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Retrospective Cohort Study

Is it possible to achieve the same oncological approach in urgent surgery for colon cancer?

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Abstract

BACKGROUND

Locoregional complications may occur in up to 30% of patients with colon cancer. As it is a frequent event in the natural history of this disease, there should be a concern in offering an oncologically adequate surgical treatment to these patients as well.

AIM

To compare the oncological radicality of urgent surgery for colon cancer in relation to elective cases.

METHODS

One-hundred-eight-nine consecutive patients with non-metastatic colon adenocarcinoma were studied over two years in a single institution, who underwent surgical resection as the first therapeutic approach, with 123 elective and 66 urgent cases. The assessment of oncological radicality was performed by analyzing the extension of the longitudinal margins of resection, the number of resected lymph nodes, and the percentage of surgeries with 12 or more resected lymph nodes. Other clinical-pathological variables were studied for comparison between the groups (sex, age, tumor location, type of urgency, surgical access, staging, compromised lymph nodes rate, differentiation grade, angiolymphatic and perineural invasion, and early mortality).

RESULTS

There was no difference between the elective and urgency group concerning the longitudinal margin of resection (average of 6.1 in elective *vs* 7.3 cm in urgency, P = 0.144), number of resected lymph nodes (average of 17.7 in elective *vs* 16.6 in urgency, P = 0.355) and percentage of surgeries with 12 or more resected lymph nodes (75.6% in elective *vs* 77.3% in urgency, P = 0.798). It was observed that the percentage of patients aged 80 and over was higher in the urgency group (13.0% in elective *vs* 25.8% in urgency, P = 0.028), as well as the early mortality (4.9% in elective *vs* 15.2% in urgency, P = 0.016, OR: 3.48, 95%CI: 1.21–10.06). Tumor location (P = 0.004), surgery performed (P = 0.016) and surgical access (P < 0.001) were also different between the groups. There was no difference in the other clinical-pathological variables studied.

CONCLUSION

It is possible to respect the oncological radicality of colon cancer surgery in both emergency and elective procedures.

Key Words: Colorectal cancer; Intestinal obstruction; Intestinal perforation; Surgical oncology; Lymph node excision

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Core Tip: The oncological radicality was compared between patients submitted to elective and urgent surgery for colon cancer. 189 patients with nonmetastatic colorectal cancer who were submitted to surgical resection as the first therapeutic approach were included over two years in a single institution. The analysis of the oncological principles of the surgery, including the longitudinal margins of resection and the number of resected lymph nodes, revealed no statistical difference between elective and urgent

surgeries. Therefore, it is possible to respect the oncological principles of colorectal surgery in urgency as well as in elective cases.

INTRODUCTION

Colorectal cancer (CRC) is a worldwide leading cause of cancer, representing 1148515 new cases a year[1]. Although many signs of progress in early detection and systemic treatment have been achieved, surgical resection remains the only curative-intent treatment for localized colon cancer[2]. Therefore, this surgery must respect some basic principles to be considered oncologically adequate[3]. Considering the inherent difficulty of urgent cases, mostly presenting with obstruction or bleeding, impact in surgical morbidity, the achievements of oncological outcomes seem to be risked in this situation. Thus, this study aimed to compare oncological radicality and surgical outcomes between patients who underwent colectomy for colon cancer in urgent or elective procedures.

MATERIALS AND METHODS

One hundred and eighty-nine consecutive patients with non-metastatic colon adenocarcinoma who underwent surgery with curative intent as the first therapeutic approach were selected, with or without colostomy, operated at urgent (66) or elective (123), from May 2016 to April 2018. All cases were operated at the General and Oncological Surgery Service of Hospital do Servidor Público Estadual de São Paulo (HSPE/SP), Brazil. The project was approved by the Universidade Federal de São Paulo Ethics Committee (CEP/UNIFESP: 0498/2019; approval decision: 3460953). The selected patients were divided into two groups: “Urgency” and “Elective”. Those admitted to the Emergency Room with a locoregional complication of colon cancer, whether obstruction or perforation, requiring a prompt surgical approach, were classified as “Urgency”. In this investigation, no patient required urgent surgery for incoercible bleeding. Conversely, those who, despite the admission to the hospital *via* the Emergency Room, had their initial emergency controlled, making it possible to

