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Impact of timing of surgery on wound complications and re-operations following closed ankle fracture fixation: a systematic review and meta-analysis

M. M. FARHAN-ALANIE[1], R. SAHEMEY[2], K. AL-HOURANI[3], A. TROMPETER[4]

[1]MBChB, BMedSci(Hons), MRCS(Ed), MSc(Dist), PgCert(MedEd), PgDip, FHEA, MFST(Ed), NIHR Doctoral Research Fellow, Warwick Medical School, University of Warwick, Coventry, CV4 7HL, UK; [2]MBBS, FRCS(Tr+Orth), Consultant Trauma & orthopaedic Surgeon, Department of Trauma & Orthopaedics, University Hospitals Birmingham NHS Foundation Trust, B15 2GW, UK; [3]MBChB, MFST, MD, PhD, FRCS(Tr+Orth), Consultant Trauma & Orthopaedic Knee Surgeon, Department of Trauma & Orthopaedics, Frimley Health NHS Foundation Trust, Frimley, GU16 7UJ, UK; [4]MBBS, BSc, FRCS(Tr+Orth), Consultant Orthopaedic Trauma Surgeon and Professor of Orthopaedic Trauma, St George's University Hospital NHS Foundation Trust and St George's University of London, UK.

Correspondence at: Muhamed M Farhan-Alanie, MBChB, BMedSci(Hons), MRCS(Ed), MSc(Dist), PgCert(MedEd), PgDip, FHEA, MFST(Ed), NIHR Doctoral Research Fellow, Warwick Medical School, University of Warwick, Coventry, CV4 7HL, UK.
Email: u1874544@live.warwick.ac.uk

Background: **The optimal timing of surgical fixation for closed ankle fractures remains uncertain. Advocates of early surgery suggest it enables faster rehabilitation without additional soft tissue insult, whereas delayed surgery is often favoured due to concerns about wound complications in the presence of swelling. This systematic review evaluated whether surgical timing influences wound complications and unplanned reoperation rates.**
Methods: **Multiple databases were searched for RCTs and cohort studies. Primary outcomes were wound complications and unplanned re-operation events. Two reviewers independently screened, assessed quality, and extracted data. Random effects meta-analysis was performed.**
Results: **Nine studies were included. Three reported significantly fewer wound complications with earlier fixation: within 24 hours (0/60 vs 16/145, p=0.004), four days (6.4% vs 18.6%, p=0.02), six days (2/56 vs 6/29, p=0.01), and seven days (2/98 vs 14/107, p=0.003). However, pooled analyses showed no differences at thresholds of 24 hours (RR 1.04, 95%CI 0.95-1.14, p=0.41), five days (RR 1.03, 95%CI 0.96-1.09, p=0.43), or seven days (RR 1.10, 95%CI 0.99-1.21, p=0.06). Four studies assessed unplanned reoperation; none found significant differences, and pooled analysis showed no difference between surgery performed within versus after five days (RD 0.04, 95%CI -0.07-0.15, p=0.49).**
Conclusions: **There is low quality evidence from three of nine studies suggesting that earlier fixation is associated with relatively reduced wound complications, but most studies showed no difference. No association was observed with unplanned reoperation. A large, prospective trial powered to wound complications is required to clarify causality. An RCT powered to investigate these outcomes is required to clarify causality.**

Keywords: Ankle, fracture, surgery, fixation, timing, wound complications.

INTRODUCTION

Ankle fractures are common injuries, affecting approximately 0.2% of the population every year[1,2], which equates to around 20,000 related admissions annually in the UK alone[3]. Over one third of patients who sustain this injury are managed operatively[3], however there is ongoing clinical uncertainty regarding the optimal timing of performing definitive fixation of closed ankle fractures[4]. Consequently, this topic remains contentious. Proponents of early fixation suggest that operative interventions allows decompression of the underlying haematoma and enables primary closure of the wound. Delaying fixation surgery also has economical implications from a healthcare and societal perspective, as post-operative length of hospital stay may be relatively longer due to slower progress in rehabilitation secondary to a longer period of preoperative immobility[5]. This may also delay patients ability to return to work. The British Orthopaedic Association Standards for Trauma (BOAST) advises early fixation on the day or day after injury in patients under 60 years

of age when the ankle mortise is unstable[6]. In contrast, others argue that delayed fixation allows a period of rest for the soft tissues, provided the ankle remains reduced, and is beneficial in helping the tissue micro-circulation recover[7], protecting against additional insult to already injured soft tissues. This strategy is thought to reduce the risk of wound complications, ranging from superficial infection to deep infection and wound dehiscence, which can be difficult to treat and may necessitate re-admission for intravenous antibiotics or further surgery, with associated costs and long-term morbidity[8].

Following closed reduction and casting of the ankle joint, patients are typically either admitted to hospital for operative fixation or discharged home with surgery scheduled at a later date. During the interim period, unstable fractures may re-displace within the plaster cast[9], either due to resolution of swelling or patient non-compliance with instructions to avoid weight bearing. This can exacerbate the soft-tissue injury through pressure-induced ischaemia and may increase the risk of post-operative wound complications[10,11].

This systematic review aimed to evaluate whether the timing of definitive fixation of closed ankle fractures in adult patients influences post-operative wound complications, including infection, and unplanned re-operations.

MATERIALS AND METHODS

Data Sources and Search Strategy

This study adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines[12] with a protocol registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42021278491). The following databases were searched from their inception up to 4th November 2021: Medline, Embase, Web of Science, Literatura Latino Americana em Ciências da Saúde (LILACS), African Journals Online (AJOL), and Cochrane Central Register of Controlled Trials (CENTRAL) and Database of Systematic Reviews. The search strategy is shown in Supplementary Table S1. The search results were independently assessed for inclusion by two authors (MFA, RS). Initial screening was by title and abstract. Further screening of selected full texts determined eligibility. Bibliographies of included articles and prior systematic reviews and meta-analyses were manually scanned to identify missed relevant articles.

Eligibility Criteria

Randomised controlled trials (RCTs) and cohort studies comparing post-operative wound complications and unplanned re-operation rates in adult patients with closed ankle fractures who have undergone primary definitive fixation surgery at different time intervals from injury or hospital presentation were eligible for inclusion. Studies investigating outcomes of primary fixation of almost united or malunited fractures were excluded. Studies in which one patient group received an additional intervention (e.g. external fixation, intermittent pneumatic foot pump) were also excluded.

Studies in English or with an accessible translation were included. Case reports and case-control studies were not eligible for inclusion. Grey literature was also not included.

