Original Article

A Retrospective Cohort Study to Compare Short-term Effects of Laparoscopic Natural Orifice Transluminal Endoscopic Surgery, Laparoscopic Assisted and Conventional Laparotomy in Patients for Right Hemicolectomy

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Key Words

Laparoscopic colectomy; Natural Orifice Transluminal Endoscopic Surgery (NOTES); Transvaginal specimen extraction; Right hemicolectomy **Objective.** The study aims to analyze the technical feasibility, safety, and short-term clinical outcomes of three surgeries: conventional laparotomy, laparoscopically assisted procedure (LAP) and Natural Orifice Transluminal Endoscopic Surgery (NOTES) in patients for right hemicolectomy. *Method.* Patients who underwent laparotomy, LAP or NOTES for right hemicolectomy in our institute were enrolled for this retrospective cohort study. The postoperative short-term effects were analyzed.

Results. Between January 2018 to July 2019, total of 75 patients (64 cancer patients and 11 non-cancer patients) subjected to right hemicolectomy were enrolled. Of these 75 patients, forty-two (56.0%) patients underwent LAP surgery, 23 (30.7%) patients for laparotomy surgery and 10 (13.3%) for NOTES. NOTES group had the smallest median wound size (2.0 cm) in comparison to LAP (8.0 cm) and laparotomy (15.0 cm) group. More percentage of patients in LAP and laparotomy groups had abdominal pain (59.5% and 65.2%) in comparison to NOTES patients (40%). NOTES patients used the smallest analgesia in comparison to LAP and laparotomy (p = 0.037) patients.

Conclusion. NOTES is feasible and had short-term benefits for patients planning for right hemicolectomy surgery, but not comprising short-term outcomes.

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Collectomy surgery to remove right colon is referred to as right hemicolectomy. It involves removal of the right side of the colon and attaching the small intestine to the remaining portion of the colon. Laparoscopy has emerged as the preferred operative approach for the most intra-abdominal pathologic conditions. Even though the first laparoscopic colectomy was reported decades ago, the majority of colectomies are still being performed via the open approach. Open surgery-related large abdominal incision increases patient discomfort, the risk of pain and wound-related morbidity.^{1,2} Minimally invasive procedures such as

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laparoscopically assisted procedures (LAP) and total laparoscopic surgery has been advanced and become the standard surgical treatments for malignant neoplasms or disease of the right colon avoiding of conventional open surgery.^{3,4} However, a new or elongation of incision (5 to 10 cm) at the abdominal wall for specimen extraction from the abdominal cavity is normally required, which might increase relevant postoperative infection, surgery-related pain or unfavorable cosmesis results to patients.⁵

The body's natural orifice can be used to perform surgical procedures to potentially decrease the body injury which occurs during traditional procedures. Natural Orifice Transluminal Endoscopic Surgery (NOTES) is to anatomic access as trans-vaginal or trans-anal, instead of abdominal incision as a way to extract the resected specimen out of the peritoneal cavity.⁶⁻⁹ This technology associating with traditional minimally invasive approaches has gained much interest among minimally invasive surgeons. According to International Alliance of International consensus on natural orifice specimen extraction surgery for colorectal cancer, the NOTES is defined as the surgical specimen resection which is performed intraabdominally, then the specimen is extracted by opening a hollow organ that communicates with the outside body, including anus, or vagina.¹⁰ In a case-control study, Park and his colleagues reported that NOTES approach is feasible with favorable short-term surgical outcomes in comparison to the conventional laparoscopically assisted approach for right hemicolectomy.¹¹ However, a standardized NOTES procedures are not yet established and its implementation in daily clinical practice for colorectal surgery, and its assumed benefits such as less pain, lower analgesia requirements, faster recovery, shorter hospital stay, better cosmetic results, and lower incisional hernia rates have yet to be studied in prospective controlled trials.¹²

To our knowledge, few reports exists on the outcomes of NOTES versus conventional laparoscopically assisted approach for right hemicolectomy. In this retrospective study, the impact of NOTES to obtain the safety and short-term postoperative benefits with cosmetic results and reduction on post-operative morbidities in comparison to LAP procedures and conventional laparotomy were analyzed.

