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AN OVERVIEW OF LOW BACK PAIN

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ΒΑΒΟΥΡΑΚΗΣ ΜΙΧΑΗΛ

Abstract

The aim of this study is to understand the very serious medical condition of low back pain, affecting approximately 80% of the population sometime in their lifetime, which can have a great impact on everyday activities of the affected individual, thus deteriorating the quality of human life.

Low back pain is considered a symptom, rather than a disease, usually running a self-limited course. Despite that, many patients presenting with an episode of low back pain will go on having recurrent episodes. Risk factors usually implicated in the development of chronic low back pain include age, obesity, occupation and other psychosocial factors.

The exact etiopathogenic mechanism behind the clinical presentation of low back pain is differentiated as being either mechanical, most commonly, or inflammatory, usually associated with a systemic rheumatic disease. To distinguish between these two entities, the presence of specific signs and symptoms should be identified through the medical history and clinical evaluation.

The use of imaging techniques, with MRI being the study of choice, is indicated either in incapacitated patients with long-lasting low back pain or when serious signs and symptoms are identified.

For the management of low back pain, proper education, daily activity modification, and, sometimes, cognitive-behavioral therapy and psychosocial support, are considered important. Active treatment with medication and physical therapy, although not always needed, is usually applied, aiming to relieve the patient from the pain and help him cope with his daily routine and responsibilities. More invasive treatment options are reserved for patients not responding to conservative treatment or with significant impairment in life quality.

Key words: low back pain, self-limiting, recurrent, mechanical, inflammatory

Περίληψη

Στόχος αυτής της μελέτης είναι η κατανόηση του οσφυοϊερού άλγους, το οποίο αναμένεται να επηρεάσει περίπου το 80% του πληθυσμού κάποια στιγμή κατά τη διάρκεια της ζωής του, έχοντας μεγάλο αντίκτυπο στις καθημερινές δραστηριότητες και την ποιότητα ζωής του ασθενούς.

Το οσφυοϊερό άλγος είναι ένα σύμπτωμα, και όχι μια ασθένεια, που συνήθως ακολουθεί μια αυτοπεριοριζόμενη πορεία. Παρ 'όλα αυτά, πολλοί ασθενείς που θα παρουσιάσουν ένα μονήρες επεισόδιο, θα έχουν συνήθως περαιτέρω υποτροπιάζοντα επεισόδια στο μέλλον. Οι παράγοντες κινδύνου που συνήθως εμπλέκονται με την ανάπτυξη χρόνιου οσφυοϊερού άλγους περιλαμβάνουν την ηλικία, την παχυσαρκία, το επάγγελμα και άλλους ψυχοκοινωνικούς παράγοντες.

Το οσφυοϊερό άλγος διαφοροποιείται ανάλογα με το αίτιο σε πόνο μηχανικής φύσεως, συνηθέστερος, ή φλεγμονώδους φύσεως, συσχετιζόμενο συνήθως με κάποια ρευματική νόσο. Η διάκριση γίνεται με τον προσδιορισμό συγκεκριμένων σημείων και συμπτωμάτων μέσω του ιατρικού ιστορικού και της κλινικής εξέτασης.

Η χρήση τεχνικών απεικόνισης, με τη μαγνητική τομογραφία να αποτελεί συνήθως την εξέταση εκλογής, ενδείκνυται σε ασθενείς με μακρόχρονο πόνο ή με ανησυχητικά σημεία και συμπτωμάτα.

Για τη διαχείριση του οσφυοϊερού άλγους, η σωστή εκπαίδευση, η τροποποίηση των καθημερινών δραστηριοτήτων, η γνωσιακή-συμπεριφορική θεραπεία, και η ψυχοκοινωνική υποστήριξη, θεωρούνται σημαντικές. Η φαρμακευτική αγωγή και η φυσιοθεραπεία έχουν ως στόχο να ανακουφίσουν τον ασθενή και να τον βοηθήσουν να ανταπεξέλθει στην καθημερηνότητά του και στις υποχρεώσεις του. Οι επεμβατικές τεχνικές προορίζονται για ασθενείς μη ανταποκρινόμενους στη συντηρητική θεραπεία ή με σημαντική έκπτωση στην ποιότητα ζωής.

Λέξεις κλειδιά: οσφυοϊερό άλγος, αυτοπεριοριζόμενο, υποτροπιάζων, μηχανικό, φλεγμονώδες

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Introduction

The aim of this study is to understand and elucidate the occurrence of low back pain, which is a topic of main importance, as it is considered amongst the top five most presenting complaints in the emergency department [1] and the most common occupational disorder worldwide [2]. Furthermore, it is the leading cause of activity limitation and work absence throughout the world [3], a major factor in escalating health-care costs [4], and the cause of both a huge economic and psychologic burden on patients and their families, affecting work performance and social responsibilities [5].

Low back pain is considered a symptom rather than a disease and is usually defined as pain, muscle tension, or stiffness, localized below the costal margin and above the inferior gluteal folds [6], with or without accompanying neurologic deficits.

It is divided into two main categories according to the cause:

1) Non-specific low back pain (approximately 90% of cases [6]), when the specific cause cannot be identified [2, 7].
2) Specific low back pain, when the condition can be attributed to a specific cause, further subdivided into mechanical and inflammatory [2, 7].

According to the duration of symptoms, the following classification exists:

1) Acute low back pain: Episode lasts less than 6 weeks.
2) Subacute low back pain: Episode duration between 6 and 12 weeks.
3) Chronic low back pain: Episode persists more than 12 weeks.

Despite this classification based on the duration of low back pain has been the gold standard for some time, nowadays an increasing tendency exists, presenting this entity as a chronic, recurrent condition, that may have one of several trajectories [8], slightly replacing the previous categorization as being either acute, subacute, or chronic [9].

1. Epidemiology

The life-time risk of each individual suffering from at least one episode of low back pain is estimated to be as high as 84% [10], while approximately 25% of them will have another episode within one year [11]. In United States, more than 25% of adult population reported an episode of low back pain that lasted at least 24 hours within the previous 3 months [12] and 7.6% reported at least one episode of severe acute low back pain within the previous year [13, 14].

Citation	Country	Age range (years)	Inclusion criteria at baseline	Case definition[a]	Incidence (%)	Standard error (%)	Risk of bias
Incidence of number of people who have a first-ever episode							
Biering-Sorensen [21]	Denmark	30–60	Never had low back pain	Low back pain over past year	6.3[c]	0.8	Low
Croft et al. [24]	United Kingdom	18–75	Never had low back pain	Low back pain over past year	15.4[c]	0.9	Moderate
Mustard et al. [30]	Canada	21–34	Never had back pain >1 day	Back pain >1 day over past year	7.5[c]	0.6	High
Incidence of number of people who have any episode (first-ever or recurrent)							
Al-Awadhi et al. [28]	Kuwait	15–99	No low back pain at baseline	Low back pain over past year	1.5[b]	0.2	High
Cassidy et al. [23]	Canada	20–69	No low back pain for 6 months prior to baseline	Low back pain over past year	18.9[b]	2.2	Low
Croft et al. [24]	United Kingdom	18–75	No low back pain at baseline	Low back pain over past year	36.0[c]	1.2	Moderate
Hestbaek et al. [20]	Denmark	30–50	No low back problems over past year	Low back problems over past year	19.3[c]	1.7	Low
Jacob et al. [25]	Israel	22–70	No activity-limiting low back pain >1day over past month	Activity-limiting low back pain >1day over past year	18.4[c]	2.7	Moderate

[a] Definition of a new episode of low back pain.
[b] Age and sex- standardized.
[c] Unadjusted.

Figure 1. *One-year incidence of low back pain in the general population [9].*

Studies show that the incidence of low back pain increases with age, reaching its peak in the third decade, and then gradually declines after the sixth decade of life [9]. Also, a female gender predominance is indicated by many studies [11], especially during pregnancy, when more than two-thirds of women suffer from low back pain [15], which tends to persist even after delivery [16-18].

2. Course and prognosis

An episode of low-back pain can be considered as a new one if:

1) The patient has been relieved from pain for at least 30 days.
2) The pain lasted for at least 24 hours.
3) The intensity of the pain is at least equal to a defined minimal clinically important change on a chosen pain intensity scale.
4) The associated functional limitation is at least equal to a defined minimal clinically important change on a chosen functional limitation scale. [19]

An acute episode of low back pain is a self-limited condition, with 72% of patients being free of symptoms within 12 months [20], without requiring any medical care [14]. Regarding the patients who do seek medical assistance, their symptoms and any form of disability improve rapidly with most of them being able to return to daily activities and work within 4–6 weeks [21]. However, one out of three had a recurrent episode of low back pain, of at least moderate intensity, within the next 12 months [22]. Furthermore, one out of five reported substantial limitations during daily activities [23]. Overall probability of progression to chronic low back pain is estimated at 23% [10].

Citation	Country	Age range (years)	Definition of what is being counted at follow-up	Follow-up period (weeks)	Remission (%)	Standard error (%)	Risk of bias
Jones et al. [42]	United Kingdom	18–65	No activity-limiting low back pain in the last week	13	61[a]	1.6	High
Hancock et al. [43]	Australia	Not given	No low back pain >1 on the Visual Analogue Scale for seven consecutive days	13	89[b]	2.0	High
Dunn et al. [38]	United Kingdom	30–59	No low back pain >1 day in the last month	26	31[b]	2.5	High
Schiottz-Christensen et al. [40]	Denmark	18–60	Complete recovery	52	54[b]	2.2	Moderate
Van den Hoogen et al. [44]	Netherlands	16–99	No low back pain for past four weeks	54	90[b]	1.4	High
Carey et al. 2000; Carey 2010 [41,46]	United States of America	18–99	Functional recovery	96	96[b]	0.5	Moderate
Vingard et al. [45]	Sweden	20–59	Improved function over past six months	104	59[b]	2.1	High

[a] Adjusted for age, sex, and socio-economic status.
[b] Unadjusted.

Figure 2. *Remission of low back pain in health facility and clinic-based studies [9].*

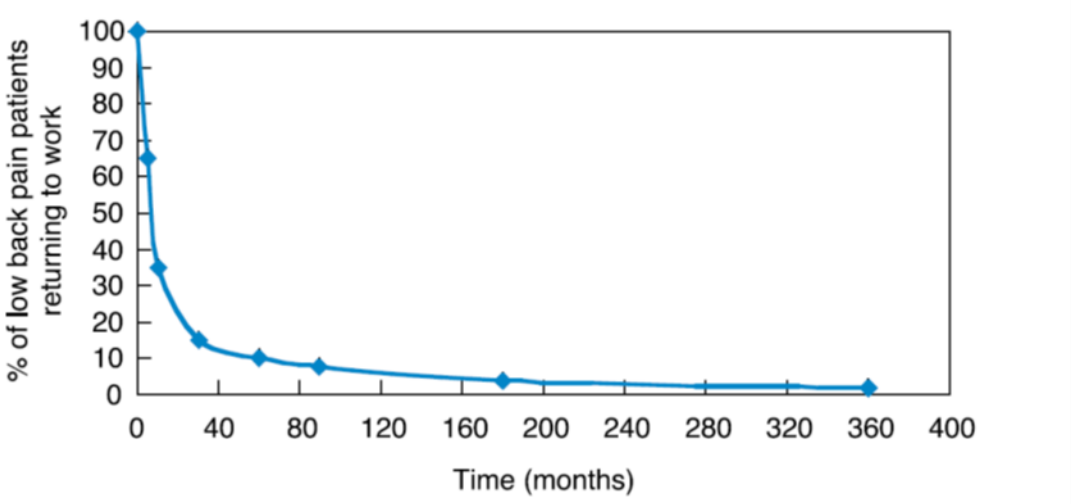


Figure 3. *Return to work after an acute attack of back pain. Reproduced, with permission from Waddell (1998) [24].*

A study found that 80% of primary care patients had a recurrence within 12 months [25], while another one found a 20% recurrence within 6 months, with the recurrence rate being increased with age [26]. Generally, recurrent episodes are more common in patients experiencing activity-limiting low back pain that lasts more than 1 day [21, 27-30].

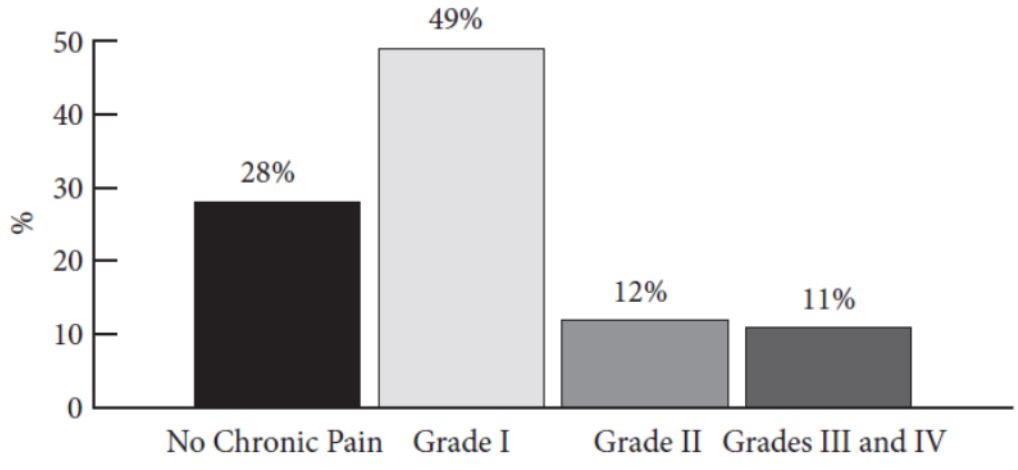


Figure 4. *Severity of low back pain (age standardized rate). Grade I, low-intensity/low-disability low back pain; Grade II, high-intensity/low-disability low back pain; Grades III and IV, high-intensity/high-disability low back pain. Created using data from Cassidy JD et al. [31].*

3. Predisposing factors

Age is considered the most important risk factor, as the incidence of low back pain steadily increases until the age of 60-65 years [9]. Excessive body weight, indicated by body mass index >30, is also a predominant factor, as it is closely associated with repeated episodes of low back pain [32, 33].

