Surgery versus conservative management of stable thoracolumbar fracture: the PRESTO feasibility RCT

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Declared competing interests of authors: Amar Rangan has received grants from the National Institute for Health Research, Orthopaedic Research UK (London, UK) and the European Commission (Horizon 2020), and grants and personal fees from DePuy Synthes Johnson & Johnson Medical Devices Ltd (Warsaw, IN, USA), all outside the submitted work. Catherine Hewitt is a member of the National Institute for Health Research Health Technology Assessment Commissioning Board (2015 to present). Joy Adamson is a member of a National Institute for Health Research Health Technology Assessment Commissioning Committee (2017 to present). David Torgerson has received grants from National Institute for Health Research during the conduct of the study; the Clinical Trials Unit is funded by the National Institute for Health Research. Catriona McDaid is a member of the National Institute for Health Research Health Technology Assessment and Efficacy and Mechanism Evaluation Editorial Board (2017 to present). She has also received funding from the British Orthopaedic Association (London, UK) to support the development of grant applications for orthopaedic trials.

Published November 2021
DOI: 10.3310/hta25620

Scientific summary

The PRESTO feasibility RCT

Health Technology Assessment 2021; Vol. 25: No. 62
DOI: 10.3310/hta25620

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

Thoracolumbar fractures are the most common fracture of the spinal column. An estimated 40–80% of these injuries are the result of a high-energy impact, such as car accidents, falls from a height or sporting activities (e.g. horse riding and skiing). This injury can also be sustained through low-energy impact and can be the result of bones being weakened by osteoporosis.

This research was undertaken in response to a commissioning brief from the National Institute for Health Research Health Technology Assessment programme. The brief requested an external pilot study to assess the feasibility of undertaking a substantive trial to assess the clinical effectiveness and cost-effectiveness of surgical fixation compared with conservative management in patients with a stable thoracolumbar fracture without spinal cord injury. The brief requested inclusion of both high- and low-energy fractures.

Objectives

The objectives of this feasibility study were to explore the following questions:

1. Are surgeons willing to randomise eligible patients and adhere to randomisation to (1) surgical fixation or (2) initial conservative management?
2. Are patients willing to be randomised and adhere to randomisation in a trial comparing the two treatments?
3. What is the completeness of follow-up in this population?
4. Are there a sufficient number of centres and surgeons (with sufficient caseloads of eligible patients) willing to participate in a future randomised controlled trial to make the trial feasible within a viable time scale?
5. What methods of establishing spinal stability and suitability for surgery or conservative management are currently used?
6. What methods of surgical fixation and conservative management are currently being used?
7. What are the barriers to successful delivery of a future trial and how can they be overcome?
8. Can the British Spine Registry be used to collect participant data in a trial?
9. What is the most suitable primary end point for a main trial?
10. How can we accurately identify, quantify and value economic data to capture the impact of the two treatments from both an NHS and societal perspective?

Methods

The Pragmatic Randomised Evaluation of Stable Thoracolumbar fracture treatment Outcomes (PRESTO) study consisted of a feasibility randomised controlled trial; a national survey of spine surgeons; a qualitative study with clinicians, recruiting staff and patients; and a costing analysis. The feasibility trial assessed objective questions 1–3 and 7–10. Questions 1, 4–7 and 9 were assessed using the survey of spine surgeons, whereas the qualitative interviews addressed questions 2, 7 and 9. The study was approved by the North East – Newcastle and North Tyneside 1 Research Ethics Committee (reference 18/NE/0008) and study-wide NHS approval was given by the Health Research Authority (Integrated Research Application System number 223912).

