REVIEW AND META-ANALYSYS

INTRACORPOREAL VERSUS EXTRACORPOREAL ANASTOMOSIS IN LAPAROSCOPIC RIGHT COLECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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Abstract: 247 words.

Main text: 2.631 words.

ABSTRACT

Purpose: Because of its technical difficulty, totally laparoscopic right colectomy with intracorporeal anastomosis is still performed by a small number of surgeons. Most of them prefer to carry out a laparoscopic assisted technique with extracorporeal anastomosis. This systematic review aims to evaluate differences in outcomes of patients undergoing right laparoscopic colectomy, either with intracorporeal or extracorporeal anastomosis.

Methods: Electronic databases were searched for studies published between 1991 to September 2011. Randomized controlled trials and case-control studies comparing intracorporeal to extracorporeal anastomosis in laparoscopic right colectomy were included in the systematic review. Meta-analytical models were used to evaluate anastomotic leak rate and short-term overall morbidity. Defined primary outcomes of interest were operating time, conversion rate, return of bowel function, anastomotic leak rate and hospital stay

Results: Randomized controlled trials were not found, confirming the paucity of literature. Five case-control studies were identified involving 412 patients undergoing right laparoscopic colectomy, 230 with intracorporeal and 182 with extracorporeal anastomosis. Best outcomes seem to be associated with totally laparoscopic right colectomy with intracorporeal anastomosis, especially in terms of return of bowel function, hospital stay and cosmetic results. Meta-analysis data show no significant difference between two techniques (Odds ratio for anastomotic leak rate = 1.05, 95% Confidence Interval: 0.29-3.78, and for short-term global morbidity = 0.71, 95% Confidence Interval: 0.40-1-26).

Conclusions: Comparative analysis of outcomes is in favor of intracorporeal anastomosis. However, meta-analysis results do not allow us to draw definitive

conclusions. Further prospective randomized trials are necessary to confirm our findings.

KEYWORDS:

Laparoscopy

Right colectomy

Anastomosis

Outcomes

Review

Meta-analysis

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INTRODUCTION

Although nowadays considered as a feasible and effective surgery in terms of short and long-term results and oncological radicality [1-5], laparoscopic right colectomy is still performed by a small number of surgeons. In an immense majority of cases this technique was performed with an extracorporeal anastomosis. Undoubtedly, one of the reasons is its increased technical difficulty, in front of left colectomy[6]. On the other hand, in recent years, the emphasis on minimizing surgical techniques, with the advent of natural orifice (NOSE, NOTES) and single port access surgery, has given new impetus to surgeons to perform an intracorporeal anastomosis[7-12].

Evidence of benefits of laparoscopic-assisted right colectomy with extracorporeal anastomosis compared to *open* or hand-assisted techniques, is widely demonstrated in the literature[13]. In addition of an equivalent oncologic results, and anastomotic leak rate, the laparoscopic approach with intracorporeal anastomosis provides an earlier return of bowel function, oral tolerance, less pain and reduced hospital stay.[13-17] However, this technique has a significant longer operative time.[14-17]

Most of the studies comparing intracorporeal vs. extracorporeal anastomosis in laparoscopic right colectomy are vey recent. Theoretically, totally laparoscopic technique, with intracorporeal anastomosis (IA), due to reduced traction on the colon and mainly on the mesocolon, should provide an even faster bowel recovery, with enhanced postoperative comfort for the patient. In contrast, the increased technical

difficulty of IA may result in a greater likelihood of anastomosis leak and a longer operating time. However, none of studies comparing intracorporeal to extracorporeal anastomosis (EA) in laparoscopic right colectomy, has provided enough evidence for which procedure is superior.

This systematic review aims to analyze the results of published series, with greater regard to operating time, conversion rate, return of bowel function, anastomotic leak rate, and hospital stay. Also, a metanalytical analysis of the published experience was performed.

METHODS

Study Selection

Two electronic databases (PubMed and Cochrane Library) were searched for studies published between 1991 to September 2011. Combinations of the following search term were used by two reviewers independently: ‘anastomosis’, ‘intracorporeal’, ‘extracorporeal’, ‘laparoscopy’, ‘laparoscopic right colectomy’ and ‘totally laparoscopic colectomy’. The “related articles” feature of PubMed was simultaneously used. A manual cross-reference search of the bibliographies of relevant studies was conducted to identify articles not found through the computerized search. There was no restriction on language, study type or publication status.

