Tattooing or Metallic Clip Placement? A Review of the Outcome Surrounding Preoperative Localization Methods in Minimally Invasive Anterior Resection Performed at a Single Center

Chang-Lin Lin, MD,*† Chou-Pin Chen, MD,* Feng-Fan Chiang, MD, PhD,* Chou-Chen Chen, MD,* Ming-Cheng Chen, MD, PhD,* Chih-Tien Chen, MD, PhD,* Chun-Yu Lin, MD,* Hou-Hsuan Cheng, MD,‡§ and Yen-Chen Shao, MD∥

Background: For minimally invasive colorectal surgery, preoperative localization is a typical procedure. We here aimed to analyze compared 2 different localization methods in terms of short-term outcomes, like the operative outcome and postoperative complication rates based on real-world data.

Materials and Methods: This was a retrospective analysis study conducted at a medical center. We enrolled patients who were presented with colonic tumor between January 1, 2016, and December 31, 2019, and they had undergone laparoscopic anterior resection in a single institution. Data included patient characteristics, operative outcome, length of hospital stay, and postoperative complications.

Results: The preoperative localization group had a better resection margin (4 vs. 3 cm; \( P < 0.001 \)) and fewer procedures of intraoperative colonoscopy (4.67% vs. 18.22%; \( P = 0.002 \)). Lymph node harvest occurred more in patients with endoscopic tattooing procedures than with metallic clip procedures (25 vs. 20; \( P = 0.031 \)). No significant difference was found regarding postoperative complications and the length of hospital stay.

Conclusions: Preoperative localization in a laparoscopic anterior resection led to better surgical planning and resection margin. The metallic clip placement was helpful in the preoperative localization and setting. The endoscopic tattooing method had a larger lymph node harvest and with fewer intraoperative colonoscopy.

Key Words: tattooing, metallic clip, colorectal surgery, laparoscopy, localization, colorectal neoplasm

Received for publication May 5, 2021; accepted August 24, 2021. From the *Division of Colorectal Surgery, Department of Surgery, Taichung Veterans General Hospital, Taichung; †Division of Colorectal Surgery, Department of Surgery, Taipei Veterans General Hospital; §Department of Surgery, School of Medicine, National Yang Ming University, Taipei; ¶Division of Colorectal Surgery, Department of Surgery, China Medical University Hsinchu Hospital, Hsinchu; and ∥Department of Surgery, Taichung Veterans General Hospital Puli Branch, Nantou, Taiwan.

The authors declare no conflicts of interest.

Reprints: Yen-Chen Shao, MD, Division of Colorectal Surgery, Department of Surgery, China Medical University Hsinchu Hospital, Hsinchu, Taiwan, No. 199, Sector 1, Xinglong Road, Zhubei City 302, Hsinchu County, Taiwan, Republic of China (e-mail: ycheneli@gmail.com).

Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

MATERIALS AND METHODS

Patients

Between January 2016 and December 2019, a total of 332 patients underwent laparoscopic anterior resection for colon tumor in our hospital. The procedure was a resection of the sigmoid colon with anastomosis beyond peritoneal reflection. Lesions were all located at the distal descending colon to the upper rectum. Those surgeries that converted to the open method were not included for this study. We initially divided these patients into 2 groups: those receiving preoperative localization and those not (ie, receiving colonoscopy only). Subsequently, patients receiving preoperative localization were further subdivided into 2 groups: a tattooing group and a metallic clip group. Data on patients were collected regarding patient characteristics, operative outcome (operative time, resection margin, lymph node
harvest, intraoperative colonoscopy usage rates, inadequate resection margin during the first attempt and later requiring a second colonic resection), length of hospital stay, and postoperative complications (wound infection, delayed weaning, anastomosis leakage, ileus, pneumonia, chylous leak, stroke, urinary tract infection).

