

Splenic flexure mobilization in sigmoid and rectal cancer resections: a meta-analysis of surgical outcomes.

Mobilização da flexura esplênica nas ressecções dos tumores de reto e sigmoide: meta-análise dos resultados cirúrgicos.

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ABSTRACT

Objective: to evaluate the influence of the splenic flexure mobilization for the main surgical outcomes of patients submitted to resection of sigmoid and rectal cancer. **Methods:** we searched the MEDLINE, Cochrane Central Register of Controlled Trials and LILACS, using the terms "splenic flexure mobilization", "colorectal surgery", "rectal cancer", "anterior resection", "sigmoid colon cancer", and "sigmoid resection". The main outcome was anastomotic dehiscence. Other outcomes analyzed were mortality, bleeding, infection and general complications. We estimated the effect sizes by grouping data from six case-control studies (1,433 patients) published until January 2018. **Results:** our meta-analysis showed that patients undergoing complete mobilization of the splenic flexure had a higher risk of anastomotic dehiscence (RR=2.27, 95%CI: 1.22-4.23) compared with those not submitted to this procedure. There was no difference between the groups in terms of mortality, bleeding, infection and general complications. **Conclusion:** splenic flexure mobilization is associated with a higher risk of anastomotic dehiscence in resections of sigmoid and rectal cancer. This surgical maneuver should be used with caution in the surgical management of sigmoid or rectal cancers.

Keywords: Rectal Neoplasms. Colorectal Surgery. Anastomotic Leak.

INTRODUCTION

Colorectal surgery has been technically improved in the recent decades. Several specific surgical steps introduced, such as total mesorectal excision, have been presenting superior oncological results for patients with colorectal cancer^{1,2}. Some technical aspects, however, remain under debate, such as the need to mobilize the splenic flexure during anterior resection of the rectum. While most surgeons believe that the splenic flexure mobilization (SFM) is required to obtain a tension-free anastomosis, others believe that this is a time-consuming maneuver, which should only be performed when a well vascularized and tension-free anastomosis cannot be readily obtained³.

The aim of this meta-analysis is to evaluate the surgical outcomes of patients undergoing resection of sigmoid or rectal colon cancer with or without complete SFM.

METHODS

We conducted this study according to current guidelines for systematic reviews and meta-analyses (PRISMA statement)^{4,5}. We registered the study protocol in the International Register of Systematic Reviews (PROSPERO) under number CRD42018083692.

Inclusion criteria

Studies were eligible for inclusion if they met the following criteria: assessed patients with sigmoid and/or rectum cancer; evaluated cases with

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and without complete SFM; reported anastomotic dehiscence (primary outcome of the study), mortality, bleeding, infection and general surgical complications (perioperative morbidity, including cardiopulmonary events, need of splenectomy, and postoperative ileus); and were case-controls.

Search strategy and study selection

We performed an electronic literature search at the US National Institutes of Health of the National Library of Medicine (PubMed.com), including MEDLINE, Cochrane Library, Latin American and Caribbean Health Sciences Literature (LILACS), without restriction of date. The descriptive terms used (MeSH) were: "splenic flexure mobilization", "colorectal surgery", "rectal cancer", "anterior resection", "sigmoid colon cancer" and "sigmoid resection". We also evaluated additional relevant references cited in retrieved articles. We limited the research to humans and to documents in English or Spanish, and we completed it in January 2018.

Two investigators independently reviewed the titles and abstracts of all retrieved articles to assess whether the studies were eligible for inclusion in the meta-analysis. Disagreements between the two researchers were presented to the third author and decided by consensus.

Data extraction and quality analysis

Two investigators extracted the data independently by using a standardized abstraction form and consensus was sought on all items obtained. When consensus could not be reached, differences in data extraction were resolved by a third reviewer.

The information extracted from each individual study were: first author's name, year of publication, number of cancer patients, number of patients undergoing SFM or not, patients demographic characteristics, surgery characteristics (duration, surgical access), tumor (TNM staging, use of neoadjuvant chemo-radiotherapy) and data on the specific outcomes of interest previously described. We applied quality assessment of case-control studies (NIH system) to all papers.

