original article

Accreditation for colorectal cancer surgery in Italy. Preliminary results of a new program in a district hospital

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SUMMARY: Accreditation for colorectal cancer surgery in Italy. Preliminary results of a new program in a district hospital.

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Accreditation for colorectal (CR) cancer surgery has become a major issue in Italy. This study aimed to analyze the early results of a newly structured program for the treatment of CR cancer in a rural district hospital. Between 2017 and 2018, a total of 214 consecutive patients underwent a CR procedure for malignancy. There were 113 men and 101 women of a mean age of 74 years. Primary CR adenocarcinoma was diagnosed in 210 patients (98%). The incidence of stage I, II, III, and IV disease was 26%, 31%, 24%, and 19% respectively. Hospital volume increased tenfold compared to previous years. Anatomical resection was performed in 204 patients. Right-sided resection and resection of the transverse colon or left angle were performed in 76 (37%) and 14 (7%) patients, respectively. A resto-

rative left sided CR resection was performed in 80 patients (39%), whereas Hartmann procedure and Miles abdominal-perineal resection were performed in 27 (13%) and 6 (3%) patients, respectively. Total colectomy with ileorectal anastomosis was performed in one patient, and two more patients underwent atypical resection. Emergency cecostomy was performed in 15 patients and a colic endoprosthesis was implanted in one patient for obstruction and seven underwent resection afterwards. Laparoscopic resection was performed in 118 patients (57.8%), and the conversion rate was 2%. Overall morbidity, reintervention, and mortality rates were 24.6%, 3,7%, and 3.2%, respectively. The incidence of AL was 4.6%, and two patients died of the consequences of it after right hemicolectomy. Five more el-derly patients died for non-surgical related medical complications. The median hospital stay was ten days, and early unplanned readmission rate was 2%. Hospital and surgeon requirements, in terms of minimum volume, organization, and surgical outcome were fulfilled. A rural district hospital can become a tertiary referral center for the surrounding districts without imposing unreasonable travel burdens for patients. CR surgery represents a capital investment for the hospital administration since it shows the effectiveness and quality of care.

KEY WORDS: Accreditation - Colorectal cancer - Surgery - Italy.

Introduction

Colorectal cancer represents the most frequent malignancy in Italian population with nearly 52.000 new cases/year, 14% of all new cancers (1). The 5-year survival rate is 50% and the incidence is likely

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to increase because of the aging population. The national screening program is going to increase as well the number of early diagnosis of premalignant lesions requiring surgical treatment (2). Surgery represents the treatment of choice and since the hospital and surgeon case load were shown to be associated with surgical and oncological outcomes, accreditation has become a major issue in Italy (3-7). A list of hospital and surgeon requirements, in terms of minimal volume and organization, have been proposed by a panel of experts in order ensure a good practice in colorectal surgery all over the country (8). According to this program, the hospital must have the amenities of a first level hospital as it must ensure directly, or through arrangements and agreement with

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other accredited structures, specialized skills. An interdisciplinary tumor board is required to ensure a diagnostic and therapeutic flowchart to all patients. Case load should be considered for a single Complex Operative Unit, and a minimum of 50 elective resections/year of intraperitoneal colorectal cancers and of 15 extraperitoneal rectal cancer, with a mortality rate of less than 5% and 3%, respectively, are required to be accredited. The accreditation program goes through a period of 3 years at the end of which it is desirable that 50% of colorectal surgery is performed laparoscopically.

"Santa Scolastica" Community Hospital of Cassino is situated in a large rural territory equidistant more than a hundred kilometers from first level hospitals of two main cities such as Rome and Naples and can serve a population of more than 300 thousand people. The hospital administration supports the ambition of the surgical Unit to become a tertiary referral center for the surrounding Districts without imposing unreasonable travel burdens for patients (9). The aim of this study is to analyze the early results of a new structured program for the treatment of colorectal cancer in a rural community hospital in order to improve the critical aspects and achieve the goal.

