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SYSTEMATIC REVIEW

Lisfranc injuries: fix or fuse?

A SYSTEMATIC REVIEW AND META-ANALYSIS OF CURRENT LITERATURE PRESENTING OUTCOME AFTER SURGICAL TREATMENT FOR LISFRANC INJURIES

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Aims

This systematic review and meta-analysis was conducted to compare open reduction and internal fixation (ORIF) with primary arthrodesis (PA) in the treatment of Lisfranc injuries, regarding patient-reported outcome measures (PROMs), and risk of secondary surgery. The aim was to conclusively determine the best available treatment based on the most complete and recent evidence available.

Methods

A systematic search was conducted in PubMed, Cochrane Controlled Register of Trials (CENTRAL), EMBASE, CINAHL, PEDro, and SPORTDiscus. Additionally, ongoing trial registers and reference lists of included articles were screened. Risk of bias (RoB) and level of evidence were assessed using the Cochrane risk of bias tools and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool. The random and fixed-effect models were used for the statistical analysis.

Results

A total of 20 studies were selected for this review, of which 12 were comparative studies fit for meta-analysis, including three randomized controlled trials (RCTs). This resulted in a total analyzed population of 392 patients treated with ORIF and 249 patients treated with PA. The mean differences between the two groups in American Orthopedic Foot and Ankle Society (AOFAS), VAS, and SF-36 scores were -7.41 (95% confidence interval (CI) -13.31 to -1.51), 0.77 (95% CI -0.85 to 2.39), and -1.20 (95% CI -3.86 to 1.46), respectively.

Conclusion

This is the first study to find a statistically significant difference in PROMs, as measured by the AOFAS score, in favour of PA for the treatment of Lisfranc injuries. However, this difference may not be clinically relevant, and therefore drawing a definitive conclusion requires confirmation by a large prospective high-quality RCT. Such a study should also assess cost-effectiveness, as cost considerations might be decisive in decision-making.

Level of Evidence: I

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Introduction

Surgeons face a major challenge when treating patients with Lisfranc injuries.[1,2] To date, it is unclear what the best operative treatment is for unstable Lisfranc injuries.[3] The generally accepted two operative techniques generally accepted are open reduction and internal fixation (ORIF) and primary arthrodesis (PA).[4] Traditionally, arthrodesis of the midfoot was seen as a salvage procedure for complicated outcome of Lisfranc injuries.[4,5] However, more recent studies have reported good patient-reported outcomes after arthrodesis as primary treatment.[6-8]

A number of meta-analyses and reviews have already been published comparing

Table I. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Published/unpublished RCTs, nRCTs, observational studies, and case series on ORIF vs PA or one of these treatments for Lisfranc injuries	Trials using ORIF or PA for other injuries than Lisfranc
All Lisfranc injuries: displaced or non-displaced, ligamentous, and bony-ligamentous	Stabilization solely with Kirschner-wires
Age ≥ 18 yrs	
PROM(s)	

nRCT, non-randomized controlled trial; ORIF, open reduction and internal fixation; PA, primary arthrodesis; PROM, patient-reported outcome measure; RCT, randomized controlled trial.

ORIF with PA in Lisfranc injuries. They all reported no significant differences in patient-reported outcome measures (PROMs) like the American Orthopaedic Foot and Ankle Society (AOFAS) score. However, these reviews reported a lack of power to support their findings, so it remains debatable which treatment is superior.[3,9-14] After these reviews, two studies on ORIF and PA have recently been published of which one RCT.[15,16] Our systematic review and meta-analysis also included cohort series that reported on either ORIF or PA, to further substantiate any results found in the meta-analysis of the included comparative studies.

Postoperative pain and secondary surgeries all have an effect on patients' wellbeing, and PROMs provide good insights into these factors. The most frequently used PROM is the AOFAS, although the Short-form 36 (SF-36) score and Visual Analogue Scale (VAS) are also used frequently.

Our systematic review and meta-analysis aims to draw a conclusion about the best available treatment, based on the most complete and recent evidence regarding PROMs and risk of secondary operations.

