

Selective sPlenic flExure mobilization for low colorEctal anastomosis after D3 lYmph node dissection (SPEEDY) trial: a study protocol

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To the Editor: Colorectal cancer (CRC) remains the second most frequent cause of cancer-related deaths worldwide. Since the concept of total mesorectal excision (TME) introduced by Heald *et al*^[1] has become a gold standard of rectal cancer surgery, there has been a significant improvement in oncological outcomes including disease-free and overall survival. Although TME is the standard procedure for rectal cancer patients undergoing either low anterior resection (LAR) or abdominoperineal resection, the optimum strategy to restore bowel continuity between colon and rectum (in case of LAR) is still debated. There is no clear consensus of the best approach both in terms of anastomotic technique^[2] (end-to-end or side-to-end) and in terms of vessel ligation (high tie or low tie ligation).

Several studies comparing high-tie with low-tie ligation reported a stage-specific survival benefit for high-tie; however, a recent study demonstrated that low-tie, without splenic flexure mobilization (SFM), decreased the complexity of the laparoscopic procedure and could reduce the operating time with comparable oncological outcomes.^[3] During a radical paraaortic lymph node dissection, the inferior mesenteric artery (IMA) is usually ligated at its origin and the arcade of Riolan provides blood supply to proximal stump of the anastomosis. Unfortunately, the arcade of Riolan is an inconstant finding. Furthermore, in about 26% of cases, the length of the remaining descending colon is not enough and SFM is required to perform a safe and tension-free anastomosis. SFM is a time-consuming component of LAR with the additional risk of iatrogenic splenic injury and maybe technically challenging during laparoscopic resection.

Therefore, we planned the prospective randomized trial to compare the anastomotic leak (AL) rate between low IMA

ligation with selective SFM and high IMA tie with routine SFM groups (trial registration: www.ClinicalTrials.gov, NCT03895255). We included patients histologically proven primary rectal adenocarcinoma located within 15 cm from anal verge without involvement of internal and/or external sphincter muscle, stage I to III according to the tumor-node-metastasis classification, American Society of Anesthesiologist classification between I and III. All patients received TME and primary colorectal anastomosis with or without neoadjuvant radio-chemotherapy. Patients were randomly divided into two groups: the first TME with high IMA tie with routine SFM and the second TME with low IMA ligation with selective SFM (76 patients per arm). The procedure was performed through-out open, laparoscopic approach. In all patient D3 lymph node dissection was performed. In both groups stapled side-to-end colorectal anastomosis was performed. The anastomoses in both groups underwent hydropneumatic leak test. Diverting loop transverse colostomy or ileostomy was performed in all patients. All patients were scheduled to return to the ambulatory clinic 4 to 6 weeks after the surgery. During these visits, post-operative data were collected and post-operative proctography was performed to evaluate the integrity of the anastomosis. If a patient fails to follow-up, the research nurse may contact the patient by all means available (phone, email, or mail) to ascertain whether the patient has had any complications and/or adverse events that were treated at another institution. If the research nurse is unsuccessful in contacting the patient, the patient will be considered as lost to follow-up.

The primary outcome of the trial was the AL rate detected within 6 weeks after surgery either clinically and/or radiologically. Secondary outcome measures included SFM rate in the first group with the low tie, IMA

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architectonics and branching, operative time, complications rate, the number of affected lymph nodes, specimen morphometry, conversion rate if laparoscopy was performed, complications of preventive stoma, length of hospital stay, short-term and long-term oncological results. Intention-to-treat analysis was performed. Quantitative variables were described as means with standard deviations, medians, range, or interquartile range as appropriate. Categorical variables were described in absolute numbers and percentages. The statistical analysis of the quantitative variables, with independent groups, was performed with the parametric Student's *t* test, provided that its conditions for application are met. Otherwise, the non-parametric Mann-Whitney *U*-test was used. Statistical analysis for categorical variables was performed using the Pearson χ^2 test or the Fisher exact test. Specifically, the above methods were used to compare the two groups in terms of baseline characteristics in order to assess whether the randomization has been effective.

It was demonstrated that routine SFM is not necessary during anterior resection for rectal cancer. A recent retrospective analysis by Mouw *et al*^[4] showed that SFM was associated with wider margins and a decreased rate of inadequate nodal staging in patients undergoing LAR. In a recent systematic review and meta-analysis by Gachabayov *et al*,^[5] laparoscopic SFM was associated with increased rate of surgical site infection and operative time without a clear decrease in AL rate; however, authors cautioned on significant selection bias and lack of standardized definition of SFM. Some authors consider ligating IMA at the level of origin, the high tie, is necessary for wide lymph node dissection, better overall survival, and precise staging. Ligation of the IMA has been demonstrated to decrease blood flow to the anastomosis, and it often requires SFM. SFM may be technically challenging with additional risks including a rate of 2.5% of splenic injury. Nevertheless, SFM is mandatory when the length of the remaining colon cannot ensure a safe anastomosis with the rectum. Some authors reported a rate of 25% of SFM in patients undergone high anterior resection of the rectum with TME. However, during LAR, many surgeons routinely perform SFM in order to ensure a tension-free anastomosis. Laparoscopic surgery has been employed since the 1990s for resection of CRC. Some surgeons perform skeletonization of IMA with lymph node dissection and preservation of LCA. In this case, SFM is

not mandatory and could be performed only if needed to perform a tension-free anastomosis (selective SFM).

Our study had several advantages compared with other researches. We have compared the high tie of IMA with SFM and low tie of IMA with selective SFM. This study may show the advantage of low IMA tie with selective SFM approach in comparison to the high IMA tie with routine SFM. This advantage may include lower risk of splenic injury, increased use of laparoscopic surgery, and shorter operation time with comparable oncological outcomes.

In conclusion, comparing the rate of complications between the two groups may allow concluding whether low IMA tie with selective SFM can be safely implemented if the proximal colon stump length is sufficient to perform anastomosis without tension. The design of this study has certain limitations, only surgical and functional outcomes are assessed. Oncological outcomes demand 3–4 years of follow-up and will be evaluated outside of this protocol.

Conflicts of interest

None.

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