Inclusion and Exclusion Criteria

After identifying relevant titles, the abstracts were read to decide if the study was eligible, and then full-text articles were obtained. Confirming the paucity of the available evidence addressing the study question, no randomized controlled trials were found. As a result, case-control studies comparing intracorporeal to extracorporeal anastomosis in laparoscopic right colectomy were included and analyzed for evidence of bias, in particular selection, observer and reporting bias. Case-control studies non-specific for right colectomy, as well as non comparative studies (case-series, case-report and technique articles) were excluded from the analysis. All assessments were undertaken independently by two reviewers, with any disagreement resolved by discussion and consensus with the third author.

Quality assessment, Risk of bias and Quality Scoring

The adequate methodology used in the selected articles was assessed according to the following criteria: type of analysis, the presence of explicit inclusion and exclusion criteria and adequate definition of studied variables. Each study was classified as being at low, intermediate or high risk for bias. Trials that reported all quality domains using appropriate methods were considered to have low risk of bias. If we could not obtain this information we considered the study to be intermediate or high risk of bias based on performance of the remaining domains.

An overall methodological quality of each included study was assessed using the MINCIR score[18], a valid and reliable scale composed of three items: study design, population sample size, adjusted according to the presence or absence of sample size in the study, and methodology used in the paper (objectives, design, eligibility criteria and their justification). According to this, a score, which represent the sum of the three items, is generated, with a final score that can vary between 6 and 36 points, 6 points being the worst methodological quality study and 36 points being the best.

Data Extraction and Outcomes of interest

All study data were extracted independently and tabulated by two reviewers: first author, year of publication, study design, number of subjects operated, and technique details. Primary outcomes of interest were: operating time, conversion rate, return of bowel function, anastomotic leak rate, and length of stay. When reported, secondary outcomes were also registered: length of larger incision, number of lymph nodes retrieved, tumor-free resection margin, and evaluation of postoperative pain.

Statistical analysis

A meta-analysis of anastomotic leak rate and overall short-term morbidity was conducted. Statistical analysis for categorical variables was carried out using the odds ratio (OR) as the summary statistic. This ratio represents the odds of an adverse event occurring in the IA group compared with the EA group. An OR of less than 1 favors the IA group, and the point estimate of the OR is considered statistically significant at the P<0.05 level if the 95 per cent confidence interval (CI) does not include the value 1. The between-study heterogeneity was assessed using I^2 and X^2 measures[19]. Substantial heterogeneity exists when I^2 exceeds 50% and P value of X^2 is below 0.05. A random-effects model was applied[20]. In this model it is assumed that there is variation between studies, thus the calculated OR has a more conservative value. Furthermore, in the absence of randomized controlled trials, meta-analysis using the random-effect model is preferable because patients included in the review have different risk profiles and selection criteria for each center. Graphical representation of the results was undertaken using Review Manager (RevMan) software version 5.0 (The Nordic Cochrane Centre, Copenhagen, Denmark).

RESULTS

A total of 72 studies were firstly identified. Of them, 59 articles were excluded for several reasons (Figure 1). Therefore, for first assessment 13 relevant studies were included [7,8,10,11,16,21-28]. Three further articles were obtained from searching reference lists[9,12,29]. After first specific analysis, 11 studies were subsequently excluded: 1 case-control non specific for right colectomy[25], the other ten regarding intracorporeal anastomosis, but without comparison to other technique: 1 case-control specific for right colectomy, comparing NOSE to totally laparoscopic conventional technique[7], 3 case-series[9,26,27], 3 case-report[8,10,12] and 3 technique articles[11,28,29].

Finally, five studies formed the basis of this review[16,21-24], involving 412 patients subjected to laparoscopic right colectomy: 230 with intracorporeal anastomosis and 182 with extracorporeal anastomosis.

Figure 1, the PRISMA diagram, is a graphical representation showing the flow of information through the different phases of the systematic review: number of records identified, included and excluded, and the reasons for exclusions.

Quality of Included Studies

In table 1, is presented the results of quality assessment using the selected domains. Three of five studies had an intermediate risk of bias and the remaining 2, a low risk of bias. The punctuation of MINCIR score ranged from 11 to 13 (mean 12,2, standard deviation: 0.84).

