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REVIEW ARTICLE

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Elbow tendinopathy and occupational biomechanical overload: A systematic review with best-evidence synthesis

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Abstract

Objectives: To evaluate the evidence of an association between occupational and non-occupational exposure to biomechanical risk factors and lateral elbow tendinopathy, medial elbow tendinopathy, and olecranon bursitis.

Methods: We carried out a systematic review of the literature. We searched MEDLINE (up to November 2019) and checked the reference lists of relevant articles/reviews. We aimed to include studies where (a) the diagnosis was based on physical examination (symptoms plus clinical signs) and imaging data (if any); and (b) the exposure was evaluated with video analysis and/or direct measurements. A quality assessment of the included studies was performed along with an evaluation of the level of evidence of a causal relationship.

Results: We included four studies in the qualitative synthesis: two prospective cohorts and two cross-sectional studies. All the included studies investigated “lateral/medial epicondylitis”, albeit the diagnosis was not supported by imaging techniques. Two cohort studies suggested that a combination of biomechanical risk factors for wrist/forearm is associated with increased risk of “lateral epicondylitis”. This association was not observed in the two included cross-sectional studies. The cohort studies suggested that a Strain Index score higher than 5 or 6.1 could double the risk of “lateral epicondylitis”. No association with increased risk of “medial epicondylitis” was observed.

Conclusions: There is limited evidence of a causal relationship between occupational exposure to biomechanical risk factors and lateral elbow tendinopathy. For medial elbow tendinopathy, the evidence is insufficient to support this causal relationship. No studies on olecranon bursitis and biomechanical overload were identified.

KEYWORDS

elbow tendinopathy, musculoskeletal diseases, occupational exposure, occupational health, systematic review, upper extremity

1 | INTRODUCTION

Elbow tendinopathy, a common painful disorder of the upper limb, may affect the tendinous insertion of the wrist extensor or wrist flexor muscles at the lateral or medial epicondyle respectively.[1,2] In the vast majority of cases, it is a self-limiting condition that can persist for over 1 year and can recur.[3] In the general Finnish population, a prevalence of 1.3% was estimated for lateral elbow tendinopathy and 0.4% for medial elbow tendinopathy.[4]

Lateral elbow tendinopathy is often referred to as "tennis elbow", while the medial elbow tendinopathy is commonly known as "golfer's elbow".[5,6]

The term "epicondylitis" (lateral and medial) has been widely used in the literature to identify these conditions: however, the use of this term should be abandoned, as it suggests an inflammatory pattern, while in many cases the condition has a degenerative origin.[1] Histopathological data highlight the possible absence of inflammatory mechanisms at any stage of elbow tendinopathy.[2] Furthermore, it is important to underline that "elbow tendinopathy" is a definition that should not be used when only symptoms are collected. In the case of epicondylar pain, "epicondylalgia" or "elbow pain" are the most appropriate terms before a diagnosis is made.[7]

Another elbow soft-tissue pathology is olecranon bursitis, also called "dart throwers' elbow".[8] It is a common inflammatory process of the olecranon bursa: in the Israel Defense Forces olecranon bursitis has a crude incidence rate of 12/10 000 person/years among administrative personnel and 97/10 000 in the case of combat duty personnel.[9]

Shiri et al found that some individual factors could be associated with lateral and medial elbow tendinopathy. In particular, smoking appeared to be a risk factor for both lateral and medial elbow tendinopathy, while obesity was associated with medial elbow tendinopathy in women.[4] It has been reported that olecranon bursitis was associated with diabetes mellitus, rheumatoid arthritis, alcoholism, and HIV infection.[10]

Apart from individual factors, elbow tendinopathy and olecranon bursitis are considered more common among manual laborers.[11-13] The extensive literature review edited by Bernard et al at NIOSH on epidemiological evidence for work-related musculoskeletal disorders concluded that elbow tendinopathy resulted associated with force and strongly associated to a combination of factors (eg force and repetition, force and posture); the evidence for causal relationship was insufficient for repetition and posture alone.[14] It should be underlined that the International Labour Organization list of occupational diseases (2010) includes "olecranon bursitis due to prolonged pressure of the elbow region" and "epicondylitis due to repetitive forceful work".[15]

van Rijn et al carried out a systematic review about the association between lateral and medial elbow tendinopathy and work-related factors[16]: they reported an association between lateral elbow tendinopathy and handling loads >20 kg at least 10 times/d, handling tools >1 kg, and repetitive hand/arm movements > 2 h/d. Risk factors associated with medial elbow tendinopathy included: handling loads >5 kg (2 times/min at a minimum of 2 h/d), handling loads >20 kg (at least 10 times/d), high hand grip forces >1 h/d, repetitive movements >2 h/d, and the use of vibrating tools >2 h/d. The authors concluded that their findings (mainly from cross-sectional studies) needed to be confirmed in longitudinal studies. Furthermore, the included studies were heterogeneous in terms of study design, exposure assessment, and diagnostic criteria.

Descatha et al. performed a systematic review of the prospective studies on lateral elbow tendinopathy and occupational exposure: a meta-analysis of the results of the five included studies was in favor of an association between lateral elbow tendinopathy and occupational exposure to biomechanical overload involving the wrist and/or elbow.[17] However, in the included studies the evaluation of exposure was mainly based on self-reported data (three out five studies).

Conversely, a prerequisite to establishing a causal relationship between an exposure and a disease is to have evidence for the disease and evidence for the exposure according to the best available science.[18] For this reason, we aimed to perform a systematic review of the available evidence on the association between occupational (and non-occupational) exposure to biomechanical risk factors and: (a) lateral elbow tendinopathy; (b) medial elbow tendinopathy; and (c) olecranon bursitis, searching for studies based on objective criteria for exposure evaluation and diagnosis.