Feasibility randomised controlled trial

The feasibility randomised controlled trial study took place in three NHS hospitals: (1) Barts Health NHS Trust, (2) Leeds Teaching Hospitals NHS Trust and (3) Cardiff & Vale University Health Board. Patients were eligible if they were aged ≥ 16 years and had sustained a high- or low-energy fracture of a thoracolumbar vertebral body between the 10th thoracic vertebra and the second lumbar vertebra confirmed by radiography, computerised tomography or magnetic resonance imaging, and met at least one of the following criteria: a kyphotic angle > 20° on weight-bearing radiographs or > 15° on supine radiographs or on computerised tomography; reduction in vertebral body height of 25%; a fracture line propagating through the posterior wall of vertebra; involvement of two contiguous vertebrae; or injury to the posterior longitudinal ligament or annulus in addition to the body fracture. Patients were excluded if they had an unstable fracture requiring surgical stabilisation, a spinal cord injury, a pathological (other than osteoporotic) fracture (e.g. tumour/infection) or if they were not considered suitable for surgery.

Participants were randomised using stratified block randomisation (permuting lengths of 2, 4, 6 and 8), with stratification by centre and type of injury (high-energy trauma or low-energy osteoporotic) used to allocate participants on a 1 : 1 basis to surgery or conservative treatment.

Conservative management consisted of mobilisation in a brace or mobilisation without a brace, as recommended by the treating surgeon in consultation with the participant. Surgical treatment could be open spinal surgery (with or without spinal fusion) or minimally invasive stabilisation surgery, with the type of surgery undertaken left to the discretion of the treating surgeon. Both procedures included placement of pedicle screws, but through different surgical approaches.

Hospital reviews were to take place at 2 weeks, 3 months and 6 months post intervention, with patient-reported outcomes collected at 3 and 6 months post intervention. Data were collected at 6 months only for those patients who reached this follow-up time point during the trial period.

Recruitment for the randomised controlled trial took place between 18 April 2018 and 31 March 2019. The primary outcome was recruitment rate, defined as the proportion of eligible participants who were randomised. Secondary outcomes included examining aspects of recruitment (the number of eligible patients, the proportion of eligible patients approached for consent, the proportion of eligible patients not approached for consent and reasons why, the proportion of patients approached who provided consent, proportion of patients approached who did not provide consent and reasons why); randomisation (the proportion of patients providing consent who were randomised, the proportion of patients randomised who did not receive the randomly allocated treatment and reasons why); crossover (the proportion of patients randomised to conservative treatment who received surgical management, at what time point and reasons why); dropout (the proportion of patients dropping out between randomisation and follow-up at each time point and reasons why); the ability to collect clinical outcome measures (the proportion of complete data for each outcome measure, the proportion successfully gathered through the British Spine Registry and the proportion of complete data); feasibility of appropriate and accurate economic data collection; and future trial design (participant treatment preferences at baseline, clinical care during the trial, details of surgical fixation and conservative management used, and the methods used to establish spinal stability).

The costing analysis aimed to identify data that would be needed for an economic analysis of a full-scale trial. Individual participant data from the trial were used to evaluate resource use, costs and health outcomes associated with the interventions.

Survey of spine surgeons

The target population of the electronic survey was NHS spine surgeons regularly treating thoracolumbar fractures. The sample frame was membership of the British Association of Spine Surgeons or the Society of British Neurological Surgeons, with additional snowball sampling being used by clinical members of the research team to ensure that spinal surgeons who were not members also

had the opportunity to participate. Responses to the survey were wholly anonymous and no person-identifying information was collected with the main survey instrument. A link to a separate survey collector was presented to participants who completed the survey. In this section, participants were given the option of being acknowledged by name as a survey participant in publications that relate to the survey and/or to volunteer to take part in an in-depth interview to explore in more detail issues regarding the feasibility of a future trial. The survey opened on 16 March 2018 and closed on 15 November 2018.

Response data were downloaded from Qualtrics® November 2018 (Qualtrics, Provo, UT, USA) into Microsoft Excel® 2016 (Microsoft Corporation, Redmond, WA, USA). Standard checks were undertaken to identify and remove errors such as outliers, inconsistencies and omissions. The response rate to individual questions was calculated using the number who had completed at least one question as the denominator. Descriptive analyses of respondent characteristics were undertaken to allow exploration of the representativeness of the sample. Descriptive analyses were undertaken of responses to questions and summary statistics are presented. All responses collected for each question were analysed, with the response rate for each question calculated using the number of responses to individual questions as the denominator. The length of time taken by respondents to answer questions was not collected and therefore no cut-off points were used.