The definitions of early and delayed surgery were extracted from the individual studies. Disagreements about study eligibility were discussed with the senior author (AT).

Data Extraction and Quality Assessment

A standardised data extraction form was used. Methodological quality was assessed on the Newcastle-Ottawa Scale[13]. This assesses three domains (selection, comparability, and outcome) across eight items with each scoring one point except for comparability which can be adapted to the specific topic to score up to two points. The two risk factors selected a priori to be most pragmatic and relevant to control for confounding between the two patient groups were body mass index and diabetes mellitu[14.] Studies scoring less than five points were judged as high risk of bias and excluded, five to seven were considered medium risk and eight or nine points were deemed low risk.

Authors were contacted by email where clarification of their methods was required or further details of their results not provided in the text was sought.

Data Synthesis and Statistical Analysis

The meta-analysis was conducted using Review Manager 5.4 (RevMan Version 5.4. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020). Summary measures were abstracted from the included studies as relative risks (RR) or, in the event where there were no events in at least one study group, as risk differences (RD). Analyses were performed using the Mantel-Haenszel method with random effects models. Outcomes were pooled, where feasible, using the most commonly reported endpoints, with analyses stratified by surgical timing intervals. Study-wise forest plots were also generated to present individual study estimates in the absence of pooled analyses. Higgins I2 test was performed to provide an estimate of the extent

of statistical heterogeneity. 95% confidence intervals (CI) were calculated for each study with statistical significance set at $p \leq 0.05$. Summary estimates of the overall effect are provided as a forest plot. Where statistical pooling was not feasible, or for additional context, findings were summarised narratively.

RESULTS

Study Identification and Selection

The literature search identified 935 articles. After excluding articles not meeting the inclusion criteria based on their title and abstract alone, 63 articles remained for full-text evaluation. Nine studies met the inclusion criteria[5,15-22]. Eight studies were retrospective cohort studies and there was one prospective cohort study. Study selection is illustrated in Figure 1 and included studies listed in Table I. An excluded studies table is provided (Table SII).

Study Characteristics and Study Quality

Of the nine studies included in the review, four were carried out in England[5,19-21], three in United States of America[15,16,18], one in Holland[22], and one in India[17]. Most studies were of small size with number of participants ranging from 50 to 235. There were data on a total of 1,313 closed ankle fractures. All participants underwent definitive open reduction internal fixation using plates and screws as a single stage procedure. Where reported or deducible, mean age of patients in the included studies ranged from 36 to 49 years, and the majority were female (59%). Where presented, the most common fracture classification was Weber B (70%) followed by Weber C (29%) and Weber A (<1%).

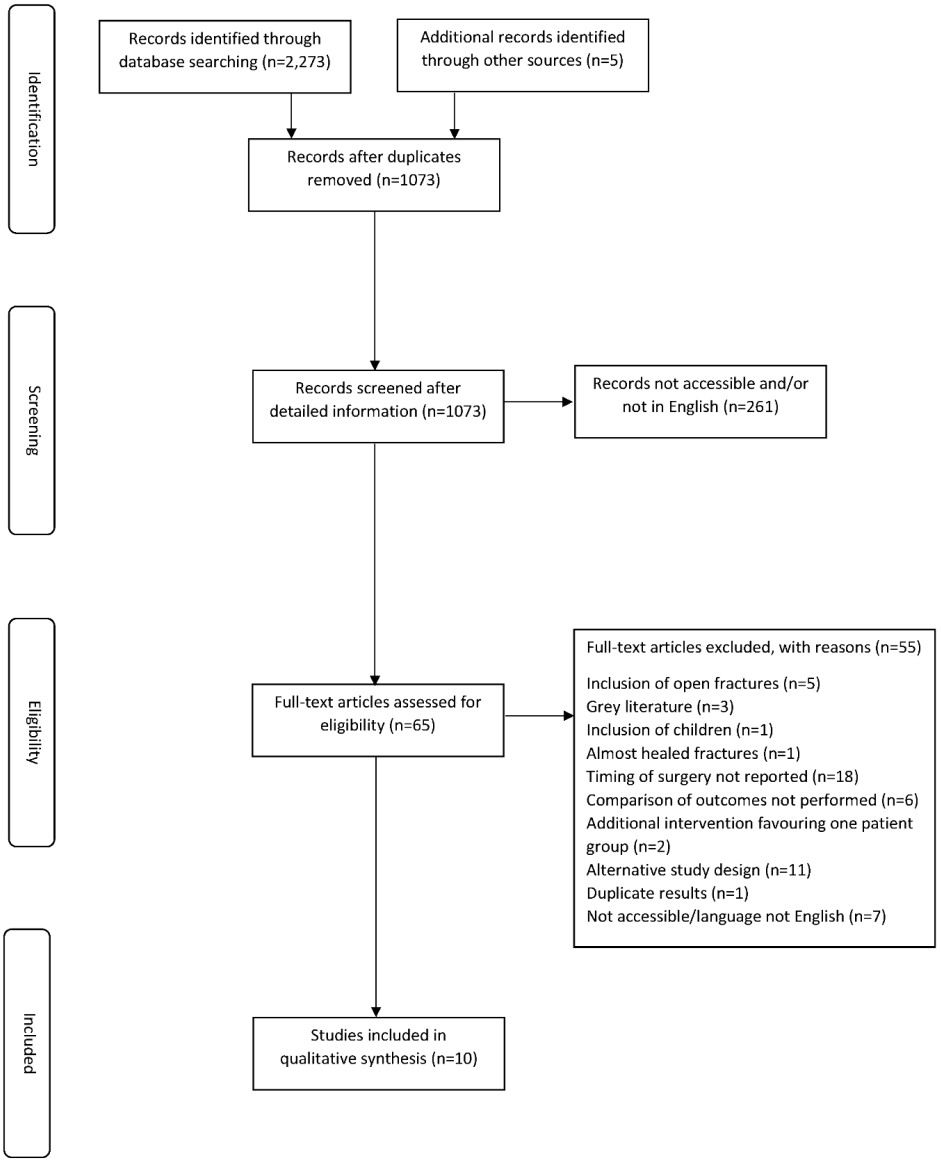

Fig. 1 — PRISMA flow diagram.

Table I. — Description of included studies.

