

Is post-operative non-weight-bearing necessary? Study protocol for a pragmatic randomised multicentre trial of operatively treated ankle fracture

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Abstract

Background:

Postoperative management regimes vary following open reduction and internal fixation (ORIF) of unstable ankle fractures. There is an evolving understanding that extended periods of immobilisation and limitation of weight-bearing may lead to poorer clinical outcomes. Traditional non-weight bearing cast immobilisation may prevent loss of fixation, and this practice continues in many centres. The purpose of this trial is to investigate the safety and efficacy of immediate weight-bearing (IWB) and range of motion (ROM) exercise regimes following ORIF of unstable ankle fractures with a particular focus on functional outcomes and complication rates.

Methods:

A pragmatic randomised controlled multicentre trial, comparing IWB in a walking boot and ROM within 24 hours versus non-weight-bearing (NWB) and immobilisation in a cast for six weeks, following ORIF of all types of unstable adult ankle fractures (lateral malleolar, bimalleolar, trimalleolar with or without syndesmotic injury) is proposed. All patients presenting to three trauma units will be included. The exclusion criteria will be skeletal immaturity and tibial plafond fractures. The three institutional review boards have granted ethical approval. The primary outcome measure will be the functional Olerud-Molander Ankle Score (OMAS). Secondary outcomes included wound infection (deep and superficial), displacement of osteosynthesis, the full arc of ankle motion (plantar flexion and dorsal flexion), RAND-36 Item Short Form Survey (SF-36) scoring, time to return to work and postoperative hospital length of stay. The trial will be reported in accordance with the CONSORT statement for reporting a pragmatic trial, and this protocol will follow the SPIRIT guidance.

Discussion:

Traditional management of operatively treated ankle fractures includes an extended period of non-weight bearing. There is emerging evidence that earlier weight-bearing may have equivocal outcomes and favourable patient satisfaction but with higher wound-related complications. These studies often preclude more complicated fracture patterns or patient-related factors. To our knowledge, immediate weight-bearing (IWB) following ORIF of all types of unstable ankle fractures has not been investigated in a controlled prospective manner in recent decades. This pragmatic randomised-controlled multicentre trial will investigate immediate weight-bearing following ORIF of all ankle fracture patterns in the usual condition of care. It is hoped that these results will contribute to the modern management of ankle fractures.

Trial registration:

The trial is retrospectively registered on the 30th of June 2019, ISRCTN - ISRCTN76410775.

<http://www.isrctn.com/ISRCTN76410775>

Administrative Information

Title {1}	Is Postoperative Non-Weight-bearing Necessary? (INWN), study protocol for a pragmatic randomised multicentre trial of operatively treated ankle fracture.
Trial registration {2a and 2b}.	'retrospectively registered' <i>ISRCTN - ISRCTN76410775 30/06/2019</i>
Protocol version {3}	Version (3) June 2019
Funding {4}	Investigator-initiated and funded
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Introduction

Background and rationale {6a}

Ankle fractures are common and affect young adults as well as the elderly(1). Typically, the treatment of an unstable ankle fracture involves surgical fixation, immobilisation and modified weight-bearing for six weeks. Immobilisation can have implications for patient function and may reduce independence, mobility and return to work.

There is emerging evidence that extended periods of immobilisation and limitation of weight-bearing may lead to poorer outcomes (2). Traditional non-weight bearing (NWB) cast immobilisation periods of six or more weeks were used to protect the soft tissue envelope and osteosynthesis (3). Newer trends in earlier

mobilisation compete with traditional NWB doctrine, and weak consensus exists as to the best postoperative strategy (4,5). This could be explained by the contradicting literature regarding the assessment of weight-bearing regimens following ankle fracture fixation (2,6–12).

Some studies have investigated early mobilisation without weight-bearing, early weight-bearing (EWB) or immediate weight-bearing (IWB) following fixation of ankle fractures, some of which reported favourable outcomes (2,6–10), and others raised concerns of increasing complication rates (9,11,13).

