

# BMJ Open The role of concomitant ligament injury in the development of post-traumatic osteoarthritis after distal radius fractures: a protocol for a systematic review

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## ABSTRACT

**Introduction** Treatment of distal radius fractures (DRFs) aims to restore anatomic position of the fracture fragments and congruity of the articular surface to optimise functional outcomes and prevent osteoarthritis in the long term. While ligament injury of the wrist is often associated with DRFs and sole ligament injuries of the wrist lead to osteoarthritis, it is plausible that concomitant ligament injury in DRFs may aggravate degenerative changes of the wrist. The relationship between concomitant ligament injury and post-traumatic osteoarthritis in patients with DRFs is unclear. This study aims to identify the types of associated ligament injury in patients with a DRF and to elucidate the association of ligament injury on the development of post-traumatic osteoarthritis.

**Methods and analysis** This protocol is written in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) guidelines. An electronic search in MEDLINE, Embase, Web of Science, Cochrane Central Register of Trials and Google Scholar has been created and performed by a Health Sciences librarian with expertise in systematic review searching. Original research articles in English literature, which report on concomitant ligament injury of the wrist in relation to post-traumatic osteoarthritis, patient-reported outcome measures or clinician-reported outcome measures in patients (aged ≥18 years) with DRFs will be included. Two reviewers will independently screen and appraise articles and perform data extraction. In case of any disagreements, a third reviewer will be consulted. A systematic qualitative synthesis will be performed using text and tables.

**Ethics and dissemination** No ethical approval is required, since this is a protocol for a systematic review. The systematic review will be submitted for publication in a peer-reviewed scientific journal and for presentation at relevant conferences.

**PROSPERO registration number** CRD42020165007.

## INTRODUCTION

Despite treatment, distal radius fractures (DRFs) often lead to incongruity of the

## Strengths and limitations of this study

- This study will be the first to systematically evaluate the relationship between concomitant ligament injury of the wrist and the development of post-traumatic osteoarthritis in patients with distal radius fractures.
- A broad approach is used to answer the aetiological research question. This may cause considerable heterogeneity of the included studies, making comparison between studies difficult.
- Study screening, data extraction and quality assessment will be performed by two independent reviewers.
- This protocol is written in accordance with the guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols.

articular surface of the radiocarpal joint which results in post-traumatic osteoarthritis.<sup>1</sup>

The incidence of post-traumatic osteoarthritis after DRFs highly varies in literature, because of heterogeneity of the studies regarding the type of DRF, follow-up duration, and the used diagnostics for assessing post-traumatic osteoarthritis.<sup>2–7</sup> The reported overall prevalence of post-traumatic osteoarthritis after intra-articular DRFs ranges from 37% to 50%.<sup>1</sup>

The pathogenesis of post-traumatic osteoarthritis is likely multifactorial. Some studies postulate that it is associated with direct damage to cartilage and/or bone during trauma, as well as chronic joint overload secondary to residual articular incongruity or malalignment, or articular instability due to soft tissue injury. The relative contribution and importance of these factors in developing post-traumatic osteoarthritis is



unknown.<sup>8–10</sup> Both are extensively studied separately in literature.

Incongruity of the articular surface caused by a step-off or gap has been shown to be a predictor for the development of post-traumatic osteoarthritis in DRFs, while other radiological factors, such as shortened radial length, dorsal angulation, radial inclination, ulnar variance and anteroposterior distance show conflicting results.<sup>1</sup> Failure to anatomically reduce fracture fragments can accelerate this degenerative process<sup>1 2 4 11–13</sup> and may compromise functional outcome.<sup>14</sup>

In addition, DRFs are often associated with multiple types of ligament injuries of the wrist. In up to 75% of DRFs soft tissue injury was reported.<sup>15–29</sup> If not diagnosed and treated correctly, additional lesions of the carpal ligaments can cause wrist disorders. The presence and extent of these soft tissue injuries in DRFs may provide a potential explanation for the variable outcomes seen after treatment of DRFs.