First Author	Publication Year	Country	Study design	Study Time Period	Surgical timing (EG/DG)	Time to surgery in days (EG/DG)	Mean age in years (EG/DG) (range/SD)	Gender (EG/DG) (Male:Female) (%)	Total Procedures (EG/DG)	EG Fracture Classification Breakdown	DG Fracture Classification Breakdown	Outcome(s) Measured	Post-operativ follow-up duration
Carragee	1991	USA	Retrospective cohort study	1983 – 1985	<4 days/ >4 days From time of injury	Mean 4.5 (SD 3.5) (overall study population)	34 (range 16 – 80) (overall study population)	40:60 (overall study population)	121 total	N/R	N/R	Wound problems Surgical site infection	Minimum 4 weeks (mean 24 weeks; range 4 – 120)
Konrath	1995	USA	Retrospective cohort study	January 1991 – January 1994	<5 days / >5 days From time of injury	Mean 1.5 / mean 13.6 Overall study population range (6 – 35)	45 / 43	27:73 / 33:67	105/97	Fractures were bimalleolar or bimalleolar equivalent. Detailed classification not reported.	Fractures were bimalleolar or bimalleolar equivalent. Detailed classification not reported.	Complications (inc. wound problems and infection) Function Length of stay Duration of surgery Reduction quality	Mean 8.1 and 7.5 months in early and delayed group respectively (range 2 – 38)
Pietzik	2006	England	Retrospective cohort study	12 month period	<48 hours / >48 hours From time of presentation	Mean 1.08 / mean 4.1	42 / 47	50:50 / 65:35	62/21	3 medial malleolar (5%) 24 lateral malleolar (39%) 26 bimalleolar (42%) 9 trimalleolar (15%)	9 lateral malleolar (43%) 10 bimalleolar (48%) 2 trimalleolar (9.5%)	Complications (incl. infection) Length of stay	Inpatient follow-up only (mean 3.9 and 5.4 days in early and delayed group respectively)
Saithna	2009	England	Retrospective cohort study	January 2004 – December 2004	≤6 days / > 6 days From time of injury	N/R	46.6 (16.4–82.2) (overall study population)	39:61 (overall study population)	56/29	N/R Overall study population included 37 unimalleolar (45%), 33 bimalleolar (40%), and 13 trimalleolar (16%)	N/R	Surgical site infection Re-operation	Minimum 12 months

Table I. — Description of included studies - continued.

First Author	Publication Year	Country	Study design	Study Time Period	Surgical timing (EG/DG)	Time to surgery in days (EG/DG)	Mean age in years (EG/DG) (range/SD)	Gender (EG/DG) (Male:Female) (%)	Total Procedures (EG/DG)	EG Fracture Classification Breakdown	DG Fracture Classification Breakdown	Outcome(s) Measured	Post-operativ follow-up duration
Schepers	2013	Holland	Retrospective cohort study	January 2004 – December 2009	<24 hours / >24 hours < 7 days / ≥ 7days From time of injury	Median 7 (IQR 1 – 11) (overall study population)	Range 16 – 65 (overall study population)	N/R	60/145 98/107	<u><24 hours</u> 26 unimalleolar (43%) 34 bi- or trimalleolar (57%)	<u>>24 hours</u> 91 unimalleolar (63%) 54 bi- or trimalleolar (37%)	Surgical site infection Function	Minimum 6 months
Singh	2015	England	Retrospective cohort study	February – July 2004, 2007 and 2010	<24 hours/ >24 hours From time of presentation	N/R	40 / 49	44:56 (overall study population)	82/132	25 lateral malleolar (30%) 30 bimalleolar (37%) 27 trimalleolar (33%) 60 Weber B (73%) 22 Weber C (27%)	1 isolated medial malleolar (<1%) 47 lateral malleolar (36%) 49 bimalleolar (37%) 35 trimalleolar (27%) 102 Weber B (77%) 29 Weber C (22%)	Complications (inc. infection) Re-operation Length of stay	Inpatient follow-up only (mean 2.9 and 5.5 days in early and delayed group respectively)

Table I. — Description of included studies - continued.

First Author	Publication Year	Country	Study design	Study Time Period	Surgical timing (EG/DG)	Time to surgery in days (EG/DG)	Mean age in years (EG/DG) (range/SD)	Gender (EG/DG) (Male:Female) (%)	Total Procedures (EG/DG)	EG Fracture Classification Breakdown	DG Fracture Classification Breakdown	Outcome(s) Measured	Post-operativ follow-up duration
Tantigate	2018	USA	Retrospective cohort study	January 2010 – December 2013	<14 days / ≥14 days	Median 7 (IQR 4 – 9) / median 19 (IQR 15 – 21)	46 (SD 17) / 51 (SD 18)	41:59 / 53:47	101/17	4 unimalleolar (4%) 40 bimalleolar equivalent (39.6%) 42 bimalleolar (41.6%) 15 trimalleolar (14.8%) 71 Weber B (70.3%) 28 Weber C (27.7%) 2 high type Weber C (2.9%)	7 bimalleolar equivalent (41.2%) 6 bimalleolar (35.3%) 4 trimalleolar (23.5%) 12 Weber B (70.6%) 5 Weber C (29.4%)	□ Complications (inc. wound problems and infection) □ Re-operation □ Function □ Duration of surgery □ Length of stay	Minimum 3 months
					<10 days / ≥10 days †	Median 5 (IQR 4 – 8) / median 15 (IQR 13 – 19)							
					<7 days / ≥7 days † From time of injury	Median 4 (IQR 2 – 5) / median 11 (IQR 8 – 15)							
Gupta	2018	India	Prospective cohort study	October 2014 – October 2015	<5 days / >5 days From time of presentation	Mean 2.88 / mean 8.56	36.2 ± 11.2 (21–60) / 36 ± 12.6 (21–60)	72:28 / 64:36	25/25	2 Weber A (8%) 6 Weber B (24%) 13 Weber C (52%) 4 Isolated medial malleolus (16%)	1 Weber A (4%) 10 Weber B (40%) 11 Weber C (44%) 3 Isolated medial malleolus (12%)	□ Complications (inc. wound problems and infection) □ Re-operation □ Length of stay	Minimum 6 months

Table I. — Description of included studies - continued.

