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Research article

Simultaneous laparoscopic colectomy and liver metastasectomy with natural orifice specimen extraction: A proof-of-concept study

Isaac Seow-En[a,*], Ye Xin Koh[b], Emile Kwong-Wei Tan[a], Ek Khoon Tan[b]

[a] Department of Colorectal Surgery, Singapore General Hospital, Singapore
[b] Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, Singapore

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ABSTRACT

Background, Natural orifice specimen extraction (NOSE) via the anus or vagina is an alternative to conventional transabdominal specimen extraction in laparoscopic colorectal cancer surgery. NOSE has been shown to be safe and effective, resulting in decreased postoperative pain, analgesia use, and improved recovery, without oncological compromise. We aimed to demonstrate the feasibility of NOSE for combined colectomy with liver metastasectomy.

Methods, From July 2022 to April 2024, all cases of laparoscopic colorectal cancer resection and synchronous liver metastasectomy with NOSE were included in the study. Selection criteria included a maximum specimen diameter of less than 5 cm and patient body mass index of less than 35 kg/m^2.

Results, Over the 22-month duration, four consecutive patients (two males, two females) underwent combined resection with NOSE. Mean age and BMI were 74.8 (range 63–81) years and 20.9 (range 19.5–22.3) kg/m^2 respectively. Patient A and D underwent anterior resection for sigmoid cancer, Patient B underwent D3 right hemicolectomy for cecal cancer, and Patient C underwent subtotal colectomy for synchronous cecal and descending colon cancer. All patients underwent liver metastasectomy at the same sitting. Patient A and D had transanal NOSE while Patients B and C underwent transvaginal NOSE. Mean operative time and blood loss was 416 (range 330–535) minutes and 338 (range 50–500) ml respectively. All patients recovered gastrointestinal function within the first two postoperative days. Infected seroma of the liver bed occurred in one patient requiring percutaneous drainage. The average maximum colon tumor diameter was 2.9 (range 1.3–4.0) cm. All resection margins were clear. Mean duration of follow-up was 7.5 (range 2–12) months.

Conclusions, Simultaneous colectomy and liver metastasectomy with NOSE for colorectal cancer is feasible and safe in highly selected patients, resulting in good postoperative outcomes. This proof-of-concept analysis paves the way for larger studies to draw definitive conclusions.

1. Introduction

Despite the introduction of national colorectal cancer screening programmes, many patients still present with late-stage disease. The liver remains the most common site of colorectal cancer metastasis due to portal venous drainage. A 2022 French registry-based cohort study including 26,813 colorectal cancer patients showed a 17 % rate of synchronous liver metastasis, with 1- and 5-year

* Corresponding author.
E-mail address: isaac.seow.en@gmail.com (I. Seow-En).

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survival of patients with synchronous liver metastasis at 42 % and 6 % respectively [1].

While overall prognosis is poor, the management strategies for resectable colorectal liver metastases are expanding. Compared to the conventional open approach, laparoscopic resection has been demonstrated to be feasible, without inferior perioperative or oncological outcomes [2]. The timing of liver resection is another area of interest. A 2018 meta-analysis of 30 studies including 5300 patients showed an average of 6 days' shorter length of hospital stay amongst patients who underwent simultaneous compared to delayed hepatectomy, without adversely affecting postoperative morbidity or survival [3]. Moreover, the METASYNC study group randomized controlled trial showed reduced overall survival with delayed resection [4].

In recent years, the viability and benefit of simultaneous laparoscopic resection of the colorectal primary and liver metastases have been widely demonstrated [2,5–11]. Several studies evaluating the use of the robotic platform for simultaneous surgery have shown similar results [12,13]. All types of colorectal and hepatic resections were performed, the latter ranging from wedge resections to major hepatectomies.

Natural orifice specimen extraction (NOSE) via the anus or vagina in laparoscopic colorectal cancer surgery is an alternative to conventional transabdominal specimen extraction using a mini midline laparotomy or Pfannenstiel incision. NOSE has been shown to be safe and effective, significantly decreasing postoperative pain and analgesia use, while resulting in improved recovery, without oncological compromise [14–18]. NOSE is most often used in gynaecological or colorectal surgery, with few reports of natural orifice extraction following hepatopancreatobiliary surgery [19,20].