Preoperative Localization Methods

The 2 methods used were: endoscopic tattooing and metallic clip placement. The tattooing method was performed using sterilized ink and is typically done with a standard puncture needle inserted in the colonic submucosa distal to the lesion circumferentially at 2 or more locations (Fig. 1, black arrows). The metallic clip method was performed using an endoscopic hemoclip. The clip was placed at the mucosa near the lesion and followed through using abdominal radiography or computed tomography (Figs. 2, 3, white arrows). The indication for use of preoperative localization is when the surgeon supposes that the lesion’s location cannot be confirmed during the perioperative period. The choice of localization method was at the surgeon’s discretion.

Statistical Analyses

Clinical data were retrospectively collected from the hospital’s database. Continuous data were presented as medians and compared with the Mann-Whitney test. Categorical data were presented in both numbers and percentages and evaluated with the $\chi^2$ test and Fisher exact test. All statistical comparisons were 2 tailed, and $P$-value < 0.05 was considered significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS).

### TABLE 1. All Patient’s Baseline Characteristics

|                          | Nonlocalization Group (N = 225) | Localization Group (N = 107) | $P$  |
|--------------------------|---------------------------------|------------------------------|------|
| Age‡                     | 62.00 (53-71)                   | 65.00 (57-77)                | 0.022*|
| Sex‡                     |                                 |                              | 0.161|
| Female                   | 104 (46.22)                     | 40 (37.38)                   |      |
| Male                     | 121 (53.78)                     | 67 (62.62)                   |      |
| BMI†                     | 24.02 (21.56-27.03)             | 24.61 (22.27-27.47)          | 0.099|
| ASA†                     | 2.00 (2-2)                      | 2.00 (2-3)                   | 0.002**|
| Stage                    |                                 |                              | 0.026*|
| 0                        | 11 (4.89)                       | 12 (11.21)                   |      |
| I                        | 55 (24.44)                      | 37 (34.58)                   |      |
| II                       | 51 (22.67)                      | 22 (20.56)                   |      |
| III                      | 83 (36.89)                      | 30 (28.04)                   |      |
| IV                       | 25 (11.11)                      | 6 (5.61)                     |      |
| Pathologic T stage‡      |                                 |                              | 0.002**|
| I                        | 37 (16.44)                      | 34 (31.78)                   |      |
| II                       | 40 (17.78)                      | 10 (9.35)                    |      |
| III                      | 112 (49.78)                     | 43 (40.19)                   |      |
| IV                       | 25 (11.11)                      | 8 (7.48)                     |      |
| TIS                      | 11 (4.89)                       | 12 (11.21)                   |      |

Continuous data were expressed as median (interquartile range). Categorical data were expressed as n (%). $\chi^2$ test.

ASA indicates American Society of Anesthesiologists; BMI, body mass index.

Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc.
TABLE 2. Localization Group Patient’s Baseline Characteristics

| Subgroup (N = 69) | Clip Subgroup (N = 38) | P   |
|-------------------|------------------------|-----|
| Age†              | 65.00 (56.79)          | 65.00 (57.75-72.25) | 0.663 |
| Sex‡             |                        |                 | 0.027*|
| Female           | 20 (28.99)             | 20 (52.63)      |      |
| Male             | 49 (71.01)             | 18 (47.37)      |      |
| BMI†             | 24.73 (23.03-28.21)    | 24.46 (21.6-27.15) | 0.327 |
| ASA†             | 2.00 (2-3)             | 2.00 (2.25)     | 0.215 |
| Stage‡           |                        |                 | 0.041*|
| 0                | 4 (5.80)               | 8 (21.05)       |      |
| I                | 22 (31.88)             | 15 (39.47)      |      |
| II               | 15 (21.74)             | 7 (18.42)       |      |
| III              | 22 (31.88)             | 8 (21.05)       |      |
| IV               | 6 (8.70)               | 0 (0)           |      |
| Pathologic T stage‡ |                    |                 | 0.036*|
| I                | 22 (31.88)             | 12 (31.58)      |      |
| II               | 5 (7.25)               | 5 (13.16)       |      |
| III              | 32 (46.38)             | 11 (28.95)      |      |
| IV               | 6 (8.70)               | 2 (5.26)        |      |
| TIS              | 4 (5.80)               | 8 (21.05)       |      |

Continuous data were expressed as median (interquartile range). Categorical data were expressed as n (%).
ASA indicates American Society of Anesthesiologists; BMI, body mass index.
†Mann-Whitney test.
‡Fisher exact test.
§Mann-Whitney test.
*P < 0.05.

