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EDITORIAL

How robotics is changing and will change the field of colorectal surgery

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Abstract

During the last decade there has been a significant upward trend in colon and rectal minimally invasive surgery which can be attributed largely to the acceptance of robotic surgery platforms such as the da Vinci® robotic system. The fourth generation da Vinci® system, introduced in 2014, includes integrated table motion, intelligent laser targeted docking and more sophisticated instrumentation and imaging. These developments have enabled more surgeons to efficiently and safely perform multi-quadrant operations. Firefly® technology allows assessment of colon perfusion and identification of ureters, and has shown potential in detecting occult recurrence or metastasis using molecular-labelled tumor markers. Wristed instrumentation has increased the technical ease of intracorporeal anastomosis (ICA) for many surgeons, leading to more common use of ICA during right colectomy. Advanced imaging has shown potential to decrease the incidence of presacral nerve injury and improve urogenital outcomes after pelvic surgery, as has been the case in robotic urologic procedures. Finally, the robotic platform lends itself to surgical simulation for surgical trainees, as a pre-operative tool for mock operations and as an ongoing assessment tool for established colorectal surgeons. Given these advantages, surgeons should anticipate continued and increased utilization of this beneficial technology.

Key words: Robotic; Colorectal; Infrared; Intracorporeal; Simulation; Skills assessment

Core tip: Firefly® technology is an integrated fluorescence capability that uses near-infrared light to visualize tissue uptake of indocyanine green, allowing for real-time,

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image-guided identification of key landmarks during surgical procedures. Wristed instrumentation, a feature of the da Vinci system, appears to enable more surgeons to perform advanced intracorporeal suturing, and thus intracorporeal anastomosis during right colectomy. Performing rectal surgery with a robotic platform may decrease risks of urogenital dysfunction compared to laparoscopic or open surgery. The robotic platform, through its master-slave configuration, digitalization of imaging, and software interface which can track kinetics, has enabled a revolution in surgical simulation.

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INTRODUCTION

When compared to open surgery, minimally invasive surgery (MIS) for patients undergoing colon and rectal procedures offers numerous benefits, including shorter hospital length of stay, lower risk of wound complications, decreased post-operative pain and faster overall recovery[1-4]. During the last decade there has been a significant upward trend in colon and rectal MIS which can be attributed largely to the acceptance of robotic surgery platforms such as the da Vinci® robotic system, approved by the Federal Drug Administration in 2000. The da Vinci® platform offers a master-slave configuration, three-dimensional, high definition imaging controlled by the surgeon, wristed instrumentation with increased degrees of freedom, tremor dampening, and advanced imaging, energy and stapler technologies.

With the introduction of the fourth generation da Vinci® system in 2014 (first Xi, and then X and SP), robotic colon and rectal surgery volume further increased due to advancements which enable more efficiency and safety in multi-quadrant operations. Integrated table motion, intelligent laser targeted docking, and further advances in instrumentation and imaging (*i.e.*, Firefly®) have all been important in the growth of robotic colon and rectal surgery procedures. The redesigned 8 mm endoscope allows for the camera to be inserted through any of the ports, which is critical to achieving multi-quadrant operations without the need for re-docking. In addition, integrated table motion allows for the patient to be repositioned without undocking or removing instruments. These advances with the newest generation platform have allowed a continued exponential increase in robotic surgery over the past five years. A 2014 multicenter study found a 1.5 fold increase in the use of MIS for patients with colon cancer and a 2.6 fold increase for rectal cancer from the years 2006-2010[5]. Currently in the United States, nearly 40% of all patients with colorectal cancer receive a minimally invasive approach[6].

DISCUSSION

Infrared light and indocyanine green

With the incorporation of robotics, there have been shifts in the practice of colon and rectal surgery by many surgeons, including more routine use of infrared light to assess vascular perfusion and increased utilization of intra-corporeal anastomosis. Additionally, recent studies suggest improved outcomes in regard to urogenital function after robotic pelvic surgery and improved oncologic dissections compared to laparoscopic or open procedures. Finally, dramatic advances in simulation are helping to change training and credentialing processes from volume-based to proficiency-based.

Anastomotic leak is one of the most dreaded complications in colorectal surgery for the patient and surgeon. Leak rates range in the literature from 3%-10%[7], with leaks thought most commonly due to poor perfusion, tension, unhealthy tissue, or technical error. Firefly® technology on the da Vinci® platform is an integrated fluorescence capability that uses near-infrared light to visualize tissue uptake of indocyanine green (ICG), allowing for real-time, image-guided identification of key landmarks during surgical procedures. Firefly® technology can be used for intraoperative perfusion assessment of bowel and particularly an anastomosis during colorectal surgery (Figure 1). For perfusion assessment, ICG (3-4 mg) is injected intravenously and

should illuminate vessels in 60 s. Near infrared lighting has been studied previously with the Pin-point® laparoscopic system and has been found to alter surgical plan and decrease rates of anastomotic leaks[8]. A 2018 study demonstrated that the use of near-infrared technology and the Pin-point® system resulted in a reduction in anastomotic leak rates from 4% to 1.9%[9]. The PILLAR II trial demonstrated a change in the surgical plan in 8% of procedures with an anastomotic leak rate of 1.4%[10]. Yet to be worked out is a more data-driven approach when using Firefly®. Currently, surgeons evaluate perfusion in a subjective manner ("green" or "not green") to determine if the desired structure illuminates. The amount of luminescence may be influenced by distance of camera from tissue, ejection fraction, density of tissue, and timing of assessment. Further studies are required to determine objective measurements of infrared illumination when using Firefly®. This approach has been studied previously for extracorporeal colorectal anastomosis with the SPY Elite® imaging system. Protyniak *et al*[11] used absolute values on a 0-256 gray scale to determine an objective measurement for anastomotic perfusion. Surgical resection was modified based upon low ICG values in 6% of patients with average ICG values in the teens. A 1% leak rate was seen in patients when Spy values ranged from 50-100, and no patient who had a change in resection site developed a leak[11]. Although there was no correlation between anastomotic leak and low SPY values, this quantitative ICG score served as an objective measurement for intraoperative anastomotic perfusion.

Firefly® technology may also offer benefits during oncological resections, particularly in reference to sentinel lymph node mapping. A recent pilot study of thirty patients with stage I colon cancer demonstrated that submucosal injection of ICG aided in oncologic resection planning in 90% of patients as mesocolic lymph node illumination provided a more specific map for resection[12]. Another area being explored regards the utility of a carcinoembryonic antigen (CEA) specific antibody conjugated with a near-infrared emitting moiety to localize occult peritoneal metastasis or recurrence. In a study from the Netherlands, 26 patients with clinically suspected occult recurrence or peritoneal metastasis based on rising CEA levels were taken to the operating room for abdominal exploration. A dose of 10 mg ICG was given 4 d preoperatively and patients underwent planned open or laparoscopic procedures. Evidence of recurrent or metastatic disease was measured first by standard tactile and visual inspection, then by infrared fluorescence. Forty-three percent of patients had lesions detected only with fluorescence, leading to treatment alterations in 35% of patients[13].

Firefly® technology may provide added safety for patients undergoing colorectal surgery by reducing iatrogenic ureteral injuries. Currently, ureter identification during complex re-operative surgery, or in patients with bulky tumors or retroperitoneal phlegmon, often requires the use of ureteral stents. Ureteral stents, however, have been shown to increase the risk of urinary tract infections, hydronephrosis, and urinary retention while showing no appreciable ability to reduce iatrogenic ureteral injuries[14-16]. In addition, there is additional cost and increased operative time that must be considered. Firefly® technology allows for accurate identification of the ureters and, though the literature is still immature, studies by Siddighi *et al*[17] and Van Manen *et al*[18] demonstrated no associated complications. Larger studies are needed to determine the ability of Firefly®-aided ureteral identification in preventing iatrogenic ureteral injuries during complex or re-operative colorectal surgery.