Reports of synchronous colorectal and liver resection with natural orifice specimen retrieval are rarely reported in the literature [21]. We aimed to demonstrate the feasibility of NOSE in a series of combined colectomy with liver metastasectomy.

2. Materials and methods

From July 2022 to April 2024, all cases of laparoscopic colorectal cancer resection and synchronous liver metastasectomy with NOSE were included in this proof-of-concept, retrospective case series. All patients underwent preoperative magnetic resonance imaging of the liver in addition to routine colorectal cancer staging. All cases included in this series were discussed at a dedicated preoperative multidisciplinary team (MDT) meeting involving senior colorectal surgeons, hepatobiliary surgeons, medical oncologists, and radiologists. The pros and cons of adjuvant chemotherapy versus upfront surgery were discussed, and the suitability of synchronous colon and liver resection was agreed upon for all cases prior to surgery. If neoadjuvant chemotherapy was recommended, MDT was repeated following completion of systemic therapy.

Appropriateness of liver metastasectomy was based on the assessment of experienced hepatobiliary specialists, without specific restrictions to the number and location of liver tumors to be removed. Predicted adequacy of R0 resection of liver tumors (confirmed intraoperatively under intracorporeal ultrasound guidance), and an estimated future liver remnant of at least 30–40 %, were necessary requirements. In addition, patients had to be deemed physiologically fit enough for synchronous minimally invasive surgery, which has a longer operative and general anesthesia time. All patients underwent preoperative anesthetist review and evaluation of comorbid status to ascertain surgical and anesthetic fitness, with possible optimization of their condition before surgery.

Selection criteria for NOSE was adapted from the 2019 International Consensus Guidelines for colorectal cancer natural orifice specimen extraction surgery [22], including a maximum specimen circumferential diameter of less than 5 cm and patient body mass index (BMI) of less than 35 kg/m^2. Patients with anal or vaginal stenosis were excluded from transanal and transvaginal NOSE procedures respectively. Prior pelvic surgery, including total hysterectomy, was not an absolute contraindication to NOSE, unless dense pelvic adhesions observed during surgery prevented safe mobilization of the rectum or creation of the posterior colpotomy.

For right sided colon resections, only transvaginal specimen retrieval was considered, as transanal NOSE would necessitate an additional rectotomy, along with the additional risk of luminal content spillage. For left sided colon resections, the transvaginal route was also preferred over transanal retrieval in view of the comparatively clean environment of the vagina, better blood supply facilitating tissue healing, and elastic walls allowing passage of larger specimens [23]. Final decision for NOSE was only made intraoperatively taking into account overall resected specimen size, inclusive of tumor and mesentery, relative to pelvic outlet and conduit diameter [23].

All patients were monitored in the surgical high dependency for at least one night after surgery. Serum hemoglobin levels, C-reactive protein, renal function, and liver function tests were obtained on postoperative day 1 and 3. Ambulatory physiotherapy was commenced on postoperative day 1, with removal of indwelling urinary catheter upon satisfactory ambulation with minimal pain. Oral intake was escalated appropriate to the recovery of gastrointestinal function, as determined by passage of flatus or stool, without nausea and vomiting. Fitness for discharge was documented after the following criteria were met: good general clinical condition, normalizing biochemical markers, tolerance of diet, and clearance by the physiotherapist. First outpatient follow-up evaluation by both the colorectal and hepatobiliary specialists was conducted 1–2 weeks after hospital discharge.

This study received SingHealth Centralized Institutional Review Board approval (Ref no. 2022/2114) and was conducted in accordance with the principles of the Declaration of Helsinki and its contemporary amendments.