Methods

Patients and organization

Between January 1, 2017 and December 31, 2018, all patients undergoing a colon and rectal procedures for malignancy or benign disease were entered prospectively in the department database. Patients' characteristics, intraoperative data and surgical outcome were collected. The preoperative assessment included colonoscopy with biopsy, thoracoabdominal TC with contrast enhancement, tumor markers, preanesthetic evaluation and in selected cases virtual colonoscopy and pelvic or liver RMI. The following factors were collected: age, sex, body mass index (BMI), presence or absence of comorbidities, ASA score, indication for surgery, intraoperative red blood cell (RBC) transfusion, duration of surgery, intraoperative findings, and postoperative complications and in-hospital mortality, reoperations, hospital stay, pathologic findings, hospitalization time and unplanned readmission within 30 days of discharge. Complications were classified according to Clavien-Dindo classification (10). Primary outcomes included the number of colorectal procedures for cancer per quarter time and in-hospital mortality, and secondary outcomes were laparoscopic rate, hospital stay, and 30-day unplanned readmission.

Patients were referred to the Surgical Unit from the Emergency Unit, and from the other medical Units of the hospital such as Gastroenterology, Internal Medicine, Geriatric, or Nephrology Units. However, most of the patients were referred as outpatients by gastroenterologist or family doctors after endoscopic diagnosis of colorectal disease to our surgical clinics. Services that are not present in "Santa Scolastica" District Hospital are located in the other two Hospitals of adjacent districts of the area such as Oncology and Radiotherapy Units in "S.S. Trinità" Community Hospital of Sora and Pathology in "Spaziani" Community Hospital in Frosinone. All patients with rectal cancers or with stage IV disease were discussed before surgery with medical oncologists and radiotherapists in order to define proper multimodal neoadjuvant treatments according to ESMO Clinical Practice Guidelines (11, 12).

Surgical approach

Mechanical bowel preparation with oral antibiotic prophylaxis and thrombosis prophylaxis with lowmolecular-weight heparin and elastic compression were routinely performed in all patients. Laparoscopic resection was the preferred technique of choice. After laparoscopic exploration of the abdominal cavity the procedures start with the primary ligation and section of the vascular pedicle followed by the posterior mobilization of the right or left colon. In case of right colectomy, the specimen is extracted through a small supraumbilical midline incision and an extracorporeal double layer hand-sewn anastomosis is performed. In case of cancer involving the splenic flexure resection is carried on in the same fashion used for right colectomy. In case of left colectomy or rectal resection, the specimen is extracted through a suprapubic transverse incision and a laparoscopic Knight-Griffen colorectal anastomosis is performed. Diverting ileostomy is routinely performed in case of neoadjuvant treatment for extraperitoneal rectal cancer. In elderly patients over 80 years old or in case of bulky locally advanced cancers a standard open approach was preferred. Hartmann colorectal resection with definitive stoma is usually performed in ultraoctagenarian patients suffering with rectal cancer that would require a low colorectal anastomosis with temporary ileostomy.

Postoperative treatment

A cautious application of early recovery after surgery (ERAS) principles was routinely applied with an increasing adherence during the study period (13, 14). ASA III, or more, and/or elderly patients received intensive care for at least 12 hours in Intensive Care Unit after surgery. Nasogastric tube was removed at the end of surgery and abdominal drainage was placed in regard of the anastomosis independent of the procedure in all patients. Oral feeding with liquids was started on postoperative day (POD) 3 for the first year, and POD 2 afterword, and patients were discharged when able to satisfy the daily needs for mobility and nutrition. Postoperative complications were classified as procedure related such as anastomotik leak (AL), haemorrhage, intraabdominal abcess, wound infection or general (pulmonary and cardiac). Postoperative infection criteria were hyperleukocytosis, combined with body temperature higher than 38.5 centigrades, positive biologic fluid cultures, such as blood, abdominal fluid, sputum. Thoraco-abdominal CT scan with intravenous and *per os* contrast enhancements was performed in all patients with infectious criteria to detect any sign of anastomotic leak, abdominal collection or pneumonia. Postoperative death was defined as any death during hospital stay. Early readmission within 30 day from discharge for any reason was recorded as unplanned.

