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ROBOTIC VERSUS LAPAROSCOPIC INTRACORPOREAL ANASTOMOSIS IN RIGHT COLON CANCER SURGERY: ANALYSIS OF PATIENTS' OPERATIVE OUTCOMES AND OPERATORS' CURRENT ATTITUDES BY MEANS OF A MONOCENTRIC CLINICAL PROSPECTIVE STUDY AND A EUROPEAN MULTICENTRIC RETROSPECTIVE STUDY

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INDEX

ABSTRACT

Background. Whereas laparoscopy proved to have better operative outcomes than open surgery over the years, robotic surgery provided no clear advantages over laparoscopy despite its more advanced technical features. However, robotic technology might help to achieve some advantageous procedures which are generally regarded as challenging, such as performing an intracorporeal anastomosis during a right colectomy. The objectives of this research project were: 1) to compare the outcomes of laparoscopic and robotic surgery in the case of a right colectomy with intracorporeal anastomosis for colon cancer; 2) to find any factors influencing surgical decisions and outcomes.

Methods. First, we conducted a meta-analysis comparing the outcomes of laparoscopic and robotic right colectomy, providing subgroup analyses for both extracorporeal and intracorporeal anastomosis. Second, we conducted a monocentric prospective clinical study comparing laparoscopic and robotic right colectomy with intracorporeal anastomosis only. Thereby, we participated in the European multicentric retrospective study MERCY (Minimally invasivE surgery for oncologic Right ColectomY). This study investigated the most relevant issues of minimally invasive right colectomy, such as the comparison between extracorporeal and intracorporeal anastomosis, the search for predictors of surgical outcomes and factors influencing the choice of surgical approach and type of anastomosis, the description of current trends in the minimally invasive surgery of right colon cancer, and the comparison between robotic and laparoscopic right colectomy with intracorporeal anastomosis.

Results. We performed the largest meta-analysis on laparoscopic vs robotic right colectomy currently available, providing the first subgroup analysis for intracorporeal anastomosis only. In the pooled data analysis, the better results of robotic surgery are presumably attributable to the clear prevalence of the intracorporeal anastomosis in the robotic group rather than to the surgical approach itself. The subgroup analysis for intracorporeal anastomosis found a shorter hospital stay after robotic right colectomy, but the retrospective nature of almost all included studies cannot be excluded as an explanation. However no higher rate of anastomotic leak was found after laparoscopic surgery, suggesting that laparoscopy is as effective and safe as robotic surgery in fashioning an intracorporeal anastomosis. Our clinical research found no differences comparing 24 laparoscopic vs 40 robotic right colectomies with intracorporeal anastomosis, except a longer operative time in the robotic group. Thereby, the MERCY study found that age, male gender, BMI, ASA score, robotic surgery, and intracorporeal anastomosis were significant predictors of surgical outcomes when performing a right colectomy for cancer. Moreover, the intracorporeal anastomosis has become increasingly widespread over the years. In this regard, age > 90 years, ASA IV, stage cT4, multivisceral resection and intraoperative hemodynamic instability were identified as factors influencing the choice of the type of anastomosis to perform. The comparison between robotic and laparoscopic right colectomy with intracorporeal anastomosis did not find any difference in terms of short-term outcomes and survivals supporting robotic surgery over laparoscopy.

Conclusions. The robotic surgery is not superior to laparoscopy in performing a right colectomy with intracorporeal anastomosis for cancer. However, the debate should be directed towards the definition of ever more effective criteria for selecting patients for a specific minimally invasive approach and a specific type of anastomosis. Finally, the evidence collected throughout our research was summarized and formalized in the elaboration of the 2021 guidelines for robotic right colectomy of the *Association Française de Chirurgie* (AFC), in which we have taken an active part.

SUMMARY

CHAPTER 1

1. INTRODUCTION

1.1. Background

1.1.1. Etymology

The word “robot” denotes a programmable machine able to carry out one or more tasks in place of man or in his support, with a variable degree of autonomy. This term comes from the Czech noun “robota” (hard labor, forced labor or servitude), which contains the same radical of the words meaning "work" in several modern Slavic languages, such as Polish, Ukrainian and Russian[1].

The word “robot” was first used by the Czech writer Karel Čapek in his science fiction work entitled “R.U.R.” (Rossumovi univerzální roboti, Rossum's Universal Robots), published in 1920. In this play set in the future, Dr. Rossum produces artificial workers in his factory to free humanity from physical fatigue. These “robots” are indistinguishable from humans and spread rapidly all over. But after a while, they start to rebel against men and finally manage to conquer the world.

In 1943, the visionary Russian-born American writer Isaac Asimov first used the word “robotics” in a short science fiction story called “Runaround”. Here, the author reports for the first time the "Three Laws" of robotics, three rules engraved in the artificial brain of autonomous humanoid robots in order to control them and prevent them from rebelling against their human creators.

Therefore, since their origin, the words “robot” and “robotics” underlie two fundamental aspects: the work done by a servant to the advantage of man and the need for man to control his servant so that he remains obedient.

1.1.2. Diffusion of robots in surgery

Knowing the history of the implementation of robotic technology in surgery is useful for appreciating the great advances currently occurring in this field. Here we report some important and interesting landmarks to provide a general overview.

1.1.2.1. From industry to surgery

At the origin of the development of robotic technology during the XX century there is the concept of “telepresence”, intended as the idea that people can appear, receive stimulations, and produce some effects in a place other than their real location as if they were really present. This idea animated the development of the first robotic arms intended to be used in hostile environments, such as the ocean floor, or to manipulate hazardous materials[2].

Already in 1951, engineer Raymond Goertz designed the first teleoperated articulated arm for the United States Atomic Energy Commission to handle radioactive material safely and reduce the risks for personnel. This system was a manipulator using just pulleys and cables as mechanical coupling between operator and machine, but it already represented a major progress in terms of design and feedback technology[3,4].

In 1954, engineer George Devol patented a programmable robotic system designed for transferring objects and conceived for a large variety of purposes. From this initial project, he developed the world's first industrial robot, Unimate. He also co-founded with engineer Joseph Engelberger the world's first robotics industry, Unimation, located in Danbury, Connecticut, and producing Unimate[4,5].

In 1961, the first Unimate robot was installed in a General Motors factory in New Jersey and consisted in a robotic arm lifting hot metal objects from die-casting machines and stacking them. Several automobile companies soon understood the potential of this technology, and a large-scale production of this robot started[4,5].

In 1969, Victor Scheinman, a researcher of the Stanford Artificial Intelligence Laboratory, developed the "Stanford Arm". It was an all-electric, computer-controlled, six-axis articulated robotic arm, able to follow random trajectories and to perform a series of instructions, unlike previous machines, which moved along one fixed trajectory and performed only one task repeatedly. Indeed, the "Stanford Arm" was specifically designed to widen the application of robots to complex tasks, such as assembly and arc welding. Its potential applications were proved in 1974, when a sensor guided experimental version of this robotic arm managed to assemble a car water pump without any human intervention[4-6].

In 1977, Scheinman sold his invention to Unimation. On this base, Unimation collaborated with General Motors and developed the Programmable Universal Manipulation Arm (PUMA), which represented the base for the production of a successful series of industrial robots[4-6].

With the production of the PUMA, the robotic technology enters the operating theatre. Indeed, the first use of a robot in a surgical procedure was documented in 1985 by Dr Yik San Kwoh, who reported a CT-guided stereotactic biopsy of a brain tumor performed in a 52-year old male patient using a Unimate PUMA 200 robotic arm at the Memorial Medical Center, Long Beach, California[7].

1.1.2.2. Surgical robots spreading

Since the second half of 1980's, several robotic surgical systems started to appear in the operating theatres. In 1988, researchers from the Imperial College of London developed the PROBOT system to perform prostatic resections. In 1992, Integrated Surgical Systems, in collaboration with IBM, released the ROBODOC system, successfully used for milling the femur in hip replacement procedures[1,2,8-11].

In the same period, a group of researchers of the National Aeronautics and Space Administration (NASA) working on virtual reality started collaborating with researchers of the Stanford Research Institute (SRI) working on accurate surgical telemanipulators for open microsurgery. After the presentation of Jacques Perrisat's laparoscopic cholecystectomy at the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) in 1989, the SRI developers were urged to adapt their telepresence surgical system to the new laparoscopic approach, which was immediately regarded as a perfect field of implementation for robotic technology[11].

Meanwhile, the U.S. Defense Advanced Research Projects Agency (DARPA) started a research program to develop a robotic surgical telemanipulator mounted on a mobile armored vehicle and remotely operated by a surgeon at a rear facility area. The aim of this project was to allow surgeons to control life-threatening injuries on the battlefield and stabilize injured soldiers before they were taken away. For this purpose, DARPA funded SRI, which developed a robotic system proving successful in performing complex surgical procedures in animal models. Finally, the project was not completed for human use, but it provided solid bases for the development of the robotic systems later used in surgery[11].

In 1993, Computer Motion, funded by NASA and DARPA, released the Automated Endoscopic System for Optimal Positioning (AESOP), an intern replacement voice-controlled robotic arm allowing an automatic control of the camera during laparoscopic surgery[11].

In 1996, the same company released ZEUS, a surgical system consisting of three robotic arms attached to the operating table, one of which was an AESOP, with originally six degrees of freedom (later become seven) and a monitor provided console for remote control[11]. In 2001, it was used by Prof. Jacques Marescaux operating in New York to perform the first transatlantic robotic cholecystectomy in a 68-year-old female patient laying on the operating table in Strasbourg, the so called "Lindbergh Operation" [12,13].

In 1995, Drs Fred Moll and John Freund, together with engineer Robert Younge, founded Intuitive Surgical after negotiating for the intellectual properties of SRI robotic surgical systems. On this bases, Intuitive Surgical developed the first prototype of da Vinci surgical system in 1997. After being ameliorated, the system received US Food and Drug Administration (FDA) approval in 2000 and, after passing through several versions, it currently represents the most widespread and used master-slave robotic surgical system in general surgery[11].

It must be noted that several other robotic systems have been used in surgery so far, but here we only selected the ones appearing to mark more deeply the evolution of robotic technology in operating rooms.

1.1.2.3. Main types of robots used in surgery

Several authors distinguish three main types of robotic surgical systems[9]:

1. "Precise path systems", consisting in robots previously programmed to perform predefined and repetitive tasks, such as several types of devices used for prostatic transurethral resections and to puncture the renal calyces.
2. "Intern replacement systems", consisting in robotic devices intended to replace surgical assistants in tasks requiring dexterity and stability, such as the AESOP system.
3. "Master-slave systems", consisting of several robotic arms remotely controlled by a surgeon through a computer console, mimicking precisely on the patient laying on the operating table the movements carried out by the surgeon at the console, and never moving without surgeon's guidance; in this context, the da Vinci surgical system has become paradigmatic.

Of course, this is not a complete summary, but it is useful to set out some important phases in the implementation of robotic technology in surgery.

1.1.3. Introduction of robotic technology in colon surgery

The first cases of robot-assisted colectomies were published in 2002[14]. In particular, Weber et al.[15] reported one case of sigmoid colectomy for diverticular disease in a 50 year-old female patient, and one case of right hemicolectomy for caecal diverticulitis in a 43-year old male patient. In both procedures, a da Vinci surgical system was used for large bowel mobilization, whereas colonic section and vascular ligations were accomplished with a laparoscopic-assisted technique, and anastomoses were performed extracorporeally. Moreover, the same surgical team published in the same year a comparative study reporting 15 laparoscopic colectomies performed using an AESOP 3000 robotic camera holder and 11 not robot-assisted laparoscopic colectomies[16].

The first cases of patients with colon cancer undergoing robot-assisted surgery with a master slave robotic system were reported by Hashizume et al.[17] in 2002, and they consisted in one ileocecal resection, one left hemicolectomy, and one sigmoidectomy performed by means of da Vinci technology for caecal, descending colon, and sigmoid colon cancer respectively[14].

Since then, many studies concerning robot-assisted surgery of the colon were published in the literature, marking a progressive amelioration of technical practices and a wide spread of competences. Among these studies, a certain attention should be paid to a case series of right and left colectomies published by Rawlings et al.[18] in 2007, where the authors reported the first cases of robot-assisted side-to-side intracorporeal anastomosis after right colectomy.

1.2. Research rationale

Over the years, numerous studies compared laparoscopic vs open approach in colon surgery, demonstrating that laparoscopy provides better outcomes, especially in terms of lower blood loss, pain reduction, faster recovery of intestinal functions, and shorter hospital stay, while assuring the same oncological adequacy[19-29].

Conversely, the advantages of robotic surgery over laparoscopy appear less evident. Indeed, the highly favorable technical features of surgical robots, such as a stable, immersive three-dimensional view, an augmented handling dexterity due to seven degrees of freedom and ambidextrous capabilities, seemed to offer the potential to overcome the limitations of conventional laparoscopy, mainly due to less favorable ergonomics. Therefore, many studies were carried out to compare the outcomes of robotic and laparoscopic colon surgery, but their results were contrasting, and clear conclusions were not possible. Moreover, the favorable technical aspects of robotic surgery were balanced by significant drawbacks, such as long operative time and high costs[30,31].

In this regard, a systematic review with meta-analysis published by Ng et al.[32] in 2019 tried to state whether robot-assisted surgery had better outcomes compared to conventional laparoscopy in colorectal cancer treatment. The authors included overall 6 randomized clinical trials and 67 among prospective/retrospective cohort studies and case-control studies, demonstrating that robotic surgery was superior to conventional laparoscopy in terms of all-cause mortality, incidence of intraoperative blood loss, time to oral diet, surgical site infection and length of hospital stay, but inferior in terms of operative time. No significant difference was found concerning anastomotic leak and disease recurrence. However, regarding to the subgroup of randomized clinical trials, no significant difference was found, except for operative time, which was higher for patients operated using robotic systems. Therefore, the authors concluded for no clear advantages of robotic approach over laparo-scopy in colorectal surgery.

By the way, several authors argue that the use of robotic technology may shorten surgeons' learning curves compared to laparoscopy[31,33,34]. They also claim that surgical robots may facilitate the execution of several procedures usually regarded as difficult and hazardous when performed in laparoscopy[31,33,34]. Among these procedures, one of the most frequently cited is the confection of an intracorporeal anastomosis during a right colectomy[35-38].

Right colectomy is one of the most common procedures performed in colorectal surgical units. Laparoscopy represents the gold standard technique for right colon cancer, showing several short-term operative advantages over laparotomy while assuring similar oncological results [39-44]. Nowadays, the minimally invasive right colectomy (laparoscopic or robotic) is more frequently performed than open surgery for benign or malignant pathologies of the right colon.[45,46] By the way, it was recently reported that while the rate of minimally invasive procedures is apparently stabilizing on the one hand, robotic surgery is starting replacing laparoscopy on the other hand[46]. Indeed, a debate still persists about what type of approach, laparoscopic or robotic, should be used to maximize the benefits of minimally invasive surgery in the case of a right colectomy.

To date, five meta-analyses[47-51] published between 2014 and 2019 compared the main short-term and pathological outcomes of laparoscopic and robotic right colectomy. Overall, they reported contrasting results, except for a significantly longer operative time for robotic surgery. However, only two studies[48,49] included a subgroup analysis on the type of anastomosis performed. In particular, both of these studies compared laparoscopic vs robotic right colectomy with extracorporeal anastomosis for both approaches, while only one[49] compared laparoscopy with extracorporeal anastomosis vs robotic surgery with intracorporeal anastomosis. In none of the studies intracorporeal anastomosis was performed by both surgical approaches.

The type of anastomosis performed, extracorporeal or intracorporeal is another crucial aspect, feeding the controversies over minimally invasive right colectomy. Notably, several recent studies[52-57], including five systematic reviews with meta-analysis[52-56,58] and a randomized clinical trial[59], compared the outcomes of patients undergoing laparoscopic right colectomy with extracorporeal or intracorporeal anastomosis. Interestingly, these studies confirmed the safety and feasibility of intracorporeal anastomosis, reporting faster postoperative recovery, shorter hospital stay, and also lower rates of conversion[57] and postoperative complications[54,55,57]. However, intracorporeal anastomosis is definitely less widespread than extracorporeal anastomosis, and its implementation in current surgical practices is limited, although its first description gets back to the early ’90.[60-63]

The supposed benefits of the intracorporeal anastomosis are probably related to a decreased need to mobilize the transverse colon, a lower risk of mesenteric traction, and a shorter laparotomy, usually placed off the midline and used only for the extraction of the surgical specimen. As shown by several retrospective series and some randomized clinical trials, the confection of an intracorporeal anastomosis may also results in faster resumption of intestinal functions[64], shorter length of hospital stay[65,66], and lower rates of surgical site infections[67] and incisional hernias[68-70]. However, most surgeons still regard the intracorporeal anastomosis as a challenging procedure, which may require a longer operative time and an increased risk of anastomotic leakage[35,52-59,63,69,71-73].

Recent retrospective studies and meta-analyses suggested that robotic right colectomy may provide additional short-term benefits over laparoscopic right colectomy, and even facilitate the confection of an intracorporeal anastomosis, despite longer operative times and higher costs[60,74,75]. However, there is no widespread consensus or international guidelines on this subject, and the choice of which type of surgical approach to use and which type of ileocolic anastomosis to perform is left the experience of the operating surgeon.

1.2.1. Surgical techniques

1.2.1.1. Laparoscopic right colectomy

Many variants of set-up for laparoscopic right colectomy have been reported in the literature. Here the most frequent setting is described.

The patient is placed in a modified lithotomy position, with the left arm along the body, the right arm abducted. The table is given a variable Trendelenburg and left tilted position. The video column is placed to the patient's right.

Four laparoscopic ports are placed in two main set-ups. The first requires: a 12 mm para-umbilical port for a 30° laparoscope, a 12 mm left pararectal port in the left flank (surgeon's right hand, L1), a 5 mm suprapubic port (surgeon's left hand, L2), a 5 mm right pararectal port in the right flank for the assistant (L3)[33]. The second differs from the first for placing the two main operating ports along the left mid-clavicular line[76]. For both configurations, a supplemental 5 mm epigastric port ay be added[77,78]. The surgeon is placed to patient's left, the first assistant to surgeon's right, the second assistant between patient's legs, the nurse to surgeon's left.

After inducing a 12 mmHg pneumoperitoneum, the abdominal cavity is inspected, the site of the tumor is confirmed, and the feasibility of a radical resection is assessed. The oncological right colectomy is generally performed with a medial to lateral approach. The ileo-colic junction is retracted laterally to tension the ileo-colic pedicle. The peritoneum is incised just below this latter one, and the dissection is carried out cephalad along the Toldt's fascia, up to the third part of the duodenum and the anterior face of pancreas's head. The ileo-colic pedicle is divided at its origin from the superior mesenteric axis. The transection of the mesocolon is continued cephalad along the same axis, dividing at their origin the vessels encountered, notably the right colic vessels (when present) and the right branches of the middle colic vessels. If an extended right colectomy is required, the entire middle colic pedicle is also divided. The peritoneum of the right colonic gutter is incised, from the caecum to the hepatic flexure, and the colo-epiploic ligament is sectioned. The dissection is then continued posteriorly to join the previously dissected Toldt's fascia. Once the right colon is completely mobilized, a mechanical stapler is used to divide the transverse colon and the distal ileal loop. Then, an extracorporeal or an intracorporeal anastomosis is performed. In the case of an extracorporeal anastomosis, a midline laparotomy or a left transverse laparotomy is generally used to fashion the anastomosis and extract the specimen. In the case of an intracorporeal anastomosis, the specimen is extracted through a suprapubic incision after the confection of the anastomosis. Drain positioning is not routinely.

1.2.1.2. Robotic right colectomy

Robot right colectomy surgical techniques have been standardized only for the da Vinci systems, whose versions Si and Xi are the most frequently used worldwide. These two versions differ from each other mainly for the configuration of their arms, which influences port placement and robot docking.

Many variants in port placement have been reported in the literature, all surgical teams developing their preferences. Here we describe four main set-ups of port positioning[79,80].

For both surgical systems, the patient is placed in a modified lithotomy position, with both arms along the body. The table is given a variable Trendelenburg and left tilted position (usually 10-15°).

Concerning the Si system, two methods of port placement can be used depending on the site of colon cancer, generally requiring three robotic ports and two laparoscopic ports, one for the camera and the other for the assistant. If the tumor is located in the caecum or in the ascending colon, the ports are placed as follows: a 12 mm optic port in a left para-umbilical position, an 12 mm robotic port 4-5 cm below the left costal margin on the mid-clavicular line (surgeon's right hand, R1), an 8 mm port 4-5 cm above the pubic symphysis on the midline (surgeon's left hand, R2), an epigastric 8 mm port to the left of the midline (assisting arm, R3), and a laparoscopic port in the left flank/left iliac fossa for the assistant. If the tumor is located in the hepatic flexure, the optic port, the robotic ports for R1 and R2 and the assistant's port are placed in the same position previously described, but the robotic 8 mm port for R3 is placed at the intersection between the right mid-clavicular line and the line running from the umbilicus to the right upper iliac spine.

After port placement, a single docking technique is used, approaching the robot to patient's right with a 15° angle. The video column is placed next to patient's left shoulder. The assistant stays to patient's left, and the nurse stays to the assistant's left.

Concerning the Xi system, two methods of port placement can be used, the "classic" set-up (or "medial to lateral"), retracing the laparoscopic right colectomy port positioning[33,81], and the "suprapubic" set-up (or "bottom to up"), which is more specific of robotic surgery[82-85]. Both methods are performed using four robotic 8 mm ports and one laparoscopic for the assistant. In the "classic" method, first an 8 mm port is placed in a para-umbilical position, then three other 8 mm ports are placed in an oblique line running from above the pubic symphysis to below the left costal margin. Finally, a laparoscopic port for the assistant is placed in the left flank. In the "suprapubic" method, the pneumoperitoneum is induced through a Palmer's needle, then four 8 mm ports are placed on a horizontal line 3-5 cm above the pubic symphysis in an equally spaced manner. Then, a laparoscopic port for the assistant is placed in the left flank. After port placement, a single docking technique is used after port placement, approaching the robot to patient's right with a 90° angle. The video column is placed next to patient's left shoulder. The assistant stays to patient's left, and the nurse stays to assistant's left.

Concerning robotic instruments, one or more among monopolar energy (hook or scissors), bipolar energy (fenestrated bipolar or bipolar Maryland), or vessel sealing devices are used. All these instruments are provided with EndoWrist technology and require an 8 mm port. For the confection of an intracorporeal anastomosis, two robotic staplers can be used, a SureForm 45 mm or a SureForm 60 mm, both needing a 12 mm robotic port.

The robotic right colectomy is performed following the same operative steps then laparoscopic right colectomy, preferring a medial to lateral approach for oncologic procedures. The use of indocyanine green may help in assessing the vascularization of ileal and colic stumps or to identify lymph nodes and guide the lymphadenectomy.

Few studies have compared da Vinci Si and Xi, probably because most centers are provided with only one platform. Anyway, robotic technology has improved considerably in the last decades, and the new generation of robotic platforms is not comparable to previous ones[86,87]. Therefore, the technical advances may have an impact on the feasibility of certain procedures and influence perioperative results[88-91]. In particular, the use of the da Vinci Xi robot might be associated with a shorter operating time compared to the da Vinci Si robot[88-92]. In an article published in 2019, Hamilton et al.[82] compared Xi vs Si and classic set-up vs suprapubic set-up. The use of the da Vinci Xi robot was associated with shorter operative time and hospital stay, although there was no significant in terms of complication rate [19] . Bianchi et al.[93] analyzed 109 right colectomies complete mesocolic excision performed using a suprapubic approach and performing an intracorporeal anastomosis, but the study was not comparative. However, the authors concluded that the suprapubic approach reduced the conversion rate and the rate of intraoperative and postoperative complications. Finally, Schulte Am Esch et al.[84] compared 24 patients operated using a suprapubic approach vs 7 patients operated using a classic approach. No difference was found apart from a larger number of lymph nodes removed with the suprapubic approach.

1.2.1.3. Extracorporeal anastomosis

After achieving the complete mobilization of the right colon, the camera hole is typically extended to create a vertical midline incision to extract the colon. Some authors prefer to extend the assistant's port incision in the right flank to create a short transverse laparotomy. Once the right colon extracted, the lymphatic resection is completed extracorporeally and an ileo-colic anastomosis is fashioned according to standard open techniques, manually or mechanically. The anastomosis is then reduced, and the laparotomy closed.

1.2.1.4. Intracorporeal anastomosis

After transecting transverse colon and terminal ileum using a laparoscopic or robotic stabler, the colic and ileal stumps are aligned in either an isoperistaltic or antiperistaltic fashion, then joined by a simple suture used for exposition. In most cases of laparoscopic and robotic right colectomy, a colotomy and an enterotomy are performed to create a common enterotomy, through which a stapled anastomosis is confectioned. The common enterotomy is then closed using a single-layer or a double-layer suturing technique. Less frequently, the anastomosis may be hand-sewn[94].

1.3. Research objectives

Given the complexity of the matter and the number of issues to take up, our research had multiple objectives.

First, we aimed to take a stock of the current knowledge about laparoscopic and robotic right colectomy in a complete and accurate way, paying a special attention to the type of anastomosis performed. After reviewing all the available literature on this matter, two questions were to be answered: 1) is there a difference in terms of operative outcomes between robotic and laparoscopic right colectomy? 2) is there a difference between laparoscopy and robotic surgery when performing a right colectomy with extracorporeal or intracorporeal anastomosis?

Second, we aimed to compare the results of laparoscopic and robotic right colectomy with intracorporeal anastomosis, to assess the impact of each minimally invasive approach when using the type of anastomosis presumed to be the most favorable for the patient but also the most difficult for the surgeon.

Thereby, we aimed to describe the evolution of surgeons' attitude in the minimally invasive treatment of right colon cancer over the years, as well as to identify any eventual critical factors influencing their choice in terms of both surgical approach and type of anastomosis.

CHAPTER 2

2. MATERIALS AND METHODS

To achieve the objectives of our research project, we proceeded as follows. First, we conducted a systematic review of the literature comparing the results of laparoscopic and robotic right colectomy, performed with extracorporeal or intracorporeal anastomosis. A meta-analysis was also carried out, to sum up the current evidence on this subject and try to clarify some unresolved issues, such as the impact of the surgical approach on postoperative recovery and hospital stay.

Second, we conducted a single-institution prospective clinical study comparing laparoscopic and robotic right colectomy both performed with intracorporeal anastomosis. The aim was to determine whether the two minimally invasive approaches had a different impact on patients' outcomes, the type of anastomosis being the same and the most advantageous for both.

Thereby, we participated to the European multicentric retrospective study MERCY (Minimally invasivE surgery for oncologic Right ColectomY) with the purpose of: 1) outlining the current trends in the minimally invasive treatment of right colon cancer; 2) comparing the outcomes of extracorporeal and intracorporeal anastomosis in minimally invasive right colectomy; 3) identifying any eventual predictor of operative outcomes; 4) assessing surgeons' preferences through a questionnaire; 5) identifying any eventual criteria influencing surgeons' decisions regarding the type of minimally invasive approach to use and the type of anastomosis to perform; 6) finally comparing laparoscopic vs robotic right colectomy, both performed with intracorporeal anastomosis, in terms of operative and survival outcomes.

2.1. Meta-analysis

Our systematic review of the literature with meta-analysis was conducted in accordance to the PRISMA checklist[95].

2.1.1. Study selection criteria

The study selection criteria were established before starting the literature search to ensure the correct identification of the eligible studies.

A study was selected when it met all the following criteria: 1) publication in English; 2) randomized or observational study, prospective or retrospective; 3) comparison between laparoscopic and robotic right colectomy on at least one operative, pathological or survival outcome.

Case reports, review articles and conference abstracts were excluded. To write the literature search equation, the PICOs[96] framework was used.

2.1.1.1. Participants

Participants were adult patients (age > 18 years) presenting with benign or malignant disease located in the right colon and requiring surgical resection.

2.1.1.2. Interventions

The interventions were laparoscopic right colectomy (LRC) and robotic right colectomy (RRC) with extracorporeal anastomosis (EA) or intracorporeal anastomosis (IA).

2.1.1.3. Compared groups

We compared the following groups:

- overall LRC (LRC) vs overall RRC (RRC)
- LRC with EA (LRC-EA) vs RRC with EA (RRC-EA)
- LRC with IA (LRC-IA) vs RRC with IA (RRC-IA).

2.1.1.4. Outcomes

We considered the length of hospital stay as the primary outcome. The secondary outcomes included: overall operative time, estimated blood loss, conversion to open surgery, time to flatus, 30-day overall complications, 30-day severe complications (Clavien-Dindo > II), anastomotic leak, ileus, surgical site infection (SSI, including both superficial and deep infections), incisional hernias, reoperation, 30-day readmission, 30-day mortality, number of harvested lymph nodes, positive resection margins, 5-year disease-free survival (DFS), 5-year overall survival (OS), and total costs.

2.1.1.5. Study design

We considered randomized clinical trials (RCTs) and both prospective and retrospective observational studies.

2.1.2. Literature search strategy

A first systematic search of the literature was conducted on April 6, 2020, using the online databases Medline (through PubMed), Scopus and Web of Science. The search equation for each database was written using the following keywords: “laparoscopic”, “robotic”, and “right colectomy”. More precisely, we used the following search equations:

- for PubMed: (((laparoscopic[Title/Abstract]) AND robotic[Title/Abstract]) AND right[Title/Abstract]) AND colectomy[Title/Abstract]
- for Scopus: (TITLE-ABS-KEY(laparoscopic) AND TITLE-ABS-KEY(robotic) AND TITLE-ABS-KEY(right) AND TITLE-ABS-KEY(colectomy))
- for Web of Science: TS=(laparoscopic AND robotic AND right AND colectomy).

The initial search was updated on April 5, 2021, using the same search equations. In addition, we searched out the references of the selected articles and of the most relevant excluded studies to identify any additional eligible publication. Only articles written in English were considered, and no time limitations were applied.

2.1.3. Study selection and quality assessment

Two independent reviewers (PG, GP) screened the literature according to the relevance of titles and abstracts. The retained articles underwent a full-text analysis. Any disagreement between the two reviewers during the selection process was resolved by discussion with a third reviewer (NdeA).

The critical assessment of the study quality and of the risk of bias was carried out by both reviewers independently. For this purpose, we used the following tools: the revised Cochrane risk of bias tool (RoB-2) for RCTs[97], and the Newcastle-Ottawa Scale (NOS) for case-control studies[98]. Additionally, the Grading of Recommendations Assessment, Development, and the Evaluation (GRADE) system was used to grade the overall "body of evidence" that emerged from this systematic review[99,100].

2.1.4. Data extraction and analysis

Data from the included studies were analyzed for qualitative and quantitative analyses. Outcome measures were extracted or estimated for each surgical approach. For continuous variables, each value was rounded to the first decimal place, which was increased by one if the second decimal place was ≥ 6.

When outcomes were reported using median (range) and median (interquartile range, IQR), the mean was estimated as described by Luo et al.[101], while the standard deviation (SD) was estimated as described by Wan et al.[102] When outcomes were reported using mean (95% confidence interval, 95% CI), the SD was estimated as described in the Cochrane handbook for Systematic Review[103]. All costs reported in Euros were converted into US dollars.

The pooled estimates of mean difference (MD) and 95% CI were calculated using a random-effects model due to the expected heterogeneity among the included studies. For dichotomous variables, the odds ratios (ORs) and the Mantel-Haenszel method were used. Heterogeneity was assessed using the I^2 statistic and interpreted according to the Cochrane handbook for Systematic Review[103]. To compare the survival rates of different approaches, hazard ratios (HRs) and 95% CI were calculated as described by Tierney et al.[104]. The pooled effect was considered significant when $p < 0.05$. For calculations, we used the statistical software Review Manager version 5.3 (Cochrane Collaboration, Copenhagen, Denmark).

2.2. Monocentric prospective clinical study

We conducted a monocentric prospective clinical study in collaboration with the Digestive and Hepato-bilio-pancreatic Surgery Unit of Henri Mondor University Hospital, University of Paris-Est Créteil, Créteil, France, as part of an international collaboration with the University of Palermo.

2.2.1. Study design

We prospectively recorded all consecutive elective laparoscopic and robotic right colectomies with intracorporeal anastomosis performed at Henri Mondor University Hospital between November 2018 and July 2021.

The right colon has been defined as the set of cecum, ascending colon and hepatic flexure. Tumor staging was performed according to the classification of the American Joint Committee on Cancer (AJCC), 8th edition. Laparoscopic procedures were performed using standard laparoscopic instruments. Robotic procedures were performed using a da Vinci Xi system.

2.2.2. Study population

Patients were included when all the following criteria were met: 1) histologically confirmed right colon cancer; 2) stage 0-III resectable tumor (subcategory T4b excluded); 3) minimally invasive elective right colectomy with intracorporeal anastomosis. Patients were excluded when one of the following criteria was encountered: 1) locally advanced cancer with involvement of adjacent structures or organs (subcategory T4b); 2) metastatic disease (stage IV); 3) double tumor localization; 4) polyposis of the colon; 5) multivisceral resections.

2.2.3. Study variables

Data were collected prospectively. The following variables were considered:

- demographic: age and sex
- clinical: body mass index (BMI), preoperative blood test parameters (hemoglobin, leukocytes and albumin), malnutrition (loss of more than 10% of body weight in 6-12 months), comorbidities (cardiovascular and respiratory diseases, renal insufficiency and diabetes), American Society of Anesthesiologists (ASA) score, AJCC 8^{th} edition tumor stage, adjuvant chemotherapy
- operative: operative time, conversion to open surgery, estimated blood loss, rate of patients transfused intraoperatively, time to flatus, time to a regular diet, postoperative complications (ileus, anastomotic fistula, intra-abdominal abscess, surgical wound infection, pancreatic fistula and digestive bleeding), Dindo-Clavien scale for postoperative complications, length of hospital stay, 60-day, and 90-day mortality
- pathological: R0 resections, number of retrieved lymph nodes (< or ≥ 12), tumor sizes and grading.

2.2.4. Surgical technique

Patients undergoing minimally invasive right colectomies did not receive any specific colic preparation, except a low-fiber diet of one week and a fasting period of at least 6 hours before surgery.

When a laparoscopic right colectomy was performed, the patient was set-up in a left-tilted anti-Trendelemburg position, with left arm along the body, the right arm abducted, and straight-legs. The ports were placed as follows: a 10 mm optic supraumbilical port for a 30° laparoscope, a 12 mm AirSeal® port in the left iliac fossa, a 5 mm port in the suprapubic region, a 5 mm port in the left flank at the umbilical line, and an optional epigastric 5 mm port.

When a robotic right colectomy was performed, the patient was set-up in a left-tilted anti-Trendelemburg position, with both arms along the body, straight-legs, and a single docking of the robot to the right was carried out. The ports were placed as follows: four equidistant robotic 8 mm, ports along an oblique line running between the suprapubic region (4 cm above the symphysis) and the point of intersection between the left mid-clavicular line and the left costal arch; a 5 mm AirSeal port on the left midclavicular line at the umbilical level.

In both minimally invasive approaches, the procedure was initiated with a bottom-to-up and medial-to-lateral dissection. First, a transverse incision below the ileo-colic pedicle was performed. Then, dissection was continued along the Gerota's fascia until the anterior face of the duodeno-pancreatic block was freed. The control of the ileo-colic and right colic pedicles was achieved using 10 mm Hem-o-lok clips, applied at about one centimeter from their origin, without previously dissecting the superior mesenteric axis. The operation continued with the dissection of the right paracolic gutter and the hepatic flexure. Once the right colon was fully mobilized, the transverse mesocolon was sectioned and the ascending branch of the middle colic pedicle interrupted between

10 mm Hem-o-lok clips. Ileal and colic sections were performed using a 60 mm EndoGIA Linear Stitcher (purple cartridge) in case of laparoscopic procedure or a 60 mm EndoWrist Stitcher (blue cartridge) in case of robotic surgery. Two Vicryl 4/0 hemostatic running sutures were performed over ileal and colic agrafes lines. The two stumps were then placed in an isoperistaltic position and joined together by a simple stich of Vicryl 4/0 later used for exposition. Two facing breaches were practiced in the stumps, and an isoperistaltic mechanical ileo-colic anastomosis was performed using a 60 mm EndoGIA in case of laparoscopy and a 60 mm EndoWrist in case of robotic surgery. The common ileo-colic breach was then closed with two 4/0 Vicryl running sutured tied together.

In both surgical approaches, the specimen was extracted through a Pfannenstiel incision, protected by an Alexis wound protector and retractor and closed using a two-layer technique. Finally, the hole of the optic port (and of the AirSeal port in case of robotic surgery) were closed using one or two stitches of Vicryl 0, skin being closed using intradermal Monocryl 3/0 or 4/0 sutures.