3. Operative technique

Over the 22-month duration, four consecutive patients (two males, two females) underwent elective combined colorectal and liver resection with NOSE. Only patients who underwent synchronous surgery for colorectal cancer and colorectal liver metastases were included. All colon resections and combined NOSE procedures were performed by a single operator (ISE) experienced in laparoscopic colorectal cancer surgery using both transvaginal and transanal routes of specimen extraction. Liver resections were performed by

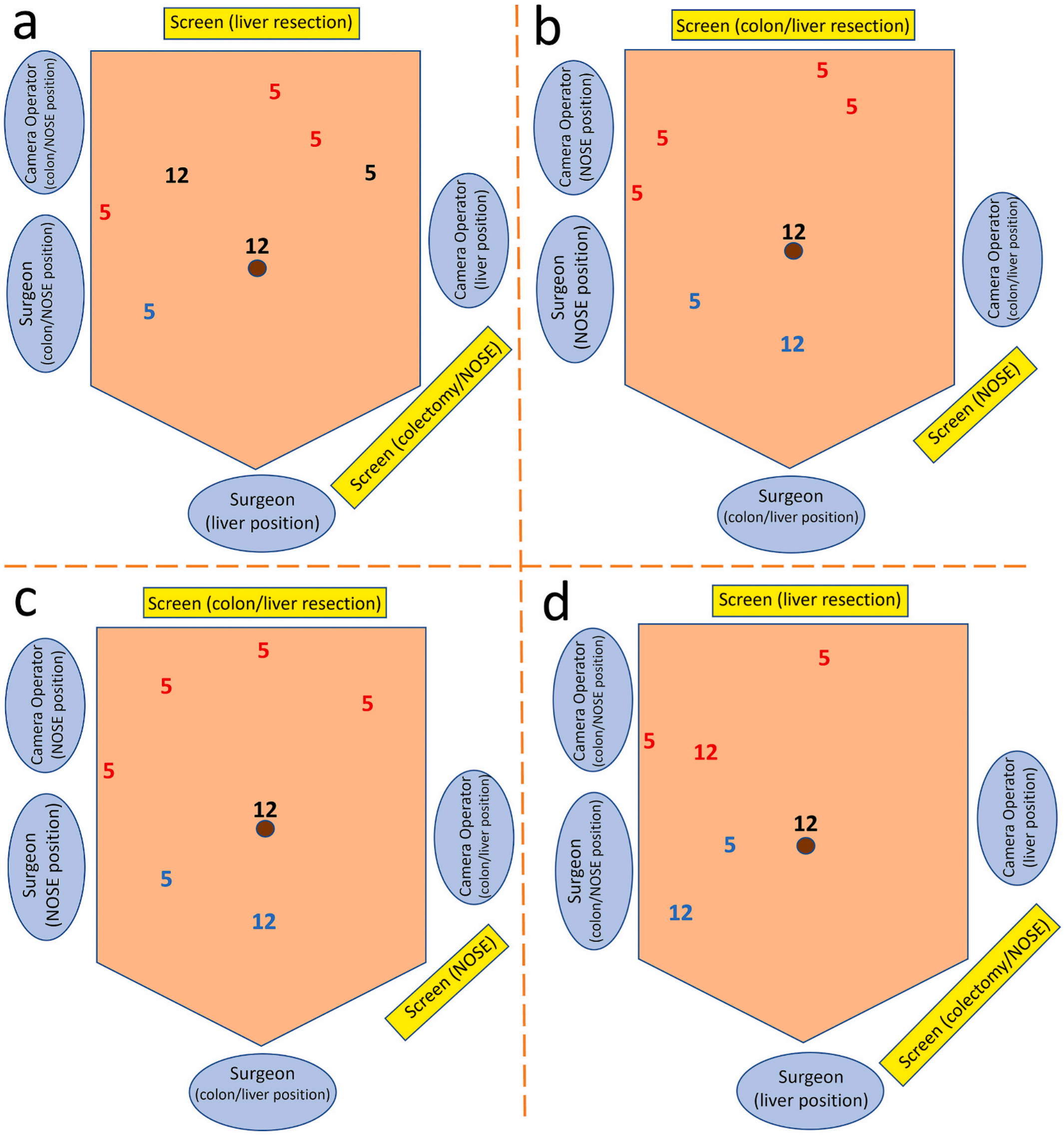

Fig. 1. Operative set-up and port placements for simultaneous liver resection and (a) (d) anterior resection with transanal NOSE, (b) D3 right hemicolectomy with transvaginal NOSE, and (c) subtotal colectomy with transvaginal NOSE. Number and placement of number denotes trocar diameter and abdominal position respectively, with red ports used for liver resection, blue ports for colectomy, and black ports for both procedures. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

hepatobiliary surgeons proficient in laparoscopic liver surgery. Intraoperative ultrasound was used in all cases to confirm position of the liver metastases, improving adequacy of resection margins. Indocyanine green fluorescence imaging was not performed.

