

Original Article

Are Preoperative Localization Methods a Benefit to Tumor Resection Margin During Laparoscopic Anterior Resection?

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Key Words

Colorectal cancer;
Laparoscopic;
Preoperative localization;
Tattoo;
Metallic clip

Purpose. Upon introduction of laparoscopic colon surgery over 20 years ago, the procedure became the standard treatment for colon cancer. Because a small colonic tumor may not easily be visualized or palpated during laparoscopic surgery, pre-operative localization of the lesion is very important. Many previously published articles have offered an opinion with regards to this, however the influence of localization on tumor resection margin has not yet been addressed in any available literature.

Methods. We identified 214 patients who had undergone elective laparoscopic colorectal surgery, and an anterior resection over the previous three-year period. Data was collected with regards to preoperative localization methods, tumor staging, intraoperative colonoscopy, tumor resection margin, lymph node dissection amount, and time need for surgery.

Results. One hundred fifty-nine (159) of 214 (74%) patients did not receive pre-operative localization. Twenty-five (25) of 214 (12%) patients underwent pre-operative localization through use of metallic clip placement. Thirty (30) of 214 (14%) patients underwent pre-operative localization via the tattoo method. The median resection margin of the non-localization group was 3 cm, which was significantly shorter than that of the localization group (4 cm, $p = 0.013$). Only 1 of 55 (2%) patients underwent an intra-operative colonoscopy in the localization group, which was significantly lower than the non-localization group (20 of 159, $p = 0.04$). In the locally advanced group (T stage 3 or 4), 115 of 214 (54%) patients were identified. The median resection margin of the non-localization group was 3 cm, with no significant difference seen when compared to the localization group (3.5 cm, $p = 0.145$). In subgroup analysis, we compared the endoscopic tattooing method to the metallic clip placement method. The resection margin, operation time, and LN dissection amount were shown not to be different between these two groups.

Conclusions. Preoperative localization in a laparoscopic anterior resection can lead to better surgical planning and resection margin, while also diminishing the need for an intraoperative colonoscopy. The choice of using either the tattooing or metallic clip method is dependent upon the surgeon's preference. More data and a longer follow-up period are still needed in order to provide a better progression free survival evaluation.

[J Soc Colon Rectal Surgeon (Taiwan) 2020;31:109-116]

Received: December 27, 2019.

Accepted: February 3, 2020.

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Upon the introduction of laparoscopic colon surgery over 20 years ago,¹ the procedure became the standard treatment for colon cancer. Because a small colonic tumor maybe not be easily visualized or palpated during laparoscopic surgery, pre-operation localization of the lesion is very important. Many previously published articles have offered an opinion with regards to this, suggesting that in laparoscopic colonic resection, preoperative lesion localization can improve surgical planning.

The marking method most popular in the world involves endoscopic tattooing. ASGE Gastrointest Endosc (2013) and SAGES Surg Endosc (2013) both suggest this method to localize lesions prior to laparoscopic colorectal surgery. This tattooing method implements dyes such as India ink which are marked on colonic mucosa by an injection needle. However, other localization techniques have been described, including metallic clip placement, intraoperative ultrasound, and preoperative colon CT.^{2,3} In our hospital, commonly used options include metallic clip placement or endoscopic tattooing as preoperative localization methods. The final decision on which option to use is dependent upon the surgeon's preference.

According to previous articles, endoscopic tattooing and metallic clip placement are both practice in preoperative localization.^{4,5} Conventional colonoscopy tumor localization error rates have been found to be approximately 14%.^{6,7} A systematic review and meta-analysis performed in 2016 showed a significantly lower incidence of tumor localization error in the tattooing group, while presenting a variable error rate (0%-40%) in the clip group.⁸ However, no guidelines exist to assist the medical community when making the choice between the tattooing or metallic clip method. Additionally, the influence of localization on tumor resection margin has not yet been addressed in published literature. The aim of this article is to evaluate the difference in resection margin between a localization group and a non-localization group at our hospital.