Methods

Reporting. The Preferred Reporting Items for Systematic review and Meta-analysis (PRISMA) guidelines were followed in conducting and reporting this review.[17]

Research question and inclusion and exclusion criteria. Is ORIF or PA a better operative treatment option for Lisfranc injuries, based on PROMs reported in the currently published literature? The outcome measures of this review are PROMs, and risk of secondary surgeries. The inclusion and exclusion criteria are summarized in Table I.

Search strategy. Two authors (NACB, AJLL) independently searched the PubMed, CENTRAL, EMBASE, CINAHL, PEDro, and SPORTDiscus databases. No restrictions were applied to this search. An independent librarian from Maastricht University checked the search strategy for errors. Additionally, ongoing trials were searched for possible useful interim analyses (last search 10 June 2020) in several national (http://www.trialregister.nl) and international trial registries (http://www.controlled-trials.com); the WHO trial register (apps.who.int/trialsearch); EU Clinical trial register (http://www.clinicaltrialsregister.eu); and ClinicalTrials.gov. Authors of potentially eligible studies were contacted by email twice for additional information, but without result (Supplementary Material).[18–20]

Study selection. After removing duplicates, references were screened on title and abstract. Full-text screening was performed independently by three authors (NACB, AJLL, GANLS) using the inclusion and exclusion criteria (Table I). Reference lists of included studies were scanned to identify any additional relevant reports.

Data extraction and analysis. Data from included articles were extracted using a data extraction form from the Cochrane Collaboration (Tables II and III).[21]

The data analysis used fixed and random effect models, using the Cochrane Review Manager 5.4 (RevMan, Cochrane Collaboration, UK) software. Outcomes were visualized in forest plots (Figure 1).

Risk of bias and levels of evidence. All PROMs reported by the included studies were assessed for risk of bias (RoB) independently by three authors (NACB, AJLL, GANLS). For RCTs, bias was assessed using the Cochrane RoB 2 tool (RoB2),[35] and for nRCTs the ROBINS-I tool.[36] The modified Newcastle Ottawa scale was used for case series.[37] In case of disagreement, agreement was achieved by discussion, and if necessary, by consulting an independent epidemiologist (MP). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to determine the level of evidence in all studies included.[38]

Results

Selection of studies. A total of 20 studies were selected for this study (Figure 2). The meta-analyses included the comparative studies: three RCTs,[8,15,23] one nRCT,[4] and eight retrospective case series,[5,6,16,22,24–27] resulting in a total of 392 patients treated by ORIF and 249 by PA. Seven non-comparative case studies reporting on ORIF and one on PA were used for a descriptive analysis to further expand our dataset.[19,28–34] Studies published between 2002 and 2020 were included.

RoB and GRADE levels of evidence. The RoB in the three RCTs and the case series was either moderate or high. Of the 15 case studies, 11 were of good quality, two of fair quality,[22,30] and two of poor quality.[26,29] GRADE levels (Table II) were low in all studies, except for the RCT from Stødle,[15] which yielded high-level evidence for the AOFAS score (Supplementary Material).

Table II. Studies comparing open reduction and internal fixation and primary arthrodesis.

