ORIGINAL ARTICLE

No inflammatory benefit obtained by single-incision laparoscopic surgery for right hemicolectomy compared with conventional laparoscopy

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Abstract

Purpose We evaluated the perioperative inflammatory mediators in a right hemicolectomy performed with single-incision laparoscopic surgery (SILS) and traditional multi-port laparoscopic surgery (MLS) to compare the postoperative inflammatory response and feasibility of SILS with that of MLS.

Methods In this retrospective study, we enrolled 56 consecutive colorectal cancer patients who underwent right hemicolectomy prospectively. Twenty patients underwent SILS, and 36 underwent MLS. The preoperative and postoperative levels of plasma vascular endothelial growth factor (VEGF), serum interleukin-6 (IL-6), and C-reactive protein (CRP) as well as the number of platelet cells were measured in all patients. The operation duration, number of harvested lymph nodes, length of the resected bowel, blood loss, and duration of hospital stay were also compared between the two groups.

Results Neither SILS nor MLS had any conversion cases. The operation duration was longer for MLS than for SILS. Blood loss tended to be lower among patients who underwent SILS than among those who underwent MLS. However, the number of harvested LNs was significantly lower with SILS than with MLS. In both pre- and postoperative blood examinations, there was no marked difference in inflammatory mediators between MLS and SILS.

Conclusion There was no systemic inflammatory advantage associated with SILS compared with MLS.

Keywords SILS · IL-6 · Systemic inflammation · Right hemicolectomy

Introduction

Minimally invasive procedures are an important topic in surgery. Since laparoscopic surgery was first introduced for cholecystectomy, the use of this technique has been expanded to various kinds of surgery. However, with laparoscopic surgery, four to six ports and sometimes a 4-cm mini-laparotomy incision have been necessary.

Recent years have seen the widespread incorporation of new surgical techniques that reduce abdominal wall destruction, such as reduced-port surgery and natural orifice transluminal endoscopic surgery (NOTES). Single-incision laparoscopic surgery (SILS), the ultimate form of reduced-port surgery, has been reported in various contexts. With respect to the number and length of surgical wounds, SILS is superior to traditional multi-port laparoscopic surgery (MLS). Many investigators have also reported the superiority of SILS in light of its reduced postoperative pain, faster recovery time, reduced blood loss and improved cosmetic results [1–4]. However, no evidence has yet been shown regarding whether or not SILS is associated with less systemic inflammation than MLS.

Therefore, in the present study, we evaluated the levels of several inflammatory mediators before and after SILS and MLS to determine whether or not SILS is superior to MLS with respect to systemic inflammation.

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Patients and methods

For this retrospective study, we enrolled 56 patients [males 27; median age 76.5 (range 52–90) years] with right-sided colon cancer (cecal 9; ascending 40; transverse 7) undergoing right hemicolectomy at Nagoya City University Hospital from January 2012 to August 2015 (Table 1). Patients with distant metastasis or unresectable tumors were excluded because the unresected lesion might cause residual inflammation. No marked physical or oncologic differences between the two groups were observed (Table 2).

The platelet count and serum interleukin (IL)-6, plasma vascular endothelial growth factor (VEGF), and C-reactive protein (CRP) levels were measured preoperatively and on postoperative days (POD) 1, 3, and 7. The operative time, blood loss, harvested lymph node number, length of the resected bowel, postoperative complications, and postoperative hospitalization duration were also compared between the two groups. Postoperative complications were classified according to the Clavien–Dindo system [5]. This study was approved by the Nagoya City University Graduate School of Medical Sciences and Nagoya City University Hospital Institutional Review Board (60160172).

Surgical procedures

On the evening before surgery, all patients underwent preoperative bowel preparation with 500 mL of magnesium citrate. Patients were placed in the supine position for the

Table 1 Clinicopathological characteristics of all 56 patients with colon cancer

Variables	($n = 56$)	%
Age (median years ± SD)	76.5 ± 7.2	
Gender		
Male	27	44.1
Female	29	55.9
Tumor location		
C	9	16.1
A	40	71.4
T	7	12.5
pT		
< 3	16	28.6
3, 4	40	71.4
Previous OP		
With	13	23.2
Without	43	76.8
Body mass index (range)	22.2 (15.3–34.3)	

SD standard deviation, *pT* depth of tumor, *C* cecum, *A* ascending colon, *T* transverse colon, *OP* operation

