

Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation

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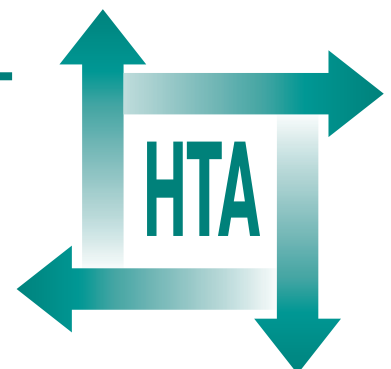
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Executive summary

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Executive summary

Previous guidance from the National Institute for Health and Clinical Excellence (NICE) on the use of laparoscopic surgery for colorectal cancer is that open surgery is the preferred procedure and that laparoscopic surgery should only be undertaken as part of a randomised controlled trial (RCT). This guidance was based on a technology assessment review conducted in 2000. New evidence has since become available, providing additional data on both the short- and long-term outcomes of surgery.

Objective of the study

The aim of this study was to determine the clinical effectiveness and cost-effectiveness of laparoscopic, laparoscopically assisted (hereafter together described as laparoscopic surgery) and hand-assisted laparoscopic surgery (HALS) in comparison with open surgery for the treatment of colorectal cancer. Where evidence allowed, possible differential effects were explored within a number of subgroups. The subgroups relate to the location of the cancer, the stage of the cancer and age at diagnosis.

Description of proposed service

In laparoscopic surgery, ports are inserted through which the laparoscopic instruments are manipulated. In practical terms, a totally laparoscopic procedure and a laparoscopically assisted procedure are considered comparable because of the size of incisions involved and hereafter are jointly described as laparoscopic surgery. In HALS, the surgeon inserts a hand into the abdomen while pneumoperitoneum is maintained.

Epidemiology and background

Colorectal cancer is the second most common malignancy in England and Wales. Approximately 36,000 new cases were diagnosed in 2002 and 17,000 people died from colorectal cancer in the same year. About 80% of all patients diagnosed with colorectal cancer (including some with advanced disease) undergo surgery.

Open resection is currently the standard method for primary resection of tumours. However, there

is significant morbidity associated with this procedure. Laparoscopic surgery is less invasive and may lead to more rapid recovery. The potential impact on cure rates is not clear. The major concerns are that tumour recurrence might occur at port sites and that clearance of the tumour may be less complete than during open surgery. However, it has also been suggested that reduced tissues trauma may lower disruption to the immune system and hence reduce the risk of recurrence. Additionally, there are disadvantages of laparoscopic surgery relating to the longer operation length, the cost of materials and the effect of surgeon experience on patient outcomes.

This review assesses the clinical effectiveness and cost-effectiveness of laparoscopic surgery and HALS in comparison with open surgery for the treatment of colorectal cancer. This was evaluated in terms of short-term, long-term and recurrence outcomes. The possible differential effects within predefined subgroups relating to the location of the cancer, the stage of the cancer and age at diagnosis were explored, although limited data were available.

Methods

Effectiveness

Electronic searches were undertaken from 2000 to May 2005 to identify published and unpublished trials of laparoscopic compared with open surgery for colorectal cancer. Systematic reviews and other evidence-based reports were identified and their lists of references searched. Selected conference proceedings were searched.

All RCTs and quasi-RCTs were eligible for inclusion if they compared laparoscopic surgery or HALS with open surgery for colorectal cancer. Also eligible were individual patient data (IPD) meta-analyses of such studies, where they provided additional data.

Two reviewers independently extracted data and assessed study quality. Dichotomous outcome data from individual trials were combined using the relative risk method and continuous outcomes



were combined using the Mantel–Haenszel weighted mean difference method. Summaries of the results from IPD meta-analyses were also presented.

Cost-effectiveness

A review of economic evaluations was undertaken by NICE in 2001. This review was updated from 2000 until July 2005. Quality assessment and data abstraction were conducted according to the guidelines for reviewers for the NHS Economic Evaluation Database.

An economic evaluation was also carried out using a Markov model incorporating the data from the systematic review. This model was first used to present a balance sheet for comparison of the surgical techniques. It was then used to estimate cost-effectiveness measured in terms of incremental cost per life-year gained and incremental cost per quality-adjusted life-year (QALY) for a time horizon up to 25 years.

Results

Number and quality of studies

In total, 46 reports on 20 studies (19 RCTs and one IPD meta-analysis) were included in the review of clinical effectiveness. The RCTs were of generally moderate quality with the number of participants varying between 16 and 1082, with 10 having less than 100 participants. The total numbers of trial participants who underwent laparoscopic or open surgery were 2429 and 2139, respectively.

Cost-effectiveness

A systematic review of four papers suggested that laparoscopic surgery is more costly than open surgery. However, the data they provided on effectiveness was poorer than the evidence from the review of effectiveness. One study compared the two forms of surgery in the context of an enhanced recovery programme. This study reported no difference in effectiveness and similar costs for both laparoscopic and open surgery. A further small study was identified comparing laparoscopic with HALS. This study also reported similar estimates of effectiveness and cost.

