limb, pelvis and lumbar spine [18,25,26], causing painful muscles, tendons and joints, often resulting in low back pain (LBP) [14-26]. It is frequent in clinical practice, that patients contact physical therapists for consultancy on LBP, which represents a common complaint of athletes [27-33]. In the 90% of the cases, LBP is defined as non-specific, because the patho-anatomical musculoskeletal causes are not clearly identifiable [34]. The LBP is one of the most common health problems in the world, that 80% of adults experience at some point in their life [35,36]. Despite many published studies on the prevalence and incidence of LBP, there is not a clear consensus regarding its actual epidemiologic impact [37-40]. Indeed, some studies reported a point prevalence estimate of LBP that ranged from 1.0% to 58.0% (mean 18,10%) [39,40]. One-year and lifetime prevalence of LBP, conducted throughout the world, ranged between 0.8%-82.5% (mean 38,10%) and 11.0-84.0% (mean 47,16%), respectively [39,40]. This great variability in prevalence rates may be due to, age of the sample, sample size, the authors definition and recall period of LBP, strategy of extracting data and methodology used.

As seen general population, a big amount of athletes also experience LBP [41]. Moreover, athletes of particular sport disciplines such as ski, rowing, golf, volleyball, track and fields, swimming or gymnastics are at greater risk of suffering from LBP than nonathletes population [33,42-47]. The incidence rates of low back pain in athletes have been reported up to 30% depending on the specific sport they are involved in [48]. However different studies exhibit also a great variability in prevalence rates, that have been reported in 66% for young athletes [49,50] to 88,5% % in elite athletes [51].

Despite several studies about the prevalence and incidence of LBP in general population and sports are retrievable [35-40], it seems that this topic has not been clearly investigated in the runners. Researches are mainly focused on RRIs in general but there are not Systematic Reviews (SRs) specifically addressing prevalence, incidence and risk factors for LBP in runners [11,18]. Moreover, earlier literature of LBP has been addressed to a wide range of sports or athletes [31,52] and no conclusive data were published peculiarly on the LBP among a specific population of runners. For this reason, the aims of this systematic review (SR) were to investigate among runners: 1) the prevalence and the incidence of LBP; and 2) specific risk factors for the onset of LBP.

2. Methods

2.1 Study Design and Protocol

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol was used to design the present SR [53]. This SR has been registered in PROSPERO database (number CRD42018102001).

2.2 Search Strategy

An electronic literature search was conducted between July 2018 to July 2019 in the following databases: PubMed, CINAHL (EBSCO), Google Scholar, Ovid, PsycINFO, PSYNDEX, Embase, SPORTDiscus, Scientific Electronic Library Online (SciELO), Cochrane Library and Web of Science. Research strategies were conducted and designed depending on the specific settings of each database with the supervision of an expert librarian. The research strings were developed according to the PICO model of clinical question (participants, interventions, comparison and outcomes). When possible MeSH (Medical Subject Headings) terms were used and combined with Boolean operators (AND, OR, NOT). Additionally, a manual research has been conducted through the bibliographies of all the assessed studies to obtain an integrative cross-references full-text selection. The full research strategy for some database is available in Appendix 1.

2.3 Eligibility Criteria

All the studies were conducted on runners without age limitation. We included any type of study design aiming to investigate prevalence, incidence and risk factors for LBP as RRIs (e.g. observational, cross-sectional, cross-sectional survey, prospective cohort, retrospective, case-control); moreover single cohort studies were also considered. We selected studies reporting at least one anatomical area included in LBP definition such as area located below the margin of the 12th rib and above inferior gluteal fold (included: pelvis/pelvis crest, sacrum and gluteus/buttock). We selected studies published in English or Italian language without limits of date of publication. Descriptive observational studies, such as case report and case series, and any study, which did not meet the inclusion criteria, were excluded

2.4 Study Selection

The selection and data collection process were done by two reviewers (FM and AC) under the supervision of a third author (MT). The whole records were screened by the management software for systematic reviews "Rayyan" [54], while references were managed by the "Mendeley" software [55]. After the removal of the duplicates, titles and abstracts were screened. Then, full-texts of the identified studies were obtained for further assessment and analyzed independently according to the eligibility criteria by two reviewers (FM and AC). Where appropriate, authors were contacted in order to obtain the full-text paper.

2.5 Data Collection

For each article the following data were extracted: study design; author, year of publication; the number and characteristics of participants/populations; international definition and/or any diagnostic criteria for LBP; analysis of the variables and the outcome of the studies; study settings/country (e.g. marathon, half-marathon, survey, lab analysis); prevalence and incidence rates; intervention and results; follow-up or study duration; theoretical perspectives on potential risk factors on the onset of LBP: reported risk factors; outcomes and measurements to associate the risks associated with the LBP (e.g. relative risk, odds ratio, etc.).

2.6 Quality Assessment

The Risk of Bias (RoB) of the included studies is analysed using the Joanna Briggs Institute Critical Appraisal tools [56] according to the specific study design (e.g., prevalence data, cross-sectional studies, case-control studies, prospective studies).

2.7 Agreement

Cohen's Kappa (K) was used to assess the interrater agreement between the two authors (FM, AC) for full-text selection (K=0.78; 0.61-0.80 IC 95%). Cohens' K was interpreted according to Altman’s definition: k<0.20 poor, 0.20<k<0.40 fair, 0.41<k<0.60 moderate, 0.61<k<0.80 good, 0.81<k<1.00 excellent [57].

2.8 Data Analysis

From each paper, we reported all the data related to the prevalence, incidence and risk factors for LBP. When needed, we estimated data on prevalence, incidence and risk factors using available data of the included articles. We reported the prevalence and incidence percentage in table form.

3. Results

3.1 Study selection process

The electronic database searches and the identification of additional references yielded 14575 records, including 3952 duplicates that were removed. After screening titles and abstracts, 10562 (including 2 full-text not available) records were excluded. Then, 61 potentially relevant papers were considered eligible for full-text assessment. Of these 61 studies, 19 articles were included in this SR for quality assessment, data extraction and analysis. The selection process is described in Figure 1 according to the PRISMA Statement [53]. Reasons for exclusions are reported in Table 1.

3.2 Characteristics of the included studies

Of the 19 articles included, 6 were cross-sectional studies [58-63], 3 were retrospective studies [64-66] and 10 were prospective studies [67-76]. They were all published in English, starting from 1981 [64] to 2019 [61,75]. Overall, follow-ups or study duration of these papers ranged from 6 weeks [71] to 2 years [74], while sample sizes varied from a minimum of 4059 to a maximum of 4380 participants [61]. All the characteristics of the studies are reported in Table 2.

3.3 Risk of Bias of the included studies

Most of the items of all the 4 RoB assessment tools used for the quality assessment were rated as low risk. For all the studies addressing prevalence data regardless of the study design [58-60,62,63,65,76], the items rated as unclear RoB were related to the sampling methods in 3 studies [58,60,65], while in one study the items rated as high risk [63]. More in depth in one study [63], another two items were rated as high risk, one regarding the reliability of the condition measurement and one regarding the validity of identification of the condition. For cross-sectional studies, the majority of studies had low and, less commonly, unclear RoB [58-63]. However, among them, in the study of Marti et al. [63], the item related to the criteria for inclusion was rated as high risk, likewise the item about the reliability of the condition measurement in the study of Chang et al. [62]. For retrospective studies [64-66] there was a low RoB across all the papers, apart from comparability of groups, matching of cases and controls, adoption of the same criteria for identification of case and controls and methods to measure the exposure in 3 studies [64-66], which were all rated as not applicable. Finally, for prospective studies [67-76], in 6 studies [68,70-73,76] items related to the similarity/recruitment of groups, methods of exposure were rated as not applicable. Also were judged as not applicable the items related to the time of follow up and loss to follow up in the study of Back et al. [67]. Moreover, in 3 studies [67,69,73] the item about strategies to address incomplete follow up was evaluated as not applicable, whereas the remaining items were commonly judged as low RoB. Details of the RoB of the included studies are presented in Table 3 to 6.

3.4 Summary of Results

Results about prevalence and incidence are reported in Table 7.

3.4.1 Prevalence of LBP

Eight [47-63,65,76] of the 19 included articles addressed prevalence of LBP among runners. Six were cross-sectional studies [58-63], one was a retrospective study [65] and one was a prospective study [76] The value of prevalence ranged from a minimum of 0,7% (point prevalence)61 and a maximum of 20,24% (lifetime) [59]. Point prevalence values were reported in two studies [58,61], five studies reported values of 1-year prevalence [60,61,63,65,76], and those about lifetime prevalence were two [58,59]. Only 1 study [61] addressed data for point and 1-year prevalence, with values of 0.7% and 13.5% respectively [61]. Also in the cross-sectional survey study of Woolf et al. [58], the point prevalence of LBP in runners was reported, and it was equal to 13,6%. The study of Marti et al. [63] reported a 1-year prevalence of LBP of 0.75%, but this value was calculated in a sample of all male runners, and it was referred only to the Grade III injuries (defined as full training involuntary interruption of running for at least two weeks duration). In the cross-sectional study of Teixeira et al. [60] the 1-year prevalence of LBP (including pain in the lumbar spine and pain in pelvic/sacral/gluteus regions) among elite marathon runners was 14%. In the retrospective descriptive study of Ellapen et al. [65] the 1-year prevalence of lower back (including hip) among recreational half-marathon runners was 14% (mean value; 13% for men, 15% for women). In the only prospective cohort study, Walter et al. [76], the 1-year prevalence of LBP among 1288 runners was 4.3%. The highest lifetime prevalence rates of LBP were reported to 20.24% in the cross-sectional study of Malliaropoulos et al. [59] in a sample of 40 ultra-trail runners. Furthermore, in another cross sectional study [62], the LBP lifetime prevalence was low, about 3.2% [62], in a sample of 893 subjects of which 80% of male runners [62].

3.4.2 Incidence of LBP

Twelve [64,66-76] of the 19 included articles addressed incidence of LBP among runners. Ten were prospective studies [67-76], and two were a retrospective study [64,66]. Overall, incidence of LBP among runners was low, findings ranged from a minimum of 0.35% (in 6 weeks) [71] and maximum value of 22% (in 1-year) [67]. The highest incidence rates of LBP was reported as equal to 22% (7 male; 3 female) in the prospective study of Bach et al. [67] in a sample of 45 runners. The minimal rate of incidence, below 1%, was found in the studies by Kluitenberg et al. [71] and Rasmussen et al. [66] with values of 0,35% and 0,49%, respectively. Furthermore, overall low incidence values, beneath 5%, were found in other six studies [64,68,70,72,73,75,76]. Among them, a value of 1,6% (in 13 weeks) was found in the prospective study of Tauton et al. [70] for the distribution of injuries in the lower back. A similar value of incidence was found in Walter et al. [76] 1,8%. In a more recent prospective cohort study of Dallinga et al. [75] an incidence rate of 1.9% (in 12 weeks) was found in a sample of recreational runners, during the training period for a running event. More in depth, the analysis of Van Der Worp et al. [72] showed a rate of 2.7% (in 12 weeks) in a sample of adult women runners. Moreover, the prospective cohort study of Von Rosen et al. [73] reported the incidence of injuries in the lower back of 2.8% of all injuries recorded between young female runners (mean age 17 years). In the study of Buist et al. [68], a value of 4,8% (in 8 weeks) was found, lastly, among a sample of novice runners, in runners with previous experience who have started running again and runners engaged in regular running. [68]. In the remaining two prospective cohort studies [69,74], the incidence rate of LBP was found to be slightly higher. Indeed, Lysholm et al. [69] reported a 1-years incidence equal to 5% among a small sample of 39 runners and in the recent study of Messier et al. [74] the incidence (in 2 years) of LBP among runners was 6%, considering the anatomical sites of back and pelvis. In the end, the retrospective analysis of Clement DB [64] among 1650 runners revealed similar findings: the two years-incidence of injuries localized in the lower back was 3.7% (3.3% for men and 4.3% for women).

3.4.3 Risk factors for LBP

The risk factors for the onset of LBP are reported in Table 8. Four studies [58,59,64,65] addressed specific risk factors for LBP in runners. Two of them were retrospective studies [64,65] and two were cross sectional studies [58,59]. The retrospective analysis of Clement et al. [64] indicated as possible risk factors for the development of non-specific back pain in runners leg-length discrepancy, poor hamstrings flexibility and poor back flexibility [64]. However, the authors did not specify the strength of the associations with LBP and the values of statistical significance. In another retrospective study (Ellapen et al.) [65] on recreational runners tightness of hip flexors and hip flexion angle measured both with the Thomas test and goniometer were defined as potential intrinsic factors predisposing to lower back/hip injuries. Indeed, the hip flexion angles of female runners who suffered lower back/hip musculoskeletal injuries, were significantly greater, than those of their non-injured runners ($p<0.01$) [65].

Moreover, the cross-sectional study of Malliaropoulos et al. [59] highlighted that having more than 6 years of experience of running could represent a predicting factor for getting injured in the lower back ($p = 0.012$) [59].

Lastly, Woolf et al. [58], in a cross sectional study conducted on a wide sample of runners, showed that runners who have previously suffered LBP reported greater shoe wear on either the inside or outside, while an equal shoe wear was less likely to relate a previous history of LBP ($p= 0.034$) [58].

In the same study [58], a previous history of LBP was reported by runners who did not use orthotics (such as insert, insole, heel, foot-bed, etc) ($p=0.011$), by who had a body mass index higher than 24 ($p<0.01$) and by who did not perform weekly traditional aerobics activity ($p<0.05$).

Moreover, again in the study of Woolf et al. [58], runners who did not regularly play contact sports (e.g. football, soccer, basketball, wrestling, boxing, rugby) were more likely ($p<0.04$) to have suffered LBP than those who do [58]. Current LBP was reported by high stature ($p<=0.02$) runners and by who perform a long time flexibility exercises routine before the training ($p<=0.05$) [58].

4. Discussion

The aim of this SR was to investigate the prevalence and incidence of LBP and to identify risk factors for the onset of LBP among runners. To the best of the authors' knowledge, this is the first SR addressing these outcomes in this specific population.

4.1 Prevalence and incidence of LBP

Despite running is one of the most practiced sports worldwide, and the prevalence rate of RRI is well documented in scientific literature [1-11], prevalence and incidence of LBP among runners are still unclear. The relatively low number of papers that we were able to include in the present review confirms the scarcity of literature on this topic.

Overall, the findings of this SR revealed that the LBP prevalence and incidence among runners, compared to the general population [35-40], were low. Indeed, in general population the point prevalence estimate of LBP ranged from 1.0% to 58.0% (mean 18,10%) [39,40] while in our review the point prevalence was reported to be in a range of 0,7% to 13,6%, however retrievable only in two studies. The one-year and lifetime prevalence of LBP, in world population, ranged between 0.8%-82.5% (mean 38,10%) and 11.0-84.0% (mean 47,16%), respectively [39,40], in our review the one-year and lifetime prevalence ranged between from 0,75% to 14% [60,61,63,65,76] and 3,2% [62] and 20,24% [59], respectively. The same considerations may be made for the incidence, indeed the 1-year incidence in general population was to 36.0% [39], while data emerging from our SR indicate that 1-year incidence ranges from 2,8%73 to 22% [67]. Moreover, it should be noted that the results of two studies reporting high prevalence (20.24% lifetime) [59], and high incidence (22% 1-year) [67], is probably depending from the very small [59,67] and the specific sample of 40 ultra-trail runners (that face with races taking place on mountain, desert, or forest and it includes uphill, downhill and is similar in duration to an ultra-marathon, that is beyond the distance of a regular marathon of 42.195 km) [59].

On usual running distance, it worths to underline that LBP prevalence in runners seems to be somehow independent from the running distance. In Besomi et al. [61] the largest sample (4380) within studies included in our SR, prevalence was assessed on a race of three difference distances (10, 21 and 42 km). The rate of prevalence in the 42 km-runners was similar (7,47%) to the rate among the 21 km-runners, (7,51%).

Moreover, the findings of this SR revealed that the LBP prevalence and incidence in runners, compared to prevalence and incidence of the other most relevant RRIs seems to be lower [2,10,11,16-20,74-80]. Indeed, the RRIs affecting lower limbs seem to have much greater prevalence rates, from 28% to 42% in the knee (i.e. patellar tendinopathy, iliotibial band syndrome, patellofemoral pain syndrome) and from 14% to 38% in the ankle (i.e. ankle sprain, achilles tendinopathy, plantar fasciopathy) [16-20,74-81].

Although prevalence and incidence of LBP appear low if compared to the general population, this conclusion should be taken cautiously. Indeed, out of the scarcity of available studies, there are many points in the included studies that weaken the generalizability of this statement.

Transversely to all the included studies, participants were heterogeneous for individual characteristics (age, gender), training level and previous injuries. Therefore, it is reasonable that various samples of populations (ex. young elite athletes or middle-aged recreational runners) may led to different prevalence or incidence rates. Furthermore, as reported in some prospective studies, not all the participants were exposed to the same running or training methods. In the cross-sectional survey study of Woolf et al. [58] for example, the rate of LBP point-prevalence, was calculated not only within experienced runners, but also between novice runners. Instead, in the study of Marti et al. [63] the 1-year prevalence of LBP, 0.75%, was estimated in a wide sample, 4358 runners, but constituted of only male runners; In the cross-sectional study of Teixeira et al. [60] which is the only one to report the IASP definition of pain [80], the prevalence of LBP was calculated among elite marathon runners who compete at international and/or national level and perform high volume of training, up to 160 km/week. In the cross-sectional study of Chang et al. [62] in a sample of 893 runners (mostly composed of male) although the lifetime prevalence rate was low, 3.2%, runners were not specifically asked if they had the symptom at the time of completing the questionnaire. Concerning the incidence, in the prospective study of Bach et al. [67] the highest rate of LBP (22%; 7 males, 3 females) was found within a small sample of 45 runners. In the two prospective cohort studies [72,73], the rate of incidence was assessed in samples made up exclusively of female runners and four studies evaluated incidence rates of LBP in only novice runners [70-72,75]. Clement et al. [64] was the only study that used the term "Non-specific lower back pain", as reported by the most recent literature [82,83] and only seven among the included studies [58,59,62,64,67,69,73], to define an injury affecting the lumbar spine, adopted specific terms such as low/lower back pain, LBP, Non specific lower back pain,.

4.2 Risk Factors

Only four studies addressed specific risk factors for the onset of LBP among runners [58,59,64,65] and great caution is required for translating their results to general practice being those studies two retrospective studies [64,65] and the two cross-sectional studies [58,59], that are not the best designs to assess risk factors. According to the Comprehensive Model for Injury Causation [84] and the Conceptual Model for the Determinants of RRIs [85], intrinsic and extrinsic factors are responsible for the increase of running injury risk. Intrinsic factors are hardly or not modifiable; they include gender, age, BMI, history of previous injury, physical fitness and psychological factor have been found to predispose runners to injury. Otherwise, extrinsic factors are modifiable, and comprise training volume or other characteristics, as sport equipment and training environment, which increase runner's susceptibility to injury. Intrinsic risk factors proposed for the onset of LBP among runners included: BMI≥24 [58]; runner's height [58]; tightness of hip flexors (measured by Thomas Test) [65] and hip flexion angles (only in female and measured by goniometer) [65]; but, as referred by the authors, there is no strong literature to explain this two last finding [65]. Moreover, the identification by Clement et al. [64] of physical impairments like reduced hamstring or back flexibility and leg length discrepancy was not supported by statistical evaluation. Even if the runners compared to non-runners seem to present significant lower degree of hip flexion with knee extended, indicating a tightness of hamstrings ($p<0.001$), nonetheless, no correlation was found between muscular tightness in runners and the incidence of LBP [67]. Due to the scarcity of available studies and the clinical impression that muscles tightness could be a risk factor for RRIs and LBP, this topic should be investigated in large samples using prospective design. The main extrinsic risk factors for the onset of LBP among runners were: high competitive level [59]; more than 6 years of experience in running [59]; some patterns of shoes' wear [58] and do not performing weekly aerobics activity [58]. Also in this case the findings extracted from the two selected papers [58,59] cannot be directly translated to the daily practice, but could only serve as possible additional elements to support the clinician in the interpretation of the athlete's condition. Indeed, the exposure to a single risk factor is often insufficient to produce an overuse injury: the RRI is the result of a number of superposing factors (like training increase, muscular impairments, unsuitable equipment, etc.) [61].

4.3 Consistency

There is a need of a standard and internationally acceptable definitions for LBP and a clearer definition and terminology of RRI. RRI is defined as an overuse injury due to an unbalance between the resistance capacity of connective tissue and the biomechanical solicitations of running [14,15]. Therefore, here the meaning of “injury” differs from usual meaning which is related to an acute trauma and, in a clinical perspective, very rare among runners [3,14,15].

In our view, a more suitable word may be “Disorder” (Running Related Disorders - RRDs) that better describes multifactorial conditions which include, beside structural aspect, also psychosocial elements often present in non-specific painful disorders like LBP [92-95].

Our SR confirmed, also for running, the findings of a recent SR [33] which concluded that the evidence about prevalence of LBP in athletes of some popular sports are scarce and derived from studies not of good methodological quality. This SR showed a quite high LBP prevalence among athletes, but this finding was relative to a wider sample of sports including volleyball, track and fields, swimming, golf, ski, gymnastics and rowing [33,42-47], not specifically including running.

4.4 Clinical Implications

Garbutt et al. [87] reported that although a significant correlation between spinal shrinkage, running speed and distance covered exists, it is not correlated to the onset or presence of LBP. Moreover, some studies suggested that running could have an anabolic role towards the intervertebral disc [89-91], among them Belavý et al. [90] reported that long-distance runners and joggers showed better hydration and glycosaminoglycan levels than the non-athletic individuals.

These findings, together with the low level of incidence and prevalence of LBP among runners, cautiously invite thinking running as a protective factor from LBP and to consider of prescribing running as a preventive exercise for LBP.

Although the data available on risk factors are weak and not conclusive, nevertheless most of proposed running related risk factors were modifiable by specific intervention and adapted training and they should be taken into consideration by physical therapists and trainers.

4.5 Implications for Research

More high-quality studies that analyse the prevalence and incidence of LBP in runners are needed before drawing strong and definitive conclusions. The actual prevalence and incidence of LBP in runners should be investigated by large cohort studies, adopting better definition of the clinical symptoms, rather than just pain distribution in anatomical districts. Moreover, a consensus on the definition of RRIs that consider the inclusion of psychosocial aspect and widens the usual pathoanatomic approach is advisable due the characteristics of conditions like LBP. Risk factors should be assessed by methodologically sound prospective studies on more homogeneous populations (in terms of demographic characteristics, training level of participants, gender, age, etc.).

4.6 Perspective

Running is one of the most practiced sports [1-11] and although evidence suggests that is one of the most effective ways to achieve a good state of health [9], recent studies indicate that it also involves a relatively high risk of injuries [10,11]. Currently a definition of RRIs is not yet fully share, this is reflected in the difficulty of analyzing the studies about of RRIs [18]. RRIs primarily affect joints of the lower limb and lumbar spine [18,25,26,86], causing painful muscles, tendons and joints, also resulting in LBP [14-26], but despite several studies about the prevalence and incidence of LBP in sports are retrievable [35-40], it seems that this topic has not been clearly investigated in the runners. Therefore, the etiology, prevalence and incidence of LBP as far as running-related injury are concerned, it is important to consider specifically how often the effectiveness of a given RRI prevention intervention is dependent on a easy modification of etiologic factors and on and their consistency with a biologically plausible causal mechanism [24]. Therefore, the investigation of how different factors affect the lumbar spine, in terms of structure-specific load and/or loadability, and the dose-response relationship between running participation and injury risk [24]. These considerations allow researchers to move beyond traditional risk factor identification. Just so, research findings could be reliable, not only in terms of the observed cause-effect association, but also translatable in clinical practice [24].

4.7 Review Limitation

This SR has several limits. Papers written in languages other than English or Italian were excluded and, due to the heterogeneity of the included studies were not possible to perform a meta-analysis. Moreover, a homogeneous definition of LBP was not adopted in all studies, populations investigated were different and prevalence, incidence or risk factors for the onset of LBP are investigated by questionnaires that are exposed to recall bias. Furthermore there is a high risk of selection bias in the studies, in that persons with low back pain may not be able to run, increasing the rate of prevalence of LBP in general population. Lastly, being unavailable a specific and validated assessment tool for retrospective studies, for the assessment of the methodological quality of the included studies was adopted the tool designed for case-control studies.

5. Conclusion

Despite the small number of included studies, the heterogeneity of the samples investigated and of running modalities did not allow to gain conclusive results, the prevalence and incidence of LBP among runners appear to be low if compared to the general population and to other RRIs. Most of the physical and training-related risk factors for the onset of LBP, even based on weak evidence, are potentially modifiable by a careful intervention of the clinician and should be considered when LBP prevention is sought.

5.1 Key points

• Prevalence and incidence of LBP among runners seem basically low if compared with general population and other popular sports activities

• Running could, cautiously, be considered a protective factors for the lumbar spine;

• Risk factors for the onset of LBP are generally physical impairments or training methods-related factors that could be partly modified and managed in clinical practice;

• Scarcity and methodological weakness of the available studies invite to conduct further research about actual prevalence and incidence as well as risk factors for LBP among runners

• LBP may be better defined as Running Related Disorder instead of Running Related Injury

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Table 1 - Excluded studies with motivations.				
N.	Author	Journal	Title	Reasons For Exclusion
1.	Sugisaki N, 2011	International Journal of Sport and Health Science	The Relationship between 30-m Sprint Running Time and Muscle Cross-sectional Areas of the Psoas Major and Lower Limb Muscles in Male College Short and Middle Distance Runners	Primary and secondary outcomes not evaluated
2.	Lee SP, 2018	Physical Therapy in Sport	Adaptations of lumbar biomechanics after four weeks of running training with minimalist footwear and technique guidance: Implications for running-related lower back pain	Primary and secondary outcomes not evaluated. The authors reported only that incorporating minimalist footwear and technique coaching into a runners' training may induce changes in lumbar biomechanics associated with reduced risk of running related LBP, without any statistical analysis
3.	Burrows M, 2003	British Journal of Sports Medicine	Physiological factors associated with low bone mineral density in female endurance runners	Primary and secondary outcomes not evaluated. This study analyze the BMD (bone mass index) of several body segments after physical exercises
4.	Cai C, 2015	Journal of Orthopaedic and Sports Physical Therapy	Low Back and Lower Limb Muscle Performance in Male and Female Recreational Runners with Chronic Low Back Pain	Primary and secondary outcomes not evaluated. This study evaluated some physical test such as muscular strength and length.
5.	Cole AJ, 1995	Journal of Back and Musculoskeletal Rehabilitation	Spine injuries in runners: A functional approach	Study design not relevant
6.	Villavicencio AT, 2006	Neurosurgical Focus	Back and neck pain in triathletes	The study population is triathlon athletes
7.	Oliveira RR, 2017	International Journal of Sports Physical Therapy	There are no biomechanical differences between runners classified by the functional movement screen	Primary and secondary outcomes not evaluated. This study evaluate the timing of TrA

				(transversus abdominis muscle) activation and the sit and reach test such as possible factors for LBP development
8.	Preece SJ, 2016	Gait & Posture	How do elite endurance runners alter movements of the spine and pelvis as running speed increases?	Primary and secondary outcomes not evaluated. This study analyze some cinematics parameters of the spine and pelvis without any consideration for LBP
9.	Sado N, 2017	Sports Biomechanics	The three-dimensional kinetic behaviour of the pelvic rotation in maximal sprint running	Primary and secondary outcomes not evaluated. This study analyze the lumbosacral cinematic to improve the sprint performance in running
10.	Schafer WE, 1985	Stress & Health	Life changes, stress, injury and illness in adult runners	LBP and LBP risk factors data not evaluated
11.	Seay JF, 2014	European Journal of Sport Science	Trunk bend and twist coordination is affected by low back pain status during running	This study analyzes the differences in trunk sagittal kinematics between 3 groups of runners, with current LBP, resolved LBP or controls. Data for LBP prevalence, incidence or risk factors not reported
12.	Tam N, 2018	Journal of Sports Sciences	Bone health in elite Kenyan runners	Primary and secondary outcomes not evaluated
13.	Lewis G, 2000	International SportMed Journal	The etiology and clinical features of low back pain in distance runners: a review	Full text not available and study design not relevant
14.	Hespanhol Junior LC, 2016	Scandinavian Journal of Medicine and Science in Sports	Health and economic burden of running-related injuries in runners training for an event: a prospective cohort study	Prevalence data for LBP not reported
15.	Franke TPC, 2019	Journal of Orthopaedic and Sports Physical Therapy	Running Themselves Into the Ground? Incidence,	This study groups the data for head,

			Prevalence, and Impact of Injury and Illness in Runners Preparing for a Half or Full Marathon	spine and trunk. For this reason is impossible to extract only LBP data
16.	Garbutt G, 1990	Medicine and Science in Sports and Exercise	Running speed and spinal shrinkage in runners with and without low back pain.	This study analyzes the spinal shrinkage in runners, without reporting data for incidence or prevalence of LBP. The only consideration of the authors about LBP is that low back pain is independent of the shrinkage induced by running
17.	Hamill J, 2009	Research in Sports Medicine	Lower Extremity Joint Stiffness in Runners with Low Back Pain	Primary and secondary outcomes not evaluated. This study evaluated the joint stiffness of hip, knee and ankle in runners with current LBP, resolved LBP and controls
18.	Winter SC, 2018	Journal of Physical Fitness, Medicine & Treatment in Sports	Centre of Mass Acceleration-Derived Variables Detects Differences between Runners of Different Abilities and Fatigue-Related Changes during a Long Distance Over ground Run	Primary and secondary outcomes not evaluated. This study evaluated the differences in running movements using a wireless accelerometers
19.	Winter SC, 2019	Research in Sports Medicine	Overuse injuries in runners of different abilities—a one-year prospective study	This study doesn’t provide the rate of incidence of injury for the single runners, but only the total amount of injuries for the groups of running level. The single anatomical site of injury for each runner was not included
20.	Kluitenberg B, 2013	BioMed Central	The NLstart2run study: health effects of a running promotion program in novice runners, design of a prospective cohort study	Study design not included
21.	Smits DW, 2018	Research in Sports Medicine	Validity of injury self-reports by novice runners: comparison with reports	This study examined the criterion validity of

			by sports medicine physicians	self-reported running related injuries, compared to an injury consultation by a sport medicine physician
22.	Tauton JE, 2002	British Journal of Sports Medicine	A retrospective case-control analysis of 2002 running injuries	This study evaluated the running-related injury in athletes of different sports such as cycling, swimming, weight-lifting, etc. who referred to had an injury during running activity
23.	Kluitenberg B, 2016	Journal of Science and Medicine in Sport	The NLstart2run study: training-related factors associated with running-related injuries in novice runners	Primary and secondary outcome not evaluated. This study analyzed the risk factors for running-related injury without referring to specific anatomical sites for each participant
24.	Wen DY, 2007	Current Sports Medicine Reports	Risk Factors for Overuse Injuries in Runners	Study design not included
25.	Damsted C, 2018	Journal of Orthopaedic and Sports Physical Therapy	Preparing for half-marathon: The association between changes in weekly running distance and running-related injuries – does it matter how the running is scheduled?	Primary and secondary outcomes not evaluated. This study evaluated only running-related injuries localized in the lower limb
26.	Nielsen RO, 2019	BMJ Open	The Garmin-RUNSAFE Running Health Study on the aetiology of runningrelated injuries: rationale and design of an 18-month prospective cohort study including runners worldwide	Study design not included
27.	Bertelsen ML, 2017	Scandinavian Journal of Medicine and Science in Sports	A framework for the etiology of running-related injuries	Study design not included
28.	Aggrawal ND, 1979	British Journal of Sports Medicine	A Study of changes in the spine in weight-lifters and other athletes	This study evaluated the spine complaints in weight-lifters and track and field athletes (data about specific runners or running related low

				back injuries in details were not provided)
29.	Noormohammadpour P, 2015	European Spine Journal	Low back pain status of female university students in relation to different sport activities	This study evaluated the LBP status in 9 sports, but not among runner (data about specific runners or running related low back injuries in details were not provided)
31.	Nielsen RO, 2013	Int J Phys Ther	Classifying running-related injuries based upon etiology, with emphasis on volume and pace.	Study design not included
32.	Jacobs S, 1989	Am J Sports Med	Injuries to runners: a study of entrants to a 10,000-meter race.	Primary and secondary outcomes not evaluated
33.	Ogon M, 1999	Foot Ankle Int	Does arch height affect impact loading at the lower back level in running?	Primary and secondary outcomes not evaluated
34.	Brill PA, 1995	Sports Med	The influence of running patterns on running injuries.	Study design not included
36.	Buist I, 2010	Am J Sports Med	Predictors of running-related injuries in novice runners enrolled in a systematic training program: a prospective cohort study.	Primary and secondary outcomes not evaluated
37.	Fredericson M, 2007	Sports Med	Epidemiology and aetiology of marathon running injuries.	Study design not included
38.	Lopes AD, 2011	J Physiother	Musculoskeletal pain is prevalent among recreational runners who are about to compete: an observational study of 1049 runners.	This study evaluated the spine complaints but data about specific LBP in details were not provided
39.	Kemler E, 2018	Phys Sportsmed	The relationship between the use of running applications and running-related injuries.	This study does not report specific data on the LBP
40.	Fokkema T, 2018	J Sci Med Sport	Prognosis and prognostic factors of running-related injuries in novice runners: a prospective cohort study.	This study does not report specific data on the LBP
41.	Linton L, 2018	J Sci Med Sport	Running with injury: a study of UK novice and recreational runners and factors associated with	This study does not report specific data on the LBP

			running related injury.	
42.	Scheer BV, 2011	Clin J Sport Med	“Al Andalus Ultra Trail”: an observation of medical interventions during a 219-km, 5-day ultramarathon stage race.	This study does not report specific data on the LBP

Table 2 Characteristics of the included studies.								
General informations (Author, years, study design, country)	**Title of the study** (Journal)	**Aims of the study**	**Population**	**Incidence or Prevalence**	**RRI definition**	**RUNNER definition**	**LBP (definition, characteristics, anatomical area)**	**Outcomes and outcome measures**
Bach KD et al, 1985 [67] **Prospective Cohort study** **USA**	A COMPARISON OF MUSCULAR TIGHTNESS IN RUNNERS AND NONRUNNERS AND THE RELATION OF MUSCULAR TIGHTNESS TO LOW BACK PAIN IN RUNNERS. (The Journal of Orthopaedic and Sports Physical Therapy)	To compare muscular tightness at the hip between runners and nonrunners, and to determine if there is a relation between muscular tightness and low back pain in runners.	N=45 Age= 18-43 years M=28 (19.4 years) F=17 (25.7 years) LBP=10 (M=7 F=3). Running experience >1 years	I=22% (1-year incidence)	Injury severe enough to temporarily give up the running activity.	Runners was defined according to the following criteria: individuals who run 18 or more miles per week, who run on a regular basis, and who have engaged in running for a minimum of 1 year	Low Back Pain	Goniometric range of motion measurements of three hip movements, abduction, flexion with the knee extended, and extension, were taken on two subject populations, runners, and non-runners, in order to determine tightness of the hip adductor, extensor, and flexor muscles, respectively.
Besomi M et al, 2019 [61] **Cross-sectional study** **Chile**	TRAINING VOLUME AND PREVIOUS INJURY AS ASSOCIATED FACTORS FOR RUNNING-RELATED INJURIES BY RACE DISTANCE: A CROSS-SECTIONAL STUDY. (Journal of Human Sport & Exercise)	To determine the relationship between weekly pre-competition running volume and the presence of running-related injuries (RRIs) by race distance.	N= 4380 Age =36 10km = 1316 21km = 2168 42km = 896 LBP= 31 (point prevalence); 307 (1-year overall prevalence; 77=10km; 163= 21km; 67= 42km) Running experience= <1 year = 704; 1-4 years= 2226; >4 years= 1450.	P= 13.5% (1-year prevalence); 0.7%(point prevalence)	A running-related injury was defined as “any injury to muscles, tendons, joints and/or bones caused by running. The injury had to be severe enough to cause or be expected to cause a reduction in distance, speed, duration, or frequency of running for at least 7 days. Conditions such as muscle soreness, blisters, and muscle cramps were not	Participants was defined as runners if have competed in one of the three SM running distances (10-21-42km)	Lower Back	

					considered as injuries".			
Buist I et al, 2008 [68] **Prospective cohort study** **Netherlands**	INCIDENCE AND RISK FACTORS OF RUNNING-RELATED INJURIES DURING PREPARATION FOR A 4-MILE RECREATIONAL RUNNING EVENT. (British Journal of Sports Medicine)	The purpose of this study is to determine the incidence of RRI and to identify sex-specific predictors of RRI among a group of novice and recreational runners training during an 8-week period for a 4-mile running event.	N=629 M=207 F=422 Age= 43.7 years Running experience= novice runners, runners with previous experience who have taken up running again or runners who were already engaged in regular running. LBP= 31	I= 4.8% (8 weeks)	A running-related injury was defined as any musculoskeletal pain of the lower limb or back causing a restriction in running (mileage, pace or duration) for at least 1 day.	The participants had to categorize themselves as novice runners, runners with previous experience who have taken up running again or runners who were already engaged in regular running. . The training program for novice runners started with ten 1-minute repetitions of running alternated by 1 minutes of walking. The training program for experienced runners started with 30 minutes of continuous running. The exposure time of running in the training program for novice and recreational runners varied, respectively, between 10–40 and 20–60	Back Lower Back Back	

						minutes per training.		
Chang W-L et al, 2012 [62] **Cross-sectional study** **Taiwan**	RUNNING INJURIES AND ASSOCIATED FACTORS IN PARTICIPANTS OF ING TAIPEI MARATHON. (Physical Therapy in Sports)	To investigate the distribution of lower extremity running injuries and their associated factors.	N=893 M= 714 (80%) F= 179 (20%) Age= 20-50 y full marathon group (38.8 11.6 years) 10 km group (33.6 9.8 years) Full marathon=127 (14.3%) ; Half marathon=337 (37.7%) ;10km= 429 (47.9%) Running experience: <1year = 179; 1-5years = 435; 5-10years = 130 ; >10 years = 146 LBP= 29; 8 (Full marathon); 11 (Half marathon); 10 (10km)	P= 3.2% (lifetime prevalence)	Questionnaire did not specifically ask the participants to identify if they currently had any symptoms. We would not know how many of the runners only had previous injuries or they also suffered from current injuries. The severity of the running symptoms was not defined in the questionnaire.	Regular running was defined as a minimum of 30 min running at least twice a week.	Lower Back Pain	
Clement DB et al, 1981 [64] **Retrospective survey** **Canada**	A SURVEY OF OVERUSE RUNNING INJURIES. (The Physician and Sportsmedicine)	To give an accurate indication of age and sex distributions, training mileage, etiological factors, and the incidence of specific disorders to physicians in sportsmedicine clinics.	N=1650 M= 987 (59.8%) F= 663 (40.2%) Age= 28.0 years Running experience= recreational runners LBP= 68 (M= 36 F= 32); Non-specific lower back pain= 54 M=27 F=27; Sciatica=10 M=10 F=3; Spondylolysis= 3 M=2 F=1; Spondylolisthesis=1 F=1;	I=3.7% (2 years)	Physician diagnosis of RRI	To be regarded as a runner, a patient had to be running at least 2 miles (3 km) three days a week at the time of injury.	Lower back injuries: Non-specific lower back pain; Sciatica; Spondylolysis; Spondylolisthesis	
Dallinga J et al, 2019 [75] **Prospective cohort study** **Netherlands**	INJURY INCIDENCE AND RISK FACTORS: A COHORT STUDY OF 706 8-KM OR 16-KM	To report (1) the injury incidence in recreational runners in preparation for a 8-km or 16-km	N= 706 M=375 F=331 Age= 43.9 years Running experience = novice and recreational runners	I=1.9% (protocol-event incidence, 12 weeks)	Every physical complaint that caused at least 1 week of training loss.	Participants was defined as runners if have competed at least in one of the two distances of the	Lower Back	OSTRC and questionnaire of running training and injury related to running

	RECREATIONAL RUNNERS. (BMJ Open Sport & Exercise Medicine)	running event and (2) which factors were associated with an increased injury risk.	LBP= 13 8km =128 16km= 521 both distances= 29			run (8-16km).		
Ellapen TJ et al, 2013 [65] **Retrospective descriptive study** **Africa**	COMMON RUNNING MUSCULOSKELETAL INJURIES AMONG RECREATIONAL HALF-MARATHON RUNNERS IN KWAZULU-NATAL. (The South African Journal of Sports Medicine)	To document the prevalence and nature of running-related musculoskeletal injuries among recreational half-marathon runners over a 12-month period (1 July 2011 - 31 June 2012).	N=200 M =120 F= 80 Age= 43.6 years Running experience= cohort regularly participated in half-marathons (21.1 km), with an average road-running history of 12.2 years. LBP= 28.	*P= 14% (overall 1-year prevalence) *P= 9% male *P= 10% female (* the data of prevalence are related to lower back/hip)	A sensation of distress or agony, and which prevented them from physical activity for a minimum of 24 hours	To be regarded as a runners, participants have to had run at least an half marathon (21.1 km)	Lower Back/Hip	
Kluitenberg B et al, 2015 [71] **Prospective cohort study** **Netherlands**	THE NLstart2run STUDY: INCIDENCE AND RISK FACTORS OF RUNNING-RELATED INJURIES IN NOVICE RUNNERS. (The Scandinavian Journal of Medicine & Science in Sports)	The purposes of the study were to assess the incidence of RRIs and to identify risk factors for RRIs in a large group of novice runners. In total,1696runnersofa6-weeksupervised“StarttoRun” program were included in the NLstart2run study.	N=1696 M= 364 F= 1332 Age= 43.3 years Running experience= novice runners LBP= 6	I= 0.35%	RRI was defined as a musculoskeletal complaint of the lower extremity or back that the participant attributed to running and hampered running ability for three consecutive training sessions at the same body part. Muscle soreness and blisters were not registered.		Pelvis/Sacrum/Buttock	
Lysholm J et al, 1987 [69] **Prospective cohort study** **Sweden**	INJURIES IN RUNNERS. (The American Journal of Sports Medicine)	To study injury-provoking factors in training and competition, and to compare differences in injury pattern between different groups runners.	N= 60 M= 39 F= 11 Age= Sprinters (20.6 ± 3.8), middle-distance runners (18.6 ±2.4), and long-distance/marathon runners (34.5 ± 7.4) Running experience= 4 years (sprinters) 3 years (middle	I= 5%	Any injuries that markedly hampered training or competition for at least 1 week were noted.	The participants have a previous experience of running training (7 hours per week or more).	Low Back Pain	

			distance) 5 years (long distance/marathon) LBP= 3						
Marti B et al, 1988 [63] **Cross-sectional survey** **Switzerland**	ON THE EPIDEMIOLOGY OF RUNNING INJURIES, THE 1984 BERN GRAND-PRIX STUDY (The American Journal of Sports Medicine)	- How frequent are jogging injuries in a representative population comparing all participants in a popular running event, and how often do such injuries lead to medical consultation and absence from work? - Is the incidence of jogging injuries related to behavior and/or characteristics of runners (training mileage, type of running shoes, age, number of years of training, etc.)? - What are the site and nature of the most common injuries? - Is there a relation between specific runner characteristics and specific running injuries?	N= 4358 M= 4358 Age = 35.0 years LBP= 30	P=0.75% overall 1-years LBP - Grade III injuries (2.2% lower back; 0.6% pelvic crest; 0.9% buttock)	Runners were asked to classify jogging injuries that had occurred during the previous 12 months according to their effect on running. Grade I injuries involved maintenance of full training activity in spite of symptoms; Grade II, a reduction of training activity, and Grade III, full training interruption, defined as involuntary complete interruption of running of at least two weeks' duration.			Lower Back Buttock Pelvic Crest	
Malliaropoulos N et al, 2015 [59] **Cross-sectional study** **Greece**	PREVALENCE OF INJURY IN ULTRA TRAIL RUNNING. (Human Movement)	The purpose of the study was to try to determine the prevalence of lower extremity and lower back	N=40 ultra-trail runners M= 36 F= 4 Age= 38.4 years (22-59)	P=42.5%	If symptoms were severe enough to forgo training for at least 1 day or causing them to quit a race.	According to the International Trail running Association, trail running takes place on various		Lower Back Lower Back Pain	

		musculoskeletal injuries in ultra-trail runners by considering injuries and related symptoms. Additionally, the predicting factors associated with these injuries were investigated in order to aid in the prevention and rehabilitation of trail running injuries.	Running experience= Level A= 13; Level B= 27; <6 years = 21; >6 years= 19 LBP= 17			natural terrain (mountain, desert, or forest) while minimizing running on paved or asphalt surfaces (no more than 20% of the total distance in competition). It can involve uphill, downhill, and horizontal trails and is similar in duration to an ultra-marathon , which is considered any race beyond the marathon distance of 42.195 km.		
Messier SP et al, 2018 [74] **Prospective cohort study** **USA**	A 2-YEAR PROSPECTIVE COHORT STUDY OF OVERUSE RUNNING INJURIES, THE RUNNERS AND INJURY LONGITUDINAL STUDY (TRAILS). (The American Journal of Sports Medicine)	To determine the risk factors that differentiate recreational runners who remain uninjured from those diagnosed with an overuse running injury during a 2-year observational period.	N= 300 M= 172 F= 128 Age= 41.15 Running experience= 11.2% LBP= 18	I= 6% (2 years)	Overuse running injuries were graded with the method defined by Marti et al: grade 1, maintained full activity in spite of symptoms; grade 2, reduced weekly mileage; and grade 3, interrupted all training for at least 2 weeks	Participants was defined as runners if they run a minimum of 5 miles per week.	Back	-Exercise Self-efficacy Scale (0, lowest self-efficacy; 100, highest self-efficacy)—which assesses beliefs in the ability to continue to run at one's training pace for periods of 1 to 8 weeks24. -12-Item Short Form Health Survey (SF-12) healthrelated quality-of-life survey (0, low; 100, high)—which measures perceived health (mental subscale) and functioning (physical subscale). -Satisfaction With Life Scale (5,

								extremely dissatisfied; 35, highly satisfied)—which assesses global judgment of life satisfaction. -Positive and Negative Affect Scale (PANAS) (10, very slightly; 50, extremely for each scale). -State-Trait Anxiety Inventory–S Scale (20, not at all; 80, very much)—which asks participants to report how they feel right now. -Visual analog scale for pain (0, no pain; 10, extreme pain).
Rasmussen CH et al, 2013 [66] **Retrospective cohort study** **Denmark**	WEEKLY RUNNING VOLUME AND RISK OF RUNNINGĒRELATED INJURIES AMONG MARATHON RUNNERS. (The International Journal of Sports Physical Therapy)	The purpose of this study was to investigate if the risk of injury declines with increasing weekly running volume before a marathon race	N= 662 M= 535 F= 127 Age= 41.4 Running experience= marathon runners: <2 years= 49; 2-5 years= 262; >5 years= 351; LBP= 3	I=0.49% point incidence	The running-related injury definition was modified based on the injury definition used by Macera et al; a running-related injury was defined as an injury to muscles, tendons, joints and/or bones caused by running; The injury had to be severe enough to cause or be expected to cause a reduction in distance, speed, duration, or frequency of running for at least 14 days. Conditions like muscle soreness, blisters, and muscle cramps were not considered as injuries.	Completion of the H.C. Andersen marathon	Lower Back	
Tauton JE et al, 2003 [70] **Prospective cohort study**	A PROSPECTIVE STUDY OF RUNNING INJURIES: THE VANCOUVER	To determine the injury pattern in a sample of the "In Training" clinics during their 13	N= 840 M= 205 F= 635 Age= 30-56 years Running experience= novice runners	I=1.6% Low back= 7% (4 men), =5% (10 women) - Hip/pelvis: =7% (4		-The novice group is primarily sedentary and deconditioned people interested	Low Back	

Canada	SUN RUN "IN TRAINING" CLINICS. (British Journal of Sports Medicine)	weeks program, and identify associated risk factors for injury.	LBP= 37	men), =10% (19 women)		in establishing a running program probably to improve health and fitness. The program for this group incorporates run/walk repeats that eventually lead to a continuous running session in the 12th week. -The intermediate program is designed for people who have completed the novice walk/run program and would like to increase their running endurance and intensity in a safe and effective way. Hill training, interval, and fartlek sessions are implemented.		
Teixeira RN et al, 2016 [60] **Cross-sectional study** **Brazil**	PREVALENCE OF MUSCULOSKELETAL PAIN IN MARATHON RUNNERS WHO COMPETE AT THE ELITE LEVEL. (The International Journal of Sports Physical Therapy)	The purpose of this research was to assess the prevalence, location and intensity of running related musculoskeletal pain over the previous 12 months in marathon runners who compete at the elite level and to verify whether certain training characteristics are	N= 199 M=164 F=35 Age= 34 (30-39) Running experience= marathon runners at elite level, on average of 11 years; LBP= 28 (Lumbar Spine 20; Pelvic/Sacral/Gluteus 8)	P=14.0% (1-year prevalence)		Runners who compete at the elite level, defined as those competing at international and/or national level; Their training is characterized by a high training volume, with weekly training loads of up to 160 km/week.	Lumbar Spine Pelvic/Sacral/Gluteus	VAS

		associated with musculoskeletal pain.						
van der Worp MP et al, 2016 [72] **Prospective cohort study** **Netherlands**	THE 5- OR 10-KM MARIKENLOOP RUN: A PROSPECTIVE STUDY OF THE ETIOLOGY OF RUNNING-RELATED INJURIES IN WOMEN. (Journal of Orthopaedic & Sports Physical Therapy)	To determine the incidence and characteristics (site and recurrence) of running-related injuries and to identify specific risk factors for running-related injuries.	N= 373 (5km=189; 10km= 184) F= 373 Age= 37.55 Running experience = novice runners LBP= 10 (4 Lower Back; 6 Buttock)	I= 2.7%	Defined as running-related pain of the lower back and/or the lower extremity that restricted running for at least 1 day.	Adult women (aged ≥ 18 years) who had signed up for the 'Marikenloop 2013' running event were eligible for inclusion. The 'Marikenloop' is a run over 5- or 10 km in Nijmegen, the Netherlands, and is a female-only event.	Lower Back Buttock	
Von Rosen P et al, 2017 [73] **Prospective cohort study** **Sweden**	ETIOLOGY OF RUNNING-RELATED INJURIES IN WOMEN. (The International Journal of Sports Physical Therapy)	The aims of this study were to describe the injury prevalence/incidence, severity grade, injury location, risk factors and the prevalence of illness in running (RU), orienteering (OR) and cross-country skiing athletes (CR).	N= 189 F= 189 Age= range 18-24 Running experience= elite athletes LBP= 5	I= 2.8%	As any physical complaint that affected participation in normal training or competition, led to reduced training volume, experience of pain or reduced performance in sports; * A substantial injury was defined as an injury leading to moderate or severe reductions in training volume, or moderate or severe reduction in performance, or complete inability to participate in sports; * A new injury was categorized as a recurrent or a non-recurrent injury, based on if the injury occurred in the same body site as the previous injury within the last year.		Low Back Pain Lower Back	OSTRC
Walter SD et al, 1989 [76]	The Ontario Cohort Study of Running-Related Injuries.	The purpose of this study was to investigate the	N= 1288 M= 985 F= 303 Age= 41.4	I=1.8% (point incidence) P=4.3% (1-year		All registered entrants to these events: 16-km (10-	Back Back	

Prospective cohort study **USA**	(Archives of Internal Medicine)	incidence and causes of running injuries.	Running experience= LBP= 23 new injuries; 56 old injuries	prevalence)		mile) race, 4-km (2.5-mile) fun run in St Catharines. 22.4-km (14mile) run and a four-member 5.6-km (3.5-mile) team relay in Burling ton were included.	Injuries	
Woolf S et al, 2002 [58] **Cross-sectional survey** **USA**	THE COOPER RIVER BRIDGE RUN OF LOW BACK PAIN IN RUNNERS AND WALKERS. (Journal of the Southern Orthopaedic Association)	The purpose of this study was to investigate the incidence, prevalence, and possible risk factors for LBP among a group of runners and walkers.	N= 436 M=227 F= 209 Age= 36.45 years Running experience= any kind of runner from novice to athletes LBP= 59	P=13.6% (point prevalence)			Low Back Pain LBP	

Table 3 Case Control Critical Appraisal			
	Clement DB. 1981 [64]	**Ellapen TJ. 2013** [65]	**Rasmussen CH. 2013** [66]
Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	Not applicable	Not applicable	Not applicable
Were cases and controls matched appropriately?	Not applicable	Not applicable	Not applicable
Were the same criteria used for identification of cases and controls?	Not applicable	Not applicable	Not applicable
Was exposure measured in a standard, valid and reliable way?	Unclear	Yes	Yes
Was exposure measured in the same way for cases and controls?	Not applicable	Not applicable	Not applicable
Were confounding factors identified?	Yes	Yes	Yes

Were strategies to deal with confounding factors stated?	Yes	Yes	Yes
Were outcomes assessed in a standard, valid and reliable way for cases and controls?	Yes	Yes	Yes
Was the exposure period of interest long enough to be meaningful?	Yes	Yes	Yes
Was appropriate statistical analysis used?	Unclear	Yes	Yes

Table 4 Cohort Critical appraisal										
	Dallinga J. 2019 [75]	**Bach DK. 1985** [67]	**Buist I. 2008** [68]	**Lysholm J. 1987** [69]	**Tauton JE. 2003** [70]	**Van der Worp MP. 2016** [72]	**Messier SP. 2018** [74]	**Kluitenberg B. 2015** [71]	**Von Rosen P. 2017** [73]	**Walter SD. 1989** [76]
Were the two groups similar and recruited from the same population?	Yes	Yes	Not applicable	Yes	Not applicable	Not applicable	Yes	Not applicable	Not applicable	Not applicable
Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Yes	Yes	Not applicable	Yes	Not applicable	Not applicable	Yes	Not applicable	Not applicable	Not applicable
Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Unclear
Were confounding factors identified?	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Were strategies to deal with confounding factors stated?	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Unclear	Yes	Unclear	Yes	Unclear	Unclear	Yes	Yes	Unclear	Unclear
Were the outcomes measured in a valid and reliable way?	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Yes	Not applicable	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Was follow up complete,	Yes	Not applicable	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

and if not, were the reasons to loss to follow up described and explored?										
Were strategies to address incomplete follow up utilized?	Yes	Not applicable	Yes	Not applicable	Unclear	No	Yes	Yes	Not applicable	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 5 Cross Sectional Critical Appraisal

	Chang W-L. 2012 [62]	**Malliaropoulos N. 2015** [59]	**Marti B. 1988** [63]	**Woolf S. 2002** [58]	**Teixeira R.N. 2016** [60]	**Besomi M., 2019** [61]
Were the criteria for inclusion in the sample clearly defined?	Yes	Yes	No	No	Yes	Yes
Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	Yes	Yes
Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes
Were objective, standard criteria used for measurement of the condition?	No	Yes	Yes	Yes	Yes	Yes
Were confounding factors identified?	Unclear	Yes	Yes	Yes	Yes	Yes
Were strategies to deal with confounding factors stated?	Unclear	Yes	Yes	Unclear	Yes	Yes
Were the outcomes measured in a valid and reliable way?	Unclear	Yes	Yes	Unclear	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes

Table 6 Prevalence Studies Critical Appraisal								
	Chang W-L. 2012 [62]	**Marti B. 1988** [63]	**Ellapen T.J. 2013** [65]	**Malliaropoulos N. 2015** [59]	**Walter SD. 1989** [76]	**Teixeira R.N. 2016** [60]	**Woolf S. 2002** [58]	**Besomi M. 2019** [61]
Was the sample frame appropriate to address the target population?	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Were study participants sampled in an appropriate way?	Yes	No	Unclear	Yes	Yes	Unclear	Unclear	Yes
Was the sample size adequate?	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes
Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the data analysis conducted with sufficient coverage of the identified sample?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were valid methods used for the identification of the condition?	Yes	No	Yes	Yes	Yes	Yes	Unclear	Yes
Was the condition measured in a standard, reliable way for all participants?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Was there appropriate statistical analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the response rate adequate, and if not, was the low response rate managed appropriately?	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes

Table 7 Results about prevalence and incidence of LBP									
Author, year	**Study design**	**Incidence**				**Prevalence**			
		lifetime	**1 year**	**point**	**other**	**lifetime**	**1 year**	**point**	**other**
Bach, 1985 [67]	Prospective Cohort		22%						
Besomi, 2019 [61]	Cross Sectional Survey						13.5%	0.7%	
Buist, 2008 [68]	Prospective Cohort				4.8% (protocol event: 8 weeks)				
Chang, 2012 [62]	Cross Sectional Survey					3.2%			
Clement, 1981 [64]	Retrospective Survey				3.7% (2 years)				
Dallinga, 2019 [75]	Prospective Cohort				1.9% (protocol event: 12 weeks)				
Ellapen, 2013 [65]	Retrospective Descriptive						14.0%		
Kluitenberg, 2015 [71]	Prospective Cohort				0.35% (protocol event: 6 weeks)				
Lysholm, 1987 [69]	Prospective Cohort		5%						
Marti, 1988 [63]	Cross Sectional Survey						0.75%		
Malliaropoulos, 2015 [59]	Cross Sectional					20,24%			
Messier, 2018 [74]	Prospective Cohort				6% (2 years)				
Rasmussen, 2013 [66]	Retrospective Cohort			0.49 %					
Tauton, 2003 [70]	Prospective Cohort				1.6% (protocol event: 13 weeks)				
Teixeira, 2016 [60]	Cross Sectional						14%		
Van der Worp, 2016 [72]	Prospective Cohort				2.7% (12 weeks)				
Von Rosen, 2017 [73]	Prospective Cohort		2.8 %						
Walter, 1989 [76]	Prospective Cohort			1.8%			4.3%		
Woolf, 2002 [58]	Cross Sectional Survey							13.6 %	

Table 8 Risk Factors for the onset LBP		
AUTHOR	**RISK FACTORS FOR LBP**	**P VALUE**
Clement DB et al (1981) [64]	- Leg-length discrepancy - Reduced hamstrings flexibility - Reduced back flexibility	/ / /
Ellapen TJ et al. (2013) [65]	- Hip flexion angles (female) -(Thomas Test + goniometer)	**$p<0.01$**
Malliaropoulos N et al. 2015 [59]	- > than 6 years of experience in running	**$P=0.012$**
Woolf S et al. (2002) [58]	- Equal wear of heels[1] - BMI ≥ 24[1] - Not performing Weekly aerobics activity[1] - Not Play in contact sports regularly[1] (i.e. football, soccer, basketball, wrestling, boxing, rugby - Not using orthotics + equal wear of heels[1] - Outside pattern of wear[a,1] - Running without Inside pattern of wear[2] - Physical height; - Flexibility exercises routine for a longer time before working out[2] - Not doing Traditional aerobics activity[2]	**$p=0.034$** **$p< 0.01$** **$p<0.05$** **$p<0.04$** **$p=0.011$** **$p=0.013$** **$p\leq0.02$** **$p\leq0.02$** **$p\leq0.05$** **$p<0.05$**
* higher credits as a sum of sex and age of the runner, difficulty level of previous races – positive height difference, the vertical climb index, and the distance in km – and performance.[1] Previous LBP; [a] Subgroup of runners without insert; [2]Current LBP;		

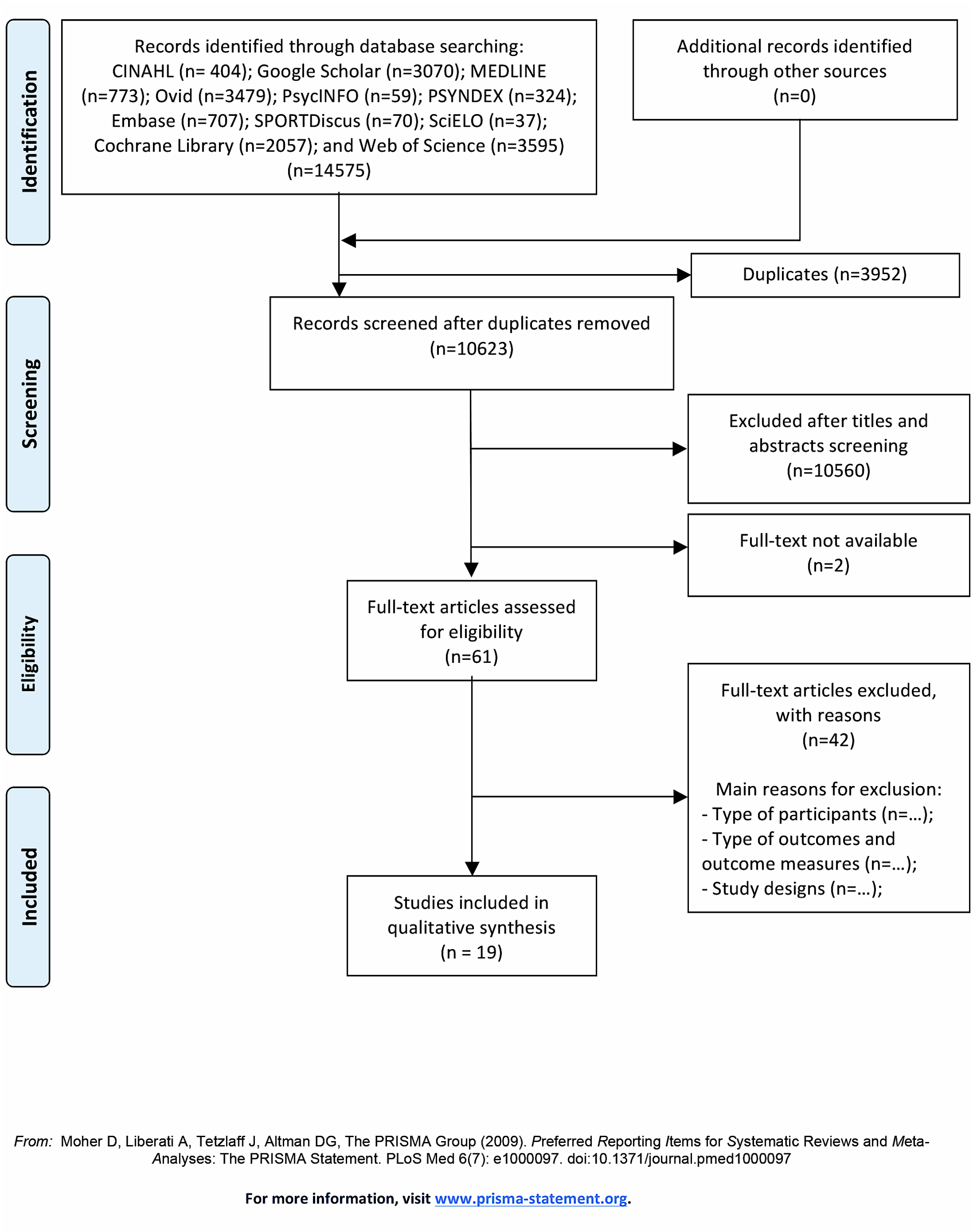

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Chart [53].