2.2.5. Statistical analysis

For the comparison between categorical variables, the χ^2 test and Fisher's exact test were used. The Student and Mann-Whitney tests were used to compare continuous variables. A difference was statistically significant if $p < 0.05$. Statistical analyses were performed using the software SPSS (Statistical Package for Social Science, IBM SPSS Statistics, Version 22 for Macintosh).

2.3. MERCY Study

We participated to the European multicentric retrospective study MERCY (Minimally invasivE surgery for oncologic Right ColectomY), which involved 21 medium-high volume colorectal surgery centers (at least 50 procedures per year) in 6 European countries (France, Ireland, Italy, Spain, Switzerland, United Kingdom). These centers contributed differently to a common database providing anonymous data obtained from prospectively updated local databases.

This study was divided into two phases:

- in the first one, extracorporeal and intracorporeal anastomoses performed during laparoscopic or robotic right colectomy for cancer were compared in terms of operative outcomes; any eventual predictor of operative outcomes was searched; the current trends in the minimally invasive treatment of right colon cancer were investigated, trying to assess surgeons' preferences and to identify any eventual criteria influencing surgeon's decisions on the type of surgical approach and anastomosis
- in the second one, laparoscopic and robotic right colectomy, both performed with intracorporeal anastomosis, were finally compared in terms of operative and survival outcomes.

2.3.1. Study design and population

Patients were included when all the following criteria were met: 1) consecutive adult patients (age ≥ 18 years); 2) non-metastatic adenocarcinoma (AJCC stages 0-III) of the right colon (cecum, ascending colon or hepatic flexure); 3) curative and elective surgery performed between January 2014 and December 2020; 4) laparoscopic right colectomy (LRC) or robotic right colectomy (RRC) (performed using one of the versions of the da Vinci robotic system, Intuitive Surgical), with extracorporeal anastomosis (EA) or intracorporeal (IA) anastomosis.

Right colectomy was performed according to standardized surgical techniques, with at least a standard D2 lymphoadenectomy[105]. All patients were treated and followed up after surgery according to standardized protocols. The procedures were performed by experienced colorectal surgeons who had already completed the learning curve in minimally invasive surgery. The type of surgical approach (laparoscopic or robotic) and the type of ileo-colic anastomosis (EA or IA) were chosen by each surgeon based on patients' clinical state, personal experience and robotic technology availability, without specific pre-established criteria. Hand-assisted procedures were excluded. The study was conducted following the STROBE[106] checklist.

2.3.2. Study variables

Data were collected retrospectively from prospectively maintained database in each participating center. The following variables were considered:

- demographic: age, sex
- clinical: body mass index (BMI), comorbidities, Charlson Comorbidity Index (CCI), American Society of Anesthesiologists (ASA) score, tumor location, stage according to the American Joint Committee on Cancer (AJCC)
- operative: operative time, conversion to laparotomy, intraoperative complications, postoperative complications (anastomotic fistula and stenosis, prolonged ileus, surgical site infection), time to flatus, time to regular oral diet, length of hospital stay, reoperation, readmission, mortality
- pathological: tumor size, pT stage, pN stage, R0 resection, number of resected lymph nodes, perineural and perivascular invasion, tumor grade
- survivals: overall survival (OS), disease-free survival (DFS).

Morbidity and postoperative mortality were defined as events occurring during hospital stay or within 90 days of surgery. Prolonged postoperative ileus was defined as the absence of bowel movements or gas transit associated with intolerance of the oral diet for more than 3 days after surgery[107]. The surgical site infection (SSI) was defined as a hospital-acquired surgical wound infection[108]. The anastomotic fistula was defined as a clinically or radiologically demonstrated anastomotic dehiscence, with or without the need for reoperation[109].

Patients were followed up after surgery according to the protocols of the individual institutions. For the present study, only the data obtained during the short-term follow-up were analyzed.

4.2.3. Statistical analysis

With regard to the first phase, statistical analyses were performed using R 4.0 statistical software. The variables with completely random missing values were imputed using median values. For variables with non-random missing values, matching patients were excluded. Concerning the descriptive analyses, mean and standard deviation [mean (SD)] were provided for the continuous variables, number of cases and percentage [n (%)] for the categorial variables.

The descriptive comparisons between groups were performed using the t-test for continuous variables and the z-test for categorical variables. The p-value was calculated considering the adjustments for multiple tests according to the method of Benjamin and Hochberg[110]. Surgical trends were analyzed with a trend-test based on a non-parametric Spearman test[111].

To describe the way surgeons chose between EA and IA during an oncologic right colectomy, we used a classification tree approach. In particular, the Recursive Partitioning and Regression Trees[112] algorithm was used to identify factors able of allocating patients in EA or IA group. In this regression tree, for each choice point, the minimum difference of observations to make a split between EA and IA was set at n = 100.

Surgeons' attitudes and practices were also assessed through an online questionnaire sent to the operators involved in the MERCY study, invited to answer anonymously according to their own experience. Finally, in order to identify significant predictors of surgical outcomes, linear and logistic regressions were carried out with a mixed model. The hospital center was considered as a random effect variable. For each mixed model, fixed effects were first selected from those reaching a p-value ≤ 0.01 in the null model, the hospital center being considered as the only random effect. Then, all possible combinations of the preselected variables were made, choosing the selecting the model with the lowest AIC criteria as the final one, as described by Burnham and Anderson[113]. Forest plots were used to visually compare the effects of predictors on different outcomes. Coefficient estimates (odds ratios, OR, for mixed logistic models) were also calculated with their 95% confidence interval (CI).

With regard to the second phase, statistical analyses were performed using SPSS statistical software (Statistical Package for Social Science, IBM SPSS Statistics, Version 28 for Macintosh, with Essential for R plug-in). The variables showing completely random missing values were imputed using median values. Mean and standard deviation [mean (SD)] were provided for the continuous variables, number of cases and percentage [n (%)] for the categorial variables. The descriptive analyses comparing RRC-IA vs LRC-IA were carried out using the t-test for continuous variables, the chi-squared test or Fisher's exact test for categorical variables over the entire study population.

To minimize the selection bias related to the retrospective nature of the study and to take into account any eventual covariates influencing the selection between RRC and LRC, a Propensity Score Matching (PSM) method was used[114]. The propensity scores of each patient were calculated by running logistic regression models including the following covariates: age, sex, obesity, ASA score, CCI, clinical T stage, and year of surgery. The type of surgical procedure (RRC-IA or LRC-IA) was entered into the regression model as the dependent variable. A 1:1 "nearest neighbor" case-control match without replacement was used [115,116]. The two matched groups were then evaluated with respect to the study outcomes.

As pointed out by several authors[117,118], Cox regression models applied to the entire cohort might often be more powerful than other tools in detecting treatment effects. Therefore, survival analyses were performed on the whole sample. OS and DFS rates at 1, 3, and 5 years after RRC-IA and LRC-IA were analyzed using the Kaplan-Meier method. Then, the two surgical groups were compared using the log rank test (Mantel-Cox). For OS and DFS, the patient's death and the disease recurrence were respectively considered as events. Censoring was performed at the last follow-up date if no event occurred. Potential prognostic factors for survivals were evaluated by the Cox regression hazard model, including in the multivariate analysis all variables reaching p value < 0.2 on the univariate analysis by using a 'backward' stepwise selection procedure. The adjusted hazard ratio (HR) was given with 95% confidence interval (CI). A p value < 0.05 was considered to be statistically significant.

CHAPTER 3

3. RESULTS

3.1. Results of the meta-analysis

The first search of the literature identified overall 448 publications, which were screened according to their title and abstract. Initially, 38 articles were selected, but two of them reported the results of the same randomized clinical trial. In particular, its authors published short-term outcomes in 2012[119] and survivals in 2019[120]. Since the two articles reported the same demographic, clinical, operative and pathological results, we retained only the most recent publication. The update of the initial literature search identified an additional eligible article[121] which had not been already selected because it was published after the first research date.

Finally, 38 articles were included in the qualitative and quantitative analyses of our meta-analysis. The flowchart of the literature search and study selection process is shown in Figure 1.

3.1.1. Characteristics of the selected studies

The 38 selected articles[18,33,60,74,76-78,91,94,120-148] were published between 2003 and 2020. They included one randomized clinical trial[120] and 37 retrospective studies[18,33,60,74,76-78,91,94,121-140,142-148], five of which were[74,94,121,147,148] multicentric. They included overall 24,233 patients: 21,417 (88.4%) undergoing LRC and 2,816 (11.6%) undergoing RRC.

The demographic and clinical data are shown in Tables 1a and 1b. The operative outcomes are shown in Tables 2a and 2b. The pathological findings and survivals are shown in Tables 3a and 3b. Total costs are shown in Table 4.

3.1.2. LRC vs RRC

Overall 20 studies[18,60,91,120,122-137], one randomized clinical trial[120] and 19 retrospective studies[18,60,91,122-137], compared LRC vs RRC without reporting precise information on the type of anastomosis performed. More precisely, 8 studies[91,122,123,125-129] compared LRC vs RRC with no information on the type of anastomosis, 6 studies[18,60,132,133,135,136] compared LRC-EA vs RRC-AI, 2 studies[120,124] (including the only RCT) compared LRC-EA + AI with prevalent EA vs RRC-EA + AI with prevalent AI, 3 studies[131,134,137] compared LRC-EA vs RRC-EA + AI, and one study[130] compared LRC-EA + AI vs RRC-AI. Eight studies[33,78,138-144] compared LRC-EA vs RRC-EA, while 10 studies[74,76-78,94,121,145-148] compared LRC-AI vs RRC-AI.

The pooled data analysis shows that LRC has longer hospital stay than RRC (MD = 0.5; 95% CI: 0.16, 0.84; $p = 0.004$; $I^2 = 58\%$). Compared to laparoscopy, robotic surgery has longer operative time, but lower blood loss, lower conversion rate, faster time to flatus, lower overall postoperative complication rate, and higher number of harvested lymph nodes. Total costs are significantly higher for RRC than LRC. Regarding to the remaining outcomes analyzed (including anastomotic leak, ileus and pathological findings), LRC and RRC are similar.

Only 2 studies[78,120] reported disease-free survival and overall survival, but estimating hazard ratio (HR), difference between observed and estimated events (O-E), and variance (V) was not possible due to the heterogeneity of the available data. Therefore, it was not possible to perform a quantitative analysis for these outcomes. The forest plots of the pooled-data analysis are shown in Figures 2a and 2b.

3.1.3. LRC-EA vs RRC-EA

Eight retrospective studies[33,78,138-144] compared LRC-EA vs RRC-EA, including overall 589 patients: 408 (69.3%) undergoing laparoscopy and 181 (30.7%) undergoing robotic surgery.

Regarding the length of hospital stay, there is no significant difference between LRC-EA and RRC-EA (MD = 0.11; 95% CI: -0.73, 0.95; p = 0.79; I2 = 38 %). However, RRC-EA has longer operative time (+ 42.91 min on the average) and higher total costs (+ 2 157.19 US dollars on the average). Regarding to the remaining outcomes analyzed, there are no difference between laparoscopy and robotic surgery.

Only one study reported data concerning severe complications[33], reoperation[33], 30-day readmission[143], incisional hernias[142] and positive resection margins[33]. No study reported data concerning survivals. Therefore, it was not possible to perform a quantitative analysis for these outcomes. The forest plots of EA subgroup analysis are shown in Figure 3.

3.1.4. LRC-IA vs RRC-IA

Ten retrospective studies[74,76-78,94,121,145-148] compared LRC-IA vs RRC-IA, including overall 1,647 patients: 716 (43.5%) undergoing laparoscopy and 931 (56.5%) undergoing robotic surgery.

The length of hospital stay is longer for LRC-IA compared to RRC-IA (MD = 0.78; 95% CI: 0.23, 1.32; p = 0.006; I^2 = 30%). Conversely, robotic surgery has longer operative time than laparoscopy. All other operative and pathological results of LRC-IA and RRC-IA are similar.

Only 2 studies[145,148] reported positive resection margin data, but in one of them[145] the percentage could not be estimated. Only one study[78] reported survivals. For these results, it was not possible to perform a quantitative analysis. Therefore, it was not possible to perform a quantitative analysis for these outcomes. The forest plots of IA subgroup analysis are shown in Figure 3.

3.1.5. Study quality assessment

The included randomized clinical trial[120] was classified at high risk of bias (Supplementary Table 1). The risk of bias for the included retrospective studies[18,33,60,74,76-78,91,94,121-140,142-148] is shown in Supplementary Table 2. According to the GRADE system, the quality of the overall scientific evidence derived from this meta-analysis is classified between low and very low (Supplementary Tables 3, 4 and 5).

3.2. Results of the monocentric prospective clinical study

Between November 2018 and July 2021, 64 minimally invasive right colectomies with intracorporeal anastomosis were performed in Henri Mondor University Hospital, 40 using a robotic surgical system and 24 using conventional laparoscopy.

The demographic and clinical characteristics of the included patients are shown in Table 5, where no significant difference between RRC-IA and LRC-IA is reported.

The operative outcomes of RRC-IA and LRC-IA are shown in Table 6. The only significant difference regards operative time, which is longer in RRC-IA group ($p = 0.03$). Conversely, in terms of conversion to laparotomy, estimated blood loss, number of transfused patients, time to flatus, time to regular diet, overall postoperative complication rate, severe postoperative complications, length of hospital stay, 60-day readmission, and 90-day mortality, RRC-IA and LRC-IA have similar outcomes.

The pathological findings of RRC-IA and LRC-IA are shown in Table 7. In particular, robotic surgery and laparoscopy have similar results in terms of tumor size, R0 resection, number of harvested lymph nodes and tumor grade.

3.3. Results of the MERCY Study - Phase I

Between 2014 and 2020, overall 1,870 patients underwent a minimally invasive right colectomy for right colon cancer. Each participating center contributed to the common database differently: the largest contribution was represented by 343 patients (18.3%), the smallest by 25 (0.6%). Eleven of the 21 participating centers were provided with a robotic system (da Vinci Si and/or da Vinci Xi). In these centers 1,223 patients (65.4%) were operated. However, 87.2% of all included patients were operated laparoscopically and only 12.8% using robotic technology.

An EA was performed in 68.1% of all procedures, an IA in 31.9%. The use of indocyanine green fluorescence was reported in only 10% of all operations (n = 187). Overall 142 (7.6%) minimally invasive right colectomies were converted to laparotomy, 129 (7.9%) laparoscopic procedures and 13 (5.4%) robotic procedures ($p = 0.193$). The rates of overall and severe postoperative complications (Dindo-Clavien ≥ III) were respectively 27.9% and 8.8%. The 90-day mortality was 1.9%. The demographic and clinical characteristics of the total study population are shown in Table 8.

Over the years, a change occurred in the way of choosing which surgical approach and which type of anastomosis. In 2014, 84.4% of all ileo-colic anastomoses were extracorporeal. This proportion gradually decreased over time, reaching 38.4% in 2020 (trend test $p = 0.002$) (Figure 5a). The same trend was also observed for the surgical approach (laparoscopic or robotic), with a decreasing use of laparoscopic EA ($p = 0.004$) and a concomitant increase in the use of laparoscopic and robotic IA. Conversely, the rate of robotic EA remained low and relatively constant ($p = 0.302$) (Figure 5b).

Due to the high rate of missing data for some variables (up to 20.7%), 808 of the total 1,870 patients were excluded. Hence, the population whose operative outcomes were finally analyzed was made up of 1,088 patients.

3.3.1. Extracorporeal vs intracorporeal anastomosis

The final study population was divided into two groups according to the type of performed anastomosis: 671 patients undergoing EA and 417 patients undergoing IA. The demographic and clinical characteristics of the two groups are shown in Table 9.

The factors most frequently associated with the choice of EA or IA are shown in the classification tree (Figure 3). Concerning robotic surgery (12%), 91% of ileo-colic anastomoses were intracorporeal. Concerning laparoscopy, EA was performed in 89% of the procedures carried out before 2017. Considering the procedures carried out since 2017 (50%), EA was performed in 73% of patients operated in centers without robotic systems and in 41% of patients operated in centers provided with surgical robots. In these latter centers, EA was performed in 60% of patients with CCI ≥ 5.5, IA in 73% of patients with CCI < 5.5.

The operative outcomes of EA and IA are shown in Table 10. Notably, compared to EA, IA is associated with longer operative time, lower estimated blood loss, lower rate of SSI, shorter time to flatus, and shorter time to oral diet resumption. A trend favoring IA is also observed for prolonged ileus and length of hospital stay. Moreover, EA and IA do not differ in terms of postoperative complications and mortality, but EA shows a higher conversion rate compared to IA (11.3% vs 1.9%). Overall, 84 patients required conversion due to the following reasons: difficult exposure (51.2%), tumor adhesions (36.9%), bleeding (9.5%), colon laceration while performing IA (1.2%) and hemodynamic instability (1.2%).

The pathological variables of EA group and IA group are shown in Tables 11. They do not differ between the two types of anastomoses, except for tumor grading. Almost all the included minimally invasive procedures (99.6%) are R0. Furthermore, in 95.5% of right colectomies with EA and in 96.6% of right colectomies with IA, at least 12 lymph nodes were resected with the surgical specimen.

3.3.2. Predictors of surgical outcomes

The significant predictors of surgical outcomes identified in the MERCY are divided into patient-related or surgery-related factors, as shown in Table 12.

The patient-related factors include: age, male gender, BMI, ASA score, and comorbidities. In particular, age is associated with shorter operative time but higher risk of postoperative complications. Male sex and BMI are associated with longer operative time, while ASA score ≥ III is predictive of higher blood loss, longer time to flatus, longer time to oral diet resumption, and longer hospital stay. The Charlson Comorbidity Index (CCI) is another predictor of longer hospital stay, while the presence of more than one comorbidity is associated with higher postoperative complication rate, as well as respiratory diseases.

The surgery-related factors include: surgical approach, type of anastomosis, and conversion to laparotomy. In particular, the robotic approach is associated with lower blood losses but longer operative time. The intracorporeal anastomosis is a predictor of faster resumption of oral diet, as well as of lower rate of SSI. Finally, conversion is associated with higher blood loss, higher postoperative complication rate, prolonged ileus, longer time to flatus, and longer hospital stay.

3.3.3. The surgeons' point of view

The questionnaire on operators' preferences was sent to 32 expert surgeons performing the operations considered in the MERCY study, being completed by 90.6% of them (n = 29). Of the surgeons participating to the survey: 1) 90% worked in university hospitals; 2) 97% were involved in surgical training and reported > 50 right colectomies per year; 3) 93% learned to perform EA before IA. Overall, 52% of surgeons perform an EA, 31% a laparoscopic IA and 17% a robotic IA.

However, 72% of surgeons affirmed to consider IA as the ideal solution for an ileo-colic anastomosis, to be performed by laparoscopy in 38% of cases and using a surgical robot in 34%. Indocyanine green is used only by 48% of the surgeons interviewed, who declared to use it systematically in case of both EA and IA (34%), or only in case of IA (14%).

When asked which patient- or disease-related factors may influence the choice to perform EA or IA, surgeons' answers were very heterogeneous. Notably, the factors receiving a consensus greater than 50% from the interviewed surgeons were the following: hemodynamic instability during the procedure (79%), need for multi-visceral resection (76%), ASA score of IV (62%), cT4 tumors (55%), and age > 90 years (55%). These data are summarized in Figure

3.4. Results of the MERCY Study - Phase II

From the overall study population of 1,870 patients, 596 of them were selected for the Phase II, 194 undergoing RRC-IA and 402 undergoing LRC-IA. (Figure 9). The demographic and clinical characteristics of the pre-PSM sample are reported in Table 13, where several significant differences may be found. Notably, RRC-IA patients showed a higher rate of cardiovascular diseases (61.9% vs 51.2%, p = 0.018) and an increased CCI (5.04 vs 4.53, p = 0.049) compared to LRC-IA patients. All anastomoses were fashioned side-to-side, but the isoperistaltic anastomosis was significantly more frequent in the LRC-IA group (p < 0.0001). Furthermore, the RRC-IA group showed lower rates of lymphovascular invasion (21.1% vs. 31.6%, p = 0.009) and adjuvant treatment (21.6% vs. 31.8%; p = 0.012) compared to the LRC-IA group, with a trend towards a greater tumor size on preoperative CT scan (p = 0.054). However, these differences between RRC-IA and LRC-IA groups were no longer found after PSM (Table 14).

3.4.1. RRC-IA vs LRC-IA: short-term outcomes

Operative and postoperative outcomes are shown in Table 15. No significant difference between RRC-IA and LRC-IA was found in terms of operative time, intraoperative complication rate, estimated blood loss, need for blood transfusion, postoperative morbidity, and mortality. Conversion to open surgery occurred in 4 cases, all robotic procedures, due to the following reasons: technical problems (difficult exposure in 3 obese or overweight patients) and colon laceration while using a robotic EndoWrist stapler. No conversion occurred in the LRC-IA group. The use of indocyanine green (ICG) fluorescence was significantly higher during robotic procedures (37% vs 15.8%, p < 0.0001). The postoperative recovery was similar in the two groups, with no significant differences in terms of time to flatus, time to regular diet, and length of hospital stay. Overall, R0 resection was obtained in 99.6% of the patients, and more than 12 lymph nodes were harvested in 92.1% of them, without group-related differences. Four patients died within 90 days of surgery, 2 for each group, accounting for an overall mortality of 1.4%.

3.4.2. RRC-IA vs LRC-IA: long-term outcomes

The survival analyses were carried out on the unmatched study sample, including overall 596 patients. Of these, 12 patients (2% of sample, 4 from the RRC-IA group and 8 from the LRC-IA group) died within 90 days after surgery and were excluded.

The mean OS was 73.94 months (95% CI: 69.39-78.48) for the RRC-IA group and 69.61 months (95% CI: 66.06-73.17) for the LRC-IA group (p = 0.824). The Kaplan-Meir curve of the OS is shown in Figure 10. The OS rates at 1, 3, and 5 years were respectively 97.8%, 84.4%, and 80.5% for the RRC-IA group and 97.6%, 90.4%, and 74.7% for the LRC-IA group (p = 0.942).

The Kaplan-Meir curve of the DFS is shown in Figure 11. The DFS rates at 1, 3, and 5 years were respectively 95.2%, 88.5%, and 85.8% for the RRC-IA group and 95.5%, 88.4%, and 81.5% for the LRC-IA group (p = 0.591).

A disease recurrence over the entire follow-up period was observed in 6.3% (n = 12) of patients undergoing RRC-IA and in 8.2% (n = 32) of patients undergoing LRC-IA ($p = 0.505$). Of these recurrent patients, 2 (4.5%) had a local recurrence, 35 (79.5%) had distant metastases, and 7 (16%) had a systemic metastatic disease, without differences between RRC-IA and LRC-IA groups ($p = 0.216$).

The significant predictors of OS and DFS are reported in Table 16. The Cox regression found pT4 and pN+ to be OS predictors, while an age > 70 years showed a trend towards a significant association with OS. Concerning DFS, only pT4 and pN+ were associated with an increased risk of a lower survival rate. The surgical approach (RRC-IA or LRC-IA) had no influence on OS ($p = 0.753$) or DFS ($p = 0.473$).

4. DISCUSSION

Here, we discuss the results of each one of the components which our research has articulated in, leaving for the end our final general conclusions.

4.1. Considerations on the meta-analysis

To date, our systematic review and meta-analysis includes the largest number of studies comparing laparoscopic vs robotic right colectomy and reports the largest number of patients in the current literature. Moreover, it provides the first subgroup analysis for intracorporeal anastomosis in both minimally invasive surgical groups.

Nine studies[18,60,120,124,132,133,135-137] compared LRC with prevalent or exclusive EA vs RRC with prevalent or exclusive IA so far. That is likely to reflect a consolidated clinical practice: to choose the type of anastomosis according to the surgical approach, reserving EA for laparoscopy and IA for robotic surgery. The reason of this attitude is probably to be found in the different degree of difficulty experienced by the surgeons when using one approach or the other. However, this finding may represent an important bias when comparing LRC vs RRC, especially due to the better results described for IA compared to EA[35,52-59,73]. That is the reason why we designed our study so as to compare subgroups which were homogeneous in terms of both surgical approach and type of anastomosis.

The first question to answer is whether the outcomes of LRC and RRC are different. Our pooled-data analysis shows that RRC provides several advantages over LRC in terms of the length of hospital stay, estimated blood loss, conversion rate, time to flatus, overall complications, and number of harvested lymph nodes. Conversely, operative time and costs are significantly higher in the robotic group.

In this matter, the conclusions of the previous meta-analyses were contradictory. In particular, only Ma et al.[47] found a shorter length of hospital stay for RRC compared to LRC. Consistent with our results, robotic surgery had lower estimated blood loss in three studies[47,49,51], lower conversion rate in two[47,48], and shorter time to flatus in three[48,49,51]. The overall complication rate was lower for RRC in two previous meta-analyses[49,51], another study showing a trend in the same direction[47]. Furthermore, a trend towards a higher number of harvested lymph nodes in the robotic group was described only by Solaini et al.[48]. The operative time was significantly longer for RRC compared to LRC in all previous meta-analyses[47-51]. Finally, total costs were significantly higher only in two studies[47,48], an important trend in the same direction being reported by another study[50].

At this point, we can make some considerations. First, among the previous meta-analyses on LRC vs RRC, Solaini et al.[48] included the largest number of patients: 7,388 undergoing laparoscopy and 869 undergoing robotic surgery. Compared to this study, the number of patients included in our meta-analysis is 2.89 times higher for LRC group and 3.24 times higher for RRC group. Hence, a higher sensibility may partly explain the differences between our conclusions and those of the previous meta-analyses.

Second, the heterogeneity in our study is often high, which may be explained by the retrospective nature of all included studies, except one. Therefore, the risk of bias is generally high. For instance, blood loss and time to flatus are hard to measure, and no precise measuring method was reported in included studies. Similarly, the definition of overall operative time was quite heterogeneous, and precise information was not available in most articles. For example, only 3 studies reported the docking time[33,76,141].

Anyway, the shorter length of hospital stay in RRC in the pooled-data analysis may be explained by the shorter time to flatus and the lower overall complication rate found in the robotic group. In this context, a critical aspect may be represented by the different proportion of intracorporeal anastomosis in the laparoscopic and robotic groups. Notably, IA is reported in 3.2% of LRC (696/21,397) and in 32.6% (911/2,796) of RRC, that is ten times more frequently during robotic procedures than laparoscopic ones. Considering that IA show better results than EA in a growing literature[35,52-59,73], this disproportion might explain the advantages of robotic surgery over laparoscopy in the pooled-data analysis.

The second question to answer is whether LRC and RRC have different outcomes when an IA or EA is performed. Our meta-analysis suggests that RRC-IA may be advantageous over LRC-IA in terms of length of hospital stay, with a mean gain of almost one day of hospitalization (0.78). This seems quite relevant, especially when considering the high number of patients included in each surgical group and the low level of heterogeneity detected for this outcome (I^2 = 30%). However, the overall complication rate is similar for LRC-IA and RRC-IA. Notably, there is no difference in the rate of anastomotic leakage between the two groups, which is in contrast with the idea that using robotic technology might ameliorate the quality of intra-corporeal anastomosis. Similarly, time to flatus shows no significant difference between LRC-IA and RRC-IA, which removes another potential explanation for the shorter length of hospital stay founded in robotic group. Furthermore, only 4 studies[76-78,146] in the IA subgroup have reported fast track protocols, but it's hard to evaluate their impact on the length of hospital stay due to a high level of heterogeneity. Hence, it cannot be excluded that the retrospective nature of almost all studies included in this meta-analysis may play an important role in explaining this apparent incoherence between a significantly shorter hospital stay for RRC and the apparent lack of reasons, even in the IA subgroup.

Conversely, EA seems to reduce the impact of robotic technology on the duration of hospital stay, with similar results for laparoscopy and robotic surgery. This finding is consistent with the results of 2 previous meta-analyses[48,49] including an EA subgroup. We have only found a trend towards lower complications and a higher number of harvested lymph nodes. In this regard, while the first finding appears quite difficult to explain, the second one may be linked to the enhanced dissection allowed by robotic technology. However, similar results have not been found in the IA subgroup; therefore, the retrospective character of studies may not be excluded as a valid explanation in this case as well.

Concerning the long-term outcomes, it was impossible to make any comparisons: 1) only 2 articles[78,120] reported complete survival data; 2) it was impossible to estimate the necessary parameters for the pooled-data analysis; 3) heterogeneity was extremely high throughout the included studies.

Total costs were considered only in the pooled-data analysis and in the EA subgroup, not in IA subgroup due to the lack of data. In both analyses, total costs were higher for robotic surgery, but the way these costs were calculated was not always clear. Moreover, it was not possible to establish if the mean difference of + 2,600 US dollars between RRC and LRC might be compensated by the mean gain of half a day in terms of length of hospital stay observed in the pooled-data analysis.

It must be underlined that the body of evidence deriving from our meta-analysis is burdened by the retrospective character of all included studies, except the only RCT found, which represents its most important limitation. Therefore, the risk of important bias is relevant and cannot be neglected. However, the current literature lacks studies of higher quality, so that our systematic review and meta-analysis represents an important instrument to summary what may be deduced from currently available data.

4.2. Considerations on the monocentric prospective clinical study

The results of the present prospective clinical trial appear to be in line with the outcomes reported in our meta-analysis. The only difference between laparoscopy and robotic surgery concerned the operative time, which was longer for RRC. The overall postoperative complication rate and, notably, the anastomotic leak rate did not differ between LRC and RRC once more. This latter outcome seems to be very significant. The anastomotic leak may depend on patient-related and surgery-related factors. If we consider that the patients included in LRC and RRC groups have similar demographic and clinical features, and that the same type of anastomosis is performed in both groups, the eventual difference between laparoscopy and robotic surgery should depend on the surgical approach itself. Indeed, the basic assumption at the base of the study was that robotic technology would eventually allow surgeons to perform more easily a safer intracorporeal anastomosis, safer meaning associated with a lower risk of anastomotic leak. In this regard, our clinical results are consistent with our meta-analysis.

Interestingly, our clinical study found that LRC and RRC had a similar length of hospital stay, while our meta-analysis had found a mean difference of 0.78 days in favor of RRC. However, of the 10 studies[90,111,129,137-14] comparing LRC-IA and RRC-IA currently available in the literature, only the retrospective study published by Mégevand et al. reported a shorter hospital stay for the robotic group. Moreover, only 2 studies found a higher conversion rate for LRC[78,146] and a shorter time to flatus for RRC[74,146]. This enforce the doubt that the shorter hospital stay of RRC-IA in our meta-analysis may depend on heterogeneity of the retrospective studies considered, since no suitable explication for that, such as a higher complication rate, may be proposed.

Conversely, the RRC group shows higher operative time in 9[74,76-78,121,145-148] studies comparing LRC-IA and RRC-IA, which is consistent with our results. Furthermore, a higher readmission rate is found in one study, and a higher rate of lymph nodes in another study. Costs are analyzed only by Merola, who found high costs of instruments and operating room for RRC-IA compared to LRC-IA, as well as higher overall costs.

The major limitations of our study are represented by its non-randomized nature, the limited number of included patients, and the absence of the cost-analysis. However, this study has been conducted prospectively and compares two groups with a low degree of heterogeneity, which makes it a good instrument to directly investigate on several hot topics of the minimally invasive surgery of the right colon.

4.3. Considerations on the MERCY Study Phase I

The first phase of the MERCY study provides updated information about on patient- and surgery-related factors predicting the outcomes of minimally invasive right colectomy for cancer. These data suggest to carefully assess patients' status prior to surgery and maximizing the advantages of minimally invasive surgery by performing a robotic right colectomy with IA whenever possible. Indeed, that is the current trend identified in the surgical community, with a progressive increase of robotic surgery and IA construction over the past 4 years and an explicit theoretical preference by the surveyed surgeons.

The picture drawn by the MERCY study provides both a large overview and detailed information concerning minimally invasive surgery for right colon cancer. Laparoscopy is the most frequent approach in case of right colectomy (87.2%), IA representing the 31.9% of all ileo-colic anastomoses performed. Overall, the minimally invasive right colectomy still has high rates of conversion (7.9 %) and postoperative complications (26.8%), consistently with the literature[63,149,150], which stresses the importance of further ameliorating surgical techniques, for example using ICG fluorescence.

The minimally invasive surgery of right colon cancer is evolving over the years. As shown by the classification tree analysis, the most relevant predictors of the choice between EA and IA is the use of an available robotic technology, with an important temporal effect (before or after 2017) probably related to the diffusion of robotic systems in a growing number of colorectal surgery units. Indeed, the robotic technology is still regarded as a tool facilitating the construction of an IA, as confirmed by the fact that RRC is associated to IA in 91% of cases. That is in line with previous studies[57,78], but in contrast with the result of our meta-analysis, which has demonstrated no direct reduction in the rate of anastomotic leak and other postoperative complications comparing RRC-IA to LRC-IA, with operative time still remaining higher.

Interestingly, the classification tree analysis has identified the Charlson Comorbidity Index (CCI) as another discriminating factor in the choice of EA or IA. Notably, in case of CCI ≥ 5.5 (correspon-ding to severe comorbidities, increased mortality, and greater use of resources[151,152]), surgeons tend to perform a laparoscopic EA, which is probably seen as a more conservative, safer, and faster technique than IA, despite higher blood losses, higher rates of ileus and SSI, and longer recovery time. This aspect, which has already been described in previous RCTs[64,153] and multicentric retro-spective studies[109,150,154,155], points out how the implementation of IA was slow over the years despite its advantages, although it seems to be currently favored by the spread of robotic systems all over[156].

Concerning the conversion rate, it was higher for EA compared to IA (11.3% vs 1.9%), consistently with other retrospective studies[109,150,154,155]. However, due to the design of these studies it is difficult to conclude on a direct relationship between conversion and type of anastomosis. Indeed, selection and reporting biases can affect these results. Surgeons are generally more inclined to perform EA for more difficult cases, which are at higher risk of conversion too. Moreover, no data concerning the stage when procedures were converted is available, conversion potentially being early and unrelated to the construction of the anastomosis.

Mixed model analyses have demonstrated that age, gender and BMI influence operative time, while ASA score and comorbidities have an impact on postoperative complications and recovery time (resulting from time to flatus, regular diet resumption, and length of hospital stay). The robotic approach is advantageous in terms of lower blood loss, while IA is a predictor of faster regular diet resumption and lower rate of SSI. Conversion to open surgery makes time to flatus longer, lengthen hospital stay longer by approximately 3 days, increases the risk of overall postoperative complications by 2 times and the risk of prolonged ileus by 4 times. Therefore, every effort should be made to prevent conversion to open surgery, starting with a careful preoperative evaluation of the patient and an accurate planning of the intervention.

Knowing the predictors of postoperative morbidity and recovery is essential to stratify patients according to their surgical risk and to perform a targeted surgical procedure[63,157]. Perioperative decision making is certainly one a difficult task, depending on many patient- and surgery-related factors. In this matter, the MERCY study has identified some of these factors, representing an important starting point for further studies aiming at finding the best surgical strategy for each clinical situation.

Overall, the findings of this large multicentric study suggest to carefully assess patients' status prior to surgery and to consider maximizing the minimally invasive approach by performing a robotic right colectomy with intracorporeal anastomosis whenever possible. Consistently, this seemed to be the current tendency of the surgical community, with robotic surgery and intracorporeal anastomosis progressively spreading during the last 4 years and representing the preferred approach of the interviewed colorectal surgeons. In this sense, it is important to consider the study published by Rausa et al.[158] in 2019. It consisted in a large meta-analysis including 5 randomized controlled trials, 18 prospective and 25 retrospective studies (overall 5,652 patients), comparing the operative outcomes of open, laparoscopic, totally laparoscopic, and robotic right colectomies, all currently performed for right colon diseases. Based on these data, the authors concluded that short-term outcomes following robotic and totally laparoscopic techniques were superior to standard laparoscopy or open surgery and thus, suggesting that the adoption of more advanced minimally invasive techniques for right colectomies may ultimately improve patients' outcomes.

The ongoing cohort study MIRCAST[159] expects to answer some unresolved questions by recruiting 1200 patients and comparing LRC-EA, LRC-IA, RRC-EA and RRC-IA in terms postoperative complications, postoperative recovery and 2-year survivals. Because of the observational design, a propensity score match analysis is planned by the researchers to counterbalance potential confounding factors. These latter ones would mainly derive from the fact that the surgical technique is not standardized in the centers involved and the choice to perform laparoscopic or robotic, EA or IA depend on the surgeons' experience[159].

The propensity score matching is certainly a valuable and popular statistical method for handling data from non-randomized studies, but it flattens the natural heterogeneity of an observed population when comparing alternative surgical techniques[160]. A different statistical method was followed in the MERCY study. Predictive models were performed to identify the perioperative factors likely to influence postoperative outcomes, without limiting the comparison between EA and IA, but including it as one of the covariates. Mixed model regressions were performed to account for a possible central effect related to the multicenter design. It should be stressed that the large population of the MERCY study provides a solid base for the generalization of its results within the context of colorectal surgery units. Moreover, in addition to objective data, surgeon's subjective report s were also provided, which revealed a lack of standardization in the choice of the operative technique but also a clear evolution towards robotic surgery, IA and ICG fluorescence use.