Materials and Methods

Patients

We performed a retrospective cohort study between

January 2016 and December 2018, where 1,713 colorectal cancer/polyp patients had been diagnosed in Taichung Veterans General Hospital. We only included patients who had undergone a laparoscopic anterior resection, with those among them who had converted to laparotomy being excluded. These patients were then divided into two groups: those who had received preoperative localization, and those who had not. The patients who had received preoperative localization were further divided into two subgroups, an endoscopic metallic clip group and a tattooing group. In the clip group, surgeons applied metallic clips distally to the tumor site and followed up immediately with an abdominal radiograph. In the tattooing group, endoscopic tattooing was performed by multiple spot circumferential distal to the tumor site, usually in two spots. Data was collected with regards to the preoperative localization method, pathological tumor staging, intraoperative colonoscopy, tumor resection margin, lymph node dissection amount, operation time, combined surgery, and need for another colon resection after intraoperative specimen evaluation.

Method of colonic lesion localization

There are two methods for colonic lesion localization which are currently used in our hospital, endoscopic tattooing and metallic clip placement. Endoscopic tattooing involves using an ink mark on the distal colonic mucosa with multiple circumferential injections. For metallic clip placement, we would immediately following abdominal radiography, so the surgeon can identify the lesion location.

Statistical analysis

Clinical data was retrospectively collected from the hospital database. Continuous data was expressed as a median (interquartile range (IQR)). Categorical data was expressed as both a number and percentage. We used the Mann-Whitney U test to compare mean. Categorical variables were compared using the Chi-Square and Fisher's exact tests. Statistical analysis was performed using the Statistical Package for the Social Science (SPSS).

Results

During the study period, 214 patients were treated with laparoscopic anterior resection. Fifty-five (55) received preoperative localization, with 25 in the endoscopic metallic clip group and 30 receiving endoscopic tattooing. One hundred fifty-nine (159) patients didn't receive either preoperative localization method. Patients' baseline demographics are shown in Table 1. The operative outcome is described in Table 2, with subgroup analyses shown in Tables 3 and 4.

The results show a significant difference in the resection margin ($p = 0.013$) and need for intraoperative colonoscopy ($p = 0.04$) (Table 2). There was however, no significant difference in results regarding operation times, LN dissected amount and need for another colon resection after intraoperative specimen evaluation. Our results showed no overall significant difference in outcome between the tattooing group and metallic clip group (Table 4).

The tumor resection margin was shown to be better in patients who received preoperative localization.

Table 1. Baseline demographic of the study sample (All)

	Preoperative location				<i>p</i> value
	No (n = 159)		Yes (n = 55)		
Age	62	(53-71)	61	(56-70)	0.628
Gender-male ^c	83	(52.20%)	34	(61.82%)	0.281
BMI	24.16	(21.76-27.17)	24.88	(22.01-27.65)	0.163
No combined surgery	146	(91.82%)	50	(90.91%)	0.784

Mann-Whitney U test. Chi-Square test. Fisher's exact test. * $p < 0.05$, ** $p < 0.01$. Continuous data were expressed as a median (IQR).

Table 2. Operative outcome

Outcome	Preoperative location				<i>p</i> value
	No (n = 159)		Yes (n = 55)		
resection margin	3	(2-4)	4	(2.5-4.5)	0.013*
OP times (單一手術)	155	(123-189.25)	164.5	(142.75-186.25)	0.247
LN dissection	22	(17-27)	21	(17-27)	0.956
Intraoperative colonoscopy	20	(12.58%)	1	(1.82%)	0.040*
Other colon resection	3	(1.89%)	0	(0%)	0.571

Mann-Whitney U test. Chi-Square test. Fisher's exact test. * $p < 0.05$, ** $p < 0.01$. Continuous data were expressed as a median (IQR). Categorical data were expressed in both number and percentage.

Table 2a. Operative outcome, pathological T-stage ≤ 2 (n = 99)

	Preoperative location				<i>p</i> value
	No (n = 64)		Yes (n = 35)		
Resection margin	3.2	(2-4)	4	(2.5-5)	0.035*
OP times (單一手術)	150	(119-189)	162	(142.75-184.25)	0.303
LN dissection	20	(15-25)	19	(15-24)	0.623
Intraoperative colonoscopy ^c	16	(25%)	1	(2.86%)	0.012*
Other colon resection	1	(1.56%)	0	(0%)	1.000

Mann-Whitney U test. Chi-Square test. Fisher's exact test. * $p < 0.05$, ** $p < 0.01$. Continuous data were expressed as a median (IQR). Categorical data were expressed in both number and percentage.