Between 1986 and 1993, Ahl et al. performed four small RCTs, with a sample size ranging from only 40 to 53 patients in each trial. They compared IMW in a cast from day one, in the first two trials, or EWB in a cast after one week, in the third and fourth trials, to NWB for seven weeks after surgical fixation of lateral malleolar and bimalleolar fracture. The results showed higher surgical site complications in the IWB group than in the EWB group, and the authors recommended delaying weight bearing until wound healing was complete.

The largest published trial in the subject by Dehgan et al. included 110 patients. They investigated early weight-bearing from 2 weeks versus late weight-bearing. Although the trial has failed to prove earlier return to work (the primary outcome) for EWB group patients, the authors recommended early weight-bearing based on early improved functional outcome and lack of increased complications rate (2). Most recently, Smeeing et al. attempted a multicenter RCT to investigate three groups of patients: unprotected non-weight-bearing, protected weight-bearing as tolerated and unprotected weight-bearing following surgical fixation of ankle supination external rotation injury only. This trial was discontinued before completing the target number due to lack of funding and the slow recruitment process. The published post hoc analysis included a total of 115 recruited patients in all three groups. The authors concluded that unprotected weight-bearing and mobilisation improved short-term functional outcomes without an increase in complication rate (10).

Our null hypothesis was that immediate weight-bearing and early mobilisation protocols are not superior to or the same as non-weight-bearing and immobilisation protocols.

Objectives {7}

The primary objective is to determine whether immediate protected weight-bearing and ankle range of motion post open reduction and internal fixation of unstable ankle fractures improve functional outcome compared to postoperative ankle immobilisation in a non-weight bearing cast. Second, to determine whether the rate of complications, such as wound infection and fixation failure, with immediate weight-bearing and ROM, is comparable to rates with the usual postoperative protocols. Finally, to determine the cost-effectiveness of this method of treatment, which can be determined by the analysis of patients' ability to return earlier to work and the detailed cost of either intervention, including the length of hospitalisation.

Trial design {8}

The study will be a prospective, pragmatic randomised controlled trial (p-RCT), un-blinded with participants allocated in a 1:1 ratio to one of two parallel groups. Patients will be randomised using computerised block randomisation (twenty patients per block). The study is multicentre and will include three major orthopaedic centres in Ireland.

Methods: Participants, Interventions And Outcomes

Study setting {9}

This pRCT will be conducted at three academic trauma units at three different urban centres in Ireland. Each centre serves a referral population of >500,000 and receives all grades of trauma from both urban and rural environments on a 24-hour basis. A trauma team is on call daily and includes two trainee surgeons and a consultant orthopaedic surgeon. Surgeries are performed in part, in total or supervised by consultant orthopaedic surgeons. Regional and general anaesthesia is used at the discretion of the anaesthetist. Ankle fracture surgery is conducted on both a day case or overnight basis. Ward-based physiotherapy is provided daily to facilitate early discharges. All hospital personnel contributing to the recruitment and patient pathways in this trial will undergo training in the objectives and methodology of the study.

Eligibility criteria {10}

Inclusion Criteria

All skeletally mature (closed distal tibial physis), acute ankle fractures treated with anatomical reduction and stable internal fixation, including AO/OTA 44A1.3 to 44A3.3, 44B and 44C.

- Isolated lateral malleolar fractures
- Isolated medial malleolar fractures
- Bimalleolar fractures
- Trimalleolar fractures
- Syndesmosis injuries that have been surgically fixed with either screw or tightrope.
- Closed, grade I, or grade II open fractures.