Table 2 Clinicopathological characteristics of each group

Variable	MLS group		SILS group		p value
	($n = 36$)	%	($n = 20$)	%	
Age (years)[a]	74.5 ± 8.2		78.5 ± 7.3		0.3
Gender					
Male	20	55.6	7	35.0	0.1
Female	16	44.4	13	65.0	
Tumor location					
C, A	32	88.9	17	85.0	0.4
T	4	11.1	3	15.0	
pT					
< 3	10	27.8	6	30.0	0.9
3, 4	26	72.2	14	70.0	
Previous OP					
With	9	25.0	4	20.0	0.7
Without	27	75.0	16	80.0	
Body mass index[a]	22.2 ± 2.3		21.7 ± 4.9		0.9

MLS multi-port surgery, *SILS* single-port surgery, *pT* depth of tumor, *C* cecum, *A* ascending colon, *T* transverse colon, *OP* operation

[a]Median ± standard deviation

operation. Epidural anesthesia or intravenous patient-controlled anesthesia (IVPCA) was performed according to the patient's bleeding risk. For SILS, an EZ access (Hakko Medical, Nagano, Japan) was placed using a 2.5-cm transverse umbilical incision. A 12-mm trocar and two 5-mm trocars were inserted into the EZ access. The operating surgeon and laparoscopist stood on the patient's left side. For MLS, a 12-mm trocar was placed at the umbilicus, and four 5-mm trocars were placed in a square. The 12-mm umbilical incision was extended to 4 cm as a mini-laparotomy for the retrieval of the specimen and anastomosis. In both procedures, the same types of straight laparoscopic instruments were used via the 5-mm ports, and a flexible 12-mm scope (Visela Pro, Olympus, Japan) was inserted via a 12-mm port. The intra-abdominal procedures were the same for SILS and MLS, as described below.

Patients were placed in the Trendelenburg position with right-sided elevation, and the ileocecal artery (ICA) and vein (ICV) were ligated at their roots. The right colic artery and right branch of the middle colic artery (MCA) were dissected according to the tumor location. In many cases, the ICA ran behind the superior mesenteric vein (SMV). In such cases, ICA ligation was performed at the right side of the SMV. The anterior side of the SMV was dissected up to an appropriate level.

From this mesenteric incision, the mesentery of the ascending and transverse colon was dissected from the duodenum by a medial approach. Once this dissection approached the omental bursa, the ascending colon mesentery was dissected by a medial approach toward the

ascending colon. Following this dissection, lateral dissection of the right side of the ascending colon and anterior dissection of the omentum enabled the specimen to be retrieved from the umbilical incision. The specimen was retrieved from the SILS port of the cecum superiorly without bowel transection. In case of a huge tumor or bulky colon mesentery interfering with retrieval, 1- or 2-cm laparotomy was performed. The oral and anal bowel margins were 10 cm apart. Anastomosis was performed by functional anastomosis with an Echeron flex. The strategy concerning the dissection area and length of the bowel cut line were the same for both SILS and MLS. Abdominal drainage was not routinely placed. However, lymphadenectomy in MLS was similar to that in SILS. Traction and countertraction were performed using the left-hand grasper of the operating surgeon and both graspers of the assistant surgeon. In brief, by lifting up the pedicle using the assistant surgeon's grasper and performing traction using the operating surgeon's left-hand grasper, the mesentery was cut using an electrocautery spatula to the root of the ICA and ICV. In the same setting, lymphadenectomy was performed as far as the root of the MCA at the surface of the SMV.

Statistical analyses

Student's *t* test was used to compare the demographic characteristics and surgical outcomes between the SIL and MLS groups. The Mann–Whitney test was used to compare laboratory values between the two groups (platelet count, plasma VEGF, serum IL-6, and CRP). A *p* value < 0.05 was considered statistically significant. Univariate analyses of the platelet count and plasma VEGF, serum IL-6, and CRP levels were performed.

Results

Measurement of inflammatory mediators

We obtained pre- and postoperative levels of serum IL-6 (Fig. 1), plasma VEGF (Fig. 2), and serum CRP (Fig. 3) as well as platelet cell numbers (Fig. 4). There were no significant differences in the levels of IL-6 either pre- or postoperatively between the SILS and MLS groups. The median levels of IL-6 peaked at POD 1 among patients who underwent either SILS or MLS. Indeed, the IL-6 levels were approximately 60-fold higher in both groups at POD 1 than the preoperative levels. The levels of IL-6 did not return to the baseline by POD 7 but remained three to fivefold higher than the preoperative levels.

Similar but non-significant trends were observed for the VEGF values between groups. The median VEGF levels

preoperatively and 1, 3, and 7 days postoperatively were 25.0 ± 26.7, 25.0 ± 26.7, 92.0 ± 81.5 and 82.0 ± 140.3 ng/mL, respectively, for the SILS group, and 43.0 ± 47.4, 94.0 ± 61.4, 58.0 ± 127.9 and 59.0 ± 97.5 ng/mL, respectively, for the MLS group.