2 | METHODS

This systematic review was conducted according to the PRISMA statement.[19] The study protocol was registered with PROSPERO at https://www.crd.york.ac.uk/prospero/ (registration number: CRD42018118228).

2.1 | Case definition

Few diagnostic criteria have been proposed for the diagnosis of lateral/medial elbow tendinopathy.[20,21] Local pain on resisted wrist extension (lateral) or on resisted wrist flexion (medial) are commonly used clinical signs.[21] However, a recent systematic review concluded that none of the physical examination tests alone was sufficient for rule in or out an elbow tendinopathy.[22] Ultrasonography (US) and magnetic

TABLE 1 Sketch of the evidence for the disease and for the exposure

	Exposure assessment			
	Objective evaluation		Indirect evaluation	
	Quantitative method of direct measurement[a]	Video analysis or video-based observations	Experts' observations	Job title, self-reported assessment, job exposure matrix
Case definition				
Objective diagnostic criteria				
Imaging (plus physical examination)	++/++	++/+	++/−	++/−−
Physical examination (symptoms plus clinical signs)	+/++	+/+	+/−	+/−−
Symptoms				
Structured interview (current and past health history)	−/++	−/+	−/−	−/−−
Self-administered questionnaire	−−/++	−−/+	−−/−	−−/−−

Note: The symbols relate to the overall assessment of a hypothetical study based on exposure data and case definition. Each combination ranks the level of evidence based on data quality for exposure assessment and diagnosis. The best scenario is depicted as (++/++), while the worst as (−−/−−). The dark grey area identifies those combinations that satisfy the inclusion criteria for the present review.

[a]It includes direct measurements like motion analysis and measurement of force.

resonance imaging (MRI) may help detecting cases of lateral/medial elbow tendinopathy.[23,24] US allows for an inexpensive dynamic examination of elbow structures and can be considered an important screening tool for diagnosis, albeit it is more operator-dependent than MRI.[23,24] In the case of chronic elbow pain, the most reliable method is the MRI, since it is able to detect tendon tears.[25] However, the use of MRI is limited due to its high costs and applicability.

With respect to olecranon bursitis, physical examination together with an accurate anamnesis may help diagnosing the two main forms of the disease (septic vs non-septic). Anteroposterior and lateral radiographs are useful to understand the causal factors of the disease, while MRI help differentiating septic and non-septic olecranon bursitis.[26]

For the present review, we included studies where the diagnosis was based on imaging or at least on physical examination (symptoms plus clinical signs). In the case diagnostic criteria were not standardized and adequately described, such studies were not considered eligible. Moreover, we excluded studies where the diagnosis was based on referred symptoms (eg epicondylalgia) reported by interview or self-administered questionnaire alone.

2.2 | Exposure assessment

Biomechanical risk factors associated to lateral/medial elbow tendinopathy included wrist/elbow repetitive movements, forceful exertions, awkward postures, hand-arm vibrations, or a combination of these.[14,16] In addition to those, olecranon bursitis has been associated with overuse or repetitive microtrauma.[13]

We included studies that reported quantitative measures of the exposure (like motion analysis, measurement of force or, at least, observations supported by video analysis). Studies reporting self-assessment of biomechanical exposure (eg through questionnaire) and/or expert's judgement were excluded. Studies using job titles as indicator/proxy of biomechanical exposure (including job exposure matrix) were excluded as well. In addition, studies investigating other risk factors than biomechanical as main exposure (with biomechanical overload treated as confounder) were not considered eligible for the present study.

2.3 | Eligibility criteria

We distinguished different levels of evidence for the diagnosis of the disease and for exposure assessment. We included only studies where (a) the evidence for the disease was based on physical examination and imaging data (if any); and (b) the evidence for the exposure was based on objective measurements. Table 1 classifies the potentially pertinent articles according to the different level of evidence for the disease and for the exposure.

2.4 | Search strategy

We conducted a systematic review of the literature included in MEDLINE (through PubMed) until November 20, 2019.

To retrieve citations regarding elbow tendinopathies and olecranon bursitis, we used PubMed Medical Subject Headings (MeSH) terms (ie elbow tendinopathy, tennis elbow) along with non-MeSH terms (such as golfer elbow, epicondylitis, olecranon bursitis).

To locate citations related to occupational exposure to biomechanical overload, the "more sensitive" PubMed search filter for occupational determinants of diseases[27] and the "more sensitive" PubMed filter for agricultural workers' diseases[28] were evoked. In addition to those search filters, we added further terms (entered as 'free text words') related to the field of ergonomics and biomechanical risk factors.

To perform an extensive search including non-occupational exposure to biomechanical overload, we added MeSH and non-MeSH terms related to the field of sport activity in general.

Electronic searches were supplemented by manual searches of reference lists of included studies and reviews about the topic of interest (if any). No language restriction was applied. Case reports and case series were excluded. The search strategy for MEDLINE (through PubMed) is reported in File S1.

2.5 | Selection of studies and data extraction

Two authors (SC and SM) independently screened titles and abstracts of the citations retrieved by the search strategy for potential inclusion. The full text of all articles potentially qualifying for inclusion was retrieved and the same pair of authors assessed whether each full article met the inclusion criteria. Disagreements were resolved by discussion. If disagreement persisted, a third author (FSV) made the final decision. The two-step process for selecting studies along with exclusion criteria is reported in File S2.

Two authors (SC and SM) independently extracted data from each eligible study. Standardized forms were used to collect information on: authors, study design, country, participants, outcome assessment, exposure assessment, main results (preferably risk estimate), and adjustment for confounders (if any). In the case of redundant (multiple) publications,[29] we aimed at excluding duplicate studies from the review.