Exclusion Criteria

- Skeletal immaturity (open distal tibial physis)
- Gustilo grade-III open fractures
- Tibial plafond fractures
- Polytraumatised patients

- Non-ambulatory status before injury
- Expected insufficient stable fracture fixation with standard surgical technique
- Pre-existent cognitive disability, neurological disease or inability to comply with non-weight-bearing mobilisation
- Grossly comminuted fragility fractures

Patient recruitment and consent: {26a}{15} (Who will take informed consent? And recruitment)

All patients admitted to the hospital with ankle fracture (AO/OTA 44A1.3 to 44A3.3, 44B and 44C) deemed appropriate for surgical intervention will be asked by the admitting trainee or consultant surgeon to participate in the trial and provided with a patient information leaflet (Appendix 1), given time to read the document and ask questions. If the patient agrees to enter the trial, they will sign the consent form in the presence of the admitting doctor on the morning of or the night before their surgery.

Interventions

Explanation for the choice of comparators {6b}

Traditional non-weight bearing (NWB) cast immobilisation is a common practice in many centres, and this protective protocol might not be necessary.

Intervention description {11a}

In accordance with a pragmatic study, the surgical approach and choice of the implant will be at the surgeon's discretion. Surgeons may or may not be authors in the study. Surgical practice at the three institutions is to achieve anatomical reduction and rigid fixation. The commonly used osteosynthesis system for fixation is the small fragment system, with a one-third tubular plate commonly used. The use of locking mode is not routinely used. Other systems are also available. All patients will be assessed by a physiotherapist for gait stability and provided with walking aids according to randomisation. Patients in the walking boot group (Group A) will be instructed to weight-bear as tolerated immediately with or without walking aids for balance. Patients in the NWB group (Group B) will be instructed to strictly bear non-weight using crutches or frames for a total of six weeks. Group A will be instructed to remove the walking boot four times a day at minimum to perform ankle range of motion exercises until they attend outpatient physiotherapy following their first postoperative visit. All patients will receive a postoperative care information sheet according to their grouping (Appendix 2 and 3).

Patients will be allocated randomly to one of two groups;

Group A:

- Will receive a walking boot orthosis postoperatively in theatre and allowed weight bearing as tolerated and range of motion (ROM) exercises immediately.

- Elevation of the affected foot in the first two weeks will be encouraged to reduce swelling.
- The first follow-up appointment will be after two weeks. This visit is for surgical site inspection, removal of sutures, check X-ray and referred to physiotherapy to continue ROM exercises and weight-bearing as tolerated progressing to full weight-bearing.

Group B:

- Will receive full below-knee cast postoperatively in theatre and prevented weight-bearing for six weeks.
- Elevation of the foot in the first two weeks will be encouraged to reduce swelling.
- The first follow-up appointment was after two weeks. This visit is for surgical site inspection, removal of sutures, check X-ray and re-application of a full below-knee cast.
- The second follow-up is after six weeks, for removal of cast and referral to physiotherapy to commence ankle ROM exercises and weight-bearing as tolerated progressing to full weight-bearing.

Criteria for discontinuing or modifying allocated interventions {11b}

The trial will be terminated early if a 20% complication rate (wound complications and fixation failure) is detected in either of the treatment groups (10,14).

Strategies to improve adherence to interventions {11c}

Surgeon:

Surgical treatment for all participants will remain unchanged in both groups, and all surgeons have agreed to participate in the trial.

Participant:

In the postoperative setting on the ward and before discharge, a physiotherapist will reinforce the patient's role in the trial and provide them with information leaflet appropriate to their grouping. At subsequent outpatient follow-up visits, patients will be reminded of the trial. The trial Case Report Form (Appendix 4) will record if the patients have received outpatient physiotherapy.

Relevant concomitant care permitted or prohibited during the trial {11d}

The choice of and duration of DVT prophylaxis will be at the surgeon's discretion.

Provisions for post-trial care {30}

None.

Outcomes {12}

The primary outcome measure is the functional Olerud-Molander Ankle Score (OMAS) at six weeks postoperatively. This score ranges from 0 to 100, with 100 representing normal ankle function (15). Secondary outcome measures include complication rate (infection and fixation failure), the full arc of ankle motion (plantar flexion and dorsal-flexion) measured in degrees using a goniometer, RAND 36-Item Short Form Survey (SF-36) scoring, the time needed to return to work in days and postoperative hospitalisation length in days.

