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ULTRASOUND DEFINITIONS AND FINDINGS IN GREATER TROCHANTERIC PAIN SYNDROME

A SYSTEMATIC REVIEW

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STUDY PROTOCOL: ULTRASOUND DEFINITIONS AND FINDINGS IN GREATER TROCHANTERIC PAIN SYNDROME: A SYSTEMATIC REVIEW

Version 2 - 7/10/2019

Version changes

from version 1 to version 2 are marked with yellow and includes:

- 1. Introduction: Last part rephrased to clarify the gaps in current research.
- 2. Objectives: Rephrased to review questions for clarity.
- 3. Population and comparators: Comorbidities will be evaluated for each study individually.
- 4. Exclusion criteria: Studies primarily focusing on tumors, hematomas, genetic disorders, and ultrasound-guided nerve block are excluded too. Injection of steroid during the last 12 months is changed from 12 to 3 months.
- 5. Inclusion criteria: Original MRI data and surgical/histopathological data are only included if there is original ultrasound data for comparison.
- 6. Selection process: Two authors will complete the process instead of one.
- 7. Data collection: One author will double-check the extracted data. Subtle changes in data extraction, see appendix 2. Due to limited resources, authors will not be contacted if data is missing.
- 8. Secondary outcomes: Surgical/histopathological outcomes added.
- 9. Assessment of methodical quality in individual studies: Epidemiological Appraisal Instrument will be used instead of Downs and Black checklist.
- 10. Data synthesis: First part rephrased for clarity.
- 11. Appendix 2: Subtle changes in data extraction form. Most importantly, MRI definitions will not be extracted and the definitions/presence of normal appearance, thickness, vascularity, bony abnormalities, enthesopathy and iliotibial band abnormalities will be extracted too.

The rationale behind the changes is to clarify and narrow the focus of this systematic review and to enhance the research quality by adding another author to the selection- and data extraction process.

Administrative information

Study protocol:

Ultrasound Definitions and Findings in Greater Trochanteric Pain Syndrome: A Systematic Review

Registration:

Our systematic review is registered for submission in the International Prospective Register of Systematic Reviews (PROSPERO). (Registration number: XXXXXXX)

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Contributions

MH has drafted the protocol with the co-operation of supervisors (MSR and JLO). All authors have read, provided feedback and approved the final manuscript.

Amendments

In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

Keywords:

Greater trochanteric pain syndrome, Gluteal tendinopathy, Trochanteric bursitis, Ultrasound, MRI

Introduction

Rationale

Greater trochanteric pain syndrome (GTPS) is a term given to chronic lateral hip pain and is most prevalent in middle-aged women (40-60 years), but is also frequently seen in runners, footballers and dancers. It is a common diagnosis and is estimated to affect between 10 - 25 % of the general population.¹

GTPS is characterized by tenderness on direct palpation of the lateral aspect of the hip and can be exacerbated by weight-bearing activities, lying on the painful site, active abduction and passive adduction of the hip joint.^{1–3} This might result in a reduction of physical activity leading to negative implications for general health, employment and well-being.⁴

In 1923 "trochanteric bursitis" was described.¹ However, cardinal symptoms of bursal inflammation like erythema, warmth and edema are usually absent and more magnetic resonance imaging (MRI), ultrasound and histopathological studies suggest that tendinopathy is a more evident reason than bursitis to GTPS.^{5–13} Nowadays GTPS is primarily thought to be due to tendinopathy/tearing of the gluteus medius tendon and/or the gluteus minimus tendon with or without coexisting bursal pathology.^{1,3}

In addition, chronic lateral hip pain can also be caused by iliotibial band friction disorders, osteoarthritis of the hip, stress fractures of the femoral neck, avascular necrosis of the femoral head, lumbar spine referred pain, nerve entrapment, pelvic pathology, myofascial pain among many other factors. These causes together with the complex etiology behind GTPS increase the risk of misdiagnosis.^{1,3,8} This emphasizes the need for good, reliable clinical tests and imaging modalities to increase the diagnostic accuracy in order to avoid mismanagement, which can lead to worsening of the prognosis and development of recalcitrant symptoms.^{3,14}

GTPS is acknowledged as a clinical diagnosis, but imaging modalities can be useful in recalcitrant cases or in cases with a mixed clinical picture.³

Plain x-ray findings are usually normal in patients with GTPS but can be used to exclude other potential causes like hip osteoarthritis and stress fractures.¹

