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## **Robotic complete mesocolic excision (CME) and central vascular ligation (CVL) for right-sided colon cancer: short-term outcomes from a case series**

Short title: Robotic CME for right-sided colon cancer

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- (II) Administrative support
- (III) Provision of study materials or patients
- (IV) Collection and assembly of data
- (V) Data analysis and interpretation
- (VI) Manuscript writing, and
- (VII) Final approval of the manuscript

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## **ABSTRACT**

*Introduction:* Despite conflicting data regarding oncologic outcomes, studies demonstrate that complete mesocolic excision (CME) and central vascular ligation (CVL) for right-sided colon cancer removes significantly more tissue and yields higher lymph node counts when compared to conventional resection. This study aims to report the safety profile of CME and CVL in patients undergoing robotic surgery for right-sided colon cancer during the introduction of this technique across two institutions.

*Methods:* Patients who underwent an elective robotic right colectomy with CME and CVL for right-sided colon cancer in a public quaternary and a private tertiary healthcare centre between November 2018 and April 2020 were included. Demographic, clinical, perioperative and histopathological variables were recorded and analysed.

*Results:* Twenty patients (13 females) with a median age of 69 (23-83) years and median BMI of 27 (19-46) were included. All of them had a preoperative diagnosis of right-sided colon adenocarcinoma. Median operative time and blood loss were 140 (130-300) min and 30 (20-100) ml, respectively. There were no conversions or intraoperative complications. There were two postoperative complications recorded (one ileus and one intraabdominal collection treated with intravenous antibiotics) and no re-interventions. Median length of stay was 4 (2-8) days. All patients had an R0 resection, and the median lymph node yield was 36 (22-80) lymph nodes.

*Conclusion:* This series demonstrates a safe introduction of robotic CME and CVL in patients with right-sided colon cancer. The lymph node harvest obtained with CME and CVL in this setting was high.

## **KEYWORDS**

Colon cancer, right hemicolectomy, robotic colectomy, complete mesocolic excision, D3 lymphadenectomy

## INTRODUCTION

Advances in medicine or surgery which dramatically alter the local recurrence (LR) or long-term survival in cancer are rare. In rectal cancer surgery, the advent and popularisation of the concept of total mesorectal excision (TME) represented one such advance; respecting the embryological planes and avoiding disruption of the resultant lymphatic package, Heald and colleagues reported significantly lowered LR rates in rectal cancer when compared to available literature at that time(1).

Analogous advances were slower to arrive in colon cancer surgery. Decades after TME introduction, Bokey et al. and other authors began to report improved survival rates in colon cancer through mobilising the colon along embryological planes(2). More recently, Hohenberger et al. have popularised the concept of complete mesocolic excision (CME) and central vascular ligation (CVL) on the premise that by similarly respecting the embryological planes, an oncologically superior colectomy could be performed(3). They showed the procedure could be carried out with low morbidity and with the potential for low locoregional recurrence. Interestingly, a nodal harvest greater than 28 lymph nodes was seen as an independent prognostic factor, even in lymph node-negative tumours.

CVL or a D3 lymph node dissection for right-sided lesions involves nodal clearance over the superior mesenteric vessels. Consequently, there has been reservation in the age of minimally invasive surgery to perform these procedures because of the perceived increased risks in Western patients(4); especially with respect to patients' higher body mass index when aiming for a more radical lymph node clearance.

Robotic-assisted surgery adds a stable surgeon-controlled camera with 3-dimensional image and wristed instruments that provide natural movements, overcoming limitations of conventional laparoscopic equipment. Limited data suggest that this platform has allowed surgeons to perform complex procedures such as CME and CVL in a minimally invasive fashion with perceived ease and safety in its adoption(5).

The study aims to report on the safety profile of CME and CVL in patients undergoing robotic right hemicolectomy for right-sided colon cancer during the introduction of this technique across two centres in Australia. Specifically, the complication profile, perioperative and histopathological data are examined.

## **MATERIALS AND METHODS**

### **Design**

A retrospective review from a prospectively maintained database at two institutions (Peter MacCallum Cancer Centre and Epworth Healthcare) was performed. Patients who underwent an elective robotic right colectomy with CME and CVL for right-sided colon cancer, between November 2018 and April 2020, were included. Patients who underwent an open or laparoscopic right hemicolectomy with CME and CVL were excluded.

SW was involved in all cases and the procedure was performed in consecutive patients with preoperative diagnosis of right-sided colon cancer amenable for a curative-intent treatment. He had performed greater than 150 robotic colorectal resections and attended many course faculty meetings in Asia, prior to commencement of CME and CVL cases. He had also performed the procedure in selected patients in an open and laparoscopic setting. The surgical approach was decided in a case-by-case basis considering multidisciplinary team recommendations and surgeons' criteria. When a minimally invasive approach was decided, procedures were performed robotically upon platform availability.

### **Variables**

Patients' demographic, clinical, perioperative and histopathological variables were recorded.

### **Definitions and outcomes of interest**

Surgical risk was classified according to the American Society of Anesthesiologist (ASA) classification. Complications and unplanned readmissions were registered up to 30 days postoperatively. Complications were classified according to the Clavien-Dindo classification(6). Ileus was defined as functional obstruction of the gastrointestinal tract, characterised by the absence of peristalsis, usually accompanied by abdominal pain, bloating, and sometimes nausea and vomiting, requiring nasogastric tube insertion for greater than 24 hours postoperatively. Anastomotic leak was defined as any clinical or radiological evidence of a defect of the intestinal wall at the anastomosis communicating the intra- and extra-luminal compartments. The histopathological staging was recorded according to the TNM classification (AJCC 8<sup>th</sup> Edition for Cancer Staging)(7).