Follow up:

Patients will be followed up in an outpatient setting at two weeks, six weeks, twelve weeks, six months and one year postoperatively. At each visit, the OMAS and RAND-36 health questionnaire will be collected. Surgeons who may or may not be authors in the study reviewing patients in either group will also, at each follow-up appointment, complete a case report form that was created by the trial team (Appendix 4). This record included surgical site assessment, any complication, X-ray evaluation, ankle range of motion (using goniometry), information regarding return to work, confirmation of physiotherapy referral and confirmation of collection of OMAS and RAND-36 questionnaire.

Participant timeline {13}

	Enrolment	Research Follow-ups				
TIMEPOINT	At admission	Two weeks	Six weeks	12 weeks	Six months	One year
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation	X					
INTERVENTIONS:						
IWB/Boot	←————→					
NWB/Cast	←————→					
ASSESSMENTS:						
Length of post-op hospitalisation	X					
OMAS		X	X	X	X	X
RAND-36		X	X	X	X	X
Return to work		X	X	X	X	X
Total ankle Arc		X	X	X	X	X
Surgical site check and complications		X	X	X	X	X
X-ray assessment		X	X	X	X	X

Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Figure of enrolment, interventions and assessments.

Key: IWB: immediate weight-bearing, NWB: non-weight-bearing, OMAS: Olerud Molander Ankle Score, RAND-36: 36-item Short-Form Health Survey.

Sample size {14}

An *a priori* power analysis for the superiority of treatment with immediate weight-bearing and ROM will be conducted for this hypothesis. To detect a clinically significant 10-point difference in the Olerud and Molander Ankle Score (OMAS) at six weeks, with a standard deviation of 19(16–19). Alpha = 0.05 and $\beta=0.20$ (80% power), two-sided test and a maximum loss of follow up of 20% (N=145), this was rounded to 160 to support the block randomisation (20 block size), and a sample size of 80 per group is necessary.

Assignment of interventions:

Allocation

Sequence generation {16a}

An online computer-generated block randomisation list (20 patients per block) will be created at the start of the trial via the website <http://www.randomization.com>. This list has a unique number that is stored safely and can be double-checked.

Concealment mechanism {16b} Implementation of randomization {16c}

Upon skin closure, a circulating theatre nurse, who is not part of the trial team, will consult the randomised block database, which is kept secure and password protected. The nurse will inform the surgical team that a walking boot (Group A) or a cast (Group B) is to be applied. The patient's details will be entered into the database, and they will be assigned a trial number. The surgeons will be blinded to the intervention until fracture fixation is complete.

Assignment of interventions:

Blinding

Who will be blinded and procedure for unblinding if needed {17a/b}

We understand there is some unavoidable risk of bias to this particular type of RCT where the intervention is impossible to blind as both cast and boot are visible. This has been a known weakness in all previous similar RCTs. Furthermore, in line with the pragmatic trial design, the patient's care must follow the routine hospital follow-up procedure. It was not feasible to introduce independent assessors to mitigate such bias. On the other hand, patient-reported outcome measures (OMAS and RAND-36) are completed solely by patients, and the assessor has no role in these data. Additionally, to reduce the risk of bias, the surgeon will be blinded until the surgical procedure is complete.

Data collection and management

Plans for assessment and collection of outcomes {18a}

At each follow-up visit, the OMAS and SF-36 Health questionnaire will be collected from the participants by outpatient clinic nurses. The attending orthopaedic consultant or NCHD fills up a case report form, which includes documentation of the following information: surgical site assessment and complication, X-ray evaluation, ankle full arc measure (goniometry), information regarding return to work, confirmation of physiotherapy referral and confirmation of collection of OMAS and RAND-36 Health survey.