Study	Study type	Sample size, n (n groups)	Sex, female (%); mean age, yrs (range/SD)	Type of injury, n*	Mean follow-up, mths (range)	PROMs	GRADE level of evidence for PROM†	Mean AOFAS (SD)
Mulier et al (2002)[22]	Case series	28 (ORIF 16, PA 12)	Sex: 10 (35.7) Age: 30.5 (15 to 47)‡	Data unavailable	30.1	PFS	Very Low	N/A
Ly and Coetzee (2006)[8]	RCT	41 (ORIF 20, PA 21)	Sex: ORIF 7 (35), PA 7 (33.3) Age: ORIF 32.4 (19 to 52), PA 32 (19 to 42)	Data unavailable	ORIF 42, PA 43.4	AOFAS VAS, FQ	Moderate Low	ORIF 57.1 (21) PA 86.9 (9.25)
Henning et al (2009)[23]	RCT	32 (ORIF 14, PA 18)	Sex: ORIF 5 (35.7), PA 6 (31.6) Age: ORIF 37 (20 to 58), PA 40 (25 to 73)	ORIF: a = 6, b = 8 PA: a = 7, b = 11	24	SF-36, SMFA	Low	N/A
Dubois-Ferrière et al (2016)[24]	Case series	61 (ORIF 50, PA 11)	Sex: 13 (21.3) Age: 37.5 (16 to 70)	a = 7 b = 54	10.9 (2.4 to 23.9)	AOFAS, VAS, SF-12, PPI. PCS	Very Low Very Low	ORIF 79.7(16) PA 77.8 (7.5)
Cochran et al (2017)[25]	Case series	32 (ORIF 18, PA 14)	Sex: 1 (3,2) Age: 28 (19 to 39)	ORIF: a = 13, b = 5 PA: a = 9, b = 5	32 (13 to 70)	FAAM, RTD	Very Low Very Low	N/A
Hawkinson et al (2017)[26]	Case series	111 (ORIF 91, PA 20)	Data unavailable§	Data unavailable	Data unavailable	RTD	Very Low	N/A
Qiao et al (2017)[6]	Case series	25 (ORIF 17, PA 8)	Sex: ORIF 5 (29.4), PA 3 (37.5) Age: ORIF 37 (18 to 65), PA 40 (34 to 52)	Data unavailable	ORIF 7.5, PA 15	AOFAS, SF-36, VAS	Very Low	ORIF 88.6 (6.4) PA 94 (8.25)
Wang et al (2017)[27]	Case series	34 (ORIF 15, PA 19)	Sex: ORIF 8 (53.3), PA 6 (31.6) Age: ORIF 38.9 (22 to 54), PA 39.6 (26 to 58)	Data unavailable	28.5 (24 to 37)	AOFAS SF-36, VAS	Low Very Low	ORIF 84.3 (9.5) PA 85.1 (8.15)
van Hoeve et al (2018)[4]	Prospective obsv.	19 (ORIF 8, PA 6, conservative 5)	Sex: 12 (63.2) Age: 40.5 (16.7/18 to 68)	b = 19	24	AOFAS FADI, SF-36	Moderate Low	ORIF 72.5 (13.5) PA 65.5 (15)
Kirzner et al (2019)[5]	Case series	39 (ORIF 21, PA 18)	Sex: ORIF 4 (19), PA 9 (50) Age: ORIF 37 (14.2), PA 49.4 (18.9)	Data unavailable	52 (13 to 114)	AOFAS MOXFQ	Low Very Low	ORIF 62.5 (19) PA 71.8 (19)
Fan et al (2019)[16]	Case series	176 (ORIF 98, PA 78)	Sex: 72 (40,9) Age: 41.4 (19 to 61)	b = 176	91 (24 to 153)	AOFAS FAOS, SF-36, VAS	Low Very Low	ORIF 74.7 (13) PA 82.8 (7.5)
Stødle et al (2020)[15]	RCT	48 (ORIF 24, PA 24)	Sex: ORIF 13 (54.2), PA 13 (52.2) Age: ORIF 34 (28 to 40), PA 30 (23 to 40)	ORIF: b = 24 PA: b = 24		AOFAS SF-36 VAS	High Moderate Low	ORIF 85 (15) PA 89 (9)

*Injury type is divided into two categories: a) purely ligamentous and b) ligamentous with any type of fracture, including avulsion fractures.
†Motivations for risk of bias assessment and GRADE assessment are shown in Supplementary Material 1-6.
‡Results of the study by Mulier et al[22] were not used in the meta-analysis due to age < 18 yrs.
§Hawkinson et al[26] describes a military population, so age ≥ 18 is to be expected.
FAAM, Foot and Ankle Ability Measure; FADI, Foot and Ankle Disability Index; FAOS, Foot and Ankle Score; FQ, functional questionnaire; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MOXFQ, Manchester Oxford Foot Questionnaire Score; N/A, not available; PFS, Baltimore Painful Foot Score; PROM, patient-reported outcome measurement; RTD, return to duty; SD, standard deviation; SMFA, Short Musculoskeletal Function Assessment.