Finally, the first phase of the MERCY study has some limitations, mainly its retrospective character. However, it should be emphasized that statistical analyses are intended to assist surgeons in their decision-making process, although a critical interpretation of current results is recommended and must be confirmed in future studies. Probably, future large prospective studies based will be the best mean to provide sufficient elements to build algorithms for choosing the best surgical approach and technique in specific clinical scenarios. Anyway, nothing will replace surgeon's judgment and clinical experience.

4.4. Considerations on the MERCY Study Phase II

The second phase of the MERCY study provides evidence that RRC-IA and LRC-IA for right colon cancer associated with comparable short- and long-term outcomes, which seems not to be influenced by the type of surgical approach chosen.

This retrospective analysis was conducted on the largest sample of patients with right colon cancer (AJCC 0-III) reported in the literature to date. By using the propensity score matching, the pretreatment clinical differences between patients in the RRC-IA and LRC-IA groups were balanced to minimize selection bias while comparing the surgical treatments on the study endpoints. Thus, the present data show that no further improvements were observed when performing RRC-IA vs LRC-IA.

Based on the most recent RCTs and meta-analyses, there is evidence to support the use of an IA instead of an EA during LRC, because it is associated with reduced short-term morbidity, faster recovery, and decreased length of hospital stay[53,55,153,161,162]. However, the rate of IA remains considerably lower than EA in clinical practice, and in the MERCY database, IA represented only 31.9% of the total procedures. This stresses the difficult implementation of a technique that demands good surgical skills and MIS experience. Robotic surgery may favor IA, as previously suggested[163], but the present results support that once the surgeon is able to successfully perform a right colectomy with an IA by a MIS approach, no significant difference may be expected between laparoscopy or robotics. Indeed, both RRC-IA and LRC-IA appeared to be safe and feasible, with no severe intraoperative complications and few conversions to open surgery.

Interestingly, no significant difference was observed in the operative time, in contrast to what was reported in previous retrospective studies comparing RRC-IA vs LRC-IA[74,76-78,121,145-148]. However, it must be noted that the MERCY study is based on data collected from European referral centers, and that all operating surgeons were highly experienced in MIS. This may particularly impact the operative time of RRC and LRC, which were not always performed by the same operator within each center.

The use of ICG fluorescence was significantly more frequent during RRC-IA than LRC-IA, although it was not systematically used. This may be related to the fact that ICG fluorescence is integrated in all robotic platforms, and it is easier to use than laparoscopy to check the vascularization of colic stump and anastomosis. Nevertheless, its utility in reducing the anastomotic leakage rate remains under debate[164,165].

Patient recovery was similar after RRC-IA and LRC-IA, with no significant differences in time to flatus, time to regular diet, and length of hospital stay. These findings are in accordance with the current literature, where only two studies found a significantly shorter hospital stay for the robotic approach[74,146]. RRC-IA and LRC-IA showed also similar postoperative complication rates, overall 34% for each group. In the literature, the reported postoperative complication rates (including all types and severity of postoperative complications) range from 14% to 75%, which points out that a high rate of patients still experience a complicated postoperative recovery, despite the standardization of the technique and the use of minimally invasive approach [74,76-78,121,145,146]. This issue may also be related to patient’s fitness for surgery, comorbidities, and cancer features. Therefore, a personalized approach, including enhanced recovery after surgery (ERAS)[166,167] and prehabilitation multimodality programs[168,169], may be important to reduce perioperative stress, to maintain postoperative physiological functions, and to promote a fast recovery after surgery, even when surgical invasiveness is minimized[77].

Concerning the long-term outcomes, only Spinoglio et al.[78] previously reported the 5-year survival rate. As in their study, no statistically significant differences were observed for OS and DFS between the RRC-IA and LRC-IA groups, which confirms the oncological adequateness of the robotic procedures. Indeed, R0 resection was obtained in 99.3% of the patients included in our study, with at least 12 lymph nodes in 92.5% of patients undergoing RRC-IA and 91.8% of patients undergoing LRC-IA. Of all factors considered, only the pT4 stage and the pN+ status were significantly associated with OS and DFS over the entire study population (n = 584), whereas the surgical approach was found to have no impact on patients' survivals.

Concerning the limitations of the second phase of the MERCY Study, the analyses were carried out on a large sample of patients, which remained relatively large even after the propensity score matching process. However, these analyses were limited to the most common and standardized operative and postoperative outcomes of the right colectomy. Some relevant outcomes, such as postoperative pain or patient satisfaction (or other patient-related outcome measures, PROMs), were unavailable. A precise and reliable estimation of the surgery-related costs for RRC-IA and LRC-IA was not feasible, because the costs of surgical instruments, operative room occupation, and hospital stay vary considerably within Europe, as well as they may be influenced by the volume of robotic procedures performed in each surgical unit. Although expected to be more expensive[120,124,147], the cost/effectiveness of RRC-IA may deserve further studies, specifically focusing on the economic sustainability of the minimally invasive surgery (MIS) approaches, which continue to be implemented in the clinical practice.

In conclusion, the second phase of the MERCY study shows that right colectomy should be performed with a minimally invasive approach an IA but points out that there is still no evidence supporting RRC-IA over LRC-IA. Most likely, the endpoints to consider should go beyond the impact of the surgical act (which is not different from laparoscopy to robotics in the case of right colectomy) and compare RRC-IA vs LRC-IA considering some performance parameters, for instance the time for a surgeon to gain proficiency in performing IA or the possibility to expand MIS indications to more difficult cases (still approached via open surgery).

4.5. Final conclusions

In the state-of-the-art definition phase, we published the largest meta-analysis on laparoscopic vs robotic right colectomy currently available in the literature, providing for the first time a homogeneous subgroup analysis for intracorporeal anastomosis. Particularly, the best results of RRC in the pooled data analysis is presumably due to the clear prevalence of the intracorporeal anastomosis in the robotic group rather than to the surgical approach itself. Furthermore, if RRC-IA has a shorter hospital stay compared to LRC-IA, this latter one has similar results in terms of post-operative recovery, complication rate, and, especially, anastomotic leak rate. That is appears to be another significant aspect, suggesting the idea that an IA performed by laparoscopy has as effective as an IA performed using robotic technology. Finally, the significant advantage showed by RRC-IA in terms of length of hospitalization (-0.78 days of average compared to LRC-IA) cannot be evaluated from an economic point of view, due to the lack of data, and might be linked to the heterogeneity of the included studies.

The clinical research conducted in collaboration with the Henri Mondor University Hospital and comparing the results of LRC-IA vs RRC-IA was intended to remove the potential effect of the type of anastomosis on patients' outcomes and evaluate the role of the chosen surgical approach only. The results were in line with the conclusions of our meta-analysis, founding no difference in terms between laparoscopy and robotic surgery , except for the operative time. The length of hospital stay, the overall complication rate and the rate of anastomotic leak were similar. Therefore, we may conclude that the choice itself of a laparoscopic or a robotic approach would not modify patients' outcomes.

The participation to the MERCY study allowed to investigate more deeply the role of the type of anastomosis and to research some patient-related or surgery-related factors influencing patients' outcomes. Notably, age, male gender, BMI, ASA score, robotic approach, and AI are predictors of surgical outcomes when performing a right colectomy for cancer. Over the years there has been an increase in AI compared to AE. In this regard, age> 90 years, ASA IV, stage cT4, the need for multivisceral resection and hemodynamic instability during the procedure were identified as factors influencing the choice of anastomosis. As MIS continues to evolve, knowing the role of these predictors can help surgeons customize surgical decision making between different MIS options for managing right colon cancer

Finally, robotic right colectomy with intracorporeal anastomosis does not appear superior to laparoscopic right colectomy with intracorporeal anastomosis. However, over time, the intracorporeal anastomosis has gained an increasing diffusion. Hence, the current effort should be directed towards the definition of increasingly effective criteria for selecting patients to be candidates for a certain minimally invasive approach and a certain type of anastomosis rather than others.

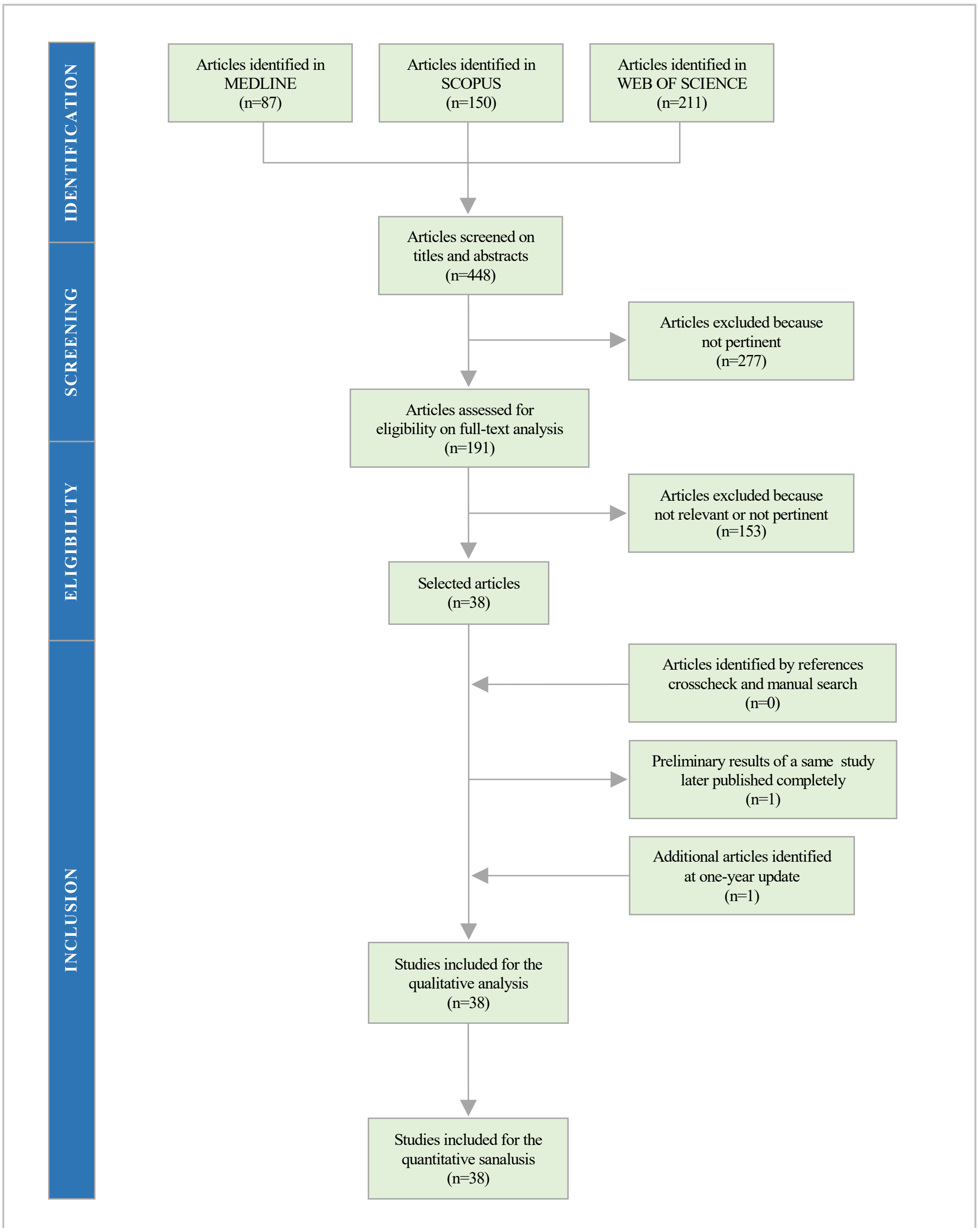
All these conclusions have been used and formalized in the elaboration of the 2021 guidelines for the robotic right colectomy of the *Association Française de Chirurgie* (AFC), in which we have participated actively. The publication process of the final version of these guidelines is ongoing.

Naturally, we believe that a higher number of randomized trials would be the best way to clear the remaining doubts on the subject, but we believe that the method followed in this research and its results provide a satisfactory answer to the main current questions concerning laparoscopic and robotic right colectomy.

5. TABLES AND FIGURES

5.1. Systematic review and meta-analysis

5.1.1. Figure 1. Flowchart of the literature search and study selection process.



5.1.2. Table 1a. Demographic and clinical characteristics of the included studies (part 1).

Year	First author	Study type and time frame	Total RCs [n]	Surgical techniques	Total patients per technique [n (%)]	IA / EA [n (%)]
2020	Ceccarelli et al.	M-RCS 2014-2019	40	3-D LRC-IA CME RRC-IA CME	20 (50.0) 20 (50.0)	20 (100) / 0 (0) 20 (100) / 0 (0)
2020	Migliore et al.	RCS 2010-2018	216	LRC-IA RRC-IA	170 (78.7) 46 (21.3)	170 (100) / 0 (0) 46 (100) / 0 (0)
2020	Milone et al.	M-RCS 2007-2017	216	LRC-IA RRC-IA	40 (18.5) 176 (81.5)	40 (100) / 0 (0) 176 (100) / 0 (0)
2019	Merola et al.	M-RCS 2012-2017	188	LRC-IA RRC-IA	94 (50.0) 94 (50.0)	94 (100) / 0 (0) 94 (100) / 0 (0)
2019	Gerbaud et al.	RCS 2013-2019	101	LRC-EA RRC- IA/EA	59 (58.4) 42 (41.6)	0 (0) / 59 (100) 19 (45.2) / 23 (54.8)
2019	Park et al.	RCT 2010-2011	70	LRC-IA/EA RRC-IA/EA	35 (50.0) 35 (50.0)	7 (20.0) / 28 (80.0) 30 (85.7) / 5 (14.3)
2019	Blumberg et al.	RCS 2003-2018	122	LRC-IA RRC-IA	101 (82.8) 21 (17.2)	101 (100) / 0 (0) 21 (100) / 0 (0)
2019	Khorgami et al.	RCS 2012-2014	7 685	LRC RRC	7 243 (94.3) 442 (5.7)	- -
2019	Solaini et al.	M-RCS 2007-2017	389	LRC-IA RRC-IA	84 (21.6) 305 (78.4)	84 (100) / 0 (0) 305 (100) / 0 (0)
2019	Yozgatli et al.	RCS 2015-2017	96	LRC-IA /EA CME RRC-IA CME	61 (63.5) 35 (36.5)	- 35 (100) / 0 (0)
2019	Mégevand et al.	RCS 2010-2015	100	LRC-IA RRC-IA	50 (50.0) 50 (50.0)	50 (100) / 0 (0) 50 (100) / 0 (0)
2018	Ngu et al.	RCS 2015-2017	32	LRC-IA CME RRC-IA CME	16 (50.0) 16 (50.0)	16 (100) / 0 (0) 16 (100) / 0 (0)
2018	Nolan et al.	RCS 2011-2016	106	LRC RRC	96 (90.6) 10 (9.4)	- -
2018	Kelley et al.	RCS 2012-2017	114	LRC-EA RRC-IA	87 (76.3) 27 (23.7)	0 (0) / 87 (100) 27 (100) / 0 (0)
2018	Spinoglio et al.	RCS 2005-2015	202	LRC-IA CME RRC-IA CME	101 (50.0) 101 (50.0)	101 (100) / 0 (0) 101 (100) / 0 (0)
2018	Scotton et al.	RCS 1998-2017	190	LRC-EA RRC-IA	160 (84.2) 30 (15.8)	0 (0) / 160 (100) 30 (100) / 0 (0)
2018	Haskins et al.	RCS 2012-2014	3 518	ORC LRC RRC	1 024 (29.1) 2 405 (68.4) 89 (2.5)	- - -
2018	Lujan et al.	RCS 2009-2015	224	LRC-EA RRC-IA	135 (60.3) 89 (39.7)	0 (0) / 135 (100) 89 (100) / 0 (0)
2017	Widmar et al.	RCS 2012-2014	463	ORC LRC RRC	181 (39.1) 163 (35.2) 119 (25.7)	- - -
2017	Dolejs et al.	RCS 2012-2014	6 780	LRC RRC	6 521 (96.2) 259 (3.8)	- -
2016	Kang et al.	RCS 2007-2011	96	ORC LRC-EA RRC-EA	33 (34.4) 43 (44.8) 20 (20.8)	NA 0 (0) / 43 (100) 0 (0) / 20 (100)
2016	de'Angelis et al.	RCS 2012-2015	80	LRC-EA RRC-EA	50 (62.5) 30 (37.5)	0 (0) / 50 (100) 0 (0) / 30 (100)
2016	Widmar et al.	RCS 2009-2014	276	LRC-EA RRC-IA/EA	207 (75.0) 69 (25.0)	0 (0) / 207 (100) 11 (16.0) / 58 (84.0)
2016	Cardinali et al.	RCS 2013-2015	90	LRC-EA RRC-IA	60 (66.7) 30 (33.3)	0 (0) / 60 (100) 30 (100) / 0 (0)
2016	Miller et al.	RCS 2013	2 849	LRC RRC	2 740 (96.2) 109 (3.8)	- -
2015	Ferrara et al.	RCS 2008-2014	28	LRC-EA RRC-EA	15 (53.6) 13 (46.4)	0 (0) / 15 (100) 0 (0) / 13 (100)
2015	Guerrieri et al.	RCS 2013-2014	29	LRC-IA/EA RRC-IA/EA	11 (37.9) 18 (62.1)	4 (36.4) / 7 (63.6) 14 (77.8) / 4 (22.2)
2015	Trastulli et al.	M-RCS 2005-2014	236	LRC-EA LRC-IA RRC-IA	94 (39.8) 40 (17.0) 102 (43.2)	0 (0) / 94 (100) 40 (100) / 0 (0) 102 (100) / 0 (0)
2014	Trinh et al.	RCS 2008-2013	22	LRC RRC	15 (68.2) 7 (31.8)	- -

2014	Casillas et al.	RCS 2005-2012	162	LRC-EA RRC-EA	110 (67.9) 52 (32.1)	0 (0) / 110 (100) 0 (0) / 52 (100)
2014	Davis et al.	RCS 2009-2011	414	LRC RRC	207 (50.0) 207 (50.0)	- -
2013	Lujan et al.	RCS 2008-2011	47	LRC-EA RRC-IA/EA	25 (53.2) 22 (46.8)	0 (0) / 25 (100) 18 (81.8) / 4 (18.2)
2013	Morprugo et al.	RCS 2008-2012	96	LRC-EA RRC-IA	48 (50.0) 48 (50.0)	0 (0) / 48 (100) 48 (100) / 0 (0)
2012	Park et al.	RT 2009-2011	70	LRC-IA/EA RRC-IA/EA	35 (50.0) 35 (50.0)	7 (20.0) / 28 (80.0) 30 (85.7) / 5 (14.3)
2012	Deutsch et al.	RCS 2004-2009	65	LRC-EA RRC-EA	47 (72.3) 18 (27.7)	0 (0) / 47 (100) 0 (0) / 18 (100)
2012	Shin et al.	RCS 2006-2011	12	LRC-EA RRC-EA	6 (50.0) 6 (50.0)	0 (0) / 6 (100) 0 (0) / 6 (100)
2010	deSouza et al.	RCS 2005-2009	175	LRC-EA RRC-EA	135 (77.1) 40 (22.9)	0 (0) / 135 (100) 0 (0) / 40 (100)
2007	Rawlings et al.	RCS 2002-2005	32	LRC-EA RRC-IA	15 (46.9) 17 (53.1)	0 (0) / 15 (100) 17 (100) / 0 (0)
2003	Delaney et al.	RCS 2001-2002	4	LRC-EA RRC-EA	2 (50.0) 2 (50.0)	0 (0) / 2 (100) 0 (0) / 2 (100)

*: median (range); **: median (interquartile range); ^: mean (95% confidence interval); a: % of patients aged ≥ 65; b: % of patients with BMI ≥ 30; c: median value; CRS: comparative retrospective study; M-: multicenter; RCT: randomized controlled study; RCs: right colectomies; LRC: laparoscopic right colectomy; RRC: robotic right colectomy; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; ORC; open right colectomy; NA: not applicable; ERAS: enhanced recovery after surgery protocol; FT: surgical unit fast-track protocol; bold: statistical difference.

5.1.3. Table 1b. Demographic and clinical characteristics of the included studies (part 2).

Year	First author	Robotic technology Da Vinci Si / Xi [n (%)]	Age years [mean (SD)]	BMI kg/m^2 [n (%)]	ASA ≥ 3 [n (%)]	Fast-track protocols
2020	Ceccarelli et al.	- Si and Xi	74.6 (13.8) 70.6 (9.9)	24.1 (2.9) 23.0 (2.4)	6 (30.0) 7 (35.0)	No
2020	Migliore et al.	- 46 (100) / 0	71.9 (10.1) 68.7 (9.2)	25.5 (4.1) 26.0 (4.0)	66 (38.8) 16 (34.8)	ERAS
2020	Milone et al.	- -	- -	- -	- -	-
2019	Merola et al.	- 35 (37.2) / 59 (62.8)	72.1 (9.5) 69.4 (10.3)	27.9 (5.7) 26.9 (4.6)	31 (33.0) 38 (40.4)	-
2019	Gerbaud et al.	- -	**72.0 (8.6)** **67.0 (8.6)**	24.0 (4.3) 26.0 (4.7)	16 (27.2) 17 (40.5)	-
2019	Park et al.	- 35 (100) / 0	66.5 (11.4) 62.8 (10.5)	23.8 (2.7) 24.4 (2.5)	2 (5.7) 4 (11.4)	No
2019	Blumberg et al.	- 21 (100) / 0	68.0 (12.0) 65.0 (10.0)	28.0 (7.0) 30.0 (7.0)	50 (49.5) 15 (71.4)	-
2019	Khorgami et al.	- -	- -	- -	- -	-
2019	Solaini et al.	- -	59 (70.2) [a] 209 (68.5) [a]	7 (8.3) [b] 44 (14.4) [b]	20 (23.8) 69 (22.6)	-
2019	Yozgatli et al.	- 0 / 35 (100)	65.0 (13.0) 65.0 (13.0)	27.0 (5.0) 29.0 (5.0)	2.0 [c] 2.0 [c]	-
2019	Mégevand et al.	- -	69.6 [c] 70.3 [c]	25.2 [c] 26.2 [c]	7 (14.0) 9 (18.0)	FT
2018	Ngu et al.	- 0 / 32 (100)	69.6 (9.6) 68.6 (10.9)	24.7 (4.2) 23.7 (3.8)	12 (75.0) 8 (50.0)	ERAS
2018	Nolan et al.	- -	- -	- -	- -	-
2018	Kelley et al.	- 0 / 27 (100)	60.0 (21.0) 60.0 (16.0)	27.0 (5.0) 28.0 (3.0)	23 (26.4) 8 (29.6)	FT
2018	Spinoglio et al.	- 101 (100) / 0	71.2 (10.6) 71.2 (10.2)	25.8 (4.4) 25.1 (4.0)	55 (54.5) 48 (47.5)	FT
2018	Scotton et al.	- 0 / 30 (100)	- -	- -	- -	-
2018	Haskins et al.	- - -	**70.7 (12.2)** **68.3 (12.6)** **68.9 (11.8)**	28.6 (6.7) 28.5 (6.3) 29.3 (6.3)	**680 (66.4)** **1 327 (55.2)** **57 (64.0)**	-
2018	Lujan et al.	- Si and Xi	72.6 (11.4) 70.9 (9.6)	27.1 (5.2) 28.4 (5.4)	- -	-
2017	Widmar et al.	- - -	64 (53-75) ** 64 (54-75) ** 68 (58-77) **	27 (24-33) ** 29 (25-32) ** 28 (24-32) **	- - -	-
2017	Dolejs et al.	- -	(48.1) [a] (54.4) [a]	(33.0) [b] (36.1) [b]	2 934 (45.0) 127 (49.0)	-
2016	Kang et al.	- - -	68.4 (11.3) 65.7 (13.2) 66.0 (9.6)	23.2 (1.9) 23.0 (3.0) 23.5 (2.4)	0 (0) 1 (2.4) 1 (5.0)	No
2016	de'Angelis et al.	- -	71.1 (12.9) 71.0 (8.5)	25.3 (4.2) 26.4 (3.2)	28 (56.0) 15 (50.0)	-
2016	Widmar et al.	- -	64.0 (22.0) ** 66.0 (20.0) **	64 (30.9) [b] 24 (34.8) [b]	- -	-
2016	Cardinali et al.	- -	70.8 (9.6) 68.7 (12.9)	26.4 (3.2) 25.4 (4.3)	9 (30.0) 21 (70.0)	-
2016	Miller et al.	- -	- -	- -	- -	-
2015	Ferrara et al.	- 13 (100) / 0	- -	- -	- -	-
2015	Guerrieri et al.	- -	65 (59-75) ** 74 (57-80) **	26 (23-28) ** 26 (24-28) **	- -	FT
2015	Trastulli et al.	- - 102 (100) / 0	70.8 (10.2) 71.5 (10.3) 68.8 (11.6)	25.4 (3.5) 26.6 (4.0) 25.6 (3.8)	39 (41.5) 14 (35.0) 39 (38.2)	No
2014	Trinh et al.	- 7 (100) / 0	- -	- -	- -	No

2014	Casillas et al.	- -	71 (12) 65 (12)	27.0 (26.1-28.1) ^ 26.9 (25.6-28.3) ^	48 (43.6) 20 (38.5)	-
2014	Davis et al.	- -	- -	- -	- -	-
2013	Lujan et al.	- -	72.6 (11.1) 71.9 (9.0)	**27.9 (6.1)** **31.4 (6.0)**	- -	-
2013	Morprugo et al.	- -	74.0 (11.0) 68.0 (8.0)	28.0 (4.0) 25.0 (3.5)	18 (37.5) 12 (25.0)	-
2012	Park et al.	- -	66.5 (11.4) 62.8 (10.5)	23.8(2.7) 24.4(2.5)	2 (5.7) 4 (11.4)	No
2012	Deutsch et al.	- -	70.8 (14.6) 65.2 (12.0)	28.0 (6.5) 25.0 (3.8)	**24 (51.1)** **5 (27.7)**	-
2012	Shin et al.	- 6 SH (100)	- -	- -	- -	-
2010	deSouza et al.	- -	65.3 (18.7) 71.3 (14.1)	26.6 (6.4) 27.3 (5.2)	51 (37.8) 21 (52.5)	-
2007	Rawlings et al.	- -	63.1 (17.5) 64.6 (11.7)	28.3 (6.4) 25.7 (4.3)	- -	-
2003	Delaney et al.	- -	63.0 (18.4) 64.5 (19.1)	25.0 (1.4) 31.5 (9.2)	1 (50.0) 1 (50.0)	-

*: median (range); **: median (interquartile range); ^: mean (95% confidence interval); a: % of patients aged ≥ 65; b: % of patients with BMI ≥ 30; c: median value; CRS: comparative retrospective study; M-: multicenter; RCT: randomized controlled study; RCs: right colectomies; LRC: laparoscopic right colectomy; RRC: robotic right colectomy; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; ORC: open right colectomy; NA: not applicable; ERAS: enhanced recovery after surgery protocol; FT: surgical unit fast-track protocol; bold: statistical difference.

5.1.4. Table 2a. Operative outcomes reported in the included studies (part 1).

First author	Surgical techniques	Overall operative time min [mean (SD)]	Estimated blood loss ml	Conversion to open surgery [n (%)]	Time to flatus days [mean (SD)]	Length of hospital stay days [mean (SD)]	30-day overall postoperative complications [n (%)]
Ceccarelli et al.	3-D LRC-IA CME RRC-IA CME	**165.9 (30.2)** **225.2 (73.0)**	- -	- -	3.0 (1.2) 3.2 (1.2)	7.8 (3.0) 7.2 (1.6)	5 (25.0) 9 (45.0)
Migliore et al.	LRC-IA RRC-IA	**187.6 (56.6)** **242.4 (47.5)**	- -	6 (3.5) 1 (2.2)	1.6 (0.8) 1.6 (1.0)	4.0 (2-40) [*] 4.0 (3-18) [*]	46 (27.1) 15 (32.6)
Milone et al.	LRC-IA RRC-IA	- -	- -	- -	- -	- -	- -
Merola et al.	LRC-IA RRC-IA	**135.5 (33.9)** **207.5 (44.9)**	- -	0 (0) 3 (3.2)	2.2 (1.2) 2.2 (0.7)	4.0 (2.0) [**] 4.0 (2.0) [**]	15 (15.9) 17 (18.1)
Gerbaud et al.	LRC-EA RRC- IA/EA	**137.0 (19.0)** **197.0 (25.3)**	31.0 (29.0) 27.0 (26.0)	1 (1.7) 0 (0)	- -	7.0 (3.1) 6.0 (2.3)	17 (28.8) 9 (21.4)
Park et al.	LRC-IA/EA RRC-IA/EA	**129.7 (43.2)** **195.0 (41.0)**	46.8 (31.3) 35.8 (36.3)	0 (0) 0 (0)	2.9 (2.2) 2.6 (1.4)	8.3 (4.2) 7.9 (4.1)	7 (20.0) 6 (17.1)
Blumberg et al.	LRC-IA RRC-IA	**212.0 (66.0)** **330.0 (100.0)**	100.0 (153.0) 100.0 (58.0)	5 (4.9) 0 (0)	- -	5.0 (1.7) 3.0 (6.4)	22 (21.7) 3 (14.3)
Khorgami et al.	LRC RRC	- -	- -	- -	- -	4.3 (2.0) 3.8 (1.6)	- -
Solaini et al.	LRC-IA RRC-IA	**160.0 (130-200)** [**] **250.0 (209-305)** [**]	- -	0 (0) 3 (1.0)	2.0 (2-3) [**] 3.0 (2-3) [**]	8.0 (6-10) [**] 7.0 (6-9) [**]	21 (25.0) 71 (23.3)
Yozgatli et al.	LRC-IA/EA CME RRC-IA CME	**132.0 (40.0)** **286.0 (77.0)**	73.0 (57.0) 75.0 (70.0)	0 (0) 0 (0)	2.0 (1.0) 3.0 (1.0)	6.0 (3.0) 6.0 (3.0)	15 (24.6) 10 (28.6)
Mégevand et al.	LRC-IA RRC-IA	**160.0 (140-180)** [**] **204.0 (180-230)** [**]	- -	**7 (14.0)** **0 (0)**	**2.5 (2-3)** [**] **2.0 (1-2)** [**]	**8.0 (6-10)** [**] **5.0 (5-7)** [**]	16 (32.0) 11 (22.0)
Ngu et al.	LRC-IA CME RRC-IA CME	**162.5 (120-285)** [*] **212.5 (160-335)** [*]	- -	0 (16) 0 (16)	2.4 (0.4-6.7) [*] 2.0 (1.1-8.8) [*]	4.5 (3-16) [*] 4.5 (2-13) [*]	12 (75.0) 12 (75.0)
Nolan et al.	LRC RRC	137.0 (105-175.5) [**] 130.5 (98-194) [**]	- -	- -	- -	4.0 (3-5) [**] 4.0 (2-5) [**]	
Kelley et al.	LRC-EA RRC-IA	**139.9 (49.0)** **255.0 (66.0)**	**35 (40.2)** [c] **2 (7.4)** [c]	1 (1.1) 0 (0)	**2.9 (1.1)** **1.2 (0.6)**	3.8 (2.2) 3.4 (1.2)	**45 (51.7)** **7 (25.9)**
Spinoglio et al.	LRC-IA CME RRC-IA CME	**236.0 (68.0)** **279.0 (80.0)**	< 50 [d] < 50 [d]	**7 (6.9)** **0 (0)**	1.8 (0.8) 1.9 (1.0)	7.9 (3.5) 7.9 (5.2)	34 (33.6) 28 (27.7)
Scotton et al.	LRC-EA RRC-IA	209.9 (64.0) 261.0 (41.0)	- -	29 (18.1) 2 (6.7)	3.1 (1.3) 2.2 (0.6)	9.9 (7.1) 8.4 (4.1)	64 (40.0) 12 (40.0)
Haskins et al.	ORC LRC RRC	**135.9 (89.2)** **142.5 (63.3)** **187.2 (81.4)**	- - -	- - -	- - -	**7.9 (7.7)** **5.2 (4.7)** **4.4 (2.4)**	- - -
Lujan et al.	LRC-EA RRC-IA	**98.8 (44.3)** **190.2 (40.7)**	**60.7 (60.0)** **37.9 (54.1)**	9 (6.7) 2 (2.3)	2.4 (1.1) 2.5 (1.2)	3.5 (2.1) 3.5 (2.7)	44 (32.6) 23 (25.8)
Widmar et al.	ORC LRC RRC	167.0 (113-245) [**] 148.0 (116-186) [**] 156.0 (131-182) [**]	- - -	**NA** **33 (20.2)** **3 (2.5)**	- - -	- - -	**68 (37.5)** **22 (13.5)** **16 (13.4)**
Dolejs et al.	LRC RRC	**133.0 (73.0)** [**] **173.0 (91.0)** [**]	- -	685 (10.5) 16 (6.2)	- -	**4.0 (3.0)** [**] **3.0 (2.0)** [**]	1 441 (22.1) 57 (22.0)
Kang et al.	ORC LRC-EA RRC-EA	**182.1 (64.3)** **236.4 (61.8)** **239.3 (59.3)**	132.1 (235.6) 101.3 (110.4) 187.0 (205.2)	NA 1 (2.3) 0 (0)	**4.0 (1-7)** [*] **3.0 (2-5)** [*] **2.0 (1-4)** [*]	**13.0 (6-41)** [*] **9.0 (4-23)** [*] **8.5 (6-27)** [*]	7 (21.2) 3 (7.0) 2 (10.0)
de'Angelis et al.	LRC-EA RRC-EA	204.1 (26.7) 200.5 (29.5)	**164.0 (24.8)** **148.6 (31.6)**	2 (4.0) 0 (0)	1.9 (0.6) 1.9 (0.5)	8.3 (4.4) 7.1 (3.1)	11 (22.0) 6 (20.0)
Widmar et al.	LRC-EA RRC-IA/EA	**128.0 (57.0)** [**] **160.0 (51.0)** [**]	- -	4 (1.9) 2 (2.9)	- -	5 (2.0) [**] 5 (2.0) [**]	71 (34.3) 22 (31.9)
Cardinali et al.	LRC-EA RRC-IA	**140.7 (32.4)** **174.0 (23.6)**	- -	5 (8.3) 1 (3.3)	3.4 (2.0) 2.7 (0.9)	8.0 (4.9) 6.8 (2.4)	10 (16.6) 5 (16.6)
Miller et al.	LRC RRC	**147.4** [h] **167.3** [h]	- -	327 (11.9) 9 (8.3)	- -	**6.2** [h] **4.9** [h]	- -
Ferrara et al.	LRC-EA RRC-EA	**167.7 (35.7)** **230.0 (34.9)**	- -	- -	- -	8.5 (4.3) 7.1 (1.5)	- -
Guerrieri et al.	LRC-IA/EA RRC-IA/EA	**145.0 (130-155)** [**] **173.0 (156-189)** [**]	- -	2 (18.2) 1 (5.6)	2.0 (2-4) [**] 1.0 (1-3) [**]	5.0 (5-10) [**] 5.0 (5-7) [**]	4 (36.4) 3 (16.7)
Trastulli et al.	LRC-EA LRC-IA RRC-IA	**208.0 (61.0)** **204.3 (51.9)** **287.4 (76.4)**	45.0 (10-500) [*] 10.0 (10-350) [*] 30.0 (10-250) [*]	8 (8.5) 6 (15.0) 4 (3.9)	**3.0 (1-6)** [*] **4.0 (1-7)** [*] **2.0 (1-8)** [*]	**7.0 (4-21)** [*] **5.5 (3-14)** [*] **4.0 (3-22)** [*]	27 (28.7) 8 (20.0) 27 (26.5)
Trinh et al.	LRC RRC	146.9 (50.0) 145.4 (39.9)	78.1 (79.6) 43.6 (29.8)	2 (13.3) 0 (0)	- -	9.4 (8.1) 6.1 (2.7)	4 (26.7) 0 (0)

Casillas et al.	LRC-EA RRC-EA	**79.0 (74-84)** ^ **143.0 (136-150)** ^	57.0 (38-84) ^ 63.0 (38-112) ^	12 (11.0) 2 (4.0)	- -	5.5 (4.6-6.5) ^ 6.2 (4.8-8.0) ^	**39 (35.0)** **9 (17.0)**
Davis et al.	LRC RRC	**179.0 (64.2)** **247.0 (90.0)**	- -	- -	- -	6.9 (7.2) 6.5 (7.4)	- -
Lujan et al.	LRC-EA RRC-IA/EA	**158.0 (38.1)** **258.0 (40.9)**	**70.2 (52.9)** **60.8 (71.3)**	0 (0) 0 (0)	- -	3.6 (2.4) 3.9 (2.7)	7 (28.0) 7 (31.8)
Morprugo et al.	LRC-EA RRC-IA	**223.0 (51.0)** **266.0 (41.0)**	- -	- -	**3.4 (1.2)** **2.4 (0.8)**	**9.0 (3.2)** **7.5 (2.0)**	22 (45.8) 8 (16.7)
Park et al.	LRC-IA/EA RRC-IA/EA	**130.0 (43.0)** **195.0 (41.0)**	46.8 (31.3) 35.8 (36.3)	0 (0) 0 (0)	2.9 (2.2) 2.6 (1.4)	8.3 (4.2) 7.9 (4.1)	7 (20.0) 6 (17.1)
Deutsch et al.	LRC-EA RRC-EA	214.4 (63.2) 219.2 (39.2)	**123.2 (89.7)** **76.4 (48.9)**	0 (0) 1 (5.6) i	3.6 (1.5) 3.0 (0.8)	6.3 (6.4) 4.3 (2.5)	20 (42.6) 6 (33.3)
Shin et al.	LRC-EA RRC-EA	250.8 (26.3) 342.5 (106.5)	241.7 (188.2) 185.0 (70.4)	2 (33.3) 0 (0)	3.6 (2.1) 3.5 (0.5)	8.8 (1.5) 10.7 (2.1)	- -
deSouza et al.	LRC-EA RRC-EA	**118.1 (38.1)** **158.9 (36.7)**	50.0 (10-600) * 50.0 (10-240) *	1 (0.7) 1 (2.5)	- -	5 (2-16) * 5 (3-10) *	40 (29.6) 10 (25.0)
Rawlings et al.	LRC-EA RRC-IA	**169.2 (37.5)** **218.9 (44.6)**	66.3 (50.7) 40.0 (24.9)	2 (13.3) 0 (0)	- -	5.5 (3.4) 5.2 (5.8)	2 (13.3) 1 (5.9)
Delaney et al.	LRC-EA RRC-EA	138.8 (31.1) 270.5 (19.1)	150.0 (1.4) 100.0 (0.0)	0 (0) 0 (0)	- -	2.5 (0.7) 3.5 (2.1)	1 (50.0) 0 (0)

*: median (range); **: median (interquartile range); ^: mean (95% confidence interval); a: > 30 days; b: ≤ 90 days; c: n (%) of cases with blood loss ≥ 90 ml; d: median value; e: up to 30 months after surgery; f: anastomotic leak rate significantly higher for open surgery than for laparoscopic or robotic surgery (p < 0.01); g: including small bowel obstruction; h: mean value; i: conversion to conventional laparoscopy; LRC: laparoscopic right colectomy; RRC: robotic right colectomy; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; ORC: open right colectomy; SD: statistical difference; bold: statistically significant difference.