Appendix 1.

PsycINFO Keywords/MeSH
(DE "Athletes" OR DE "College Athletes" OR DE "Athletic Participation" OR DE "Athletic Performance" OR DE "Athletic Training") OR
DE "Physical Activity" OR DE "Actigraphy" OR DE "Exercise" OR DE "Aerobic Exercise" OR
(DE "Running") OR TX runn* OR
TX jogg*
(DE "Injuries")
#1 OR #2 OR #3 OR #4 OR #5
DE "Back Pain" OR
DE "Lumbar Spinal Cord" OR
TX back pain OR
TX lumb* N5 pain OR
TX back N5 disorder* OR
TX lumb* W1 pain OR
TX "SPONDYLOLISTHESIS" OR TX "SPONDYLOLYSIS" OR
TX lumbago OR
TX sciatica OR
TX dorsalgia OR
TX sciatic* N5 pain
#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
(DE "Epidemiology") OR (DE "Risk Factors")
TX prevalance OR TX incidence
TX risk factors
TX cross-sectional stud* OR
TX cohort stud* OR
TX longitudinal stud* OR
(DE "Prognosis")
#19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25
#6 AND #18 AND #27

SPORTDiscuss Keywords/MeSH
(DE "TRACK & field athletes") OR
(DE "ATHLETES") OR
(DE "RUNNING") OR (DE "RUNNERS (Sports)" OR DE "RUNNING" OR DE "RUNNING injuries" OR DE "RUNNING race training" OR DE "RUNNING races" OR DE "RUNNING techniques" OR DE "RUNNING training") OR
(DE "JOGGING" OR DE "JOGGING injuries" OR DE "JOGGING training")
(DE "Injuries")
#1 OR #2 OR #3 OR #4 OR #5
TX dorsalgia OR
TX lumb* W1 pain OR
TX back N5 disorder* OR
TX lumb* N5 pain OR
(DE "BACKACHE") OR TX "backache" OR
(DE "LUMBAR pain" OR DE "LUMBAR vertebrae" OR DE "LUMBAR vertebrae physiology" OR DE "LUMBOSACRAL region") OR
(DE "COCCYX") OR TX "coccydynia" OR
DE "SPONDYLOLISTHESIS" OR DE "SPONDYLOLYSIS" OR TX "SPONDYLOLISTHESIS" OR TX "SPONDYLOLYSIS" OR
DE "SCIATICA" OR TX "sciatica" OR
#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
DE "DISEASE prevalence" OR DE "DISEASE risk factors" OR DE "DISEASES" OR
(DE "EPIDEMIOLOGY") OR
DE "COHORT analysis" OR
TX cross-sectional stud* OR
TX cohort stud* OR
TX longitudinal stud* OR
(DE "Prognosis")
#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
#6 AND #17 AND #26

CINAHL Keywords/MeSH
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(MH "Athletes+") OR (TX athlet*)
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(MH "Extreme Sports") OR (MH "Triathlon")
(MH "Running+") OR "running" OR (MH "Running, Distance") OR (MH "Running Injuries+") OR (TX runn*) OR
#1 OR #2 OR #3 OR #4 OR #5
TX dorsalgia OR
TX lumb* W1 pain OR
TX back N5 disorder* OR
TX lumb* N5 pain OR
(MH "Low Back Pain") OR
(MH "Back Pain+") OR TX "backache" OR
(MH "Coccydynia") OR TX "coccydynia" OR
(MH “Spondylolisthesis”) OR (MH “Spondylolysis”) OR TX “Spondylolisthesis” OR TX “Spondylolysis” OR
(MH "Sciatica") OR (MH "Piriformis Syndrome") OR TX sciatica OR
(MH "Lumbar Vertebrae") OR lumbar N2 vertebra* OR
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TX cohort stud* OR
TX longitudinal stud* OR
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#6 AND #19 AND #28

PUBMED Keywords/MeSH
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(running[MeSH Terms]) OR runn* OR
(jogging[MeSH Terms]) OR jogg*
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dorsalgia [Title/Abstract] OR
Back Pain[Mesh] OR "Low Back Pain"[Mesh] OR
(backache[Title/Abstract]) OR back pain[Title/Abstract] OR
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back disorder*[Title/Abstract] OR
low back pain[Title/Abstract] OR
backache[Title/Abstract]
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Incidence[Mesh] OR incidence OR
Epidemiology[Mesh] OR "epidemiology" [Subheading] OR epidemiolog* OR
Risk Factors[Mesh] OR "risk factor*" OR
Cross-Sectional Studies[Mesh] OR cross-sectional studies OR
Longitudinal Studies[Mesh] OR longitudinal studies OR
"Cohort Studies"[Mesh] OR cohort OR
Observational Study [Publication Type]
#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26
#6 AND #18 AND #28

ScIELO Keywords/MeSH
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track and field OR athlet* OR runn* OR jogg* OR marathon* OR triath*
#1 OR #2 OR #3 OR #4
dorsalgia OR coccy* OR sciatica OR spondylolisthesis OR spondylolysis OR "back injur*" OR lumbago OR "low back pain" OR backache OR "back pain"
dorsalgia OR coccy* OR sciatic* OR spondyl* OR lumbago OR low back pain OR backache OR back injur*
(running OR runners OR jogging OR athletes OR athlete OR athletic OR "track and field") AND (back pain OR low back pain OR backache)
#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 #17
prevalence OR incidence OR cross-sectional studies OR longitudinal studies OR cohort OR epidemiolog*
adolescen* OR child* OR paediatric OR pediatric
#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26
#6 AND #18 AND #28
(ab:((track AND field) OR athlet* OR runn* OR jogg*)) AND (dorsalgia OR coccy* OR sciatic* OR spondyl* OR lumbago OR "low back pain" OR backache OR "back pain")

Google Scholar
Keywords/MeSH
(running OR jogging) AND (low back pain OR backache) AND (prevalence OR incidence OR cross-sectional studies OR longitudinal studies OR cohort OR epidemiology) AND adults NOT (adoles* OR child*)
2013 - 2018
#1 OR #2 OR #3 OR #4
(running OR runner OR runners OR jogging) AND (low back pain OR backache) AND adults -adolescent -children -child -adolescents -pediatric -paediatric
(running OR runners) ("low back pain" OR backache) (prevalence OR incidence) (adult OR adults) -adolescent -children -child -adolescents -pediatric -paediatric
2013-2018
(running OR runners OR jogging) ("back pain" OR backache) (prevalence OR incidence) (adult OR adults) -adolescent -children -child -adolescents -pediatric -paediatric
2013-2018
#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 #17
#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26
#6 AND #18 AND #28

CHAPTER III

KNOWLEDGE AND MANAGEMENT AS LOW BACK PAIN AS RELATED RUNNING INJURIES AMONG ITALIAN PHYSICAL THERAPISTS: FINDINGS FROM A NATIONAL SURVEY

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Knowledge and management of Low Back Pain as Related Running Injuries among Italian Physical Therapists: findings from a national survey

Abstract

Objectives: To investigate the beliefs, the knowledge, the attitudes, the behavior and the management procedures of Italian physical therapists (with specialization in orthopaedic manipulative physical therapy - OMPTs) towards running and its correlation with low back pain (LBP).

Design: A cross-sectional online survey.

Setting: A national cross-sectional survey, according to the Checklist for Reporting Results of Internet E-Surveys guidelines (CHERRIES) and STrengthening the Reporting of OBservational Studies in Epidemiology (STROBE), was performed in 2019.

Participants: 1218 Italian OMPTs.

Methods: Survey Monkey software was used to deliver the survey. The questionnaire was self-reported and included 23 questions. Descriptive statistics and frequencies described the actual number of respondents to each question. A wide sample of Italian OMPTs belonging to national association was involved.

Results: Out of 2,000 eligible physical therapists with OMPTs specialization, 1364 answered (68,20%) and 1218 questionnaires (60,90%) were valid for the analysis. A high proportion worked as private practice (n=845; 69.38%; 95%CI 66.69-71.94). The majority of respondents (n=806.; 66.17%; 95% CI 63.43-68.82) reported that running is not a relevant risk factor for the onset of LBP. The majority of participants (n=679; 55.75%; 95% Ci 52.90-58.55) adopted, as a

therapeutic choice in runners with LBP, the combination between manual therapy (MT) and therapeutic exercise (TE).

Conlusions: A great knowledge on LBP in running in clinical practice has emerged among Italian OMPTs. The academic education of OMPTs seems in line with recent literature, albeit the studies that analyzed LBP, as like RRI, are very few. The research on LBP in runners and physical therapy has to be considered in its early stages. Therefore, further quantitative studies evaluating knowledge, beliefs, attitudes, behavior and attitudes on LBP as like RRI among OMPTs and also non-specialized physical therapists across different countries, are strongly recommended.

1. Introduction

Running is one of the most practiced sport activities around the world [1-6]. Despite its general health benefits and popularity, many studies indicate that running also involves a relatively high risk of associated injuries [2,5].

Each year, researches have reported that 11%-85% of recreational runners experience one Running Related Injuries (RRIs) [1,4]. The rate of prevalence of RRIs among middle and long-distance runners has been reported ranging between 19% and 92% [3,7-11]. About 80% of RRIs are due to overuse, resulting from an imbalance between loadability of connective tissue and the biomechanical load of running [9,12,13]. Others theories claim that the etiology of overuse RRIs is multifactorial, and can result from the interaction between many extrinsic (e.g., environmental conditions, running surface, footwear, and weekly training mileage) and intrinsic factors (e.g., age, gender, foot strike pattern, and gait biomechanics) [1,4,14]. Prolonged exposure to these intrinsic and extrinsic risk factors may lead to overuse RRIs [15].

Actually, a definition of RRIs is not yet fully shared among scholars, due to the divergences in the type of runners involved, follow-up provided, study design, etiology and terminology of RRIs adopted in the studies [1,3,7-12,15-19], thus limiting a direct comparison between studies9.

Evidence confirm that RRIs mainly affects the joints of the lower limb, pelvis and lumbar spine [9,15,20], causing painful muscles, tendons, joints and low back pain (LBP) [1,3,7-12,15-20]. LBP is one of the most common health problems in the world, which 80% of adults experience one time in their lives [21,22]. Similar to the general population, a large number of athletes also experience LBP [23] and it is common, in clinical practice, that patients contact physical therapists for advice on LBP [24-30]. Furthermore, athletes of particular types of sports, such as skiing, rowing, golf, volleyball, track and fields, swimming or gymnastics, present a greater risk of LBP compared to the non-athletic population [29,33-36].

Despite many studies are available on prevalence and incidence of LBP in the general population and sports [21,22,37-40], up to now LBP has not been optimally investigated in runners. The recent literature is mainly focused on RRIs in lower limbs, but there are not no studies specifically addressing prevalence, incidence and risk factors for LBP, or its management, in runners or among a specific population of runners, [1-3,7,9].

Albeit the socio-economic and health impact of LBP is very important, this lack of studies on LBP as RRIs also reflected in the lack of studies that investigated physical therapists' point of view during the management of runners with LBP.

Experienced physical therapists have higher levels of knowledge in managing musculoskeletal (MSK) conditions [41,42] and in primary care they represent the first point of contact for patients with simple or complex MSK conditions43; thus it is essential to know how experienced physical therapists manage runners with LBP.

These data could have implications for health and educational standards related to the utilization and preparation of clinical practice of experienced physical therapists in the Orthopaedic Manipulative Physical Therapy (OMPT), as to better decision making processes in the management of athletes, runners in details.

Therefore, the aim of the present study was to explore: a) the beliefs; b) the knowledge; c) the attitudes; d) the behavior; and e) the management procedures of Italian physical therapists specialized in OMPT, towards the running and its correlation with LBP.

2. Material and Methods

2.1 Design

A web-based, national cross-sectional survey, herein reported according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) guidelines [44] and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [45], was performed, between February and April 2019. The Liguria Clinical Experimental Ethics Committee (357REG2017, accepted on 21/01/2019) approved the present study.

2.2 Participants and Setting

A national sample of Italian physical therapists specialized in OMPT was the target population identified from the complete email database of the GTM – Gruppo di Terapia Manuale Full Member of International Federation of Orthopaedic Manipulative Physical Therapist (IFOMPT) (n = 2000). This group captures almost all of the Italian PT specialized as OMPTs and it represents the four academic post-graduate program in manual therapy presented in Italy (Genoa University, Padova University, Roma "Tor Vergata" University and Bologna University), based upon the standards established by the IFOMPT [46]. Within the established population, we investigated those OMPTs who: a) presented a valid e-mail account, b) understood the Italian language; and c) were working as clinicians at the time of the survey. Taking into consideration previous surveys, conducted on running patients in the field [47-50], where the response rate was from 30%–60%, approximately 600 to 1200, responses were expected from the total population target of 2000 OMPT. The application of these estimated sample size to the formula, considering a single population proportion with the population proportion set at 50%, produced a two-sided 95% confidence level within 1.8% to 3.3% points of the true value and a relative standard error ranging from 1.8–3.4 [51].

2.3 Questionnaire developments and pre-testing

To the best of our knowledge, this is the first survey that reported beliefs, knowledge, attitudes, behavior and management procedure of Italian physical therapists towards the running and its correlation with LBP. Therefore, a survey was developed using items from the existing surveys on running extracted from the literature [33,47-50]. Moreover, the survey was developed with distinct and iterative steps [52]. The initial list included 30 questions that were critically evaluated for face validity and content validity [52] by a panel of 15 experts OMPTs, with an extensive experience in survey design, in the diagnosis and in the management of RRI. These experts worked independently and then agreed on the final list, by proving feedback on content accuracy, wording, question order and survey structure. Considering the emerged feedback, progressively adjustments were included. When full agreement among experts was achieved, a preliminary version of the survey made of 26 questions was self-administered and piloted in a convenient sample of 15 OMPTs (North, n = 5; Centre, n = 5; South of Italy, n = 5).

Once the pilot stage was concluded, a telephone debriefing session was performed [52]. The panel of experts conducted one-to-one interviews among the sample of 15 OMPTs on possible difficulties encountered when filling in the survey (e.g., identifying questions that required further explanation, words that were too difficult to be read or semples in which respondents seemed to find confusing) and the OMPTs' experience in answering the questions. At the end of the pilot stage, the interview was satisfactory, thus no changes or others comments/integrations were necessary. The sample of pilot stage reported that items of questions were not ambiguous, phrasing was easy and simple to be understood and the sharing experience was good.

Questionnaire implementation

A self-administered questionnaire (translated into English, Supplementary File 1 and in original language Supplementary File 2 in Appendix 1) divided into 4 sections (A, B, C and D) was used.

The socio-demographic variables were investigated using 2 open-ended questions (e.g., age, geographic region) in section A. Six closed multiple-choice questions, were included in section B. The questions of section B investigated the professional variables (e.g., years of experience, numbers of patients in a week).

The third section (C) consisted of 4 closed multiple-choice questions that investigated the running variable, while the last section (section D) consisted of 15 closed multiple-choice questions on LBP in running. More specifically, the questions were exploring the knowledge of LBP as like RRI and its management. This last section also explored participants' beliefs on how running could or could not be a risk factor or not in the onset of LBP.

2.4 Data collection procedure

The SurveyMonkey (Survey-Monkey, Palo Alto, California, www.surveymonkey.com) online survey tool was used. The survey was administered over an 8 weeks period between 5th February 2019 and 15th April 2019. After permission was obtained from GTM, all OMPTs were contacted by blast email [52]. An email, containing the survey and a brief note that underlined the aim of the study, was delivered. Moreover, the email contained the data handling, the anonymity and invitation to complete the survey.

Specifically, the statement within the email informed that by clicking on the survey link, respondents were providing their consent to participate in the study [52]. Two email reminders were sent 2 and 4 weeks after the initial contact, to encourage those who did not participate in the survey. Seven to 10 minutes were needed to complete the survey, corresponding to the adequate completion time needed to optimize response rates in online surveys [53].

Participation was voluntary and no incentives were offered to participants; there was the option to decline to answer specific questions or to leave the entire questionnaire blank [52]. Participants were able to review or change responses using a back button, before submitting their answers. Data were downloaded and stored in an encrypted computer, and only the project manager had access to the information during all stages of the study. Participants were ensured that their identities would not be disclosed to investigators. All data were de-identified (name and email address) to maintain confidentiality and data protection [52].

2.5 Data analysis

Survey data were downloaded from SurveyMonkey into Excel spreadsheets and reviewed for accuracy and missing values. A questionnaire was considered incomplete if >20.0% of data were missing [54].

For questions allowing a single choice, descriptive statistics (mean, standard deviation) for continuous variables were used, including 95% confidence intervals (CI), while absolute frequencies and percentages were applied to dichotomous, nominal and ordinal variables. The demographic variable age (transformed into an ordinal variable considering a decade as variable levels), years of work experience, type of degree, type of the advanced degree (PG Graduation), type of work regimen, numbers of patients visited per week and numbers of runners visited each month were used for correlation analysis, as described below. For questions with more than one choice, the absolute frequency and percentages for each combination of responses provided by each participant was calculated.

For example, considering that the fields (n) asked in the domain 'anatomical segment' were five with dichotomous responses (r), we calculated the absolute frequency and percentages of the five possible fields and of their 32 combinations, given by the formula r^n, to better describe the responses given by each participant.

The presence of any relationship between the individual characteristics (section A of the survey) and the responses given (sections B and C of the survey) was investigated with Cramer's V, which is a measure of strength and direction of association derived from chi-square statistics. Only correlation values higher >0.60 were deemed acceptable and, therefore, here reported. R software, version 3.4.4 [55] was used for data analysis with the packages psych [56] and ggplot2 [57].

3. Results

3.1 Participant's characteristics

Out of the 2000 invited OMPTs, a total of 1364 responded (68.0%). One hundred forty-six incomplete surveys were excluded from data analysis, leaving 1218 questionnaires to be considered as valid (60,90%) for the analysis. The OMPTs had a mean age of 35.72 (SD = 9.84; 95%CI 35.16–36.27; Range 21-69). The most represented region in the sample of all participants was Lombardy with 18.34% (95%CI 16.24-20.66), the least represented was Valle d'Aosta with 0,27% (95%CI 0.10-0.90). Globally, the regions of sample of all participants are presented in Figure 1. A small percentage, 14.70% (n=179; 95%CI 12.78-16.84) of participants, reported less than 3 years of clinical experience, while the 42.61%. and 42.69% reported from 4 to 10 years and more than 10 years of clinical experience (n=519; n=520; 95%CI 39.82-45.45; 95%CI 39.90-45.53), respectively. A high proportion worked as private practice (n=845; 69.38%; 95%CI 66.69-71.94). Moreover, 58.29% of participants treat more than 20 patients per week (n=710; 95%CI 55.46-61.07); 71.92% (n=876; 95%CI 69.29-74.41) of respondents reported treating less than 5 runners per month. The respondents' characteristics are described in Table 1A e 1B.

3.2 Running Section Characteristics

The majority of OMPTs reported that it is clinically relevant to ask runners how long they have been running (n=1191; 97.78%; 95% CI 96.75-98.51) and information about running footwear (n=1115; 91.54%; 95% CI 89.80-93.02). A large proportion of participants visits non-competitive runners (n=1061; 87.11%; 95% CI 85.07-88.91). Participants were asked to identify what was the anatomical district or the combinations of body segments for which runners most frequently complain for pain. The single part of body with most percentage of response was the knee (n=114; 9.36%; 95% IC 7.81-11.17), while the most cited combination was the ankle, the knee and the lumbar spine (n=242; 19.87%; 95% IC 17.68-22.24). In the questionnaire also shoulder and thoracic spine were presents, but did not receive responses (n=0; 0%). Globally, the single items and their combinations are presented in Figure 2. The overall overview of data of this section is reported in Table 2.

3.3 Beliefs and knowledge towards the running

We asked respondents if running may or not be a significant risk factor in the onset of LBP. For this question, the majority of respondents (n=806.; 66.17%; 95% CI 63.43-68.82) reported that the running is not a relevant risk factor for the onset of LBP. The reported reasons for this item were: “it does not burden for the lumbar spine (not harmful)”, “if done correctly, it prevents the onset of LBP” and “it has no higher incidence than other sports”. The percentage of this reasons were 21.92% (n=267; 95% CI 19.65-24.37) 22.99% (n=280; 95% CI 20.67-25.48) and 21.26% (n=259; 95% CI 19.02-23.69), respectively.

The response "YES" were four and mentioned as follows, “for continuous stress/impact with the ground/soil”, “if the biomechanics of running is altered”, “if there is an imbalance between load and load capacity”, “if there is a reduced strength/ elasticity of the lower limb/lumbar spine”, with the following percentages results: 9.28% (n=113; 95% CI 7.74-11.08), 8.21% (n=100;

95% CI 6.76-9.93), 7.96% (n=97; 95% CI 6.53-9.66); 8.37 (n=102; 95% CI 6.91-10.11), respectively.

A similar proportion 37.52% (n=457; 95% CI 34.80-40.32) and 46.63% (n=568; 95% CI 43.81-49.48) of respondents reported that the evaluation and treatment adopted for runners with LBP was compared with other patients without using dedicated technology aids (visual assessment of the running mechanics), respectively. Only a small percentage of participants (n=193; 15.84%; 95% CI 13.86-18.05), reported the use of dedicated technology aids (i.e., treadmills, video analysis, sensors, etc.) for specific evaluation and treatment. The majority of participants (n=679; 55.75%; 95% CI 52.90-58.55) adopted as a therapeutic choice the combination between manual therapy (MT) and therapeutic exercise (TE) in runners with LBP. The minimal percentage of participants (n= 16; 1.31%; 95% CI 0.78-2.17) reported to use only therapeutic modalities (TM) (i.e., TENS, LASER therapy, etc.). A large amount of participants reported the use of taping techniques, sometimes (n=668; 54.84%; 95% CI 51.60-57.66) and orthotics/insole with runners with LBP (n=754; 61.90%; 95CI 59.10-64.63). The overall overview of data of this section is reported in Table 3.

3.4 Management LBP in runners

We asked respondents about their clinical practice, during specific running exercise planning given to prevent the onset of LBP in runners: they consider more relevant to work on frequency, intensity, duration of training, foot strike pattern, cadence (step rate/step frequency) or step length (stride length). The 28.24% of respondents (n=344; 95% CI 25.75-30.88) declared to work on intensity (run kilometers per week or running session time per week)), while the 22% (n=268; 95% CI 19.73-24.46) stated to work on frequency (number of training session per week). Only the 6.40% (n=78; 95% CI 5.12-7.96) reported to work on stride length. In presence of a common LBP in runners, the high percentage of participants (n=1033; 84.81%; 95% CI 82.64-86.75) recommends to modify training and to suspend competitions. Only 2.95% (n= 36; 95% CI 2.11-4.11) reported to totally suspend both training and competitions. When asked how many days they would indicate to stop training in case of LBP, most respondents (n=748; 61.41%; 95% CI 58.60-64.15) reported less than 3 days. Differently, when asked how many days would they recommend to modify training, most respondents (n=471; 38.67%; 95% CI 35.93-41.48) reported to advise runners to modify it for 7 days. The recommendation to stop and to modify training for a common LBP in a runner had the most similar response rate, 18.96%-20.85% and 24.05-26.03%, respectively. The given reasons to stop training were: "to recover an optimal load capacity" (n=231; 18.96%; 95% CI 16.82-21.31), "wait for the expected improvement from physiotherapy" (n=244; 20.03%; 95% CI 17.84-22.41), "wait for symptoms resolution or acute phase regression" (n=248; 20.36%; 95% CI 18.15-22.76), "avoid symptoms worsening" (n=241; 19.79%; 95% CI 17.61-22.16) and "replace running with walking/exercise" (n=254; 20.85%; 95% CI 18.63-23.27). The reasons chosen to modify the training were: "not to decondition the athlete" (n=300; 24.63%; 95% CI 22.25-27.17), "to learn new motor strategies" (n=317; 26.03%; 95% CI 23.60-28.60), "to modify/improve running biomechanics" (n=308; 25.29%; 95% CI 22.89-27.84), "to allow a progressive load exposure" (n=293; 24.05%; 95% CI 21.70-26.58).

In case of modifying training, the highest percentage of respondents (n=319; 26,19%; 95% CI 23.76-28.77) reported to take action on training times, while the lowest percentage (n=147; 12.07%; 95% CI 10.32-14.06) reported to take action on footwear. When asked how many days did runners with LBP improve in their clinical practice, , most of the respondents replied 15 days (n=491; 40.31%; 95% CI 37.55-43.13) or more than 15 days (n=504; 41.38%; 95% CI 38.60-44.21); only 4.68% (n=57; 95% CI 3.59-6.06) reported that their patients improve in less than 3 days. The overall overview of data of this section is reported in Table 4.

3.5 Correlation between variables

No significant correlations (Cramer's V <0.60) were found between individual characteristics (section A of the survey) and the responses given (sections B and C of the survey). The overall data are reported in Table 5.

4. Discussion

To the best of our knowledge, this is the first study that evaluates beliefs and management of LBP in running among OMPTs. Although 70% of the respondents treat few runners per month (less than 5 runners per month), the main finding of our research identifies that, in order to opinion and clinical practice of OMPTs, running does not represent a risk factor for the onset LBP. These data are in line with recent literatures, confirming a low LBP prevalence and incidence among runners, when compared to general population [21,22,37-40,58-60]. In accordance with evidence, running could play an anabolic role towards the intervertebral disc [58-60]: Belavý et al. [60] reported that long-distance runners and joggers showed better hydration and glycosaminoglycan levels than the non-athletic individuals.

The largest number of respondents indicates that the knee is the most frequently anatomical district complained of as painful, immediately followed by the ankle, in single responses, as confirmed by the literature [7,9,11,48,49,61-63]. When looking at combined responses, although a clear prevalence of lower limb is detected as the most frequently complained district by runners, our data, in absolute terms, reveal that multiple answer of the ankle, lumbar and knee involvement achieved the greatest number of responses. This choice could be interpreted in many ways, speculating on the various reasons that led to this answer, from the possible desire of the respondents to insert all the possible choice options (max. 3), to the possibility that runners, complaining about knee and ankle, may implement altered running strategies affecting the carrying capacity of the lumbar spine. We, as authors, given the single and combined answers to two choices, tend more for the first reason described, than for a real interest of the lumbar spine.

The OMPTs seem to be careful in relation to the evaluation methods used to assess runners; indeed, most of them specifically evaluate this kind of patient by taking into consideration the analysis of running and its biomechanics [64-67]. However, only a small percentage of professionals uses advanced tools to conduct such type of analysis. Probably, due to the high cost of such equipment or to the small number of runners treated in a month, OMPTs tend not to invest in this technology. Almost half of the sample prefers to assess runners in a similar way to other patients with non-specific musculoskeletal disorders. This motivation could be linked to the type of training that the OMPTs receive, or, as already said, depend from the restated number of runners treated per month, which pushes physiotherapists not to carry out specific training on running.

When asked, the sample interviewed on how they treat these patients, however, declared to use a combination of manual therapy and therapeutic exercise:

these data seem in line with the new therapeutic guidelines in relation to the musculoskeletal disorders, which indicate as first solution to these disorders the combination of multiple instruments and therapeutic strategies or choices oriented towards the bio-psycho-social approach, like information and pain neuroscience education (PNE) [68-71].

In a situation of dualism that derives from the apparent "hands-off" characterization of the neuroscience of pain (more oriented towards the psychosocial aspect) and the pure MT "hands-on" approach68 (more oriented towards the "bio" aspect), a transition zone must be clarified by PNE [69]. PNE is fundamental to balance the "bio" component with the psychosocial dimensions of pain [71,72] establishing a valid aid for the modern MT [68] and creating a solid integration between the two approaches.

A recent systematic review [70] compared studies that use only PNE with those that use PNE combined with therapeutic exercise and/or MT. PNE alone does not appear to be able to significantly reduce patient pain. In contrast, when associated with exercise, subjects reported a significant reduction in pain [73-75]. PNE and exercise also positively influence pain modulation more than the “therapeutic” effect obtained on the structurally damaged muscles and tendons [68,76,77]. Indeed, an increasing number of publications have witnessed the clinical effect of TE in patients with chronic diseases [78] and made it necessary to introduce this treatment modality more frequently within the prescribed therapies, with equal and sometimes greater efficacy than drug therapy [78,79]. In addition, PNE is superior to ergonomic education in patients with chronic pain and the related effects are detectable even after one year [80].

In relation to the use of taping, many OMPTs reply that they do not use these tools in their clinical practice when they treat runners with LBP. Moreover, most of them respond that they only use them sometimes. These data also are in line with the new therapeutic orientations in order to taping. Despite the use of taping is frequent in lower extremity disorders in runners [81-84], the effect of taping on runners with LBP has yet not been studied: evidence-based literature suggests the use of taping with caution due to slight and temporary beneficial effect on LBP [85-88]. Effects are very small to be considered clinically relevant and meaningful when compared with placebo taping [85,87]. In fact, patients who received a physical therapy program consisting of exercise and manual therapy did not get additional benefit from the use taping and it cannot be considered a substitute for traditional physical therapy or exercise [86,88].

In order to use of orthotics/insole, OMPTs reply that, as like taping, they do not use or use these tools sometimes in their clinical practice, when they have to treat runners with LBP. Also these data also are in line with the new therapeutics orientations, indeed, while the orthotics are used often in lower extremity disorders in runners because they appear to reduce the risk of some running-related lower extremity injuries [89-94], even if rarely named in studies where LBP is analysed in running [47,95].

According to the opinion of the OMPTs, during the planning of specific exercises to prevent the onset of LBP in runners, it seems to be more important to work on frequency (number of training sessions per week) and intensity (km courses per week).

These data would seem in line with the theories of load and loadability: gradual exposure allows to increase loads, balancing between the resistance capacity of the connective tissue and the biomechanical load of running [12,96,97]. Also, the reasons expressed for stopping or modifying training also seem in line with the theories of load and load capacity [12,96,97].

In presence of a common LBP in runners the majority of OMPTs respondents recommend to modify training and to stop competitions. This recommendation seems highly in line with the clinical practice guidelines on LBP that advice on returning to normal activities, staying active and avoiding bed rest [98-100].

Although acting on cadence seems to be a useful strategy to reduce the RRI of lower extremities [67,101], there are no available data on this strategy in relation to the LBP in runners: such reasons could be the basis of the answers given by the OMPTs interviewed, who prefer to act on changing running surface, on reducing the km travelled, on modifying the training time, in order to the theories of load and loadability, as well [12,96,97].

According to the OMPTs interviewed, if it is recommended to stop training, it is only necessary for less than 3 days, while if it is recommended to modify it, most of them report between 7 and 15 days. Based on their clinical experience, the highly part of OMPTs reported that runners with LBP improve between 15 and just over 15 days: our data confirms the characteristics of the international consensus which defines the RRI as a musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running activities, causing a total restriction or suspension of running for at least seven or more days, requiring medical/physiotherapy assistance10. Moreover, our data are much similar to data obtained from general population, that at 2 weeks after onset, over 35% of patients no longer have symptoms, at 4 weeks over 60% [102]. For these reasons, we cautiously invite to think running as a protective factor from LBP and to consider to prescribe running as a preventive exercise for LBP.

4.1 Strengths and weaknesses of the study

A high response rate was achieved (60,90%), confirming the willingness of Italian OMPTs to participate to the survey [103]. To the authors' knowledge, there are not existing other similar studies on PT investigating LBP in runners conducted through questionnaires. Therefore, we cannot compare our data with our study. A specific group of Italian OMPTs (n = 845), educated on how to mainly manage musculoskeletal disorders in private healthcare sector104, was involved. Therefore, their responses might differ from those of group of non-OMPT-specialized PT [104]. Moreover, demographical characteristic of the respondents, such as the regional distribution of Italy, where respondents are based in (North vs Centre and South), other characteristics like more than 20 years of clinical practice and majority of physiotherapists treating less than 5 runners per months, may have influenced the participants' adoption, knowledge, beliefs and management of LBP in runners. A survey tool was adopted to understand the perspectives of the target population [105]. The questionnaire included different items (e.g., close-ended questions), to increase the likelihood of capturing the complexity of the phenomena under study [106]. However, our methodological choice was based on the impossibility to have a previously standardized questionnaire for a national online survey for similar data, thus mimicking a past survey experience previously reported in running survey performed only on runners [47-50]. Given that data were self-reported and retrospective in nature, recall bias can threaten the validity of the findings [107-109].

5. Conclusion

A great knowledge on LBP in running in clinical practice has emerged among Italian OMPTs. The academic education of OMPTs seem in line with recent literature, albeit the studies that analyzed LBP, as like RRI, are very few. Due to this, to ensure appropriate competence, awareness, and the ethical use of the knowledge on these topics, these issues should be included in physical therapy graduate and postgraduate study programs and in OMPTs long-life learning courses. The research on LBP in runners and physical therapy has to be considered in its early stages. Therefore, further quantitative studies evaluating knowledge, beliefs, attitudes, behavior and attitudes on LBP as like RRI among OMPTs and also non-specialized physical therapists across different countries, are strongly recommended. To develop a more comprehensive understanding of the phenomena, there is also a need to investigate patients' perceptions on LBP and running in physical therapy practice.

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TABLE 1A | Demographic Participant's Characteristics (*N* = 1,218). (section A and B of questionnaire)

	Min-Max	Mean	95% CI*
Q1. Age (SD)*	21.0-69.0	35.72(9.84)	35.16-36.27
Q2. Italian Region	**N***	**%***	**95% CI***
Lombardy	223	18.34	16.24-20.66
Veneto	176	14.50	12.59-16.62
Tuscany	134	10.97	9.30-12.89
Piedmont	106	8.68	7.19-10.44
Emilia Romagna	101	8.27	6.82-9.99
Puglia	97	7.94	6.52-9.64
Lazio	89	7.29	5.92-8.93
liguria	63	5.16	4.02-6.59
Friuli Venezia Giulia	34	2.78	1.96-3.91
Marche	33	2.70	1.90-3.82
Trentino Alto Adige	32	2.62	1.83-3.72
Sicily	28	2.29	1.56-3.34
Campania	20	1.64	1.03-2.56
Sardinia	19	1.56	0.97-2.47
Umbria	18	1.47	0.90-2.37
Abruzzo	17	1.39	0.84-2.27
Calabria	10	0.82	0.42-1.55
Basilicata	8	0.65	0.30-1.34
Molise	7	0.57	0.25-1.23
Valle d'Aosta	3	0.27	0.10-0.90

*CI: Confidence Interval; SD: Standard deviation; N: numbers; %: percentage

TABLE 1B | Professional Participant's Characteristics (*N* = 1,218). (section A and B of questionnaire)

	N*	%*	95% CI*
Q3. Years of PT's* clinical practice:			
<3	179	14.70	12.78-16.84
4-10	519	42.61	39.82-45.45
>10	520	42.69	39.90-45.53
Q4. Academic Title:**			
University degree	86	7.06	5.72- 8.68
Masters of Science	109	8.95	7.43-10.73
Bachelor of Science	925	75.94	73.42-78.30
Antecedent title	82	6.73	5.42-8.32
PhD*	16	1.31	0.78-2.17
Q5. PG* certification:			
- only MSDs***	594	48.77	45.93-51.62
- Sports	74	6.07	4.83-7.60
- Others type	550	45.16	42.34-48.00
Q6. Job Position:			
private practice	845	69.38	66.69-71.94
employee	331	27.18	24.71-29.78
mixed	36	2.96	2.11-4.11
other	6	0.49	0.20-1.13
Q7. N* of patients/we*:			
<10	102	8.37	6.91-10.11
11-20	406	33.33	30.70-36.07
>20	710	58.30	55.46-61.07
Q8. N of runners/mo*:			
<5	876	71.92	69.29-74.41
5-10	279	22.91	20.59-25.39
>10	63	5.17	4.03-6.61

**CI: Confidence Interval; SD: Standard deviation; N: numbers; %: percentage; PT: Physiotherapy

PhD: Phylosophy Doctorate; PG: Post Graduate (this Title in Italy is called Master; we:week; mo: month

**this item reflects italian legislation (www.miur.gov.it/processo-di-bologna)

***MSDs (Musculoskeletal Disorders and Orthopaedic Manipulative);

TABLE 2 | Running Section Characteristics (N = 1,218). (section C of questionnaire)			
	N*	%*	95% CI*
Q9. Based on your opinion, would you consider it clinically relevant to ask runners-patients how long they have been practicing running?			
No	27	2.22	1.49-3.25
Yes	1191	97.78	96.75-98.51
Q10. Based on your opinion would you consider it clinically relevant to ask runners-patients for information about running footwear ?			
No	103	8.46	6.98-10.20
Yes	1115	91.54	89.80-93.02
Q11. What type of runner do you treat most?			
Competitive	157	12.89	11.09-14.93
Non-competitive	1061	87.11	85.07-88.91
Q12. Based on your clinical experience, which is the anatomical district for which runners-patients more frequently complain**			
Ankle (A)	78	6.40	5.12-7.96
Knee (B)	114	9.36	7.81-11.17
Lumbar spine (C)	41	3.37	2.45-4.58
Cervical spine (D)	2	0.16	0.03-0.66
Hip (E)	11	0.90	0.47-1.66
AB	228	18.72	16.59-21.05
AC	84	6.90	5.57-8.50
AE	20	1.64	1.03-2.57
BC	141	11.58	9.86-13.54
BD	1	0.08	0.00-0.53
BE	21	1.72	1.098-2.67
CD	2	0.16	0.03-0.66
CE	8	0.66	0.30-1.34
ABC	242	19.87	17.68-22.24
ABD	5	0.41	0.15-1.01
ACD	5	0.41	0.15-1.01
ABE	130	10.67	9.02-12.58
ACE	22	1.81	1.16-2.77
ADE	2	0.16	0.03-0.66
BCD	7	0.57	0.25-1.24
BCE	52	4.27	3.23-5.60
BDE	1	0.08	0.00-0.53
CDE	1	0.08	0.00-0.53

***CI: Confidence Interval; SD: Standard deviation; N: numbers; %: percentage;

**in the questionnaire there were presents also shoulder and thoracic spine that have not received responses

TABLE 3 | Beliefs, knowledge, attitudes, behavior LBP Runners Section (*N* = 1,218). (section D of questionnaire)

	N*	%*	95% CI*
Q13. Based on your opinion, running is a significant risk factor for the onset of low back pain?			
No	806	66.17	63.43-68.82
Yes	412	33.83	31.18-36.57
Q14. Why?:			
If No:			
- It does not burden for the lumbar spine (not harmful)	267	21.92	19.65-24.37
- if done correctly it prevents of the low back pain	280	22.99	20.67-25.48
- it has no higher incidence than other sports	259	21.26	19.02-23.69
If Yes:			
- Due to continuous stresses/impacts with grounds/soils	113	9.28	7.74-11.08
- if the running biomechanics is altered	100	8.21	6.76-9.93
- if there is an imbalance between load and load capacity	97	7.96	6.53-9.66
- if there is a reduced strength/ elasticity of the lower limb/lumbar spine	102	8.37	6.91-10.11
Q15. In your clinical practice, how do you manage runners with low back pain?			
- Assessment and treatment similar to the one used with other patients non runners	457	37.52	34.80-40.32
- Specific assessment and treatment (running biomechanics	568	46.63	43.81-49.48
	193	15.84	13.86-18.05

evaluation) without technological dedicated tools) - Specific assessment and treatment, WITH technological dedicated tools (i.e. treadmills, video analysis, sensors, etc.)			
Q16. In your clinical practice, which therapeutic choice do you adopt in runners with low back pain?			
- Mainly Therapeutic Modalities (TM) (i.e. TENS, LASER therapy, ETC.)	16	1.31	0.78-2.17
- Mainly Therapeutic Exercise (TE) (including pain education)	78	6.40	5.12-7.96
- Mainly Manual Therapy (MT) (i.e. mobilizations, manipulations, pain education, etc.)	88	7.22	5.86-8.86
Combination of:			
- MT+TE	679	55.75	52.90-58.55
- MT+TM	52	4.27	3.23-5.60
- ET+TM	35	2.87	2.04-4.02
- MT+TE+TM	270	22.17	19.88-24.63
Q17. In your clinical practice, do you adopt taping techniques in runners with low back pain?			
No	384	31.53	28.94-34.23
Yes, always	24	1.97	1.29-2.96
Yes, often	142	11.66	9.94-13.63
Yes, sometimes	668	54.84	51.60-57.66
Q18.. In your clinical practice, do you consider it useful to adopt orthotics/insole during the treatment of runners with low back pain?			
No	373	30.62	28.06-33.31
Yes, always	11	0.90	0.47-1.66
Yes, often	80	6.57	5.27-8.14
Yes, sometimes	754	61.90	59.10-64.63

**CI: Confidence Interval; SD: Standard deviation; N: numbers; %: percentage;

TABLE 4 | Management LBP Runners Section (*n* = 1,218). (section D of questionnaire)

	Count	%	95% CI
Q19. During specific exercise planning, for prevent onset of low back pain in runners, do you think it is more important to work on			
- frequency (number of training session per wk)	268	22.00	19.73-24.46
- intensity (run km*/wk -** running session time per wk**)**	344	28.24	25.75-30.88
- training duration (in terms of minutes in a single session)	182	14.94	13.01-17.10
- foot strike pattern	190	15.60	13.63-17.79
- cadence/step rate/step frequency	156	12.81	11.01-14.84
- Stride length	78	6.40	5.12-7.96
Q20. In the presence of a common low back pain in a runner you recommend			
- To stop training	59	4.84	3.74-6.24
- To stop training and competition	36	2.95	2.11-4.11
- To modify training and to stop competitions	1033	84.81	82.64-86.75
- To continue training but to stop competitions	90	7.39	6.01-9.04
Q21. Just in case you recommend to stop training for a common low back pain: for how many days?			
<3	748	61.41	58.60-64.15
7	394	32.35	29.74-35.07
15	62	5.09	3.95-6.52
>15	14	1.15	0.65-1.97
Q22. Just in case you recommend to modify training for a common low back pain: for how many days?			
<3	242	19.87	17.68-22.24
7	471	38.67	35.93-41.48
15	316	25.94	23.52-28.52
>15	189	15.52	13.55-17.70
Q23. Just in case you recommend to stop training for a common back pain: for which reason?			

- To recover an optimal load capacity	231	18.96	16.82-21.31
- To wait for the expected improvement from physiotherapy	244	20.03	17.84-22.41
- To wait for symptoms resolution/acute phase regression	248	20.36	18.15-22.76
- To avoid symptoms worsening	241	19.79	17.61-22.16
- To replace running with walking/exercise	254	20.85	18.63-23.27
Q24. Just in case you recommend to modify training for a common low back pain: for which reason?			
- Not to decontion the athlete	300	24.63	22.25-27.17
- To learn new motor strategies	317	26.03	23.60-28.60
- To modify/improve running biomechianics	308	25.29	22.89-27.84
- To allow a progressive load exposure	293	24.05	21.70-26.58
Q25. Just in case you recommend to modify training for a common low back pain, what would you mainly do?			
- Running surface	304	24.96	22.57-27.51
- Run km	288	23.64	21.30-26.15
- Training time	319	26.19	23.76-28.77
- Footwear	147	12.07	10.32-14.06
- cadence/step rate/step frequency	160	13.14	11.32-15.19
Q26. Based on your clinical experience, on how many days on average do your running patients with low back pain improve			
<3	57	4.68	3.59-6.06
7	166	13.63	11.78-15.71
15	491	40.31	37.55-43.13
>15	504	41.38	38.60-44.21

*km:kilometers; **wk:week;

TABLE 5 ∣ Correlation between variables																	
	Q9	Q10	Q11	Q13	Q14	Q15	Q16	Q17	Q18	Q19	Q20	Q21	Q22	Q23	Q24	Q25	Q26
Age (ordinal)	0,05	0,06	0,11	0,14	0,09	0,05	0,11	0,11	0,07	0,05	0,15	0,10	0,08	0,05	0,05	0,04	0,06
Years/PT's*	0,05	0,04	0,10	0,10	0,09	0,06	011	0,11	0,05	0,06	0,13	0,09	0,06	0,05	0,06	0,02	0,06
Academic Title	0,10	0,03	0,05	0,11	0,09	0,07	0,11	0,10	0,07	0,05	0,10	0,07	0,06	0,04	0,05	0,05	0,07
PG* Title	0,03	0,06	0,04	0,20	0,14	0,04	0,14	0,08	0,06	0,05	0,10	0,09	0,04	0,03	0,05	0,06	0,05
Job Position	0,01	0,04	0,10	0,14	0,11	0,06	0,11	0,06	0,04	0,08	0,05	0,04	0,06	0,04	0,05	0,05	0,05
N* pts/wk*	0,05	0,05	0,10	0,06	0,08	0,06	0,09	0,04	0,05	0,07	0,03	0,05	0,06	0,06	0,04	0,04	0,04
N rns*/mo	0,05	0,04	0,28	0,07	0,08	0,13	0,09	0,03	0,04	0,05	0,04	0,06	0,06	0,07	0,04	0,05	0,08

*PT: Physiotherapist; PG: post graduate; N: Numbers; pts: patients; wk: week; rns: runners; mo: month
Note: The presence of any relationship between the individual characteristics and the responses given was investigated with Cramer's V

Figure 1- The italian regions of OMPTs participants'

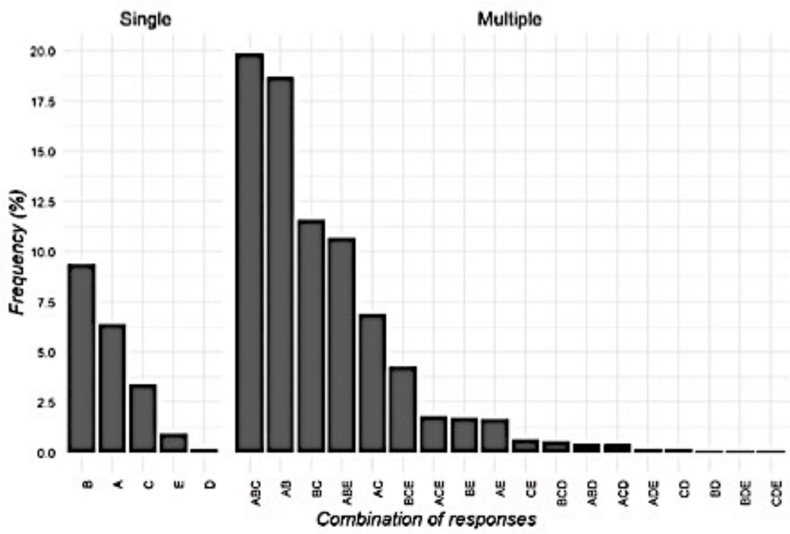

Figure 2- Most complained painfull anatomical regions by runners according to OMPTs. Note: Ankle (A); Knee (B); Lumbar spine (C); Cervical spine (D); Hip (E); OMPTs: Orthopaedic Manipulative Physical Therapists

Appendix 1
QUESTIONARIO – ITA
Running, Lombalgia e Fisioterapisti

Introduzione:

Gentile Collega
Tra le pratiche sportive più praticate nel mondo, la corsa sta riscontrando un enorme successo anche in Italia, grazie all'impatto benefico sulla salute. Tuttavia il maggior inconveniente associato alla corsa è il rischio relativamente elevato di procurarsi lesioni a carico delle strutture muscolo-scheletriche. In letteratura esistono attualmente diverse incongruenze inerenti il tema degli infortuni nella corsa e la mancanza di dati certi nella ricerca rende difficile confrontare i diversi risultati degli studi. I distretti corporei più colpiti sono l'arto inferiore ed il rachide lombare e la correlazione fra la corsa ed il mal di schiena è ad oggi ancora poco conosciuta e scarsamente indagata.
Questo questionario intende indagare la sua personale esperienza ed opinione in relazione a questo tema.
La compilazione dell'intero questionario è volontaria e richiede 5-7 minuti. Le sue risposte sono completamente anonime e saranno utilizzate solamente per gli scopi di questa ricerca
Si tenga conto che nel questionario consideriamo come "corridore" la persona che pratica abitualmente la corsa da almeno 3 mesi, per un tempo di 30 minuti o 5 km per sessione, per almeno due volte a settimana.

A. Sezione Anagrafica

1. Età ______________________________
2. Regione _____________________________

B. Sezione Professione

3. Da quanti anni è fisioterapista?
   □ <3 □4-10 □>10

4. Quale titolo accademico possiede?
   □ PhD
   □ Laurea Magistrale
   □ Laurea triennale
   □ Diploma Universitaria
   □ Titolo antecedente

5. Ha conseguito un Master Universitario oltre Terapia Manuale/Riabilitazione Muscoloscheletrica?
   □ Soltanto in Terapia Manuale/Riabilitazione Muscoloscheletrica
   □ Anche in Fisioterapia Sportiva
   □ Anche altro tipo______________________

6. Qual è il suo regime lavorativo?
   □ libero professionista
   □ dipendente
   □ misto

□ altro________________________

7. Quanti pazienti vede/tratta a settimana
□<10 □11-20 □>20

8. Mediamente quanti pazienti corridori visita o tratta in un mese?
□ nessuno
□<5 □5-10 □ >10

C. Sezione Running

9. In base alla sua opinione riterrebbe clinicamente rilevante chiedere ai pazienti corridori, da quanto tempo pratichino la corsa ?
□ si
□ no

10. In base alla sua opinione riterrebbe clinicamente rilevante chiedere ai pazienti corridori, informazioni riguardo le calzature per la corsa?
□ si
□ no

11. Tratta corridori più frequentemente?
□ agonisti
□ non agonisti

12. Nella sua esperienza clinica quale è il distretto anatomico per il quale i suoi pazienti corridori, lamentano dolore con maggior frequenza (è possibile selezionare più risposte, massimo 3)
□ ginocchio
□ caviglia-piede
□ anca
□ rachide lombare
□ rachide toracico
□ rachide cervicale
□ spalla
□Altro______________________________

D. Sezione Lombalgia

13. Secondo la sua opinione, la pratica della corsa costituisce un rilevante fattore di rischio per l'insorgenza del mal di schiena?
□ no □ si

14. □ no □ perché:
□ non ha un'incidenza maggiore di altri sport
□ non grava sul rachide lombare in maniera dannosa
□ se svolta correttamente previene il mal di schiena

□ si □ perché:
□ per continue sollecitazioni/impatto con il terreno/suolo

□ se la biomeccanica della corsa è alterata
□ se c'è uno squilibrio tra carico e capacità di carico
□ se c'è una ridotta forza/elasticità dell'arto inferiore/rachide lombare

15. Nella sua pratica clinica come gestisce i corridori con mal di schiena?
□ valutazione e trattamento simile a quello utilizzato con altri pazienti non corridori
□ valutazione e trattamento specifico (valutazione della meccanica della corsa senza ausili di tecnologia dedicata)
□ valutazione specifica , con ausili di tecnologia dedicata (p.es: tapis roulant, video analisi, sensori, ecc) e trattamento

16. Nella sua pratica clinica, con i corridori affetti dal mal di schiena quale scelta terapeutica adotta?
□ principalmente terapia manuale (es: mobilizzazioni articolari, manipolazioni,
educazione del paziente sul dolore, ecc.)
□ principalmente esercizio terapeutico (inclusa educazione del paziente sul dolore)
□ principalmente elettromedicali (es: tecar, tens, laser, ultrasuoni, ecc.)
□ combinazione di terapia manuale ed esercizio terapeutico
□ combinazione di terapia manuale ed elettromedicali
□ combinazione di esercizio terapeutico ed elettromedicali
□ combinazione di esercizio terapeutico, terapia manuale ed elettromedicali

17. Nella sua pratica clinica, con i corridori affetti dal mal di schiena, utilizza tecniche di taping?
□ no
□ si talvolta
□ si spesso
□ si sempre

18. Nella sua pratica clinica, con i corridori affetti dal mal di schiena considera utile nel trattamento l'adozione di plantari/ortesi?
□ no
□ si talvolta
□ si spesso
□ si sempre

19. Nella pianificazione di specifici esercizi per la corsa, per prevenire l'insorgenza del mal di schiena, ritiene più rilevante intervenire su: (può segnare fino a tre opzioni)
□ frequenza (numero di allenamenti settimanali)
□ intensità (km percorsi o tempo di percorrenza a settimana)
□ durata di allenamento (in termini di minuti nella singola sessione)
□ tipologia di appoggio
□ cadenza
□ lunghezza del passo
□ altro____________________________________

20. In presenza di un comune mal di schiena consiglia di:
    □ sospendere l’allenamento
    □ sospendere l’allenamento e le competizioni
    □ modificare l’allenamento
    □ continuare gli allenamenti ma sospendere le competizioni

21. Nel caso consigli di sospendere l’allenamento per un comune mal di schiena:
    per quanti giorni? □ <3 □ 7 □ 15 □>15

22. Nel caso consigli di modificare l’allenamento per un comune mal di schiena:
    per quanti giorni? □ <3 □ 7 □ 15 □>15

23. Nel caso consigli di sospendere l’allenamento per un comune mal di schiena: per quale motivo?
    □ per recuperare un’ottimale capacità di carico
    □ per attendere il miglioramento della fisioterapia proposta
    □ per attendere la risoluzione dei sintomi/fase acuta
    □ per non aggravare i sintomi
    □ sostituire la corsa con cammino/esercizio terapeutico

24. Nel caso consigli di modificare l’allenamento per un comune mal di schiena: per quale motivo?
    □ per non decondizionare l'atleta
    □ per apprendere nuove strategie motorie
    □ modificare/migliorare la biomeccanica della corsa
    □ consentire una progressiva esposizione al carico

25. Nel caso consigliasse di modificare l’allenamento per un comune mal di schiena, su cosa interverrebbe principalmente?
    □ i km percorsi
    □ il tempo di allenamento
    □ la cadenza
    □ le calzature
    □ la superficie di corsa
    □ altro______________________________

26. Nella sua esperienza, in quanti giorni in media migliorano i suoi pazienti corridori con mal di schiena?
    □ <3 □ 7 □ 15 □>15

SURVEY – ENG
Running, low back pain and physiotherapists

Introduction:

Dear Collegue,
Among the most practiced sports in the world, running is having a huge success in Italy, thanks to its beneficial impact on health. However, the major drawback associated with running is the relatively high risk of injuries of the musculoskeletal structures. Currently, in literature several inconsistencies related to the topic of running injuries are present; the lack of reliable data in research makes it difficult to compare the different results of the studies. The most affected body districts are the lower limb and the lumbar spine, and the correlation between running and back pain is still poorly understood and poorly investigated to date.
This questionnaire aims to investigate your personal experience and opinion in relation to this topic.
The compilation of the survey is voluntary and it takes 5-7 minutes. Your answers are completely anonymous and will only be used for the purposes of this research.
Consider that in the questionnaire we define as "runner" a person who habitually practices running at least from 3 months, for a time of 30 minutes or 5 km per session, at least twice a week.