AOFAS Midfoot Scale. Eight comparative studies used the AOFAS score and were eligible for meta-analysis.[4–6,8,15,16,24] The total study population consisted of 252 and 183 patients undergoing ORIF and PA, respectively. A significant mean difference in the AOFAS score was found in favour of PA (-6.34 (95% CI -11.88 to –0.80)). There was significant heterogeneity among these studies: $Tau^2 = 44.60$; $Chi^2 = 31.83$; df = 7 ($p < 0.0001$); and $I^2 = 78\%$. The study by Ly and Coetzee[8] found a larger mean difference than the other studies, which adds to the reported heterogeneity (Figure 1a). Mean AOFAS score in the non-comparative case studies was 78.6 (71.0 to 89.4) for ORIF and 81 for PA (Table III).[34]

VAS. Seven studies reported VAS score, and were eligible for meta-analysis (Figure 1b).[6,8,15,16,24,25,27] They reported no difference in mean VAS score between ORIF and PA (0.63 (95% CI -0.86 to 2.13)). Heterogeneity among these studies was high ($Tau^2 = 3.96$; $Chi^2 = 2725.17$; df = 6 ($p < 0.00001$); $I^2 = 100\%$). The non-comparative studies found VAS scores of 1.8 (standard deviation (SD) 2) and 1.1 (SD 0.7), respectively.[19] These non-comparative studies support the findings of the comparative studies.[4,6,8,16,25,27]

SF-36 Score. No difference in SF-36 score (-1.20 (95% CI -3.86 to 1.46)) was found between ORIF and PA.[15,16,27] Heterogeneity among these studies was moderate (Figure 1c). The SF-36 score found by the non-comparative study was 51.4 (SD 11.9), which is relatively low in comparison with the comparative studies included in our meta-analysis.[34]

Revision surgery and hardware removal. Patients who underwent ORIF had a risk ratio of 1.53 (95% CI 1.15 to 2.03) for hardware removal, compared to PA.[5,6,8,15,23,25,26] No difference was found in revision surgery (RR 2.23 (95% CI 0.94 to 5.32)).[5,6,8,15,16,23,25,26] Heterogeneity for hardware

Table III. Non-comparative studies on either open reduction and internal fixation or primary arthrodesis for Lisfranc injuries.

Study	Sample size, n	Sex, female (%); mean age, yrs (range)	Injury type, n*	Mean follow-up, mths (range)	Mean AOFAS (SD)†	Mean VAS (SD)	Other mean PROMs (SD)	Occurrence of post-traumatic osteoarthritis, %	Removal of hardware, %
Demirkale et al (2013)[28]	32 (ORIF)	Sex: 11 (34.4) Age: 34.5 (19 to 55)	NI	43.3 (22 to 96)	74.7 (N/A)	N/A	FADI 59.6 (N/A)	15.6	65.6
Ghate et al (2012)[29]	19 (ORIF and CRIF)	Sex: 4 (21.2) Age: 41 (21 to 58)	a: 6 b: 13	30 (24 to 40)	a: 73.5 (N/A) b: 79 (N/A)	N/A	MFS 77.7 (N/A)	21	N/A
Kuo et al (2000)[30]	48 (ORIF)	Sex: 16 (33.3) Age: 39.2 (15 to 77)	a: 13 b: 29	52 (12 to 114)	a: 78.8 (N/A) b: 80.68 (N/A)	N/A	MFA 19 (13.75)	25	N/A
Rajapakse et al (2005)[31]	16 (ORIF)	Sex: 9 (36) Age: 33.2 (16 to 76)	a: 9 b: 7	42.6 (11 to 69)	a: 74.9 (N/A) b: 80.9 (N/A)	N/A	N/A	N/A	N/A
Rammelt et al (2008)[32]	22 (ORIF)	Sex: 5 (22.7) Age: 35 (17 to 76)	a: 0 b: 22	37 (24 to 89)	81.4 (9.5)	N/A	MFS 85 (7.5)	N/A	N/A
Teng et al (2002)[33]	11 (ORIF)	Sex: 6 (54.2) Age: 40.6 (21 to 58)	a: 0 b: 11	41.2 (14 to 53)	71.0 (16.25)	N/A	N/A	73	N/A
Wu et al‡ (2020)[19]	14 (ORIF)	Sex: 7 (50) Age: 32.7 (22 to 49)	N/A	13 (9 to 24)	89.4 (4.5)	1.1 (0.7)	SF-12 48.8 (3.3)	N/A	71.4
Reinhardt et al (2012)[34]	25 (PA)	Sex: 17 (68) Age: 46 (20 to 73)	a: 12 b: 13	42 (24 to 96)	a: 83.3 (12.75) b: 78.5 (18.75)	1.8 (2)	SF-36 51.4 (11.9)	12	16