Patients and Methods

Patients

Data was collected retrospectively of all consecutive patients who underwent right hemicolectomy surgeries due to malignant neoplasms or other indicated colon diseases from January 2018 to July 2019 in Tung's' Taichung MetroHarbor Hospital. Patient demographic and surgical outcomes were collected by chart review. All surgeries were performed by three experienced surgeons (G.-S.C).

Surgical technique

The choice of surgical approach (NOTES, or laparoscopically assisted procedures, or laparotomy) was determined by a preoperative joint decision between the patient and physician and by intraoperative findings, including characteristics of the tumor and vaginal status. The surgery was performed following clinical standard procedures,¹³⁻¹⁵ and is briefly summarized below.

Laparotomy

Under adequate general endotracheal anaesthesia, the patient was placed on supine position. Midline incision was made and a self-retaining retractor was placed into the abdomen cavity. Small intestine and transverse colon were packed away. The right colon was mobilized by making incision at the lateral peritoneal reflection and followed by combining blunt and sharp incision. Hepatic flexure was carefully taken down, possible bleeders was carefully clamped and ligated. Right half of omentum included in the specimen, and omental vessels was carefully isolated, clamped, and divided. Right half of gastrocolic ligament was also carefully isolated and ligated. Mesenteric tissue including mesenteric vessels from the divided bowels leading towards the pedicle was carefully isolated, clamped, divided and ligated. The specimen was removed. Side to side anastomosis between terminal ileum and transverse colon was accomplished with autosutures. Specimen was retracted and the incision wound was closed layer by layer.

Laparoscopically assisted procedures (LAP)

The patient was placed on the operative table in the supine position. General endotracheal anesthesia was induced. The abdomen was prepared and draped in the usual sterile fashion. A 2 cm incision was made at umbilicus as camera port by open method. Pneumoperitonium was made. The other 3 trocar holes were made: two at left site, and one at right site. The small bowel loops were pulled upward. Dissection was made since lower portion of ileocolic vessels by medial to lateral method. Dissection was made upward to gallbladder and laterally till abdominal wall. After ligation, ileocolic vessels were transected. Lateral white line was dissected since mesoappendix and upward to hepatic flexure. Carefully divided and ligated the right, and middle colic artery and vein. The lesser sac was entered after gastrocolic omentum was divided along gastroepiploic artery.

The camera trocar hole was enlarged, and the right site mobilized colon was pull out. Side-to-side anastomosis was done by autosuture. Mersilk suture was performed interruptedly by Lembert sutures over the anastomosis sites. A J-vac drain was placed in Morrison pouch. The fascia was closed by figure eight method. The skin was closed with nylon.

NOTES

The transvaginal route was used for specimen extraction for all NOTES patients in this study which was done by one experienced physician. The patient's tumor/potential extracted sample must be less than 8 cm and the suitable patients were informed and agreed to this surgery. Briefly, under ETGA, the patient was placed in supine lithotomy position. Three Troca (12, 12, and 12 mm at L't axillary, supra-umbilicus, and R't lower axillary line) pneumoperitoneum was created. Ilocolic artery and vein was ligated. Side-to-side anastomosis was done by autosutures. Specimen was placed in tissue bag. One 2 cm incision line was created at vagina and specimen was extracted from vaginal orifice. Vaginal wound was closed by 1-0 Vicryl. A J-vac drain was placed in Morrison pouch. The fascia was closed by figure eight method. The skin was closed with nylon.

Outcome variables

The surgical data including operation time, estimated blood loss, and intraoperative adverse events; pathology data including tumor size, location of tumor, resection margin status, wound size, and number of harvested lymph nodes; and postoperative data including length of hospital stay, morbidity were analyzed.

Perioperative analgesia exposure was measured using WHO Defined Daily Dose (DDD) standardised cumulative analgesia prescribing.¹⁶

Statistical analysis

Continuous variables were expressed as mean \pm standard deviation and tested by Mann-Whitney U test. Categorical variables were expressed as counts (percentage), chi-square test was conducted to determine difference. All statistical assessments were two sided and evaluated at the 0.05 level of significance. Statistical analyses were performed by IBM SPSS statistical software version 22 for Windows (IBM Corp., Armonk, New York, USA).

