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Case Series

Autologous blood for preoperative colorectal TUMOR'S localization: A Vietnamese preliminary experience

Ngoc Hung Nguyen [a], The Hiep Nguyen [a,c], Cong Long Nguyen [b], Xuan Vinh Vu [a,c], Tuan Hiep Luong [c,**], Thanh Khiem Nguyen [a,*]

[a] Department of Gastrointestinal and Hepato-Pancreato-Biliary Surgery, Bach Mai Hospital, Hanoi, Viet Nam
[b] Gastroenterology & Hepatology Center, Bach Mai Hospital, Hanoi, Viet Nam
[c] Department of Surgery, Hanoi Medical University, Hanoi, Viet Nam

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ABSTRACT

Introduction: Laparoscopic colorectal surgery (LCRS) is the optimal choice for cases of early cancer. However, due to their early stage, one of this procedure's challenges is tumoral localization. So that, there are many methods of locating tumors preoperatively that have been studied by authors. Recently, Korean authors have reported a method of injecting autologous blood to mark the tumor before surgery with high efficiency and safety. This article aims to evaluate the effectiveness by analyzing the section biopsy's results, as well as the safety of this procedure.

Materials and method: This study is descriptive cross-section study with analysis of retrospective occurrences of case series of colonoscopy with autologous blood before surgery from October 2020 to December 2021.

Results: 16 patients were recruited to the study. The average age was 62.9 ± 13.1 with male/female ratio was 8/8. 50% (8/16 patients) of all cases was early carcinomas, and by location, 62.5% of all cases was sigmoid colon tumors. All 16 patients (100%) found the tumor marking position. None of the patients had complications of marked endoscopy such as intestinal perforation, peritonitis, abdominal abscess, intestinal adhesions, etc.

Conclusion: The method of autologous blood injection to locate the tumor before laparoscopic colorectal surgery is a technique that can be performed effectively and safely.

1. Introduction

Laparoscopic colorectal surgery is the optimal choice for cases of early cancer (small or flat tumors), large adenomatous polyps that cannot be removed through gastrointestinal endoscopy, and malignant polypectomy lesions requiring radical colorectal resection [1]. These are tumors that are difficult to locate during laparoscopic surgery because the lesion has not invaded the serosa to be visible as well as cannot be directly palpated to find it. Therefore, determining the tumor location for surgery by preoperative tattooing is very important [2].

There are many methods of locating tumors that have been studied in literature around the world: methylene blue injection, Indian ink or Indocyanine green (ICG), endoscopic lesion clipping, intraoperative colonoscopy, etc [3]. Method of injecting methylene blue, the dye does not last long enough at the marked location and spreads around and into other locations [4]. With the Indian ink injection method, many studies have reported complications: Focal peritonitis, inflammatory pseudotumor, intestinal perforation, intestinal infarction, intestinal adhesions, etc [5]. Another animal study by Price N et al. showed that injection Indian ink and ICG cause mild to severe mucosal ulceration and inflammation at injection sites, either concentrated or diluted [6].

Therefore, the choice of method for tumor's location marking is still a matter of debate among endoscopists and gastrointestinal surgeons. Recently, Korean authors have reported a method of injecting autologous blood to mark the tumor before surgery with high efficiency and safety [3,5]. However, in all these articles, authors had concentrated in the safety as well as analyzed the complications of this method. Therefore, the study was carried out to evaluate the effectiveness by analyzing the section biopsy's results, as well as the safety of our procedure of autologous blood injection to locate the tumor before laparoscopic colorectal surgery.

* Corresponding author.
** Corresponding author.
E-mail addresses: nnh@bachmai.edu.vn (N.H. Nguyen), bacsithehiep@gmail.com (T.H. Nguyen), nguyenconglongbvbm@gmail.com (C.L. Nguyen), vuxuanvinh@hmu.edu.vn (X.V. Vu), hiep1995hsgs@gmail.com (T.H. Luong), ntk@bachmai.edu.vn (T.K. Nguyen).

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Abbreviations

AB	Autologous blood
ICG	Indocyanine green
LCRS	Laparoscopic colorectal surgery

2. Material and methods

2.1. Study population

Approval was obtained from the Institutional Review Board (IRB). 'This case series has been reported in line with the PROCESS Guideline' at the end of the methods section (and include citation in the references section) [7] and was registered in accordance with the declaration of Helsinki (ID: researchregistry7579, https://www.researchregistry.com/register-now#home/registrationdetails/61ed43ab56b89f001e390d10/). Data was retrospectively collected from patient's database with diagnosis of colorectal early cancer (small or flattened), large adenomatous polyps that cannot be removed through gastrointestinal endoscopy and malignant lesions after polypectomy in our institute from October 01, 2020 through 31/12/202. Cut off of December 31, 2021 was used to have a meaningful follow-up period. From the clinical database, 16 patients who underwent colonoscopy with autologous blood before surgery from October 01, 2020 through December 31, 2021 were recruited in the study.

