

PRAGMATIC RANDOMISED TRIAL TO EVALUATE LAPAROSCOPIC SURGICAL REPAIR FOR INGUINAL HERNIA - PROPOSAL TO EXTEND RECRUITMENT WITHIN EXISTING RESOURCES

This proposal seeks to justify reallocation of resources within the ongoing MRC trial of laparoscopic surgical repair for inguinal hernia to allow patient recruitment to continue for an additional year. Despite initial problems with recruitment, the substudies addressing more 'explanatory' aspects of the evaluation (such as effects on pulmonary function, metabolic response, and analgesia use) have been completed ahead of schedule. Without further recruitment it is likely that the more important 'pragmatic' aspects of the trial will not be addressed reliably. These include possible effects on return to normal activity, hernia recurrence, chronic pain and other rare but serious complications. These are the aspects which will have greatest impact on decision making within the NHS.

Background

Funding was agreed in 1993 for a multi-centre pragmatic randomised controlled trial to evaluate the new laparoscopic approach to surgical repair for inguinal hernia with particular reference to patient outcomes and costs including:

1. analgesic use
2. pulmonary function
3. metabolic response
4. hospital stay
5. complications
6. return to normal activity
7. general health status
8. hernia recurrence
9. cost to national health service
10. value to the community

An additional objective was to assess the impact of a 'learning curve' on outcome. Differential effects on analgesia use, pulmonary function, and metabolic response were to be assessed on early patients recruited in Glasgow. The impact on other longer term outcomes was to be evaluated within a broader-based multi-centre study, in which 16 surgeons had already agreed to participate.

A requirement for participation in the randomised trial component was that a surgeon had to have completed at least 10 laparoscopic hernia repairs. Nevertheless, to assess the learning curve all patients managed laparoscopically were to be registered and studied alongside the formal trial.

Progress

Good progress has been made in the following respects:

a. Assessing the learning curve

More than 750 people whose inguinal hernias were repaired laparoscopically have been registered in the study. These data will be used to assess the impact of learning on surgical performance.

b. Substudies based in Glasgow

The substudies on analgesia use, pulmonary function, and metabolic response are now completed and a report of the findings has been submitted for publication. This has been completed ahead of schedule with (as described further below) significant resource savings.

c. Health economics

As planned, data are being collected to measure the pre-operative costs, operative costs (such as medical and nursing theatre time, operating time, and use of instruments), and post-operative costs, such as hospital stay and post-operative investigations. This aspect of the trial is up to schedule.

d. Assessment of differential effects on other measures of short-term outcome

More than 700 people have already agreed to join the multi-centre trial and been randomly allocated to either laparoscopic or conventional repair. This number will provide a sufficiently precise estimate of any differential effects on hospital stay and general health status up to three months after the operation.

Reasons for recruiting fewer randomised patients than anticipated

The current study would allow only an imprecise estimate of differences between the group in the important, but less common adverse outcomes, such as rare operative complications, recurrence, and chronic pain. The reasons for the initial difficulties in recruitment are important because they reflect the difficulties of evaluating an emerging technology that requires training and skill.

a. Developments in laparoscopic techniques

Methods of laparoscopic hernia repair have continued to develop since the trial started. Concerns that the transabdominal approach occasionally causes bowel obstruction led to the development of a totally extra-peritoneal method in preference to the transabdominal pre-peritoneal approach described in the original submission.

b. Developments in conventional methods of hernia repair

Somewhat paradoxically, the new laparoscopic techniques for hernia repair have contributed to fundamental changes in conventional surgical approaches. Specifically, the new tension-free methods using a mesh (associated with the name Lichtenstein) have been widely adopted, because they are technically easy, appear to be less painful, and seem to have acceptable failure rates. This made the laparoscopic approach less attractive to surgeons.

c. Surgeons' having a change of mind about participation

Changes in surgical techniques were one reason why 50% of the surgeons who had originally said they would collaborate, in the event decided not to participate. Another reason was difficulties persuading Trust Managers to provide funds to cover the additional service costs of an 'experimental' treatment. Increasing constraints on inpatient theatre facilities and a move to use day case surgery led some purchasers and providers to limit hernia repairs to day cases and few if any day-case units allowed laparoscopic repair. Reflecting this move to day-care surgery, hernia operations are increasingly being performed by staff grade surgeons rather than consultants, limiting the numbers of hernia operations performed by surgeons with appropriate training in laparoscopic techniques.