TABLE 3. Surgical Outcome of Nonlocalization and Localization Groups

| Resection margin (cm)§ | Nonlocalization Group (N = 225) | Localization Group (N = 107) | P   |
|------------------------|----------------------------------|-----------------------------|-----|
| 3.00 (2-4)             | 4.00 (2.8-4.5)                   | < 0.001*                    |
| Operative time (min)‡  | 164.00 (129.75-198)              | 169.00 (144.75-184)         | 0.750 |
| Lymph node harvest§    | 22.00 (18-29.5)                  | 24.00 (18-29)               | 0.719 |
| Intraoperative colonoscopy‡ | 41 (18.22)              | 5 (4.67)                    | 0.002*|
| Another colonic resection† | 6 (2.67)                    | 1 (0.93)                    | 0.436 |
| Hospital stay (d)‡     | 7.00 (6-9)                      | 7.00 (6-9)                  | 0.662 |
| Postoperative complication |                                 |                             |      |
| Wound infection†       | 5 (2.22)                        | 2 (1.87)                    | 1.000 |
| Delayed weaning (48 h)† | 4 (1.78)                      | 1 (0.93)                    | 1.000 |
| Anastomotic leakage‡   | 2 (0.89)                        | 0 (0)                       | 1.000 |
| Ileus‡                 | 17 (7.56)                       | 5 (4.67)                    | 0.453 |
| Pneumonia‡             | 1 (0.44)                        | 3 (2.80)                    | 1.000 |
| Chylous leak‡          | 2 (0.89)                        | 4 (3.74)                    | 0.088 |
| Stroke‡               | 1 (0.44)                        | 0 (0)                       | 1.000 |
| Urinary tract infection‡ | 3 (1.33)                      | 0 (0)                       | 0.554 |

Continuous data were expressed as median (interquartile range). Categorical data were expressed as n (%).
Note: Another colonic resection: inadequate resection margin during first attempt.
†Fisher exact test.
‡Mann-Whitney test.
*P < 0.01.

RESULTS

There were 332 patients receiving laparoscopic anterior resection during our study period. Among them, 107 received preoperative localization, and 225 received an only preoperative colonoscopy. Of the 107 patients with preoperative localization, 38 metallic clip placements, while 69 had the tattoo method. All patients’ baseline characteristics are shown in Tables 1 and 2.

Between the preoperative localization and colonoscopy alone groups (Table 3), we found a statistical difference in the resection margin and the usage of intraoperative colonoscopy. No statistical difference was found between postoperative complications and the length of hospital stay.

Between the tattooing subgroup and metallic clip subgroup (Table 4), while we found no significant differences in resection margin, we found a statistical difference in the number of lymph node harvest. The tattooing subgroup had more lymph node harvests than the metallic clip subgroup (25 vs. 20, P = 0.031). Also, we found more postoperative chylous leakage between subgroups, but the difference was statistically insignificant (5.8% vs. 0%, P = 0.295). The intraoperative colonoscopy usage rate was lower in the tattooing subgroup (10.53% vs. 1.45%, P = 0.053). No differences were found regarding postoperative complications and the length of hospital stay.

DISCUSSION

In our article, we only included patients with laparoscopic anterior resection. Previous studies suggested that for lesions at the right side of the colon or rectum, preoperative localization is unnecessary.3,8 We were able to identify right