A. Registry section

1. Age ____________________________
2. Region ____________________________

B. Profession section

3. How many years have you been a physiotherapist ?
   □ <3 □4-10 □>10

4. What academic title do you have?
   □ PhD
   □ Master of science
   □ Bachelor degree
   □ Univerisity degree
   □ Antecendent title

5. Did you achieved Post Graduate besides Manual Therapy/Muscoloskeletal Rehabilitation?
   □ Only Manual Therapy/Muscoloskeletal Rehabilitation
   □ Sport Physiotherapy
   □ Other type _______________________

6. What is your job position?
   □ Private Practice
   □ Employee
   □ Mixed

☐ Other ______________________

7. How many patients do you treat per week?
☐ <10
☐ 11-20
☐ >20

8. On average, how many runners do you treat per month?
☐ none
☐ <5
☐ 5-10
☐ >10

C. Running section

9. Based on your opinion, would you consider it clinically relevant to ask runners-patients how long they have been practicing running?
☐ Yes
☐ No

10. Based on your opinion, would you consider it clinically relevant to ask runners-patients information about running footwear?
☐ Yes
☐ No

11. What type of runner do you treat most?
☐ Competive
☐ Non-competive

12. Based on your clinical experience, which is the anatomical district for which runners- patients more frequently complain (multiple answer can be selected, max 3)
☐ Knee
☐ Ankle-foot
☐ Hip
☐ Lumbar spine
☐ Thoracic spine
☐ Cervical spine
☐ Shoulder
☐ Other ___________________________

D. Low Back Pain section

13. Based on your opinion, running is a significant risk factor for the onset of low back pain?
☐ No
☐ Yes

14. ☐ If not ☐ Why?

□ It has no higher incidence than other sports
□ It does not burden the lumbar spine (not harmful)
□ If done correctly, it prevents low back pain

□ If yes □ Why?
□ Due to continuous stresses/impacts with grounds/soils
□ If running biomechanics is altered
□ If there is an imbalance between load and load capacity
□ If there is a reduced strength/elasticity of the lower limb/lumbar spine

15. In your clinical practice, how do you manage runners with low back pain?
□ Assessment and treatment similar to the one used with other patients non runner
□ Specific assessment and treatment (running biomechanics evaluation) without technological dedicated tools
□ Specific assessment and treatment, with technological dedicated tools (i.e. treadmills, video analysis, sensors, etc.)

16. In your clinical practice, which therapeutic choice do you adopt in runners with low back pain?
□ Mainly manual therapy (eg: joint mobilization, manipulation, pain education, etc.)
□ Mainly therapeutic exercise (including pain education)
□ Mainly modalities (eg: diathermy, TENS, laser, ultrasounds, etc.)
□ Combined manual therapy and therapeutic exercise
□ Combined manual therapy and modalities
□ Combined therapeutic exercise and modalities
□ Combined therapeutic exercise, manual therapy and modalities

17. In your clinical practice, do you adopt taping techniques in runners with low back pain?
□ No
□ Yes, sometimes
□ Yes, often
□ yes, always

18. In your clinical practice, do you consider it useful to adopt orthotics during the treatment of runners with low back pain ?
□ No
□ Yes, sometimes
□ Yes, often
□ yes, always

19. During specific exercise planning, for prevent onset of low back pain in runners, do you think it is more important to work on: (choose up to three options)
□ Frequency (number of training session per week)
□ Intensity (run kilometers per week/running session time per week)

☐ Training duration (in terms of minute in a single session)
☐ Foot strike pattern
☐ Cadence/step rate/step frequency
☐ Stride length
☐ Other___________________________________

20. In presence of a common low back pain in a runner, you recommend?
☐ To stop training
☐ To stop training and competitions
☐ To modify training but to stop competitions
☐ To continue training, but to stop competitions

21. Just in case you recommend to stop training for a common low back pain: for how many days?
☐ <3
☐ 7
☐ 15
☐>15

22. Just in case you recommend to modify training for a common low back pain: for how many days?
☐ <3
☐ 7
☐ 15
☐>15

23. Just in case you recommend to stop training for a common low back pain: for which reason?
☐ To recover an optimal load capacity
☐ To wait for the expected improvement from physiotherapy
☐ To wait for symptoms resolution/acute phase regression
☐ To avoid symptoms worsening
☐ To replace running with walking/exercise

24. Just in case you recommend to modify training for a common low back pain: for which reason?
☐ Not to decontion the athlete
☐ To learn new motor strategies
☐ To modify/improve running biomechianics
☐ To allow a progressive load exposure

25. Just in case you recommend to modify training for a common low back pain, what would you mainly do?
☐ Run kilometers
☐ Training time
☐ Cadence/step rate/step frequency
☐ Footwear
☐ Running surfaces
☐ Other__________________________

26. Based on your clinical experience, on how many days on average do your running patients with low back pain improve
    □ <3
    □ 7
    □ 15
    □>15

CHAPTER IV

LOW BACK PAIN AMONG ITALIAN RUNNERS: A CROSS-SECTIONAL SURVEY

Submitted as:
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Low Back Pain Among Italian Runners: A Cross-Sectional Survey

Abstract

Background: Low Back Pain is commonly reported as a very frequent disorder in sports, but it remains still unclear if its prevalence in running is higher than in other sports, or even in a non-athletes group.

Objectives: To determine prevalence of low back pain (LBP) and possibly related risk factors in a wide sample of Italian runners

Design: A cross-sectional online survey.

Setting: A national cross-sectional survey, according to the Checklist for Reporting Results of Internet E-Surveys guidelines (CHERRIES) and STrengthening the Reporting of OBservational Studies in Epidemiology (STROBE), was performed in 2019.

Partecipants: 2539 Italian runners.

Methods: Survey Monkey software was used to deliver the survey. The questionnaire was self-reported and included 38 questions. Descriptive statistics and frequencies described the actual number of respondents to each question. A wide sample of Italian runners belonging to national Italian runners associations was involved.

Results: Out of 4,000 eligible runners, 2600 (65.00%) answered and 2539 questionnaires (63.475%) were valid for the analysis. The 22.57% of respondents reported they have experieced LBP in the past year: The mean of highest intensity of pain perceived in the last episodes, measured by NPRS was 4.33. For the 76.96% of participants run was not cause of their LBP. No significant

correlations (Cramer's V <0.60) were found between individual characteristics and the other variables.

Conclusion: The LBP prevalence in Italian runners is low. These data seem in line with recent literature, albeit the studies that analyzed LBP, as like RRI, are very few. Our study did not revealed relevant risk factors for the onset of LBP but, probably, the exposure to a single risk factor is often insufficient to produce an overuse injury. The research on LBP in runners has to be considered in its early stages. Therefore, further quantitative studies should be developed.

1. Introduction

Low Back Pain (LBP) is the most frequently encountered muscoloskeletal disorders (MSDs) in general population [1-4] and one of most common health problems in the world; about the 80% of adults experience LBP at some point in their life, indeed [5,6 35,36]. Moreover, MSDs are a major clinical and social burden, since LBP is the first leading cause of Years Lived with Disability (YLDs), according to Global Burden of Disease 2013 [1].

As in general population, a great numbers of athletes also suffered LBP [7]. Particular sport disciplines such as ski, rowing, golf, volleyball, track and fields, swimming or gymnastics are at greater risk of suffering from LBP than nonathletes population [8-14]. Besides, LBP accounts about 30% of the common complaints occurring among the athletic population [15-17].

Some studies reported a point prevalence estimate of LBP that ranged from 1.0% to 58.0% (mean 18,10%) [18,19], while one-year and lifetime prevalence of LBP, conducted throughout the world, ranged between 0.8%-82.5% (mean 38,10%) and 11.0-84.0% (mean 47,16%), respectively [18,19]. Others different studies exhibited also a great variability in prevalence rates, that have been reported in 66% for young athletes [20,21] to 88,5% % in elite athletes [22]. These great variabilities in prevalence rates may be due to age of the sample, sample size, types of sport, types of athletes, the authors definition and recall period of LBP, strategy of extracting data and methodology used.

Albeit much studies about rate of the prevalence and incidence of LBP in world population and in different types of sport are available [5,6,18,19,23-25], it seems that this disorder has not been clearly investigated in runners population. Specifically, there are no data in this area in the population of Italian runners.

In fact, the health benefits associated with running are well documented [26-31], but, recent studies indicate that it also involves a relatively high risk of associated injuries [32,33]. Several studies have reported that 11%-85% of recreational runners have at least one Running Related Injuries (RRIs) each year [32] and the rate of prevalence of RRIs among middle and long-distance runners has been reported to range between 19% and 92% [34-39]. However, existing discrepancies among studies limit the comparison of data due to the divergences in the type of runners studied, follow-up provided, study design, etiology and definition of RRIs [34-47]. Therefore, RRIs primarily affect joints of the lower limb, pelvis and lumbar spine [37,47,48], causing painful muscles, tendons and joints, often resulting in low back pain (LBP) [35-39,41-48]. Yamato et al. [39], in 2015, defined the RRIs as musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running, causing a total restriction or interruption of running for at least seven or more days and requiring therapeutic assistance [39]. Currently, a definition of RRIs is not yet fully shared, and this reflected in the difficulty of analyzing the studies about of RRIs [37]. In last years, the studies mainly focused on RRIs in general, but actually there are not currently studies specifically addressing on prevalence, incidence and risk factors for LBP in runners [33,37]. Moreover, earlier literature of LBP has been addressed to a wide range of sports or athletes [4,25] and no conclusive data were published peculiarly on the LBP among a specific population of runners. For this reason, the aim of the present study was to explore and to investigate among nationwide sample of Italian runners: 1) the prevalence of LBP; and 2) if specific risk factors exist for LBP onset.

2. Material and Methods

2.1 Design

A web-based, national cross-sectional survey, herein reported according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) guidelines [49] and STrengthening the Reporting of Observational Studies in Epidemiology (STROBE) [50], was performed, between February and April 2019. The Liguria Clinical Experimental Ethics Committee (357REG2017, accepted on 19/09/2017) approved the present study.

2.2 Participants and Setting

A national sample of Italian runners was the identified target population through the websites of the major Italian running events (e.g. "Running Heart", Bari, Italy;) and from the email databases or facebook profiles of the Italian runners association, that accepted to partecipate.

The number of eligible people who responded to the survey was 2.539. Within the established population, we investigated those runners who: a) own a valid e-mail account, b) understood the Italian language; and c) were runner at the time of the survey. Taking into consideration previous surveys, conducted on runners [52-57] where the response rate ranged from 30%–60%, approximately 1200 to 2400 responses were expected from the total population target of 4000 runners.

With these sample sizes, a relative standard error ranging from 2 - 2.9 of the true estimate in the population with a 95% confidence level within 2 to 2.8%

points was expected, using a simple random sampling approach and with a population proportion set to 50% [51].

2.3 Questionnaire development and pre-testing

To the best of our knowledge, this is the first survey that investigated the prevalence of LBP and the main self-reported risk factors for the onset of LBP among a group of Italian runners. Therefore, a survey was developed using items from the existing surveys on running extracted from the literature [14,52-57].

Moreover, a survey was developed distinct and with iterative steps [58]. The initial list included 42 questions that were critically evaluated for face and content validity [58] by a panel of 15 runners and 15 OMPTs experts with an extensive experience in survey design, in the diagnosis and in the management of RRI. These runners and experts worked independently and then agreed on the final list by proving feedback on content accuracy, wording, question order and survey structure. Considering the feedbacks that received, the improvements were progressively included. When full agreement among runners and experts was achieved, a preliminary version of the survey made of 38 questions was self-administered and piloted in a convenient sample of other 15 runners (North, n = 5; Centre, n = 5; South of Italy, n = 5).

Once the pilot stage was concluded, a telephone or email debriefing session was performed [58]. The panel of experts conducted one-to-one interviews among the sample of 15 runners on the possible difficulties encountered when doing the survey (e.g., identifying questions that required further explanation, wording that was too difficult to read or that respondents seemed to find confusing) and the runners' experience in answering the questions. At the end of the pilot stage, the report was satisfactory, thus no changes or others comments/integrations were necessary. The sample of pilot stage reported that items of questions were not ambiguous; phrasing was easy and simple to be understood and the sharing experience was good.

2.4 Questionnaire implementation

A self-administered questionnaire (translated into English, Supplementary 1 File and in original language Supplementary 2 File in Appendix 1) divided into 4 sections (A, B, C and D) was used.

To deal with the risk of social desirability, the questionnaire guaranteed anonymity and its compilation was carried out via computer/tablet/mobile phone. To minimize the conceptual ambiguity, we included our definition of low back pain and a bodychart, which marked the part that had to be considered painful on the first page of the questionnaire.

The socio-demographic, professional variables and anthropometric variables were investigated using 7 open-ended questions (e.g., age, gender, weight, geographic region) in section A. Three closed multiple-choice questions, included in section B, investigated, sleep, smoke and drink, daily habits (e.g., numbers of cigarettes, hours sleep per night).

The third section (C) consisted of 14 closed multiple-choice questions investigated running variables (e.g., years of experience, kilometers (Km) run per week, training program, surface). This section, also investigated the presence of RRIs and the episodes of LBP. In the questionnaire the definition of RRIs was presented to minimize the conceptual ambiguity.

The last section (section D) lists 14 closed multiple-choice questions investigated the LBP in running. More specifically, the questions directed to know more about the episodes of LBP for example, intensity of pain, medical/physiotherapy consultation, participants' beliefs on cause of LBP during running, participants' knowledge on footwear, etc.

2.5 Data collection procedure

The SurveyMonkey (Survey-Monkey, Palo Alto, California, www.surveymonkey.com) online survey tool was used. The survey was administered over a 35 weeks period between 1th October 2018 and 1th June 2019. After permission was obtained from administrators of websites of the major Italian running events and administrators of the Italian runners association, all runners were contacted by blast email [58]. An email containing the survey and a brief note that underlined the aim of the study was delivered. Moreover, the email contained the data handling, the anonymity and invitation form to complete the survey.

Specifically, the statement within the email informed that by clicking on the survey link, respondents were providing their consent to participate in the study [58]. Three email reminders were sent 4, 8 and 12 weeks after the initial contact to encourage those who did not participate in the survey. Seven to 10 minutes were needed to complete the survey, corresponding to the completion time found to optimize response rates in online surveys [59]. Participation was voluntary and no incentives were offered to participants; there was the option to decline to answer to specific questions or to leave the entire questionnaire blank [58]. Participants were able to review or change responses using a back button, before submitting their answers. Data were downloaded and stored in an encrypted computer, and only the project manager could access to the information during all stages of the study. Participants were ensured that their identities would not be disclosed to investigators. All data were de-identified (name and email address) to maintain confidentiality and data protection [58].

2.6 Data analysis

Survey data were downloaded from SurveyMonkey into Excel spreadsheets and reviewed for accuracy and missing values. A questionnaire was considered incomplete if >20.0% of data were missing [60].

For questions that allowed a single choice, descriptive statistics (mean, standard deviation) for continuous variables were used, including 95% confidence intervals (CI), while absolute frequencies and percentages were applied to dichotomous, nominal and ordinal variables. The demographic variable age (transformed into an ordinal variable considering a decade as variable levels), gender, Body Mass Index (BMI) (transformed into five weight classes), job/profession type, smoke, alcohol daily, hours of sleep per night, muscoloskeletal deformities, duration of symptoms, change footwear between training/competition, time of running experience, every how many Kilometers (Km)/replace your footwear, Km/run per week, other sports practice, hours a week/training beyond running, type of footwear, time of run with same footwear, training program followed, stress periods, type of runner, type of ground/surface, were used for correlation analysis, as described below. For multiple-choiche questions, the absolute frequency and percentages for each combination of responses provided by each participant was calculated.

The presence of any relationship between the individual, daily habits and running, characteristics (section A, B, C of the survey) and the responses given (sections D of the survey) was calculated with Cramer's V, which is a measure of strength and direction of association derived from chi-square statistics. Only correlation values higher >0.60 were deemed acceptable and, therefore, here reported. R software, version 3.4.4 [61] was used for data analysis with the packages psych [62] and ggplot2 [63].

3. Results

3.1 Participant's characteristics

Out of the 4000 invited runners, a total of 2600 (65.00%) responded. Sixty-one incomplete surveys were excluded from data analysis, leaving 2539 questionnaires to be considered as valid (63.475%) for the analysis.

Runners had a mean age of 40.42 (SD 10.61; 95% CI 40.01-40.83; Range 18.0-77.0). The most represented region in the sample of the participants was Lombardy with 14.02% (95% CI 12.71-15.45), the least represented was Basilicata with 0.47% (95% CI 0.26-0.85). Mean of weight and height reported were 72.34 kilograms (Kg) (SD 9.66; 95% CI 71.97-72.72; range 42.00-160.00) and 169.74 centimeters (cm) (SD 9.65; 95% CI 169.36-170.11; range 111.00-216.00), respectively. These data were used to calculate the BMI of all participants: the mean resulting was 25.18 of BMI index (SD 3.41; 95% CI 25.05-25.31; range 15.40-34.29). A great proportion of runners worked as freelance/private practice (n=1550; 61.05%; 95% CI 59.11-62.94).

The reported musculoskeletal deformity diagnosed in the past in sample of participants were scoliosis and hyperkyphosis in 22,80% and 11,07% of the sample, respectively (n=579; 22.80%; 95% CI 21.19-24.50; n=281; 11.07%; 95% CI 9.89-12.37). Instead, the muscolosckeletal disorder reported were osteoarthritis of the spine and the hip (n=731; 28.79%; 95% CI 27.04-30.60; n=926; 36.47%; 95%

CI 34.60-38.38, respectively). The respondents' characteristics are described in Table 1.

3.2 Daily habits section

In this section we aimed to have information about some daily habits, such as smoking cigarettes, drinking alcohol, night hours of sleep. The majority of runners reported not to smoke (n=1068; 42.06%; 95% CI 40.14-44.01); moreover between smokers, the majority reported to smoke less than 5 cigarettes (n=698; 27.49%; 95% CI 25.77-29.28) or to smoke between 5 and 10 cigarettes (n=654; 25.76%; 95% CI 24.07-27.51). A very small percentage reported to smoke more than 20 cigarettes per day (n=12; 0.47%; 95% CI 0.26-0.85). A large proportion of runners (n=1306; 51.44%; 95% CI 49.47-53.40) reported to drink between 3 and 5 glasses of alcohol (e.g. wine, beer, per day). The percentage that reported not to drink alcohol was also wide (n=869; 34.23%; 95% CI 32.39-36.11). In relation to the request for daily hours of sleep, the majority of participants reported that they slept between 5 and 8 hours per night (n=1157; 45.57%; 95% CI 43.62-47.53). Sleeping between 3 and 5 hours was reported by 30.48% of the participants (n=774; 95% CI 28.70-32.32), while less than 3 hours or more than 8 hours it were reported by 19.49% and 4.45% of participants, respectively (n=495; 95% CI 17.98-21.10; n=113; CI 3.70-5.34). The overall overview of data of this section is reported in Table 2.

3.3 Running Section

Most runners reported running between 6 and 12 months (n=916; 36.08 %; 95% CI 34.21-37.98) but a large proportion of runners reported running between 3 and 6 months (n=732; 28.83%; 95% CI 27.08-30.64) and 36 months (n=516; 20.32 %; 95% CI 18.78-21.95), respectively. Less than 3 months (n=120; 4.73%; 95% CI

3.95-5.64) and between 12 and 36 months (n=255; 10.04%; 95% CI 8.91-11.29) were the periods of running experience that obtained the lowest percentage. Moreover, the majority of participants were non-competitive runners (n=1671; 65.81%; 95% CI 63.92-67.65) and not registered with some sport club (n=1473; 58.02%; 95% CI 56.06-59.94). When asking runners about number of kilometers run per week, the great numbers of runners reported running between 10 and 20 or 21 to 30 Km, respectively (n=833; 32.81%; 95% CI 30.99-34.68; n=766; 30.17%; 95% CI 28.39-32.00). Small percentages reported running less than 10km or more than 70km per week, instead (n=350; 13.78%; 95% CI 12.48-15.20; n=205; 8.07%; 95% CI 7.06-9.22). Participants were asked to report on which type of ground/surface most frequently run. The majority of runners reported to run on hard surfaces (e.g. asphalt, tartan, sidewalk) (n=1188; 46.79%; 95% CI 44.83-48.75); the minority of runners reported to run on combined/mixed surfaces (n=541; 21.31%; 95% CI 19.74-22.96). When asked if runners changed the type of footwear between training and competition, the large percentage reported that not change (n=1660; 65.38%; 95% CI 63.49-67.22). Over fifty percent (56.20%; 95% CI 54.24-58.14) of participants declared having changed running footwear between 600 and 1000 km (n=1427), while a small percentages reported to change footwear over 1000 km (n=330; 13.00%; 95% CI 11.73-14.38). Other questions about the footwear concerned the type of footwear that runners wore most frequently and how long they run with them. The majority of participants reported that they run with Motion Control footwear (n=1008; 39.70%; 95% CI 37.79-41.64), while the minority of them reported running with minimalist/barefoot footwear (n=149; 5.87%; 95% CI 5.00-6.87), (in the questionnaire example of footwear pictures and characterisics were presented for each type, see Supplementary 1 and Supplementary 2 Files in Appendix 1). About thirty-three percent of respondents reported changing the run footwear every 6-12 months (n=841; 33.12%; 95% CI 31.30-35.00), instead about thi instead about the thirteen percent of runners reported changing the run footwear after 12 months (n=352; 13.86%; 95% CI 12.55-15.28).

Most of participants reported to follow a training program prepared of a coach (n=859; 33.83%; 95% CI 32.00-35.71) or given by a teammate (n=833; 32.81%; 95% CI 30.99-34.68), only 10,48% (95% CI 9.32-11.75) declared they downloaded it from Internet (n= 266). Five hundred eighty-one participants (22.88%; 95% CI 21.27-24.58) reported that they did not follow any training program. Runners were also asked if they did other sports besides running and, most of them reported no (n=734; 28.90%; 95% CI 27.16-30.72), about thirty percent (n=721; 28.40%; 95% CI 26.66-30.20). The same percentage reported to do cycling, as well, while about tweenty percent reported doing soccer or gymnastics/fitness (n=557; 21.4%; 95% CI 20.35-23.61; n=527; 20.76%; 95% CI 19.20-22.40, respectively). A greater part of partecipants reported that they trained beyond running for less 3 hours per week (n=1209; 47.61%; 95% CI 45.66-49.58), only small part of participants for more ten hours per week (n=85; 3.35%; 95% CI 2.70-4.14). The major part of participants declared to have any other suffering RRIs in the past (n=862; 33.95%; 95% CI 32.11-35.83), conversly participants reported to have RRIs in the last 18 and 24 months in high percentages (n=646; 25.45%; 95% CI 23.77-27.19; n=661; 24.06%; 95% CI 22.42-25.78, respectively). Finally, we asked respondents about their experience of LBP, hence we asked if they have had LBP episodes in the past year and what average duration lasted these episodes. A high percentage, 77.43% (95% CI

75.74-79.03) of respondents (n=1966), reported none episode of LBP. The remaining 22.57% of respondents reported they have experieced LBP in the past year: in detail, the 11.46% (n=291; 95% CI 10.26-12.78) of runners reported duration of episode LBP between 1 and 3 days, the 6,06% (n=154; 95% CI 5.18-7.08) reported duration of LBP between 3 and 7 days, the 3.51% (n=89; 95% CI 2.84-4.31) reported than 10 days and the 1.54% (n=39; 95% CI 1.11-2.11) reported between seven and 10 days. The mean value of reported numbers of episodes was 2.50 (95% CI 2.44-2.55; Sd 1.39; range 1-9). The overall overview of data of this section is reported in Table 3.

3.4 Low back pain section

In this section only the data relating to the sample that suffered LBP in the last year are reported. In presence of LBP, the high percentage of participants (n=220; 38.39%; 95% CI 34.42-42.53) reported to limit their daily activities/routines for the less than 50%, while the majority of runners with LBP reported that they did not limit their activities/routines (n=278; 48.52%; 95% CI 44.36-52.69). The 24.26% of particpants reported to stop the training for less of seven days (n=139; 95% CI 20.84-28.02). Only 2.27% reported they always limit their activities/routines (n=13; 95% CI 1.27-3.95). Moreover, in presence of LBP, the highest percentage of participants (n=315; 54.97%; 95% CI 50.79-59.09) reported not to stop training, while the percentages of partecipants that stopped training for over 90 and 180 days were 1.74% (95% CI 0.89-3.29) and 1.40% (95% CI 0.65-2.84) respectively (n=10; n=8). The highest percentage of respondents (n=373; 65.09%; 95% CI 61.01- 68.97) reported to not change the way of run, in case not stopping training, due to their LBP. Among those who responded to change the way they run, the lowest percentage of runners reported they modified the foot strike pattern (n=39; 6.81%; 95% CI 4.94-9.27), they reduced the time and the km traveled, with 7.50% (95% CI 5.54-10.05) and 20.59% (95% CI 17.40-24.19) proportion of response, respectively (n= 43; n= 118). In case of health treatment or consultation, the majority of respondents reported they referred to a physiotherapist (n=208; 36.30%; 95% CI 32.38-40.40), while the 10.82 (95% CI 8.45-13.72) percentage of runners to a general practitioner (n=62) and only the 2.79 (95% CI 1.66-4.59) reported to refer to other healthcare professional (n=16); the highest proportion of partecipants reported not to resort any health consultation or treatment (n=287; 50.09%; 95% CI 45.92-54.25). A total part of respondents of the sample with LBP, reported to used drugs (NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) to reduce LBP (n= 573). The NSAIDS were recommended by a general pratictioner in 60.56% of cases (n=347; 95% CI 56.41-64.56), while only 7.33% (n=42; 95% CI 5.39-9.86) was recommended by friend or relatives and in the 32.11% by self- medication (n=184; 95% CI 28.33-36.13).

In presence of LBP, the high percentage of participants (n=240; 41.88%; 95% CI 37.83-46.05) referred that laying down was an activity to reduce the symptoms of LBP; the 24.96% (95% CI 21.50-28.75) reported instead that walking was an activity to reduce LBP (n=143); the lowest percentage of runners reported that none activity reduced LBP (n=40; 6.98%; 95% CI 5.09-9.46). Conversely, 12.04 percentage of runners reported that walking increased LBP (n=69; 10.28%; 95% CI 9.55-15.06), but the same percentage of participants, as in the activities that reduced LBP, reported that none activities increased LBP (n=40). The mean of highest intensity of pain perceived in the last episodes, measured by NPRS [64] was 4.33 (range 1-10; 95% CI 4.25-4.40; SD 1.91). When asked if in addition to their LBP, did you experience radiating pain down to your lower limb most of the respondents replied no had experience (n=344; 60.03%; 95% CI 55.88-64.05); the 24.08% (n= 138; 95% CI 20.68-27.84) reported experience radiating pain up to the knee, only 15.88% (n=91; 95% CI 13.04-19.19) reported experience radiating up to the feet. Small percentages reported other unpleasant sensations in lower limb, 15.18% (95% CI 12.40-18.45), 17.80% (95% CI 14..80-21.24) and 8.90% (95% CI 6.76-11.61) reported tingling, burning and weakness (n= 87; n= 102; n= 51), respectively. Answers given to the question "Do you think running is the cause of your LBP?" spread out as follows: for the great part of sample, run was not cause of their LBP (n=441; 76.96%; 95% CI 73.25-80.31), in the 16.58% (n=95; 95% CI 13.68-19.94) respondents thinked the run was a cause of their LBP and for 6.46% (n=37; 95% CI 4.65-8.87) of participants, they declared not to know if the run was or not the cause of LBP. For the majority of participants the episode of LBP does not coincided with any running related activities (n=276; 48.17%; 95% CI 44.01-52.34), while for lowest part of participants the episodes of LBP coincided with competition (n=27; 4.71%; 95% CI 3.19-6.87). For the other parts, LBP coincided with training, athletic training and recovery after a stop, 24.61% (95% CI 21.17-28.39), 7.68% (95% CI 5.69-10.25) and 14.83% (95% CI 12.08-18.07) respectively (n= 141; n=44; n=85).

In case of LBP episodes overlapped with training periods, the 13.61% of respondents (n=78; 95% CI 10.97-16.76) reported that the episodes overlaped with repeats session (high intensity), furthermore the 15.36% (n=88; 95% CI 12.56-18.63) reported that episodes overlaped with slow cross-country race (low intensity running), the 10.64% (n=61; 95% CI 8.30-13.53) reported that overlaped with medium cross-country race (mid intensity running) and 7.85% (n=45; 95%

CI 5.84-10.44) reported that overlaped with unloading workout. The majority of runners (n=301; 52.53%; 95% CI 48.35-56.67) reported that the episodes did not match with training periods. Moreover if LBP episodes overlapped with intense stress periods (school, job, family) a great percentage of participants reported that LBP episodes coincided with intense stress periods due to job (n=236; 41.19%; 95% CI 37.14-45.35); a little percentage of participants reported that episodes coincided with intense stress periods due to school or family (n=25; 4.36%; 95% CI 2.90-6.46; n=49; 8.55%; 95% CI 6.45-11.22), respectively. The highest percentage of runners reported that not coincide of none intense stress periods (n=263; 45.90%; 95% CI 41.77-50.08). Finally, we asked participants if they noticed whether or not LBP episodes coincided with footwear change: almost all of the participants reported no, that the episodes of LBP did not coincide with the change of footwear (n=502; 87.61%; 95% CI 84.56-90.14). The overall overview of data of this section is reported in Table **4.**

3.5 Correlation between variables

No significant correlations (Cramer's V <0.60) were found between individual characteristics (section A, B and C of the survey) and the responses given (sections D of the survey).

4. Discussion

To the best of our knowledge, this is the first study that evaluates prevalence, beliefs and risk factors of the onset of LBP in wide sample of Italian runners.

This study analyzed characteristics of prior LBP episodes like as RRIs, related to gender, BMI, smoke, hours of sleep, training volume (time and kilometers), stress periods, type of footwear and others running characteristics.

Among the social characteristics, the male gender is the most represented, with over 60% of the participants, with an average age in the sample of about 40 years. Among the demographical characteristic of the respondents, instead , the sample is most rappresented in the northern part of Italy, respect to (vs) South and Islands vs Centre, probably due to the number of regions which compose such areas.

The majority of the sample of runners work as freelance/private practice nel 60% of the cases. All these characteristics highlight a sample of runners, as already described in many other studies, in which men are much more than women, with an average age of 40 years, like our sample as well [52-54,56,57,65-74].

The sample examined seems to be composed by healthy runners and pursuing healthy lifestyles. Indeed, most of the respondents have a BMI of 25.18, which corresponds to slighty overweight persons, more than 50% of the sample sleeps between 5 and 8 or more hours and over 34% of the sample does not drink alcohol or only moderately (between 3 and 5 glasses of wine or beer per day) in the 50% of sample, respectively. Moreover, non-smoker represent more than 40% of the sample and about 30% smokes less than 5 cigarettes per day. Although athletes who sleep <8h per night have, on average, 1.7 times much more risk of injury than athletes who sleep ≥ 8h per night [75], no positive associations were found in our sample between hours of sleep and number of episodes of LBP, pain intensity or duration of symptoms in days:

probably this phenomenon happens due to the association of a combination of correct daily living habits in our sample. Moreover, sleep deprivation appears to be associated with injuries in an adolescent athletic population, rather than adults [75]. Albeit these findings, evidence indicates that current and former smokers have a higher prevalence and incidence of LBP than non-smokers [76]: the 30% of our smoker participants sample did not have correlation with LBP, even if the evidence confirmed that this association is fairly modest and the association between low back pain is stronger in adolescents than in adults [76]. Overweight and obesity have the strongest association with seeking care for LBP and chronic LBP: in fact, compared with non-overweight people, overweight people had a higher prevalence of LBP but a lower prevalence of LBP compared to obese people [77]. In our respondents' sample, mean BMI value was 25.18, which corresponds to a slighty overweight: this may be the reason of aformentioned results.

Several analyzed characteristics define in the sample a part of amateur or recreational runners. In fact, more than 60% of them reported to have been running for no more than a year. Only a small part of the sample, around 20%, seems to be build up of more experienced runners, since they have been running for more than 36 months. In this study it was more likely that we were faced with less experienced runners, based on their time of running, km travelled (more than 70% of runners told they did not run more than 30 km per week), the type of runner, (e.g. non-competitive runners versus competitive runners), they are not registered in sports clubs. About 20% of participants run more km per week, between 50 and 70, and this could represent that part of sample running for more than 36 months.

Despite subjects in this study were more likely to be recreational runners, injury rates and patterns observed agree with previous data on LBP, such as RRIs among runners with a different experience years (e.g. > 4 years) and type (e.g. full marathon) [52-57].

The findings of our cross-sectional survey revealed that the LBP prevalence among runners, compared to the general population [5,6,18,23,24], is low. The one-year prevalence of LBP, in world population, ranges between 0.8%-82.5% (mean 38,10%) [18,19], while in our study the one-year prevalence is 22.57%, as confirmed in other studies, indeed [54,55,57,66,74].

Moreover, our findings revealed that the LBP prevalence in runners, compared to the prevalence of the other most relevant RRIs, seems to be lower [32-39,72-74,78-81]. Furthermore, the RRIs affecting lower limbs seem to have much greater prevalence rates, from 28% to 42% in the knee (i.e. patellar tendinopathy, iliotibial band syndrome, patellofemoral pain syndrome) and from 14% to 38% in the ankle (i.e. ankle sprain, achilles tendinopathy, plantar fasciopathy) [35-39, 72-74,78-82].

The study also identified that the type of footwear, the time or run kilometers before changing footwear, the training type or duration and surface were not significantly associated with running related LBP. Conversely what has been confirmed instead in other studies that analyzed the RRIs of the lower limbs [32-39,43,54-57,72,73,83,84].

Practicing other sports, including cycling, soccer, and gym/fitness, was also found not to be related to the onset of LBP episodes. This seems in line with other studies, indicating that doing other activities, especially gymnastics, seems to be a protective factor [52].

In presence of a LBP, the majority of runners respondents reported that run is not the cause of onset of their LBP; furthermore over 45% did not reduce their daily activities and in over 50% did not stop the training program. The reason for this could reside in the low pain intensity reported by the sample of runners interviewed (NPRS 4.33) [64] or also because runners of our study were active and fit subjects. These findings seems highly in line with the clinical practice guidelines on LBP, which advices to retunr to normal activities, staying active and avoid bed rest [85-87].

According to the runners interviewed, about 22%, reported that episodes of LBP improve between 1 and just over 10 days: our data confirms the characteristics of the international consensus which defines the RRI as a musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running activities, causing a total restriction or suspension of running for at least seven or more days, requiring medical/physiotherapy assistance [39]. Moreover, our data are much similar to data obtained from general population, which at 2 weeks after onset (over 35% of patients) and at 4 weeks (over 60% of patients) have no longer symptoms, respectively [88].

For these reasons, we cautiously invite to think running as a protective factor from LBP and to consider prescribing running as a preventive exercise for LBP.

4.1 Strengths and weaknesses of the study

A high response rate was achieved (63.47%), confirming the willingness of Italian runners to participate to the survey such as in others survey developed on Italian sportsmen [14]. To the authors' knowledge, there are not existing other similar studies investigating LBP on Italian runners and conducted through questionnaires. Therefore, we cannot compare our data with other studies. A specific group of Italian runners (n =2539), more likely recreational runners, was involved. Therefore, their responses might differ from that group of runners with more experience. Moreover, demographical characteristic of the respondents, such as the regional distribution of Italy, where respondents are based in (North vs Centre and South), and other characteristics like age of the sample, may have influenced the participants' knowledge, beliefs and other characteristics of LBP in running. A survey tool was adopted to understand the perspectives of the target population [52-57]. The questionnaire included different items (e.g., close-ended questions), to increase the likelihood of capturing the complexity of the phenomena under study [89]. However, our methodological choice was based on the impossibility to have a previously standardized questionnaire for a national online survey for similar data, hence we mimicked a past survey experience previously reported in running survey performed on runners the others nationality [52-57]. Given that data were self-reported and retrospective in nature, recall bias can threaten the validity of the findings [73,90,91].

5. Conclusion

Overall, the findings of this cross-sectional study revealed that the LBP prevalence in runners, compared to prevalence of the other most relevant RRIs, seems to be lower [32-39,72-74,78-81]. These data seem in line with recent literature, albeit the studies that analyzed LBP, as like RRI, are very few. Our study did not revealed relevant risk factors for the onset of LBP in Italian runners but, probably, the exposure to a single risk factor is often insufficient to produce an overuse injury: the RRI is the result of a number of superposing factors (like training increase, muscular impairments, unsuitable equipment, etc.) [55].

The research on LBP in runners has to be considered in its early stages. Therefore, further quantitative studies that evaluating beliefs, attitudes, behaviors and risk factors for the onset of LBP, as like RRI among runners, should be developed. To develop a more comprehensive understanding of the phenomena, there is a strong need to investigate patients' perceptions on LBP and running.

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TABLE 1 | Participant's Characteristics (*N* = 2.539).
(section A of questionnaire) (In brackets only the values of the sample with LBP)

	Min-Max	Mean	95% CI*	SD*
Q1. Age:	18.0-77.0	40.42	40.01-40.83	10.61
Q2. Gender:				
- M	1758 (374)	69.24 (65.27)	67.40-71.02 (61.19-69.14)	
- F	781 (199)	30.76 (34.73)	28.97-32.60 (30.86-38.81)	
Q3. Weight (Kg):**	42.00-160.00	72.34	71.97-72.72	9.66
Q4. Height (cm):**	111.00-216.00	169.74	169.36-170.11	9.65
- BMI:**	15.40-34.29	25.18	25.05-25.31	3.41
	N*	**%***	**95% CI***	
Q5. Job/Profession:				
- Practice/Freelance	1550 (362)	61.05 (63.18)	59.11-62.94 (59.06-67.11)	
- Employee	989 (211)	38.95 (36.82)	37.05-40.88 (32.89-40.94)	
Q6. Italian Region:	**N**	**%**	**95% CI**	
Abruzzo	79	3.11	2.49-3.88	
Basilicata	12	0.47	0.26-0.85	
Calabria	137	5.40	4.56-6.36	
Campania	115	4.53	3.77-5.43	
Emilia Romagna	191	7.52	6.54-8.63	
Friuli Venezia Giulia	15	0.59	0.34-1.00	
Lazio	56	2.21	1.68-2.87	
Liguria	71	2.80	2.20-3.53	
Lombardia	356	14.02	12.71-15.45	
Marche	157	6.18	5.29-7.21	
Molise	83	3.27	2.63-4.06	
Piedmont	277	10.91	9.74-12.20	
Puglia	172	6.77	5.84-7.84	
Sardegna	115	4.53	3.77-5.43	
Sicilia	212	8.35	7.32-9.51	
Trentino Alto Adige	72	2.84	2.24-3.58	
Toscana	171	6.73	5.80-7.80	
Umbria	30	1.18	0.81-1.70	
Valle d'Aosta	**74**	2.91	2.31-3.66	
Veneto	144	5.67	4.82-6.66	
Q7. Musculoskeletal deformities/disorders diagnosed in the past*:**				
- Scoliosis	579 (122	22.80 (21.29)	21.19-24.50 (18.05-24.92)	
- Hyperkyphosis	281 (96)	11.07 (16.75)	9.89-12.37 (13.84-20.12)	
- Osteoarthritis				
- spine	731 (141)	28.79 (24.61)	27.04-30.60 (21.17-28.39)	
- hip	926 (213)	36.47 (37.17)	34.60-38.38 (33.23-41.29)	
- None	22 (1)	0.87 (0.17)	0.56-1.33 (0.01-1.12)	

*N: numbers; SD: standard deviation; CI: Confidence Interval; %: percentage;
**BMI: Body Mass Index; Kg: kilograms; cm: centimeters;
***in questionnaire other deformities were presented and they do not received any answers.

TABLE 2 ǀ Daily habits section (*N* = 2.539). (section B of questionnaire) (In brackets only the values of the sample with LBP)	N*	%*	95% CI*
Q8. Do you smoke (cigarettes/day)?			
- Yes			
- <5	698 (41)	27.49 (7.15)	25.77-29.28 (5.24-9.66)
- 5-10	654 (32)	25.76 (5.58)	24.07-27.51 (3.91-7.88)
- 10-20	107 (21)	4.21 (3.66)	3.48-5.09 (2.34-5.64)
- >20	12 (1)	0.47 (0.17)	0.26-0.85 (0.01-1.12)
- No	1068 (478)	42.06 (83.42)	40.14-44.01 (80.06-86.32)
Q9. Do you drink alcohol daily?			
- Yes			
- 1-3 glasses	331 (277)	13.04 (48.34)	11.76-14.42 (44.19-52.52)
- 3-5 glasses	1306 (19)	51.44 (3.31)	49.47-53.40 (2.06-5.22)
- >5 glasses	33 (8)	1.30 (1.40)	0.91-1.84 (0.65-2.84)
- No	869 (269)	34.23 (46.94)	32.39-36.11 (42.81-51.13)
Q10. How many hours on average do you sleep per night?			
- < 3h*	495 (31)	19.49 (5.41)	17.98-21.10 (3.76-7.68)
- 3-5h	774 (83)	30.48 (14.48)	28.70-32.32 (11.76-17.70)
-5-8h	1157 (445)	45.57 (77.66)	43.62-47.53 (73.98-80.96)
-> 8h	113 (14)	4.45 (2.44)	3.70-5.34 (1.39-4.17)

*N: numbers; CI: Confidence Interval; %: percentage; h: hours;

TABLE 3 ǀ Running section (*N* = 2.539). (section C of questionnaire) (In brackets only the values of the sample with LBP)	N*	%*	95% CI*
Q11. How long have you been running?			
- <3 months	120 (72)	4.73 (12.56)	3.95-5.64 (10.02-15.62)
- 3-6 months	732 (81)	28.83 (14.14)	27.08-30.64 (11.44-17.32)
- 6-12 months	916 (81)	36.08 (14.14)	34.21-37.98 (11.44-17.32)
- 12-36 months	255 (94)	10.04 (16.04)	8.91-11.29 (13.52-19.75)
- >36 months	516 (245)	20.32 (42.76)	18.78-21.95 (38.68-46.93)
Q12. Are you registered with some sport club?			
- Yes	1066 (310)	41.98 (54.10)	40.06-43.93 (49.92-58.23)
- No	1473 (263)	58.02 (45.90)	56.06-59.94 (41.77-50.08)
Q13. Are you a runner:			
- Competitive	868 (260)	34.19 (45.37)	32.35-36.07 (41.26-49.56)
- Non-competitve	1671 (313)	65.81 (54.62)	63.92-67.65 (50.44-58.74)
Q14. How many km do you run per week:			
- <10	350 (123)	13.78 (21.46)	12.48-15.20 (18.22-25.10)
- 10-20	833 (123)	32.81 (21.46)	30.99-34.68 (18.22-25.10)
- 21-30	766 (112)	30.17 (19.55)	28.39-32.00 (16.42-23.08)
- 30-50	385 (150)	15.16 (26.18)	13.80-16.63 (22.66-30.02)
- >70	205 (65)	8.07 (11.34)	7.06-9.22 (8.92-14.30)
Q15. Which type of			

ground/surface do you run most frequently on?			
- Hard (asphalt, tartan, sidewalk)	1188 (408)	46.79 (71.20)	44.83-48.75 (67.27-74.84)
- Soft (wood, topsoil, sand)	810 (44)	31.90 (7.68)	30.10-33.76 (5.69-10.25)
- Combined/mixed surfaces	541 (121)	21.31 (21.12)	19.74-22.96 (17.89-24.74)
Q16. Do you change the type of footwear between training and competition?			
- Yes	879 (148)	34.62 (25.83)	32.77-36.51 (22.33-29.65)
- No	1660 (425)	65.38 (74.17)	63.49-67.22 (7034-77.67)
Q17. How often do you replace your footwear on average with which you run most often?			
- <600 Km*	782 (177)	30.80 (30.89)	29.01-32.64 (27.16-34.88)
- 600-1000 Km	1427 (331)	56.20 (57.77)	54.24-58.14 (53.59-61.83)
- >1000 Km	330 (65)	13.00 (11.34)	11.73-14.38 (8.92-14.30)
Q18. Which type of footwear do you use most frequently*:**			
- Motion Control	1008 (219)	39.70 (38.22)	37.79-41.64 (34.25-42.35)
- Stability	596 (130)	23.47 (22.69)	21.85-25.18 (19.36-26.38)
- Light Stability	630 (168)	24.81 (29.32)	23.15-26.55 (25.66-33.26)
- Neutral	156 (41)	6.14 (7.15)	5.26-7.17 (5.24-9.66)
- Minimalist/Barefoot	149 (15)	5.87 (2.62)	5.00-6.87 (1.53-4.38)
Q19. How long did you run with the same footwear?			
- <3 months	654 (195)	25.76 (34.03)	24.07-27.51 (30.18-38.09)
- 3-6 months	692 (172)	27.25 (30.02)	25.54-29.04 (26.32-33.98)
- 6-12 months	841 (76)	33.12 (13.26)	31.30-35.00 (10.65-16.38)
- >12 months	352 (130)	13.86 (22.69)	12.55-15.28 (19.36-26.38)
Q20. Do you follow a training program?			
- Yes			
- A coach	859 (148)	33.83 (25.83)	32.00-35.71 (22.33-29.65)
- A teammate	833 (84)	32.81 (14.66)	30.99-34.68 (11.92-17.88)
- Internet	266 (51)	10.48 (8.90)	9.32-11.75 (6.76-11.61)
- No	581 (290)	22.88 (50.61)	21.27-24.58 (46.44-54.77)
Q21. Do you practice other sports?			
- Yes**			
- football soccer	557 (205)	21.94 (35.78)	20.35-23.61 (31.87-39.87)
- cycling	721 (204)	28.40 (35.60)	26.66-30.20 (31.70-39.69)
- gym/fitness	527 (150)	20.76 (26.18)	19.20-22.40 (22.66-30.02)
- No	734 (14)	28.90 (2.44)	27.16-30.72 (1.39-4.17)
Q22. For how many hours a week do you train beyond running?			
- <3h	1209 (365)	47.61(63.70)	45.66-49.58 (59.59-67.62)
- 3-5h	816 (136)	32.14 (23.73)	30.33-34.00 (20.35-27.48)
- 5-10h	429 (54)	16.90 (9.42)	15.47-18.42 (7.22-12.19)
- >10h	85 (18)	3.35 (3.14)	2.70-4.14 (1.93-5.01)
Q23. Have you ever had any RRIs** (excluding LBP)?**			
- Yes, in the last 12 months	420 (136)	16.54 (23.73)	15.13-18.06 (20.35-27.48)
- Yes, in the last 18 months	646 (44)	25.45 (7.68)	23.77-27.19 (5.69-10.25)

- Yes, in the last 24 months	611 (87)	24.06 (15.18)	22.42-25.78 (12.40-18.45)
- No	862 (306)	33.95 (53.40)	32.11-35.83 (49.22-57.54)
Q24. Have you had LBP* episodes in the past year (Average duration in days)?			
- No	1966	77.43	75.74-79.03
- Yes, 1-3 days	291	11.46	10.26-12.78
- Yes, 3-7 days	154	6.06	5.18-7.08
- Yes, 7-10 days	39	1.54	1.11 -2.11
- Yes, more than 10 days	89	3.51	2.84-4.31
	Min-Max	**Mean**	**95% CI*/ SD***
If Yes numbers of episodes	1-9	2.50	2.44-2.55/ 1.39

*Km: Kilometers; N: numbers; CI: Confidence Interval; %: percentage;
**this question have had free choice, the three sports indicated are the only ones reported by the participants;
***in questionnaire example of footwear pictures were presented for each type.
****RRIs: Running Related Injuries; in the questionnaire was presented the definition of RRIs;

TABLE 4 | Low back pain section (*N* = 573). (section C of questionnaire)

	N*	**%***	**95% CI***
Q25. Has LBP* limited you in daily routines?			
- Yes, always	13	2.27	1.27-3.95
- Yes, less than 50%	220	38.39	34.42-42.53
- Yes, more than 50%	62	10.82	8.45-13.72
- No	278	48.52	44.36-52.69
Q26 Did you stop training, due to LBP*?			
- Yes < 7 days	139	24.26	20.84-28.02
- Yes > 7 days	73	12.74	10.18-15.81
- Yes > 30 days	28	4.89	3.33-7.07
- Yes > 90 days	10	1.74	0.89-3.29
- Yes > 180 days	8	1.40	0.65-2.84
- No	315	54.97	50.79-59.09
Q27. If you did not stop training, due to your LBP* did you change your way to run?			
- Yes, I reduced the traveled Km**	118	20.59	17.40-24.19
- Yes, I reduced time	43	7.50	5.54-10.05
- Yes, I modified the foot strike pattern	39	6.81	4.94-9.27
- No	373	65.09	61.01- 68.97
Q28. Did you have to resort to medical treatment or consultation?			
- No	287	50.09	45.92-54.25
- Yes, General practitioner	62	10.82	8.45-13.72
- Yes, Physiotherapist	208	36.30	32.38-40.40
- Yes. Other healthcare professional	16	2.79	1.66-4.59

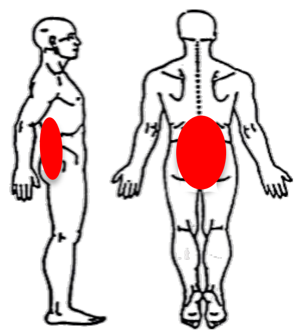
Q29. Did you use drugs to reduce LBP*,specify who recommended you?			
- Medical prescription	347	60.56	56.41-64.56
- Suggested by friends/relatives	42	7.33	5.39-9.86
- Self-medication	184	32.11	28.33-36.13
If you answered Yes		NSAIDs^	
- specify which ones***			
Q30. Which activities or positions reduced LBP*?			
- Laying down	240	41.88	37.83-46.05
- Sitting down	86	15.01	12.24-18.26
- Standing up straight	64	11.17	8.77-14.11
-Walking	143	24.96	21.50-28.75
- None	40	6.98	5.09-9.46
Q31. Which activities or positions increased LBP*?			
- Laying down	77	13.44	10.81-16.57
- Sitting down	169	29.49	25.82-33.44
- Standing up straight	218	38.04	34.08-42.18
- Walking	69	12.04	9.55-15.06
- None	40	6.98	5.09-9.46
	Min-Max	**Mean**	**95% CI* /SD***
Q32. Which was the highest intensity of pain perceived in the last episode? (measured by NPRS)	1-10	4.33	4.25-4.40/1.91
	N*	%*	**95% CI***
Q33. In addition to your LBP*, did you experience radiating pain down to your lower limb, if yes?			
- Yes, up to the knee	138	24.08	20.68-27.84
- Yes, up to the feet	91	15.88	13.04-19.19
- No	344	60.03	55.88-64.05
In addition to pain, were there other unpleasant sensations in the lower limb?			
- tingling	87	15.18	12.40-18.45
- burning	102	17.80	14..80-21.24
- weakness	51	8.90	6.76-11.61
- none	333	58.11	53.95-62.17
Q34. Do you think running is the cause of your LBP*?			
- Yes	95	16.58	13.68-19.94
- I do not know	37	6.46	4.65-8.87
- No	441	76.96	73.25-80.31
Q35. LBP* episodes coincide with periods of:			
- training	141	24.61	21.17-28.39
- athletic training	44	7.68	5.69-10.25
- recovery after a stop	85	14.83	12.08-18.07
- competition	27	4.71	3.19-6.87
- they do not match with any sport related activities	276	48.17	44.01-52.34
Q36. LBP* episodes			

overlap with training periods:			
- slow cross-country race (low intensity running)	88	15.36	12.56-18.63
- medium cross-country race (mid intensity running)	61	10.64	8.30-13.53
- repeats (high intensity)	78	13.61	10.97-16.76
- unloading workout	45	7.85	5.84-10.44
- they do not match with training periods	301	52.53	48.35-56.67
Q37. LBP episodes overlap with intense stress periods (school, job, family)			
- Yes, for the school	25	4.36	2.90-6.46
- Yes, for the job	236	41.19	37.14-45.35
- Yes, for the family	49	8.55	6.45-11.22
- No, do not coincide	263	45.90	41.77-50.08
Q38. Did you notice whether or not LBP* episodes coincide with footwear change?			
- Yes	71	12.39	9.86-15.44
- No	502	87.61	84.56-90.14

*N: numbers; SD: standard deviation; CI: Confidence Interval; %: percentage;
*LBP: Low Back Pain;** Km: Kilometers; *NSAIDs: Nonsteroidal Anti-Inflammatory Drugs
***this question have had free choice, the Drug indicated is the only ones reported by the participants;
**** NPRS: Numeric Pain Rating Scale [64];

Appendix 1

QUESTIONARIO – Running e Lombalgia

Definizione di Mal di Schiena	
Il mal di schiena, tecnicamente Lombalgia, è definibile come un dolore e/o limitazione funzionale compreso tra il margine inferiore dell'arcata costale e le pieghe glutee inferiori con eventuale irradiazione posteriore alla coscia ma non oltre il ginocchio.	

