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The *fusion fascia of Fredet*. An important embryological landmark for complete mesocolic excision and D3-lymphadenectomy in right colon cancer.

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Running title: Fredet's fascia – a laparoscopic landmark

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Abstract

Background: The fusion fascia of Toldt is a well-known landmark used by colorectal surgeons. On the contrary, the fusion fascia of Fredet (the plane between the ascending mesocolon and the visceral duodenal-pancreatic peritoneum) still remains a neglected embryological structure. Aim of this study was to provide an anatomic description of this fascia and its application to minimally-invasive D3-lymphadenectomy (D3-L) and complete mesocolic excision (CME) for right colon cancer.

Methods: First phase: Cadaveric dissection and anatomic description of the fascia of Fredet. Second phase: prospective evaluation of its surgical application in consecutive series of laparoscopic right hemicolectomies with CME and D3-L at a tertiary hospital.

Results: The fascia of Fredet was identified and dissected in one fresh and two formalin-fixed cadavers. The trunk of Henle and the medial border of the superior mesenteric vein defined the medial limit of this embryologic plane. Seventeen patients were operated on. Laparoscopic dissection of the fascia of Fredet was possible in every patient. Median operative time was 210 (120-380) minutes. There were no major postoperative complications. All cases were adenocarcinomas, except one adenomatous polyp. T stage was Tis in three, T2 in two, T3 in seven, and T4 in five patients. Median number of harvested lymph nodes was 24 (9-39). Lymphatic invasion was found in six patients. All resections were classified as satisfactory mesocolic excision and R0. Median postoperative length of stay was 6 (4-20) days. Median follow-up time was 28 (16-41) months. Local and distal recurrence rate was 0.

Conclusion: The fusion fascia of Fredet is useful to achieve CME and D3-L in right colon cancers with reduced risk of intraoperative complications. This structure is particularly suitable for minimally invasive surgery; therefore, we encourage awareness of the fascia of Fredet by colorectal surgeons.

Key-words: laparoscopy; colorectal surgery; fascia; surgical anatomy; Fredet; training.

Introduction

Complete mesocolic excision (CME) and D3-lymphadenectomy (D3-L) are two concepts which involve different steps, namely respecting the embryological planes during surgical dissection, high ligation of the vessels feeding the tumor, and dissection of the lymphoadipose tissue lying on the medial border of the superior mesenteric vein (SMV) and on the gastrocolic trunk of Henle. (1,2)

The fascia of Toldt, which runs between the ascending colon and the retroperitoneum, is a well-known landmark used by colorectal surgeons. (3) On the contrary, the *fusion fascia of Fredet*, which was described by Fredet as the adhesion plane between the ascending mesocolon and the visceral duodenal-pancreatic peritoneum (named after him by Rouvière in 1924 (4) still remains a neglected anatomical structure. Awareness and knowledge of its development and location can be useful to perform minimally-invasive D3-lymphadenectomy, reducing the risk of intraoperative bleeding from the SMV.

Aim of this study was to provide an anatomic and surgical description of the fascia of Fredet, combining cadaver dissection with clinical application of the findings on a prospective series of patients with colon cancer, who underwent laparoscopic resection.

Material and Methods

This study was performed in two different stages. The first part consisted of a cadaveric study of the anatomy of the right colon, and the second part consisted of a prospective assessment of oncological laparoscopic right hemicolectomy following the principles of CME. The study was performed at a tertiary centre under the care of a multidisciplinary colorectal team.

First Phase

The anatomical phase was performed in collaboration with the Department of Human Anatomy and Embryology of the University of Valencia. Cadavers were obtained through regulations subject to the Spanish National law.

Dissections of fresh and embalmed cadavers were carried out by a colorectal surgeon (AGG) with expertise in human anatomy and by a human anatomist (AAVN). Cadavers with previous abdominal surgery were excluded.

A right hemicolectomy with CME and D3-L was simulated.

CME was defined as: (1,5)

- dissection between the right mesocolon and the retroperitoneum, following the embryological plane defined by the fusion fascia of Toldt and the fusion fascia of Fredet
- high tie of ileocolic vessels, right colic vessels, and right branch of middle colic vessels

D3-L was defined as: (6,7)

- dissection of the lymphoadipose tissue covering the medial side of the SMV.
- dissection of the lymphoadipose tissue covering the head of pancreas after section of the superior right colic vein (SRCV) at its confluence in the gastrocolic trunk of Henle (GCTH).