## Procedure

All patients received mechanical bowel preparation. General anaesthetic was given and prophylactic antibiotics were administered at induction. An indwelling urinary catheter was inserted, and the patient placed in a supine position with both arms tucked by the sides. All patients had sequential compression devices placed before the operation. Low molecular weight heparin was given on induction, and throughout the inpatient stay.

The patient was placed in a slight reverse Trendelenburg position. The four-port robotic technique was adopted utilising a da Vinci Xi platform (Intuitive Surgical, Sunnyvale, CA, USA). Early in the introduction of this technique, an intracorporeal anastomosis was standardised. Hence, for most of those cases a small Pfannenstiel extraction port was placed with a Gelpoint Mini (Applied Medical, Rancho Santa Margarita, CA, USA) or Alexis wound retractor (Applied Medical, Rancho Santa Margarita, CA, USA) with a cap. This was often performed at the start of the case to establish pneumoperitoneum. For most cases, pneumoperitoneum was maintained with the aid of an AirSeal® System (Conmed, Connecticut, USA) set at a 12-mmHg pressure. The port positions are shown in Figure 1. The omentum was reflected above the colon to highlight the vascular pedicles. In all cases, two left arms and one right arm were used. A dissecting scissor, and or vessel sealer was utilised in the right arm, while a tip-up instrument was utilised in arm 1, and a fenestrated bipolar instrument was used in arm 2.

Wherever possible, video recording and photographs were used to highlight the vascular anatomy.

### *Superior mesenteric vein (SMV) approach*

A superior mesenteric vein-first approach was adopted for all cases (Figure 2)(8). Arm 1 was used to retract the ileocolic pedicle and the assistant port to retract the transverse mesocolon. The peritoneum overlying the SMV was exposed on its medial side well below the level of the ileocolic vein. The superior mesenteric artery (SMA) was also exposed in many cases.

On further cranial dissection along the vascular pedicle, first, the ileocolic vein was identified and separated from the artery. These were often clipped with a robotic Hem-o-lok (Teleflex Headquarters International, Ireland). The ileocolic artery position varied in keeping

with previously described variations(9,10); in many cases, the artery ran anterior to the SMV. Where the ileocolic artery was coursing anteriorly, it was taken flush with the SMA; however, where it was coursing posteriorly, the vessel was taken flush with the SMV medial border. This is demonstrated in Figure 3.

Following further dissection, the right colic vein was taken. The duodenum and pancreatic tissue were preserved, but all lymphovascular tissue above the pancreas removed (Figure 4). The middle colic vein was taken flush with the SMV when performing an extended right hemicolectomy. Henle's trunk with its colic, gastroepiploic and pancreatic branches was seen (Figure 5). The colic branches of the GCT were taken while gastroepiploic and pancreatic branches were preserved. The vascular anatomy variations in laparoscopic right hemicolectomy have been described previously(9). The right branch of the middle colic artery was ligated proximally. In cases where the tumour was located in the hepatic flexure or the transverse colon, the middle colic artery was taken flush with the SMA.

Following ligation of the vessels, the colonic mobilisation was completed in a medial to lateral fashion, the hepatic flexure mobilised, and lateral attachments taken in the usual manner. The mesenteric vascular window was kept carefully intact as this represents a quality marker of the CME (Figure 6).

#### *Complements*

In most cases, Indigo Carmine Green (ICG) was used intravenously to highlight the vascular supply to the colon and small bowel prior to the anastomosis. In select cases, the ICG was injected peritumorally to highlight the lymph node package. The authors have published on this technique previously(11).

Where an intracorporeal anastomosis was performed, division of the ileum and the distal division of the colon was performed using the robotic stapling device. An isoperistaltic side-to-side mechanical anastomosis was performed using stay sutures, enterotomies and a linear robotic stapler. Enterotomies were then closed with a running absorbable 3-0 barbed suture, with a second layer of interrupted 3-0 Vicryl above this.

The specimen was extracted using a Pfannenstiel incision following completion of the intracorporeal anastomosis. Postoperatively, the ERAS (Enhanced Recovery After Surgery) protocol, was followed.

### **Statistical analysis**

All characteristics were summarised using descriptive statistics, including counts and frequencies for categorical variables, and median and range for continuous variables. All statistical analyses were performed using Microsoft Excel 2010.

### **Ethics**

Institutional Review Board ethics approval were obtained from both sites. Reference numbers: PMCC2020-64038 and EH2020-564.

## RESULTS

### *Demographic and pre-treatment details*

Twenty patients (13 females) with a median age of 69 (23-83) years and median BMI of 27 (19-46) were included. Sixteen patients were ASA I or II, whilst the rest were ASA III. The surgical indication for all patients was colon adenocarcinoma. Tumour location was distributed in the caecum in 6, ascending colon in 7 and hepatic flexure in 7 patients (Table 1).