5.1.5. Table 2b. Operative outcomes reported in the included studies (part 2).

First author	Surgical techniques	Anastomotic leak [n (%)]	Ileus [n (%)]	Surgical site infection [n (%)]	Incisional hernia [n (%)]	30-day Dindo-Clavien class > II [n (%)]	30-day readmission [n (%)]	Reoperation [n (%)]
Ceccarelli et al.	3-D LRC-IA CME RRC-IA CME	- -	- -	0 (0) 1 (5.0)	- -	1 (20.0) 0 (0)	- -	- -
Migliore et al.	LRC-IA RRC-IA	- -	7 (4.1) 6 (13.0)	- -	- -	6 (3.5) 1 (2.2)	4 (2.4) 1 (2.2)	5 (2.9) 0 (0)
Milone et al.	LRC-IA RRC-IA	0 (0) 3 (1.7)	- -	- -	- -	- -	- -	- -
Merola et al.	LRC-IA RRC-IA	1 (1.1) 1 (1.1)	- -	- -	- -	4 (4.2) 3 (3.2)	1 (1.1) 0 (0)	0 (0) 0 (0)
Gerbaud et al.	LRC-EA RRC- IA/EA	1 (1.7) 2 (4.8)	1 (1.7) 1 (2.4)	3 (5.1) 2 (4.8)	- -	6 (10.1) 4 (9.5)	2 (3.3) 3 (7.1)	4 (6.7) 4 (9.5)
Park et al.	LRC-IA/EA RRC-IA/EA	0 (0) 1 (2.8)	1 (2.8) 1 (2.8)	3 (8.6) 2 (5.7)	- -	1 (2.8) 1 (2.8)	2 (5.6) [a] 1 (2.8) [a]	1 (2.8) [a] 1 (2.8) [a]
Blumberg et al.	LRC-IA RRC-IA	0 (0) 1 (4.8)	1 (0.9) 0 (0)	6 (5.9) 0 (0)	1 (0.9) 0 (0)	17 (16.8) 3 (14.3)	- -	1 (0.9) 1 (4.8)
Khorgami et al.	LRC RRC	- -	- -	- -	- -	- -	- -	- -
Solaini et al.	LRC-IA RRC-IA	3 (3.6) 8 (2.6)	- -	7 (8.3) 25 (8.1)	- -	7 (8.3) 19 (6.2)	3 (3.6) [b] 1 (0.3) [b]	- -
Yozgatli et al.	LRC-IA/EA CME RRC-IA CME	3 (4.9) 0 (0)	8 (13.1) 2 (5.7)	2 (3.3) 4 (11.4)	- -	4 (6.5) 1 (2.8)	0 (0) 2 (5.7)	3 (4.9) 1 (2.8)
Mégevand et al.	LRC-IA RRC-IA	5 (10.0) 2 (4.0)	4 (8.0) 4 (8.0)	0 (0) 1 (2.0)	- -	- -	0 (0) 0 (0)	6 (12.0) 2 (4.0)
Ngu et al.	LRC-IA CME RRC-IA CME	0 (0) 0 (0)	- -	- -	- -	0 (0) 1 (6.2)	1 (6.2) 2 (12.5)	- -
Nolan et al.	LRC RRC	- -	- -	- -	- -	- -	- -	- -
Kelley et al.	LRC-EA RRC-IA	1 (1.1) 0 (0)	**24 (27.5)** **1 (3.7)**	7 (8.0) 0 (0)	- -	8 (9.2) 1 (3.7)	11 (12.6) 1 (3.7)	2 (2.2) 0 (0)
Spinoglio et al.	LRC-IA CME RRC-IA CME	1 (0.9) 1 (0.9)	10 (9.9) 10 (9.9)	10 (9.9) 5 (4.9)	0 (0) 0 (0)	6 (5.9) 4 (3.9)	- -	1 (0.9) 1 (0.9)
Scotton et al.	LRC-EA RRC-IA	8 (5.0) 0 (0)	- -	19 (11.9) 3 (10.0)	4 (2.5) -	- -	- -	5 (3.1) 0 (0)
Haskins et al.	ORC LRC RRC	- - -	**198 (19.3)** **235 (9.8)** **11 (12.4)**	115 (11.2) 180 (7.5) 5 (5.6)	- - -	- - -	- - -	48 (4.7) 79 (3.3) 2 (2.2)
Lujan et al.	LRC-EA RRC-IA	5 (3.7) 1 (1.1)	15 (11.1) 4 (4.5)	6 (4.4) 3 (3.4)	5 (7.1) [e] 0 (0) [e]	10 (7.4) 1 (1.1)	7 (5.2) 2 (2.3)	3 (2.2) 1 (1.1)
Widmar et al.	ORC LRC RRC	**DS** [f]	5(2.7) [g] 5(3.1) [g] 1(0.8) [g]	**46 (25.4)** **12 (7.4)** **7 (5.8)**	- - -	**27 (14.9)** **4 (2.4)** **3 (2.5)**	- - -	- - -
Dolejs et al.	LRC RRC	143 (2.2) 6 (2.3)	626 (9.6) 28 (10.8)	528 (8.1) 18 (7.0)	- -	678 (10.4) 29 (11.2)	489 (7.5) 21 (8.1)	- -
Kang et al.	ORC LRC-EA RRC-EA	- - -	3 (9.1) [g] 1 (2.3) [g] 0 (0) [g]	**3 (9.1)** **0 (0)** **0 (0)**	- - -	- - -	- - -	- - -
de'Angelis et al.	LRC-EA RRC-EA	2 (4.0) 0 (0)	0 (0) 1 (3.3)	1 (2.0) 0 (0)	- -	2 (4.0) 0 (0)	- -	2 (4.0) 0 (0)
Widmar et al.	LRC-EA RRC-IA/EA	1 (0.5) 0 (0)	10 (4.8) 4 (5.8)	26 (12.6) 10 (14.5)	46 (22.2) 12 (17.4)	2 (1.0) 2 (2.9)	19 (9.2) [b] 5 (7.2) [b]	- -
Cardinali et al.	LRC-EA RRC-IA	1 (1.7) 0 (0)	1 (1.7) 0 (0)	1 (1.7) 3 (10.0)	- -	- -	- -	1 (1.7) 0 (0)
Miller et al.	LRC RRC	- -	- -	- -	- -	- -	- -	- -
Ferrara et al.	LRC-EA RRC-EA	- -	- -	- -	- -	- -	- -	- -
Guerrieri et al.	LRC-IA/EA RRC-IA/EA	- -	- -	- -	- -	- -	- -	- -
Trastulli et al.	LRC-EA LRC-IA RRC-IA	2 (2.1) 0 (0) 3 (2.9)	3 (3.2) 1 (2.5) 2 (2.0)	6 (5.9) 4 (3.9) 7 (6.9)	- - -	- - -	- - -	2 (2.1) 0 (0) 7 (6.8)
Trinh et al.	LRC RRC	- -	2 (13.3) 0 (0)	1 (6.7) 0 (0)	- -	- -	- -	- -

Casillas et al.	LRC-EA RRC-EA	7 (6.0) 0 (0)	**13 (12.0)** **1 (2.0)**	7 (6.0) 1 (2.0)	- -	- -	- -	- -
Davis et al.	LRC RRC	- -	- -	- -	- -	- -	- -	- -
Lujan et al.	LRC-EA RRC-IA/EA	- -	3 (12.0) 3 (13.6)	1 (4.0) 1 (4.5)	- -	- -	- -	- -
Morprugo et al.	LRC-EA RRC-IA	**4 (8.3)** **0 (0)**	- -	7 (14.6) 5 (10.4)	**4 (8.3)** **0 (0)**	- -	- -	- -
Park et al.	LRC-IA/EA RRC-IA/EA	0 (0) 1 (2.8)	1 (2.8) 1 (2.8)	3 (8.6) 2 (5.7)	- -	1 (2.8) 1 (2.8)	- -	- -
Deutsch et al.	LRC-EA RRC-EA	1 (2.1) 1 (5.6)	10 (21.3) 2 (11.1)	0 (0) 1 (5.6)	2 (4.3) 0 (0)	- -	- -	- -
Shin et al.	LRC-EA RRC-EA	- -	- -	- -	- -	- -	- -	- -
deSouza et al.	LRC-EA RRC-EA	- -	11 (0.7) 3 (7.5)	10 (8.1) 2 (5.0)	- -	- -	**2 (1.5)** **4 (10.0)**	- -
Rawlings et al.	LRC-EA RRC-IA	0 (0) 1 (5.9)	1 (6.7) 0 (0)	- -	- -	- -	- -	1 (6.7) 1 (5.9)
Delaney et al.	LRC-EA RRC-EA	- -	- -	- -	- -	- -	- -	- -

*: median (range); **: median (interquartile range); ^: mean (95% confidence interval); a: > 30 days; b: ≤ 90 days; c: n (%) of cases with blood loss ≥ 90 ml; d: median value; e: up to 30 months after surgery; f: anastomotic leak rate significantly higher for open surgery than for laparoscopic or robotic surgery (p < 0.01); g: including small bowel obstruction; h: mean value; i: conversion to conventional laparoscopy; LRC: laparoscopic right colectomy; RRC: robotic right colectomy; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; ORC: open right colectomy; SD: statistical difference; bold: statistically significant difference.

5.1.6. Table 3a. Pathological results and survivals reported in the included studies (part 1).

First author	Surgical techniques	Carcinoma [n (%)]	pTNM stage [n (%)]			
			0	1	2	3
Ceccarelli et al.	3-D LRC-IA CME RRC-IA CME	20 (100) 20 (100)	- -	- -	- -	- -
Migliore et al.	LRC-IA RRC-IA	163 (95.9) 43 (93.5)	- -	- -	- -	- -
Milone et al.	LRC-IA RRC-IA	- -	- -	- -	- -	- -
Merola et al.	LRC-IA RRC-IA	94 (100) 94 (100)	- -	13 (13.8) 10 (10.6)	56 (59.6) 52 (55.3)	23 (24.5) 31 (33.0)
Gerbaud et al.	LRC-EA RRC- IA/EA	37 (62.8) 30 (71.5)	- -	- -	- -	- -
Park et al.	LRC-IA/EA RRC-IA/EA	35 (100) 35 (100)	- -	10 (28.6) 9 (25.7)	16 (45.7) 16 (45.7)	9 (25.7) 10 (28.6)
Blumberg et al.	LRC-IA RRC-IA	43 (42.0) 9 (43.0)	58 (57.4) 12 (57.2)	13 (12.9) 4 (19.0)	15 (14.9) 4 (19.0)	9 (8.9) 1 (4.8)
Khorgami et al.	LRC RRC	- -	- -	- -	- -	- -
Solaini et al.	LRC-IA RRC-IA	- -	- -	- -	- -	- -
Yozgatli et al.	LRC-IA /EA CME RRC-IA CME	35 (100) 61 (100)	3 (4.9) 2 (5.7)	7 (11.5) 5 (14.3)	20 (32.8) 13 (37.1)	29 (47.5) 12 (34.3)
Mégevand et al.	LRC-IA RRC-IA	50 (100) 50 (100)	15 (30.0) 9 (18.0)	7 (14.0) 10 (20.0)	9 (18.0) 16 (32.0)	16 (32.0) 12 (24.0)
Ngu et al.	LRC-IA CME RRC-IA CME	15 (93.7) 14 (87.5)	- -	- -	- -	- -
Nolan et al.	LRC RRC	- -	- -	- -	- -	- -
Kelley et al.	LRC-EA RRC-IA	67 (77.0) 21 (77.7)	- -	- -	- -	- -
Spinoglio et al.	LRC-IA CME RRC-IA CME	101 (100) 101 (100)	- -	26 (26.0) [b] 21 (21.0) [b]	28 (28.0) [b] 38 (38.0) [b]	33 (33.0) [b] 37 (37.0) [b]
Scotton et al.	LRC-EA RRC-IA	160 (100) 30 (100)	- -	- -	- -	- -
Haskins et al.	ORC LRC RRC	1 024 (100) 2 405 (100) 89 (100)	- - -	- - -	- - -	- - -
Lujan et al.	LRC-EA RRC-IA	80 (59.3) 46 (51.6)	6 (7.4) [c] 6 (13.0) [d]	28 (34.6) [c] 14 (30.4) [d]	22 (27.2) [c] 10 (21.7) [d]	19 (23.5) [c] 13 (28.3) [d]
Widmar et al.	ORC LRC RRC	181 (100) 163 (100) 119 (100)	- - -	**23 (13.0)** **36 (22.0)** **27 (23.0)**	**38 (21.0)** **62 (38.0)** **46 (39.0)**	**33 (18.0)** **55 (34.0)** **38 (32.0)**
Dolejs et al.	LRC RRC	3 247 (49.8) 116 (44.8)	- -	- -	- -	- -
Kang et al.	ORC LRC-EA RRC-EA	33 (100) 43 (100) 20 (100)	- - -	3 (9.1) 7 (16.3) 5 (25)	18 (54.5) 16 (37.2) 7 (35)	12 (36.4) 20 (46.5) 8 (40)
de'Angelis et al.	LRC-EA RRC-EA	50 (100) 30 (100)	- -	18 (36.0) 8 (26.7)	21 (42.0) 13 (43.3)	11 (22.0) 9 (30.0)
Widmar et al.	LRC-EA RRC-IA/EA	- -	- -	- -	- -	- -
Cardinali et al.	LRC-EA RRC-IA	60 (100) 30 (100)	- -	37 (61.7) 18 (60.0)	11 (18.3) 8 (26.7)	11 (18.3) 3 (10.0)
Miller et al.	LRC RRC	- -	- -	- -	- -	- -
Ferrara et al.	LRC-EA RRC-EA	15 (100) 13 (100)	- -	- -	- -	- -
Guerrieri et al.	LRC-IA/EA RRC-IA/EA	11 (100) 18 (100)	- -	- -	- -	- -
Trastulli et al.	LRC-EA LRC-IA RRC-IA	88 (93.6) 32 (80.0) 88 (86.3)	5 (5.3) 2 (5.0) 7 (6.9)	26 (27.7) 7 (17.5) 23 (22.5)	26 (27.7) 10 (25.0) 26 (25.5)	27 (28.7) 9 (22.5) 30 (29.4)
Trinh et al.	LRC RRC	- -	- -	- -	- -	- -

Casillas et al.	LRC-EA RRC-EA	- -	- -	- -	- -	- -
Davis et al.	LRC RRC	- -	- -	- -	- -	- -
Lujan et al.	LRC-EA RRC-IA/EA	12 (48.0) 10 (45.4)	- -	- -	- -	- -
Morprugo et al.	LRC-EA RRC-IA	48 (100) 48 (100)	- -	11 (23.0) 20 (41.7)	15 (31.2) 18 (37.5)	18 (37.5) 7 (14.6)
Park et al.	LRC-IA/EA RRC-IA/EA	35 (100) 35 (100)	- -	10 (28.6) 9 (25.7)	16 (45.7) 16 (45.7)	9 (25.7) 10 (28.6)
Deutsch et al.	LRC-EA RRC-EA	24 (51.0) 5 (27.7)	- -	- -	- -	- -
Shin et al.	LRC-EA RRC-EA	- -	- -	- -	- -	- -
deSouza et al.	LRC-EA RRC-EA	66 (48.9) 18 (45.0)	- -	- -	- -	- -
Rawlings et al.	LRC-EA RRC-IA	6 (40.0) 2 (11.7)	- -	- -	- -	- -
Delaney et al.	LRC-EA RRC-EA	1 (50.0) 1 (50.0)	- -	- -	- -	- -

*: median (range); **: median (interquartile range); ^: mean (95% confidence interval); a: patients showing relapse and no other indication of time; b: over 100 cases; c: over 81cases; d: over 47 cases; e: n (%) of cases with ≥ 12 nodes harvested; f: mean value; g: median value; LRC: laparoscopic right colectomy; RRC: robotic right colectomy; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; ORC; open right colectomy; bold: statistically significant difference.

5.1.7. Table 3b. Pathological results and survivals reported in the included studies (part 2).

First author	Surgical techniques	Tumour size (cm)	Number of harvested nodes [n (SD)]	Positive resection margins [n (%)]	5-year free disease survival (%)	5-year overall free survival (%)
Ceccarelli et al.	3-D LRC-IA CME RRC-IA CME	4.0 (2.2) 4.1 (1.9)	19.8 (8.8) 19.5 (11.6)	- -	- -	- -
Migliore et al.	LRC-IA RRC-IA	- -	19.9 (8.2) 19.4 (6.8)	- -	- -	- -
Milone et al.	LRC-IA RRC-IA	- -	- -	- -	- -	- -
Merola et al.	LRC-IA RRC-IA	- -	22.3 (3.8) 21.9 (5.9)	- -	- -	- -
Gerbaud et al.	LRC-EA RRC- IA/EA	4.2 (1.9) 3.8 (2.0)	23.0 (7.0) 26.0 (11.0)	1 (1.7) 2 (4.7)	4 [a] 1 [a]	- -
Park et al.	LRC-IA/EA RRC-IA/EA	- -	30.8 (13.3) 29.9 (14.7)	- -	83.6 ^ 77.4 ^	91.0 ^ 91.1 ^
Blumberg et al.	LRC-IA RRC-IA	- -	14.0 (8.0) 19.0 (11.0)	0 (0) 0 (0)	- -	- -
Khorgami et al.	LRC RRC	- -	- -	- -	- -	- -
Solaini et al.	LRC-IA RRC-IA	- -	19.0 (15.0-27.0) [**] 22.0 (18.0-29.0) [**]	0 (0) 1 (0.3)	- -	- -
Yozgatli et al.	LRC-IA /EA CME RRC-IA CME	5.0 (3.0) 5.0 (2.0)	**33.0 (10.0)** **41.0 (12.0)**	0 (0) 0 (0)	- -	- -
Mégevand et al.	LRC-IA RRC-IA	- -	23.0 (15.0-33.0) [**] 20.5 (16.0-22.0) [**]	- -	- -	- -
Ngu et al.	LRC-IA CME RRC-IA CME	- -	31.0 (12.0-47.0) [*] 41.0 (20.0-89.0) [*]	- -	- -	- -
Nolan et al.	LRC RRC	- -	- -	- -	- -	- -
Kelley et al.	LRC-EA RRC-IA	- -	- -	- -	- -	- -
Spinoglio et al.	LRC-IA CME RRC-IA CME	- -	30.4 (13.1) 28.2 (10.6)	- -	83.0 85.0	73.0 77.0
Scotton et al.	LRC-EA RRC-IA	- -	20.5 (11.2) 21.8 (6.8)	- -	11 [a] 0 [a]	- -
Haskins et al.	ORC LRC RRC	- - -	**18.0 (12.0)** **19.0 (11.0)** **18.0 (9.0)**	**24 (2.3)** **22 (0.9)** **0 (0)**	- - -	- - -
Lujan et al.	LRC-EA RRC-IA	- -	11.9 (9.7) 14.1 (12.1)	- -	- -	- -
Widmar et al.	ORC LRC RRC	- - -	**28.0 (12.0)** **29.0 (14.0)** **34.0 (17.0)**	- - -	- - -	- - -
Dolejs et al.	LRC RRC	- -	- -	- -	- -	- -
Kang et al.	ORC LRC-EA RRC-EA	5.5 (3.0) 4.4 (3.1) 4.0 (2.7)	31.8 (16.9) 32.3 (16.5) 32.2 (18.1)	- - -	87.7 84.0 89.5	86.4 79.2 73.1
de'Angelis et al.	LRC-EA RRC-EA	5.2 (1.2) 4.9 (1.1)	44.0 (88.0) [c] 25.0 (83.0) [c]	1 (2.0) 1 (3.3)	- -	- -
Widmar et al.	LRC-EA RRC-IA/EA	- -	- -	- -	- -	- -
Cardinali et al.	LRC-EA RRC-IA	3.3 (1.5) 3.3 (1.4)	17.7 (8.7) 15.3 (6.8)	- -	- -	- -
Miller et al.	LRC RRC	- -	- -	- -	- -	- -
Ferrara et al.	LRC-EA RRC-EA	- -	18.0 (6.4) 24.2 (13.4)	- -	- -	- -
Guerrieri et al.	LRC-IA/EA RRC-IA/EA	- -	14.0 (9-20) [**] 14.0 (8-20) [**]	- -	- -	- -
Trastulli et al.	LRC-EA LRC-IA RRC-IA	- - -	19.5 (7.7) 19.0 (10.1) 20.3 (7.7)	- - -	- - -	- - -
Trinh et al.	LRC RRC	- -	- -	- -	- -	- -

Casillas et al.	LRC-EA RRC-EA	- -	24.0 (21.0-26.0) ^ 28.0 (24.0-32.0) ^	- -	- -	- -
Davis et al.	LRC RRC	- -	- -	- -	- -	- -
Lujan et al.	LRC-EA RRC-IA/EA	- -	18.3 (10.3) 22.5 (6.2)	- -	- -	- -
Morprugo et al.	LRC-EA RRC-IA	- -	25.0 (13.0) 26.0 (13.0)	- -	- -	- -
Park et al.	LRC-IA/EA RRC-IA/EA	4.7 (2.9) 4.1 (2.4)	30.8 (13.3) 29.9 (14.7)	- -	- -	- -
Deutsch et al.	LRC-EA RRC-EA	- -	18.7 [f] 21.1 [f]	- -	- -	- -
Shin et al.	LRC-EA RRC-EA	- -	18.8 (6.8) 25.8 (16.4)	- -	- -	- -
deSouza et al.	LRC-EA RRC-EA	3.5 (2.1) 3.2 (1.4)	16.0 [g] 17.0 [g]	- -	- -	- -
Rawlings et al.	LRC-EA RRC-IA	- -	- -	- -	- -	- -
Delaney et al.	LRC-EA RRC-EA	- -	- -	- -	- -	- -

*: mediana (range); **: mediana (range interquartile); ^: media (intervallo di confidenza al 95%); a: pazienti con recidiva senza indicazioni temporali; b: su 100 casi; c: su 81 casi; d: su 47 casi; e: n (%) di casi con un numero di linfonodi resecati ≥ 12; f: valore mediano; SRC: studio retrospettivo comparativo; M-: multicentrico; RT: *Randomized Trial*; CDL: colectomia destra laparoscopica; CDR: colectomia destra robotica; AI: anastomosi intracorporea; AE: anastomosi extracorporea; CDA: colectomia destra aperta; ECM: escissione completa del mesocolon; grassetto: differenza statisticamente significativa.

5.1.8. Table 4. Total costs reported in the included studies.

Year	First author	Surgical technique	Total costs (€/$)
2019	Merola et al.	LRC-IA RRC-IA	**6,196.0 (1,444.0) €** **11,576.0 (1,915.0) €**
2019	Park et al.	LRC- IA/EA RRC-IA/EA	**10,319.7 (1,607.7) $** **12,235.0 (1,907.9) $**
2019	Khorgami et al.	LRC RRC	**12,516.0 (5,281.0) $** **15,027.0 (6,049.0) $**
2016	Kang et al.	ORC LRC-EA RRC-EA	**9,009.0 (2,506.0) $** **9,911.0 (3,064.0) $** **12,492.0 (3,911.0) $**
2015	Guerrieri et al.	LRC- IA/EA RRC-IA/EA	**7,326.0 (7,326-9,492) €** ** **7,326.0 (7,326-7,326) €** **
2014	Davis et al.	LRC RRC	16,396.0 (12,497.0) $ 18,515.0 (9,803.0) $
2012	Park et al.	LRC- IA/EA RRC-IA/EA	**10,319.7 (1,607.7) $** **12,235.0 (1,907.9) $**
2010	deSouza et al.	LRC-EA RRC-EA	**12,361.5 (7,796-79,440) $** * **15,192.0 (9,801-38,453) $** *
2007	Rawlings et al.	LRC-EA RRC-IA	8,073.0 (2,805.0) $ 9,255.0 (5,075.0) $

*: median (range); **: median (interquartile range); LRC: laparoscopic right colectomy; RRC: robotic right colectomy; IA: intracorporeal anastomosis; EA: extracorporeal anastomosis; ORC: open right colectomy; €: Euros; $: US dollars; bold: significant difference.

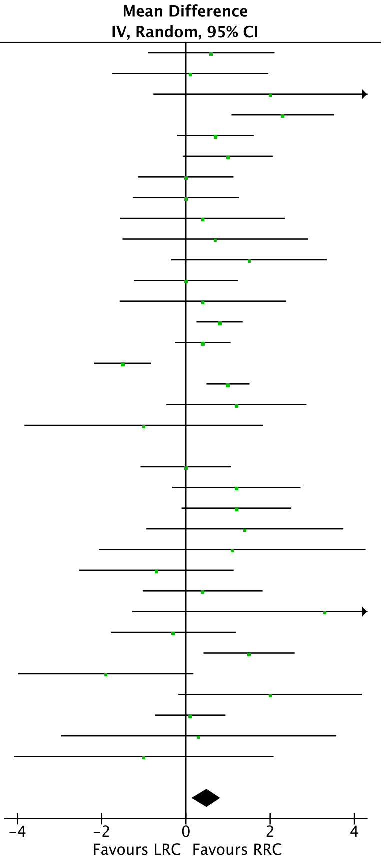
5.1.9. Figure 2a. Forest plots concerning the pooled-data analysis LRC vs RRC (part 1).

Length of hospital stay *

Study or Subgroup	LRC Mean	LRC SD	LRC Total	RRC Mean	RRC SD	RRC Total	Weight	Mean Difference IV, Random, 95% CI	Year
Ceccarelli et al. 2020	7.8	3	20	7.2	1.6	20	2.9%	0.60 [−0.89, 2.09]	2020
Migliore et al. 2020	5.3	9.7	170	5.2	3.9	46	2.3%	0.10 [−1.74, 1.94]	2020
Blumberg et al. 2019	5	1.7	101	3	6.4	21	1.2%	2.00 [−0.76, 4.76]	2019
Mégevand et al. 2019	8	3.9	50	5.7	1.9	50	3.6%	2.30 [1.10, 3.50]	2019
Solaini et al. 2019	8	3.9	84	7.3	2.9	305	4.5%	0.70 [−0.20, 1.60]	2019
Gerbaud et al. 2019	7	3.1	59	6	2.3	42	4.0%	1.00 [−0.05, 2.05]	2019
Merola et al. 2019	4	3.9	94	4	3.9	94	3.9%	0.00 [−1.11, 1.11]	2019
Yozgatli et al. 2019	6	3	61	6	3	35	3.5%	0.00 [−1.25, 1.25]	2019
Park et al. 2019	8.3	4.2	35	7.9	4.1	35	2.1%	0.40 [−1.54, 2.34]	2019
Ngu et al. 2018	6.2	3.4	16	5.5	2.9	16	1.8%	0.70 [−1.49, 2.89]	2018
Scotton et al. 2018	9.9	7.1	160	8.4	4.1	30	2.3%	1.50 [−0.33, 3.33]	2018
Spinoglio et al. 2018	7.9	3.5	101	7.9	5.2	101	3.6%	0.00 [−1.22, 1.22]	2018
Nolan et al. 2018	4	1.9	96	3.6	3.1	10	2.1%	0.40 [−1.56, 2.36]	2018
Haskins et al. 2018	5.2	4.7	2405	4.4	2.4	89	5.7%	0.80 [0.27, 1.33]	2018
Kelley et al. 2018	3.8	2.2	87	3.4	1.2	27	5.3%	0.40 [−0.25, 1.05]	2018
Lujan et al. 2018	3.5	2.1	135	5	2.7	89	5.3%	−1.50 [−2.16, −0.84]	2018
Dolejs et al. 2017	4	5.9	6521	3	3.9	259	5.8%	1.00 [0.50, 1.50]	2017
de'Angelis et al. 2016	8.3	4.4	50	7.1	3.1	30	2.6%	1.20 [−0.45, 2.85]	2016
Kang et al. 2016	9.9	4.9	43	10.9	5.5	20	1.2%	−1.00 [−3.82, 1.82]	2016
Miller et al. 2016	6.2	0	2740	4.9	0	109		Not estimable	2016
Widmar et al. 2016	5	3.9	207	5	3.9	69	4.0%	0.00 [−1.06, 1.06]	2016
Cardinali et al. 2016	8	4.9	60	6.8	2.4	30	2.9%	1.20 [−0.31, 2.71]	2016
Trastulli et al. 2015	6.1	2.8	40	4.9	4.9	102	3.4%	1.20 [−0.09, 2.49]	2015
Ferrara et al. 2015	8.5	4.3	15	7.1	1.5	13	1.6%	1.40 [−0.92, 3.72]	2015
Guerrieri et al. 2015	6.8	5.1	11	5.7	2	18	1.0%	1.10 [−2.05, 4.25]	2015
Casillas et al. 2014	5.5	5.1	110	6.2	5.7	52	2.3%	−0.70 [−2.52, 1.12]	2014
Davis et al. 2014	6.9	7.2	207	6.5	7.4	207	3.1%	0.40 [−1.01, 1.81]	2014
Trinh et al. 2014	9.4	8.1	15	6.1	2.7	7	0.5%	3.30 [−1.26, 7.86]	2014
Lujan et al. 2013	3.6	2.4	25	3.9	2.7	22	3.0%	−0.30 [−1.77, 1.17]	2013
Morprugo et al. 2013	9	3.2	48	7.5	2	48	4.0%	1.50 [0.43, 2.57]	2013
Shin et al. 2012	8.8	1.5	6	10.7	2.1	6	1.9%	−1.90 [−3.96, 0.16]	2012
Deutsch et al. 2012	6.3	6.4	47	4.3	2.5	18	1.8%	2.00 [−0.16, 4.16]	2012
deSouza et al. 2010	5.4	3.6	135	5.3	1.8	40	4.8%	0.10 [−0.72, 0.92]	2010
Rawlings et al. 2006	5.5	3.4	15	5.2	5.8	17	0.9%	0.30 [−2.95, 3.55]	2006
Delaney et al. 2003	2.5	0.7	2	3.5	2.1	2	1.0%	−1.00 [−4.07, 2.07]	2003
Total (95% CI)			**13971**			**2079**	**100.0%**	**0.50 [0.16, 0.84]**	

Heterogeneity: $Tau^2 = 0.46$; $Chi^2 = 76.13$, df = 33 ($P < 0.0001$); $I^2 = 57\%$

Test for overall effect: Z = 2.86 (P = 0.004)

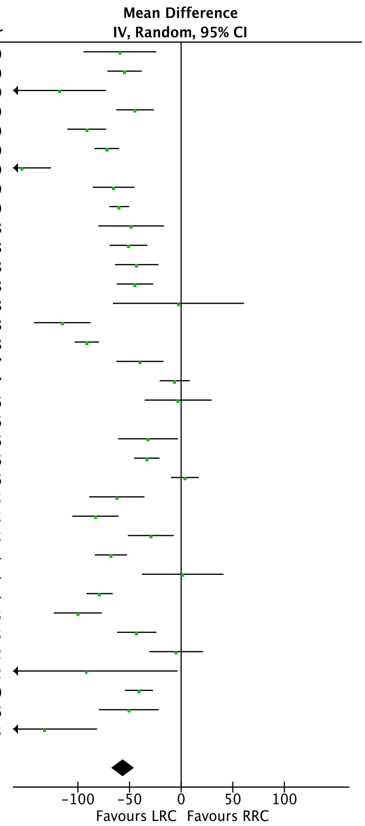


Overall operative time *

Study or Subgroup	LRC Mean	LRC SD	LRC Total	RRC Mean	RRC SD	RRC Total	Weight	Mean Difference IV, Random, 95% CI	Year
Ceccarelli et al. 2020	165.9	30.2	20	225.2	73	20	2.5%	−59.30 [−93.92, −24.68]	2020
Migliore et al. 2020	187.6	56.6	170	242.4	47.5	46	3.2%	−54.80 [−70.95, −38.65]	2020
Blumberg et al. 2019	212	66	101	330	100	21	2.2%	−118.00 [−162.66, −73.34]	2019
Mégevand et al. 2019	160	39.9	50	204.7	49.8	50	3.1%	−44.70 [−62.39, −27.01]	2019
Solaini et al. 2019	163.5	69.5	84	254.9	95	305	3.1%	−91.40 [−109.69, −73.11]	2019
Merola et al. 2019	135.5	33.9	94	207.5	44.9	94	3.3%	−72.00 [−83.37, −60.63]	2019
Yozgatli et al. 2019	132	40	61	286	77	35	2.8%	−154.00 [−181.41, −126.59]	2019
Park et al. 2019	129.7	43.2	35	195	41	35	3.1%	−65.30 [−85.03, −45.57]	2019
Gerbaud et al. 2019	137	19	59	197	25.3	42	3.3%	−60.00 [−69.06, −50.94]	2019
Ngu et al. 2018	175.8	43.8	16	224.2	46.4	16	2.7%	−48.40 [−79.67, −17.13]	2018
Scotton et al. 2018	209.9	64	160	261	41	30	3.1%	−51.10 [−68.81, −33.39]	2018
Spinoglio et al. 2018	236	68	101	279	80	101	3.0%	−43.00 [−63.48, −22.52]	2018
Haskins et al. 2018	142.5	63.3	2405	187.2	81.4	89	3.1%	−44.70 [−61.80, −27.60]	2018
Nolan et al. 2018	139.3	69.9	96	141.9	98.9	10	1.6%	−2.60 [−65.47, 60.27]	2018
Kelley et al. 2018	139.9	49	87	255	66	27	2.8%	−115.10 [−142.04, −88.16]	2018
Lujan et al. 2018	98.8	44.3	135	190.2	40.7	89	3.3%	−91.40 [−102.68, −80.12]	2018
Dolejs et al. 2017	133	144.3	6521	173	180.2	259	3.0%	−40.00 [−62.22, −17.78]	2017
Widmar et al. 2017	150.1	69.4	163	156.3	50.6	119	3.2%	−6.20 [−20.21, 7.81]	2017
Kang et al. 2016	236.4	61.8	43	239.3	59.3	20	2.6%	−2.90 [−34.78, 28.98]	2016
Miller et al. 2016	147.4	0	2740	167.3	0	109		Not estimable	2016
Widmar et al. 2016	128	112.9	207	160	101.4	69	2.8%	−32.00 [−60.44, −3.56]	2016
Cardinali et al. 2016	140.7	32.4	60	174	23.6	30	3.3%	−33.30 [−45.07, −21.53]	2016
de'Angelis et al. 2016	204.1	26.7	50	200.5	29.5	30	3.3%	3.60 [−9.29, 16.49]	2016
Ferrara et al. 2015	167.7	35.7	15	230	34.9	13	2.8%	−62.30 [−88.50, −36.10]	2015
Trastulli et al. 2015	204.3	51.9	40	287.4	76.4	102	3.0%	−83.10 [−104.97, −61.23]	2015
Guerrieri et al. 2015	143.2	25.7	11	172.6	33.4	18	3.0%	−29.40 [−51.05, −7.75]	2015
Davis et al. 2014	179	64.2	207	247	90	207	3.2%	−68.00 [−83.06, −52.94]	2014
Trinh et al. 2014	146.9	50	15	145.4	39.9	7	2.4%	1.50 [−37.41, 40.41]	2014
Casillas et al. 2014	109	45.5	110	188	32.3	52	3.3%	−79.00 [−91.22, −66.78]	2014
Lujan et al. 2013	158	38.1	25	258	40.9	22	3.0%	−100.00 [−122.70, −77.30]	2013
Morprugo et al. 2013	223	51	48	266	41	48	3.1%	−43.00 [−61.51, −24.49]	2013
Deutsch et al. 2012	214.4	63.2	47	219.2	39.2	18	2.9%	−4.80 [−30.38, 20.78]	2012
Shin et al. 2012	250.8	26.3	6	342.5	106.5	6	1.0%	−91.70 [−179.48, −3.92]	2012
deSouza et al. 2010	118.1	38.1	135	158.9	36.7	40	3.3%	−40.80 [−53.86, −27.74]	2010
Rawlings et al. 2006	168.2	37.5	15	218.9	44.6	17	2.8%	−50.70 [−79.15, −22.25]	2006
Delaney et al. 2003	138	31.1	2	270.5	19.1	2	2.0%	−132.50 [−183.08, −81.92]	2003
Total (95% CI)			**14134**			**2198**	**100.0%**	**−56.50 [−67.30, −45.69]**	

