ARTÍCULO ORIGINAL

Short-term and oncological outcomes in laparoscopic colectomy in colon cancer stage I-III with 3-year follow-up

Morbimortalidad posquirúrgica y resultados oncológicos con 3 años de seguimiento en colectomía laparoscópica por cáncer de colon en estadio I-III en nuestra población

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Abstract

Background: *Laparoscopic colectomy (LC) presents similar short-term results and oncological outcomes to conventional colectomy (CC) in colon cancer.* **Objectives:** *Compare short-term and oncological outcomes at 3-year follow up between LC and CC.* **Materials and methods:** *Patients who underwent LC and CC for colon cancer between January 2010 and December 2017 were retrospectively analyzed. Short-term results and oncological outcomes were studied.* **Results:** *Two hundred sixty-nine patients were included in the study. CC was performed in 37.5% and LC in 62.5%. LC presented shorter operative time (157 vs. 175 min, p = 0.01), shorter length of stay (8.4 vs. 10.5 days, p = 0.02), lees readmission (6% vs. 15%, p = 0.02), and lower morbidity (40% vs. 56%, p = 0.01). No differences were found for overall survival (OAS) (LC = 87.1% vs. CC = 82.8%, p = 0.28) and disease-free survival (DFS) (LC = 78.2% vs. CC = 75.3%, p = 0.47). Recurrence was observed in 37 patients (LC = 16.1% vs. CC = 18.3%, p = 0.53). No differences were found for local recurrence (LC = 6.5% vs. CC = 8.6%, p = 0.49) and distant recurrence (LC = 12.1% vs. CC = 16.1%, p = 0.3). Stage analysis showed no difference for recurrence, OAS, and DFS.* **Conclusions:** *LC is a safe procedure with short-term outcomes, OAS, DFS, and recurrence similar to CC. LC should be the initial indication in non-metastatic colon cancer in our population.*

Key Words: *Colonic neoplasms. Colectomy. Laparoscopy. Morbidity. Survival analysis.*

Resumen

Antecedentes: *La colectomía laparoscópica (CL) presenta resultados a corto plazo y oncológicos similares a los de la colectomía convencional (CC) en cáncer de colon.* **Objetivo:** *Comparar los resultados a corto plazo y oncológicos a 3 años de seguimiento entre la CL y la CC.* **Material y métodos:** *Pacientes intervenidos de CL y CC por cáncer de colon entre enero de 2010 y diciembre de 2017. Se estudiaron los resultados a corto plazo y oncológicos.* **Resultados:** *Se incluyeron 269 pacientes (62.5% CL y 37.5% CC). La CL presentó menor tiempo quirúrgico (157 vs. 175 min; p = 0.01), menor estadía hospitalaria (8.4 vs. 10.5 días; p = 0.02), menor reinternación (6% vs. 15%; p = 0.02) y menor morbilidad (40 vs. 56%; p = 0.01). No se observan diferencias para sobrevida global (87.1% CL y 82.8% CC; p = 0.28) y sobrevida libre de enfermedad (78.2% CL y 75.3% CC; p = 0.47). Hubo recidiva en 37 pacientes (16.1% CL y 18.3% CC; p = 0.53). No se encontraron diferencias*

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Fecha de recepción: 09-06-2019
Fecha de aceptación: 08-10-2019
DOI: 10.24875/CIRU.19001353

Cir Cir. 2020;88(3):314-320
Contents available at PubMed
www.cirugiaycirujanos.com

en recidiva local (6.5% CL y 8.6% CC; p = 0.49), a distancia (12.1% CL y 16.1% CC; p = 0.3), al dividir la recidiva, la sobrevida global y la sobrevida libre de enfermedad por estadios. **Conclusiones:** *La CL es un procedimiento seguro, con una sobrevida global, una sobrevida libre de enfermedad y una tasa de recidiva similares a las de la CC. La CL debería ser la indicación inicial en el cáncer de colon no metastásico en nuestra población.*

Palabras Clave: *Neoplasia colónica. Colectomía. Laparoscopía. Morbilidad. Análisis de supervivencia.*

Introduction

In times when multimodal management of colon cancer is undisputed, surgery continues to be the gold standard[1,2]. Multiple studies showed that laparoscopic colectomy (LC) presents similar results to conventional colectomy (CC)[1-3].