Surgical technique

Tables 2 and 3 summarize several technical aspects in each surgical technique. In one of the studies, there is no a clear explanation of surgical technique. In all studies, the anastomosis is performed using stapler in a side-to-side fashion. Regarding other technical steps there is large variation among published series. The specimen is preferentially extracted by all the authors using a Pfannestiel incision in patients with intracorporeal anastomosis. Only one group[16] used the right lower quadrant trocar site incision for this purpose. However in the cases of EA, the extraction specimen's site is more variable.

Primary outcomes

In tables 4 and 5 there is the main findings regarding outcomes in both series. Regarding operative time the analysis showed variable results: no difference between techniques was found in one study[22]; two series reported a less time for EA[21,24] and two series showed favorable data for IA[16,23]. The conversion rate was also nonconclusive among series. Hellan *et al* [24] report no conversions to open technique; in the study by Franklin *et al* [16] there is no comparison. One paper describes no difference [22], Fabozzi *et al* [23] report an advantage for EA. Only one study describe fewer conversions IA, but without statistically significant differences (p=0.09) [21]. All the authors[21-24], with the exception of one series[16] reported a clear advantage of IA for bowel recovery function, considered as the first movement or first flatus. In two series[21,22] there is statistical significant difference between two techniques (p=0.04 and p=0.043). Two studies reported no anastomotic leak on group series[16,22]. In contrast, two authors reported better results with EA, without

statistical significance [21,24] and the later [23] described a significant less anastomotic leak with IA.

Secondary outcomes

The majority of studies [16,22-24], presented some advantages in terms of cosmetic results of abdominal incision, for IA technique. While there were some variations in terms of number of lymph nodes retrieved, there was unanimity for the advantage of IA technique in terms of T-free resection margins [21-23]. Only two series described the postoperative pain [22,23] and revealed better results for IA.

Meta-analysis

In figures 2 and 3 are represented the forest plots of meta-analysis results of analysed series focusing on anastomotic leak rate and overall short-term morbidity. In one published series [16] only one value of overall morbidity has been reported and therefore it was excluded from the analysis. There were no significant differences between IA and EA groups in the incidence of both outcomes. Odds Ratio was 1.05 (95% CI 0.29 to 3.78) for anastomotic leak rate and 0.71 (95% CI 0.40 to 1.26) for overall short-term morbidity, although Fabozzi *et al* [23] do not describe any postoperative complication in 50 patients undergoing totally laparoscopic right colectomy with intracorporeal anastomosis. The results of funnel plots (Figs. 4, 5) demonstrated a significant publication bias for morbidity outcome.

DISCUSSION

Right colectomy is a widely used technique in clinical practice [17]. Its laparoscopic feasibility has been demonstrated and there are two techniques of anastomosis: extracorporeal or intracorporeal [2-4]. Overall, although by comparative analysis best outcomes seem to be associated with intracorporeal anastomosis, the present meta-analysis results for anastomotic leak rate and overall short-term morbidity showed no significant differences between two techniques.

Given the paucity of literature, this systematic review has the strength to be the first study comparing intracorporeal and extracorporeal anastomosis in laparoscopic right colectomy. However, the main limitation of this study is the lack of homogeneity between the different included studies. The absence of published randomized controlled trials on this issue, has forced us to include only an observational studies. Therefore, some heterogeneity has been found regarding methodology (study design, inclusion criteria, operative technique) and outcomes.

It is well known that laparoscopic approach for colon resection improved short-term outcomes compared to open surgery[1-5,30-32]. However, while laparoscopic colectomy with intracorporeal anastomosis is a common practice on the left colon and rectum, laparoscopic right colon using intracorporeal anastomosis is still rarely performed[6]. The explanation rises for technical difficulties and for the need to perform in most of cases, laparoscopic handsewn sutures. In this line most surgeons still prefer to carry out an extracorporeal anastomosis using laparotomy assistance.

Although there are examples of anastomosis performed through exclusive use of stapler[16,33], is recognized that handsewn closure of enterostomies minimizes the risk of inadvertent leak or stricture[26]. According to this hypothesis, with the exception of one group[16], the authors included in our review, at the end of intracorporeal anastomosis they closed enterostomies by handsewn sutures [21,22,24].

No reliable indications for the benefit by one of the two techniques can be drawn from results of our review about conversion rate. Bergamaschi et *al* [26] in a series of 111 unselected patients undergoing totally laparoscopic right colectomy with intracorporeal anastomosis reported an average of 120 min for procedure, and a 5.4% the conversion rate.