2.6 | Assessment of the study quality

A quality assessment of the included studies was performed. The quality of the studies was independently assessed by two authors (SC and SM). Disagreements were resolved by consensus. The quality assessment was derived from a pre-existing tool developed for the evaluation of other musculoskeletal outcomes[30] and adapted accordingly. It covers five major topics, namely:

a. Study design (1-3): cross-sectional study (1), cohort with a follow-up ≤1 year (2), cohort with a follow-up >1 year (3);
b. Study population (0-3), sum of: adequate description of inclusion and exclusion criteria (1), participation rate ≥70% (1), and sufficient description on completers vs withdrawals (1);
c. Outcome assessment (1-3): physical examination (symptoms and clinical signs) (1), physical examination (symptoms and clinical signs) plus imaging techniques (2), blinding for exposure status (+1);
d. Exposure assessment (1-3): observation and video analysis (1), observation, video analysis and quantitative measurements (2), blinding for outcome status (+1);
e. Data analysis (0-5): confounders reported in descriptive tables only (1), control for confounding (age and/or gender) (2), control for confounding (age and/or gender and other confounders) (3), analysis adjusted for non-occupational biomechanical risk factors (eg sport, hobby, housekeeping) (+1), robustness of the results to the presence of missing data (+1).

The quality score of the included studies was calculated as the sum of each item (minimum score of 3 and maximum of 17). Based on the tertile distribution of the quality score, studies were classified in: low quality (3-7), medium quality (8-12), and high quality studies (13-17).

2.7 | Best-evidence synthesis

We reported a comprehensive summary of all the findings of the included studies. Data were analysed using the best-evidence synthesis as first introduced by Slavin.[31]

The studies were classified according to the type of study design (where the prospective cohort study was judged as the preferred one) and ranked by their methodological quality score.

To evaluate the causal relationship between the disease under study (ie elbow tendinopathy) and the exposure to biomechanical risk factors we used the widely accepted convention: "a positive relationship has been observed between the exposure and disease in studies in which chance, bias and confounding could be ruled out with reasonable confidence". This is the requirement set by the International Agency for Research on Cancer for establishing sufficient evidence for carcinogenicity in humans.[32] However, this definition does not specify "how many" studies are necessary. For the purpose of this review, we adopted the slightly modified criteria proposed by The Scientific Committee of the Danish Society of Occupational and Environmental Medicine for the study of other musculoskeletal outcomes.[30] The following levels of evidence were used:

a. Strong evidence: positive relationship observed between exposure and outcome in two or more high quality cohort studies and several high-quality observational studies other than cohort studies;
b. Moderate evidence: positive relationship observed between exposure and outcome in one high quality cohort study and several high-quality observational studies other than cohort studies;

c. Limited evidence: positive relationship observed between exposure and outcome in some observational studies; it is not unlikely that this relationship could be explained by chance, bias or confounding;
d. Insufficient evidence: the available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association;
e. No evidence is provided when no studies could be found.

3 | RESULTS

3.1 | Study selection

The flow diagram of the study selection is summarized in Figure 1 (see File S3 for the PRISMA Checklist). The electronic search retrieved 2266 potentially relevant references, of which 42 were assessed in full-text. Of these, 37 did not meet the inclusion criteria. No additional potentially eligible articles were identified through hand searching. Four studies were included in qualitative synthesis. Of note, one of the four studies was reported in two articles.

3.2 | Study characteristics

The main characteristics of the included studies were reported in Table 2. The included studies consisted in two prospective cohorts[33-35] and two cross-sectional studies.[36,37] Two studies were conducted in the USA,[33-35] one in Colombia,[36] and the other one in Taiwan.[37]

One study investigated "lateral epicondylitis" alone,[35] while the other three studies examined both "lateral epicondylitis" and "medial epicondylitis".[33,34,36,37] No studies on olecranon bursitis were identified according to inclusion criteria.

For all the included studies, the diagnosis of "lateral/medial epicondylitis" was provided by physical examination on the base of symptoms and clinical signs.[33-37] None of the studies reported the use of imaging techniques as diagnostic criteria.