### *Perioperative outcomes*

Sixteen patients underwent a right hemicolectomy while four had an extended right hemicolectomy. The median operative time and blood loss were 140 (130-300) min and 30 (20-100) ml, respectively. The extraction site was a Pfannenstiel incision in 11 cases; a midline incision was used in two patients with midline hernias that were concurrently repaired and a transverse periumbilical incision in the other two. There were no conversions to conventional laparoscopy or open surgery in this series. Eighteen patients received an intracorporeal anastomosis; the other two patients had a midline hernia repaired concomitantly and therefore received an extracorporeal anastomosis. During the study period, two patients had a Clavien-Dindo I to II complications; one had an ileus, and the second an intraabdominal collection, treated with antibiotics. No grade III or IV complications were observed; notably, there was no vascular injury or secondary haemorrhage, nor postoperative haematomas or anastomotic leaks were encountered. There were no re-interventions in this series. The median length of stay was 4 (2-8) days. Only the patient with the intraabdominal collection was readmitted 16 days after discharge for intravenous antibiotic treatment and pain management. There was no mortality in this series (Table 2).

### *Histopathological outcomes*

Nineteen patients had a confirmed diagnosis of colon cancer by histopathology, and all of them had an R0 resection. One patient was thought to have a clinical-stage II cancer without definitive preoperative histologic confirmation; in this case, histopathology revealed no malignancy in the surgical specimen. The mean lymph node yield was  $39 \pm 13,5$  with a

median of 36 (22-80) lymph nodes. The pathological TNM staging details are summarised in Table 2.

## DISCUSSION

The current paper shows that CME and CVL for right-sided colon cancer can be safely performed using a robotic platform provided appropriate surgical expertise and training is present. This series represents a bi-institutional learning curve with an acceptable complication profile whilst introducing this technique. The results are consistent with series from Eastern countries and more recently adopted by large centres in the West(12). Also, despite interunit variabilities in pathological reporting, the nodal harvest from this technique was very high and may be used as a surrogate marker of surgical quality. The pathologists were unaware of the audit, thus the lymph node sampling techniques were not modified for this study.

The concept of CME and CVL as described by Hohenberger and colleagues, was to facilitate sharp dissection along embryological tissue whilst ensuring that all lymphovascular tissue was removed. The central vascular component of the operation involves a high vascular ligation with lymphatics overlying the SMV removed. Such an approach removes lower peripancreatic tissue and clears central nodes (N3) which have been reported to be positive in 1 to 22 percent of right-sided colon cancers(13). The initial open description involved kocherisation of the duodenum, an approach that has not been adopted in newer modified approaches in both the East and West. Hohenberger et al. in their early series were able to show improvements in locoregional recurrence and importantly distant recurrence following the adoption of CME. In their series of 1329 patients, the 5-year survival improved from 82% to 89%, whilst in node-negative patients a nodal harvest was independently associated with survival (96% vs 90%,  $P<0.018$ )(3). Our standardised approach, as described in the methods section was to perform a SMV first approach. In our series, the median lymph node yield was 36 lymph nodes and acted as a surrogate marker of quality for CME and CVL performance. The authors also ensured photos were taken routinely of the vascular access, and wherever possible videos were saved.

Notwithstanding promising results with CME and CVL regarding long-term oncologic outcomes for colon cancer, most of the data is based on retrospective studies with limited high-quality studies supporting this approach. CME and CVL has two key components; achieving a specimen with a complete mesocolic envelope, and maximising the nodal harvest by removing central lymph nodes. While there is evidence linking the quality of the mesocolic envelope with long-term outcomes(16), evidence to support a more radical lymph

node dissection is less clear. Maximizing the nodal harvest is still a matter of debate since it has not clearly demonstrated to independently impact survival. Interestingly, an extended lymphadenectomy for colon cancer does not seem to improve staging(17)and moreover, removal of positive nodes in the N3 barrier is associated with poor oncologic outcomes regardless of surgical radicality(18). Another point of debate is whether this approach should be undertaken in every cancer case or on a selective basis. Despite publications showing survival benefits of a more radical lymph node dissection even in early stage cancers(19), data is still scarce and there is no convincing theoretical explanation for this phenomena so far(13).

The results from the current study are consistent with other key publications suggesting a strong safety profile in experienced hands(4). Bertelsen's publication from Danish data showed 258 patients of 529 underwent minimally invasive CME procedures, with a conversion rate approaching 20 per cent. In the entire series, a 6.2% mortality was seen, an intraoperative organ injury of 9.1%, SMV injury rate of 1.7%, and sepsis rate of 6.6%(4). The complication profile, therefore, was of concern. However, Athanasiou et al. systematic review of laparoscopic versus open CME that included one randomised and seven case-control studies showed that a laparoscopic approach was not associated with any significant difference in ileus, surgical site infection, anastomotic leakage or 30-day mortality; there was a trend towards a shorter length of stay for the laparoscopic group. However, it was associated with longer operative times(14). Many Eastern centres have not seen the level of morbidity that was initially described. In our early experience, the operative time is longer, however, the morbidity profile is exceptional and consistent with these Eastern publications.

More recently, results from the Danish cohort exclusively focusing on the effect of CME and CVL in patients with right-sided colon cancer have been published(15). Amongst 1069 patients, 286 had CME and CVL. The 5.2-year cumulative incidence of recurrence was 17.9% for conventional right colectomy compared to an 8.2% for CME and CVL. Furthermore, 60-day major postoperative complication rates were 17% for the control group versus 18% for CME and CVL.