A very important point of discussion in determining the success of each technique is the anastomotic leak rate. According to the results analyzed, there is some benefit for EA [21,24]. However, the only study that reaches statistical significance was in favor of IA [23]. Other series studies reported encouraging results with 3,8% and 0% of anastomosis leak rate, respectively [26,27]. Another unpleasant drawback that may occur performing the laparoscopic assisted technique is the incorrect alignment of the mesentery after extraction, resulting in a volvulus of the anastomosis [24]. A completely intracorporeal anastomosis may reduce the likelihood of intestinal twist.

Regarding bowel function, all authors agree on the advantage for intracorporeal anastomosis in some series (with statistical significant differences) [21,22]. Although there is no scientific evidence, the explanation may be attributed to reduced bowel manipulation and less traction on the mesentery and pancreaticoduodenal block. As

a consequence, it may improve patient comfort and shorten the hospital stay, as proven by Chaves *et al* [21] and Fabozzi *et al* [23] .

One of the main aims of totally right laparoscopic colectomy is to avoid a mini-laparotomy, performing a significantly smaller incision. A benefit from this approach was achieved with statistical significance by three of five authors considering this outcome [22-24]. The main part of groups who performed an intracorporeal anastomosis, carried out a Pfannestiel incision [21,22,24], with statistically significant result in terms of shorter incision length. The advantage of totally laparoscopic technique is the ability to use any abdominal location for specimen extraction, while in laparoscopic assisted technique the incision is often conditioned by where the anastomosis is planned. Pfannestiel incision is known for excellent cosmetic results and protective factor against incisional hernia, with a rate of 0%-2% [36,37]. The incisional hernia rate in laparoscopic colon surgery is 17%-24% with a higher rate for midline versus off-midline incisions [38,39]. Furthermore, smaller incisions achieved by a completely intracorporeal approach, may decrease pulmonary complications [40].

This issue it is especially relevant for obese patients, as reported by Raftopoulos *et al* [41]. Frequently, in these patients the terminal ileum cannot be adequately exteriorized because of their short and heavy mesentery and their thick abdominal wall. Moreover, an excessive mesenteric traction during externalizing maneuvers increases the risk of vascular accident including mesenteric and portal vein thrombosis[42]. These factors make it necessary to increase the incision length to extract the specimen and perform the anastomosis, if carried out extracorporeal. A conversion to open technique cannot often be avoided. Therefore, in obese patients,

a totally laparoscopic approach with intracorporeal anastomosis may decrease larger incision length and high conversion rate that occur in laparoscopic assisted right colectomy with extracorporeal anastomosis[43], reducing increased incisional hernia risk and pulmonary complications. And in addition, as widely shown in literature[44-46], other wound-related outcomes that may receive a benefit by smaller incisions are postoperative pain and length of stay.

Finally in this systematic review we aimed to analyze also the oncological results. Thus advantages seem to emerge from intracorporeal anastomosis. An increased number of lymph nodes retrieved[21,24] and a larger T-free resection margin[21-23] have been achieved performing this technique. The reason may depend on several factors that make it difficult the exposure of the base of mesentery in laparoscopic assisted technique with extracorporeal anastomosis: not precise location of the abdominal incision for specimen extraction, the need to maintain a small incision, obese patients (short mesentery and thick abdominal wall). All these factors may compromise a high mesenteric ligation and limit the extension of the resection[45,47]. To overcome this problem, many authors carry out extracorporeal anastomosis after intracorporeal high-vessel ligation[34, 35, 45, 47].

In summary, results of comparative analysis of considered outcomes seem to be in favor of totally laparoscopic right colectomy with intracorporeal anastomosis, especially in terms of return of bowel function, hospital stay, oncological and cosmetic results. Furthermore, encouraging findings seem to emerge also regarding the operating time performing an IA. However, meta-analysis data arising from nonrandomized retrospective comparative studies included in the review do not allow

us to determine the technique of choice. Therefore, the quality of studies must be improved, and prospective randomized trials are necessary in the future.

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FIGURE LEGENDS

Figure 1. PRISMA flow diagram showing selection of articles for review.

Figure 2. Forest plot of studies comparing anastomotic leak rate between intracorporeal and extracorporeal anastomosis in right laparoscopic colectomy.

Figure 3. Forest plot of studies comparing short-term global morbidity between intracorporeal and extracorporeal anastomosis in right laparoscopic colectomy.

Figure 4. Funnel plot demonstrating the absence of publication bias between the studies for anastomotic leak rate.

Figure 5. Funnel plot demonstrating the presence of publication bias between the studies for short-term global morbidity.