First Author	Publication Year	Country	Study design	Study Time Period	Surgical timing (EG/DG)	Time to surgery in days (EG/DG)	Mean age in years (EG/DG) (range/SD)	Gender (EG/DG) (Male:Female) (%)	Total Procedures (EG/DG)	EG Fracture Classification Breakdown	DG Fracture Classification Breakdown	Outcome(s) Measured	Post-operativ follow-up duration
Lee	2021	England	Retrospective cohort study	March 2014 – December 2016	<24 hours / >24 hours From time of injury	Mean 3.5±4.23 (range 0 to 23) (overall study population)	48±18.25 (18-88) / 49±19.97 (18-93)	44:64 / 43:67	108 / 127	38 bimalleolar (35%) 25 trimalleolar (23%) 40 lateral malleolar (37%) 5 medial malleolus/ maisonneuve fracture (5%)	44 bimalleolar (35%) 15 trimalleolar (12%) 46 lateral malleolar (36%) 21 medial malleolus/ maisonneuve fracture (17%) 1 other (<1%)	▯ Wound complications (inc. infection) ▯ Length of stay	Minimum 2 years
Hawkins	2023	USA	Retrospective cohort study	July 2011 – July 2018	<3 days / 4 – 7 days / >8 days From time of injury	Mean 9.4±6.5 (overall study population)	53.9±14.2 (overall study population)	N/R	39/50/126	Article reports fracture classification and severity not significantly different between groups. Detailed classification not provided.	Article reports fracture classification and severity not significantly different between groups. Detailed classification not provided.	▯ Wound complication (inc. infection) ▯ Function ▯ Union	Minimum 12 weeks. Median 26 weeks (range 12 – 305 weeks)

† supplementary material; N/R: Not reported.

Studies classifying fractures by involvement of number of malleoli demonstrated majority were unimalleolar (43%) followed by bimalleolar (38%) and trimalleolar (20%). The criteria for diagnosing surgical site infections were reported in only two studies[15,22] which applied the Centres for Disease Control and Prevention (CDC) definition[23]. All but two studies[5,20] reported on post-operative follow-up duration of patients following hospital discharge which ranged from a minimum of four weeks to two years. A detailed summary of the study characteristics is provided in Table I.

Table II details the results of the bias assessment; none of the eligible studies were excluded. Body mass index and presence of diabetes mellitus were not significantly different between patient groups in the two studies reporting these characteristics.

Overlapping results data occurred in two identified articles for outcome wound complications[16,24]. The paper containing the larger study population was included in the review[16].

Wound complications

All nine (n=9) studies reported on wound complication rate.

Tantigate et al.[15] found no statistically significant differences in wound complications (surgical site infection, wound dehiscence, and wound erythema) between patient groups undergoing surgery within or on and after seven, ten, and fourteen days from time of injury. Wound complications occurred in 3/57 (5.4%) compared to 4/61 (6.5%) patients (p=0.583) (RR 1.01, 95%CI 0.93 to 1.11), 3/83 (3.6%) compared to 4/35 (11.5%) patients (p=0.178) (RR 1.09, 95%CI 0.96 to 1.23), and in 5/101 (5%) compared to 2/17 (11.8%) patients (p=0.447) (RR 1.08, 95%CI 0.90 to 1.29), when surgery was performed within seven, ten, and fourteen days respectively.

Gupta et al. investigated differences in superficial and deep wound infection between patients undergoing surgery within versus after five days of injury[17]. Superficial wound infections occurred in 1/25 patients (4%) in the early surgery group compared to 2/25 (8%) patients in the delayed surgery group. Deep wound infection occurred in one patient in the delayed surgery group (1/25; 4%). When considering all wound infections combined, the relative risk was 1.09 (95%CI 0.92 to 1.29). A post hoc Fisher's exact test comparing the results of these two groups for illustrative purposes revealed p=0.609.

Schepers et al.[22] demonstrated that a significantly higher number of patients experienced surgical site infections when operated on or after 24 hours (0/60 versus 16/145; p=0.004) (RD 0.11, 95%CI 0.05 to 0.17). The 16 complications in the delayed group consisted of six superficial and ten deep surgical site infections. Further analysis using seven days as the cut-off interval also demonstrated statistically significant differences between patient groups favouring early surgery (2/98 versus 14/107; p=0.003) (RR 1.13, 95%CI 1.04 to 1.22). Two patients in the early group suffered a deep infection whereas in the delayed surgery group, ten and four patients suffered a superficial and deep infection, respectively.

Carragee et al.[16] reported that major complications which includes deep surgical site infection were significantly higher in the patient group who underwent surgery more than four days following their injury when considering all fracture types (18.6% versus 6.4%, p=0.02), and simple fractures defined as displacement of <10mm in any plane (12.5% versus 2.1%, p=0.03). In contrast, minor complications which included superficial surgical site infection and wound dehiscence were not found to be significantly different between groups when analysing all fracture patients

Table II. — Summary of judgements on each risk of bias category for each included cohort study.

First author (Year)	Selection	Comparability	Outcome	Total Score
Hawkins (2023)	★★★★	★	★★	7
Lee (2021)	★★★★	–	★★	6
Tantigate (2018)	★★★★	★★	★	7
Gupta (2018)	★★★★	–	★★	6
Singh (2015)	★★★★	–	★	5
Schepers (2013)	★★★★	–	★	5
Saithna (2009)	★★★★	–	★★	6
Pietzik (2006)	★★★★	–	★	5
Konrath (1995)	★★★★	–	★★	6
Carragee (1991)	★★★★	–	★★	6

(11.5% versus 20.9%, p=0.08) and those with simple fractures only (2.1% and 9.3%, p=0.08).

Saithna et al.[21] found that wound infection occurred in 3.6% (2/56) of patients undergoing surgery within six days compared with 20.7% (6/29) in those operated on later, representing a significantly lower risk with early surgery (p=0.010; RR 1.22, 95% CI 1.00 to 1.47). Kaplan-Meier analysis showed a trend towards increasing probability of infection with increasing time to surgery. The cumulative probability of infection at six, nine and sixteen days was 0.03 (95% CI 0.00-0.07), 0.19 (95% CI 0.04 – 0.35) and 0.51 (9%% CI 0.10-0.89) respectively.

No statistically significant differences in surgical site infection were found by Singh et al. who compared surgery within versus after 24 hours from presentation – 6/82 (7%) versus 15/132 (11%) (p=0.589; RR 1.05, 95% CI 0.96 to 1.14)[5].

Konrath et al.[18] compared effects of surgery within versus after five days of injury on minor and major complications defined by the requirement for additional surgical management. No major wound complications occurred and no significant differences in minor wound complications were observed – 5/105 (4.8%) versus 6/97 (6.2%) (p=0.56; RR 1.02, 95%CI 0.95 to 1.09).

Lee et al.[19/] compared incidence of major wound complications, defined as admission for intravenous antibiotics or surgical management, between patients undergoing surgery within versus after 24 hours of injury. Five of the 108 patients (4.6%) and two of 127 (1.6%) patients in the early and delayed surgery groups experienced major wound complications respectively (p>0.05; RR 0.97, 95% CI 0.92 to 1.02).