The introduction of new technology carries unique safety challenges and certainly adopting a Halstedian method to resect colon cancers may be viewed as controversial in an age where tailored minimalism and more chemotherapy is being practised. In this case, the

primary surgeon involved in the introduction of robotic CME and CVL is an early adopter of the technique and follows other large units and Eastern centres showing that a standardised approach for right colectomies is possible(12). Our policy has been to include two Consultants during the procedures. Also, additional time has been spent to analyse the preoperative imaging with relation to the vascular anatomy. This work has been undertaken within a highly specialised colorectal unit, with broad experience in vascular dissection including pelvic exenterations and pelvic side-wall dissections. All surgeons were beyond the robotic learning curve for standard colorectal resections. Moreover, steps have been taken with close auditing of data. The challenge with this technique will come when moving beyond the early adopter phase to the dissemination phase, as seen with other techniques. In order to achieve a low morbidity profile, specialised courses and proctorship, as well as rigorous case audit, will be required, with surgical observation and critiques from world experts required to make this more available in other centres.

As with many feasibility case series, the results presented are not in the setting of a comparative study and represent the surgeons' learning curve limited by a bi-institutional experience. Furthermore, the current manuscript does not intend to review oncological follow-up, but subsequent follow-up data of this patient group will be published to assess long-term cancer outcomes.

## **CONCLUSION**

This early series demonstrates a safe introduction of robotic CME and CVL in patients with right-sided colon cancer. The lymph node yield with CME and CVL in this setting was high.

## **DISCLOSURE STATEMENT**

Conflict of interest: Jose T. Larach is a Robotic Colorectal Fellow supported by Device Technologies, Australia. The rest of the authors declare that they have no conflict of interest

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## FIGURES AND TABLES

**Figure 1.** Port placement. Note the left upper quadrant 12-mm robotic port for the stapling device and a left flank or left iliac fossa assistant port (EP)

**Figure 2.** Superior mesenteric vein (SMV) first approach. The peritoneum over the SMV is opened to expose the SMV, perform a central vascular ligation and clear the N3 barrier lymph nodes. ICA = ileocolic artery; ICV = ileocolic vein

**Figure 3.** Ileocolic artery (ICA) variations. ICA running posteriorly (left-side picture) and anteriorly (right-side picture) to the superior mesenteric vein (SMV)

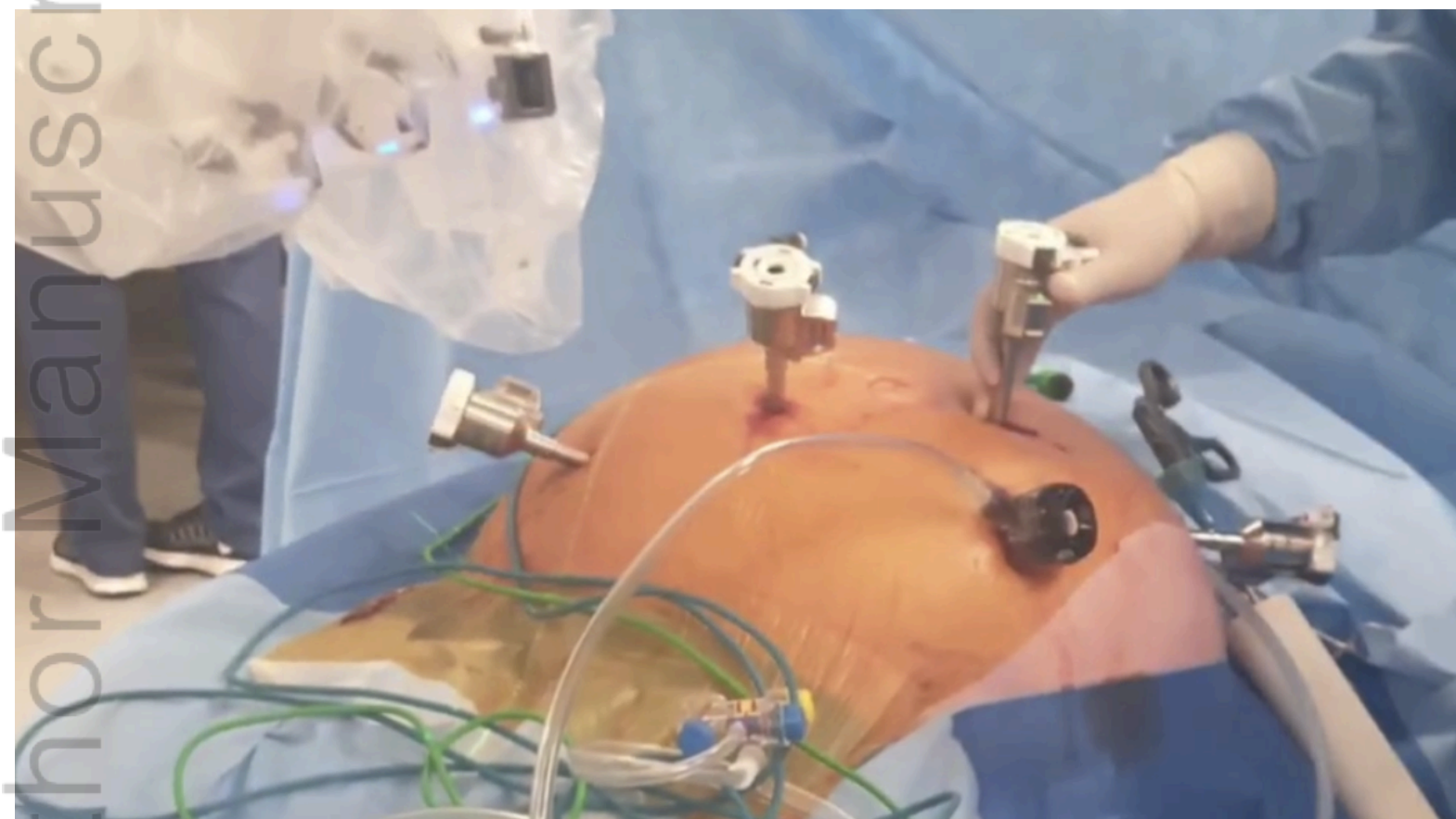
**Figure 4.** Superior mesenteric vein (SMV) anatomical relations during complete mesocolic excision and central vascular ligation. UP = uncinate process of the pancreas; DUO = second and third portion of the duodenum; ICA = ileocolic artery; ICV = ileocolic vein

