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Minimally Invasive Colorectal Surgery - Present and Future Trends

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Abbreviations:

BMI – Body Mass Index;
RCT – Randomized Control Trial;
MIS – Minimally Invasive Surgery;
ESMO – European Society for Medical
Oncology;
NCCN – National Comprehensive Cancer
Network;
TME – Total Mesorectal Excision;
CRM – Circumferential Resection Margin;
RC – Robotic Colonic Surgery;
LC – Laparoscopic Colonic Surgery.

Rezumat

Abordul minimal invaziv în chirurgia colo-rectală – prezent și perspectivă

În ultimele decenii am asistat la dezvoltarea tehnicilor chirurgicale în paralel cu progresul tehnologic, cu apariția unor dispozitive din ce în ce mai sofisticate care au ca scopuri o intervenție chirurgicală cât mai puțin traumatizantă pentru pacient dar și obținerea unor rezultate cât mai bune perioperator și la distanță. După publicarea rezultatelor trialurilor randomizate, ghidurile actuale recomandă laparoscopia ca opțiune de tratament pentru cancerul de colon acolo unde există expertiză. Spre deosebire de colectomiile laparoscopice, rezecțiile de rect prin abord laparoscopic sunt intervenții dificile tehnic și sunt asociate cu o rată de adopție mică, o rată de conversie ridicată, rezultate funcționale și oncologice discutabile. Aceste dezavantaje au creat nevoia unui instrument mai bun. Sistemul robotic a fost conceput pentru a depăși limitele laparoscopiei în ceea ce privește vizibilitatea și manevrabilitatea instrumentelor. Abordul laparoscopic este indicat în cancerul de colon și de rect superior, în timp de abordul robotic facilitează mult intervențiile pentru cancer de rect mediu și inferior (în special la bărbați - pelvis îngust și la pacienții cu IMC ridicat). În aceste cazuri avantajele tehnice oferite de sistemul robotic facilitează mult abordul minimal invaziv și permite, de cele mai multe ori, preservarea plexurilor nervoase, conducând implicit la o calitate a vieții mai bună. Datorită costului ridicat și disponibilității scăzute a acestei metode, este greu de anticipat dacă va duce o creștere semnificativă a ratei de adopție a chirurgiei minimal invazive în cancerul colorectal.

Cuvinte cheie: chirurgie robotică, chirurgie laparoscopică, chirurgie minimal invazivă, cancer de rect, cancer de colon

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Abstract

In the last decades, surgical techniques have evolved, introducing better, more sophisticated devices, aimed at providing the least traumatizing surgical operations, with improved perioperative and long-time results. Based on the results of randomized control trials, current guidelines recommend laparoscopic approach for the treatment of colonic cancer where there is appropriate expertise. Compared with colonic resection, laparoscopic rectal resections are technically challenging procedures associated with a low adoption rate, high conversion rate, debatable functional and oncological results. These drawbacks created the need for a better tool. Robotic surgery emerged to overcome the limits of laparoscopy in terms of visibility and instrument maneuverability. Laparoscopic approach is best suited for colon and superior rectal cancers, while robotic approach is best indicated in medium and inferior rectal cancers (especially in men with a narrow pelvis and in patients with high BMI). In these cases the robotic approach greatly facilitates the minimally invasive approach and, most of the time, allows preservation of the pelvic autonomic nerves leading to a better quality of life. Due to increased costs and relative unavailability of this method, it is difficult to anticipate if the adoption rate of minimally invasive surgery in colorectal cancer will increase significantly.

Key words: robotic surgery, laparoscopic surgery, minimally invasive surgery, rectal cancer, colon cancer

Parallel to technological progress, in the last decades, surgical techniques have evolved, introducing better, more sophisticated devices, aimed at providing the least traumatizing surgical operations, with improved perioperative and long-time results. These techniques however come with a long learning curve and therefore are not easily acquired by surgeons. Thus, when laparoscopic technique emerged, it was used enthusiastically, but especially in operations without a great degree of complexity, such as cholecystectomy, excision of ovarian cysts or gastric fundoplication. In the case of complex surgical procedures and particularly in oncologic surgery, laparoscopy has been adopted slowly and even presently is performed only in a small number of centers. Although short-term clinical outcomes following laparoscopy were better when compared to open surgery (reduced pain, reduced length of stay and reduced ileus), there were concerns regarding port site metastasis and oncological outcomes.

Almost 10 years after the first laparoscopic colectomy was reported in 1991 (1), the first RCT comparing laparoscopic and open colectomy was published by Lacy et al. in 2002 (2) showing that laparoscopic colonic resections were not only

similar, but better than open colectomy regarding morbidity rate, hospital stay, tumor recurrence, and cancer-related survival. The following trials comparing laparoscopic to open colectomy demonstrated that the long-term oncological results (local recurrence, distant recurrence, disease-free and overall survival) were comparable for the two approaches (3-5).

