

# Laparoscopic colorectal cancer surgery: panacea, placebo or just good fun?

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**“Numerous well-constructed multicenter trials have now demonstrated that the laparoscopic approach results in similar locoregional disease control and offers equivalent long-term oncological outcomes.”**

The timely collision of technological development of miniature video cameras, on-screen display and surgical opportunities led to the emergence of minimally invasive surgery, which has been met with open arms by surgeons and patients alike. Ever since the first laparoscopic cholecystectomy in 1987, the surgical world has been fascinated with broadening the potential indications for laparoscopic surgery. In the early 1990s, laparoscopic colorectal surgery was an emerging technique with unproven outcomes. Case reports documenting port site tumor recurrence raised concerns in the medical community, questioning the oncological outcomes and potential sacrifices that were being made in order to perform the resection in a minimally invasive manner.

The initially steep learning curve and evolving technology meant longer operating times and higher costs compared with open surgery, with perhaps minimal gains in terms of length of stay, opiate use and return of bowel function. Early adapters looked for the potential advantages of laparoscopic surgery and continued to refine techniques, thus reducing operating times and subsequent associated costs. However, issues still remain as surgeons moved from ‘what can we do?’ to ‘what should we do?’; the question arose as to whether laparoscopic colectomy could achieve an oncologically sound resection with an equivalent extent of dissection and lymph node yield without creating new patterns of disease recurrence. It has

taken almost 20 years from the initial trial designs to publication of the long-term results to clarify this. There are four landmark trials that have helped map the path forward. Interestingly, none of these trials were designed to determine whether or not laparoscopic surgery was superior to open surgery.

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The first substantive results to be published were from the COST study group and were reported in the *New England Journal of Medicine* in 2004 [1]. This was a noninferiority designed randomized controlled trial that recruited 872 patients from 48 institutions between August 1994 and August 2001. After a median follow-up of 4.4 years, the results showed no difference in overall survival or local recurrence.

The COLOR trial group reported their noninferiority design study in *Lancet Oncology* in 2009 [2]. They had recruited patients from March 1997 to March 2003. Exclusion criteria included those with a BMI over 30 – a somewhat

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interesting exclusion given the modern day obesity epidemic. They randomized 627 patients to laparoscopic surgery and 621 to open surgery with the primary end point being cancer-free survival at 3 years. The median follow-up was 53 months (range: 0.03–60 months). This study showed a trend towards increased disease-free survival in patients undergoing an open operation. The difference in overall survival at 3 years was 2.4% (95% CI: 2.1–7.0; hazard ratio: 0.95 [0.74–1.22]).

In January 2013, the UK Medical Research Council CLASICC trial long-term results were published in the *British Journal of Surgery* [3]. They had recruited 794 patients who underwent laparoscopic and open surgery at a ratio of 2:1, respectively, between July 1996 and July 2002. With a median follow-up of 62.9 months (range: 22.9–92.8), this noninferiority study found no difference in overall or disease-free survival; however, they did note that after 10 years of follow-up, right-sided colon cancer had an increased propensity for local recurrence (14.7 vs 5.2% for left-sided cancers).

Two meta-analyses of the literature have concluded equivalent oncological outcomes with laparoscopic colectomy. In 2007, the COST, CLASICC and COLOR trials combined their data sets, along with those from the Barcelona trial [4], to look at 3-year outcome data on patients who had undergone surgery before 1 March 2000 [5]. A total of 1765 patients were identified, from which a surprising 229 (13.0%) were excluded, leaving 796 laparoscopic open surgery and 740 open surgery patients. The overall 3-year survival was 82.2% for laparoscopic surgery patients and 83.5% for open surgery patients (95% CI of the difference: -3 to 5%). The associated hazard ratio was 1.07 (95% CI: 0.83–1.37;  $p = 0.61$ ).

A Cochrane review published in 2008 examined 12 randomized controlled trials involving 3346 patients [6]. They found no difference in local recurrence, the development of metastatic disease or long-term survival. They also found no difference in the development of incisional hernia ( $p = 0.32$ ) or need for reoperation for adhesions ( $p = 0.30$ ).