Patient A and D underwent anterior resection for sigmoid cancer, Patient B underwent D3 right hemicolectomy for cecal cancer, and Patient C underwent subtotal colectomy for synchronous cecal and descending colon cancer. All patients underwent liver metastasectomy at the same sitting. Patient A and D had transanal NOSE while Patients B and C underwent transvaginal NOSE. Patient B had prior hysterectomy performed while Patient C's uterus was intact.

Operative set-up and port placement for each surgery is shown in Fig. 1a - d. Bowel preparation with 2L of polyethylene glycol was used for Patient A, C, and D. No bowel preparation was administered for Patient B. Patients A, B, C underwent laparoscopic liver resection before colon surgery.

For Patient A, the splenic flexure and left colon were mobilized, including high ligation of the inferior mesenteric artery. The distal colonic mesentery was then divided, and the bowel lumen was occluded with a silk tie. Rectal washout was performed before the distal bowel was sharply transected distal to the occluding tie. NOSE retrieval of the colon and liver specimens was performed. The proximal bowel was then delivered via the open rectal stump, with extracorporeal proximal bowel transection and application of the circular anvil (Fig. 2a and b). The bowel was then returned into the abdominal cavity, and the rectal stump was closed using a linear stapler. An

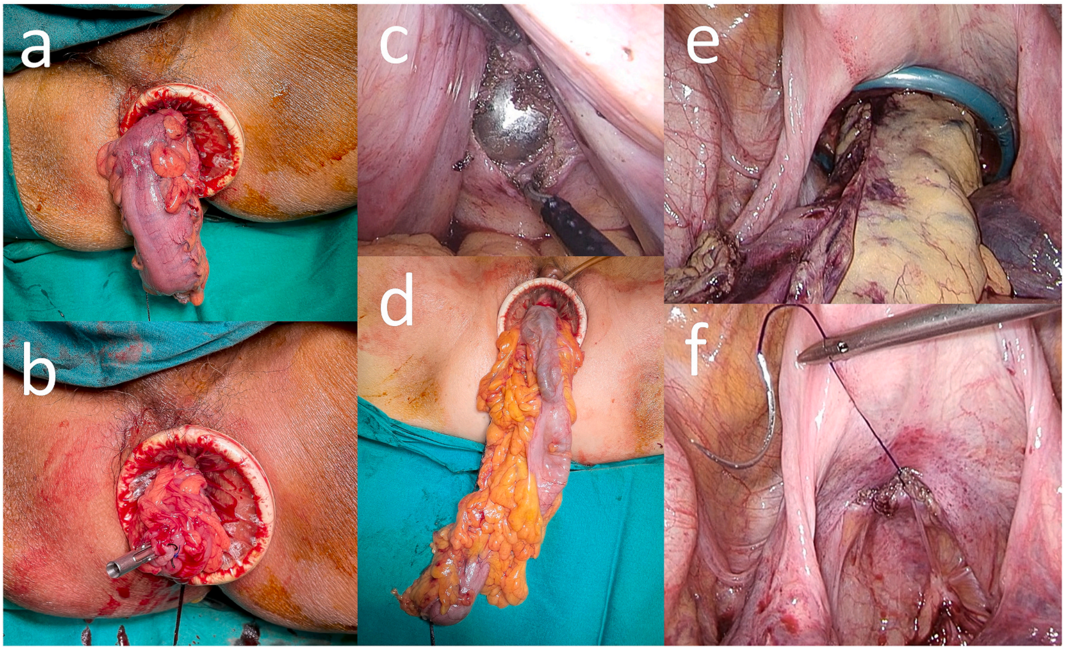

Fig. 2. (a) For Patient A, the proximal bowel was delivered transanally and transected, with (b) extracorporeal application of the circular stapler anvil. (c) Posterior vaginotomy in Patient B with prior hysterectomy and (d) transvaginal NOSE. (e) A double ring wound protector is positioned within the NOSE conduit. (f) Closure of vaginotomy with a continuous barbed suture.

end-to-end colorectal anastomosis was made using a circular stapler.