Meta-analyses

We performed a separate meta-analysis for each study variable. Relative risk (RR) was the measure of the effect size used to compare the two procedures: SFM and no splenic flexure mobilization (NSFM). The RR were grouped using the Mantel-Haenzel method and the random effects model with the DerSimonian and Laird estimator. We chose the random effects model to incorporate the expected heterogeneity between individual studies. We used the Mantel-Haenzel method because it provides interval estimates with greater precision than those produced by the conventional inverse variance method when the RR is the effect size. We used the Cochran's Q test and I² statistics to assess heterogeneity between studies. All statistical tests were bilateral and significance was set at $p < 0.05$. We performed statistical analyzes with the R version 3.2.1 (R Foundation for Statistical Computing).

RESULTS

Study selection

Figure 1 shows a flow diagram illustrating the strategy used to select studies for the meta-analysis.

We retrieved 211 potentially relevant citations by searching the electronic databases and 195 of them were deleted during the review of titles and abstracts. The 16 articles that seemed eligible at the time had their full texts evaluated. After a critical reading, we excluded ten other studies because they had ineligible study designs, duplicated results, and no comparison between groups according to SFM.

Studies included in the meta-analysis

Six case series met the eligibility criteria and were included in our meta-analysis⁶⁻¹¹. Four studies consisted of retrospective analysis of medical records and institutional databases^{6,7,10,11}. In two studies, data were collected prospectively^{8,9}. In all studies, SFM was performed selectively.

The main characteristics of the studies are presented in table 1. In total, they analyzed 1,433 patients with colorectal cancer: 577 patients with

complete SFM and 856 patients without SFM. In five studies, the SFM was compared to NSF. Gezen *et al.*⁹ compared complete with partial SFM, which did not include the dissection of gastrocolic and pancreaticomesocolic attachments. Gouvas *et al.*¹¹ included 21 patients with tumors located in the descending colon who underwent left colectomy. Considering that SFM is a routine step of a left colectomy, we excluded these 21 cases from our meta-analysis.

Four studies^{6,7,9,10} reported tumor staging; three^{6,8,9} described neoadjuvant chemo-radiotherapy. In the study conducted by Brennan *et al.*⁶, the only surgical access used was the laparotomic (open) one. In the studies by Gezen *et al.*⁹ and Gouvas *et al.*¹¹, only laparoscopic resections were performed.

The quality index of the studies is shown in table 1. We classified all six included studies as having good quality.