Result

Between January 2018 and July 2019, a total of 75 patients who undergoing right hemicolectomy were recruited, the median (Q1, Q3) of age was 65.0 (57.0, 77.0) years, most of male (54.67%). From 75 patients, 42 (56.0%) patients underwent LAP surgery for right hemicolectomy, 23 (30.7%) patients for laparotomy surgery and 10 (13.3%) for NOTES. All 10 patients (8 cancer patients and 2 non-cancer patients) who received NOTES were female using transvaginal route for specimen extraction. For pathology parameters, the median (Q1, Q3) proximal margins of samples resected through LAP, NOTES, and laparotomy methods were 9.8 (8.0, 17.0), 12.5 (7.8, 17.0), and 8.0 (5.5,

14.0) cm, respectively, while median distal margins were 6.0 (4.0, 9.1), 6.5 (4.5, 7.5), and 7.0 (6.0, 10.0) cm respectively. There was no significant difference of specimen margins between different surgery methods.

The number of dissected lymph node in the specimen and blood loss among three surgeries were similar as well. NOTES had the longest median surgery time (168.0 min), followed by LAP with 155.5 min, and laparotomy with 116.0 min. The median days (Q1, Q3) of hospital stay after three surgeries were 13.0 (10.0, 17.0), 12.0 (10.0, 17.0), and 14.0 (10.0, 15.0) days, respectively. NOTES method had the smallest maximum wound size (2.0 cm) in comparison to LAP (8.0 cm) and laparotomy (15.0 cm). Therefore, patients receiving laparoscopic NOTES used the smallest defined daily dose (DDD, median (Q1, Q3) at 0.4 (0.2, 0.9) of analgesia in comparison to LAP with 0.6 (0.4, 1.1) and laparotomy with 1.1 (0.4, 3.1).

Patients receiving NOTES surgery, LAP and laparotomy have similar analgesics drug use day at 3.50 ± 2.17 , 3.45 ± 2.25 and 3.39 ± 1.47 , respectively (Table 1). Table 1 revealed the distribution of three different surgery methods in these 75 patients. NOTES had the oldest age, longest surgery time, fewest analgesia frequency and smallest wound in these three groups. Table 2 showed the distribution of three different surgery methods in these 64 cancer patients. Laparotomy had significant largest tumor size in those three groups. NOTES had the oldest age, longest surgery time, shortest hospital stay and smallest wound in these

		Total patients			
	Total $(n = 75)$	Laparoscopic NOTES		Laparotomy	<i>p</i> -value ^a
Age	65.0 (57.0, 77.0)	66.0 (58.0, 81.0)	74.5 (65.0, 79.0)	60.0 (48.0, 71.0)	0.093
Gender					-
Male	41 (54.67%)	22 (52.4%)	0 (0.00%)	12 (52.2%)	
Female	34 (45.33%)	20 (47.6%)	10 (100.0%)	11 (47.8%)	
Cancer					0.869
No	11 (14.7%)	6 (14.3%)	2 (20.0%)	3 (13.0%)	
Yes	64 (85.3%)	36 (85.7%)	8 (80.0%)	20 (87.0%)	
Proximal margin	9.75 (7.05, 15.0)	9.8 (8.0, 17.0)	12.5 (7.8, 17.0)	8.0 (5.5, 14.0)	0.260
Distal margin	6.5 (4.63, 9.08)	6.0 (4.0, 9.1)	6.5 (4.5, 7.5)	7.0 (6.0, 10.0)	0.303
Tumor size	4.5 (2.53, 7.38)	7.38 ± 12.94	8.06 ± 7.55	7.11 ± 3.29	0.057
Dissect lymph node	17.0 (14.0, 22.0)	19.0 (14.0, 22.0)	18.0 (14.5, 27.0)	15.0 (14.0, 21.0)	0.664
Blood loss (cc)	20.0 (20.0, 50.0)	25.0 (20.0, 100.0)	25.0 (20.0, 50.0)	20.0 (20.0, 50.0)	0.884
Surgery time (min)	150.0	155.5	168.0	116.0	0.001
	(115.0, 195.0)	(125.0, 196.0) ^b	$(155.0, 210.0)^{\rm c}$	(101.0, 150.0) ^{b,c}	
Analgesia frequency	4.0 (2.0, 5.0)	3.5 (1.5, 5.0) ^b	4.0 (2.0, 5.0)	$6.0(3.0,7.0)^{b}$	0.041
Length of hospital stay	13.0 (10.0, 17.0)	13.0 (10.0, 17.0)	12.0 (10.0, 17.0)	14.0 (10.0, 15.0)	0.846
Maximum wound (cm)	8.0 (6.0, 12.0)	$8.0(7.0, 8.0)^{b,d}$	$2.0(2.0,2.0)^{b,c}$	15.0 (14.0, 15.0) ^{c,d}	< 0.001
DDD					
Median (Q1, Q3)	0.6 (0.4, 1.5)	0.6 (0.4, 1.1)	0.4 (0.2, 0.9)	1.1 (0.4, 3.1)	0.115
Analgesics drug use (days) (mean \pm SD)	3.28 ± 1.76	3.45 ± 2.25	3.50 ± 2.17	3.39 ± 1.47	0.884
Median (Q1, Q3)	3 (2.0, 4.75)	3 (2.0, 5.0)	3 (2.0, 4.3)	3 (2.0, 5.0)	
Max, Min	(1, 9)	(1, 11)	(2, 9)	(1, 6)	
Abdominal pain					0.618
No	31 (41.3%)	17 (40.5%)	6 (60.0%)	8 (34.8%)	
Yes	44 (56.7%)	25 (59.5%)	4 (40.0%)	15 (65.2%)	

