

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of laparoscopic versus open surgery on hospital costs for colon cancer: a population-based retrospective cohort study
AUTHORS	Laudicella, Mauro; Walsh, Brendan; Munasinghe, Aruna; Faiz, Omar

VERSION 1 - REVIEW

REVIEWER	Tarik Sammour MD Anderson Cancer Center Houston, Tx USA
REVIEW RETURNED	27-Jun-2016

GENERAL COMMENTS	<p>The authors have conducted an exhaustive propensity matched hospital cost analysis of a large dataset of NHS patients, comparing laparoscopic vs open surgery for colon cancer. The statistics appear well executed and the paper is expertly written. The authors are also to be commended for conducting research on cost considerations, an issue which is going to be at the forefront of our practice in the coming years.</p> <p>Some issues to discuss:</p> <ol style="list-style-type: none">1. The authors propensity matched for age, Charlson comorbidity index score, number of diagnoses, deprivation index and year of procedure. Why did they not propensity match for procedure type (e.g. r hemicolectomy, extended right, sigmoid, total etc)? This would have been more valid potentially than a post-hoc sensitivity analysis. If there is no strong reason for this, a line in the limitations should be added to discuss this issue.2. There needs to be frank discussion that this kind of study cannot account for opportunity cost differences between groups. Laparoscopic procedures take on average 60-90min longer to perform than open procedures in most randomized studies. What is the opportunity cost to the NHS in cumulative lost operating theatre time, given that in a typical colorectal practice, one or two smaller extra smaller cases could be performed with that time, or even more thought provoking is that fact that most surgeons could potentially perform 3 open colectomies in the time it takes to perform 2 laparoscopic ones. I would suggest the authors dedicate a paragraph in the discussion dealing with this issue which is not often discussed.
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REVIEWER	Marco E. Allaix Department of Surgical Sciences University of Torino, Italy
REVIEW RETURNED	01-Jul-2016

GENERAL COMMENTS	This is an interesting paper on costs of laparoscopic and open colon resection for cancer. However, the retrospective nature of the study does not allow to draw any conclusions, even though the authors performed statistical analyses to mitigate this major drawback. The two study population may be different. For instance, patients with larger tumors might have received open surgery. In addition, the difference in intraoperative costs between the two approaches was estimated by using results from other studies.
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REVIEWER	Antonio Biondi University of Catania Italy
REVIEW RETURNED	11-Aug-2016

GENERAL COMMENTS	<p>This is an interesting paper on the impact on hospital costs of laparoscopic versus open surgery in patients with colon cancer. Overall the manuscript is good and it is a current topic already widely debated in Literature. The statistical analysis has been well conducted and results are clearly presented. Figures and tables are exhaustive. I would only suggest to include some references on the topic in the discussion section:</p> <p>1)Marventano S et al, Evaluation of four comorbidity indices and Charlson comorbidity index adjustment for colorectal cancer patients. <i>Int J Colorectal Dis.</i> 2014; 2)Biondi A et al, Predictors of conversion in laparoscopic-assisted colectomy for colorectal cancer and clinical outcomes. <i>Surg Laparosc Endosc Percutan Tech.</i> 2014; 3)Biondi A et al, Laparoscopic vs. open approach for colorectal cancer: evolution over time of minimal invasive surgery. <i>BMC Surg</i> 2013; 4)Biondi A et al, Laparoscopic-assisted versus open surgery for colorectal cancer: short- and long-term outcomes comparison. <i>J Laparoendosc Adv Surg Tech A.</i> 2013</p>
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VERSION 1 – AUTHOR RESPONSE

*** Response to Reviewer #1

We thank Reviewer #1 for his positive comments. We cannot use procedure subtypes, such as hemicolectomy, extended right, and sigmoid, in the list of matching variables as they can be considered post-treatment assignment variables. The data generating process can be summarised in the following two steps: (1) the surgeon assesses the patient and tumour characteristics; (2) the surgeon assigns the patient to a laparoscopic or open procedure and to the most appropriate procedure subtype. Procedure subtypes are unsuitable as matching variables as they may not affect assignment to laparoscopic or open treatment. Moreover, it can be argued that procedure subtypes and the laparoscopic/open approach are too closely linked for assessing their effect separately, and this is outside the scope of our study. In sensitivity analyses, we showed evidence that the distribution of procedure subtypes is similar between laparoscopic and open interventions (Table A2), and thus they are unlikely to affect the results of our analysis.

We added a clarification on this point in the manuscript section “Sensitivity Analyses”:

“Amongst both laparoscopic and open surgery groups, the distribution in operation subtypes was broadly similar. The most common procedure in each group was extended right/right hemicolectomy followed by sigmoid colectomy (Appendix Table A2). Procedure subtypes were not included in the list of matching variables as they may not affect the allocation of patients to a laparoscopic or open intervention, and can be considered as part of the intervention.”

We agree with Reviewer #1 that the operation time needed to perform a laparoscopy is shorter than for open surgery. However, post-operative length of stay and length of stay associated with 90 days readmissions are shorter in patients receiving a laparoscopic procedure. Assessing opportunity costs is challenging and requires careful considerations of broader aspects associated with the two procedures that are outside the scope of this study. For instance, it is not straight forward to establish the alternative use for the extra bed days associated with post-operative length of stay and 90 days readmissions, and such an alternative use might differ across hospitals depending on the local demand for care. Our cost analysis focuses on the direct cost of the intervention and direct costs associated with readmissions occurring within 90 days from discharge. This approach is in line with the cost analysis performed in previous Health Technology Assessments (HTA) and Randomised Clinical Trials (RCT).