LC presents a faster recovery, lower morbidity, mortality, and hospital length of stay compared to CC[1-3]. Likewise, multiple studies have demonstrated the oncological safety of LC for colon cancer with respect to overall survival (OAS), disease-free survival (DFS), and recurrence[4-13] at 3- and 5-year follow-up.

Since the first published series in 1991 by Jacobs et al.[14], the use of laparoscopy for colorectal surgery has been spreading through the different high complexity surgical services. In underdeveloped countries, as in South America, this situation is different as we present certain limitations. Among them are the lack of accessibility to the necessary technology, the lack of trained surgeons and the difficulty of accepting the laparoscopic technique that some surgical services still present nowadays. Therefore, we believe that the results presented by the large series published so far should be taken with caution since they cannot be extrapolated to our environment.

The objectives of this study are to compare short-term and oncological outcomes at 3-year follow-up between LC and CC in two tertiary care academic hospitals.

Materials and methods

We performed a retrospective study including every LC and CC for colon cancer performed between January 2010 and December 2017 in Hospital Privado Universitario de Córdoba and Hospital Raúl Ferreyra. Colectomies for colon cancer stage I to III confirmed by biopsy were included in the study. We excluded patients older than 85 years, colectomies for stage IV, benign tumors, other histological types of colon cancer, and rectal surgery.

Demographics, conversion rate, surgical indication, and surgical time were studied. Short-term outcomes were analyzed at 30 days follow-up and classified according to Clavien-Dindo. Complications among 30 days were recorded and divided into global morbidity including all of them; minor complications for those $\leq$ 3a; and major complications for those $\geq$ 3b according to Clavien-Dindo criteria. The hospital length-of-stay, readmission, surgical site infection, dehiscence of anastomosis and reintervention were also analyzed. Regarding oncological results, we evaluated the number of lymph nodes resected, the presence of compromised margins and histopathology.

For those patients who had completed a 3 years follow-up, we analyzed OAS, DFS, and recurrence (global, local, and distant). OAS was calculated from the date of surgery to the date of death from any cause. Patients alive or lost to follow-up were censored at the date last known to be alive. DFS was calculated from the date of surgery to the date of recurrence or death (from any cause). Patients alive without recurrence disease or lost follow-up were censored at the date last known to be alive or recurrence-free. Time to global, local, or distant recurrence was calculated from the date of surgery to the date of recurrence. Patients without evidence of recurrence at death were censored at the date of death. Follow-up after 3 years from surgery was censored in all analyses.

Qualitative variables were analyzed with the chi-square test while the quantitative variables were analyzed with the Student's t-test. OAS, DFS, and recurrence were analyzed using Kaplan–Meier method and tested with logrank test. We analyzed variables independently associated with OAS, DFS, and recurrence from the multivariate analysis. The IBM SPSS Statistics 25 program was used for the statistical analysis.

Results

We included 269 patients who underwent colectomy for colon cancer between January 2010 and December 2017. In the same period, 386 patients were excluded from the study. CC was performed in 37.5% (n = 101) and LC in 62.5% (n = 168) of the cases. Demographic variables are shown in table 1.

Table 1. Demographic variables

Variables	Laparoscopic n (%)	Conventional n (%)	p
Age (median and SD)	64 (11)	66 (12)	0,12
Sex			0,63
Man	44 (74)	66 (67)	
Women	56 (94)	34 (34)	
ASA			0,73
1	1.5 (3)	1 (1)	
2	67 (112)	53 (53)	
3	30 (50)	45 (46)	
4	1.5 (3)	1 (1)	
Hypertension	52 (88)	59 (60)	0,26
Smoking	43 (72)	40 (40)	0,64
Diabetes	9 (16)	10 (10)	0,91
Renal disease	3 (5)	7 (7)	0,12
Heart disease	14 (24)	13 (13)	0,74

SD: standard deviation; ASA: American Society of Anesthesiologists score.