Intracorporeal anastomosis

Wristed instrumentation, a feature of the da Vinci system, appears to enable more surgeons to perform advanced intra-corporeal suturing, and thus intracorporeal anastomosis (ICA), specifically during right colectomy. Performing an ICA may lead to reduced manipulation of bowel, less mobilization of colon and less traction on the mesentery. Additionally, ICA affords more freedom to choose extraction sites that can be placed off midline and potentially lower the risk of incisional hernias[19,20]. In a retrospective study, Lujan *et al*[21] found significantly lower incisional hernia rates, smaller incisions and decreased conversion rates with robotic ICA when compared to laparoscopic extracorporeal anastomosis (ECA) for right colectomies. A recent meta-analysis found no difference in anastomotic leak rate or ileus, but did demonstrate decreased short-term morbidity and length of stay with ICA[22]. Trastulli *et al*[23] similarly found that ICA had better outcomes including shorter length of stay and faster time to flatus when compared to ECA. Others have not seen benefits with ICA. A recent study examined short- and long-term outcomes of ICA versus ECA and found no difference in perioperative mortality, overall survival, number of lymph nodes harvested, operative time, complications or estimated blood loss[24]. More long-term data is needed to clarify what, if any, advantages are gained by performing intra-corporeal anastomosis during colorectal surgery.

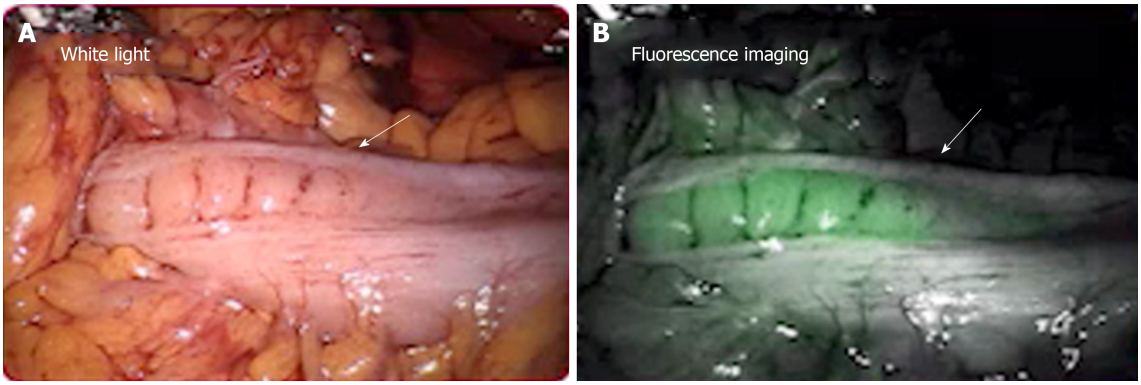

Figure 1 Intraoperative picture of integrated fluorescence using near-infrared light to visualize tissue uptake of indocyanine green. A: Colon perfusion assessment after mesenteric vessel ligation, visualized with standard white light; B: Same area of colon assessed for perfusion after injection with indocyanine green, visualized with infrared light. Well-perfused tissue appears bright green. In both images, arrow points to area of demarcation. Above images obtained from Intuitive Surgical with permission for publication.

Urinary and sexual function

Performing rectal surgery with a robotic platform may decrease risks of urogenital dysfunction compared to laparoscopic or open surgery. Approximately 31% of patients experience temporary urogenital dysfunction and as many as 5% of patients suffer permanent bladder or sexual dysfunction after proctectomy[25]. Post-operative urogenital dysfunction is often due to iatrogenic injury to the hypogastric nerves during pelvic dissection[26]. The robotic platform offers precise visualization and fine instrument movement during pelvic dissection, perhaps leading to decreased nerve injury[27]. One recent meta-analysis demonstrated better sexual function at 3 mo and better bladder function at 12 mo in the robotic group compared to the laparoscopic group in patients undergoing total mesorectal excision (TME) for rectal cancer[28]. Mean urologic function scores post-operatively were superior in the robotic group in all categories except initiation and straining. Mean sexual function scores for the robotic group were superior in all domains over the laparoscopic group[28]. Panteleimonitis *et al*[29] demonstrated improved sexual and urogenital function in the robotic subgroup when comparing males undergoing robotic versus laparoscopic TME. Kim *et al*[30] found earlier recovery of normal voiding and sexual function after robotic TME compared to laparoscopic TME, with international prostate scores returning to baseline at 3 mo for the robotic group versus 6 mo for the laparoscopic group.

Oncologic dissection

Recent studies have demonstrated improved oncologic outcomes in regard to circumferential resection margins (CRM) with robotic TME. Xiong *et al*[31] reported a positive CRM after TME in 2.74% of patients undergoing robotic approach *vs* 5.78 % of patients undergoing a laparoscopic approach. Wang *et al*[32] similarly demonstrated decreased CRM positivity with robotic TME, as well as a lower conversion rate, lower EBL and shorter time to return of bowel function. Other authors have concluded little or no difference exists between robotic TME and laparoscopic TME. One recent randomized controlled trial demonstrated that TME quality, resection margins, number of harvested lymph nodes, morbidity and return of bowel function did not differ between robotic or laparoscopic approach. These authors did find post-operative sexual function to be superior in the robotic group[33]. Updated studies are needed to understand the true impact of the newer generation robotic platforms on TME quality and oncologic outcomes, as the majority of these studies were conducted on older generation da Vinci® systems. In addition, many of the meta-analyses available regarding robotic TME evaluate the same small number of patients in the literature which are based on studies that are retrospective and non-randomized.

Simulation

The robotic platform, through its master-slave configuration, digitalization of imaging, and software interface which can track kinetics, has also enabled a revolution in surgical simulation. Simulation exercises (whether done in a dry lab, in vivo, or via virtual reality) enable trainees to develop and hone skills that are directly transferrable to the operating room, and provide a record to track their progress. Volume-based learning is being replaced with proficiency-based learning, as metrics are used to measure progress rather than number of procedures or years in training.

Bric *et al*[34] demonstrated that medical students with no prior robotic surgery experience progressed to proficiency on Fundamental Skills of Robotic Surgery with an average of 164.3 min of console time. Simulation has likewise proven useful for established surgeons as it allows easier assessment for re-credentialing purposes, provides advanced procedural-based training, and can function as a warm-up exercise prior to actual surgery[35]. A recent feasibility study used standard preoperative imaging and 3D reconstruction to generate surgical models of complex renal tumors in order to perform surgical rehearsals on the robotic platform. A subsequent comparison of resection times between the model and the actual tumor in a patient-specific manner found mean resection times between the model and patient to be equivalent. The study concluded that the robotic platform could be used as a feasible and realistic simulator for complex tumor anatomy[36].

Skills assessment

Finally, the robotic platform allows for continued assessment of robotic skills. This is most evident in a recent study involving Global Evaluative Assessment of Robotic Skills (GEARS). GEARS is a clinical assessment tool for robotic surgical skills that was developed and validated in an intraoperative environment. Modeled after the Global Operative Assessment of Laparoscopic Skills (GOALS), GEARS consists of six domains (depth perception, bimanual dexterity, efficiency, force sensitivity, autonomy, and robotic control) that are scored on a 5-point Likert scale with anchors at one, three, and five. Aghazadeh *et al*[37] validated the ability of GEARS to classify 47 surgeons as experts, intermediates or novices based on assessment of tasks in a porcine model.

CONCLUSION

The advent of the robotic platform has dramatically changed the surgical landscape across specialties, and the advancements in colorectal surgery are broad-ranging. Firefly® enables assessment of colon (and specifically anastomotic) perfusion, identification of ureters and potentially assessment of occult recurrence or metastasis using molecular-labelled tumor markers. Wristed instrumentation has increased the technical ease of ICA leading to more common use of ICA in many surgeons' practices. Some studies suggest this may result in improved postoperative outcomes, including faster recovery times and decreased incisional hernia rates. Advanced imaging has the potential to decrease the incidence of nerve injury and improve urogenital outcomes after pelvic surgery, as has been the case in robotic urologic procedures. Additionally, the robotic platform lends itself to surgical simulation for surgical trainees, as a pre-operative tool for mock operations and as an ongoing assessment tool for established colorectal surgeons. Given these advantages, surgeons should anticipate continued and increased utilization of this beneficial technology.