As is known, sole ligament injury of the wrist in the absence of a fracture, in particular scapholunate (SL) ligament injury in combination with injury to the secondary stabilisers,<sup>30</sup> may lead to a change in the carpal kinematics, instability, chronic wrist pain and possibly secondary degenerative changes.<sup>31 32</sup> The natural course of chronic isolated SL ligament injury is unclear and multiple studies show different results in the long term regarding the incidence of degenerative arthritic changes and decreased wrist function after isolated SL ligament injury.<sup>33–35</sup> However, current concepts are to restore ligament continuity and carpal kinematics within 4–6 weeks to produce a painless and stable wrist to prevent chronic instability and osteoarthritis in the long term.<sup>30 35 36</sup>

Even though instability and incongruity often coexist after intra-articular fractures and both may exacerbate chronic cartilage loading,<sup>9</sup> the primary focus of treatment of DRFs is to restore the anatomical position and congruity of the articular surface. The evaluation of ligament injury is not performed standardly. If instability is a potent determinant of post-traumatic osteoarthritis, the physician should ensure both joint stability and joint congruity.<sup>9</sup>

Therefore, the primary aim of this systematic review is to identify the types of associated ligament injury in patients with a DRF and to elucidate the association of ligament injury on developing post-traumatic osteoarthritis. This allows for more understanding of the pathomechanics of secondary osteoarthritis in DRFs.

## Objectives

1. To determine the incidence and types of concomitant ligament injury in DRFs.
2. To assess the difference in the incidence of post-traumatic osteoarthritis in patients with DRFs with ligament injury compared with patients without ligament injury and whether a relationship between ligament injury and radiological degree of osteoarthritis is reported.

**Table 1** Inclusion and exclusion criteria for the studies

	Inclusion criteria	Exclusion criteria
Study design	(pseudo-)RCTs Cohort studies Case-control studies Case series >5 patients	Case series ≤5 patients Case-reports Commentaries Editorials Letters Conference abstracts Book chapters
Participants	Patients with all types of DRFs Aged ≥18 years	Animal or cadaveric studies Aged <18 years
Report characteristics	Concomitant ligament injury* in relation to post-traumatic osteoarthritis, PROMs or CROMs	TFCC injury DRUJ injury
Language	English language	Other language

\*See online supplemental file 2 for a list of all included injuries and ligaments.

CROM, clinician-reported outcome measure; DRF, distal radius fracture; DRUJ, distal radioulnar joint; PROM, patient-reported outcome measure; RCT, randomised controlled trial; TFCC, triangular fibrocartilage complex.

3. To assess the difference in patient-reported outcome measures (PROMs) and clinician-reported outcome measures (CROMs) in patients with DRFs with ligament injury compared with patients without ligament injury.

## METHODS AND ANALYSIS

The systematic review protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42020165007) at <https://www.crd.york.ac.uk/PROSPERO/#myprosperto>. This protocol is written in accordance with the guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). The PRISMA-P checklist can be found in online supplemental file 1.<sup>37 38</sup>

### Eligibility criteria

See [table 1](#) for an overview of the inclusion and exclusion criteria.

### Study designs

Randomised controlled trials (RCTs), pseudo-RCTs and non-randomised studies, including cohort studies and case-control studies will be included. Prospective and retrospective studies will be included. Case series with a population of ≤5 patients, case-reports, commentaries, editorials, letters, conference abstracts and book chapters will be excluded.

### Participants

Studies with patients, aged ≥18 years, with DRFs will be included. Both intra-articular and extra-articular DRFs