perform complete staging, preoperative exams and assessments, and colon preparation according to the institution's routine, were classified as “Electives”, along with the cases scheduled on an outpatient basis. This study excluded patients with rectal cancer, metastatic disease, whether diagnosed before or during surgery, those who underwent other therapeutic interventions before surgical resection (colonic prosthesis, derivative surgery, neoadjuvant), histological types other than adenocarcinoma, as well as patients with insufficient medical record data. Clinical-pathological variables were selected to compare the “Elective” and “Urgency” groups. Histopathological analysis was performed by the Pathology Service of Hospital do Servidor Público Estadual, and no slide review was necessary to carry out this investigation. All variables were collected by the main researcher, retrospectively, through electronic medical records review. The clinical-pathological variables evaluated were longitudinal margin (cm), number of resected lymph nodes, percentage of surgeries with 12 or more resected lymph nodes, sex, age (years), tumor location, surgery performed, type of urgency, access route used, staging according to AJCC UICC 8th edition (2017), rate of compromised lymph nodes, degree of differentiation, angiolymphatic and perineural invasion, and early mortality (up to 30 days). The oncological radicality for colectomies was assessed by the minimal longitudinal margin of resection of 5 cm and the harvesting of at least 12 Lymph nodes (representing proximal ligature of colic vessels). Inferential analysis was performed using the R program version 3.5.2 R Core Team (2016). Pearson's chi-square test or Fisher's exact test was applied when comparing groups for categorical variables. For numerical variables, the t-Student test for independent samples or Mann-Whitney test was applied, using the Shapiro-Wilk test to investigate the normality of numerical variables. In all conclusions obtained through inferential analyzes, an alpha significance level of 5% ($P < 0.05$) was used.

RESULTS

Regarding the 189 patients, respectively 66 operated at urgent (34.9%) or 123 patients in the elective group (65.1%). There was no difference between groups in terms of

distribution by sex (P = 0.632). Higher mean age was observed in the emergency room (71.8 *vs* 68.1 years in the elective group, P = 0.031), with 25.8% of patients aged 80 years or older in the emergency room, against 130% in the elective group (P = 0.028). Regarding the type of urgency that led to surgery in the emergency room, 47 (71.2%) were due to obstruction and 19 (28.8%) to perforation, with no patient being operated on for bleeding. These general characteristics are summarized in Table 1. Emergency operated patients had higher early mortality (up to 30 d) than in the elective group (15.2% *vs* 4.9%, P = 0.016, OR: 3.48, 95%CI: 1.21-10.06) and there was no difference in the interval for starting systemic chemotherapy when indicated (average of 75.2 *vs* 71.8 d, P = 0.535). There was a difference between the groups regarding the surgery performed, directly related to the location of the tumor (Table 2). In both groups, there was a predominance of location in the sigmoid, followed by the ascending colon. The surgical access also differed between groups, with a higher frequency of surgeries performed by laparoscopy in the elective group (43.1% *vs* 0 in emergency, P < 0.001).

Pathological characteristics are summarized in Table 3. It was observed that there was no statistical difference between the groups concerning the T and N classification, staging, degree of differentiation, and presence of angiolymphatic and perineural invasion. It was noted that, in both groups, more than 80% of patients had advanced stages (II or III). The rate of compromised lymph nodes was also found to be similar between groups (8.1% *vs* 7.9%, P = 0.785). Regarding the variables referring to the oncological principles for colon cancer surgery, there was also no statistically significant difference in the urgency group when compared to the elective ones (Table 4). The stratified analysis by the location of the tumor is summarized in Table 5. Tumors located in the cecum, ascending, and 3 cases of transversus, were considered to be the right colon; and the left colon, those located at the splenic, descending, sigmoid, and 2 cases of transversus. Four cases of transverse tumors (2 elective and 2 urgent) were excluded from this stratification as they underwent transversectomy, not being possible to allocate them in the right or left colon. There was a difference in the longitudinal margin in the analysis of the left colon (4.8 in the elective *vs* 7.6 cm in urgency, P =

0.003), with all other variables being similar between the groups. Early mortality was analyzed (up to 30 d) in patients who underwent emergency surgery. It was observed that the mean age was significantly higher in patients who died (84.0 *vs* 69.6 years, $P < 0.001$, 95%CI: 7.2-21.6). Of the 10 patients who died, 8 (80.0%) were 80 years old or older, in contrast to the 56 patients who survived, in which only 9 (16.1%) were in this age group ($P < 0.001$). There was no statistically significant difference regarding early mortality in the other clinical-pathological characteristics between the groups, as shown in Table 6.