For Patient B, right hemicolectomy was performed with complete mesocolic excision, central vascular ligation of the ileocolic vessels, and D3 lymphadenectomy. A fully stapled intracorporeal antiperistaltic side-to-side ileocolic anastomosis was then created as previously described [24]. A posterior colpotomy was created for transvaginal extraction of specimens (Fig. 2c and d). The colpotomy was then closed laparoscopically using a continuous barbed suture (STRATAFIX PDS 2-0). For Patient C, oncological subtotal colectomy was performed with the bowel mobilized from right to left, with sequential ligation of vessels. An intracorporeal isoperistaltic side-to-side colocolic anastomosis was fashioned, using one linear stapler reload followed by sutured closure of the common channel. Posterior colpotomy was created for transvaginal NOSE (Fig. 2e), and subsequently repaired as in Patient B (Fig. 2f).

Following anterior resection for Patient D, the circular stapler anvil was anchored intracorporeally to the proximal bowel using the intracorporeal antimesenteric ancillary trocar (IAAT) technique. This approach was recently reported in detail by our unit [25]. In contrast to extracorporeal application of the anvil by exteriorizing the proximal colon (as in Patient A), the IAAT method introduces the circular anvil with the attached ancillary trocar through the anus into the abdominal cavity. The spike of the ancillary trocar was then brought out several centimeters proximal to the open end of the proximal colon via the antimesenteric border. Stapled closure of the open colon was then performed. Following specimen retrieval with NOSE, the rectal stump was stapled closed and an intracorporeal side-to-end colorectal anastomosis was fashioned. The IAAT technique requires less tissue dissection, eliminating the need for splenic flexure mobilization, and is our current approach of choice for anterior resection with NOSE.

In each case, a double ring wound protector was applied prior to specimen extraction to protect the conduit of choice from the theoretical risk of tumor cell seeding (Fig. 2a–e). The wound protector was removed prior to posterior colpotomy repair or stapled closure of the rectal stump. While described at some units, a separate sterile bag was not used to contain the colonic specimen prior to extraction, as specimens tended to bunch up within the bag, increasing specimen diameter and adding to the difficulty of NOSE. As resected liver specimens were friable and prone to tear when grasped directly, these were placed in an endoscopic bag to facilitate subsequent grasping and retrieval.

For Patients A, B, and C, liver resection preceded colon resection. The liver specimens were placed in a laparoscopic bag within the abdomen prior to colon surgery. Following colonic resection, natural orifice retrieval of the colon and bag containing the liver specimen(s) was performed. In patient D, sigmoid colon resection was first performed with transanal NOSE of the anterior resection specimen. The transanal wound protector was then twisted externally to occlude the channel, preventing loss of pneumoperitoneum during liver metastasectomy.

Patient A [26] and B [27] were previously described as individual case reports with accompanying step-by-step operative video vignettes.

Table 1
Patient and surgery characteristics for patients who underwent simultaneous laparoscopic colectomy and liver metastasectomy with natural orifice specimen extraction.

Patient	Age (years)	ASA score	BMI (kg/m^2)	Colon tumor location	Surgery
A	75 M	3	19.5	Sigmoid	Anterior resection, liver wedge resections (S4, S6), transanal NOSE
B	81F	3	19.7	Cecum	D3 right hemicolectomy, liver wedge resections (S4, S7), transvaginal NOSE
C	80F	2	21.9	Synchronous cecum and descending	Subtotal colectomy, liver wedge resection (S5/8), transvaginal NOSE
D	63 M	3	22.3	Sigmoid	Anterior resection, liver wedge resections (S7, S8), transanal NOSE

NOSE natural orifice specimen extraction, *ASA* American Society of Anesthesiologists score, *BMI* body mass index.

Table 2
Intraoperative and early postoperative outcomes following natural orifice specimen extraction for simultaneous laparoscopic colectomy and liver metastasectomy.