Table 1. Methodological quality assessment of included trials.

Author	Type of analysis	Explicit inclusion and exclusion criteria	Adequate variables definition	Risk of bias
Franklin et al.[16]	Prospective	Yes	Yes	Low
Hellan et al. [24]	Retrospective	Yes	Yes	Intermediate
Fabozzi et al. [23]	Retrospective	No	Yes	Intermediate
Scatizzi et al. [22]	Prospective	Yes	Yes	Low
Chaves et al. [21]	Retrospective	Yes	Yes	Intermediate

Table 2. Included studies: Totally laparoscopic right colectomy and intracorporeala anstomosis (IA) technique.

	Chaves *et al* [21] (2011)	Scatizzi *et al* [22] (2010)	Fabozzi *et al*[23] (2010)	Hellan *et al* [24] (2009)	Franklin *et al* [16] (2004)
No. of patients	35	40	50	23	82
Type of anastomosis	stapled	stapled	NR	stapled	stapled
Fashion of anastomosis	side-to-side NR	side-to-side isoperistaltic	NR NR	side-to-side isoperistaltic	side-to-side NR
Closure of enterotomies	handsewn	handsewn	NR	handsewn	stapled
Extraction of the specimen	Pfannestiel incision	Pfannestiel incision	NR	Pfannestiel incision	right lower quadrant trocar site

NR= not reported

Table 3. Included studies: Laparoscopic assisted right colectomy and extracorporeal anastomosis (EA) technique.

	Chaves *et al*[21] (2011)	Scatizzi *et al*[22] (2010)	Fabozzi *et al*[23] (2010)	Hellan *et al*[24] (2009)	Franklin *et al*[16] (2004)
No. of patients	25	40	50	57	10
Type of anastomosis	stapled / handsewn	stapled	NR	stapled	stapled / handsewn
Fashion of anastomosis	side-to-side NR	side-to-side isoperistaltic	NR NR	side-to-side NR	NR NR
Closure of enterotomies	stapled	handsewn	NR	91% stapled 9% handsewn	NR
Extraction of the specimen	midline trocar site / subcostal / suprapubic	right flank incision	NR	umbilical trocar site midline incision	right lower quadrant trocar site

NR= not reported

Table 4. Primary outcomes: Totally laparoscopic and IA vs. Laparoscopic assisted and EA technique.

	Chaves *et al*[21] (2011)	Scatizzi *et al*[22] (2010)	Fabozzi *et al*[23] (2010)	Hellan *et al*[24] (2009)	Franklin *et al*[16] (2004)
Operating time	EA (p=0.06)	ND (p=0.167)	**IA (p< 0.05)***	EA (p NS)	IA (p NR)
Conversion rate (to "open")	IA (p=0.09)	ND (p=1.000)	EA (p NR)	0	no comparison
Return of bowel function	**IA (p=0.04)***	**IA (p=0.043)***	IA (p NS)	IA (p NS)	NC
Anastomosis leak rate	EA (p=0.13)	0	**IA (p < 0.05)***	EA (p NS)	0
Length of stay	IA (p=0.09)	ND (p=0.085)	**IA (p < 0.05)***	ND (p NS)	NC

*Statistically significant (P<0.05); IA, intracorporeal anastomosis; EA, extracorporeal anastomosis; ND, no difference; NR, not reported; NS, not significant; NC, not considered

Table 5. Other outcomes: Totally laparoscopic and IA v.s Laparoscopic assisted and EA technique.

	Chaves *et al*[21] (2011)	Scatizzi *et al*[22] (2010)	Fabozzi *et al*[23] (2010)	Hellan *et al*[24] (2009)	Franklin *et al*[16] (2004)
Length of larger incision / Cosmetic result	NC	**IA (p=0.019)***	**IA (p < 0.05)***	**IA (p=0.004)***	IA (p NR)
Nº lymph nodes retrieved	**IA (p=0.03)***	EA (p=0.084)	EA (p NS)	IA (P NS)	no comparison
T-free resection margin	IA (p=0.57)	**IA (p=0.026)***	**IA (p < 0.05)***	NC	no comparison
Postoperative pain / Use of analgesic drugs	NC	ND (p=0.748)	**IA (p < 0.05)***	NC	NC

*Statistically significant (P<0.05); IA, intracorporeal anastomosis; EA, extracorporeal anastomosis; ND, no difference; NR, not reported; NS, not significant; NC, not considered