Pietzik et al. (20) compared surgery within versus after 48 hours of injury. One patient in the delayed surgery group experienced a superficial wound infection – 1/42 versus 0/47 (post hoc Fisher's exact test p=0.472; RD -0.02, 95% CI -0.09 to 0.04).

Figure 2 illustrates the study-level estimates for wound complications. Figure 3 shows the pooled

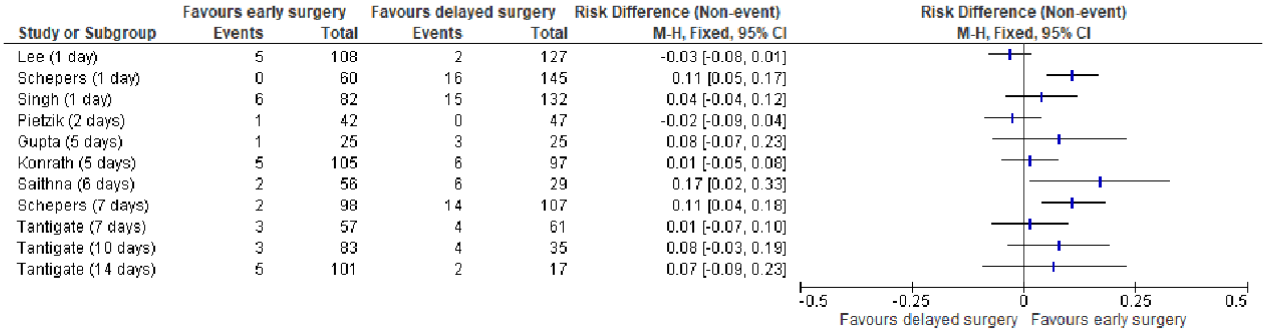

Fig. 2 — Forest plot of study-level estimates for outcome wound complications (parenthesis denote surgical timing intervals).

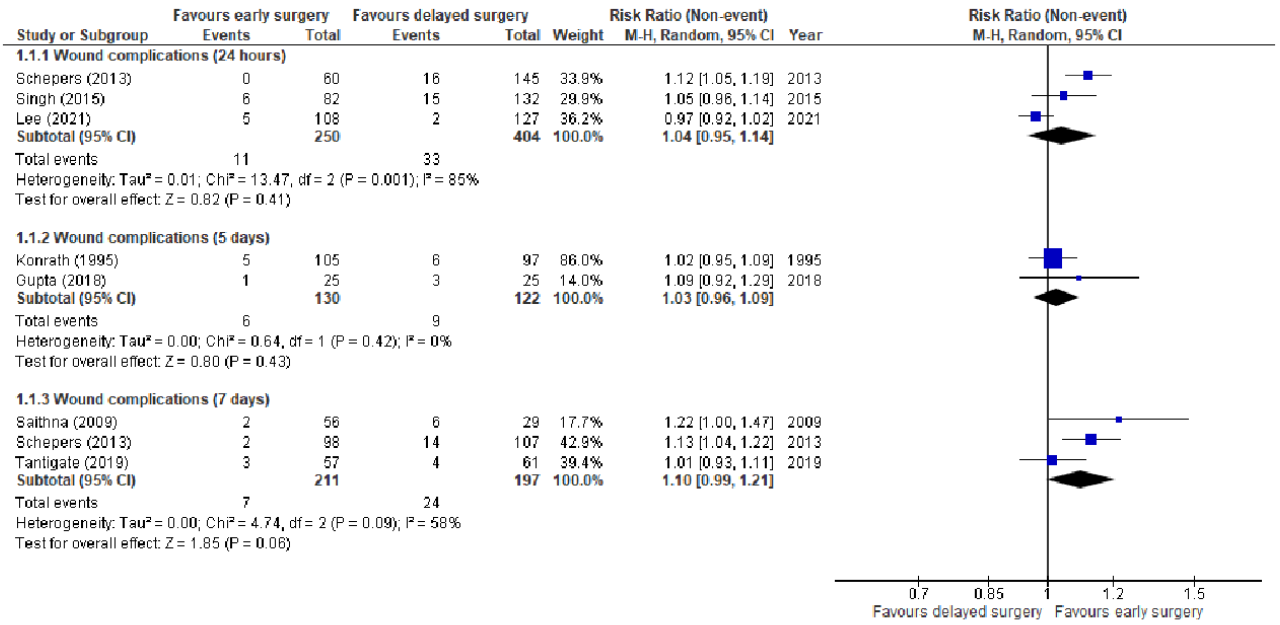

Fig. 3 — Comparison of wound complication risk ratios between patient groups, stratified by surgical timing intervals.

analyses restricted to studies that reported common surgical timing intervals, which demonstrated no significant differences in wound complications between early and delayed surgery at 24 hours (RR 1.04, 95% CI 0.95 to 1.14, p=0.41), 5 days (RR 1.03, 95% CI 0.96 to 1.09, p=0.43), and 7 days (RR 1.10, 95% CI 0.99 to 1.21, p=0.06).

Unplanned re-operation rate

Four (n=4) studies reported on unplanned re-operation rate.

No statistically significant differences in re-operation rate were observed between patients who underwent surgery within versus after 14 days of injury in the in the study by Tantigate et al.[15] – 22.8% (23/101) versus 5.9% (1/17) respectively (p=0.625; RR 3.87, 95%CI 0.56 to 26.81). The majority of these were performed for hardware removal (86.8% and 100% in the early and delayed groups respectively). The indications for re-operation for the remaining three patients in the early surgery group were debridement for surgical site infection, ankle replacement for post traumatic arthritis, and osteophyte resection. Additional analyses using seven and ten days as the cut-off time point for the early and delayed surgery groups was also performed however this only altered the distribution of patients who underwent hardware removal with findings also not being statistically significant.

Gupta et al.[17] found no statistically significant differences in unplanned re-operation rate in patients operated within versus after five days of injury. In contrast to the early surgery group where no patients (0/25) required additional surgery, three patients (3/25) in the delayed surgery group underwent a subsequent procedure for indications including infection, exposed metalwork, and implant irritation (RD -0.12, 95%CI -0.26 to 0.02). A post hoc Fisher's exact test comparing these two groups' results for illustrative purposes revealed p=0.235.