Plans to promote participant retention and complete follow-up {18b}

We have developed a patient tracking system to allow researchers to monitor follow-up carefully. As part of this system, a weekly list of expected patients is provided to the research nurse in the OPD, and this list

is reviewed daily to record attendance. In case of a patient being absent from the clinic, another appointment for the following week will be arranged, the RAND-36 and the OMAS score will be posted to the patients with prepaid envelope enclosed, and the patient will be contacted to encourage follow-up.

Data management {19}

Three forms are collected and checked at each follow-up visit and then stored securely in the trial locker: two patient-reported outcomes measure (PROM), the OMAS and RAND-36, and the case report form. Every two weeks, all data are transferred to a temporal database located within the hospital computer system by two researchers, and a read-only copy is stored in a separate folder. This is then cross-checked before data are transferred to the statistical software for statistical analysis and reporting by the statistician and the research team.

The RAND-36 requires multiple steps analysis; this will be performed with oblique scoring and the orthogonal-factor analytic model (20). Normative data for the Irish population will be used as a reference (21).

Confidentiality {27}

Data management will be in accordance with the *General Data Protection Regulation*

(GDPR) Health Service Executive (HSE) and Health Research regulations (22,23). Data will be kept anonymously in the database within the HSE local hospital computer system in protected folders to ensure confidentiality. Paperwork will be stored in the trial locker in a locked researcher office within the hospitals.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Not applicable as there is no laboratory evaluation or biological specimen collection in this study.

Statistical methods

Statistical methods for primary and secondary outcomes {20a and b}

Continuous outcomes and other key variables will be described by their means and SDs, medians and IQRs, and total range. Categorical variables will be described by counts and respective proportions.

The primary outcome, OMAS score at six weeks, will be analysed using multiple linear regression with fixed effects for study arm and centre, from which we will report the centre-adjusted difference in mean OMAS scores between the two arms with its 95% confidence interval (CI) and exact p-value. The complete set of longitudinal OMAS scores, from 2 weeks to 1 year, will be analysed with the corresponding linear mixed-effects model (with the identity link function), with fixed effects for the centre, arm, and time (dummy coded) and an interaction term between arm and time. Time-specific differences in mean OMAS

scores between arms will be calculated from the model's results, along with 95% CIs, and the exact p-value from the time by arm interaction.

Longitudinally measured secondary outcomes will be similarly analysed and reported: ankle range of motion with the same linear mixed-effects model; and RAND-36 scores with an ordinal mixed-effects model with a logit link function (i.e. the "proportional odds model). Time to return to work (in the subset working at baseline) and length of stay will be analysed using Cox proportional hazards models, with fixed effects for centre and treatment arm. Infection (any) and fixation failure at any point during study follow-up will be similarly analysed using logistic regression.

There will be no formal adjustments for multiplicity, but we will report all estimated treatment effects alongside exact p-values, allowing the reader to make whatever adjustments they prefer. Any deviations from the above plan will be fully described and justified in the final report of the trial results. All analyses, as well as the production of tables and plots, will be conducted using R (version 3.6.3, R Project for Statistical Computing) and Stata16 software. All analyses will be conducted or supervised by the Principal Statistician of the HRB Clinical Research Facility Cork under their quality system and relevant standard operating procedures and following regulatory guidance (e.g., ICH E9).

Because outcomes at week six are collected as part of routine care, we do not anticipate and have intentionally aimed to avoid any missing values at that time point. However, if there are missing values, then we will carefully consider the reasons why data are missing and employ appropriate methods, which could range from complete case analysis in the presence of very little missing data that is deemed MCAR, to multiple imputations under assumptions of MAR. For missing longitudinal data, we will take advantage of full-information maximum likelihood estimation for the mixed-effects models to retain all patients in the models. Irrespective of the actual approach taken (which cannot be optimally decided on without consideration of the actual study data), we will explore choices and their potential impact on inferences with sensitivity analyses.