Heterogeneity: $Tau^2 = 890.21$; $Chi^2 = 387.12$, df = 34 ($P < 0.00001$); $I^2 = 91\%$

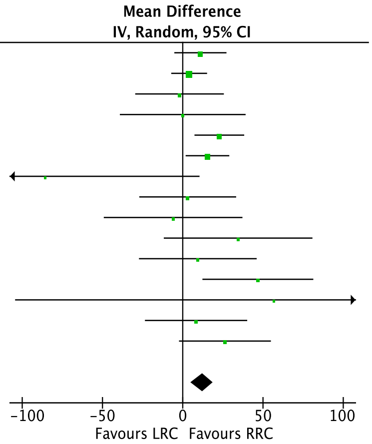
Test for overall effect: Z = 10.25 (P < 0.00001)



Estimated blood loss *

Study or Subgroup	LRC Mean	LRC SD	LRC Total	RRC Mean	RRC SD	RRC Total	Weight	Mean Difference IV, Random, 95% CI	Year
Park et al. 2019	46.8	31.3	35	35.8	36.3	35	13.1%	11.00 [-4.88, 26.88]	2019
Gerbaud et al. 2019	31	29	59	27	26	42	20.8%	4.00 [-6.80, 14.80]	2019
Yozgatli et al. 2019	73	57	61	75	70	35	5.6%	-2.00 [-29.25, 25.25]	2019
Blumberg et al. 2019	100	153	101	100	58	21	3.0%	0.00 [-38.80, 38.80]	2019
Lujan et al. 2018	60.7	60	135	37.9	54.1	89	14.0%	22.80 [7.67, 37.93]	2018
de'Angelis et al. 2016	164	24.8	50	148.6	31.6	30	16.6%	15.40 [2.17, 28.63]	2016
Kang et al. 2016	101.3	110.4	43	187	205.2	20	0.5%	-85.70 [-181.49, 10.09]	2016
Trastulli et al. 2015	44.2	88.1	40	41.1	61.6	102	4.8%	3.10 [-26.70, 32.90]	2015
Casillas et al. 2014	57	123.1	110	63	132.9	52	2.5%	-6.00 [-48.83, 36.83]	2014
Trinh et al. 2014	78.1	79.6	15	43.6	29.8	7	2.2%	34.50 [-11.43, 80.43]	2014
Lujan et al. 2013	70.2	52.9	25	60.8	71.3	22	3.4%	9.40 [-26.90, 45.70]	2013
Deutsch et al. 2012	123.2	89.7	47	76.4	48.9	18	3.8%	46.80 [12.62, 80.98]	2012
Shin et al. 2012	241.7	188.2	6	185	70.4	6	0.2%	56.70 [-104.08, 217.48]	2012
deSouza et al. 2010	73.4	151.2	135	65.1	59.6	40	4.4%	8.30 [-23.19, 39.79]	2010
Rawlings et al. 2006	66.3	50.7	15	40	24.9	17	5.3%	26.30 [-1.96, 54.56]	2006
Total (95% CI)			**877**			**536**	**100.0%**	**12.14 [5.20, 19.08]**	

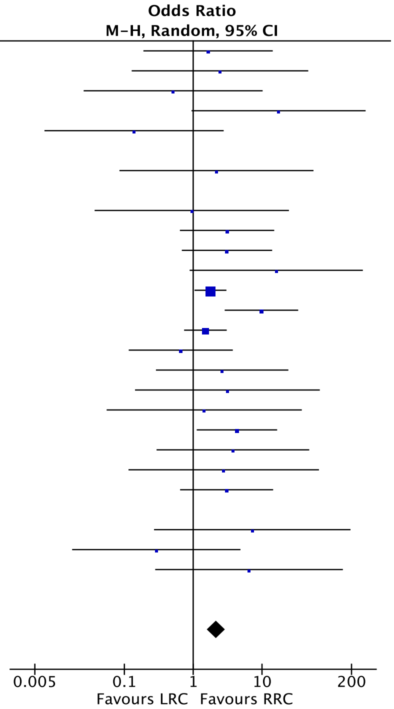
Heterogeneity: $Tau^2 = 29.91$; $Chi^2 = 16.98$, df = 14 (P = 0.26); $I^2 = 18\%$
Test for overall effect: Z = 3.43 (P = 0.0006)



Conversion to laparotomy *

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	6	170	1	46	2.0%	1.65 [0.19, 14.03]	2020
Blumberg et al. 2019	5	101	0	21	1.1%	2.45 [0.13, 46.01]	2019
Solaini et al. 2019	0	84	3	305	1.1%	0.51 [0.03, 10.00]	2019
Mégevand et al. 2019	7	50	0	50	1.1%	17.41 [0.97, 313.73]	2019
Merola et al. 2019	0	94	3	94	1.1%	0.14 [0.01, 2.72]	2019
Yozgatli et al. 2019	0	61	0	35		Not estimable	2019
Gerbaud et al. 2019	1	59	0	42	0.9%	2.18 [0.09, 54.82]	2019
Park et al. 2019	0	35	0	35		Not estimable	2019
Kelley et al. 2018	1	87	0	27	0.9%	0.95 [0.04, 24.09]	2018
Lujan et al. 2018	9	135	2	89	3.9%	3.11 [0.66, 14.73]	2018
Scotton et al. 2018	29	160	2	30	4.2%	3.10 [0.70, 13.75]	2018
Spinoglio et al. 2018	7	101	0	101	1.1%	16.11 [0.91, 285.97]	2018
Dolejs et al. 2017	685	6521	16	259	35.1%	1.78 [1.07, 2.97]	2017
Widmar et al. 2017	33	163	3	119	6.4%	9.82 [2.93, 32.85]	2017
Miller et al. 2016	327	2740	9	109	19.4%	1.51 [0.75, 3.01]	2016
Widmar et al. 2016	4	207	2	69	3.2%	0.66 [0.12, 3.69]	2016
Cardinali et al. 2016	5	60	1	30	1.9%	2.64 [0.29, 23.64]	2016
de'Angelis et al. 2016	2	50	0	30	1.0%	3.14 [0.15, 67.73]	2016
Kang et al. 2016	1	43	0	20	0.9%	1.45 [0.06, 37.09]	2016
Trastulli et al. 2015	6	40	4	102	5.3%	4.32 [1.15, 16.25]	2015
Guerrieri et al. 2015	2	11	1	18	1.5%	3.78 [0.30, 47.56]	2015
Trinh et al. 2014	2	15	0	7	0.9%	2.78 [0.12, 65.79]	2014
Casillas et al. 2014	12	110	2	52	4.0%	3.06 [0.66, 14.21]	2014
Lujan et al. 2013	0	25	0	22		Not estimable	2013
Shin et al. 2012	2	6	0	6	0.9%	7.22 [0.28, 189.19]	2012
deSouza et al. 2010	1	135	1	40	1.2%	0.29 [0.02, 4.76]	2010
Rawlings et al. 2006	2	15	0	17	1.0%	6.48 [0.29, 146.53]	2006
Delaney et al. 2003	0	2	0	2		Not estimable	2003
Total (95% CI)		**11280**		**1777**	**100.0%**	**2.17 [1.60, 2.95]**	
Total events	1149		50				

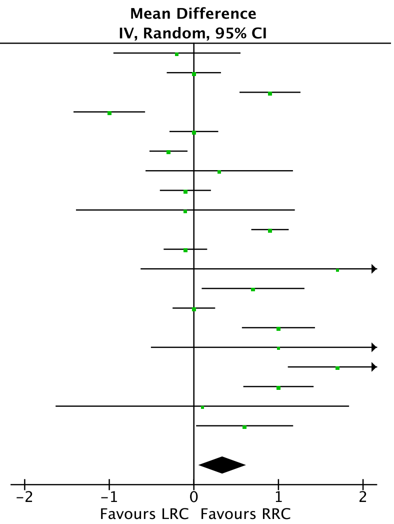
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 23.04$, df = 23 (P = 0.46); $I^2 = 0\%$
Test for overall effect: Z = 4.96 (P < 0.00001)



Time to flatus *

Study or Subgroup	LRC Mean	LRC SD	LRC Total	RRC Mean	RRC SD	RRC Total	Weight	Mean Difference IV, Random, 95% CI	Year
Ceccarelli et al. 2020	3	1.2	20	3.2	1.2	20	4.6%	-0.20 [-0.94, 0.54]	2020
Migliore et al. 2020	1.6	0.8	170	1.6	1	46	6.1%	0.00 [-0.31, 0.31]	2020
Mégevand et al. 2019	2.5	0.9	50	1.6	0.9	50	6.0%	0.90 [0.55, 1.25]	2019
Yozgatli et al. 2019	2	1	61	3	1	35	5.8%	-1.00 [-1.42, -0.58]	2019
Merola et al. 2019	2.2	1.2	94	2.2	0.7	94	6.2%	0.00 [-0.28, 0.28]	2019
Solaini et al. 2019	2.3	0.9	84	2.6	0.9	305	6.4%	-0.30 [-0.52, -0.08]	2019
Park et al. 2019	2.9	2.2	35	2.6	1.4	35	4.1%	0.30 [-0.56, 1.16]	2019
Lujan et al. 2018	2.4	1.1	135	2.5	1.1	89	6.2%	-0.10 [-0.39, 0.19]	2018
Ngu et al. 2018	2.8	1.7	16	2.9	2	16	2.8%	-0.10 [-1.39, 1.19]	2018
Scotton et al. 2018	3.1	1.3	160	2.2	0.2	30	6.4%	0.90 [0.69, 1.11]	2018
Spinoglio et al. 2018	1.8	0.8	101	1.9	1	101	6.3%	-0.10 [-0.35, 0.15]	2018
Kelley et al. 2018	2.9	11	87	1.2	0.6	27	1.2%	1.70 [-0.62, 4.02]	2018
Cardinali et al. 2016	3.4	2	60	2.7	0.9	30	5.1%	0.70 [0.10, 1.30]	2016
de'Angelis et al. 2016	1.9	0.6	50	1.9	0.5	30	6.3%	0.00 [-0.24, 0.24]	2016
Kang et al. 2016	3.1	0.8	43	2.1	0.8	20	5.8%	1.00 [0.58, 1.42]	2016
Guerrieri et al. 2015	2.7	2	11	1.7	2	18	2.3%	1.00 [-0.50, 2.50]	2015
Trastulli et al. 2015	4	1.5	40	2.3	1.8	102	5.2%	1.70 [1.12, 2.28]	2015
Morprugo et al. 2013	3.4	1.2	48	2.4	0.8	48	5.8%	1.00 [0.59, 1.41]	2013
Shin et al. 2012	3.6	2.1	6	3.5	0.5	6	1.9%	0.10 [-1.63, 1.83]	2012
Deutsch et al. 2012	3.6	1.5	47	3	0.8	18	5.3%	0.60 [0.03, 1.17]	2012
Total (95% CI)			**1318**			**1120**	**100.0%**	**0.34 [0.05, 0.63]**	

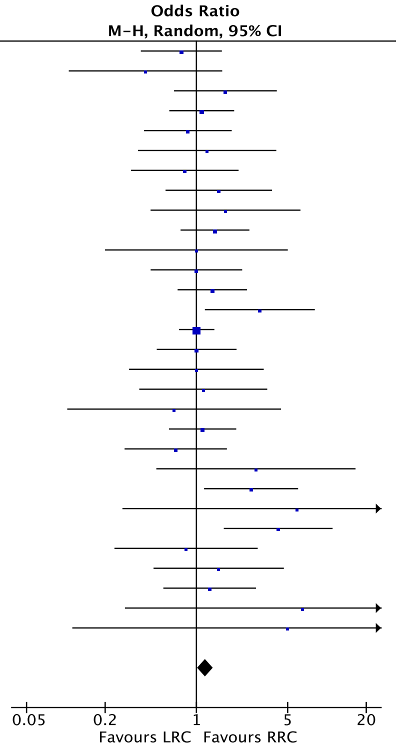
Heterogeneity: $Tau^2 = 0.32$; $Chi^2 = 186.65$, df = 19 (P < 0.00001); $I^2 = 90\%$
Test for overall effect: Z = 2.33 (P = 0.02)



Overall postoperative complications *

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	46	170	15	46	4.4%	0.77 [0.38, 1.55]	2020
Ceccarelli et al. 2020	5	20	9	20	1.2%	0.41 [0.11, 1.56]	2020
Mégevand et al. 2019	16	50	11	50	2.7%	1.67 [0.68, 4.08]	2019
Solaini et al. 2019	21	84	71	305	6.9%	1.10 [0.63, 1.92]	2019
Merola et al. 2019	15	94	17	94	3.7%	0.86 [0.40, 1.84]	2019
Park et al. 2019	7	35	6	35	1.5%	1.21 [0.36, 4.04]	2019
Yozgatli et al. 2019	15	61	10	35	2.5%	0.82 [0.32, 2.08]	2019
Gerbaud et al. 2019	17	59	9	42	2.5%	1.48 [0.59, 3.75]	2019
Blumberg et al. 2019	22	101	3	21	1.3%	1.67 [0.45, 6.20]	2019
Lujan et al. 2018	44	135	23	89	6.1%	1.39 [0.76, 2.52]	2018
Ngu et al. 2018	12	16	12	16	0.8%	1.00 [0.20, 4.95]	2018
Scotton et al. 2018	64	160	12	30	3.4%	1.00 [0.45, 2.22]	2018
Spinoglio et al. 2018	34	101	28	101	6.0%	1.32 [0.73, 2.41]	2018
Kelley et al. 2018	45	87	7	27	2.4%	3.06 [1.17, 7.98]	2018
Dolejs et al. 2017	1441	6521	57	259	24.0%	1.01 [0.74, 1.36]	2017
Widmar et al. 2017	22	163	16	119	4.5%	1.00 [0.50, 2.01]	2017
Cardinali et al. 2016	10	60	5	30	1.6%	1.00 [0.31, 3.24]	2016
de'Angelis et al. 2016	11	50	6	30	1.7%	1.13 [0.37, 3.45]	2016
Kang et al. 2016	3	43	2	20	0.6%	0.68 [0.10, 4.40]	2016
Widmar et al. 2016	71	207	22	69	6.4%	1.12 [0.62, 2.00]	2016
Trastulli et al. 2015	8	40	27	102	2.7%	0.69 [0.28, 1.69]	2015
Guerrieri et al. 2015	4	11	3	18	0.7%	2.86 [0.50, 16.36]	2015
Casillas et al. 2014	39	110	9	52	3.2%	2.62 [1.16, 5.95]	2014
Trinh et al. 2014	4	15	0	7	0.2%	5.87 [0.27, 125.58]	2014
Morprugo et al. 2013	22	48	8	48	2.4%	4.23 [1.64, 10.92]	2013
Lujan et al. 2013	7	25	7	22	1.4%	0.83 [0.24, 2.91]	2013
Deutsch et al. 2012	20	47	6	18	1.7%	1.48 [0.47, 4.62]	2012
deSouza et al. 2010	40	135	10	40	3.3%	1.26 [0.56, 2.83]	2010
Rawlings et al. 2006	2	15	0	17	0.2%	6.48 [0.29, 146.53]	2006
Delaney et al. 2003	1	2	0	2	0.2%	5.00 [0.11, 220.62]	2003
Total (95% CI)		**8665**		**1764**	**100.0%**	**1.18 [1.02, 1.36]**	
Total events	2068		411				

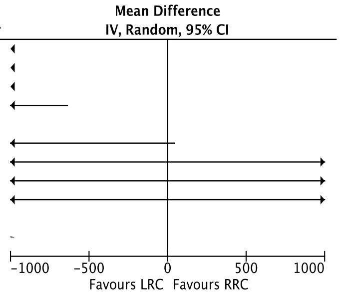
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 28.72$, df = 29 (P = 0.48); $I^2 = 0\%$
Test for overall effect: Z = 2.18 (P = 0.03)



Total costs *

Study or Subgroup	LRC Mean	LRC SD	LRC Total	RRC Mean	RRC SD	RRC Total	Weight	Mean Difference IV, Random, 95% CI	Year
Merola et al. 2019	6,784.9	1,581.25	94	12,676.3	2,097	94	15.3%	-5891.40 [-6422.33, -5360.47]	2019
Park et al. 2019	10,319.7	1,607.7	35	12,235	1,907.9	35	15.0%	-1915.30 [-2741.86, -1088.74]	2019
Khorgami et al. 2019	12,516	5,281	7243	15,027	6,049	442	15.3%	-2511.00 [-3087.89, -1934.11]	2019
Kang et al. 2016	9,911	3,064	43	12,492	3,911	20	12.7%	-2581.00 [-4524.36, -637.64]	2016
Guerrieri et al. 2015	8,494.8	640.7	11	8,022.3	0	18		Not estimable	2015
Davis et al. 2014	16,396	12,497	207	18,515	9,803	207	12.2%	-2119.00 [-4282.71, 44.71]	2014
deSouza et al. 2010	15,228.7	18,361.7	135	16,987.5	7,424.6	40	8.3%	-1758.80 [-5617.26, 2099.66]	2010
Rawlings et al. 2006	8,073	2,805	15	9,255	5,075	17	10.6%	-1182.00 [-3981.09, 1617.09]	2006
Delaney et al. 2003	2,287	83.4	2	3,783	2,005.3	2	10.7%	-1496.00 [-4277.56, 1285.56]	2003
Total (95% CI)			**7785**			**875**	**100.0%**	**-2589.46 [-4206.21, -972.72]**	

Heterogeneity: $Tau^2 = 4367668.60$; $Chi^2 = 109.47$, df = 7 (P < 0.00001); $I^2 = 94\%$
Test for overall effect: Z = 3.14 (P = 0.002)



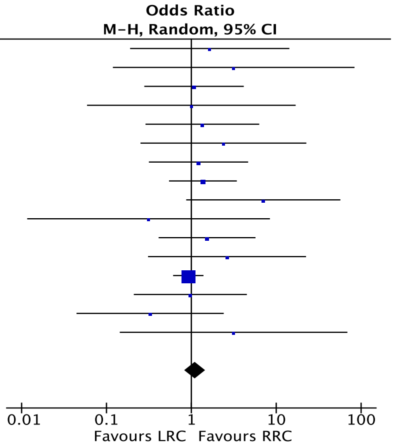
*: statistically significant difference.

5.1.10. Figure 2b. Forest plots concerning the pooled-data analysis LRC vs RRC (part 2).

Severe postoperative complications

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	6	170	1	46	1.8%	1.65 [0.19, 14.03]	2020
Ceccarelli et al. 2020	1	20	0	20	0.8%	3.15 [0.12, 82.16]	2020
Gerbaud et al. 2019	6	59	4	42	4.8%	1.08 [0.28, 4.07]	2019
Park et al. 2019	1	35	1	35	1.1%	1.00 [0.06, 16.65]	2019
Merola et al. 2019	4	94	3	94	3.6%	1.35 [0.29, 6.20]	2019
Yozgatli et al. 2019	4	61	1	35	1.7%	2.39 [0.26, 22.24]	2019
Blumberg et al. 2019	17	101	3	21	4.8%	1.21 [0.32, 4.59]	2019
Solaini et al. 2019	7	84	19	305	10.4%	1.37 [0.56, 3.37]	2019
Lujan et al. 2018	10	135	1	89	2.0%	7.04 [0.89, 55.99]	2018
Ngu et al. 2018	0	16	1	16	0.8%	0.31 [0.01, 8.28]	2018
Spinoglio et al. 2018	6	101	4	101	5.0%	1.53 [0.42, 5.60]	2018
Kelley et al. 2018	8	87	1	27	1.9%	2.63 [0.31, 22.06]	2018
Dolejs et al. 2017	678	6521	29	259	54.5%	0.92 [0.62, 1.37]	2017
Widmar et al. 2017	4	163	3	119	3.7%	0.97 [0.21, 4.43]	2017
Widmar et al. 2016	2	207	2	69	2.2%	0.33 [0.05, 2.37]	2016
de'Angelis et al. 2016	2	50	0	30	0.9%	3.14 [0.15, 67.73]	2016
Total (95% CI)		**7904**		**1308**	**100.0%**	**1.10 [0.82, 1.48]**	
Total events	756		73				

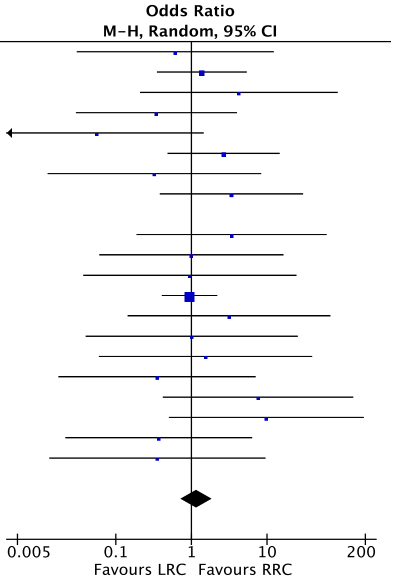
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.67$, df = 15 (P = 0.89); $I^2 = 0\%$
Test for overall effect: Z = 0.66 (P = 0.51)



Anastomotic leak

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Milone et al. 2020	0	40	3	176	2.6%	0.61 [0.03, 12.08]	2020
Solaini et al. 2019	3	84	8	305	12.6%	1.38 [0.36, 5.30]	2019
Yozgatli et al. 2019	3	61	0	35	2.6%	4.25 [0.21, 84.67]	2019
Gerbaud et al. 2019	1	59	2	42	3.9%	0.34 [0.03, 3.93]	2019
Blumberg et al. 2019	0	121	1	21	2.2%	0.06 [0.00, 1.43]	2019
Mégevand et al. 2019	5	50	2	50	8.0%	2.67 [0.49, 14.44]	2019
Park et al. 2019	0	35	1	35	2.2%	0.32 [0.01, 8.23]	2019
Lujan et al. 2018	5	135	1	89	4.9%	3.38 [0.39, 29.47]	2018
Ngu et al. 2018	0	16	0	16		Not estimable	2018
Scotton et al. 2018	8	160	0	30	2.8%	3.40 [0.19, 60.48]	2018
Spinoglio et al. 2018	1	101	1	101	2.9%	1.00 [0.06, 16.21]	2018
Kelley et al. 2018	1	87	0	27	2.2%	0.95 [0.04, 24.09]	2018
Dolejs et al. 2017	143	6521	6	259	33.5%	0.95 [0.41, 2.16]	2017
de'Angelis et al. 2016	2	50	0	30	2.4%	3.14 [0.15, 67.73]	2016
Widmar et al. 2016	1	207	0	69	2.2%	1.01 [0.04, 25.07]	2016
Cardinali et al. 2016	1	60	0	30	2.2%	1.54 [0.06, 38.88]	2016
Trastulli et al. 2015	0	40	3	102	2.6%	0.35 [0.02, 6.95]	2015
Casillas et al. 2014	7	110	0	52	2.8%	7.61 [0.43, 135.80]	2014
Morprugo et al. 2013	4	48	0	48	2.6%	9.81 [0.51, 187.40]	2013
Deutsch et al. 2012	1	47	1	18	2.9%	0.37 [0.02, 6.24]	2012
Rawlings et al. 2006	0	15	1	17	2.1%	0.35 [0.01, 9.38]	2006
Total (95% CI)		**8047**		**1552**	**100.0%**	**1.18 [0.73, 1.90]**	
Total events	186		30				

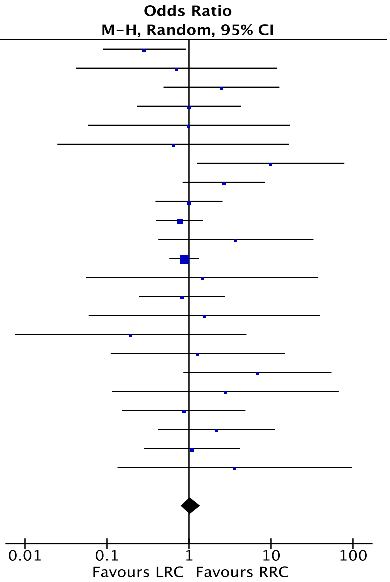
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 14.60$, df = 19 (P = 0.75); $I^2 = 0\%$
Test for overall effect: Z = 0.67 (P = 0.50)



Ileus

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	7	170	6	46	5.6%	0.29 [0.09, 0.90]	2020
Gerbaud et al. 2019	1	59	1	42	1.0%	0.71 [0.04, 11.63]	2019
Yozgatli et al. 2019	8	61	2	35	2.9%	2.49 [0.50, 12.45]	2019
Mégevand et al. 2019	4	50	4	50	3.6%	1.00 [0.24, 4.24]	2019
Park et al. 2019	1	35	1	35	1.0%	1.00 [0.06, 16.65]	2019
Blumberg et al. 2019	1	101	0	21	0.7%	0.64 [0.03, 16.29]	2019
Kelley et al. 2018	24	87	1	27	1.8%	9.90 [1.27, 77.08]	2018
Lujan et al. 2018	15	135	4	89	5.7%	2.66 [0.85, 8.28]	2018
Spinoglio et al. 2018	10	101	10	101	8.3%	1.00 [0.40, 2.52]	2018
Haskins et al. 2018	235	2405	11	89	15.3%	0.77 [0.40, 1.46]	2018
Widmar et al. 2017	5	163	1	119	1.7%	3.73 [0.43, 32.39]	2017
Dolejs et al. 2017	626	6521	28	259	30.5%	0.88 [0.59, 1.31]	2017
Kang et al. 2016	1	43	0	20	0.7%	1.45 [0.06, 37.09]	2016
Widmar et al. 2016	10	207	4	69	5.2%	0.82 [0.25, 2.72]	2016
Cardinali et al. 2016	1	60	0	30	0.8%	1.54 [0.06, 38.88]	2016
de'Angelis et al. 2016	0	50	1	30	0.7%	0.19 [0.01, 4.94]	2016
Trastulli et al. 2015	1	40	2	102	1.3%	1.28 [0.11, 14.55]	2015
Casillas et al. 2014	13	110	1	52	1.8%	6.84 [0.87, 53.74]	2014
Trinh et al. 2014	2	15	0	7	0.8%	2.78 [0.12, 65.79]	2014
Lujan et al. 2013	3	25	3	22	2.6%	0.86 [0.16, 4.79]	2013
Deutsch et al. 2012	10	47	2	18	2.9%	2.16 [0.42, 11.01]	2012
deSouza et al. 2010	11	135	3	40	4.2%	1.09 [0.29, 4.13]	2010
Rawlings et al. 2006	1	15	0	17	0.7%	3.62 [0.14, 95.78]	2006
Total (95% CI)		**10635**		**1320**	**100.0%**	**1.05 [0.79, 1.39]**	
Total events	990		85				

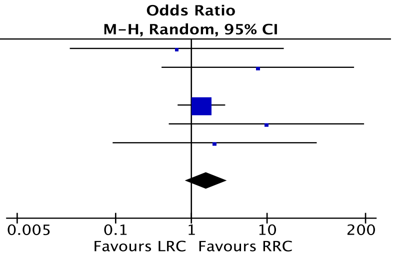
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 23.26$, df = 22 (P = 0.39); $I^2 = 5\%$
Test for overall effect: Z = 0.35 (P = 0.73)



Incisional hernias

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Blumberg et al. 2019	1	101	0	21	3.9%	0.64 [0.03, 16.29]	2019
Lujan et al. 2018	5	135	0	89	4.8%	7.54 [0.41, 138.14]	2018
Spinoglio et al. 2018	0	101	0	101		Not estimable	2018
Widmar et al. 2016	46	207	12	69	82.3%	1.36 [0.67, 2.74]	2016
Morprugo et al. 2013	4	48	0	48	4.7%	9.81 [0.51, 187.40]	2013
Deutsch et al. 2012	2	47	0	18	4.3%	2.03 [0.09, 44.42]	2012
Total (95% CI)		**639**		**346**	**100.0%**	**1.60 [0.84, 3.03]**	
Total events	58		12				

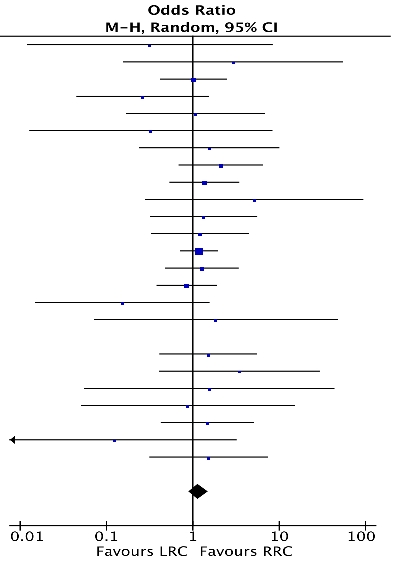
Heterogeneity: Tau² = 0.00; Chi² = 3.22, df = 4 (P = 0.52); I² = 0%
Test for overall effect: Z = 1.44 (P = 0.15)



Surgical site infection

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Ceccarelli et al. 2020	0	20	1	20	0.6%	0.32 [0.01, 8.26]	2020
Blumberg et al. 2019	6	101	0	21	0.8%	2.93 [0.16, 53.95]	2019
Solaini et al. 2019	7	84	25	305	8.6%	1.02 [0.42, 2.44]	2019
Yozgatli et al. 2019	2	61	4	35	2.1%	0.26 [0.05, 1.52]	2019
Gerbaud et al. 2019	3	59	2	42	2.0%	1.07 [0.17, 6.71]	2019
Mégevand et al. 2019	0	50	1	50	0.6%	0.33 [0.01, 8.21]	2019
Park et al. 2019	3	35	2	35	1.9%	1.55 [0.24, 9.88]	2019
Spinoglio et al. 2018	10	101	5	101	5.3%	2.11 [0.69, 6.41]	2018
Haskins et al. 2018	180	2405	5	89	7.9%	1.36 [0.54, 3.39]	2018
Kelley et al. 2018	7	87	0	27	0.8%	5.12 [0.28, 92.69]	2018
Lujan et al. 2018	6	135	3	89	3.3%	1.33 [0.32, 5.47]	2018
Scotton et al. 2018	19	160	3	30	4.0%	1.21 [0.34, 4.39]	2018
Dolejs et al. 2017	528	6521	18	259	27.8%	1.18 [0.72, 1.92]	2017
Widmar et al. 2017	12	163	7	119	7.1%	1.27 [0.49, 3.33]	2017
Widmar et al. 2016	26	207	10	69	10.7%	0.85 [0.39, 1.86]	2016
Cardinali et al. 2016	1	60	3	30	1.2%	0.15 [0.02, 1.53]	2016
de'Angelis et al. 2016	1	50	0	30	0.6%	1.85 [0.07, 46.83]	2016
Kang et al. 2016	0	43	0	20		Not estimable	2016
Trastulli et al. 2015	4	40	7	102	4.0%	1.51 [0.42, 5.46]	2015
Casillas et al. 2014	7	110	1	52	1.5%	3.47 [0.42, 28.93]	2014
Trinh et al. 2014	1	15	0	7	0.6%	1.55 [0.06, 42.91]	2014
Lujan et al. 2013	1	25	1	22	0.8%	0.88 [0.05, 14.87]	2013
Morprugo et al. 2013	7	48	5	48	4.4%	1.47 [0.43, 5.00]	2013
Deutsch et al. 2012	0	47	1	18	0.6%	0.12 [0.00, 3.16]	2012
deSouza et al. 2010	10	135	2	40	2.7%	1.52 [0.32, 7.24]	2010
Total (95% CI)		**10762**		**1660**	**100.0%**	**1.16 [0.90, 1.50]**	
Total events	841		106				

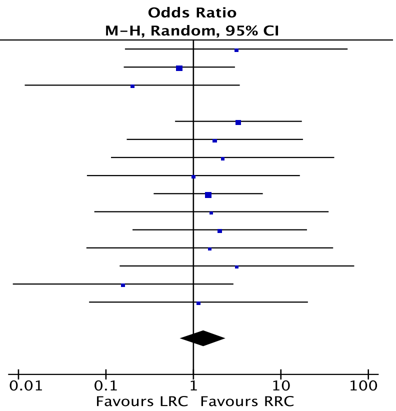
Heterogeneity: Tau² = 0.00; Chi² = 13.86, df = 23 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.13 (P = 0.26)



Reoperation

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	5	170	0	46	4.3%	3.09 [0.17, 56.92]	2020
Gerbaud et al. 2019	4	59	4	42	17.3%	0.69 [0.16, 2.93]	2019
Blumberg et al. 2019	1	101	1	21	4.6%	0.20 [0.01, 3.33]	2019
Merola et al. 2019	0	94	0	94		Not estimable	2019
Mégevand et al. 2019	6	50	2	50	13.3%	3.27 [0.63, 17.07]	2019
Yozgatli et al. 2019	3	61	1	35	6.8%	1.76 [0.18, 17.58]	2019
Scotton et al. 2018	5	160	0	30	4.2%	2.16 [0.12, 40.04]	2018
Spinoglio et al. 2018	1	101	1	101	4.7%	1.00 [0.06, 16.21]	2018
Haskins et al. 2018	79	2405	2	89	18.0%	1.48 [0.36, 6.11]	2018
Kelley et al. 2018	2	87	0	27	3.8%	1.61 [0.07, 34.53]	2018
Lujan et al. 2018	3	135	1	89	7.0%	2.00 [0.20, 19.54]	2018
Cardinali et al. 2016	1	60	0	30	3.5%	1.54 [0.06, 38.88]	2016
de'Angelis et al. 2016	2	50	0	30	3.8%	3.14 [0.15, 67.73]	2016
Trastulli et al. 2015	0	40	7	102	4.3%	0.16 [0.01, 2.82]	2015
Rawlings et al. 2006	1	15	1	17	4.4%	1.14 [0.07, 20.02]	2006
Total (95% CI)		**3588**		**803**	**100.0%**	**1.30 [0.71, 2.37]**	
Total events	113		20				

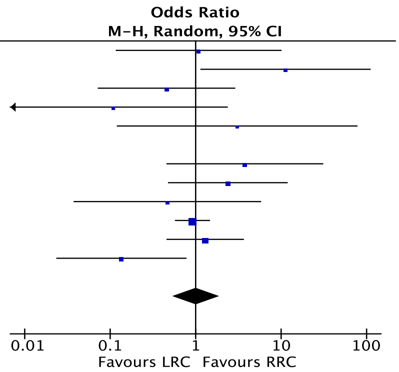
Heterogeneity: Tau² = 0.00; Chi² = 6.78, df = 13 (P = 0.91); I² = 0%
Test for overall effect: Z = 0.85 (P = 0.40)