d. The learning curve

It is now clear that there is a steep learning curve for the laparoscopic technique (and our data should define this). Some surgeons, however, chose to drop out of the study because of poor outcome, particularly recurrence in the first few patients, before they had gained experience.

e. Adverse publicity

Adverse publicity, particularly during 1994, slowed the trial's progress. There were anecdotal reports in the medical press of serious adverse effects such as trauma to great vessels and nerves from misuse of staples. These certainly contributed to the reluctance of some surgeons to participate. Some of these concerns were later elaborated by lay journalists and this led to adverse publicity, most strikingly during

a television documentary in 1994. This undoubtedly affected recruitment; patients who had agreed to join the study telephoned to withdraw, and others refused to participate.

f. Changes in personnel at the Health Services Research Unit in Aberdeen.

In retrospect, it was unfortunate that recruitment started in the 'interregnum' between two Directors of the Health Services Research Unit in Aberdeen. One of the original applicants, Ian Russell, moved towards the end of 1993 and was not replaced by Adrian Grant until the middle of 1994. This led to some aspects of the trial co-ordination being suboptimal. A centralised telephone randomisation system was put in place late in 1994, but by this time clear evidence had emerged that the envelopes system used until then had been corrupted in some centres. For this reason, data for a few surgeons can only be used for observational analyses in the context of assessing the learning curve.

Reasons for thinking that extending recruitment would be worthwhile

Despite these difficulties, the trial is now recruiting relatively well. About 30 consultant surgeons have recruited patients to the randomised comparison, but most have been in the trial for only a relatively short period of time (median 9 months). This has been reflected in an encouraging increase in recruitment rates recently up to 40 to 50 people per month. Furthermore, now that the in-depth studies based in Glasgow have been completed, all resources can be focused on the pragmatic, longer term, outcomes.

Extending recruitment for another 12 months would not require any additional resources, only a re-distribution of those already granted by MRC. This is because our resources have been husbanded sensibly in the light of the difficulties and delays described above. For example, the original grant application envisaged a full-time research nurse in Edinburgh from the start of recruitment; in the event, however, it was judged appropriate only to employ a nurse from April 1995 and on a part-time basis. The completion of the in-depth studies in Glasgow seven months ahead of schedule has meant that the research registrar has been able to turn his attention to patient recruitment and follow-up, so that the part-time research nurse based in Glasgow is no longer necessary.

Modified plan of investigation

The plan proposed is to extend recruitment to 31 December 1996. All participating surgeons are willing to continue and strongly support this proposal. Follow-up of patients would also be extended to allow a minimum period of one year. By the end of 1996, over 1000 patients should have been randomised. This would allow reasonable power to identify differences in recurrence and chronic pain rates at one year. Estimates of likely rates in the control conventional group are uncertain, but may be as low as 2-4% that is, lower than anticipated in the original grant application. A trial with a 1000 participants would have 80% power to identify difference between the groups of 2.5-3.5% ($P < 0.05$). And a trial of this size would also allow exploration of differential effects within subgroups, such as those with bilateral or recurrent hernias and type of surgeon characterised by different approaches to laparoscopic and conventional repair, particularly in respect of the more common short-term outcomes. Another stratified analysis will allow investigation of whether specialist 'laparoscopic' surgeons have better results than 'general' surgeons. These secondary analyses may allow the identification of 'the appropriate place' of laparoscopic hernia repair. In some centres, information has been collected about all patients having herniorrhaphy whether or not in the trial. This will allow an assessment of whether those recruited to the trial are typical of all patients in those centres and hence may aid generalisation.

We are aware, however, that even a trial with a 1000 patients will not be sufficient to address all issues. For this reason, we shall be actively contributing to a collaborative review group on laparoscopic hernia repair within an international group headed by Dr Peter Goh in the Netherlands.

Justification for reallocation of existing funds

The original award from MRC was in two parts. The first was a grant to the University of Aberdeen. This was for support for the trial's data co-ordination and the health economics study within the Health Services Research Unit and the Health Economics Research Unit, and for a research nurse based in Edinburgh to support local collaborating clinicians. The second part was a grant to the University of Glasgow to support the clinical co-ordinating centre including the in-depth studies. We are asking for a reallocation of resources within both these ongoing grants. It should be emphasised that this is not a request for any new money.