Ultrasound is highly effective in evaluating gluteal tendons and bursae and can further be used therapeutically to guide injection of steroid.¹ Connell et al. describe that ultrasound can be used to identify gluteal tendinopathy in patients with GTPS and further that ultrasound also can be used to characterize the severity of disease and to discriminate tendinosis from partial- and full thickness tears.⁷ Another study found a positive predictive value of 100 % for gluteal tendons tears in 24 patients with GTPS and also describes the ability of ultrasound to detect bursa pathology.⁶ In addition, ultrasound is a simple, dynamic, inexpensive and radiation-free diagnostic tool and as such, it is an

excellent imaging modality. However, ultrasound requires trained personnel, is vulnerable to interpersonal differences and cannot exclude intra-articular and bony causes to hip pain.^{1,7}

MRI is usually restricted to patients in whom conservative measures have failed due to its expensiveness and lack of availability. Though, MRI is a highly sensitive diagnostic tool regarding GTPS and is also sensitive to other causative pathologies of chronic lateral hip pain. In addition, no interpersonal differences are seen.^{1,7} On the other hand, MRI findings are also seen in asymptomatic people and may therefore not be entirely specific.^{11,15,16} For that reason Grimaldi et al. recommends that positive MRI findings always should be backed up by positive palpation of the hip and at least one active clinical test in order to diagnose GTPS as the cause to chronic lateral hip pain.¹⁷

A limitation in identifying specific structural diagnoses is that both ultrasound and MRI rely on radiological interpretation. Docking et al. states that there is no consensus around the features that differentiate between the most common finding in GTPS: Tendinosis, partial- and full-thickness tears and bursitis. This lack of consensus leads to inability to reliably distinguish between the various categories and contributes to poor accuracy.¹³

To our knowledge, no golden standard is recognized in the diagnostic approach of GTPS. MRI is highly sensitive and often used as golden standard, but detection of abnormalities on MRI is a poor predictor of pain because pathological MRI findings are seen in both symptomatic and asymptomatic patients. For that reason, a study by Ganderton et al. states that MRI does not provide an accurate evaluation of GTPS and that a diagnostic golden standard of GTPS yet has to be identified.^{15,16} Some studies have used surgical and histopathological findings as golden standard, but these studies are demanding and have a low sample size ranging from 5-24 patients, lowering their power.^{6,7,12,13}

All together ultrasound seems to be an excellent first choice of imaging modality to diagnose the etiology behind GTPS due to its high sensitivity, ease of access and low cost. However, there are no clear ultrasound definitions on the most common findings in GTPS and the prevalence of these findings is not systematically described. Additionally, the diagnostic accuracy of ultrasound plus the association between ultrasound- and MRI findings in patients suffering from GTPS are last systematically described in 2012 by McMahon et al.¹⁴ More studies have been published since,^{13,18,19} justifying an updated systematic review of the literature.

Review questions

Primary objectives

- How are the classical ultrasound findings in GTPS methodical defined across different studies? (e.g. tendinitis, tendinosis, partial and full-thickness tears, bursitis and calcifications?)
- 2. What is the prevalence of ultrasound findings in patients with clinical GTPS?

Secondary objectives

- 3. How accurate is ultrasound in the diagnosis of patients with GTPS compared to surgical/histopathological findings?
- 4. What is the association between ultrasound- and MRI findings in patients diagnosed with GTPS?

Methods

We will conduct a systematic review following the PRISMA statement and prospectively register the review in PROSPERO.²⁰

Search strategy and information sources

We will carry out a systematic search in the following bibliographic databases: PubMed, Embase and Cochrane Central Register of Controlled Trials. A hand search of the reference lists of relevant articles will also be conducted for other relevant references. There will be no restrictions in year of publication, but only articles reported in English or Danish will be included. Unpublished studies and abstracts will not be included.

The following search strategy was tested to be the most efficient across databases and will be applied in all databases mentioned above, see appendix 1:

Target condition

(("lateral") AND "hip") AND "pain"	OR
"trochanter" OR "trochanteric"	OR
"gluteal" OR "gluteus"	OR
"gtps"	OR
"iliotibial"	OR
"peritrochanteric"	
	AND
Imaging modalities	
"ultrasound"	OR
"ultrasonography"	OR
"mri"	OR

There will be performed a re-run of the search just prior to the final analyses.

Eligibility criteria

"magnetic resonance"

Study design and setting

To increase the number of eligible studies we will include any type of study design and setting, except case reports, case series and evidence synthesis such as systematic reviews.