Singh et al.[5] reported results on additional surgery for the management of postoperative surgical site infection. No statistically significant differences were observed between the early and delayed surgery groups – 3/82 (3.7%) versus 7/132 (5.3%) respectively (p=0.63; RR 0.69, 95%CI 0.18 to 2.59).

In the study by Konrath et al.[18] none of the patients in the early and delayed surgical group required additional surgery for the management of wound complications and its sequela – 0/105 versus 0/97 patients (RD 0.00, 95%CI -0.02 to 0.02).

Figure 4 presents the study-level estimates for unplanned reoperations. Figure 5 illustrates the pooled analysis restricted to studies that reported common surgical timing intervals, which showed no significant difference in unplanned reoperation between patients who underwent surgery within five days of injury compared with those operated on after five days (RD 0.04, 95%CI -0.07 to 0.15, p=0.49).

Summary of findings

Using the GRADE approach, the certainty of evidence was rated as very low for both wound complications and unplanned reoperation. Downgrading was primarily due to risk of bias inherent to observational study designs, inconsistency arising from heterogeneity among studies included in the meta-analysis, and imprecision resulting from wide confidence intervals and few events (Table III).

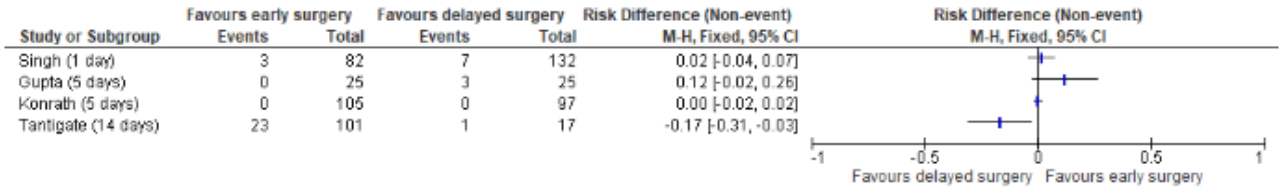

Fig. 4 — Forest plot of study-level estimates for outcome unplanned reoperations (parenthesis denote surgical timing intervals).

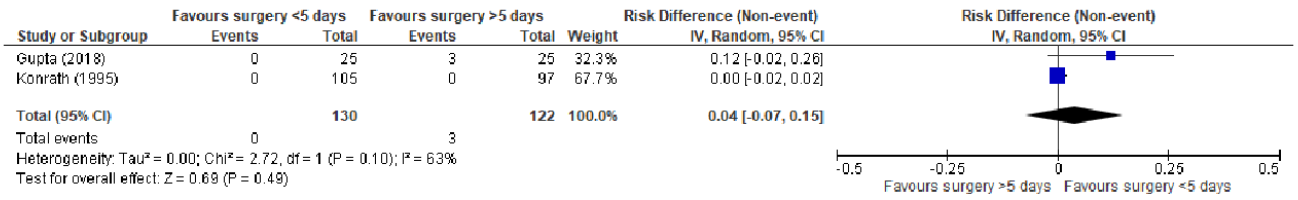

Fig. 5 — Risk differences in unplanned reoperation between patients undergoing initial surgery within versus after five days of their injury.

Table III. — Certainty of evidence (GRADE) for wound complications and unplanned reoperation.

Summary of findings: Impact of timing of surgery on wound complications and re-operations in patients with closed ankle fracture fixation: a systematic review					
Patient or population: Patients undergoing internal fixation for closed ankle fracture Setting: Hospitals Intervention: Early surgery Comparison: Delayed surgery					
Outcomes	Number of studies	Number included in meta-analysis	Effect (RD, 95%CI, p-value)	Certainty of evidence	Reasons for downgrading
Wound complications	9 observational	7 observational	Interval timing of 24 hours: RD 0.04, 95%CI -0.05 to 0.13, p=0.41 Interval timing of 5 days: RD 0.02, 95%CI -0.03 to 0.08, p=0.41 Interval timing of 7 days: RD 0.08, 95%CI -0.07 to 0.23, p=0.32	Very low	Risk of bias, inconsistency, and imprecision
Unplanned reoperation	4 observational	2 observational	RD 0.04, 95%CI -0.07 to 0.15, p=0.49	Very low	Risk of bias, inconsistency, and imprecision
CI: confidence interval, RD: risk difference, N/A: not applicable GRADE Working Group grades of evidence High quality: Further research is very unlikely to change our confidence in the estimate of effect. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate.					

DISCUSSION

This is the most comprehensive systematic review investigating the effects of the timing of surgical fixation of closed ankle fractures in adults on post-operative wound complications and unplanned re-operations. Our review identified three of nine cohort studies demonstrating a statistically significant reduction in wound complications in patients who received relatively earlier surgery within 24 hours (0/60 versus 16/145, p=0.004), four days (6.4% versus 18.6%, p=0.02), six days (2/56 versus 6/29, p=0.01), and seven days (2/98 versus 14/107, p=0.003)[16,21,22]. This suggests that the risk of wound complications potentially increases when fixation is delayed beyond four to seven days. This may relate to progressive subluxation of the ankle joint within the cast as swelling subsides, leading to additional insult to the soft tissues. However, the pooled analysis found no statistically significant differences, although despite variation in surgical timing interval across studies, the results demonstrated a consistent direction of effect with comparable effect sizes, suggesting a signal of benefit associated with earlier fixation. For unplanned re-operation, none of the four studies investigating this outcome demonstrated statistically significant differences, which was consistent with the findings in the pooled analyses.

Only one previous systematic review on this topic has been performed, and was published in 2013 by Schepers et al[22]. This review was embedded within their article reporting the results of their cohort study[22]. Their review focussed solely on wound complications and pooled analysis of 11 studies, including their own, found that delayed surgery was associated with a significantly higher incidence of wound complications – 24/673 (3.6%) versus 66/513 (12.9%); p<0.0001 (summary estimate, precision, and statistical heterogeneity not reported). However, it is important to mention that three of the included studies in their review contained patients who sustained open fractures. Furthermore, their pooled analysis did not stratify outcomes by a consistent surgical timing interval but instead adopted each study's own definition of early and late surgery. Given these intervals varied considerably (range 24 hours to 14 days), the two groups are not directly comparable. However, the variation in surgical timing being compared within these studies suggests a lack of agreement in the literature regarding the optimal timing of ankle fracture fixation surgery. Similarly, several healthcare and orthopaedic organisations have published differing recommendations on the timing of ankle fracture fixation surgery. The National Institute for Care and Excellence (NICE) recommends surgery on the day of injury or the