A recent paper published in 2018 in the USA, shows yet another benefit of minimally invasive approach (both laparoscopic and robotic) – the fact that MIS approaches are associated with less delay in the initiation of adjuvant systemic therapy and improved survival in patients with stage III colon adenocarcinoma. The authors recommend MIS approaches for the treatment of stage III colon adenocarcinoma whenever possible (6).

In both ESMO (European Society for Medical Oncology) and NCCN (National Comprehensive Cancer Network) guidelines, laparoscopy is recommended for the treatment of colonic cancers. It is emphasized that the surgeon's experience is one of the main factors in choosing the surgical approach. ESMO guidelines indications for laparoscopic approach are: lack of serious abdominal adhesions due to prior major abdomi-

nal surgery and locally advanced disease (absence of acute bowel obstruction and/or perforation)(7).

NCCN guidelines have the following exclusion criteria when it comes to the use of laparoscopy: locally advanced cancers, perforation and acute bowel obstruction. The "Japanese Society for Cancer of the Colon and Rectum guidelines for the treatment of colorectal cancer" note that: "the indications for laparoscopic surgery are determined by considering the surgeon's experience and skills, as well as tumor factors, such as the location and degree of progression of the cancer, and patient factors, such as obesity and history of open abdominal surgery" (8).

There are significant differences between various countries, between high and low volume centers and, as expected, between the rural and urban areas, when it comes to the adoption rate of laparoscopy for the treatment of colorectal cancer. A recently published article shows that, in the US the rate of adoption of laparoscopy in colorectal cancer has increased from 51.3% in 2009 to 59.3% in 2012 (9).

In Asian countries this rate is even higher. According to the results of the JCOG0404 trial, in Japan, laparoscopy was not shown to be inferior compared with open surgery for overall survival, and its adoption rate had increased to approximately 70-75% (10).

Korea has also seen a significant increase in the rate of adoption of laparoscopy for colorectal cancers, from 42.6 to 64.7% in 2013 (11).

Compared with colonic resection, laparoscopic rectal resections are technically challenging procedures that require careful consideration as a result of additional concerns regarding an accurate total mesorectal excision and, consequently, the possibility of compromising the oncological outcome in cases of incomplete TME. Technical difficulties are related to the anatomy of the pelvis - a narrow space, where it is difficult to operate with straight laparoscopic instruments - this is why the conversion rate to open surgery is higher than the one for laparoscopic colectomy. Additional concerns are related to the functional outcome; there is a relatively high

rate of sexual and urinary dysfunction, therefore, laparoscopic rectal resection is even less widespread than laparoscopic colectomy.

There are some debates about the oncological results of laparoscopic surgery compared to open surgery for rectal cancer. First of the randomized trials comparing open to laparoscopic surgery for rectal cancer - UK CLASSIC Trial - concluded that laparoscopic anterior resection for cancer of the rectum can not be yet recommended as a routine procedure, based on their observation that the rate of increased positivity of the circumferential resection margin was higher in the laparoscopic group (12% versus 6%, $P = .19$) (12,13).

Published almost 10 years after, The CORE-AN trial (14) and Color II study (15) were both non inferiority studies which have concluded that laparoscopic resection for rectal cancer are similar in terms of oncological outcomes (disease free survival) as open resection, which justifies its use.

Two recent randomized control trials, conducted in different parts of the world showed concerning results, and failed to show the non-inferiority of laparoscopic rectal resection to open rectal resection, when analyzing the pathological outcomes. The ACOSOG Z6051 RCT was conducted in 35 institutions in the United States and Canada; nearly 500 patients with stage II or III mid or inferior rectal cancer (12 cm of the anal verge) were randomized after completion of neo-adjuvant therapy to laparoscopic or open resection. The criteria for assessing efficacy included all of the following: circumferential radial margin greater than 1 mm, distal margin without tumor, and a complete mesorectal excision. A 6% non-inferiority margin was chosen according to clinical relevance estimation. In the laparoscopic group a successful resection was performed in 81.7% of cases and in the open resection group in 86.9% of cases and did not support non-inferiority; P for noninferiority = .41 (16).

The Ala Cart RCT was conducted in 24 institutions from Australia and New Zealand; 475 patients with T1-T3 rectal adenocarcinoma were randomized to laparoscopic or open

resection. The primary end point was a successful resection, defined by all of the following criteria: complete excision of the mesorectum, circumferential margin ≥ 1 mm and a distal resection margin of at least 1 mm or greater. In the laparoscopic group a successful resection was obtained in 194 patients representing 82% and in the open surgery group in 208 patients representing 89%, ($P = .38$) for non-inferiority. The circumferential resection margin in the laparoscopic surgery group was negative in 222 patients representing 93% of cases and in the open surgery group in 228 patients which represents 97% of cases. The study showed a negative distal margin in 236 patients (99%) in the laparoscopic group and in 234 patients (99%) in the open group (17).