**Table 2** Diagnosis of concomitant ligament injury of the wrist

	All ligament injury and carpal instabilities	SL ligament injury	LT ligament injury <sup>55</sup>
Physical examination	No specific requirements.	<ul style="list-style-type: none"> <li>▶ Watson's scaphoid shift test—elicits a palpable and/or audible reduction of the subluxated scaphoid and elicits symptomatic pain, usually on the dorsal side.<sup>56</sup></li> <li>▶ Finger extension test—elicits pain when performing maximum finger extension against resistance during simultaneous volar flexion of the wrist.</li> </ul>	<ul style="list-style-type: none"> <li>▶ Ulnar snuffbox test—elicits pain when performing lateral pressure on the triquetrum between the flexor carpi ulnaris and extensor carpi ulnaris tendons.</li> <li>▶ Shear test—laxity compared with the contralateral side or elicitation of recognisable symptoms when performing a dorsal force on the triquetrum/pisiform and volar force on the lunate.</li> <li>▶ LT ballottement test—elicits pain when rocking the triquetrum back and forth on the stabilised lunate.</li> <li>▶ Click provocation test—elicits a click during ulnar deviation with the wrist pronated under axial compression.</li> </ul>
X-ray	No specific requirements.	<ul style="list-style-type: none"> <li>▶ SL interval of &gt;3 mm on PA view.</li> <li>▶ SL angle of &gt;60° on lateral view.</li> <li>▶ CL angle of &gt;30° on lateral view (taking into account the SL angle).</li> <li>▶ Exaggerated cortical ring of the distal scaphoid on PA view.</li> </ul>	<ul style="list-style-type: none"> <li>▶ A break in Gilulas arcs compared with the contralateral side on PA view.</li> <li>▶ SL angle of &lt;30° on lateral view.</li> <li>▶ CL angle of &gt;30° on lateral view (taking into account the SL angle).</li> </ul>
MRI scan, CT scan, fluoroscopy, cinematography, other <sup>57</sup>	No specific requirements.	No specific requirements.	No specific requirements.
Arthroscopy	Geissler classification <sup>15</sup> or other relevant classification.		

CL, capitollunate; LT, lunotriquetral; PA, posteroanterior; SL, scapholunate.

will be eligible. Animal studies or cadaveric studies will be excluded.

### Exposure

Patients with a DRF and concomitant ligament injury of the wrist are eligible. Lesions of the triangular fibrocartilage complex and the distal radioulnar joint are not included, since these are a separate entity in DRFs. See online supplemental file 2 for a list of all included injuries and ligaments.

Ligament injury of the wrist must be diagnosed by history, physical examination, radiology or arthroscopy or other relevant diagnostics as stated by the article. See table 2 for details on the diagnosis of ligament injury and carpal instabilities.

### Comparator

Patients with DRFs without ligament injury.

### Outcomes

Outcomes are incidence or prevalence of post-traumatic osteoarthritis or an association, correlation or regression between post-traumatic osteoarthritis and ligament injury. Post-traumatic osteoarthritis must be assessed on X-ray, CT scan or MRI scan of the wrist. All classification systems for osteoarthritis will be eligible, such as the Kellgren and Lawrence classification,<sup>39</sup> Scapholunate Advanced

Collapse classification,<sup>40</sup> Knirk and Jupiter classification<sup>4</sup> or other relevant classification as stated by the article.

Other outcomes are functional outcomes, such as PROMs and CROMs (eg, grip strength and range of motion).

See online supplemental file 2 for the exact PECO research question with a list of all search terms.

### Setting and time frame

Studies will need a minimum length of 1 year of follow-up after trauma to assess post-traumatic osteoarthritis. However, studies with a shorter period of follow-up will be included, because otherwise relevant studies for determining the incidence of concomitant ligamentous injury might be missed. In addition, it is expected that only a few studies evaluate the exposure versus the comparator. Therefore, the comparator will not be used as an inclusion criterion during our selection process.

### Report characteristics

Only published data in English will be included. A list of possible relevant titles in other languages will be provided as an appendix. There will be no limitation on the year in which the study was performed or published. Only full text articles will be included.

## Search strategy

An electronic search in MEDLINE ALL via Ovid, Embase via Embase.com, Web of Science Core Collection, Cochrane Central Register of Trials via Wiley and Google Scholar has been created and performed on 24 October 2019 by a Health Sciences librarian with expertise in systematic review searching (WMB). The initial list of relevant search terms used during the preparation of the search strategy was drawn up by a senior hand surgeon (GAK), orthopaedic researcher (NMCM) and medical doctor (MES). Animal studies, conference abstracts, case reports, book chapters and dissertation abstracts were excluded from the MEDLINE and Embase search strategies. The search strategies of the databases are included in online supplemental file 3.