*Injury type is divided into two categories: a) purely ligamentous and b) ligamentous with any type of fracture, including avulsion fractures.
†Results of outcome measurements at last follow-up.
‡Wu et al compared acute ORIF with delayed ORIF; the present review only included the patients treated with acute ORIF.
AOFAS, American Orthopedic Foot and Ankle Society score; CRIF, closed reduction and internal fixation; MFA, Musculoskeletal Function Assessment; MFS, Maryland Foot Scale; N/A, not available; ORIF, open reduction and internal fixation; PROM, patient-reported outcome measure; SD, standard deviation; VAS, visual analogue scale.

removal surgery and revision surgery was 65% and 5%, respectively (Figure 1).

Purely ligamentous versus bony ligamentous injuries. Four studies distinguished between PROMs for different injury types.[29–31] Three of these described the AOFAS score for patients who underwent ORIF for purely ligamentous injuries and for those with injuries involving any type of fractures.[29–31] None of these studies found a significant difference in AOFAS score between the ligamentous and bony ligamentous groups. The retrospective case series did not find significant differences between these groups for PA patients either.[34]

Discussion

This study aimed to compare ORIF and PA, based on the latest and most complete available evidence, to finally draw a conclusion about the best available treatment for unstable Lisfranc injuries regarding PROMs and risk of secondary surgery, and draw a recommendation for further research in this field.

Our meta-analysis is the first to report a significant difference favouring PA, as measured by the AOFAS Midfoot Scale. Although it is questionable, this difference does reach clinical significance since the difference was 6.8 points on the 100-point outcome scale, it does support the growing belief that PA for unstable Lisfranc injury might yield the better outcome. Significant heterogeneity between studies was found for most parameters. This may be explained by the heterogeneous injury pattern, with varying extent of joint involvement, fracture pattern, and ligamentous disruption. This heterogeneous injury pattern is a good representation of the patients encountered in common practice. The study by Ly and Coetzee[8] is an apparent outlier; this prospective RCT is one of the main causes of heterogeneity in this meta-analysis. The mean AOFAS score (57.1 (SD 21)) for ORIF in Ly and Coetzee[8] is lower than reported in the other studies (62.5 to 89.4, median 77.6). One explanation could be that at the time of the last follow-up, five out of 20 patients in the ORIF group had undergone secondary arthrodesis (SA) for post-traumatic arthritis, which has a negative effect on the functional outcome.

Additionally, Fan et al[16] found a statistically significant difference in scores with respect to several components of the Foot and Ankle Outcome Score (FAOS), in favour of PA (e.g. quality of life ORIF: 79.95, PA: 86.67, $p < 0.001$). Other outcome measures did not show any significant differences (Tables II and III).

