Surgical versus non-surgical management of lateral compression type-1 pelvic fracture in adults 60 years and older: the L1FE RCT

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Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, or available in the toolkit on the NIHR journals Library report publication page at https://doi.org/10.3310/LAPW3412.

Primary conflicts of interest: Peter Bates holds educational contracts with Johnson and Johnson and Zimmer Biomet, for delivering teaching, visitations and webinars. He is one of the design surgeons for a pelvic plating system, '*Phoenix*' manufactured by ITS. This plating system is not used in the treatment of fragility lateral compression type-1 (LC-1) pelvic fractures. He is a senior lecturer at Queen Mary University of London (QMUL), in Orthopaedic Trauma Sciences. Catherine Hewitt is a member of the National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) Commissioning Board (2015–present) and Deputy Chair (2019–present). Catriona McDaid is a member of the NIHR HTA and EME Editorial Board (2017–present), NIHR Pre-doctoral Fellowship Selection Committee (2019–present) and NIHR Programme Grants for Applied Research Sub-committee B (2020–present). Catherine Hilton received NIHR Pre-doctoral Clinical and Practitioner Academic Fellowship Bridge (2021–2).

Published March 2024
DOI: 10.3310/LAPW3412

Scientific summary

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Health Technology Assessment 2024; Vol. 28: No. 15
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NIHR Journals Library www.journalslibrary.nihr.ac.uk

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Background

Lateral compression type-1 (LC-1) pelvic fractures are a common fragility fracture in older adults. Older patients who do not get back walking following an LC-1 fracture due to ongoing pain are at greater risk of immobility-related complications. In the UK, standard treatment for LC-1 fragility fracture is to 'mobilise as pain allows', involving prescribing pain relief, getting patients up within a few days of injury with physiotherapy input and encouraging them to mobilise with an assistive device until the fracture heals. This is unlike fragility hip fractures (fractures involving the upper end of the femur) where there is evidence that early surgery (within 1–2 days) is associated with reduced risk of death and pressure sores and these fractures are usually treated surgically. Despite LC-1 fractures being similarly disabling for some patients in terms of pain and immobility and occurring in the same patient group as hip fractures, to date, it has not been shown whether elderly patients with LC-1 fractures would have a better recovery with surgery than non-surgical management.

Objectives

To assess the clinical and cost effectiveness of surgical fixation with internal fixation device (INFIX) compared to non-surgical management of LC-1 fragility fractures in older adults (L1FE trial):

- undertake a 12-month internal pilot to obtain robust estimates of recruitment and confirm trial feasibility
- undertake a parallel group multicentre randomised controlled trial (RCT) to assess the effectiveness of surgical fixation with INFIX versus non-surgical management of LC-1 fragility fractures in older adults
- undertake an economic evaluation to compare the cost effectiveness of surgical fixation compared to non-surgical management, to determine the most efficient provision of future care and to describe the resource impact on the NHS for the two treatment options
- undertake a long-term review of patient well-being [EuroQol-5 Dimensions, five-level version (EQ-5D-5L) and mortality] 12 months after entering the trial.

Design

Pragmatic, randomised controlled superiority trial, with 12-month internal pilot to assess recruitment assumptions, and an economic evaluation. Participants were randomised between INFIX surgical fixation and non-surgical management of LC-1 pelvic fracture with a 1 : 1 allocation ratio. The target sample size was 600 participants. For the internal pilot the target was to set up a minimum of 19 recruitment sites and randomise 148 participants in order to meet the target sample size in the main trial. To progress to the main trial, an average recruitment rate of one participant per centre per month was required.

Setting and participants

Participants were recruited from Major Trauma Centres (MTCs) in the UK. Adults aged 60 years or older with an LC-1 pelvic fracture, arising from a low-energy fall from standing height or less, and unable to mobilise independently to a distance of around 3 m and back due to pelvic pain 72 hours after injury were eligible for inclusion.

Interventions

Internal fixation device surgical fixation and non-surgical management (both groups received pain relief and were seen by a physiotherapy team who worked to mobilise the patients as pain allowed).

Internal fixation device surgery uses an INFIX to stabilise the pelvis. INFIX devices have screws that are secured into the pelvic bone, and these are connected by a metal bar across the front of the patient. The INFIX device sits entirely under the patient's skin.

Main outcome measures

Primary outcome – average patient health-related quality of life, over 6 months, assessed by the patient-reported outcome measure, EQ-5D-5L utility score. Collected at baseline, 2 weeks, 6 weeks, 12 weeks and 6 months post-randomisation time points.