Table 2. Surgical indication

Variables	Laparoscopic n (%)	Conventional n (%)
Sigmoidectomy	19 (32)	21 (21)
Right colectomy	50 (84)	42 (42)
Left colectomy	29 (48)	27 (27)
Transverse colectomy	-	4 (4)
Total colectomy	2.4 (4)	7 (7)

LC presented shorter operative time than CC (157 vs. 175 min, p = 0.01). Conversion was required in 8.3% (n = 14). Surgical indication is detailed in table 2. Patients who underwent LC required less hospital length-of-stay than the CC (8.4 vs. 10.5 days, p = 0.02). The 30-day mortality was 1.2% (n = 2) in LC and 3% (n = 3) in CC (p = 0.36). LC presented lower overall morbidity than CC (40% vs. 56%, p = 0.01). When we divided them by major and minor complications, no statistically significant differences were observed although the trend was always in favor of LC and is detailed in table 3. In addition, LC required lees readmission than CC (6% vs. 15%, p = 0.02). No differences were found between both procedures for reintervention (CL 7% vs. CC 8%, p = 0.81). Patients who underwent CC required more transfusions (32% vs. 19%, p = 0.01) and presented more surgical site infection (31% vs. 19%, p = 0.02) than those in the LC group.

No positive distal margins were found in both procedures. The mean number of resected lymph nodes

Table 3. Morbidity and mortality

Variables	Laparoscopic n (%)	Conventional n (%)	p
Mortality	1.2 (2)	3 (3)	0.36
Morbidity	40 (68)	56 (57)	0.01
Minor complication	29 (49)	39 (39)	0.11
Major complication	11 (19)	17 (17)	0.19
Surgical time (median and SD)	157 (57)	176 (62)	0.01
Length-of-stay (median and SD)	8.4 (7)	10.5 (7)	0.02
Reintervention	7 (12)	8 (8)	0.81
Readmission	6 (11)	15 (15)	0.02
Transfusions	19 (32)	32 (32)	0.01
Hemorrhage	0.6 (1)	2 (2)	0.55
Pneumonia	1.2 (2)	4 (4)	0.2
Urinary infection	1.2 (2)	1 (1)	0.9
Catheter infection	0.6 (1)	2 (2)	0.55
Surgical site infection	19 (33)	31 (32)	0.02
Dehiscence of anastomosis	14 (23)	17 (17)	0.48

SD: standard deviation.

Table 4. Oncologic outcomes

Variables	Laparoscopic n (%)	Conventionwal n (%)	p
Stage I	22 (37)	13 (13)	0.11
Stage II	38 (63)	43 (43)	0.41
Stage III	41 (68)	45 (45)	0.12

was 15 for CC and 18 for LC (p = 0.03). No statistically significant difference was found in the rest of the oncological results and is shown in table 4.

At the time of analysis, the median follow-up was 40 months, 48 in CC and 37 in LC. A total of 217 patients completed the 3-year follow-up and were included in the survival analysis, 57.1% of them corresponded to LC and 42.9% to CC. Follow-up was lost in 8.6% in CC and in 3.2% in LC. No differences were found regarding to OAS (87.1% in LC vs. 82.8% in CC, p = 0.28, Fig. 1) and DFS (78.2% in LC vs. 75.3%, p = 0.47, Fig. 2) at 3-year follow-up between both groups. There was also no difference between the two procedures when the analysis was performed by stage (Table 5) (Fig. 3).

Recurrence was observed in 37 patients during follow-up, 16.1% in LC and 18.3% in CC (p = 0.53). In the recurrence analysis at 3-years follow-up, no differences