TABLE 4. Surgical Outcome of Tattoo and Clip Groups

| Subgroup (N = 69) | Clip Subgroup (N = 38) | P   |
|-------------------|------------------------|-----|
| Resection margin (cm)§ | 3.50                  | 4.00 (3-5) | 0.421 |
| Operative time (min)‡ | 171.00               | (124-184.75) | 0.172 |
| Lymph node harvest§    | 25.00 (18-31.5)       | 20.00 (16.75-27) | 0.031*|
| Intraoperative colonoscopy‡ | 1 (1.45)             | 4 (10.53) | 0.053 |
| Another colonic resection† | 1 (1.45)           | 0 (0)     | 1.000 |
| Hospital stay (d)‡     | 7.00 (6-9)            | 7.50 (7-9) | 0.323 |
| Postoperative complications |                                 |                             |      |
| Wound infection†       | 1 (1.45)             | 1 (2.63)   | 1.000 |
| Delayed weaning (48 h)† | 0 (0)                | 1 (2.63)   | 0.355 |
| Anastomotic leakage‡   | 0 (0)                | 0 (0)      | —     |
| Ileus‡                 | 3 (4.35)             | 2 (5.26)   | 1.000 |
| Pneumonia‡             | 2 (2.90)             | 1 (2.63)   | 1.000 |
| Chylous leak‡          | 4 (5.80)             | 0 (0)      | 0.295 |
| Stroke‡               | 0 (0)                | 0 (0)      | —     |
| Urinary tract infection‡ | 0 (0)               | 0 (0)      | —     |

Continuous data were expressed as median (interquartile range). Categorical data were expressed as n (%).
Note: Another colonic resection: inadequate resection margin during first attempt.
†Fisher exact test.
‡Mann-Whitney test.
*P < 0.05.
side colonic lesions through the use of an ileocecal valve. When located at the rectum, these lesions could be identified by the use of a Huston valve. For the above reason, we believed that limiting the procedure to only an anterior resection likely reduced bias.

A systematic review in 2016 found a higher accuracy for colonic localization in the endoscopic tattooing method when compared with the preoperative conventional colonoscopy alone.9 Also, there is no consensus as to which method is better, that is, between endoscopic tattooing and other localization methods. According to our present findings, the localization group showed a better resection margin and surgical plan by having more accurate lesion localization. The more accurate resections in the localization group are reflected in the boxplots (Fig. 4). As for the tattooing and metallic clip subgroups, the only statistical difference was lymph node harvest. Dye-containing lymph nodes were likely better detected during surgery. Adequate numbers of lymph nodes in the specimen are known to be critically important for patients with colorectal cancer.10,11 Adequate harvests of lymph nodes (eg, >12) help avoid understaging and are strongly associated with better outcomes.12–14 Most specialists consider the benefits of endoscopic tattooing in lymph node retrieval,15–17 while others disagree.18 In our present study, tattooing led to more lymph node harvest than metallic clip placement (25 vs. 20, P = 0.031), although both subgroups had adequate numbers of dissected lymph nodes (>12). The usage of intraoperative colonoscopy was higher in the metallic clip subgroup, a result that is consistent with expectation. As the proportion of early cancer staging was also higher in the metallic clip subgroup, we cannot exclude the likely existence of some bias. The tattooing technique has been discussed for >20 years.19,20 One study in 2017 reported that an intraluminal circumferential multiple spot injection improves localization accuracy.21 This can avoid having a tattoo located retroperitoneally or colonic serosa being covered by omentum, a condition which cannot be easily seen. Endoscopic tattooing with localized accuracy is dependent on the surgeon’s skills and may fail due to insufficient injections of the submucosal dye. If the puncture needle perforates the colonic wall, the dye may cause peritonitis or abscesses, making the operation more challenging.22 In our study, only 1 patient in the tattooing group required an additional colonic resection due to poor localization. In the case, the error was due to dye spreading to the proximal colonic serosa, misleading the surgeon in performing the correct segmental resection of the colon (Fig. 5). Few cases in the tattooing subgroup showed unsatisfied resection margins (only about 1 cm) (Fig. 6). One possibility of such error may be due to the fact that the tattoo procedure was not performed by the chief surgeon. Also, distances between the tattooing site and the lesion site were inconsistent across patients. All these factors should be considered when performing the endoscopic tattoo.