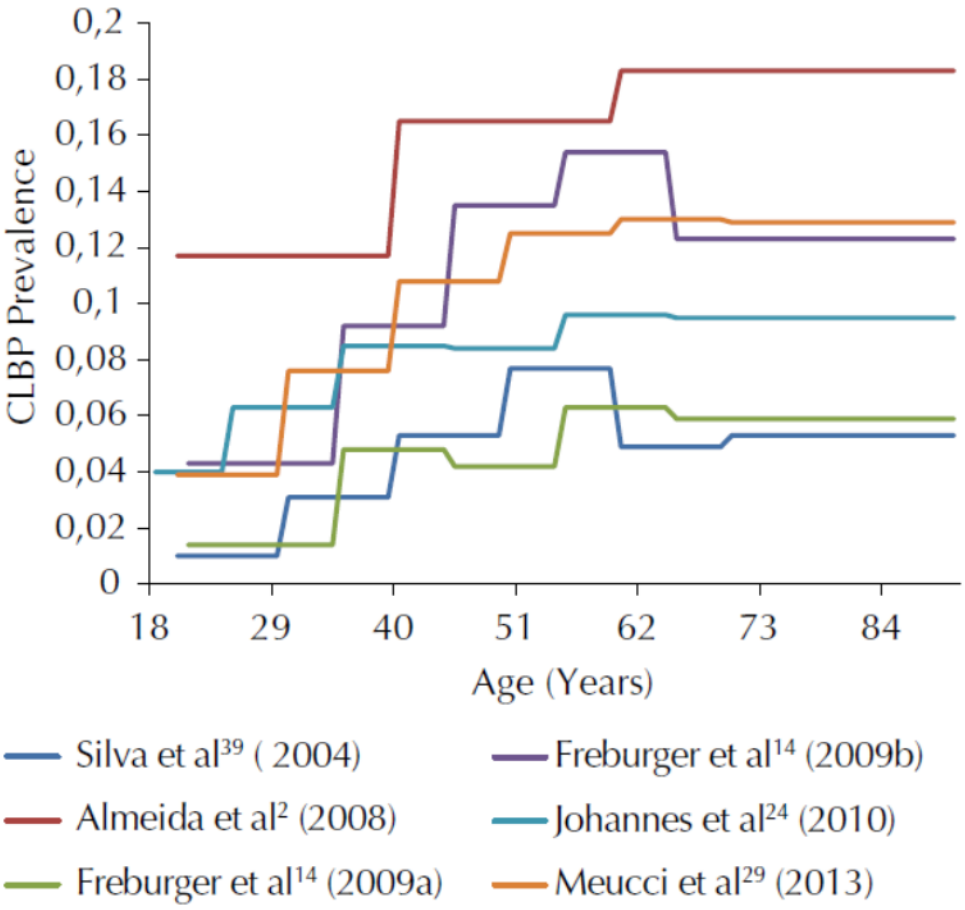


Figure 5. *Chronic low back pain prevalence (CLBP) according to age (six estimates) [34].*

Another crucial predisposing factor is occupation, as these accompanied by high physical demands, exposure to whole-body vibration, and prerequisites such as bending, twisting and manual handling, have been linked with a high number of low back pain incidents [35]. Sometimes, even job dissatisfaction seems to play an important role [6].

Other factors usually implicated is smoking [36] and psychosocial factors, such as depression, anxiety and stress, although a clear relationship between them and the presence of low back pain has not been established [6, 37-43].

Association with a low educational status [44-47] is speculated, with many studies indicating a lower prevalence of low back pain in developing countries, which can be also attributed to better access to industrial insurance and healthcare services due to higher incomes, higher pain thresholds, more physical activity and shorter height [48].

	Occurrence	**Chronicity**
Individual factors	Age	Obesity
	Physical fitness	Low educational level
	Strength of back and abdominal muscles	High levels of pain and disability
	Smoking	
Psychosocial factors	Stress	Distress
	Anxiety	Depressive mood
	Mood/emotions	Somatization
	Cognitive function	
	Pain behavior	
Occupational factors	Manual handling of materials	Job dissatisfaction
	Bending and twisting	Unavailability of light duty on return to work
	Whole body vibration	Job requirement of lifting for ¾ of the day
	Job dissatisfaction	
	Monotonous tasks	
	Work relations/social support	

Table 1. *Risk factors for occurrence and chronicity [6].*

4. Clinical evaluation

Starting with the medical history, the presence of conditions such as osteoporosis, active infections, history of malignancy, or endocrine disorders, must be investigated [49]. Then, attention must be focused on the possible presence of systemic or characteristic local signs and symptoms, raising suspicion for an inflammatory condition.

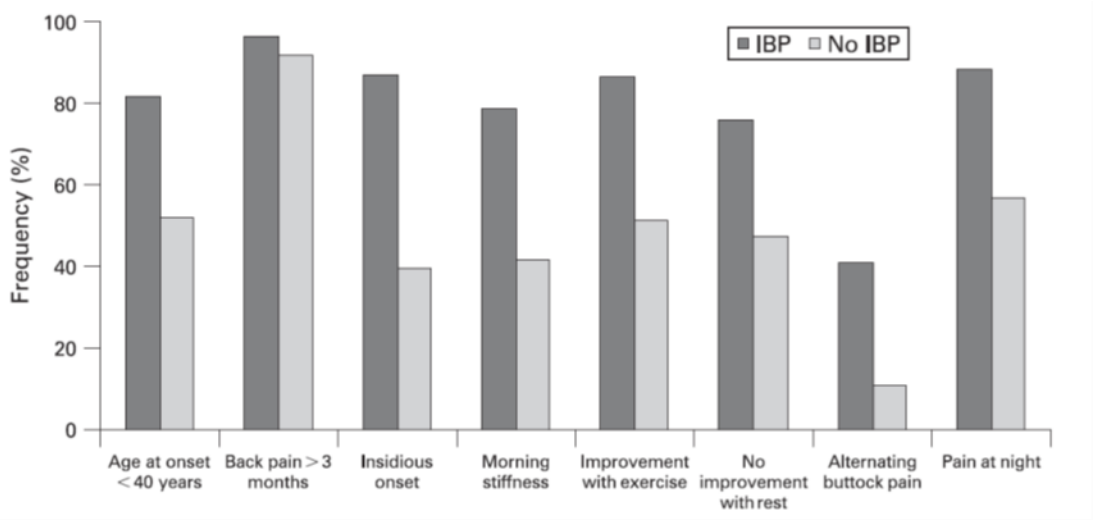


Figure 6. *Frequencies of individual parameters of inflammatory back pain (IBP) in patients considered by Assessment of Spondylarthritis International Society (ASAS) experts to have IBP and considered not to have IBP [51].*

A thorough history regarding the specific characteristics of the lower back pain itself should be focused on 4 main points:

1) Detailed description of the pain, aiming to collect information about exact location, duration, severity, and possible triggering or relieving factors.
2) Neurologic involvement, by determining irradiation into one or both legs, in a dermatomal distribution [49].
3) Identification of the so-called “red flag” symptoms, which indicate an increased possibility of a serious underlying etiology requiring urgent intervention [50].

Previous history of cancer
Chronic steroid use
History of intravenous drug abuse
Immunosuppression
Weight loss
Fever, chills, night sweats
Age > 50
Abnormal neurologic examination
Pain worsening when supine
Bowel or bladder dysfunction
Saddle anesthesia

Table 2. *"Red flag" signs and symptoms [50].*

Duration
Acute low back pain: less than 6 weeks
Subacute low back pain: 6 weeks to 3 months
Chronic low back pain: more than 3 months
Pain Description
Location
Severity (pain scale, type of pain, activities affected)
Timing (morning, evening, constant, intermittent)
Aggravating and relieving factors (ambulation/rest, sitting/standing/laying, inclines/declines, back flexion/extension)
Radiation (dermatomal or non-dermatomal)
Deficits
Motor weakness
Sensory changes (numbness, tingling, paresthesias, dermatomal or non-dermatomal)
Urinary or bowel incontinence, urgency, or frequency

Table 3. *Historical factors that must be considered in the evaluation of a patient with low back pain [49].*

Moving forward to the physical examination, observation of body posture and gait may provide valuable information. Cervical range of motion in extension is assessed by tragus to wall test (typical for ankylosing spondylitis), rotatory movements are also checked. Rib mobility is assessed by measuring chest expansion. Schober's test should be performed to assess patient's ability to flex the lower back [12]. To detect the exact location of the pain, palpation of the bony elements of the pelvis and the spine can be helpful [49]. To evaluate each dermatome/myotome, basic motor examination is performed [12]:

1) L2-L4: Femoral stretch test
2) L5-S1: Straight leg raise and crossed straight leg raise tests, ankle dorsiflexion, great toe extension
3) Hip or sacroiliac joint pathology: Patrick's (FABER), Gaenslen's and Yeoman's tests
4) Deep tendon reflexes (differentiation between CNS deficit – hyperreflexia and PNS deficit – hyporeflexia [49]): Patellar reflex (L2-L4), Achilles tendon reflex (S1).

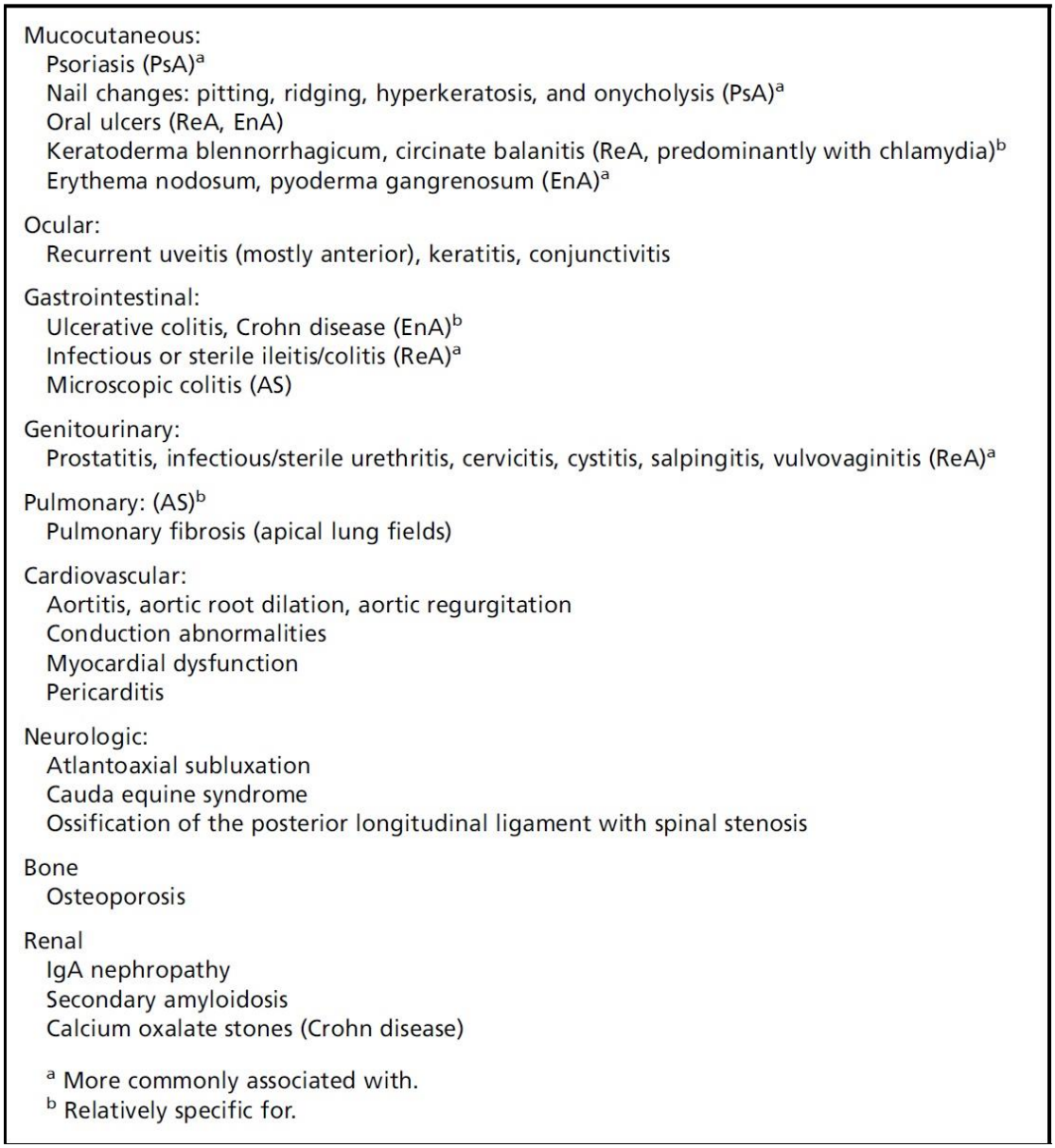
In case of neurological deficit, presence of hypoesthesia or hyperesthesia to pinprick and light touch may occur within a specific dermatome. Similarly, a decrease in muscle tone may occur within a specific myotome [12].