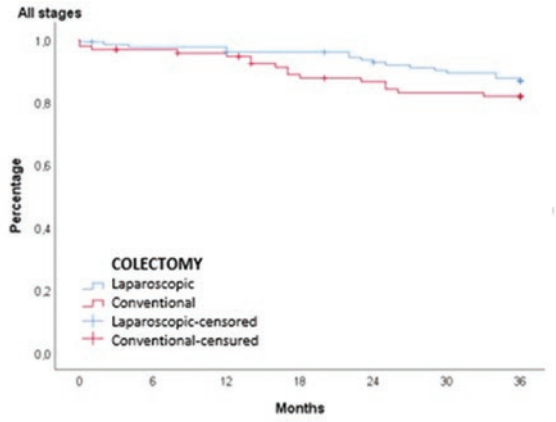

Figure 1. *Overall survival in all stages.*

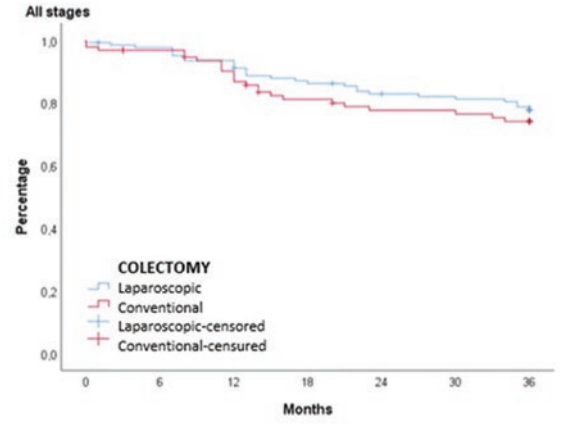

Figure 2. *Disease-free survival in all stages.*

were found, overall local recurrence was 7.4% (6.5% in LC vs. 8.6% in CC, p = 0.49) while overall distant recurrence was 13.8% (12.1% in LC vs. 16.1% in CC, p = 0.3). The stage analysis showed no statistical difference between both procedures (Table 6).

The multivariate analysis showed no variables independently associated with OAS, DFS, and recurrence.

Discussion

Multiple studies have shown that LC presents similar results to CC in the treatment of colon adenocarcinoma because it is a procedure with lower morbidity and mortality and good long-term oncological results[1-5,7]. This study allowed us to confirm these results in our population and establish LC as a feasible therapeutic option for colon adenocarcinoma stage I-III.

As we mentioned before, in underdeveloped countries, we present certain limitations to reach these outcomes. Despite this, there is recent evidence that

Table 5. DFS at 3-year follow-up by stage

Variables	Laparoscopic (%)	Conventional (%)	p
Global DFS	78.2	75.3	0.47
Stage I	92.6	83.3	0.37
Stage II	78	74.4	0.66
Stage III	70.2	73.8	0.9

DFS: Disease-free survival.

Table 6. Recurrence

Variables	Laparoscopic (%)	Conventional (%)	p
Stage I			
Global recurrence	7.4	8.3	0.86
Local recurrence	3.7	8.3	0.54
Distant recurrence	3.7	7.7	0.49
Stage II			
Global recurrence	12	17.9	0.43
Local recurrence	6	12.8	0.27
Distant recurrence	8	12.8	0.45
Stage III			
Global recurrence	25.5	21.4	0.84
Local recurrence	8.5	4.8	0.53
Distant recurrence	21.3	21.4	0.83

LC is a safe procedure in our region. Bernal et al.[15] in Medellin (Colombia) compared 33 LC with 38 CC and found no differences between both procedures to short-term and oncologic results. Vendramini et al.[16] in Florianopolis (Brazil) analyzed 110 colectomies and compared short-term outcomes in both procedures and found that LC presents longer surgical time, shorter hospital length-of-stay, and morbidity.

We have shown that LC is a safe procedure with post-operative results similar to CC. Surgical time was shorter in LC (157 vs. 176 min, p = 0.02). Nelson et al.[7] and Guillou et al.[17] reported a longer duration of surgery in LC (150 vs. 95 min, p = 0.001; 180 vs. 135 min). Furthermore, time spent in the operating theatre was shorter in patients assigned for CC than for those assigned LC (170 vs. 202 min, p = 0.0001) in Colon cancer laparoscopic or open resection (COLOR)[18] trial. Results presented in this study demonstrate that LC is a procedure 19 min shorter than CC. This could be explained because of the learning curve was already reached before the study. In addition, since this study was performed in an academic hospital, residents have more participation in CC which may extend the surgical time. Despite this result, we do not believe that LC provides an advantage in terms of shorter surgical time and these results are due to a purely statistical issue rather than a real advantage.