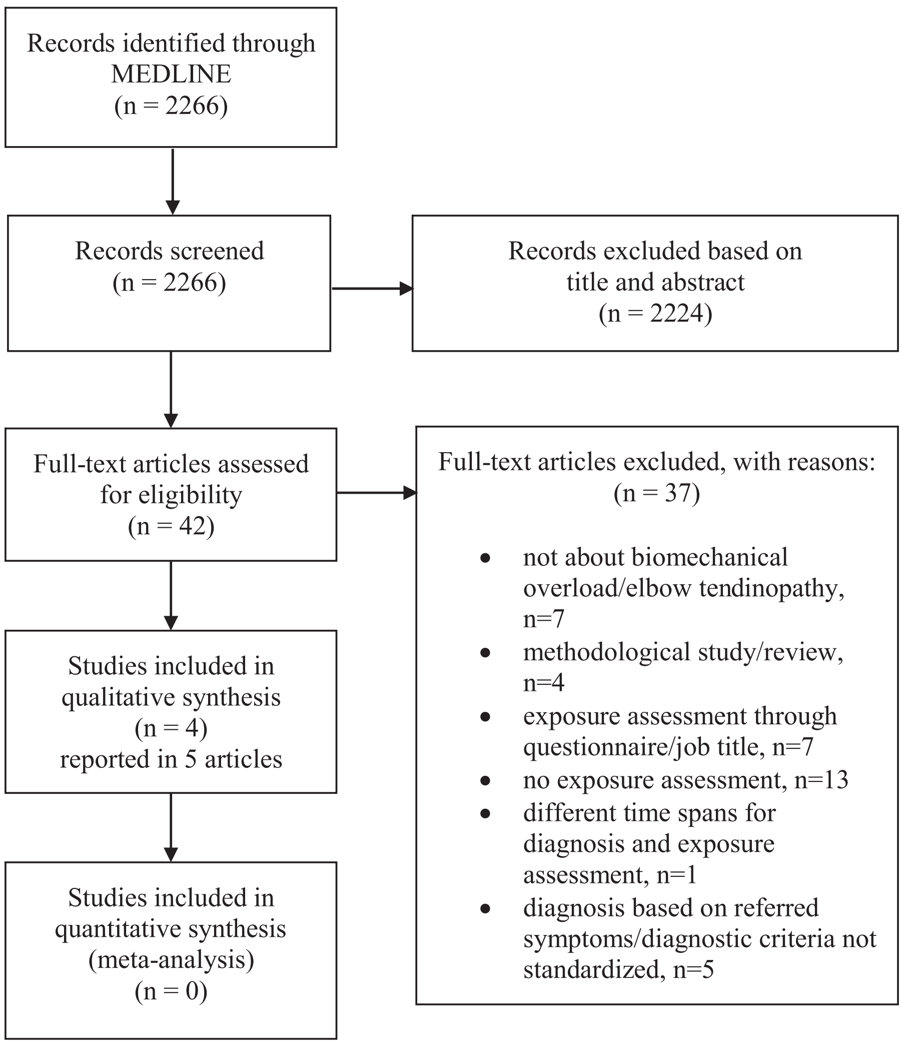

FIGURE 1 Flow diagram of the study selection

TABLE 2 Main characteristics of included studies

Study	Authors	Study design	Country	Participants	Outcome assessment	Exposure assessment	Main results	Notes
#1	Fan 2014[33]	Prospective cohort	USA	611 workers from 12 different manufacturing and service sector plants followed for an average of 3.5 y	*Case definition*: "lateral epicondylitis" of the dominant side assessed by physical examination (symptoms plus clinical signs). *Assessment*: Positive elbow or forearm symptoms were defined as: (a) any pain, aching, stiffness, burning, numbness, or tingling in the elbow or forearm region in the past 7 d AND (b) symptoms that lasted more than 1 wk or occurred more than three times in the previous 12 mo AND (iii) no previous sudden injury at the elbow/forearm area at the time of the onset of symptoms Positive physical exam was defined as pain in the lateral humeral epicondylar region on resisted wrist extension A positive clinical case of "lateral epicondylitis" was defined as positive symptoms at the elbow or forearm plus a positive physical exam on the symptomatic side	*Evaluation*: observation by ergonomists, video analysis (at task level) and use of quantitative methods for forceful exertions *Description:* All subjects were observed by ergonomists on-site and videotaped while they performed their typical tasks. Depending on task type and cycle time, video recording was performed for a minimum of 15 min. Using data on task distribution, job-level exposures were then computed using the time-weighted average approach Estimation of 5 variables for wrist/forearm postures, 5 for different types of frequency and percentage of time of forceful exertions, and 20 for posture-force combination Forceful exertions were defined as pinch grip force $\geq$ 0.9 kg of object weight or with 1.8-kg pinch grip force, power grip forces as $\geq$4.5 kg of object weight or with 4.5-kg power grip, lifting/lowering as object weights $\geq$4.5 kg, and pushing/pulling forces as $\geq$4.5 kg force Object weights and push/pull forces were measured using force gauges Pinch and power grip forces were measured with a grip dynamometer (using a force-matching technique), as well as estimated by the ergonomists and the workers themselves Duration and frequency of power tool use was estimated	Multivariable analyses (age/gender adjusted): the combined effect of forearm pronation $\geq$45° for $\geq$40% time and time spent in forceful exertion, including any power grip (HR = 2.8, 95% CI [1.35-5.77]), lifting for $\geq$3% of time (HR = 2.50, 95% CI [1.19-5.24]), and duty cycle for $\geq$10% (HR = 2.25, 95% CI [1.09-4.66]), were significant predictors of "lateral epicondylitis", whereas neither longer duration of the awkward posture nor any of the forceful exertion alone was significant	Hobbies or sports requiring: (a) high hand force; (b) high repetitive hand activities; were recorded Data were reported as yes/no in the univariate analysis Comorbidities including hypertension, diabetes mellitus, gout, thyroid diseases (collapsed into one variable), and obesity were reported in the univariate analysis

(Continues)

TABLE 2 (Continued)