Supplemantary Table I. — Medical subject headings and free words used in the literature search across the six databa-

Medline and Embase	((ankle* or unimalleol* or bimalleol* or trimalleol* or malleol* or fibul*) adj3 fracture*).ti. OR ((ankle* or unimalleol* or bimalleol* or trimalleol* or malleol* or fibul*) adj3 fracture*).ab. AND ((earl* or dela* or tim* or exped* or immediate* or late) adj6 (surger* or operat* or fixation*)).ab. OR ((earl* or dela* or tim* or exped* or immediate* or late) adj6 (surger* or operat* or fixation*)).ti. AND ORIF*.kw,ti,ab. OR nail*.kw,ti,ab. OR plate*.kw,ti,ab. OR fixation*.kw,ti,ab. OR treat*.kw,ti,ab OR swelling.kw,ti,ab OR swollen.kw,ti,ab
The Cochrane Library	(((ankle* or unimalleol* or bimalleol* or trimalleol* or malleol* or fibul*) near/3 fracture*)):ti,ab AND (((earl* or dela* or tim* or exped* or immediate* or late) near/6 (surger* or operat* or fixation*))):ti,ab AND (ORIF* or nail* or plate* or fixation* or treat* or swelling or swollen):ti,ab
Web of Science	TOPIC ((ankle* or unimalleol* or bimalleol* or trimalleol* or malleol* or fibul*) NEAR/3 fracture*) AND TOPIC (ORIF* or nail* or plate* or fixation* or treat* or swelling or swollen) AND TOPIC ((earl* or dela* or tim* or exped* or immediate* or late) NEAR/6 (surger* or operat* or fixation*))
Literatura Latino Americana em Ciências da Saúde (LILACS)	ankle [Words] AND fracture [Words]
African Journals Online (AJOL)	Ankle fracture

next day[25]. The British Orthopaedic Association Standards for Trauma (BOAST) advises early fixation on the day or day after injury in patients under 60 years of age when the ankle mortise is unstable[6]. The AO/ASIF Manual of Internal Fixation recommends performing surgery in the first 6-8 hours following injury or after 4-6 days when the swelling has subsided[26]. Although early surgery is preferred by patients[27], it may not always be feasible. Factors such as condition of the skin and soft tissues, the need for medical optimisation, or other patient related issues may necessitate delay. In addition, operational constraints, including limited theatre capacity, competition with higher priority trauma cases, and staffing availability, represent important determinants of time to surgery[17,28]. Together, these clinical and logistical considerations contribute to the variation observed in practice.

This review synthesised evidence from nine studies conducted across multiple institutions, including patients of a varying ages and fracture patterns, which enhances the generalisability of our findings to a broad population. However, there are several limitations which should be considered when interpreting the results of this review. All included studies were observational in design, and most were conducted retrospectively, which introduces the risk of confounding and causality cannot be inferred. Confounding by indication is also possible, as patients selected for delayed fixation may have presented with more severe soft tissue compromise at baseline, thereby predisposing them to poorer outcomes. None of the studies provided a breakdown of the reasons for delays to surgery however degree of soft tissue swelling around the ankle was frequently cited as the cause. The method of ankle immobilisation following closed reduction and prior to surgery was inconsistently reported across the included studies. The definition of early and delayed surgery in most studies was largely arbitrary, with the exception of the study by Schepers et al.[22] who used the median time to surgery of their study population as the surgical timing interval cut-off value. Few studies reported time from injury to hospital presentation, and delays to closed reduction may have different between groups, particularly in the included studies conducted in countries where universal healthcare is unavailable[29]. Furthermore, most studies contained small sample sizes potentially underpowered to detect differences between the patient groups for wound complications and unplanned re-operations, which are infrequent events[30]. Also, the definitions of surgical site infection

Supplemantary Table II. — List of excluded studies along with reasons for exclusion.