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Recent long-term follow-up data from the ALCCaS, which recruited 601 patients between January 1998 and April 2005, reported on 587 patients with a median follow-up of 52 months (range: 1 week to 11.4 years) [7]. This study concluded that despite some differences in short-term surrogate oncological markers, laparoscopic surgery was not inferior to open surgery as assessed by 5 year survival and recurrence. The laparoscopic patients were older at randomization and their pathology specimens had smaller distal margins. The open patients had some worse pathology parameters but there was no difference in disease stage. Interestingly, further subgroup analyses revealed that it may be elderly patients who stand to benefit most from

minimally invasive surgery. The ALCCaS data revealed that overall complication rates were reduced in patients who underwent laparoscopic resection as opposed to open surgery. This finding was largely attributed to a significant reduction in the postoperative complication rate in patients aged 70 years or older in the intention-to-treat laparoscopic group [8].

Implementation of enhanced recovery or fast track pathways has been a major advance in colorectal surgery over the past 15 years. This evidence-based multidisciplinary approach has resulted in better postoperative recovery, this has perhaps negated some of the initial advantages of laparoscopic surgery. Even within a fast track program, laparoscopic colorectal surgery may have advantages over open surgery. A recent meta-analysis of randomized trials comparing laparoscopic with open colorectal resections within a fast track program showed a significantly shorter in-hospital stay in the laparoscopic group of approximately 2 days without any significant difference in morbidity, mortality and hospital readmissions [9].

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So where does minimally invasive colorectal surgery stand in the year 2013? Numerous well-constructed multicenter trials have now demonstrated that the laparoscopic approach results in similar locoregional disease control and offers equivalent long-term oncological outcomes. The short-term advantages of laparoscopic surgery have been noted across many trials with small but important benefits, including reduced blood loss, less postoperative pain, earlier recovery of bowel function, earlier mobilization, reduced pulmonary complications and improved cosmesis.

However, one must consider the timing of the above mentioned trials. The patient accrual for these large multicenter trials occurred early in the learning curve of laparoscopic colorectal surgery, when surgical techniques and technology were evolving and surgeons were relatively inexperienced with the laparoscopic approach compared to major colonic resection. Modern colorectal surgeons have often grown up in the era of laparoscopy. They are likely to have completed more cholecystectomies and appendectomies laparoscopically than during open surgery, and in many centers the same bias applies to colonic resections. The laparoscopic technology that is currently available has vastly improved since the trials were conducted, with development of articulating laparoscopic stapling devices, intraluminal staplers, ultrasonic dissecting devices capable of coagulating and cutting tissues and high-definition optics with the ability to view in 3D, to mention but a few. One would expect that such rapid advances in minimally invasive surgical equipment coupled with the exponential rises in surgical experience would correlate to even greater benefits for the patient having their colonic resection

completed laparoscopically. Furthermore, recent data appear to confirm what was long suspected; patients who have undergone laparoscopic colorectal resections have a lower risk of developing clinically significant intra-abdominal adhesions, with lower rates of subsequent surgical intervention to deal with the complications of such adhesions [10]. Given the significant morbidity associated with adhesions, including small bowel obstruction, infertility and the increased duration and complexity of reoperative surgery, one cannot underestimate the potential gains of reduced adhesion formation.

With rapid advances in medical technology, new surgical techniques need to undergo the same rigorous assessment as novel drugs. High-quality trials are undertaken to ensure that corners are not being cut when new techniques are introduced, thus confirming that oncological outcomes remain equivalent – if not better – than the traditional gold-standard approach. Laparoscopic colorectal surgery has repeatedly undergone such assessment in numerous multicenter randomized trials, which have cemented its place in modern day oncology surgery.

Whether the potential gains from laparoscopic surgery outweigh the increased costs and operating times are beyond the scope of this editorial; however, recent trials suggest it may be that elderly patients have the most to gain from a minimally invasive approach. Given the aging population and high incidence of colon and rectal cancer worldwide, the potential advantages of minimally invasive surgery should be considered carefully. In addition, rapid advances in surgeons' laparoscopic skills and experience coupled with vast advances in minimally invasive surgical technology may mean that early trials have underestimated the potential gains of a laparoscopic approach to major colonic surgery.

#### Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

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