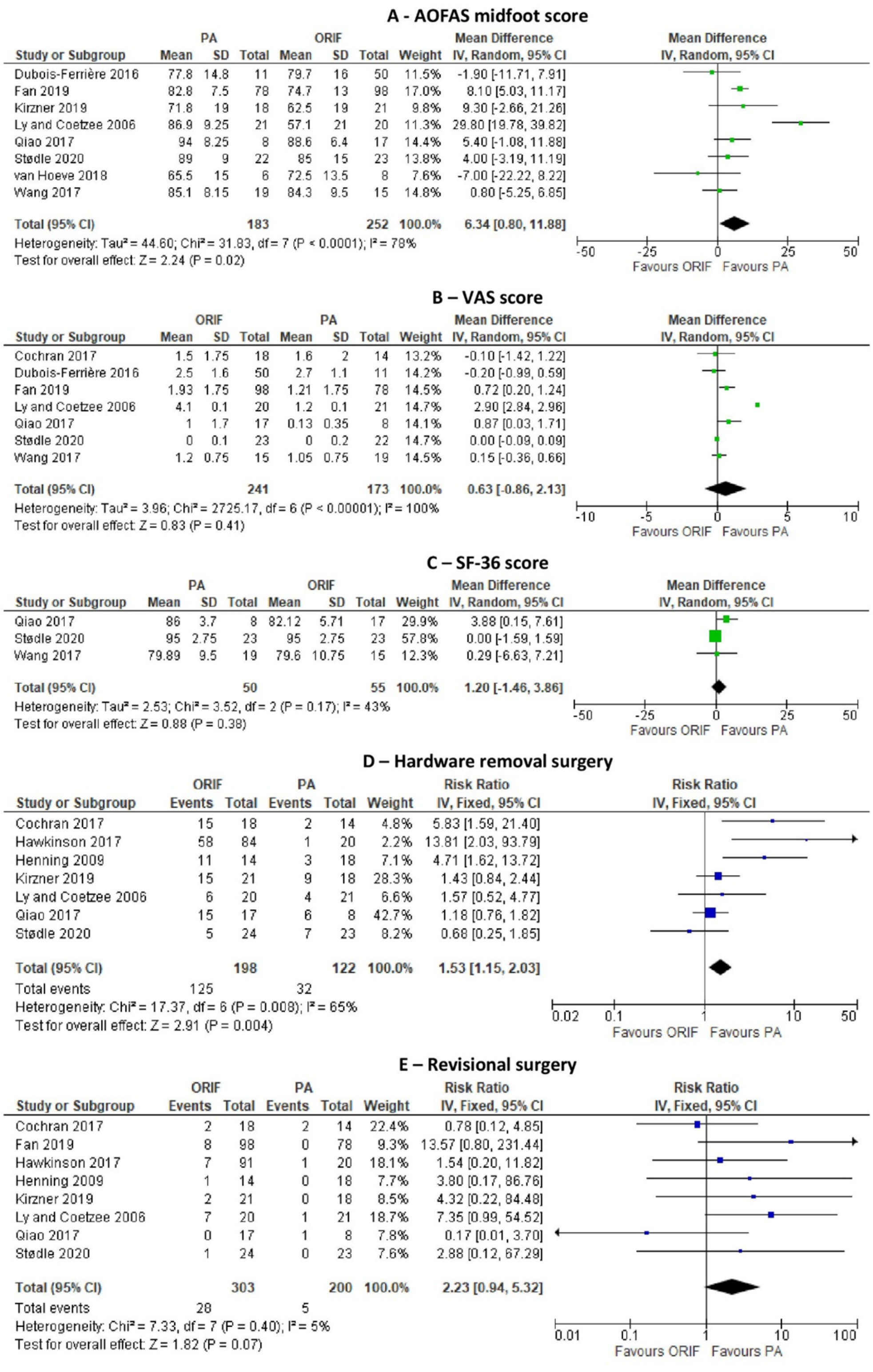

Fig. 1

Meta-analysis of comparative studies. AOFAS, American Orthopedic Foot and Ankle Society; CI, confidence interval; IV, inverse variance; ORIF, open reduction and internal fixation; PA, primary arthrodesis; SD, standard deviation; SF-36, 36-Item Short-Form Health Survey questionnaire; VAS, visual analogue scale.