Embryological fasciae were defined as follows:

- Fusion fascia of Toldt: adhesion plane between visceral peritoneum of the ascending mesocolon and the retroperitoneum. (8) **(Figure 1)**
- Fusion fascia of Fredet: adhesion plane between visceral peritoneum of the mesocolon of ascending colon and hepatic colonic flexure and the visceral peritoneum of duodenum and pancreas. (3,9) **(Figure 2)**
- Fusion fascia of Treitz: adhesion plane between the visceral peritoneum of the duodenum and pancreas and the retroperitoneum. (3,9) **(Figure 2)**

The Surgical Area of the Gastrocolic Trunk of Henle (SAGCTH) (10) was defined as the area of the SMV located at the head of the pancreas, defined by the venous confluence of the following three veins [6]: right gastroepiploic vein, anterosuperior pancreatic-duodenal vein and SRCV. **(Figure 3)**

A detailed description of the fusion fascia of Fredet was performed during the dissections, with particular emphasis on its relationship with the second duodenal portion, the head of pancreas, the GCTH, and the SMV.

Second Phase

This consisted of a prospective evaluation of a consecutive series of laparoscopic right hemicolectomies with CME and D3-L performed by an individual consultant colorectal surgeon (AGG) at a tertiary hospital between July 2015 and August 2017.

Only patients who underwent elective resection were included. In all of the procedures, the surgeon looked for and identified the fusion fascia of Fredet, and used it as anatomical landmark to perform CME and D3-lymphadenectomy of the lymphoadipose tissue covering the head of pancreas.

Immediately after surgery, the specimen was injected with methylene blue through the ileocolic artery, aiming at identifying the highest number of nodes possible. (11)

Complications were graded according to Clavien-Dindo Classification (12). Mortality and short-term postoperative complications within the first 30 postoperative days (or during the entire hospital stay if longer than 30 days) were recorded.

Postoperative ileus was defined as no tolerance of solid food and no defecation by postoperative day 6 (13).

Postoperative bleeding was defined as bleeding requiring at least one transfusion of packed red cells during surgery or in the subsequent 48 hours.

The anatomopathological assessment was performed by two dedicated pathologists based on available guidelines of reporting (14, 15).

Pathology reports included histology, lymph node status and margins status. The pathological resection margin status was considered R0 (microscopically clear resection margins of at least 1 mm); R1 (microscopically involved resection margin with tumour within 1 mm of the resection margin); and R2 (macroscopically involved resection margin).

High-resolution digital colour photographs were prospectively taken on a consecutive series of fresh specimens by the operating surgeon immediately after resection, including anterior and posterior views alongside a metric scale for calibration, using a standardized fashion. The quality specimen was graded as good mesocolic plane (smooth intact mesocolic excision with high vascular ties), intramesocolic plane (disruption of the mesocolon, but the incisions do not reach down to the muscularis propria), or intramuscularis propria plane (exposed muscularis propria) according to the standard definitions (16). The mesentery was laid out flat without external tension, and the sites of the tumor and vascular ties were made identifiable.

Demographic, operative, and histopathologic data were recorded. The study was approved by the local Ethical Committee and all the patients signed an informed consent before inclusion.

Statistical Analysis

Continuous variables are reported as median (range), whereas categorical variables are reported as number of patients and percentage.

Results

First Phase

For the purpose of this study, we used three cadavers, one fresh cadaver and two formalin-fixed cadavers. Median age was 84 (75-90) years, and two were women.

The fascia of Toldt was dissected between the visceral peritoneum of the ascending mesocolon and the retroperitoneum. **Figure 4. (Video 1)**

The fascia of Fredet was identified and dissected in all cadavers. Starting from this embryological plane, identification and separation of the second and third portion of the duodenum and of the head of pancreas was easy, and it did not require section of any vascular structure or duodenal manipulation. **Figure 5. (Video 2)**

The SAGTCH and the medial border of the SMV defined the medial limit of this embryologic plane. **(Figure 6). (Video 2)** Section of the SRCV at this level allowed including the lymph nodes of this area in the specimen of the simulated CME right hemicolectomy.

Second Phase

Seventeen patients were operated on, with a median age of 74 (49-88) years, nine of whom were women (53%). Indication to surgery was colonic adenocarcinoma in all but one, who underwent surgery for a polyp not amenable to endoscopic removal. None of them presented preoperative distal metastasis.

In 10 patients, the tumor was located in the caecum, in 4 in the ascending colon, and in 3 in the hepatic flexure of the colon. The latter underwent an extended right hemicolectomy, dividing the middle colic vessels at their origin.