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REVIEW

Use of absorbable meshes in laparoscopic paraesophageal hernia repair

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Abstract

Paraesophageal hernia (PEH) repair is one of the most challenging upper gastrointestinal operations. Its high rate of recurrence is due mostly to the low quality of the crura and size of the hiatal defect. In an attempt to diminish the recurrence rates, some clinical investigators have begun performing mesh-reinforced cruroplasty with nonabsorbable meshes like polypropylene or polytetrafluoroethylene. The main problem with these materials is the occurrence, in some patients, of serious mesh-related morbidities, such as erosions into the stomach and the esophagus, some of which necessitate subsequent esophagectomy or gastrectomy. Absorbable meshes can be synthetic or biological and were introduced in recent years for PEH repair with the intent of diminishing the recurrence rates observed after primary repair alone but, theoretically, without the risks of morbidities presented by the nonabsorbable meshes. The current role of absorbable meshes in PEH repair is still under debate, since there are few data regarding their long-term efficacy, particularly in terms of recurrence rates, morbidity, need for revision, and quality of life. In this opinion review, we analyze all the presently available evidence of reinforced cruroplasty for PEH repair using nonabsorbable meshes (synthetic or biological), focusing particularly on recurrence rates, mesh-related morbidity, and long-term quality of life.

Key words: Paraesophageal hernia; Laparoscopy; Mesh; Absorbable; Biological

Core tip: Paraesophageal hernia repair is one of the most challenging laparoscopic operations. This type of hernia is large and frequently associated with a short esophagus and poor quality of the diaphragmatic crura. Different types of mesh have been used to lower recurrence rates but many of them, mostly nonabsorbable, have been associated

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with significant morbidity (*i.e.*, erosions). In this paper, we discuss the use of absorbable meshes (synthetic and biologic) in paraesophageal hernia repair.

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INTRODUCTION

There are four types of hiatal hernias (HHs). Type I (sliding HH) are the most common, and their surgical indication is usually for gastroesophageal reflux disease (GERD). Types II [true paraesophageal hernia (PEH)]; fundus herniation with an abdominal esophagogastric junction), III (fundus and esophagogastric herniation) and IV (fundus, esophagogastric junction as well as another abdominal organ, such as colon) are usually referred as PEHs. The PEHs are uncommon, accounting for only 5%-10% of HHs, but with more than 90% of them being type III.

The proper management of PEH is controversial and even their surgical indication is now under debate. Historically, all PEHs were operated because of a higher complication rate observed after conservative treatment. Today, their management has shifted to a case-by-case decision, since the risk of the repair can be high in elderly patients with multiple comorbidities and the risk of complications (according to observation) seems to be lower than in the historical reports[1].

One of the main problems of laparoscopic PEH repair is a high recurrence rate - being 12%-42% in some large series[2], while other series have shown up to 60%[3]. To improve these results, some clinical investigators began to use prosthetic materials to reinforce the crural closure. The first mesh-reinforced cruroplasties used nonabsorbable materials like polypropylene or polytetrafluoroethylene (PTFE)[4]. The occurrence of serious morbidity, in some patients, after the nonabsorbable mesh placement (*i.e.*, erosions into the stomach or the esophagus, some of which required esophagectomy or gastrectomy) has kept the use of these materials from becoming standard[5-7].

The ideal mesh material should be able to help reduce tension of the crural closure, without causing erosion or dysphagia, and with provision of long-term duration. This ideal material has not yet been found.

Absorbable meshes were introduced to maintain the theoretical benefit of reducing the recurrence rate without the associated morbidity of the nonabsorbable materials. They can be synthetic, such as Vicryl® (Ethicon, Somerville, NJ, United States) or Bio-A® (Gore Medical, Newark, DE, United States), or biological, such as Surgisis® (Cook Medical, Bloomington, IN, United States), AlloDerm® (Allergan PLC, Dublin, Ireland), or Strattice™ (Allergan PLC) (Table 1). Although they seem to be safe, with very low short- and long-term morbidity rates, the main questions regarding their applicability are long-term efficacy and, in some cases (biological), their high costs.

A recent survey, conducted by the Society of American Gastrointestinal Endoscopic Surgeons (known as SAGES) and answered by more than 2500 members, revealed that among surgeons using mesh for HH repair, 67% preferred absorbable material. Among the high-volume surgeons (> 20 cases of PEH repair per year), 23% reported using mesh reinforcement in the majority of their cases, while the remaining 77% of surgeons reported using it in approximately half of their cases[8]. PEH repairs continue to be so controversial that a clinical guideline for the management of HH concluded that there is not sufficient evidence to support or to speak against the use of mesh to reinforce crural closure[9].

We conducted a thorough search of the Medline and PubMed databases that would allow us to discuss the various results published by different groups worldwide, using all kinds of absorbable meshes for laparoscopic PEH repair.

EXPERIENCES WITH ABSORBABLE SYNTHETIC MESHES

One of the first publications of crural reinforcement with an absorbable mesh (Bio-A®) described work by Massullo *et al*[10]. This initial experience consisted of only 11 patients with GERD or PEH. All patients received a reinforced laparoscopic

Table 1 Different types of absorbable meshes

Type of material	Composition	Commercial name
Synthetic	Polyglactin 910	Vycril®
Synthetic	Polyglycolic acid (67%)	Bio-A®
	Trimethylene carbonate (33%)	
Biological	Porcine small intestine submucosa	Surgisis®
Biological	Acellular human dermis	AlloDerm®
Biological	Bovine pericardium collagen matrix	Veritas®
Biological	Porcine acellular dermal collagen	Permacol®[1]
Biological	Porcine-derived acellular dermal matrix	StratticeTM

[1]Medtronic, Minneapolis, MN, United States.

cruroplasty with Bio-A® mesh, after which they underwent either Nissen or Toupet fundoplication. Mean follow-up was 13 mo, with 1 case of recurrence (9%) and no mesh-related complications (MRCs). The clinical value of this initial experience was limited, however, because of the small number of patients and the short follow-up.

A later prospective series of 70 patients, consisting of 48 PEH and 22 large type I HH, was published in 2013 by Powell and coworkers[11]. The crural reinforcement was also performed with Bio-A® mesh but without the classical U-shape. Instead, the investigators cut the mesh only to cover the crural closure, in an attempt to make no contact with the dissected esophagus. On short-term follow-up, there were no MRCs.

Iossa *et al*[12] recently published a retrospective series reporting their mid-term results on 120 patients with Bio-A® mesh-reinforced cruroplasty. Mean follow-up was 42 mo, and recurrence rates were 5.4% in the obese group and 7.1% in the nonobese population. No MRCs were recorded. The value of this paper is limited, however, since most of the patients were obese and having undergone concomitant bariatric surgery (sleeve gastrectomy) and the rest of the patients having been operated because of GERD, with only 6 cases representing PEH. Nevertheless, the study showed that mesh placement was safe, with no MRCs, and recurrence rate was low.

Asti *et al*[13] published a retrospective experience of 100 cases of reinforced cruroplasty with Bio-A® mesh, after which all patients received a Toupet fundoplication. The indications for mesh placement were weak or frail crura and large HH (90% of the cases were PEH). No MRCs were observed and the recurrence rate was 9%, with a mean follow-up of 30 mo, and mostly in patients with type III PEH. Although this is a retrospective series, it has the value of showing the safety of Bio-A® mesh placement with a low recurrence rate in the mid-term. Other small retrospective series have yielded similar results[14,15].

Zehetner and coworkers[16] published their experience with reinforced cruroplasty using polyglactin mesh (Vycril®) secured with a biological glue (BioGlue® surgical adhesive; CryoLife Inc, Kennesaw, GA, United States). This material has a degradation time between 6 wk and 8 wk. Of the 35 patients with an intrathoracic stomach (defined as > 50% of the stomach inside the thoracic cavity), 21 completed a 1-year follow-up, at which point they were evaluated by esophagogram, pH monitoring, and upper endoscopy. The recurrence rate was 9.5% (2 cases; 1 having GERD symptoms and 1 being asymptomatic). No MRCs were observed. These different experiences are summarized in Table 2.

EXPERIENCES WITH ABSORBABLE BIOLOGIC MESHES

Oelschlager *et al*[17] published, in 2006, a multicenter prospective and randomized trial, comparing suture alone *vs* reinforced cruroplasty with Surgisis® for the treatment of PEH. A total of 108 patients with symptomatic large PEH were enrolled, 51 in the Surgisis arm and 57 in the suture-alone arm. All demographic and PEH type distributions were similar among both groups. At 6-mo follow-up, there was a significant improvement in all the symptoms that had been described in the preoperative period. The majority of patients (90%) underwent an upper gastrointestinal contrast study, the data from which showed a statistically significant difference in recurrence rate in favor of the Surgisis group (24% *vs* 9% respectively). On multivariate analysis, the only factor associated with a lower risk of recurrence was the placement of Surgisis®.