For patients suffering from bowel and/or urinary bladder dysfunction, further investigation for anal wink reflex, rectal tone, and saddle anesthesia, should be performed to assess for cauda equina syndrome.

When an inflammatory condition is suspected to be the cause of low back pain, accompanying systemic manifestations may be present. An asymmetric peripheral oligoarthritis affecting both small and large joints outside the spine, largely in the lower extremities, is a common finding. Enthesitis presenting with tenderness at insertion sites of large tendons, commonly involving the elbow, knee and Achilles' tendon, as well as generalized tenosynovitis, presenting with erythema, edema and limitation in the range of movement, can be present. Furthermore, dactylitis presenting as swelling of an entire digit ("sausage digit") is a typical finding in systemic inflammatory conditions [51].

Extra-articular manifestations are also typical for systemic inflammatory conditions. A detailed examination of the oral mucosa for possible ulcers as well as further investigations concentrated to other specific gastrointestinal findings pointing to the presence of an inflammatory bowel disease should be performed. A thorough skin examination for identification of possible psoriatic lesions is necessary. Additionally, the nails should be examined closely for presence of conditions like onycholysis or pitting. Ocular examination is of great importance, as uveitis is the most common extra-articular finding in patients with spondylarthropathies, presenting in up to 37% of all cases [52, 53]. Main features include eye redness, blurred vision, photophobia, increased lacrimation and itching/pain. Cardiac and respiratory findings, together with non-specific systemic features, such as fever, weight loss and night sweats, may be present.

Finally, on the laboratory blood testing, the presence of increased inflammatory markers and non-specific findings, such as anemia, leukocytosis and thrombocytosis, can raise suspicion for the presence of a systemic inflammatory disorder in patients presenting with low back pain [54].



Mucocutaneous:
- Psoriasis (PsA)[a]
- Nail changes: pitting, ridging, hyperkeratosis, and onycholysis (PsA)[a]
- Oral ulcers (ReA, EnA)
- Keratoderma blennorrhagicum, circinate balanitis (ReA, predominantly with chlamydia)[b]
- Erythema nodosum, pyoderma gangrenosum (EnA)[a]

Ocular:
- Recurrent uveitis (mostly anterior), keratitis, conjunctivitis

Gastrointestinal:
- Ulcerative colitis, Crohn disease (EnA)[b]
- Infectious or sterile ileitis/colitis (ReA)[a]
- Microscopic colitis (AS)

Genitourinary:
- Prostatitis, infectious/sterile urethritis, cervicitis, cystitis, salpingitis, vulvovaginitis (ReA)[a]

Pulmonary: (AS)[b]
- Pulmonary fibrosis (apical lung fields)

Cardiovascular:
- Aortitis, aortic root dilation, aortic regurgitation
- Conduction abnormalities
- Myocardial dysfunction
- Pericarditis

Neurologic:
- Atlantoaxial subluxation
- Cauda equine syndrome
- Ossification of the posterior longitudinal ligament with spinal stenosis

Bone
- Osteoporosis

Renal
- IgA nephropathy
- Secondary amyloidosis
- Calcium oxalate stones (Crohn disease)

[a] More commonly associated with.
[b] Relatively specific for.

Figure 7. *Extra-articular manifestations [51].*

5. Mechanical low back pain

Mechanical back pain refers to the pain caused by an anatomical deformity, injury, or due to overuse, in individuals with normal anatomic configuration. This entity represents almost 95% of disorders resulting in low back pain.

Age at presentation	Independent
Onset	Acute
Duration of symptoms	Variable, usually < 1 month
Morning stiffness	< 30 minutes
Effect of exercise	Deterioration
Pain at rest	Improvement
Nocturnal pain	No
Alternating gluteal pain	Rare
Irradiation/neurologic deficit	Common, Radicular/Yes
Sacroiliac joint sensitivity	No
Systemic symptoms	No
Positive family history	Variable, usually irrelevant
Correspondence to NSAIDs	Moderate

Table 4. *Clinical characteristics of mechanical low back pain [55].*

Clinical observation	**Muscle strain**	**Herniated disc**	**Osteoarthritis**	**Spinal stenosis**
Age (years)	20-40	30-50	> 50	> 60
Straight leg raising test	No	Yes	No	Yes (only after walking)
Pain pattern				
Location	Back (unilateral)	Back/leg (unilateral)	Back (unilateral)	Leg (unilateral or bilateral)
Onset	Acute	Acute	Insidious	Insidious
Change while standing	Increase	Decrease	Increase	Increase
Change while sitting	Decrease	Increase	Decrease	Decrease
Change while bending	Increase	Increase	Decrease	Decrease
Evidence from imaging				
X-ray	None	None	Disc space narrowing	Arthritis
MRI	None	Disc abnormality	Facet joint arthritis	Canal/foramen narrowing

Table 5. *Characteristics of specific disorders causing mechanical low back pain [56].*

5.1 Lumbar sprain

Defined as a non-radiating ache or muscle spasm in the lower back with its onset usually linked to the adoption of a prolonged abnormal body posture or repetitive overuse. Other possible etiologies include a sudden increase in mechanical stress or an isolated traumatic incident [57]. It reflects an injury to ligamentous, muscular, or fascial structures of the lower back and typically worsens with motion, especially bending. It is considered the most common cause of mechanical low back pain accounting for 60% to 70% of all cases [58]. The diagnosis is determined by medical history and by identifying a localized pain with palpation or during movement on physical examination.

5.2 Vertebral compression fracture

Fractures occurring either slowly over time or acutely from a mild trauma (e.g. fall from a standing height) are considered fragility fractures due to osteoporosis. The most common type of osteoporotic fracture is vertebral compression fracture [59] and the most commonly affected part of the vertebral column is the thoracolumbar junction [60]. Studies indicate that during their lifetime, at least 25% of American post-menopausal women will experience an osteoporotic vertebral compression fracture [61]. Additionally, a history of an osteoporotic fracture is considered a risk factor for subsequent fractures, as 19% of patients will suffer another one in the next year [62].

Although many acute episodes will go on unnoticed as being asymptomatic, this is not the case for every patient. Typical clinical manifestation is that of acute localized pain or tenderness over the involved level, following an activity such as weight lifting, standing from a seated position, bending forward, even a vigorous cough or sneeze [63]. Pain may extend unilateral or bilateral into the flanks, or the posterior superior iliac spine [64], and is usually aggravated by any movement, especially walking down stairs, sitting, and spine flexion or extension [65, 66].Upon physical examination, pressure appliance over the corresponding spinous process usually triggers the pain. Neurological findings are typically absent. Sometimes focal kyphosis or loss of lumbar lordosis may be observed, although kyphosis as well as height loss are mostly found in cases of multiple vertebral fractures [67].

Radiographic evaluation is the main principal, not only for the detection of a vertebral compression fracture (appearance of a classic ‘‘wedge’’ fracture), but also for determining its severity staged as follows [68]:

- Grade 1: 20-25% height deformity
- Grade 2: 25-40% height deformity
- Grade 3: > 40% height deformity

Even though most acute episodes usually resolve over a 4 to 6 week time period, approximately 75% of symptomatic cases will go on developing chronic back pain and suffering from functional impairment [69, 70]. This is mainly attributed to the presence of more than one vertebral fractures or abnormal healing after an acute episode [57].

For the management of a vertebral compression fractures, prevention of osteoporosis is equally important to a specific treatment scheme. Treatment of an acute vertebral compression fracture is conservative with proper immobilization and analgesia being applied. For patients with persistent pain lasting more than 6 weeks, except of the medical treatment, vertebral augmentation should be considered [60].

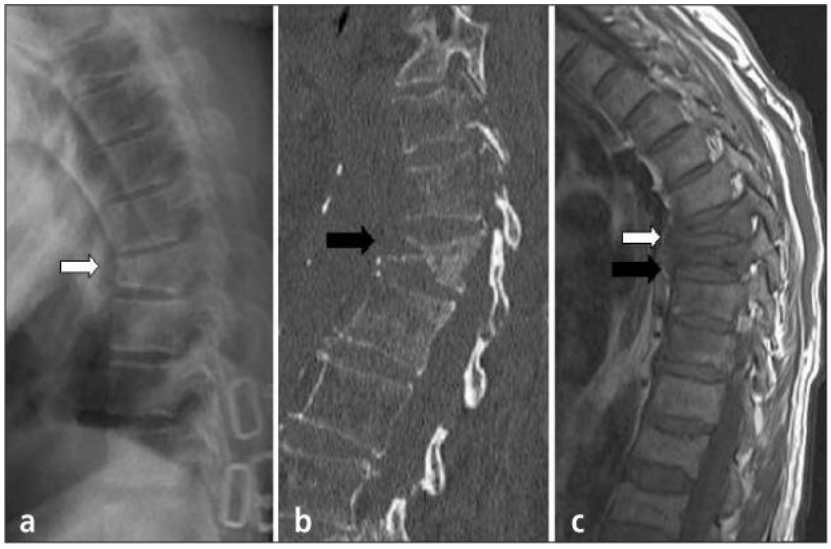


Figure 8. *X-ray images of vertebral compression fracture: a) x-ray images of vertebral compression fracture with anterior wedging (white arrow) b) computed tomography scan of biconcave vertebral compression fracture (black arrow) c) T2 weighted magnetic resonance images of wedge vertebral compression fracture (white arrow), and biconcave vertebral compression fracture (black arrow) [71].*

5.3 Intervertebral disc herniation

One of the main manifestations of ageing is degeneration of intervertebral discs. With time, the elastic properties of nucleus pulposus are diminished, thus losing its resistance to compressive forces, while annulus fibrosus degenerates and fissures. As a result, with the appliance of excessive pressure nucleus pulposus protrudes outside annulus fibrosus, forming a hernia. Disc herniation accounts for approximately 5% to 10% of mechanical low back pain.

Beneath each vertebra there is a pair of neural foramina through which a pair of spinal nerve roots, recurrent meningeal nerves and radicular blood vessels pass to the periphery. Formation of a disc hernia can lead to compression of the spinal root at the corresponding level during its passage through the root canal, hence leading to development of radiculopathy [72].

The lumbosacral part is the most susceptible to disc herniation, especially at the level of L4-L5 and L5-S1, which accounts for 90% to 95% of cases because of its mobility [57].

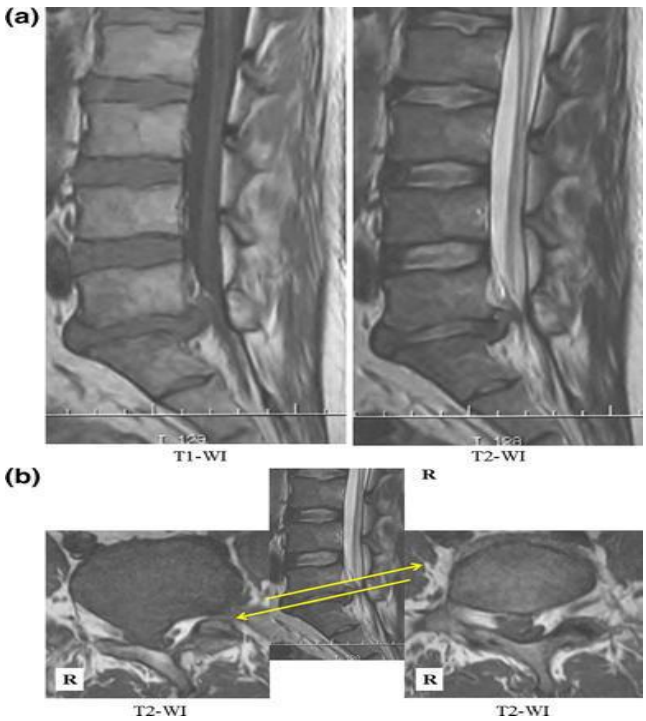


Figure 9. *(a) MR sagittal images showing disc herniation at L5-S1 intervertebral disc level. (b) Axial MR T2-weighted images showing the herniated nucleus pulposus (HNP,* left panel*), which migrated cranially (b,* right panel*) [73].*

The clinical presentation of lumbosacral intervertebral disc herniation is that of lower back pain, with or without accompanying motor/sensory deficits, spreading over a dermatomal distribution. It is typically relieved by standing and worsened in sitting position [49]. The exact range of symptoms vary according to the level at which a nerve root or roots are compressed [74]:

- L1 radiculopathy: Uncommon as disc herniation at the level of L1 is rare. The inguinal region is mostly affected where pain, paresthesia and sensory loss can be present.
- L2/L3/L4 radiculopathy: Considered a common entity, as the corresponding spinal nerve roots are responsible for innervation of the anterior thigh muscles which makes their differentiation based to symptoms difficult. Patients present with acute low back pain radiating around the anterior aspect of the thigh, down into the knee and often down the medial aspect of the lower leg, as far as the arch of the foot. On physical examination weakness in hip flexion, knee extension and hip adduction may be observed. An accompanying reduction in patellar reflex is common.
- L5 radiculopathy: Maybe the most common radiculopathy. Presents with acute low back pain radiating down the lateral aspect of the leg into the dorsum of the foot. On physical examination, weakness in foot dorsiflexion, toe extension, foot inversion and foot eversion may be observed.
- S1 radiculopathy: The second most common radiculopathy. The pain starts from the lower back, near the sacroiliac joints, radiating down the posterior aspect of the leg into the plantar aspect of the foot. On physical examination, weakness of plantar flexion is more prominent, while weakness of leg extension and knee flexion may coexist. A loss of Achilles tendon reflex is typical.
- S2/S3/S4 radiculopathy: Disc herniation at these levels is less common, but a radiculopathy may be caused by compression of nerve roots from a large hernia at a higher level, usually at L5-S1 level. Pain located at the sacral or buttocks area may be present with radiation down to the posterior aspect of the leg or into the perineum. It is usually accompanied by urinary and fecal incontinence, as well as sexual dysfunction.