Metallic clip placement has been used by gastrointestinal tract endoscopists for a long time. It was described as a method to evaluate the depths of the colonoscopy tip in the colon23 and has also been used for precise localization of colon lesions in laparoscopic surgery.24 Accurate placement

![FIGURE 5. Surgical specimen. Black arrow: Tattoo on wrong colonic segment serosa. White arrow: True lesion proximal colonic mucosa been tattooed. Black dotted line: Inadequate colonic resection at first attempted (this specimen was repaired with simple suture). White dotted line: Another colonic resection with adequate resection margin.](image-url)

![FIGURE 4. Boxplot of resection margin between localization and nonlocalization groups.](image-url)

![FIGURE 6. Boxplot of resection margin between tattooing and metallic clip groups.](image-url)
of the metallic clip is known to cover a wide range. Error localization rates range from 0% to 40%.25,26 Interestingly, one 2016 study a 100% accurate level even without using the tattooing method. In that study, only the method of metallic clip or colonoscopy was applied.27 The benefit of this method is that a surgeon knows the lesion’s relative location before surgery. Furthermore, surgeons can decide in advance on the port site, patients’ position, and endo-videosurgery monitor placement. After a selected colon segment is dissected retroperitoneally, the surgeon can pull it through and check the colonic lesion by manual palpation. If the lesion is too small to be palpable, an intraoperative colonoscopy may be needed. Clip migration may lead to erroneous localization and other complications such as perforation or colonic ulcer.28

This observational study is limited by its retrospective nature. Our laparoscopic anterior resections were carried out by different surgeons, with surgeon-dependent choices of the localization method. Different surgeons with different experiences could have well influenced the number and the quality of lymphadenectomy. The intraoperative colonoscopy usage rate was statistically lower in the localization group, but that also required longer surgical time. Selection bias could have contributed different results.

Each of the 2 methods has different features. Tattooing is aimed to facilitate intraoperative localization, but this is not possible with clip placement, which is not visible intraoperatively. Tattooing methods also can map the surgical field for better surgical outcomes. Metallic clip placement is helpful in the preoperative setting based on imaging results, especially for difficult lesions localized in the transverse colon/splenic flexure. It is noteworthy that a case series study describing new marking methods like fluorescent clips may have advantages of both methods.29

In conclusion, preoperative localization produced better resection margins and surgical plans. Metallic clip placement is a simple method for preoperative localization and setting. The endoscopic tattooing method offered more lymph node harvest and less usage of an intraoperative colonoscopy. If you can only choose one of these 2 methods, we would recommend the endoscopic tattooing method. However, we believe the usage of both techniques would create the best surgical plan.

ACKNOWLEDGMENTS

The authors thank Dean S. Dowers and Paul W.F. Poon for editing the manuscript, supported by the Taichung Veterans General Hospital, as well as the Biostatistics Task Force of Taichung Veterans General Hospital for performing the study.