The long-term follow-up of this experience[17] was published in 2011. Of the original

Table 2 Experiences with absorbable synthetic mesh

Publication	Study design	*n*	Type of mesh	Recurrence	MRC	Median FU in mo
Massullo *et al*[10]	Retrospective	11	Bio-A®	9%	No	13
Iossa *et al*[12]	Retrospective	120	Bio-A®	7.1%	No	42
Asti *et al*[13]	Retrospective	100	Bio-A®	9%	No	30
Zehetner *et al*[16]	Retrospective	35	Vicryl®	9.5%	No	12

FU: Follow-up; MRC: Mesh-related complication.

108 patients, the investigators were able to contact 72, now with a median follow-up of 58 mo. No differences were observed between the two groups in terms of frequency or severity of upper gastrointestinal symptoms. Recurrence rates were 59% in the suture-alone group and 54% in the Surgisis group. The conclusion of the study is that the initial advantage for the use of biologic reinforcement of the cruroplasty was erased in long-term follow-up (5 years). However, the high recurrence rate observed in this experience might be biased by the fact that the diagnosis was made only by experienced radiologists and any herniation into the hiatal space was considered as a recurrence. The responses on quality of life (QOL) questionnaires remained satisfactory[18].

Lee *et al*[19] from the Nebraska University retrospectively reviewed their experience with reinforced cruroplasty with AlloDerm® mesh. This material is biologic and is supposed to be fully incorporated in the recipient tissue at 9 mo postapplication. The study evaluated 52 patients, with a median follow-up of 16 mo. No MRCs were observed, and the recurrence rate was 3.8%.

A more recent experience from the same group consisted of a retrospective review of their experience with 35 patients who submitted to reinforced cruroplasty with Strattice™ mesh. All patients had PEH at least of 5 cm on upper endoscopy, with a mean hernia size of 10 cm. At a short follow-up of 12 mo, 5 recurrences were observed (14%). The investigators concluded that the use of this mesh was safe, producing short-term results similar to those of other comparable materials[20].

In a study designed to identify factors associated with PEH recurrence after reinforced cruroplasty with biologic material, Lidor and coworkers[21] from Johns Hopkins University found that the risk of recurrence was higher in patients with intrathoracic stomach. The material used in this study was the Veritas mesh (Baxter International, Deerfield, IL, United States) and the recurrence rate was 27% at 1-year follow-up, with most of the patients reporting a better QOL despite recurrence. No MRCs were reported. At 36 mo, most patients reported overall satisfaction but symptoms such as heartburn, early satiety and nausea remained as in the preoperative period. The investigators' conclusion was that, despite a high recurrence rate, most of the patients remained asymptomatic and reported "good" on QOL questionnaires. These different experiences using biological meshes are summarized in Table 3.

EXPERIENCES COMPARING MULTIPLE MATERIALS

Tam *et al*[22] retrospectively reviewed 795 patients, of which 106 received crural mesh reinforcement, with 84% of the cases receiving a biological mesh. The recurrence rate was similar between both groups. This might be explained by the fact that most patients requiring mesh placement were older and had bigger hernias with poor quality crura, with some even having a completely intrathoracic stomach. Three patients (2.8%) had MRCs. Two patients suffered from a severe fibrosis around a biological mesh causing dysphagia, with one requiring several endoscopic dilatations and the other esophagectomy. One patient suffered a cardiac tamponade that required sternotomy and right coronary artery hemostasis, due to a tacker injury. The investigators recommend selective use of mesh cruroplasty.

Parsak *et al*[23] published an interesting prospective and randomized trial comparing crural reinforcement with polypropylene *vs* polyglactin mesh in patients operated for GERD. A total of 150 patients were included in the study (75 receiving polypropylene and 75 receiving polyglactin). Postoperative morbidity was similar for both groups, with no MRCs. At a mean follow-up period of approximately 36 mo, the recurrence rate was 7.5%, similar between both arms of the study. No erosion was reported in any group.

Table 3 Experiences with biological mesh

Author	Study design	*n*	Type of Mesh	Recurrence	MRC	Median FU in mo
Oelschlager *et al*[17]	RCT	108 (51 with mesh)	Surgisis®	9%	No	6
Oelschlager *et al*[18]	RCT	72 (33 with mesh)	Surgisis®	54%	No	58
Lee *et al*[19]	Retrospective	52	AlloDerm®	3.8%	No	16
Lomelin *et al*[20]	Retrospective	35	Strattice™	14%	No	12
Lidor *et al*[21]	Prospective non-randomized	111	Veritas®	27%	No	36

FU: Follow-up; MRC: Mesh-related complication; RCT: Randomized-controlled trial.

Zehetner *et al*[24] published in 2011 a retrospective evaluation comparing open vs laparoscopic PEH repair. In this experience, they used multiple mesh materials (Surgisis®, Vycril®, and Bio-A®) and the recurrence rate was 18%, similar between the open and laparoscopic approach groups, with the latter being superior in terms of shorter hospital stay and reduced morbidity.

An interesting prospective and randomized trial was conducted by Watson *et al*[26]. They compared suture cruroplasty (43 cases) *vs* reinforced cruroplasty with absorbable mesh (41 cases receiving Surgisis®) and nonabsorbable mesh (42 cases receiving TiMESH (PFM Medical Titanium gmbh, Nürnberg, Germany) in patients with large PEH. No differences were observed in term of recurrence between the three arms of the study and - as seen in most of the other studies previously cited in this review - most were asymptomatic. A limitation of this study is its short follow-up of only 12 mo, since this duration might not allow for detection of late recurrences and late complications of nonabsorbable meshes (*i.e.*, erosion)[25]. A later evaluation of QOL performed on these patients at 24-mo follow-up showed no differences between the groups.

Jones *et al*[27] published, in 2015, one of the few papers reporting on long-term follow-up of reinforced cruroplasty with the use of an absorbable mesh. Most large hernias in this study were operated using biological material (AlloDerm® and Strattice™), whereas synthetic material (Bio-A®) was used mostly for the smaller ones. No MRC was observed. At 5 years after surgery, radiologic recurrence was 39%, but most of the preoperative symptoms were significantly better in the postoperative period.

Finally, a recent meta-analysis by Huddy *et al*[28], evaluating results of suture-alone cruroplasty *vs* absorbable mesh-reinforced cruroplasty *vs* nonabsorbable mesh-reinforced cruroplasty found that the addition of the mesh significantly reduces recurrence rate, with more benefits being obtained with the nonabsorbable material. The rate of surgical revisions was also significantly reduced with the addition of a mesh. There were no reports of erosions in the study, probably because of a short-term follow-up. These different experiences using multiple materials are summarized in Table 4.

CONCLUSION

Laparoscopic crural reinforcement with absorbable material (synthetic or biological) is becoming accepted by the surgical community, as has been revealed by a large survey conducted by SAGES. This event is probably related more to their safety profiles (few MRCs reported) instead of their long-term recurrence rates. More studies with longer follow-up periods are needed to clarify this. The actual evidence shows, however, that despite high recurrence rates, most patients remain asymptomatic, with good QOL, and very few require surgical revisions.

Table 4 Experiences with multiple mesh materials

Author	Study design	*n*	Type of mesh	Recurrence	MRC	Median FU in mo
Tam *et al*[22]	Retrospective	106	Mostly biological	22%	2.8%	NS
Parsak *et al*[23]	RCT	150	75 Polypropylene/75 Polyglactin	7.5%	No	36
Watson *et al*[25]	RCT	126	43 Suture alone 41 Surgisis® 42 Nonabsorbable	Similar, about 20%	No	12

FU: Follow-up; NS: Not stated; RCT: Randomized-controlled trial.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Impact of age on feasibility and short-term outcomes of ERAS after laparoscopic colorectal resection

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Abstract

BACKGROUND

There is still large debate on feasibility and advantages of fast-track protocols in elderly population after colorectal surgery.

AIM

To investigate the impact of age on feasibility and short-term results of enhanced recovery protocol (ERP) after laparoscopic colorectal resection.