Results

Between January 2017 and December 2018, a total of 248 consecutive patients were admitted at the Department of General Surgery at "Santa Scolastica" District Hospital of Cassino and underwent a colorectal surgical procedure. Thirty-four patients that underwent resective surgery for benign disease were excluded from the analysis. The charts of 214 patients that were admitted for malignancy were the object of this study. Patients characteristics and diagnosis are listed in Table 1. There were 113 male and 101 women of a median age of 74 years old. Median body mass index was 25.4 and median ASA score was 3. Primary colorectal adenocarcinoma was diagnosed in 210 patients, whereas in four patient colorectal resections was performed because of colon invasion from giant abdominal metastases in two cases (for renal cell carcinoma and melanoma) in one case for lo-

TABLE 1 - PATIENTS AND DISEASE CHARACTERISTICS. AGE, BMI, ARE EXPRESS IN MEAN.

Patients (number)		214	
Gender Male		113	
Age		74 [18-96]	
BMI		25,4	
ASA score		3 [2-3]	
Diagnosis	Primary adenocarcinoma	210	
	Gastric GIST	1	
	Metastases from Melanoma	1	
	Metastasis from RCC	1	
	Abdominal wall Desmoid tumor	1	
Stage of disease	Ι	50 (26%)	
-	II	64	
	III	48	
	IV	38	

cally advanced gastric stromal tumor and, in one case for abdominal wall desmoids tumor.

A total of 221 surgical procedure were performed in 214 patients, as depicted in Table 2. All patients were operated on within 30 days from diagnosis. Cecostomy was performed in 15 patients admitted for left sided CR cancer presenting with obstruction. A colic endoprosthesis was implanted before resection in one patient. A total of 204 anatomical resections and one local resection and one atypical resection were performed. Right hemicolectomy and ileocecal resection were performed in 73 and 3 patients (37%), respectively, whereas resection of the transverse colon or left angle in 3 and 11 patients (7%), respectively. In all these procedures a hand sewn anastomosis was performed. A left sided resection was performed in 113 patients. A restorative resection was performed in 80 patients (39%), whereas Hartmann procedure and Miles abdominal-perineal resection were performed in 27 (13%) and 6 (3%) patients, respectively. Particularly, resection of rectal cancer was performed in 34 patients, nine of whom have had a covering stoma done. Total colectomy with ileorectal anastomosis was performed in one patient, in one patient an atypical colectomy was performed and one patient underwent local excision of rectal adenoma. Resection was planned with curative intent in 164 patients, whereas 38 patients

TABLE 2 - TYPE OF OPERATION.

were diagnosed with stage IV disease and underwent resection after discussion at the interdisciplinary tumor board. Seven patient underwent to a cecostomy before the resection. Laparoscopic resection was performed in 118 patients (57%), and conversion rate was 3.5%. Intraoperative transfusion is necessary in 8 patients (3.9%), and median operative time was 137 minutes.

Morbidity, reintervention and mortality rates were 24.7% and 3.7%, 3.2%, respectively. After 171 restorative resections, the overall AL rate was 4.6%, being 5.2% after right sided resection with hand sewn ileocolic anastomosis, 0% after resection of the transverse colon or left angle with hand sewn colocolic anastomosis, and 5% after left sided resection with mechanical circular stapled anastomosis, respectively. After right sided resection mortality rate was 5.2%, and two patients died of the consequences of AL (1%) and two ASA IV patients, that underwent palliative resection, died of cardiac failure and renal failure, respectively. After left sided resection, three octogenarian apparently healthy patients died because of cardiac arrest, respiratory failure, and septic shock, respectively, accounting for a mortality rate of 2.6%. In this series, five patients, aged between 77 and 84 years, died of medical complications in absence of any detected surgical complication. The types of complications are listed in

Type of Resection		
	Cecostomy	8
	Ileocecal resection	3
	Right hemicolectomy	73
	Transverse colon resection	3
	Left angle colon resection	11
	Left hemicolectomy	31
	Sigmoid resection	15
	Rectal anterior resection	25
	Rectal anterior resection with ileostomy	9
	Hartman resection	27
	Addominoperineal resection	6
	Total Colectomy	1
	Other	2
Intraoperative trasfusion		8
Laparoscopic Approach		114
Convertion Rate		4 (3.5%)
Operative Time		137 min

