Multicentre randomised clinical trials in trauma care

We need to inform clinical decisions in trauma management using the best available evidence. Randomised controlled trials are generally considered the benchmark for unbiased assessment of treatment effects, and produce the highest level of unfiltered information on the pyramid of evidence-based medicine.1 However, although necessary for guiding clinical practice, relatively few randomised trials are conducted in orthopaedic trauma surgery. Indeed, partly as a consequence of the practical difficulties intrinsic in conducting these studies, almost 90% of published orthopaedic research is observational and non-randomised.2 In some countries national registries have helped generate hypotheses for testing, and helped identify underperforming implants. For similar reasons, the role of such registries for trauma implants is worthy of debate.

There is a growing professional recognition of the need for randomised trials to produce good-quality evidence in certain key areas of orthopaedic trauma care: typical examples are fragility fractures and major trauma. Fragility fractures are an increasing public health problem with considerable implications for use of resources. The management of major trauma is primarily resource intensive, with outcome largely dependent on the organisation of services. The introduction of a national trauma leadership structure in the United Kingdom under the leadership of Professor K. Willet, National Clinical Director for Trauma, has created new opportunities to streamline services and to develop research into trauma care. There is the potential to define future directions and strategies for trauma research under this administrative umbrella, which may help attract the allocation of funds to support such a program.

Despite long-held convictions, it is clearly important that clinicians step forward and test hypotheses using level 1 studies if we are to produce high-level evidence to inform practice. Some randomised multicentre trials in trauma have been successfully completed or are being conducted in some parts of the world.3-9

In many areas of orthopaedic trauma care only a well-performed randomised trial with adequately powered, clinically relevant outcome measures and appropriately long follow-up is likely to produce the evidence required to inform and change practice. There are some in progress. Independently funded multicentre randomised clinical trials have recently been commissioned in the United Kingdom to answer some key questions of high priority in orthopaedic trauma care. A typical example is the ProFHER trial,10 which is a pragmatic multicentre randomised trial designed to answer the fundamental question of whether surgery improves outcomes in the majority of displaced fractures of the proximal humerus in adults. Other similar projects are the United Kingdom Heel Fracture Trial, the Ankle Injury Management Trial and the Distal Radius Acute Fracture Fixation Trial.11

Randomised trials in surgical practice pose a significant challenge, including the need to overcome surgeons’ reluctance to become involved. Confidence in the surgical techniques, consent for trial participation and the level of research infrastructure in collaborating centres present difficulties that can only be overcome with education and investment. Appropriate levels of independent funding, a multidisciplinary team and management by a recognised clinical trials unit are essential to ensure compliance with research governance and successful project completion.
In the United Kingdom, the Integrated Research Application System and the Co-ordinated System for gaining Permission have helped streamline the process of approval by ethics committees and research and development departments in individual hospitals. The Comprehensive Local Research Networks play a key role in supporting recruitment into these trials by facilitating the appointment of research associates in the participating centres. An important aspect of these publicly commissioned trials has been the establishment of a network of active research units to develop collaborative trials in trauma and orthopaedic surgery. The willingness of all the parties involved, at local, regional and national level, to continue to work to produce level 1 evidence puts the United Kingdom in a favourable position for conducting multicentre randomised trials; a large patient population can be studied in a scientifically sound way in a collaborative fashion between the various centres. Although many trials have been published in trauma surgery, most have included small sample sizes, reporting large average treatment effects (> 50% relative risk reduction) correlated with a smaller number of total outcome events.12,13 The results of such small studies with few events should be interpreted with caution. Considering the prevalence of trauma, single-centre studies will generally find it difficult to achieve an adequate sample size within a reasonable period of time. Such studies also have limited generalisability. Trauma trials pose some unique challenges, including, for example, controlling for level of injury, and the recruitment of unconscious patients following major trauma. Such barriers can be successfully overcome by involving an appropriate multidisciplinary team and by collaborative research. In addition to individually randomised trials, cluster randomised controlled trials should be considered, despite their greater complexity of design and analysis, and a requirement for more participants to obtain comparable statistical power, because they are more appropriate to use in certain areas, for example, a study of strategies for injury prevention.

We are advocates of multicentre trials in orthopaedic trauma. Given the intrinsic constraints of designing and performing level 1 studies, results may take some time to report but they will provide a well-grounded indication of what is more effective in our field. We believe that multicentre randomised clinical trials should become an integral part of future research into orthopaedic trauma care, and appropriate investment to support these trials is essential.

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References