The reviewers searched PROSPERO and existing databases for any ongoing or existing systematic review on this topic prior to writing this protocol. No such review has been identified.

The search will be updated towards the end of the review to retrieve the most recent eligible studies. Reference lists of the included studies and relevant reviews will be screened to identify additional potentially eligible studies which are not identified in the electronic searches.

## Study records

### Selection process

Literature search results will be uploaded to Endnote.<sup>41</sup> Duplicate records of the same report will be removed from the results.<sup>42</sup> Two reviewers (MES and EMS) will independently screen the title and abstracts for potential relevancy.

Relevant full text articles will be uploaded to the Covidence website, where the review will be managed.<sup>43</sup> This is an internet based software programme that facilitates collaboration among reviewers during the study selection process. The two independent reviewers will screen the full text articles using a standardised form based on the eligibility criteria. This form will be piloted on the 10 most recent citations prior to the selection process. Multiple reports of the same study will be linked.

The reason for exclusion will be recorded for articles that do report on ligament injury in patients with DRFs but do not meet the inclusion criteria. The search and selection process will be presented in study flow diagram according to the PRISMA statement.<sup>44</sup>

### Data management and collection

To minimise errors and reduce potential biases, data will be extracted by the two independent reviewers onto piloted, standardised data collection forms designed for this study on the Covidence website.<sup>43</sup>

### Data items

Patient characteristics (eg, age, sex), fracture characteristics (eg, intra-articular versus extra-articular, type of DRF), treatment, incidence or prevalence of osteoarthritis, degree of osteoarthritis, PROMs, grip strength,

range of motion, incidence or prevalence of concomitant ligament injury, type and grade of ligament injury and how it was diagnosed will be extracted. In addition, study characteristics (ie, trial design, trial size, primary and secondary outcomes of the study, duration of follow-up, source of financial support) and information for quality assessment will be extracted.

### Outcomes and prioritisation

The primary outcome of the systematic review is an association or correlation between osteoarthritis and concomitant ligament injury after DRFs. If no association or correlation is reported, the incidence or prevalence of osteoarthritis in relation to concomitant ligament injury will be reported. Outcomes will be subdivided for different types of DRFs and different intervention groups where appropriate. If studies vary at different time points, the incidence and prevalence of osteoarthritis will be subdivided as follows:

- ▶ Early onset of osteoarthritis, 1–2 years after trauma.
- ▶ Middle late onset of osteoarthritis, 2–5 years after trauma.
- ▶ Late onset of osteoarthritis, over 5 years after trauma.

Secondary outcomes of the systematic review will be PROMs, such as the Patient-Reported Wrist Evaluation (PRWE),<sup>45</sup> (Quick) Disabilities of Arm Shoulder and Hand ([Quick]DASH),<sup>46</sup> Michigan Hand Outcome Questionnaire (MH[O]Q),<sup>47</sup> the Australian Canadian Osteoarthritis index (AUSCAN),<sup>48</sup> Visual Analogue Scale (VAS) or numeric rating scale (NRS) for pain or other PROM as reported by the study. Other secondary outcomes of the systematic review are CROMs, such as grip strength and range of motion.

Outcomes will be presented for the latest evaluated time points according to the study.

### Risk of bias in individual studies

The two independent reviewers will assess the risk of bias for each included study.

The Cochrane Collaboration's Risk of Bias tool 2.0 (RoB 2.0) will be used for RCTs.<sup>49</sup> The Risk Of Bias In Non-Randomized Studies-of Interventions (ROBINS-I) will be used for non-randomised studies or quasirandomised studies.<sup>50</sup> The Newcastle-Ottawa Scale (NOS) will be used for quality assessment of prospective and retrospective cohort studies, which do not compare interventions, as well as for case-control studies and small case-series.<sup>51</sup> The NOS will be adapted to meet the specific needs of this systematic review.

Discrepancies between the independent reviewers will be clarified through discussion after every step of the selection process, data extraction process and the risk of bias assessment. A third reviewer (GAK) will be consulted if no consensus is achieved. Furthermore, authors will be contacted if more information is needed to make final decisions on the inclusion of studies (ie, clarification of study eligibility), and if data are unclear or missing from reports.