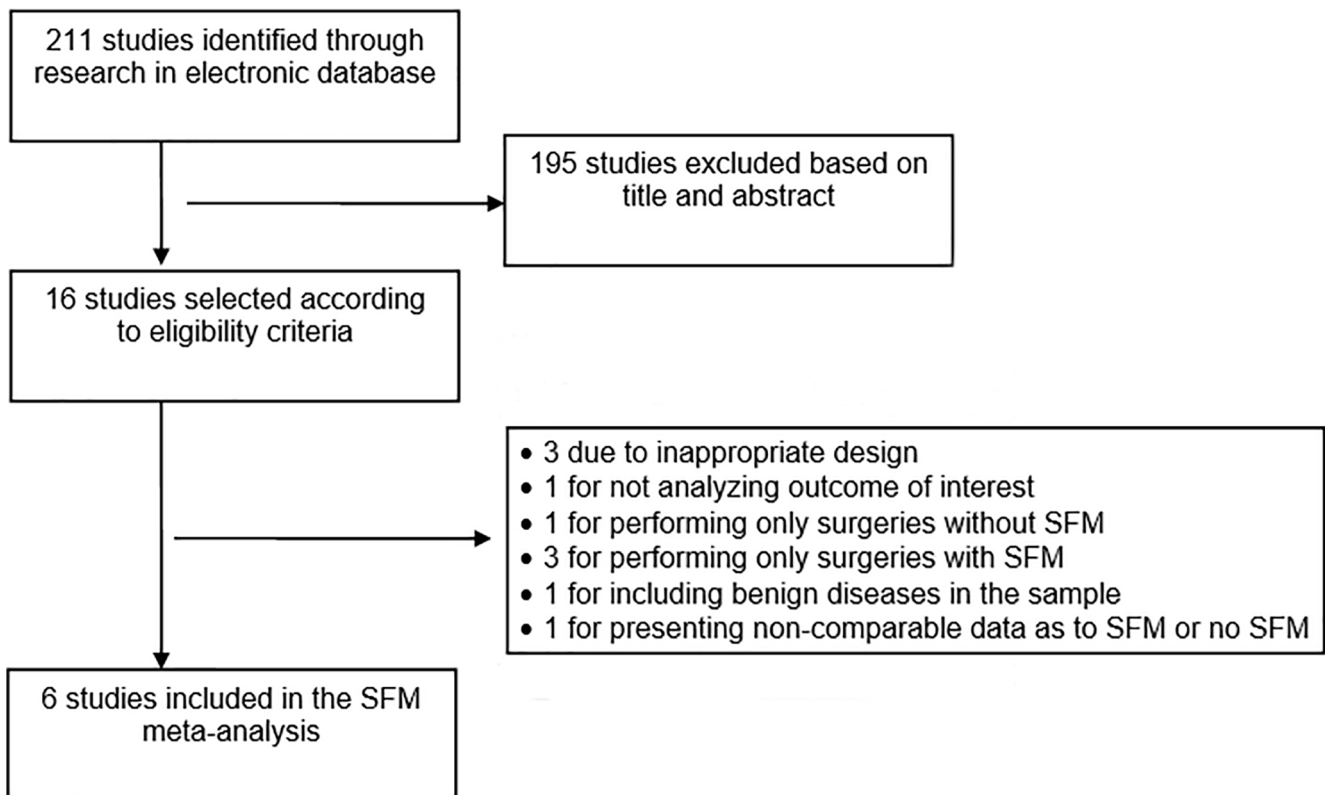


Figure 1. PRISMA flowchart of the study selection process.

Table 1. Characteristics of studies included in the meta-analysis.

	Study (first author)					
	Brennan ⁶	Katory ⁷	Marsden ⁸	Gezen ⁹	Ouaïssi ¹⁰	Gouvas ¹¹
CSFM ¹	26	176	97	86	53	139
ISFM ²	74	531	119	36	27	69
Age in years (range)	63 (44-84)	66 (22-93)	69 (30-89)	58 (45-71)	69 (34-93)	64 (51-76)
Men	62 (62%)	353 (50%)	136 (63%)	77 (63%)		107 (51%)
TNM					0- 13 (16,2%) ³	
	I- 25 (25%)	I- 63 (9%)		I- 9 (7%)	I- 15 (18%)	
	II- 45 (45%)	II- 255 (36%)		II- 18 (15%)	II- 15 (18%)	
	III- 28 (28%)	III- 224 (32%)		III- 80 (66%)	III- 22 (27,5%)	
		IV- 121 (17%)		IV- 0 (0%)	IV- 15 (18%)	
Neoadjuvant radiotherapy	28 (28%)		17 (8%)	74 (61%)		
Surgical access						
Laparoscopic	0 (0%)	177 (25%)	138 (64%)	122 (100%)		208 (100%)
Open	100 (100%)	531 (75%)	78 (36%)	0 (0%)		0 (0%)
Duration in minutes						
CSFM ¹	167		225±55	225		
ISFM ²	120			224		
Country	Ireland	Singapore	England	Turkey	France	Greece
Quality	Good	Good	Good	Good	Good	Good

¹ CSFM: complete splenic flexure mobilization; ² ISFM: incomplete splenic flexure mobilization; ³ premalignant lesions. Data are expressed as mean (+/-) the standard deviation or median values and range.