Laparoscopic dissection of the fascia of Fredet was possible in all of the patients, and the SRCV was identified in all of them after this step **(Figure 7) (Video 3)**. Three patients required conversion to open surgery, two because of the size of the tumor, and the other one for adhesions from previous abdominal surgery. In two out of three patients that required conversion to open surgery, the dissection of the fascia of Fredet and of the GCTH was performed laparoscopically, before the conversion. Median operative time in patients who did not need conversion was 210 (120-380) minutes.

No patients required reoperation, and there were no major postoperative complications. Minor complications included hematoma of the ileocolic anastomosis, which did not require any interventions, and postoperative ileus in three patients. Perioperative mortality was nil.

Intraoperative, pathological and postoperative data are reported in **Table 1**.

All cases were reported as adenocarcinoma except one adenomatous polyp. The median number of harvested lymph nodes was 24 (9-39). Lymphatic invasion was found in six patients. All resections were classified as R0. Retroperitoneal margin was negative in all patients. All specimens were graded as satisfactory mesocolic excision. **(Figure 8)**

T stage was Tis in three, T2 in two, T3 in seven, and T4 in five patients. Median postoperative length of stay was 6 (4-20) days.

The median follow-up time was 28 (16-41) months. Five patients received postoperative chemotherapy. Local recurrence rate was 0% and none of the patients had distal metastasis.

Discussion

Knowledge of the embryologic development and associated formation of anatomical planes is pivotal, in order to perform ontologically correct laparoscopic colorectal surgery.

The concept of CME has been popularized with the aim of improving oncologic clearance after right colectomy (1). D3-L for right colon cancer is a technically demanding procedure that has been proposed in order to further reduce the risk of local recurrences by obtaining a more extended lymph node removal; however, a clear relation with a survival benefit is yet to be confirmed (17). CME and D3-L rely on some important manoeuvres: dissection of the mesocolon and retroperitoneum, following the embryological planes (8); high tie of the vessels feeding the tumor; dissection of the lymphoadipose tissue at the medial border of the SMV (known as surgical trunk of Guillot) (7,9); dissection of SAGCTH (7,18).

The avascular plane referred to as fusion fascia of Toldt is well known among laparoscopic colorectal surgeons, as it facilitates the dissection of the right mesocolon and peritoneum, as well as the identification of the ileocolic vessels at their origin in order to obtain a high tie (19).

Laparoscopic dissection of the surgical trunk of Gillot and of the GCTH increases the risk of injuries to the SMV and perioperative bleeding. One of the reasons, is their anatomic location, derived from rotation of the digestive tract during the embryologic development (20).

The mesocolon attaches to the meso-duodenum and to the greater omentum, and becomes fused to them by the 12th week of pregnancy. The surgical planes around the SMV are complex, because of the secondary modifications due to vascular development (21).

In order to better understand the origin of fusion fasciae, one should consider that the rotation of the digestive tube represents a key step of the embryological development of the digestive system. Fusion fasciae are generated by the adhesion occurring between two peritoneal leaves. The most commonly known is the fusion fascia of Toldt, which originates from the coalescence between the visceral fascia of the right mesocolon and the retroperitoneal fascia. During the embryological development, the pancreas is formed from two endodermal portions from the ventral and dorsal surface of the duodenum, so that the visceral peritoneum of the duodenum is the same of the pancreas. The fascia of Treitz is formed between the retroperitoneal fascia and the retro-duodenal-pancreatic fascia; and the fascia of Fredet is formed between the visceral supra-duodenal-pancreatic fascia and the visceral fascia of the right mesocolon (3). This fascia was described for the first time by Rouvière in 1924, who named it fascia of Fredet (4). Subsequently, it has been sparsely described, and it has been referred to as “anterior pancreatic fascia” by Mike in 2015, whereas the space created by dissecting this fascia has been named “ventral space of Fredet” (9).

The fusion fascia of Treitz has been used as surgical reference in patients with pancreatic cancer (22) with the aim of obtaining tumor-free retroperitoneal margins.

The fusion fascia of Fredet is not widely known among colorectal surgeons. During the last years, several approaches and manoeuvres have been proposed in order to obtain an adequate CME and dissection of the GCTH (23), but no one has incorporated the fusion fascia of Fredet as an anatomical landmark (24). In 2015, Mike et al highlighted the importance of being aware that the right fusion fascia of Toldt is divided into the posterior pancreatic fascia of Treitz (dorsally) and the anterior pancreatic fascia (ventrally), at the level of the second duodenal portion (9). As observed in the first stage of our study, these are three different fasciae, so that dissecting the anatomic space between the mesocolon and the fascia of Fredet allows to obtain a CME.