Interim analyses {21b}

No planned interim analysis.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Any protocol non-adherence will be disclosed and handled accordingly. An effort will be made to prevent missing data as much as possible. Unavoidable missing data, such as withdrawals from the study or loss to follow-up data, will be analysed on an intention-to-treat basis, including sensitivity analysis. Multiple imputations using Chain Equations MICE will be used for missing data. (24–26).

Plans to give access to the full protocol, participant level-data and statistical code {31c}

The full protocol is available at the registry website and will be published in one of the trial protocol journals.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

Four authors at the coordinating centre (University Hospital Waterford) take responsibility for the scientific validity of the study protocol, assessment of study quality and conduct, as well as for the scientific quality of the final study report.

Composition of the data monitoring committee, its role and reporting structure {21a}

The authors understand the composition for a standard data monitoring committee (DMC) for this trial is challenging and might be impossible. Lack of funding is the main barrier. Unlike a clinical trial where a DMC and interim analysis must be formulated, this non-interventional trial, with relatively small numbers, does not investigate a pharmacological or medicinal product and does not expose patients to significant harm. Both treatment methods are already part of routine practice. As such, the trial team will closely monitor any adverse event or harm that might arise and act accordingly on a daily basis (see below).

Adverse event reporting and harms {22}

Collected case report forms will be checked daily by the research team before being stored in the trial locker; any adverse events or harm will be communicated with the study team.

Frequency and plans for auditing trial conduct {23}

The trial conduct is continuously audited in the departmental audit meeting (three monthly).

Plans for communicating important protocol amendments to relevant parties (e.g., trial participants, ethical committees) {25}

Any change to the trial protocol will be communicated with the ethical committees and trial registry.

Dissemination plans {31a}

The results of this trial will be published in one of the peer-reviewed medical journals.

Discussion

The National Institute for Health and Care Excellence (NICE) has recommended the subject as worthy of further research (27), and this has been reinforced by a recent audit of the UK Practice (3). Furthermore, the latest systematic review and meta-analysis by Smeeing et al. in 2015 reviewed the effect of early

mobilisation and early weight-bearing. Analysis of short- and long-term functional outcomes after weight-bearing was not possible due to the lack of studies and proper reporting. Furthermore, only three studies with a total number of 67 patients were included in the return to work analysis and had substantial heterogeneity (28).

To our knowledge, immediate weight-bearing (IWB) following ORIF of all types of unstable ankle fractures has not been investigated in a controlled prospective manner in recent decades. This will be the largest pragmatic randomised-controlled multicentre trial that investigates the safety and efficacy of IWB following ORIF of all ankle fracture patterns in the usual condition of care and will help in formulating a widely accepted guideline for postoperative management of ankle fractures.

Abbreviations

ORIF: open reduction and internal fixation

IWB: immediate weight-bearing

ROM: range of motion

NWB: non-weight bearing

OMAS: Olerud-Molander Ankle Score

EWB: early weight-bearing

HSE: Health Service executive

LOCF: Observation carried forward

BOCF: baseline observation carried forward

GDPR: *General Data Protection Regulation*

DMC: Data Monitoring Committee

ITT: intention-to-treat

Declarations

Ethics approval and consent to participate {24}

The following research ethics committees approved the study:

1/ Research Ethics Committee of Waterford University Hospital on the 14th of November 2018.

2/ Research Ethics Committee of Galway University Hospital, reference number: CA 2248 on the 20th of September 2019.

3/ Research Ethics Committee of Cork University Hospital, reference number: ECM 4 (z) on 22nd of October 2019.

Informed consent will be obtained from all study participants.

Trial status

Recruitment started on the 7th of January 2019. One-year follow-up is planned. At the time of the manuscript submission, 90 patients were recruited. This protocol is the 6th version and dated 20th of June 2020.

Authors' contributions {31b}

RK conceived this trial, initiated the trial and wrote the protocol. Invited the three contributing centres and granted ethical approval from each. RM is a site lead investigator and a contributor in formulating and writing the manuscript. FR contributed to setting up the inclusion and exclusion criteria and reviewed and adjusted the protocol. MS contributed to data collection and analysis. SK is a site lead investigator. DV is a site co-investigator and data manager. MT is a site co-investigator and data manager. CT is a site lead investigator. MC is the senior author and has a contributor in adjusting and reviewing the protocol. All authors read and approved the manuscript.