Continuous variables were presented as median (Q1, Q3).

^a Chi-square test or Kruskal Wallis test.

Significant value was in bold.

The same superscript letters indicate significant differences.

	Cancer patients $(n = 64)$				
	Laparoscopic	NOTES	Laparotomy	- <i>p</i> -value ^a	
Age	66.5 (59.5, 81.0)	76.0 (71.0, 80.5) ^b	61.5 (50.0, 73.5) ^b	0.027	
Gender				0.024	
Male	19 (52.8%)	0 (0.0%)	9 (45.0%)		
Female	17 (47.2%)	8 (100.0%)	11 (55.0%)		
Proximal margin	9.8 (8.0, 17.0)	12.5 (7.8, 17.0)	8.0 (5.5, 14.0)	0.260	
Distal margin	6.0 (4.0, 9.1)	6.5 (4.5, 7.5)	7.0 (6.0, 10.0)	0.303	
Tumor size	4.43 ± 3.28	6.45 ± 7.26	6.84 ± 3.13	0.023	
Dissect lymph node	18.0 (14.0, 22.0)	18.0 (14.5, 27.0)	15.5 (14.5, 21.5)	0.811	
Blood loss (cc)	25.0 (20.0, 100.0)	20.0 (20.0, 40.0)	20.0 (20.0, 40.0)	0.777	
Surgery time (min)	153.5 (124.0, 198.5) ^b	184.0 (149.5, 250.5) ^c	115.0 (101.0, 142.5) ^{b,c}	0.001	
Analgesia frequency	$3.0(1.0, 5.0)^{b}$	5.0 (2.0, 5.0)	$6.0(3.0,7.0)^{b}$	0.040	
Length of hospital stay	13.0 (10.5, 17.0)	12.0 (10.0, 30.0)	14.5 (11.0, 16.0)	0.989	
Maximum wound (cm)	$8.0(6.5, 8.0)^{b,d}$	$2.0(2.0, 2.0)^{b,c}$	15.0 (14.0, 15.0) ^{c,d}	< 0.001	
DDD					
Median (Q1, Q3)	0.6 (0.4, 0.9)	0.4 (0.2, 1.1)	1.3 (0.5, 3.1)	0.037	
Analgesics drug use (days) (mean \pm SD)	3.0 ± 1.77	3.75 ± 2.38	3.45 ± 1.43	0.506	
Median (Q1, Q3)	3 (1, 4)	3 (2, 4.75)	3 (2.25, 5)		
Max, Min	(1, 8)	(2, 9)	(1, 6)		
Abdominal pain				0.725	
No	15 (41.6%)	5 (62.5%)	8 (40.0%)		
Yes	21 (58.4%)	3 (37.5%)	12 (60.0%)		

Tab	le 2.	ANOV	A test b	between	three	surgery	of	cancer patients
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Continuous variable were presented as median (Q1, Q3).