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Patients with complications		53 (24,7 %)
Clavien Dindo Grade	Ι	16 (7.8%)
	II	21 (10.2%)
	IIIa/IIIb	1/7 (3.9%)
	IV	1 (0.5%)
	V - mortality	7 (3.4%)
Surgical complications	Anastomotic Leak*	8 (4.6%)*
0	Abdominal abscess	3
	Bleeding	8
	Paralytic ileus	7
	Urinary complication	6
	Wound infection	3
	Occlusion	1
General complication	Cardiorespiratory	12
Re-intervention		8 (3.7%)
Length of Stay		10 days
Readmission rate		2%

TABLE 3 - INCIDENCE AND TYPE OF COMPLICATIONS IN 204 RESECTIVE PROCEDURE.

* in 171 restorative procedures

Table 3. Median hospital stay was 10 days, and an improvement of the length of stay was recorded during the study period of our experience (Figure 1). Thirty day readmission rate was 2% (cholecistitis, urinary retention, occlusion, ileocolic anastomosis

phlegmon without leak, and with wound dehiscence). Only one patient required reintervention after discharge because of early dehiscence of aponeurotic plane, and a direct abdominal wall closure was required.

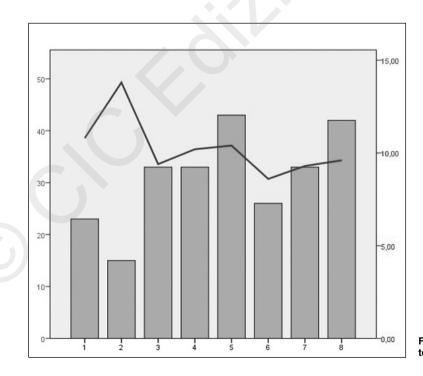


Figure 1 - Number of resection according to quarter time. Green Curve represent length of stay.

Discussion

Colorectal (CR) surgery remains a major challenge for all hospitals, especially those with minor ancillary supports, because morbidity and mortality rates remain high in both emergency and elective settings. In large nationwide studies the mortality rate after CR surgery ranges between 1% and 5% in elective procedures and between 10 and 25% in emergency (15-20). The incidence of colorectal disease is high, and it represents the ideal testing ground to determine the effectiveness and quality of care. This study provides insight in two years of practicing in a new CR cancer surgery program in a rural district hospital, and shows that surgeon skill and experience represent the keystone for creation and development of a new program. In the five previous years, 5-10 colorectal resection/year for cancer were performed at the same hospital. Implementing the surgical team with an experienced surgeon (SR) in cancer surgery, and particularly in CR laparoscopic surgery, resulted in a tenfold increase of the case load and the standard requirements recommended for accreditation were quickly reached (21). A total of 206 colorectal resection for cancer were performed in the two-year study period and Figure 1 shows the number of resections according to quarter time, reaching peaks of 15 colorectal resection per month. During the same period, 34 resections for benign disease were performed. As the case load increased, the working hours in the operating room necessarily doubled thanks to a novel planning and implementation of the anesthesiologist and nurse teams.