Study	Authors	Study design	Country	Participants	Outcome assessment	Exposure assessment	Main results	Notes
	Fan 2014[34]	Prospective cohort	USA	607 workers from 12 different manufacturing and service sector plants followed for an average of 3.5 y	*Case definitions*: "lateral epicondylitis" and "medial epicondylitis" of the dominant side assessed by physical examination (symptoms plus clinical signs) *Assessment*: Positive elbow or forearm symptoms were defined as: (a) any pain, aching, stiffness, burning, numbness, or tingling in the elbow or forearm region in the past 7 d AND (b) symptoms that lasted more than 1 wk or occurred more than three times in the previous 12 mo AND (c) no previous accident or sudden injury at the elbow/forearm area at the time of the onset of symptoms Positive physical exam for "lateral epicondylitis" was defined as pain in the lateral humeral epicondylar region on resisted wrist extension or tenderness on palpation of the lateral epicondyle Positive physical exam for "medial epicondylitis" was defined as pain in the medial epicondylar region on resisted wrist flexion or tenderness on palpation of the medial epicondyle A positive clinical case of "lateral or medial epicondylitis" was defined as positive symptoms at the elbow or forearm plus a positive physical exam on the symptomatic side	*Evaluation*: observation by ergonomists, video analysis (at task level) *Description*: Exposure was assessed according to the SI method. For each subject, the SI score was calculated considering multiple forces/tasks and re-evaluated for physical exposure when a job change occurred SI score was categorized into: (a) "safe and hazardous" (SI ≤ 3 and SI > 7, respectively) and (b) "low and high exposure" (SI ≤ 5 and SI > 5, respectively) and (c) three categories of equal number of jobs within: cut points at SI 5 and 12	Multivariable analyses (age/gender/poor general health adjusted): the association between job risk classification of Safe, Action, and Hazardous jobs (SI ≤ 3, SI 3.1-7, and SI > 7, respectively) and "lateral epicondylitis" or "medial epicondylitis" was not statistically significant The job risk classification of High exposure vs Low exposure (SI > 5 vs ≤5) was associated with an adjusted HR of 2.06 (95% CI 1.16-3.64) and 1.41 (95%CI 0.64-3.12) for "lateral epicondylitis" or "medial epicondylitis" respectively The job risk classification divided in three levels of exposure (SI > 12 and SI 5.1-12 vs SI ≤ 5) indicated significant relationships for "lateral epicondylitis": HR 2.00 (95% CI 1.04- 3.87) for SI 5.1-12, and HR 2.12 (95% CI 1.11-4.05) for SI > 12. No sign of an association for "medial epicondylitis"	Hobbies or sports requiring: (a) high hand force; (b) high repetitive hand activities; were recorded Data were reported as yes/no in the univariate analysis Comorbidities including hypertension, diabetes mellitus, gout, thyroid diseases (collapsed into one variable), and obesity were reported in the univariate analysis

(Continues)

TABLE 2 (Continued)

Study	Authors	Study design	Country	Participants	Outcome assessment	Exposure assessment	Main results	Notes
#2	Garg 2014[35]	Prospective cohort	USA	495 workers from 10 industrial plants, followed for 6 y	*Case definition*: "lateral epicondylitis" either in the left, right or both sides assessed by structured interview and physical examination (symptoms plus clinical signs) *Assessment*: Symptoms and history of disorders were recorded in a structured interview for each arm separately The structured interview included: (a) intensity of pain at the elbow (at or near lateral epicondyle) on a 10-point pain scale, (b) when the pain began, (c) what percentage of time pain was experienced, (d) history of specific musculoskeletal disorders Standardized physical examination included: (a) palpation, (b) physical examination maneuvers, (c) evaluation for signs of certain disorders such as rheumatoid arthritis The case definition for "lateral epicondylitis" required: (a) pain at or near the lateral epicondyle, (b) pain upon palpation in one or more of six points (ACOEM Practice Guide lines) when applying approximately 4 kg of force, (c) lateral epicondylar region pain upon either resisted wrist extension or third digit extension	*Evaluation*: observation by ergonomists and video analysis *Description*: Exposure was assessed according to the SI method and ACGIH TVL for HAL Baseline job physical exposure data were collected for each individual worker and for each hand separately and subsequently at 3-mo interval Peak hand force, frequency of exertion, and duration were estimated using frame by frame video analysis When a job change occurred, physical exposures were re-measured using the same methods as at baseline The "typical exposure" approach was used to assign exposure at the worker level (ie the task the worker performed for the largest percentage of a work shift) SI score was categorized into low risk ($SI \leq 6.1$) and high risk ($SI > 6.1$) TLV for HAL scores were classified into one of the three categories: below the AL (score < 0.56), between the AL and TLV ($0.56 \leq$ score≤ 0.78), and above the TLV (score > 0.78)	Multivariable analyses (age/family problems/ swimming adjusted): the risk for "lateral epicondylitis" increased with an increase in SI score up to ≤ 9.0 (HR = 1.18 per unit increase, 95% CI [1.02-1.37]). The HR at SI = 9.0 was 4.43 relative to unexposed. For SI scores > 9.0 there was no further increase in risk. In the adjusted model, SI treated as a categorical variable using the Moore et al [2006] recommended limit of SI = 6.1 was significantly associated with increased risk of "lateral epicondylitis" (HR = 2.3, 95% CI [1.12-4.75]) TLV for HAL introduced as a continuous variable showed a non-statistically significant trend for increased risk of "lateral epicondylitis"; the same when it was treated as a categorical variable	Hobbies and activities outside of work were recorded In the adjusted model, increased risk of "lateral epicondylitis" was not associated with physical activities outside of work (hobbies and sports) other than swimming (entered as binary variable) Comorbidities (including diabetes mellitus, hypertension, hypercholesterolemia, rheumatoid/inflammatory arthritis, osteoarthritis, and distal upper extremity musculoskeletal disorders other than "lateral epicondylitis"), and BMI were reported in the univariate analysis

(Continues)

TABLE 2 (Continued)

Study	Authors	Study design	Country	Participants	Outcome assessment	Exposure assessment	Main results	Notes
#3	Barrero 2012[36]	Cross sectional	Colombia	158 workers from eight different flower companies	*Case definition*: "lateral epicondylitis" and "medial epicondylitis" either in the left, right or both sides assessed by physical examination (symptoms plus clinical signs) *Assessment*: The presence of signs and symptoms for "lateral and medial epicondylitis" was considered positive if there was pain exacerbated or not with wrist extension and wrist flexion respectively	*Evaluation*: observation, self-reported work exertion, video analysis and use of quantitative methods for kinematics, posture and forceful exertions *Description*: All subjects responded to an interview to investigate the duration of tasks. A sample of the initially recruited subjects (with at least three subjects randomly selected from each working area) were video-taped during daily task for 45-75 min. Video recordings were analyzed to assess cycle durations based on time-motion analyses. A subsample was randomly selected to analyze motion and posture measurements. Finally, a subgroup of subjects underwent surface EMG Magnitude of grip force, wrist posture (in flexion—extension and radial—ulnar deviation), dynamics of wrist motion, and the frequency of repeated motions were assessed: (a) exertion was self-reported by the workers using an RPE Borg scale, (b) cycle duration was assessed by a trained observer using video recordings, (c) postures of the hands and forearm were analyzed by movement sensors, (d) muscular activity of upper-limb was assessed by surface EMG Exposure estimates were carried out in a representative sample Exposure assessment was performed on those tasks that were more frequently performed on a working day, entailing repetitive and/or forceful exertions (ie flower cutting, flower classification, flower bunching, and a combination of these tasks)	The prevalence of "lateral epicondylitis" and/or "medial epicondylitis" was higher in workers performing classification and bunching tasks No information is provided about statistical significance of observed differences between tasks	No control group Descriptive data about BMI were reported for the study population as a whole