METHODS

Data from 225 patients undergoing laparoscopic colorectal resection and ERP between March 2014 and July 2018 were retrospectively analyzed. Three groups were considered according to patients' age: Group A, 65 years old or less, Group B, 66 to 75 years old and Group C, 76 years old or more. Clinic and pathological data were compared amongst groups together with post-operative outcomes including post-operative overall and surgery-specific complications, mortality and readmission rate. Differences in post-operative length of stay and adherence to ERP's items were evaluated in the three study groups.

RESULTS

Among the 225 patients, 112 belonged to Group A, 57 to Group B and 56 to Group C. Thirty-day overall morbidity was 32.9% whilst mortality was nihil. Though the percentage of complications progressively increased with age (25.9% *vs* 36.8% *vs* 42.9%), no differences were observed in the rate of major complications (4.5% *vs* 3.5% *vs* 1.8%), prolonged post-operative ileus (6.2% *vs* 12.2% *vs* 10.7%) and anastomotic leak (2.7% *vs* 1.8% *vs* 1.8%). Significant

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differences in recovery outcomes between groups were observed such as delayed urinary catheter removal (P = 0.032) and autonomous deambulation (P = 0.013) in elderly patients. Although discharge criteria were achieved later in older patients (3 d *vs* 3 d *vs* 4 d, P = 0.040), post-operative length of stay was similar in the 3 groups (5 d *vs* 6 d *vs* 6 d).

CONCLUSION
ERPs can be successfully and safely applied in elderly undergoing laparoscopic colorectal resection.

Key words: Colorectal surgery; Laparoscopic surgery; Enhanced recovery protocol; Age; Elderly

Core tip: Feasibility and safety of enhanced recovery protocols in elderly populations undergoing minimally invasive colorectal surgery have been questioned by recent literature. Age has been considered an obstacle for enhanced recovery and a risk factor for surgical outcomes. Our study investigated the impact of age on fast-track after laparoscopic colorectal resection. Early removal of urinary catheter and walking resumption were the most difficult goals achieved by the elderly. Nevertheless, general compliance to fast-track items was good and, although discharge criteria were fulfilled later in older patients, no differences in length of stay and major complications rate were observed.

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INTRODUCTION

Laparoscopy and enhanced recovery protocols (ERPs) represent two major innovations in colorectal surgery. ERP is a multi-disciplinary model of peri-operative care for patients undergoing different types of major surgery[1] and it is considered the gold standard for patients undergoing colorectal surgery[2]. The purpose of these protocols is to minimize the response to surgical related stress and promote faster restoration of homeostasis. Many studies have proved that fast-track programs are safe and effective in reducing post-operative morbidity and length of hospital stay (LOS) after colorectal surgery[3-5]. The association of minimally invasive techniques and ERPs leads to a faster recovery and definitively produces an improvement of short-term outcomes[6,7].

Early ERPs excluded elderly patients from enrollment since their frailty was considered a contraindication to fast-track pathways. Recent experiences show that elderly patients may benefit from ERP though critics have argued that successful programs are difficult to be achieved due to a lower adherence to many fast-track components[8,9]. Although the elderly have higher levels of comorbidity, frailty and social care requirements[10,11], it is not proven that they may not be able to complete an ERP or that they have different outcomes with such management[12]. The aim of this retrospective observational study was to assess the safety, feasibility and efficacy of ERP according to patients' age after laparoscopic colorectal surgery.

MATERIALS AND METHODS

Inclusion criteria and population under study

Enhanced recovery after surgery program was introduced at the Division of General and Hepatobiliary Surgery, University of Verona Hospital Trust, in March 2014. Between March 2014 and July 2018 patients undergoing elective laparoscopic colorectal resection, with or without stoma formation, were preferentially enrolled in

the ERP. All patients aged 18 years or more, undergoing elective surgery for tumor of the colon and rectum or diverticular disease were offered to enter the protocol. Exclusion criteria were: inflammatory bowel disease (IBD), familial adenomatous polyposis (FAP), palliative surgery, body mass index above 35 kg/m^2, American Society of Anaesthesiologists (ASA) physical status above 3, coagulopathy, impaired kidney function, uncontrolled diabetes, severe cardiovascular impairment or chronic obstructive pulmonary disease, psychiatric disorders, drug and alcohol addiction, duration of anesthesia above 6 h and denied consent. Reasons for pre-operative and intra-operative exclusion criteria have been previously described in detail[13]. Informed consent was obtained from all the patients for the surgical procedure proposed and the protocol was approved by the local Ethics Committee.

ERAS protocol and outcome measures

The protocol was devised in accordance to the recommendations of the ERAS Society[1]. The objective of the ERP was to provide all the items to all patients as far as possible. Surgical approach, anesthesiologic management, post-operative analgesia and post-operative care according to ERAS items were previously described in detail[13,14].

Post-operative morbidity was defined as any deviation from the expected course and complications were graded according to the Clavien-Dindo Classification[15]. Thirty-day readmission rate and mortality were registered. During hospital stay, patients were clinically reviewed at least twice a day by a trained member of the surgical team and adherence to ERP items was registered together with the presence of nausea, vomiting, passage of flatus and stools, tolerance to liquid and solid diet and level of pain according to a Visual Analog Scale (VAS). Diet was considered tolerated when patient's oral intake would be deemed enough to avoid starvation and be independent of intravenous fluids. Out of bed mobilization was considered as patient sitting on chair for at least 2 h per day while active mobilization was considered as assisted or autonomous walking or sitting on chair for more than 6 h per day.

LOS was measured from the date of surgery to the date of discharge from hospital. Time to readiness for discharge (TRD) was defined as the number of days needed to fulfill discharge criteria[16]: Patients were considered fit for discharge when bowel function was restored (stool or repeated flatus), adequate amount of food and liquid intake was tolerated, normal mobilization restored, pain well controlled with oral analgesics (VAS < 4) and CRP < 120 mg/dL on the third post-operative day (POD)[17]. Discharge delay (DD) was defined as the difference between TRD and the actual discharge from hospital. Since the aim of our ERAS protocol was not to pursue very early discharge, the TRD was considered as an indicator of how comfortable patient felt with returning home and effective presence of post-hospitalization assistance.

Data analysis

All demographic and clinical data, after treatment consent acquisition, were anonymously collected in a PC dataset. Statistical analysis was performed using IBM SPSS software version 21.0. Descriptive variables were reported as frequencies and continuous variables were reported as mean (± SD) or median (range).

Short-term outcomes and adherence to ERP items were compared in 3 groups according to patients' age: Group A, 65 years old or less, Group B, 66 to 75 years old and Group C, 76 years old or more. These cut-off values defining elderly and old elderly patients were defined according to the World Health Organization definition[18].

Adherence to ERP items and clinical outcomes were analyzed as a binary outcome (yes/no). Discrete variables were compared with the chi-square test. For continuous outcomes, Student's *t*-test, ANOVA and Mann-Whitney tests were used when indicated. All statistical tests were two-sided with statistical significance expressed as $^aP < 0.05$ and $^bP < 0.01$.

RESULTS

During the study period, a total of 317 patients underwent laparoscopic colorectal resection at our institution; among these, 73 patients did not meet pre-operative inclusion criteria while 19 patients were excluded due to post-operative exclusion criteria. Younger patients (Group A) were most frequently excluded due to surgical indication and refusal to participate in ERP whilst, in Group B and C the most frequent causes for exclusion were the presence of severe comorbidities and lack of collaboration (Figure 1). The final cohort was represented by 225 patients: 112 patients belonged to Group A, 57 patients to Group B and 56 patients to Group C.