Summary of quantitative data

Figure 2 shows the main results of the present study. The six evaluated studies analyzed anastomotic dehiscence. Our meta-analysis revealed that patients undergoing complete SFM had a significantly higher risk of presenting anastomotic dehiscence (RR=2.2; 95%CI: 1.2-4.2) compared with those not undergoing the procedure. There were no significant differences in mortality (RR=1.94; 95%CI: 0.78-4.8) and surgical infection (RR=1.2; 95%CI: 0.7-2.2) between groups.

Three studies analyzed surgical bleeding^{8,9,11}. Bleeding was reported when it was considered a reason for reoperation⁸, or when presenting as intra-abdominal bleeding or as prolonged bloody drainage⁹. Gouvas *et al.*¹¹

did not provide a definition of bleeding, but all cases were related to splenic hemorrhage. We obtained the calculated evidence from 322 patients with complete SFM and 224 without complete SFM, without significant differences between them (RR=2.4; 95%CI: 0.6-8.6).

Five studies made available data on general surgical complications, including 401 patients in the complete SFM group and 325 in the group without complete SFM. Again, there were no significant differences between study groups.

DISCUSSION

Although management of colorectal cancer has been improved by evidence-based clinical and surgical practices, such as total resection of the

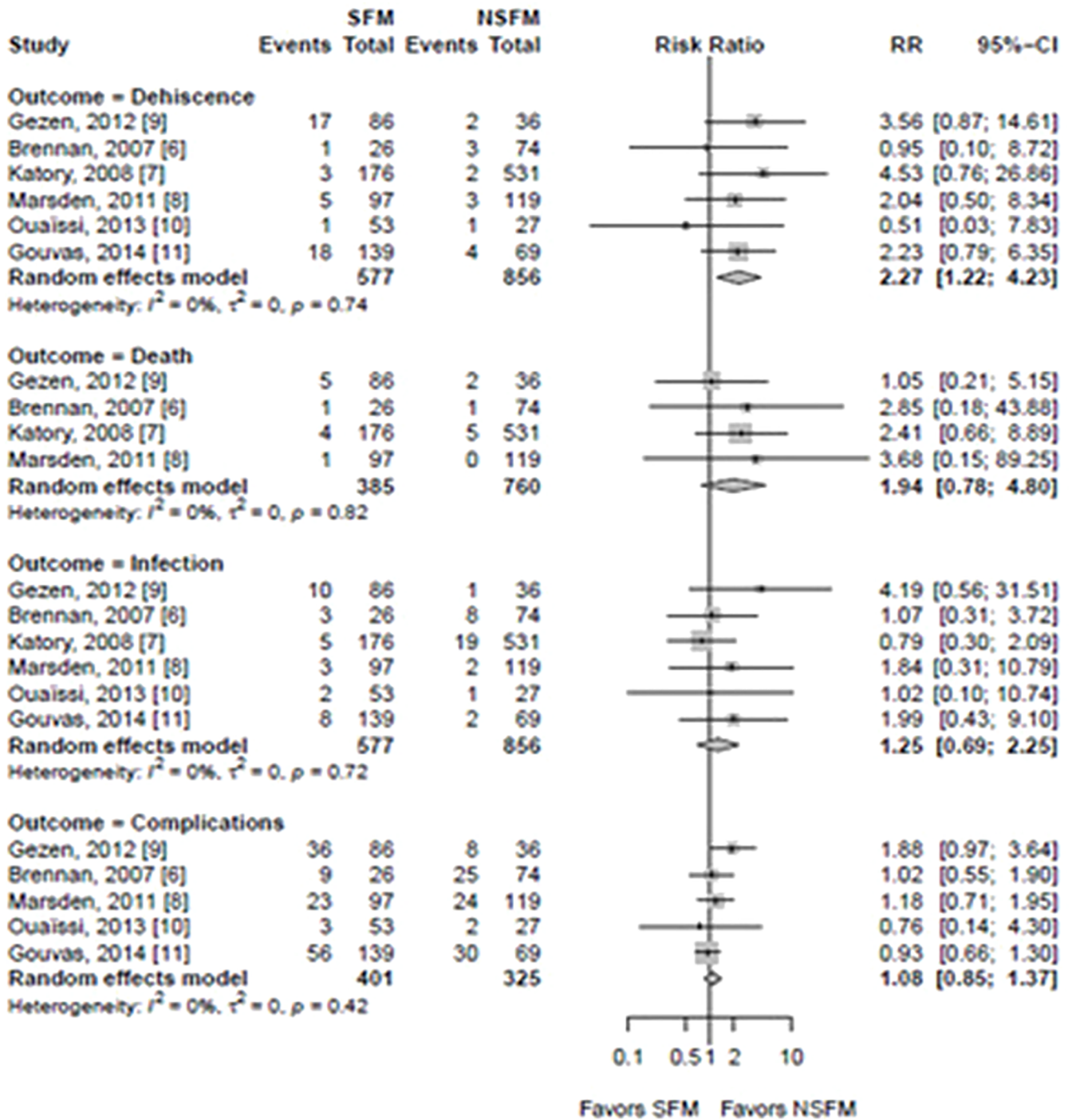


Figure 2. Forrest graphs showing endpoints of interest in groups with SFM and no SFM (NSFM).

mesorectum and neoadjuvant chemo-radiotherapy, much of what surgeons still practice in the operative field remains based on institutional surgical routine, since there are often no controlled trials and high quality evidence available. SFM is one of those controversial points for which scientific evidence is limited.

To the best of our knowledge, this is the first meta-analysis that assesses the main surgical outcomes of colorectal cancer patients according to whether or not they undergo SFM. It was possible to demonstrate that patients submitted to complete SFM had a significantly higher risk of anastomotic