Table 2b. Operative outcome, pathological T-stage 3-4 (n = 115)

	Preoperative location				p value
	No (n = 95)		Yes (n = 20)		
Resection margin	3	(2-4)	3.5	(2.58-4.5)	0.145
OP times (單一手術)	160	(131.5-194)	169.5	(132.25-208)	0.295
LN dissection	23	(18-27)	25.5	(19-36.75)	0.091
Intraoperative colonoscopy	4	(4.21%)	0	(0%)	1.000
Other colon resection	2	(2.11%)	0	(0%)	1.000

Mann-Whitney U test. Chi-Square test. Fisher's exact test. * $p < 0.05$, ** $p < 0.01$.

Continuous data were expressed as a median (IQR).

Categorical data were expressed in both number and percentage.

Table 3. Baseline demographic of the subgroup patients

	Localization method				p value
	Tattooing (n = 30)		Metallic clip (n = 25)		
Age	61	(54.75-71.5)	61	(57.5-69.5)	0.926
Gender-male ^c	22	(73.33%)	12	(48%)	0.100
BMI	24.87	(22.57-27.93)	24.97	(21.57-27.72)	0.648
No combine surgery	26	(86.67%)	24	(96%)	0.362

Mann-Whitney U test. Chi-Square test. Fisher's exact test. * $p < 0.05$, ** $p < 0.01$.

Continuous data were expressed as a median (IQR).

Categorical data were expressed in both number and percentage.

Table 4. Subgroup operative outcome

Outcome	Method				p value
	Tatto (n = 30)		Clip (n = 25)		
Resection margin	3	(2.38-4.5)	4	(3-5)	0.079
OP times (單一手術)	167	(149.75-209)	158	(125.25-184)	0.168
LN dissection	22.5	(18-27.75)	19	(16.5-26)	0.360
Intraoperative colonoscopy	0	(0%)	1	(4%)	0.455
Other colon resection	0	(0%)	0	(0%)	---

Mann-Whitney U test. Chi-Square test. Fisher's exact test. * $p < 0.05$, ** $p < 0.01$.

Continuous data were expressed as a median (IQR).

Categorical data were expressed in both number and percentage.

In consideration of locally advanced tumors being visualized during laparoscopy, these patients were then separated into two groups; either tumors exceeding pathological T2 or within T2. There was shown to be no specific difference in tumor resection margin in the colonic lesion for the exceed T2 group ($p = 0.145$) (Table 2b). Additionally, this result showed a significant difference in resection margin ($p = 0.035$), along with the intraoperative colonoscopy ($p = 0.012$) usage rate in tumor within pathological T2 (Table 2a).

Discussion

As there has been an increased utilization of laparoscopic or robotic modalities, accurate tumor localization preoperatively appears to now be more important. We can identify lesion at the right side colon by its ileocecal valve location; which is found below the middle rectum having been identified by the Huston valve. In contrast to a right side lesions, left side lesions are difficult to recognize due to lack of an obvious landmark such as the ileocecal valve, particularly

at a descending colon or sigmoid colon. A T-colon maybe identified by its triangular configuration or hepatic flexure. A gray-blue colored impression of the liver maybe seen at this point. For the above reason, we limited our study to the patients who had undergone laparoscopic anterior resection.

Our data shows a significant difference in the resection margin between the preoperative localization group and the non-localization group. Boxplot (Fig. 1) displays more distributary data regarding the resection margin for the non-preoperative localization group. Such a result has a very plausible explanation. Our countermeasures to laparoscopic anterior resection in the non-preoperative localization group are intraoperative colonoscopy and intraoperative specimen evaluation, for the purpose of confirming whether the tumor was within the resection colonic segment or not. Outliers existed in the non-preoperative localization group, which presented an unnecessary resection of the colon. If the tumor had been localized at the middle sigmoid colon and just happened to be a redundant S-colon, this may lead to an overly long resection margin (> 8 cm). This result presented a better accuracy localization in the preoperative localization group.