Qualitative study

It was intended that qualitative interviews were to be undertaken with patients (both those who consented to participate in the randomised controlled trial and those who declined to participate). Interviews were also conducted with trial recruitment staff and spine surgeons, identified both from participating hospitals and through the survey of spine surgeons. All interviews were conducted over the telephone, were semistructured and followed a topic guide. Recruitment to the qualitative element was ongoing throughout the recruitment period of the randomised controlled trial. Thematic analysis was adopted to ensure a systematic approach and was centred on the following stages defined by Braun and Clarke (Braun V, Clarke V, Hayfield N, Terry G. Thematic Analysis. In Liamputtong P, editor. *Handbook of Research Methods in Health Social Sciences*. Singapore: Springer; 2019. pp. 843–60): familiarisation, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and data reporting.

Results

Feasibility randomised controlled trial

Two hundred and eleven patients were assessed for eligibility and, of these, 28 met the criteria (13.3%). Initial discussion with participating centres indicated that 120 eligible patients would be seen in the recruitment period; our figure is 23.3% of this. Only a small proportion of patients screened were eligible to be entered into the trial; therefore, a full trial is unlikely to be feasible.

Of the 28 patients assessed as eligible, 12 were randomised, giving a recruitment rate (proportion of eligible patients recruited) of 0.43 (95% confidence interval 0.24 to 0.63). The proportion of eligible patients who were not approached for consent was zero (95% confidence interval 0.00 to 0.12). The combined total of site recruitment months was 30.7, which gives an overall average recruitment rate per month of 0.39 per site. The individual rates for each site were 0.44 for Bart's Health NHS Trust, 0.11 for Leeds Teaching Hospitals NHS Trust and 0.61 for Cardiff & Vale University Health Board.

Two patients (17%) withdrew from hospital follow-up (one in each arm) and no patients withdrew completely. At 3 months, 75% of questionnaires were returned (surgery, $n = 5$; conservative, $n = 4$) and 73% (surgery, $n = 4$; conservative, $n = 4$) were returned at month 6. Attendance at the 2-week hospital follow-up was 100%, at the3-month hospital follow-up was 82% and at the 6-month hospital follow-up was 50%.

The follow-up rates (questionnaire return and visit attendance) are lower than the 80% that would be required in a main trial. However, it is likely that the feasibility study underestimated this and the rate could be increased.

Of the six patients who underwent surgery, four (66.7%) underwent minimally invasive surgery and two had open surgery (33.3%). All surgeries involved the fusion method, with one (16.7%) also using the stabilisation method. All participants who received conservative treatment wore a non-customised brace.

Among the seven patients who completed measures using the British Spine Registry at both time points, the proportion of complete responses for EuroQol 5 Dimensions, five-level version, visual analogue scale and Oswestry Disability Index components was 0.92 (95% confidence interval 0.86 to 0.96). The missing data were spread across all the measures and time points and data were complete for only one patient. No patients completed the health resource use questions via the British Spine Registry at any time point.

The cost and logistics of using the British Spine Registry and the incompleteness of data collected mean that it would not be feasible to use the British Spine Registry as the sole method of data collection in a full-scale study.

The EuroQol 5 Dimensions, five-level version, appeared to be sensitive to problems in the study population. Data were gathered on treatments, length of hospital stay, rehabilitation, time to return to work and time to return to normal activities for all trial patients who returned postal questionnaires or attended the follow-up visits.

Qualitative study

Five patients who agreed to take part in the feasibility randomised controlled trial were interviewed. No interviews were conducted with patients who declined to take part in the study. Interviews were also conducted with 19 surgeons and trial recruiters. Eleven participants were surgeons, physiotherapists or research associates involved in recruiting patients to the feasibility randomised controlled trial. The remaining eight participants were surgeons who routinely treat patients with thoracolumbar fractures, but were from non-participating sites.