**Figure 5.** Gastrocolic trunk. GCT = gastrocolic trunk; RCV = right colic vein; SRCV= superior right colic vein; RGEV = right gastroepiploic vein; UP = uncinate process of the pancreas; DUO = second and third portion of the duodenum; ICV = ileocolic vein

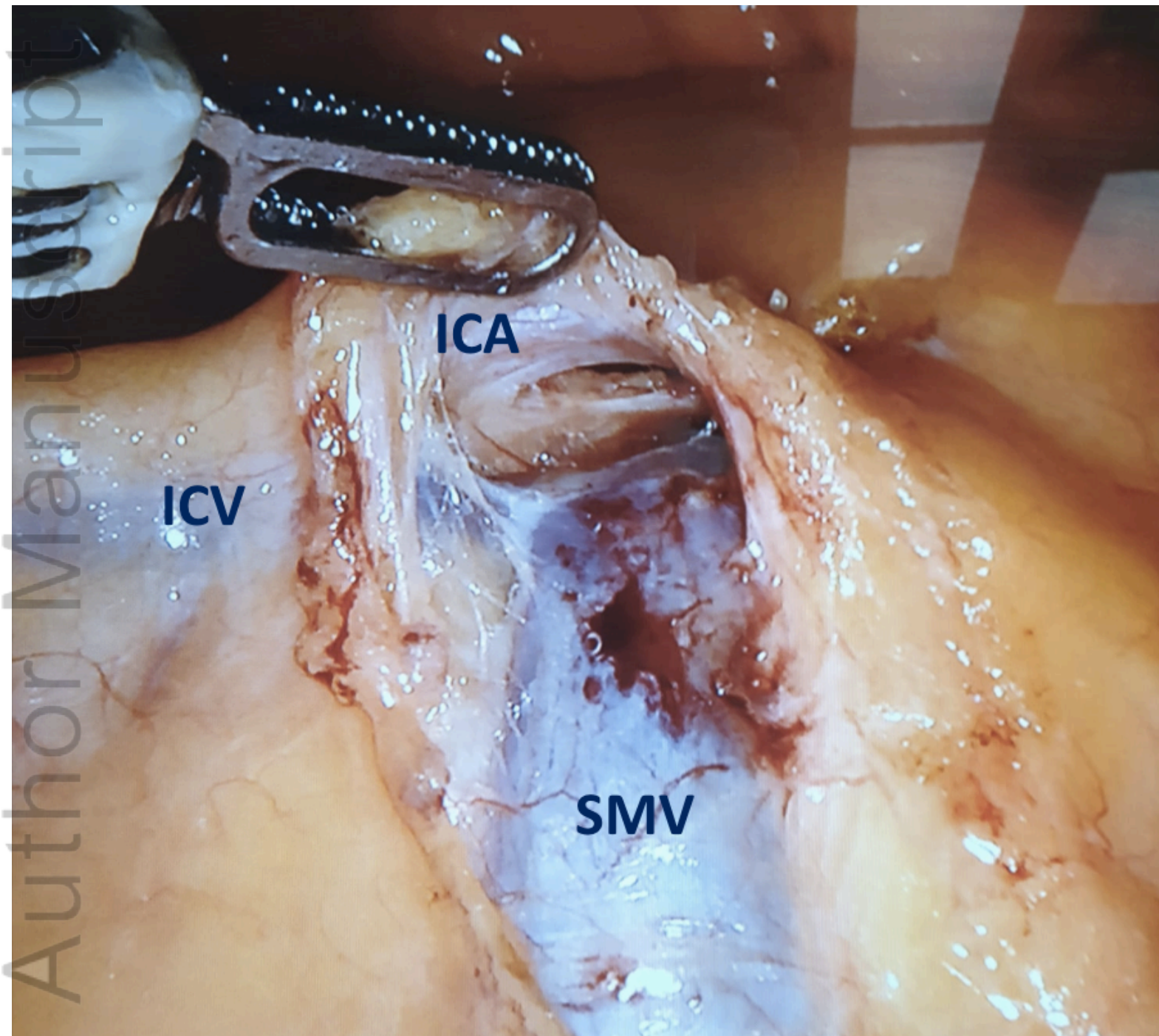
**Figure 6.** Specimen from a robotic right hemicolectomy with complete mesocolic excision and central vascular ligation. Note the intact mesenteric vascular window. RCV = right colic vein