In addition, no significant differences were observed in the number of platelet cells between the SILS and MLS procedures. In both groups, the peak median platelet numbers were observed at POD 7 (269.0 ± 49.1 for SILS and 294.0 ± 91.0 for MLS).

There were also no significant differences in the levels of the traditional inflammatory mediator CRP between the SILS and MLS groups, either pre- or postoperatively. Indeed, the levels of CRP preoperatively and 1, 3, and 7 days postoperative were 0.2 ± 0.6, 7.69 ± 3.9, 11.2 ± 5.7 and 1.9 ± 4.2 mg/dL, respectively, for SILS, and 0.2 ± 0.2, 7.8 ± 1.2, 8.6 ± 1.3 and 2.1 ± 1.8 mg/dL, respectively, for MLS.

Quality of operation

The median SILS operative time (180.5 min) was less than that of MLS (236.5 min), and this difference in the operation duration was significant ($p < 0.0001$). Similarly, the median blood loss was lower with SILS (21.0 mL) than with MLS (85.0 mL) ($p = 0.009$). The median number of lymph nodes harvested during SILS (10) was significantly lower than that during MLS (13) ($p = 0.03$). However, the length of the resected bowel was almost the same in SILS (20.0 cm) and MLS (22.5 cm) ($p = 0.7$) (Table 3).

Short-term outcomes

The median hospital stay after SILS (9 days) was almost the same as that following MLS (9 days) ($p = 0.8$). There were three postoperative complications after MLS (anastomotic bleeding in two; colitis in one) and three after SILS (ileus in two; venous emboli in one). All complications were Clavien–Dindo grade 1, regardless of the procedure type (Table 3).

Discussion

Since the original report of single-port surgery in the 1990s [6–8], the use of this technique has spread to various surgery types. At first, this technique began with simple surgeries, such as appendectomy or cholecystectomy. Presently, this technique is performed for comparatively difficult surgeries, such as nephrectomy or rectal resection [9]. SILS has been reported to be superior to MLS, with respect to cosmetics and pain control [2]. To date, several studies have compared
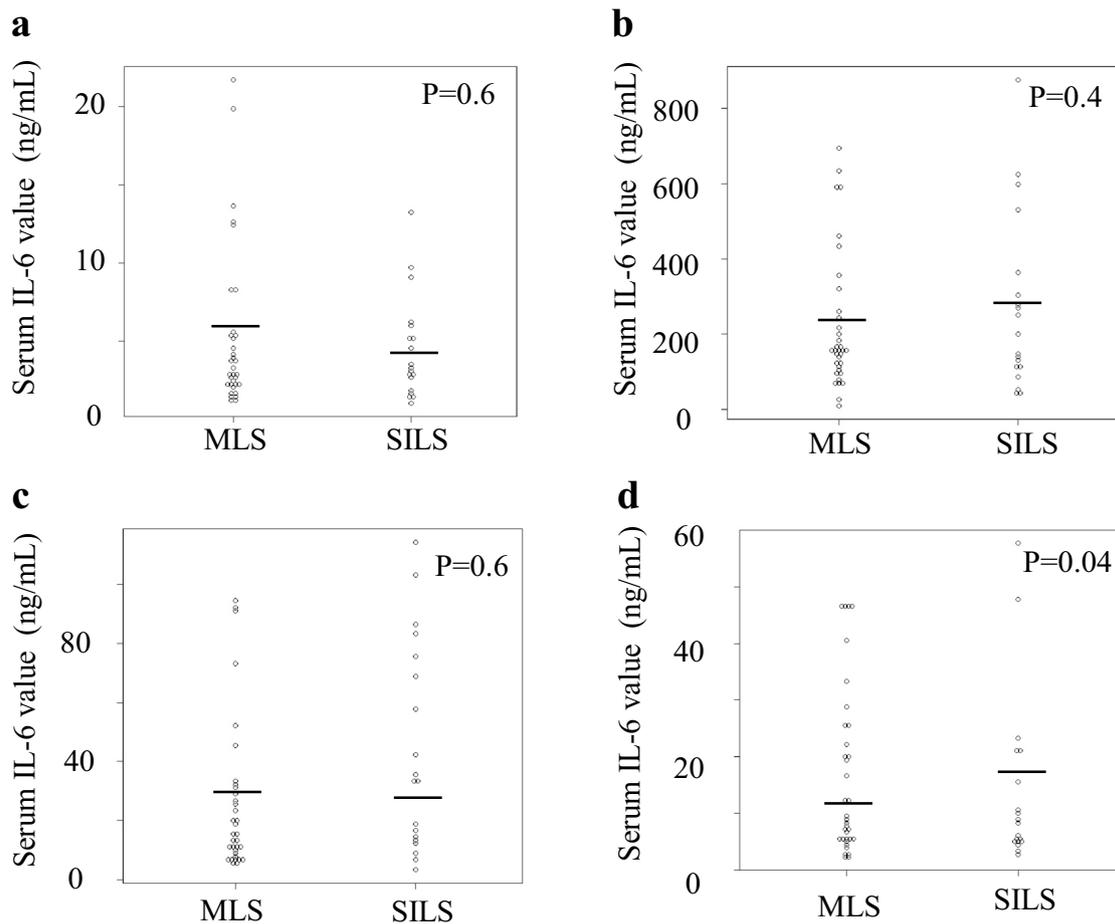
a