Patient	Operative time (min)	Blood loss (ml)	Time to first flatus/BO (days[a])	Postoperative LOS (days)	30-day postoperative complications
A	350	50	2/2	3	Nil
B	330	500	1/2	3	Nil
C	535	300	1/2	3	Nil
D	450	500	2/2	6	Infected liver bed seroma

NOSE natural orifice specimen extraction, *BO* bowel opening, *LOS* length of stay.
[a] Post-operative days.

Table 3
Histopathological results and follow-up duration following natural orifice specimen extraction for simultaneous laparoscopic colectomy and liver metastasectomy.

Patient	Primary tumor site and TMN stage	Margins	Tumor CDmax (cm)	Total LN harvest	Disease recurrence (months)
A	Sigmoid cancer pT4N1	Clear	2.0	32	9
B	Cecal cancer pT3N2a	Clear	3.8	19	6
C	Cecal cancer ypT3N1	Clear	3.5	27	Nil
	Descending cancer ypT1N0		1.3	11	
D	Sigmoid cancer pT3N2	Clear	4.0	26	Nil

NOSE natural orifice specimen extraction, *CDmax* maximum circumferential diameter, *LN* lymph node.

4. Results

Patient and surgery characteristics are shown in Table 1. Mean age and BMI were 74.8 (range 63–81) years and 20.9 (range 19.5–22.3) kg/m^2 respectively.

Table 2 provides the intraoperative and early postoperative outcomes. Mean operative time and blood loss was 416 (range 330–535) minutes and 338 (range 50–500) ml respectively. Patient controlled analgesia was not used in any instance, with no patients requiring the use of postoperative opioids or rescue analgesia. All patients recovered gastrointestinal function within the first two postoperative days. Patients A, B, and C were fit for discharge on postoperative day three. Patient D developed a fever and was diagnosed with a liver resection bed infected seroma on postoperative day 2, which resolved with percutaneous drainage and antibiotic treatment. There were no other postoperative complications in this series.

Histopathological results are given in Table 3. The average maximum colon tumour diameter was 2.9 (range 1.3–4.0) cm on histopathologic examination. All colon and liver resection margins were clear. Postoperative abdominal appearance and specimen images are shown in Fig. 3(a–d) and Fig. 4(a-d) respectively.

Patient A had a premorbid history of cardiac bypass surgery four years prior, heart failure, and atrial fibrillation. He underwent 8 cycles of adjuvant chemotherapy but developed bilobar liver recurrence nine months postoperatively and died three months later from pneumonia. Patient B had premorbid history of hypertension and diabetes mellitus complicated by chronic renal failure. She declined postoperative chemotherapy and developed pleural recurrence six months following surgery, passing soon after from respiratory failure. Both Patients A and B had documented good quality of life prior to disease recurrence. Patient C underwent 4 cycles of neoadjuvant chemotherapy and 4 cycles of adjuvant chemotherapy. She remains alive and well without evidence of disease recurrence ten months after surgery. Patient D also remains well and disease free two months postoperatively. Mean overall duration of follow-up in the series was 7.5 (range 2–12) months.