	Inclusion of open fractures
1.	Breederveld RS, van Straaten J, Patka P, van Mourik JC. Immediate or delayed operative treatment of fractures of the ankle. Injury. 1988;19(6):436-8.
2.	Balaratnam S, Naidu V, Singh BI. Early versus delayed surgery for ankle fractures: A comparison of results. Eur J Orthop Surg Traumatol. 2005;15(1):23–7.
3.	Gonzalez Quevedo D, Sanchez Siles JM, Rojas Tomba F, Tamimi Marino I, Bravo Bardaji MF, Villanueva Pareja F, et al. Blisters in Ankle Fractures: A Retrospective Cohort Study. J Foot Ankle Surg. 2017;56(4):740–3.
4.	Meng JH, Sun T, Zhang FQ, Qin SJ, Li Y, Zhao HT. Deep surgical site infection after ankle fractures treated by open reduction and internal fixation in adults: A retrospective case-control study. Int Wound J. 2018;15(6):971–7.
5.	Ahluwalia R, Cook J, Raheman F, Karuppaiah K, Colegate-Stone T, Tavakkolizadeh A, et al. Improving the efficiency of ankle fracture care through home care and day-surgery units: Delivering safe surgery on a value-based healthcare model. Surgeon. 2021;19(5):e95–102.
	Conference abstract
6.	Derias M, Upadhyay P, Laing G, Edres K, Shah N, Ajis A. 'why can't i elevate my ankle at home doctor?'-formulating ankle fracture pathway. Br J Surg. 2020;107(SUPPL 3):138.
7.	Silva A, Platt S. Preoperative ankle swelling and the effect on postoperative wound complications following ankle fracture surgery. Foot Ankle Int. 2018;39(2 SUPPL):114S.
8.	Bazzoni D, Mazzucco A, Occhipinti V, Gadaleta M, Trentani L, Merlo M. Immediate surgery advantages in ankle fractures-dislocations. J Orthop Traumatol. 2011;12(SUPPL. 1):S90.
	Children included
9.	Westacott DJ, Abosala AA, Kurdy NM. The Factors Associated with Prolonged Inpatient Stay after Surgical Fixation of Acute Ankle Fractures. J Foot Ankle Surg. 2010;49(3):259–62.
	Almost healed fractures
10.	Toker S, Morgan S, Hak DJ. Fixing the almost healed ankle fracture. Are surgery, reduction, and complication rate different from acute open reduction and internal fixation? Curr Orthop Pract. 2012;23(1):34–7.
	Timing of surgery not reported
11.	Shah NH, Sundaram RO, Velusamy A, Braithwaite IJ. Five-year functional outcome analysis of ankle fracture fixation. Injury. 2007;38(11):1308–12.
12.	Burwe HN, Charnley AD, Burwell HN, Charnley AD. The treatment of displaced fractures at the ankle by rigid internal fixation and early joint movement. JBone Jt Surg. 1965;47(4):634–60.
13.	Eventov I, Salama R, Goodwin DR, Weissman SL. An evaluation of surgical and conservative treatment of fractures of the ankle in 200 patients. J Trauma. 1978;18(4):271-4.
14.	Srinivasan CMS, Moran CG. Internal fixation of ankle fractures in the very elderly. Inj J CARE Inj. 2001;32(7):559–63.
15.	Beauchamp CG, Clay NR, Thexton PW. Displaced ankle fractures in patients over 50 years of age. J Bone Joint Surg Br. 1983;65(3):329-32.
16.	Bhandari M, Sprague S, Ayeni OR, Hanson BP, Moro JK, Ayeni OR, et al. A prospective cost analysis following operative treatment of unstable ankle fractures: 30 Patients followed for 1 year. Acta Orthop Scand. 2004;75(1):100–5.
17.	Shah R, Ahad A, Faizi M, Mangwani J, Mangwani Rohi; ORCID: http://orcid.org/0000-0001-9717-9825 JAO-S. Foot and ankle trauma management during the COVID-19 pandemic: Experiences from a major trauma unit. J Clin Orthop trauma. 2021;16:285–91.
18.	McCreary DL, White M, Vang S, Plowman B, Cunningham BP. Time-Driven Activity-Based Costing in Fracture Care: Is This a More Accurate Way to Prepare for Alternative Payment Models?. J Orthop Trauma. 2018;32(7):344–8.
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20.	Sun R, Li M, Wang X, Li X, Wu L, Chen Z, et al. Surgical site infection following open reduction and internal fixation of a closed ankle fractures: A retrospective multicenter cohort study. Int J Surg. 2017;48:86–91.
21.	Jones CB, Sietsema DL, Gilde A. Treatment of syndesmotic injuries of the ankle: A critical analysis review. JBJS Rev. 2015;3(10):1–15.
22.	Godoy-Santos AL, Schepers T, Rammelt S, Sakaki MH, Mateluna CO, Sposeto RB, et al. SOFT-TISSUE INJURY TO THE FOOT AND ANKLE: LITERATURE REVIEW AND STAGED MANAGEMENT PROTOCOL. ACTA Ortop Bras. 2019;27(4):223–9.
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24.	Baessler A, Mullis B, Loder R, Corn K, Mavros C. Overlapping Surgery for Ankle Fractures: Is It Safe?. J Orthop Trauma. 2020;34(8):e282–6.
25.	Sung KH, Kwon SS, Yun YH, Park MS, Lee KM, Nam M, et al. Short-Term Outcomes and Influencing Factors After Ankle Fracture Surgery. J FOOT ANKLE Surg. 2018;57(6):1099-+.
26.	Bohl DD, Idarraga AJP, Lee S, Hamid KS, Lin J, Holmes GB, et al. Timing of Early Complications Following Open Reduction and Internal Fixation of Closed Ankle Fractures. Foot Ankle Spec. 2021;14(2):140–7.
27.	Fournier MN, Cline JT, Seal A, Smith RA, Throckmorton TW, Bettin CC, et al. Initial evaluation by a nonsurgeon provider does not delay the surgical care of operative ankle fractures in a walk-in orthopaedic clinic: A retrospective cohort study. Curr Orthop Pract. 2019;30(6):561–5.
28.	Stupay KL, Miller CP, Staffa S, McTague MF, Weaver MJ, Kwon Kristen L.; ORCID: http://orcid.org/0000-0002-1715-9873 AO - Miller, Christopher P.; ORCID: http://orcid.org/0000-0001-8259-7629 JYAO-S. Risk Factors for Aseptic Revision of Operatively Treated Ankle Fractures. Foot Ankle Int. 2021;

Supplemantary Table II. — List of excluded studies along with reasons for exclusion - continued.

Comparison of outcomes not performed
29. McKissack HM, Viner GC, Alexander BK, Jha AJ, Wilson JT, McMurtrie JT, et al. Does Insurance Status Affect Access to Care Among Ankle Fracture Patients? An Institutional Retrospective Study. J Foot Ankle Surg. 2021;60(3):520–2.
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32. Ashton F, Hamid K, Sulieman S, Eardley W, Baker P. Factors Influencing patient experience and satisfaction following surgical management of ankle fractures. Injury. 2017;48(4):960-5.
33. Naumann MG, Sigurdsen U, Utvag SE, Stavem K. Associations of timing of surgery with postoperative length of stay, complications, and functional outcomes 3-6 years after operative fixation of closed ankle fractures. Injury. 2017;48(7):1662-9.
34. Hoiness P, Engebretsen L, Stromsoe K. The influence of perioperative soft tissue complications on the clinical outcome in surgically treated ankle fractures. Foot Ankle Int. 2001;22(8):642-8.
Additional intervention favouring one patient group
35. Tanoglu O, Gokgoz MB, Ozmeric A, Alemdaroglu KB. Two-Stage Surgery for the Malleolar Fracture-Dislocation With Severe Soft Tissue Injuries Does Not Affect the Functional Results. J FOOT ANKLE Surg. 2019;58(4):702–5.
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Alternative study design or review article
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Duplicate results
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Not accessible/article language not English
49. Vasli S. Operative treatment of ankle fractures. Acta Chir Scand Suppl. 1957;226:1-74.
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varied between studies, with only two applying the CDC criteria, which represents a potential source of between-study heterogeneity. Lastly, the use of broad time intervals in some analyses may also have introduced greater variability, diluting potential signals that might have been evident within narrower windows. More granular comparisons of specific time periods may therefore have yielded more meaningful insights.

CONCLUSIONS

Ankle fracture fixation is associated with some of the highest rates of post-operative complications in orthopaedic trauma surgery[31,32], including fracture-related infection, which represents considerable morbidity[33]. There is therefore a need to evaluate the impact of modifiable factors such as timing of surgery to improve the outcomes of patients undergoing ankle fracture fixation. At present, no high level evidence exists to guide the optimal timing of fixation for closed ankle fractures, and the heterogeneity in time intervals being compared across studies suggests that the ideal window remains unknown. Given the methodological limitations of the existing literature, no definitive recommendations can be made regarding timing of surgery to reduce wound complications or unplanned reoperations. Before further research is carried out on this topic, consensus work is needed to refine study methods, and future studies should adopt standardised definitions of surgical site infection to strengthen methodological rigour.

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