b

c

d

Fig. 1 Multi-port and single-incision laparoscopic surgery perioperative serum interleukin-6 values. Measured (dot) and mean (bar) preoperative (**a**) and postoperative days 1 (**b**), 3 (**c**), and 7 (**d**) interleukin-6 values

SILS right hemicolectomy with MLS right hemicolectomy [1, 3, 4, 10–15]. These reports have shown SILS to be advantageous with respect to cosmetics [1] and shorter hospital stays [3, 4]; however, no benefit concerning the short-term surgical outcome has been shown [1, 10]. In many reports, SILS was performed as safely as MLS [1, 3, 4, 11–14] with no conversion cases [3, 14] but with a longer operative time [12]. Our findings regarding the short-term outcomes and quality of SILS and MLS operations were very similar to those of previous reports. Despite the technical difficulty of SILS, we found that the short-term outcomes associated with this procedure were feasible when compared with those of MLS. It is not clear why the number of harvested lymph nodes was significantly different between these two groups despite the fact that we used the same strategy for creating the dissection area and that both procedures were associated with similar lengths of resected bowel.

However, the systemic inflammation with SILS was quite different from what we had expected. Serum IL-6 has been used as a marker of systemic inflammation for laparoscopic and open surgery for the past two decades [16, 17]. These studies showed that laparoscopic surgery is associated with lower postoperative values of serum IL-6, thereby suggesting that laparoscopic surgery is less invasive than open surgery. However, our results revealed no marked difference in the postoperative levels of IL-6 between SILS and MLS. In this study, several inflammatory mediators, such as IL-6, VEGF, and the platelet cell count, were evaluated as well as the traditional inflammatory mediator CRP. The levels of the angiogenetic factor VEGF are increased in an inflammatory state, which is reported to cause postoperative cancer metastasis after inflammation [18]. The platelet cell count often increases under conditions of inflammation induced by several cytokines. In addition, we found no difference in
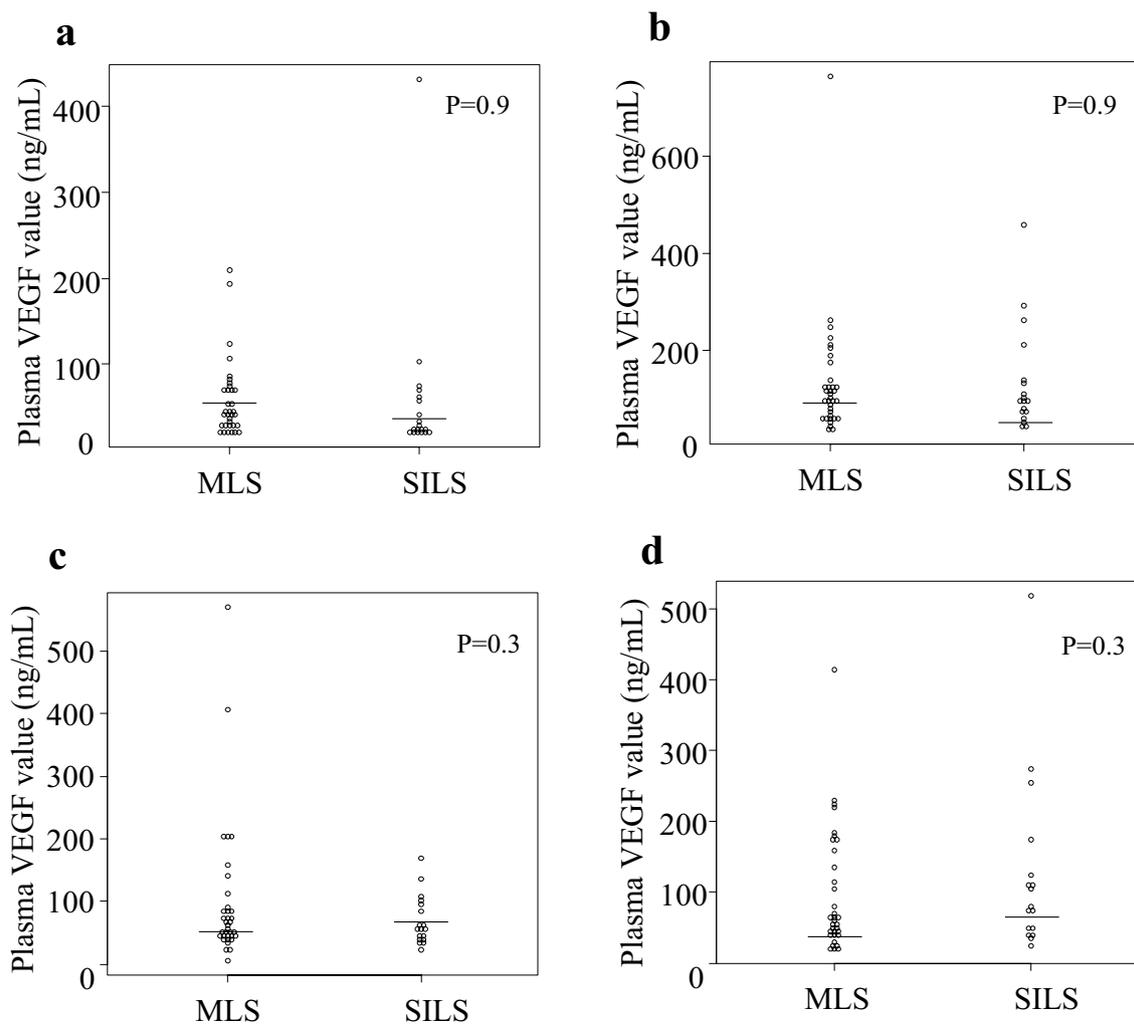
Fig. 2 Multi-port and single-incision laparoscopic surgery perioperative plasma vascular endothelial growth factor values. Measured (dot) and mean (bar) preoperative (**a**) and postoperative days 1 (**b**), 3 (**c**), and 7 (**d**) vascular endothelial growth factor values