Lumbar nerve root	Muscle group	Sensory distribution	Deep tendon reflex
L2	Hip flexors	Anterior medial thigh	None
L3	Quadriceps	Anterior thigh to knee	Patellar
L4	Anterior tibialis	Medial calf/ankle	Patellar
L5	Extensor hallucis longus	Lateral ankle/dorsum of foot	None
S1	Calf muscles	Plantar-lateral foot	Achilles

Table 6. *Lower extremity myotomes, dermatomes, and reflexes by lumbar nerve root [49].*

Management of intervertebral disc herniation is in most cases conservative, while surgical treatment is considered for patients suffering from intractable pain or in case of radiculopathy accompanied by neurologic deficits.

5.4 Spondylolysis and spondylolysthesis

Spondylolysis refers to a defect, usually a fracture, in the bony part of pars interarticularis, which serves as a connection between two adjacent facet joints. Almost 90% of cases occur at the level of L5 [75]. Spondylolysis can be unilateral or bilateral (80% of cases [76]), with bilateral defects usually leading to slippage of a vertebral body onto the one below, a condition known as spondylolisthesis [77]. Most commonly, the superior vertebra slips anteriorly over its inferior one, a condition called anterolisthesis, while posterior slippage is called retrolisthesis [78].

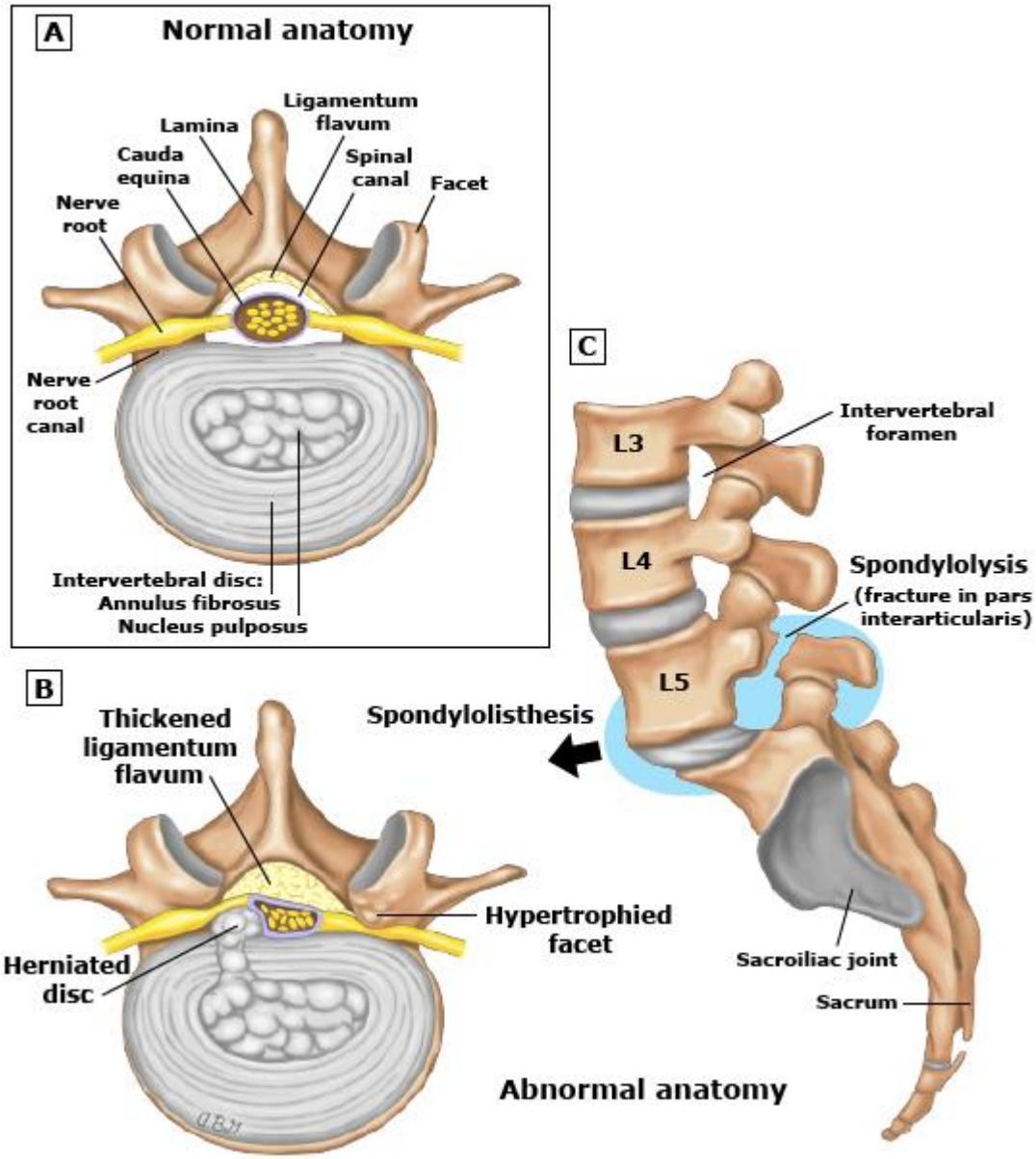


Figure 10. *Common pathoanatomical conditions of the lumbar spine [79].*

Wiltse classification [80] is used to categorize spondylolisthesis based on the etiology:

- Type I – dysplastic: Attributed to a congenital dysplasia of the first sacral vertebra.
- Type II – isthmic: The most common type, usually seen in young athletes. It can present as separation of the pars interarticularis following a fatigue fracture (type IIa), elongation of pars interarticularis due to healing after repetitive fractures (type IIb), or acute fracture of pars interarticularis (type IIc).

- Type III – degenerative: More common in elderly population as it is attributed to degenerative changes at the facet joints, leading to ligamentous instability and subsequent subluxation of the affected vertebral body. The most common site in degenerative spondylolisthesis is L4 [89].
- Type IV – traumatic: Injury of a supporting bone, other than pars interarticularis, caused by a high-impact type of injury.
- Type V – pathologic: Due to a local or generalized bone disease.

Meyerding classification [78] is used to categorize the grade of spondylolisthesis according to the degree of vertebral displacement beyond its inferior one:

- Grade I: 0-25%
- Grade II: 25-50%
- Grade III: 50-75%
- Grade IV: 75-100%
- Grade V: complete displacement (spondyloptosis)

The clinical presentation is that of insidious back pain radiating into the buttocks or down to the posterior thigh of one or both legs, which is exacerbated by flexion or extension. Motor or sensory changes are typically present and include paresthesias, numbness, or weakness [57]. During physical examination, main findings are lumbosacral and hamstring tightness, while abnormal gait – typically crouch gait, with hips and knees flexed – can be present [78].

Management of low-grade spondylolisthesis is conservative with NSAIDs and physiotherapy, with bracing being used sometimes to support stability and avoid extension. Surgical treatment is reserved for grade III or higher spondylolisthesis.

5.5 Spinal stenosis

Spinal canal narrowing leading to compression of the spinal cord and its spinal nerve roots [56]. It is classified as being either primary (congenital) or secondary (acquired) [81]. By far the most common etiology is degenerative spondylosis, a condition usually appearing in persons older than 50 years [82].

Congenital/developmental	Acquired
Idiopathic	**Degenerative**
Genetic/metabolic	Spondylosis
Morquino syndrome	Intervertebral disc narrowing
Achondroplasia	Lateral recess nerve entrapment
Down syndrome	Spondylolisthesis
Other	Adult scoliosis
Childhood scoliosis	Intraspinal synovial cyst
	Metabolic/endocrine
	Osteoporosis with fracture
	Acromegaly
	Calcium pyrophosphate dehydrate disease
	Hypoparathryroidism
	Epidural lipomatosis
	Postoperative
	Traumatic
	Fracture
	Miscellaneous
	Paget disease
	Diffuse idiopathic skeletal hyperostosis
	Amyloidosis

Table 7. *Causes of Lumbar Spinal Stenosis [83].*

In degenerative spondylosis, a variety of age-related degenerative or arthritic changes take place leading to the end-result, the spinal canal stenosis. At first, intervertebral discs are affected. Their desiccation and subsequent flattening results in disc bulging and collapse [84]. The most commonly affected intervertebral disc is L4–5, followed by L3–4, L5–S1, and L1–L2 [85-87]. This disc disintegration is responsible for an increase in stress applied on facet joints and ligamentum flavum, thus resulting in osteophyte formation and its thickening. Each of these changes play an important role in the narrowing of spinal canal [88].

The clinical picture arising from the compression of the neuronal elements passing through the spinal canal is known as neurologic claudication or pseudoclaudication, not to be confused with vascular claudication. It usually has an insidious onset with the first symptoms being morning stiffness and low back pain relieved by activity [89]. Then, it progresses to lumbar neurogenic claudication, which is characterized by bilateral, asymmetrical heaviness, cramping and pain on the lower limbs, typically triggered by walking or prolonged standing and worsening with lumbar extension [90]. Symptoms tend to progress until the patient is unable to keep walking or standing, and cease only by a change in body position, mainly sitting or leaning forward [91]. Some patients adopt the so called “simian stance”, a position with hip and knee slightly flexed [92]. Signs and symptoms of radiculopathy, such as numbness and other sensory deficits are not present, but in a few cases, while motor deficits are generally mild [93, 94].

Differentiating between vascular and neurologic claudication is always crucial. In contrast to the neurologic one, vascular claudication ceases even with rest at a standing position. There is also a difference in the way of distribution, as neurogenic pain tends to radiate distally, while vascular tends to radiate proximally from the foot to the thigh [56]. Other typical characteristics of vascular claudication include changes in skin temperature and color as well as diminished distal pulses in the lower extremities [95].

Characteristic	Vascular (Iiliofemoral arterial insufficiency)	Neurogenic (Ilumbosacral nerve root entrapement)
Mechanism	Ischemic	Ischemic and/or mechanical
Pain	Present (cramping)	Present or absent (radicular)
Pain location	Exercised muscles	Lumbosacral (sciatic)
Pain relieved by	Rest	Flexion posture or sitting
Motor deficit	Rare	Variable, exacerbated by walking
Pulses	Decreased	Normal
Arterial bruit	May be present	Absent
Aortography	Diagnostic	Normal
Lumbar MRI, CT, myelogram	Normal	Diagnostic

Table 8. *Vascular versus Neurogenic Claudication [83].*

Conservative treatment is the first option, at least for mild cases, with surgical treatment being reserved for incapacitated patients with a bad quality of life [96]. The gold standard method is a typical open laminectomy with bilateral foraminotomies, which is performed via a single large incision. Alternatively, minimally invasive techniques can be used via several small incisions [97]. In case of preexisting spinal instability, it is usually followed by spinal fusion [98]. Finally, implantation of expander devices may be tried in mild to moderate cases [99].

5.6 Vertebral osteoarthritis

The hallmark of osteoarthritis consists of joint pain, stiffness, deformity and functional impairment. It is considered one of the leading causes of disability in the elderly population [100].

Lumbar osteoarthritis is a diagnosis of exclusion with the only confirmatory sign being the presence of non-specific radiographic alterations of the vertebral column [56]. It mainly affects the zygapophyseal (facet) joints and intervertebral discs, creating the so called facet syndrome [101].

Manifestations of facet syndrome may mimic these of lumbar spinal stenosis, meaning localized low back pain radiating to the gluteal region and down to one or both legs, typically ending above the knee, although persistent neurological deficits are typically not present [56].

The end result of lumbar osteoarthritis can be that of degenerative scoliosis or spondylolisthesis [102], as the unevenly distributed pressure applied on the intervertebral discs and corresponding joints results in articular cartilage loss and remodeling, which in turn leads to progressive curvature of the spine and joint subluxation [103].

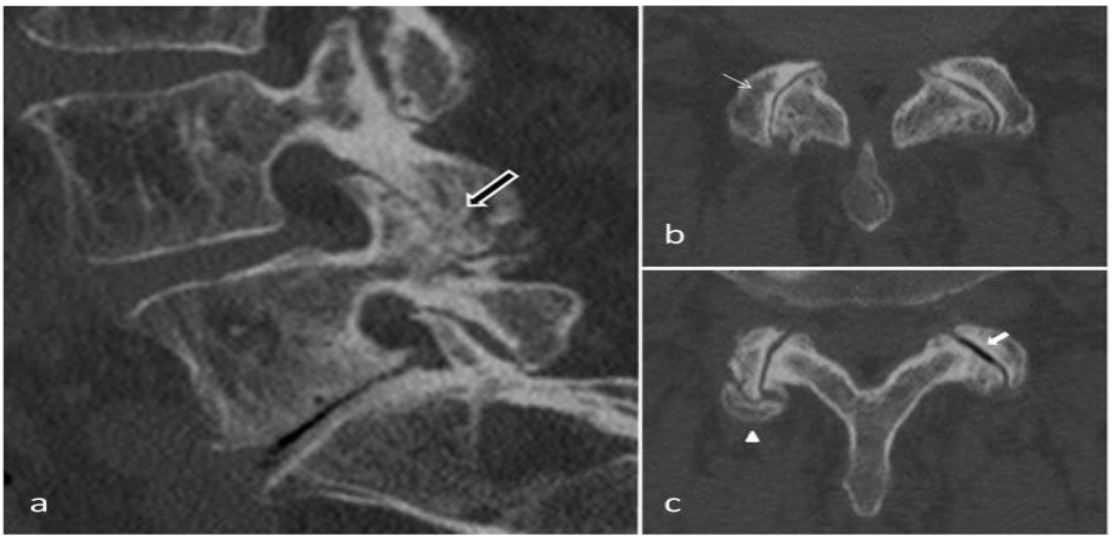


Figure 11. *Degenerative facet joint osteoarthritis (FJOA): Sagittal (a) and axial (b, c) CT views. Hypertrophy of the posterior articular process (black arrow). Joint space narrowing (thin white arrow). Joint capsule calcification (arrow head) and vacuum phenomenon (white arrow) [104].*

6. Inflammatory low back pain

Of the patients suffering from low back pain, approximately 5% will end up being diagnosed with a systemic inflammatory condition [105, 106]. These are rheumatic diseases characterized by the absence of both rheumatoid factor (RF) and anti-nuclear antibodies (ANAs), thus being called seronegative spondylarthropathies. They show a 3:1 male-to-female predominance, while the most common age of presentation is between the second and third decade of life [107].