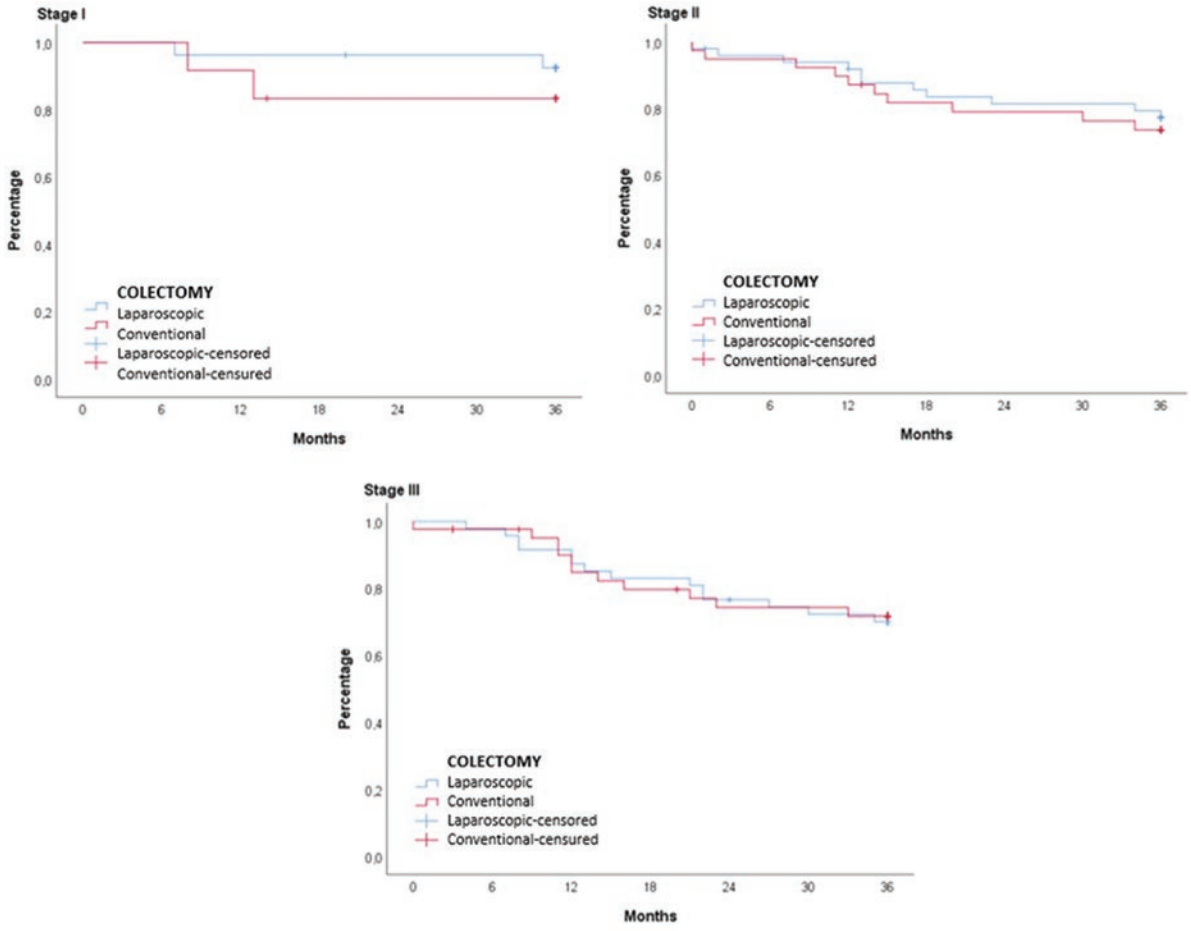

Figure 3. *Disease-free survival by stages. 1-stage I. 2-stage II. 3-stage III.*

In our series, LC presented a shorter hospital length of stay (8 vs. 10 days, p = 0.02) and less readmission (6% vs. 15%, p = 0.02). Lower hospital length of stay was previously demonstrated by Nelson et al.[7] (5 vs. 6) and Veldkamp et al.[18] (8 vs. 9). There was no difference in reintervention (7% vs. 8%, p = 0.81). Similar results presented Veldkamp et al.[18], where no differences were found between both procedures and the percentage was similar (7% vs. 5%, p = 0.13). In addition, LC was converted in 8.3%. The largest series published so far showed a need for conversion of LC of 15-20% in small-volume centers and 10% in reference centers[7,11,17,18].

Multiple studies analyzed global morbidity with no difference found[7,17,18]. In our study, it was lower in LC (40% vs. 56%, p = 0.01). Lacy et al.[11] presented similar results for LC (relative risk [RR] = 0.49, 95% CI = 0.30-0.82, p = 0.001). When morbidity was divided in major and minor complications, no differences were found in our population, although the trend was always in favor of LC (11% vs. 17%, 29% vs. 39%, respectively). The same results were found in mortality where no differences were found between both procedures (1.2% vs. 3%, p = 0.36). In addition, LC required less blood transfusions (19% vs. 32%, p = 0.01) and presented less surgical site infection (19% vs. 31%, p = 0.02). Similar outcomes were shown by Veldkamp et al.[18] and Lacy et al.[11] who found that LC had less blood loss than CC (p = 0.001).