Readmission

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	4	170	1	46	6.2%	1.08 [0.12, 9.94]	2020
Solaini et al. 2019	3	84	1	305	6.0%	11.26 [1.16, 109.68]	2019
Gerbaud et al. 2019	2	59	3	42	8.3%	0.46 [0.07, 2.86]	2019
Yozgatli et al. 2019	0	61	2	35	3.6%	0.11 [0.01, 2.34]	2019
Mégevand et al. 2019	1	50	0	50	3.3%	3.06 [0.12, 76.95]	2019
Merola et al. 2019	0	94	0	94		Not estimable	2019
Kelley et al. 2018	11	87	1	27	6.8%	3.76 [0.46, 30.58]	2018
Lujan et al. 2018	7	135	2	89	10.0%	2.38 [0.48, 11.72]	2018
Ngu et al. 2018	1	16	2	16	5.1%	0.47 [0.04, 5.73]	2018
Dolejs et al. 2017	489	6521	21	259	25.5%	0.92 [0.58, 1.45]	2017
Widmar et al. 2016	19	207	5	69	16.4%	1.29 [0.46, 3.61]	2016
deSouza et al. 2010	2	135	4	40	8.9%	0.14 [0.02, 0.77]	2010
Total (95% CI)		**7619**		**1072**	**100.0%**	**1.02 [0.55, 1.90]**	
Total events	539		42				

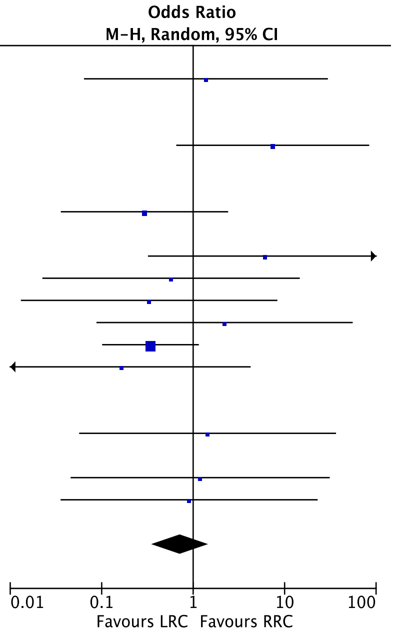
Heterogeneity: Tau² = 0.34; Chi² = 16.03, df = 10 (P = 0.10); I² = 38%
Test for overall effect: Z = 0.07 (P = 0.95)



Mortality

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Ceccarelli et al. 2020	0	20	0	20		Not estimable	2020
Migliore et al. 2020	2	170	0	46	5.4%	1.38 [0.07, 29.24]	2020
Mégevand et al. 2019	0	50	0	50		Not estimable	2019
Park et al. 2019	0	35	0	35		Not estimable	2019
Solaini et al. 2019	2	84	1	305	8.6%	7.41 [0.66, 82.79]	2019
Merola et al. 2019	0	94	0	94		Not estimable	2019
Blumberg et al. 2019	0	101	0	21		Not estimable	2019
Haskins et al. 2018	8	2405	1	89	11.5%	0.29 [0.04, 2.37]	2018
Kelley et al. 2018	0	87	0	27		Not estimable	2018
Lujan et al. 2018	4	135	0	89	5.8%	6.13 [0.33, 115.18]	2018
Scotton et al. 2018	1	160	0	30	4.8%	0.57 [0.02, 14.41]	2018
Spinoglio et al. 2018	0	101	1	101	4.9%	0.33 [0.01, 8.20]	2018
Widmar et al. 2017	1	163	0	119	4.9%	2.21 [0.09, 54.63]	2017
Dolejs et al. 2017	26	6521	3	259	34.8%	0.34 [0.10, 1.14]	2017
de'Angelis et al. 2016	0	59	1	30	4.8%	0.17 [0.01, 4.18]	2016
Widmar et al. 2016	0	207	0	69		Not estimable	2016
Trastulli et al. 2015	0	40	0	102		Not estimable	2015
Casillas et al. 2014	1	110	0	52	4.9%	1.44 [0.06, 35.91]	2014
Morprugo et al. 2013	0	48	0	48		Not estimable	2013
Deutsch et al. 2012	1	47	0	18	4.8%	1.19 [0.05, 30.65]	2012
deSouza et al. 2010	1	135	0	40	4.8%	0.90 [0.04, 22.61]	2010
Total (95% CI)		**10772**		**1644**	**100.0%**	**0.72 [0.36, 1.47]**	
Total events	47		7				

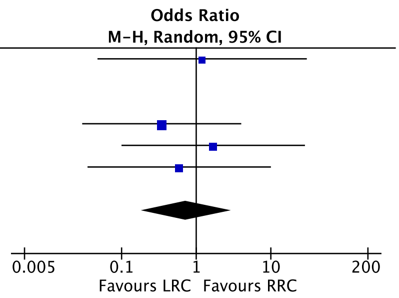
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 10.30$, df = 11 (P = 0.50); $I^2 = 0\%$
Test for overall effect: Z = 0.90 (P = 0.37)



Positive resection margins

Study or Subgroup	LRC Events	LRC Total	RRC Events	RRC Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Solaini et al. 2019	0	84	1	305	18.7%	1.20 [0.05, 29.75]	2019
Yozgatli et al. 2019	0	61	0	35		Not estimable	2019
Blumberg et al. 2019	0	101	0	21		Not estimable	2019
Gerbaud et al. 2019	1	59	2	42	32.5%	0.34 [0.03, 3.93]	2019
Haskins et al. 2018	22	2405	0	89	24.4%	1.69 [0.10, 28.08]	2018
de'Angelis et al. 2016	1	50	1	30	24.4%	0.59 [0.04, 9.83]	2016
Total (95% CI)		**2760**		**522**	**100.0%**	**0.73 [0.18, 2.93]**	
Total events	24		4				

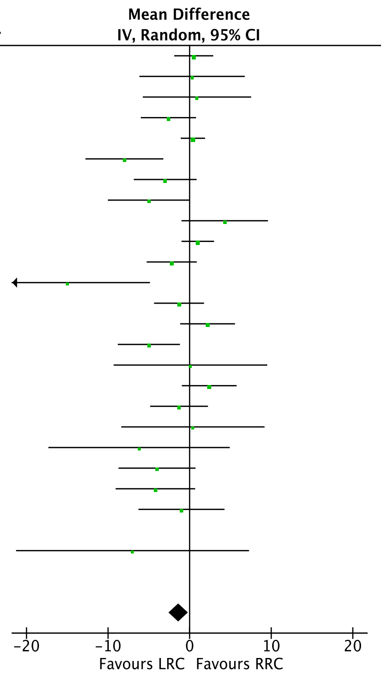
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.82$, df = 3 (P = 0.84); $I^2 = 0\%$
Test for overall effect: Z = 0.44 (P = 0.66)



Number of harvested lymph nodes

Study or Subgroup	LRC Mean	LRC SD	LRC Total	RRC Mean	RRC SD	RRC Total	Weight	Mean Difference IV, Random, 95% CI	Year
Migliore et al. 2020	19.9	8.2	170	19.4	6.8	46	7.0%	0.50 [−1.82, 2.82]	2020
Ceccarelli et al. 2020	19.8	8.8	20	19.5	11.6	20	2.6%	0.30 [−6.08, 6.68]	2020
Park et al. 2019	30.8	13.3	35	29.9	14.7	35	2.5%	0.90 [−5.67, 7.47]	2019
Solaini et al. 2019	20.4	11.9	84	23	18.9	305	5.5%	−2.60 [−5.91, 0.71]	2019
Merola et al. 2019	22.3	3.8	94	21.9	5.9	94	8.3%	0.40 [−1.02, 1.82]	2019
Yozgatli et al. 2019	33	10	61	41	12	35	3.9%	−8.00 [−12.70, −3.30]	2019
Gerbaud et al. 2019	23	7	59	26	11	42	4.9%	−3.00 [−6.78, 0.78]	2019
Blumberg et al. 2019	14	8	101	19	11	21	3.7%	−5.00 [−9.96, −0.04]	2019
Mégevand et al. 2019	23.7	17.9	50	19.4	5.9	50	3.4%	4.30 [−0.92, 9.52]	2019
Haskins et al. 2018	19	11	2405	18	9	89	7.6%	1.00 [−0.92, 2.92]	2018
Lujan et al. 2018	11.9	9.7	135	14.1	12.1	89	6.0%	−2.20 [−5.20, 0.80]	2018
Ngu et al. 2018	30.5	9.3	16	45.5	18.3	16	1.3%	−15.00 [−25.06, −4.94]	2018
Scotton et al. 2018	20.5	11.2	160	21.8	6.8	30	6.0%	−1.30 [−4.29, 1.69]	2018
Spinoglio et al. 2018	30.4	13.1	101	28.2	10.6	101	5.6%	2.20 [−1.09, 5.49]	2018
Widmar et al. 2017	29	14	163	34	17	119	5.0%	−5.00 [−8.73, −1.27]	2017
Kang et al. 2016	32.3	16.5	43	32.2	18.1	20	1.4%	0.10 [−9.24, 9.44]	2016
Cardinali et al. 2016	17.7	8.7	60	15.3	6.8	30	5.6%	2.40 [−0.88, 5.68]	2016
Trastulli et al. 2015	19	10.1	40	20.3	7.7	102	5.3%	−1.30 [−4.77, 2.17]	2015
Guerrieri et al. 2015	14.4	11.3	11	14	12.1	18	1.6%	0.40 [−8.31, 9.11]	2015
Ferrara et al. 2015	18	16.4	15	24.2	13.4	13	1.1%	−6.20 [−17.24, 4.84]	2015
Casillas et al. 2014	24	13.4	110	28	14.4	52	3.9%	−4.00 [−8.65, 0.65]	2014
Lujan et al. 2013	18.3	10.3	25	22.5	6.2	22	3.8%	−4.20 [−9.00, 0.60]	2013
Morprugo et al. 2013	25	13	48	26	13	48	3.4%	−1.00 [−6.20, 4.20]	2013
Deutsch et al. 2012	18.7	0	47	21.1	0	18		Not estimable	2012
Shin et al. 2012	18.8	6.8	6	25.8	16.4	6	0.7%	−7.00 [−21.21, 7.21]	2012
deSouza et al. 2010	16	0	135	17	0	40		Not estimable	2010
Total (95% CI)			**4194**			**1461**	**100.0%**	**−1.38 [−2.59, −0.17]**	

Heterogeneity: $Tau^2 = 4.08$; $Chi^2 = 51.31$, df = 23 (P = 0.0006); $I^2 = 55\%$
Test for overall effect: Z = 2.23 (P = 0.03)



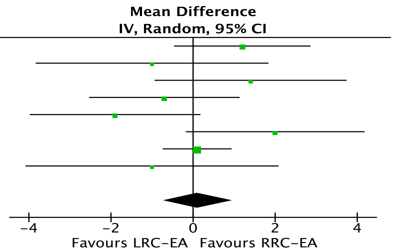
*: statistically significant difference.

5.1.11. Figure 3. Forest plots concerning the subgroup analysis LRC-EA vs RRC-EA.

Length of hospital stay

Study or Subgroup	LRC-EA Mean	LRC-EA SD	LRC-EA Total	RRC-EA Mean	RRC-EA SD	RRC-EA Total	Weight	Mean Difference IV, Random, 95% CI	Year
de'Angelis et al. 2016	8.3	4.4	50	7.1	3.1	30	15.1%	1.20 [−0.45, 2.85]	2016
Kang et al. 2016	9.9	4.9	43	10.9	5.5	20	7.1%	−1.00 [−3.82, 1.82]	2016
Ferrara et al. 2015	8.5	4.3	15	7.1	1.5	13	9.6%	1.40 [−0.92, 3.72]	2015
Casillas et al. 2014	5.5	5.1	110	6.2	5.7	52	13.4%	−0.70 [−2.52, 1.12]	2014
Shin et al. 2012	8.8	1.5	6	10.7	2.1	6	11.3%	−1.90 [−3.96, 0.16]	2012
Deutsch et al. 2012	6.3	6.4	47	4.3	2.5	18	10.6%	2.00 [−0.16, 4.16]	2012
deSouza et al. 2010	5.4	3.6	135	5.3	1.8	40	26.6%	0.10 [−0.72, 0.92]	2010
Delaney et al. 2003	2.5	0.7	2	3.5	2.1	2	6.2%	−1.00 [−4.07, 2.07]	2003
Total (95% CI)			**408**			**181**	**100.0%**	**0.11 [−0.73, 0.95]**	

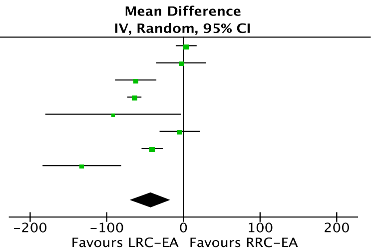
Heterogeneity: Tau² = 0.52; Chi² = 11.29, df = 7 (P = 0.13); I² = 38%
Test for overall effect: Z = 0.26 (P = 0.79)



Overall operative time *

Study or Subgroup	LRC-EA Mean	LRC-EA SD	LRC-EA Total	RRC-EA Mean	RRC-EA SD	RRC-EA Total	Weight	Mean Difference IV, Random, 95% CI	Year
de'Angelis et al. 2016	204.1	26.7	50	200.5	29.5	30	14.9%	3.60 [−9.29, 16.49]	2016
Kang et al. 2016	236.4	61.8	43	239.3	59.3	20	12.6%	−2.90 [−34.78, 28.98]	2016
Ferrara et al. 2015	167.7	35.7	15	230	34.9	13	13.4%	−62.30 [−88.50, −36.10]	2015
Casillas et al. 2014	79	26.7	110	143	25.1	52	15.2%	−64.00 [−72.45, −55.55]	2014
Shin et al. 2012	250.8	26.3	6	342.5	106.5	6	5.7%	−91.70 [−179.48, −3.92]	2012
Deutsch et al. 2012	214.4	63.2	47	219.2	39.2	18	13.5%	−4.80 [−30.38, 20.78]	2012
deSouza et al. 2010	118.1	38.1	135	158.9	36.7	40	14.9%	−40.80 [−53.86, −27.74]	2010
Delaney et al. 2003	138	31.1	2	270.5	19.1	2	9.9%	−132.50 [−183.08, −81.92]	2003
Total (95% CI)			**408**			**181**	**100.0%**	**−42.91 [−69.34, −16.49]**	

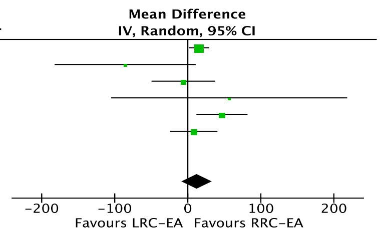
Heterogeneity: Tau² = 1177.97; Chi² = 103.85, df = 7 (P < 0.00001); I² = 93%
Test for overall effect: Z = 3.18 (P = 0.001)



Estimated blood loss

Study or Subgroup	LRC-EA Mean	LRC-EA SD	LRC-EA Total	RRC-EA Mean	RRC-EA SD	RRC-EA Total	Weight	Mean Difference IV, Random, 95% CI	Year
de'Angelis et al. 2016	164	24.8	50	148.6	31.6	30	37.3%	15.40 [2.17, 28.63]	2016
Kang et al. 2016	101.3	110.4	43	187	205.2	20	4.2%	−85.70 [−181.49, 10.09]	2016
Casillas et al. 2014	57	123.1	110	63	132.9	52	15.2%	−6.00 [−48.83, 36.83]	2014
Shin et al. 2012	241.7	188.2	6	185	70.4	6	1.6%	56.70 [−104.08, 217.48]	2012
Deutsch et al. 2012	123.2	89.7	47	76.4	48.9	18	19.9%	46.80 [12.62, 80.98]	2012
deSouza et al. 2010	73.4	151.2	135	65.1	59.6	40	21.7%	8.30 [−23.19, 39.79]	2010
Delaney et al. 2003	150	1.4	2	100	0	2		Not estimable	2003
Total (95% CI)			**393**			**168**	**100.0%**	**13.28 [−7.34, 33.90]**	

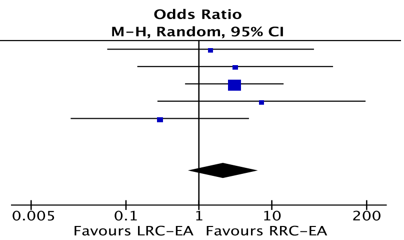
Heterogeneity: Tau² = 251.00; Chi² = 8.93, df = 5 (P = 0.11); I² = 44%
Test for overall effect: Z = 1.26 (P = 0.21)



Conversion to laparotomy

Study or Subgroup	LRC-EA Events	LRC-EA Total	RRC-EA Events	RRC-EA Total	Weight	Odds Ratio M−H, Random, 95% CI	Year
Kang et al. 2016	1	43	0	20	11.2%	1.45 [0.06, 37.09]	2016
de'Angelis et al. 2016	2	50	0	30	12.5%	3.14 [0.15, 67.73]	2016
Casillas et al. 2014	12	110	2	52	50.1%	3.06 [0.66, 14.21]	2014
Shin et al. 2012	2	6	0	6	11.1%	7.22 [0.28, 189.19]	2012
deSouza et al. 2010	1	135	1	40	15.1%	0.29 [0.02, 4.76]	2010
Delaney et al. 2003	0	2	0	2		Not estimable	2003
Total (95% CI)		**346**		**150**	**100.0%**	**2.18 [0.73, 6.45]**	
Total events	18		3				

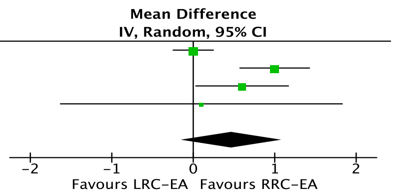
Heterogeneity: Tau² = 0.00; Chi² = 2.83, df = 4 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.40 (P = 0.16)



Time to flatus

Study or Subgroup	LRC-EA Mean	LRC-EA SD	LRC-EA Total	RRC-EA Mean	RRC-EA SD	RRC-EA Total	Weight	Mean Difference IV, Random, 95% CI	Year
de'Angelis et al. 2016	1.9	0.6	50	1.9	0.5	30	33.3%	0.00 [−0.24, 0.24]	2016
Kang et al. 2016	3.1	0.8	43	2.1	0.8	20	30.2%	1.00 [0.58, 1.42]	2016
Deutsch et al. 2012	3.6	1.5	47	3	0.8	18	27.1%	0.60 [0.03, 1.17]	2012
Shin et al. 2012	3.6	2.1	6	3.5	0.5	6	9.4%	0.10 [−1.63, 1.83]	2012
Total (95% CI)			**146**			**74**	**100.0%**	**0.47 [−0.14, 1.09]**	

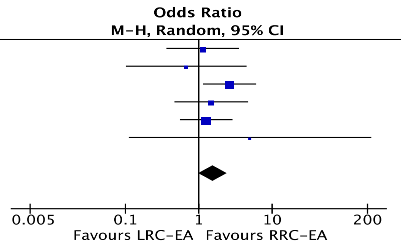
Heterogeneity: Tau² = 0.28; Chi² = 17.36, df = 3 (P = 0.0006); I² = 83%
Test for overall effect: Z = 1.51 (P = 0.13)



Overall postoperative complications

Study or Subgroup	LRC-EA Events	LRC-EA Total	RRC-EA Events	RRC-EA Total	Weight	Odds Ratio M−H, Random, 95% CI	Year
de'Angelis et al. 2016	11	50	6	30	16.1%	1.13 [0.37, 3.45]	2016
Kang et al. 2016	3	43	2	20	5.7%	0.68 [0.10, 4.40]	2016
Casillas et al. 2014	39	110	9	52	30.1%	2.62 [1.16, 5.95]	2014
Deutsch et al. 2012	20	47	6	18	15.6%	1.48 [0.47, 4.62]	2012
deSouza et al. 2010	40	135	10	40	31.0%	1.26 [0.56, 2.83]	2010
Delaney et al. 2003	1	2	0	2	1.4%	5.00 [0.11, 220.62]	2003
Total (95% CI)		**387**		**162**	**100.0%**	**1.56 [1.00, 2.44]**	
Total events	114		33				

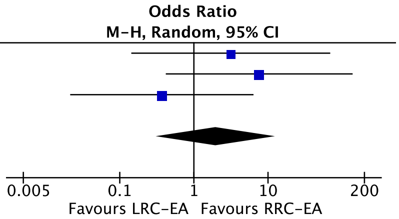
Heterogeneity: Tau² = 0.00; Chi² = 3.29, df = 5 (P = 0.66); I² = 0%
Test for overall effect: Z = 1.94 (P = 0.05)



Anastomotic fistula

Study or Subgroup	LRC-EA Events	LRC-EA Total	RRC-EA Events	RRC-EA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis et al. 2016	2	50	0	30	30.7%	3.14 [0.15, 67.73]	2016
Casillas et al. 2014	7	110	0	52	34.1%	7.61 [0.43, 135.80]	2014
Deutsch et al. 2012	1	47	1	18	35.2%	0.37 [0.02, 6.24]	2012
Total (95% CI)		**207**		**100**	**100.0%**	**2.00 [0.31, 12.77]**	
Total events	10		1				

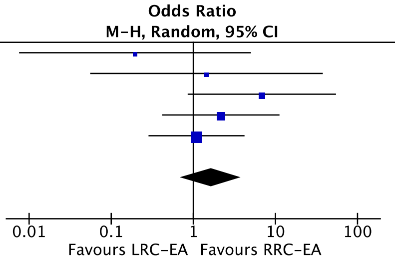
Heterogeneity: Tau² = 0.46; Chi² = 2.41, df = 2 (P = 0.30); I² = 17%
Test for overall effect: Z = 0.73 (P = 0.46)



Ileus

Study or Subgroup	LRC-EA Events	LRC-EA Total	RRC-EA Events	RRC-EA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis et al. 2016	0	50	1	30	7.1%	0.19 [0.01, 4.94]	2016
Kang et al. 2016	1	43	0	20	7.1%	1.45 [0.06, 37.09]	2016
Casillas et al. 2014	13	110	1	52	17.4%	6.84 [0.87, 53.74]	2014
Deutsch et al. 2012	10	47	2	18	27.6%	2.16 [0.42, 11.01]	2012
deSouza et al. 2010	11	135	3	40	40.8%	1.09 [0.29, 4.13]	2010
Total (95% CI)		**385**		**160**	**100.0%**	**1.64 [0.69, 3.89]**	
Total events	35		7				

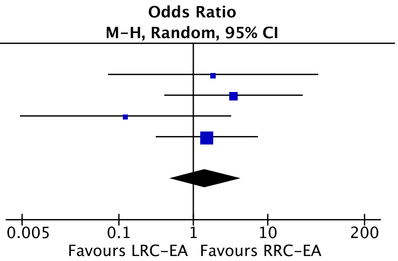
Heterogeneity: Tau² = 0.02; Chi² = 4.07, df = 4 (P = 0.40); I² = 2%
Test for overall effect: Z = 1.11 (P = 0.27)



Surgical site infection

Study or Subgroup	LRC-EA Events	LRC-EA Total	RRC-EA Events	RRC-EA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Kang et al. 2016	0	43	0	20		Not estimable	2016
de'Angelis et al. 2016	1	50	0	30	11.6%	1.85 [0.07, 46.83]	2016
Casillas et al. 2014	7	110	1	52	27.0%	3.47 [0.42, 28.93]	2014
Deutsch et al. 2012	0	47	1	18	11.5%	0.12 [0.00, 3.16]	2012
deSouza et al. 2010	10	135	2	40	49.9%	1.52 [0.32, 7.24]	2010
Total (95% CI)		**385**		**160**	**100.0%**	**1.45 [0.48, 4.38]**	
Total events	18		4				

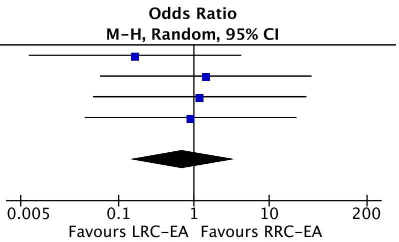
Heterogeneity: Tau² = 0.00; Chi² = 2.89, df = 3 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.66 (P = 0.51)



Mortality

Study or Subgroup	LRC-EA Events	LRC-EA Total	RRC-EA Events	RRC-EA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis et al. 2016	0	59	1	30	25.0%	0.17 [0.01, 4.18]	2016
Casillas et al. 2014	1	110	0	52	25.2%	1.44 [0.06, 35.91]	2014
Deutsch et al. 2012	1	47	0	18	24.7%	1.19 [0.05, 30.65]	2012
deSouza et al. 2010	1	135	0	40	25.1%	0.90 [0.04, 22.61]	2010
Total (95% CI)		**351**		**140**	**100.0%**	**0.71 [0.14, 3.58]**	
Total events	3		1				

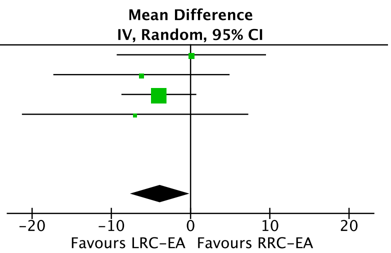
Heterogeneity: Tau² = 0.00; Chi² = 1.09, df = 3 (P = 0.78); I² = 0%
Test for overall effect: Z = 0.41 (P = 0.68)



Number of harvested lymph nodes

Study or Subgroup	LRC-EA Mean	LRC-EA SD	LRC-EA Total	RRC-EA Mean	RRC-EA SD	RRC-EA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kang et al. 2016	32.3	16.5	43	32.2	18.1	20	16.2%	0.10 [−9.24, 9.44]	2016
Ferrara et al. 2015	18	16.4	15	24.2	13.4	13	11.6%	−6.20 [−17.24, 4.84]	2015
Casillas et al. 2014	24	13.4	110	28	14.4	52	65.3%	−4.00 [−8.65, 0.65]	2014
Shin et al. 2012	18.8	6.8	6	25.8	16.4	6	7.0%	−7.00 [−21.21, 7.21]	2012
Deutsch et al. 2012	18.7	0	47	21.1	0	18		Not estimable	2012
deSouza et al. 2010	16	0	135	17	0	40		Not estimable	2010
Total (95% CI)			**356**			**149**	**100.0%**	**−3.80 [−7.56, −0.05]**	

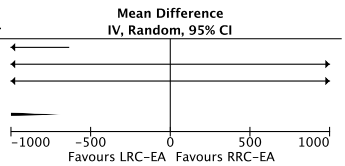
Heterogeneity: Tau² = 0.00; Chi² = 1.05, df = 3 (P = 0.79); I² = 0%
Test for overall effect: Z = 1.98 (P = 0.05)



Total costs *

Study or Subgroup	LRC-EA Mean	LRC-EA SD	LRC-EA Total	RRC-EA Mean	RRC-EA SD	RRC-EA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kang et al. 2016	9,911	3,064	43	12,492	3,911	20	57.4%	−2581.00 [−4524.36, −637.64]	2016
deSouza et al. 2010	15,228.7	18,361.7	135	16,987.5	7,424.6	40	14.6%	−1758.80 [−5617.26, 2099.66]	2010
Delaney et al. 2003	2,287	83.4	2	3,783	2,005.3	2	28.0%	−1496.00 [−4277.56, 1285.56]	2003
Total (95% CI)			**180**			**62**	**100.0%**	**−2157.19 [−3629.69, −684.70]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 2 (P = 0.80); I² = 0%
Test for overall effect: Z = 2.87 (P = 0.004)



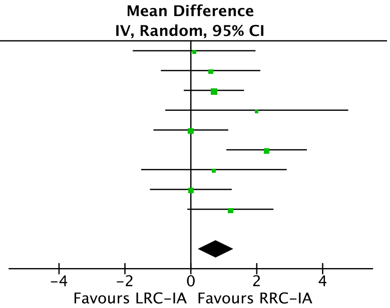
*: statistically significant difference.

5.1.12. Figure 4. Forest plots concerning the subgroup analysis LRC-IA vs RRC-IA.

Length of hospital stay *

Study or Subgroup	LRC-IA Mean	LRC-IA SD	LRC-IA Total	RRC-IA Mean	RRC-IA SD	RRC-IA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Migliore et al. 2020	5.3	9.7	170	5.2	3.9	46	7.2%	0.10 [−1.74, 1.94]	2020
Ceccarelli et al. 2020	7.8	3	20	7.2	1.6	20	10.1%	0.60 [−0.89, 2.09]	2020
Solaini et al. 2019	8	3.9	84	7.3	2.9	305	19.2%	0.70 [−0.20, 1.60]	2019
Blumberg et al. 2019	5	1.7	101	3	6.4	21	3.6%	2.00 [−0.76, 4.76]	2019
Merola et al. 2019	4	3.9	94	4	3.9	94	15.0%	0.00 [−1.11, 1.11]	2019
Mégevand et al. 2019	8	3.9	50	5.7	1.9	50	13.6%	2.30 [1.10, 3.50]	2019
Ngu et al. 2018	6.2	3.4	16	5.5	2.9	16	5.4%	0.70 [−1.49, 2.89]	2018
Spinoglio et al. 2018	7.9	3.5	101	7.9	5.2	101	13.3%	0.00 [−1.22, 1.22]	2018
Trastulli et al. 2015	6.1	2.8	40	4.9	4.9	102	12.4%	1.20 [−0.09, 2.49]	2015
Total (95% CI)			**676**			**755**	**100.0%**	**0.78 [0.23, 1.32]**	

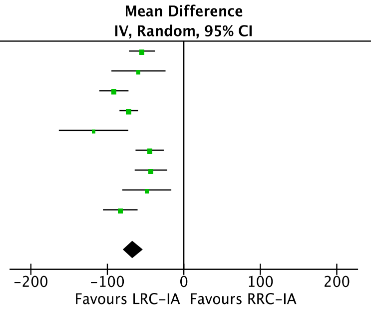
Heterogeneity: Tau² = 0.20; Chi² = 11.35, df = 8 (P = 0.18); I² = 30%
Test for overall effect: Z = 2.76 (P = 0.006)



Overall operative time *

Study or Subgroup	LRC-IA Mean	LRC-IA SD	LRC-IA Total	RRC-IA Mean	RRC-IA SD	RRC-IA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Migliore et al. 2020	187.6	56.6	170	242.4	47.5	46	13.4%	−54.80 [−70.95, −38.65]	2020
Ceccarelli et al. 2020	165.9	30.2	20	225.2	73	20	7.9%	−59.30 [−93.92, −24.68]	2020
Solaini et al. 2019	163.5	69.5	84	254.9	95	305	12.7%	−91.40 [−109.69, −73.11]	2019
Merola et al. 2019	135.5	33.9	94	207.5	44.9	94	14.9%	−72.00 [−83.37, −60.63]	2019
Blumberg et al. 2019	212	66	101	330	100	21	5.8%	−118.00 [−162.66, −73.34]	2019
Mégevand et al. 2019	160	39.9	50	204.7	49.8	50	12.9%	−44.70 [−62.39, −27.01]	2019
Spinoglio et al. 2018	236	68	101	279	80	101	12.0%	−43.00 [−63.48, −22.52]	2018
Ngu et al. 2018	175.8	43.8	16	224.2	46.4	16	8.7%	−48.40 [−79.67, −17.13]	2018
Trastulli et al. 2015	204.3	51.9	40	287.4	76.4	102	11.5%	−83.10 [−104.97, −61.23]	2015
Total (95% CI)			**676**			**755**	**100.0%**	**−66.05 [−79.41, −52.69]**	

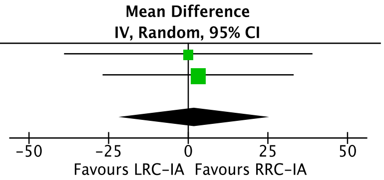
Heterogeneity: Tau² = 277.86; Chi² = 29.65, df = 8 (P = 0.0002); I² = 73%
Test for overall effect: Z = 9.69 (P < 0.00001)



Estimated blood loss

Study or Subgroup	LRC-IA Mean	LRC-IA SD	LRC-IA Total	RRC-IA Mean	RRC-IA SD	RRC-IA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Blumberg et al. 2019	100	153	101	100	58	21	37.1%	0.00 [−38.80, 38.80]	2019
Trastulli et al. 2015	44.2	88.1	40	41.1	61.6	102	62.9%	3.10 [−26.70, 32.90]	2015
Total (95% CI)			**141**			**123**	**100.0%**	**1.95 [−21.69, 25.59]**	

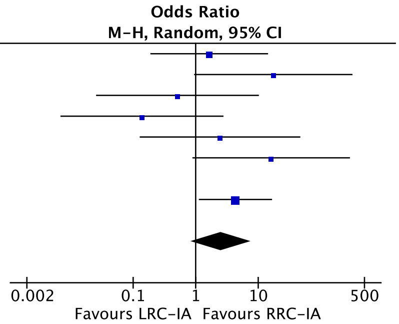
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.16 (P = 0.87)



Conversion to laparotomy

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	6	170	1	46	17.0%	1.65 [0.19, 14.03]	2020
Mégevand et al. 2019	7	50	0	50	11.2%	17.41 [0.97, 313.73]	2019
Solaini et al. 2019	0	84	3	305	10.7%	0.51 [0.03, 10.00]	2019
Merola et al. 2019	0	94	3	94	10.7%	0.14 [0.01, 2.72]	2019
Blumberg et al. 2019	5	101	0	21	11.0%	2.45 [0.13, 46.01]	2019
Spinoglio et al. 2018	7	101	0	101	11.3%	16.11 [0.91, 285.97]	2018
Ngu et al. 2018	0	16	0	16		Not estimable	2018
Trastulli et al. 2015	6	40	4	102	28.0%	4.32 [1.15, 16.25]	2015
Total (95% CI)		**656**		**735**	**100.0%**	**2.57 [0.85, 7.81]**	
Total events	31		11				

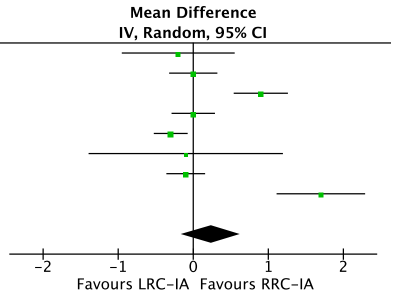
Heterogeneity: Tau² = 0.69; Chi² = 8.79, df = 6 (P = 0.19); I² = 32%
Test for overall effect: Z = 1.66 (P = 0.10)



Time to flatus

Study or Subgroup	LRC-IA Mean	LRC-IA SD	LRC-IA Total	RRC-IA Mean	RRC-IA SD	RRC-IA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Ceccarelli et al. 2020	3	1.2	20	3.2	1.2	20	10.0%	−0.20 [−0.94, 0.54]	2020
Migliore et al. 2020	1.6	0.8	170	1.6	1	46	14.3%	0.00 [−0.31, 0.31]	2020
Mégevand et al. 2019	2.5	0.9	50	1.6	0.9	50	13.9%	0.90 [0.55, 1.25]	2019
Merola et al. 2019	2.2	1.2	94	2.2	0.7	94	14.5%	0.00 [−0.28, 0.28]	2019
Solaini et al. 2019	2.3	0.9	84	2.6	0.9	305	15.0%	−0.30 [−0.52, −0.08]	2019
Ngu et al. 2018	2.8	1.7	16	2.9	2	16	5.9%	−0.10 [−1.39, 1.19]	2018
Spinoglio et al. 2018	1.8	0.8	101	1.9	1	101	14.8%	−0.10 [−0.35, 0.15]	2018
Trastulli et al. 2015	4	1.5	40	2.3	1.8	102	11.7%	1.70 [1.12, 2.28]	2015
Total (95% CI)			**575**			**734**	**100.0%**	**0.24 [−0.15, 0.63]**	

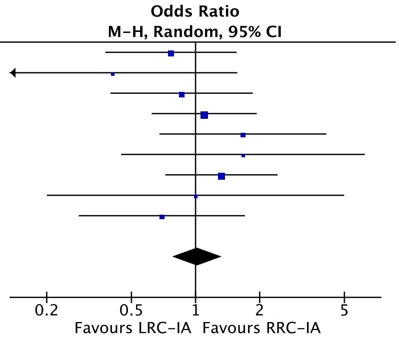
Heterogeneity: Tau² = 0.26; Chi² = 65.28, df = 7 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.19 (P = 0.23)



Overall postoperative complications

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	46	170	15	46	14.7%	0.77 [0.38, 1.55]	2020
Ceccarelli et al. 2020	5	20	9	20	4.0%	0.41 [0.11, 1.56]	2020
Merola et al. 2019	15	94	17	94	12.5%	0.86 [0.40, 1.84]	2019
Solaini et al. 2019	21	84	71	305	23.1%	1.10 [0.63, 1.92]	2019
Mégevand et al. 2019	16	50	11	50	9.1%	1.67 [0.68, 4.08]	2019
Blumberg et al. 2019	22	101	3	21	4.2%	1.67 [0.45, 6.20]	2019
Spinoglio et al. 2018	34	101	28	101	20.2%	1.32 [0.73, 2.41]	2018
Ngu et al. 2018	12	16	12	16	2.8%	1.00 [0.20, 4.95]	2018
Trastulli et al. 2015	8	40	27	102	9.2%	0.69 [0.28, 1.69]	2015
Total (95% CI)		**676**		**755**	**100.0%**	**1.02 [0.78, 1.33]**	
Total events	179		193				

