



Robotic-assisted laparoscopic surgery in treatment of rectal cancer

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One of the major benefits of conventional laparoscopic surgery has been the reduction of surgical trauma. Compared with laparotomy, conventional laparoscopic surgery has reduced blood loss, post-operative pain, and recovery time (1). Therefore, conventional laparoscopic surgery is now considered the treatment of choice for many abdominal procedures. The number of laparoscopic colorectal procedures in treatment of cancer has also increased in frequency in the last two decades (2), as laparoscopic surgery has demonstrated comparable oncological outcomes to laparotomy (3-6).

Several minimal invasive surgical options have evolved in recent years. Robotic-assisted laparoscopic surgery is gaining widespread usage in urological, gynecological, as well as abdominal surgical procedures. The benefits of robotic-assisted laparoscopic surgery such as 3-dimensional field of vision with depth perception, articulating instruments with wrist-like motion, and reduced tremor contribute to more precise dissection. These attributes may be valuable when performing surgery in difficult areas, such as the deep and narrow pelvis. Consequently, there is an increase in rate of colorectal procedures performed by robotic-assisted laparoscopic surgery (7).

Although a growing interest in robotic surgery is generating an increasing amount of literature on the subject, the ROLARR trial (8) is the first large randomized study designed to compare robotic-assisted laparoscopic surgery with conventional laparoscopic surgery in treatment of patients with rectal cancer. The study reports results of a total of 471 patients randomized to either robotic-assisted

(n=237) or laparoscopic surgery (n=234). The primary endpoint measured risk of conversion to open laparotomy and showed no significant difference between robotic-assisted laparoscopic surgery as compared with conventional laparoscopic surgery (8.1% *vs.* 12.2%, unadjusted difference, 4.1%; 95% CI: -1.4%–9.6%), and no difference with respect to odds of conversion (OR =0.61; 95% CI: 0.31–1.21; P=0.16). There was furthermore not found significant difference in any of the secondary endpoints including circumferential resection margin positivity, intra- and post-operative complications, 30-day mortality, or bladder and sexual function at 6 months. A difference was seen in the mean operative time, which was 37.5 minutes longer for the robotic-assisted group compared with conventional laparoscopic group (298.5 *vs.* 261.0 minutes). Additionally, the mean health care cost was, as expected, higher in the robotic-assisted laparoscopic group (mean difference =\$1,132; 95% CI: 191–2,072; P=0.001).

It has long been advocated for the superiority of robotic-assisted laparoscopic surgery over open surgery in the field of urological procedures and robotic-assisted prostatectomy is now considered as standard of choice in many clinics (9). However, a recent Cochrane review only identified two eligible randomized studies on robotic-assisted and laparoscopic versus open radical prostatectomy for prostate cancer, and concluded no significant benefits in terms of oncological outcome or urinary and sexual quality of life (10). The implementation of robotic-assisted surgery in the field of colorectal surgery has undergone the same success without clear evidence of benefits. In

contrast to other surgical fields where robotic-assisted laparoscopic surgery is compared with open procedures, the potential benefits of such comparisons are meaningless, as laparoscopic surgery for colorectal cancer is well implemented and has shown reduced morbidity and similar oncological outcomes (1,4). Consequently, robotic-assisted laparoscopic surgery must stand its trial against laparoscopy.

The many potential benefits of robotics are why robotic-assisted laparoscopic surgery is especially appealing in pelvic surgery. The deep and narrow pelvis presents challenges, especially in male and obese patients or patients with bulky tumors. The technical advantages of robotics could overcome some of the challenges of conventional laparoscopy and reduce conversion rates.

Two meta-analyses found significantly lower conversion rates for robotic-assisted laparoscopic surgery for rectal cancer (11,12). However, only one of the studies included in the meta-analysis was randomized (no difference regarding conversion to open surgery), allowing for selection bias, and the only two studies that found lower conversion rates had fewer than 100 patients. The ROLARR trial did not, however, show any significant decrease in conversion rate. A possible explanation may be that the sample size calculations were based on conversion rates from the CLASICC trial (34% conversion rate) (3). Since, the rate of conversion for laparoscopic rectal cancer surgery has reduced notably (4-6), and the most recent randomized trial reports conversion to open surgery in 9% of patients (6).