REFERENCES

1. Lee SW. Laparoscopic procedures for colon and rectal cancer surgery. Clin Colon Rectal Surg. 2009;22:218–224.
2. Liu ZH, Liu JW, Chan FS, et al. Intraoperative colonoscopy in laparoscopic colorectal surgery: a review of recent publications. Asian J Endosc Surg. 2020;13:19–24.
3. Kim SH, Milsom JW, Church JM, et al. Perioperative tumor localization for laparoscopic colorectal surgery. Surg Endosc. 1997;11:1013–1016.
4. National Comprehensive Cancer Network. Colon Cancer (Version 2.2021). 2021. Available at: www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed March 2, 2021.
5. Cho YB, Lee WY, Yun HR, et al. Tumor localization for laparoscopic colorectal surgery. World J Surg. 2007;31:1491–1495.
6. Montorsi M, Opochoer E, Santambrogio R, et al. Original technique for small colorectal tumor localization during laparoscopic surgery. Dis Colon Rectum. 1999;42:819–822.
7. ASGE Standards of Practice Committee, Fisher DA, Shergill AK, et al. Role of endoscopy in the staging and management of colorectal cancer. Gastrointest Endosc. 2013;78:8–12.
8. Zerey M, Hawyer LM, Awad Z, et al. SAGES evidence-based guidelines for the laparoscopic resection of curable colon and rectal cancer. Surg Endosc. 2013;27:1–10.
9. Acuna SA, Elmi M, Shah PS, et al. Preoperative localization of colorectal cancer: a systematic review and meta-analysis. Surg Endosc. 2017;31:2366–2379.
10. Chen SL, Bilchik AJ. More extensive nodal dissection improves survival for stages I to III of colon cancer: a population-based study. Ann Surg. 2006;244:602–610.
11. Kim CH, Huh JW, Kim HR, et al. Prognostic comparison between number and distribution of lymph node metastases in patients with right-sided colon cancer. Ann Surg Oncol. 2014;21:1361–1368.
12. Washington MK. Colorectal carcinoma: selected issues in pathologic examination and staging and determination of prognostic factors. Arch Pathol Lab Med. 2008;132:1600–1607.
13. Onitilo AA, Stankowski RV, Engel JM, et al. Adequate lymph node recovery improves survival in colorectal cancer patients. J Surg Oncol. 2013;107:828–834.
14. Lykke J, Roikjaer O, Jess P. Danish Colorectal Cancer Group. The relation between lymph node status and survival in stage II/III colon cancer: results from a prospective nationwide cohort study. Colorectal Dis. 2013;15:559–565.
15. Kang J, Park HS, Kim I, et al. Effect of preoperative colonoscopic tattooing on lymph node harvest in T1 colorectal cancer. Int J Colorectal Dis. 2015;30:1349–1355.
16. Goo JI, Ryu DG, Kim HW, et al. Efficacy of preoperative colonoscopic tattooing with indocyanine green on lymph node harvest and factors associated with inadequate lymph node harvest in colorectal cancer. Scand J Gastroenterol. 2019;54:666–672.
17. Wang Q, Chen E, Cai Y, et al. Preoperative endoscopic localization of colorectal cancer and tracing lymph nodes by using carbon nanoparticles in laparoscopy. World J Surg Oncol. 2016;14:231.
18. Fico CV, Portinari M, Zuolo M, et al. Preoperative endoscopic tattooing to mark the tumour site does not improve lymph node retrieval in colorectal cancer: a retrospective cohort study. J Negat Results Biomed. 2015;14:9.
19. McArthur CS, Roayaie S, Waye JD. Safety of preoperative endoscopic tattoo with india ink for identification of colonic lesions. Surg Endosc. 1999;13:397–400.
20. Nizam R, Siddiqi N, Landas SK, et al. Colonic tattooing with India ink: benefits, risks, and alternatives. Am J Gastroenterol. 1996;91:1804–1808.
21. Letarte F, Webb M, Raval M, et al. Tattooing or not? A review of current practice and outcomes for laparoscopic colorectal resection following endoscopy at a tertiary care centre. Can J Surg. 2017;60:394–398.
22. Yang M, Pepe D, Schlachta CM, et al. Endoscopic tattoo: the importance and need for standardised guidelines and protocol. J R Soc Med. 2017;110:287–291.
23. Lehman GA, Maveety PR, O’Connor KW. Mucosal clipping—utility and safety testing in the colon. Gastrointest Endosc. 1985;31:273–276.
24. Ellis KK, Fennerty MB. Marking and identifying colon lesions. Tattoos, clips, and radiology in imaging the colon. Gastrointest Endosc Clin N Am. 1997;7:401–411.
25. Narahiro S, Yoshida M, Ohdaira H, et al. A novel fluorescent marking clip for laparoscopic surgery of colorectal cancer: a case report. Int J Surg Case Rep. 2019;64:170–173.
26. Warnick P, Chopra SS, Raubach M, et al. Intraoperative localization of occult colorectal tumors during laparoscopic surgery by magnetic ring markers-a pilot study. *Int J Colorectal Dis.* 2013;28:795–800.

27. Ohdaira T, Konishi F, Nagai H, et al. Intraoperative localization of colorectal tumors in the early stages using a marking clip detector system. *Dis Colon Rectum.* 1999;42:1353–1355.

28. Cai Z, Pan R, Ma J, et al. Tumor localization for laparoscopic colorectal resection without endoscopic tattooing. *Surg Laparosc Endosc Percutan Tech.* 2016;26:230–235.

29. Naruhito S, Yoshida M, Ohdaira H, et al. Effectiveness and safety of tumor site marking with near-infrared fluorescent clips in colorectal laparoscopic surgery: a case series study. *Int J Surg.* 2020;80:74–78.