2.2. Selection criteria

All cases of colorectal early cancer (small or flat tumor, cancerous polyp), large adenomatous polyp that cannot be removed through gastrointestinal endoscopy and post-malignant polypectomy lesions in our department from October 01, 2020 through December 31, 2021 were recruited to our study.

2.3. Data collection

Data collected included patient demographics, clinical data of patients (general information, disease's characteristics), the characteristics of autologous blood technique (marking positions, time of tattooing, volume of blood injection), the technique's results (number of intraoperative visible marking positions, section biopsy's results, technical complications).

2.4. Statistical methods

Continuous variables are presented as a mean with standard deviation, or as median with range or interquartile range, depending on the distribution of the data. All statistical analyses were performed using SPSS, version 22.0 for Windows statistical software.

2.5. Technical protocol

The marking was proceeded in about 24–48 h before laparoscopic surgery, we took 10 ml of the patient's venous blood (without anticoagulant) as a marker just before the colonoscopy. Submucosa injection with 5 ml of the patient's venous blood into the site below the lesion (2 cm from the lower border of the tumor) and 5 ml into the site above the lesion (2 cm from the upper border of the tumor) (Fig. 1).

3. Results

100% cases had upper and lower R0-section. No complications was found that related to technique.

4. Discussion

Our study showed that 100% of patients found the marker position during laparoscopic surgery. In which, 12/16 patients (75%), both upper and lower marked positions had been seen, these cases had showed the exact location of the tumor (between the two markers) (Fig. 2). 4/16 patients (25%) had been seen one marker site (upper or lower), which would show the appreciated exact location of the tumor (the tumor could be below or above the marker).

According to Seung HL et al., there were 23/25 (92%) finding the marking position intraoperatively, and in two failure cases, the author identified the cause as too deep injection and not enough deep injection. In case of too deep injection, blood will spread to the peritoneum adjacent to the colon, making it difficult to determine the exact location. In cases where the injection was not deep enough, the blood cannot spread to the serosa to be visible intraoperatively [3]. Eui JK. et al. revealed that 47/51 patients (92.2%) found the marker position intraoperatively. Analysis of 4 patients with failure marking found that: In the first patient, with a history of cirrhosis and thrombocytopenia, endoscopic manipulation formed subserosal hematomas, so the location of the marker could not be distinguished with these injuries; In the second patient, with a BMI $\geq$30 kg/m2, the marker site could not be detected because the lesion was covered with intraperitoneal fat; In the third patient, blood spilled around and caused intestinal adhesions, which required open surgery; In the fourth patient, the serosal surface tattoo could not be detected, but only a hematoma in the colonic wall was seen on pathology, in this patient, the authors believed that the cause was due to the technique of the endoscope: insufficient blood injection or not deep enough injection [5].

In our study, there were no cases where both markers could not be seen, however, there were 4 patients who only saw one marking position, the cause may also be due to technical factors that blood injection was not deep enough for the blood to spread to the serosa. With these 4 patients, only the tumoral location could be determined relatively accurately: it was located about 2 cm (cm) above or below the hematoma site, in these cases our experience is that more extensive resection was required above and below the marker site to ensure that all tumor cells were removed. The results showed that the postoperative pathology was very good: 93,8% of all cases had the distance from the upper section to the tumor greater than 5 cm (with both colon tumor group of twelve patients and rectal tumor group of four patients); The distance from the lower section to the tumor of the colon tumor group and the rectal tumor group were: 5.5 $\pm$ 1.7 cm and 2.4 $\pm$ 1.1 cm, respectively; 100% of the upper and lower sections had no tumor cells (R0-resection). It is not clear how long the mark will be valid. Since it is blood, it will disappear over time. So that, in all cases, we had proceeded operation in the following day after this procedure, with two purposes: Firstly, to preserve the autologous blood masks, and secondly, to avoid the complication of intestinal infarction and perforation. And we hadn't used anticoagulants, so in this procedure, we had inject autologous blood right after blood sampling to avoid blood's coagulant.

In aspect of safety, our study had result of no cases with any complications of endoscopic markers such as intestinal perforation, peritonitis. intestinal adhesions, etc. The longest interval from the time of endoscopic marking to the time of surgery was 4 days in one patient, in this patient in laparoscopic surgery still clearly saw 2 marked locations (upper, lower) and did not have any complications. Because autologous blood wasn't a foreign ingredients like Indian ink, it was believed that this technique was safer than other methods of marking injection by methylene blue injection, Indian ink or Indocyanine green (ICG). Research by Seung HL. et al. in 25 cases, there were no cases of complications of blood tattooing, the author considered that using autologous blood to inject markers has high safety because there was no foreign elements rarely presented [3]. Research by Eui JK. et al. revealed that 3/51 patients (5.9%) had complications of blood tattooing, in which one case had peritonitis and another two cases of abdominal

hemorrhaging [5]. In other hand, there are diverse hazardous materials in India ink like ethylene glycol, phenol, shellac, and gelatin which could cause adverse events. A systematic review by Acuna et al. revealed that the most frequent adverse events of tattooing were ink spillage, with a rate of about 10–15% in some research [2,8,9].