The analysis of the results showed that morbidity and mortality rates were consistent with the recommended standards. Postoperative mortality was 3.2% in this series. Two patients died of the septic consequences of an AL after right hemicolectomy, however five patients, aged between 77 and 84 years, died of medical complications in absence of any detected surgical complication. AL represents the most important complication and the greatest fear for a colorectal surgeon, since it is likely to develop sepsis and multisystem organ failure and it still represents a major cause of postoperative death. Right hemicolectomy and ileocolic anastomosis do not represent the most challenging procedure in CR surgery, however, it remains the Achille's talon of colorectal surgery because of the devastating short-term outcome of AL (22, 23). A recent review shows that the incidence of AL after right hemicolectomy ranges between 4 and 6% (24) and in our series it occurred in four patients (5.2%). Two of these patients were admitted for obstruction and a dilated ileum might have played a role in the genesis of the leakage. Despite retrospective and prospective series found no significant difference in the incidence of AL between hand-sewn and stapled anastomosis (25-27), the experience of the surgeon performing the procedure was found to impact the risk of leak. Moreover, a recent study demonstrated a 2-fold increase in AL after stapled versus handsewn ileocolic anastomoses (23). In our experience, the technical choice of the hand-sewn anastomosis was based on the previous personal experience of the surgeon (SR) and its selfconfidence. The incidence of anastomotic leak after left sided resection varies between 0,5% and 20 (24). Male gender, obesity, malnutrition, bulky tumor, neoadjuvant therapy and the low level of anastomosis represent the major risk factors for anastomotic leak. Performing a covering stoma in high risk patients or difficult anastomosis is very effective in the reduction of the clinically adverse effect of an anastomotic leak, including fecal peritonitis and septicemia, and thus mortality. Despite ERAS program suggests to abandon the use of abdominal drainage, in this initial phase of the program we preferred to routinely place the drainage in regard of all anastomosis and it was wery helpful in the early diagnosis and treatment of the leak (28, 29). In our series, the rate of other major surgical complication such as haemorrhage and surgical site infections was low. Careful preoperative radiological evaluation of the technical risks and planning of the procedure using a cautious bloodless surgical technique was effective in preventing intraoperative or postoperative bleedings. Prevention of the surgical site infection represented a major issue in the education and surgical process organization through effective and persistent skin antisepsis, meticulous operative technique, appropriate antibiotic prophylaxis and glucose control preventing hyperglycaemia.

In this single center series, the median age was

significantly higher compared to that reported in multicentric studies and general complications represented the main cause of postoperative death (4, 5, 16). Age older than 70 years represent one of the four independent risk factors for mortality in the AFC score for colorectal surgery (30) and in our series, median age was 74 years. Multidisciplinary discussion and preoperative assessment of the preoperative risk factors represented another major issue during our experience. Anesthetists evaluated high risk patients after cardiologic and pulmonary consult, and surgery was planned with the support of postoperative intensive care unit. An internal audit and critical review was undertaken but we did not find any substantial failure in the surgical process that could make non surgical related postoperative deaths preventable. Advanced stage disease increases as well the risk of 90-day mortality (20). Thirtyeight patients with stage IV disease underwent resection, however, two of them did not recover after surgery without any detected surgical complication. Decision for palliative resection was taken since there was no other treatment modalities for their disease, and these ASA IV patients (cardiac failure and renal failure) with perfect level of consciousness were treated for 10 days before operation for this purpose. In such high risk patients, it is difficult for surgeon alone to decide not to go ahead with surgery, and the right decision should be patient-centered, based on good evidence, clearly communicated and made in a supportive environment. Surgeon, other health professionals, the patient and the family have the right and a responsibility to be included in the decision making. Paradoxically, since high volume hospitals take care of more complicated cases, the more the indications are extended to high risk patients the more the morbidity and mortality rates can increase. The incidence of Hartmann resection in this series was quite high (13%) because of the high incidence of ultra octogenarian patients or locally advanced rectal cancers, and it remains a good indication in high risk patients, and in this subset of patient no postoperative death were recorded. Prehabilitation represents a new field in the development of ERAS program that has been shown to improve significantly postoperative outcome. Immunonutrition and supplemented diet can improve postoperative results as well as early mobilization and walking especially in fragile and elderly patients (31, 32).

The laparoscopic approach represented the technique of choice (21), however, developing the laparoscopic approach resulted a difficult task. Technical devices and instruments had to be updated and required continuous education of all the surgeons and the rotating nursing staff. It took one year to make CR laparoscopic surgery familiar and routinely performed. The laparoscopic approach rate of 55% in this series is quite high, taking into account also the unselected patients population, and it largely fulfilled the requirements for accreditation (33). However, we agree that the laparoscopic approach should be selectively proposed in fragile elderly patients, and open standard resection was undertaken in bulky tumors or in patients with severe cardiopulmonary disease (29, 34).

Hospital stay showed a significant reduction during the study period, and the readmission rate was very low, demonstrating that a cautious and tailored application of the ERAS principles can rapidly provide excellent results without affecting postoperative outcome even in a rural context.