Population and comparators

The study populations must include patients suffering from GTPS. Subjective symptoms, as well as patients diagnosed with GTPS in a clinical setting, will be accepted. However, possible causes to GTPS anticipated to be included are gluteus medius or minimus tendinopathies or tears and

trochanteric bursitis. An asymptomatic control group for comparison is desirable but is not a requirement.

Only studies examining adults (18 years or older) will be included. Though, studies addressing both adults and children with separate data will be included too. The influence of potential comorbidities will be evaluated for each study individually. Otherwise, there will be no restrictions regarding gender, disease status and level of physical activity.

Exclusion criteria

Studies including patients with injections of steroid during the last 3 months, patients who had undergone hip arthroplasty, and studies primarily focusing on hip fractures, intraarticular pathology, tumors, hematomas, genetic disorders, infections and ultrasound-guided nerve blocks will be excluded. Finally, studies on animals and cadavers will be excluded too.

Imaging modalities and outcomes

This systematic review will investigate the properties of ultrasound in the diagnostic process of GTPS and secondly evaluate the association between ultrasound-, MRI- and surgical/histopathological findings. Therefore, studies must include original ultrasound data in order to be included. Details about gluteus medius, gluteus minimus or bursae of the lateral hip region must be obtainable. Original MRI data and surgical/histopathological data will only be included if there is original ultrasound data on the same group of patients for comparison.

Selection process

Studies identified through the search process will be downloaded to "Covidence", whereupon duplicates are removed. Then, two authors (MH and MSR) will screen for potential studies based on titles and abstracts and subsequently perform a full-text evaluation of the selected studies. Studies which fulfil the eligibility criteria will be included in the review. Disagreement between the two authors will be solved by discussion. If consensus is not achieved, a third author will be involved (JLO).

Data collection

One author will collect data from the included studies using a specifically designed standardized data extraction form (Appendix 2), while another author (MSR) will double-check the extracted data. The following data will be extracted:

- General study information
- Study design and setting
- Characteristics of study population and participants
- Ultrasound definitions of GTPS pathology (normal appearance, thickness, vascularity, bursitis, tendinosis, tendinitis, partial- and full-thickness tears, calcifications, bony abnormalities, enthesopathy and iliotibial band abnormalities)
- Outcome measures

- The presence of pathological changes verified by ultrasound
- The presence of pathological changes verified by surgery/histopathology in order to calculate diagnostic accuracy of ultrasound
 - Whenever possible, data will be extracted or analyzed to provide sensitivity, specificity, positive predictive value and negative predictive value.
- Original MRI data compared to original ultrasound data

Primary outcomes

The primary outcomes are how the included studies define the typical ultrasound findings in GTPS (normal appearance, thickness, vascularity, bursitis, tendinosis, tendinitis, partial- and full-thickness tears, calcifications, bony abnormalities, enthesopathy and iliotibial band abnormalities) and the presence of these ultrasound findings in patients with GTPS.

Secondary outcomes

Secondary outcomes are the presence of MRI findings and surgery/histopathological findings in patients with GTPS.

Assessment of methodical quality in individual studies

This systematic review potentially includes both randomized controlled trials and non-randomized studies why the Epidemiological Appraisal Instrument (EAI) will be used to assess the methodical quality in the included studies. Only circumstances concerning ultrasound definitions and -findings will be evaluated. EAI is a 43 items tool, which is a valid and reliable appraisal instrument for systematic reviews. Its applicable for multiple types of study designs and assesses various components like study description, subject selection, measurement quality, data analysis and generalization of results.²¹ Items will be scored yes (score = 2), partial (score = 1), no (score = 0), unable to determine (score = UTD) or not applicable (NA). The items concerning exposure (item 2, 25-27) will be interpreted as the characterization of GTPS. Characteristics of study participants (item 8) must include age, gender, disease duration and BMI to score "yes". Observers need to be blinded for symptoms, clinical test results and possible reference standards to score "yes" (item 29).

To further assess the methodical quality in primary diagnostic accuracy studies included in this review, QUADAS-2 will be applied. This checklist assesses the risk of bias across 4 different categories: Patient selection (bias in the selection of patients?); index test (bias in the interpretation of the index test?); reference standard (bias when comparing to the reference standard?) and flow and timing (bias in the flow of patient? e.g. was there an appropriate interval between index and reference test?). Each category will be judged as high- or low risk of methodological quality issues. If insufficient information is provided the term "unclear" will be given.²²

The assessments will be completed by one author (MH) and supervisors (MSR and JLO) will be involved in ambiguous cases.