the VEGF or CRP levels or the platelet cell count between the two procedures. The levels of these mediators peaked at postoperative days 1 (IL-6 and VEGF), 3 (CRP), and 7 (platelet cell number). The peak levels of IL-6, VEGF, and CRP tended to be higher in the SILS group than in the MLS group; however, there were no significant differences between the groups, suggesting that SILS and MLS are associated with similar levels of systemic inflammation. Furthermore, this result failed to indicate the oncological benefit of SILS caused by reducing the plasma VEGF level.

To date, only three studies have investigated the levels of IL-6 following MLS and SILS. One study was conducted in pigs, and the remainder investigated inflammation following cholecystectomy [19–21]. These reports showed no

inflammatory difference between MLS and SILS. To our knowledge, ours is the first report to evaluate the differences in IL-6 levels following laparoscopic colectomy.

One possible reason why we observed no marked difference in inflammation between SILS and MLS is the small difference in invasiveness between the incision and abdominal procedures. Certainly, the incision of SILS is smaller than that of MLS. However, its difference is no more than 2–3 cm in length. Conversely, the dissection area in the abdominal cavity is ≥ 20 cm from the colon bowel and its mesentery. It is clear that the 2- to 3-cm difference in incision is minimally invasive compared with large intra-abdominal dissection. Similar results were observed in the NOTES study [22, 23]. Another study in
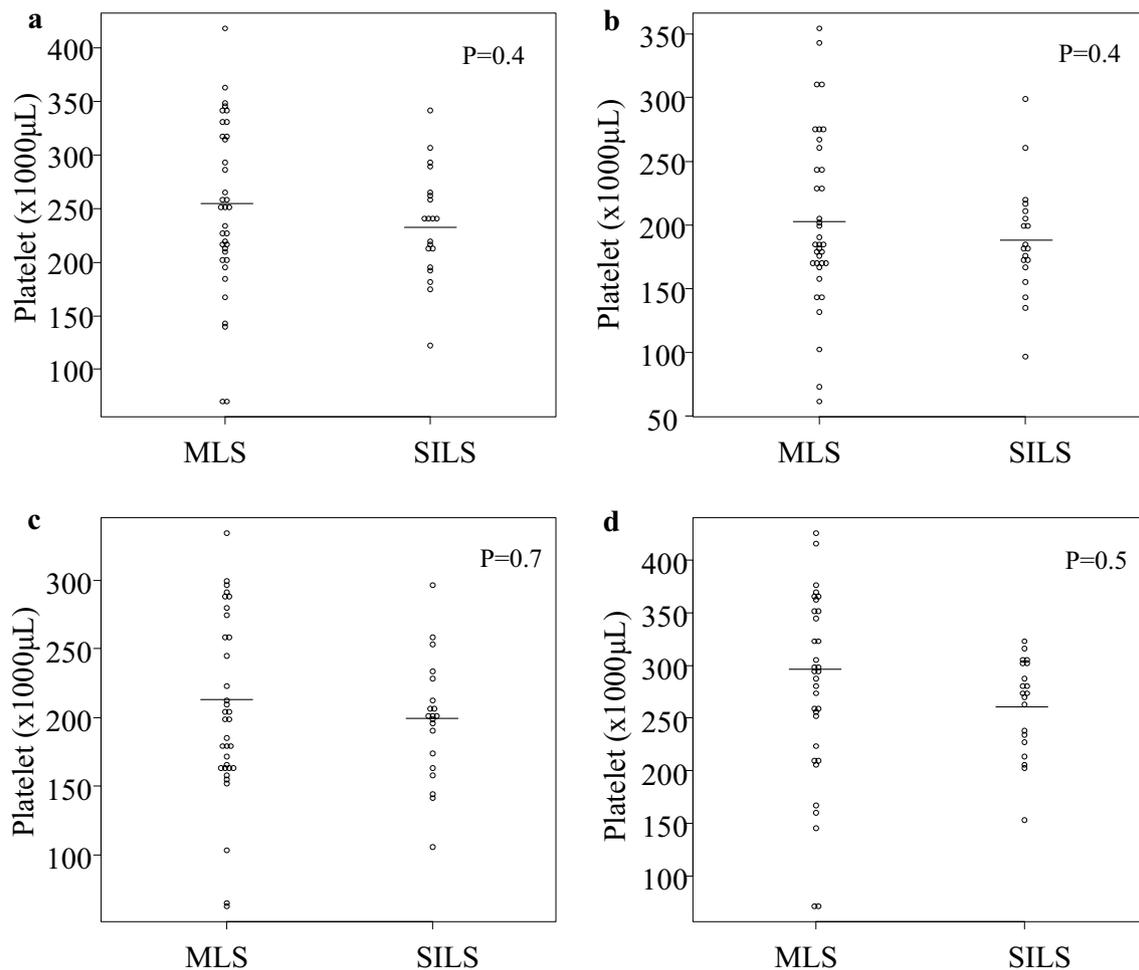
Fig. 3 Multi-port and single-incision laparoscopic surgery perioperative platelet counts. Measured (dot) and mean (bar) preoperative (**a**) and postoperative days 1 (**b**), 3 (**c**), and 7 (**d**) platelet counts

a rat model showed that the serum IL-6 level was higher in the NOTES group than in the conventional laparoscopic group [24]. This technique does not require a mini-laparotomy to retrieve the specimen. In some cases, even the incision for trocars can be omitted. Several studies have reported that systemic inflammation was similar between this less invasive surgery and conventional surgery. These findings suggest that such a small difference in invasiveness may not translate into reduced inflammation for either the NOTES procedure or SILS.

Nevertheless, it is clear that fewer and smaller incisions are superior when considering cosmetics, especially for young female patients. Our results showed that SILS is safe and of similar quality to MLS. However, SILS was not shown to be less invasive than MLS.