This study shows that the staff is essential and education represents the most important factor for team building. Continuous medical education remain mandatory with the aim of implementing the ERAS program and further improve surgical outcomes (35). The hospital medical engineer and pharmacist also should become part of the team and take part to the drafting of a shared protocol because such a program includes crucial technical instruments and drugs. One of the most important aspects that emerged from the daily clinical practice, that cannot be directly demonstrated by data, was the rapidly improving expertise in this field by all the surgical team including surgeon and nursing staff of the ward and operating room. A significant change in mindset, resulting in improved collaboration and lower stress level in everyday clinical practice. Behavioral changes and process optimization was promoted in all the surgical process with the aim to prevent the surgical site infections that represent a major issue in colorectal surgery.

In conclusion, rural community hospital can be-

come referral centers for CR cancer and avoid unreasonable travel burdens for patients. The selection of an appropriate qualified surgeon is crucial to develop such a program, form a multidisciplinary team and achieve the requirements for accreditation. CR surgery represent a capital investment for the hospital administration since it shows the effectiveness and quality of care.

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References

- 1. AIOM, AIRTUM. I numeri del cancro in Italia 2018. 8° Edizione.
- 2. Osservatorio Nazionale Screening. Report ONS 2017.
- Lenzi J, Lombardi R, Gori D, Zannini N, Tedesco D, Masetti M, Ovine E, Fantini MP. Impact of procedure volumes and focused practice on short-term outcomes of elective and urgent colon cancer resection in Italy. PLoS One. 2013;8:1-7.
- Buurma M1, Kroon HM1, Reimers MS2, Neijenhuis PA1. Influence of Individual Surgeon Volume on Oncological Outcome of Colorectal Cancer Surgery. Int J Surg Oncol. 2015;2015:464570. doi: 10.1155/2015/464570. Epub 2015 Sep 3.
- Liu CJ, Chou YJ, Teng CJ, Lin CC, Lee YT, Hu YW, Yeh CM, Chen TJ, Huang N. Association of surgeon volume and hospital volume with the outcome of patients receiving definitive surgery for colorectal cancer: A nationwide population-based study. Cancer. 2015 Aug 15;121(16):2782-90. doi: 10.1002/cncr.29356. Epub 2015 Apr 17. PMID:25892632.
- Schrag D, Cramer LD, Bach PB, Cohen AM, Warren JL, Begg CB. Influence of hospital procedure volume on outcomes following surgery for colon cancer. JAMA. 2000 Dec 20;284(23):3028-35.
- Cornish JA, Tekkis PP, Tan E, Tilney HS, Thompson MR, Smith JJ. The national bowel cancer audit project: the impact of organisational structure on outcome in operative bowel cancer within the United Kingdom. Surg Oncol. 2011 Jun;20(2):e72-7. doi: 10.1016/j.suronc.2010.10.005. Epub 2010 Nov 10. Review.
- Ruffo G, Barugola G, Rossini, R and Sartori CA. Colorectal surgery in Italy. Criteria to identify the hospital units and the tertiary referral centers entitled to perform it. Updates Surg. 2016;68:123-128.

- Versteeg SE, Ho VKY, Siesling S, Varkevisser M. Centralisation of cancer surgery and the impact on patients' travel burden. Health Policy. 2018 Sep;122(9):1028-1034. doi: 10.1016/j.healthpol.2018.07.002. Epub 2018 Jul 6.
- Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg. 2009 Aug;250(2):187-96. doi: 10.1097/SLA.0b013e3181b13ca2.
- 11. Van Cutsem E, Cervantes A, Adam R, Sobrero A, Van Krieken JH, Aderka D, Aranda Aguilar E, Bardelli A, Benson A, Bodoky G, Ciardiello F, D'Hoore A, Diaz-Rubio E, Douillard JY, Ducreux M, Falcone A, Grothey A, Gruenberger T, Haustermans K, Heinemann V, Hoff P, Köhne CH, Labianca R, Laurent-Puig P, Ma B, Maughan T, Muro K, Normanno N, Österlund P, Oyen WJ, Papamichael D, Pentheroudakis G, Pfeiffer P, Price TJ, Punt C, Ricke J, Roth A, Salazar R, Scheithauer W, Schmoll HJ, Tabernero J, Taïeb J, Tejpar S, Wasan H, Yoshino T, Zaanan A, Arnold D. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol. 2016 Aug;27(8):1386-422. doi: 10.1093/annonc/mdw235. Epub 2016 Jul 5.
- Glimelius B, Tiret E, Cervantes A, Arnold D; ESMO Guidelines Working Group. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013 Oct;24 Suppl 6:vi81-8. doi: 10.1093/annonc/mdt240.
- Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controller trials. World J Surg. 2014;38(6):1531-41.
- 14. Arrik L, Mayson K, Hong T, Warnock G. Enhanced recovery

after colorectal surgery: Impact of protocol adherence on patient outcomes. J Clin Anesth. 2018;55:7-12.