**Table 1.** Demographic and clinical data

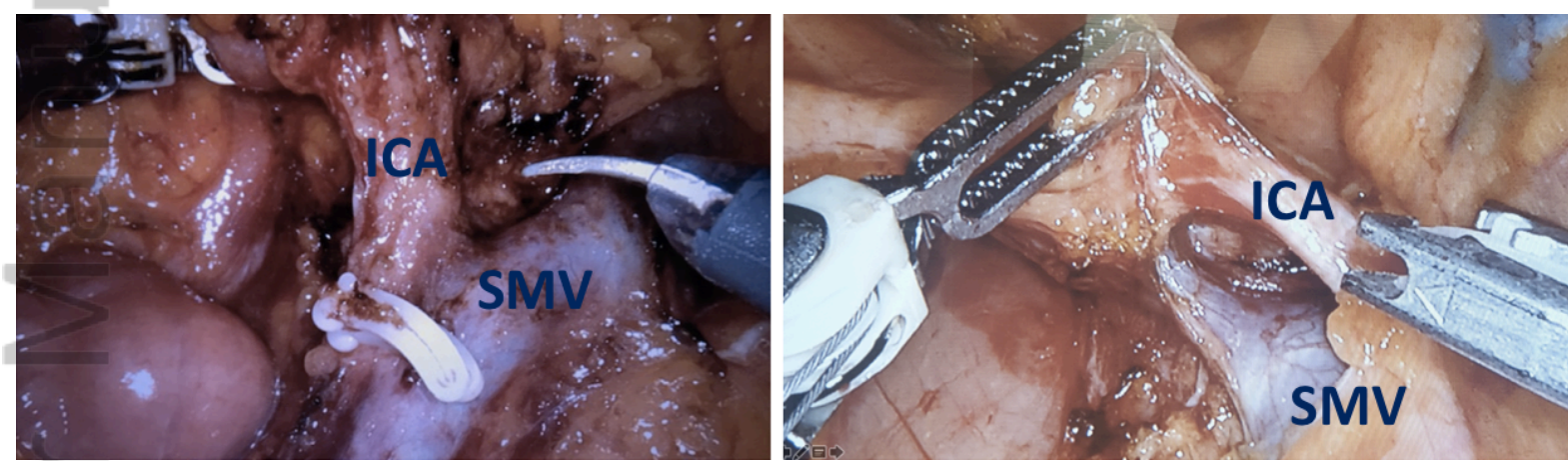
**Table 2.** Perioperative and histopathological data



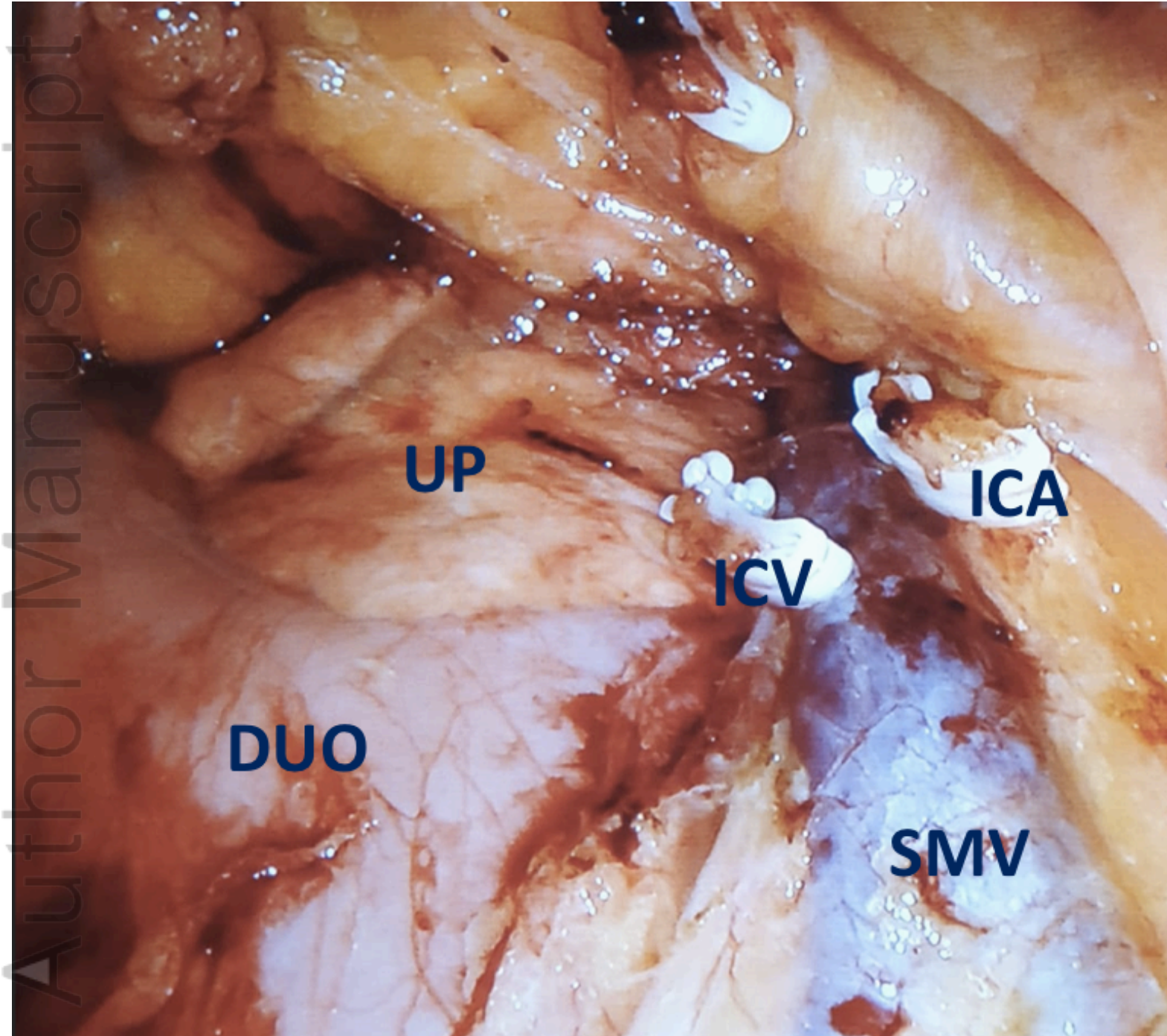
ANS\_16224\_Figure 1. Port placement.png