Perioperative colonoscopy has proven to be an unsuitable technique for tumoral localization in most cases because of the potential for increased error due to loopholes in the colonoscope, moreover, if it is determined accurately, in laparoscopy is itself also very difficult to estimate the tumor position through the screen. Colonoscopy method to identify tumor in surgery often has many inconveniences and after colonoscopy often occurs colorectal distention and reduces the surgical field. Cho et al. reported an accuracy rate of 88.7% using colonoscopy alone [10]. In 1958, Sauntry and Knudtson firstly reported the technique of marker injection using blue dye at the base of the polyp [11]. Subsequently, Knoernchild reported series of 190 patients who underwent endoscopic marker injection [12]. The most common used dye was Indian ink, as first described in 1975 by Ponsky and King [13]. However, injection marked with Indian ink showed off many complications and side effects, the dye spread around leading to inaccurate assessment of tumor location [14]. Indian ink had been proved that also been implicated in fat necrosis, inflammatory pseudo-tumoral formation, colonic abscesses, and intestinal adhesions [15,16]. The technique of injecting a marker with methylene blue has also been reported, however, the dye does not persist long enough at the marker site and can spread rapidly around, making it difficult to locate the exact location [17]. Tumoral markers with indocyanine green (ICG) on an enhanced fluorescence screen have also been described [18]. Although this technique was reported to be safe and effective, but significantly extra costs due to the need for additional lighting and fluorescent screens.

In our research, there have been just one case of ascending colon tumor. For tumors in the ascending colon, we conducted using metal clips additionally next to the tumor, an abdominal X-ray film was performed could show the location of the tumor on the colonic frame (Fig. 3). In case the tumor in the transverse colon was partially covered by the great omentum, to confirm firmly, we will conduct both using clips next to the tumor and the injection of autologous blood, injecting both the 2-cm-in-distance upper and lower parts of the tumor and an additional site on the opposite side of the tumor (in case the tumor markers the upper and lower the tumor are covered by the great omentum and are not visible during surgery). And finally, the autologous blood mark seems somewhat vague as compared to Indian ink and may sometimes be difficult to find. But in all cases, we use two positions to inject autologous blood, so that the blood tattooing was quite clearly visible and easy to determine laparoscopically in most cases. With superior aspect in reducing adverse events comparing with Indian ink, we think this inconvenience was acceptable.

5. Conclusions

In conclusion, we see that marking with autologous blood is a method that can be implemented effectively and safely, overcome the disadvantages of colonoscopy, clipping, ICG injection; as well as limit the side effects of using Indian ink and other dyes. However, its results are highly dependent on the qualifications and experience of the endoscopists. At the same time, this study has a small sample size, so the results are only preliminary, it will be necessary to conduct future studies with larger sample sizes to get more certain results.

Ethics approval

The study was approved by the Research Ethics Committee of Bach Mai Hospital. The procedures used in this study adhere to the tenets of the Declarations of Helsinki.

Sources of funding

The authors declare no funding for this study.

Authorship contribution statement

Ngoc Hung NGUYEN: the main doctor conceived the original idea and operated the patients, summed up, revised manuscript. The Hiep NGUYEN: the doctor conceived the original idea and operated the patients, wrote manuscript. Cong Long NGUYEN: the doctor proceeded the technique in patients, revised manuscript. Xuan Vinh VU: the doctor conceived operated the patients, revised manuscript. Tuan Hiep LUONG: operated the patients, followed up, wrote manuscript. Thanh Khiem NGUYEN: the doctor conceived the original idea and operated the patients. All authors contributed to the interpretation of the results, discussed the results. All authors read and approved the final manuscript to submit.

Availability of data and material

Data is available upon reasonable request and with permission of Bach Mai Hospital.

Guarantor

Ngoc Hung NGUYEN, MD, PhD.

Consent

The written informed consent was obtained from the recruited patients.

Provenance and peer review

Not commissioned, externally peer reviewed.

Declaration of competing interest

The authors declare that they have no conflicts of interests.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103345.