dehiscence (RR=2.27, 95%CI: 1.22-4.23) when compared with those not undergoing this procedure. Therefore, the decision not to conduct a SFM during a sigmoid or rectum cancer resection, whenever it is possible to avoid this surgical step, can be considered a protective factor for anastomotic leak. This finding is clearly in contrast with the opinion of many colorectal surgeons. An international survey of 368 surgeons who performed laparoscopic rectal resection showed that 71.2% routinely perform SFM¹². The objective of SFM is to obtain a well-vascularized and tension-free anastomosis¹³, recognized as an independent risk factor for dehiscence¹⁴. In addition, upper ligation of the inferior mesenteric artery, which is often used to achieve radical lymph node resection, potentially increases the risk of distal colon ischemia³.

SFM is considered a technically difficult surgical step. Jamali *et al.*¹⁵ surveyed the surgical approach of 28 renowned laparoscopic colorectal surgeons from Europe and the United States to quantify the degree of difficulty involved in various laparoscopic colorectal procedures. Analyzing the degree of complexity of each individual surgical step, SFM was considered the most difficult step, ahead of rectal mobilization. The difficulty of SFM is related to the need for extensive posterior dissection without injury of the mesenteric artery, retroperitoneal structures and spleen. Consequently, the SFM increases the surgical time and adds specific risks to the operation, which could only be justifiable if a real benefit of the procedure could be demonstrated. Our meta-analysis showed no significant differences between the groups in terms of mortality, surgical infection, bleeding, and general surgical complications.

Most of our findings agree with the results reported by Carlson *et al.*¹⁶, who performed a retrospective cohort analysis of all elective anterior anastomotic resections (open and laparoscopic) between January 2005 and December 2009 at the National College of Surgeons (Surgical Quality Improvement Program). This series was not included in our meta-analysis, because more than 60% of their cases had other diagnosis than colon and rectum cancer, and because anastomotic dehiscence rates were not recorded. However, infectious, renal and pulmonary adverse events, as well as operative times, were compared between patients with SFM (3,890 cases, 35%) and those without SFM (7,222 cases, 65% of cases). Splenic flexure mobilization was associated with an increase in surgical time (204 *versus* 172 minutes, $p < 0.0001$). There were no differences in organ space infections (3.9% *versus* 3.7%, $p = 0.7$) or return to the operating room between the two groups. However, patients who underwent SFM had significantly more superficial surgical site infections (10.6% *versus* 8.4%, $p < 0.0002$).