Spondylarthropathies compose a heterogeneous group of disorders that share characteristic clinical features with the most common, and usually the initial symptom, being inflammatory back pain [108] as well as a genetic predisposition related to the HLA-B27 allele. Despite this connection, it must be noted that less than 5% of the HLA-B27 positive population will develop spondylarthropathy [51].

Age at presentation	< 40
Onset	Insidious
Duration of symptoms	> 3 months
Morning stiffness	> 30 minutes
Effect of exercise	Improvement
Pain at rest	Deterioration
Nocturnal pain	Yes
Alternating gluteal pain	Common
Irradiation/neurologic deficit	Diffuse/Rare
Sacroiliac joint sensitivity	Common
Systemic symptoms	Yes
Positive family history	Common
Correspondence to NSAIDs	Strong

Table 9. *Clinical characteristics of inflammatory back pain [55]*.

Spondylarthropathies are subdivided to predominantly axial spondylarthritis, predominantly peripheral spondylarthritis, or mixed, according to their clinical presentation [109]. Axial spondylarthritis leads to inflammatory and structural changes mainly in the spine and sacroiliac joints, while in the peripheral ones, changes are more prominent in other joints [110].

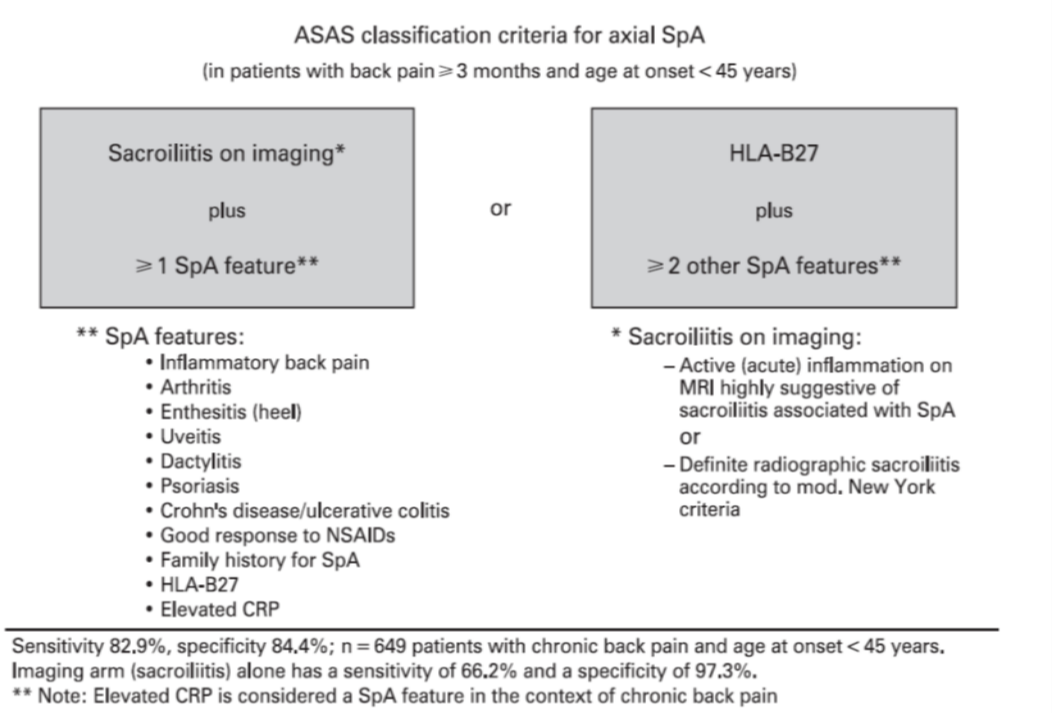


Figure 12. *Classification criteria for axial spondylarthritis (SpA) selected by the Assessment of Spondylarthritis international Society (ASAS) [111].*

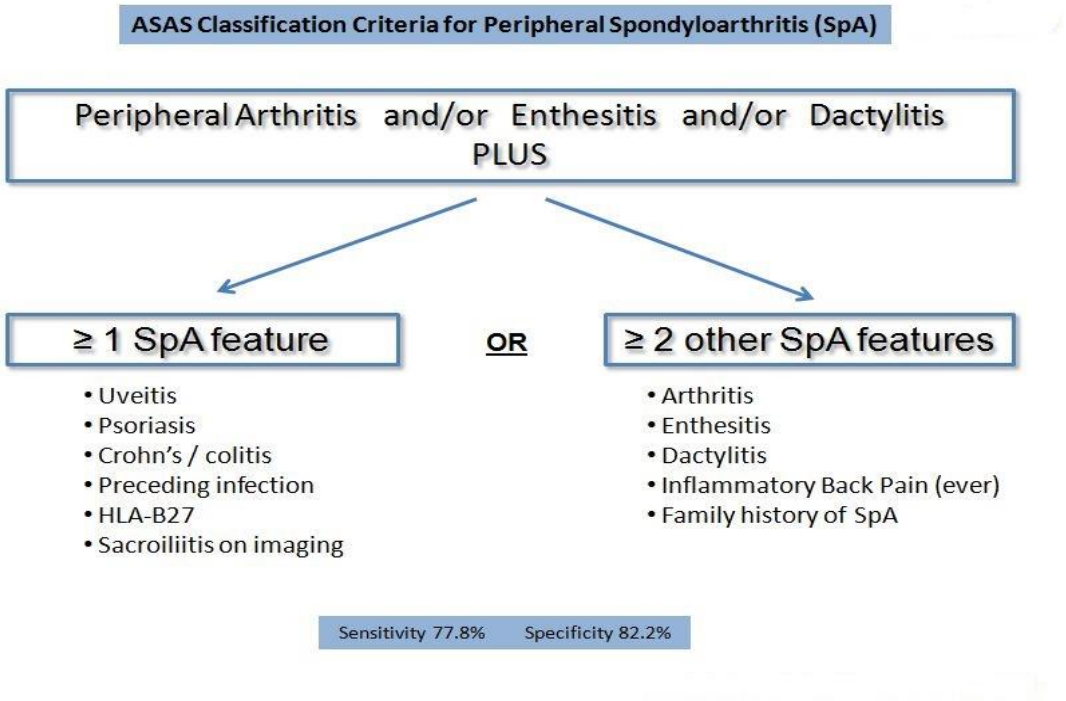


Figure 13. *Classification criteria for peripheral spondylarthritis (SpA) selected by Assessment of Spondylarthritis international Society (ASAS) [112].*

The presence of HLA-B27 gene is associated with an increased risk of axial involvement, younger age of disease onset, higher incidence of extra-articular manifestations, and more prominent diagnostic delay [113].

The most important problem related to spondylarthritis is the significant delay between the initial symptoms and the development of radiographic sacroiliitis, which is a very important diagnostic tool. The average time period needed for the establishment of a definite diagnosis is estimated to be 8–11 years [107], with the disease meanwhile progressing to irreversible structural damage of the sacroiliac joints and the spine [114].

To confirm or exclude the diagnosis of spondylarthritis, the following algorithm has been developed.

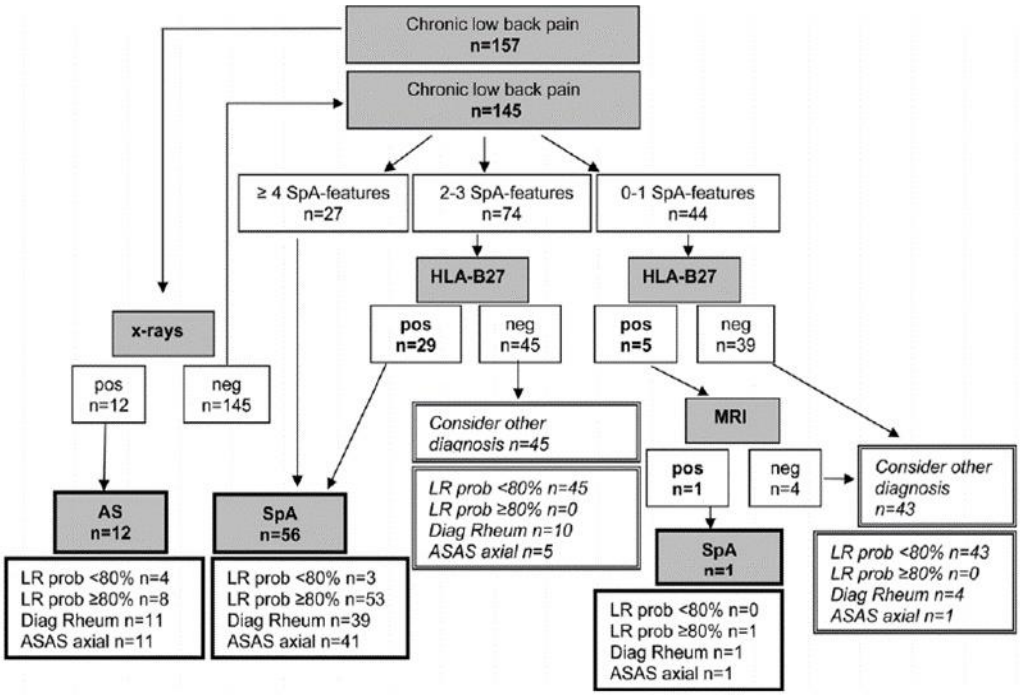


Figure 14. *ASAS modification of the Berlin algorithm [115].*

6.1 Ankylosing spondylitis

A systemic inflammatory disease usually presenting as chronic back pain with progressive spinal stiffness. It is considered the most common and the most severe

disease within the group of spondylarthropathies, with worldwide prevalence ranging up to 0.9% [116].

Ankylosing spondylitis is divided into two subtypes [117]:

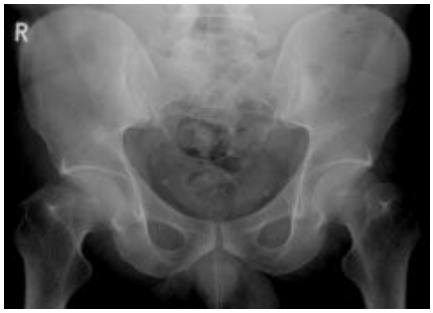
1) Radiographic axial spondylitis: Patients who present with radiographic sacroiliitis. This group represents the typical definition of ankylosing spondylitis, but it may take several years for such a finding to develop.
2) Non-radiographic axial spondylitis: Patients with typical symptomatology and active sacroiliac joint inflammation on MRI.

Typically, ankylosing spondylitis onset is mostly seen in the second or third decade of life [116] and is related to a male predominance of 3:1 [117]. Moreover, the spine and chest wall are most commonly affected in men, while the pelvis, hips, knees, ankles and wrists, are the areas mostly involved in women [118]. Additionally, the disease seems to run a more serious course in men [119].

The leading feature of the disease is persistent inflammatory back pain of gradual onset, over several months, accompanied by excessive fatigue. It may radiate to the gluteal or thigh region, but not below the knee. It is typically worse during inactivity, especially at night or early in the morning and relieved by exercise. The most commonly involved sites are the sacroiliac joints and the spine [117]. The association with articular and periarticular extraspinal features is typical, manifesting as enthesitis (up 70%), peripheral arthritis (up to 40%), and dactylitis (up to 8%) [117]. Extra-articular manifestations are usually present, with acute anterior uveitis being the most common, appearing as a single episode in approximately 40% of ankylosing spondylitis patients, while repeating episodes present in 33% [118].

The diagnosis of ankylosing spondylitis is based on the characteristic clinical findings and the presence of sacroiliitis on imaging. To identify the nature and severity of involvement of the sacroiliac joints the New York grading system is used [120]:

1) Grade I: Suspicious changes
2) Grade II: Minimal evidence of erosion and sclerosis
3) Grade III: Moderate to advanced sacroiliitis characterized by erosions, sclerosis and partial ankylosis
4) Grade IV: Total ankylosis of sacroiliac joints



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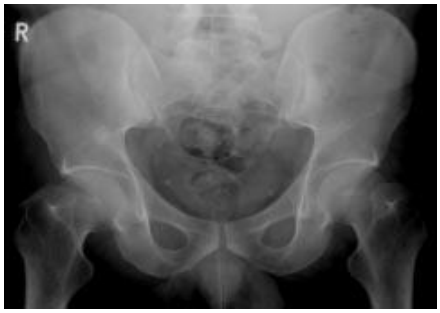

(b)

Figure 15. *(a) Pelvic radiograph of a patient with AS showing sacroiliitis grade II on the right side and grade II–III on the left, (b) Pelvic radiograph of a patient with AS showing bilateral sacroiliitis grade III [121].*

Laboratory investigations can be used if ankylosing spondylitis is suspected, but they are not diagnostic. HLA-B27 gene is present in more than 90% of patients [122]. Also, an increase in acute phase reactants is observed in 50–70% of the patients with active disease [123].