Appendix

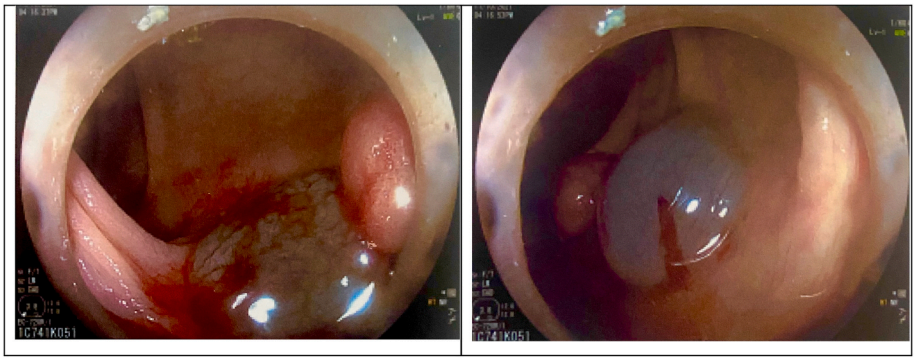

Fig. 1. Colonoscopy submucosa autologous blood injection

Table 1
General information of targeted patients

Index		N	%
Mean age (years old)		62,9 ± 13,1	
Male: Female ratio		8 : 8	
Tumoral classification	Early cancer	8	50,0
	Large adenomatous polyp	6	37,5
	Post-malignant polypectomy lesions	2	12,5
Tumoral position	Descending colon tumor	2	12,5
	Sigmoid colon tumor	9	56,3
	Rectal tumor	4	25,0
	Ascending colon tumor	1	6,3

Table 2
Technical characteristics

Index		N	%
The interval time from endoscopic marking to the surgery	Less than 24 h	15	93,8
	More than 24 h	1	6,2
Number of visible marking positions	All two marking positions	12	75,0
	One marking position	4	25,0
	No marking position	0	0,0
Distance from the upper section to the tumor	Greater than 5 cm	15	93,8
	Lower than 5 cm	1	6,2
Distance from the lower section to the tumor (mean ± SD, cm)	Group of colon tumors	5,5 ± 1,7	
	Group of rectal tumors	2,4 ± 1,1	

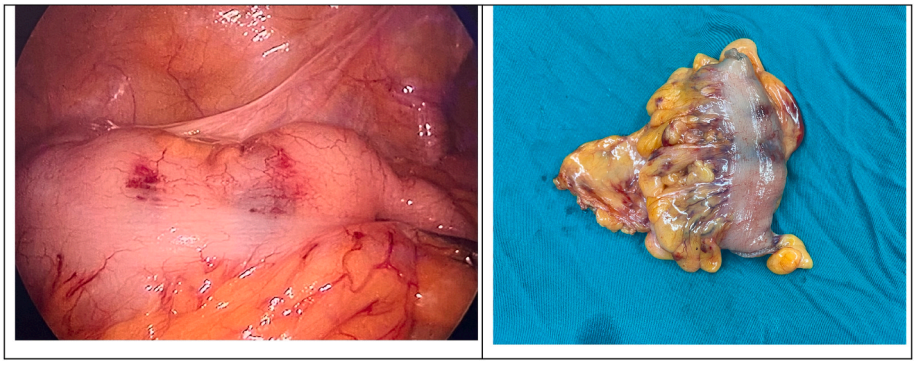

Fig. 2. Intraoperative imaging found all two marking positions

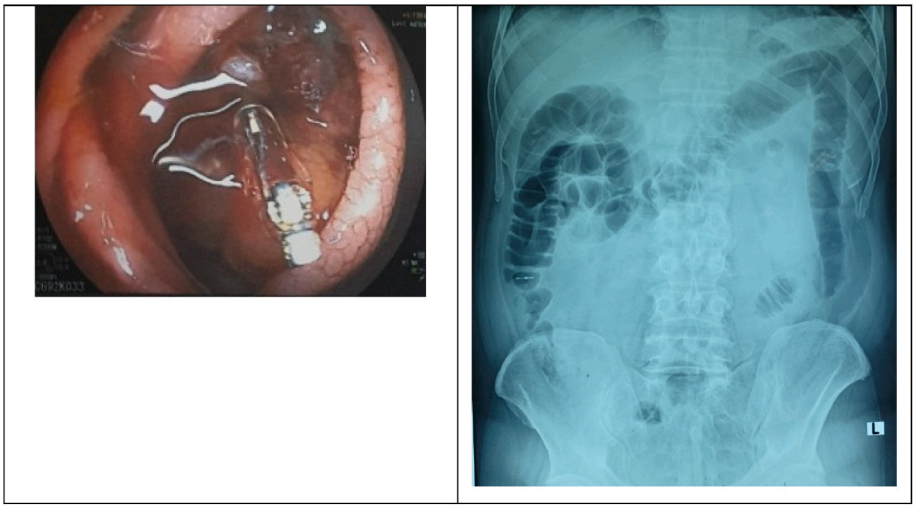

Fig. 3. Using additionally metal clips next to the tumor, an abdominal X-ray film was performed could show the location of the tumor on the colonic frame

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