Data synthesis

The primary focus for this systematic review is a narrative synthesis. At first, the characteristics of the included studies will be presented followed by an evaluation of methodical quality. After this, the primary outcomes will be discussed. Here the various definitions of ultrasound findings in GTPS will be presented and the presence of these findings in patients with GTPS will be explored. Subsequently, the diagnostic accuracy of ultrasound in patients suffering from GTPS with surgery/histopathology as reference standard will be discussed. At last, MRI findings and ultrasound findings will be compared in patients with GTPS.

The focus for the data synthesis will be on studies reporting detailed definitions of ultrasound findings, on studies presenting ultrasound findings in both symptomatic and asymptomatic patients and on studies comparing ultrasound findings to either MRI or surgery/histopathological findings.

Studies of any level of methodical quality will be retained in the analysis.

If sufficient data is available in the included studies a meta-analysis will be performed. In this the aim will be to investigate the likelihood of ultrasound findings in patients with and without GTPS.

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PubMed Database search results			
Line	Search Term	Results	
1	(("lateral") AND "hip") AND "pain"	1442	
2	("trochanter") OR "trochanteric"	7987	
3	("gluteal") OR "gluteus"	8433	
4	"gtps"	249	
5	"iliotibial"	1007	
6	"peritrochanteric"	188	
7	1 or 2 or 3 or 4 or 5 or 6	18155	
8	"ultrasound"	256894	
9	"ultrasonography"	310325	
10	"mri"	232298	
11	"magnetic resonance"	702150	
12	8 or 9 or 10 or 11	1141696	
13	7 and 12	2012	

Appendix 1 – Preliminary search results 5/8/2019

Em	Embase Database search results		
Line	Search Term	Results	
1	(("lateral") AND "hip") AND "pain"	3253	
2	("trochanter") OR "trochanteric"	11311	
3	("gluteal") OR "gluteus"	12643	
4	"gtps"	327	
5	"iliotibial"	1309	
6	"peritrochanteric"	252	
7	1 or 2 or 3 or 4 or 5 or 6	27284	
8	"ultrasound"	459458	
9	"ultrasonography"	202324	
10	"mri"	408668	
11	"magnetic resonance"	1263525	
12	8 or 9 or 10 or 11	1797613	
13	7 and 12	4306	

Cochrane Database search results

Line	Search Term	Results
1	(("lateral") AND "hip") AND "pain"	
2	("trochanter") OR "trochanteric"	
3	("gluteal") OR "gluteus"	
4	"gtps"	

5 "iliotibial"

6	"peritrochanteric"	
7	1 or 2 or 3 or 4 or 5 or 6	18
8	"ultrasound"	
9	"ultrasonography"	
10	"mri"	
11	"magnetic resonance"	
12	8 or 9 or 10 or 11	292
13	7 and 12	4

Appendix 2 – Data extraction form

General study information

Title	
Study ID (surname of first author and year first	
full report of study was published e.g. Smith	
2001)	
Journal	
Country	
Notes:	

Study design and setting

Aim of study	
Design	
Setting	
Recruitment period	
Notes:	

Study population and participants

Study population description	
Inclusion criteria	
Exclusion criteria	
Notes	

Baseline characteristics

Variables	Total	With GTPS	Without GTPS	Subgroup X
	n =	n =	n =	n =
Age				
Gender (W/M)				
Height				
Weight				
BMI				
Duration of				
symptoms until				
imaging				
Other				
Notes				

Data collection

Ultrasound – Definitions	
Equipment	
Investigator	
Procedure	
Normal	
Thickness	
Vascularity	
Bursitis	
Tendinosis	
Tendinitis	
Partial tear	
Full thickness tear	
Calcifications	
Bony abnormalities	
Enthesopathy	
Iliotibial band abnormalities	
Notes:	

Outcomes

Ultrasound – Findings

Normal	
Thickness	
Vascularity	
Bursitis	
Tendinosis	
Tendinitis	
Partial tear	
Full thickness tear	
Calcifications	
Bony abnormalities	
Enthesopathy	
Iliotibial band abnormalities	
Notes:	

Ultrasound – Diagnostic accuracy

Condition: e.g. tendinosis,	Surgery/Histopathology		
full-thickness tear, bursitis	Condition Condition		Total
	positive	negative	

Ultrasound	Test outcome positive		
	Test outcome		
	negative		
	Total		

Sensitivity	
Specificity	
Positive predictive value	
Negative predictive value	
+ Likelihood ratio	
- Likelihood ratio	
Accuracy	

Original MRI data for comparison

Conclusion

Primary outcome:	
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