



Intracorporeal vs. extracorporeal anastomosis for laparoscopic right colectomy: state of the art in 2020

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Laparoscopic right colectomy with intracorporeal anastomosis was pioneered as early as in 1992 and subsequently standardized in 2004 (1). However, due to the technical difficulties related to perform intracorporeal hand-sewn sutures, to close the enterotomies, to the prolonged operative time and to the long learning curve, this technique was not initially embraced by the surgical community and had limited diffusion worldwide. In the last 10 years, mainly due to an increased ability of dedicated laparoscopic surgeons, this technique has gained popularity and interest as testified by the several meta-analyses comparing intracorporeal (IA) *vs.* extracorporeal (EA) anastomosis after laparoscopic right colectomy published in the international literature since 2013 (2-9). Based on these results, there seems to be an advantage in favor of IA, since it is apparently associated to a better postoperative recovery, to a shorter hospital stay without any increase in major complications. Nevertheless, in all the meta-analyses published before 2020, quite all data were extracted from non-randomized or retrospective studies with inherent limitations. Moreover, we must also keep in mind that among the included studies, a high heterogeneity was reported as claimed by the majority of authors (3-9). This applies particularly to the conversion to open surgery which was not universally reported and to the anastomotic leak which includes different definitions. Van Oostendorp in a recent meta-analysis stressed that the Clavien-Dindo classification for the definition of postoperative complications was used only in 25% of cases (7). In addition, Milone in another meta-analysis on

the same subject including 1,862 patients (5) noted that Clavien-Dindo was used in only 914 patients, which is likely too few to obtain robust results, also considering the fact that more than half of this number (512 patients) came from only one author (10). The heterogeneity in the surgical techniques chosen to fashion the anastomosis, in particular the extracorporeal one, which included hand-sewn, totally stapled (both anastomosis and insertion holes closure) and stapled anastomosis with hand-sewn closure of the insertion holes represents another object of controversial and discussion (2-4,6,7). In addition among studies included in the abovementioned meta-analyses, the majority were small series of retrospective nature, which makes difficult to obtain statistically significant results and to reach reasonable conclusions about state of one technique's superiority over the other, and thus the majority of the authors concluded their analysis suggesting an RCT study on this topic (2-7,10). Two RCT trials only were published before 2019, however only 60 patients were randomized in both studies (11,12). Mari *et al.* randomized 30 patients to EA and 30 patients to IA and the analysis was focused on surgical stress response following the two different techniques. The paper was adequately statistically powered to show significant lower postoperative levels of interleukin-6 and C-reactive protein and an earlier recovery of bowel function in the intracorporeal group (11). Vignali *et al.* in an interim analysis from an RCT on the same topic showed a favorable effect of IA in term of postoperative recovery of bowel function and postoperative ileus (12). However, we had to wait until 2020, before the results of

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two large RCT trials were available in the international literature. The first one published, was from Italy by Allaix *et al.* (13), while the second one was from Spain, by Bollo *et al.* (14). In both studies 70 patients per group were randomized to IA or EA for a total of 140 patients in each trial. The results of the two aforementioned RCT seems to confirm the advantages of IA in term of recovery of digestive function and less paralytic ileus. However, the earlier recovery of bowel function and the lower incidence of paralytic ileus did not translate in a shorter length of stay, which was the main outcome in both studies. Data from the two RCT studies, show that patients in the IA group experienced a lesser postoperative pain as assessed by VAS scale. Moreover, in the RCT by Bollo, the lesser pain reported in the IA group translated into a lesser postoperative analgesia requirement (14). Despite underpowered to detect difference in complication rate, a similar incidence of overall postoperative complication rates was reported in the IA and EA groups in both trials. Data from two large meta-analyses published in the last 6 months including 3,699 and 4,450 patients, respectively, reach similar conclusions (8,9). Nevertheless, in the effort of convincing the surgical community to change their surgical practice in favor of a new technique, the main argument should be ideally represented by a robust evidence of a lower incidence of anastomotic leak in the IA group, by a lower incidence of overall postoperative complications or severity of complications assessed by Clavien-Dindo classification. Anastomotic leak, in fact, still represents the most feared complication in colorectal surgery, whose consequences are particularly dramatic following right colectomy both in term of severity of the peritonitis as well as for the mortality rate which is higher when compared to left colic or rectal operation (15). Contrasting data are coming from the two recent RCT trials with respect to the incidence of anastomotic leak. Allaix reports a non-significant higher incidence in the IA group (8.6% *vs.* 2.9% in the EA), while Bollo reported a non-significant higher leak rate in the EA (7% *vs.* 4% in the IA). Of interest in the paper of Allaix, in the EA group a stapled iso-peristaltic side to side anastomosis was fashioned only in 51% of patients, while in the remaining patients a hand-sewn extracorporeal anastomosis was fashioned. In the paper by Bollo, a side to side mechanical anti-peristaltic anastomosis was fashioned in both groups, but in the EA group, the two bowel ends were closed with a TA stapler, while in the IA, a double layer running suture was used to close the enterotomy defect.

Contrasting results in term of anastomotic leak rate were

also reported by the large meta-analyses published in the last 3 years showing no difference (4,6-8) or a significantly higher odds ratio for anastomotic leak for extracorporeal anastomoses (9). Of note, in the only meta-analysis showing a significant difference in the anastomotic leak rate between the two groups, in the EA group, 44% of the anastomoses were hand-sewn, and as previously mentioned, the definition of anastomotic leak was different among the included studies or no reported. The heterogeneity in the way the anastomosis was fashioned in the EA group as emerged both from RCT trials and retrospective studies included in the aforementioned meta-analyses should not be underestimated. A Cochrane review published in 2011, in fact indicate that stapled anastomoses are at lower risk of anastomotic leak when compared to the hand-sewn anastomoses (16). Moreover, the method used for close the enterotomy at the staple line, represents another matter of debate and must be taken into account, since in our experience on 426 consecutive laparoscopic colectomies with IA, anastomotic leak was due to a defect at the enterotomy closure site in 72.3% of the cases (data not shown).

According on these findings, in our opinion the end of the discussion is not near, also taking into account that the statistical significance not necessarily translates into clinical significance in light of the limitations cited above. At present time, based on the available evidence in literature we could not reach definitive conclusion in term of anastomotic leak when EA and IA are considered and further larger multicentric RCT trials with restrictive and homogeneous criteria in the surgical technique chosen for fashioning the EA anastomosis are warranted. The same criteria apply also for the issue of postoperative complications.

Several randomized studies and a large international, multicentric prospective observational study which aim to analyze outcomes from IA and EA are ongoing: The MIRCAS trial (NCT03650517), The IVEA study (NCT03990714), The RICART study (NCT03862781), IN EXTREMO study (NCT01679756). Once these trials will be complete, hopefully the debate will be bringing to a conclusion with robust evidence.

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