- Engel AF, Oomen JL, Knol DL, Cuesta MA. Operative mortality after colorectal resection in the Netherlands. Br J Surg. 2005 Dec;92(12):1526-32. PMID:16273529.
- Alves A, Panis Y, Mathieu P, Mantion G, Kwiatkowski F, Slim K; Association Française de Chirurgie. Postoperative mortality and morbidity in French patients undergoing colorectal surgery: results of a prospective multicenter study. Arch Surg. 2005 Mar;140(3):278-83, discussion 284.
- Borowski DW, Kelly SB, Bradburn DM, Wilson RG, Gunn A, Ratcliffe AA; Northern Region Colorectal Cancer Audit Group. Impact of surgeon volume and specialization on shortterm outcomes in colorectal cancer surgery. Br J Surg. 2007 Jul;94(7):880-9.
- Contant CM, Hop WC, van't Sant HP, Oostvogel HJ, Smeets HJ, Stassen LP, Neijenhuis PA, Idenburg FJ, Dijkhuis CM, Heres P, van Tets WF, Gerritsen JJ, Weidema WF. Mechanical bowel preparation for elective colorectal surgery: a multicentre randomised trial. Lancet. 2007 Dec 22;370(9605):2112-7.
- Masoomi H, Kang CY, Chen A, Mills S, Dolich MO, Carmichael JC, Stamos MJ. Predictive factors of in-hospital mortality in colon and rectal surgery. J Am Coll Surg. 2012 Aug;215(2):255-61. doi: 10.1016/j.jamcollsurg.2012.04.019. Epub 2012 May 27.
- Theile DE, Philpot S, Blake M, Harrington J, Youl PH. Outcomes following colorectal cancer surgery: Results from a population-based study in Queensland, Australia, using quality indicators. J Eval Clin Pract. 2018 Dec 21. doi: 10.1111/jep.13087. [Epub ahead of print].
- Santoro E, Carboni F, Ettorre GM, Lepiane P, Mancini P, Santoro R, Santoro E. Early results and complications of colorectal laparoscopic surgery and analysis of risk factors in 492 operated cases. Updates Surg. 2010 Dec;62(3-4):135-41. doi: 10.1007/s13304-010-0029-4.PMID:21181332.
- 22. 2015 European Society of Coloproctology collaborating group. The relationship between method of anastomosis and anastomotic failure after right hemicolectomy and ileo-caecal resection: an international snapshot audit. Colorectal Dis. 2017 Mar 6. doi: 10.1111/codi.13646. [Epub ahead of print].
- Nordholm-Carstensen A, Schnack Rasmussen M, Krarup PM. Increased Leak Rates Following Stapled versus Handsewn Ileocolic Anastomosis in Patients with Right-sided Colon Cancer: A Nationwide Cohort Study. Dis Colon Rectum. 2018 Nov 26. doi: 10.1097/DCR.000000000001289. [Epub ahead of print]bPMID:30489322.
- Sciuto A, Merola G, De Palma GD, Sodo M, Pirozzi F, Bracale UM, Bracale U. Predictive factors for anastomotic leakage after laparoscopic colorectal surgery. World J Gastroenterol. 2018 Jun 7;24(21):2247-2260. doi: 10.3748/wjg.v24.i21.2247. Review. PMID:29881234.
- Milone M, Elmore U, Di Salvo E, Delrio P, Bucci L, Ferulano GP, Napolitano C, Angiolini MR, Bracale U, Clemente M, D'ambra M, Luglio G, Musella M, Pace U, Rosati R, Milone F. Intracorporeal versus extracorporeal anastomosis. Results from a multicentre comparative study on 512 right-sided colorectal cancers. Surg Endosc. 2015 Aug;29(8):2314-20. doi: 10.1007/s00464-014-3950-7. Epub 2014 Nov 21. PMID:25414066.

