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Clinical research in fragility fractures

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ABSTRACT

The Fragility Fracture Network is coordinating international initiatives to promote collaborative research, multidisciplinary care, and the secondary prevention of fragility fractures. This review discusses the use of national audit processes and the collection of common outcomes to facilitate research, as well as the key role played by patient and public involvement, and strategies to overcome research barriers.

Introduction

In the year 2000 there were an estimated 9 million new fragility fractures and an estimated 50 million people worldwide suffering from the sequelae of these fractures [1]. In the European Union (EU27) the associated costs to healthcare systems and individuals were estimated annually in 2010 at 37 billion Euros with 1,180,000 quality adjusted life years lost [2]. This challenge will intensify. Hip fractures alone are predicted to rise from 1.31 million in 1990 [3] to an estimated 6.26 million globally by 2050 [4] and the associated costs are expected to rise by 25% in 2025 [2].

In this review, we discuss how national audit processes facilitate collection of outcomes data for multicentre research trials in fragility fracture, how patient involvement has become a key component of research, and how the Fragility Fracture Network (a global organisation whose mission is to optimise the multidisciplinary management of patients with fragility fractures including secondary prevention) is developing initiatives which promote international collaboration to drive research and improvements in patient care.

National audit programmes & core outcome sets

The seminal work of the Swedish national hip fracture registry (Rikshöft 1988) paved the way for a number of other countries to develop their own programmes of national hip fracture audit [5–8]. The implementation of national audit programmes has been shown to improve outcomes [9], and annual reports on these national level data act as 'feedbacks' on how well we deliver services and care for patients [10]. A recent review of national audit reports from eight countries (Sweden, Denmark, Norway, Ireland, Australia, New Zealand, Scotland, and England, Wales & Northern Ireland) compared the international approach to hip fracture care in these countries [11]. The authors found significant variation in a number of key areas including the classification of fracture type, the approach to defining cognitive impairment, the type of surgical implant, and anaesthetic technique used during surgery. The reasons for these differences most likely reflect a combination of individual or institutional preferences, lack of high quality evidence, differences in health systems/infrastructure, and financial influences. Exploring and rationalising these differences is challenging but raises the exciting possibility of establishing international treatment pathways with common outcomes which would establish a powerful international framework for research.

To begin to address this, the Fragility Fracture Network (FFN) has developed a minimum common dataset (MCD) of outcomes and performance indicators [12]. This initiative has completed a successful pilot phase in five European countries (Spain, Slovenia, Germany, Malta, and Germany) and ongoing work is underway to expand the data collection to other countries [13]. This initiative aims to promote international collaboration and comparison, to drive improvements in patient care, and to establish a framework within which to undertake research.

In the UK, the World Hip Trauma Evaluation study (WHiTE) has tested the use of existing national audit frameworks to facilitate the collection of outcomes data for research [14]. The WHiTE

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cohort recruits all hip fracture patients at participating sites and augments the routine collection of the national audit data (NHFD) [15] with the UK core outcome data set (UK COS) for hip fracture [16]. The UK COS was developed using a consensus approach involving patients, carers, clinicians, and methodologists, all whom collaborated to identify a set of core outcomes which patients themselves consider important in their recovery. Choosing an appropriate outcome measure for fragility fracture research has presented significant challenges due to a lack of specific measures addressing the complex health and social care needs of this patient group. The UK COS has addressed this by bringing together a minimum set of outcome measures which patients themselves consider to be important. The consensus process recommended the use of single item measures of mortality and mobility (indoor/outdoor walking status), and the EuroQol 5-D (EQ-5D) as the most simple and practical method of measuring quality of life in hip fracture patients [16,17]. The EQ-5D is a generic health-related quality-of-life outcome tool which consists of a visual analogue scale (VAS) for self-rated health on a scale from 'best imaginable health state' to 'worst imaginable health state', and a health status instrument with a five-level response (no problems, slight problems, moderate problems, severe problems and extreme problems) for the following five domains: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression [18]. The UK COS has now been adopted by NICE in their most recent Hip Fracture Guidelines [10].

By using existing national infrastructure for routine data collection the WHiTE study has efficiently delivered a number of randomised controlled trials embedded within the cohort with a number of studies in recruitment and planned [19–21]. The work of the FFN in establishing international collaboration and collection of common outcome data will no doubt facilitate future international multi-centre research collaborations.

