A randomised trial comparing abdominal, vaginal and laparoscopic methods of hysterectomy

EVALUATE hysterectomy trial: a multicentre randomised trial comparing abdominal, vaginal and laparoscopic methods of hysterectomy

R Garry,[1*] J Fountain,[2] J Brown,[2] A Manca,[3] S Mason,[2] M Sculpher,[3] V Napp,[2] S Bridgman,[4] J Gray[5] and R Lilford[6]

[1] ng Edward Memorial Hospital, University of Western Australia, Australia
[2] Clinical Trials Research Unit, University of Leeds, UK
[3] Centre for Health Economics, University of York, UK
[4] Newcastle under Lyme Primary Care Trust, Directorate of Public Health, Newcastle under Lyme, UK
[5] Clinical Trials Unit, University of Newcastle, UK
[6] Department of Public Health and Epidemiology, University of Birmingham, UK

* Corresponding author

Executive summary

Health Technology Assessment 2004; Vol. 8: No. 26

Health Technology Assessment
NHS R&D HTA Programme

Executive summary

Introduction

The introduction of a third method of hysterectomy [laparoscopic hysterectomy (LH)] resulted in the urgent need to determine the appropriate role for the new laparoscopic approach before it became established into routine clinical practice. In 1992–3, before the introduction of LH, abdominal hysterectomy (AH) was used in 81% of the 72,269 hysterectomies performed in England and Wales. Direct comparison between the established techniques was difficult because most gynaecologists regarded the clinical indications for each procedure to be different. A study was therefore set up to compare both standard abdominal and vaginal (VH) methods of hysterectomy with LH, to give indications about the relative roles of all three procedures in this most commonly performed and important surgical operation.

Design

The study was of two parallel, unblinded, multi-centre randomised trials that compared LH with AH and VH. Patients were allocated to either the vaginal or abdominal trial by the individual surgeon according to their usual clinical practice. After allocation to a particular trial, the patient was then randomised to receive either LH or the default procedure in an unbalanced 2:1 manner; 63.5% of patients were allocated to the AH trial and 36.5% to the VH trial.

Setting

A total of 43 surgeons from 28 centres throughout the UK and two centres in South Africa took part in the study.

Subjects

A total of 1380 patients were recruited to the study, of whom 876 were included in the AH trial and 504 in the VH trial. In the AH trial, 584 patients had a laparoscopic type of hysterectomy (designated ALH) and 292 had a standard AH. In the VH trial 336 had a VLH and 168 had a standard VH.

Objectives

The objective of the study was to test the null hypothesis of no significant difference between LH and AH and VH with regard to each of the outcome measures of the trial, and also to assess the cost-effectiveness of the alternative procedures.

Outcome measures

The primary end-point of the trial was the occurrence of death or major complications (haemorrhage requiring blood transfusion, haematoma requiring transfusion/surgical drainage, bowel, bladder or urinary tract trauma, unintended laparotomy, wound dehiscence, pulmonary embolus and major anaesthetic problems). The secondary end-points were minor complication rates, blood loss (intraoperatively), pain assessment, sexual activity, body image, health status, quality of life (QoL) and resource use.

Sample size

The sample size for the AH trial was calculated from a previous study which indicated a 9% major complication rate in AH cases. From previous work we expected a 50% reduction in major complications with LH, which would require 487 patients in each arm to detect. In the same study, the rate of complications noted for VH was only 4%. To detect a similar rate of reduction would require 1141 patients per treatment arm. As VH was relatively infrequently performed, we did not expect to recruit this number but rather to collect as much data as possible as it would represent the largest such trial of VH ever performed and potentially be of value in a meta-analysis.