A. Sezione Anagrafica

1. Età ___________________________
2. Genere: M□ F □
3. Peso (kg)___________________________
4. Altezza (cm) ___________________________
5. Professione: Libero Professionista □ Dipendente □
6. Regione ___________________________

7. Deformità/Disordini muscoloscheletriche diagnosticate in passato
   □ Scoliosi
   □ Ipercifosi
   □ Osteoartrosi
      □ rachide
      □ anca
      □ ginocchio
   □ Osteocondrosi
      □ rachide
      □ anca
      □ tuberosità tibiale
   □ Ginocchia vare □ Ginocchia valghe)
   □ piedi piatti □ piedi cavi
   □ Eterometria arti inferiori (gamba più lunga dell'altra)
      □ Usi un plantare per questo?
   □ altro_____________
   □ nessuna

B. Sezione Abitudini Quotidiane

8. Fumi □ si □ no se si quante sigarette al giorno □ <5 □5-10 □ 10-20 □>20
9. Bevi alcoolici giornalmente (per esempio, vino, birra)?
   se si □1-3 bicchieri □3-5 bicchieri □>5 bicchieri □ no
10. Quante ore dormi mediamente a notte □ <3h □3-5h □ 5-8h □>8h

C. Sezione Running

11. Da quanto tempo pratichi la corsa
    □ <3 mesi
    □ 3 -6 mesi
    □ 6 -12 mesi
    □ 12 -36 mesi
    □ >36 mesi

12. Sei tesserato con qualche società sportiva □ si □ no

13. Sei un corridore
    □ agonista
    □ non agonista

14. Quanti Km percorri a settimana □ <10 □ 10-20 □ 21-30 □ 30-50 □ >70

15. Su quale tipologia di superfice corri con maggior frequenza
    □Dura (asfalto, tartan, marciapiede)
    □Morbida (legno, terra, sabbia)
    □Superfici combinate

16. Cambi tipologia di di scarpa fra l'allenamento e la competizione?
    □ si □ no

17. Ogni quanti Km mediamente sostituisci le tue scarpe con le quali corri più spesso
    □ <600 km □ 600-1000 Km □ >1000 Km

18. Quale tipologia di calzatura utilizzi più frequentemente*:

□  Motion Control

□  Stability

□  Light Stability

□  Neutral

□  Minimalist - Barefoot

19. Per quanto tempo hai corso con le stesse calzature
    □<3mesi □3-6 mesi □6-12 mesi □>12 mesi

20. Segui un programma di allenamento ? □ si □ no
    se si consegnato da □ un tecnico □ un compagno di corsa □ internet

21. Pratichi altri sport □ si □ no se si quale________________________

22. Per quante ore alla settimana ti alleni oltre la corsa
    □ <3h □ 3-5h □ 5-10h □ >10h

23. Hai mai avuto degli infortuni correlati alla corsa**
    □ si, negli ultimi 12 mesi
    □ si, negli ultimi 18 mesi
    □ si, negli ultimi 24 mesi
    □ no

24. Nell'ultimo anno hai avuto episodi di mal di schiena?^
    □ si □ no
    Se hai risposto SI,
    N° episodi ______
    Durata media in giorni
    □ 1-3 giorni
    □ 3-7 giorni
    □ 7-10 giorni
    □ più di 10 giorni

    ^(Se ha risposto NO a questa domanda la sua indagine è terminata. Grazie)

D. Sezione Lombalgia

25. Il mal di schiena ti ha limitato nelle attività quotidiane? □ si □ no
    Se hai risposto SI, □ Sempre □ Si meno del 50% □ Si più del 50% □ No

26. Hai sospeso gli allenamenti a causa del mal di schiena? □ si □ no
    Se hai risposto SI, □ <7 gg □ >7gg □ >30gg □ >90gg □ >180gg

27. Se non hai sospeso gli allenamenti, a causa del mal di schiena hai modificato il tuo modo di correre
    □ si, diminuendo i Km percorsi
    □ si, diminuendo il tempo
    □ si, modificando la tipologia di appoggio
    □ no

28. Sei ricorso a cure o consulto sanitario □ si □ no
    □ medico di famiglia □ fisioterapista □ altro operatore sanitario____________________

29. Hai utilizzato farmaci per ridurre il mal di schiena □ si □ no
    Se hai risposto SI, specifica quali_______________________________________
    Specifica chi ti ha consigliato?
    □ Su prescrizione medica
    □ Suggeriti da amici/parenti
    □ Automedicazione

30. Quali attività o posizioni riducevano il mal di schiena?
    □ sdraiarsi
    □ sedersi
    □ stare in piedi fermo
    □ camminare
    □ Nessuna

31. Quali attività o posizioni aumentavano il mal di schiena?
    □ sdraiarsi
    □ sedersi
    □ stare in piedi fermo
    □ camminare
    □ Nessuna

32. Qual è stata l'intensità massima di dolore percepita nell'ultimo episodio? (segna con una croce in base alla tua esperienza)
    □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10
    Minima
    Massima

33. Oltre alla schiena, hai avuto anche dolore irradiato lungo l'arto inferiore
    □ si □ no
    Se hai risposto SI, □ fino al ginocchio □ fino al piede
    Oltre al dolore erano presenti altre sensazioni spiacevoli all'arto inferiore?
    □ formicolio
    □ bruciore
    □ debolezza

34. Pensi che la corsa sia la causa del tuo mal di schiena?
    □ si □ no □ non so

35. Gli episodi di mal di schiena coincidono con periodi di:
    □ allenamento
    □ preparazione
    □ alla ripresa dopo periodo di stop
    □ competizione
    □ non corrispondono con attività legate allo sport

36. Gli episodi di mal di schiena coincidono con periodi di allenamento:
    □ fondo lento (corsa a bassa intensità)
    □ fondo medio (a media intensità)
    □ ripetute (alta intensità)
    □ allenamento di scarico
    □ non corrispondono con periodi di allenamento

37. Gli episodi di mal di schiena coincidono con periodi di intenso stress (scuola, lavoro, famiglia)
    □ si, per la scuola
    □ si, per il lavoro
    □ si, per la famiglia
    □ no, gli episodi di mal di schiena NON coincidono con periodi di intenso stress

38. Hai notato se gli episodi di lombalgia coincidono con il cambio di calzatura
    □ no □ si

*Massimo ammortizzamento (Le scarpe con massimo ammortizzamento possono offrire il massimo comfort grazie all'elevato potere ammortizzante dal peso che supera i 300 gr.)

Stabili (Le scarpe stabili garantiscono il massimo del sostegno, della protezione e della stabilità, pesano generalmente oltre i 300 gr.)

Stabili Intermedie (Le scarpe intermedie hanno un peso compreso tra 240 e 295 gr. garantiscono in generale un buon livello di ammortizzamento, possono presentare leggeri stabilizzatori mediali per il controllo)

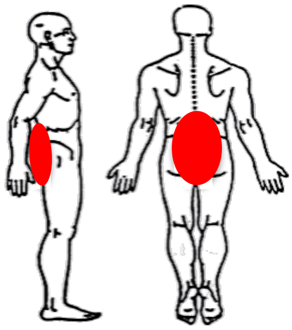
Superleggere (Le scarpe superleggere pesano meno di 250 gr. sono reattive ed elastiche, ed estremamente flessibili)

Scarpe Minimaliste (Le scarpe minimaliste sono estremamente leggere, generalmente pesano dai 150/300 gr, progettate per favorire il naturale movimento delle articolazioni del piede e garantire una posizione biomeccanica ottimale)

**Gli infortuni correlati alla corsa sono un dolore muscoloscheletrico o disturbo fisico degli arti inferiori o della schiena dovuto della corsa, che causa una totale limitazione o interruzione della corsa per almeno sette o più giorni e richiedono assistenza sanitaria.

Appendix 1

SURVEY – Running and Low back pain

Definition of low back pain	
Back pain, properly low back pain, can be defined as a pain and/or a functional limitation between the lower edge of the rib arch and the lower gluteal folds with a possible posterior irradiation to the tight, but not beyond the knee.	

A. Registry section

1. Age ____________________________
2. Gender: M□ F □
3. Weight (Kg)____________________________
4. Height (cm) ____________________________
5. Job/Profession Private Practice/Freelance □ Employee □
6. Region ____________________________

7. Muscoloskeletal deformities/disorders diagnosed in the past
   □ Scoliosis
   □ Hyperkyphosis
   □ Osteoarthritis
      □ spine
      □ hip
      □ Knee
   □ Osteochondrosis
      □ spine
      □ hip
      □ tibial tuberosity
   □ Varus knees □ Valgus knee
   □ Flat feet □ Hollow feet
   □ Lower limbs heterometry (one leg longer than the other)
      □ Do you use any orthotics for this problem?
   □ Other ____________________
   □ None

B. Daily habits section

8. Do you smoke? □ Yes □ No If yes, how many cigarettes per day □ <5 □5-10 □ 10-20 □>20
9. Do you drink alcohol daily (e.g. wine, beer)?
   If yes, □1-3 glasses □3-5 glasses □>5 glasses □ No
10. How many hours on average do you sleep per night? □ <3h □3-5h □ 5-8h □>8h

C. Running section

11. How long have you been running?
    □ <3 months
    □ 3-6 months
    □ 6-12 months
    □ 12-36 months
    □ >36 months

12. Are you registered with some sport club? □ Yes □ No

13. Are you a runner:
    □ Competitive
    □ Non-competitve

14. How many kilometers do you run per week
    □ <10
    □ 10-20
    □ 21-30
    □ 30-50
    □ >70

15. Which type of ground/surface do you run most frequently on?
    □ Hard (asphalt, tartan, sidewalk)
    □ Soft (wood, topsoil, sand)
    □ Combined/mixed surfaces

16. Do you change the type of footwear between training and competition?
    □ Yes □ No

17. How often do you replace your footwear on average with which you run most often? (Expressed in run kilometers)
    □ <600 Km
    □ 600-1000 Km
    □ >1000 Km

18. Which type of footwear do you use most frequently*:

□  Motion Control

□  Stability

□  Light Stability

□  Neutral

□  Minimalist - Barefoot

19. How long did you run with the same footwear?
□<3 months □3-6 months □6-12 months □>12 months

20. Do you follow a training program? □ Yes □ No
If yes, delivered by □ A coach □ A teammate □ Internet

21. Do you practice other sports? □ Yes □ No If yes, which one________________________

22. For how many hours a week do you train beyond running?
□ <3h
□ 3-5h
□ 5-10h
□ >10h

23. Have you ever had any running related injuries**?
□ Yes, in the last 12 months
□ Yes, in the last 18 months
□ Yes, in the last 24 months
□ No

24. Have you had low back pain episodes in the past year?^
□ Yes □ No
If you answered yes, numbers of episodes ____
Average duration in days
□ 1-3 days
□ 3-7 days
□ 7-10 days
□ more than 10 days

^(If you answered NO to this question, your investigation is ended. Thanks)

D. Low back pain section

25. Has low back pain limited you in daily routines? □ Yes □ No
    If you answered yes ,
    □ Always
    □ Yes, less than 50%
    □ Yes, more than 50%
    □ No

26. Did you stop training due to low back pain? □ Yes □ No
    If you answered yes,
    □ <7 days
    □ >7 days
    □ >30 days
    □ >90 days
    □ >180 days

27. If you did not stop training, due to your low back pain did you change your way to run?
    □ Yes, I reduced the traveled kilometers
    □ Yes, I reduced time
    □ Yes, I modified the foot strike pattern
    □ No

28. Did you have to resort to medical treatment or consultation? □ Yes □ No
    □ General practitioner □ Physiotherapist □ Other healthcare professional
    ____

29. Did you use drugs to reduce back pain? □ Yes □ No
    If you answered YES, specify which ones
    ____
    Specify who recommended you?
    □ Medical prescription
    □ Suggested by friends/relatives
    □ Self-medication

30. Which activities or positions reduced low back pain?
    □ Laying down
    □ Sitting down
    □ Standing up straight
    □ Walking
    □ None

31. Which activities or positions increased low back pain?
    □ Laying down
    □ Sitting down
    □ Standing up straight
    □ Walking
    □ None

32. Which was the highest intensity of pain perceived in the last episode? (mark with a cross based on your experience)

□ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ 8 □ 9 □ 10

Minimum

Maximum

33. In addition to your low back pain, did you experience radiating pain down to your lower limb, indeed? □ Yes □ No
If you answered YES, □ up to the knee □ up to the feet
In addition to pain, were there other unpleasant sensations in the lower limb?
□ tingling
□ burning
□ weakness

34. Do you think running is the cause of your low back pain?
□ Yes □ No □ I do not know

35. Low back pain episodes coincide with periods of:
□ training
□ athletic training
□ recovery after a stop
□ competition
□ they do not match with any sport related activities

36. Low back pain episodes overlap with training periods:
□ slow cross-country race (low intensity running)
□ medium cross-country race (mid intensity running)
□ repeats (high intensity)
□ unloading workout
□ they do not match with training periods

37. Low back pain episodes overlap with intense stress periods (school, job, family)
□ Yes, for the school
□ Yes, for the job
□ Yes, for the family
□ No, do NOT coincide with periods of intense stress

38. Did you notice whether or not low back pain episodes coincide with footwear change?
□ No □ Yes

*Maximum cushioning (Shoes with maximum cushioning can offer maximum comfort thanks to the high cushioning power with a weight that exceeds 300 gr.)

Stable (Stable shoes guarantee maximum support, protection and stability, they generally weigh over 300 gr.)

Stable Intermediate (The intermediate shoes have a weight between 240 and 295 gr. Generally guarantee a good level of cushioning, they can have light medial stabilizers for control)

Superlight (Superlight shoes weigh less than 250 gr. Are reactive and elastic, and extremely flexible)

Minimalist shoes (Minimalist shoes are extremely light, generally weighing from 150/300 gr, designed to favor the natural movement of the foot joints and ensure an optimal biomechanical position)

**RRIs as musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running, causing a total restriction or interruption of running for at least seven or more days and requiring therapeutic assistance

CHAPTER V

DIFFERENTIAL DIAGNOSIS IN PHYSICAL THERAPY PRACTICE

GENERAL INTRODUCTION

The lack of systematic data on the differential diagnosis in the literature and on the identification of red flags in sports clinical practice, in particular for analyzed the LBP in running, has prompted me to investigate this issue in the context of the physiotherapy's clinical practice, with the final production of one narrative and one systematic reviews. In fact, the only data that can be found on this topic, in the running context, are purely medical and linked to serious pathologies that can hardly be assessed in a physiotherapy direct access setting. Most of them are Cardiovascular, Respiratory, Central Nervous System, Gastrointestinal, Metabolic and Infective illness. Notably, the majority are reported during the race activities [1-2].

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THE USE OF RED FLAGS IN SCREENING PATIENTS IN PHYSIOTHERAPY. NARRATIVE REVIEW

Submitted as:

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The use of red flags in screening patients in physiotherapy.

Narrative Review

Abstract

When a cluster of Red Flags (RFs) are identified through either the history or the clinical examination, the physiotherapist needs to refer the patient to an appropriate specialist to avoid inappropriate treatments. Therefore the first item of importance for a physiotherapist is to identify, RF that indicate the presence of a serious pathology. The objectives of this narrative review are to define RF as not all health care professionals use RF, collect information concerning the screening process, identify the diagnostic accuracy of RF and analyze their utility in order to improve the patient's prognosis. In the past, the identification of RF has been a reference point for screening the patient for a serious pathology. Recently authors have questioned the use of RF as a screening tool due to a low diagnostic accuracy and a high level of false positives. Authors have noted that articles questioning RF have identified low methodological quality as most articles on RF are either case reports or qualitative studies. In this narrative review, we identified 238 RFs involving with the following focus: advanced age, unintentional weight loss, history of trauma or malignancy and no improvements with treatment. While it is true that the diagnostic accuracy is generally low for an individual RF, when RFs are combined their use improves the screening process which improves early diagnosis benefitting the patient. A thorough medical history has been suggested by authors as the most effective approach to identify the presence of a serious pathology. Clinicians have recently debated the reliance on the physical examination to determine the presence of a serious pathology. As most

studies involving differential diagnosis are case reports, the evidence is lacking on a standardized screening approach to help physiotherapists during their clinical practice.

1. Background

The origin of the term Red Flag (RF) is unknown, but its first use in the medical literature dates back to 1911, when Thomas D. Luke published the first report on RF to identify cancer [1]. The term RF was introduced in Medline in 1973 and in physical therapy by Waddell in 1998 [2]. In 1994, the Clinical Standards Advisory Group (CSAG) in the UK and the United States Agency for Health Care Policy and Research (AHCPR) included their own list of RFs in the "Guidelines for the Assessment and Treatment of Acute Lumbago in Adults," without showing substantial differences between the various RF (Table 1).

Recently, two clinical practice guidelines for the management of non-specific LBP [3-4] were published and excluded any references of RF. Specifically within the physiotherapist (PT) literature, the Orthopaedic Section of the American Physical Therapy Association (APTA) identify significant RF that arelinked to the International Classification of Functioning, Disability, and Health" (2012) [5] (Table 2).

This suggests that the use of RFs are not used across disciplines. The definition of a RF is unclear and authors lack agreement on the definition [6-22]. RFs are defined as signs and symptoms found in the patient history and clinical examination that may be associated with a serious pathology [23]. However this definition suggests that signs and symptoms are the only method to identify a RF. Arnold et al. [6], suggest RFs are "signs and symptoms of an abnormal course of disease or of an unknown motor strategy." Textbooks on differential diagnosis define RFs as "signs and symptoms that can mimic neuromuscular or musculoskeletal dysfunction" [24]. In the Guide for Physical Therapy practice, RFs are defined as "the activity of determining the need for further examination or consultation by another health care professional" [25]. Thus, there are multiple definitions of RF. RFs can be classified in terms of severity to indicate how a clinician should react to a RF using three categories [7]: (a) category I: RFs that requires immediate attention, showing a clear correlation between the patient's clinical conditions and a serious pathology. This category indicates physical therapy examination and treatment are not indicated; (b) category II: RFs that require additional questions and/or involves contraindications to manual therapy or therapeutic exercise. This category indicates that there may be a link between the patient's medical condition and serious pathologies and that evaluation and treatment must be carefully conducted; (c) category III: RFs that require additional testing. This category indicates that the PT should be careful during physical examination and treatment due to the patient presentation. Clinicians face a conundrum as clinical tests that have been routinely used have now been identified as unreliable such as Homans sign; this sign is generally unreliable as a clinical sign of Deep Vein Thrombosis (DVT) since its accuracy ranges from 8% to 56% of cases of diagnosed DVT and being positive in greater than 50% of symptomatic patients without DVT [26]. As not all professions use RFs to identify a serious pathology, clinicians should screen patients for RF even if the patient was referred from another healthcare provider. In fact, it has been reported that less than 5% of clinicians screen for RF during the initial medical session. Screening for RFs are important, as medical errors are the third leading cause of death in the US [27,28]. Screening patients for RFs are vital to decision-making. The initial examination for a PT consists of an evaluation of past medical history, assessment of risk factors, an analysis of the patient's clinical presentation, association of signs and symptoms of systemic diseases and a review of systems [24]. An evaluation of all the components of the examination determines the diagnosis in order to decide the best pathway for the patient [29,30]. The RFs that require immediate medical intervention (category I RF) are: loss of consciousness, quick progression of neurological deficits, abdominal pulsating masses and abnormal vital signs (breath, pulse, blood pressure and temperature) [7]. Table 3 and Table 4 report a multitude of serious pathologies and their respective RFs [24,31-35].

Differential diagnosis in physiotherapy may not focus on identifying the underlying pathology that the patient presents with, but instead establishes the appropriateness of the intervention. For example, it is outside of the scope of practice for a PT to identify a specific cancer based on a patient presentation but it is within the scope of practice to recognize the RFs associated with cancer in a patient presentation. This process for PTs is described as screening for referral [24]. The screening for referral process that identifies category I RFs improves the healthcare system response thus improving the patient's prognosis and, in some cases, life expectancy [8,24,36,37]. Screening for referral results in three potential possibilities (a) referral to another health specialist; (b) treat and referral; (c) or treating the patient. These options are not mutually exclusive as a patient may return to the care of a PT or medical consultation may be necessary [38]. During the screening for referral process (Figure 1), RFs are considered in terms of severity to direct immediacy of care as well as within clusters of RFs (Figure 2) to determine what system may be involved so the patient can be referred to the appropriate practitioner. The screening for referral process is vital in a Direct Access (DA) environment. For the APTA, DA is: "the right of an individual to choose to get treatment from a PT, where and when he or she wants it"; even in the absence of a preliminary medical examination. The first states to allow DA were California and Nebraska in 1957. The majority of the US followed these two states beginning in 1980 [39]. Globally, Australia received DA in 1976 [40]. Evidence for physical therapy services is safe, has greater patient satisfaction rates and lower costs to the National Health System [39].

The authors of this narrative review present evidence in this paper in order to: a) suggest a comprehensive definition of the term RF; b) support the use of RF during the decision-making process considering diagnostic accuracy levels; c) detail an approach for identifying RF; and d) identify the clinical utility of RF identification to improve patient prognosis.

RED FLAGS DEFINITION

What is the shared and comprehensive definition of the term Red Flags?

Currently there are multiple definitions for RF that range from: warning signs [6,9-11]; signs and symptoms [6-8,12-14]; clinical indicators [6,15]; prognostic variables [16]; clinical features [17,18,41]; screening questions [19,20]; and serious pathologies; biomedical or risk factors [6].

Table 5 provides a breakdown of the definitions and the multiple sources that provide the definitions. When considering all of these resources, the authors suggest the following definition: signs and symptoms of alarm that emerge from the physical examination that are associated with an increased risk of serious pathology. This definition suggests that the screening for referral process is needed to identify patients that require further investigation to prevent an adverse outcome [6-22]. This definition includes life-threatening pathologies as well as clinical conditions that may need a treat and refer approach for the patient to receive the optimal care. An example of this latter situation is a patient with radicular complaints that might benefit from a Solumedrol treatment to optimize physiotherapy. Table 5 provides definitions of RF including: "signs and symptoms of alarm, emerging from the anamnesis and the physical examination, associated with an increased risk of serious pathologies, even musculoskeletal, which need a proper screening for referral process, in order to identify those patients which require further investigations or intervention by an appropriate specialist, in order to avoid a worse prognosis, a contraindicated treatment and adverse or irreversible outcome" [6-22]. The authors' definition of a RF is supported by the literature.

RED FLAGS SCREENING PROCESS

Which clinical screenings are needed to identify Red Flags?

Medical history and physical examination are essential components of the RF screening for referral process [7,9,12,13,16-18,41,42]. The Optimal Screening for Prediction of Referral and Outcome (OSPROS), [43] is a useful tool to consider to efficiently review systems and more evidence needs to be gathered on the effectiveness of this screening tool. Although evidence for several special tests have been suggested to be poor, it is the composite of the physical examination that needs to be considered [7,14,17,19,21,44-46]. Examples include tests used for detecting lumbar radiculopathy such as Straight Leg Raise (SLR) and Prone Knee Bending (PKB) (Sn 0.18-0.91; Sp 0.26-0.83; LR + 1, 2; LR- 0.34) [7,17,19,44]; pain during spine palpation to detect fractures, infections and malignancy (Sn

0.15-0.73; Sp 0.59-0.60; LR + 0.4-0, 73; LR- 1.37) [7,14,17,19,21,45] and the presence of abnormal reflexes in fractures, radiculopathy and CES (Sn 0.08-0.12; Sp 0.89-0.95) [7,19,44,46].

Regional Red Flags

Lumbar spine

RFs are often related to spinal pathologies such as vertebral fracture, malignancy, CES and infection [6,7,9-14,16-22,44-55]. The first three conditions are frequently referenced in the literature [6,11,12,14,17,18,21,51]. The main RFs identified for the lumbar spine are: advanced age; female gender; prolonged use of corticosteroids; history of trauma or malignancy; bladder or bowel dysfunction; and saddle anaesthesia [6,11,12,14,17,18,21,51].

Systemic disorders linked to LBP cited in the literature are inflammatory and rheumatic diseases, such as osteomyelitis, spondylitis ankylosis, rheumatoid arthritis, gout, polymyalgia rheumatica, and specific conditions such as Abdominal Aortic Aneurysm (AAA), osteoporosis, lumbar stenosis, lumbar radiculopathy, tuberculosis and myelopathy [13,15,28,41,47,49,52,53,56-60].

There are a large number of RFs especially regarding LBP. Evidence for unexplained weight loss [6,7,10-16,18,19,22,31-33,44-46,47-50,57,61,62] and constitutional symptoms, such as fever or chills, night sweat, discomfort, fatigue, nausea, vomiting, [6,7,10-16,18-20,22,31,32,34,44,45,47-50,56,57] as major RF, showing a rather good diagnostic accuracy, with a good specificity (Sp) [0.88-0.99 vs 0.93-0.99] but low sensitivity (Sn), LR + and LR- [Sn 0.08-0.15 vs 0.00-0.12; LR + 1.87-3.00 vs 1.71-25.00; LR- 0.87-0.96 vs 0.95-1.00]. Often an important aspect that is not considered influential as a RF is the age of the patient. In terms of RF for fracture, cancer and infection, the most important RF identified is age >50 years [6,7,10,11,13,14,16-19,22,31,35,44,47-50,56-58,61] [Sn 0.50-0.79; Sp 0.32-0.71; LR + 1.1-2.7; LR- 0.1]; the most important RF for inflammatory disorders and malignancy is age <20 years [6,13,14,22,47,49]. The most important RF for fracture, malignancy and osteomyelitis is age >70 [13,17,18,44,47,49] [Sn 0.03-0.50; Sp 0.80-0.96; LR + 1.55-11.2; LR- 0.86] or more generally advanced age [11,12,45,46,51,56] [Sn 0.50-1.00; Sp 0.66-0.77; LR + 1.9-4.6; LR- 0.3-0.7]. The main RFs for malignancy and vertebral fracture are a previous history of cancer [LR+ 31.5] [6,7,10-14,16,18-20,22,35,44-49,57,61,62] and trauma [LR+12.8] [6,7,9-11,13,14,16-20,34,44,46,47,49,51,57]. Night pain that specifically wakes the patient during the night or that does not permit sleeping, is often related to sinister pathologies [6,10,11,13,14,16,20,22,31,35,45,47-49,51,62], even if the diagnostic accuracy is generally low. Multiple authors [6,10-14,20,31,37,45,46-49,52,61] consider conservative treatment failure (i.e. within 1 month), use of corticosteroids [6,7,11,13,14,16,17,20,46,47,49,51,57] and bladder or bowel dysfunctions [6,7,10,11,13,14,16,20-22,34,47,49,53,63] as RFs for serious lumbar pathologies [LR + ranging from 18.00 and 48.50]. Resting pain [6,10-14,18-20,47-49,64] and saddle anesthesia [6,7,10,11,13,14,16,20-22,47,49,53] show heterogeneous diagnostic accuracy values (Table 6). Lower extremity neurological signs are related to lumbar (radiculopathy, stenosis, malignancy) and upper extremity neurological signs are related to cervical (instability, myelopathy, basal impression) spine conditions [6,7,10,13-15,20,21,31,34,47,49]. RFs related to the lumbar spine with low diagnostic accuracy can be located in Table 6 and Table 7 (Appendix I).

Cervical spine

Neck pain (NP) is one of the most common complaints that leads patients to seek conservative management from PTs with a prevalence ranging from 30% to 50% [33,65-68]. Many medical pathologies of the neck may mimic musculoskeletal conditions making the diagnosis for NP and its associated disorders are challenging for clinicians. Although encountering medical pathology in physiotherapy practice is a rare occurrence (i.e. 0.4-6%) [33,65,68], the incidence of delayed diagnosis ranges from 5% to 20% in the cervical region [68] leading to a lack of recognition that can have life-threatening consequences in those patients with serious pathology [7]. The main medical pathologies screened by PTs described in the literature are: malignancy, infections, fracture, cervical spine instability (i.e. craniovertebral ligamentous damage and fracture), vascular pathologies of the neck (i.e. dissection of the vertebral arteries (VA) or internal carotid arteries (ICA or craniovertebral congenital anomalies (CVCA) (i.e. basilar impression (BI) and Chiari type malformation) [23,33,34,65-69].

Usually, cancer in the neck involves the oropharynx, thyroid and are lymphomas [69]. Infection usually involves retropharyngeal abscess or vertebral infection (osteomyelitis and tuberculosis) [69]. RFs for NP are derived from RFs that exist in the LBP literature [68]. A recent case report described craniopharyngioma (CP), a rare benign neoplasm caused by maldevelopment that presents as reproducible NP and cervicogenic headache symptoms. CP occurs in both children and adults in the sellar and suprasellar regions of the brain. The authors of this case report describe alarming primary findings caused by increased intracranial pressure, visual and endocrine system symptoms [68].

Vascular pathologies of the neck include conditions affecting the VA and ICA which can lead to cerebral ischaemia, stroke, or death [33]. Notably, often the early presentation is non-ischemic in origin for the dissection of both the VA and ICA. Patients with this presentation typically complain of ipsilateral NP and headache. Furthermore, dissections might not be recognized, particularly in the absence of clear ischemic (or neurological) features. Therefore, transient antecedent neurological signs and symptoms are essential to recognize in these patients. Ischemic signs occur more commonly in VA than in ICA dissection but may be delayed by days or weeks [66]. The most common RFs for a VA dissecting event are unsteadiness, ataxia, imbalance, dysphagia, dysarthria and aphasia, ptosis, facial palsy and weakness, especially of the upper extremities [23]. Ischemic stroke occurs in in 67-77% of cases and the neurological presentation depends on the area of the brain supplied by the dissected artery [33,66]. CVCAs are rare, extremely life-threatening conditions of the neck. Diagnosis of a CVCA is challenging as the patient may present without symptoms and this condition may not be recognized until adulthood [34]. Preceding transient neurological symptoms appear to occur commonly and may assist in the identification of a CVCA. Notably, these are often subtle and transient and may not be recognized as significant by the patient or the clinician [23,66]. Common RFs are occipital or cough headache, lower cranial nerve palsies, corticospinal signs, cerebellar dysfunction, syringomyelia and syringobulbia [34]. Interestingly, the literature describes that these patients may present with musculoskeletal symptoms but may present with risk factors related to instability (i.e. neck fracture and craniovertebral ligaments damage) recognized by screening following the Canadian Cervical Spine Rules (CCSR)

[65]. The CCSR is a valid clinical decision rule that accurately screens (Sn: 99.4%; Sp 42.5%) vertebral fracture after blunt trauma [65]. The most often patient described RFs for CVCA instability are vertigo, tinnitus, dizziness, facial pain, arm pain, and migraine headaches [67]; patients with fracture at the lower cervical spine (C3-C7) present muscle spasms, crepitation, paraesthesia in addition to NP [67]. Infection usually involves a retropharyngeal abscess or vertebral infection (osteomyelitis and tuberculosis) [69]. The main RFs for upper cervical spine instability (C0-C2) are: vertigo, tinnitus, dizziness, facial pain, arm pain, and migraine headaches [33,67]. In the lower cervical spine (C3-C7) the main RFs are: muscle spasms, crepitation, paraesthesia in addition to chronic NP [33,67]. In patients with trauma, the use of the CCSR guides the use of cervical-spine radiography [65]. It appears to be a good screening tool to rule out a vertebral fracture (Sn: 99.4%; Sp 42.5%) [65].

Upper Extremity

Pain can be a RF in certain conditions involving the upper extremities. That is, early symptoms of sinister pathologies, like a Pancoast tumour (i.e. tumour of the lung's apex), is pain in the shoulder [70]. In the presentation of pain as the only RF, there are many potential possibilities. PTs must weigh the patient'spast medical history, family history, history of clinical presentation and the clinical examination findings to determine the next step for this patient [71].

Upper extremity RFs that may indicate systemic causes of shoulder pain (Table 6) could be related to the neck (i.e. bone or spinal cancer and metastases), the thorax (i.e. myocardial infarction, aneurysm, breast cancer, lung cancer, herpes zooster, Pancoast's malignancy, pacemaker, lung and heart diseases), the abdomen region (i.e. liver diseases, spinal metastases, diaphragmatic irritation) or systemic diseases (i.e. diabetes, gout and rheumatic diseases) [31]. The clinician should consider the importance of bilateral signs (rash, nodules, pain) and constitutional symptoms (nausea, vomiting, fatigue, paleness, diarrhea, weight loss, dizziness) [31]. It is common to encounter patients with heart disease mimicking upper extremity pain. The main RFs for these conditions are age >50 years, menopause, female gender, family history of heart pathologies [31]. Furthermore, clinicians must consider other secondary causes of shoulder pain such as thoracic complaints (Dissecting Aortic Aneurysm, Thoracic outlet syndrome, endocarditis, pericarditis, hiatal hernia, pneumothorax, breast cancer, Pulmonary embolism) and abdominal pathologies referring to the shoulder (gallbladder diseases, pancreatic disease, liver diseases, ruptured of spleen) [72]. Acute or traumatic injuries of the scapular girdle such as fractures (i.e. scapular or glenoid fractures, coracoid, clavicular and humeral fractures, floating shoulder), glenohumeral or acromion-clavicular dislocations, traumatic tendon ruptures and septic arthritis are related to traumatic events so the clinician needs to ask about recent trauma or occupational hazards that the patient encounters [73]. The literature regarding the RFs of the upper extremities are scarce, a few case reports describe rare conditions such as osteochondritis dissecans of the radial head of the elbow [74]; spontaneous multidirectional shoulder dislocation secondary to involuntary muscular spasms [75]; carcinoma in the coracoid process [76]; lymphoma [77]; osteochondroma of the anterior aspect of the lower or supero-medial scapular angle [29,78,79]; subscapular lipomas [80]; and osteosarcoma of the trapezius muscle [81].

Peripheral neuropathy, as brachial plexus diseases [29], Pagette Shroetter syndrome [82], and Personage-turner syndrome have to be considered during the differential diagnosis process of the upper extremity [83].

Embryological development, the multilevel organ innervation, and compression of the diaphragm are the main mechanisms of visceral origin of shoulder pain [31]. That is, visceral pain origin must be suspected when shoulder pain is: directly related to pleural signs and symptoms (i.e. symptoms provocation during coughing, and breathing and symptoms reduction when laying on the involved side); when symptoms are exacerbated during effort not related to shoulder movement; when the patient presents with cardiac or gastrointestinal (i.e. nausea, vomiting, abdominal pain, diarrhea) or urologic (i.e. haematuria, painful and frequent urination, urine change colour) signs and symptoms [31]. Another condition that must be considered cautiously are large rotator cuff tears. Clinical presentation is characterized by pain, strength deficits, and local bruising when related to trauma [84]. However, degenerative changes related to disuse atrophy are not alarming and do well with conservative management [85-87]. More attention must be paid to traumatic rotator cuff tears in patients presenting with post traumatic acute shoulder pain and weakness [88]. Evidence suggests that adhesive capsulitis seems to be associated with diabetes, hyperthyroidism, ischemic heart disease, infections and lung diseases. If there is a combination of 3 or more RFs for these conditions associated with risk factors: alcohol, smoking, obesity, sedentary lifestyle, drug abuse, overseas travel, radiation exposure, multiple sexual partners, age, or occupation; the clinician must consider the referral of that patient [31].

Elbow pain is a common presenting symptom in the primary care setting [89]. Pathology can arise from any component of the joint including tendons, bursa, bones, or nerves. It is a commonly dislocated joint, especially in children (‘pulled elbow’) [89]. Rheumatoid (inflammatory), post-traumatic, and primary osteoarthritis are three primary patterns of arthritis affecting the elbow [89]. In the physical examination, the first action is to exclude red flags such as: (a) swelling and dislocation following trauma; (b) a tender, swollen joint; (c) a rapidly increasing mass [89]. The evidence supports that when a patient presents with bilateral elbow pain with stiffness and joint swelling, loss of full range of motion (ROM), involvement of other joints besides the upper extremities, and systemic symptoms, that the clinician should consider inflammatory arthritis [90]. For example, 20–50% of patients with rheumatoid arthritis have bilateral involvement of their elbows [90]. Neurological symptoms like numbness and tingling must be assessed in the patient with elbow pain. Ulnar nerve radiculopathy is common in medial epicondylitis, osteoarthritis (50% of patients), and inflammatory arthritis [91].

In many case reports analyzed, the onset of pain is insidious and generally associated with a reduction in Range of Motion (ROM) and function. In the case of oncologic pathologies, the masses are often palpable and when they are not, they can be inferred from Magnetic Resonance Imaging (MRI) as an incidental finding such as angiosarcoma with pulmonary metastases (slight pain, insidious for 2 months, associated with palpable painless and firm mass) [92]; pigmented villonodular synovitis (enlarged palpable masses, in the absence of pain but with forearm numbness and sensitivity reduction) [93]; neurothekeomas mass of radial nerve (intense remitting pain to treatment, paresthesia of the entire forearm) [94]; elbow septic arthritis (pain, redness, swelling, skin lesions, fever resistant to antibiotic treatment) [95]; intra-articular nodular fasciitis (reduction of the grip strength of the hand, pain for more than 12 months) [96]; osteoma-osteoid (severe pain for more than 12 months, worsening at night, reduction in muscular trophism, passive elbow extension only) [97]; osteochondroma with radial head dislocation (persistent pain from 18 months, joint limitation in flexion-extension and pronation-supination, structural deformity and palpable bone mass anteriorly) [98]; osteochondroma (articular block, pain, slight reduction in flexion-extension, significantly limited pronation-supination, sudden symptoms but swelling for 15 years) [99]; synovial osteochondromatosis (recurrent increase in intra-articular volume with reduction of flexion-extension, joint blockages and crepitus) [100]; epithelioid hemangioendotelioma (palpable non-pulsating and painless mass in the cuboid fossa for 48 months, paresthesia along the median nerve) [101]; Ewing's sarcoma (pain and palpable mass) [102]; colon cancer with metastasis (insidious pain for 4 years, with typical signs of inflammation at the elbow) [103]; Kimura's disease (bilateral painful and palpable mass, for about 12 months) [104]; African histoplasmosis (shoulder swelling, fever, weight loss, dizziness, palpable mass in the left elbow, pallor, muscle weakness, left hand numbness) [105].

Patients with regional enteritis (i.e. Crohn's disease in 25% of cases) or a bacterial infection may experience elbow joint pain that is preceded by diarrhea approximately 1 to 3 weeks in advance. Patients with this presentation may present with monoarthritis (i.e., asymmetric pattern affecting one joint at a time) [24].

L**ower** Extremity

Lower extremity serious pathologies are mainly described by case reports in the literature. The RFs for these conditions (Table 6) show various and generally low diagnostic accuracy levels [35,41,54, 55,60,62,63,106-113]. Many specific conditions mimic the musculoskeletal system in presentation. For example, peripheral arterial disease (PAD) mimics LBP and sciatica [41,107]. There are other serious pathologies of the lower extremity that PTs need to be aware to improve recognition of these conditions. Ewing Sarcoma is an aggressive malignant tumor characterized by "small round blue cells (on microscopic investigation) with a peak incidence between 10 and 25 years and a mortality rate within 5 years of diagnosis. Authors have reported on two different patients with LBP and lower extremity pain [63]; and a child identified with medial tibial stress syndrome that was ultimately diagnosed with osteosarcoma [62]. Pelvic Osteomyelitis may present as groin and medial thigh pain [46]; hip bone marrow edema presenting as LBP [63]; bone and soft tissue malignancy with different clinical presentations that are often confounded with osteoarthritis or radiculopathy [35]; and superficial peroneal nerve schwannoma presenting as lumbar radicular syndrome [54] were also described. Stress fractures are a bone-related injury primarily occurring in the lower extremity with an increased incidence potentially due to the number of older adults. Periacetabular fractures for both the ischio-pubic and ileum-pubic ramus [108], hip fracture [112], neck/head stress fracture [113], osteonecrosis of the femoral head and avulsion fracture could be encountered in clinical practice [85]. Risk factors and RF for these conditions are diabetes, history of chemotherapy, pain in the hip and anteromedial part of the thigh, progressive worsening weight-bearing status, older age, hypertension, antalgic gait with abduction of the hip, painful and limited hip ROM, pain on palpation of the hip and palpable warmth at the fracture site [35]. Stress fractures may be identified using a combination of special tests such as the patellar-femoral percussion test (PFPT), tuning fork test and ultrasound [109-112]. In order to identify ankle fractures, clinicians can confidently rely on the Ottawa Ankle Rules (OAR), a highly sensitive clinical decision rule (Sn 97%; Sp 29%), in addition to the highly specific (Sn 69%; Sp 45%) Bernese Ankle Rules (BAR) [110]. Integration of the Tuning Fork test to the OAR and BAR increases the diagnostic accuracy of the clinical examination (Sn 100%; Sp 91%) [110].

Systemic disorders

There is a lack of RF studies investigating serious pathologies related to systemic disorders, especially those related to chest pain as a consequence of pulmonary, cardiac or gastroesophageal diseases. Cardiovascular disorders are well represented RFs in the literature. Systemic RFs are pain radiating to the upper extremities, dyspnea, palpitations, syncope, exertional pain and family history of cardiovascular diseases [114-116]. Concerning pulmonary disorders, the main RFs are: cough, tachycardia and hemoptysis, but no specific diagnostic accuracy is provided [114-116]. Gastroesophageal disorders are less analysed in the literature and the signs and symptoms most common are stomach ache, meal-related pain, vomiting, unintentional weight loss and decreased appetite [116].

What is the diagnostic accuracy of Red Flags?

According to Williams et al. [17] RF, especially if used alone, provide a high number of false positives. However, combining multiple RFs increases the diagnostic accuracy. The literature supports a cluster of RFs for back pain [6,19,37,44,61] (i.e. age> 50 years, history of previous malignancy, unexplained weight loss and 1-month conservative treatment failure) [Sn 1.00, Sp 0.60-1.00; LR + 2.4; LR- 0.06]. Verhagen et al. [11] suggested clustering RFs (i.e. age> 50 years, first episode of severe LBP, history of cancer in the last 15 years, unexplained weight loss and conservative treatment failure after 4 weeks) in order to accurately detect the presence of malignancy; however, diagnostic accuracy level are not provided [14]. Henschke et al. [22] identified a cluster of RFs for screening for fractures: female gender, age> 70 years, major trauma and prolonged use of corticosteroids. The LR + values are positively correlated to the number of RF detection: 1 RF, LR + 1.8; 2 RF, LR + 15.5; 3 or 4 RF, LR + 218.3. Therefore, the use of RFs increases the probability of detecting a serious pathology [6-9,12,14-17,18-20,41] and multiple RFs improves this process. This evidence supports the screening for referral process and directs the PT to refer a patient to the appropriate specialist [10,14,15,20] and identify patients who need further diagnostic investigations with imaging [7,8,19,20].

RED FLAGS AND CLINICAL PRACTICE

Does screening for Red Flags improve the patient's prognosis?

A few authors have reported information about prognosis related to RF use. According to Briggs et al [15] and Arnold et al. [6] screening of RFs may result in positive changes leading to patient care optimization, allowing a reduction in the delay for appropriate treatment and appropriately determining the need for further diagnostic investigations. Goodman [31,32] confirms the importance of conducting a RF screening for referral process in order to prevent the onset of comorbidities and/or complications. In addition, Ferguson et al. [59] underline the essential role of detecting RFs to guarantee the patient's safety. Cook et al. [8] recommend a careful monitoring symptom change over time through the "watchful waiting" and to link RFs directly to outcomes, prognosis and health status of the patient rather than to diagnostic testing. According to Todd [21] and Peterson et al. [35] an early diagnosis from RF screening avoids irreversible damage. In case reports of CES and lower extremity malignancy, the authors suggest that early diagnosis improved the quality of life and survival rate reducing healthcare costs. Other examples of the direct implications in early recognition of RFs for emergency management have previously been described by Esser M & Baima J [58] and Hawkins [60].

Direct access physiotherapy safety and professional ability in Red Flags screening

The incidence of musculoskeletal disorders account for 18% of all primary care visits and are estimated to represent 30% of a general practitioners caseload [117]. The increase of older adults, the decline of general practitioners (GP), the burden of health costs, the expected increased workload on primary care services, the rising incidence of chronic pain disorders, and the high number of referral of patients complaining of musculoskeletal disorders to secondary care has resulted in an increase in physiotherapy DA models [118]. DA physiotherapy has been defined as a primary visit with a PT without being visited by a physician first [119]. Emerging evidence suggest that this model seems to be a potential pathway to improve healthcare costs, disability, quality of life, and patient satisfaction [120]. Moreover, DA physiotherapy reduces waiting time, imaging prescriptions, and referral to secondary care [121]. Notably, in a recent systematic review investigating 65,351 DA physiotherapy evaluations, none were associated with an adverse event [120]. Moreover, a substantial reduction in referrals to physicians with a high appropriateness rate was reported [118]. This suggests that patients complaining of musculoskeletal disorders could be assessed and managed safely and independently by PTs. Therefore, DA, PTs possess the knowledge and skill set to identify when a patient's signs and symptoms are outside of their scope and in need of appropriate medical referral.

Conclusion

Although ruling-out life-threatening and medical serious pathology are the primary goals when patients present to physiotherapy, the RF literature is extensive but mainly based on lower level evidence. The authors suggest that a RF be defined as signs and symptoms of alarm that emerge from the physical examination that are associated with an increased risk of serious pathology. Identifying these RFs during a screening for referral process may help clinicians recognize a presentation that warrants investigation or intervention by referral to an appropriate specialist. It is essential, that the RFs are identified during the anamnesis to improve appropriate care. The physical examination is an essential part of assessment to identify RFs. The most described RFs in the literature that are able to identify sinister conditions are unexplained weight loss, constitutional symptoms, age > 50 years, previous history of malignancy, and trauma. Notably, combining RFs increases diagnostic accuracy leading to a core set of RFs for identifying serious pathologies (Sn: 1.00 and Sp: 0.60-1.00). The most accepted RF core set is age >50 years, previous history of cancer, unexplained weight loss and conservative treatment failure after 1 month of care. From a prognostic and clinical relevance perspective, screening for referral optimizes patient healthcare, reduces treatment delay and may lead the clinician to consider further investigation. The screening for referral process is essential for an early diagnosis that improves safety, prevents comorbidities and further complications, avoids irreversible damage, and improves the quality of life while reducing healthcare costs. The increased demand for DA physiotherapy raises the need for an evidence-based standardized approach. This manuscript supports the need for further research on this topic.

Limits

The main limitation of our debate is the overall quality of the evidence that is inherent in narrative reviews, expert or editorial opinion and case reports.

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CSAG (1994)	AHCPR (1994)
Age of onset <20 or >55	Age of onset <20 or >50
Violent trauma such as a fall from a height or a traffic accident	Violent trauma such as a fall from a height or a traffic accident
Constantly progressive, non-mechanical pain	Constantly progressive, non-mechanical pain
Chest pain	Chest pain
History of carcinoma	History of carcinoma
Systemic steroid intake	Systemic steroid intake
Drug abuse, human immunodeficiency virus (HIV)	Drug abuse, human immunodeficiency virus (HIV)
Continuous state of malaise	Continuous state of malaise
Weight loss	Weight loss
Persistent severe restriction of lumbar flexion	Persistent severe restriction of lumbar flexion
Very widespread neurological deficit	Very widespread neurological deficit
Structural deformity	Structural deformity
	Pain that worsens from supine
	Severe night pain

Table 1 - Comparison of RFs between the CSAG (1994) and the AHCPR (1944). (Note: Differences are noted in blue)

RF's list modified from Clinical Practice Guidelines	
Back-related tumor	Constant pain not affected by position or activity; worse weight bearing, worse at night Age over 50 History of cancer Failure of conservative intervention (failure to improve within 30 days) Unexplained weight loss No relief with bed-rest
Cauda equina syndrome (CES)	Urine retention Fecal incontinence Saddle anesthesia Sensory or motor deficit in the feet (L4, L5, S1 areas)
Back-related infection	Recent infection (eg. Urinary tract or skin), intravenous drug user/abuser Concurrent immunosuppressive disorder Deep constant pain, increases with weight bearing Fever, malaise, and swelling Spine rigidity; accessory mobility may be limited Fever: tuberculosis osteomyelitis Fever: pyogenic osteomyelitis Fever: spinal epidural abscess
Spinal compression fracture	History of major trauma, such as vehicular accident, fall form a height, or direct blow to the spine Age over 50 Age over 75 Prolonged use of corticosteroids Point tenderness over site of fracture Increased pain with weight bearing
Abdominal aneurysm (≥ 4 cm)	Back, abdominal, or groin pain

	Presence of peripheral vascular disease or coronary artery disease and associated risk factors (age over 50, smoker, hypertension, diabetes mellitus) Smoking history Family history Age over 70 Non-Caucasian Female Symptoms not related to movement stresses associated with somatic low back pain Abdominal girth <100 cm Presence of a bruit in the central epigastric area upon auscultation Palpation of abnormal aortic pulse Aortic pulse 4 cm or greater Aortic pulse 5 cm or greater

Table 2 - RF's list modified from Clinical Practice Guidelines JOSPT 2012.

RF patient's history	RF physical examination
• Fever (>37,5/38,3°), chills • Night-time temperature changes • Diaphoresis (unexplained sweating) • Night sweating • Nausea, vomiting • Sphincter disorders • Diarrhoea, pain in defecation • Paleness, jaundice • Skidding, fainting, unexplained excessive fatigue • Fatigue not related to physical exertion, weakness, malaise • Unexplained weight loss (4,5kg or >5-10% of body weight) in 3-6 months • itching	• general appearance • structural deformity • atypical muscle spasms • masses of the musculoskeletal system • masses or nodules on the body (lymph nodes) • inability to lie supine on a bed • unusual neurological deficit • Persistent severe restriction of spinal movements (lumbar flexion) • Aortic aneurysm • outcomes of traumas (fractures, bruises, edema, abrasions, bruises) • rash or skin changes • Lower extremity atrophy or upper extremity atrophy • local pain, load pain

Table 3 - RF in patient's history and physical examination [24,31-35].

Body System	Examples of diseases
Cardiac	Heart attack, pericarditis, angina pectoris
Pulmonary	Pneumonia, pleurisy pneumothorax, obliterative bronchiolitis
Genitourinary	kidney stones, nephrolithiasis, pyelonephritis
Gastrointestinal	liver disorders, gallbladder disease, pancreatitis, peptic or duodenal ulcer, esophagitis
Neurologic	Cauda equina syndrome (CES), myelopathy, vertebrobasilar insufficiency / cervical artery dysfunction (CAD), stroke
Musculoskeletal	Rheumatic diseases (gout, ankylosing spondylitis), fractures, avascular necrosis
Vascular	deep vein thrombosis (DVT), abdominal aortic aneurysm
Immunological	infection, HIV
Other	Cancer

Table 4 - Examples of serious pathology cited in many of RF studies

STUDIES	RF DEFINITION
Briggs et al. 2013	clinical indicators of possible serious underlying conditions requiring further medical intervention; manifestations that suggest that the physician referral may be warranted
Cook et al. 2018	signs or symptoms that are related to a serious underlying pathology and may indicate more diagnostic testing is necessary before the appropriate care can be delivered
Enthoven et al. 2016	alarm symptoms, resulting from history and/or physical examination, that may be associated with serious diseases
Greenhalg & Selfe 2009	prognostic variables for serious pathology, i.e. benign or malignant tumour, infection, fracture or CES. However, the prognostic strength of a single RF or combined RFs is not yet known. The importance of anamnesis is emphasized
Cooney et al. 2017	clinical features from the history and physical examination of a patient that are associated with an increased risk of a serious underlying condition
Leerar et al. 2007	alarm signals that suggest that physician referral may be warranted
William et al. 2013	features from the patient's medical history and physical examination which are thought to be associated with a higher risk of serious pathology
Henschke et al. 2007	screening questions to alert clinicians to the presence of serious disease and indicate when further investigation is required
Henschke et al.	features from the patient's clinical history and physical

2013	examination which are thought to be associated with a higher risk of serious pathology
Verhagen et al. 2016	alarm signals
Sizer et al. 2007	signs and symptoms found in the patient history and clinical examination that may tie a disorder to a serious pathology; in general, RF may warrant further diagnostic workup and potentially immediate treatment by a specialist
Todd NV. 2017	RF indicate the presence of a hazard and are useful for the diagnosis and treatment of patients before irreversible damage
Verhagen et al. 2017	signs and symptoms, collected during the clinical assessment, that indicate an underlying serious condition requiring attention
Tsiang et al. 2019	a series of questions used to screen low back pain patients for potentially serious underlying pathologies such as malignancy, vertebral fractures, spinal infections, and CES. Patients that screen positive for RF warrant further clinical investigation, particularly with imaging or consultation with a specialist. Delaying treatment for these serious and complex pathologies can result in adverse outcomes for patients
Ramanayake et al. 2018	signs and symptoms found in the patient history and clinical examination that may tie a disorder to a serious

	pathology
Buchberger M. 2007	signs and symptoms suggesting the possible presence of serious spinal and non-spinal conditions requiring immediate specialist examination with targeted treatment
Arnold et al. 2009	linked to the possible presence of a severe disease. Synonyms used are: indicators, signs and symptoms, severe disease, risk factors, biomedical factors, warning signals and danger signals

Table 5 – RF definitions

RED FLAGS	N° STUDIES	DIAGNOSTIC ACCURACY				PATHOLOGIES
		SN	SP	LR+	LR-	
Age>50years (6,7,13,14,16-17,21,22,31,35,44,45,47,50,56-58,61) ok	21	0,50-0,79	0,32-0,71	1,1-2,7	0,1	General RF, back, LBP, tumor, infection, fracture, lung cancer, cardiovascular diseases, lumbar stenosis, rheumatic polymyalgia
Age>54 years (17)	1	0,63-0,83	0,52-0,76	-	-	fracture
Age <52 years (17)	1	0,95	0,39	-	-	fracture
Age >64 years (17)	1	0,63-0,78	0,68-0,91	-	-	fracture
Age >60 years (47)	1	-	-	-	-	Abdominal aortic aneurysm, lumbar stenosis
Age >65 years (47)	1	0,77	0,69	-	-	Lumbar stenosis
Age >74 years (17)	1	0,25-0,45	0,89-0,98	-	-	Fracture
Age ≥75 years (17)	1	0,45	0,85	3,1	0,6	Fracture
Women >54 years (17)	1	0,50	0,96	-	-	Fracture
Women >64 years (17)	1	0,59-0,63	0,79-0,96	-	-	Fracture
Age >70 years (16,17,21,22,47,50)	5	0,03-0,50	0,80-0,96	1,55-11,2	0,86	fracture, tumor
Women >74 years (17)	1	0,25-0,45	0,89-0,98	-	-	Fracture
Older age (32,33,44,53,56,47)	6	0,50-1,00	0,66-0,77	1,9-4,6	0,3-0,7	Tumor, LBP, osteomyelitis
Age <20 years (6,16,17,47,50)	5	-	-	-	-	LBP, tumor,

						inflammatory disorders
Age <45 years (47)	1	-	-	-	-	inflammatory disorders
High ERS (7,14,44)	3	-	-	-	-	Back pain, tumor
ERS ≥20mm/h (45)	1	0,78	0,67	2,3	0,37	tumor
ERS ≥50mm/h (45)	1	0,56	0,97	18,0	0,46	tumor
ERS ≥100mm/h (45)	1	0,22	1,00	55,6	0,75	Tumor
Hematocrit <30% (45,47)	2	0,09	0,99	18,2	0,88	Tumor
Anomaly in serous protein electrophoresis (47)	1	-	-	-	-	Tumor
Anaemia (16,45)	2	0,55	0,86	3,9	0,53	Tumor, esophageal carcinoma, perforated petide ulcer
WBC ≥12000 (45,47)	2	0,22	0,94	4,1	0,80	Tumor, infection
High VES, low hematocrit (44,47,47)	4	-	-	18,2	-	Tumor, inflammatory disorders, General RF
History of previous cancer 6,7,13-18,21,22,35,43-46,47,50,47,62)	20	0,20-1,00	0,77-0,98	6,4-31,7	0.06-0,8	General RF, back pain, LBP, tumor, infection
Strong clinical suspicion (14,15)	2	0,43-1,00	0,96-0,99	12,0-54,2	0,6	Tumor
Unexplained weight loss (6,7,13-18,21,22,31,32,15,44-46,47,50,47,61,62)	24	0,08-0,15	0,88-0,99	1,87-3,00	0,87-0,96	General RF, LBP, back pain, tumor, infection, tuberculosis, lung cancer, Felty's syndrome
Progressive symptoms (14,15,31)	3	-	-	-	-	Tumor, General RF
Night pain/that awakens from sleep (6,13,14,16-18,31,35,43,44,47,50,51,62)	16	0,16-0,37	0,47-0,87	0,85	1,07	General RF, LBP, tumor, infection, inflammatory disorders, abdominal aortic aneurysm
Blood in sputum (7,31,47)	3	-	-	-	-	General RF
Loss of consciousness or altered mental state (7,47,47)	3	-	-	-	-	General RF, fracture
Neurological deficit not associated with radiculopathy (7,47)	2	-	-	-	-	Back pain, General RF
Failure of conservative therapy after 4 weeks/1 month (6,15-17,31,35,44-46,47,50,52)	14	0,25-0,31	0,84-0,90	3,00-3,2	0,75-0,8	LBP, tumor, infection, lumbar radiculopathy, General RF
Persistent pain from 4-6 weeks (14,16,21,45,47,47)	6	0,50	0,81	2,6	0,62	Cancer, General RF
Pain for at least 3 months (47)	1	-	-	-	-	Inflammatory disorders
Constitutional symptoms (fever or chills, night sweat, discomfort, fatigue, nausea, vomiting) (6,7,13-18,21,31,32,34,15,43-45,47,50,56,47,61)	24	0,00-0,12	0,93-0,99	1,71-25,00	0,95-1,00	General RF, back pain, LBP, tumor, infection, tuberculosis, lung cancer, basilar impression, osteomyelitis, Felty's syndrome, abdominal aortic

						aneurysm, pneumonia, pleuritis
Paraparesis (14,15,31)	3	-	-	-	-	Tumor, General RF
Trauma (major or minor or weightlifting in elderly patients with osteoporosis) (6,7,12-14,16-17,21,22,34,43,45,46,47,50,51,47)	17	0,00-1,00	0,51-0,97	0,2-12,8	0,37-1,18	General RF, back pain, LBP, fracture, RCS instability, tumor, basilar impression
gradual onset before 40 years (21,47)	2	-	-	-	-	Tumor, inflammatory disorders
Familial LBP (21)	1	-	-	-	-	Tumor
Insidious onset (21,31,35,45,47)	5	0,62	0,42	1,00	0,94	Tumor, General RF, inflammatory disorders
Abrasions/contusions (17,46)	2	0,08	0,97	-	-	LBP, fracture
Immunodepression (6,13,14,16,17,47,50,56)	8	-	-	-	-	LBP, infection, tumor, osteomyelitis
Recent infection (gastrointestinal, urinary tract, cutaneus) (6,7,13,14,16,17,22,47,59)	9	0,24	0,97	0,31	0,78	Back pain, LBP, tumor, infection, General RF
Bites/stitches (47)	1	-	-	-	-	infection
History of metabolic disorder (7,47,47)	3	-	-	-	-	Back pain, infection, General RF
Abnormal clinical presentation (17,31)	2	-	-	-	-	LBP, General RF
Pain at rest, which worsens at night or from lying down/supines (6,13-17,21,43-44,47,50,64)	13	0,00-0,90	0,46-0,93	0,7-1,00	0,46-1,3	LBP, tumor, infection, paediatric osteosarcoma, inflammatory disorders, abdominal aortic aneurysm, lumbar radiculopathy
Severe pain (7,14,16,21,45,47,47)	8	0,23	0,85	1,7	0,88	Infection, fracture, General RF, tumor, abdominal aortic aneurysm
Non mechanical, constant and progressive pain (7,31,16,17,21,47,50,47)	10	-	-	-	-	Back pain, LBP, tumor, General RF, infection
Worsening deep pain (35)	1	-	-	-	-	tumor
Band-like trunk pain (18)	2	-	-	-	-	Tumor, General RF
Multiple sites pain (14)	1	-	-	-	-	tumor
Saddle anesthesia/hypoesthesia (6,7,13,14,16-18,43,47,47,50,63)	13	0,00-0,75	0,75-0,99	-	-	General RF, LBP, CES, tumor, myelopathy
Bladder and/or bowel dysfunction (6,7,13,14,16-18,34,43,47,47,50,53,63)	14	0,13-0,90	0,73-0,98	2,31-18	0,1-0,91	General RF, LBP, CES, tumor, myelopathy, basilar impression, lumbar radiculopathy
Lower and/or upper extremity neurological deficit (motor and sensitive) (6,7,13,16,17,31,34,15,45,47,47,50)	12	0,00-0,80	0,91	0,4	1,06	LBP, tumor, CES, lumbar radiculopathy and stenosis, basilar impression, RCS instability, cervical myelopathy, General RF