For the management of ankylosing spondylitis, NSAIDs are considered the first-line treatment, as they are effective in relieving pain and stiffness in 80% of cases. Physical therapy and the adoption of a healthy lifestyle have also some effect [51]. In cases where NSAIDs are ineffective or contraindicated, anti-TNF and anti-IL 17 medication, notably etanercept and secukinumab respectively [124], are considered the treatment of choice [118]. Disease-modifying antirheumatic drugs may have some effect on peripheral arthritis, but are not considered an effective treatment for axial disease [51]. Additionally, topical injection of corticosteroids into large joints seems to provide pain relief for several months [118].

The activity of the disease and its response to a specific treatment scheme is assessed using either the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) or the Ankylosing Spondylitis Disease Activity Score (ASDAS) [125].

For severe cases resistant to conservative treatment, presenting with functional, clinical, or radiographic deterioration, spinal surgery is the treatment option recommended by ASAS [126]. In particular, corrective osteotomy is mainly used. In case of vertebral compression fractures, which appear to be more frequent in ankylosing spondylitis than in other rheumatic diseases [127], vertebral augmentation techniques may be applied.

6.2 Psoriatic arthritis

A type of chronic inflammatory arthritis occurring in relation to psoriasis. It is estimated that approximately 30% of the patients with psoriasis will develop psoriatic arthritis [128]. In most cases, approximately 70% to 75%, cutaneous disease occurs prior to arthritis, in 10% a simultaneous onset is observed, while in the remaining 15% cutaneous disease follows after arthritis onset ("psoriatic arthritis sine psoriasis") [129, 130].

The overall prevalence of psoriatic arthritis is low, estimated around 0.3% to 1.0%, although a highly increased prevalence, ranging from 6% up to 42%, is seen in patients with existing psoriasis [131]. Incidence of the disease peaks at the age of 30 to 50 years [130], with male-to-female ratio being 1:1 [132].

Patients generally present with the typical symptoms of inflammatory arthritis affecting both axial and peripheral joints [133, 134]. It is considered a disease with great heterogeneity as five different clinical subtypes have been described [135]:

1) Asymmetric oligoarthritis: The most common subtype in which up to 4 joints are affected in an asymmetric distribution.
2) Symmetric polyarthritis: This subtype involves 5 or more joints that are symmetrically affected, resembling rheumatoid arthritis.
3) Distal arthritis: Affects the distal interphalangeal joints of hands and/or feet. It usually occurs simultaneously with some other subtype, with isolated presentation being rare (only 5%).
4) Mutilating arthritis: A destructive form that causes bone resorption and/or osteolysis, resulting in deformities. Telescoping and flail digits are characteristic findings.
5) Spondyloarthropathy: Axial presentation affecting the spine (spondylitis) and/or the sacroiliac (sacroiliitis) joints. It manifests as typical inflammatory back pain.

Sometimes these patterns may overlap each other or may change over time [136]. About 10% to 25% of psoriatic arthritis patients are found to be positive for the HLA-B27 gene. In cases of axial involvement, HLA-B27 positivity is a more common finding [137, 138].

Pattern of arthritis	Incidence
Asymmetric oligoarticular/monoarticular	Up to 70% of cases
Symmetric	5%-20%, associated with a poorer prognosis
Joint-predominant disease: Distal interphalangeal joints	5%-10%
Arthritis mutilans	5%
Axial-predominant disease: Spondylitis with or without sacroiliitis	Up to 50% over time when associated with peripheral disease (bilateral sacroiliitis often associated with HLA-B27 gene), 2%-4% in isolation

Table 10. *Patterns of psoriatic arthritis [133, 134].*

Other common musculoskeletal clinical manifestations include enthesitis, tenosynovitis and dactylitis, which occur in up to 40% of the cases [133, 134]. Observing for any psoriatic skin lesions is crucial. Typically affected areas include the scalp, ears, groin, umbilical area and other areas where pressure is applied [132]. Characteristic nail lesions, such as pits and onycholysis, which present in up to 90% of patients with psoriatic arthritis, but in only 45% of patients with skin psoriasis as well as the presence of axial involvement, support the diagnosis [139].

On classic radiographic studies the affected joints present with bone erosion, ankylosis and fluffy periostitis. For the definite diagnosis of psoriatic arthritis the CASPAR classification criteria, being highly sensitive (91–100%) and specific (97–99%), have been established [140, 141].

Criteria	Points
Current evidence of psoriasis	2
Past of family history of psoriasis	1
Current nail lesions, including pits or onycholysis	1
Negative rheumatoid factor	1
Dactylitis (current or documented by a rheumatologist)	1
Fluffy periostitis detected on radiographs	1

Table 11. *Criteria for the Diagnosis of Psoriatic Arthritis. Diagnosis of psoriatic arthritis can be made based on accrual of three points [141].*

Variable	Psoriatic arthritis	Rheumatoid arthritis	Gout	Osteoarthritis
Joint distribution at onset	Asymmetric	Symmetric	Asymmetric	Asymmetric
No. of hands or feet involved	Oligoarticular	Polyarticular	Monoarticular or oligoarticular	Monoarticular or oligoarticular
Sites of hands involved	Distal	Proximal	Distal	Distal
Areas involved	All joints of a digit	Same joint across digits	Usually monoarticular	Same joints across digits
Tenderness (kg on a dolorimeter)	7	4	NA	NA
Purplish discoloration	Yes	No	Yes	No
Spinal involvement	Common	Uncommon	Absent	Non-inflammatory
Sacroiliitis	Common	Absent	Absent	Absent

Table 12. *Differentiation among Various Forms of Arthritis [132].*

The heterogeneity in the presentation of psoriatic arthritis makes its treatment more complicated and challenging. In cases of mild oligo-articular presentation, a combination of NSAIDs and intra-articular injected corticosteroids is usually effective. For patients presenting with poly-articular involvement or more severe symptoms, disease-modifying antirheumatic drugs (methotrexate, leflunomide) are typically the treatment of choice [142]. For refractory cases, in which symptomatic improvement is not achieved after 3 months of administration of one or a combination of DMARDs [130], biologic agents are used. In particular, anti-TNF and anti-IL 17 agents have been found to suppress skin and joint inflammation and delay radiographic progression, while anti-IL 12/23, anti-APC/T cell and PDEA4 inhibitors have also demonstrated positive results [143]. Patients developing functional disabilities are candidates for surgical treatment. Joint damage is assessed as being mild or severe by the so-called Steinbrocker functional capacity activity grading system, which is used to evaluate the degree of disability [144, 145].

6.3 Enteropathic arthritis

Chronic inflammatory arthritis which is attributed mainly to inflammatory bowel diseases (Crohn's disease, ulcerative colitis), but can also result from other gastrointestinal disorders including celiac disease, Whipple's disease and intestinal bypass surgery [146]. Arthropathy is the most common extra-intestinal manifestation, presenting in up to 50% of patients suffering from an inflammatory bowel disease. In some cases articular manifestations may precede the typical clinical manifestations of bowel disease [147].

An active bowel disease, a positive family history, lifestyle habits like cigarette smoking, as well as the presence of additional extra-intestinal features, are considered predisposing factors for the development of inflammatory arthritis in patients with inflammatory bowel disease [148].

Inflammatory bowel disease has been associated with 3 different types of arthritis [149]. The first one manifests as an axial disease, ranging from a type of ankylosing spondylitis to an isolated sacroiliitis, while the second and the third one manifest as two distinct types of peripheral arthritis [150]. Type 1 peripheral arthritis is a self-

limiting acute oligoarthritis, affecting less than five joints. It is usually involves large joints of the lower extremities with the knee being the most commonly affected site. It presents with remissions and flare ups closely related to the activity of inflammatory bowel disease. Type 2 peripheral arthritis is a persisting polyarthritis involving mostly small-joints in a symmetrical pattern. The metacarpophalangeal joints are most commonly affected. It typically lasts for a median duration of 3 years and is not associated with inflammatory bowel disease activity [146]. The axial group, as well as type 1 peripheral arthritis, are classified as spondylarthritides related to inflammatory bowel disease [109].

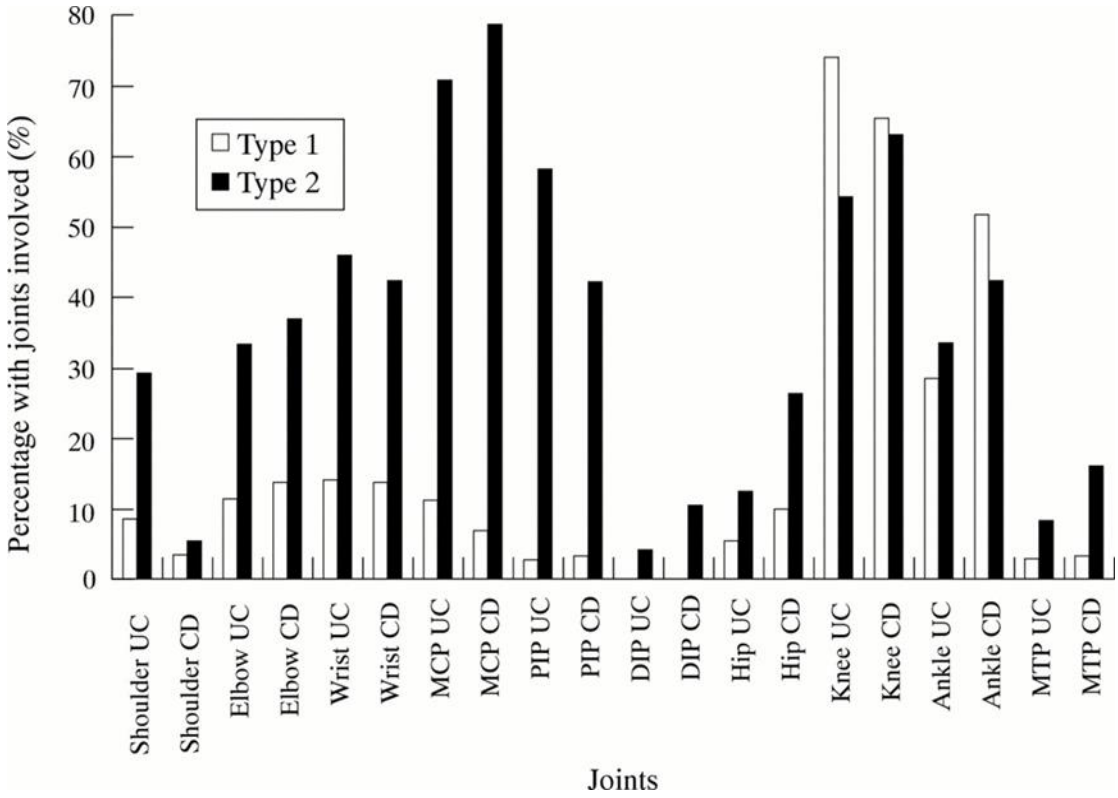

Figure 16. *Articular distribution of peripheral arthropathies in inflammatory bowel disease. UC, ulcerative colitis; CD, Crohn's disease; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint; DIP, distal interphalangeal joint; MTP, metatarsophalangeal joint [151].*

The prevalence of spondylarthritis in inflammatory bowel disease is estimated at 11.5% to 45.7% [151, 152], while the typical inflammatory back pain presents in 5% to 50% of the patients [153, 154]. More specifically, an axial involvement is more commonly seen in patients with Crohn's disease rather than those with ulcerative colitis. Approximately 50% to 75% of the patients with IBD-associated axial arthritis are found to be positive for the HLA-B27 allele [148]. On the other hand, the prevalence of peripheral arthritis is 2.8% to 30.6% [155, 156], with peripheral joint involvement in patients with Crohn's disease and ulcerative colitis being 10% to 20% and 5% to 14% respectively [148].

Periarticular manifestations such as enthesitis, tenosynovitis and dactylitis are typical findings. As for the extra-articular manifestations, the most common include acute anterior uveitis (25%) and cardiac disturbances, mainly aortic insufficiency (4%–10%) and cardiac conduction disturbances (3%–9%). Additionally, skin lesions such as erythema nodosum and pyoderma gangrenosum occur in 10%–25% of the patients. These symptoms are found to be associated with axial involvement and HLA-B27 positivity [146].

Until now, no gold standard criteria have been developed to diagnose enteropathic arthritis. For the diagnosis of enteropathic spondylarthritis, the European Spondyloarthropathy Study Group (ESSG) criteria are used, as the presence of inflammatory bowel disease is considered the most important criterion. Therefore, a patient suffering from inflammatory bowel disease and presenting with inflammatory back pain and/or arthritis of the lower extremities, is diagnosed with spondylarthritis [146]. In case of an established disease, these criteria are highly sensitive (86%) and specific (87%) [109].

In early imaging studies of patients with inflammatory bowel disease, typical findings of axial spondylarthritis, mainly sacroiliitis, are present in up to 19% on plain X-ray [157, 158] and in up to 29% on CT [159]. Of these patients only 3% were symptomatic at the time.