Funding {4}

Investigator-initiated and funded.

Availability of data and materials {29}

No personal data will be available. The coded datasets used and analysed during this trial will be available from the corresponding author on reasonable request following the GDPR and Health Research Regulations 2018(22,23).

Consent for publication {32}

Consent to publish anonymised data was explicit within the consenting process. No identifiable personal data will be published.

Competing interests {28}

The authors declare that they have no competing interests and no financial benefit.

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References

1. Court-Brown CM, Caesar B. Epidemiology of adult fractures: A review. *Injury*. 2006 Aug;37(8):691–7.
2. Dehghan N, McKee MD, Jenkinson RJ, Schemitsch EH, Stas V, Nauth A, et al. Early Weightbearing and Range of Motion Versus Non-Weightbearing and Immobilization After Open Reduction and Internal Fixation of Unstable Ankle Fractures: A Randomized Controlled Trial. *J Orthop Trauma*. 2016 Jul;30(7):345–52.
3. BONE Collaborative. Weight-bearing in ankle fractures: An audit of UK practice. *Foot Edinb Scotl*. 2019 the 14th of February;39:28–36.
4. Coles CP, Tornetta P, Obremsky WT, Spitler CA, Ahn J, Mirick G, et al. Ankle Fractures: An Expert Survey of Orthopaedic Trauma Association Members and Evidence-Based Treatment Recommendations. *J Orthop Trauma*. 2019 Sep;33(9):e318–24.
5. Swart E, Bezhani H, Greisberg J, Vosseller JT. How long should patients be kept non-weight bearing after ankle fracture fixation? A survey of OTA and AOFAS members. *Injury*. 2015 the 1st of June;46(6):1127–30.
6. van Laarhoven C, Meeuwis J, van der Werken C. Postoperative treatment of internally fixed ankle fractures: a prospective randomised study. *J Bone Joint Surg Br*. 1996;78(3):395-399.
7. Black JDJ, Bhavikatti M, Al-Hadithy N, Hakmi A, Kitson J. Early weight-bearing in operatively fixed ankle fractures: A systematic review. *The Foot*. 2013 the 1st of June;23(2):78–85.
8. Gul A, Batra S, Mehmood S, Gillham N. Immediate unprotected weight-bearing of operatively treated ankle fractures. 2007;73:6.
9. Thomas G, Whalley H, Modi C. Early Mobilization of Operatively Fixed Ankle Fractures: A Systematic Review. *Foot Ankle Int*. 2009 the 1st of July;30(7):666–74.
10. Smeeing DPJ, Houwert RM, Briet JP, Groenwold RHH, Lansink KWW, Leenen LPH, et al. Weight-bearing or non-weight-bearing after surgical treatment of ankle fractures: a multicenter randomised controlled trial. *Eur J Trauma Emerg Surg Off Publ Eur Trauma Soc*. 2018 the 24th of September;