Secondary outcomes – health-related quality of life using the EQ-5D-5L visual analogue scale (VAS); physical function using the eight-item Patient-Reported Outcome Measures Information System (PROMIS) lower extremity function (LEF) (mobility) – Short Form and Timed Up and Go (TUG) test; mental health using the PROMIS Scale v1.2 – Global Health Mental 2a subscale; pelvic pain using a VAS; delirium using the Abbreviated Mental Test Score (AMTS) and 4AT Rapid Assessment Test for Delirium; displacement of the pelvis based on a radiological assessment at the 12-week visit; mortality; complications and adverse events including lateral cutaneous nerve injury which was an adverse event of special interest (AESI); resource use; long-term review of patient well-being using the EQ-5D-5L and mortality at 12 months (optional follow-up for those recruited early in the trial). Information on resource use such as length of hospital stay, medication use, surgery details and details of rehabilitation therapy received was collected throughout the follow-up period to assess the impact on the NHS as part of the economic evaluation.

Sample size

Sample size was calculated based on the primary outcome, EQ-5D-5L. To be conservative, we took the lowest published estimate of the minimal clinically important differences (MCID) (0.074) with an estimated standard deviation (SD) of 0.25 (estimated from the 0.30 reported for the 3L version and adjusted down to account for the 5L version's greater sensitivity). Based on these assumptions we would have needed to analyse 480 participants (240 per group) and, after accounting for loss to follow-up of 20%, we would have needed to recruit and randomise 600 participants for a study with 90% power ($2p = 0.05$).

Randomisation

Intervention allocation was assigned using an online data management system developed for the L1FE study by the software team at York Trials Unit (YTU). There was independent and concealed random allocation (1 : 1 ratio), using computer-generated random permuted blocks of random sizes (4, 6 and 8), stratified by centre, following confirmation of eligibility and written consent.

Analysis

The originally planned primary analysis was a mixed-effects linear regression model, with EQ-5D-5L scores at 2, 6 and 12 weeks and 6 months follow-up as the dependent variable, adjusting for baseline

EQ-5D-5L, randomised group and other pertinent baseline characteristics as fixed effects. The plan was to control for potential clustering at hospital site level by including it in the model as a random effect and to account for the correlation of scores within patients over time by means of an appropriate covariance structure. Due to the small sample size and stopping at the end of the internal pilot, a descriptive analysis was undertaken with no formal hypothesis testing. All reported summary statistics are given at both a treatment group and overall level.

The planned economic analysis was to examine the overall difference in EQ-5D-5L index scores between the two groups using regression methods, consistent with the model selected in the statistical analysis. The EQ-5D-5L health states were to be valued in accordance with National Institute for Health and Care Excellence (NICE) guidance. Quality-adjusted life-years (QALYs) were to be calculated by plotting the utility scores at each of the four time points and estimating the area under the curve and regression methods used to express the incremental cost per QALYs gained. Results were to be presented using incremental cost-effectiveness ratios (ICERs) and cost-effectiveness acceptability curves (CEACs).

Results

The trial closed early, at the end of the internal pilot due to low recruitment. The internal pilot took place in two separate phases (August 2019 to March 2020 and March 2021 to September 2021) because of a 1-year recruitment pause due to the coronavirus disease 2019 (COVID-19) pandemic.

Site set-up

Eleven sites in England and Wales were opened during the first phase of the internal pilot. Ten of these re-opened following the study recruitment pause. A further 10 sites, including 3 in Scotland, were interested in participating and were in various stages of set-up prior to study closure. The 11 sites were open for a combined total of 92 months.

Patient screening

During the internal pilot, 316 patients were assessed for eligibility, of whom 43 were eligible (13.6%). The main reasons for ineligibility were: patient able to mobilise independently 3 m and back (n = 161), concomitant injury that impedes mobilisation (n = 57), surgery contraindicated (n = 40), patient did not have a low-energy LC-1 pelvic fracture (n = 38), unable to schedule surgery within 10 days of injury (n = 34), patient was under 60 years of age (n = 23) and/or the patient was non-ambulatory or required assistance prior to injury (n = 22).

Recruitment, withdrawals and follow-up

Of the 43 eligible participants, 36 (83.7%) were approached for consent, of whom 11 (30.6%) provided consent. Eleven (100%) of the consenting patients were randomised into the study. The most common reason for eligible patients not consenting to take part was that they were unwilling to be randomised to a treatment (n = 10).

The average recruitment rate per site per month was 0.175, well below the target rate of one patient per site per month.