- 26. 2015 European Society of Coloproctology Collaborating Group. The impact of stapling technique and surgeon specialism on anastomotic failure after right-sided colorectal resection: an international multicentre, prospective audit. Colorectal Dis. 2018 Nov;20(11):1028-1040. doi: 10.1111/codi.14308. Epub 2018 Jul 12.
- Marinello FG, Baguena G, Lucas E, Frasson M, Hervás D, Flor-Lorente B, Esclapez P, Espí A, García-Granero E. Anastomotic leakage after colon cancer resection: does the individual surgeon matter? Colorectal Dis. 2016 Jun;18(6):562-9. doi: 10.1111/codi.13212. PMID:26558741.
- ERAS Compliance Group. The Impact of Enhanced Recovery Protocol Compliance on Elective Colorectal Cancer Resection: Results From an International Registry. Ann Surg. 2015 Jun;261(6):1153-9. doi: 10.1097/SLA.000000000001029. PMID:25671587.
- Braga M, Pecorelli N, Scatizzi M, Borghi F, Missana G, Radrizzani D; PeriOperative Italian Society. Enhanced Recovery Program in High-Risk Patients Undergoing Colorectal Surgery: Results from the PeriOperative Italian Society Registry. World J Surg. 2017 Mar;41(3):860-867. doi: 10.1007/s00268-016-3766-9.
- 30. Alves A, Panis Y, Mantion G, Slim K, Kwiatkowski F, Vicaut E. The AFC score: validation of a 4-item predicting score of postoperative mortality after colorectal resection for cancer or diverticulitis: results of a prospective multicenter study in 1049 patients. Ann Surg. 2007 Jul;246(1):91-6.
- Stethen TW, Ghazi YA, Heidel RE, Daley BJ, Barnes L, Patterson D, McLoughlin JM. Walking to recovery: the effects of missed ambulation events on postsurgical recovery after bowel resection. J Gastrointest Oncol. 2018 Oct;9(5):953-961. doi: 0.21037/jgo.2017.11.05.
- Lirosi MC, Tirelli F, Biondi A, Mele MC, Larotonda C, Lorenzon L, D'Ugo D, Gasbarrini A, Persiani R. Enhanced Recovery Program for Colorectal Surgery: a Focus on Elderly Patients Over 75 Years Old. J Gastrointest Surg. 2018 Sep 5. doi: 10.1007/s11605-018-3943-2. [Epub ahead of print]. PMID:30187323.
- 33. Elmore U, Vignali A, Rosati R, Valeri A, Silecchia G; SICE colorectal collaborative group. SICE national survey: current state on the adoption of laparoscopic approach to the treatment of colorectal disease in Italy. Updates Surg. 2018 Nov 23. doi: 10.1007/s13304-018-0606-5. [Epub ahead of print].
- 34. Chern YJ, Tsai WS, Hung HY, Chen JS, Tang R, Chiang JM, Yeh CY, You YT, Hsieh PS, Chiang SF, Lai CC, Lin GP, Hsu YR, You JF. The dark side of laparoscopic surgery for colorectal cancer patients aged 75 years or older. Int J Colorectal Dis. 2018 Jul 15. doi: 10.1007/s00384-018-3130-7. [Epub ahead of print]. PMID:30008115.
- 35. Vincent X. Liu, MD, MS, Efren Rosas, MD, Judith Hwang, MD, MBA, Eric Cain, MD, MBA, Anne Foss-Durant, RN, MSN, FNP, MBA, Molly Clopp, RN, MS, MBA, Mengfei Huang, MSc, Derrick C Lee, MD, Alex Mustille, BS, Patricia Kipnis, PhD, and Stephen Parodi, MD. Enhanced Recovery After Surgery Program Implementation in 2 Surgical Populations in an Integrated Health Care Delivery System. JAMA Surg. 2017 July 19;152(7):e171032. doi:10.1001/jamasurg. 2017.1032.