Conclusions

In this study, we demonstrated the equivalent feasibility and surgical quality of SILS and MLS. Although SILS was associated with a reduced operation time and blood loss, we did not note any remarkable inflammatory benefit of SILS compared with MLS. Further larger-scale randomized studies will be necessary to confirm these findings.
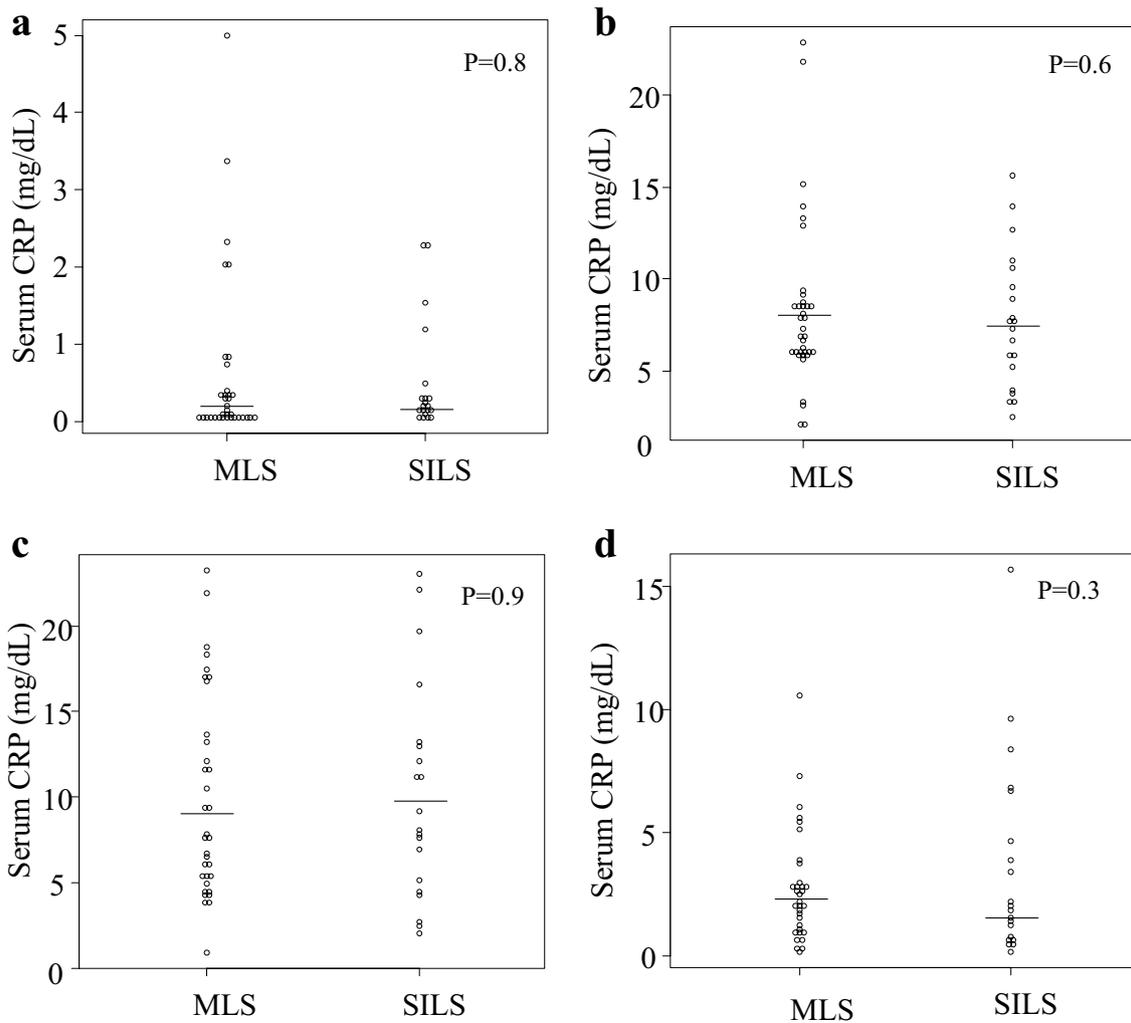
Fig. 4 Multi-port and single-incision laparoscopic surgery perioperative serum C-reactive protein values. Measured (dot) and mean (bar) preoperative (**a**) and postoperative days 1 (**b**), 3 (**c**), and 7 (**d**) C-reactive protein values

Table 3 Short-term outcomes and quality of the operation of MLS and SILS

Variable	MLS (n = 36)	SILS (n = 20)	p value
Operation time (min)[a]	236.5 ± 54.8	185.5 ± 45.7	< 0.0001
Blood loss (g)[a]	85.0 ± 101.4	21.0 ± 44.6	0.009
Harvested lymph node[a]	13 ± 7.8	10 ± 4.9	0.03
Length of resected bowel (cm)[a]	22.5 ± 9.0	20.0 ± 7.9	0.7
Postoperative complication			1.0
Clavien–Dindo grade < 3	3	3	
Clavien–Dindo grade ≥ 3	0	0	
Hospital day[a]	9.0 ± 10.8	9.0 ± 10.5	0.8

MLS multi-port surgery, *SILS* single-port surgery

[a]Median ± standard deviation

Compliance with ethical standards

References

1. Chen WT, Chang SC, Chiang HC, Lo WY, Jeng LB, Wu C, Ke TW. Single-incision laparoscopic versus conventional laparoscopic right hemicolectomy: a comparison of short-term surgical results. Surg Endosc. 2011;25:1887–92.

2. Hiraki M, Takemasa I, Uemura M, Haraguchi N, Nishimura J, Hata T, Mizushima T, Yamamoto H, Doki Y, Mori M. Evaluation of invasiveness in single-site laparoscopic colectomy, using "the PainVision system" for quantitative analysis of pain sensation. Surg Endosc. 2014;28:3216–23.

3. Keshava A, Young CJ, Richardson GL, De-Loyde K. A historical comparison of single incision and conventional multiport laparoscopic right hemicolectomy. Colorectal Dis. 2013;15:e618–22.

4. Ramos-Valadez DI, Patel CB, Ragupathi M, Bartley Pickron T, Haas EM. Single-incision laparoscopic right hemicolectomy: safety and feasibility in a series of consecutive cases. Surg Endosc. 2010;24:2613–6.

5. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibanes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien–Dindo classification of surgical complications: five-year experience. Ann Surg. 2009;250:187–96.