The AOFAS Midfoot Scale score may be limited in validity and internal consistency for long-term outcome evaluation.[39] The AOFAS even published a position statement discouraging further use in 2011.[40] Although this

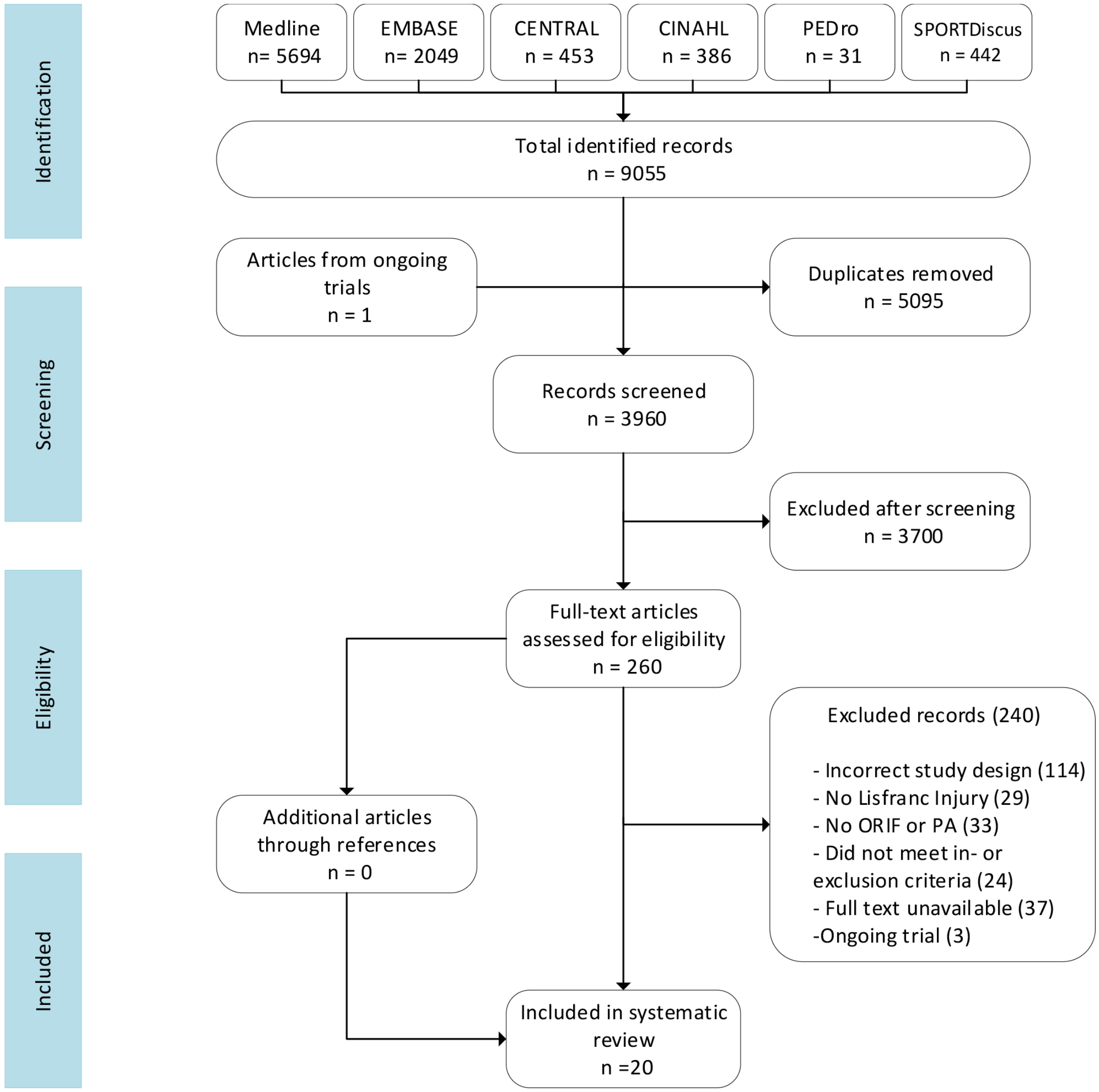

Fig. 2

Flowchart of included studies.

might constitute a limitation, the AOFAS Midfoot Scale is the most commonly used outcome measure for patients treated for Lisfranc injury, and there is no better measure to replace this scale to date.[41] Smith et al[11] stated that with the currently available evidence, future studies should continue to include the AOFAS score for comparative purposes.