## Data synthesis

Since the research question is aetiological and broader in nature, a systematic, narrative, qualitative summary will be performed according to the PRISMA statement, to explore the findings and relationship between ligament injury and the incidence of osteoarthritis within studies and between the included studies.<sup>44</sup> Studies which are eligible based on patient, exposure and outcomes will be described. These studies do report on concomitant ligament injury in patients with DRF but do not compare their results to patients with DRF without ligament injury. If it turns out that  $\geq 5$  studies are eligible in terms of exposure and comparator, the systematic review will be based on these studies only. Hence, the systematic review will be based on studies with a comparator and higher overall quality.

Information will be presented in the text and tables to summarise and explain the characteristics and findings of the included studies. A table of summary will first be sorted on studies that compare both groups of patients with and without ligament injury in relation to post-traumatic osteoarthritis and functional outcomes and subsequently the studies that did not report on both groups. Second, it will be sorted on type of study design and will be graded from low risk of bias to high risk of bias within type of study design. In addition, a risk of bias table will be presented. All studies which are included will be reported, regardless of the risk of bias. However, low risk of bias studies will be emphasised in the qualitative summary.

No meta-analysis will be performed since we expect heterogeneity of the studies. Thus, a quantitative synthesis may not be appropriate.

## Meta-bias

Assessment of meta-bias will not be performed.

## Confidence in cumulative evidence

Not applicable.

## Patient and public involvement

No patients are involved during this study.

## ETHICS AND DISSEMINATION

No ethical approval is required, since this is a protocol for a systematic review. The systematic review will be submitted for publication in a peer-reviewed scientific journal and for presentation at relevant conferences.

## DISCUSSION

Aims of this systematic review are to summarise existing literature on the effect of concomitant ligament injury in adult patients with DRFs on the incidence and radiological degree of osteoarthritis, and its effect on functional outcomes, as well as to identify any existing gaps in knowledge. To our knowledge, no systematic review in English literature has reported on the incidence of post-traumatic

osteoarthritis and clinical outcomes of patients with DRFs without ligament injury compared with those with ligament injury on the long term. Two (systematic) reviews have been performed on the use of wrist arthroscopy in the management of DRFs. These mainly focus on the indications and additional value of wrist arthroscopy in DRFs in terms of functional outcomes and radiological osteoarthritis. Part of these reviews entails concomitant ligament injury seen during arthroscopy; however, no association was reported on the type and grade of ligamentous injuries and radiological degree of osteoarthritis. Also, the authors did not compare outcomes between patients with isolated DRFs and patients with DRFs with concomitant ligament injury.<sup>52 53</sup> Likewise, Fowler performed a non-systematic review on SL and lunotriquetral ligament injuries associated with acute DRFs. The effect on the development of post-traumatic osteoarthritis was not addressed in this article.<sup>54</sup>

It is possible that none of the eligible studies address our primary research question and only briefly report on osteoarthritis. Therefore, a broad approach to our synthesis was set up. Realistically, this may result in substantial heterogeneity of the studies in terms of study design, types of DRFs and their treatment, how ligament injury was assessed and what classification is used and outcomes assessed at different time points. Therefore, no meta-analysis will be performed. Findings of this review could clarify the role and relevance of concomitant ligament injury of the wrist on the development of post-traumatic osteoarthritis in patients with DRFs and whether this topic needs to be addressed in future studies on management of preventing post-traumatic osteoarthritis of the wrist after DRFs.

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**Contributors** MES conceived the idea of the study, contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria, drafted the manuscript of the protocol, will perform the selection process and data collection as an independent reviewer, and will draft the manuscript of the systematic review. GAK provided expertise on osteoarthritis of hand and wrist, contributed to the development of the selection criteria, the risk of bias assessment strategy, data extraction criteria and is the third reviewer in case of any disagreements during the selection and data extraction process. WMB developed the search strategy and provided expertise on the methodology. JWC provided expertise on osteoarthritis of hand and wrist, contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. NMCM contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. All authors read and approved the final manuscript.

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