DISCUSSION

One of the necessary criteria to achieve oncological radicality concerns the extension of the longitudinal margin of the colon, which must be 5 cm to 7 cm[4,5]. Regarding the radial margin, block resection of adjacent structures should be performed in case of direct invasion, given their tumoral involvement by contiguity[2,6]. Another oncological preconized principle is the complete resection of the main vascular pedicles with the corresponding lymphadenectomy[7]. The number of resected lymph nodes directly influences the prognosis of the patient with colon cancer[8,9], considering that at least 12 Lymph nodes must be resected and evaluated for lymphadenectomy to be considered oncologically adequate[3]. A situation inherent to colon cancer is the presence of possible locoregional complications that lead to the need for urgent surgery[10], which can occur in up to 30% of cases[11]. Intestinal obstruction is the most common locoregional complication, followed by intestinal perforation[12]. Incoercible bleeding is a less frequent cause of urgent indication for colon cancer because, in most cases, bleeding stops or reduces, either spontaneously or through endoscopic or hemodynamic therapies, allowing the elective surgery to be performed[13,14]. In the face of an emergency, whether perforation or obstruction, surgical resection should be proposed as the first therapeutic approach, provided that patients are in clinical conditions for this purpose[15,16].

In emergency surgeries, however, it is observed that the oncological principles described above cannot always be contemplated, considering that locoregional complications can lead to abdominal sepsis, as well as may complicate pre-existing underlying diseases[17]. Thus, the surgeon must choose a less aggressive procedure to save the patient's life, avoiding any complications associated with more extensive surgeries[18]. In contrast, it is known that, despite the urgency, many patients are still able to undergo surgery with all the necessary oncological radical approaches.[19] As it is a frequent situation in the natural history of colon cancer, it is essential to be concerned regarding the oncological principles also in urgent surgeries. Teixeira *et al*[19] and Enciu *et al*[20] showed that it is possible to respect the oncological principles for colon cancer even in an emergency. In both studies there was no control group and, therefore, does not allow inferential analyzes to be carried out related to elective cases. As in this present study, Weixler *et al*[21] studied clinical and pathological data of patients with colorectal cancer who underwent emergency surgery adopting elective patients as a control group. In that investigation, 747 patients were selected over 24 years, with 663 (88.8%) elective and 84 (11.2%) urgent. The percentage of patients who underwent emergency surgery was lower than that reported in the literature (about 30%), and the period of capturing patients was longer than most studies on the topic[12,19,20]. The study showed that there was a statistically significant difference in relation to the percentage of surgeries with 12 or more resected lymph nodes (P = 0.016) and the presence of compromised margins (P = 0.014), showing a difference in the pattern of elective and urgent surgery. Despite these differences, the study demonstrated that overall and disease-free survival were not impacted by surgical urgency[21].

Data available in the literature, therefore, are not able to show whether the emergency surgery for colon cancer is being performed with the same technical standard as the elective ones. The strength of the present study is based on the collected data from emergency and elective patients, in the same period, over two years, and in a single institution, which allowed the homogenization of the group of surgeons and pathologists. Elective patients constituted the ideal control group for the analysis of

oncological radicality in the emergency room, which is the object of this investigation. In the hospital where the study was carried out, the same service is responsible for elective and emergency oncological surgeries. Thus, in both situations, surgeons are duly qualified for colonic oncology surgeries, ensuring the technical standard approach. It is known that the surgeon's experience and the volume of surgery at the institution have an impact on the short and long-term prognosis of patients with colon cancer[22]. Although some patients underwent therapeutic interventions before surgical resection, such as colonic prosthesis or derivative surgery, they represented a small number of patients and there would be a difficulty to allocate them between the elective and urgency groups. Thus, they were excluded from this study population. Evaluating the two main variables of the study, longitudinal margin, and the number of resected lymph nodes, there was no statistically significant difference between the groups. Thus, it was observed that, even in an emergency, it is feasible to perform an oncologically adequate surgery. Also, the percentage of surgeries with 12 or more resected lymph nodes was also similar between groups, showing the same technical pattern of oncological radicality in urgency and elective approaches. The percentage values observed in this study are compatible with previous literature data[19,20]. The analysis of demographic characteristics revealed a statistically significant difference related to age. It was observed that, in the emergency room, patients were older than elective ones. This data can be explained by the fact that elderly patients perform fewer screening tests for colon cancer, which increases the chance of presenting with symptomatic or complicated lesions. In addition, this hypothesis confirmation is not within the scope of this investigation. As for the type of urgency, it was observed that the prevalence of cases of perforation (28.8%) was slightly higher than that reported in most of the literature, which is around 20%[11,12], yet similar distributions have also been demonstrated[23].