(Continues)

TABLE 2 (Continued)

Study	Authors	Study design	Country	Participants	Outcome assessment	Exposure assessment	Main results	Notes
#4	Chiang 1993 [37]	Cross sectional	Taiwan	207 workers from 8 fish processing factories	*Case definition*: "lateral epicondylitis" and "medial epicondylitis" of the dominant side assessed by a standardized questionnaire and clinical screening (symptoms plus clinical signs) *Assessment*: The criteria for the diagnosis "epicondylitis" were: local tenderness, pain during resisted extension or flexion of the wrist and fingers, and decreased hand grip compared with that of the opposite hand	*Evaluation*: observation by an industrial hygienist, video analysis and use of quantitative methods for forceful exertions *Description*: Movements of the three workers, each representing one of the three groups under study, were observed by an industrial hygienist and recorded for at least 30 m or three work cycles Highly repetitive jobs were defined as those with a cycle time of less than 30 s or performing the same type of fundamental cycles for more than 50% of the cycle time The hand-force requirements of the jobs were estimated by bilateral surface electromyographic recordings from the forearm flexor muscles. The high force jobs were those with an estimated average hand force of more than 3 kg Workers were divided in three groups based on repetitiveness and force required by regular daily tasks: (a) group I: low repetitiveness and low forceful movement of the upper limbs, (b) group II: high repetitiveness or highly forceful movement of the upper limbs, (c) group III: high repetitiveness and highly forceful movement of the upper limbs Exposure estimates were carried out in a representative sample	30/207 (14.5%) of the workers were classified as having "lateral epicondylitis" and/or "medial epicondylitis": (a) group I: 6/61 (9.8%), (b) group II: 18/118 (15.3%), (c) group III: 5/28 (17.9%) The reported data did not distinguish between "lateral epicondylitis" and "medial epicondylitis" Differences between groups were not statistically significant	Subjects who suffered from hypertension, diabetes mellitus, a history of traumatic injuries to the upper limbs, arthritis, and collagen diseases were excluded

Abbreviations: ACGIH, American Conference of Governmental Industrial Hygienists; AL, action limit; BMI, body mass index; CI, confidence interval; EMG, electromyography; HAL, hand activity level; HR, hazard ratio; RPE, rating of perceived exertion; SI, Strain Index; TLV, threshold limit value.

TABLE 3 Quality assessment of the included studies

Study	Authors	Study design (1-3)	Study population (0-3)	Outcome assessment (1-3)	Exposure assessment (1-3)	Data analysis (0-5)	Total quality score
#1	Fan 2014[33]	3	1	2	3	2	11
	Fan 2014[34]	3	1	2	2	3	11
#2	Garg 2014[35]	3	1	2	2	5	13
#3	Barrero 2012[36]	1	2	1	2	1	7
#4	Chiang 1993[37]	1	1	2	2	2	8

Note: The quality score was calculated as the sum of each item (minimum score of 3 and maximum of 17). High quality studies were defined as those with a total score ≥ 13.

In the four studies, the exposure was assessed by experienced observers with the support of video recordings.[33-37] Of these, one study applied the Strain Index (SI) for the exposure assessment,[34] while the SI and the American Conference of Governmental Industrial Hygienists' (ACGIH) threshold limit value (TLV) for hand-activity level (HAL) were used in another one.[35]

Forceful exertions were estimated by surface electromyography in two studies[36,37] and by force gauges and grip dynamometer in one study.[33] Postures of the hands and forearm were assessed by sensors for movement analysis in one study.[36]

3.3 | Quality assessment

The quality assessment of the included studies is reported in Table 3. The quality score ranged from 7 to 13. The most frequently missing items were the lack of information about completers and withdrawals, the participation rate higher than 70%, and the lack of control for confounders (including non-occupational biomechanical risk factors). Only one cohort study was classified as high quality (total score of 13 out of 17).[35] The other three studies were ranked with medium/low quality score.[33,34,36,37] The assessment of each item is reported in File S4.

3.4 | Summary of study results

The included studies used similar case definitions. However, they were heterogenous in terms of: (a) type and number of biomechanical risk factors studied; (b) methods adopted to estimate or measure the single risk factor; (c) indices or composite measures of exposure.

Among the four included studies, the cohort study by Garg et al reported the highest quality score.[35] At the multivariable analysis, the risk for "lateral epicondylitis" increased with the increase in the SI score (up to the value of 9) with a hazard ratio (HR) of 1.18 per unit increase (95% confidence interval [95% CI], 1.02-1.37). In the case of applying the recommended SI limit value of 6.1, the risk of "lateral epicondylitis" was more than doubled as compared to less exposed (HR 2.3, 95% CI [1.12-4.75]). TLV for HAL introduced as continuous or categorical variable showed a non-statistically significant trend for increased risk of "lateral epicondylitis".