A previous study presents that approximately 20% of the patients who haven't received preoperative localization prior to laparoscopic colorectal surgery are relying on a table endoscopy and intraoperative specimen analysis.⁹ An intraoperative colonoscopy leads to a prolonged surgery time. The impact of bowel resection margins in colon cancer has been mentioned in several studies.^{10,11} A longitudinal margin of colon resection < 5 cm may result in diagnostic under staging, hence increasing the recurrence rates. Our resection margin data was recorded in a pathological report written by pathologists. The numerical value was always lower than the value of the resection margin recorded in our operation notes. The effect of formalin fixation on resection margins has been discussed in another article.¹² The mean reduction after formalin fixation was 17.48 mm. Although our resection margin was approximately 3-4 cm in average, it was expected to be more than 5 cm when seen in laparoscopic vision. We would attempt to provide an evaluation of both the recurrent and survival rates in our

patients after a longer follow-up period.

According to the AJCC (American Joint Committee on Cancer) colon and rectum cancer staging 7th edition, primary tumor (T) T2 do not invade through the muscularis propria. Therefore, colonic tumor within T2 is usually invisible under laparoscopic view. It is possible however for some of them to be sensed by the instrument's feedback. However, a primary T3 lesion is defined as having invaded through the muscularis propria into the pericolorectal tissues, which are usually visible under laparoscopic view. Otherwise, it can be touched easily by the instrument. We divided our patients into two subgroups, either primary tumor within T2 or exceeding T2. In the primary tumor within T2 group, the results presented a specific difference in resection margin between the preoperative localization group and the non-localization group. In contrast, there showed no significant differ-

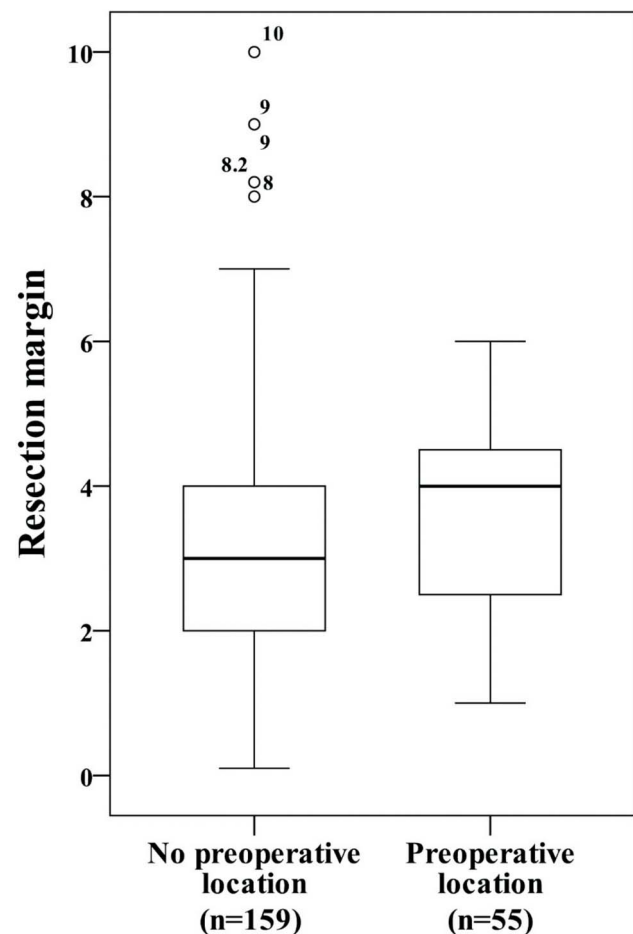


Fig. 1. Boxplot of all group.

ence in resection margin, LN dissection, intraoperative colonoscopy use, and operation time in the primary tumor exceeding T2 group. Therefore, preoperative localization is much more important when the patient is at the early stages of colon cancer.

In subgroup analysis, we compared the tattoo method to the metallic clip placement method and found no significant differences between the two groups. The Dotpolt (Fig. 2) shows a more aggregated distribution in the clip group. However, this result was unexpected. We reviewed the chart of the tattoo group patients and found that some tattooing involved injections on the colonic mucosa very close to the lesion, which led to a shorter resection margin. In the clip group, the surgeon was able to identify the lesion location according to abdominal radiography and colonoscopy findings. Here, only 1 of 30 patients required an intraoperative colonoscopy for localization.