SFM is associated with risk of iatrogenic splenic injury that often leads to splenectomy¹⁷. Incidental splenectomy during colorectal resections was associated with poorer short-term surgical outcomes¹⁸ and also the reduction of survival rates after sigmoid or rectal cancer resection¹⁹. According to a recent retrospective study by Mangano *et al.*²⁰, the laparoscopic approach can reduce the rate of splenic injury by almost 3.5 times compared to open rectal resection. Holubar *et al.*²¹ reported their experience over a 15-year period, during which over 13,000 colectomies were performed at the Mayo Clinic.

A total of 59 patients had spleen injury, resulting in a splenic injury rate during colectomy of 0.5%. A subsequent study showed that SFM was independently associated with an increased risk of splenic injury (OR: 18.4 [2.1-161]; $p=0.0085$) during colectomies. Survival of patients with splenic injury tended to be lower both in 30 days (98% vs. 88%; $p=0.06$) and in five years (58% vs. 55%), with a hazard ratio of 1.6 (1.0-2.6; $p=0.05$)²². No splenectomies were reported in the studies included in our meta-analysis due to the still limited number of cases available for analysis. However, two of the studies identified a higher (but not significant) risk of bleeding in the SFM group^{8,9}.

It is important to take into account that estimates summarized with meta-analyses need to be interpreted with caution, as they can often be influenced by publication bias and heterogeneity between studies. Despite these intrinsic methodological limitations, the meta-analysis

remains a valid instrument for assessing clinical and surgical situations for which a prospective randomized trial would be ethically and technically difficult to perform. This is exactly the case with studies evaluating the systematic use of SFM in colorectal surgery.

Although our meta-analysis does not definitively establish a causal role for SFM in anastomotic dehiscence, it demonstrates that there is no proven benefit in subjecting all rectal and sigmoid cancer patients to this surgical maneuver. Although dehiscence usually results from a combination of factors, SFM cannot be considered a protective factor for this surgical complication, being in fact significantly associated with a higher risk of dehiscence. These results contrast with the current concept of SFM adopted by many influent colorectal surgeons. Future prospective studies comparing routine *versus* selective SFM are still needed to determine if this maneuver is associated with increased risk of dehiscence in colorectal anastomoses.

R E S U M O

Objetivo: avaliar a influência da mobilização da flexura esplênica nos principais resultados cirúrgicos de pacientes submetidos à ressecção de câncer do cólon sigmoide ou reto. **Métodos:** os bancos de dados MEDLINE, Cochrane Central Register de Ensaios Controlados e LILACS foram pesquisados usando os termos "mobilização da flexura esplênica", "cirurgia colorretal", "câncer retal", "ressecção anterior", "câncer de cólon sigmoide", "ressecção de sigmoide". O desfecho principal foi a deiscência da anastomose. Outros desfechos analisados foram mortalidade, sangramento, infecção e complicações gerais. Os tamanhos dos efeitos foram estimados por meio do agrupamento dos dados de seis estudos de caso-controle (1.433 pacientes) publicados até janeiro de 2018. **Resultados:** nossa meta-análise revelou que pacientes submetidos à mobilização completa da flexura esplênica tinham um risco maior de deiscência anastomótica (RR=2,27, IC95%: 1,22-4,23) em comparação àqueles não submetidos a esse procedimento. Nenhuma diferença pôde ser demonstrada entre os grupos em termos de mortalidade, sangramento, infecção e complicações gerais. **Conclusão:** a mobilização da flexura esplênica está associada a um maior risco de deiscência anastomótica nas ressecções de câncer de reto ou cólon sigmoide. Esta manobra cirúrgica deve ser utilizada com cautela no manejo cirúrgico dos tumores colorretais.

Descritores: Neoplasias Retais. Cirurgia Colorretal. Fístula Anastomótica.

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