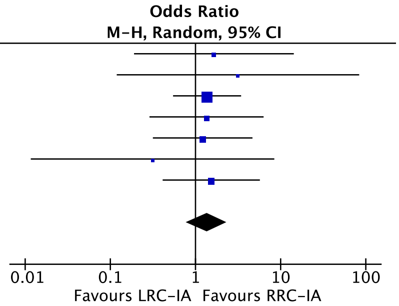
Heterogeneity: Tau² = 0.00; Chi² = 5.83, df = 8 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.14 (P = 0.89)



Severe postoperative complications

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Migliore et al. 2020	6	170	1	46	6.8%	1.65 [0.19, 14.03]	2020
Ceccarelli et al. 2020	1	20	0	20	2.9%	3.15 [0.12, 82.16]	2020
Solaini et al. 2019	7	84	19	305	38.1%	1.37 [0.56, 3.37]	2019
Merola et al. 2019	4	94	3	94	13.3%	1.35 [0.29, 6.20]	2019
Blumberg et al. 2019	17	101	3	21	17.6%	1.21 [0.32, 4.59]	2019
Ngu et al. 2018	0	16	1	16	2.9%	0.31 [0.01, 8.28]	2018
Spinoglio et al. 2018	6	100	4	100	18.4%	1.53 [0.42, 5.60]	2018
Total (95% CI)		**585**		**602**	**100.0%**	**1.36 [0.78, 2.37]**	
Total events	41		31				

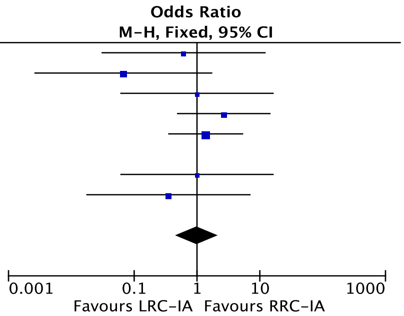
Heterogeneity: Tau² = 0.00; Chi² = 1.12, df = 6 (P = 0.98); I² = 0%
Test for overall effect: Z = 1.08 (P = 0.28)



Anastomotic fistula

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Milone et al. 2020	0	40	3	176	10.1%	0.61 [0.03, 12.08]	2020
Blumberg et al. 2019	0	101	1	21	19.1%	0.07 [0.00, 1.71]	2019
Merola et al. 2019	1	94	1	94	7.7%	1.00 [0.06, 16.23]	2019
Mégevand et al. 2019	5	50	2	50	14.0%	2.67 [0.49, 14.44]	2019
Solaini et al. 2019	3	84	8	305	26.0%	1.38 [0.36, 5.30]	2019
Ngu et al. 2018	0	16	0	16		Not estimable	2018
Spinoglio et al. 2018	1	101	1	101	7.7%	1.00 [0.06, 16.21]	2018
Trastulli et al. 2015	0	40	3	102	15.3%	0.35 [0.02, 6.95]	2015
Total (95% CI)		**526**		**865**	**100.0%**	**1.01 [0.47, 2.19]**	
Total events	10		19				

Heterogeneity: Chi² = 4.75, df = 6 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.97)



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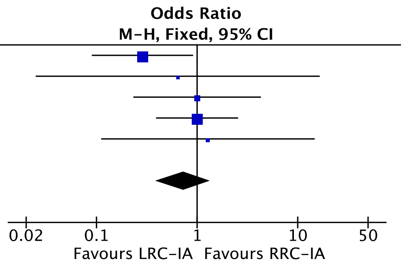
Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Migliore et al. 2020	7	170	6	46	38.3%	0.29 [0.09, 0.90]	2020
Blumberg et al. 2019	1	101	0	21	3.4%	0.64 [0.03, 16.29]	2019
Mégevand et al. 2019	4	50	4	50	15.6%	1.00 [0.24, 4.24]	2019
Spinoglio et al. 2018	10	101	10	101	38.1%	1.00 [0.40, 2.52]	2018
Trastulli et al. 2015	1	40	2	102	4.6%	1.28 [0.11, 14.55]	2015
Total (95% CI)		**462**		**320**	**100.0%**	**0.73 [0.39, 1.34]**	
Total events	23		22				

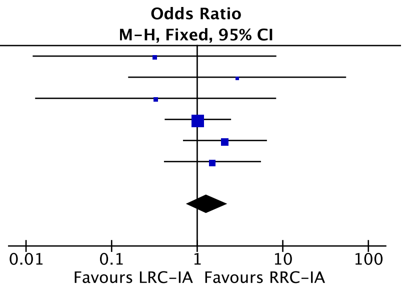
Heterogeneity: Chi² = 3.41, df = 4 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.02 (P = 0.31)



Surgical site infection

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Ceccarelli et al. 2020	0	20	1	20	6.8%	0.32 [0.01, 8.26]	2020
Blumberg et al. 2019	6	101	0	21	3.6%	2.93 [0.16, 53.95]	2019
Mégevand et al. 2019	0	50	1	50	6.9%	0.33 [0.01, 8.21]	2019
Solaini et al. 2019	7	84	25	305	45.7%	1.02 [0.42, 2.44]	2019
Spinoglio et al. 2018	10	101	5	101	20.8%	2.11 [0.69, 6.41]	2018
Trastulli et al. 2015	4	40	7	102	16.4%	1.51 [0.42, 5.46]	2015
Total (95% CI)		**396**		**599**	**100.0%**	**1.30 [0.75, 2.25]**	
Total events	27		39				

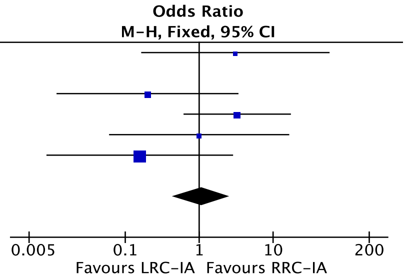
Heterogeneity: Chi² = 2.80, df = 5 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.93 (P = 0.35)



Reoperation

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Migliore et al. 2020	5	170	0	46	8.1%	3.09 [0.17, 56.92]	2020
Merola et al. 2019	0	94	0	94		Not estimable	2019
Blumberg et al. 2019	1	101	1	21	17.5%	0.20 [0.01, 3.33]	2019
Mégevand et al. 2019	6	50	2	50	18.8%	3.27 [0.63, 17.07]	2019
Spinoglio et al. 2018	1	101	1	101	10.6%	1.00 [0.06, 16.21]	2018
Trastulli et al. 2015	0	40	7	102	45.0%	0.16 [0.01, 2.82]	2015
Total (95% CI)		**556**		**414**	**100.0%**	**1.08 [0.44, 2.62]**	
Total events	13		11				

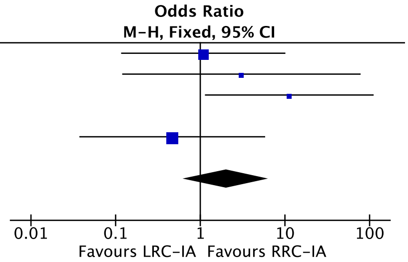
Heterogeneity: Chi² = 5.33, df = 4 (P = 0.26); I² = 25%
Test for overall effect: Z = 0.16 (P = 0.87)



Readmission

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Migliore et al. 2020	4	170	1	46	35.6%	1.08 [0.12, 9.94]	2020
Mégevand et al. 2019	1	50	0	50	11.2%	3.06 [0.12, 76.95]	2019
Solaini et al. 2019	3	84	1	305	9.7%	11.26 [1.16, 109.68]	2019
Merola et al. 2019	0	94	0	94		Not estimable	2019
Ngu et al. 2018	1	16	2	16	43.5%	0.47 [0.04, 5.73]	2018
Total (95% CI)		**414**		**511**	**100.0%**	**2.02 [0.64, 6.38]**	
Total events	9		4				

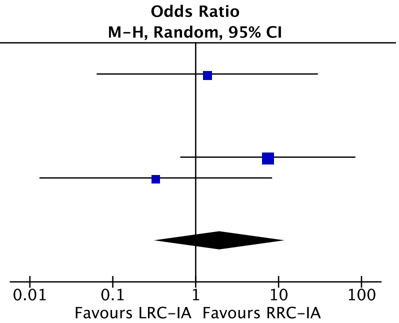
Heterogeneity: Chi² = 3.87, df = 3 (P = 0.28); I² = 22%
Test for overall effect: Z = 1.20 (P = 0.23)



Mortality

Study or Subgroup	LRC-IA Events	LRC-IA Total	RRC-IA Events	RRC-IA Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Ceccarelli et al. 2020	0	20	0	20		Not estimable	2020
Migliore et al. 2020	2	170	0	46	29.6%	1.38 [0.07, 29.24]	2020
Blumberg et al. 2019	0	101	0	21		Not estimable	2019
Merola et al. 2019	0	94	0	94		Not estimable	2019
Mégevand et al. 2019	0	50	0	50		Not estimable	2019
Solaini et al. 2019	2	84	1	305	43.2%	7.41 [0.66, 82.79]	2019
Spinoglio et al. 2018	0	101	1	101	27.2%	0.33 [0.01, 8.20]	2018
Trastulli et al. 2015	0	40	0	102		Not estimable	2015
Total (95% CI)		**660**		**739**	**100.0%**	**1.93 [0.31, 11.88]**	
Total events	4		2				

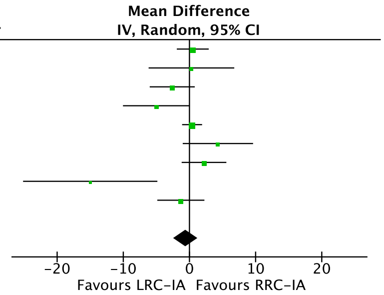
Heterogeneity: Tau² = 0.47; Chi² = 2.44, df = 2 (P = 0.30); I² = 18%
Test for overall effect: Z = 0.71 (P = 0.48)



Number of harvested lymph nodes

Study or Subgroup	LRC-IA Mean	LRC-IA SD	LRC-IA Total	RRC-IA Mean	RRC-IA SD	RRC-IA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Migliore et al. 2020	19.9	8.2	170	19.4	6.8	46	16.4%	0.50 [-1.82, 2.82]	2020
Ceccarelli et al. 2020	19.8	8.8	20	19.5	11.6	20	6.1%	0.30 [-6.08, 6.68]	2020
Solaini et al. 2019	20.4	11.9	84	23	18.9	305	12.9%	-2.60 [-5.91, 0.71]	2019
Blumberg et al. 2019	14	8	101	19	11	21	8.6%	-5.00 [-9.96, -0.04]	2019
Merola et al. 2019	22.3	3.8	94	21.9	5.9	94	19.5%	0.40 [-1.02, 1.82]	2019
Mégevand et al. 2019	23.7	17.9	50	19.4	5.9	50	8.0%	4.30 [-0.92, 9.52]	2019
Spinoglio et al. 2018	30.4	13.1	101	28.2	10.6	101	13.0%	2.20 [-1.09, 5.49]	2018
Ngu et al. 2018	30.5	9.3	16	45.5	18.3	16	3.0%	-15.00 [-25.06, -4.94]	2018
Trastulli et al. 2015	19	10.1	40	20.3	7.7	102	12.5%	-1.30 [-4.77, 2.17]	2015
Total (95% CI)			**676**			**755**	**100.0%**	**-0.56 [-2.42, 1.30]**	

Heterogeneity: Tau² = 4.11; Chi² = 20.17, df = 8 (P = 0.010); I² = 60%
Test for overall effect: Z = 0.59 (P = 0.55)



*: statistically significant difference.

5.2. Monocentric prospective clinical study

5.2.1. Table 5. Demographic and clinical characteristics of patients undergoing RRC or LRC with IA for right colon cancer at Henri Mondor University Hospital.

Variables	RRC (n = 40)	LRC (n = 24)	*p*
Gender (F/M) [n]	23/17	12/12	0.720
Age (years) [mean (SD)]	67.8 (7.3)	66.1 (9.8)	0.678
BMI (kg/m^2) [mean (SD)]	23.8 (5.9)	22.9 (4.4)	0.673
Pre-operative Hemoglobin (g/L) [mean (SD)]	13.2 (1.9)	13.4 (1.8)	0.910
Pre-operative Leukocytes (10^9/L) [mean (SD)]	7.67 (2.43)	7.88 (2.24)	0.787
Albumin Serum Level (g/L) [mean (SD)]	38.76 (5.6)	38.23 (6.3)	0.535
Weight Loss (> 10%) [n (%)]	5 (14.7)	3 (12.5)	0.567
Kidney Failure [n (%)]	1 (2.9)	1(4.2)	1
Diabetes [n (%)]	8 (20)	5 (20.8)	0.688
Cardiovascular and Pulmonary Diseases [n (%)]	20 (58.8)	16 (66.7)	0.879
ASA Score [n (%)] I II III IV	 10 (25.0) 23 (57.5) 6 (15) 1 (2.5)	 6 (25.0) 14 (58.3) 4 (16.7) 0 (0)	0.980
TNM AJCC Stage [n (%)] 0 I II III	 0 (0) 12(30) 20(50) 8 (20)	 0 6(25.0) 14(58.3) 4(16.7)	0.358
Adjuvant chemotherapy [n (%)]	20 (50)	18 (75.0)	1

Bold: significant statistical difference.

5.2.2. Table 6. Operative outcomes of patients undergoing RRC or LRC with IA for right colon cancer at Henri Mondor University Hospital.

Variables	RRC (n = 40)	LRC (n = 24)	*p*
Operative time (min) [mean (SD; range)]	223.0 (40.21; 150-365)	187.1 (45.3; 110-280)	**0.03**
Conversion to laparotomy [n (%)]	0	0	NA
Operative blood loss (ml) [mean (SD)]	115 (35.9)	110 (40.5)	0.611
Number of transfused patients [n (%)]	1 (2.9)	0	1
Time to flatus (days) [mean (SD; range)]	1.5 (0.67; 1-4)	1.9 (0.87; 1-4)	0.08
Return to regular diet (days) [mean (SD; range)]	2.5 (0.59; 2-5)	2.7 (0.91; 2-6)	0.575
Post-operative complications [n (%)] - ileus - anastomotic leakage - intra-abdominal abscess - wound infection - pancreatic fistula - intestinal bleeding	 1 (2.9) 1 (2.9) 2 (5.9) 2 (5.9) 0 (0) 1 (2.9)	 2 (8.3) 0 (0) 0 (0) 4 (16.7) 0 (0) 0 (0)	0.816
Dindo-Clavien classification [n (%)] - I - II - ≥ III	5 (14.7) 1(2.9)	4 (16.7) 2 (8.3)	0.567
Mortality within 90 days [n]	0	0	NA
Length of hospital stay (days) [mean (SD; range)]	5.5 (3.5; 3-14)	6.2 (2.3; 4-14)	0.579
Re-admission within 60 days [n (%)]	0	0	NA
Bold: significant statistical difference.			

5.2.3. Table 7. Pathologic findings of patients undergoing RRC or LRC with IA for right colon cancer at Henri Mondor University Hospital.

Variables	RRC (n = 40)	LRC (n = 24)	*p*
R0 resection [n (%)]	40 (100)	24 (100)	1
Number of lymph nodes harvested [n (%)] - < 12 lymph nodes - ≥ 12 lymph nodes	 0 (0) 40 (100)	 0 (0) 24 (100)	1
Tumor size max diameter (cm) [mean (SD; range)]	6.5 (2.0; 3-15)	5.9 (2.1; 3-14)	0.431
Adenocarcinoma [n (%)] - well differentiated - moderately differentiated - mucinous	 23 (57.5) 14 (35) 3 (7.5)	 16 (6.7) 8 (3.3) 0 (0)	0.979
Bold: significant statistical difference.			

5.3. MERCY Study (Phases I and II)

5.3.1. Table 8. MERCY Phase I: demographic and clinical characteristics of the entire study population.

Variables	MERCY Study Entire Population (n = 1870)
Male [n (%)]	935 (50.0)
Age [mean (SD)]	72.3 (11.2)
Age >75 [n (%)]	827 (44.2)
BMI [mean (SD)]	26.2 (4.4)
Obesity [n (%)]	304 (16.3)
ASA [n (%)] - I - II - III - IV	 153 (8.2) 897 (48) 771 (41.2) 49 (2.6)
Cardiovascular diseases [n (%)]	1032 (55.2)
Pulmonary diseases [n (%)]	275 (14.7)
Kidney diseases [n (%)]	176 (9.4)
Neurocognitive disorders [n (%)]	150 (8)
Diabetes [n (%)]	435 (23.3)
Comorbidity > 1 [n (%)]	905 (48.4)
Charlson score [mean (SD)]	5.4 (2.4)
Previous abdominal surgery [n (%)]	773 (41.3)
Tumor location [n (%)] - cecum - ascending colon - hepatic flexure	 679 (36.3) 792 (42.4) 399 (21.3)
Surgical approach [n (%)] - laparoscopic - robotic	 1630 (87.2) 240 (12.8)
Type of anastomosis [n (%)] - extracorporeal anastomosis (EA) - intracorporeal anastomosis (IA)	 1274 (68.1) 596 (31.9)
AJCC stage [n(%)]* - 0 - 1 - 2 - 3	 34 (1.8) 543 (29) 716 (38.3) 552 (29.5)
*missing data: 25 (1.3%); bold: significant statistical difference.	

5.3.2. Table 9. MERCY Phase I: demographic and clinical characteristics of included patients, divided into EA and IA groups.

Variables	EA group (n = 671)	IA group (n = 417)	*p**
Male [n (%)]	329 (49)	205 (49.2)	0.977
Age [mean (SD)]	73.5 (10.3)	72.1 (10.6)	0.049
Age >75 ans [n (%)]	345 (48.6)	184 (44.1)	0.610
BMI [mean (SD)]	26.1 (4.3)	26.6 (4.3)	0.100
Obesity [n (%)]	116 (17.3)	84 (20.1)	0.955
ASA [n (%)] - I + II - III + IV	 323 (48.1) 348 (51.9)	 221 (53) 196 (47)	0.676
Cardiovascular diseases [n (%)]	372 (55.4)	224 (53.7)	0.779
Pulmonary diseases [n (%)]	114 (17)	58 (13.9)	0.779
Kidney diseases [n (%)]	53 (7.9)	39 (9.4)	0.805
Neurocognitive disorders [n (%)]	64 (9.5)	23 (5.5)	0.779
Diabetes [n (%)]	132 (19.7)	106 (25.4)	0.610
Comorbidity > 1 [n (%)]	310 (46.2)	213 (51.1)	0.600
Charlson score [mean (SD)]	5.7 (2.5)	4.7 (2.2)	**< 0.001**
Previous abdominal surgery [n (%)]	278 (41.4)	176 (42.2)	0.955
Tumor location [n (%)] - cecum or ascending colon - hepatic flexure	 540 (80.5) 131 (19.5)	 331 (79.4) 86 (20.6)	0.890
Surgical approach [n (%)] - laparoscopic - robotic	 659 (98.2) 12 (1.8)	 299 (71.7) 118 (28.3)	**< 0.001**

*p-values adjusted for multiple testing using Benjamini & Hochberg method; bold: significant statistical difference.

5.3.3. Table 10. MERCY Phase I: operative outcomes of EA and IA groups.

Variables	EA group (n = 671)	IA group (n = 417)	*p**
Operative time (min) [mean (SD)]	168.3 (52.5)	181.2 (55.3)	**< 0.001**
Intraoperative complications [n (%)]	18 (2.7)	6 (1.4)	0.995
Estimated blood loss (ml) [mean (SD)]	96.4 (94.9)	74.3 (56.2)	**< 0.001**
Use of ICG fluorescence [n (%)]	11 (1.6)	116 (27.8)	**< 0.001**
Conversion to open surgery [n (%)]	76 (11.3)	8 (1.9)	**< 0.001**
Patients with postoperative complication(s) [n (%)]	183 (27.3)	109 (26.1)	0.995
Severe postop. complications (Dindo-Clavien ≥ III) [n (%)]	49 (7.3)	33 (7.9)	0.995
Anastomotic leakage [n (%)]	31 (4.6)	16 (3.8)	0.995
Prolonged ileus [n(%)]	21 (3.1)	3 (0.7)	0.066
Surgical site infection [n (%)]	76 (11.3)	8 (1.9)	**< 0.001**
Time to flatus (days) [mean (SD)]	2.5 (1.4)	2.3 (1.2)	**0.001**
Time to regular diet (days) [mean (SD)]	4.8 (4.6)	3.5 (2.3)	**< 0.001**
Hospital stay (days) [mean (SD)]	8.8 (7)	7.9 (7.7)	0.081
Readmission [n (%)]	26 (3.9)	16 (3.8)	0.995
Mortality at 90 days [n (%)]	11 (1.6)	4 (1)	0.995
Adjuvant therapy needed [n (%)]	166 (24.7)	115 (27.6)	0.995

*p-values adjusted for multiple testing using Benjamini & Hochberg method; bold: significant statistical difference.

5.3.4. Table 11. MERCY Phase I: pathological findings of EA and IA groups.

Variables	EA group (n = 671)	IA group (n = 417)	*p**
Tumor size (cm) [mean (SD)]	4.7 (2.6)	4.4 (2)	0.086
Complete tumor resection (R0 status) [n (%)]	669 (99.7)	415 (99.5)	0.995
Lymph nodes retrieved			
- total number [mean (SD)]	22.5 (9)	23.1 (9.7)	0.337
- ≥ 12 lymph nodes [n (%)]	641 (95.5)	403 (96.6)	0.873
pT stage [n (%)]			
- 1	60 (8.9)	50 (12)	0.890
- 2	131 (19.5)	101 (24.2)	0.820
- 3	417 (62.1)	216 (51.8)	0.058
- 4	63 (9.4)	50 (12)	0.890
pN stage [n (%)]			
- 0	463 (69)	292 (70)	0.890
- 1	140 (20.9)	88 (21.1)	0.966
- 2	68 (10.1)	37 (8.9)	0.890
AJCC stage [n (%)]			
- 0	1 (0.1)	0 (0)	-
- 1	168 (25)	130 (31.2)	0.873
- 2	294 (43.8)	162 (38.8)	0.873
- 3	208 (31)	125 (30)	0.995
Perivascular invasion [n (%)]	160 (23.8)	123 (29.5)	0.873
Perineural invasion [n (%)]	143 (21.3)	81 (19.4)	0.890
Tumor grade [n (%)]			
- well differentiated	128 (19.1)	146 (35)	**0.020**
- moderately differentiated	397 (59.2)	190 (45.6)	**0.019**
- poorly differentiated	146 (21.8)	81 (19.4)	0.890

*p-values adjusted for multiple testing using Benjamini & Hochberg method; bold: significant statistical difference.

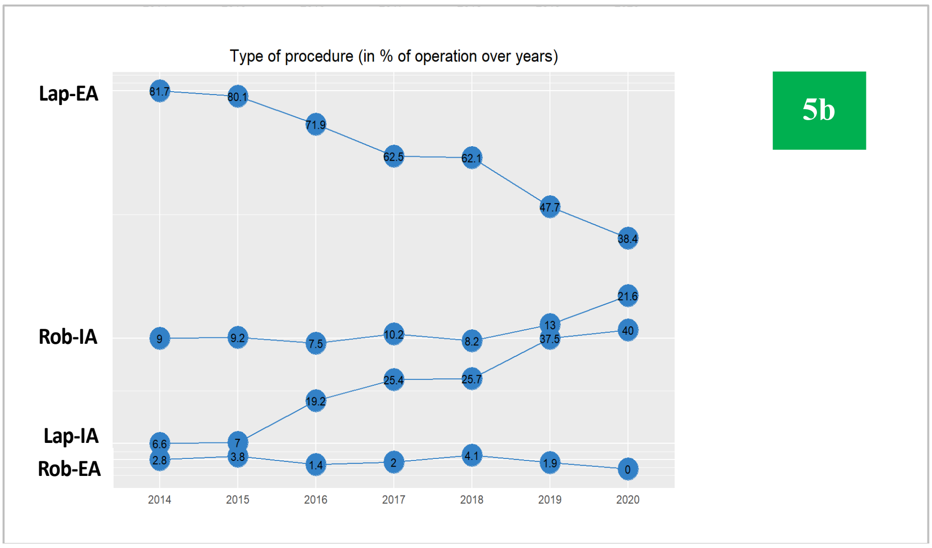
5.3.5. Table 12. MERCY Phase I: significant predictors of surgical outcomes.

	Data are expressed as coefficients (95%CI) obtained by linear mixed models					Data are expressed as OR (95%CI) obtained by logistic mixed models		
	Operative time (min)	Blood loss (mL)	Time to flatus (days)	Time to regular diet (days)	LOS (days)	Postop. cx.	SSI	Prolonged ileus
Patient-related factors								
Age	**-0.28 [-0.53; -0.03]**					**1.02 [1.01; 1.04]**		
Male	**8.93 [3.68; 14.18]**							
BMI	**1.24 [0.6; 1.87]**							
ASA III-IV		**10.11 [1.16-19.07]**	**0.28 [0.12; 0.43]**	**0.64 [0.23; 1.05]**	**1.08 [0.16; 2.01]**			
CCI		1.52 [-0.67; 3.71]			**0.31 [0.1; 0.52]**			
Comorbidity ≤ 1						**0.66 [0.49; 0.9]**		
Pulmonary diseases						**1.47 [1.02; 2.12]**		
Surgery-related factors								
Robotic approach	**13.48 [4.84; 22.12]**	**-16.94 [-30.97; -2.92]**						
Intracorporeal anastomosis		-4.79 [-16.11; 6.52]		**-1.11 [-1.63; -0.6]**			**0.03 [0.01; 0.08]**	
Conversion to open surgery		**50.19 [34.67; 65.71]**	**0.45 [0.16; 0.73]**		**3.25 [1.65; 4.85]**	**1.99 [1.24; 3.18]**		**4.11 [1.53; 11.02]**

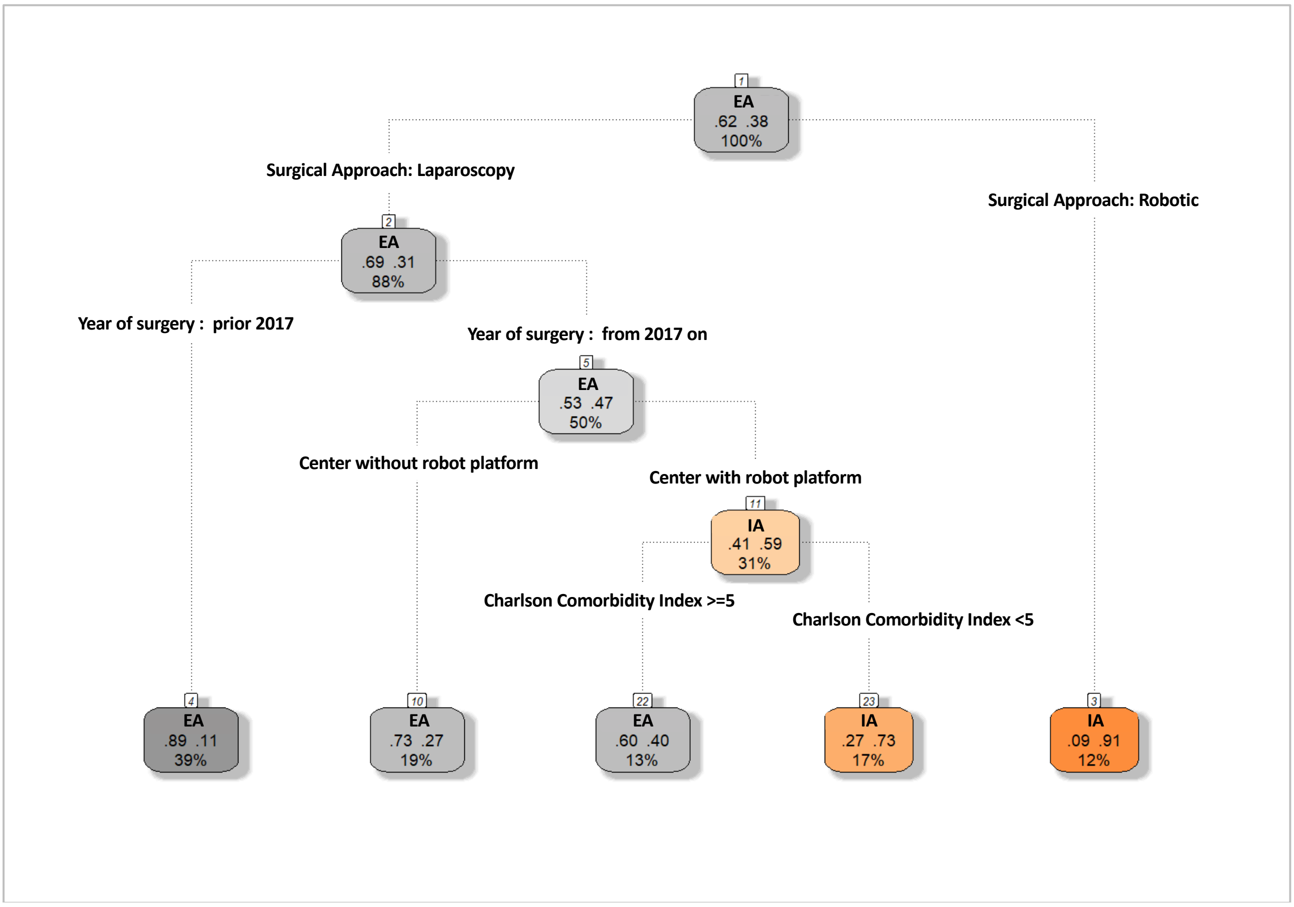
LOS: length of hospital stay; cx: complications; SSI: surgical site infection; CCI: Charlson Comorbidity Index; bold: significant statistical difference.

5.3.6. Figure 5a. Surgical trends in minimally invasive right colectomy over time: fashioning EA or IA.

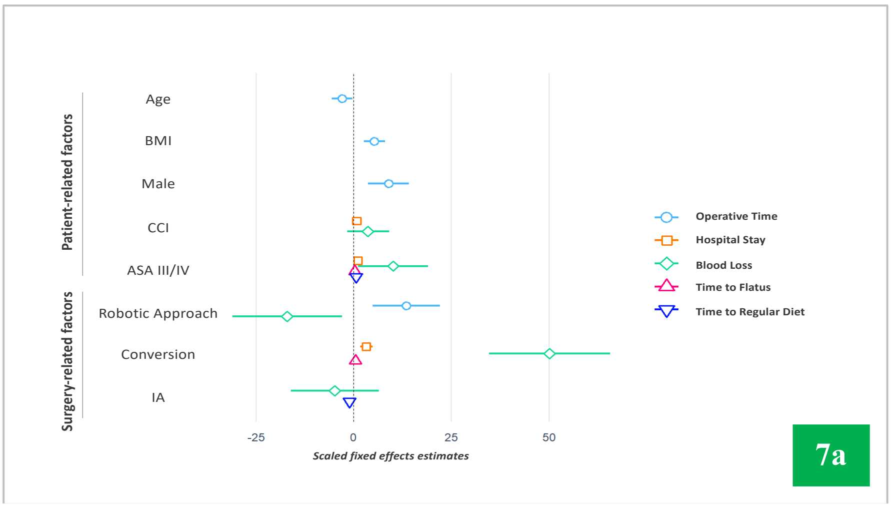
5.3.7. Figure 5b. Surgical trends in minimally invasive right colectomy over time: use of robotic and laparoscopic approach with EA or IA.



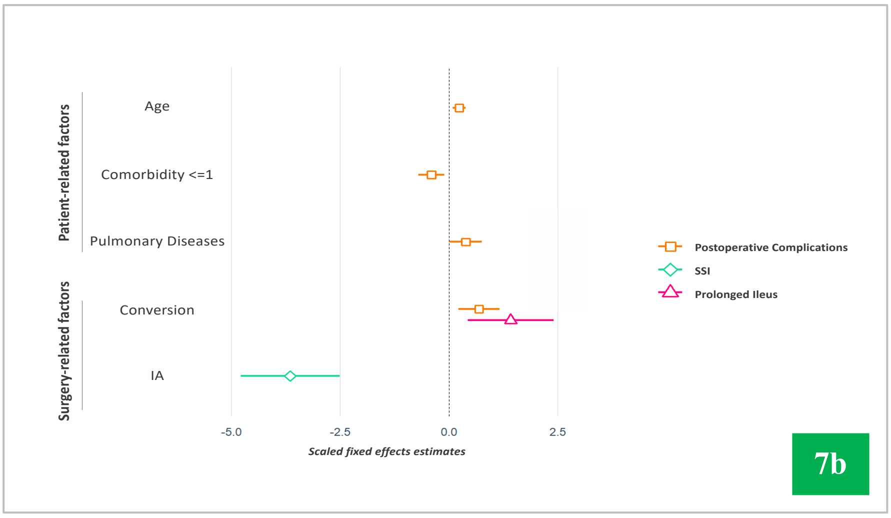
5.3.8. Figure 6. Classification tree describing the factors influencing the choice between EA and IA during minimally invasive right colectomy.



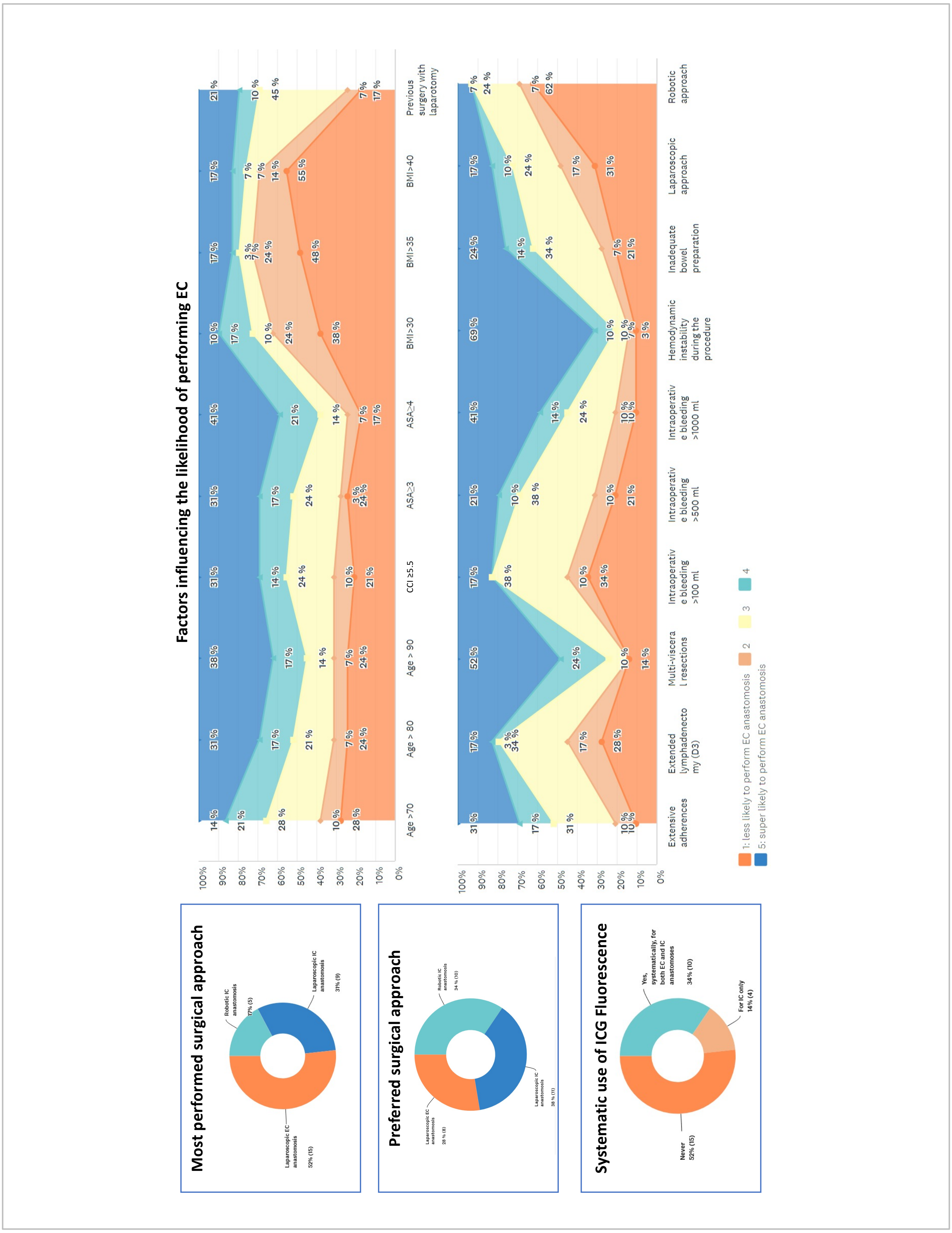
5.3.9. Figure 7a. Forest plots of the predictors of surgical outcomes: linear mixed models for continuous outcomes.