An analysis of different types of injuries (purely ligamentous vs displaced bony ligamentous vs non-displaced bony ligamentous injuries) was not possible. Most studies do not clearly describe which type of injuries were taken into account, and the data on different injury patterns are commonly presented as one dataset. Some authors excluded major intra-articular fractures, so selection bias is to be expected.[23] Additionally, some authors reported avulsion fractures as purely ligamentous injuries, which might also influence the results.[3,8,12,14]

We found no difference between ORIF and PA in the risk of secondary surgeries for postoperative complications. Hardware removal was carried out more often in ORIF patients. However, this was greatly affected by routine hardware removal in the ORIF group.[6,15,16,23] Analysis of hardware removal on indication did not show a significant difference.[5,8,25,26] No significant difference was found for secondary surgery without implant removal. However, one of the presumed advantages of PA is to prevent post-traumatic arthritis and the consequent need for SA. This might be explained by the fact post-traumatic osteoarthritis is not always symptomatic. In addition, spontaneous fusion is seen after joint-preserving surgery, with reported better PROMs.[19]

The need to deliver healthcare efficiently has increased substantially in recent years.[42] Two studies have reviewed the costs of ORIF and PA: one found that PA was significantly more expensive and, in contrast, one found PA to be more cost-effective.[43,44] All of the reported studies measuring the cost-effectiveness only measured the medical costs, such as professional care and diagnostic tests. We suggest also measuring the patient and family costs caused by reduced productivity and hospital visits, since Lisfranc injuries may often cause long-term complaints.[44–46]

Several limitations of this meta-analysis have to be mentioned. All case studies, and most prospective studies, rated low or very low level of evidence. Furthermore, all prospective studies, except for the RCT by Stødle et al,[15] had a high RoB. Another limitation is the heterogeneity of the studies; we could not make a separate analysis for different injury types as described above. Although caution is advised with regard to drawing any firm conclusions in case of pooling of non-randomized study results, our study offers the most recent and best comprehensive overview of the currently available data, and therefore is the only study to include all available evidence in this field. Compared to previous systematic reviews and meta-analyses, our study included additional data from non-comparative studies to support our meta-analysis, and included one recently published RCT for meta-analysis.[15] Our analysis of this resulting larger dataset further substantiates the growing notion that PA could be considered as the primary intervention for Lisfranc injuries. These insights will be noteworthy as, until now, there has been no golden standard (although this may not represent a clinical difference, and the bias of the studies available makes definitive conclusions difficult). This highlights the need for further robust RCTs to answer this important question.

In conclusion, our systematic review and meta-analysis is the first to suggest that, based on the AOFAS, PA might be a better option for Lisfranc injuries than ORIF. However, the limitations of the methodological quality of the individual studies, and the pooling of non-randomized study results, make it difficult to favour one intervention over the other. Therefore, in order to draw a definitive conclusion regarding the best treatment, there is an urgent need for a large prospective high-quality RCT. Such a study should also assess cost-effectiveness, as cost considerations could be crucial in decision-making, especially when both treatments are equal based on PROMs.

Take home message

- Based on the American Orthopedic Foot and Ankle Score, primary arthrodesis may be a better option for Lisfranc injuries than open reduction and internal fixation.
- In order to draw a definitive conclusion regarding the best treatment, there is an urgent need for a larger prospective high-quality randomized controlled trial. Please see the current controlled trial: NCT04519242 with registration date: 08/13/2020 (retrospectively registered; protocol date and version: Version 4 05/06/2020).

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Supplementary material

Screening tools for the risk of bias and Grading of Recommendations Assessment, Development and Evaluation level of evidence, and additional information about the database search.

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