Economic evaluation methods

A cost–utility analysis was undertaken based on a 1-year time horizon. Costs were estimated from the perspective of the UK NHS. Resource use data included theatre resources, hospital stay and costs incurred during the postoperative period. Quality-adjusted life years (QALYs) were estimated using

the EQ-5D, which was administered at baseline and at 6 weeks, 4 months and 1 year after hospital discharge. Two comparisons were undertaken: VLH (n = 324) versus VH (n = 163) and ALH (n = 573) versus AH (n = 286). To account for the skewed nature of the data, 95% confidence intervals for the differential costs and QALYs were calculated using bias-corrected non-parametric bootstrapping. Missing resource use and EQ-5D data were imputed using a multivariate multiple imputation procedure. To account for uncertainty due to sampling variation, cost-effectiveness acceptability curves were plotted. Given the data collected within the trial, this curve shows the probability of laparoscopic-assisted hysterectomy being more cost-effective than conventional hysterectomy for different maximum levels that the decision-maker may be willing to pay for an additional QALY.

Results

Clinical

Compared with AH, LH was associated with a higher rate of major complications (11.1 versus 6.2%, p = 0.02), less postoperative pain (visual analogue scale score of 3.51 versus 3.88, p = 0.01) and shorter hospital stay (3 versus 4 days), but took longer to perform (84 versus 50 minutes). Securing the ovarian pedicles with laparoscopic sutures was used in only 7% of cases but was associated with 25% of the complications. At the 6 weeks postoperative point, ALH was associated with a significantly better physical component of the health survey questionnaire (SF-12), better body image scale (BIS) scores and a significantly increased frequency of sexual intercourse than AH. These differences were not observed at either 4 months or 12 months after surgery. There were no significant differences in any measured outcome between LH and VH except that VLH took longer to perform (72 versus 39 minutes) and was associated with a higher rate of detecting unexpected pathology (16.4 versus 4.8%, $p < 0.001$).

Economic

Compared with VH, VLH had a higher mean cost per patient of £401 [95% confidence interval (CI) £271 to £542] and higher mean QALYs of 0.0015 (95% CI –0.015 to 0.018), resulting in an incremental cost per QALY gained of £267,333. The probability that VLH is cost-effective was < 50% for a large range of willingness to pay values for an additional QALY. Compared with AH, ALH had a higher mean cost per patient of £186 (95% CI –£26 to £375) and higher mean QALYs of 0.007 (95% CI –0.008 to 0.023), resulting in an incremental cost per QALY gained of £26,571. If the NHS is willing to pay £30,000 for additional QALYs, the probability that ALH is cost-effective is 56%. The cost-effectiveness of laparoscopic procedures was sensitive to assumptions about the balance of reusable and disposable theatre equipment.

Conclusions

ALH is associated with a significantly higher risk of major complications and takes longer to perform than AH. ALH is, however, associated with less pain, quicker recovery and better short-term QoL after surgery than AH. The cost-effectiveness of ALH is finely balanced and depends on the threshold value the NHS attaches to an additional QALY and the error probability that the system is willing to accept in making its decision. Cost-effectiveness is also influenced by the balance of reusable equipment versus disposable consumables used during ALH. Individual surgeons must determine the optimum balance between patient-orientated benefits and the risk of severe complications. The clinical results from the vaginal trial were inconclusive as the study was under-powered. VLH was not cost-effective relative to VH.

Recommendations for future research

1. Application and relevance of QoL measures following hysterectomy, and long-term follow-up.
2. Patient preferences – balance between risks and benefits of the various forms of hysterectomy.
3. Reducing complication rates.
4. Improving gynaecological surgical training.
5. Surgeon effect in surgery trials.
6. Care pathways for hysterectomy.
7. Additional pathology identification in LH.
8. Meta-analysis/further trial of VH versus LH.

Publication

Garry R, Fountain J, Brown J, Manca A, Mason S, Sculpher M, *et al*. EVALUATE hysterectomy trial: a multicentre randomised trial comparing abdominal, vaginal and laparoscopic methods of hysterectomy. *Health Technol Assess* 2004;**8**(26).

NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, consumer groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including consumers) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or designing a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a limited time period.

Criteria for inclusion in the HTA monograph series
Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 94/16/03 (ISRCTN 93016131). As funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. 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 referees 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.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.