What had been stated so far confirms LC as a safe procedure with similar postoperative results to CC in our population. LC is a procedure that presented less surgical time, hospital length of stay, reintervention, overall morbidity, blood transfusions, and surgical site infection.

The mean number of resected lymph nodes was higher in LC (18 vs. 15, p = 0.03). There are several study groups that did not find differences in the number of lymph nodes harvested. Veldkamp et al.[18] and Buunen et al.[4] presented similar results with no differences between both procedures (10 nodes in both procedures, p = 0.35 and p = 0.32, respectively). Guillou et al.[17], on the other hand, presented a median of 13.5 in CC and 12 in LC without statistically significant

differences. On the other hand, Kuhry et al.[8] in a Cochrane meta-analysis that included 3346 patients found that LC presents fewer resected nodes than CC (p = 0.003).

No differences were found between both procedures for the commitment of distal margins or staging. In preoperative evaluation, colonoscopy was performed in all patients with biopsy and methylene blue marking of the tumor. Moreover, oncological criteria were respected avoiding short segmental block resections. All specimens were analyzed macroscopically in the operating room before finishing surgery to define the need to expand resection. Furthermore, if there was any doubt during surgery, intraoperative endoscopy was performed to define margins of resection. In addition, in this study stage IV tumors and rectal surgery were excluded, so delimiting margins of resection did not present any difficulty since being marked and without the need to search for distal margin in the pelvis allowed us to grant a good macroscopic surgical margin.

As has been shown until today, most of the authors did not find differences with respect to OAS and DFS[1,4,6,7,8]. CLASICC group[12] did not find differences in the 3-year follow-up in OAS (CC = 66.7% vs. LC 68.4%, p = 0.55) and DFS (CC = 67.7% vs. LC = 66.3%, p = 0.7). Same results were found when it was analyzed for 5-year follow-up[5]. COLOR group[4], on the other hand, analyzed the same results at 3-year between LC and CC, finding an OAS of 81.8% versus 84.2% (p = 0.45) and a DFS of 74.2% versus 76.2% (p = 0.7), respectively. In our population, we found similar results (OAS CL = 87.1% vs. CC = 82.2% and DFS LC = 78.2% vs. CC = 75.3%) without significant differences. When performing the same analysis divided by stages, we did not find differences either, so we can affirm that we present similar results to those obtained in large series[7,4,12].

Recurrence was analyzed at 3-year in terms of global, local, and distant recurrence and no differences were found. Same results were found when recurrence was analyzed by stage. LC presented local recurrence in 6.5% and distant recurrence in 12.1% while CC presented local recurrence in 8.6%, and distant recurrence in 16.1%. CLASICC group[12] published a 3-year local recurrence of 7.3% in LC and 6% in CC (p = 0.68). Moreover, they showed similar results in terms of distant recurrence (LC = 11.3% vs. CC = 12.5%). COLOR[4] group presented no differences in local, distant, and global recurrence (p = 0.24) in 3-year follow up. Moreover, Nelson et al.[7] presented a global recurrence rate in LC which did not differ significantly in CC (17% vs. 19%, p = 0.32). The present study demonstrates that LC is a safe procedure with similar recurrence rates (global, local, and distant) to CC at 3-year follow-up.

This study has some limitations. Among them, it stands out that it is a non-randomized retrospective study that presents a reduced number of patients. However, we believe that it demonstrates the safety of LC in colon cancer in terms of post-operative morbimortality and oncological safety in 3-year follow-up in our population.

Conclusions

The findings of this study confirm LC as a safe procedure with post-operative results similar to CC in our population. In addition, it presents similar OAS, DFS, and recurrence (global, local, and distant) at 3-year follow-up, which is why we can affirm that it is a procedure with proven oncological safety. Based on what it has been exposed, LC should be the initial indication in patients with non-metastatic colon cancer in our population.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Funding

The authors declare that there was no funding used for this research project.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals in this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy an informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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