Patients' demographics and clinical characteristics according to age grouping are

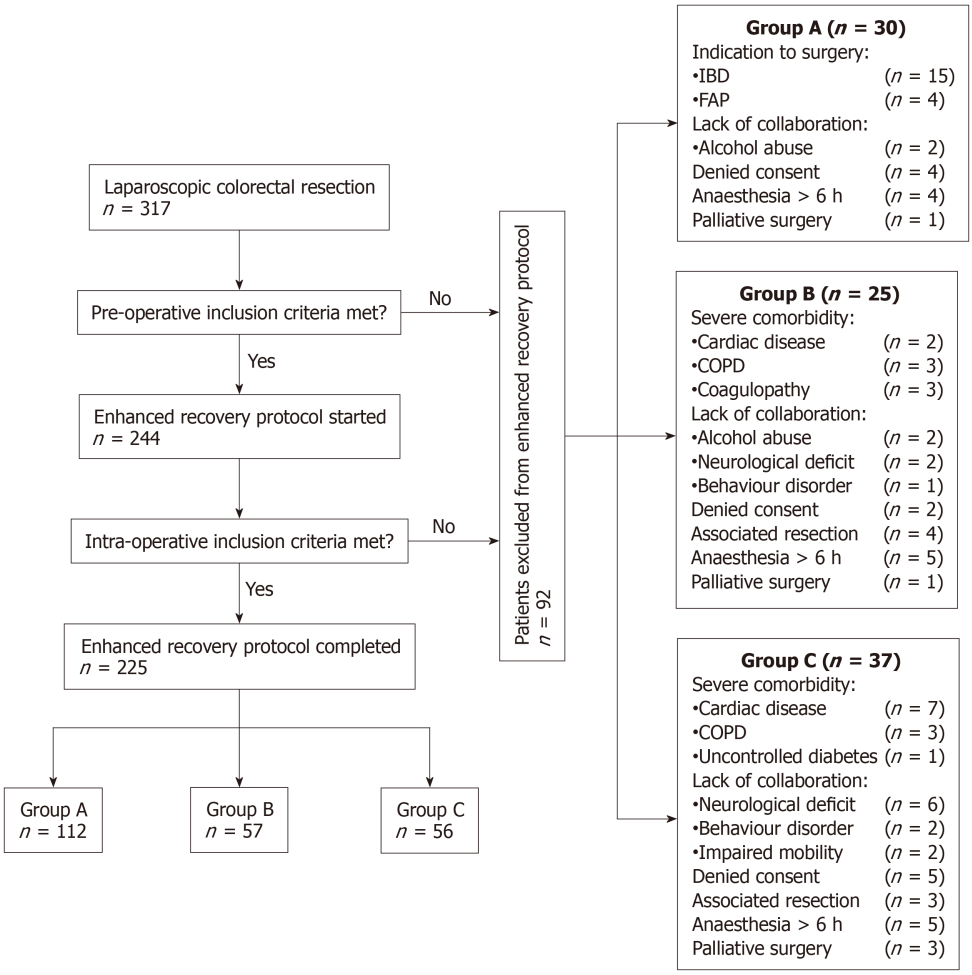

Figure 1 Exclusion criteria among the 317 patients undergoing laparoscopic colorectal resection from March 2014 to July 2018. IBD: Inflammatory bowel disease; FAP: Familial adenomatous polyposis; COPD: Chronic obstructive pulmonary disease.

reported in Table 1. In Group A, most patients were classified as ASA ≤ 2 while, in Group B and Group C, the number of patients classified as ASA 3 was significantly higher (4.5% *vs* 24.6% *vs* 33.9%; $P < 0.001$). Similarly, a significantly higher rate of patients with comorbidities ≥ 2 was observed in Group B and C (20.5% *vs* 47.4% *vs* 58.9%; $P < 0.001$). Colonic cancer was the main indication for surgery in the three groups although, rectal cancer was more frequent in younger patients (28.6% *vs* 8.8% *vs* 14.3%; $P = 0.007$). The three groups did not differ in terms of extent of surgery, surgical procedure duration, blood loss and new stoma formation. Conversion to open surgery was comparably low in the subgroups (2% *vs* 7% *vs* 3.6%).

Compliance outcomes

Adherence to the 14 ERP items selected for this study is summarized in Table 2. Respiratory training, routine antiemetic therapy, nasogastric tube removal immediately after surgery, TAP block administration were equally dispensed in almost all the patients independently from age.

Compliance to early fluid intake on the day of surgery and soft diet on POD 1 was overall low and similar among groups. Discontinuation of intravenous fluid within POD2 was generally more difficult in Group C ($P = 0.032$) and the compliance for carbohydrate rich drink consumption was twofold in Group A and B compared to Group C (42.9% *vs* 45.6% *vs* 23.2%; $P = 0.022$).

Independently from age, early mobilization on chair was accomplished in a large majority of patients on POD 0 or on the morning after surgery, while walking on POD 1 was less frequently achieved in Group B and C (50.9% *vs* 40.4% *vs* 37.5%; $P = 0.032$).

Considering the whole cohort, older patients presented lower rates of early urinary catheter removal (58.9% *vs* 70.2% *vs* 42.9%; $P = 0.013$) but opioid analgesia avoidance was more frequently regarded in this group ($P = 0.007$).

Global compliance (GC), defined as the percentage of protocol goals achieved by each patient, was similar among groups. Good compliance was defined as adherence

Table 1 Clinic-pathological characteristics and operative data according to age grouping for the 225 patients under study, *n* (%)

	Age group			*P* value
	Group A (*n* = 112)	Group B (*n* = 57)	Group C (*n* = 56)	
Age, yr[b]	57.1 (18-65)	68.9 (65.5-74.2)	80 (75-91.6)	
Male sex	62 (55.4)	35 (61.4)	24 (42.9)	NS
BMI, Kg/m2	25 (3.8)	25.6 (3.7)	24.9 (3.2)	NS
ASA classification[b]				< 0.001
I	23 (20.5)	2 (3.5)	1 (1.8)	
II	84 (75)	41 (71.9)	36 (64.3)	
III	5 (4.5)	14 (24.6)	19 (33.9)	
Indication for surgery[b]				0.007
Colon cancer	46 (41.1)	37 (64.9)	37 (66.1)	
Rectal cancer	32 (28.6)	5 (8.8)	8 (14.3)	
Benign	34 (29.4)	15 (26.4)	11 (19.7)	
Presence of comorbidities[b]				< 0.001
None	48 (42.9)	12 (21.1)	8 (14.3)	
1	41 (36.6)	18 (31.6)	15 (26.8)	
≥ 2	23 (20.5)	27 (47.4)	33 (58.9)	
Previous surgery	49 (43.7)	33 (57.9)	31 (55.4)	NS
R0 resection	75 (96.2)	42 (100)	45 (100)	NS
TNM Stage				NS
Stage ≤ II	53 (67.9)	28 (66.7)	36 (80)	
Stage III	23 (29.5)	11 (26.2)	19 (20)	
Stage IV	2 (2.6)	3 (7.1)	-	
Extent of surgery				NS
Right hemicolectomy	26 (23.2)	19 (33.3)	23 (41.1)	
Left hemicolectomy	46 (41)	28 (49.2)	21 (37.5)	
Rectal resections[1]	32 (28.6)	5 (8.8)	8 (14.3)	
Abdominoperineal resection	6 (5.4)	1 (1.7)	-	
Others	2 (1.8)	4 (7)	4 (7.1)	
Stoma formation				NS
Ileostomy	20 (17.9)	2 (3.6)	5 (8.9)	
Colostomy	6 (5.4)	1 (1.8)	1 (1.8)	
Time of surgery, min	235 (125-360)	216 (145-340)	220 (125-320)	NS
Estimated blood loss, mL	50 (20-400)	40 (10-400)	50 (20-250)	NS
Conversion to open surgery	2 (1.8)	4 (7)	2 (3.6)	NS

[1]Includes extended resections to the upper rectum, anterior resection, low anterior resection and intersphincteric resection. Data are expressed as number of patients (%), mean (standard deviation) or median (range).
[b]$P < 0.01$. BMI: Body mass index; ASA: American Society of Anaesthesiologists.

to more than 75% of the ERP items while, adherence to < 50% and 50%-75% of the items was classified as poor and borderline compliance, respectively (Table 2). No statistical correlation was demonstrated between age groups and GC, suggesting that ERAS goals can be achieved by elderly patients as well.