11. Lehtonen H, Järvinen TLN, Honkonen S, Nyman M, Vihtonen K, Järvinen M. Use of a cast compared with a functional ankle brace after operative treatment of an ankle fracture. A prospective, randomised study. *J Bone Joint Surg Am*. 2003 Feb;85(2):205–11.
12. Early mobilisation in a removable cast compared with immobilisation in a cast after operative treatment of ankle fractures: a prospective randomise... - PubMed - NCBI [Internet]. [cited 2019 Dec 29]. Available from: <https://www.ncbi.nlm.nih.gov.ezproxy.library.qmul.ac.uk/pubmed/17257532>
13. Vioreanu M, Dudeney S, Hurson B, Kelly E, O'Rourke K, Quinlan W. Early mobilisation in a removable cast compared with immobilisation in a cast after operative treatment of ankle fractures: a prospective randomised study. *Foot Ankle Int*. 2007 Jan;28(1):13–9.
14. Zaghloul A, Haddad B, Barksfield R, Davis B. Early complications of surgery in operative treatment of ankle fractures in those over 60: a review of 186 cases. *Injury*. 2014 Apr;45(4):780–3.
15. Olerud C, Molander H. A scoring scale for symptom evaluation after ankle fracture. *Arch Orthop Trauma Surg Arch Orthopadische Unf-Chir*. 1984;103(3):190–4.
16. O WT, E BK, P A, E W, M MM, M C-BC. A prospective randomised controlled trial of the fibular nail versus standard open reduction and internal fixation for fixation of ankle fractures in elderly patients. *Bone Jt J* [Internet]. 2016 Sep 1 [cited 2020 Jan 8]; Available from: <http://online.boneandjoint.org.uk/doi/abs/10.1302/0301-620X.98B9.35837>
17. Matthews PA, Scammell BE, Ali A, Coughlin T, Nightingale J, Khan T, et al. Early motion and directed exercise (EMADE) versus usual care post ankle fracture fixation: study protocol for a pragmatic randomised controlled trial. *Trials*. 2018 the 31st of May;19(1):304.
18. Weil NL, Termaat MF, Rubinstein SM, El Moumni M, Zuidema WP, Derksen RJ, et al. WARRIOR-trial - is routine radiography following the 2-week initial follow-up in trauma patients with wrist and ankle fractures necessary: study protocol for a randomised controlled trial. *Trials*. 2015 Feb 27;16(1):66.
19. Carter TH, Oliver WM, Graham C, Duckworth AD, White TO. Medial malleolus: Operative Or Non-operative (MOON) trial protocol - a prospective randomised controlled trial of operative versus non-operative management of associated medial malleolus fractures in unstable fractures of the ankle. *Trials*. 2019 Sep 12;20(1):565.
20. Laucis NC, Hays RD, Bhattacharyya T. Scoring the SF-36 in Orthopaedics: A Brief Guide. *J Bone Joint Surg Am*. 2015 the 7th of October;97(19):1628–34.
21. Blake C, Codd MB, O'Meara YM. The Short Form 36 (SF-36) Health Survey: normative data for the Irish population. *Ir J Med Sci*. 2000 the 1st of July;169(3):195.
22. reg_2014_536_en.pdf [Internet]. [cited 2020 Feb 2]. Available from: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf
23. Harris S. DATA PROTECTION ACT 2018 (SECTION 36(2)) (HEALTH RESEARCH) REGULATIONS 2018. :18.
24. Bell ML, Fiero M, Horton NJ, Hsu C-H. Handling missing data in RCTs; a review of the top medical journals. *BMC Med Res Methodol*. 2014 Nov 19;14(1):118.

25. National Research Council (US) Panel on Handling Missing Data in Clinical Trials. The Prevention and Treatment of Missing Data in Clinical Trials [Internet]. Washington (DC): National Academies Press (US); 2010 [cited 2019 Dec 28]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK209904/>
26. Trials NRC (US) P on HMD in C. Conclusions and Recommendations [Internet]. National Academies Press (US); 2010 [cited 2020 Jan 3]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK209905/>
27. Fractures (non-complex): assessment and management [Internet]. NICE. [cited 2018 Sep 19]. Available from: <https://www.nice.org.uk/researchrecommendation/post-operative-weight-bearing-in-people-with-ankle-fractures-what-is-the-most-clinically-effective-and-cost-effective-strategy-for-weight-bearing-in-people-who-have-had-surgery-for-internal-fixation-of-an-ankle-fracture>
28. Smeeing DPJ, Houwert RM, Briet JP, Kelder JC, Segers MJM, Verleisdonk EJMM, et al. Weight-Bearing and Mobilization in the Postoperative Care of Ankle Fractures: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Cohort Studies. PLOS ONE. 2015 Feb 19;10(2):e0118320.

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