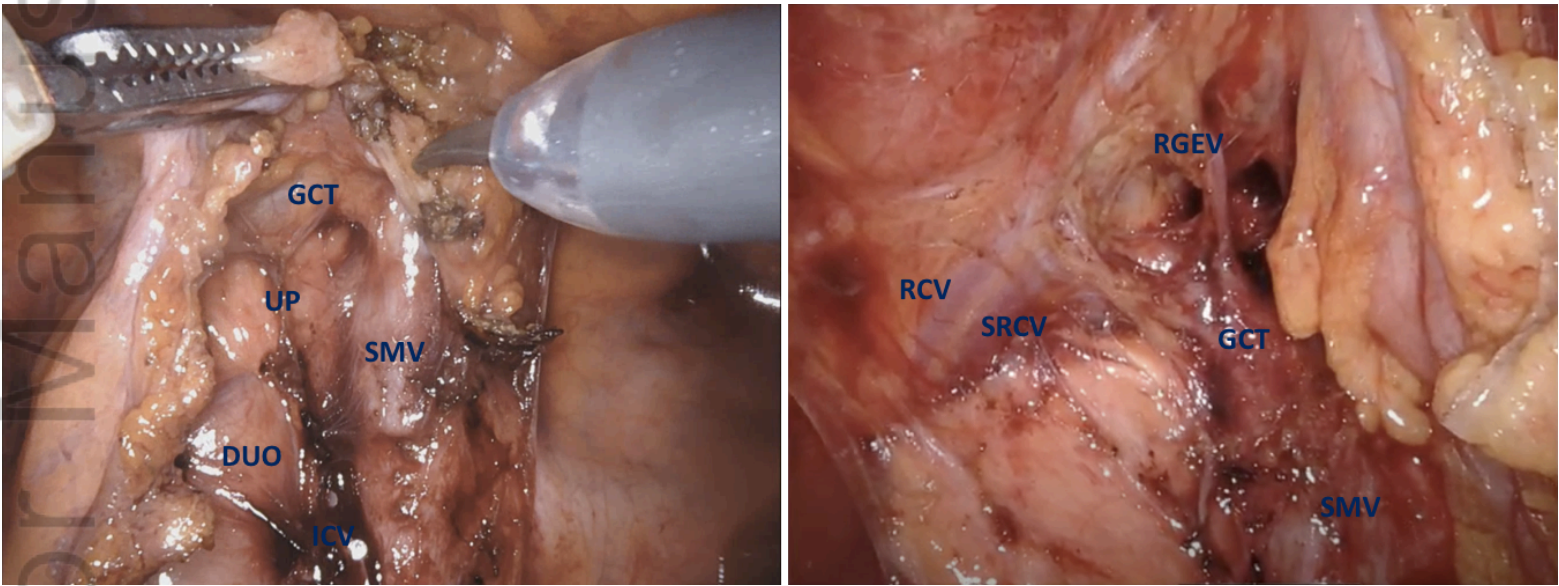
ANS\_16224\_Figure 2. SMV first approach.png