The medicaments used for the treatment of enteropathic arthritis are similar to those for the other seronegative spondylarthritides. More specifically, NSAIDs, which are considered the first-line treatment, have shown good results by reducing both intestinal inflammation and arthritis in type 2 peripheral polyarthritis. For refractory cases, TNF_{α} and IL 17 inhibitors have been found to be highly effective and constitute the last-resort conservative treatment [160].

On the contrary, the treatment of both type 1 peripheral oligoarthritis and axial spondylarthritis seems to be more complicated, as articular inflammation usually remains unaffected despite the possible reduction in intestinal inflammation. Moreover, prolonged administration of NSAIDs may be helpful by reducing articular and periarticular manifestations in many cases, but at the same time they can provoke an exacerbation of the inflammatory bowel disease [146].

Surgical treatment with colectomy of the affected intestinal part have been found ineffective in cases with axial involvement. In case of peripheral arthritis, colectomy can induce remission in patients with ulcerative colitis, but not in those with Crohn's disease [51].

6.4 Reactive arthritis

Defined as an aseptic inflammatory arthritis triggered by a bacterial infection localized at a distant site rather than at the joint itself [161]. Symptoms usually arise 1 to 4 weeks after a gastrointestinal or a genitourinary tract infection [162]. It was previously known as Reiter's syndrome, which nowadays is considered a subgroup not covering the whole spectrum of the disease [163].

An acute episode of reactive arthritis usually resolves after a period of 6 months, or even less, although in many patients it may last for up to 1 year. When the symptoms persist even more, reactive arthritis is considered as chronic [161].

The prevalence of reactive arthritis is estimated as 0,03-0,04% and appears to affect both genders equally [131]. Nevertheless, this number is just an approximation as an exact estimation is difficult to be made due to the lack of a precise disease definition and existence of different diagnostic criteria [164].

A great number of microorganisms have been associated to reactive arthritis with the most common being Chlamydia trachomatis, Salmonella and Shigella. Despite this, approximately 40% of cases are found not to be related to an infectious agent [162].

Enteric infections	Urogenital infections
Salmonella enterica	*Chlamydia trachomatis*
Serovars: *Typhimurium enteriditis paratyphi B, C*, others	*Ureaplasma urealyticum*
	Mycoplasma genitalium
Shigella:	*Neisseria gonorrhoeae*
S. Flexneri	*Gardnerella vaginalis*
S. dysenteriae	Respiratory infections
S. sonnei	*Chlamydia pneumoniae*
Yersinia	Group A beta-hemolytic Streptococcus
Y. enterocolitica (O:3, O:8, and O:9)	Miscellaneus
Y. pseudotuberculosis	HIV
Campylobacter jejuni	B-19 parvovirus
C. jejuni	*Borrelia burgdorferi*
C. coli	*Brucella abortus*
Clostridium difficile	*Calmette-Guerin Bacillus*
Escherichia coli: diarrhogenic strains	*Chikungunya virus*
Bacillus cereus	
Amoebae	
Cryptosporidium	
Giardia lamblia	
Helicobacter pylori, cinaedi	
Strongyloides spp	
Tropheryma whippelii	

Figure 17. *Arthritogenic agents associated with the development of reactive arthritis [165, 166].*

The disease is typically characterized by the clinical triad of conjunctivitis, non-gonococcal urethritis and arthritis, however all these symptoms are present simultaneously only in one-third of the cases [51].

Common clinical manifestations are asymmetric oligoarthritis, predominantly affecting joints of the lower limbs, enthesitis, tenosynovitis, bursitis, and dactylitis. Axial involvement is less common, with sacroiliitis presenting in 15–30% of patients, while the lumbar spine is affected in approximately 50% of patients. In cases with axial involvement, classical inflammatory low back pain is the main finding [51].

Major criteria

1. Arthritis, with 2 of 3 of the following findings

   * Asymmetric
   * Mono- or oligoarthritis
   * Affection predominantly in lower limbs
2. Preceding symptomatic infection, with 1 or 2 of the following findings

   * Enteritis (diarrhoea for at least 1 day, 3 days to 6 weeks before the onset of arthritis)
   * Urethritis (dysuria or discharge for at least 1 day, 3 days to 6 weeks before the onset of arthritis)

Minor criteria, at least 1 of the following

1. Evidence of triggering infection

   * Positive nucleic acid amplification test in the morning urine or urethral/cervical swab for *Chlamydia trachomatis*
   * Positive stool culture for enteric pathogens associated with ReA
2. Evidence of persistent synovial infection (positive immunohistology or PCR for Chlamydia)

Definition of reactive arthritis

Definite ReA: Both major criteria and a relevant minor criterion
Probable ReA: 1) Both major criteria, but no relevant minor criteria or 2) Major criteria 1 and one or more of minor criteria

Exclusion criteria

Other causes for acute arthritis

Figure 18. *Preliminary classification criteria for reactive arthritis, modified from Braun et al., 2000 [164].*

Except of the musculoskeletal system, the disease affects also extra-articular tissues. Ocular manifestations include conjunctivitis, keratitis and uveitis. Skin features such as keratoderma blennorhagica and erythema nodosum are typical, while oral mucosa ulcerations may be present. Genitourinary tract is typically affected with urethritis, circinate balanitis, prostatitis, cervicitis and hemorrhagic cystitis being common findings. Gastrointestinal symptoms like diarrhea are also common. If any of the above mentioned symptoms is identified, a thorough investigation for any active infection should be prompted. Finally, cardiac manifestations, mainly rhythm abnormalities and pericarditis, are rarely seen [167].

Septic arthritis (inflammatory monoarthritis or oligoarthritis)
Disseminated gonococcal infection (genitourinary symptoms, arthritis)
Enteroviral infection (diarrhea, arthritis)
Whipple's disease (acute oligoarthritis or chronic polyarthritis)
Inflammatory bowel disease (diarrhea, arthritis)
Behcet's disease (diarrhea, arthritis, skin and genital ulcers, rash, uveitis)
Crystalline arthropathy
Lyme disease
Post-streptococcal arthritis

Table 13. *Differential diagnosis of reactive arthritis [161].*

Similarly to other spondylarthritides, an association with HLA-B27 gene is found in 50%-80% of patients with reactive arthritis [161]. Furthermore, HLA-B27 positivity bears an increased risk for a more severe course of disease and a higher probability for chronicity [168].

The treatment of reactive arthritis is basically similarly to the rest of spondylarthropathies, with NSAIDs being the first-line medication and biologic agents as well as systemic or intra-articular corticosteroids providing some pain relief. The key difference lies in the possible presence of an active infection, in which case the appropriate antibiotic treatment should be administered as a first step [51].

6.5 Undifferentiated spondylarthritis

The term undifferentiated spondylarthritis is used to describe patients with typical symptoms of spondylarthritis that do not fulfil the classification criteria for any of the subgroups mentioned above. These cases usually remain undifferentiated for a very long period of time [169].

A conflict exists, as this entity is considered by many reports an early phase of ankylosing spondylitis similar to the non-radiographic axial one [131, 170]. Some reports have shown that the number of cases subsequently developing radiographic changes typical for ankylosing spondylitis reach up to 68% at 10 years [171, 172], while others indicate progression to ankylosing spondylitis being only 10% at 2 years [173] and 24% at 10 years [174]. The same applies for a possible association with HLA-B27, as positivity is found at 61.3 % of patients by some studies [174], in contrast to others placing it at only 37.5% [175].

The clinical spectrum of undifferentiated spondylarthritis is wide as it consists mainly from a combination of the clinical and radiological manifestations found in the other spondylarthropathies [176]. The most frequent features related to this entity are low back pain (87.5%), peripheral arthritis (62.5%), enthesitis (62.5%) and low-grade radiographic sacroiliitis (45.0%) [177]. On the other hand, a decreased incidence of extra-articular manifestations is found in cases of undifferentiated spondylarthritis [178].

7. Management

7.1 Imaging techniques

Further investigation with the use of imaging techniques is not indicated in patients with low back pain lasting less than 6 weeks, unless any "red flag" signs or symptoms are identified through the history and physical examination [179, 180]. In this case, imaging studies are mandatory. Other conditions for which imaging should be considered include failure of multiple therapies, history of spinal surgery due to previous injury, coexisting psychiatric dysfunction, pain intensity disproportionate to clinical findings and history of substance abuse [50].

Computed tomography (CT) and magnetic resonant imaging (MRI) are the most commonly used modalities. MRI is usually the study of choice, especially in the presence of neurologic symptoms, as it allows for optimal visualization of the intervertebral discs, nerve roots and spinal cord. In case of a clinically significant intervertebral disc herniation, the specificity and sensitivity are approximately 77% and 75% respectively for MRI [181], almost identical with these of CT, which are about 73% and 57%–64% respectively [182]. CT sensitivity for disc herniation improves to 76% with the addition of myelography [183]. Similarly, regarding the detection of spinal stenosis, the sensitivity and specificity of MRI is 75% and 87%–96% [184] in comparison to 75% and 80%–96% for CT [185]. However, for the detection of nerve root compression, MRI is by far the best modality with sensitivity and specificity reaching 90% and 100% respectively [186].

In case of spondylarthritis, CT has the ability to identify bony changes at a relative early stage [187], but MRI is still much more sensitive in identifying local inflammation [188]. The so-called 'Romanus lesions', typically located at the corners of vertebra are characteristic axial inflammatory changes [189]. Additionally, in spondylarthritis, MRI has a double role, as it serves for both diagnosis and therapy monitoring. Last but not least, MRI may have a higher cost but it does not expose the patient to ionizing radiation in contrast to CT [190].

Additional imaging methods that can be used are of less value. Although plain film radiograph is the most commonly utilized imaging modality due to low cost and high availability, it does not allow for visualization of nerve roots and spinal canal structures. Even lytic lesions cannot be easily detected using plain films, except in significantly advanced cases [191]. Sensitivity and specificity for detection of such lesions is 60% and 99% respectively [192]. In advanced cases of spondylarthritis, changes such as 'shiny corners' of vertebral bodies, syndesmophytes, ankyloses and spinal fusion may be depicted on X-ray. Finally, sacroiliitis, which is considered the hallmark of ankylosing spondylitis is also a late finding [190].

Bone scintigraphy is another modality which can be useful in differentiating degenerative changes from disorders like vertebral fracture, malignancy, or infection. It has the ability to detect characteristic changes at an early stage of spondylarthritis, however in cases of sole sacroiliitis, distinguishing between normal bony uptake and the disease, at a specific site, is relative difficult [193].

Ultrasound can be a useful tool, mainly in peripheral arthritis, as it can show superficial soft tissue inflammation such as enthesitis and synovitis [194]. Ultrasound is found to be more sensitive than physical examination for detecting this kind of manifestations [195].

7.2 Conservative treatment

Active treatment is not always needed for low back pain as most episodes have a self-limited course and tend to resolve within 6 to 8 weeks. Nevertheless, a treatment plan is usually followed, aiming to relief the patient from the pain and help him cope with his daily routine and responsibilities.

As a first step, a treatment plan should focus on proper patient education with details regarding the specific problem as well as the possible provoking and relieving factors being thoroughly explained. It was found that a medical doctor is the most appropriate person to provide this kind of education compared to a nurse or a physiotherapist [196]. Also, both cognitive-behavioral therapy and psychosocial support seem to have a strong positive impact in chronic cases [12].

Traditionally, strict bed rest for at least 15-20 days was advised for patients suffering from low back pain. Nowadays, this belief tends to be replaced by relative rest, meaning activity modification by excluding the pain-provoking ones, as studies have shown a better outcome regarding maintenance of functional status and pain relief compared to strict bed rest [197].

Equally important is pharmacotherapy, which aims mainly to pain relief rather than cure of the specific condition. For mechanical low back pain the most efficient regimen consists of a combination between nonsteroidal anti-inflammatory drugs and muscle relaxants [198]. Some studies indicated that also antidepressants, notably inhibitors of 5-hydroxytryptamine and noradrenaline reuptake, have a positive impact on relieving chronic low back pain [199]. Antiepileptic medications, specifically gabapentin and pregabalin, are efficient in treating peripheral neuropathic pain conditions [200]. Systemic steroids is another entity to be considered, although no significant benefit have been observed in most studies [201].

For inflammatory low back pain, non-steroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors (COXIBs) are considered the first-line treatment aiming to reduce pain and inflammation [202]. Disease modifying antirheumatic drugs (DMARDs) can be administered mainly to control inflammation on peripheral joints, but have less or no effect on axial disease. The most commonly used medicaments of this category are leflunomide, methotrexate, sulfasalazine and cyclosporin [203, 204].

In spite of their wide availability, their effectiveness on the radiological progression of articular changes remains questionable, thus are not commonly used nowadays [205, 206]. Biologic agents, mainly the tumor necrosis factor-alpha (TNF_{α}) and interleukin (IL) 17 inhibitors, are considered the most advanced treatment for spondylarthritis, as they appear to be equally effective for both the axial disease as well as the peripheral articular and periarticual manifestations. They show good results in both reducing pain and improving functional disabilities. Infliximab, etanercept, adalimumab (anti-TNF_{α}), and secukinumab (anti-IL 17) are the main drugs administered [203, 204, 207, 208]. Contrary to DMARDs, results related to biologic agents present evidence indicating a reduction on the radiological progression of articular changes [209]. Opioid analgesics are reserved for patients suffering from severe chronic low back pain, unresponsive to other kinds of treatment.