Post-operative outcomes

Post-operative outcomes are shown in Table 3. Major complication, reoperation and readmission rates were comparably low among the 3 groups. Besides a higher overall complication rate in Group B and C (25.9% *vs* 36.8% *vs* 42.9%), no differences were detected in surgery specific complications such as post-operative prolonged ileus or anastomotic leak. Older patients needed post-operative red blood cells transfusion (RBC) more frequently, even though the percentage was anyhow low (5.4% *vs* 3.5% *vs*

Table 2 Adherence to the enhanced recovery protocol's items according to age grouping for the 225 patients under study, *n* (%)

	Age group			
	Group A (*n* = 112)	Group B (*n* = 57)	Group C (*n* = 56)	*P* value
Laparoscopy (no conversion)	110 (98.2)	53 (93)	53 (94.6)	NS
Carbohydrate rich drink[a]	48 (42.9)	26 (45.6)	13 (23.2)	0.022
Respiratory training	106 (94.6)	54 (94.7)	55 (98.2)	NS
Prophylactic antiemetics	109 (97.3)	52 (91.2)	52 (92.9)	NS
Intra-operative warming	108 (96.4)	52 (91.2)	55 (98.2)	NS
No nasogastric tube	101 (90.2)	53 (93)	48 (85.7)	NS
TAP block	62 (55.4)	29 (50.9)	37 (66.1)	NS
Oral liquids POD0	31 (27.7)	14 (24.6)	9 (16.1)	NS
Solid food POD1	46 (41.1)	18 (31.6)	16 (28.6)	NS
Early mobilization	101 (90.2)	51 (89.5)	50 (89.3)	NS
Walking POD1[a]	57 (50.9)	23 (40.4)	21 (37.5)	0.032
Early UC removal[a]	66 (58.9)	40 (70.2)	24 (42.9)	0.013
Stop iv fluids POD2[a]	67 (59.8)	36 (63.2)	23 (41.1)	0.032
Opiates avoidance[a]	56 (50)	22 (38.6)	38 (67.9)	0.007
GC, %	70.3 (36-100)	64.3 (21-100)	64.3 (36-100)	NS
GC < 50%	20 (17.9)	10 (17.5)	13 (23.2)	
GC 50%-75%	51 (45.5)	23 (40.4)	29 (51.8)	
GC > 75%	41 (36.6)	24 (42.1)	14 (25)	

[a]*P* < 0.05. TAP: Transversus abdominis plane; POD: Post-operative day; UC: Urinary catheter; GC: Global compliance.

9%). No post-operative mortality was observed during the study period.

As showed in Table 4, median LOS was one day shorter in Group A (5 d *vs* 6 d *vs* 6 d), although the difference did not reach statistical significance. According to the defined discharge criteria, the number of patients who could have been discharged on POD 3 progressively decreased according to age (64.3% *vs* 61.4% *vs* 48.2%). Median TRD was significantly shorter in Group A and B (*P* = 0.040) though DD did not differ in the 3 groups.

DISCUSSION

Colorectal cancer is still the 2nd most common cause of death from neoplastic disease in men and the 3rd in women with a peak incidence between the 7th and 8th decades; over 70% of colorectal cancers are currently diagnosed in patients over the age of 65 [19]. Life expectancy, defined as the average number of years that a person at a defined age can be expected to live, is increasing worldwide. In 1985 in Italy, life expectancy at the age of 65 years was assumed to be 14.2 years for males and 17.4 years for females, in 2016 it is increased to 19.4 years for males and 22.9 years for females. Likewise, life expectancy at 75 years is expected to be 12 years for males and 14.5 years for females, one of the highest among Western countries[20]. In this regard, a steadily increasing number of colorectal cancers are expected to be operated on in older patients in the next future[21]. Most of the studies analyzing safety and feasibility of ERPs did not include elderly since, full adhesion to all fast-track items was assumed to be unfeasible in consideration of physical impairment and accompanying comorbidities[22]. This idea seems to be supported by a systematic review from Bagnall *et al*[23] which highlighted the lack of evidence to support ERP application at advanced ages. Conversely, several experiences focused on ERP application in the elderly highlighting its safety and efficacy on post-operative outcomes[24-28].

Our study reports the results of ERP application in a complete laparoscopic series of patients undergoing colorectal resection without age limit. Most of the recent studies still consider heterogeneous cohorts with open and laparoscopic approach[24-27] and this could lead to an underestimation of ERP benefits. We believe that minimally

Table 3 Post-operative complications according to age grouping for the 225 patients under study, *n* (%)

	Age group			
	Group A (*n* = 112)	Group B (*n* = 57)	Group C (*n* = 56)	*P* value
Overall complications	29 (25.9)	21 (36.8)	24 (42.9)	NS
Major complications				NS
(Clavien-Dindo ≥ III)	5 (4.5)	2 (3.5)	1 (1.8)	
General complications[a]	9 (8.1)	13 (22.8)	11 (19.6)	0.045
Cardiovascular	2 (1.8)	3 (5.3)	7 (12.4)	
Respiratory	3 (2.7)	3 (5.3)	2 (3.6)	
Urinary tract	1 (0.9)	4 (7)	2 (3.6)	
Anemia	1 (0.9)	1 (1.8)	-	
Others	2 (1.8)	2 (3.5)	-	
Surgical complications	22 (19.6)	11 (19.3)	13 (23.2)	NS
Anastomotic leak	3 (2.7)	1 (1.8)	1 (1.8)	
Bowel obstruction	1 (0.9)	2 (3.5)	-	
Prolonged post-operative ileus	7 (6.3)	7 (12.2)	6 (10.7)	
Bleeding	2 (1.8)	1 (1.8)	1 (1.8)	
Gastrointestinal bleeding	1 (0.9)	-	-	
Surgical site infection	2 (1.8)	-	4 (7.1)	
Others	6 (5.4)	-	1 (1.8)	
Infective complications	6 (5.4)	4 (7)	7 (12.5)	NS
RBC transfusion	6 (5.4)	2 (3.5)	5 (9)	NS
Redo Surgery	4 (3.6)	2 (3.5)	1 (1.8)	NS
Anastomotic leak	3 (3.6)	-	1 (1.8)	
Internal hernia	1 (.9)	2 (3.5)	-	
30-d readmission	3 (3.6)	-	1 (1.8)	NS
30-d mortality	-	-	-	

[a]$P < 0.05$. Data are expressed as number of patients (%). RBC: Red blood cells.

invasive surgery is one of the cornerstones of a successful fast-track program since it reduces surgical stress[6,7] and improves compliance to ERP items[6,25]. For this reason, we privileged to analyze the impact of age on fast-track results in a large and fully laparoscopic cohort.

Since the very beginning of ERP adoption in our unit, elderly patients were included in the protocol, consequently our results are probably affected negatively by the enlarged inclusion criteria. As previously documented[29], a good implementation of ERP requires a starting period for personnel training and acquaintance with some innovating items. We believe that most of the poorer results here described for the elderly are related to the need of more time for ERP implementation in this subgroup. For this reason, further investigation analyzing fast-track results in age groups in different periods is advisable.

When analyzing global compliance for ERP interventions, an adherence higher than 60% was achieved independently from age. The aim of a 90% compliance was obtained in 4 items: fully laparoscopic procedure without conversion to open surgery, post-operative respiratory training program, prophylactic antiemetics administration and intra-operative patient warming. Good results in early mobilization were achieved independently from age thanks to an optimal pain management. In our experience, one of the key aspects in post-operative pain management was the use of transversus abdominis pain (TAP) block that proved to reduce significantly the use of opioid analgesics and to ensure an optimal pain control[13,30], without the adverse effects of epidural analgesia, such as vasodilatation and hypotension. Limiting the side effects of opioids and epidural seems of particular benefit in elderly that are more sensitive to sedation and blood pressure variations.