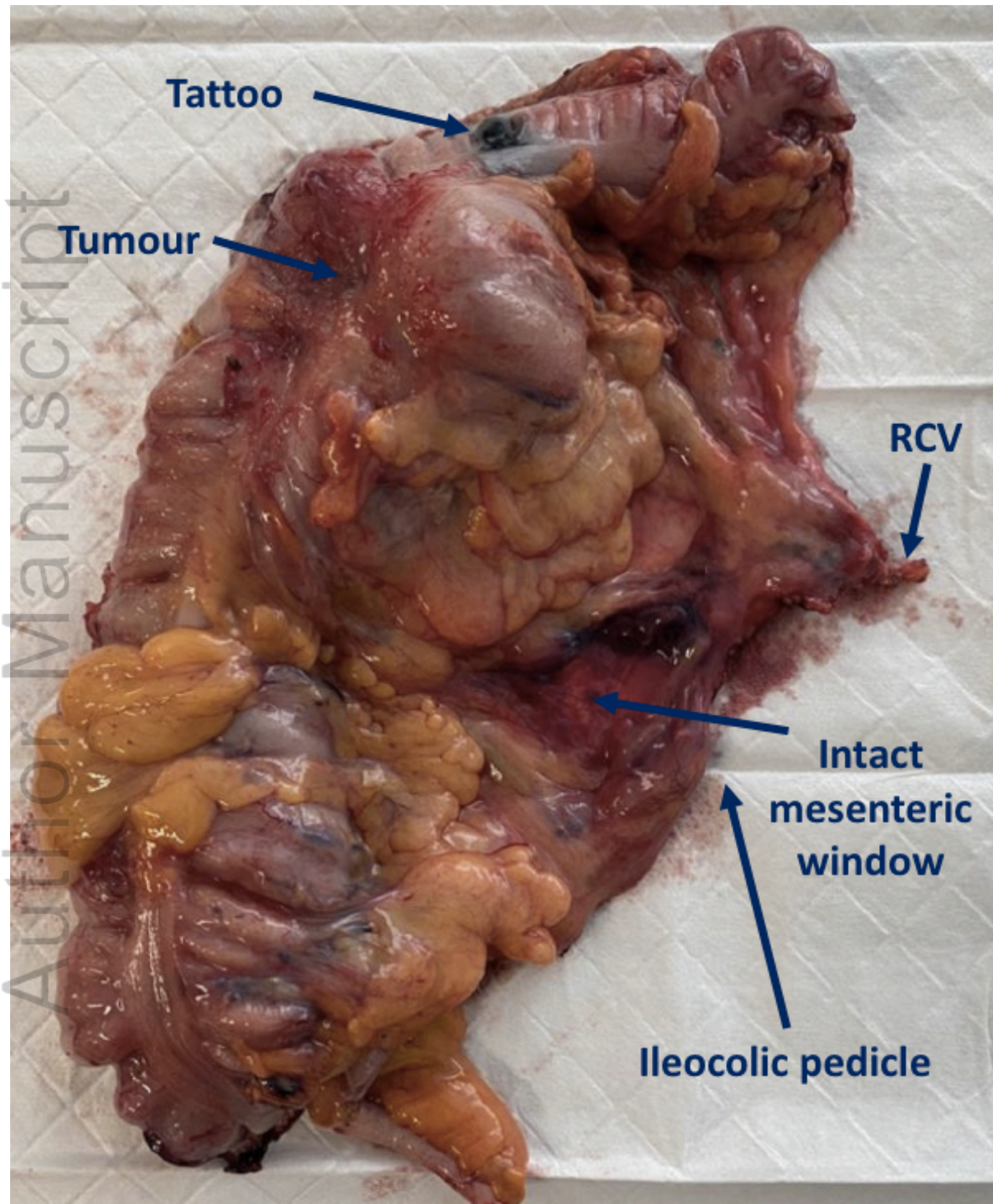
ANS\_16224\_Figure 3. ICA variations.png



ANS\_16224\_Figure 4. Anatomical relationships.png



ANS\_16224\_Figure 5. GCT.png



ANS\_16224\_Figure 6. Specimen.png

**Table 1.** Demographic and clinical data

<b>Demographic and clinical data</b>	<b>n = 20</b>
<b>Age, median (range)</b>	69 (23-83)
<b>Female sex, n (%)</b>	13 (65)
<b>BMI, median (range)</b>	27 (19-46)
<b>ASA, n (%)</b>	
I	3 (15)
II	13 (65)
III	4 (20)
<b>Indication for surgery, n (%)</b>	
Cancer	20 (100)
<b>Tumour location, n (%)</b>	
Caecum	6 (30)
Ascending colon	7 (35)
Hepatic flexure	8 (35)

BMI = body mass index; ASA = American Society of Anaesthesiologists Surgical Risk Classification

**Table 2.** Perioperative and histopathological data

<b>Perioperative and histopathological results</b>	<b>n = 20</b>
<b>Procedure</b>	
Right hemicolectomy	16 (80)
Extended right hemicolectomy	4 (20)
<b>Anastomosis type, n (%)</b>	
Intracorporeal	18 (90)
Extracorporeal	2 (10)
<b>Conversion, n (%)</b>	0 (0)
<b>Operative time (min), median (range)</b>	140 (130-300)
<b>Blood loss (ml), median (range)</b>	30 (20-100)
<b>Extraction site, n (%)</b>	
Midline incision	2 (10)
Pfannenstiel	11 (55)
Transverse periumbilical incision	7 (35)
<b>Post-operative length of stay, median (range)</b>	4 (2-8)
<b>Morbidity (Clavien-Dindo), n (%)</b>	
I	0 (0)
II	2 (10)
III	0 (0)
<b>Anastomotic leak, n (%)</b>	0 (0)
<b>Reoperations, n (%)</b>	0 (0)
<b>Non-programmed readmissions, n (%)</b>	1 (5)
<b>Mortality, n (%)</b>	0 (0)
<b>pTNM*, n (%)</b>	
<b>pT</b>	
is	2 (11)
1	2 (11)
2	3 (16)
3	11 (58)
4	1 (5)
<b>pN</b>	
0	15 (79)
1	3 (16)
2	1 (5)
<b>pStage</b>	
I	4 (21)
II	10 (52)
III	3 (16)
IV	2 (11)
<b>Number of lymph nodes harvested, mean <math>\pm</math> SD (median, range)</b>	39 $\pm$ 13,5 (36,22-80)

p = Pathological; is = in situ