A. Systemic drug treatment
1. Peripheral arthritis
NSAIDs and COXIBs
Sulfasalazine, methotrexate, leflunomide or cyclosporin
Corticosteroids (in arthritis flares; 40 mg/day dose of methylprednisolone [or lower] that should be tapered quickly, according to the clinical response)
Anti-TNF-α or anti-IL 17 (in more severe cases)
2. Axial involvement
Celecoxib (in continuative administration)
Anti-TNF-α or anti-IL 17
B. Local drug treatment
Intra-articular injections of corticosteroids (when one ore few peripheral joints are involved)
Soft-tissues injections of corticosteroids

Table 14. *Treatment of spondylarthritis [202].*

Other treatment options like epidural steroid injections can be used, especially in cases where neurologic symptoms are present, as short-term pain relief can be achieved for up to 3 months [210, 211]. However, this option raises questions as many side effects, including nerve damage and even paralysis, have been reported in the US making the Food and Drug Administration (FDA) issue a warning label to such products [212]. Therefore, epidural steroid injections are not recommended as a first-line treatment and must be used with caution. Intra-articular or soft tissue injection of a semi-soluble corticosteroid together with an anesthetic modestly decreases pain [213, 214]. The use of botulinum toxin A injection into the paraspinal muscles is supported by little evidence [215], showing a pain improvement at a period of 3 to 4 weeks [216].

The use of physical therapy and chiropractic manipulation have shown a moderate to low effectiveness, while succor of techniques like massage and acupuncture remain controversial [49].

	Acute low back pain	Chronic low back pain
Beneficial	Advice to stay active	Exercise therapy
	NSAIDs	Behavioral therapy
	Muscle relaxants	Multidisciplinary treatment programs
Likely to be beneficial	Analgesics	Analgesics
	Spinal manipulation	Back schools in occupational settings
		Massage
		NSAIDs
Unknown effectiveness	Acupuncture	Acupuncture
	Back schools	Antidepressants
	Epidural steroid injections	Epidural steroid injections
	Lumbar supports	Lumbar supports
	Massage	Muscle relaxants
	Transcutaneous electrical nerve stimulation	Spinal manipulation
	Trigger point injections	Transcutaneous electrical nerve stimulation
	Thermal therapy	Trigger point injections
	Ultrasound	Thermal therapy
	Traction	Ultrasound
Unlikely to be beneficial	Specific exercises	Bed rest
		Electromyogram biofeedback
Ineffective or harmful	Bed rest	Facet joint injections
		Traction

Table 15. *Evidence of treatments for acute and chronic low back pain [6].*

For patients with persistent symptoms, despite the conservative treatment, a follow-up and re-evaluation for possible emergence of “red flag” signs and symptoms is suggested at 4 weeks. If none are identified, continuation of conservative treatment with the addition of physiotherapy may be considered. If the patient remains symptomatic after 6 to 8 weeks, further re-assessment of the patient for “red flags” should be considered in combination with utilization of imaging studies.

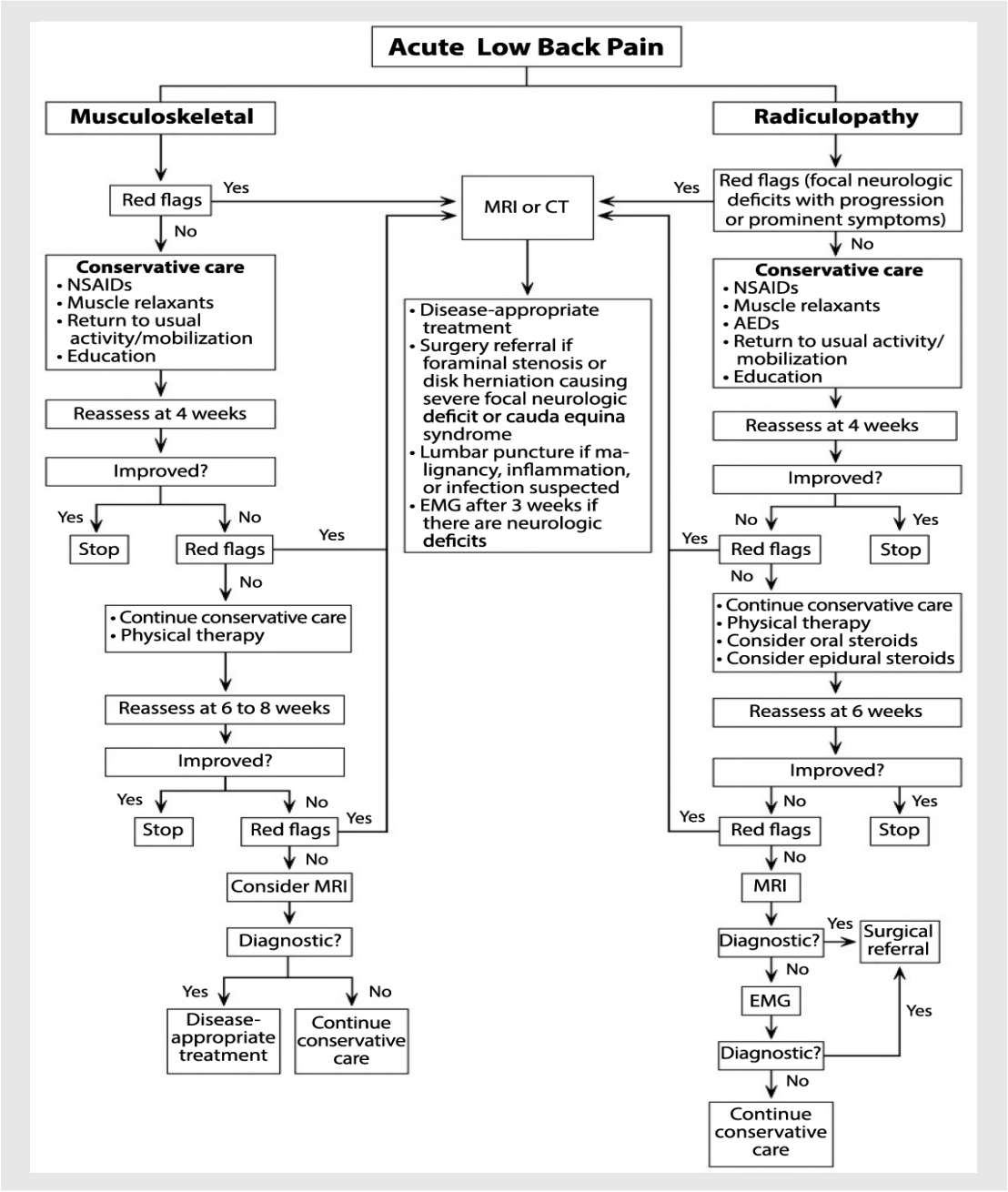

Figure 19. *Treatment algorithm for acute low back pain [12].*

The McKenzie method was developed for patients with low back pain in order to identify whether a treatment scheme or physical therapy is beneficial for them. End-range of joint motion movements are used to assess the patient's mechanical and symptomatic response [217].

Two main examination features are described:

1) The centralization phenomenon, a rapid change in the location of pain from a peripheral or distal location to a more proximal or central location in response to treatment [218]. It can be used as prognostic indicator as a better outcome is observed in patients presenting with it at initial evaluation [219].
2) Directional preference, a rapid and lasting positive change in symptom, function, or range of motion, occurring from repeated end-range joint movement testing in one specific direction of movement. Directional preference is determined from a decrease in pain intensity without a change in pain location.

According to a randomized trial, when centralization or directional preference are matched with a treatment in the same direction, patient's condition is more likely to have a positive outcome [218] with moderate evidence indicating pain reduction and function improvement [217, 220, 221].

Classification	Conceptual model	Clinical findings
Derangement syndrome	Internal articular displacement causing a disturbance in the joint, which produces pain and impairment	Rapid and lasting changes in pain intensity and location occurring for a few minutes to a few days; often accompanied by mechanical improvements; symptom centralization/peripheralization may be present
Dysfunction syndrome	Pain resulting from deformation of structurally impaired soft tissue surrounding or within the spine resulting from previous trauma, degeneration, or development of an imperfect repair; examples include contraction, scarring, adherence, and adaptive shortening	Pain is felt consistently when the abnormal tissue is loaded at the end range of motion and abates when the loading is released; range of motion is restricted; no rapid change in pain is seen
Posture syndrome	Mechanical deformation of normal soft tissues arising from prolonged postural stresses that lead to pain; local mechanical pain occurs after prolonged positioning at joint end range (e.g., sitting slouched)	Local mechanical pain occurs only after prolonged positioning at joint end range (e.g., sitting slouched); and abates when position changes; range of motion is full and repeated motions have no effect
Other	Does not fit criteria for derangement, dysfunction, or posture syndrome	No lasting change in pain location or intensity in response to therapeutic loading strategies

Figure 20. *McKenzie Method Diagnostic Classifications for Low Back Pain [217].*

7.3 Invasive treatment

In refractory cases with rapid progression or presence of disabling symptoms, leading to a significant impairment in life quality, surgical intervention is often warranted. Choice of surgical approach depends on the underlying pathology and the degree of structural changes [12].

Spinal fusion: A procedure in which two or more vertebral bodies are joined together in continuity. It aims to provide stability (e.g. in spondylolisthesis) as well as pain relief by motion restriction and removal of possible triggers (e.g. degenerated intervertebral disc). It is the most common type of surgery used for chronic nonspecific low back pain [222].

Lumbar disc replacement: Replacement of a degenerative intervertebral disc with an artificial one. It is considered a new alternative to spinal fusion, gaining more support with time, as it targets the preservation of spine mechanics and physiological range of motion, thus reducing the long-term degenerative changes that usually follow spinal fusion [222].

Discectomy and laminectomy: Removal of the herniated part of an intervertebral disc which is usually followed by removal of the vertebral lamina to relieve further pressure. The traditional open discectomy involved a standard surgical incision. Nowadays, it has been widely replaced by microdiscectomy, which is performed through an operating microscope, via a significantly smaller incision, and is commonly followed by a hemilaminectomy. It is considered the gold standard method with success rate exceeding 90% [96].

Minimally invasive procedures: Endoscopic discectomy, laser discectomy, percutaneous discectomy, percutaneous manual nucleotomy and radiofrequency nucleoplasty are newer techniques emerging. Endoscopic transforaminal discectomy appears to have results similar to microdiscectomy when performed by a well-trained physician [223]. On the other hand, non-endoscopic percutaneous methods may be less invasive but they also seem to have an increased risk of additional surgery within the following years [224], ranging between 60% and 70% [225].

Another disadvantage is related to the pain relief, which shows a slower decrease rate, extending through several weeks before disappearing. Hence, these techniques are mostly reserved for older patients or those with less severe clinical manifestations.

Vertebral augmentation: Kyphoplasty is a technique in which inflatable bone tamps are introduced into a fractured vertebra elevating it to its original level, while vertebroplasty involves the percutaneous injection of bone cement into a fractured vertebra under image guidance [226]. It must be noted that despite a successful procedure, 25% of the patients report recurrent pain within the first 6 months of treatment [227].

Implant devices: Implantation of expander devices between vertebral bodies is a newer, less invasive method that can be used in order to relieve spinal compression [99]. The so called "X-stop" is the first approved implant of this type indicated for mild to moderate cases [228, 229].

Osteotomy and stabilization: Corrective osteotomy followed by stabilization is the most common surgical procedure indicated in severe cases of axial spondylarthritis. Osteotomy is differentiated into being open, closed, or poly-segmental. Fewer complications are found in cases of closed osteotomy [230].

Conclusion

Low back pain is an extremely common problem, affecting approximately 80% of people at some point in their life. Incidence increases with age until the sixth decade of life, when it gradually declines. It has a huge impact on individuals, families, communities, governments and business throughout the world.

Most cases are characterized as being non-specific, in which no clear pathology is found. The natural history of acute episodes of low back pain is favorable in most patients, running a self-limiting course lasting up to 12 months, however many of them will develop chronic low back pain facing recurrent episodes. Predisposing factors leading to chronicity include age, educational status, psychosocial factors, occupational factors and obesity.

Evaluation of these patients includes completing an appropriate history as well as performing a comprehensive physical examination. In patients with low back pain lasting more than 6 to 8 weeks, unresponsive to conservative treatment, or presenting with any “red flag” signs or symptoms, an imaging must be obtained. In such cases, the study of choice is usually the MRI.

In case of specific low back pain, identification of the exact etiopathogenesis is very important. Mechanical back pain, which constitutes the most common type, is usually characterized by an acute onset, improves with rest and is commonly accompanied by radiculopathy. Conditions that belong to this category are lumbar sprain, vertebral osteoarthritis, vertebral compression fracture, intervertebral disc herniation, spondylolysis/spondylolisthesis and spinal stenosis. On the other hand, inflammatory back pain usually presents with an insidious onset, morning stiffness, improvement with exercise, alternating gluteal pain and is associated with bot systemic articular and extra-articular manifestations. Diseases such as ankylosing spondylitis, reactive arthritis, psoriatic arthritis, enteropathic-related arthritis and undifferentiated spondylarthritis are known as spondylarthropathies and can present with axial involvement and inflammatory low back pain.

An acute episode of low back pain is typically treated conservatively with relative rest, activity modification, pharmacotherapy and physical therapy. In chronic cases, patient education, cognitive-behavioral therapy and psychosocial support are also imperative. Surgical treatment is considered as last resort in patients unable to keep up with daily routine and responsibilities due to disease progression, despite following a conservative treatment scheme, or if “red flag” signs and symptoms requiring urgent intervention are present.

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