Widespread neurological deficit (7,17-17,21,45,47,50,64)	11	0,00-0,29	0,88-0,97	7,5	0,78	General RF, back pain, CES, fracture, LBP, tuberculosis, tumor, paediatric osteosarcoma, lumbar radiculopathy and stenosis
Alterated sensation from trunk down (21,47)	2	-	-	-	-	Tumor, fracture, CES, radicolopatia e lumbar stenosis
Uni or bilateral radicolopaty (7,17,31,47,47)	4	-	-	-	-	Back pain, LBP, CES, General RF
Lower extremity pain with mono or bilateral sciatica (6,14,17,17,31,47,50)	7	0,00-0,80	0,85-0,91	-	-	LBP, CES, fracture, General RF, lumbar radiculopathy and stenosis
Absence of buttocks/legs pain (17)	1	0,32	0,86	-	-	fracture
Lower extremity weakness and gait abnormalities (6,7,31,14,17,15,43,47)	11	0,17-0,66	0,78-0,94	-	-	Back pain, LBP, CES, myelopathy, tumor, RCS instability, cervical myelopathy, heart diseases, lumbar stenosis and radiculopathy
Vague abdominal or pelvic symptoms, not specific at lower extremity (18,56)	2	-	-	-	-	General RF, osteomyelitis
Decreased mobility (18)	1	-	-	-	-	General RF
Recent back surgery (6,14,16,17,47,50)	6	-	-	-	-	LBP, infection
Penetrating and not healing wound (7,15,47,47)	4	-	-	-	-	Infection, General RF
HIV or intravenous drug abuse (6,13,14,17,18,47,50,56)	9	-	-	-	-	General RF, LBP, infection, tumor, osteomyelitis
Injections (17,50)	2	-	-	-	-	LBP, infection
Pathological changes in the gastrointestinal system (47)	1	-	-	-	-	General RF
Thoracic pain (6,7,12,17,21,31,15,45,50,51,61)	11	0,17-0,42	0,78-0,84	1,2-1,9	0,7-0,96	LBP, RT, fracture, tumor, lung cancer, pleuritis, pericarditis, General RF, abdominal aortic aneurysm
Spinal tenderness (47)	1	0,86	0,60	2,2	0,23	Tumor, infection, fracture
Permanent urinary catheter (47)	1	-	-	-	-	infection
Unexplained referred pain (7,31)	2	-	-	-	-	Back pain, General RF
Structural defomrmity (6,14,17,47,50,51)	6	0,12	1,00	21,6-46,4	-	LBP, fracture, infection
BMI <23 (17)	1	0,37	0,83	-	-	fracture
Decreasing of pain from sitting (17,47)	2	0,29-0,79	0,81-0,93	6,6	-	Fracture, lumbar stenosis
Absence of gait abnormalities (17)	1	0,66	0,23	-	-	fracture
Tenderness at spinous processes palpation (7,14,17,17,21,45)	6	0,15-0,73	0,59-0,60	0,4-0,73	1,37	Fracture, osteomyelitis/infection, tumor
Spasm (17,21,45)	3	0,12-0,25	0,66-0,91	0,5	1,25	Fracture, tumor

Corticosteroid use (6,7,14,16-17,43,46,47,50,47,51)	14	0,00-0,25	0,84-0,99	48,5		General RF, fracture, LBP, back pain, infection
Osteoartrosis (17)	1	0,50	0,52	-	-	fracture
First motoneuron disease, multiple sclerosis, diabetes, alcoholism, cervical myelopathy, peripheral neuropathy, lower extremity edema for cardiovascular diseases, spinal stenosiss, nerve root compression (18)	1	-	-	-	-	Red Herrings of serious spinal pathologies
Not regular exercise (17)	1	0,82	0,44	-	-	fracture
History of previous fracture (14,51)	2	-	-	-	-	Fracture, LBP
Low body weight (14)	1	-	-	-	-	Fracture
Increased kyphosis (14)	1	-	-	-	-	Fracture
Subtract age from weight (kg), multiply by 0.2 and put under integral; score ≤-1 to confirm risk (64)	1	0,83-0,95	0,37-0,71	-	-	Osteoporosis Self-Assessment Screening Tool
Osteoporosis (12,14,16,15,43,47,51)	7	0,17-0,58	0,87-0,88	3,2	0,7	Fracture, LBP
Back pain ≥7 (12)	1	0,67	0,63	1,8	0,5	fracture
First episode of LBP in life <20 or >50 years (6)	1	-	-	-	-	LBP in general
Clinical judgment (44,45,47)	3	0,00-1,00	0,94-0,98	2,9-12,6	0,00-0,77	Tumor, fracture, CES, back pain
History of previous cancer+ weight loss+ age >50 years + failure of conservative therapy after 1 month (6,37,44,45,47)	5	1,00	0,60-1,00	2,4	0,06	LBP in general, tumor, back pain
Age >50years+ first episode of severe LBP and history of carcinoma in the last 15 years+ unexplained weight loss+ failure of conservative therapy after 4 weeks (14)	1	-	-	-	-	tumor
Female gender+ age >70 years+ severe trauma+ prolonged corticosteroid use (22)	1	-	-	1/4: 1,8 2/4: 15,5 3/4: 218,3	-	fracture
Pain and stiffness (47)	1	-	-	6,7-7,2	0,42-0,44	fracture
Severe central pain that improves when lying down (47)	1	-	-	-	-	fracture
Diabetes/alcoholism/chronic renal insufficiency (47,50)	2	-	-	-	-	infection
Female gender (14,31,47,50,51,59)	6	-	-	1,3	0,65-0,67	fracture, LBP, osteoporosis, cardiovascular diseases
Menopause (31,59)	2	-	-	-	-	Osteoporosis, cardiovascular diseases
Fracture with minor trauma (15)	1	-	-	-	-	Osteoporosis
Loss in height (15)	1	-	-	-	-	Osteoporosis
Caucasian race (59)	1					osteoporosis
pain so intense that it's hard to understand where it came from (47,50)	2	-	-	1,7	0,78	fracture
general physical appearance: tired face, paleness or flushing, sweating,	3	-	-	-	-	LBP and RF in genera

altered skin color, tremors or agitation, manifestation of excessive tiredness, halitosis (31,32,50)						
spinal rigidity in response to percussion (50)	1	0,86	0,60	-	-	infection
Sudden scoliotic deviation (50)	1	-	-	-	-	osteoma
Mass of the musculoskeletal system (35,50)	2	-	-	-	-	tumor
Inability to lie supine on the couch (50)	1	-	-	-	-	tumor
Lumbar kyphois (6)	1	-	-	-	-	LBP in general
Sacral pain without trauma (6)	1	-	-	-	-	LBP in general
Edema /swelling of lower extremity (6)	1	-	-	-	-	LBP in general
Bilateral symptom (rash, nodules, pain) (31)	1	-	-	-	-	General RF
Shoulder pain of visceral origin (31,32,47)	3	-	-	-	-	General RF
Severe and constant abdominal, flank pain +LBP (6,47,50,47)	4	-	-	-	-	Abdominal aortic aneurysm
Irradiated buttock pain (47)	1	-	-	-	-	Abdominal aortic aneurysm
Atherosclerosis (47,47)	2	-	-	-	-	Abdominal aortic aneurysm
Caucasian race, family history of smoking, hypertension, coronary heart failure (47)	1	-	-	-	-	Abdominal aortic aneurysm
Male gender (47)	1	-	-	-	-	Abdominal aortic aneurysm
Pain that does not change with different positions (35,47,50,47)	4	-	-	-	-	Abdominal aortic aneurysm
Absence of aggravating characteristics (47)	1	-	-	-	-	Abdominal aortic aneurysm
Abdominal pulsating mass (6,7,17,47,50,47)	6	-	-	-	-	Abdominal aortic aneurysm, general RF
Unexplained weakness of upper or lower extremity (7,33,17,61)	4	0,02-0,23	0,89-0,99	-	-	Back pain, myelopathy, fracture, lung cancer, CAD
RCS instability (15)	1	-	-	-	-	Cervical myelopathy
Loss of manual dexterity (7)	1	-	-	-	-	myelopathy
Stiff neck (7)	1	-	-	-	-	myelopathy
Altered sensation of upper and lower extremity (18,17,17,62) (7,17,31)	4	0,00-0,27	0,88-0,98	-	-	Myelopathy, fracture, general RF
Hyperreflexia, spasticity, Babinski sign, Romberg, clonus by sustained foot dorsiflexion, clones (7,17,15,47,50,47)	7	0,13-0,53	0,91-1,00	-	-	Spinal compression/myelopathy, multiple sclerosis, RCS instability, lumbar stenosiss, general RF
Spurling test (7)	1	-	-	-	-	Cervical radiculopathy
Abnormal reflexes (7,17,47,47)	4	0,08-0,12	0,89-0,95	-	-	radiculopathy, fracture, CES, General RF
SRL or PKB (7,17,17,47)	4	0,18-0,91	0,26-0,83	1,2	0,34	Lumbar radiculopathy, RL, fracture, CES
Atrophy (7,31)	2	-	-	-	-	radiculopathy, General RF

pain worsening with cough/sneeze/Valsava (47)	1	-	-	-	-	radiculopathy
Cruciate SRL + (47)	1	0,29	0,88	2	-	Lumbar radiculopathy
Pain decreases from walking, standing, supine with bent legs (47)	1	-	-	-	-	Lumbar radiculopathy
Pain worsens from bending forward and sitting (47)	1	-	-	-	-	Lumbar radiculopathy
Hyperextension test (47)	1	0,63	Con SRL crociato + 0,93	4	-	Lumbar radiculopathy
Bell test (47)	1	0,71	-	-	-	Lumbar radiculopathy
loss of lordosis and/or scoliosis from sciatica (47)	1	-	-	-	-	Lumbar radiculopathy
Intolerable radicular pain despite medications (52)	1	-	-	-	-	Lumbar radiculopathy
Severe (<3 MRC, movement against gravity is possible) or progressive (that worsens in a few days) motor deficits (52)	1	-	-	-	-	Lumbar radiculopathy
Neurogenic claudicatio (47)	1	0,60	-	-	-	stenosis
Improvement with lumbar flexion (47)	1	0,79	-	-	-	Stenosis
Broad-based walking (47)	1	-	0,97	-	-	Stenosis
Peripheral vascular deficiency (47)	1	-	-	-	-	Stenosis
Worsening with extension, standing, walking downhill (47)	1	-	-	1,00	0,97	stenosis
Movement-related, intermittent and pulling lower extremity pain, rarely appears at rest, subjective loss of strength in the same area, tingling, cold feeling, hypercholesterolemia, absence of impairment at physical examination (20)	1	-	-	-	-	OAD
Absence of the left foot dorsal artery's wrists (20,47)	2	-	-	-	-	OAD, aortic aneurysm
Morning stiffness (6,16,47)	3	-	-	-	-	Morbus Bechterew, ankylosing spondylitis, other inflammatory disorders
Improvement with exercises (16,47)	2	-	-	-	-	ankylosing spondylitis, other inflammatory disorders
Severe and persistent restriction of lumbar flexion (6,17,47,50)	4	-	-	-	-	LBP, inflammatory disorders
Family history of arthritis or osteoporosis (47)	1	-	1,00	-	-	Inflammatory disorders
Alternating buttocks pain (16,47)	2	-	-	-	-	ankylosing spondylitis, other inflammatory disorders
Younger age (16)	1					ankylosing spondylitis, other inflammatory disorders

Limitation of spinal movements (7,16,47,50)	4	-	-	-	-	ankylosing spondylitis, other inflammatory disorders, tuberculosis, RT, infection, lumbar radiculopathy
Hypersensitivity to NSAIDs (47)	1	-	-	-	-	inflammatory disorders
Reduced thoracic expansion (47)	1	-	0,99	9	-	inflammatory disorders
Reduced lumbar lateral flexion (47)	1	0,52	0,82	2,9	-	inflammatory disorders
Peripheral joint involvement (47)	1	-	-	-	-	inflammatory disorders
Skin rashes (47)	1	-	-	-	-	inflammatory disorders
Uveitis/synovitis/psoriasis (47)	1	-	-	-	-	inflammatory disorders
Pain in the thoracolumbar junction (50)	1	-	-	-	-	tuberculosis
Abscess in the groin, trochanteric or gluteal zone (50)	1	-	-	-	-	tuberculosis
History of previous tuberculosis (50)	1	-	-	-	-	tuberculosis
Posterior spine dysfunction, low hairline, short and webbed neck (34)	1	-	-	-	-	basilar impression
Symptoms of vertebro basilar insufficiency (15)	1	-	-	-	-	RCS instability
Alterated sensation of tongue and mouth (15)	1	-	-	-	-	RCS instability
5 D: Diplopia, dysphagia, dysarthria, drop attack, dizziness (7,33)	2	-	-	-	-	vertebrobasilar insufficiency, CAD
passive cervical spine tests with provocation of symptoms in end range (2)	1					vertebrobasilar insufficiency, RCS instability
Dental injury (2)	1	-	-	-	-	RCS instability
Cervical pain (2,34,15)	3	-	-	-	-	RCS instability, basilar impression, cervical myelopathy
Restricted cervical ROM (7,34)	2	-	-	-	-	RCS instability, basilar impression
worsening symptoms with head flexion (headache, fatigue, upper extremity paresthesias) (2)	1	-	-	-	-	RCS instability
ligament instability test + (e.g. Sharp-Purser) (2)	1	0,88	0,96	-	-	RCS instability
Limp or refusal to walk and bone pain, lasts for >14 days, is localized, is associated with swelling or deformity, and does not improve with NSAIDs S (64)	1	-	-	-	-	Paediatric osteosarcoma
Lymphadenopathy (56,64)	2	-	-	-	-	Paediatric osteosarcoma, osteomyelitis
onset of headache after 50 years, focal pain on the temporal artery (16)	1	-	-	-	-	Temporal arteritis
onset >50 years, progressive in severity and frequency, focal neurological signs, papillary edema, "thunderclap" headache (16)	1	-	-	-	-	Cerebral mass injury

sudden onset of "thunderclap" headache (16)	1	-	-	-	-	subarachnoid haemorrhage
progressive in severity and frequency, headache resulting from trauma (16)	1	-	-	-	-	subdural haematoma, drug abuse, epidural haematomas and intracranial haemorrhages
signs of systemic diseases such as fever, cervical stiffness, photophobia, general malaise, papilledema (16)	1	-	-	-	-	meningitis/encephalitis
focal neurological signs such as progressive visual disturbances, weakness, loss of balance, clumsiness (16)	1	-	-	-	-	stroke and vascular malformation
pregnancy or immediately after postpartum (16)	1	-	-	-	-	venous sinus thrombosis, CAD, preeclampsia
Ipsilateral cranio-cervical and posterior-occipital pain (33,34)	2	-	-	-	-	CAD
dysfunction of the cranial or peripheral nerves (33,34)	2	-	-	-	-	CAD
Tinnitus (33,34)	2	-	-	-	-	CAD
Horner's syndrome (myosis, ptosis, anhydrosis, asymmetriy of the pupils) (33,34)	2	-	-	-	-	CAD
Headache with characteristics of migraine/fronto-temporal but unlike previous episodes, stress in cervical rotation/cervical trauma, hypertension, 3N: nystagmus, numbness, nausea, ataxia, , short-term memory loss, weakness of the lower and upper extremities, ipsilateral carotid bruit, orbital pain, scalp tension, neck swelling, amaurosi fugax, TIA/stroke, retinal infarction, functional positional VBI tests (rotation, extension), young patient with diabetes, previous stroke (33)	1	-	-	-	-	CAD
Gout Risk Criteria: male, previous arthritis attack, onset within one day, joint redness, first metatarsal involvement, hypertension or more of one cardiovascular disease, uric acid level in serum >5.88 mg/dl; score 0-13 (59)	1	se ≤4 0,99	-	-	-	Gout
acute intermittent monoarticular attack, predisposition for metacarpophalanxes (58)	1	-	-	-	-	Gout
age ≥50 years, bilateral pain, stiffness for more than one month, most involved joints are cervical, shoulders, pelvic girdle and hips, ERS ≥40mm/h, rapid response to prednisone ≤20 mg/day, body weight reduction; it's important the differential diagnosis with Systemic Lupus Erithematosus (thrombocytopenia, leukopenia, pleurisy or pericarditis), polymyositis	1	-	-	-	-	Reumathic polymyalgia

(muscle weakness rather than pain, increased muscle enzymes), spondyloarthropathy (oligoarthritis, distal edema, minimal axial involvement, elevated ERS, dactylitis, distal enthesitis, uveitis, HLA-B27 association, Rx with signs of sacroiliitis), fibromyalgia (younger age of onset, variable and heterogeneous symptoms, irritable bowel syndrome, tender points, normal ERS), tumours (poor response to corticosteroid therapy, absence of movement pain or stiffness, fever, night pain, weight loss), calcium pyrophosphate deposition disease (tibiofemoral osteoarthritis, tendon calcifications, typical of elderly patients) (58)						
FT treatment is not contraindicated, only if there are related disorders. Often associated with structural changes in the atlanto-occipital joint (chronic and severe occipital-cervical pain, ear, mastoid and facial pain, severe neurological deficits such as ataxia, paresis in the limbs, transient ischemic attacks, sleep apnea, ophthalmoplegia, spastic quadriparesis, diplegia, nystagmus) and Rest Leg Syndrome (sleep disorders, early fatigue, stress, fibromyalgia, pain); may mimic or hide paraneoplastic rheumatic syndrome (fever ≥40°, weight loss, unusual and chronic inflammatory arthritis, asymmetric distribution, high CPR, rare bone deformities, often negative ANA) (58)	1	-	-	-	-	Reumathoid arthritis
Reynaud's phenomenon, cyanosis, telangiectasia, skin thickening, calcinous, sclerodactyly, visceral complications of the lungs, gastroenteric system (with esophageal dismobility), cardiovascular and renal system (58)	1	-	-	-	-	Systemic sclerosis
Flank pain, slow urine flow, history of previous kidney stones: increase of post-test probability up to 25% (with CT up to 90%) (59)	1	-	-	-	-	Kidney stones
History of malignacy and surgery (6 points); Storia di tumor e di chirurgia (6 punti); presence of at least 3 classic sign of inflammation without fever (weakness, relapsing pain and functional deterioration, 5 points); 11 points: probable osteomyelitis, to make it sure 18 points are needed, achievable with additional microbiological analysis and imaging (56)	1	-	-	-	-	osteomyelitis
chronic use of internal catheter, history	1	-	-	-	-	Osteomyelitis

of bedsores, recent surgery, infection of the surgical wound, lethargy, anorexia, vomiting, edema and localized erythema, no neurological signs, abdominal tension, pain worsened by abduction of the hip and symphysis palpation (56)						
Stiffness and dull lumbar pain with insidious and progressive onset, deep anterior thigh pain with heavy feeling, symptoms get worse at work, with walking, prolonged sitting position, lumbar movements and squat while improve with rest or by night, negative neurological examination, limited and painful hip AROM and PROM (internal rotation, flexion+abduction, passive flexion with limited and painful rotation), no change of lower extremity symptoms after failure of FT lumbar treatment, response of symptoms to loading movements, tuning fork +, single hop test +, percussion test + (60)	1	-	-	-	-	Hip bone marrow edema
Faddir test + (60)	1	0,99	0,25	-	-	Hip bone marrow edema
Scour test + (60)	1	0,50	0,29	-	-	Hip bone marrow edema
Patellar pubic percussion test + (60)	1	0,94	0,95	-	-	Hip bone marrow edema
poor weight-bearing tolerance, antalgic gait with abduction and extrarotation of the hip, warmth (35)	1	-	-	-	-	Lower extremity tumor
diabetes, history of chemotherapy, pain in the hip and anteromedial part of the thigh, progressive worsening weight-bearing status (35)	1	-	-	-	-	Avascular necrosis of the femoral head
older age, diabetes, hypertension, hip and anteromedial part of the thigh pain (35)	1	-	-	-	-	Hip or pelvic fracture
poor weight-bearing tolerance, antalgic gait with abduction and extrarotation of the hip, painful and limited hip ROM, pain on palpation of the hip, also palpable warmth for the fracture (35)	1	-	-	-	-	Avascular necrosis of the femoral head, Hip or pelvic fracture
previous DVT, recent surgery, progressive weakness/femoral nerve palsy or paresis, loss of sensation; score of +1, moderate risk of DVT, at the Wells Prediction Rule (Appendix VI) (35)	1	-	-	-	-	DVT
Skin thinning, painful peripheral neuropathy (15)	1	-	-	-	-	Steroid-induced diabetes mellitus
Frequent bacterial infections, splenomegaly (15)	1	-	-	-	-	Felty's syndrome
'Red eye', eye pain, photophobia, decreased visual acuity, dry/itchy eye (15)	1	-	-	-	-	Episcleritis, scleritis,retinal vasculitis
Dry eyes and mouth. Skin, nose and	1	-	-	-	-	Sjögren's syndrome

vaginal dryness also present (15)						
Acute sensory and/or motor neuropathy, occurring as a result of vasculitis, compression, or diabetes (15)	1	-	-	-	-	Mononeuritis multiplex, peripheral neuropathy
Signs of ischaemia or necrosis in affected organs/tissues (15)	1	-	-	-	-	Vasculitis
Petechiae/purpura (red or purple skin lesions that do not blanch on pressure). Leg ulcers and peripheral gangrene (15)	1	-	-	-	-	Major cutaneous vasculitis
Single or multiple subcutaneous nodules, >5 mm diameter. Usually painless and on extensor surfaces (15)	1	-	-	-	-	Reumathoid nodules
Swollen and painful tendon, crepitus on movement; warmth; evidence of swelling (15)	1	-	-	-	-	Tenosinovitis
Pain on resisted movement/load. loss of function; deformity, loss of tendon function, joint instability and tendon discontinuity. Discordance between active and passive joint movement. (15)	1	-	-	-	-	Tendon rupture and/or joint dislocations of the hand/wrist or foot/ankle joints
Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist, combination of flexion of proximal IP joint and hyperextension of distal IP joint. (15)	1	-	-	-	-	Boutonnière deformity
Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist., combination of flexion at MCP joint, hyperextension of the proximal IP joint and flexion of the distal (15)	1	-	-	-	-	Swan neck deformity
nausea, vomiting, pain, diarrhea, constipation, altered motility caused by tobacco, caffeine, alcohol, physical and emotional stress, lifestyle; abdominal pain, dysphagia (difficulty swallowing), odinophagy (swallowing pain), bleeding, epigastric pain with radiation corresponding to the back, symptoms worsen with food intake, failure to evoke symptoms with shoulder movements, arthralgia. One of the causes of shoulder pain related to intestinal causes are complications from NSAIDs (31,32,47)	3	-	-	-	-	RF gastrointestinal system
40-45 years or older at first presentation, family history of gastric cancer with onset age<50 years, severe or persistent dyspepsia, chronic gastrointestinal bleeding, persistent vomiting, difficulty swallowing, palpable abdominal mass, nocturnal aspiration or coughing spells, previous peptide ulcer, prolonged aspirin intake (16,47)	2	-	-	-	-	Esophageal/stomach carcinoma, perforated peptide ulcer
right shoulder pain, tremor,	2	-	-	-	-	RF liver/biliary

paresthesias, skin changes (paleness, orange or green skin, jaundice, itching, palmar erythema, spider angiomas) and nail bed changes (white stripes, i.e. leukonychia, clubbing, koilonychia, the latter not specific for liver diseases); musculoskeletal signs and symptoms (interscapular thoracic pain, shoulder pain, upper trapezium and right subscapular area pain, osteoarthropathy of ankles and wrists, new myopathies with a history of statin intake); neurological symptoms (confusion, sleep disorders, tremors, hyperreflexia, movement disorders, asterixes, i.e. inability to maintain the extension of the wrist to the upper extremities flexed forward, peripheral neuropathies) (31,47)						system
infections, inflammations, obstructions, renal failure; ipsilateral shoulder pain, posterior costovertebral and subcostal region pain, generalized abdominal pain with nausea, vomiting, impaired intestinal motility, testicular pain in males, constant pain, deafness, taking NSAIDs; for cancer we have blood in the urine, weight loss, fever and pain (31,47,47)	3	-	-	-	-	RF renal disorders
sudden and acute pain, chills, nausea, vomiting, renal colic, typical symptoms of urinary tract infection, residence in a warm environment, and moist, history of kidney stones or recurrent episodes; acute color, severe, fever, disturbances in urine elimination (pain, burning, excessive frequency in the stimulus, cloudy color, smelly). Recent or coexisting urinary tract infection (urinary stagnation, pregnancy), enlarged prostate, recent kidney stones or past episodes and predisposing factors such as diabetes, debilitating diseases. Minor symptoms, possible periods of exacerbation, risk of destruction of renal tissue resulting in loss of function; back and hip pain; TLJ or back pain; TLJ and back pain (31,47)	2	-	-	-	-	Nephrolithiasis, acute or chronic pyelonephritis
paleness, sweating, dyspnea, nausea, sensation of indigestion, shortness of breath, weakness, numbness, fainting, sudden darkness or loss of sight and speech; Fever, chills, weakness, coughing, increased pain with the patient positionated on his left side or supine, by movements associated with deep breathing (laughing, coughing, deep inhalation), by movements of the trunk (lateroflexion and inclination),	1	-	-	-	-	IMA, pericarditis, angina

relieved with bending forward, sitting position or by holding the breath; **A. stable/chronic:** oppression that occurs after exertion or emotional stress. Position, duration, intensity and frequency of thoracic pain are consistent over time. Symptoms improve with nitroglycerin and rest. **A. pectoris unstable:** sudden change in frequency intensity, duration, high risk of IMA. Does not respond to nitroglycerin and rest. **A. from rest:** pain that occurs at rest and in supine position, often at the same time every day. Pain is not caused by exercise or relieved by rest. **A. of Prinzmetal:** symptoms are similar to those of the atypical but given by the spasm of the arteries which are usually free of plates or modifications. Occurs at rest, especially early in the morning, difficult to reproduce with exercise; severe thoracic and/or back pain, retrosternal pain (pain may extend to the left arm, jawbone, teeth); acute thoracic pain that may be referred laterally to the neck, shoulders retrosternally, upper back, upper part of the trapezoid muscle, left supraclavicular area; thoracic and/or back pain (47)						
pleuritic pain, fever, chills, headache, malaise, nausea, catarrhal cough; pain that increases during inhalation, difficulty in ventilating or expanding the thoracic cage, hyperresonance to percussion, decreased respiratory sounds, recent cough attacks, intense exercise or trauma¸ pain sometimes even in the abdomen, history or risk factors of DVT, dyspnoea; pain may be felt in the shoulder; thoracic pain; thoracic and shoulder pain (47)	1	-	-	-	-	Pneumonia, pneumothorax, pulmonary embolism
dyspnoea-related activity, coughing, pain worsening with inhalation, smoker, chronic obstructive pulmonary disease (COPD), dysphagia, change in respiratory pattern, wheezing, hoarseness, hemoptysis (61)	1	-	-	-	-	Lung cancer
Cough (31,15,47,47)	4	-	-	-	-	interstitial lung disease, obliterative bronchiolitis, pleuritis
Dyspnoea (31,15,47)	3	-	-	-	-	obliterative bronchiolitis, interstitial lung disease, pleuritis, pneumonia, pericarditis

Wheezing/crackles on auscultation (31,15)	2	-	-	-	-	obliterative bronchiolitis
Sneezing (15)	1	-	-	-	-	Pleuritis
Palpitations (31,15)	2	-	-	-	-	Pericarditis, cardiovascular diseases
acute and severe pain ("knifelike pain"), dyspnoea, decreased thoracic range, pleuritic pain, recent history of recurrent respiratory disorders such as infections, pneumonia, tumours, tuberculosis; thoracic and interscapular pain (47)	1	-	-	-	-	Pleuritis
family history of heart problems (31)	1	-	-	-	-	Heart diseases
Shoulder pain with exacerbation in recumbency, with effort and not related to shoulder movement, diaphoresis (31)	1	-	-	-	-	Heart diseases
Shoulder pain with cough, reproduction of the symptom with breathing (31)	1	-	-	-	-	Lung diseases
diabetes, hyperthyroidism, ischaemic heart disease, infections and lung diseases (31)	1	-	-	-	-	Adhesive capsulitis
pain on swallowing, feeling that food is struggling to go down, vomiting, nausea, stomach pains, sputum regurgitation and decreased appetite; retrosternal thoracic pain (47)	1	-	-	-	-	Esophagitis
epigastrial pain, dull and dazzling, burning sensation, symptoms are relieved by eating, painful right epigastrium, constipation, bleeding, vomiting, tarry stools, coffee-colored emesis, history of NSAIDs; pain in the thoracolumbar junction area (TLJ) and central thoracic area, supraclavicular (31,47)	2	-	-	-	-	Peptide ulcer
dull, constant pain that does not decrease with NSAIDs, VAS 8-9/10, aggravated by sitting, standing and twisting movements; pain that worsens at the end of the day; night pain. Tenderness to abdominal palpation, joint dysfunction; Medium thoracic pain and in the TLJ and lumbar area (31,47)	2	-	-	-	-	Duodenal ulcer
pain in the upper quadrant accompanied by nausea, vomiting, fever, jaundice and urine are often very dark; pain in the TLJ with radiation to the right upper extremity (47)	1	-	-	-	-	Liver disorders
pain like colic, symptoms may worsen with ingestion of fatty foods but do not increase with activity nor are relieved by rest; pain often after meal; nausea; vomiting; fever; tachycardia; jaundice and malaise; scapular and right upper abdominal quadrant pain; central	2	-	-	-	-	Cholecystitis, cholelithiasis

thoracic and in the TLJ pain (31,47)						
tenderness to upper right abdominal palpation; penetrating abdominal pain in the middle epigastrium that radiates to the back, increases in intensity and can last more than a week. Fever, the pain worsens by standing and is alleviated by a supine position, sitting and bending forward; persistent pain, recurrent epigastritis. It can last from a few hours to weeks. Often the pain begins 12-24 hours after an episode of intoxication; abdominal and epigastric area pain with radiation to the back, possible presence of abdominal mass, the pain may worsen after a meal or in the supine position, sitting position and by bending forward. Anorexia, weight loss, jaundice secondary to obstruction of the bile duct. Dark urine; pain in the TLJ and medium thoracic area; TLJ pain and middle thoracic area; upper lumbar region pain; TLJ and middle thoracic area pain (31,47)	2	-	-	-	-	acute or chronic pancreatitis, cancer
age <40 years, acute episode, traumatic event, PROM limitation, previous acute episode or instability, deformity, risk of related fracture if it's the first episode, age >40 and contusive trauma (the absence of these 3 factors has a Sn of 97%), for acromioclavicular dislocation further signs are contact sports, men and upper shoulder pain, for sternal-clavicular collision with vehicles, contact sports, shoulder or anterior chest pain, paresthesias, dysphagia, breath's shortness [73]	1	-	-	-	-	Shoulder dislocation
rotator cuff, pectoralis, biceps (acute and traumatic episode, muscle weakness) [73]	1	-	-	-	-	Tendon rupture
proximal humerus (age >40 years, especially women >60 years, balance problems, previous falls, insulin-dependent diabetes, gait abnormalities, maternal history of hip fractures, trauma, PROM limitation, pain aggravated by movement, deformity, necessary neurovascular examination), clavicle (men between 15-30 years with high impact trauma from sport or accident or women >80 years after fall; deformity, ecchymosis, necessary neurovascular evaluation) [73]	1	-	-	-	-	Scapular girdle fracture
children (irritability, fever, tachycardia, pain at every movement of the limb) and adults (vague symptoms and swelling, age >80 years, diabetes mellitus, rheumatoid arthritis,	1	-	-	-	-	Upper extremity septic arthritis

recent surgery, immunodepression, intravenous drug abuse, skin infections, prosthesis, pain exacerbated by movement, visible wounds) [73]						
continuous, deep, sharp, shooting pain of the left leg. symptoms worsened during prolonged driving and long distance running, previous diagnose of lumbar radicular irradiation in the leg. Physiotherapical management without any improvement, nodular formation in the soft tissue [54]	1	-	-	-	-	Superficial peroneal nerve schwannoma
OAR [110]	1	0,97	0,29	-	-	Ankle fractures
BAR [110]	1	0,69	0,45	-	-	Ankle fractures
OAR+ BAR+ Tuning Fork test [110]	1	1,00	0,91	-	-	Ankle fractures

Table 6 – Red Flags of serious pathologies

LIST OF 141 SINGLE RED FLAGS APPEARED ON INDIVIDUAL STUDIES
Age>54 years (17)
Age <52 years (17)
Age >64 years (17)
Age >60 years (47)
Age >65 years (47)
Age >74 years (17)
Age ≥75 years (17)
Women >54 years (17)
Women >64 years (17)
Women >74 years (17)
Age <45 years (47)
ERS ≥20mm/h (45)
ERS ≥50mm/h (45)
ERS ≥100mm/h (45)
Anomaly in serous protein electrophoresis (47)
Pain for at least 3 months (47)

Familial LBP (21)
Bites/stitches (47)
Worsening deep pain (35)
Multiple sites pain (14)
Absence of buttocks/legs pain (17)
Decreased mobility (18)
Pathological changes in the gastrointestinal system (57)
Spinal tenderness (47)
Permanent urinary catheter (47)
BMI <23 (17)
Absence of gait abnormalities (17)
Osteoartrosis (17)
First motoneuron disease, multiple sclerosis, diabetes, alcoholism, cervical myelopathy, peripheral neuropathy, lower extremity edema for cardiovascular diseases, spinal stenosiss, nerve root compression (18)
Not regular exercise (17)
Low body weight (14)
Increased kyphosis (14)
Subtract age from weight (kg), multiply by 0.2 and put under integral; score ≤-1 to confirm risk (64)
Back pain ≥7 (12)
First episode of LBP in life <20 or >50 years (6)
Age >50years+ first episode of severe LBP and history of carcinoma in the last 15 years+ unexplained weight loss+ failure of conservative therapy after 4 weeks (14)
Female gender+ age >70 years+ severe trauma+ prolonged corticosteroid use (47)
Pain and stiffness (47)
Severe central pain that improves when lying down (47)
Fracture with minor trauma (15)
Loss in height (15)
Caucasian race (59)

spinal rigidity in response to percussion (50)
Sudden scoliotic deviation (50)
Inability to lie supine on the couch (50)
Lumbar kyphois (6)
Sacral pain without trauma (6)
Edema /swelling of lower extremity (6)
Bilateral symptom (rash, nodules, pain) (31)
Irradiated buttock pain (47)
Caucasian race, family history of smoking, hypertension, coronary heart failure (47)
Male gender (47)
Absence of aggravating characteristics (47)
RCS instability (15)
Loss of manual dexterity (7)
Stiff neck (7)
Spurling test (7)
pain worsening with cough/sneeze/Valsava (47)
Cruciate SRL + (47)
Pain decreases from walking, standing, supine with bent legs (47)
Pain worsens from bending forward and sitting (47)
Hyperextension test (47)
Bell test (47)
loss of lordosis and/or scoliosis from sciatica (47)
Intolerable radicular pain despite medications (52)
Severe (<3 MRC, movement against gravity is possible) or progressive (that worsens in a few days) motor deficits (52)
Neurogenic claudicatio (47)
Improvement with lumbar flexion (47)
Broad-based walking (47)
Peripheral vascular deficiency (47)

Worsening with extension, standing, walking downhill (47)
Movement-related, intermittent and pulling lower extremity pain, rarely appears at rest, subjective loss of strength in the same area, tingling, cold feeling, hypercholesterolemia, absence of impairment at physical examination (20)
Family history of arthritis or osteoporosis (47)
Younger age (16)
Hypersensitivity to NSAIDs (47)
Reduced thoracic expansion (47)
Reduced lumbar lateral flexion (47)
Peripheral joint involvement (47)
Skin rashes (47)
Uveitis/synovitis/psoriasis (47)
Pain in the thoracolumbar junction (50)
Abscess in the groin, trochanteric or gluteal zone (50)
History of previous tuberculosis (50)
Posterior spine dysfunction, low hairline, short and webbed neck (34)
Symptoms of vertebro basilar insufficiency (15)
Alterated sensation of tongue and mouth (15)
passive cervical spine tests with provocation of symptoms in end range (2)
Dental injury (2)
worsening symptoms with head flexion (headache, fatigue, upper extremity paresthesias) (2)
ligament instability test + (e.g. Sharp-Purser) (2)
Limp or refusal to walk and bone pain, lasts for >14 days, is localized, is associated with swelling or deformity, and does not improve with NSAIDs (64)
onset of headache after 50 years, focal pain on the temporal artery (16)
onset >50 years, progressive in severity and frequency, focal neurological signs, papillary edema, "thunderclap" headache (16)
sudden onset of "thunderclap" headache (16)
progressive in severity and frequency, headache resulting from trauma (16)
signs of systemic diseases such as fever, cervical stiffness, photophobia, general

malaise, papilledema (16)
focal neurological signs such as progressive visual disturbances, weakness, loss of balance, clumsiness (16)
pregnancy or immediately after postpartum (16)
Headache with characteristics of migraine/fronto-temporal but unlike previous episodes, stress in cervical rotation/cervical trauma, hypertension, 3N: nystagmus, numbness, nausea, ataxia, , short-term memory loss, weakness of the lower and upper extremities, ipsilateral carotid bruit, orbital pain, scalp tension, neck swelling, amaurosi fugax, TIA/stroke, retinal infarction, functional positional VBI tests (rotation, extension), young patient with diabetes, previous stroke (33)
Gout Risk Criteria: male, previous arthritis attack, onset within one day, joint redness, first metatarsal involvement, hypertension or more of one cardiovascular disease, uric acid level in serum >5.88 mg/dl; score 0-13 (59)
acute intermittent monoarticular attack, predisposition for metacarpophalanxes (58)
age ≥50 years, bilateral pain, stiffness for more than one month, most involved joints are cervical, shoulders, pelvic girdle and hips, ERS ≥40mm/h, rapid response to prednisone ≤20 mg/day, body weight reduction; it's important the differential diagnosis with Systemic Lupus Erithematosus (thrombocytopenia, leukopenia, pleurisy or pericarditis), polymyositis (muscle weakness rather than pain, increased muscle enzymes), spondyloarthropathy (oligoarthritis, distal edema, minimal axial involvement, elevated ERS, dactylitis, distal enthesitis, uveitis, HLA-B27 association, Rx with signs of sacroiliitis), fibromyalgia (younger age of onset, variable and heterogeneous symptoms, irritable bowel syndrome, tender points, normal ERS), tumours (poor response to corticosteroid therapy, absence of movement pain or stiffness, fever, night pain, weight loss), calcium pyrophosphate deposition disease (tibiofemoral osteoarthritis, tendon calcifications, typical of elderly patients) (58)
PT treatment is not contraindicated, only if there are related disorders. Often associated with structural changes in the atlanto-occipital joint (chronic and severe occipital-cervical pain, ear, mastoid and facial pain, severe neurological deficits such as ataxia, paresis in the limbs, transient ischemic attacks, sleep apnea, ophthalmoplegia, spastic quadriparesis, diplegia, nystagmus) and Rest Leg Syndrome (sleep disorders, early fatigue, stress, fibromyalgia, pain); may mimic or hide paraneoplastic rheumatic syndrome (fever ≥40°, weight loss, unusual and chronic inflammatory arthritis, asymmetric distribution, high CPR, rare bone deformities, often negative ANA) (58)
Reynaud's phenomenon, cyanosis, telangiectasia, skin thickening, calcinous, sclerodactyly, visceral complications of the lungs, gastroenteric system (with esophageal dismobility), cardiovascular and renal system (58)
Flank pain, slow urine flow, history of previous kidney stones: increase of post-test probability up to 25% (with CT up to 90%) (59)
History of malignancy and surgery (6 points); Storia di tumor e di chirurgia (6 punti);

presence of at least 3 classic sign of inflammation without fever (weakness, relapsing pain and functional deterioration, 5 points); 11 points: probable osteomyelitis, to make it sure 18 points are needed, achievable with additional microbiological analysis and imaging (56)
chronic use of internal catheter, history of bedsores, recent surgery, infection of the surgical wound, lethargy, anorexia, vomiting, edema and localized erythema, no neurological signs, abdominal tension, pain worsened by abduction of the hip and symphysis palpation (56)
Stiffness and dull lumbar pain with insidious and progressive onset, deep anterior thigh pain with heavy feeling, symptoms get worse at work, with walking, prolonged sitting position, lumbar movements and squat while improve with rest or by night, negative neurological examination, limited and painful hip AROM and PROM (internal rotation, flexion+abduction, passive flexion with limited and painful rotation), no change of lower extremity symptoms after failure of FT lumbar treatment, response of symptoms to loading movements, tuning fork +, single hop test +, percussion test + (60)
Faddir test + (60)
Scour test + (60)
Patellar pubic percussion test + (60)
poor weight-bearing tolerance, antalgic gait with abduction and extrarotation of the hip, warmth (35)
diabetes, history of chemotherapy, pain in the hip and anteromedial part of the thigh, progressive worsening weight-bearing status (35)
older age, diabetes, hypertension, hip and anteromedial part of the thigh pain (35)
poor weight-bearing tolerance, antalgic gait with abduction and extrarotation of the hip, painful and limited hip ROM, pain on palpation of the hip, also palpable warmth for the fracture (35)
previous DVT, recent surgery, progressive weakness/femoral nerve palsy or paresis, loss of sensation; score of +1, moderate risk of DVT, at the Wells Prediction Rule (Appendix VI) (35)
Skin thinning, painful peripheral neuropathy (15)
Frequent bacterial infections, splenomegaly (15)
'Red eye', eye pain, photophobia, decreased visual acuity, dry/itchy eye (15)
Dry eyes and mouth. Skin, nose and vaginal dryness also present (15)
Acute sensory and/or motor neuropathy, occurring as a result of vasculitis, compression, or diabetes (15)

Signs of ischaemia or necrosis in affected organs/tissues (15)
Petechiae/purpura (red or purple skin lesions which do not blanch on pressure). Leg ulcers and peripheral gangrene (15)
Single or multiple subcutaneous nodules, >5 mm diameter. Usually painless and on extensor surfaces (15)
Swollen and painful tendon, crepitus on movement; warmth; evidence of swelling
Pain on resisted movement/load. loss of function; deformity, loss of tendon function, joint instability and tendon discontinuity. Discordance between active and passive joint movement (15)
Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist, combination of flexion of proximal IP joint and hyperextension of distal IP joint (15)
Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist, combination of flexion at MCP joint, hyperextension of the proximal IP joint and flexion of the distal (15)
paleness, sweating, dyspnea, nausea, sensation of indigestion, shortness of breath, weakness, numbness, fainting, sudden darkness or loss of sight and speech; Fever, chills, weakness, coughing, increased pain with the patient positionated on his left side or supine, by movements associated with deep breathing (laughing, coughing, deep inhalation), by movements of the trunk (lateroflexion and inclination), relieved with bending forward, sitting position or by holding the breath; **A. stable/chronic:** oppression that occurs after exertion or emotional stress. Position, duration, intensity and frequency of thoracic pain are consistent over time. Symptoms improve with nitroglycerin and rest. **A. pectoris unstable:** sudden change in frequency intensity, duration, high risk of IMA. Does not respond to nitroglycerin and rest. **A. from rest:** pain that occurs at rest and in supine position, often at the same time every day. Pain is not caused by exercise or relieved by rest. **A. of Prinzmetal:** symptoms are similar to those of the atypical but given by the spasm of the arteries which are usually free of plates or modifications. Occurs at rest, especially early in the morning, difficult to reproduce with exercise; severe thoracic and/or back pain, retrosternal pain (pain may extend to the left arm, jawbone, teeth); acute thoracic pain that may be referred laterally to the neck, shoulders retrosternally, upper back, upper part of the trapezoid muscle, left supraclavicular area; thoracic and/or back pain (57)
pleuritic pain, fever, chills, headache, malaise, nausea, catarrhal cough; pain that increases during inhalation, difficulty in ventilating or expanding the thoracic cage, hyperresonance to percussion, decreased respiratory sounds, recent cough attacks, intense exercise or trauma¸ pain sometimes even in the abdomen, history or risk factors of DVT, dyspnoea; pain may be felt in the shoulder; thoracic pain; thoracic and shoulder pain (57)
dyspnoea-related activity, coughing, pain worsening with inhalation, smoker, chronic obstructive pulmonary disease (COPD), dysphagia, change in respiratory pattern,

wheezing, hoarseness, hemoptysis (61)
Sneezing (15)
acute and severe pain ("knifelike pain"), dyspnoea, decreased thoracic range, pleuritic pain, recent history of recurrent respiratory disorders such as infections, pneumonia, tumours, tuberculosis; thoracic and interscapular pain (57)
family history of heart problems (31)
Shoulder pain with exacerbation in recumbency, with effort and not related to shoulder movement, diaphoresis (31)
Shoulder pain with cough, reproduction of the symptom with breathing (31)
diabetes, hyperthyroidism, ischaemic heart disease, infections and lung diseases (31)
pain on swallowing, feeling that food is struggling to go down, vomiting, nausea, stomach pains, sputum regurgitation and decreased appetite; retrosternal thoracic pain (57)
pain in the upper quadrant accompanied by nausea, vomiting, fever, jaundice and urine are often very dark; TL pain with radiation to the right upper extremity (57)
children (irritability, fever, tachycardia, pain at every movement of the limb) and adults (vague symptoms and swelling, age >80 years, diabetes mellitus, rheumatoid arthritis, recent surgery, immunodepression, intravenous drug abuse, skin infections, prosthesis, pain exacerbated by movement, visible wounds) (73)
proximal humerus (age >40 years, especially women >60 years, balance problems, previous falls, insulin-dependent diabetes, gait abnormalities, maternal history of hip fractures, trauma, PROM limitation, pain aggravated by movement, deformity, necessary neurovascular examination), clavicle (men between 15-30 years with high impact trauma from sport or accident or women >80 years after fall; deformity, ecchymosis, necessary neurovascular evaluation) (73)
rotator cuff, pectoralis, biceps (acute and traumatic episode, muscle weakness) (73)
age <40 years, acute episode, traumatic event, PROM limitation, previous acute episode or instability, deformity, risk of related fracture if it's the first episode, age >40 and contusive trauma (the absence of these 3 factors has a Sn of 97%), for acromioclavicular dislocation further signs are contact sports, men and upper shoulder pain, for sternal-clavicular collision with vehicles, contact sports, shoulder or anterior chest pain, paresthesias, dysphagia, breath's shortness (73)
OAR (110)
BAR (110)
OAR+ BAR+ Tuning Fork test (110)

Table 7 – List Of 141 Single Red Flags Appeared On Individual Studies

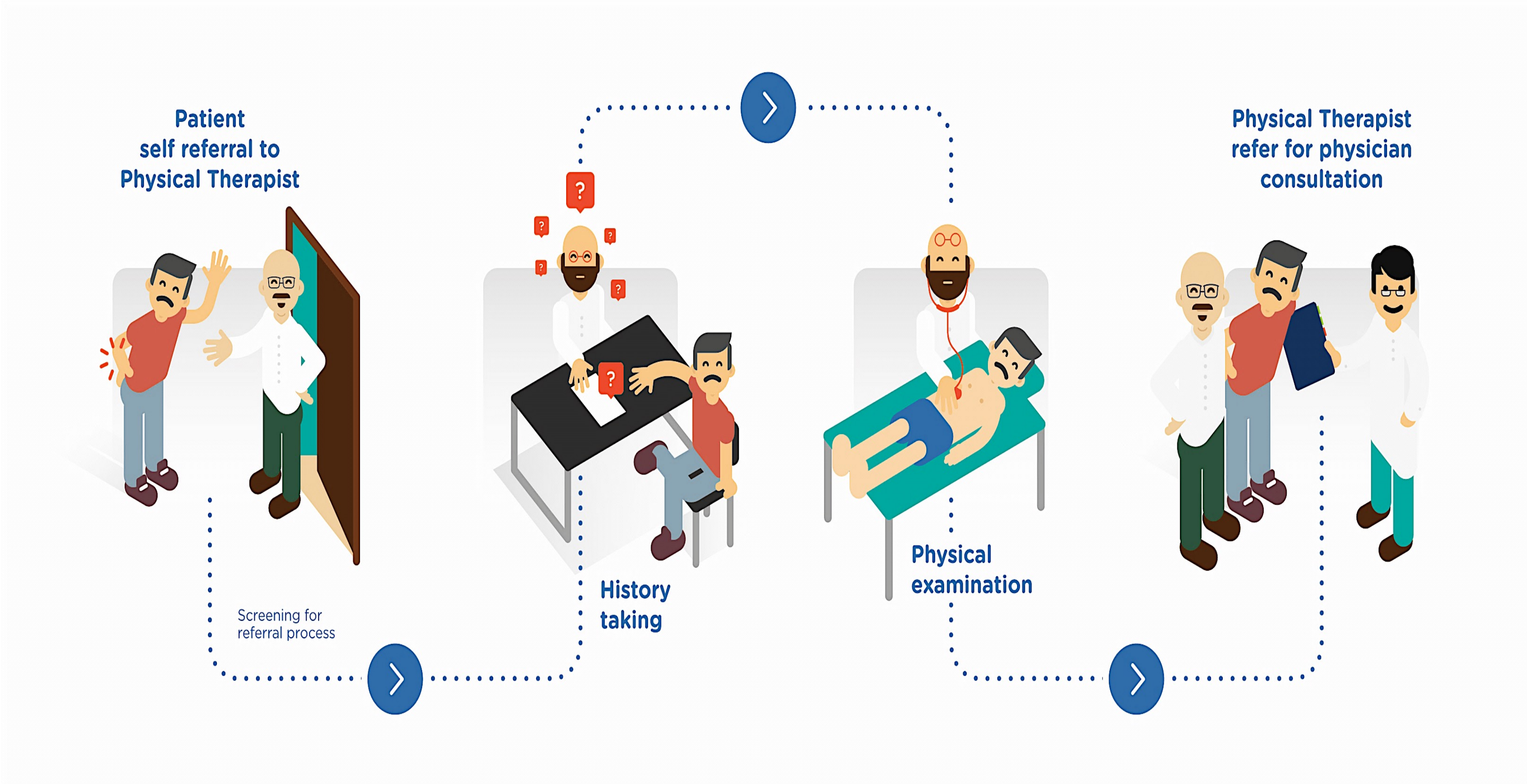

Figure 1: Screening for Referral Process

Figure 2: Physical Therapy Clinical Reasoning

THE DIAGNOSTIC VALUE OF RED FLAGS IN THORACOLUMBAR PAIN: A SYSTEMATIC REVIEW

Submitted as:

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The diagnostic value of Red Flags in thoracolumbar pain: a systematic review

Abstract

Objective: Red Flags (RFs) are considered specific signs and symptoms useful for the screening of serious pathologies mimicking a musculoskeletal pain. Current literature is questioning the RFs use due to low diagnostic accuracy and several rates of false-positive. The aims of the systematic review are: (a) to identify; and (b) to evaluate the most important RFs that could be found by a health care professional during the assessment of patients with low and upper back pain to screen serious pathologies.

Data Sources: Pubmed, Web of Science, Cochrane Library, Pedro, Scielo, CINAHL, and Google Scholar. were searched between September 2018 to March 2019 using a combination of search terms with synonyms of low back pain, chest pain, differential diagnosis, red flag, serious disease.

Review Methods: A systematic review of the literature was conducted. Searches were performed on 7 databases. Risk of bias was assessed with the Newcastle Ottawa Scale and interrater agreement between authors for full-texts selection was evaluated with Cohen's Kappa. Where possible the diagnostic accuracy was recorded for Sensitivity (Sn), Specificity (Sp) and positive/negative Likelihood Ratio (LR+/LR-).

Results: 36 observational studies were included. In Low Back Pain (LBP), 6 studies stated malignancy and vertebral fracture described as serious medical condition. In Chest Pain (CP), significant pathologies were less analysed. Overall, the included studies were judged as low risk of bias. The main RFs identified were: advanced age; neurological signs; history of trauma;

malignancy; female gender; corticosteroids use; night pain; unintentional weight loss; bladder or bowel dysfunction; loss of anal sphinter tone; saddle anesthesia; constant pain; recent infection; family or personal history of heart or pulmonary diseases; dyspnea; fever; postprandial CP; typical reflux symptoms; hemoptysis; sweating; pain radiated to upper limbs; hypotension; exertional pain; diaphoresis; and tachycardia. Despite the diagnostic accuracy of RFs was low on a stand-alone basis, the combination of multiple RFs increase the probability to identify a serious pathology.

Conclusion: The use of single RF is not recommended for clinical practice. The RFs should be used in combination to increase their diagnostic accuracy, becoming an excellent screening tool for Thoracolumbar pain.

1. Introduction

1.1. Rationale

Low back pain (LBP) is a common condition throughout the world experienced by 50–80% of adults during life. In 90% of cases, LBP is defined as non-specific because the musculoskeletal causes are not clearly identifiable [1,2]. In contrast, between 1 and 4% of cases, LBP is considered to present a specific etiology, including fractures, malignancy, infections or cauda equina syndrome (CES) [3]. Upper back pain (UBP) is defined as pain the area of the spine above the base of the rib cage and below the neck [4], particularly, in the region of the thoracic spine, between the boundaries of T1–T12 and across the posterior aspect of the trunk[5]. Given that the 12-month prevalence for UBP ranges from15–34.8% in the adult population, it is a common presentation in primary clinical practice[5]. Chest pain (CP) represents the second cause of access to the Emergency Department (ED) with a prevalence of 25% [6]. Although only in 20% of cases CP has a non-musculoskeletal cause, this condition continues to be a challenge for professionals; in fact, 50-80% of patients are discharged from ED without clear diagnosis [6]. The most significant serious pathologies mimicking CP are pulmonary, cardiovascular or gastrointestinal disorders and it would be estimated that less than 35% of subjects with CP need a healthcare intervention such as physiotherapy and rehabilitation [7]. Considered together, LBP , UBP and CP represent the painful areas between the front trunk and the back (from chest to the back between T1 vertebra and the inferior gluteal fold) [8]. In the context of this systematic review, we refer to Thoracolumbar pain (TLP) as pain experienced in the region of lumbar and sacral spine, including L1-S4 segments to the lower back down to the inferior gluteal fold, and thoracic spine between

T1-T12 and across the posterior aspect of the trunk. Furthermore we included the area of the chest wall, from breastbone to the costal region on the anterior aspect of the trunk. According to the definition, RFs consist of signs and symptoms indicating the presence of a serious pathology justifying the screening process for patient referral [9] to a medical specialistic evaluation. In clinical practice, TLP is challenging and RFs may be not present at the healthcare provider's consultation (i.e. doctors, nurses, physiotherapists, chiropractors, etc). Four clinical guidelines suggest a careful history taking and physical examination as the optimal approach aimed at the recognition of red flags (RFs) [9–12]. For a long time, RFs have been a reference point in the healthcare providers' clinical practice aimed to reduce the risk of a contraindicated intervention and identify as soon as possible an appropriate treatment for the patient [9]. Over the last years, 6 systematic and narrative reviews concerning spinal pain were published proving that RFs have low diagnostic accuracy and several rates of false-positive, especially when used alone [11,13–17].