Fan et al reported the findings of their study in two articles where they evaluated several occupational risk factors along with their combination by applying different methods of exposure assessment: (a) video analysis plus quantitative methods for forceful exertions computation[33]; and (b) video analysis plus assessment of biomechanical overload using the SI.[34] In the first case, at the multivariable analysis, forearm pronation (≥45° for ≥40% time) combined with (1) any power grip; (2) lifting for ≥3% of time; and (3) and duty cycle for ≥10% reported a HR of 2.8 (95% CI,1.35-5.77), 2.50 (95% CI, 1.19-5.24); and 2.25 (95% CI, 1.09-4.66) for "lateral epicondylitis" respectively. Neither longer duration of the awkward posture nor any of the forceful exertion alone increased significantly the risk of "lateral epicondylitis".[33] In the second case, the SI scores were used to categorize job risk classifications by proposed cut-off values.[34] At multivariable analysis, the job risk classification of High exposure (SI > 5) was associated with an adjusted HR of 2.06 (95% CI 1.16-3.64) and 1.41 (95% CI 0.64-3.12) for "lateral epicondylitis" and "medial epicondylitis", respectively, as compared to Low level of exposure (SI ≤ 5). On the other hand, the three-level classification of Safe, Action, and Hazardous jobs (SI ≤ 3, SI 3.1-7, and SI > 7, respectively) was not associated with "lateral epicondylitis" or "medial epicondylitis". On the basis of the distribution of the study population, the job risk classification was further divided in three levels of exposure (SI > 12 and SI 5.1-12 vs SI ≤ 5). This classification indicated significant relationships for "lateral epicondylitis" (HR 2.00, 95% CI [1.04-3.87] for SI 5.1-12; and HR 2.12, 95% CI [1.11-4.05] for SI > 12), while no sign of an association for "medial epicondylitis" was present.

The cross-sectional study by Chiang et al reported the prevalence of workers suffering from "lateral/medial epicondylitis" classified according to three levels of exposure based on repetitiveness and force required by regular daily tasks.[37] Workers exposed to high repetitiveness and highly forceful movement of the upper limbs reported the highest prevalence (17.9%, 5/28). However, the differences between groups were not statistically significant.

The cross-sectional study performed in eight flower companies showed a higher prevalence among workers performing classification and bunching tasks[36]; however, no control group was used. In addition, no information was provided about statistical significance of observed differences between tasks.

With respect to non-occupational exposure to biomechanical risk factors, two studies collected information about hobbies and sports.[33-35] Only in one study, the authors carried out a multivariable analysis where an increased risk of "lateral epicondylitis" was associated with swimming (introduced as binary variable), but not with other physical activities performed outside of work.[35]

Finally, data about comorbidities (such as diabetes mellitus and hypertension) and high body mass index (BMI) were collected in two studies and reported in the univariate analysis.[33-35] No study performed multivariable analyses adjusted for comorbidities.

4 | DISCUSSION

This systematic review showed that there is limited evidence of a causal relationship between occupational exposure to biomechanical risk factors and lateral elbow tendinopathy. For medial elbow tendinopathy, the evidence is insufficient to support this causal relationship. We included two cohorts—reported in three articles—and two cross-sectional studies investigating "lateral/medial epicondylitis". Conversely, no studies on olecranon bursitis and biomechanical overload were identified.

To study the occupational origin of a disease, we first need the evidence of the disease that should be preferably based on the most reliable diagnostic method.[18] However, the case definition of the four included studies was based on symptoms and physical examination signs, but not confirmed by imaging techniques (such as US or MRI). This means that, even if the term "epicondylitis" was used, these studies were actually investigating the putative occupational origin of referred or provoked epicondylalgia.[38] It could be argued that sometimes it is not possible to collect state-of-the-art diagnosis and it is quite common to use surrogate for diagnosis in large scale epidemiological studies. Nevertheless, it should be imperative to establish in advance the minimal diagnostic requirements that a study should satisfy in order to provide a meaningful contribution to a specific field of investigation. In the case of elbow tendinopathy, we believe that the scientific community should start a debate on the case definition to be used in epidemiological studies, as it was done for carpal tunnel syndrome more than two decades ago.[39]

In the second place, evidence is needed for the objective evaluation of exposure assessment.[18,40] In the four included studies the exposure assessment was performed by experienced ergonomists with the support of video analysis.[33-37] One of these studies applied the ACGIH TLV for HAL and the SI,[35] which combine two or more biomechanical risk factors for upper extremity musculoskeletal disorders and report summary measures of the risk.[41,42] The exposure was evaluated using the SI alone in another study.[34] Applied force and forceful exertions were evaluated on the basis of observational methods in one study.[35] On the other hand, two studies measured forceful exertions by surface electromyography,[36,37] while another one used force gauge and dynamometer in addition to ergonomists' and workers' esteem.[33] The analysis of the postures of the hands and forearm was assessed by sensors for movement analysis in one study only.[36]

Two cohort studies suggested that a combination of biomechanical risk factors for wrist/forearm is associated with increased risk of "lateral epicondylitis", albeit the diagnosis was not supported by imaging techniques.[33-35] Furthermore, this putative association was not observed in the other two cross-sectional studies included in the qualitative synthesis.[36,37]

The combined measures of exposure as well as the methods adopted to estimate or measure the biomechanical risk factors differed between the first article published by Fan et al[33] and the study by Garg et al.[35] Conversely, the latter together with the second article published by Fan et al[34] adopted the SI as a method to estimate the biomechanical overload, even if using different cut-off values in the analysis. Both studies suggested that a SI score higher than 5[34] or 6.1[35] could double the risk of "lateral epicondylitis".

No association with increased risk of "medial epicondylitis" was reported in the cohort study by Fan et al.[34] Indeed, this possible association was not supported by the findings from the two included cross-sectional studies, as well.[36,37]

Taken together, these findings suggest that the evidence of a causal relationship between lateral elbow tendinopathy and exposure to biomechanical risk factors is still limited, whereas for medial elbow tendinopathy the evidence of this relationship is insufficient.