The estimates from the systematic review of clinical effectiveness were incorporated into a Markov model used to estimate cost-effectiveness for a time horizon of up to 25 years. In terms of incremental cost per life-year, laparoscopic surgery appeared more costly and no more effective than open surgery. With respect to incremental cost per

QALY, few data were available to differentiate between laparoscopic and open surgery. The results of the base-case analysis indicate that there is an approximately 40% chance that laparoscopic surgery is the more cost-effective intervention at a threshold willingness to pay for a QALY of £30,000. A second analysis assuming equal mortality and disease-free survival found that there was an approximately 50% likelihood at a similar threshold value.

Sensitivity analyses

Broadly similar results were found in the sensitivity analyses. A threshold analysis was performed to investigate the magnitude of QALY gain associated with quicker recovery following laparoscopic surgery required to provide an incremental cost per QALY of £30,000. The implied number of additional QALYs required would be 0.009–0.010 compared with open surgery.

Limitations of the calculations (assumptions made)

Much information available for some outcomes was reported in a form that was unsuitable for entry into the meta-analyses. The main limitations related to the quantity and quality of the data available. For example, the best data on mortality and disease-free survival were only available for a 3-year follow-up.

The nature of the data available also had an impact on the economic evaluation, which extrapolated outcomes for up to 25 years. More importantly, the data available to estimate costs were limited and the data used to estimate QALYs were highly suspect. The UK-based multicentre Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC) trial is due to report its economic evaluation soon and a draft version of a cost analysis conducted alongside the CLASICC trial was incorporated within the economic model as sensitivity analysis. The results of this analysis are not contained in this report as the data were supplied in confidence. Nevertheless, it is expected that this study will provide additional data on costs and will provide utility scores relevant to the UK.

Conclusions

Summary of benefits

Laparoscopic resection is associated with a quicker recovery (shorter time to return to usual activities and length of hospitalisation) and no evidence of a difference in mortality or disease-free

survival up to 3 years following surgery. However, operation times are longer and a significant number of procedures initiated laparoscopically may need to be converted to open surgery. The rate of conversion may be dependent on experience in terms of both patient selection and performing the technique.

Costs

Laparoscopic resection appears more costly to the health service than open resection, with an estimated extra total cost of between £250 and £300 per patient.

Cost-effectiveness

In terms of relative cost-effectiveness, laparoscopic resection is associated with a modest additional cost, short-term benefits associated with more rapid recovery and similar long-term outcomes in terms of survival and cure rates up to 3 years. Assuming equivalence of long-term outcomes, a judgement is required as to whether the benefits associated with earlier recovery are worth this extra cost.

Other important issues regarding implications

Should the use of laparoscopic surgery be increased from its current level of 0.1% to 25% of total resections, then the extra cost to the NHS has been estimated at £2.1 million per year.

The increased adoption of laparoscopic techniques may allow patients to return to usual activities faster. This may, for some people, reduce any loss of income. However, current provision is very limited and few patients have access to laparoscopic surgery.

For the NHS, increased use of laparoscopic surgery would lead to an increased requirement for training, which may be costly. Owing to the limited number of surgeons currently providing laparoscopic surgery, it may take some time before the provision of laparoscopic surgery can be increased.

Both open and laparoscopic surgery may be provided in the context of an enhanced recovery programme. Such an approach may reduce length of stay for both procedures but may not lead to reduced total costs to the NHS.

Notes on the generalisability of the findings

The 19 trials were conducted in a wide range of settings but data relating to the subgroups were limited. With respect to the data on costs, only two UK studies were identified, one of which was a preliminary analysis. Such cost data as were

available may not reflect practice within the UK. Further data, when available from the CLASICC trial, would improve the confidence with which the findings can be generalised.

Need for further research

Although useful data on long-term outcomes were available from the IPD meta-analysis identified as part of the review, this study only reported data from four RCTs for up to 3 years. The long-term follow-up of the RCT cohorts would be very useful and ideally these data should be incorporated into a wider IPD meta-analysis.

Few data were available on the long-term complications of surgery such as incisional hernias. Given the apparent similarity between the procedures in survival and disease-free survival, attention might be given to identifying differences in outcomes such as persisting pain, that may affect a patient's quality of life.

Key limitations of the economic model were the limited data on both costs and utilities. Once available, such data should be included in an updated model. At this point, further consideration should then be given as to whether additional data should be collected within ongoing trials.

Few data were available to assess the relative merits of HALS. Ideally, there should be more data from methodologically sound RCTs.

Further research is needed on whether the balance of advantages and disadvantages of laparoscopic surgery varies within subgroups based on the different stages and locations of disease.

Laparoscopic surgery for colorectal cancer is, like other laparoscopic procedures, technically challenging and performance is likely to improve with experience. This issue is important in its evaluation and further methodologically sound research related to this is warranted in the context of both trials and meta-analyses of trial data.

Publication

Murray A, Lourenco T, de Verteuil R, Hernandez R, Fraser C, McKinley A, *et al.* Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation. *Health Technol Assess* 2006;**10**(45).

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 Health and 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.

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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, service-users groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including service users) 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 conducting a trial to produce new evidence where none currently exists.

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