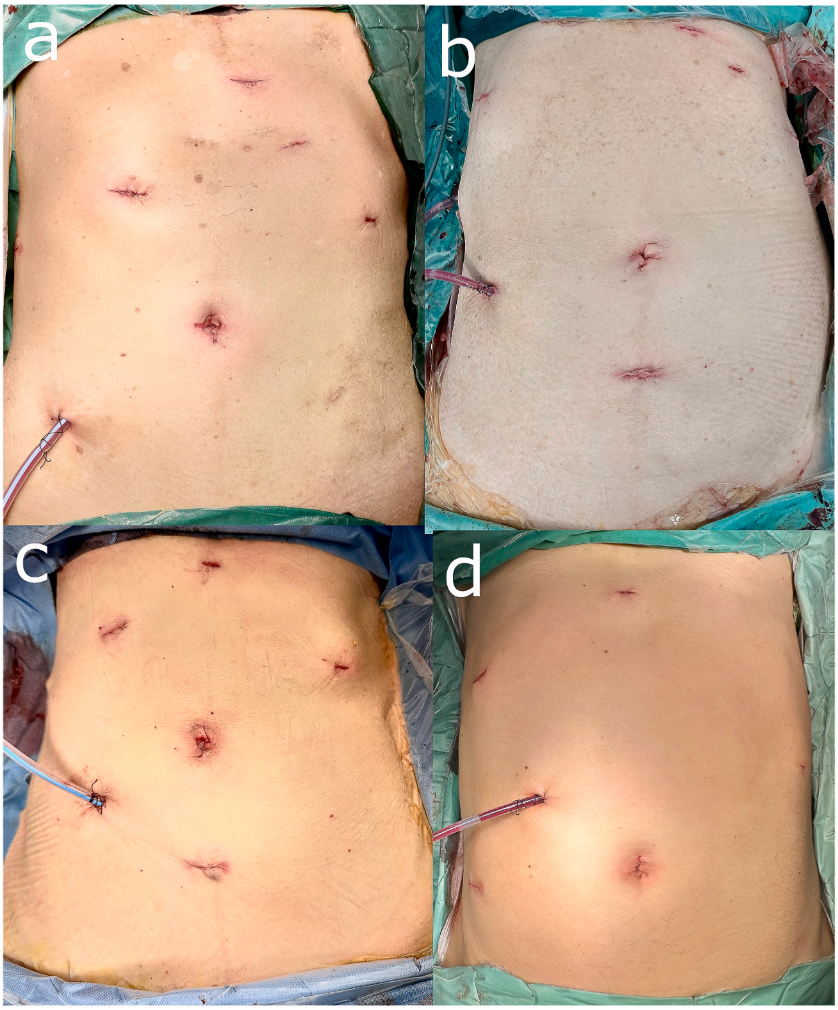

Fig. 3. Immediate postoperative abdominal appearance following simultaneous liver resection and (a) (d) anterior resection with transanal NOSE, (b) D3 right hemicolectomy with transvaginal NOSE, and (c) subtotal colectomy with transvaginal NOSE.

5. Discussion

Steady progress in surgical innovation and operator experience have led to the adoption of minimally invasive surgical techniques even for complex abdominal procedures, including colorectal cancer resection [28], gynaecological cancer surgery [29], and liver resection [30]. NOSE has been described as a logical progression of minimally invasive surgery, and a major step towards the goal of scarless surgery [31]. At least five meta-analyses have been published on colorectal NOSE surgery within the past two years [14–18], reflecting the increasing popularity of the technique following colorectal resection. Comparatively, reports of natural orifice extraction in hepatopancreatobiliary surgery are scarce.

Meng et al. recently described three cases of laparoscopic pancreaticoduodenectomy for periampullary tumors with transanal specimen extraction, showing good postoperative, functional, and oncological outcomes [19]. Hwang et al. showed the viability of transvaginal extraction in a series of different organ resections, including two liver specimens [20]. In 2020, Gundogan et al. demonstrated the first transanal NOSE following anterior resection for sigmoid adenocarcinoma with synchronous liver metastasectomy [21].

To our knowledge, this is the first case series of combined colon and liver resection with NOSE, demonstrating the feasibility of the technique and postoperative safety across a range of colon resection types. Only non-anatomical liver wedge resections were performed, allowing for smaller specimens to facilitate natural orifice retrieval. Tumor recurrences in half the patients of the series is likely reflective of the advanced nature of the disease rather than a consequence of the natural orifice extraction procedure, as none of the recurrences occurred in proximity of the extraction conduit or within the pelvis.

The advantages of reduced incision size with NOSE were apparent in this small cohort of patients. Decreased early postoperative pain allowed avoidance of opioid analgesia, quicker time to ambulation, and return of gastrointestinal function. This facilitated enhanced recovery and discharge, which was particularly noteworthy considering the extensive multiorgan surgery and advanced