Eleven patients were randomised, five to INFIX surgical fixation and six to non-surgical management. Three participants in the non-surgical management group were withdrawn from the study. One participant died, one participant lost capacity and their family member no longer wanted them to take part in the study and one participant had sight problems and considered themselves too frail to continue. Of the five participants randomised to surgical fixation, all received surgery and no one in the non-surgical management group received surgery. All participants in the surgical fixation group completed the 6-month questionnaires and the remaining participants in the non-surgical management group provided data at 6 months (3/6).

The average age of participants was 83.0 years (interquartile range 76.0–89.0) and the EQ-5D-5L utility score at 6 months post randomisation (n = 8) was 0.32 (SD 0.37).

Barriers to recruitment and actions taken

There were multiple barriers to recruitment, which, combined with the impact of COVID-19 on the NHS, resulted in a very low recruitment rate. These included:

- Fewer patients than anticipated were screened and screening activity was variable across sites. Patients had multiple entry points to hospital for treatment with onward admissions to several possible departments (Geriatric ward, Orthopaedic ward, Medical ward or an Admissions unit). This made screening resource-intensive for the research teams at sites. This became particularly challenging following the recruitment pause, as recruiting staff at sites were not all back to full capacity.
- A substantial proportion of patients were able to mobilise by 72 hours post injury and therefore did not meet the eligibility criteria for the trial. There was also variation across sites in how the assessment of mobility was undertaken and the extent of assistance provided to patients.
- The COVID-19 pandemic led to a concerted focus on avoidance of hospital admissions where possible, thereby minimising hospital stays. Because the pre-trial standard care for LC-1 pelvic fragility fractures was non-surgical management, there were challenges in the delivery of the L1FE trial. Patients were increasingly being discharged before the 72-hour assessment to nursing homes, residences with care packages or rehabilitation hospitals and could not be screened for the trial.
- There was evidence of a lack of equipoise amongst both surgical and non-surgical healthcare professionals, with a preference for non-surgical management in some centres. For example, some surgeons felt that INFIX was not a good treatment for this patient cohort, or they felt that most patients could mobilise fairly quickly.
- The recruiting window was relatively small. There were 3 days before the initial approach was permitted, with the surgery required to take place before day 10 (but in reality, this was often shorter due to 1 day per week operating lists or no operating at weekends at some sites). Making a decision about participating in a trial where the interventions are very different in intensity and risks is potentially a daunting one for patients and their consultees (where patients lacked capacity). From the perspective of recruiting staff, the resulting consent process was experienced as time consuming, involving difficult conversations and a lot of back-and-forth, waiting for patients to discuss the trial with their relatives and/or surgeon, or for next of kin to do so. This was exacerbated by the COVID-19 pandemic. Where patients lacked capacity, discussions with consultees had to take place remotely and recruitment staff felt that it was more difficult to build rapport and trust. There was a perception amongst staff that patients' next of kin were also reluctant to consent on behalf of the patient whom they were unable to see due to COVID-19 visiting restrictions, in order to have a better idea of how they were doing, or get a better sense of the study.

We used multiple strategies to mitigate against the barriers identified. We used cross-site meetings with the aim of bringing together research staff at recruiting sites to discuss the challenges with recruitment experienced at each site, share knowledge and provide support from the central trial team. We obtained approval for changes to the protocol clarifying how the 72-hour mobility inclusion criterion was implemented. During the recruitment pause we developed new resources to support recruitment staff: a short video introduction to the trial that sites could share across departments; a narrated animation on identifying patients across departments; a video resource on how to undertake the 72-hour mobility assessment for the trial; a patient-facing consent video; and updated consent guidance. We obtained approval for the associate principal investigator (API) scheme to be extended to orthogeriatricians to increase their engagement with the study. The trial team including the chief investigator (CI), physiotherapist, orthogeriatrician and trial co-ordinators provided support to address issues at individual sites. With the input of our patient and public involvement (PPI) group, the patient information sheet (PIS) was also revised. Despite the efforts of the central trial team and recruiting teams at sites, the strategies did not sufficiently mitigate against the barriers.

Conclusions

It is not feasible to recruit to this trial in the current context.

Further research to understand the treatment and recovery pathways of this group of patients, along with their outcomes, would be needed prior to undertaking a future trial.

Trial registration

This trial is registered as ISRCTN16478561.

Funding

This award was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme (NIHR award ref: 16/167/57) and is published in full in *Health Technology Assessment*; Vol. 28, No. 15. See the NIHR Funding and Awards website for further award information.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.6

A list of Journals Library editors can be found on the NIHR Journals Library website

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This manuscript

The research reported in this issue of the journal was funded by the HTA programme as award number 16/167/57. The contractual start date was in October 2018. The draft report began editorial review in June 2022 and was accepted for publication in November 2022. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' manuscript and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this manuscript.

This manuscript presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care.

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