In current literature there are no published systematic reviews regarding RFs for TLP. Otherwise, specifically for LBP, six systematic reviews examinating vertebral fracture and/or malignancy have already been published [10,11,15,18–20], but never associated to CP or other serious pathologies and the included studies are mostly dated. Namely the main RFs identified with the highest post-test probability to detect vertebral fracture are: older age; use of corticosteroids; major trauma; distracting painful injury; tenderness; female gender; and presence of contusion or abrasion [3,11,15,18,20]. Concerning malignancy, the most important RF is the previous history of cancer. Up to now, there are only narrative reviews regarding CP and the main RFs are: previous history of cardiovascular disorders; dyspnea; pain radiating to upper limbs; and caugh [21–23].

Regarding the methodological quality of the current systematic and narrative reviews on TLP, only 4 systematic reviews [11,15,18,20] explicitly stated that the methods were established prior to the commencement of the review and only 3 [10,15,18] used a comprehensive literature search strategy. Only Downie and Williams et al. [15,18] thoroughly explained the selection of study designs for inclusion in the review, analysed the included studies in detail and provided a list of excluded studies with reasons for the exclusion. In a low number of reviews, the data extraction process was performed by at least two authors and the majority of the studies did not use an adeguate tool for quality assessment of the included primary studies. Verhagen et al. [3] in 2016 compared RFs included in the main international guidelines, observing that only 3 out of the 16 guidelines have any evidence to support RF screening. However, the main international guidelines still recommend their use [3,19,20]. Most guidelines do not endorse the same set of RFs and most recommendations are not supported by research and accompanied by diagnostic accuracy data [3]. Especially concerning CP, the methodological quality is generally low and with statements based upon expert opinion whose references to primary research are not provided [24].

According to recent literature [3,18–20,25], there is a strong need to investigate which are the main RFs for TLP and their clinical utility in daily practice to help the screening process of serious pathologies by healthcare providers.

1.2. Objectives of the Study

The aims of this systematic review was: (a) to identify; and (b) to evaluate the most important RFs to take into account during the assessment of patients with TLP by healthcare professionals in clinical practice.

2. Materials and Methods

2.1. Protocol

This systematic review was conducted in line with the PRISMA Statement for reporting in systematic reviews [26]. The panel of the authors of this systematic review: (a) has extensive experience in performing systematic reviews; and (b) presented specific clinical expertise and training in the screening of patients with TLP. Overall, Cohen's Kappa (K) was used to quantify the inter-rater agreement between the two authors (FM, MP) for full-text selection. Cohens' K was interpreted according to Altman's definition [27]: k<2 poor, 0.2<k<0.4 fair, 0.41<k<0.60 moderate, 0.61<k<0.80 good, 0.81<k<1.00 excellent [28]. A confidence interval of 95% was calculated (CI 95%). Disagreements were solved by a third reviewer (MT) not involved in the data extraction process.

2.2. Search Strategy

An electronic search was performed independently by two reviewers (FM and MP) under the supervision of a third author (MT) between September 2018 to March 2019 on Pubmed, Web of Science, Cochrane Library, Pedro, Scielo, CINAHL, and Google Scholar. The search strings were developed according to the PI(C)O model of clinical question (participants, interventions and outcomes) [26]. To make the search strategies sensitive, we did not insert key words for comparisons. The PICO model is explained in table 1. The full search strategy for all databases is available in the supplementary materials (Supplementary

Files 1). Where possible MeSH (Medical Subject Headings) terms were used and combined with Boolean operators (AND, OR, NOT). Additionally, we conducted a manual search of all bibliographies of the studies assessed for the subsequent full-text selection. In addition, grey literature was screened (i.e. thesis, conference reports, expert opinions, books) via web.

Population	Patients with chest and/or thoracic and lumbar pain
Intervention	Differential diagnosis of a health care professional through RFs identification
Comparison	None
Outcome	Detection of non-musculoskeletal pathologies by health care professional

Table 1. Systematic review's PICO

2.3. Eligibility Criteria

To be eligible, full-texts had to be observational studies published in English or Italian language. Publication date was restricted from 01/01/1999 to nowadays. No age of participants restrictions was applied.

2.4. Study Selection

All titles and abstracts were screened independently by two reviewers (FM and MP) under the supervision of a third author (MT). All the studies investigating the identification and/or the evaluation of RFs or specific sign and symptoms of serious pathologies in TLP patients were included. Where appropriate authors were contacted in order to obtain the full-text paper. Finally, full-texts were independently screened and assessed for eligibility by two reviewers (FM, MP).

2.5. Inter-rater agreement

Cohen's Kappa (K) was used to quantify the inter-rater agreement between two authors (FM, MP) for full-text selection, between three authors (FM,MP,GR) for the data extraction and between four authors (FM, MP, VB, LS) for the quality assessment. Cohens' K was interpreted according to Altman's definition [27]: k<2 poor, 0.2<k<0.4 fair, 0.41<k<0.60 moderate, 0.61<k<0.80 good, 0.81<k<1.00 excellent.

2.6. Data Extraction

Three authors (FM, MP, GR) individually extracted data using a data extraction form developed in line with the PI(C)OS model of the clinical question and adapted from the Cochrane Collaboration guidelines (Cochrane Handbook 5-1) [26,29,30]. Data extraction was organized as follows: (a) authors; (b) publication year; (c) study design; (d) study population ; (e) study objectives ; (f) RFs identified; and (g) diagnostic accuracy levels for each RF. All RFs for serious pathologies were identified and where possible diagnostic accuracy was analised: positive likelihood ratio (LR+); negative likelihood ratio (LR-); sensibility (Sn); and specificity (Sp). The LRs use the sensitivity and specificity of the test to determine whether a test result usefully changes the probability that a condition (such as a disease state) exists. Reference values for LR are reported in table 2 [31]. The results were screened using the Ryyan software for the mangement of systematic reviews [32]. Bibliography was handled using the Mendeley software [33].

LR+	LR-	Report interpretation
> 10	< 0.1	Great variation
5 - 10	0.1 – 0.2	Moderate variation
2 - 5	0.2 – 0.5	Small variation
1 - 2	0.5 - 1	Very small variation

Table 2. LR data interpretation (LR+: Likelihood ratio positive; LR-: Likelihood ratio negative).

2.7. Quality Assessment

Four authors (FM, MP, VB, LS) performed the quality assessment of the included studies using the Newcastle-Ottawa Quality Assessment for observational studies [34], in accordance with the recommendations reported in the Cochrane Collaboration guidelines (Cochrane Handbook 5-1) [30].

3. Results

3.1. Study Selection

The electronic database searches delivered 1563 results. Grey literature provided additional 18 studies. After removal 306 duplicates, we excluded 1230 records because they did not meet the inclusion criteria, leaving 45 studies eligible for full-text assessment. 9 out of 45 records were excluded after full-text reading, reasons for te exclusions are reported in the Supplementary files 2. In total, 36 observational studies were included [24,25,35–67]. The full search process is reported in figure 1. The agreement between the authors was good (Cohen's K: 0.790; 95% CI: 0.686 to 0.893) for the screening process. (see **Figure 1** – Flowchart, inserted at the end of the chapter)

3.2. Study Characteristics

Thirthy-six primary studies were included in this systematic review[24,25,35–67]. Details of each paper are given in table 3. Total patients recruited were 43450 between 16 to 91 years of age, with a F/M equal ratio. Eighteen studies concerned patients with LBP [25,35,37–39,46,50,54,55,57,58,63–66,68–70] and 16 were focused on CP [24,40–44,46–52,57,60,61], all patients were screened by a physician in a clinical setting or at the emergency department, through a physical assessment [36,46,57,60,62] or by a questionnaire [24,25,53,55,68]. (see **Table 3.** Characteristics of the included papers, inserted at the end of the chapter)

3.3. Risk of bias

Most of the studies were judged as low risk of bias. The main methodological limitations concerned non-representative cohort of patients, uncomplete reporting of follow-up data, lack of statistics about lost to follow-up patients, set of RFs for identical pathologies were differently analysed, differences in reference standards for RFs among studies. Only 3 studies [25,57,58] were judged as high methodological quality. Agreement between authors was good (Cohen's k: 0.777; 95% CI: 0.571 to 0.983). Methodological quality assessment is reported in table 4 (inserted at the end of the chapter).

3.4. Synthesis of results

The extraction process shows a substantial agreement between authors . Serious pathologies identified through the RFs screening as a cause of TLP were: vertebral fracture [25,45,55–58,62–64,67,68,70]; malignancy [25,46,50,58,63–65,68]; infection [25,35,57,58,66,69,70]; CES [25,37–39,54,55,57,58]; cardiovascular disorders [24,40,41,43,44,49,60]; pulmonary disorders [42,46–48,61];

gastroesophageal disorders [50–52]; and inflammatory disorders [57]. For each of these, we listed RFs and relative diagnostic accuracy data in table form (tables 5,6,7,8). Frequency of RFs among studies are reported in figure 2 (inserted at the end of the chapter).

3.4.1. Vertebral fracture

Vertebral fracture represents the most frequently encountered serious pathology in LBP patients with a prevalence between 0.4% and 5.6 [25,57]. The most useful RFs to identify a vertebral fracture were: advanced age; history of trauma; midline tenderness; female gender; neurological signs; pain Numeric Rating Scale >7; prolonged use of corticosteroids; osteopororis; osteoarthritis; and distracting painful injury [25,45,55–58,62–64,67,68,70]. In the physical examination is it important to pay attention to: gait abnormalities; palpable midline step; bruising; positive percussion test; decrease in height and neurological signs [45,56,62].

Seven out of eleven studies (65%) identified history of trauma, advanced age, prolonged corticosteroids use and female gender as key RFs for vertebral fractures [25,55,57]. Henschke et al. [57] investigated the combination of these 4 features obtaining promising results with a post-test probability to detect fracture increased up to 52%: 1 positive RF (Sn: 88% / Sp: 50% / LR +: 1.8); 2 positive RFs (Sn: 63% / Sp: 96% / LR +: 15.5); 3 or more positive RFs (Sn: 38% / Sp: 100% / LR +: 218.3). Enthoven et al. [55] identified a diagnostic prediction model combining multiple RFs: 1 positive RF (Sn 0.88; Sp 0.42; LR+ 1.5; LR- 0.3); 2 positive RFs (Sn 0.70; Sp 0.81; LR+ 3.6; LR- 0.4); ≥3 positive RFs (Sn 0.30 ; Sp 0.95; LR+ 5.8; LR- 1.0). Even Roman et al. [45] combined 3 RFs, improving diagnostic accuracy data (Sn 76%; Sp 68%; LR+ 2.5; LR- 0.34). According to

Premkumar et al. [25] increasing diagnostic accuracy was achieved associating a history of recent trauma to age > 50 years (LR + 2.54) or > 70 years (LR + 4.35), respectively, by 13.1% and 20.5%. Finally, greater diagnostic accuracy can was observed when multiple RFs are combined, but only 5 primary studies supported these data [25,45,55,57,58]. The overall diagnostic accuracy data are reported in table 5 (inserted at the end of the chapter).

3.4.2. Malignancy

The prevalence of malignancy in LBP ranged from 0.1% to 1.6% and the spine was the most common site for bony metastases, affecting up to 30% to 70% of patients with cancer [57,65]. Early detection was the most important screening aimed to prevent the spread of any metastatic disease and development of further complications such as spinal cord compression [25,54,62].

The most reliable RFs to identify a malignancy were: previous history of cancer; older age; unexplained weight loss; absence of improvements in conservative treatments; positive clinical judgment; night pain and steady back pain unrelieved by rest. The previous history of cancer was the RF with highest diagnostic accuracy (LR+ 7.25) and carries a 10.6% probability of having a vertebral malignancy [25]. During the physical examination, absence of pain during any lumbar movements raises the probability to rule-out malignancy (Sn 100%; LR- 0.01) [65]. Data of diagnostic accuracy are reported in 5 primary studies [25,58,63–65], and the results are presented in table 6. According to Henschke et al. [57], the RFs with the highest number of false positives (>10%) were: unrestful sleep; insidious onset; and age <20 years or >55 years. Two studies identified night pain as a false-positive in almost 85% of subjects with malignancy, when no other RF symptoms are present [25,53]. Premkumar et al.

[25] evaluated the combination of multiple RFs which increased the probability of a serious pathology up to 14.3%. (LR+ 10.25), in case of personal history of malignancy and unexplained weight loss. Four predictors (anticoagulant use; decreased sensibility on physical examination; worsening of pain at night; and persistent pain despite appropriate treatment) identified serious pathology (91% sensitivity; 55% specificity) [70]. (see Table 6. Malignancy and diagnostic accuracy, inserted at the end of the chapter).

3.4.3. Infection

Tuberculosis (TB) and Staphylococcus Aureus represented the main source of spinal infection reported among the included studies. Early diagnosis is essential as the infection could hesitate to an extradural spinal abscess (ESA) with neurological signs and symptoms [35]. Spinal infection occurs between 0.3% and 1.2% [25,57] and thoracolumbar joint is the most common vertebral sites affected (62-65%) [9,69]. The main RFs valuable to detect an infection were: fever; sweating; chills; recent infection; night pain; unexplenable weight loss; neurological signs; and constant pain not relieve by rest. Five out of seven studies (70%) reported the presence of fever as the most important RF, showing a good Sp (97-99%) [15,25]. Diagnostic accuracy was evaluated in 3 papers [25,58,63] and data are presented in table 7 (inserted at the end of the chapter). According to Premkumar et al. [25]: a recent history of infection determines a 10.2% probability of having a spinal infection (LR+ 9.31); the presence of weight loss would increase the probability of 3%; and the history of fever, chills or sweating, if present alone, would lead to an increase of 2%. The same authors [25] assessed that combination of fever, chills and sweating, associated with a recent infection, increases the probability to detect spinal infection (LR + 13.15 /

LR - 0.93), with post-test probability of 13.8%. Night-awaking caused by pain is a false-positive in more than 96% of cases, when no other RFs are present [25]. Henschke et al. [57] highlighted that many RFs have a false- positive prevalence up to 10% such as: systemically unwell; constant pain; neurological signs; and recent infection.

3.4.4. Cauda Equina Syndrome

CES, along with fractures, malignancy and infections, is considered the most frequent serious pathology of TLP, with a prevalence lower than 1% [25,57]. The most helpful RFs to recognize CES were: bladder or bowel dysfunction; neurological signs; saddle anaesthesia and loss of anal sphincter tone. The associated presence of bladder or bowel dysfunction was underpinned by 100% of the studies increasing the probability of CES by 1.2% (Sn 8.3%; Sp 97.2%; LR+ 3.0; LR- 0.94) [25]. Raison et al. [54] reported as main RFs saddle anesthesia and bladder/bowel dysfunction. Also they observed that combination of 3 RFs determines an improvement of the diagnostic accuracy (LR + 3.46 / Sn: 0.27 / Sp: 0.92). Tsiang et al. [58] analysed dysregulation of bladder or bowel, identifying a Sn of 50% and a Sp of 86.5%. The diagnostic accuracy is reported in 4 papers [25,54,58,63] and presented in table 8 (inserted at the end of the chapter).

3.4.5. Cardiovascular Disorders

Patients with CP can reach more than 5% of ED visits and early identification is essential to avoid life-threatening disorders such as acute coronary syndrome and acute myocardial ischemia [41]. The main RFs useful to identify cardiovascular disorders were: exertional pain; personal or family history of cardiac diseases; diaphoresis; dyspnea; sweating; hypotension; pain radiating to upper limbs; neck or back; and CP described as squeezing, burning, oppressive, crashing or retrosternal. The main RF is the radiated pain to upper limbs which were included by 100% of the studies, showing high potential to detect a serious heart disorder. Only 3 papers [24,40,44] included diagnostic accuracy data, and the latter are reported in table 9. Schillinger et al. [40] evaluated the combination of multiple RFs on increasing the probability to identify cardiovascular disorders, but their diagnostic accuracy data were weak (LR+ 1.15 to 1.85; LR- 1.05-3.0). (see Table 9 inserted at the end of the chapter).

3.4.6. Pulmonary Disorders

Pulmonary disorders had a prevalence of 10% of CP representing the most frequent and potentially life-threatening diseases. Notably, pulmonary embolism (PE) and deep venous thrombosis remain a diagnostic challenge due to low sensitivity and specificity of their signs and symptoms [48]. The main RFs able to recognize pulmonary disorders were: history of pulmonary pathologies; recent surgery or immobilization; active cancer; female gender; hemoptysis; cough; syncope; dyspnea; tachycardia; leg swelling; oxygen saturation less than 95%; palpitations; fever; tachypnoea; cyanosis; abnormal lower limb examination; shortness of breath; age >40; pleural rub; hypoxemia; and pleuritic or substernal CP. Patients reported CP (72%) and dyspnea (70%) as the most common presenting symptoms [46]. Only Wells et al. [47] evaluated the diagnostic accuracy data, elaborating a scoring system to detect PE: the combination of multiple RFs show a LR+ value between 0.13 and 6.75.

3.4.7. Gastroesophageal Disorders

Non-cardiac chest pain is defined as a recurrent retrosternal angina-like pain in patients with normal cardiac evaluations with a prevalence between 25% to

35% [51]. Gastroesophageal disorders are the most common causes of NCCP, followed by chest wall syndromes and psychosomatic disorders [52]. It is a benign condition without an impact on mortality, though it decreases quality of life . Therefore, screening for the referral process may be required [50]. The most common pathologies are Gastroesophageal reflux diseases, peptic ulcers diseases and gastritis [51]. The main RFs suitable to identify gastroesophageal disorders were: typical reflux symptoms; postprandial CP; use of anti-reflux drugs for pain relief; obesity; smoking; diabetes; heartburn; and acid regurgitation. None study evaluated the diagnostic accuracy data or the combination of multiple RFs.

3.4.8. Inflammatory Disorders

Only Henschke et al. [57] analysed inflammatory disorders as a cause of CP, which has a prevalence of 0.2% (0.1-0.6). The RFs identified by the authors were: gradual onset before age 40 years; tired sleep without relief; insidious onset; systemically unwell; constant, progressive, nonmechanical pain; morning back stiffness lasting > 0.5 hours; peripheral joint involvement; persisting limitation of spinal movements in all directions; iritis; skin rashes (psoriasis); colitis; urethral discharge; family history of arthritis or osteoporosis; pain improvement with exercise; and clinically diagnosed inflammatory disorders.

No diagnostic accuracy data were provided and many RFs have a false-positive prevalence higher than 10% ,such as: no relief with bed rest; insidious onset; morning back stiffness lasting > 0.5 hours; family history of arthritis or osteoporosis; and pain improvement with exercise. Diagnostic accuracy data or a combination of multiple RF are not provided.

4. Discussion

4.1. Summary of evidence

To best of the authors' knowledge, this is the first systematic review concerning signs and symptoms suggestive of RF aimed at guiding healthcare providers during the evaluation of patients with TLP . It represents a novelty in the field, due to the absence of other systematic reviews regarding CP or LBP connected to other serious pathologies excluding fracture and malignancy [10,11,15,18–20]. The 36 included primary studies [24,25,35–67] have analysed 8 serious pathologies as a cause of TLP such as: vertebral fracture; malignancy; infection; CES; cardiovascular; pulmonary; gastroesophageal; and inflammatory disorders. Many RFs have been identified, but only the 45% (n: 16/36) of the included studies evaluated the diagnostic accuracy of the RFs, therefore we could analysed the clinical utility of less than 50% of the identified signs and symptoms. However, the majority of patients without serious pathology presented more than one positive RFs, showing a very high false-positive rates [57]. Features of good screening tools include high LR- and Sn, but according to Premkumar et al [25] almost no RF has a Sn greater than 75% and most of them have values below 60% [25]. Combining multiple RFs is recommended to increase the diagnostic accuracy levels, and to help healthcare providers to screen specific pathologies [25,52,54]; however, it was evaluated only in the 30% (n: 11/36) of the included studies and some studies have investigated different set of RFs for the same pathologies. Our systematic review provides the first list of RFs useful for the screening of patients with TLP presenting with non-musculoskeletal signs and symptoms related to cardiovascular, pulmonary or gastroesophageal disorders. The patient's assessment in case of these disorders remains challenging for healthcare providers, due to the high risk of misdiagnosis [40]. Indeed, nowadays there is a low number of primary studies on the topic and sparse evidence on the screening process since only 4 papers has been published [24,40,44,47] evaluating the diagnostic accuracy data.

Cardiovascular disorders are the most frequent life-threatening pathologies and 8 RFs have been identified showing a low diagnostic accuracy [24,40,44]: pain radiating to upper limbs and exertional pain are the main and show a good probability to rule-in a serious heart disorder, but the Sn is never greater than 55.6% and usually have values below 30% [24,44]. Only one study evaluate the combination of multiple RF and show no increasing in the diagnostic accuracy [40]. Regarding pulmonary disorders many RFs have been identified, but only a scoring system created to detect PE shows a moderate probability to identify the pathology while no other diagnostic accuracy data are analysed [46–48].

About gastroesophageal and inflammatory disorders there are no diagnostic accuracy data available therefore we can just report the main RFs without any information about their clinical utility [51,52,57], limiting their applicability in healthcare settings. Regarding vertebral fractures and malignancies, our results agree with current systematic reviews [10,11,15,18–20], identifying almost the same set of RFs. However, analysing the diagnostic accuracy of each RF, we highlighted the low diagnostic accuracy of the most widespread sign and symptoms used in clinical settings, thus their reliability should be reconsidered.

Vertebral fracture is the most analysed pathology and the most cited RFs are: advanced age; history of trauma; corticosteroids use; and female gender. However, the use of corticosteroids reported a Sn between 18% and 25%, thus resulting not so useful during the clinical practice. Furthermore, the female gender usually is merely considered as a risk factor, not a relevant RF [71] Many patients could have a fracture without having a history of trauma, since only Tsiang et al. provide a Sn of 81.1% among other 3 papers showing values between 21% and 25% [25,55,58,62]. Female gender shows a better diagnostic accuracy if combined with advanced age and history of trauma. All findings obtained during the physical examination demonstrate a low clinical utility. The combination of multiple RFs is suitable during the screening process, increasing up to 52% the post-test probability to detect vertebral fracture (Sn 88%; Sp 95-100%) [55,57].

The history of cancer; an unexplained weight loss; an advanced age; and a night pain represent the main RFs suggestive for malignacy [25,46,50,58,63–65,68]. The absence of one or two RFs do not significantly decrease the LR-: indeed 64% of subjects with spinal malignancy present no RF during the medical interview [25]. The history of malignancy is the RF with the best diagnostic accuracy [25]. The unexplained weight loss, included by a few narrative reviews [72–74], show a very low Sn (8.3%) [25]. The age <20 years or >55 years displays a high false-positive rate. Night pain is reported by more than 55% of patients, but it is a false positive in the 85% of patients [25,53]. Combining a history of malignancy and unintentional weight loss the probability to rule-in the pathology increase up to 14.3% (LR+ 10.25) [25]. CES and infection are examinated in a few narrative reviews with a low methodological quality and statement generally based on expert opinion [72–79], thus reducing their clinical impact. In case of spinal infection the presence of fever, sweat, chills and recent infection are important RFs to screen showing a good Sp (93.2% to 99.6%), but a very low Sn (11.7% to 24.2%) [25,58]. Few authors [72–74] endorse as important

RFs: the presence of unintentional weight loss; neurological signs; and constant pain not relieved by rest. However, no primary study analyse their diagnostic accuracy thus reducing their clinical utility. Different authors identify RFs with high false-positive rate such as neurological signs; constant pain [57]; and the presence of night pain [25]. The screening process of CES include the following RFs: bladder or bowel dysfunction; neurological signs; saddle anesthesia; and loss of anal sphincter tone. However, no primary study evaluate the diagnostic accuracy of loss of anal sphincter tone even if is one of the most endorsed RF. Saddle anesthesia is analysed only by Raison showing a Sn of 24%, thus limiting its utility for the clinician [54]. Bladder or bowel dysfunction are cited by all the included papers [25,37–39,54,55,57,58] with an heterogeneous diagnostic accuracy (Sn between 13.9% to 100%). The combination of multiple RFs improves the probability to rule-in CES (Sp 92% to 97.2), but not to rule-out it (Sn 8.3% to 27%). Concerning the internal validity of the results emerged from out systematic review is supported by a fairly good quality assessment of the included papers even if a few methodological limitations have been identified. The external validity of this systematic review is reduced by two elements. Firstly, the screening of RFs has been generally performed by a medical provider using an interview [36,46,57,60,62] or a questionnaire [24,25,53,55,68], thus possibly influencing the conclusion of this sistematic review since our aim is to inform every healthcare providers. Secondly, a low number of studies analyse the diagnostic accuracy of RFs, thus limiting the report of their clinical utility.

4.2. Limitations

This SR has several limits. Firstly, we can not rule out a publication bias because the exclusion of those papers published before 01/01/1999[80]. However, we have screened 7 databases and "grey" literature in order to make our search strategy sensitive and to improve the probability to retrieve the higher number of studies [26]. Secondly, we created a review protocol before the commencement of the review, but we did not submit such protocol on the reference database (PROSPERO) [81]. However, we followed the PRISMA guidelines to design the study and to guarantee a management methodology, relevance of results and clarity of optimal reporting [26]. Thirdly, only the 45% of primary studies analyse the diagnostic accuracy of RFs due to the low prevalence of serious pathologies. Therefore we decided to provide information concerning RFs clinical utility only on signs and symptoms whose diagnostic accuracy was reported.

5. Conclusion

We analysed 36 primary studies concerning TLP and several RFs have been identified. However, according to current literature, RFs screening, especially if used alone, is not advisable to guide healthcare providers' clinical practice since almost no RF significantly increase the probability to identify a serious pathology. The combination of multiple RFs shows a higher diagnostic accuracy resulting in an excellent screening tool, but only 30% of the included papers evaluate it. Healthcare providers should consider history of trauma, female gender and advanced age as 3 RFs to combine in case of vertebral fracture; history of cancer is the most relevant RF for malignancy and shows a higher diagnostic accuracy if combined with unintentional weight loss. For spinal infection, we recommend the combination of fever, sweats, chills and recent infection; to detect CES, healthcare professionals should screen for bladder or bowel dysfunction and saddle anaesthesia. Pain radiating to upper limbs and extertional pain are the 2 main RFs for cardiovascular disorders, but their combination has not been evaluated. Several RFs regarding pulmonary, gastrointestinal or inflammatory disorders exist, but since diagnostic accuracy data are not available, we are not able to provide information about clinical utility of such RFs. Since the screening process aimed to exclude serious pathologies should be performed using the combination of multiple RFs, we recommend for future research to conduct more high quality primary studies in order to increase diagnostic accuracy data of RFs and to gain more applicability for all healthcare professionnels in clinical practice. Some SRs regarding fracture and malignancy already exist, but their included studies are often dated. There is a need for forthcoming studies to evaluating specific serious pathologies such as pulmonary or gastroesophageal disorders which are less studies in current literature.

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AUTHORS	OBJECTIVE	METHODS	RESULTS
Roman 2010 [45]	To identify clinical characteristics associated with a diagnosis of osteoporotic vertebral compression fracture (OVCF).	Retrospective, cross-sectional study of 1448 consecutive patients seen at a spine surgery center.	RFs for OVCF: Age > 52 years; BMI < 22; female gender; no gait abnormality; does not exercise regularly; sitting decreases pain; concomitant Osteoarthritis; no leg or buttock pain. Combining more RFs there is a better diagnostic accuracy with a posttest probability increasing up to 20.4%.
Cook 2011 [65]	To investigate the diagnostic accuracy of lumbar movement restrictions and pain in patients with metastatic bone cancer.	Retrospective cohort study of 1109 patients with LBP.	Pain-free lumbar movements rule-out malignancy: Sn 55%, Sp 59% LR+ 1.3, LR- 0.8.
De Schepper 2015 [68]	To investigate the prevalence of spinal pathology.	Cross-sectional, cohort study of 2975 patients presenting for an MRI lumbar examination.	RFs for vertebral fracture are: age>70 years, history of trauma and female gender. The RFs for malignancy are: age at onset over 50 years, continuous back pain, back pain at night, history of malignancy, unexplained weight loss.
Hsu 2003 [56]	To determine a clinical diagnostic pathway for the imaging of the thoracolumbar (TL) spine.	Retrospective study of 200 traumatic patients.	RFs for TL fracture are: back pain/midline, palpable midline step, back bruising, abnormal neurological signs and history of trauma.
Holmes 2003 [62]	To analyze if clinical screening criteria can identify all patients with TL spine injuries.	Prospective, observational cohort study of 2404 patients undergoing TL spine radiographs following blunt trauma.	RFs: complaints of TL spine pain; TL spine tenderness on midline palpation; decreased level of consciousness; abnormal peripheral neurologic examination; distracting painful injury; evidence of intoxication with ethanol or drugs.
Van den Bosch 2004 [63]	To evaluate the prevalence of abnormalities findings on radiographic by age.	Retrospective study of 2007 radiographic reports of patients referred with low back pain for lumbar spine radiography.	The prevalence of reported degenerative changes in case of fracture, malignancy and infection increased with age in patients > 55 years and older (62%).
Donner-Banzhoff 2006 [64]	To evaluate the diagnostic validity of a simple heuristic based on the patient's view of the familiarity of LBP.	Cross-sectional diagnostic study of 1378 patients presenting with LBP.	Diagnostic validity of a simple heuristic based on patient's view is Sn: 50%; Sp: 83%; LR+ 2.95; LR- 0.6.
Harding 2005 [53]	To assess the importance of the symptom of night pain.	Prospective longitudinal study of 482 patients attending a back pain triage clinic with night pain.	A total of 213 (44%) patients had night pain, with 90 having pain every night. No serious pathology was identified. The presence of night is not a specific sign to detect serious pathologies.
Raison 2014 [54]	To assess the effectiveness of RF used in the ED to identify spinal cord compression and CES.	Retrospective cohort study of 206 patients with back pain attending the ED.	RFs: saddle anesthesia and bladder or bowel dysfunction. The combination of the RFs increase the diagnostic accuracy.
Enthoven 2016 [55]	To identify the prevalence of back pain and to assess associations between RF and vertebral fractures.	Prospective cohort study of 669 patients with back pain.	RFs for vertebral fracture: age > 70 years, female gender, corticosteroids use, history of trauma, reduction in height, positive percussion test, great disability, painful injury, NRS > 7/10, hip or knee osteoarthritis and CP.
Henschke 2009 [57]	To determine the prevalence of serious pathology in patients with acute LBP, and to evaluate their diagnostic accuracy.	Cohort study of 1172 consecutive patients receiving primary care for acute LBP.	Only 3 of the red flags for fracture were informative: corticosteroids use, major trauma, age > 70 years. Clinical judgement had a very good Sp. The combination of multiple RFs increase the diagnostic accuracy.
Tsiang 2019 [58]	To quantify the sensitivity and specificity of patient-reported RF.	Retrospective nested case-control study of 500 patients with LBP.	Patient-reported. RFs malignancy: history of cancer; fracture: corticosteroids use, history of trauma; infection: fever; for CES: bladder or bowel dysfunction. Provider-reported red

			flags. Malignancy: history of cancer; fracture: osteoporosis and history of trauma; infection: fever; CES: bladder dysfunction and lower limbs weakness.
Premkumar 2018 [25]	To examine the effectiveness of RF questions as a screening tool.	Retrospective observational study of 9940 patients with LBP.	RFs for vertebral fracture: age > 50/70 years, history of recent trauma; RF for malignancy: unexplained weight loss, history of cancer. RFs for infection: fever, chills and sweating, recent infection. RFs for CES: loss of bladder or bowel control. The combination of multiple RFs increase the diagnostic accuracy data.
Dugas 2011 [36]	To evaluate the presenting signs and symptoms of SCC and CES and to determine the incidence of emergency department (ED) misdiagnosis.	Retrospective study of 1231 patients who had visited the ED for a related complaint.	The main RFs are: pain, difficulty ambulating, weakness, motor or sensory deficits.
Ahad 2015 [37]	To underline clinical signs could predict the presence of CES.	Retrospective study of 79 consecutive patients undergoing MRI of the spine.	RFs: decreased anal tone, fecal incontinence, urinary retention, bladder, incontinence, constipation, saddle anesthesia.
Domen 2009 [38]	To overlooking a potential diagnosis of (CES).	Retrospectively studied 58 consecutive cases of suspected CES.	RFs: bilateral sciatica, subjective urinary retention or rectal incontinence symptoms.
Balasubramanian 2010 [39]	To evaluate the efficacy of clinical assessment in the diagnosis of CES.	Retrospective cohort study of 80 patients who presented with clinical features of CES.	Saddle anesthesia is the only clinical feature with a statistically significant association with MRI positive CES. Other RFs: unilateral or bilateral leg pain, bladder or bowel dysfunction.
Everden 2018 [66]	To reviewed the epidemiology, management and outcome of all cases of bone and joint TB (BJTB).	Retrospective study of 21 cases of BJTB.	Thoracic and lumbar spine are the most common sites affected (62%). RFs: localized pain, fever and weight loss.
Broderick 2018 [67]	To determine the demographics, presentation and investigation of patients with a TB infection.	Retrospective observational study of 31 patients with positive TB cultures	Main RFs: pain and swelling. Fever, sweats and weight loss are uncommon.
Kempthorne 2009 [35]	To define the presentation, findings and prognosis of extradural spinal abscesses (ESA).	Retrospective study of 42 patients diagnosed with ESA.	RFs: severe back pain, not relieved by rest or sleep, patient's clinical history and examination findings (nature and duration of their back pain).
Schillinger 2004 [40]	To investigate the predictive value of MI atypical characteristics for the exclusion of acute or subacute coronary events.	Prospective study of 1288 consecutive patients presenting with acute CP at a non-trauma ED.	RFs: left-sided or substernal chest pain defined as squeezing or crushing, burning; radiation of CP to the left or both arms, neck or back; exercise-induced , undulating, relieved with rest or nitroglycerine; dyspnea, nausea; diaphoresis; personal or family history of cardiac disorders; smoking ; obesity; hypertension ; diabetes; hyperlipidemia.
Sánchez 2007 [41]	To establish a triage flowchart to rule out ACS.	Prospective observational study of 1000 consecutive patients with CP on an ED.	RFs: age <40 years, absence of diabetes, no previously known coronary artery disease, no oppressive pain, and no retrosternal pain.
Albarran 2002 [49]	To investigate whether there were differences in pain radiation between those with and without MI and according to gender	Prospective study of 541 patients presenting with CP.	Radiation to neck, back and upper limbs are common features in MI. women with MI described more radiation to the right arm, upper right region than those without MI.
Milner 2002 [43]	To evaluate typical and atypical symptoms to detect ACS.	Observational study of 246 women and 276 men seen in the ED with symptoms	RFs: CP, discomfort, dyspnea, diaphoresis, upper limbs pain, diaphoresis (women), dizziness or faintness(men).

		suggestive of ACS.	
Goodacre 2002 [44]	To measure the predictive value and diagnostic performance of clinical features used to diagnose coronary syndromes.	Prospective, observational cohort study of 893 patients presenting at the ED with acute CP.	RFs for AMI: pain radiating to shoulders or both arms; exertional pain; absence of chest wall tenderness. RFs for ACS: pain radiating to shoulders, left arms or both arms; exertional pain.
Body 2010 [24]	To assess the value of individual historical and examination findings for diagnosing AMI and other cardiac events.	Prospective observational study of 796 ED patients with CP.	RFs for AMI: pain radiating to the right arm or both arms, vomiting, central CP and sweating. The presence of rest pain or pain radiating to the left arm did not significantly modify the probability of AMI.
Courtney 2010 [46]	To measure the predictive value of variables for pulmonary embolism.	Prospective observational study of 7940 patients with pulmonary embolism.	RFs: patient history of pulmonary embolism or deep venous thrombosis or thrombophilia, unilateral leg swelling, recent surgery, estrogen use, hypoxemia, active cancer, pleuritic or substernal CP, female gender and oxygen saturation less than 95%.
Wells 2000 [47]	To determine a scoring system, that combined with D-dimer results, exclude PE.	Prospective cohort study of 1211 patients.	RFs: Symptoms of DVT, no alternate diagnosis more likely than PE, heart rate >100 beats per minute, immobilization or surgery in past 4 weeks, previous objectively diagnosed DVT or PE, hemoptysis and malignancy.
Bagattini 2004 [48]	To evaluate clinical characteristics that allow to predicting alternative diagnoses other than PE by ruling out venous thromboembolism.	Retrospective study of 1090 consecutive patients admitted for clinically suspected of PE.	RFs: tachycardia, recent immobilization, dyspnea, age > 40, hemoptysis.
Timmons 2003 [42]	To compare the clinical presentation of younger and older patients with acute pulmonary embolism	Retrospective study of 60 consecutive patients with PE.	RFs: Collapse, dyspnea, cough, hemoptysis, palpitations, hypotension, tachycardia, tachypnea, fever , cyanosis, abnormal lower limb examination and pleural rub.
Karlaftis 2013 [50]	To determine clinical characteristics that could identify GERD in patients with NCCP.	Observational study of 52 patients with NCCP.	RFs: typical reflux symptoms, postprandial CP and use of anti-reflux drugs for pain relief.
Sung-Hun Park 2015 [51]	To evaluate the risk factors and prevalence of gastroesophageal reflux diseases (GERD) in NNCP	Retrospective non-interventional observational study of 904 consecutive patients with NCCP.	RFs: obesity, smoking, and diabetes.
Ko 2012 [52]	To examine GERD in young patients with NCCP and to evaluate their symptomatic characteristics.	Observational study of 118 patients with NCCP.	RFs: heartburn and acid regurgitation. In young NCCP patients, the prevalence of GERD was relatively low compared to average-aged.
Thiruganasambandamoorthy 2014 [59]	To identify risk factors associated with serious pathology.	Observational study of 329 patients with nontraumatic LBP.	RFs: anticoagulant use, decreased sensation on physical examination, pain that is worse at night and pain that persists despite appropriate treatment.
Punukollu 2005 [61]	To evaluate the clinical characteristics and outcome of acute PE in elderly patients.	Observational study of 136 patients with a confirmed diagnosis of acute PE.	RFs: shortness of breath, pleuritic CP, syncope, active cancer, immobilization, tachycardia.
Svensson 2003	To evaluate factors which predict the	Prospective observational study of 538	RFs: history of myocardial infarction or angina pectoris or hypertension ECG changes and

[60]	development of ACS or AMI.	patients who called for an ambulance due to CP and suspected ACS.	the elevation of serum markers (CKMB).

Table 3. Characteristics of the included papers.

LR+: Likelihood Ratio positive; LR-: Likelihood Ratio negative; Sn: Sensitivity; Sp: Specificity; RFs: Red Flags; LBP: Low Back Pain; CP: Chest Pain; TLP: Thoracolumbar pain; ED: Emergency Department; CES: Cauda Equina Syndrome; NRS: Numeric Rating Scale; BMI: body Mass Index; AMI: Acute Myocardial Infarction; ACS: Acute Coronary Syndrome; NCCP: Non Cardiac Chest Pain; GERD: Gastroesophageal Reflux Diseases; PE: Pulmonary Embolism.

Included studies	Selection	Comparability	Outcome	Total score (out of 9)
Roman 2010 [45]	3	2	2	7
De Schepper 2015 [68]	3	2	2	7
Hsu 2003 [56]	2	2	1	5
Holmes 2003 [62]	3	1	1	5
Van den Bosch 2004 [63]	3	1	1	5
Donner-Banz 2006 [64]	3	2	3	8
Cook 2011 [65]	3	1	2	6
Everden 2018 [66]	2	2	3	7
Broderick 2018 [67]	2	2	3	7
Kempthorne 2009 [35]	3	1	2	6
Dugas 2011 [36]	3	2	2	7
Ahad 2015 [37]	3	1	3	7
Domen 2009 [38]	2	2	2	6
Balasubramani 2010 [39]	3	1	2	6
Schillinger 2004 [40]	3	2	2	7
Sanchez 2007 [41]	3	2	2	7
Albarran 2002 [49]	3	1	2	6
Milner 2002 [43]	2	1	2	5
Goodacre 2002 [44]	2	1	3	6
Body 2010 [24]	3	2	3	8
Courtney 2010 [46]	3	2	1	6
Wells 2000 [47]	3	2	1	6
Bagattini 2004 [48]	3	2	2	7

Timmons 2003 [42]	3	1	2	6
Karlaftis 2013 [50]	2	2	1	5
Park SH 2015 [51]	3	2	3	8
Ko 2012 [52]	2	2	1	5
Premkumar 2018 [25]	4	2	3	9
Harding 2005 [53]	3	1	3	7
Raison 2014 [54]	3	2	2	7
Enthoven 2016 [55]	3	2	3	8
Henschke 2009 [57]	4	2	3	9
Tsiang 2019 [58]	4	2	2	8
Thiruganasam 2014 [59]	3	2	2	7
Punukollu 2005 [61]	2	1	2	5
Svensson 2003 [60]	2	1	1	4

Table 4. Risk of Bias of the included studies. (Newcastle-Ottawa Quality Assessment for observational studies: Good quality: 3 or 4 points in selection domain AND 1 or 2 points in comparability domain AND 2 or 3 points in outcome/exposure domain; Fair quality: 2 stars in selection domain AND 1 or 2 points in comparability domain AND 2 or 3 points in outcome/exposure domain; Poor quality: 0 or 1 point in selection domain OR 0 point in comparability domain OR 0 or 1 point in outcome/exposure domain)

Author	Red Flag	Sn	Sp	LR+	LR-
Roman 2010 [45]	Age > 50	95% (83-95%)	39% (38-40%)	1.5 (1.3-1.5)	0.14 (0.03-0.45)
Van d Bosch 2004 [63]	Age > 55	-	-	1.5 - 8	-
Premkumar 2018 [25]	Age > 50	74%	32.9%	1.1 (1.05-1.16)	0.79 (0.69-0.91)
Premkumar 2018 [25]	Age > 70	39%	80%	1.55 (1.36-1.76)	0.86 (0.82-0.91)
Enthoven 2016 [55]	Age > 75	45%(0.28-0.62)	85%(0.82-0.88)	3.1(2.0-4.7)	0.6(0.5-0.9)
Henschke 2009 [57]	Age >70	50%	96%	11.0 (4.65–19.48)	0.52 (0.23–0.82)
Roman 2010 [45]	Body Mass Index <22	38% (24-55%)	83% (82-84%)	2.3 (1.4-3.4)	0.74 (0.54-0.91)
Enthoven 2016 [55]	Female gender	67%(51-83%)	41%(37-44%)	1.1(0.9-1.4)	0.8(0.5-1.3)
Roman 2010 [45]	Female gender	90% (76-96%)	41% (41-42%)	1.5 (1.3-1.6)	0.26 (0.10-0.60)
Roman 2010 [45]	Gait abnormality	66% (50-79%)	23% (22-23%)	0.86 (0.65-1-02)	1.5 (0.91-2.2)
Roman 2010 [45]	No regular exercise	81% (65-91%)	44% (43-45%)	1.5 (1.2-1.6)	0.43 (0.20-0.80)
Roman 2010 [45]	Sitting decrease pain	29% (27-32%)	81% (79-83%)	1.6 (1.2-1.9)	0.87 (0.82-0.92)
Roman 2010 [45]	Osteoarthritis	50% (35-65%)	52% (51-52%)	1.1 (0.70-1.4)	0.97 (0.67-1.3)
Enthoven 2016 [55]	Osteoarthritis	16%(03-28%)	69%(65-72%)	0.50(0.2-1.1)	1.2(1.0-1.4)
Roman 2010 [45]	No leg pain	31% (16–49%)	86% (85–87%)	2.2 (1.2–3.6)	0.81 (0.58–0.97)
Enthoven 2016 [55]	Corticosteroids use	18%(05-31%)	93%(91-95%)	2.5(1.1-5.3)	0.90(0.8-1.0)
Henschke 2009 [57]	Corticosteroids use	25%	100%	48.5 (11.62-165.22)	0.75 (0.41–0.93)

Tsiang 2019 [58]	Corticosteroids patient reported	64.8%	58.5%	-	-
Enthoven 2016 [55]	History of trauma	21%(07-35%)	97%(95-98%)	6.2(2.8-13.5)	0.80(0.5-1.3)
Henschke 2009 [57]	History of trauma	25%	98%	10.0 (2.76–26.36)	0.77 (0.42–0.95)
Premkumar 2018 [25]	History of trauma	24.7%	88.6%	2.17 (1.86-2.54)	0.84 (0.81-0.89)
Tsiang 2019 [58]	History of trauma	81.1%	79.1%	-	-
Tsiang 2019 [58]	Trauma patient reported	64.8%	58.5%	-	-
Enthoven 2016 [55]	Sudden decrease in height	9%(01-19%)	97%(95-98%)	2.9(0.9-9.4)	0.90(0.8-1.0)
Enthoven 2016 [55]	Percussion tenderness of the spine	21%(07-35%)	81%(78-84%)	1.1(0.6-2.2)	1.0(0.8-1.2)
Enthoven 2016 [55]	Severe disability	30%(14-46%)	87%(84-90%)	2.3(1.3-4.2)	0.8(0.6-1.0)
Enthoven 2016 [55]	Numeric Rating Scale >7	67%(51-83%)	63%(59-67%)	1.8(1.4-2.3)	0.50(0.3-0.9)
Enthoven 2016 [55]	Painful injury	30%(15-46%)	64%(60-68%)	0.8(0.5-1.4)	1.1(0.9-1.4)
Enthoven 2016 [55]	Thoracic back pain	42%(26-59%)	78%(75-81%)	1.9(1.3-3.0)	0.7(0.5-1.0)
Tsiang 2019 [58]	Osteoporosis	81.1%	79.1%	-	-
Hsu 2003 [56]	Midline tenderness	62.1%	91.5%	-	-
Hsu 2003 [56]	Palpable midline step	13.8%	100%	-	-
Hsu 2003 [56]	Back bruising	6.9%	98.6%	-	-
Hsu 2003[56]	Abnormal neurological signs	41.4%	95.8%	-	-

Table 5. Fracture and diagnostic accuracy. (Sn: sensibility; Sp: specificity; LR+: Likelihood ratio positive; LR-: Likelihood ratio negative)

Author	Red Flag	Sn	Sp	LR+	LR-
Premkumar 2018 [25]	Age > 50	71.7%	32.6%	1.06 (0.96-1.17)	0.87 (0.68-1.11)
Van d Bosch 2004 [63]	Age > 55		--	1.5 - 8.0	-
Premkumar 2018 [25]	Age > 70	22.6%	79.5%	1.1 (0.82-1.47)	0.97 (0.9-1.06)
Premkumar 2018 [25]	Night pain	55.4%	41.8%	0.85 (0.83-1.1)	1.07 (0.9-1.27)
Premkumar 2018 [25]	Unexplained weight loss	8.2%	95.6%	1.87 (1.1-3.17)	0.96 (0.92-1.01)
Premkumar 2018[25]	History of malignancy	32%	95.6%	7.25 (5.65-9.3)	0.71 (0.64-0.79)
Tsiang 2019 [58]	History of malignancy	91.7%	77.8%	-	-
Tsiang 2019 [58]	Malignancy patient reported	75%	78.7%	-	-
Cook 2011 [65]	No pain during flexion	67% (55-77)	41% (40-42)	1.1 (0.9–1.3)	0.80 (0.56–1.1)
Cook 2011 [65]	No pain during extension	65% (54–75)	50% (49–51)	1.3 (1.1–1.5)	0.70 (0.49–0.94)
Cook 2011 [65]	No pain during right side flexion	96% (88–98)	4% (04–05)	0.94 (0.85–1.0)	1.0 (0.92–1.0)
Cook 2011[65]	No pain during left side flexion	96% (88-98)	4% (03-04)	0.99 (0.91–1.0)	1.1 (0.37–3.2)
DonnerBanz 2006 [64]	Clinical judgment	50%	83%	2.95	0.6

Table 6. Malignancy and diagnostic accuracy. (Sn: sensibility; Sp: specificity; LR+: Likelihood ratio positive; LR-: Likelihood ratio negative)

Author	Red Flag	Sn	Sp	LR+	LR-
Premkumar 2018 [25]	Fever	11.7%	93.2%	1.71 (1.04-2.81)	0.95 (0.89-1.01)
Tsiang 2019 [58]	Fever	12.5%	99.6%	-	-
Tsiang 2019 [58]	Fever patient reported	25%	97.6%	-	-
Premkumar 2018 [25]	Chills	11.7%	93.2%	1.71 (1.04-2.81)	0.95 (0.89-1.01)
Premkumar 2018 [25]	Night pain	57.5%	41.8%	0.99	1.02
Premkumar 2018 [25]	Sweating	11.7%	93.2%	1.71 (1.04-2.81)	0.95 (0.89-1.01)
Premkumar 2018 [25]	Persistent night sweating	17.5%	86.1%	1.26 (0.85-1.86)	0.96 (0.88-1.04)
Premkumar 2018 [25]	Recent infection	24.2%	97.4%	9.31 (6.63-13.07)	0.78 (0.7-0.86)
Van d Bosch 2004 [63]	Age > 55	-	-	1.5 – 8.0	-

Table 7. Infection and diagnostic accuracy. (Sn: sensibility; Sp: specificity; LR+: Likelihood ratio positive; LR-: Likelihood ratio negative)

Author	Red Flag	Sn	Sp	LR+	LR-
Premkumar 2018 [25]	Bladder dysfunction	22.2%	90.4%	2.31 (1.25-4.27)	0.86 (0.72-1.03)
Raison 2014 [54]	Bladder dysfunction	65% (44-82%)	73% (66-80%)	2.45	-
Tsiang 2019 [58]	Bladder dysfunction	100%	76.9%	-	-
Tsiang 2019 [58]	Bladder dysfunction patient rep	50%	86.5%	-	-
Premkumar 2018 [25]	Bowel dysfunction	13.9%	95%	2.78 (1.23-6.3)	0.91 (0.8-1.03)
Raison 2014 [54]	Bowel dysfunction	65% (44 - 82%)	73% (66 - 80%)	2.45	-
Tsiang 2019 [58]	Bowel dysfunction patient rep	50%	86.5%	-	-
Raison 2014 [54]	Saddle dysfunction	27% (12-48%)	87% (81-92%)	2.11	-
Tsiang 2019 [58]	Lowe limbs weakness	100%	76.9%	-	-
Van d Bosch 2004 [63]	Age > 55	-	-	1.5 – 8.0	-

Table 8. CES and diagnostic accuracy. (Sn: sensibility; Sp: specificity; LR+: Likelihood ratio positive; LR-: Likelihood ratio negative)

Author	Red Flag	Sn	Sp	LR+	LR-
Goodacre 2002 [44]	Pain radiating to upper limbs-AMI	38.2% (23.9-55.0%)	90.6% (88.5-92.4%)	4.07 2.53-6.54)	0.68 (0.52-0.89)
Goodacre 2002 [44]	Pain radiating to upper limbs-ACS	55.6% (44.7-65.9%)	65.6% (62.3-68.8%)	1.62 (1.30-2.01)	0.68(0.53, 0.87)
Body 2010 [24]	Pain radiating to upper limbs	13.5% (8.2–17.5%)	94.8% (93.2-96.8%)	2.58 (1.55-4.29)	0.91 (0.87–0.97)
Body 2010 [24]	Pain radiated to the right arm	18.9% (12.3-22.8%)	91.8% (89.8-94.3%)	2.31 (1.47-3.34)	0.88 (0.84–0.96)
Goodacre 2002 [44]	Exertional pain - AMI	35.3% (21.5-52.1%)	85% (82.4-87.2%)	2.35 (1.45-3.80)	0.76 (0.59-0.98)
Goodacre 2002 [44]	Exertional pain - ACS	29.6% (20.8-40.3%)	85.6% (83.0-87.8%)	2.06 (1.41-2.99)	0.82 (0.71-0.95)
Goodacre 2002 [44]	Absence of chest wall syndrome	91.7% (74.2-97.7%)	27.8% (24.6-31.2%)	1.27 (1.12-1.44)	0.30 (0.08-1.14)
Body 2010 [24]	Vomiting	16.2%(9.8-19.7%)	94.8%(93.2-96.8%)	3.09(1.82-4.85)	0.88(0.85-0.95)
Body 2010 [24]	Sweating	59.5%(49.0-62.7%)	54.3%(50.4-58.6%)	1.30(1.06-1.43)	0.75(0.68-0.96)
Body 2010 [24]	Sweating observed	36.5%(22.0-34.5%)	94.3%(92.4-96.2%)	6.39(3.42-7.63)	0.67(0.70-0.83)
Body 2010 [24]	Central CP	85.1%	34.1%	1.29	0.44
Body 2010 [24]	Pain left anterior	11.5%	68.2%	0.36	1.30
Body 2010 [24]	Duration >1 h	77%(65.0–77.5%)	44.9%(41.2-49.4%)	1.40(1.17-1.46)	0.51(0.50-0.79)
Body 2010 [24]	Hypotension	6.8%(4.4–12.0%)	97.7%(97.1-99.3%)	2.92(2.21-10.98)	0.95(0.90-0.98)
Body 2010 [24]	Basal crackles	16.2%(11.8-22.3%)	90.6%(88.9-93.6%)	1.72(1.30–2.90)	0.92(0.85–0.97)
Body 2010 [24]	Acute ischemic ECG changes	71%(51.3–65.0%)	81.3%(79.1-85.4%)	3.80(2.69-4.08)	0.36(0.43-0.60)
Body 2010 [24]	Similar to previous ischemia	22.3%	69.4	0.73	1.12

Table 9. Cardiovascular disorders and diagnostic accuracy. (Sn: sensibility; Sp: specificity; LR+: Likelihood ratio positive; LR-: Likelihood ratio negative; AMI: Acute Myocardial infarction; ACS: Acute Coronary Syndrome; ECG: Elecrocardiogram)

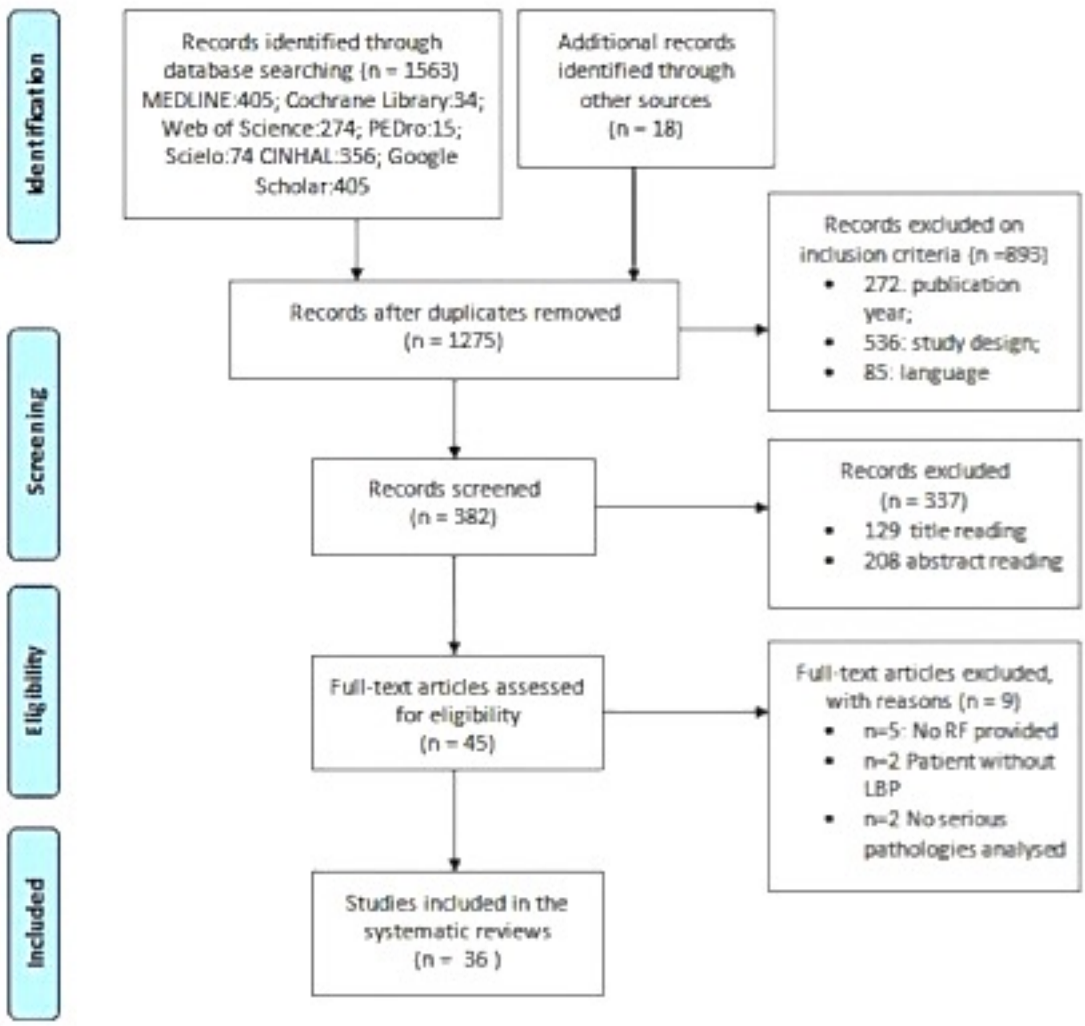

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Chart [26].