We added the following paragraph to the “Study limitations” section of the manuscript:

“Finally, this study focuses on direct hospital costs and does not consider the opportunity costs associated with the two interventions. On one hand, open resections are associated with shorter operating theatre time, which might offer the opportunity of performing more interventions per day. On the other hand, laparoscopic resections are associated with shorter post-operative length of stay and lower probability of a 90 days readmission, which might free up hospital beds and resources for treating other patients. Assessing opportunity costs is challenging as theatre time and hospital beds can be allocated to a number of alternative uses depending on the local demand for care and the local organization of health services.”

*** Response to Reviewer #2

We thank Reviewer #2 for his comments. We acknowledge that our study design cannot control for some of the patient characteristics that might determine treatment assignment, such as patient tumour size. However, a number of previous studies referenced in our manuscript adopted a similar observational study design for the analysis of the outcomes of laparoscopic and open resections in colorectal cancer patients:

Burns EM, Currie A, Bottle A, et al. Minimal-access colorectal surgery is associated with fewer adhesion-related admissions than open surgery. *Br J Surg* 2013;100:152–9.

Mamidanna R, Burns EM, Bottle A, et al. Reduced risk of medical morbidity and mortality in patients selected for laparoscopic colorectal resection in England: A population-based study. *Arch Surg* 2012;147:219–27.

Burns EM, Mamidanna R, Currie A, et al. The role of caseload in determining outcome following laparoscopic colorectal cancer resection: an observational study. *Surg Endosc* 2014;28:134–42.

We also acknowledge that the cost data used in this study do not report the difference in theatre costs associated with the two procedures, which we estimated by using a weighted average of the difference reported by two most recent RCTs on colon cancer patients.

We added a discussion on these two points in the “Study limitations” section of the paper:

“This study is based on a retrospective analysis of administrative data from HES. The study design does not allow us to control for a number of factors that are likely to influence patients’ allocation to a laparoscopic or open intervention and potentially result in selection bias. The HES data do not include information on some patient characteristics that might make them unfit for laparoscopic surgery, such as obesity and multiple previous abdominal operations. The use of stomas has also not been factored into the analysis, which may influence length of stay and readmission rates. Finally, cancer staging is not reported and we are unable to stratify for this variable in our analysis. Larger or more advanced tumours may be selected for open surgery over laparoscopy and these may be associated with more extensive procedures with increased postoperative complications and costs.[9] We use a number of techniques to mitigate potential selection bias from unreported patients’ characteristics.

First, our analysis is restricted to elective admissions only as emergency presentation are more likely to capture advanced tumours in a screened population. A similar approach has been used in a number of earlier studies using HES data to compare the outcomes of laparoscopy and open resections in colon cancer patients.[2,7,9,10,20,29]

Second, our study examines the difference in costs between the two procedures in 2006-2012 when laparoscopy reached a similar level of diffusion as open surgery reducing the scope for selection bias from early adopters. We use PSM techniques to create a similar sample of patients undergoing the two treatments in a large population of colon cancer patients. Although PSM cannot assure the same level of randomisation as an RCT, the issue of patient selection should be less relevant in our study population as the prevalence of laparoscopy is similar to open resection in the examined years. PSM allows us to analyse retrospective data on a very large population of patients reducing the problem of heterogeneity and increasing the power of the statistical analysis and external validity of results. Finally, we are able to produce robust evidence at a fraction of the cost of an RCT.

Third, we conducted a number of sensitivity analyses to test the robustness of our findings to potential sample selection bias. We examined a highly restricted sample of patients who had routine and uncomplicated elective admissions, and who are less likely to be frail and having comorbidities; differences in outcomes and cost savings are still present. We also repeated our analysis using 2012-13 data only in order to reduce the scope for selection bias from early adopters who are likely to select easier cases as the prevalence of laparoscopic surgery moves from 13.1% in 2006-07 to 54.5% in 2012-13. We find very similar results suggesting that the difference in costs and outcomes are explained by laparoscopic surgery rather than selection bias from early adopters.

This study combines retrospective data on hospital admissions from HES with data on service costs from the NSRC creating a powerful tool of analysis. The validity of these data for cost analysis has been demonstrated elsewhere [34] and the data have been successfully applied in a number of empirical investigations on the costs of care. [23–25] However, NSRC data do not report the difference in theatre costs associated with the two procedures, which was estimated using a weighted average of the difference reported by two most recent RCTs on colon cancer patients.[16,26]”

*** Response to Reviewer #3

We thank Reviewer #3 for his positive comments. We added references #3 and #4 from his suggested list to the manuscript.

VERSION 2 – REVIEW

REVIEWER	Tarik Sammour MD Anderson Cancer Center Houston Texas USA
REVIEW RETURNED	29-Sep-2016

GENERAL COMMENTS	The authors have addressed the reviewers concerns by adding additional information to limitations section and updating references. While it would have been nice to see additional analyses performed, I think the manuscript as it stands currently is suitable for publication.
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