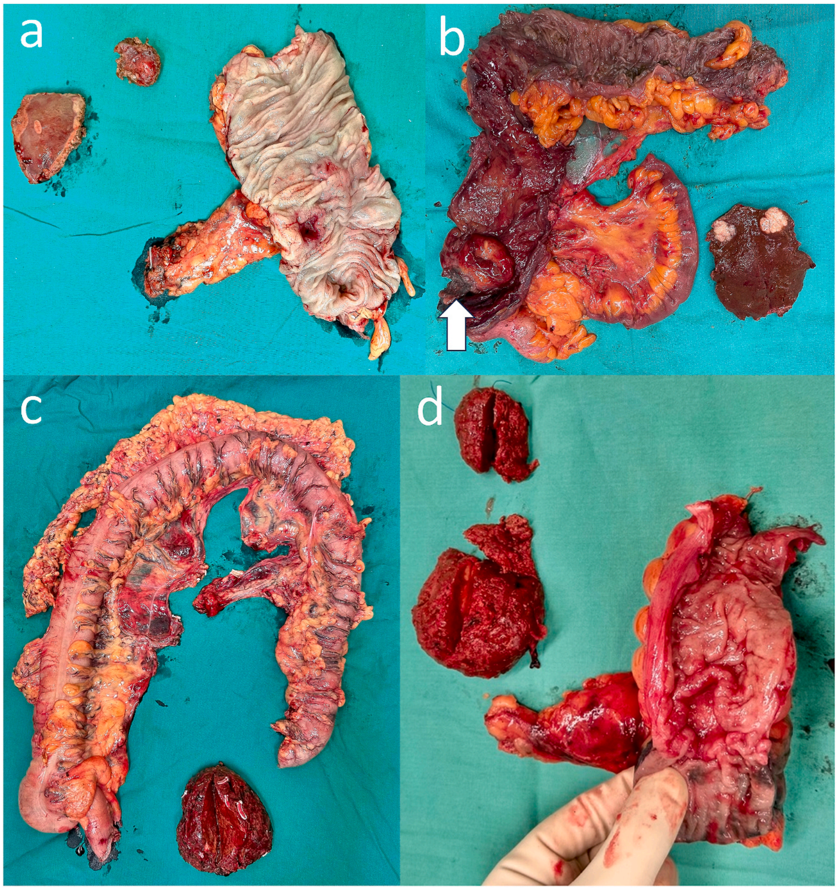

Fig. 4. Resected specimens following simultaneous liver resection and (a) (d) anterior resection with transanal NOSE, (b) D3 right hemicolectomy with transvaginal NOSE, and (c) subtotal colectomy with transvaginal NOSE.

patient age within the series. No patients experienced major postoperative complications, anastomotic or wound problems, or complications related to the NOSE procedure per se.

Our study is limited by the very small number of patients. Strict selection of patients in whom synchronous colon and liver resections was deemed feasible, with relatively smaller sized tumors fulfilling the criteria for NOSE, resulted in few patients available for inclusion in the series. Moreover, there were no instances of anatomical liver resections in our study. Although not demonstrated in the study cohort, we believe that larger liver specimens can be safety extracted on a case-by-case basis.

While NOSE only describes the method of specimen removal, successful NOSE surgery necessitates laparoscopic expertise and intracorporeal bowel anastomosis, without compromising oncological outcomes. It is therefore crucial for surgeons to be proficient in conventional laparoscopic colorectal and hepatic surgery prior to attempting combined resection with NOSE. With increasing evidence demonstrating the benefit of synchronous colorectal surgery with liver metastasectomy, combined resection NOSE may be a beneficial option for experienced operators. Future areas of study include quality of life outcomes and long-term oncological results.

6. Conclusions

Simultaneous colectomy and liver metastasectomy with natural orifice retrieval for colorectal cancer is feasible and safe in highly selected patients, resulting in good postoperative outcomes. This proof-of-concept analysis paves the way for larger studies to draw definitive conclusions.

Declarations

Ethical approval statement

This study received SingHealth Centralized Institutional Review Board approval (Ref: 2022/2114) and was conducted in accordance with the principles of the Declaration of Helsinki and its contemporary amendments.

Funding statement

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Participant consent

All participants provided written consent for publication of clinical images in this study.

Data availability statement

The data associated with this study has not been deposited into a publicly available repository. Data is available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Isaac Seow-En: Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ye Xin Koh:** Writing – review & editing, Resources. **Emile Kwong-Wei Tan:** Writing – review & editing, Supervision. **Ek Khoon Tan:** Writing – review & editing, Resources.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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