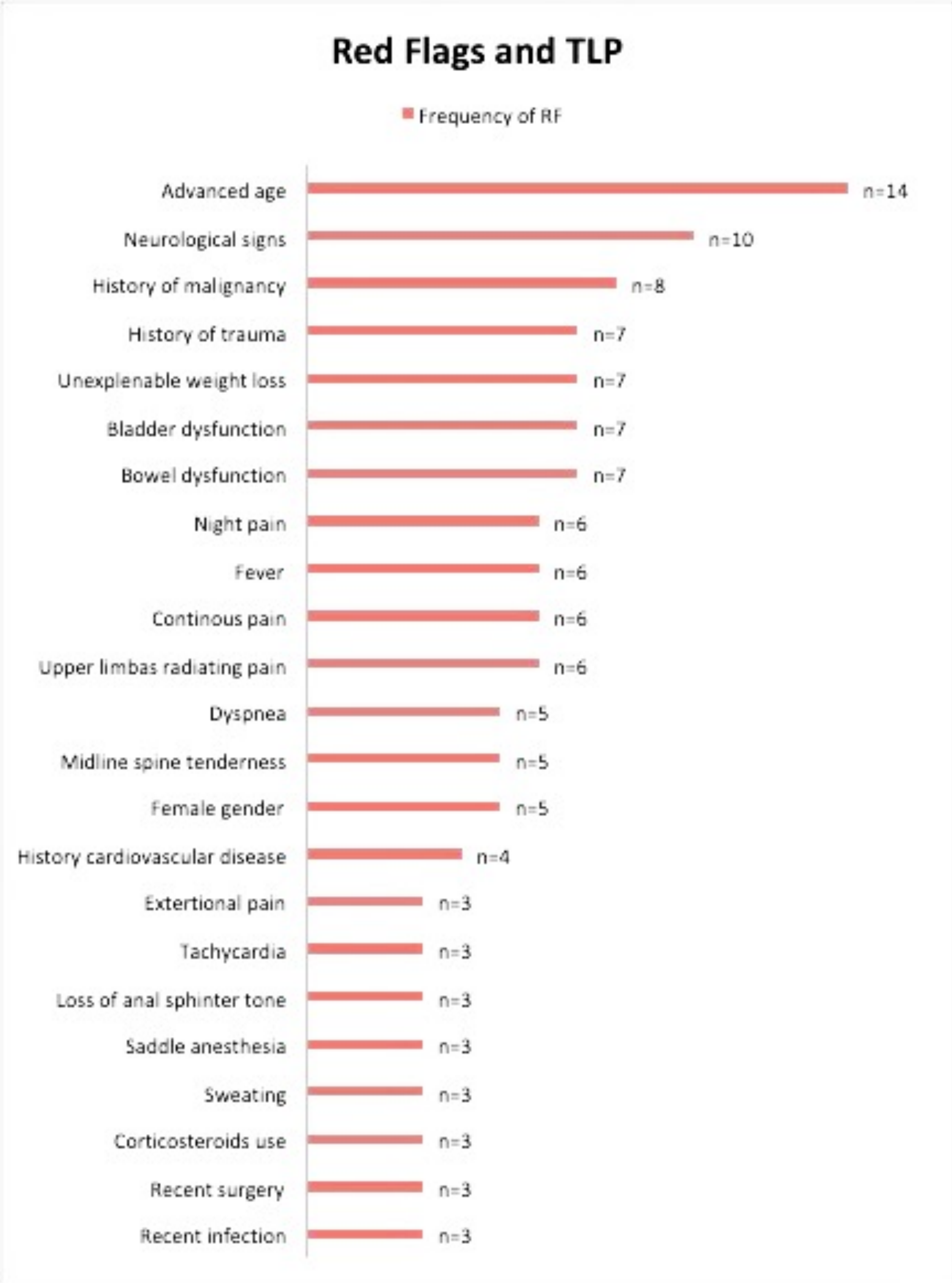

Figure 2: Frequency of RFs in TLP

CHAPTER VI
RED FLAGS IDENTIFICATION AS AN IMPORTANT STEP TO SCREENING FOR REFERRAL PROCESS IN RUNNERS WITH LOW BACK PAIN
- CASES REPORTS -

THE IMPORTANCE OF SCREENING IN PHYSICAL THERAPY: VERTEBRAL FRACTURE OF THORACO-LUMBAR JUNCTION IN A RECREATIONAL RUNNER

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The Importance of screening in physical therapy: Vertebral fracture of Thoraco-Lumbar Junction in a recreational runner

Abstract

Running is one of the most popular sports worldwide. Studies suggest that 11%-85% of recreational runners have at least one Running Related Injuries (RRIs) each year, resulting in a reduction or interruption of training. High risk of RRIs represents an important inconvenience counterbalancing its beneficial effects of running. RRIs primarily affects joints of lower limb and lumbar spine. Noteworthy, in some cases, the clinical presentation of signs and symptoms is confusing and may hide serious conditions, thus clinicians have to pay special attention when potential factors arise such as the presence of red flags. As reported in this case report, patients can present with Low Back Pain (LBP) as a primary problem mimicking a red flag such as a fracture of the spine. The aim of this case report was to describe a case of a recreational runner presenting with LBP as the sole symptom of an underlying thoraco-lumbar fracture.

1. Background

Running is one of the most popular sports worldwide due to the low demand for expensive technical materials and beneficial impacts on health. [1,2] The benefits of running include prevention of cardiovascular disease, reductions in mortality risk, obesity and other chronic health disorders. [1-4] Media coverage of health and fitness issues has increased in the last decade, leading to a growing interest in running both at competitive and recreational levels. [3-6] Although running is one of the most effective ways to achieve a general healthy status, [7] recent studies highlight a relatively high risk of associated injuries. [8,9] Previous studies have reported that 11%-85% of recreational runners have at least one Running Related Injuries (RRIs) each year, [8] resulting in a reduction or interruption of training in in a large percentage of runners. [9,10] Acute RRIs are described as rare: approximately 80% of RRIs are due to overuse, resulting from an imbalance between the resistance capacity of connective tissue and the biomechanical load of running, and acute RRIs are described as rare. [11,12] The prevalence of RRIs among middle and long-distance runners have been reported to range between 19% and 92%. [2, 13-16] However, comparisons between studies are difficult due to the discrepancies in the type of runners studied, follow-up provided, study design, etiology and definition of RRI. [1,2,11-22] In 2015, an international consensus was reached and RRI was defined as musculoskeletal pain or physical complaint of the lower limbs or of the back/trunk due to running activities, causing a total restriction or suspension of running for at least seven or more days and requiring medical assistance. [17]

RRIs primarily affect joints of the lower limb and lumbar spine, including the pelvis, [15,22,23] resulting in painful muscles, tendons and joints. [11-23] Patients normally contact physical therapists for a clinical evaluation aimed at resolving RRIs with low back pain (LBP) being a common complaint of RRIs. [24-30] Noteworthy, in some cases, the clinical presentation of signs and symptoms is confusing and may mimic more serious conditions, thus clinicians have to pay special attention when factors arise such as the presence of red flags (RF). For these reasons it is necessary to adopt a careful process of clinical reasoning and of decision making in order to screen for potential RF, and eventually direct these patients towards an appropriate diagnostic-therapeutic pathway. [25,31] As reported in this case report, patients can present with LBP as a primary problem mimicking a red flag such as a fracture of the spine. Vertebral fractures, [24,27] are one of the most common serious pathologies of the spine but despite this, more than 2/3 of vertebral fractures remain undiagnosed on initial examination. [32] Stress fractures are common in running, accounting for 15% of the overall injuries, [33-37] and one of most common sites of stress fractures is the pelvis. [33-37] LBP may be the sole complaint in an initial stage of a vertebral fracture. For this reason, clinicians involved in caring for patients with sport injuries, and especially in RRI, have to pay special attention in such cases to screen for RF. Indeed, less than 5% of primary care physicians routinely examine for RF during an initial screen. [38] The first aim of this case report was to describe a case of a recreational runner presenting with LBP as the sole and most important symptom of an underlying post-traumatic thoraco-lumbar fracture.

Moreover, this case report highlights the diagnostic value of further imaging besides the traditional scan (i.e. radiography), thus offering the opportunity to reflect on the risk to miss serious complications. Relying on the original diagnosis for the patient could have been dangerous for the patient and for the physical therapist.

2. **Case Presentation**

A 37-year-old man, working as a dentist, self-referred to an outpatient physical therapist, with a chief complaint of a stabbing LBP. He described the pain as a continuous and deep pain in the central thoraco-lumbar junction area, rated as an 8 out of 10 on the numeric pain rating scale (NPRS). [39] He also reported a concomitant more superficial pain in his lower posterior back (NPRS 3/10) that began after the patient fell backwards to the ground, during a middle-distance uphill running training session (10 Km), 1 day before the physical therapy consultation. He presented on initial examination with difficulty walking and he was accompanied by his wife who supported him in ambulation. In the history, he described aggravating activities such as walking, sitting for a short time (10 minutes) and breathing. Moreover, he reported lying in bed as the most aggravating activity that limited his sleep. In his past medical history, he reported sporadic episodes of LBP that resolved spontaneously after a few days. However, this episode of LBP was much worse than previous episodes of pain. The patient complained of sporadic numbness and tingling to his bilateral feet throughout the day. He reported his pain as continuous during the day, gradually worsening throughout the night. The patient denied serious symptoms such as unexplained recent weight loss or gain and any bowel or bladder symptoms.

3. Investigations

3.1 First Examination

On observation, no deformity was noted during the visual analysis of posture but the assessment of active movements revealed decrease of active range of motion (aROM) of the thoraco-lumbar junction (T12-L2) in flexion, and less decreased aROM in combined movement with extension on the right. The assessment of bilateral side bending and rotation was not possible secondary to pain. All active spinal movements were accompanied by an intense pain (NPRS 9/10) while in standing that resulted in pain (NPRS 8/10) in the central thoraco-lumbar junction of the spine and more superficial pain in the lower posterior back (NPRS 3/10). The hypothesized diagnosis was a fracture as a result of trauma that occured 1 day before physical therapy consultation, as LBP presents as the sole symptom of its initial presentation. [24-26] To confirm this diagnosis different additional provocative tests were performed, such as the tuning fork test, [40,41] the percussion test (boney vibration test) [42] and percussion to the effected vertebrae. [43] All of these tests were positive, thus no other over-pressure testing were performed in order to avoid exacerbation of the patient's pain. No loss of function were detected during the neurological examination thus, on the basis of the anamnestic report (trauma, night pain, unable to lie - supine sign, [43] pain over 9/10 NPRS) and the results of the clinical examination, a clinical diagnosis of specific LBP was made considering a possible vertebral fracture in the thoraco-lumbar junction. In accordance with literature and clinical best practice, [3,24-27,29,31,44,45] the patient was referred to the emergency unit for a consultation. The patient was asked to inform the physical therapist about the outcome of the emergency unit visit or any change in their symptoms of LBP.

4. Differential Diagnosis

Spinal fracture is reported to be 1-4% of all patients presenting with LBP to a primary care clinic. [26] A potential cause of spinal fracture is malignancy and the incidence of malignancy causing a spinal fracture is less than 1% of those patients presenting to a primary care clinic. [46] Among scholars there has been debate on the importance of RF for those patients that present with LBP, discussing its value during the decision-making process. Koes et al reported there were 26 red flags that suggest spinal fracture. [47] Downie et al, [48] suggested that for those patients that present to primary care clinics, the following RF should be used: older age, prolonged steroid use, severe trauma, and contusion or abrasion. [48] Downie et al, [48] reported that when one of these RF is present, there is a 10-33% increased probability of a spinal fracture. [48] They also suggested that when the patient presents with several of these RF, the probability of fracture increases to 42 to 90%. [48] Downie et al, [48] note that the European guidelines for non-specific LBP endorses 10 RF for fracture: patient aged <20 or >55, non-mechanical pain, thoracic pain, history of cancer, steroid use, structural changes, general unwellness, loss of weight, and diffuse neurological deficit. [48] Moreover, Downie et al, results suggested that age>55, thoracic pain, non-mechanical pain, structural change, and loss of weight were uninformative as RF. [48]

Differentiating the patient presentation by utilizing RF did not clarify the patient's diagnosis for this case report. The patient is middle aged which does not fit the Downie et al suggestions [48] indeed the patient: 1) did not have a history of prolonged steroid use; 2) did present trauma as the patient did fall during an uphill training session, and 3) did not have a contusion or abrasion at the thoraco-lumbar junction where the patient was complaining of 8/10 pain on the NPRS. Therefore, the patient only presented with LBP as the sole symptom of its initial presentation.

5. Treatment

5.1 Diagnostic Imaging and First Intervention

In the emergency department (ED), a physician, after carefully considering the patient's medical history and observation, performed plain film radiographs of the lumbar and thoracic spine, which showed a closed fracture of the first lumbar vertebrae without involvement of the spinal cord [Figure 1]. After, the patient was referred to an orthopaedic surgeon; the surgeon prescribed absolute rest and the use of a corset (Camp C35) for 45 days. NSAID (ibuprofen) and pain killer (tramadol) were prescribed for 2 weeks to assist in controlling the amount of pain the patient was experiencing. However, approximately 12 hours after the ED consultation, the patient presented to our clinic reporting an aggravation of pain during rest and during sitting on the bed while wearing the corset. Furthermore, he noted numbness and tingling in bilaterally his feet that was now much more aggravated than at initial physical therapist's evaluation. For this reason, the physical therapist went to the patient's home in order to analyze the change in clinical presentation and to consider if the corset was appropriately donned and worn by the patient.

5.2 Diagnostic Imaging and Second Intervention

During the home consultation the patient informed the physical therapist that the pain became more and more unbearable and the feeling of numbness in the lower limbs had become much worse. The sitting position was impossible to maintain, even while wearing the corset. While the patient was lying in bed, the physical therapist performed a neurological examination, which displayed a reduction of Osteotendinous Reflexes (OTR) (the patellar reflex was non-evocable bilaterally, the Achilles tendon reflex was slightly evocable, expecially on the left leg) and sensitivity; the muscle strength was not evaluated to avoid intense efforts that may potentially aggravate the patient's lumbar pain. Taking into account the radiographic results, the physical therapist hypothesized an aggravation of symptoms due to potential medullar compression and for this reason we advised the patient to call an ambulance and return to the emergency unit. At the emergency hospital, the physician decided to perform a computed tomography scan (CTs), which revealed a burst fracture of the first lumbar vertebrae with a spinal cord compression [Figure 2]. The patient was immediately taken for surgery and an arthrodesis surgery with percutaneous stabilization was performed with pedicle bars and screws T12-L2 [Figure 3].

6. Outcome And Follow-Up

Two days after spinal surgery, the patient started to walk with a front-wheeled walker and began an active and active-assisted mobilization of the lower limbs. [49] Five days after spinal surgery, the patient was discharged with pharmacologic therapies (Heparin, Ceftriaxone, Ibuprofen, Tramadol) and was referred for physical therapy in order to fully regain function so he could return to work activities and running. After spinal surgery, the patient's symptoms decreased gradually (one week), especially LBP and numbness in the lower limbs. From the second week after surgery, the patient started physical therapy, completing a total of 30 visits over the course of 48 weeks. The large number of visits over an extended period of time was agreed with patient, who decided to pay individually for treatment aimed at returning to run. The details of physical therapy programs are reported below. Patient follow-up was performed up to one year after surgery. In the first phase (time: 2 weeks, total: 6 visits, scheduling: 3 visits each week), manual therapy (i.e. passive joint mobilization, stretching, myofascial release and mobilization with movement) directed to the region of the thoracic and lumbar spine, was performed to improve full aROM and to relieve pain. Relief of pain should be a priority in order to build the patient's confidence and facilitate active engagement to optimize long-term outcomes. [50-56] In the second phase (time: 3 weeks, total: 9 visits, scheduling: 3 visits each week) the patient was instructed to perform an exercise program following the physical therapist's instructions. Exercises were dosed and progressed according to pain levels and number of repetitions reached. Subsequently (3 times/week for 3 weeks) the treatment program was progressively increased with functional exercises and load progressing from non-weight bearing to a weight bearing position following the patient's tolerance.

In this phase, functional exercises for motor control have been included: [57-59] i.e. bird dog (i.e. four point kneeling, pressing the hands and shins towards the floor with neutral lumbar spine); side bridge (i.e. side-lying with bent knees, pressing supporting forearm on the floor, or side sitting with upper knee upwards, pressing supporting hand down); single leg stretch; shoulder bridge; weight transfer, side lunge and one leg stand; "cat – cow – downwards facing dog". [57] Weekly meetings were scheduled to ensure proper execution of exercises and gradual progression of loads (i.e. side-lying hip abduction, supine two-leg bridge, plank, etc.). [54]

Evidence [59,60], suggests functional exercises ameliorate motor control strategies with short-term effects [58] redistributing the neuromuscular activities within and between muscles, decreasing aberrant movements, and improving the motor pattern variability of the thoraco-lumbar junction. [60] However, recent motor control theories, [60-64] suggest the adoption of functional exercises for long-term effects aimed at [60]: 1) increasing the overall load capacity of the spine; 2) enhancing the ability to perform activities of daily living and 3) improving patients' self-efficacy. [59]. Therefore, functional exercises represent a new way for physical therapists to reduce the recurrence and to alleviate the persistence of pain after a spinal fracture. [60] In the third phase (time: 12 weeks; scheduling: 5 sessions per week; details: alternating walking and running, with two rest days), a graded running retraining program was initiated. [54-56] Various strategies required consideration such as: 1) increasing step rate; 2) reducing overstride, 3) altering the strike pattern, 4) reducing impact loading variables, 5) increasing step width and 6) altering proximal kinematics. The primary goals of these strategies was to optimize the dosage of loading stress to reduce the risk of RRIs even if it does not always lead to an improvement in the running biomechanics immediately upon implementation [Figure 4]. [54-56,65-69] The physical therapy program was balanced with other interventions to include the management of psychosocial aspects of the pain experience, negative illness perceptions, education, maladaptive cognitions, coping strategy [50-53,60]

7. Discussion

In accordance with clinical guideline, [47] LBP is usually considered a musculoskeletal disorder with a positive prognosis commonly treated by physical therapist using education, manual therapy and exercises. However, in a low percentage of cases LBP could be secondary to a serious pathology, such as malignancy, infection, cauda equina syndrome or fracture. [24-27] In the literature, the most common of serious spinal pathologies, which may initially manifest as LBP, is vertebral fracture. [24-27]

From a clinical perspective, the aim of this case report was to discuss the relevant aspects of the screening, the differential diagnosis and the therapeutic management concerning the severity of fracture of thoraco-lumbar junction in a runner presenting as back pain in a direct access physical therapy setting. Authors have observed, in this case report, that the most common of serious spinal pathologies among runners, which may initially manifest as LBP, is vertebral fracture. [24-27]

Among the athletes that the physical therapist regularly evaluates, runners, both recreational and competitive, enjoy running as it is one of the most popular sports activities practiced all over the world. [1,2] Physical therapists routinely assess patients and athletes whose primary complaint is back pain alone, [24-30] but when the clinical presentation is not clear, other clinical conditions must be considered with attention to an accurate process of clinical reasoning and screening for referral. [25,31]

The ability to recognize a serious pathology is a key component of physical therapist practice. [29] Differential diagnosis in physical therapy practice is the result of a complex process of clinical reasoning and decision-making encompassing the patient’s history, physical examination, and results of imaging when ordered. [70] Clinical reasoning improves the diagnosis rate of each system if a systematic approach is performed on each patient. [70] The patient's history is a milestone in the evaluation of physical therapy to obtain information on the clinical conditions of patients with apparent musculoskeletal disorders, [71] facilitating the therapist to improve or reduce the likelihood ratio of serious pathologies. [72]

In this case report, various elements of the patient’s in history, have been collected (i.e. trauma, pain intensity, numbness of the lower limbs, supine positive sign) and included in the clinical reasoning process in order to guide the consequent physical examination. [73] Physical therapists must ask themselves questions through self-reflection during assessment and treatment to identify the presence/absence of risk factors. [74]

In particular, in presence of a change in patient’s clinical situation (i.e. aggravation of symptoms), the time until care is rendered by the physical therapist can significantly change the patient's medical prognosis. This occurred in this case and may have resulted in in a life-changing clinical presentation like cord compression due to fracture. [75,76] It is important to remember that less than 5% of Primary Care Physicians routinely examine for Red Flags during an initial screen. [38]

This case highlights the importance of a thorough physical assessment in the presence of an atypical clinical presentation. The patient's history, clinical pattern of pain presentation and confirmation by imaging led the physical therapist to matching an effective intervention to the patient. This case report describes the history, assessment and treatment of a runner with a serious LBP caused by a vertebral fracture that was exacerbated with running.

After surgery, treatment focused on education and loading the tissues over many weeks through a graded program of loaded functional exercises and running retraining. In the running retraining there is a strong need to pay attention to: the specific capacity of the structure during the progression of sessions; the cumulative load of the structure for the current session; the reduction of the specific capacity of the structure during a session in progress, and not exceeding the specific capacity of the structure and running at the regular pace. [54-56,65-69,77,78] Indeed running speeds below 12km/h, seem to be ideal and reduce the risk of injury of the joint. [77,78] It is important to note that the patient was educated on his clinical condition, the neurophysiology of pain that influenced his behavior and conception; the knowledge of lumbar anatomy, surgery and the running retraining. This approach has enforced and improved his expectation to expect full recovery which motivated the patient to strive towards a better outcome. [50-53] Pain education and exercise positively influenced the patient in terms of pain modulation. This case report encourages physical therapists to use biopsychosocially-oriented treatments to obtain good outcomes and facilitate return to running in a patient with a thoraco-lumbar fracture that was ultimately stabilized with surgery. [50-53] In summary, this case report describes the clinical condition of a recreational runner presenting with post traumatic thoraco-lumbar fracture, thus highlighting the importance of appropriate screening for physical therapists to facilitate the identification of potential pathologies that masquerade as a musculoskeletal condition by performing a thorough clinical examination. [31]

Figure 1:

Radiograph showing a closed compression fracture of the first lumbar vertebrae without involvement of the spinal cord (yellow arrow).

Figure 2:

CT images showing a comminuted, burst fracture of the vertebral body of L1, with displaced fragments of the right and posterior walls, and a displaced fracture of the anterior vertebral wall with loose fragments in the vertebral canal, impinging on the dural sac. Also shown, are fractures of the right pedicle and left lamina next the spinous process. Left side: Axial plane; right side: sagittal plane (yellow arrow).

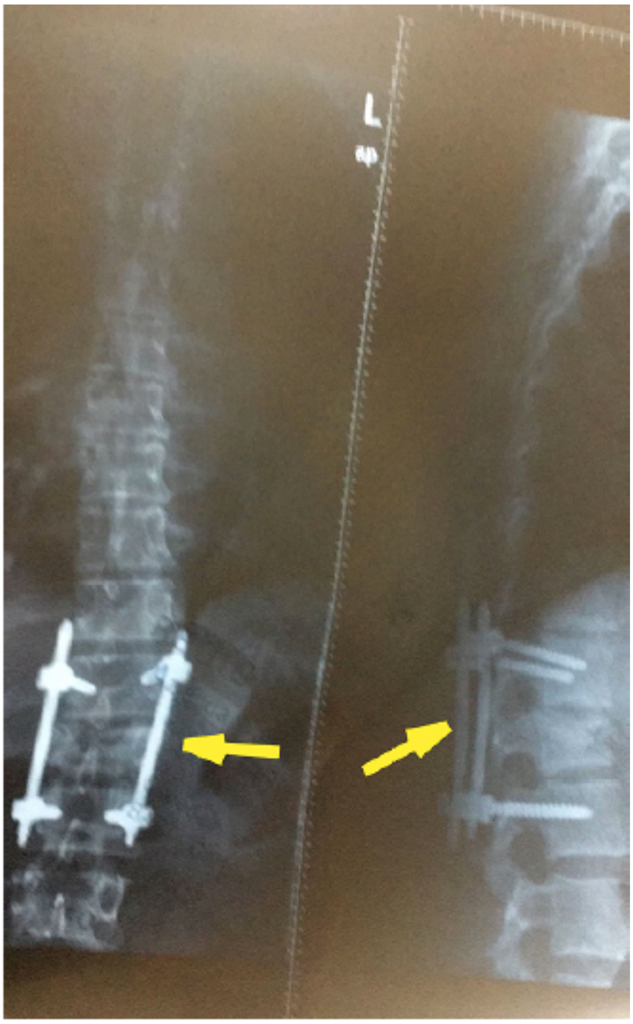

Figure 3:

Radiograph showing open reduction and internal fixation of the L1 vertebral fracture with stabilising pedicle bars and screws D12-L2; left side: posterior view; right side: sagittal view.

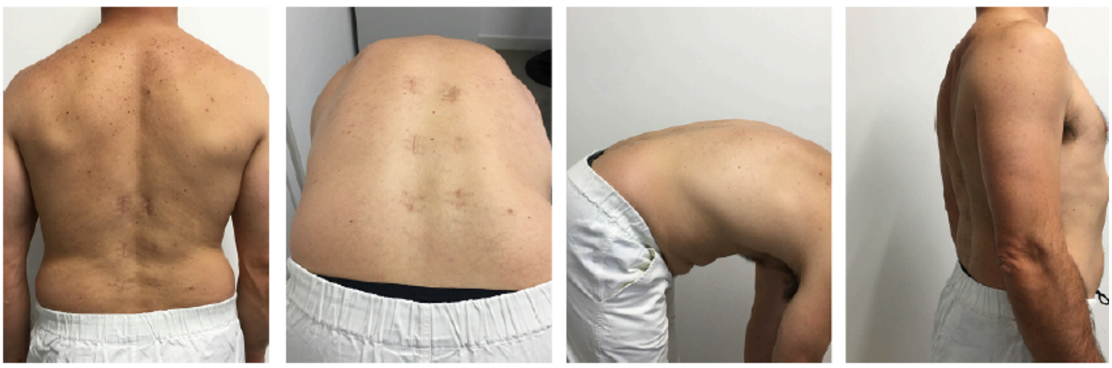

Figure 4:

Photographs of the patient in a standing position and performing forward flexion movements.

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LOW BACK PAIN AND CALF PAIN IN A RECREATIONAL RUNNER MASKING PERIPHERAL ARTERY DISEASE: A CASE REPORT

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Low Back Pain and calf pain in a recreational runner masking Peripheral Artery Disease: a case report

Abstract

Background: Running is one of the most popular sports worldwide due to its low costs and its beneficial impact on health. Recent evidence suggests 11% to 85% of recreational runners experience at least one running-related injury each year and most of these are related to musculoskeletal conditions. The aim of this case report is to describe the clinical decision-making process that guided a physiotherapist to suspect a non-musculoskeletal cause in a recreational runner presenting with low back pain and calf pain secondary to Peripheral Artery Disease.

Case Presentation: This case report describes the clinical history, clinical exam, laboratory and imaging tests, and surgical procedure of a 65 y.o. amateur runner suffering low back pain and left calf pain for 3 months. The patient's clinical findings suggested that referral to another health-care provider was required to explore potential non-musculoskeletal sources of pain. An angioplasty was necessary to solve the patient's clinical situation. **Discussion and Conclusion:** In this patient case, clinical findings along with a comprehensive family and personal history, ruled out a musculoskeletal condition and implicated a vascular condition.

1. Background

Running is one of the most popular forms of sport activities in the world [1,2] secondary to the low cost of equipment and the beneficial impact on health ranging from the improvement of the cardiovascular system, the reduction of mortality risk, the reduction of the incidence of obesity, and the improvement of chronic health complaints [3]. The benefits of health associated with running are documented in the literature [2]. The awareness induced by media towards health, diet, fitness and competitive athletics has led to an increase in the level of individual physical activity, often without adequate preparation or training [1].

Despite researchers describing running as one of the most effective strategies to improve health and fitness, recent evidence suggests that it involves a relatively high risk of running related injury (RRI) [4]. Several studies have found that 11% to 85% of recreational runners experience a RRI every year [5], with a heterogenous incidence (3.6% to 79%) [3,6,7] and prevalence (3.5% to 92%), in middle-distance and long-distance runners [3,6-9], resulting in the reduction or need to stop training in 30% to 90% of cases [10]. The primary risk of running is the relatively high risk of lower extremity injuries [2]. Emergent research confirms that 80% of RRI are due to overuse resulting from a mismatch between the resistance capacity of supporting connective tissue and biomechanical loads that occur during running [11].

The RRI affects several body regions, particularly in the lower limb where the knee (42%), the foot and the ankle (16.9%), and the lumbar and sacral spine (3.4%) were the most frequently injured joints [12,13]. Evidence from research regarding RRI, has also indicated non-musculoskeletal system problems as contributing factors. For example, several researchers have investigated the relationship between cardiovascular risks (e.g., atherosclerosis) and running [14,15]. From a clinical perspective, the identification of runners at cardiovascular risk is challenging [16]. One study suggested that the higher prevelance of peripheral atherosclerosis in marathon runners is related to cardiovascular risk factors and to the coronary atherosclerotic burden which induces a significant remodeling of the peripheral arteries [17]. This suggests that marathon runners that are tasking their cardiovascular system need to be screened appropriately, as vascular conditions such as atherosclerosis and underlying potential cardiovascular risk factors may prevail in marathon runners [17]. The importance of considering and weighing each risk factor for vascular disease should be considered in the running population [16].

This case report describes the patient presentation and the clinical decision-making process that led a physiotherapist to suspect a non-musculoskeletal condition in a recreational runner presenting with Low Back Pain (LBP) and calf pain. From the authors' knowledge this is the first case report that describes a recreational runner presenting with Peripheral Artery Disease (PAD). The aims of this case report were: 1) to discuss the relevant concepts related to the pathophysiology, screening and differential diagnosis of PAD; and 2) to describe the relevant findings from the history and physical examination in a patient that presents with a condition that mimics a musculoskeletal presentation.

2. Case Description

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. Details of the patient's history are shown on the Timeline (see Figure 1). Three months before presenting to a physiotherapy private practice clinic, the patient was evaluated by a general practictioner (GP). The GP diagnosed the patient with LBP and radicular irradiation to the left leg and ordered lumbar magnetic resonance imaging (MRI) and physiotherapy for 20 visits. The initial physiotherapy management was performed for one month in another physiotherapy outpatient setting and included exercise for improving lumbar spine motion and physiotherapy modalities (e.g., TENS), but did not result in the patient improving the amount of pain in his back or within the left calf.

The patient presented to our outpatient rehabilitation clinic with low grade LBP (2/10 NPRS - Numeric Pain Rating Scale) and a constant disabling left calf pain (7/10 NPRS) with daily activities (see Figure 2 - Body Chart number 1). He was a 65-year-old man, retired farmer, and smoked 20-cigarettes/day since he was 16 y.o. The patient stated he initiated a recreational running program three years previous to this episode of care, training for 10 km 2-3 times/week.

The patient stated the LBP (2/10 NPRS) and calf pain started three months prior to seeking physical therapy. The patient's past medical history included similar episodes of LBP that previously resolved spontaneously without any specific treatment. This episode of care presented differently as the patient now reported 8/10 calf pain. The onset of calf pain was gradual and without apparent cause: at the initial onset of symptoms, the patient described the pain as 2/10, annoying, sporadic and intermittent pain. The patient stated that the calf pain increased with level of activity noting that every time he tried to run (about 8 km), to walk a lot (about 1 hour) or climb the stairs (about 3 floors), he felt the quality of the pain changed from annoying pain to a stabbing pain in his left calf that at times radiated to the plantar and medial side of the heel. He rated the calf pain on these occasions as 5/10 (see Figure 3 - Body Chart number 2).

The patient reported the LBP was stable and negligible, since onset three months presiously but the left calf pain increased in severity and became constant during the day and increased on the NPRS to a 7/10. The patient also noted an associated numbness sensation on the left foot specifially in the toes in the plantar zone. When the patient was questioned about the calf pain regarding what makes the calf pain worse, the patient noted that when he walked for a few minutes, the calf pain became so intense (NPRS 8/10) that he was forced to limp and required seated rest breaks until the calf pain decreased. The patient noted there was no difference in LB pain when comparing walking uphill or downhill but the patient did note that the calf pain increased as he walked uphill. The patient noted that the calf pain disappeared when he laid down on the bed and rested (NPRS 0/10) whereas the calf pain decreased (NPRS 2/10) when taking a seated rest break.

During the review of systems and medical history, the patient did not report symptoms of involvement of any other systems besides his back pain and calf pain. The patient did report a previous surgical procedure for a left rotator cuff tear 10 years prior and for a right inguinal hernia in nine years prior. The patient reported significant family history to include: myocardial infarction; lung cancer; and amputation secondary to severe PAD.

Two months prior to this examination and one month after the onset of pain, he stopped running, because his calf pain became severe (NPRS 8/10), affecting activities of daily living (ADL) and walking capacity. The intensity of his calf pain influenced the patient's decision to seek a second physical therapy opinion.

2.1 Clinical Examination

The patient was diagnosed by the patient's physician as having back pain with a radicular component referring to the left calf. The physiotherapist initially suspected LBP [18]. However, the physical examination of the patient did not fit the clinical pattern of this diagnosis. The patient's lumbar spine range of motion (ROM) was normal and almost pain free (NPRS 1/10) in end range active flexion and extension without exacerbation by overpressure or repeated movements. The findings of a neurological examination were not significant: no motor deficits were noted testing muscles of the lower extremity; and no sensory abnormalities were revealed by dermatomic light touch for epicritic sensitivity or by diapason for protopatic sensitivity. Lasegue's test was negative bilaterally and deep tendon reflexes were negative and comparable bilaterally. The patient shared the report from the imaging prescribed by his GP: the MRI scans for lumbar and the sacral spine revealed a "small left-convex scoliosis and L1 bulging disc". The negative clinical examination findings of the patient's lumbar spine were considered along with the imaging that reported findings that did not explain the patient's calf symptoms (L1 bulging and scoliosis). That is, the physiotherapist focused specifically on the symptomatic lower extremity to screen for non-musculoskeletal sources of the patient's pain [19,20].

2.2 Non-musculoskeletal System Screening

During inspection of the symptomatic lower extremity, the patient's left calf did not reveal edema, pitting edema sign, ecchymosis, or skin rashes or pigmentation abnormalities. There was no difference in temperature between the patient's lower extremities, decreased hair growth or evidence of capillary refill concerns. Neither shiny skin or nor hypertrophic nails were noted. An active standing evaluation for movements of hip, knee and ankle performed to assess impairments of mobility was negative for active ROM reduction or pain provocation. The patient was placed in a supine position and the physiotherapist performed a passive ROM evaluation for screening the hip, knee and ankle. Passive ROM was noted to be comparable between the lower extremities without evoking pain or discomfort. The stress test for plantar and dorsal flexion of the ankle did not elicit pain. A stabbing pain was noted with compression of the first one/third of left calf referred to as Pratt's sign. Pratt's sign is a simple test that may suggest suspicion of vascular disease but lacks sensitivity or specificity [20].

Based on clinical experience and the clinical examination and the non-musculoskeletal system screening, the physiotherapist had a high index of suspicion of lower extremity vascular compromise and determined that a pedal plantar flexion exercise test was appropriate for further examination [21]. Yamamoto et al. [22] compared treadmill walking to a pedal plantar flexion test. The authors reported that the pedal plantar flexion test may serve as an alternative to treadmill testing (r=0.74) in evaluating patients with intermittent claudication that are unable to handle treadmill testing. Sensitivity and specificity has not been reported to date for this test. This exercise/test was chosen compared to treadmill because: 1) a treadill was not available in our office practice; 2) the pedal plantar flexion test's diagnostic performance was similar to values recorded after treadmill exercises; and 3) the pedal plantar flexion test is a simple screening test to perform in the clinic [23] (McPhail, Spittell, Weston, and Bailey, 2001). The patient was asked to stand flat-footed and perform 50 sequential, symptom-limited calf raises to investigate the ability of the ankle plantar flexors to raise the heels maximally off the floor (McPhail, Spittell, Weston, and Bailey, 2001) [23]. During the exercise, the patient's calf pain was reproduced after the 8th repetition and the patient was unable to continue after the 12th repetition. The physiotherapist chose to assess the arterial pulses for acquiring more information about the lower limb vascular perfusion. Arterial pulses were present at the inguineal area, (2+) bilaterally. In comparing the right knee to the left knee, the pulse flow on the left appeared weak (1+) in comparison to the right side. No left dorsal foot arterial pulse was appreciated, scoring 0 as opposed to a 2+ or normal pulse. Although there is no sensitivity and specificity for the Pratt's sign and the pedal plantar flexion test, clusters of tests and the lack of normal arterial pulses in the lower extremity suggested that the pain the patient was having was more likely to be related to a vascular compromise than due to LBP.

The Ankle Brachial Index (ABI) is a quick and cost-effective strategy to establish or to refute compromised blood perfusion in the lower limbs [21,24,25]. An ABI evaluation has been validated and compared to angiography to determine its sensitivity and specificity as a lower extremity vascular diagnostic tool [26]. The diagnostic performance of an ABI has been well-established with a sensitivity of 91%, specificity of 86%, 6.5 positive likelihood ratios and 0.1 negative likelihood ratios [27]. Gerhard-Herman et al. [28] demonstrated that the ABI provides better discrimination than the absolute ankle pressure alone in distinguishing between normal limb arteries and those with lower extremity perfusion disease. Moreover, an abnormal ABI can suggest PAD and together these parameters are predictive of other conditions such as systemic atherosclerotic disease. Moreover, the presence of a low ABI is predictive of cardiovascular mortality with a relative risk of cardiovascular mortality in the low ABI cohort reported as increased by approximately 3- to 4-fold [29]. The formula that was used in this case report was "systolic ankle pressure/systolic arm pressure" as described by Fowkes [30] and reported in Table 1 [30].

Table 1. Ankle-Brachial Index (ABI) value interpretation (Fowkes et al. [30]

VALUES	INTERPRETATION OF ABI
>1.30	Non Comprensible
1.00 – 1.29	Normal
0.91–0.99	Border Line
0.41–0.90	Mild to Moderate PAD
0.00–0.40	**Severe PAD**

Note: ABI value's from Fowkes et al. [30]. Patient in this case report had a critical value indicating Severe PAD (in bold)

The resting ABI is used to establish the presence of a lower extremity PAD in patients with suspected lower extremity vascular compromise. The clinical diagnosis of a patient with PAD is defined as an individual with exertional leg symtoms with or without non-healing wounds, who are 50 years or older and have a history of smoking [28]. The patient presented in this case report met this definition. To perform an ABI evaluation, the systolic blood pressure is measured from different arteries of the lower limbs such as the dorsalis pedis and the posterior tibial arteries after a patient rests in supine for 10 minutes. These lower extremity systolic pressure measurments serve as the numerator in the index equation. The brachial systolic pressure from the upper extremity serves as the denominator. Interarm differences for systolic blood pressure of the left upper extremity was <12 mm/Hg (118 mm/Hg for right arm and 120 mm/Hg for left arm) indicating no subclavian or axillary arterial stenosis. The physiotherapist then measured the blood pressure bilaterally in both ankles. The right ABI measure was 1.05 mm Hg (normal values 1.00-1.29 mm Hg) and the left ABI measure was 0.40, indicating severe deficit of blood perfusion at the ankle [21].

Because the ABI evaluation was significant for the left lower extremity at rest, the physiotherapist avoided any further testing or evaluations. The physiotherapist asked the patient to complete the Italian version of the SF-36 [31], to assess the patients' subjective health status. The scale revealed a low value (20 points) with all the domains seriously compromised. During the anamnesis and the clinical examination, the patient presented a high self-efficacy, an adequate coping strategy, an active and a positive attitude: he was a man with a strong personality, active, with a medium-low cultural level, and with a supportive family. The patient appeared worried about his calf pain, mostly because it prevented him from running which he considered an important activity for his overall well-being. The patient's goals were to: 1) to heal completely, 2) to return to a normal life, and 3) to return to running.

2.3 Physical Therapy Diagnosis and Recommendation for Referral

Elements of the patient's medical and family history and clinical examination suggested to the physiotherapist that this patient needed to be referred for further testing. The findings of the musculoskeletal examination and systems screening suggested that the vascular system might be compromised and this needed further investigation by another heath professional. The patient was referred to a radiologist with a suggestion that screening of the arterial circulation via a Color Doppler Duplex Ultrasound (CDU) might be appropriate [21].

2.4 Diagnostic Imaging

A CDU investigating the arterial trunks of the lower limbs was performed by an interventional radiologist. The CDU report stated the following:

"right limb diffuse atheromas, but normal fluxes until tibial artery are present. Atheromas in the lower limbs at the arterial axes. On left lower limb, three-phase flow on common femoral artery and superficial femoral artery. Presence of calcific plaques with signifigant stenosis at the Hunter canal. After this point blood flow became demodulated in the popliteal artery, anterior and posterior tibial arteries. Computed Tomography scan (CT) for arterial flows for abdominal artery and lower limb's arterial axes and interventional radiology's assessment are suggested" (see Figure 4). The report of arterial CT listed the following findings:

"dynamic multislice volumetric technique during the administration of non-ionic water-soluble iodides as contrast substance. Subsequent reconstructions MPR (multiplanar reconstruction), MIP (multiplanar informations) and 3D (tridimensional volume rendering screening) in the radial coronal planes was performed. It revealed a diffuse arteriosclerosis on the lumbar aorta and its terminals characterized by intimal thickening and multiple calcific atheromatous plaques. Approximately 50% of stenosis on the ostium of the right common iliac followed by ectasia with medial extrinsic pseudoaneurysm before the internal and the external bifurcation. There was a 90% stenosis of the left superficial femoral artery at the junction with the poplitea area. At this level an anastomotic circle of popliteal compensation is observed, atheromatous calcification on the residual popliteal and reduced opacification of the anterior tibial and peroneal arteries with poor appreciation of the ipsilateral foot dorsal artery" (see Figures 5, 6).

3. Intervention

3.1 Medical Intervention

The radiologist diagnosed PAD with a "steno-occlusion of the left popliteal artery and recommended hospitalization for angioplasty". As suggested by the Clinical Practice Guideline of the American College of Cardiology/American Heart Association Task Force [28], the radiologist prescribed Clopidogrel, ASA (acetylsalicydic acid), and Ranitidine. Blood analysis was also performed revealing abnormal lab values. The lab values were as reported in Table 2.

Table 2. Lab exams and values interpretation.

lab exams	Normal values	Patient' values
triglycerides	< 150 mg/dl	**194 mg/dl**
total cholesterol (normal value	<200 mg/dl	**292 mg/dl**
cholesterrol HDL (High density lipoprotein)	51 mg/dl	**>56 mg/dl**
cholesterol LDL (Low density lipoprotein)	<100 mg/dl; (*values > 190 mg/dl suggested coronaric cardiopathy assessment rate)	**226 mg/dl**

GFR (glomerular filtration rate)	>90 ml/min/1.73m^2	**78 ml/min/1.73m^2**
Total protein	6.6-8.8 g/dl	**6.3 g/dl**
Albumin	55.8-66%	**66.9%,**
Gamma Globulins	11.1-18.8%	**9.6%,**
Albumin/globulins rate	1.08-1.86	**2.02**

Note: Blood analysis performed revealing patient's abnormal values (in bold). mg/dl: micrograms/decilitre; ml/min/1.73 m2: milliliters/minute/1.73 square meters; g/dl: grams/decilitre.

In accordance with the clinical guideline of Gerhard-Herman et al. [28] an angioplasty was performed (see Figures 7, 8). The surgical procedure led to a return of an optimal perfusion of the left limb. The patient had a 2-day hospitalization without complications and was discharged from the hospital. Ten days post operation, the surgeon noted blood perfusion control with the CDU and reported: "follow-up of popliteal artery angioplasty. Bilaterally loose the femuro-popliteal arterial flows, with atheroma and three-phasic flows" (see Figure 9, 10). Secondary to the excellent results of clinical observation of the patient and corresponding CDU results, the surgeon recommended a follow-up visit in 6 months and iniated physiotherapy for a progressive and gradual resumption of working and sporting activities.

3.2 Physiotherapy Intervention

The patient came back to the physiotherapy private practice clinic 15 days after surgery. He was referred with an absence of LBP (0/10 NPRS) or calf pain (0/10 NPRS) that dissipated one week after surgery. Three days following surgery, he started to walk daily for 20 minutes. During the visit, the physiotherapist assessed arterial pulses and reassesedthe patient with the pedal plantar flexion test and ABI. Arterial pulses were present in the inguineal area, popliteal fossa and at the dorsal foot equally (2+). The patient's performance of the pedal plantar flexion test was 40 sequential calf raises without any symptoms and the last 10 repetitions were with little effort but no pain, showing a improvement from the first visit. ABI values were border line (0.96) (Table 1). Therefore, the patient started a supervised physiotherapy program composed of supervised exercises and home non-supervised exercises: concentrating on the patient's capacity to to improve walking distance, quality of life, and functional status. All of these items are considered important for a comprehensive biosocial functional restoration program for patients post-lower-limb bypass surgery [32]. Among patients with PAD, quality of life is reduced and the distance walked is impaired, affecting the overall ability to meet the personal, social, and occupational demands of daily living [32]. Therefore it was indicated to adopt this training aimed at improving the patients' functional capacity.

The physiotherapy program was composed of a warm-up phase of 5–10 min with dynamic breathing and stretching exercises and then track walking, stair climbing, treadmill exercise; at the end of 45 minutes section, a 5–10 min cool-down phase of static and dynamic breathing and stretching exercises. In accordance with Haas et al. [33], intensity of training was established between 60%–85% of maximum heart rate. Exercises were performed for a minimum of 30–45 min/session at least 3 times/week for 12 weeks [34,35].The physiotherapist provided home recommendations such as walk for at least 30 min/day, three to five times a week, and to increase walking time as often as possible [32].

4. Outcomes

The patient returned to running 4.5 months after surgery at his pre-injury level. At the last visit (three months after surgery), the patient completed an SF-36 questionnaire, resulting in a score of 62 points. The SF-36 showed improvements in psychological, physical pain and general health domains. Furthermore, the patient completed the SF-36 before returning to running and scored a high level of health status (87 points).

At the end of 6 months of follow-up, the patient stated that at the initiation of physiotherapy he did not think that his calf pain would dissipate and he would be able to reach his goals to return to normal and run again. The impact of this situation led the patient to diminish and eventually stop smoking. The patient expressed gratitude to both the surgeon and the physiotherapist for the efficient but complete assessment and referral to a specialist for further investigation.

5. Discussion And Conclusion

In this case report, correlation between the patient's symptoms and the lower limb musculoskeletal presentation did not match the clinical examination. This inconsistancy suggested the need to carefully consider other serious clinical conditions through a process of screening and differential diagnosis [36]. The anamnesis is a milestone in the assessment for the physiotherapist working in an outpatient clinic setting for obtaining information about patients with apparent musculoskeletal dysfunction [37]. Different anamnestic elements were collected (e.g., characteristics of symptoms, mechanisms of pain, expectations and psychosocial factors of patients), weighed and included in the clinical reasoning process and guided the subsequent physical examination [38]. The use of the acronym VINDICATES is useful for clinicians to consider systems or elements that need to be screened. VINDICATES stands for Vascular, Inflammatory, Neoplastic, Drugs, Infectious, Congenital, Autoimmune, Trauma, Endocrine, and Psychosocial. This diagnostic reasoning mnemonic tool was used in this case and led immediately to referral of this patient. In this case, the patient met the criteria for an increased risk of PAD [39]: age 50–64 years; risk factors for atherosclerosis (e.g., diabetes mellitus, history of smoking, hyperlipidemia, hypertension) with a family history of vascular diseases (e.g., father’s heart attack and his sister’s foot amputation secondary to PAD); walking impairments; leg discomfort with exertion and “non-injuries related limb symptoms” [40, 41]. In accordance with the Clinical Practice Guideline of the American College of Cardiology/American Heart Association Task Force [28], the patient’s history, clinical presentation, and positive ABI score suggested the need for an accurate clinical evaluation to rule-out vascular pathology. PAD encompasses a range of non-coronary arterial syndromes that are caused by an altered structure and function of the arteries supplying the brain, visceral organs, and limbs [21]. Atherosclerosis is the most common cardiovascular pathophysiological process [42], representing an important consideration in the differential diagnosis of lower extremity pain in outpatient physical therapy for primary musculoskeletal-like symptoms [43]. Particularly, in a patient that presents with a similar clinical presentation as lumbar pain with radicular symptoms, when the initial diagnosis is erroneous. Time can significantly change the evolution of a patient's medical history and, as reported in this case, an even later diagnosis could result in a life-changing patient outcome such as a stroke [44]. The clinical manifestations of PAD are a major cause of acute and chronic illness associated with a reduction in functional capacity and quality of life. In extreme cases PAD may cause: limb amputation; ischemic renal failure; mesenteric ischemia; aneurysmal rupture; myocardial infarction; stroke and potentially death [45]. Running at the right pace is beneficial [46]. Running speeds below 12 km/h seems to reduce the risk of musculoskeletal injuries in the lower limb joints, expecially at the knee and ankle [47]; however clinicians need to consider an active runner's individual The possibility of cardio-circulatory disorders capable of mimicing a musculoskeletal disorder must be considered in the process of differential diagnosis [48]. Despite the fact that habitual endurance exercise improves the cardiovascular risk profile, it does not preclude the risk for damage of the cardiovascular system [49]. Clinical reasoning improves the rate of diagnosis of each system if a systematic approach is conducted on every patient. A systematic approach decreases the rate of consequences related to vascular diseases such as PAD. Morevoer the investigation of anamnestic data such as smoking, diabetes, hyperlipidemia, dyslipidemia, patient and family history [14-16] are very important risk factors to consider especially in an outpatient setting. Physiotherapists need to query patients about these risk factors as many patients may not offer this information or may not consider this important to share with the physiotherapist. Laboratory analysis data are also important: lipid abnormalities that are associated with lower extremity PAD include elevated cholesterol values (total and LDL), a decreased HDL cholesterol, and hypertriglyceridemia [50-52]. In the clinical presentation, the observation of claudication is considered the symptomatic marker of lower extremity PAD. Clinical tests such as an abnormal ABI along with vital signs such as blood pressure measurements facilitate clinical assessment [21]. It is important to consider that physical activity and training must be adapted to the individual's state of health and cardio-respiratory risk [53]. Physiotherapists should carefully consider the impact of a cumulative exposure to cardiovascular risk for smoking, being overweight, abnormal laboratory values, and pre-existing activity levels [54]. The association between atherosclerosis and the initiation of a running program is gaining recognition [17]. Physiotherapists can play an important role in the prevention of atherosclerosis by educating their patients about these concerns and by determining the risk profile of their patients to provide appropriate advice to those who are considering initiation of a running program [1]. In summary, this case report highlights the need for physiotherapists practicing as primary care clinicians to facilitate the identification of potential pathologies that masquaerade as a musculoskeletal condition by performing a thorough clinical examination [55]. Physiotherapists should complete a comprehensive history and be competent in screening for non-musculoskeletal medical conditions using tools such as VINDICATES. This approach avoids the delivery of physiotherapy that does not benefit the patient, may avoid harm to the patient, or may delay appropriate care.

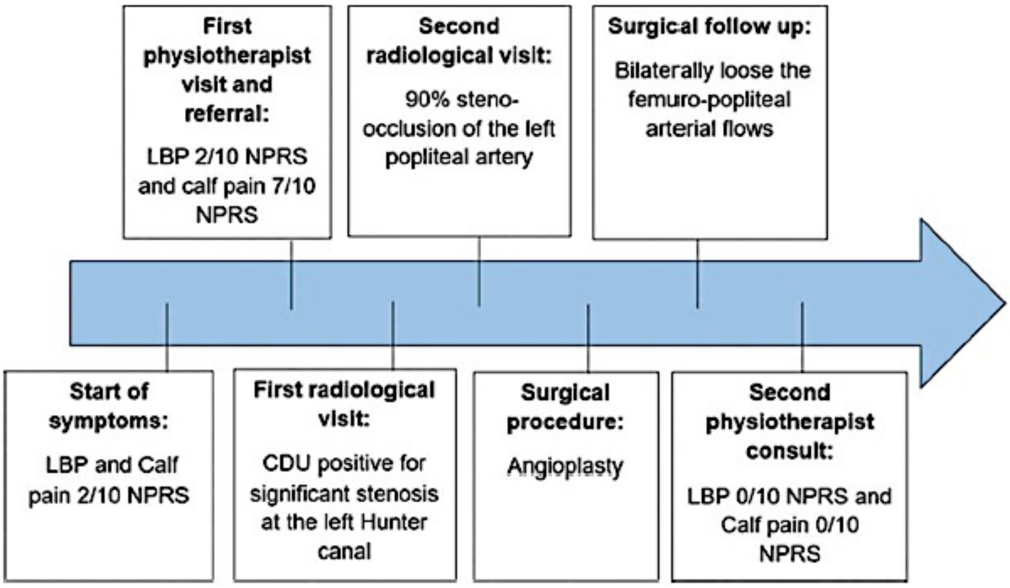

Figure 1: TIMELINE. (Note: Patient's history evolution from the physiotherapist's initial visit to discharge).

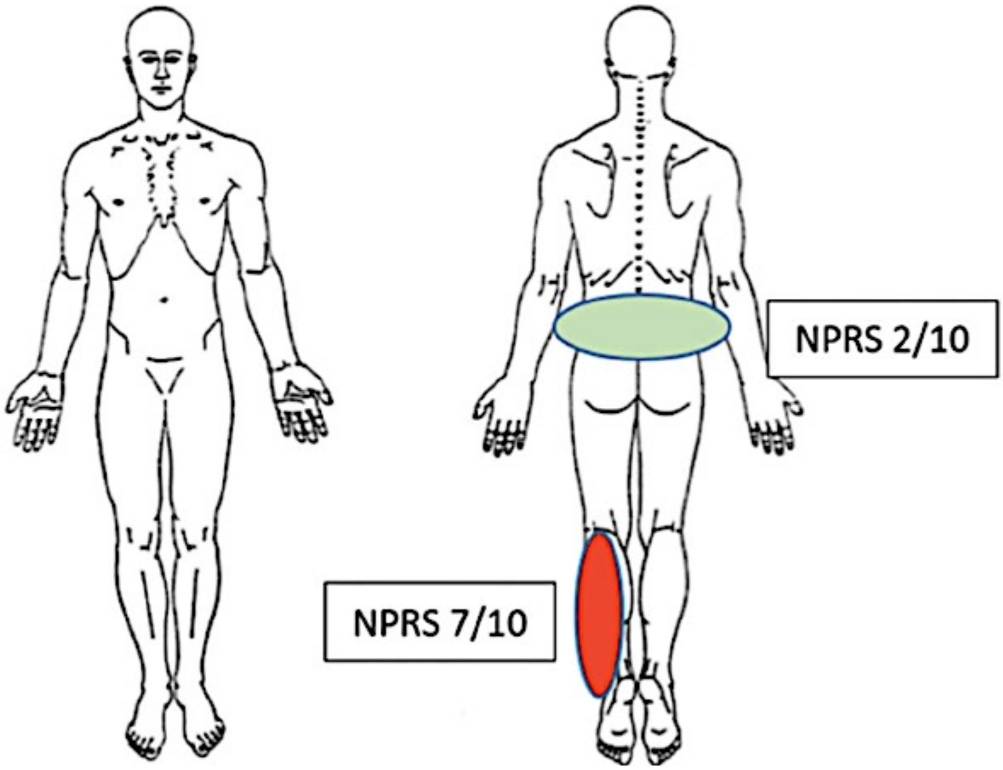

Figure 2: BODY CHART number 1. (Note: Body chart of the patient at access in author's outpatient rehabilitation clinic).

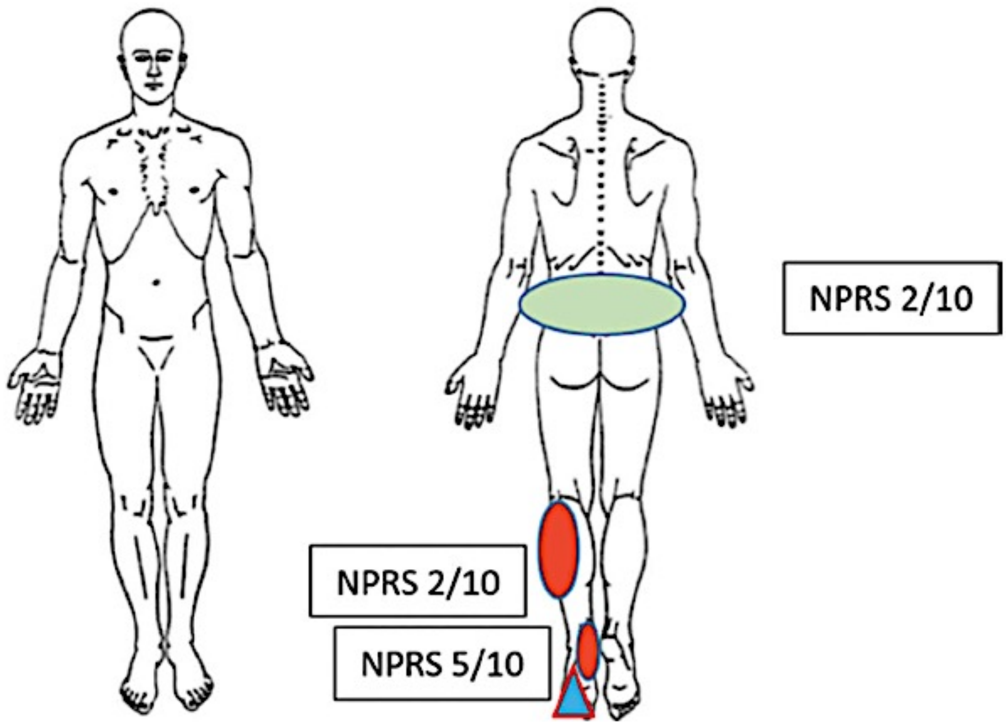

Figure 3: BODY CHART number 2. (Note: Body chart of the patient at the beginning of clinical history. Blue triangle stans for numbness).