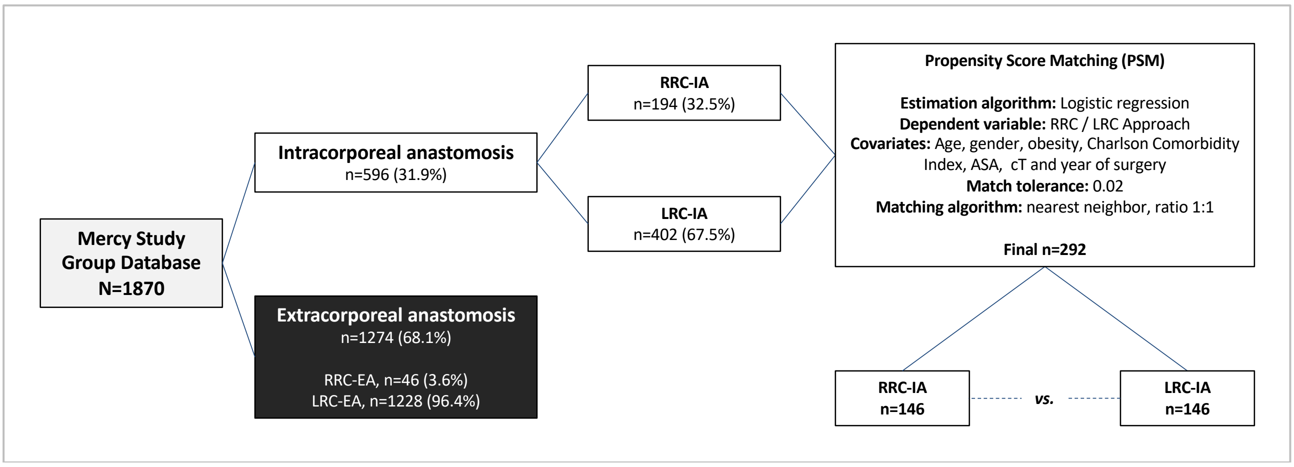
5.3.10. Figure 7b. Forest plots of the predictors of surgical outcomes: logistic mixed models for categorical outcomes.



5.3.11. Figure 8. Factors influencing the likelihood of performing EA or IA.



5.3.12. Figure 9. MERCY Phase II: flowchart of the study population selection and PSM



5.3.13. Table 13. MERCY Phase II: demographic, clinical and tumor characteristics of patients undergoing RRC-IA or LRC-IA before PSM.

Variables	RRC-IA (n = 194)	LRC-IA (n = 402)	*p*
Demographic and clinical variables			
Male [n (%)]	201 (50)	94 (48.5)	0.728
Age [mean (SD)]	70.72 (10.72)	71.35 (12.03)	0.209
Age >70 [n (%)]	113 (58.2)	244 (60.7)	0.593
BMI [mean (SD)]	27.23 (3.65)	26.74 (4.37)	0.076
Obesity (BMI > 30 kg/m^2)	45 (23.2)	78 (19.4)	0.283
ASA [n (%)] - 0 - I - II - III	 14 (7.2) 111 (57.2) 65 (33.5) 4 (2.1)	 25 (6.2) 207 (51.5) 157 (39.1) 13 (3.2)	0.438
Cardiovascular diseases [n (%)]	120 (61.9)	206 (51.2)	**0.018**
Pulmonary diseases [n (%)]	27 (13.9)	52 (12.9)	0.797
Kidney diseases [n (%)]	22 (11.3)	32 (8)	0.222
Neurocognitive disorders	18 (9.3)	23 (5.7)	0.121
Diabetes [n (%)]	57 (29.4)	103 (25.6)	0.705
Comorbidity > 1 [n (%)]	102 (52.6)	202 (50.2)	0.601
Charlson score [mean (SD)]	5.04 (1.86)	4.53 (2.12)	**0.049**
Previous abdominal surgery [n (%)]	73 (37.6)	18 (4.5)	0.215
Anastomosis fashion side-to-side [n (%)] - Isoperistaltic - Antiperistaltic	 164 (84.5) 30 (15.5)	 4.26 (2.20) 183 (45.5)	**< 0.0001**
Preoperative imaging assessment on CT scan			
Largest clinical tumor size (cm) [mean (SD)]	4.49 (2.02)	135 (33.6)	0.054
Tumor location [n (%)] - cecum - ascending colon - hepatic flexure	 74 (38.1) 75 (38.7) 45 (23.2)	 84 (20.9) 50 (12.4) 7 (1.7)	0.231
Cases with suspected extra colic involvement [n (%)]	22 (11.3)	127 (31.6)	0.789
Histological and oncological variables			
AJCC stage [n (%)] - 0 - 1 - 2 - 3	 6 (3.2) 60 (30.9) 73 (37.6) 55 (28.4)	 140 (34.8) 128 (31.8) 127 (31.6) 74 (18.4)	0.589
Lymphovascular invasion [n (%)]	41 (21.1)	125 (31.1)	**0.009**
Perineural invasion [n (%)]	28 (14.4)	18 (4.5)	0.247
Tumor grade [n (%)] - well differentiated - moderately differentiated - poorly differentiated	 61 (31.4) 101 (52.1) 32 (16.5)	 4.26 (2.20) 203 (50.5) 74 (18.4)	0.845
Largest histological tumor size (cm) [mean (SD)]	4.61(2.14)	4.41(2.15)	0.106
Adjuvant treatment [n (%)]	42(21.6)	128(31.8)	**0.012**
Bold: significant statistical difference.			

5.3.14. Table 14. MERCY Phase II: demographic, clinical and tumor characteristics of patients undergoing RRC-IA or LRC-IA after PSM.

Variables	RRC-IA (n = 146)	LRC-IA (n = 146)	*p*
Demographic and clinical variables			
Male [n (%)]	69 (47.3)	75 (51.4)	0.558
Age [mean (SD)]	70.77 (11.05)	71.53 (12.45)	0.182
Age **>70** [n (%)]	87 (47.3)	97 (66.4)	0.275
BMI [mean (SD)]	26.97 (3.81)	26.94 (4.69)	0.831
Obesity (BMI > 30 kg/m^2)	32 (21.9)	29 (19.9)	0.774
ASA [n (%)] - 0 - I - II - III	 10 (6.8) 78 (53.4) 54 (37) 4 (2.7)	 11 (7.5) 73 (50) 59 (40.4) 3 (2.1)	0.902
Cardiovascular diseases [n (%)]	89 (61)	84 (57.5)	0.634
Pulmonary diseases [n (%)]	18 (12.3)	22 (15.1)	0.610
Kidney diseases [n (%)]	18 (12.3)	12 (8.2)	0.335
Neurocognitive disorders	14 (9.6)	9 (6.2)	0.385
Diabetes [n (%)]	42 (28.8)	36 (24.7)	0.509
Comorbidity > 1 [n (%)]	75 (51.4)	80 (54.8)	0.639
Charlson score [mean (SD)]	4.78 (1.54)	4.74 (2.09)	0.653
Previous abdominal surgery [n (%)]	52 (35.6)	60 (41.1)	0.4
Anastomosis fashion side-to-side [n (%)] - Isoperistaltic - Antiperistaltic	 127 (87) 19 (13)	 137 (93.8) 9 (6.2)	0.072
Preoperative imaging assessment on CT scan			
Largest clinical tumor size (cm) [mean (SD)]	4.41 (1.99)	4.15 (2.12)	0.177
Tumor location [n (%)] - cecum - ascending colon - hepatic flexure	 59 (40.4) 55 (37.7) 32 (21.9)	 71 (48.6) 45 (30.8) 30 (20.5)	0.338
Cases with suspected extra colic involvement [n (%)]	15 (10.3)	15 (10.3)	1
Histological and oncological variables			
AJCC stage [n (%)] - 0 - 1 - 2 - 3	 4 (2.7) 45 (30.8) 55 (37.7) 42 (28.8)	 3 (2.1) 51 (34.9) 51 (34.9) 41 (28.1)	0.878
Lymphovascular invasion [n (%)]	31 (21.2)	40 (27.4)	0.275
Perineural invasion [n (%)]	20 (13.7)	19 (13)	1
Tumor grade [n (%)] - well differentiated - moderately differentiated - poorly differentiated	 43 (29.5) 78 (53.4) 25 (17.1)	 44 (30.1) 75 (51.4) 27 (18.5)	0.929
Largest histological tumor size (cm) [mean (SD)]	4.55 (2.16)	4.39 (2.11)	0.385
Adjuvant treatment [n (%)]	35 (24)	45 (30.8)	0.238

Bold: significant statistical difference.

5.3.15. Table 15. MERCY Phase II: operative and pathological outcomes of patients undergoing RRC-IA or LRC-IA after PSM.

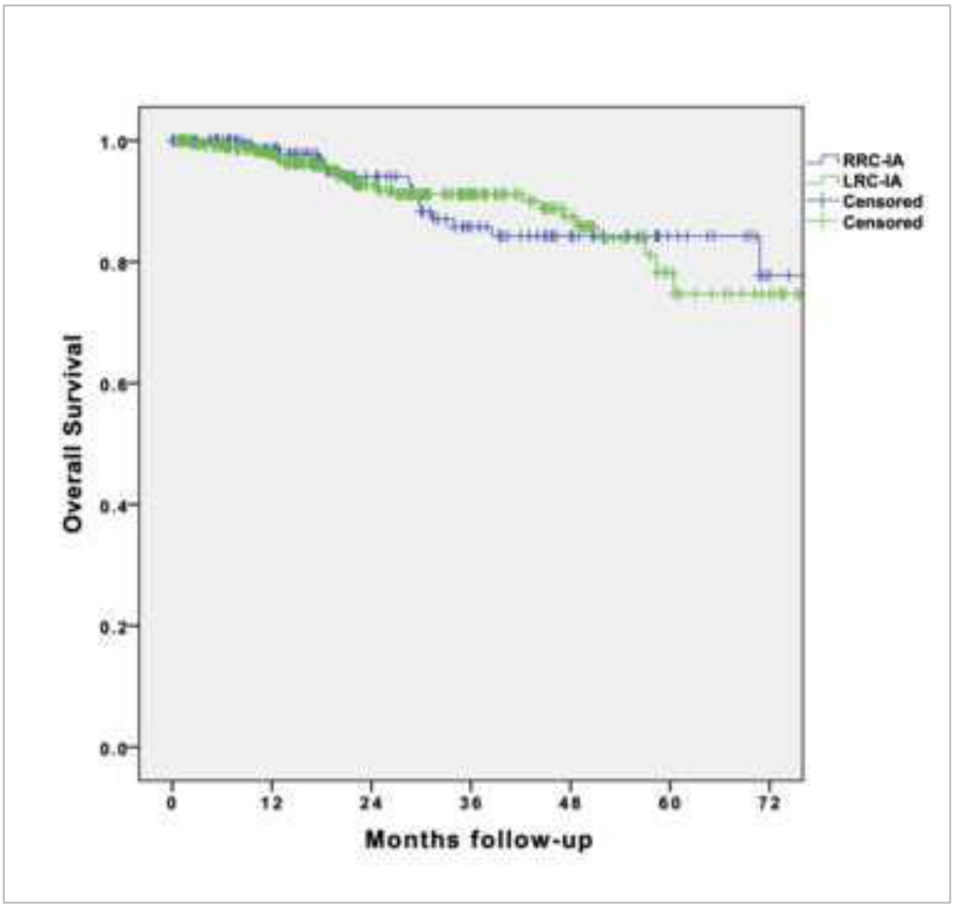
Variables	RRC-IA (n = 146)	LRC-IA (n=146)	*p*
Operative outcomes			
Operative time (min) [mean (SD)]	191.63 (52.05)	183.58 (62.83)	0.241
Intraoperative complications [n (%)]	3 (2.1)	0	0.247
Estimated blood loss (ml) [mean (SD)]	67.54 (48.34)	74.78 (57.6)	0.279
Blood transfusion [n (%)]	15 (10.3)	16 (11)	1
Use of ICG fluorescence [n (%)]	54 (37)	23 (15.8)	**< 0.0001**
Conversion to open surgery [n (%)]	4 (2.7)	0	0.122
Patients with postoperative complication(s) [n (%)]	34 (23.3)	34 (23.3)	1
Severe postop. complications (Dindo-Clavien ≥ III) [n (%)]	14 (41.2)	11 (32.4)	0.615
Reoperation [n (%)]	9 (6.2)	3 (2.1)	0.138
Anastomotic leakage [n (%)]	9 (6.2)	5 (3.4)	0.412
Anastomotic stenosis [n (%)]	0 (0)	0	NA
Prolonged ileus [n (%)]	0 (0)	1 (0.7)	1
Surgical site infection [n (%)]	0 (0)	2 (1.4)	0.498
Time to flatus (days) [mean (SD)]	2.1 (1.15)	2.31 (1.14)	0.154
Time to regular diet (days) [mean (SD)]	3.13 (1.92)	3.49 (1.6)	0.999
Length of hospital stay (days) [mean (SD)]	7.77 (8.27)	8.18 (4.85)	0.604
Readmission [n (%)]	5 (3.4)	4 (2.7)	1
Mortality at 90 days [n (%)]	2 (1.4)	2 (1.4)	1
Pathological outcomes			
Complete tumor resection (R0 status) [n (%)]	145 (99.3)	146 (100)	1
Lymph nodes retrieved - total number [mean (SD)] - ≥ 12 lymph nodes [n (%)]	 22.04 (9.42) 135 (92.5)	 23.66 (10.28) 134 (91.8)	 0.192 1
Multivisceral resection [n (%)]	8(5.5)	10(6.8)	0.809
pT stage [n (%)] - Tis - 1 - 2 - 3 - 4	 4 (2.7) 25 (17.1) 30 (20.5) 72 (49.3) 15(10.3)	 3 (2.1) 22 (15.1) 32 (21.9) 74 (50.7) 15 (10.3)	0.980
pN stage [n (%)] - 0 - 1 - 2	 104 (72.2) 30 (20.5) 12 (8.3)	 105 (71.9) 28 (19.2) 13 (8.9)	0.716
Bold: significant statistical difference.			

5.3.16. Table 16. Multivariate Cox regression models for overall survival (OS) and disease-free survival (DFS).

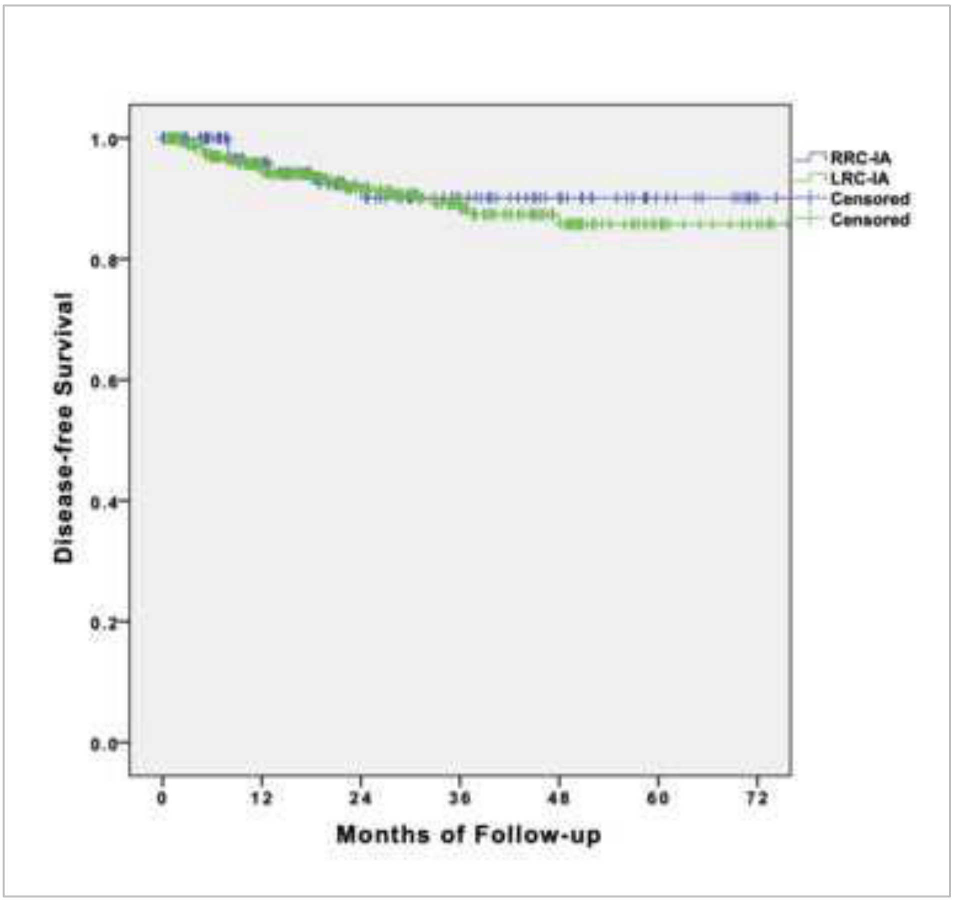
Variables	Overall cohort (n = 584) [a]			
	Overall Survival		Disease-Free Survival	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Age > 70yr	1.86 (0.97-3.56)	0.061		
pN+ vs pN0	2.91 (1.55-5.49)	**0.001**	6.83 (3.14-14.88)	**< 0.0001**
pT4 vs pT1-3	2.55 (1.31-4.97)	**0.006**	3.39 (1.79-6.37)	**< 0.0001**

a: after removing patients deceased within 90 days post-surgery (n = 12); HR: hazards ratio (HR < 1 indicates a survival improvement (positive prognostic factor); HR > 1 indicates a survival worsening (negative prognostic factor); CI: confidence interval; bold: significant statistical difference.

5.3.17. Figure 10. Kaplan-Meier curve of the overall survival (OS).



5.3.18. Figure 11. Kaplan-Meier curve of the disease-free survival (DFS).



5.4. Supplementary Tables

5.4.1. Supplementary Table 1. RoB-2 tool for randomized clinical trials (RCTs).

Park et al. 2019	
🟢	Domain 1: Risk of bias arising from the randomization process
🔴	Domain 2: Risk of bias due to deviations from the intended interventions
🟢	Domain 3: Risk of bias due to missing outcome data
🟢	Domain 4: Risk of bias in measurement of the outcome
🟢	Domain 5: Risk of bias in selection of the reported result
🔴	Overall risk of bias

🟢 low risk 🟡 some concerns 🔴 high risk

5.4.2. Supplementary Table 2. Newcastle-Ottawa Scale quality assessment for retrospective studies.

Year	First author	Selection				Comparability*	Exposure			Total
		Is the case definition adequate?	Representativeness of the cases	Selection of controls	Definition of controls		Ascertainment of exposure	Same ascertainment method for cases and controls	Non-response rate	
2020	Ceccarelli	*	*	*	*	**	*	*	-	8
2020	Migliore	*	*	*	*	**	*	*	-	8
2020	Milone	*	*	*	*	-	*	*	-	6
2019	Merola	*	*	*	*	**	*	*	-	8
2019	Gerbaud	*	*	*	*	*	*	*	-	6
2019	Blumberg	*	*	*	*	**	*	*	-	8
2019	Khorgami	*	*	*	*	-	*	*	-	6
2019	Solaini	*	*	*	*	**	*	*	-	8
2019	Yozgatli	*	*	*	*	**	*	*	-	8
2019	Mégevand	*	*	*	*	**	*	*	-	8
2018	Ngu	*	*	*	*	**	*	*	-	8
2018	Nolan	*	*	*	*	-	*	*	-	6
2018	Kelley	*	*	*	*	**	*	*	-	8
2018	Spinoglio	*	*	*	*	**	*	*	-	8
2018	Scotton	*	*	*	*	-	*	*	-	8
2018	Haskins	*	*	*	*	-	*	*	-	6
2018	Lujan	*	*	*	*	*	*	*	-	7
2017	Widmar	*	*	*	*	*	*	*	-	7
2017	Dolejs	*	*	*	*	**	*	*	-	8
2016	Kang	*	*	*	*	**	*	*	-	8
2016	de'Angelis	*	*	*	*	**	*	*	-	8
2016	Widmar	*	*	*	*	*	*	*	-	7
2016	Cardinali	*	*	*	*	**	*	*	-	8
2016	Miller	*	*	*	*	-	*	*	-	6
2015	Ferrara	*	*	*	*	-	*	*	-	6
2015	Guerrieri	*	*	*	*	*	*	*	-	7
2015	Trastulli	*	*	*	*	**	*	*	-	8
2014	Trinh	*	*	*	*	-	*	*	-	6
2014	Casillas	*	*	*	*	**	*	*	-	8
2014	Davis	*	*	*	*	-	*	*	-	6
2013	Lujan	*	*	*	*	*	*	*	-	7
2013	Morprugo	*	*	*	*	**	*	*	-	8
2012	Deutsch	*	*	*	*	*	*	*	-	7
2012	Shin	*	*	*	*	-	*	*	-	6
2010	deSouza	*	*	*	*	**	*	*	-	8
2007	Rawlings	*	*	*	*	*	*	*	-	7
2003	Delaney	*	*	*	*	**	*	*	-	8

*: Age and ASA > 2

5.4.3. Supplementary Table 3. GRADE system for the comparison LRC vs RRC.

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Laparoscopic surgery	Relative (95% CI)	Absolute (95% CI)		
Length of hospital stay												
34	observational studies	serious [a]	not serious	not serious	not serious	none	13951	2059	-	MD **0.5 higher** (0.15 higher to 0.85 higher)	⊕◯◯◯ VERY LOW	CRITICAL
Operative time												
35	observational studies	serious [a,b]	not serious	not serious	not serious	none	14114	2178	-	MD **56.43 lower** (67.43 lower to 45.43 lower)	⊕◯◯◯ VERY LOW	IMPORTANT
Estimated blood loss												
15	observational studies	very serious [b]	not serious	not serious	very serious [b]	none	877	536	-	MD **12.14 higher** (5.2 higher to 19.08 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Conversion												
28	observational studies	not serious	not serious	not serious	not serious	none	50/1777 (2.8%)	1149/11280 (10.2%)	OR 2.17 (1.60 to 2.95)	**96 more per 1.000** (from 52 more to 149 more)	⊕⊕◯◯ LOW	IMPORTANT
Time to flatus												
19	observational studies	very serious [b]	not serious	not serious	very serious [b]	none	1298	1100	-	MD **0.37 higher** (0.07 higher to 0.66 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Overall complications												
29	observational studies	serious [c,d]	not serious	not serious	not serious	none	2063/8645 (23.9%)	402/1744 (23.1%)	OR 1.19 (1.03 to 1.38)	**32 more per 1.000** (from 5 more to 62 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Total costs												
9	observational studies	serious [b]	not serious	not serious	serious [b]	none	7785	875	-	MD **2589.46 lower** (4206.21 lower to 972.72 lower)	⊕⊕◯◯ LOW	IMPORTANT
Anastomotic leakage												
21	observational studies	serious [c]	not serious	not serious	not serious	none	186/8047 (2.3%)	30/1552 (1.9%)	OR 1.18 (0.73 to 1.90)	**3 more per 1.000** (from 5 fewer to 17 more)	⊕◯◯◯ VERY LOW	IMPORTANT

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Laparoscopic surgery	Relative (95% CI)	Absolute (95% CI)		
Ileus												
23	observational studies	serious [c,d]	not serious	not serious	serious [c,d]	none	990/10635 (9.3%)	85/1320 (6.4%)	OR 1.05 (0.79 to 1.39)	**3 more per 1.000** (from 13 fewer to 23 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Surgical site infection												
24	observational studies	serious [c,d]	not serious	not serious	not serious	none	841/10742 (7.8%)	105/1640 (6.4%)	OR 1.17 (0.90 to 1.51)	**10 more per 1.000** (from 6 fewer to 30 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Mortality												
20	observational studies	not serious	not serious	not serious	not serious	none	47/10752 (0.4%)	7/1624 (0.4%)	OR 0.72 (0.36 to 1.47)	**1 fewer per 1.000** (from 3 fewer to 2 more)	⊕⊕◯◯ LOW	IMPORTANT
Number of harvested lymph nodes												
25	observational studies	not serious	not serious	not serious	not serious	none	4174	1441	-	MD **1.44 lower** (2.68 lower to 0.19 lower)	⊕⊕◯◯ LOW	IMPORTANT
Ceccarelli et al. included after performing the present quality assessment.												

5.4.4. Supplementary Table 4. GRADE system for the comparison LRC-EA vs RRC-EA.

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Laparoscopic surgery	Relative (95% CI)	Absolute (95% CI)		
Length of hospital stay												
8	observational studies	serious [a]	not serious	not serious	not serious	none	408	181	-	MD **0.11 higher** (0.73 lower to 0.95 higher)	⊕◯◯◯ VERY LOW	CRITICAL
Operative time												
8	observational studies	serious [a,b]	not serious	not serious	not serious	none	408	181	-	MD **42.91 lower** (69.34 lower to 16.49 lower)	⊕◯◯◯ VERY LOW	IMPORTANT
Estimated blood loss												
7	observational studies	very serious [b]	not serious	not serious	very serious [b]	none	393	168	-	MD **13.28 higher** (7.34 lower to 33.9 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Conversion to laparotomy												
6	observational studies	not serious	not serious	not serious	not serious	none	18/346 (5.2%)	3/150 (2.0%)	OR 2.18 (0.73 to 6.45)	**55 more per 1.000** (from 14 fewer to 209 more)	⊕⊕◯◯ LOW	IMPORTANT
Time to flatus												
4	observational studies	very serious [b,c]	not serious	not serious	very serious [c,d]	none	146	74	-	MD **0.47 higher** (0.14 lower to 1.09 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Overall complication rate												
6	observational studies	serious [c,d]	not serious	not serious	not serious	none	387	162	-	MD **1.56 higher** (1 higher to 2.44 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Total costs												
3	observational studies	serious [b]	not serious	not serious	serious [b]	none	180	62	-	MD **2157.19 lower** (3629.69 lower to 684.7 lower)	⊕◯◯◯ VERY LOW	CRITICAL
Anastomotic leakage												
3	observational studies	serious [c]	not serious	not serious	not serious	none	10/207 (4.8%)	1/100 (1.0%)	OR 2.00 (0.31 to 12.77)	**10 more per 1.000** (from 7 fewer to 104 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Laparoscopic surgery	Relative (95% CI)	Absolute (95% CI)		
Ileus												
5	observational studies	serious [c,d]	not serious	not serious	serious [c,d]	none	35/385 (9.1%)	7/160 (4.4%)	OR 1.64 (0.69 to 3.89)	**26 more per 1.000** (from 13 fewer to 107 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Surgical site infection												
5	observational studies	serious [c,d]	not serious	not serious	not serious	none	18/385 (4.7%)	4/160 (2.5%)	OR 1.45 (0.48 to 4.38)	**11 more per 1.000** (from 13 fewer to 76 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Mortality												
4	observational studies	not serious	not serious	not serious	not serious	none	3/351 (0.9%)	1/140 (0.7%)	OR 0.71 (0.14 to 3.58)	**2 fewer per 1.000** (from 6 fewer to 18 more)	⊕⊕◯◯ LOW	IMPORTANT
Number of harvested lymph nodes												
6	observational studies	not serious	not serious	not serious	not serious	none	356	149	-	MD **3.8 lower** (7.56 lower to 0.05 lower)	⊕⊕◯◯ LOW	IMPORTANT
Ceccarelli et al. included after performing the present quality assessment.												

5.4.5. Supplementary Table 5. GRADE system for the comparison LRC-IA vs RRC-IA.

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Robotic surgery	Laparoscopic surgery	Relative (95% CI)	Absolute (95% CI)		
Length of hospital stay												
8	observational studies	serious [a]	not serious	not serious	not serious	none	656	735	-	MD **0.8 higher** (0.18 higher to 1.42 higher)	⊕◯◯◯ VERY LOW	CRITICAL
Operative Time												
8	observational studies	serious [a,b]	not serious	not serious	not serious	none	656	735	-	MD **66.71 lower** (81.08 lower to 52.34 lower)	⊕◯◯◯ VERY LOW	IMPORTANT
Estimated blood loss												
2	observational studies	very serious [b]	not serious	not serious	very serious [b]	none	141	123	-	MD **1.65 higher** (21.69 lower to 25.59 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Conversion to laparotomy												
8	observational studies	not serious	not serious	not serious	not serious	none	31/656 (4.7%)	11/735 (1.5%)	OR 2.57 (0.85 to 7.81)	**23 more per 1.000** (from 2 fewer to 91 more)	⊕⊕◯◯ LOW	IMPORTANT
Time to flatus												
7	observational studies	very serious [b]	not serious	not serious	very serious [b]	none	555	714	-	**0.29 higher** (0.13 lower to 0.71 higher)	⊕◯◯◯ VERY LOW	IMPORTANT
Overall complication rate												
8	observational studies	serious [c,d]	not serious	not serious	not serious	none	174/656 (26.5%)	184/735 (25.0%)	OR 1.06 (0.80 to 1.40)	**11 more per 1.000** (from 40 fewer to 68 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Severe complication rate												
6	observational studies	not serious	not serious	not serious	not serious	none	40/565 (7.1%)	31/582 (5.3%)	OR 1.32 (0.75 to 2.33)	**16 more per 1.000** (from 13 fewer to 63 more)	⊕⊕◯◯ LOW	IMPORTANT
Anastomotic leakage												
8	observational studies	serious [c]	not serious	not serious	not serious	none	10/526 (1.9%)	19/865 (2.2%)	OR 1.01 (0.47 to 2.19)	**0 fewer per 1.000** (from 12 fewer to 25 more)	⊕◯◯◯ VERY LOW	CRITICAL
Ileus												
5	observational studies	serious [c,d]	not serious	not serious	serious [c,d]	none	23/462 (5.0%)	22/320 (6.9%)	OR 0.73 (0.39 to 1.34)	**18 fewer per 1.000** (from 41 fewer to 21 more)	⊕◯◯◯ VERY LOW	IMPORTANT

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Robotic surgery**	**Laparoscopic surgery**	**Relative (95% CI)**	**Absolute (95% CI)**		
Surgical site infection												
5	observational studies	serious [c,d]	not serious	not serious	not serious	none	27/376 (7.2%)	38/579 (6.6%)	OR 1.37 (0.78 to 2.40)	**22 more per 1.000** (from 14 fewer to 79 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Reoperation												
6	observational studies	not serious	not serious	not serious	not serious	none	13/556 (2.3%)	11/414 (2.7%)	OR 1.08 (0.44 to 2.62)	**2 more per 1.000** (from 15 fewer to 40 more)	⨁⨁◯◯ LOW	IMPORTANT
Readmission												
5	observational studies	not serious	not serious	not serious	not serious	none	9/414 (2.2%)	4/511 (0.8%)	OR 2.02 (0.64 to 6.38)	**8 more per 1.000** (from 3 fewer to 40 more)	⨁⨁◯◯ LOW	IMPORTANT
Mortality												
7	observational studies	not serious	not serious	not serious	not serious	none	4/640 (0.6%)	2/719 (0.3%)	OR 1.93 (0.31 to 11.88)	**3 more per 1.000** (from 2 fewer to 29 more)	⨁⨁◯◯ LOW	IMPORTANT
Number of harvested lymph nodes												
8	observational studies	not serious	not serious	not serious	not serious	none	656	735	-	MD **0.65 lower** (2.65 lower to 1.34 higher)	⨁⨁◯◯ LOW	IMPORTANT
Ceccarelli et al. included after performing the present quality assessment.												

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SCIENTIFIC PRODUCTS

List of publications or other products consistent with the topic of the doctoral project, performed within the time frame of the project (from the beginning of the PhD):

1. de'Angelis, N., Piccoli, M., ... Genova, P., ... & Espin, E. for the MERCY Study Collaborating Group Members (**2022**). Right Colectomy with Intracorporeal Anastomosis: a European Multicenter Propensity Score Analysis of Robotic vs. Laparoscopic Procedures - *Techniques in Coloproctology* - **SUBMITTED**
2. de'Angelis, N., Lupinacci, R., Abdalla, S., **Genova, P.**, Beliard, A., Cotte, E., Denost, Q., Goasguen, N., Lakkis, Z., Lelong, B., Manceau, G., Meurette, G., Perrenot, C., Pezet, D., Rouanet, P., Valverde, A., Pessaux, P. (**2021**). Robotic-assisted right colectomy. Official expert recommendations delivered under the aegis of the French Association of Surgery (AFC) - *Journal de Chirugie Viscérale* - **IN PRESS**
3. **2020 MERCY Study collaborating Group** (**2021**). Predictors of surgical outcomes in minimally invasive right colectomy: results from a large European multicentric database - *International Journal of Colorectal Disease* - **IN PRESS**
4. **Genova, P.,** Pantuso, G., Cipolla, C., Latteri, M. A., Abdalla, S., Paquet, J. C., Brunetti, F., de'Angelis, N., Di Saverio, S. (**2020**). Laparoscopic versus robotic right colectomy with extra-corporeal or intra-corporeal anastomosis: a systematic review and meta-analysis. *Langenbeck's Archives of Surgery*, 1-23. DOI: 10.1007/s00423-020-01985-x
5. **Genova, P.**, Pantuso, G., Abdalla, S., Memeo, R., Gaiani, F., Gavriilidis, P., de'Angelis, N. (**2020**). Milestones in robotic colorectal surgery development: an historical overview. *Mini-invasive Surgery*, 4, 2. DOI: 10.20517/2574-1225.2019.30

List of other publications or products (carried out by the PhD student within the time frame of the project):

1. Graceffa, G., Vieni, S., Mannino, V., Gennari, V., **Genova, P.**, Cipolla, C. (**2021**) Effectiveness of early administration of a single dose of steroids and escin after loss of signal on electromyographic signal recovery during neuromonitored thyroidectomy. *Am J Surg*. Oct 15:S0002-9610(21)00606-1. DOI: 10.1016/j.amjsurg.2021.10.016
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3. Cipolla, C., Vieni, S., **Genova, P.**, Contino, S., Latteri, M., Graceffa, G. (**2021**) Value of Neuro-stimulation Plus Laryngeal Palpation to Predict Postoperative Vocal Fold Motility. *The Journal of surgical research*, *267*, 506–511. DOI: 10.1016/j.jss.2021.06.003
4. Fazzotta, S., Genova, G., Pantuso, G., Buscemi, S., Palumbo, V. D., Damiano, G., ... & **Genova, P.** (**2021**). Intraoperative Cholangiography during Cholecystectomy Using a Biliary-nose Tube: Routinely Used in Patients with Main Bile Duct Stones. *World*, *14*(1), 16. DOI: 10.5005/jp-journals-10033-1425
5. Fazzotta, S., Buscemi, S., Palumbo, V., Damiano, G., Geraci, G., Licciardi, M., Licciardi M., Palumbo F.S., Fiorica, C., Cudia, B.M., **Genova, P.**, Lo Monte, A.I. (**2020**). Nanofibrillar scaffold resists to bile and urine action: experiences in pigs. *KLINICESKAA I EKSPERIMENTAL'NAA HIRURGIA, 8(4), 29-34.* DOI: 10.33029/2308-1198-2020-8-4-29-34

6. **Genova, P.**, Palumbo, V. D., Lo Monte, A. I., Cipolla, C., Genova, G. (**2020**). Unexplained neoplastic anastomotic recurrence after right hemicolectomy: a case report. Journal of Medical Case Report. *J Med Case Reports*, *14*, 196. DOI: 10.1186/s13256-020-02529-z
7. **Genova, P.**, Memeo, R., Brunetti, F. (**2020**). Robotic transanal surgery: perspectives for application. *Mini-invasive Surgery 4:*20. DOI: 10.20517/2574-1225.2019.47
8. de'Angelis, N., Martínez-Pérez, A., Winter, D. C., Landi, F., Vitali, G. C., Le Roy, B., ... & Espin, E., on behalf of the **SFC Study Group** (**2020**). Extended right colectomy, left colectomy, or segmental left colectomy for splenic flexure carcinomas: a European multicenter propensity score matching analysis. *Surgical Endoscopy*, 1-12. DOI: 0.1007/s00464-020-07431-9
9. Destan, C., Brouquet, A., De Carbonnières, A., **Genova, P.**, Fessenmeyer, C., De Montblanc, J., ... & Benoist, S. (**2020**). What are the risk factors of failure of enhanced recovery after right colectomy? Results of a prospective study on 140 consecutive cases. *International Journal of Colorectal Disease*, 1-9. DOI: 10.1007/s00384-020-03590-2
10. Martínez-Pérez, A., Reitano, E., Gavriilidis, P., **Genova, P.**, Brunetti, F., de'Angelis, N. (**2019**). What is the best surgical option for the resection of transverse colon cancer? *Ann Laparosc Endosc Surg, 4, 69-80* DOI: 10.21037/ales.2019.07.01
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