There are some articles which have documented adverse events regarding colonoscopic tattooing, with most of them involving intraperitoneal spillage. The tattoo spill rates ranged from 4% to 9.5%.^{13,14} However, even this incidence is rare. Severe complications involving endoscopic tattooing, such as an abscess or peritonitis have also been reported.¹⁵ In our series, no complications were noted after tattooing injection.

Conclusion

In conclusion, preoperative localization in laparoscopic anterior resection will lead to both better surgical planning and resection margin, while diminishing the need for an intraoperative colonoscopy. And it is much more important when the patient is at the early stages of colon cancer (primary tumor within T2). The choice of using the tattooing or metallic clip method remains dependent upon the surgeon's preference. More data and a longer follow-up period are still needed for a more complete progression free survival evaluation.

Conflict of Interest Statement

The authors declare no conflict of interest in the study.

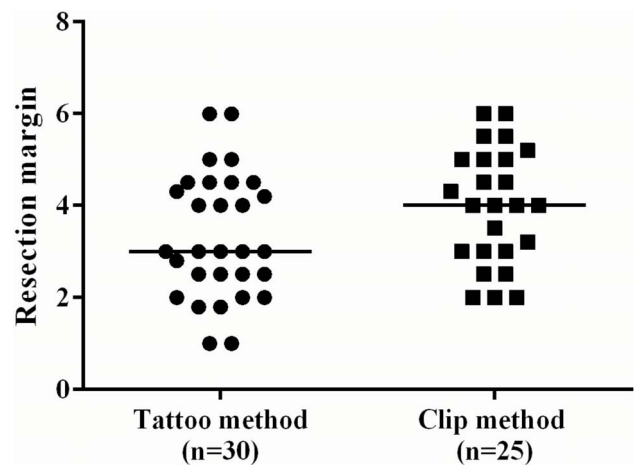


Fig. 2. Dotpolt of preoperative group.

Role of the Funding Source

The authors declare no role of funding source in the study.

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原 著

對於腹腔鏡前位切除而言，術前定位是否對於腫瘤切除邊緣有幫助

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目的 大腸直腸腹腔鏡手術至今已經超過 20 多年，已經成為世界各地大腸直腸癌的標準治療方法。由於在腹腔鏡下，比較小的大腸病灶不容易用肉眼看到或是觸摸到，術前的定位就顯得非常重要。之前有不少文章對於術前定位有提供不少建議，但是對於腫瘤切除邊緣是否有幫助仍然沒有文章提及。

方法 我們蒐集了台中榮民總醫院過去三年中，接受常規腹腔鏡前位切除手術的病人共 215 位。資料來源根據病歷記載，蒐集了關於術前定位方法，腫瘤階段，是否使用術中大腸鏡，腫瘤切除邊緣長短，淋巴結廓清術，以及手術時間。

結果 總共 159 位病人 (74%) 沒有接受術前定位，25 位病人 (12%) 使用大腸鏡金屬止血夾定位，30 位病人 (14%) 使用大腸鏡黏膜染色定位。沒有術前定位組的腫瘤切除邊緣中位數為 3 公分，統計上顯著比有定位組的短 (4 公分)。有定位組中只有 1 位病人 (2%) 接受術中大腸鏡檢查，統計上顯著比沒定位組的少 (13%)。在這全部 214 位病人之中，分類屬於局部進階的腫瘤 (T3-T4) 有 115 位 (54%)。在這群病人中沒有定位組的腫瘤切除邊緣中位數為 3 公分，統計上跟有定位組沒有差異 (3.5 公分)。我們還有比較使用大腸鏡黏膜染色定位或大腸鏡金屬止血夾定位之間的差異，結果在於腫瘤切除邊緣、淋巴廓清數量、手術時間都沒有統計上的差異。

結論 對於腹腔鏡前位切除手術，術前定位能夠帶來更好的手術計畫和腫瘤切除邊緣，降低術中大腸鏡的使用。至於要使用哪種定位方法就根據外科醫師的個人偏好。在未來，我們需要更多的病人資料以及更長的追蹤時間來評估對於腫瘤預後有無影響。

關鍵詞 大腸直腸癌、腹腔鏡、術前定位、染色、金屬夾。