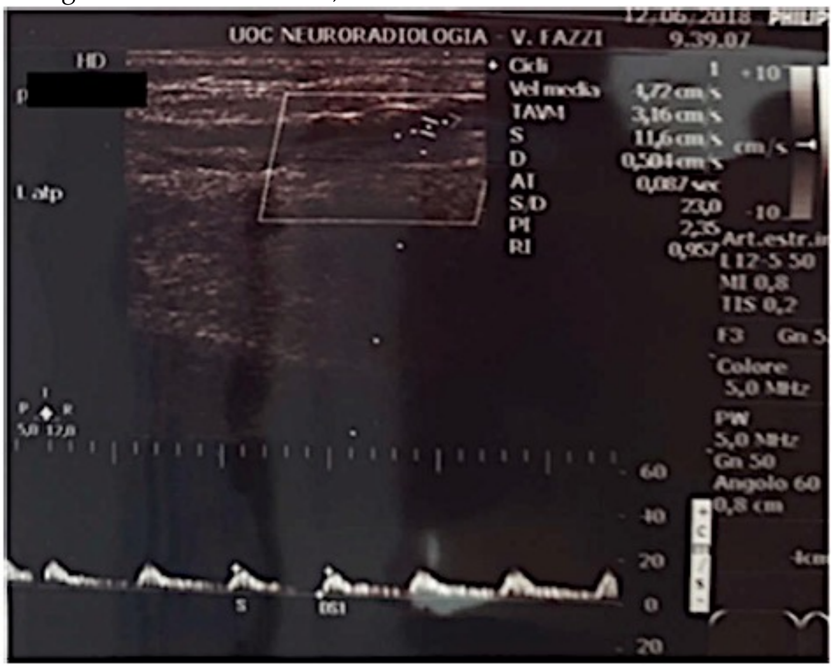

Figure 4: Findings from Color Doppler Ultrasound examination.(Note: on right limb diffuse atheromas but normal fluxes until tibials artery are present. Atheromas in lower limbs arterial axes. On left lower limb three-phase flow on common femoral artery and superficial femoral artery. Presence of calcific plaques with significative stenosis at Hunter cantal. After this point, bloody flows became demodulated in the popliteal artery, anterior and posterior tibal arteries).

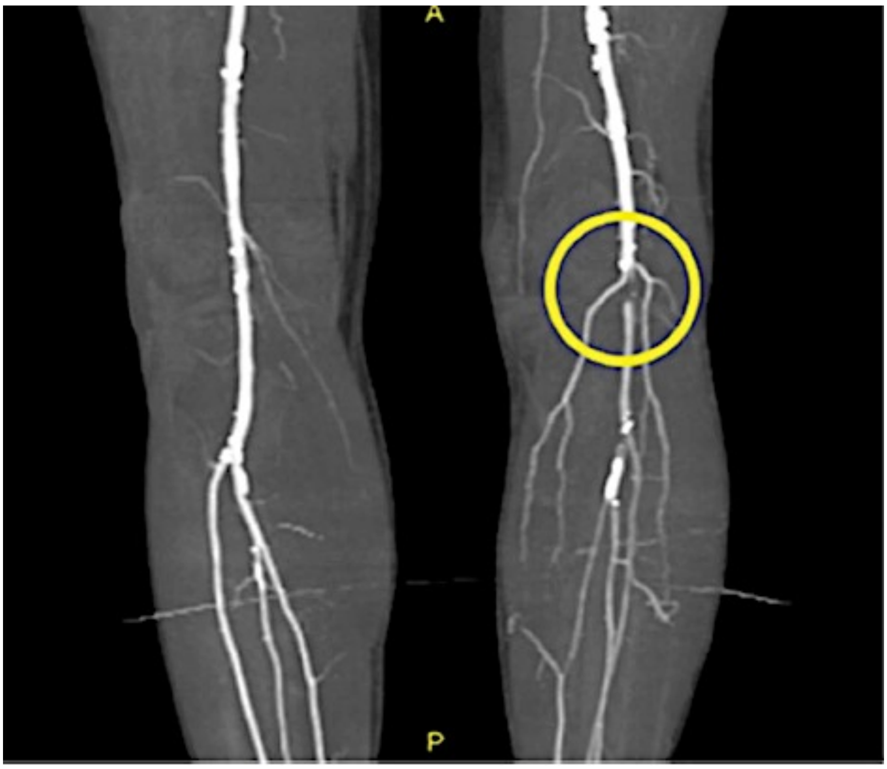

Figure 5: Findings from Tomography scan (Orizzontal plane). (Note: Orizzontal plane. Stenosis at about 90% of left superficial femoral artery at the junction with the poplitea area. At this level an anastomatic circle of popliteal compensation is observed, atheromatous calcification on the resudial popliteal and reduced opacification of the anterior tibal and peroneal arteries with poor appreciation of the ipsilateral foot dorsal artery).

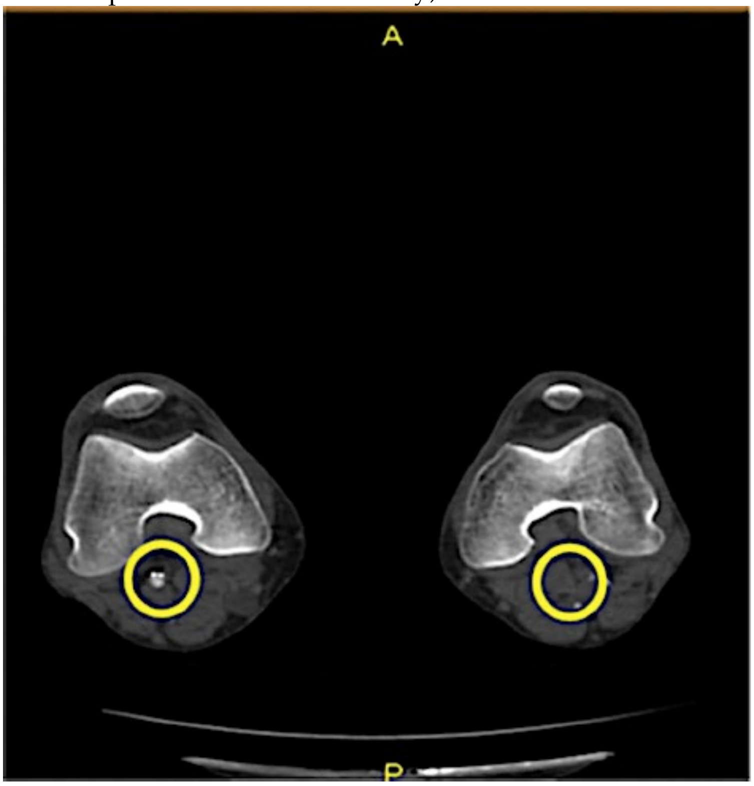

Figure 6: Findings from Tomography scan (Transverse plane). (Note: Transverse plane. Stenosis at abut 90% of left superficial femoral artery at the junction with the poplitea area. The artery is not appreciable in this scan in its position behind the knee).

Figure 7: Angioplastic procedure. (Note: Angioplastic procedure of the left popliteal artery).

Figure 8: Findings from angioplastic procedure. (NOTE: Blood perfusion permitted after the angioplasty.

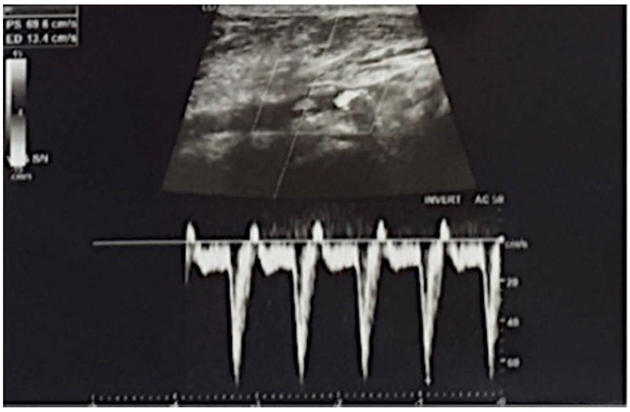

Figure 9: Findings from Color Doppler Ultrasound examination follow-up (pulse). (Note: Follow up of popliteal artery angioplasty. High intensity of arterial flow stated the patency of the vessel).

Figure 10: Findings from Color Doppler Ultrasound examination follow-up (flow). (Note: Follow up popliteal artery angioplasty. Bilaterally loose the femuro-popliteal arterial flows, with atheroma and threephasic flows).

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SUPERFICIAL PERONEAL NERVE SCHWANNOMA PRESENTING AS LUMBAR RADICULAR SYNDROME IN A NON-COMPETITIVE RUNNER

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Superficial Peroneal Nerve Schwannoma presenting as lumbar radicular syndrome in a non-competitive runner

Abstract

Introduction: Running is one of the most common sports practices in the world due to the beneficial impact on the health, despite the relatively high risk of getting injuries. In fact, running is one of the most common sports capable to induce overuse injuries of the lower back and leg. In previous studies, the symptoms in the lower limb have been attributed to lumbosacral degenerative pathology. When the symptoms are unclear, they must be studied with great attention by carrying out an accurate process of screening and differential diagnosis.

Materials and Methods: A 42-year-old non-competitive male runner who complained of left leg pain was referred to a physiotherapist. He reported a continuous, deep, sharp, shooting pain of the left leg. The symptoms began one year earlier. Symptoms worsened during prolonged driving and long distance running. The patient had been previously diagnosed with lumbar radicular irradiation in the leg by a general practitioner. Initial management, in another physical therapy outpatient setting, was without any improvement.

Results: After surgical excision, symptoms gradually regressed shortly and the patient was referred to a physiotherapist in order to fully recover and restore work and running activities.

Conclusion: This case report describes the history, assessment and treatment of a runner with a rare cause of leg pain. After surgery excision, treatment focused on education and loading the tissues over many weeks through a graded

program of loaded exercises and running retraining.

1. Introduction

Running is one of the most common sports practices in the world, due to the low running costs and the beneficial impact on the health ranging from the improvement of the cardiovascular system and the reduction of mortality risk to the reduction of the incidence of obesity and the improvement of many chronic health problems [1,2]. The importance induced by the media concerning health, diet, fitness and competitive athletics has brought an increase in levels of physical activity even in subjects without preparation and training methodology [3], thus identifying the relatively high risk of getting injuries as the primary drawback of running [1,2]. In fact, running is one of the most common sports capable to induce overuse injuries of the lower back and the leg [4]. In particular, the incidence of lower extremity injuries in runners ranges from 19.4% to 79.3% [1]. The most common diagnoses for pain in lower leg include dysfunctions such as patellofemoral pain; medial tibial stress syndrome (shin splints); achilles tendinopathy; iliotibial band syndrome; plantar fasciitis; and stress fractures of the metatarsals and tibia [1,5–8]. In other cases, the symptoms in the lower limb have been attributed to lumbosacral degenerative pathologies [9–11] such as low back pain (LBP) or lumbar radicular syndrome [12]. LBP and radicular syndrome are considered benign conditions and are usually managed quite easily [13,14]. When the symptoms are unclear, these clinical conditions must be considered with great attention by carrying out an accurate process of screening and differential diagnosis [13]. In fact, in this case the correlation between symptoms and serious pathology was not always clear and the lumbar radicular syndrome could delay the diagnosis and more appropriate treatment. This case report represents an emblematic example. The patient presented symptoms in the lower left leg and had been diagnosed with LBP with radicular syndrome, but it turned out he was affected by schwannoma in the superficial peroneal nerve.

2. Case presentation

A 42-year-old non-competitive male runner who complained of left leg pain was referred to a physiotherapist. He reported a continuous, deep, sharp, shooting pain and a superficial burning sensation in the anterolateral aspect of the left leg. The symptoms began one year earlier with an insidious onset and were not associated with any trauma or injury. Symptoms worsened during prolonged driving and long distance running (i.e. 10–15 km). Symptoms began in concomitance with the start of the running training, and pain was almost constant with an intensity of 7/10 at Numeric Pain Rating Scale (NPRS) [15]. The patient was previously diagnosed with LBP and radicular irradiation in the leg by a general practitioner (GP) that prescribed a lumbar Magnetic Resonance Imaging (MRI). Initial management, in other physical therapy outpatient settings, included physiotherapy (lumbar massage, exercise for lumbar spine), physical therapy modalities (i.e. tens), and spinal manipulation, all without any improvement.

2.1. Physical assessment

During the history examination, the patient reported a previous episode of LBP in the past, but noted that it always resolved spontaneously without any specific treatment. In fact, he presented LBP with an intensity of pain of 1-2/10 NPRS. Our physical examination did not reveal any impairments on the lumbar spine (range of motion (ROM)) were normal and the pain was not exacerbated by back movements or coughing). Neurological examination was also normal; no obvious motor or sensory deficit was noted, Lasegue's test was negative and osteotendinous reflexes were normal. Furthermore, the patient was healthy and had no past medical problems. Furthermore, the MRI scans of his lumbar and sacral spine were normal. To make a diagnosis, the lumbar spine was excluded and the screening process focused specifically on the leg. Additional provocative and functional tests were performed on the symptomatic leg. The fulcrum sign, single leg hops and peroneal percussion test were negative and the ROM of the knee and ankle were normal. However, there was a significant increase of the familiar patient symptoms during superficial palpation close to the fibular head and during resisted dorsiflexion of the foot. An accurate local deep palpation of the upper third of the anterior part of the left leg, around the fibular head, revealed an isolated oblong soft-tissue mass sensitive to percussion, which has been gradually increasing in size for more than one year but was never mentioned by the patient in other medical examinations. A nodular formation in the soft tissue raised the suspicion of a neurinoma of superficial peroneal nerve [9,14,16].With this diagnostic hypothesis the patient was referred for ultrasonography that showed an oval formation in proximity of the fibular head (Figure 1). A successive MRI (Figures 2 and 3) confirmed the diagnosis of neurinoma of peroneal nerve.

2.2. Therapy and evolution

After surgical excision of the neurinoma (Figure 4), symptoms gradually regressed and the patient was referred for physical therapy in order to fully recover and restore work activities and running. A schwannoma of superficial peroneal nerve was diagnosed through histological analysis. The patient completed a total of 12 visits over the course of 24 weeks. In the first phase, manual therapy (passive joint mobilization and mobilization with movement) was performed for restoring the full knee and ankle range and pain relief. The patient visited three times a week. Relief of these symptoms should be a priority in order to gain patients' trust, to facilitate active engagement and to optimize long-term outcomes [17]. In the second phase, the patient was instructed to undergo an exercise program. He was asked to perform prescribed exercises three times a week for three weeks. Exercises were dosed and progressed according to pain levels and the number of repetitions reached. Subsequently, three times a week for three weeks, the treatment program aimed to progressively increase the exercises functional demand and load, progressing exercises from no-weight bearing to weight bearing. Weekly meetings were scheduled to ensure proper execution of exercises and gradual pro gression of loads [17]. In the third phase, in line with the literature, the running retraining program was performed [18] for five weeks. Various options required consideration, including strategies to step rate manipulation, reduce overstride, altering strike pattern, reducing impact loading variables, increasing step width and altering proximal kinematics. In fact, by optimizing the amount and frequency of loading stress, injuries could be avoided [4]. The patient received a personalized running program over 12 weeks (five sessions per week, alternating between running and walking, with two rest days between).

3. Discussion

Schwannoma, also called neurinoma or neurilemmoma, is a benign peripheral nerve sheath tumor [9], and is the most common of its sort [19–21]. They make up 5% of benign soft tissue tumors [16], and are frequently seen between the ages of 20 and 50 [16]. Cases of common peroneal nerve schwannomas are very rare in the literature [16], and diagnosis can be delayed for a long period of time, since symptoms are usually attributed to lumbosacral degenerative pathology [9–11]. Schwannomas usually have a clinically silent course, though the present case highlights how a peroneal nerve schwannoma can become symptomatic due to mechanical compression, resulting in pain, swelling or a lump [16]. A mismatch between the resilience of the viscoelastic properties of the connective and supporting tissue during running [22] and an increase in levels of physical activity without preparation and training methodology [3], could have triggered the symptoms in this case report. In fact, literature confirmed that patients after changing their load rapidly cause a deterioration of their symptoms [23], given the dynamic nature of the relationship between applied stress and injury [4]. Schwannomas are benign lesions and their surgical excision is generally definitive and malignant transformation is rare [16].

4. Conclusion

In sports medicine, history and physical examination are considered the core for making the diagnosis [24]. A reliable diagnosis is important for both clinical practice and research. From a clinical practice and research perspective, it is important to identify lower leg injuries in a correct and reliable manner, as this may change the prognosis and treatment in practice, and may alter the eligibility of the candidate athlete for participation in a clinical trial. Therefore, it is important to consider differential diagnoses [24]. The current case highlights the importance of a thorough physical assessment in the presence of an atypical clinical manifestation as it specifically targeted the investigation by imaging and prompt investigation, which helped to make the correct diagnosis and initiate appropriate treatment. This case report describes the history, assessment and treatment of a runner with a rare cause of leg pain. After surgery excision, treatment focused on education and loading the tissues over many weeks through a graded exercise program and running retraining.

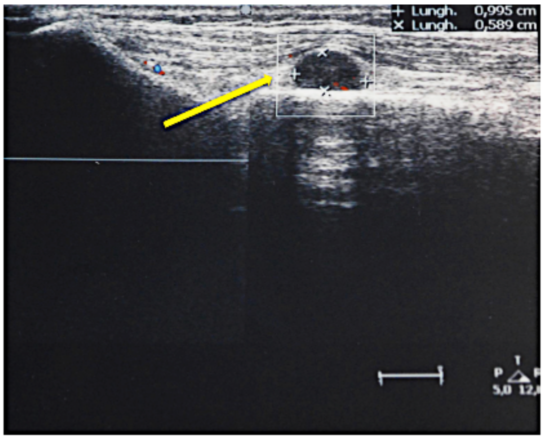

Figure 1.

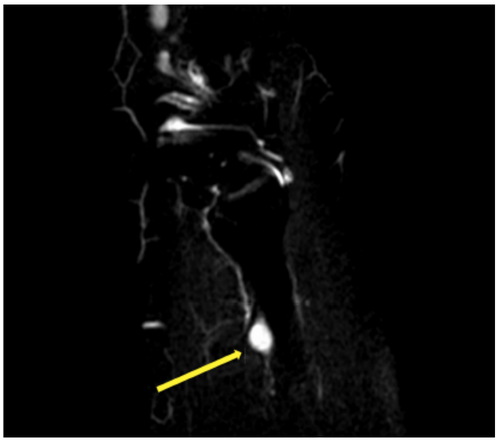

Figure 2.

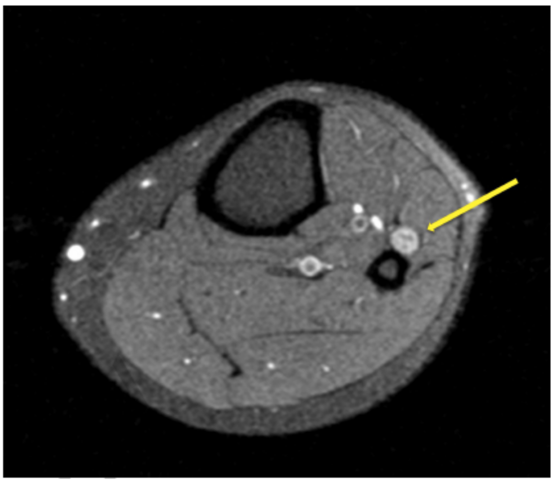

Figure 3.

Figure 4.

Figure 1. Longitudinal ultrasonography image reveals oval formation in proximity of the fibular head (yellow arrow).

Figure 2. Sagital view. MRI (in T2 with fat suppression) imaging studies of the patient's left leg. Tumor visible on the lateral leg compartment below the level of the left fibular head (yellow arrow).

Figure 3. Axial view. The Schwannoma with high signal intensity in T1 weighted axial left leg MRI. Tumor visible on the lateral aspect of the left fibular head (yellow arrow).

Figure 4. Lateral view. Scar of surgical excision in the left leg (yellow arrow).

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COULD A HAGLUND'S SYNDROME MIMIC A SCIATICA? A RARE CASE IN A LONG-DISTANCE RUNNER WITH 3 YEARS FOLLOW-UP.

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Could a Haglund's syndrome mimic a sciatica? A rare case in a long-distance runner with 3 years follow-up.

Abstract

Background and Purpose: Running is one of the most popular sport worldwide and running-related benefits are well documented in the scientific scenario. However, running also generates a substantial number percentage of running-related injuries (RRIs) such as plantar fasciopathy, ankle sprains and lower limb tendinopathies. Across all RRIs, overuse syndromes are common and characterized by repetitive loads on the foot often associated with various bony deformities, such as Haglund’s syndrome, which consists of an abnormality of the posterosuperior part of the calcaneus just lateral to the Achilles tendon. For both systemic and musculoskeletal clinical assessment and screening, the diagnosis of Haglund’s syndrome is challenging for all healthcare professionals. The purpose of this case report is to describe history, clinical examination and systems review which conducted to the Haglund’s syndrome differential diagnosis in a long distance runner.

Case Description: 41-year-old male amateur runner presented to an outpatient physical therapy clinic with intense right heel pain radiating up to the posterior leg, tight and right posterolateral surface of lumbopelvic region due to an increase of training load. After a misdiagnosis of low back pain and sciatica made by two healthcare professionals, the patients was referred to imaging deepening and orthopaedic assessment from the physical therapist due to the suspicion of achilles tendinopathy associated with Haglund’s syndrome. Once confirmed the latter diagnosis from x-rays and magnetic resonance imaging, the

patient underwent surgical intervention and subsequent physical therapy treatment by which gained full return to sport.

Outcomes: The follow-up 3 years after the first reported full restoration of functional activities, including running, no pain, no limits to any activities or restriction to patient's participation.

Discussion: This case report underlines the crucial importance of physical therapist – as primary care health professionals – in differential diagnosis processes and in identifying clinical conditions that may require referral for medical evaluation or imaging, in particular in direct access settings. The ability to screen for red flags and, then, the differential diagnosis for several musculoskeletal conditions should be an indispensable requirement for physical therapists, in particular for clinicians working in direct access contexts.

1. Background and Purpose

Running is one of the most popular sports around the world across the adult population, involving a broad variety of people [1,2]. In the last decades, running has rapidly become popular because of the low cost of the equipment [3], the increased interest in disease prevention [4], and the growth of recreational running events in several cities of the western society [3,5]. Also, the number of runners is steadily increasing since 2000 [5] and, in 2015, in Europe almost 50 million people reported to run regularly [6].

In health research, benefits of running such as effects on several indices of health [7], on the reduction of cardiovascular mortality risks, on psycho-social well-being [8-10], on positive effects related to biomechanical properties of the intervertebral discs [10,11], are already well documented in the scientific scenario. However, from a musculoskeletal perspective, running also generates a considerable percentage of running related injuries (RRIs) [3,12], with a reported incidence of RRIs between 19% to 79% [13]. The reason of the latter wide range of percentage related to RRIs is probably due to the lack of consensus in the definition of RRIs [14]. The most common injuries reported by half-marathon and long-distance runners are those involving foot and ankle districts [15]. In detail, in a recent review, Lopes et al. reported that the 3 of the top 5 most common ankle and foot injuries in runners are Achilles tendinopathy, plantar fasciopathy, and ankle sprains [16]. The overall RRIs in foot and ankle are estimated to compose almost 5.7% to 39% [13,17], while it has been calculated that about 8-10% of runners suffer for heel pain [18]. From an aetiological point of view, those conditions could be related to some risk factors such as previous injury, age, sex, BMI, foot posture, leg-length discrepancy, use of orthotics/inserts and shoe wear [3,14,19,20].

Although still poorly understood, a common cause of hind foot pain is Haglund's syndrome [21]. Firstly described in 1927 by Patrick Haglund [22], it consists in a posterior superior exostosis of the calcaneus in a lateral view, typically matched by mechanically induced insertional Achilles tendinopathy and retrocalcaneal bursitis [23,24], which may lead to a painful syndrome [25,26]. Albeit merely suggestive, one study reported a 25% rate of concomitant Haglund's syndrome in patients with insertional Achilles tendinopathy [27]. Haglund's syndrome is usually based on idiopathic aetiology, but several factors contribute to the clinical manifestation such as altered subtalar joint biomechanics, runner's over-practice [28,29], forefoot strike strategy during running[30], unsuited shoe wear, generally low back or stiff-backed shoes and chronic stress [24]. However, also other anatomical factors such as hindfoot varus and pes cavus may play a role in these terms [23].

In respect to the treatment of Haglund's syndrome, conservative management is effective in most of cases [21,31]. Namely, anti-inflammatory drugs, physiotherapy and shoe wear modification may be used to manage pain and relieve the tension in the Achilles tendon and the irritability of the retrocalcaneal bursa [32]. Surgery is required only in resistant cases [21]: specifically, operative treatment should be considered in non-respondent patients after 6 months of conservative management or after 3 months in high-demand athletes [33]. Clinical diagnosis of Haglund's syndrome is based on a combination of medical history and physical assessment, both supported out of imaging findings [33,34]. Given that Haglund's deformity and insertional

Achilles tendinopathy may present simultaneously, physicians and healthcare professionals are required to recognize and manage both pathologies distinctly [32]. Nonetheless, establishing an accurate diagnosis can be challenging due to the complex regional anatomy and the close proximity of potential pain generators [31]. Moreover, the aetiological mechanisms underlying some types of tissue injury within the foot are not clearly understood [35].

In respect to the screening procedure during the clinical assessment for both physicians and healthcare professionals, the first step of the differential diagnosis process should be aimed to exclude vascular, infectious, oncologic or systemic causes as potential pain sources [36]. However, subacute and chronic foot, ankle or heel pain are most commonly due to repetitive microtrauma or compression of neurologic structures [36], and may be possible referred symptoms in presence of discogenic, osteoarthritis or nerve roots problems [37]. Hence, also an appropriate differential diagnosis process intended to exclude other neuromusculoskeletal contributors to patients' symptoms should be performed. Since most of the musculoskeletal pain origins are multifactorial [38], and the possibility of coexisting painful areas is a clinical common scenario [39], namely for patients presenting with ankle and foot complaints or heel pain, healthcare professionals in direct access must be careful and vigilant about the differential diagnosis due to the complex clinical presentation of these patients.

Therefore, the aim of this case report is 1) to report the key elements of anamnesis and clinical assessment of a patient presenting to an outpatient physical therapy clinic with complaints of mild low back pain (LBP) with intense right heel pain radiating up to the leg and 2) the clinical reasoning which led to the differential diagnosis of Haglund's syndrome and concomitant Achilles tendinopathy.

2. Case Description

2.1 Patient History and Systems Review

A 41-year-old male amateur runner employed in a lighting technology company presented to the physical therapy outpatient clinic complaining deep, stinging and burning pain wrapping up all the right leg, from the posterior aspect of the plantar surface of the foot radiating up to the posterior aspect of the leg, thigh and posterolateral area of the lumbopelvic region (see Body Chart in Figure 1). Pain intensity reduced as long as it moved cranially up to the thigh: Numeric Pain Rating Scale (NPRS) [40] 8/10 from the heel to the calf, NPRS [40] 6/10 from the calf to the popliteal fossa and NPRS [40] 3/10 at the mid-thigh. The patient complained also mild right LBP at the time of consultation (NPRS [40] 3/10).

The patient ordinarily run since 15 years and took part to one or two marathons per year after adequate physical preparation and presented him-self with a sporty appearance and denied any past history of smoking or drinking. He trains daily with a single day off per week with exercise regimen ranging from 50 to 80 km per week based on the athletic training. At the time of the first visit the patient stopped running 3 months before.

The subject describes an initial onset of moderate pain (NPRS [40] 2-3/10) in the leg and in the lower back 6 months before the first consultation, managed autonomously with ice, rest and training regimen modification for 3 months.

Then, the patient experienced an important worsening of pain intensity due to an increase of both running mileage and training load focused on lower limbs due to the preparation for a marathon.

The patient was firstly assessed by a general practitioner (GP) and diagnosed with LBP and sciatica based on the clinical assessment and the previous prescribed X-rays and lumbar Magnetic Resonance Imaging (MRI) – which were unremarkable – and was discharged with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) (600mg dose of ibuprofen for two times a day per ten days) for the management of pain. After an other consultation due to the persistence of symptoms the GP referred the patient to physical therapy management.

The physical therapist the patient was firstly referred to treated the runner with electrotherapies and massages directed to the lower back, thigh and leg for 4 weeks without any improvements of the clinical condition. In fact, pain worsened especially in the leg so much to affect also simple activities of daily living such as wake up and walk, sit-up from the chair, drive for a long time.

Three months after the onset of pain, the patient brought him-self to attention of a second physical therapist.

2.2 Clinical impression #1

The patient denied any traumas, constitutional symptoms, no weight loss, history of malignancy, constant e non-modifiable pain and then the hypothesis of a serious pathology was firstly rejected – to be confirmed as the first step of the physical examination. However, a deepen and careful differential diagnosis of the other systems was still required and necessary due to the unusual clinical picture (no improvements of pain and disability with previous treatments, NSAIDs or interruption of training).

Although the interview did not completely satisfy the clinical criteria of a lumbar radiculopathy or radicular pain (pain onset and type, the caudo-cranial direction of the expansion of symptoms, alleviating and provocative factors), the first step was to exclude radiculopathy in terms of priorities (e.g. to exclude a potential positive neurological examination).

Then, due to the characteristics of patient (runner, middle-aged) and the trend of symptoms (load-related onset of pain and no improvements with no recommended therapies for overload injuries in runners), the physical therapist took into account the hypothesis of Achilles tendinopathy with or without concomitant plantar fasciopathy and myofascial pain) and/or low back-related leg pain (referred pain). Moreover, the physical therapist considered also a potential contribution of central pain processing since it may be present in patients with Achilles tendinopathy [41,42], particularly in those with chronic pain.

2.3 Physical therapist examination #1

The patient showed no abnormalities or antalgic postures in the lower back which had full range of motion without any modification of symptoms in the back, thigh, leg and foot. Straight leg raise [43], neurological examination (strength, reflexes and sensory testing) and lumbar provocative test (compression test, distraction test and springing test) were unremarkable or did not evoke patient's symptoms.

During the foot examination, a swollen, red, deformed and highly painful on palpation heel characterized with a prominent tubercle on the posterior superior lateral aspect of the heel was noted.

Functional tests such as heel walk and walk on toes were both possible but the heel walk exacerbated the familiar and intense pain at the right heel (NPRS [40] 7/10). Moreover, heel raises on two legs were painful (NPRS [40] 5/10) and one-leg-heel raises were extremely painful and suspended after 2 repetitions (NPRS [40] 9/10). Manual resisted test of the several muscles of the lower limb (plantar flexors, knee flexors, medium and maximus gluteus) and palpation of such muscles were painful and reproduced the familiar pain localized in the posterior aspect of the leg and thigh, as well as in the right lumbopelvic region.

2.4 Clinical impression # 2

Based on findings of the clinical examination, the suspected diagnosis were achilles tendinopathy with concomitant Haglund's syndrome [21]. Hence the patient was referred to the orthopaedic surgeon for deepening through imaging to corroborate such hypotesis.

2.5 Diagnostic imaging

X-ray of the ankle and the foot showed an abnormal bony prominence on the posterosuperior aspect of the calcaneal (calcaneal exostosis) (Figure 2). In agreement with the physical therapist, the surgeon also prescribed Magnetic Resonance Imaging (MRI). MRI has been used to detect the degenerative changes in the Achilles tendon, bony oedema and the presence of secondary retrocalcaneal bursitis. Indeed, the MRI showed retrocalcaneal bursitis associated with tendonitis phenomenons and spongious oedema in the insertional region of achilles tendon in the calcaneus where bone erosions were also noted (Figure 3). Due to imaging results and clinical picture, the patient was referred to a orthopaedic surgeon for further assessment.

2.6 Final diagnosis

According to findings rising from MRI, combined with the clinical symptoms, the final diagnosis made by the orthopaedic surgeon was Haglund's syndrome and consequent achilles tendinopathy [44].

2.7 Medical Intervention: surgical procedures

The orthopaedic decided to perform a posterior ankle endoscopic calcaneoplasty and removal of the bursitis and endoscopic resection of the calcaneal exostosis (See Figure 4 show MRI post surgery view; Figure 5 and 6 for surgery's results observation). During the recovery at the hospital, antibiotic (Amoxicillin/clavulanic acid 875 mg/125mg twice a day per five days) and antithrombosis prophylaxis (enoxaparin 4000ui 0,4ml once a day per five days) were administered. The patient was discharged after a regular post-operative period and adviced to take enoxaparin 4000ui 0,4ml once a day per 15 days and acetaminophen 500 mg as needed, maximum 3 times per day. Orthopaedic advices constited on a prohibition of load on the right lower limb for 15 days and suggested the patient to use 2 crutches. For a more detailed description of the timeline from injury to diagnosis to management, see the timeline in Figure 7.

2.8 Post-operative physical therapy intervention

Within the first month post-intervention, post-operative physical therapy program was aimed to restore ankle and foot joints mobility, to reduce pain and swelling as well as to re-establish activities of daily living. Over the second post-operative month, a cautious program of progressive load on the lower limb, a strength training protocol gradual return to functional activities and to sport throughout running retraining were followed (see Figure 8, 9 and 10) . The subject was evaluated on an instrumented treadmill (MyRun, Technogym, FC, Italy) at a preferred running pace of 6,5 minutes/km . Foot strike pattern was determined visually by looking at the slow motion video recording.

3. Outcomes

The following clinical performance tests have been used as outcome measures for the rehabilitation program: reduction in NPRS [40] level of pain in the heel, calf and lower back; reconditioning of 3:30':00" marathon run time; run rhythm of 5km/min; running cadence; number of painless heel raises.

To achieve running retraining have been analyzed 4 benchmarks: cadence (steps per minute), ground contact time (time of foot contact with the ground during each step), and vertical oscillation [the amount that the torso moves vertically with each step, while running, measured in centimeters (cm)], and foot-strike pattern, collected using OPTO-JUMP NEXT software (Microgate, Italy). In the first analysis, the subject had a rearfoot strike pattern, running cadence was 167 steps per minute, ground contact time was 277 ms, and vertical oscillation was 8 cm. NPRS [40] was 7/10 at right heel, 6/10 from the heel to the calf, 2/10 in the lower back.

At 3 months post-intervention, namely the first follow up, the subject enhanced foot-strike to a midfoot-strike pattern. Cadence improved to 181 steps per minute, time of ground contact was 252 ms, and vertical oscillation 7 cm, while run rhythm was on average of 5 km/min. NPRS [40] was 0/10 throughout the body. After 1-year from surgery, the patient returned to run regularly and took part in the marathon. Finally, at 3 years of post-surgical intervention, the patient denied any pain, limitations of activities as well as no restriction to social participation.

4. Discussion

This is the first case report describing a runner with concomitant Achilles tendinopathy and Haglund's Syndrome with such unusual clinical presentation (pain type and descriptors, topography of pain, caudo-cranial expansion of pain and evolution over time) and, moreover, symptoms that could mimic a LBP and sciatica. Indeed, a similar article exist in literature [45], but the jogger patient recruited in such study was older than the one of this paper and his clinical features and therapeutic process were substantially different: left heel pain and diagnosis of Haglund's syndrome, surgery and new right heel pain with a other diagnosis of Haglund's syndrome [45].

The runner of this case report presented him-self with all clinical features of Achilles tendinopathy (i.e. morning pain, well-localized tenderness on palpation, palpable nodule and thickening of the tendon, asymmetry to the contralateral side, painful resisted test for plantar flexors muscles) [44], reasonably based on a previous existent Haglund's syndrome. The latter aspect may deserve more attention. Indeed, such clinical presentation is not unusual. In previous case reports describing individuals with a diagnosis of Haglund's syndrome, patients presented to the clinical examination with a bulge Achilles tendon and pain on palpation in a 37-years-old woman [46], or pain in the area of insertion of Achilles tendon, symptoms more pronounced with sit-to-stand activities or in the morning and a noticeable bump and tender swelling in the attachment of Achilles tendon in a 60-year-old woman [47]. These aspects may be took into account from physical therapist treating patients with direct access and heel pain, mainly for those patients whose pain last for several months.

It is already know that Haglund's syndrome is a painful condition caused by a bony deformity in the posterior superior aspect of calcaneus, often associated with a chronic insertional Achilles tendinopathy and retrocalcaneal bursitis [23,24,48,49], and due to altered foot or ankle joints biomechanics, unsuited footwear or chronic load stress [34]. Furthermore, Haglund's syndrome is a common condition in adults, particularly among runners [27,50]. As a rule, the diagnosis process is made clinically [51,52], and conservative management is the first rehabilitation strategy [21,31], while surgery is required only in non-respondent patients [21].

The following clinical features of Haglund's syndrome have been described in the literature:

- posterior superior enlargement of the calcaneus bone [19,21,22];
- pain on palpation at back of heel [19,21,32];
- redness and swelling of the calcaneal bump[19,21,22];
- stiffness of the triceps surae muscles [19,21,22];
- pain and impaired function in gait or running and in plantar flexion movements [19,21,22].

Despite the all clinical signs and symptoms of Haglund's syndrome are clearly reported in literature, it must be kept in mind that patients may present with a widespread variety of clinical features that may led misdiagnosis. Indeed, this case report underpins the central role of the clinical reasoning process of primary care clinicians, such as physical therapists, in identifying musculoskeletal conditions that may be present simultaneously and, therefore, could mimic specific pathologies, such as radicular pain or radiculopathies as in this specific case. An exhaustive differential diagnosis is mandatory for physical therapists in order to recognize pathologies outside their scope of practice that may need referral for imaging, medical assessment or surgical interventions, even if subjects have been previously evaluated by other healthcare professionals. In respect to the latter considerations, the patient presented in a direct access outpatient physical therapy clinic to the physical therapist after a specialistic consultation with a physiatrist and an unsuited rehabilitation program. Then, the physical therapist decided to refer the patient to an orthopaedic surgeon due to his suspected diagnostic hypothesis.

Risk factors are well known from the current literature for those patients with Haglund's syndrome. Adults with anatomical features of foot [21][21], or those who usually wear improper tight shoes, are specifically at risk [21,31]. Like the subject described in this case report that was training in preparation for a marathon run, the risk of developing Haglund's syndrome increases in those individuals that over-practice run between the third or fourth decades of age, particularly in presence of altered ankle/foot biomechanics [28-30]. Missing the diagnosis of overuse pathologies, which includes Haglund's syndrome, in adult runners could lead to an increased risk of Achilles tendon rupture [53].

Risk factors and physical examination findings must be carefully assessed and weighed in order to consider possible diagnoses. This case report describes the clinical features (i.e. history of related injury mechanism; an increased reactivity to mechanical stimuli to the calcaneus, the delay in symptoms reduction, the distal to proximal course of symptomatology; and the appropriate demographic risk factors), and the clinical reasoning that should prompt any clinician in a direct access setting to be suspicious of multiple musculoskeletal concomitant condition in adult sport population. That is to consider the many risk factors (i.e. sport loading activities, a history of long time sports activity, etc.), the behaviour and progression of symptoms especially related to the load .

Lastly, this case report describes the natural history and the post-surgical management of Haglund's deformity removal in an adult marathon runner. Early stage attempts to restore functional abilities and to reduce pain, followed by a long-term post-operative program aimed to achieve successful return to sport.

5. Conclusion

To the best of authors' knowledge this is the first case describing the diagnostic and therapeutic process of a runner with concomitant Achilles tendinopathy and Haglund's syndrome with this unusual clinical presentation. The diagnostic process in which the patient was involved in underlines the importance of the differential diagnosis in physical therapy, even if the patients have been already assessed or treated from other healthcare professionals. The patient gained full return to sport after the surgical intervention and the subsequent physical therapy management. However, through the diagnostic process physical therapists should be able to screen for both all the other systems for referral and, at the same time, be capable to apply an appropriate clinical reasoning process for the identification of different musculoskeletal affections.

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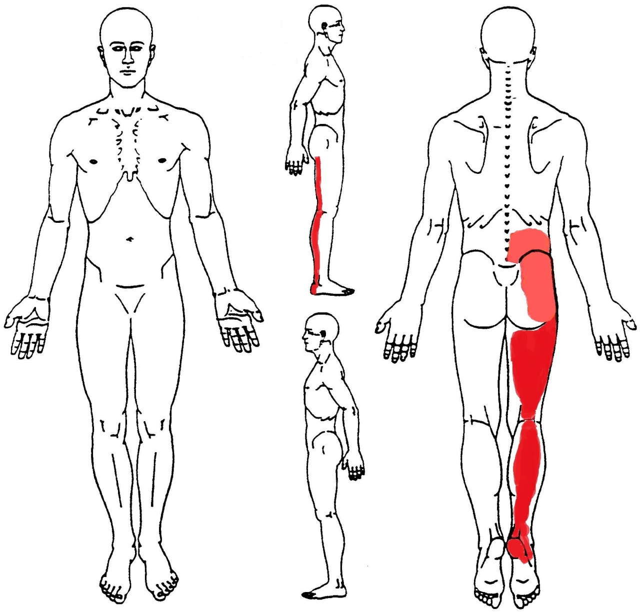

Figure 1. Body chart;

Figure 2: Radiograph showing a lateral view of ankle and foot. Thick yellow arrow indicates a showed an abnormal bony prominence on the posterosuperior aspect of the calcaneal;

Figure 3. Sagittal T1-weighted sequence of the ankle and foot shows bony prominence on the posterosuperior aspect of the calcaneal, retrocalcaneal bursitis and localised calcaneal bone marrow oedemaa (yellow arrow indicates) (pre-surgery clinical condition);

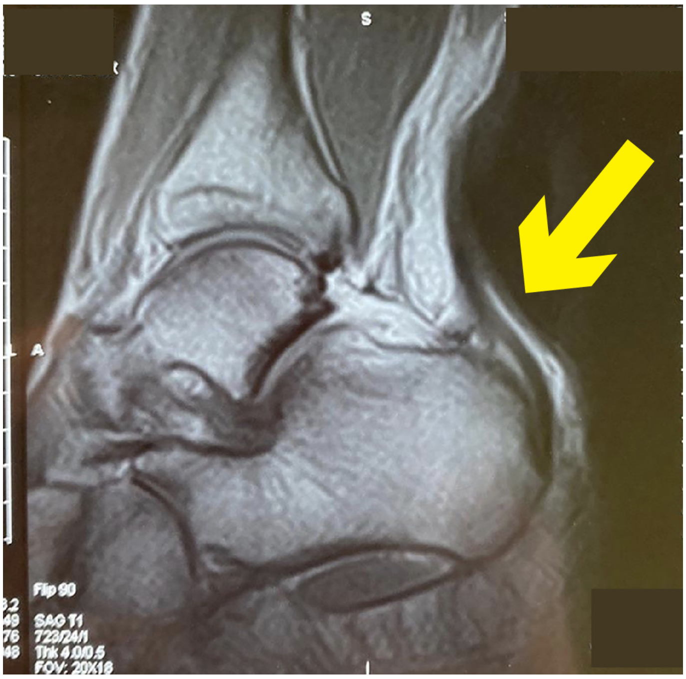

Figure 4. Sagittal T1-weighted spin-echo sequence of the foot and ankle shows the outcomes of surgical procedures. The complete removal of the bursitis and endoscopic resection of the calcaneal exostosis (yellow arrow indicates);

Figure 5: Photographs of the patient shows medial view of foot/ankle complex, in early phase post surgical procedures.

Figure 6. Photographs of the patient shows posterolateral view of foot/ankle complex, in early phase post surgical procedures.

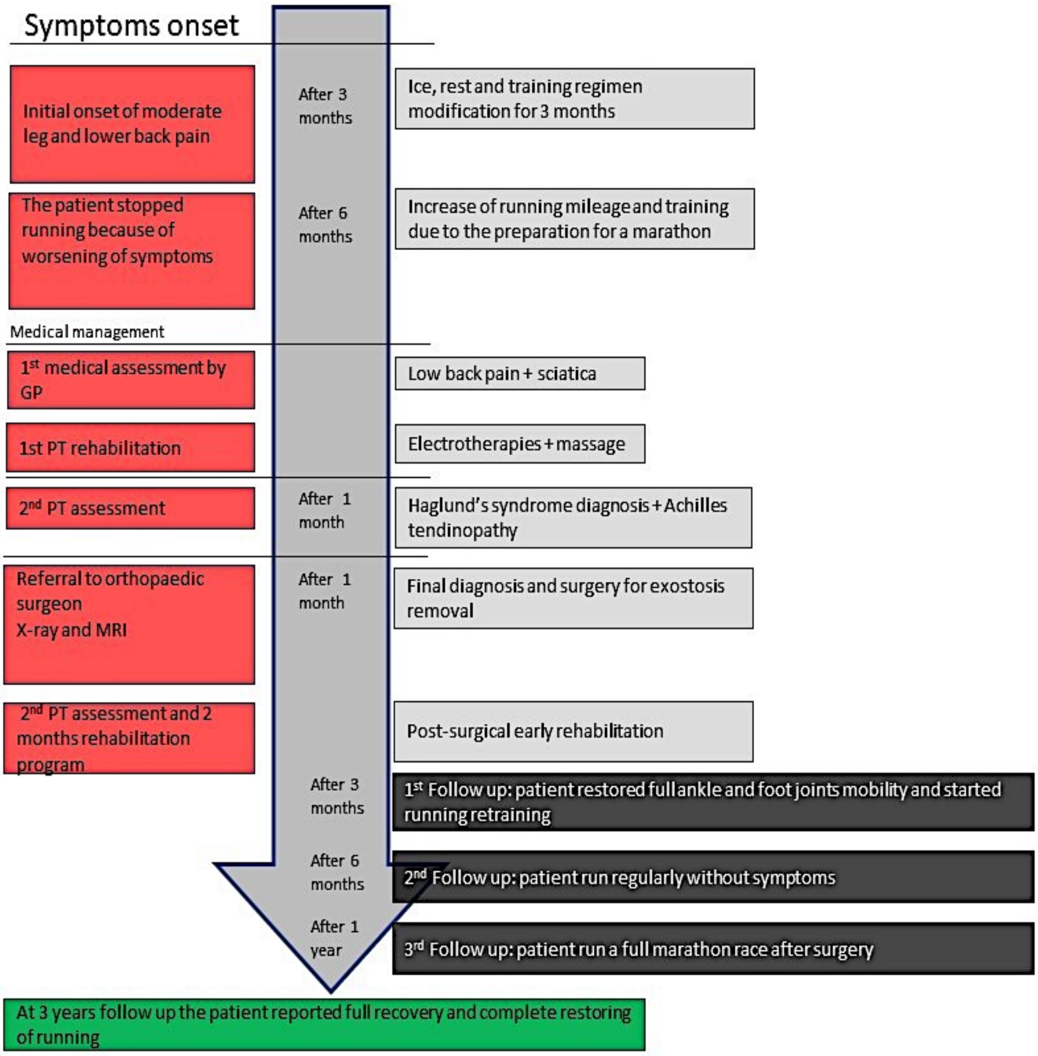

Figure 7: Timeline of case' progression.

Figure 8. Photographs of the patient performing a squat with an elastic band.

Figure 9. Photographs of the patient performing step down with an elastic band

Figure 10. Photographs of the patient in a one leg standing position with an elastic band performing exercise on unstable surface

CHAPTER VII

GENERAL DISCUSSION

Every chapter of this thesis contains a thorough discussion concerning the specific topic investigated. In this last section some critical points, which emerged from the discussions of each chapter, are analysed, offering some suggestions that may be helpful for future developments and implementation of the study of LBP in running and research in physical therapy's clinical practice.

Implication for physical therapy discipline

As demonstrated in this PhD project, although several studies on the prevalence and incidence of LBP in general population and sports are available [1-6], it seems that this topic has not been clearly investigated in the runners. Even though the lumbar spine was identified as the common sites for injury in runners [7,8], no conclusive data were published on the Low Back Pain (LBP) among runners.

Overall, the findings in this PhD revealed that the LBP prevalence in runners, compared to prevalence of the other most relevant Running Related Injuries (RRIs), seems to be lower [7,9-22]. These data seem in line with recent literature, albeit the studies that analyzed LBP, as like RRI, are very few.

Moreover, few, studies addressed specific risk factors for the onset of LBP among runners [23-26] and great caution is required for translating their results to general practice [64,65] [23-26].

According to the Comprehensive Model for Injury Causation [27] and the Conceptual Model for the Determinants of RRIs [28], intrinsic and extrinsic factors are responsible for the increase of running injury risk. Intrinsic factors are hardly or not modifiable; they include gender, age, BMI, history of previous injury, physical fitness and psychological factor have been found to predispose runners to injury. Otherwise, extrinsic factors are modifiable, and comprise training volume or other characteristics, as sport equipment and training environment, which increase runner's susceptibility to injury. Intrinsic risk factors proposed for the onset of LBP among runners included: BMI≥24 [23]; runner's height [23]; tightness of hip flexors [26] and hip flexion angles (only in female) [26]; but, there is no strong literature to explain this two last finding [26]. Moreover, the identification [64] of physical impairments like reduced hamstring or back flexibility and leg length discrepancy was not supported by statistical evaluation. Due to the scarcity of available studies and the clinical impression that muscles tightness could be a risk factor for RRIs and LBP, this topic should be investigated in large samples using prospective design. The main extrinsic risk factors for the onset of LBP among runners were: high competitive level [24]; more than 6 years of experience in running [24]; some patterns of shoes' wear [23] and do not performing weekly aerobics activity [23]. Also in this case the findings extracted from the studies [23,24] cannot be directly translated to the daily practice, but could only serve as possible additional elements to support the clinician in the interpretation of the athlete's condition.

This Phd study did not revealed relevant risk factors for the onset of LBP in Italian runners also, but, probably, the exposure to a single risk factor is often insufficient to produce an overuse injury: the RRI is the result of a number of superposing factors (like training increase, muscular impairments, unsuitable equipment, etc.) [29].

Furthermore, as demonstrated in this PhD project, furthermore, a great knowledge on LBP in running in clinical practice has emerged among Italian OMPTs. The academic education of OMPTs seem in line with recent literature, albeit the studies that analyzed LBP, as like RRI, are very few.

Implication for future studies

The results of the present PhD project represent a starting point for future researches in the study of LBP in running and its assessment in physical therapy' clinical practice, part of which has already been initiated in the scientific world.

The possibility to study the prevalence, incidence and risk factors for onset of LBP in running and its effects allows the scientific community to measure their impact on different outcomes through primary studies. Due to this, to ensure appropriate competence, awareness, and the ethical use of the knowledge on these topics, these issues should be included in physical therapy graduate and postgraduate study programs and in OMPTs long-life learning courses.

The scarcity and methodological weakness of the available studies invite to conduct further research about risk factors for LBP among runners.

Therefore, further quantitative studies that evaluating beliefs, attitudes, behavior and risk factors for the onset of LBP, as like RRI among runners should be developed.. To develop a more comprehensive understanding of the phenomena, there is a strong need to investigate patients' perceptions on LBP and running.

This lack of studies on LBP as RRIs, is also reflected in the lack of studies that investigated physical therapists' point of view during the management of runners with LBP.

Currently the management of runners with LBP does not seem very dissimilar to the management of non-runner with LBP [30-33]. For these reason, the future researchs should be oriented towards study of the specific procedures of assessments and the specific treatments for runners with LBP.

Strength and limitations of the PhD project

The use of different study designs represents the strength of this PhD project. The findings in relation to prevalence, incidence, risk factors for onset of LBP in running have been investigated using a clear and defined methodology as reported in chapter II (systematic review) and chapter III and IV (national online survey), thus reducing the possible source of bias and improving the overall quality of the project (34, 35). Moreover, the topic has been discussed using a multidisciplinary broad-spectrum analysis ranging from clinical to research points of view, helping the reader to understand the topic from different perspectives and increasing the PhD student's reflective process (36). The analyze of screening for referral process inphysical therapy and the defintion of red flags through non systematic-review methods for physical therapy' clinical practice outcomes (chapter V), and through case reports (chapter VI), could represent a possible weakness of this PhD project. However, narrative review, debate and letter to the editor have been considered an accepted method for discussion (35).

Conclusion

The principal aim of this PhD project has been to investigate the prevalence, incidence and risk factors for onset of LBP in running and to analyze the screening for referral process of the runners that presented serious clinical condition, above all in direct access physical therapy's practice.

This goal has been achieved through different study designs, in order to present the prevalence of LBP in a wide italian sample runners, to present the knowledge and attitudes of Italian OMPTs in order to assessment runners with LBP, to present the ability of physical therapists to screen the runners with serious clinical condition that mimicking non specific LBP

Five main findings emerged:

1) The prevalence rate in italian runners is low

2) Has been not revealed relevant risk factors for the onset of LBP in Italian runners

3) A great knowledge on LBP in running in clinical practice has emerged among Italian OMPTs.

4) Red Flags Identification is an important step to screening for Referral Process in runners with Low Back Pain.

5) In our view, a more suitable word may be “Disorder” (Running Related Disorders - RRDs) that better describes multifactorial conditions which include, beside structural aspect, also psychosocial elements often present in nonspecific painful disorders like LBP [37-38].

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APPENDIX

In the Appendix, two different corollary papers, conducted during the three years of this PhD are presented.

Some runners with serious pathology was analyzed during this period and although they did not have LBP their cases deserved to be investigated and described in case reports

Therefore, in this section I will present two clinical cases of runners whit seriuos clinical condition that mimicked the muscoloskeletal disorders who have had a favorable prognosis after a physical physiotherapist's assessment and screening process for referral to medical doctor. All the presented research has been reported in abstracts

APPENDIX 1

THE USE OF RUSI (REHABILITATIVE ULTRASOUND IMAGING) TECHNIQUE IN A PHYSICAL THERAPY'S DIFFERENTIAL DIAGNOSIS IN RECREATIONAL RUNNER WITH PAIN IN FIFTH TOE: A CASE REPORT.

Submitted as:

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Case Reports in Orthopedics (2020) Under Review

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The use of RUSI (Rehabilitative UltraSound Imaging) technique in a physical therapy's differential diagnosis in recreational runner with pain in fifth toe: A Case Report.

Abstract

Background and Purpose: Running often leads to several injuries. Mostly, injured joints in runner involve lower limbs: frequently, the foot district is affected and acute ankle sprains represent one of the most common injury in runners, as a result of the fracture of the fifth metatarsal base.

Case Description: A 55-year-old recreational runner presented to an outpatient physical therapist after a right ankle injury, happened during sport competition with physician's clinical diagnosis of lateral ankle sprain. The physical therapist, based on the patient's clinical history and examination, suspected the presence of a serious pathology (i.e. fracture) After screening process a high possibility of fracture of the 5th metatarsal was hypothesized. Therefore, using Rehabilitative UltraSound Imaging, to further verify diagnostic suspicion of metatarsal fracture. The ultrasound examination revealed an alteration of the fifth metatarsal bone cortex. The patient was referred to the orthopedic surgeon who prescribed a foot X-ray; the exam revealed an acute "Jones" fracture, that is an oblique compound fracture of the base of the fifth metatarsus of the right foot. The physician in agreement

with the physical therapist decided to follow a conservative treatment approach.

Outcomes: At the end of a 14 weeks rehabilitation program, the assessment scales reported a score of 0/10 for the NPRS and a score of 98% and sport 0%, standing for complete ability to perform sport activities, for the FADI, respectively; the patient was considered clinically recovered and able to return to full sport practice.

Discussion: This clinical case shows how a thorough clinical examination performed by the PT can contribute to the correct diagnosis of a serious ongoing pathology. In the end, the diagnosis was made by orthopedic surgeon, but timely referral led to an early identification of the case, improving the prognosis of the patient.

APPENDIX 2

AN UNUSUAL PRESENTATION OF ACUTE MYOCARDIAL INFARCTION IN PHYSICAL THERAPY DIRECT ACCESS.

Submitted as:

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Physiotherapy Theory and Practice (2019) Under Review

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An Unusual Presentation Of Acute Myocardial Infarction In Physical Therapy Direct Access.

Abstract

Background: Shoulder pain (SP) may originate from both the musculoskeletal system and visceral conditions. Physical therapists (PT) in a direct access setting may encounter patients with life-threating pathologies with symptoms mimicking SP, such as acute myocardial infarction (AMI). To our knowledge, this is the first documented case of AMI presenting with an atypical upper limb pain pattern recognized by a PT in a direct access clinic, after 2 misdiagnoses in ED.

Case Presentation: A 46 years old male recreational runner went to an outpatient physical therapy clinic for SP, occurred during the past week, and worsened the night before. Previously, two access in ED for the same shoulder symptoms confirmed right SP syndrome. The patient, however, had a shift of the pain on the left side. The PT referred him to GP. The GP identified the signs and symptoms of cardiac disease and immediately referred the patient to ED, where finally an AMI has diagnosed. This case report underlines the clinical reasoning of a PT, which allows distinguishing signs and symptoms of MSDs or visceral diseases.

Conclusion: This case report highlights the importance of the patient's assessment by a PT even in the case of medical diagnosis or prescription.