Concerning early mortality, an incidence was found about three times higher in urgency than in elective (15.2% *vs* 4.9%). Morris *et al*[24] conducted an extensive population study in England, involving 160920 individuals undergoing surgical

resection for colorectal cancer, having also found a difference in early mortality with a similar proportion (14.9% *vs* 5.8%). Other studies have reported an incidence of early emergency mortality in the range of 8.3%–34.0%, that is, it can be said that the mortality observed in this study is within the expected range according to previous literature data[19–22]. In this research, when analyzing the clinical-pathological characteristics between emergency patients who died and those who survived, a statistically significant difference was observed in relation to age. The prevalence of the elderly was higher among those who died, in which 80% of the patients were 80 years of age or over. Differently from reported in the literature[25], there was no difference in pathological characteristics between those who died and survived, revealing those factors intrinsic to the patient would be more important than tumor staging for the outcome of early mortality. There was a statistically significant difference related to the resection approach employed, and it was observed that 43.1% of the elective cases were performed by laparoscopy, while all urgent surgeries were opened. The laparoscopic approaches in the Urgency group were less expected based on their indissociable indications for urgency procedures (70.2% of bowel obstruction, and 28.8% of bowel perforation), and in older patients, possibly with more comorbidities. Nevertheless, the results suggest that even for patients in these unfavorable scenarios, patients of the Urgency group obtained similar oncological outcomes concerning margin and node status to patients who underwent elective procedures. Laparoscopy was offered in the Elective group, as much as possible, based on the current evidence in the literature that supports the oncological safety of minimally invasive colorectal surgery[26–28]. Thus, all patients regardless of their surgical approaches were used, in order not to exclude a certain group of patients or surgeons based on their practice. Ghazi *et al*[25] demonstrated the presence of more advanced tumors in the emergency room, with a higher prevalence of more advanced staging, greater angiolymphatic and perineural invasion, and a higher rate of compromised lymph nodes. However, our study did not reveal any significant difference between the elective and urgency groups in terms of staging, degree of differentiation, angiolymphatic invasion, perineural invasion and

compromised lymph node rate. It is noteworthy that the present study revealed a low prevalence of early stages even in the elective group, which may be one of the reasons for not having observed this difference. Regarding the location of the tumor, some studies show a worse prognosis in the right colon compared to the left colon[29]. Furthermore, the extent of lymphadenectomy for colon cancer is still an object of study in the literature[30], most of which refer to the right colon, where there is a greater difficulty in standardizing the lymphadenectomy[9]. As there was a statistically significant difference between groups in terms of the location of the tumor in this study, this could bias the results regarding the oncological principles of surgery. However, in the analysis stratified by location, it was observed that, on the right, there was no difference between groups in relation to longitudinal margins, number of lymph nodes resected, or percentage of surgeries with 12 or more lymph nodes resected. On the left, lymphadenectomy was also similar between the groups, but there was a difference concerning the longitudinal margins, being lower in the elective group. The assessment of possible causes for this difference is out of the scope of this study.

As any retrospective study, this study has limitations regarding the impact of inferential analyzes. In terms of long-term survival analyses, the study's limitations for these objectives are those associated with the immeasurable biases seen in all retrospective studies, particularly those addressing oncologic outcomes. Selection bias based on several nonobjective criteria could have contributed to some of the differences between the two study groups. Because detailed data on systemic treatment, radiotherapy, or their toxicity were not reasonably available to analyze, they were not addressed in this study. However, for the investigation of oncological approach in urgency compared to electives, this is a useful and applicable model. The allocation to the elective or emergency group takes into account the patient's clinical presentation, not being possible any type of randomization. Considering 30-d mortality, our sample presented a small number of deceased patients to perform an adequate multivariate model. Thus, only univariate analysis is presented, and confounding bias cannot be excluded. In summary, we do believe that this study provides subsidies to recommend

the oncologically adequate surgery to be performed even in an emergency for most patients. However, it also suggests that a more specific assessment of patients over 80 years is appropriate, especially due to the observed mortality. It should be noted that this conduct should be reserved for surgeons with experience in oncology surgery for colon cancer, as well as institutions with a high volume of this disease, as occurred in this study.

CONCLUSION

It is possible to respect the oncological radicality of colon cancer surgery in both emergency and elective procedures.

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