These findings were apparently in contrast with those of previous systematic reviews.[16,17] In 2009 van Rijn et al found an association between several work-related risk factors and lateral/medial elbow tendinopathy.[16] Considering that the authors included studies rather heterogeneous in terms of study design, evaluation of the exposure and diagnostic criteria and their findings were mainly based on cross-sectional studies, they stated that the evidence for causality was still debatable. The meta-analysis performed by Descatha et al strongly supported an association between lateral elbow tendinopathy and occupational exposure to biomechanical overload involving the wrist and/or elbow.[17] Although this systematic review aimed to include only prospective studies, the majority of them (three out five) were based on self-reported data in terms of exposure assessment.

In addition, it is worth noting that a recent pooled analysis of baseline cross-sectional data of three occupational cohorts (presumably two of three were those studied by Fan et al[33,34] and Garg et al[35]) reported a strong association between "lateral epicondylitis" and cardiovascular risk factors expressed using a modified Framingham score.[43] This association remained after adjustment for known and potential confounders, including the measure of job physical demand evaluated with the SI. At multivariable analysis (adjusted for BMI, cardiovascular risk score and job satisfaction), the odds ratio for SI was 0.97 (95% CI, 0.95-1.00) for "lateral epicondylitis" defined as both symptoms and at least one positive physical examination test.[43] Hence, it should be underscored that it is not unlikely that the positive relationship between referred or provoked lateral epicondylalgia and exposure to biomechanical risk factors could be explained by chance, bias, or confounding.

With respect to olecranon bursitis, no studies about the putative occupational origin of the disease were found; some anecdotal links to occupational activities involving frequent traumas to the elbow were reported.[26] This was not expected considering that the International Labour Organization includes the "olecranon bursitis due to prolonged pressure of the elbow region" in the list of occupational diseases (revised 2010) which represents the latest worldwide consensus on diseases internationally accepted as caused by work.[15]

It should be underlined that in epidemiological setting (in contrast with the clinical one) the diagnosis of work-related musculoskeletal disorders is made by the medical investigator who is looking for diseased subjects in an (assumed) healthy population. Consequently, one would expect that in the epidemiology of work-related musculoskeletal disorders—conditions which have a high spontaneous incidence even in non-exposed populations—case definitions were based on the best available diagnostic techniques, exposures were directly measured with an appropriate tool and studies were performed with blind techniques (exposure/outcome).[40] In addition to that, direct measurements and video-based observation of exposure are more desirable considering that these methods are assumed to have a higher level of accuracy than subjective assessment and self-reports, which tend to be more prone to misclassification of the exposure.[44,45]

The quality score of the included studies ranged from 7 to 13 (out of 17). It is worth noting that the only high-quality study is, at the same time, the only one in which the exposure was estimated using an observational method, but where a direct measurement is lacking.[35] In addition, the outcome was blinded with respect to exposure assessment in two studies,[33-35] whereas blinding for exposure status in the case of outcome assessment was reported in three studies.[33-35,37]

It is unexpected that in the case of elbow tendinopathy (ie "tennis/golfer's" elbow) the data collected on hobbies and sports were so limited, if not missing. Actually, only Garg et al reported multivariable analysis controlled for non-occupational biomechanical risk factors, such as swimming.[35]

Observational studies are prone to various biases including reverse causality.[46] Concerns may be raised for cross-sectional studies, where it may be difficult to ascertain the temporal order of exposure and disease. This aspect is often neglected as potential explanation for apparent or unexpected association. In the present review, we classified the included studies according to study design and applied the criteria developed by the Scientific Committee of the Danish Society of Occupational and Environmental Medicine to evaluate the causal relation between elbow tendinopathy and exposure to biomechanical risk factors.[30] Cohort studies were judged as the preferred ones and all included studies were then ranked by their methodological quality score.

One of the strengths of this study is to search for articles concerning non-occupational exposure to biomechanical overload, using terms related to the field of sport activity in general. Moreover, we applied two sensitive search filters tailored for occupational etiology of disease,[27,28] adding terms related to the field of ergonomics and biomechanical risk factors.

We searched through PubMed only. However, in the field of occupational medicine, the vast majority of high-quality articles are indexed in PubMed.[47] Hence, the probability of retrieving other studies satisfying the inclusion criteria in another database of the scientific literature is very low.

5 | CONCLUSIONS

There is the need for well-planned and properly designed cohort studies in which, making a distinction between lateral and medial elbow tendinopathy, outcome, and exposure are assessed and measured with the best available techniques, including blinding of exposure and outcome assessment. A consensus on the minimal diagnostic criteria to be applied in epidemiological studies of elbow tendinopathies is needed as well as on objective exposure assessment. Future cohort studies have to consider all possible confounders (including non-occupational biomechanical risk factors and comorbidities) and minimize potential biases. Until that, even meta-analyses and systematic reviews cannot provide definitive answers to research questions on elbow tendinopathies and, more in general, occupational musculoskeletal diseases.

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DISCLOSURE

Approval of the research protocol: N/A. *Informed consent*: N/A. *Registry and the registration no. of the study/trial*: PROSPERO (registration number: CRD42018118228).

Animal studies: N/A. *Conflict of interest*: Authors declare no conflict of interests.

AUTHOR CONTRIBUTIONS

SC was involved in the conception and design, acquisition of data, analysis and interpretation of the data, and drafting of the article. SM was involved in the acquisition of data, analysis and interpretation of the data, and assisted in writing of the article. RB and AF were involved in the analysis and interpretation of the data. FSV was involved in the conception and design, analysis and interpretation of the data. All authors revised it critically for important intellectual content, approved the final version to be published and agreed to be accountable for all aspects of the work.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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