Cognitive impairment and consent

Up to 40% of patients presenting with a hip fracture have cognitive impairment [22]. This impairment may be either permanent (dementia) or temporary (acute delirium), and compounded by the acute nature of the injury and the effects of pain relieving opioids. Patients with cognitive impairment are frequently excluded from research [23,24] due to the complexities of obtaining consent and in completing follow-up (see section on Core Outcome Set), yet the inclusion of patients with cognitive impairment in fragility fracture research is vital if the results are to be applicable to the population as a whole [24].

In the UK, the Mental Capacity Act 2005 regulates research in the emergency setting where patients lack capacity [25] and the approach used for research involving fragility fractures has been previously described [26]. In 'life and death' cases (e.g. cardiac arrest) the act allows the research team to proceed under a waiver of consent, subject to having obtained approvals by the relevant Research Ethics Committee. However, in the majority of cases involving the care of fragility fractures the research team will have time to seek 'agreement' from either a personal consultee (e.g. a family member or next of kin) or where not available, then a nominated consultee is approached. The nominated consultee is typically a carer or member of the clinical team caring for the patient, but critically the nominated consultee must not be a member of the research team. At all times, every effort is made to respect the patient's autonomy and to involve the patient in the decision making process.

Fragility fractures encompass a spectrum of injury of varying severity including wrist fractures, hip fractures, and open fragility fractures of the ankle. Assessment of capacity and the emergent nature of treatment should be assessed on a case-by-case basis together with the potential for the patient to regain capacity. For example, in fragility wrist fractures requiring operative intervention the patient often achieves a degree of pain relief with cast immobilisation and where capacity is regained then consent to inclusion in research can proceed with informed prospective patient consent. However, in more severe injuries such as open fragility fractures, and indeed hip fractures, which require emergent surgical treatment and the use of opioid-based analgesia, then consent from a consultee (ideally a personal consultee) may be more appropriate where patients lack capacity.

Patient & public involvement in research

Patient and public involvement (PPI) has flourished in all aspects of research from the identification of research priorities, to developing study designs and documentation, identifying outcome measures, assisting with recruitment, and disseminating results. In the UK, the National Institute of Health Research (NIHR) has driven PPI in research such that it is now a key part of the design, conduct, and delivery of research in health and social care [27]. Researchers submitting grant applications are expected to engage with PPI members in their study design and to justify how patients will benefit from the output of their proposed research. This process been greatly supported, both in the UK and internationally, by a number of charities, research networks, and organisations such as INVOLVE (a UK based national advisory group dedicated to the advancement and promotion of PPI involvement) [28] and the Health Technology Assessment International (an international organisation with a patient and citizen involvement interest group) [29]. Recently, an international consensus study has developed the first evidence based guidance for reporting patient and public involvement in research [30]. The GRIPP2 guidelines (Guidance for Reporting Involvement of Patients and the Public) aim to promote the consistent and transparent reporting of PPI involvement in research and will further the evidence base for the role of PPI in research [30].

Within fragility fracture research, a series of priority setting partnerships (PSPs) are underway in conjunction with the James Lind Alliance – a non-profit making organisation which coordinates PSPs to identify the Top 10 research uncertainties within a health research area [31]. These PSPs bring together patients, carers and clinicians with a variety of specialist interests to identify and prioritise research questions which are then forwarded to funders of health research. The research questions are initially identified through national surveys which are designed and piloted in collaboration with PPI members. The first in a series of PSPs in fragility fracture will report the Top 10 research priorities for pelvic and lower limb fractures in 2018 with the priorities for upper limb fragility fractures to follow soon after [32].

Trainee involvement in multicentre trials

One of the challenges of conducting large-scale multicentre research studies is establishing and maintaining recruitment across the contributing centres. In the UK, and increasingly in other countries around the world, a number of trainee-led initiatives have demonstrated the effectiveness of trainee networks in recruiting to multi-centre randomised controlled trials [33,34]. Trainees are well placed to lead recruitment into research for a number of reasons: they are on the 'front-line' of patient care, provide out-of-hours (evenings and weekends) clinical service when research teams typically are not present, they usually work across a number of hospital sites, and proof of involvement in research and audit is a mandatory component of their training [35]. Recently, a UK based trainee led regional research collaborative [36] completed recruitment to a multicentre trial in 1000 hip

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