NCCN guidelines, recommend caution in choosing the minimally invasive approach for the treatment of rectal cancer because of the conflicting published results, especially the association between laparoscopy and a high rate of positive CMR and incomplete TME; the minimally invasive treatment is reserved for experienced surgeons and is not indicated in cases of locally advanced disease with a chance of positive circumferential margin based on staging.

Oncological concerns, technical difficulties, low adoption rate and high conversion rate associated with laparoscopy in the treatment of rectal cancer created the need for a better tool. As a natural step in technological development, robotic surgery emerged to overcome the limits of laparoscopy: 2D vision without depth perception of the surgical field, unarticulated instruments with limited mobility, the transmission and amplification of the surgeon's physiological tremor. Robotic surgery compensates all of these limitations of laparoscopic surgery, bringing the surgeons 3D surgical field, improved dexterity, precision and comfort. All these improvements allow tackling complex surgical procedures that can now be executed safely and with improved results (18,19).

Data published so far support the equivalence of robotic and laparoscopic surgery in terms of perioperative morbidity, adequate

oncological resection as CRM, harvested lymph nodes, and integrity of the mesorectal sheath at the end of resection for the treatment of rectal cancer (20).

Current evidence suggests a trend in reducing functional complications associated with robotic rectal surgery (urinary and sexual complications) (21-23).

Even though a recent RCT that compares laparoscopic with robotic TME – the ROLARR study showed a decrease in conversion rate favorable for the robotic approach - 8.1% in the robotic-assisted laparoscopic group and 12.2% in the conventional laparoscopic group (the decrease was not statistically significant) - it failed to prove the superiority of the robotic approach in terms of intraoperative complications, postoperative complications, plane of surgery, 30-day mortality, bladder dysfunction, and sexual dysfunction. Authors suggest a possible benefit in male patients, obese patients and for low anterior resection particularly, but these were results of a subgroup analysis and thus, require further research for confirmation (24).

Another thing that must be taken into account is the fact that the learning curve for robotic colorectal procedures seems to be between 15 and 30 cases, significantly less compared to laparoscopic colorectal surgery (50-60 cases) (25-27).

Because of the increased costs of robotic surgery, this surgical approach is far from imposing itself in current practice, despite its significant technical advantages. A recently published article focuses on two of the main shortcomings of robotic surgery: prolonged operative times compared to open surgery and increased costs.

An analysis of the National Surgical Quality Improvement Project database, has identified approximately 44.000 cases of colon cancers operated in a minimally invasive fashion in a three-year time-span, and these cases were compared (laparoscopic vs robotic approach). The results showed that there was a significant increase in robotic approach over time and that conversion rates dropped as well (6.0% among RC versus 11.5% among LC,

P <.001). RC operations however, tended to last longer (226 min versus 178 min, P <.001). Unadjusted complication rates were higher in the LC cohort (17.5% versus 15.2%, P <.001). In conclusion, after consideration of operative duration and patient covariates, RC was associated with similar rates of postoperative morbidity, but with decreased conversion rates and shorter hospitalization. The conclusion of the analysis suggested a potential solution for reducing the costs of robotic surgery - reducing the conversion rate and the number of hospitalization days (28).

The first laparoscopic procedure with curative intent for rectal cancer was performed in our Department in 1995 – an abdomino-perineal resection (29) and was followed shortly by the first laparoscopic sphincter preserving resection for rectal cancer (30).

Right from the beginning, 3 surgical teams for minimally invasive surgery were formed, which started undertaking more and more difficult cases. This evolution was sustained by the development of the laparoscopic instruments and every new instrument used in our current practice (ultrasonic, bipolar devices, Ligasure) allowed safe and accurate laparoscopic colorectal surgery while drastically reducing the length of the operations, which is one of the biggest shortcomings of laparoscopic surgery.

Every year, the number of laparoscopic operations performed for the treatment of colorectal cancer increased, but only slightly. In the first 15 years (1995-2010) we have performed 84 laparoscopic rectal resections; with a high percentage of abdomino-perineal resections (40%).(31)

In our Department, laparoscopy hasn't been a popular choice, only 3 out of 33 surgeons have overcome the steep learning curve for laparoscopic colorectal surgery, and another 3 surgeons are still in the learning process.

In 2008, through the technological platform „George Emil Palade”, the Surgical Department of the „Carol Davila” School of Medicine and Pharmacy acquired a „DaVinci S” robotic system with which over 1000 robotic operations were performed in the Center of

General Surgery and Liver Transplant of Fundeni Clinical Institute (32,33).