6. Esposito C. One-trocar appendectomy in pediatric surgery. Surg Endosc. 1998;12:177–8.

7. Navarra G, Pozza E, Occhionorelli S, Carcoforo P, Donini I. One-wound laparoscopic cholecystectomy. Br J Surg. 1997;84:695.

8. Piskun G, Rajpal S. Transumbilical laparoscopic cholecystectomy utilizes no incisions outside the umbilicus. J Laparoendosc Adv Surg Tech Part A. 1999;9:361–4.

9. Chen CW, Hsiao KH, Chang YJ, Lai CW. (2013) Single-incision laparoscopic surgery using a homemade transumbilical port for synchronous colon and hepatic lesions: a case report. Surg Laparosc Endosc Percutaneous Tech 23:e164–167.

10. Curro G, Cogliandolo A, Lazzara S, La Malfa G, Navarra G. Single-incision versus three-port conventional laparoscopic right hemicolectomy: is there any real need to go single? J Laparoendosc Adv Surg Tech Part A. 2012;22:621–4.

11. Chew MH, Chang MH, Tan WS, Wong MT, Tang CL. Conventional laparoscopic versus single-incision laparoscopic right hemicolectomy: a case cohort comparison of short-term outcomes in 144 consecutive cases. Surg Endosc. 2013;27:471–7.

12. Lim SW, Kim HR, Kim YJ. Single incision laparoscopic colectomy for colorectal cancer: comparison with conventional laparoscopic colectomy. Ann Surg Treat Res. 2014;87:131–8.

13. Mufty H, Hillewaere S, Appeltans B, Houben B. Single-incision right hemicolectomy for malignancy: a feasible technique with standard laparoscopic instrumentation. Colorectal Dis. 2012;14:e764–70.

14. Su Y, Wu, Kong J, Yu H, Fan Y, Tian Y. Single incision laparoscopic colorectal surgery using conventional laparoscopic instruments: initial experience with 44 cases. J Investig Surg. 2015.

15. Chambers WM, Bicsak M, Lamparelli M, Dixon AR. Single-incision laparoscopic surgery (SILS) in complex colorectal surgery: a technique offering potential and not just cosmesis. Colorectal Dis. 2011;13:393–8.

16. Stage JG, Schulze S, Moller P, Overgaard H, Andersen M, Rebsdorf-Pedersen VB, Nielsen HJ. Prospective randomized study of laparoscopic versus open colonic resection for adenocarcinoma. Br J Surg. 1997;84:391–6.

17. Harmon GD, Senagore AJ, Kilbride MJ, Warzynski MJ. Interleukin-6 response to laparoscopic and open colectomy. Dis Colon Rectum. 1994;37:754–9.

18. Pascual M, Alonso S, Salvans S, Mayol X, Mojal S, Gil MJ, Grande L, Pera M. Postoperative serum vascular endothelial growth factor is an independent prognostic factor of disease free survival and overall survival in patients with non metastatic colon cancer. Am J Surg. 2018;216:255–9.

19. Luna RA, Nogueira DB, Varela PS, Rodrigues Neto Ede O, Norton MJ, Ribeiro Ldo C, Peixoto AM, de Mendonca YL, Bendet I, Fiorelli RA, Dolan JP. A prospective, randomized comparison of pain, inflammatory response, and short-term outcomes between single port and laparoscopic cholecystectomy. Surg Endosc. 2013;27:1254–9.

20. Ypsilantis P, Didilis V, Tsigalou C, Pitiakoudis M, Karakatsanis A, Margioulas A, Simopoulos C. Systemic inflammatory response after single-incision laparoscopic surgery versus standard laparoscopic approach. Surg Laparosc Endosc Percutaneous Tech. 2012;22:21–4.

21. Froghi F, Sodergren MH, Wright VJ, Coomber R, Courtney AP, Darzi A, Paraskeva P. Single-center experience in systemic stress and short-term morbidity of single-incision cholecystectomy. Surg Innov. 2012;19:117–22.

22. Sohn DK, Jeong SY, Park JW, Kim JS, Hwang JH, Kim DW, Kang SB, Oh JH. Comparative study of NOTES rectosigmoidectomy in a swine model: E-NOTES vs. P-NOTES. Endoscopy. 2011;43:526–32.

23. Wolthuis AM, Fieuws S, Van Den Bosch A, de Buck van Overstraeten A, D'Hoore A. Randomized clinical trial of laparoscopic colectomy with or without natural-orifice specimen extraction. Br J Surg. 2015;102:630–7.

24. Guo J, Pasricha NP, Shenoy MM, Liu L, Mehta K, Pasricha PJ. Transgastric versus laparoendoscopic single-site peritoneoscopy in a rat model: effects on motility, inflammation, and nociception. Surg Endosc. 2012;26:747–53.