^a Chi-square test or Kruskal Wallis test.

Significant value was in bold.

The same superscript letters indicate significant differences.

 e *p*-value = 0.08.

three groups. In addition, terms of age, gender, tumor size, surgery time, analgesia frequency, maximum wound and DDD were significant difference between three surgery methods (p < 0.05). It was a remarkable fact that DDD had a significant difference between three groups but had not significant difference in posteriori comparisons. A total of six patients had postoperative complications, three in LAP group (1 ileus, 1 wound infection, 1 pneumonia) and three in laparotomy group (1 poor wound healing, 1 ileus stress, 1 ulcer upper GI bleeding). No postoperative complication was reported in NOTES group.

Discussion

This is a retrospective cohort study to compare short-term benefits of NOTES procedure with clinical

standard surgery method LAP and conventional laparotomy surgery in consecutive cohort patients who underwent right hemicolectomy surgery in single medical center. The results indicated that NOTES method for right hemicolectomy resulted in smallest maximum wound size with better cosmetic outcome, significantly lower analgesic requirement. These findings suggested that NOTES approach for right hemicolectomy surgery is preferred due to favorable shortterm surgical outcomes. The similar conclusion was reported in a case-control study compared the clinical outcomes of totally laparoscopic hemicolectomy with NOTES and the conventional LAP for right-sided colonic cancer.¹¹

Post-operative pain reduction is critical among patients with right hemicolectomy surgery. Intense postoperative pain might cause long-term adverse outcome.¹⁷ A large abdominal incision is used to extract sisted procedure, the cut site below umbilicus is expanded to at least 5 cm for specimen extraction. In this study, the maximum wound size below umbilicus was 8.0 cm in LAP group and 15.0 cm in laparotomy group while it was only 2.0 cm in NOTES group. Here, we found that in LAP group showed a larger maximum wound size (8.0 cm) than usual laparoscopy surgery. This result might be caused by the original tumor size were larger in several patients in LAP group. Clearly, NOTES right hemicolectomy significantly avoids incisional pain, and then reduce postoperative stress. Minimally abdominal wound size also brought better cosmetic effect to patients.

Previous large randomized controlled study has proven that LAP and open colectomy for colon cancer resulted in similar recurrent rate to solve initial concerns regarding the adequacy of oncologic margins and trocar site believed to occur with laparoscopy.¹⁸ Now minimally invasive colectomy is widely accepted since this method is associated with significantly low risk of major perioperative complications, lower total hospital costs.¹⁹ In this study, we found three postoperative complications in LAP group, including one wound infection. No postoperative complication was noted in NOTES group. However, the major concern is with the successful specimen extraction from natural orifice, as in the case of tumor resection by transanal or transvaginal route with enough tumor margins with no contamination of trocar site. The present study showed that tumor samples in NOTES group had similar safe proximal and distal margins to those in LAP and laparotomy groups and their dissect lymph node numbers were same as well. The NOTES route has the same ability to extract specimen in right hemicolectomy as well as LAP and laparotomy. This indicates that these patients might have the same long-term prognosis while NOTES patients had an additional short-term benefits such as smaller wound size, less analgesic prescription.

About 20% of initial laparoscopic colectomies for cancer might require conversion to equivalent open procedures.²⁰ Tong et al. compared laparoscopic (n = 77) and open (n = 105) right hemicolectomy for several variables, including surgery time, and length of

hospital stays.²¹ They found a mean operating time was shorter for the open procedure (115.4 min) and seven laparoscopic cases (9%) required conversion to an open procedure. Median hospital stay was longer for open (7 days) than for laparoscopic surgery (6 days) and was significantly longer (9 days) in the converted-to-open group. In this study, we also found laparotomy procedure had the shorter median surgery time (116 min). This is consistent with previous reports.^{21,22} NOTES had numerical shorter median duration of hospital stay (12 days) in comparison to laparotomy (14.5 days) with no statistical significance. In this study, no initial LAP or NOTES procedures was converted to laparotomy right hemicolectomy.