Establishing clear indications for robotic surgery is an ongoing process and, after radical prostatectomy (the first indication of robotic surgery), rectal cancer and gynecological cancer surgery seem to follow.

Between 2008 and 2013, when the National Program for robotic surgery was supported by the Ministry of Health, approximately 150 robotic operations were performed annually, with various indications. Quite soon, it became clear that robotic surgery was extremely useful in operations that were difficult to perform laparoscopically and especially in areas difficult to approach such as the pelvis and the sub-diaphragmatic area (19).

Probably as a natural course of evolution, the same surgeons skilled in laparoscopic surgery have become involved into robotic surgery. Even though many publications cite that laparoscopic training is not necessary in order to perform robotic operations, we believe that this previous experience is especially useful, both for the main operator, but more so for the surgeons assisting the main operator (34).

In order to clearly define the right indications for robotic surgery, we have also performed operations for colon cancer robotically (approximately 50 operations), and as we gained experience, it became clear that surgery for rectal cancer benefits most from the advantages of the robotic approach. Especially in the case of medium and inferior rectal tumors, which require total mesorectal excision, the DaVinci system clearly facilitates the surgical operation. Our first 100 cases of rectal cancer operated robotically comprised an article published in 2013 in the Romanian journal “Chirurgia” (35), and at that time, based on the number of cases, represented one of the top single center experiences worldwide. The conclusion of the article that robotic surgery was advantageous for both surgeon (improved dissection in a narrow pelvis) and patient (good quality of life by preservation of sexual and urinary function in the vast majority of patients, low morbidity and good midterm

oncological outcomes) was confirmed by studies published thereafter.

After performing nearly 200 robotic rectal resections, we have observed a very low conversion rate (2%). Regarding operative time, after rapidly overcoming the learning curve, the operative time was comparable with laparoscopic surgery (the median operative time for sphincter-saving procedures was 192 min, the median time for robotic abdomino-perineal resection was 150 min). Surgical morbidity was 12% associated with good functional results as well (four patients presented transitory post-operative urinary dysfunction; severe erectile dysfunction was reported in 3 patients).

After 2013, without financial support, the number of robotic operations decreased drastically, reaching a third of the number of procedures performed previously, which is why the indications had to be revised: in our current opinion, colon cancer can very well be operated laparoscopically. Rectal cancer, gynecological cancers and redo surgery for eso-gastric junction pathology remained good indications for robotic surgery.

After 2013, when the program of the Ministry of Health stopped, we resumed laparoscopic approach of colorectal cancer, acquiring an experience of over 700 cases. The number of cases has continued to slowly increase, so that in the last year, in one single team, over 50 laparoscopic colo-rectal operations were performed.

Nearly 25 years from our first laparoscopic operation for colorectal cancer, having acquired an experience of nearly 1000 minimally invasive cases (700 laparoscopy operations and 250 robotic ones), we believe that laparoscopic approach is best suited for colon and superior rectal cancers, while robotic approach is best indicated in medium and inferior rectal surgery. Robotic surgery in these cases is expected to overcome the low penetration rate of laparoscopy in this field. Unfortunately, even in our Department, due to the small number of experienced surgeons in minimally invasive surgery, the rate of adoption of laparoscopy does not exceed 15-

20%. From the data comprised from national surgery conferences, we conclude that minimally invasive approach remains the attribute of specialized centers, and that the rate of adoption of laparoscopy in Romania does not exceed 5%.

Concerning colonic cancer, the laparoscopic approach is virtually indicated in all cases, with few exceptions: locally invasive cancers on imaging studies, voluminous palpable tumors which require a large incision for removal and occlusive tumors where a laparoscopic field can't be achieved. Previous open surgery, in a patient's history, is not a contraindication for laparoscopy; the operation may begin with laparoscopic exploration and, judging by the case and the experience of the surgeon it may continue laparoscopically or be converted to a classic approach.

Robotic approach is indicated in medium and inferior rectal cancers, especially in men (due to a narrower pelvis) and in patients with high BMI, cases where the technical advantages provided by the robotic approach greatly facilitate the minimally invasive approach and, most of the time, allow preservation of the nervous structures leading to a better quality of life.

Although, internationally, the rate of adoption of laparoscopic surgery in colon cancer is in a continuous ascent, and current guidelines recommend laparoscopic approach for the treatment of colonic cancer, in Romania, laparoscopy proved itself an unpopular choice among surgeons. Robotic surgery for rectal cancer, with its shorter learning curve, lower conversion rate, comparable oncologic results and better functional results, is an alternative to be considered. Due to increased costs and relative unavailability of this method, it is difficult to anticipate if the adoption rate of minimally invasive surgery in colorectal cancer will increase significantly.

Conflict of Interest

The authors declare no conflicts of interests.

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