The main differences in favor of younger patients were observed in carbohydrate rich drink consumption, independence from intravenous fluid stop and early

Table 4 Meeting criteria for discharge according to age grouping

	Age group			*P* value
	Group A (*n* = 112)	Group B (*n* = 57)	Group C (*n* = 56)	
Fluid intake[a]	1 (0-5)	1 (0-7)	1 (0-7)	0.039
Soft diet	2 (1-6)	2 (1-13)	2 (1-9)	NS
Early mobilization	1 (0-3)	1 (0-7)	1 (0-4)	NS
Walking	1 (0-4)	2 (1-8)	2 (1-8)	NS
Bowel open to gas	1 (0-6)	1 (0-4)	1 (0-4)	NS
Bowel open to stools[a]	2 (0-8)	3 (1-9)	3 (1-9)	0.002
Pain control with oral analgesics	3 (2-4)	3 (1-5)	3 (1-4)	NS
Length of stay	5 (2-40)	5 (3-26)	6 (3-22)	NS
Ready for discharge on POD 3, *n* (%)	72 (64.3)	35 (61.4)	27 (48.2)	NS
Time to readiness for discharge[a]	3 (3-35)	3 (3-22)	4 (3-18)	0.040
Discharge delay	1 (0-8)	2 (0-8)	2 (0-4)	NS

[a]$P < 0.05$. Data are expressed as number of patients (%) or median (range). POD: Post-operative day.

walking. In our opinion these data should be interpreted as the result of the association of a more protective attitude of health personnel and a stronger reluctance of the elderly to get out of bed or drink after the day of surgery. These results confirm the experience of Feroci *et al*[31] which reported significant differences both in early liquid and solid diet intake when comparing patients younger or older than 75 years old. The need for an extra effort from the caregivers should be stressed together with a stronger information on ERP items safety for personnel and patients. Later resumption of walking in the elderly was probably related to a lower rate of early UC removal. In a recent review of the literature[32], this item has proved to be one of the most difficult goals to achieve, although the presented results should be considered generally good[24,35]. In our opinion, room for further improvement in GC, is to be found in strict adhesion to early UC removal and iv fluid withdrawal which should lead to a higher rate of patients' early mobilization.

Regarding 30-d post-operative outcomes, no mortality was observed in the 225 patients. Our data showed that 57% of patients aged more than 75 years old did not experience any complication and only one patient experienced a major complication requiring reiterative surgery (anastomotic leak); readmission rate was low as well. As previously assessed[27], these results confirm the safety of ERPs at all ages despite a significantly higher comorbidity rate. Considering the 3 groups, the occurrence of surgery-related adverse events was comparable whilst, the rate of general complications was almost doubled in Groups B and C compared to Group A. This difference was mainly related to the progressive increase in cardiovascular complications observed with age increasing (2% *vs* 5% *vs* 12%). Conversely, no differences were found in respiratory complications rate that, in accordance with recent literature (2%-7%), was less than 5% in the 3 groups[25,28]. These results confirm the role of ERPs in preventing pulmonary complications and support the data denying a relationship between early oral intake and higher risks of inhalation.

Surgery specific complications were equally distributed among the 3 groups, with an overall anastomotic leak rate of 2.2% and prolonged post-operative ileus rate of 8.9%, in line with those reported in other studies[24,26,33]. In our experience, the median overall LOS of 5 d (2-40) was in line with the recent European literature[24-27]. Elderly patients equally benefitted from ERP as younger patients in terms of LOS although, fewer patients fulfilled the clinical discharge criteria on POD 3 so that, in accordance to the results from the PeriOperative Italian Society Registry, time to readiness for discharge was one day longer in patients aged more than 75 years[25]. When analyzing the causes for a delayed discharge, logistical challenges such as home care or hosting structure availability, are the most important factors[24]. Social and organizational issues or further care factors can account for about 11.5% of failures to discharge[22,34]. In our study delayed discharge was similar in the 3 groups proving that adequate counselling and family information on post-operative fast-track course reduce the time delay between time to readiness for discharge and the actual return to home or hosting structure for elderly patients.

Our study has some major limitations that should be mentioned. First, although

data were prospectively acquired, the study design is retrospective. Therefore, data on specific scores evaluating patients at risk for surgery as ColoRectal Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (CR-POSSUM) score, were not included in data collection. Although colorectal CR-POSSUM and other frailty indexes[11] have proved to identify patients at risk for possible failure of ERPs[24,35], these scores tend to overestimate morbidity and mortality, since firstly elaborated for open surgery[36]. Considering this drawback and the limited use in clinical practice, such information was not considered in data collection. We should also consider that the limited number of patients in Group B and C could have limited the evaluation of confounding factors such as the higher number of rectal resections in Group A. Analysis of larger populations also considering multicentric study design should be carried out to reduce influence of confounding factors. Second, lack of analysis of patients pre-operatively excluded from the ERP. At the time we started our ERP, we established to include all patients independently from age and extent of colorectal resection. But severe comorbidities were considered as exclusions criteria since perioperative management could have been altered greatly. Recently, Braga *et al*[25] reported that older patients with high ASA grade (III-IV) do not require a specifically tailored pathway and can benefit from ERP both in terms of morbidity and LOS[25]. In our experience patients older than 75 years required post-operative ITU stay in 52% of the cases (15 out of 29; data not shown). Furthermore, two third of patients were excluded from study protocol due to their own or family refusal and due to severe neurological impairment, that hampered their participation into ERP (Figure 1). A specifically designed protocol with tailored goals has now been implemented in our practice since, it is our belief that the two subgroups need to be managed differently in order to optimize post-operative results in both populations.

Third, a complete prehabilitation program considering all aspects influencing post-operative short-term results, such as nutritional status, anemia correction, improvement of muscle function, *etc*., was not regularly accomplished; herein the idea that short-term outcomes could be further improved. A comprehensive prehabilitation program has been recently implemented in our clinical practice for all patients undergoing colorectal resection although, a major benefit is expected for elderly population.

CONCLUSION

Our study confirms that ERP can be safely and successfully applied to most of the elderly patients undergoing laparoscopic colorectal resection who are able and willing to participate in fast-track protocols. Although patients aged more than 75 years showed a lower GC rate and required a longer time to achieve discharge criteria (TRD), complication rate, readmission rates and LOS were comparable to those of younger patients. The value added from standardized prehabilitation protocols in improving short-term outcomes in elderly population should be further evaluated.

ARTICLE HIGHLIGHTS

Research background

Life expectancy is increasing worldwide, and a growing number of colorectal resections are expected to be operated in older patients in the next future. Age has been traditionally considered a risk factor for poor surgical outcomes and delayed recovery after surgery. After the advent of laparoscopy, more recently, enhanced recovery protocols (ERP) aimed at further improvement in surgical results for elderly patients.

Research motivation

Fast-track protocols have proved their efficacy in improving length of stay, morbidity and recovery after colorectal surgery. Nevertheless, most studies have excluded elderly patients assuming greater frailty and lower compliance to ERP. Moreover, few papers have evaluated the most challenging recovery goals for this population.

Research objectives

The main objectives of this study were to evaluate the feasibility and safety of ERP in elderly patients undergoing colorectal resection with minimally invasive approach. Global compliance to fast-track items was evaluated together with its impact on discharge delay.

Research methods

Our prospectively maintained departmental database of patients undergoing colorectal resection between March 2014 and July 2018 was examined to identify patients enrolled in fast-track

protocol. According to the World Health Organization's definition of elderly and old elderly, patients were divided in 3 groups (Group A, ≤ 65 years old, Group B, 66-75 years old and Group C, > 76 years old). Clinic and pathologic characteristics of the three groups were compared. Further analysis included short-term outcomes and recovery results considering fast-track protocol compliance as the amount of ERP's items successfully achieved.

Research results

Of 317 patients who underwent laparoscopic colorectal resection during the study period, 225 met the inclusion criteria and were divided in Group A (n = 112), Group B (n = 57) and Group C (n = 56). Although a higher rate of patients with more than two comorbidities was observed in Group B and C (P < 0.001), major complication, reoperation and readmission rates were comparably low among the three groups. Whilst the median time to fulfil the proposed discharge criteria was significantly shorter in Group A and B (P = 0.040), median length of hospital stay (LOS) was comparable within groups. The most difficult ERP goals to be achieved in the elderly were carbohydrate rich drink consumption (P = 0.022) and walking resumption on the first post-operative day (P = 0.032). Furthermore, Group C resulted less efficient in early urinary catheter removal (P = 0.013).

Research conclusions

This study found no age-related differences in the main short-term outcomes after laparoscopic colorectal resection performed within a fast-track protocol. Morbidity, reoperation and surgical complication rates were similar in the three groups. Even tough elderly patients required more time to fulfil discharge criteria no differences in LOS were observed. Global compliance within Group B and C was satisfying although room for specific items' improvement was highlighted.

Research perspectives

Our results suggest that elderly patients can be safely enrolled within ERP. Reasons for fast-track goals failure should be registered in prospectively collected databases and considered for further research. The evidence of characteristic age-related difficulties in achieving ERP objectives could then lead to the definition of specific targets for prehabilitation programs.

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