As for any new procedure, the learning curve may have an impact on the measured outcomes. The learning curve for robotics cannot, however, be expected to be as steep as for conventional laparoscopy, as surgeons performing robotic-assisted laparoscopic surgery are already well accustomed to laparoscopic surgery. A sensitivity analysis in the ROLARR trial revealed potential benefits of robotic surgery when the procedure was performed by a surgeon with 100 or more previous robotic-assisted laparoscopic procedures. Previous studies found a mean number of 39 cases required for the surgeon to be considered as an expert in robotic rectal cancer surgery (13). Subgroup analyses could not be performed in the ROLARR trial due to insufficient number of patients. However, a significant reduction in conversion rates was shown for robotic-assisted laparoscopic surgery in male patients. These analyses should be interpreted with caution due to very wide confidence intervals, indicating an underpowered study. Along with the narrow male pelvis, obesity is one of the main reasons for conversion to open

surgery. Robotic-assisted laparoscopic surgery has not yet proven to be valuable in such patients.

The advantages of articulating instruments and tremor filtering, with potential improvements in dissection precision, has been postulated to enhance the quality of resected specimen and in time improved survival. The benefit regarding reduction in circumferential margin positivity has failed to demonstrate in both smaller retrospective, larger retrospective and propensity score-adjusted, and now in the randomized ROLARR trial (8,14-18). The long-term oncological results are however not available yet.

Another major problem for patients operated for rectal cancer is sexual function and bladder dysfunction and is caused by damage to the pelvic autonomic nerves (19). The 3-dimensional view and articulating movements is what may allow the surgeon operating with robotic-assisted laparoscopy to improve the nerve-sparing technique when performing total mesorectal excision. Nonetheless, the positive effects of robotic-assisted laparoscopic surgery on sexual function and bladder function seen in smaller, non-randomized studies (20-23) could not be confirmed in the ROLARR trial.

When significant benefits on preoperative, oncological or functional outcomes of robotic-assisted laparoscopic surgery fail to demonstrate themselves, the issue of cost becomes growingly important. It was calculated in the ROLARR trial that the mean difference of the health care cost was higher in the robotic-assisted laparoscopy group than in the conventional laparoscopy group [mean difference =£980 or \$1,132 (95% CI: \$191-\$2,072); P=0.02]. The higher costs were a result of longer use of the operating room (longer operative time) and cost of instruments. The highest cost is however the purchase and maintenance of the robotic system, which was not included in the analysis due to variation between centers. The estimated cost of purchase of a robotic system varies between \$0.6 and \$2.5 million, with maintenance costs between \$80,000 and \$170,000 per year (24). In countries where the healthcare system is mainly government-funded, the issue of cost-effectiveness is crucial. As with all new technology, one could expect that the high cost of robotics will fall in the future. New companies increase the competition on the market, which will probably bring the cost of robotics down. With a cost reduction and similar or better outcomes, robotics may gain even wider spread in the surgical community.

So far, the literature has failed to demonstrate the superiority of robotic-assisted laparoscopic surgery in

treatment of patients with rectal cancer. It is understandable that randomized trials for technical innovations such as robotic-assisted laparoscopic surgery and other minimal invasive procedures are difficult to undertake. The surgeon must be allowed to gain experience with the new procedure and overcome the learning curve. A decrease of the wide implementation of robotic-assisted surgery across hospitals would not only reduce healthcare costs, but also contribute in keeping the robotic-assisted laparoscopic surgery in fewer hands, and hereby creating opportunities for better assessment of potential benefits. The gained knowledge and experience with robotic-assisted laparoscopic surgery should be preserved and further developed in order to improve patient outcomes. Additional randomized controlled trials are warranted as the experience with robotic-assisted laparoscopic surgery increases. It is likely that, as seen with improved conversion rates with increased use of laparoscopy, the benefits of robotics will present overtime.

The pathological specimen quality obtained with robotic-assisted laparoscopic surgery in the general rectal cancer patient may not have shown any significant improvement yet. However, randomized trials and meta-analyses with substantial number of patients to perform subgroup analysis on male, obese, and patients requiring low anterior resection should be undertaken in order to further investigate possible benefits in oncological and functional outcomes in selected patients.

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appropriately investigated and resolved.

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