Of the natural orifice, the vagina is considered a viable route for specimen retrieval during LAP.^{10,23} In comparison to NOTES which is mainly applicable to extract small tumors or samples, NOTES is available for female patients with a bulky specimen that cannot be removed through the anus and NOTES should be avoided in young women who have not completed their family.¹⁰ In the present study, all 10 patients underwent NOTES were female and transvaginal route was used for specimen extraction. The patients' tumor size was less than 8 cm based on pre-surgery examination and the size of tumor sample was suitable for transvaginal extraction. In addition, those 10 patients for NOTES with average 75 years old were evaluated for their vagina sex function, and total consent informed since a 2 cm incision was cut in their vaginal wall for specimen extraction in a plastic bag. Care should be carried out when selecting individuals for transvaginal specimen extraction. A careful review of gynecologic history and preoperative consultation is required when selecting appropriate female patients. In general, transvaginal access is not recommended for patients who have vaginal narrowing, virginity, or a history of endometriosis, or for patients who are planning a pregnancy or for whom the cosmetic result is not a concern.

The outcomes from 64 cancer patients were almost similar to the outcomes analyzed based on total 75 patients (Table 2). This might indicate that laparoscopic surgery also can provide short-term benefits for right hemicolectomy patients with non-cancer colon diseases. Unfortunately, the number of non-cancer patient was small. In the future, more data are needed to confirm the advantages of NOTES for right hemicolectomy surgery for patients due to non-cancer disease.

The major limitation of this study is the retrospective characteristic and the results have to be confirmed with prospective studies of larger sample size. The number of patients in NOTES is relatively smaller. The outcome of this study is short-term effect. Longterm observation is needed to evaluate impact of NOTES on patients with right hemicolectomy. To our knowledge, this is the first report of NOTES on right hemicolectomy in comparison to LAP and open surgery in Taiwanese. Further, studies with long-term follow-up is warranted to establish the role of NOTES technique in the treatment of colon diseases.

In conclusion, in the case of the same safety and prognosis, the NOTES method had smaller wounds, fewer pain medications and shorter length of hospital stay than traditional surgery method.NOTES can bring short-term benefits to patients for right hemicolectomy regarding wound size, analgesia using, and duration of hospital stay while it has same ability and safety to cut and extract the tumor samples with less postoperative complications.

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<u>原 著</u>

回逤性研究使用自然孔洞標本取出術與 傳統腹腔鏡和常規剖腹術對右半結腸 切除術的短期預後比較

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目的 回溯姓研究使用自然孔洞標本取出術與傳統腹腔鏡和常規剖腹術對右半結腸切除 術的短期預後比較。

方法 本研究為回溯性病歷回顧,評估了從 2018 年 1 月至 2019 年 7 月間,醫療社團法 人童綜合醫院大腸直腸外科自然孔洞標本取出術與傳統腹腔鏡和常規剖腹術對右半結腸 切除術的短期預後比較。

結果 本研究將75位接受右半結腸切除術患者進行臨床表徵分類,其中64位癌症病人, 11 位非癌症病人,42 位 (56%) 行腹腔鏡切除合併腹壁標本取出,23 位 (30.7%) 行常 規剖腹術,10 位 (13.3%) 行腹腔鏡切除合併自然孔洞標本取出,在比較三組族群,腹 腔鏡切除合併自然孔洞標本取出族群擁有最小平均傷口大小 (2 cm),在常規剖腹術與腹 腔鏡切除合併腹壁標本取出術族群病人在術後較有疼痛情形 (65.2% 與 59.5%),腹腔鏡 切除合併自然孔洞標本取出族群擁有較少術後疼痛狀況 (40%),在比較三組族群,腹腔 鏡切除合併自然孔洞標本取出族群擁有最少的術後止痛藥使用量 (*p*=0.037)。

結論 自然孔洞標本取出術與傳統腹腔鏡和常規剖腹術對右半結腸切除術的短期預後上 能使病人擁有較小傷口,減少術後疼痛,與減少止痛藥的使用量。

關鍵詞 腹腔鏡切除合併自然孔洞標本取出術、右半結腸切除術、回溯性回顧。

張家齊等