All patients who participated in the qualitative study reported having a preference for surgery prior to randomisation, largely because of perceived quicker recovery times. However, return to work, comfort, ease of commuting, positive experiences of previous surgery, the influence of family members having received a brace, the impact of the brace on daily life and concerns about compliance with a brace also contributed to these preferences.

Although a couple of patients also had prior knowledge of randomisation, with these individuals demonstrating an awareness of why research is required, for others randomisation was a new concept that was considered ‘a little bit odd at first’. Patient knowledge of randomisation during interviews was therefore variable. Although a couple of participants could describe randomisation clearly, others showed a lack of understanding, which was, in some cases, influenced by capacity issues.

Surgeon views of the treatment that should be provided to patients with stable thoracolumbar fractures were strong, irrespective of whether they advocated conservative or surgical management. Usual practice is known to vary throughout the UK, largely according to individual consultant preferences. The majority of surgeons in our sample reported a preference for managing stable thoracolumbar fractures conservatively, perceived by many to be the most commonly prescribed treatment for stable thoracolumbar fractures in the UK. However, what was considered conservative treatment varied. For example, some were opposed to the use of braces and preferred ‘monitoring only’, whereas others routinely prescribed braces. There was a lack of clinical consensus regarding the

implementation of the eligibility criteria in practice and what constitutes a stable fracture, alongside strongly polarised views about the appropriateness of surgical intervention for stable fractures.

There was a lack of consensus among surgeons regarding a primary outcome measure for a definitive trial. In particular, there was no agreement on an appropriate measure for trauma or acute injury that was also appropriate at different stages in the follow-up, despite this being raised as a concern during the qualitative interviews.

Survey of spine surgeons

Ninety participants agreed to take part in the survey and 86 responded to at least one question. Sixty-five respondents (72%) completed the whole survey. This means that not all participants provided answers to all of the questions. It is not possible to calculate a response rate, given the variety of approaches to recruitment and there is no definitive way to determine the number of people the survey reached. The total number of participants responding to each individual question was used as the denominator to calculate percentages.

Fifty out of the 65 (77%) respondents confirmed that they would be willing to randomise patients with a stable high-energy fracture to either surgical or conservative management. When asked about willingness to randomise patients with a stable low-energy fracture (e.g. resulting from a fall from standing height in osteoporotic or osteopenic patients) to either surgical or conservative management, 46 out of 66 respondents (70%) said that they would be willing.

Participants in the survey rated neurological deficit as the most important factor when establishing spinal stability. Participants also rated both computerised tomography and standing radiography as the most important imaging measures used to establish spinal stability, with segmental kyphosis and magnetic resonance imaging findings also being of importance. Other important factors included mechanism of injury, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association 2018 classification and trunk control.

Conclusions

The findings of the PRESTO study demonstrate that the trial design tested in the feasibility randomised controlled trial element would be unlikely to result in a successful definitive trial at this time, principally because of the small number of people meeting the eligibility criteria.

The recruitment and follow-up rates were slightly lower than anticipated; however, there is room to increase these based on information gathered during the feasibility study and because there was support in the surgical community for a future trial.

There were some contradictions from the different sources of data. Although there was support for the eligibility criteria used as part of the feasibility trial in the national survey, there was a lack of consensus about the definition of fracture stability, which is central to defining the study population identified in the qualitative research. Further consensus work defining the eligible population would be required in advance of any definitive trial.

Trial registration

This trial is registered as ISRCTN12094890.

Funding

This project was funded by the National Institute for Health Research (NIHR) Health Technology Assessment programme and will be published in full in *Health Technology Assessment*; Vol. 25, No. 62. See the NIHR Journals Library website for further project information.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.014

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, the Cochrane Library and Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

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This report

The research reported in this issue of the journal was funded by the HTA programme as project number 15/154/07. The contractual start date was in September 2017. The draft report began editorial review in October 2019 and was accepted for publication in March 2020. 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' report 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 report.

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