We support the assumption of Mike et al, which lead us to study systematically, in cadavers, the structures encountered once the dissection is continued on the embryological plane corresponding to the fascia of Fredet. We found that the medial limit of the fascia of Fredet is represented by the SMV and GCTH. In fact, the dissection of the fascia of Fredet allowed us to enter this area safer, with better exposure, and it offered a correct mesocolic plane, thus reducing the risk of injuries and bleeding from the SMV. The optimal knowledge of this anatomical landmark is crucial to avoid injuries to the SMV, which can lead to life-threatening complications (20).

Patients with colon cancers resected with an intact mesocolon achieve 5-year overall survival by 15% better than those who had mesocolic defects on the specimens (16). Among the points that need further research in future studies, one should consider whether the fascia of Fredet also has three detectable layers (like in Toldt's fascia) and, related to the latter, whether the fusion fascia should stay on the pancreas or on the mesocolon during CME for right colon cancer (8).

In our series, early oncologic outcome was excellent, in line with the recommendations of available guidelines for the management of colon cancer. Complications were kept to the minimum and no intraoperative bleeding occurred. Conversion to open surgery only consisted of strategic conversion and was not secondary to intraoperative complications.

Conclusion

The anatomical knowledge of the embryologic fusion fascia of Fredet is crucial to achieve CME an D3-L in right colon cancers, and it can effectively reduce the risk of intraoperative complications. This structure is particularly suitable for minimally invasive surgery, therefore awareness of the fascia of Fredet by colorectal surgeons is warranted.

Authors Disclosures

Drs. Alvaro Garcia-Granero, Gianluca Pellino, Matteo Frasson, Delfina Fletcher Sanfeliu, Fernando Bonilla, Luis Sánchez-Guillén, Alberto Domenech Dolz, Vicent Primo Romaguera, Luis Sabater Ortí, Francisco Martinez-Soriano, Eduardo Garcia-Granero, Alfonso A. Valverde-Navarro have no conflicts of interest or financial ties to disclose.

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Legends to Figures

Figure 1. Drawing showing the embryological development of the fusion fascia of Toldt. This will be formed between the visceral peritoneum of the mesocolon and the parietal peritoneum of the retroperitoneum.

Figure 2. Drawing showing the embryological development of the fusion fascia of Treitz and of the fusion fascia of Fredet. The fascia of Treitz will be formed between the retroperitoneum and the posterior visceral peritoneum of the pancreatoduodenal region. The fascia of Fredet will be formed between the anterior visceral peritoneum of the pancreatoduodenal region and the visceral peritoneum of the right mesocolon.

Figure 3. Drawing showing a lateral view of the fusion fascia of Fredet in adults. A. The fusion fascia of Fredet (red) not dissected. B. The fusion fascia of Fredet divided and removed. The medial border of the fascia consists of the gastrocolic trunk of Henle (GCTH).

Figure 4. Dissection of the fusion fascia of Toldt in a cadaver of an adult male individual. Blue arrow: fusion fascia of Toldt. In purple: retroperitoneum. In blue: retroperitoneal margin of the mesocolon of the right colon.

Figure 5. Demonstration of the fusion fascia of Fredet in a cadaver of an adult male individual. Purple line: border of the retroperitoneum. Blue line: border of the mesocolon. Yellow line: border of the pancreas. Red line: border of the fusion fascia of Fredet.

Figure 6. Demonstration of the superior mesenteric vein (SMV) and venous flow derived from the ileocolic vein and the gastrocolic trunk of Henle. SAGCTH: Surgical area of the gastrocolic trunk of Henle. 1: superior mesenteric vein; 2: ileocolic vein; 3: superior right colic vein; 4: right gastroepiploic vein; 5: anterosuperior pancreatoduodenal vein.

Figure 7. Pictures of the patients operated on with laparoscopy for right colon cancer. Demonstration of the different stages of dissection of the fusion fascia of Fredet, which is used as a landmark to enter the surgical area of the gastrocolic trunk of Henle (SAGCTH). Red arrow: fusion fascia of Fredet. Blue arrow: superior right colic vein.

Figure 8. Anterior and posterior views of a surgical specimen from a laparoscopic right hemicolectomy with complete mesocolic excision (CME) and D3 lymphadenectomy. White circle: tumour. 1: high tie of the ileocolic vessels; 2: lymphoadipose tissue covering the superior mesenteric vein; 3: high tie of the superior right colic vein; 4: satisfactory mesocolic plane (smooth intact mesocolon).

Table 1: Outcome of 17 consecutive procedures for right colon cancer.

Results are shown as n (%) or median (range)

Women	9 (53)
Age, years	74 (49-88)
Conversion to open	3 (17.6)
Operative time, minutes	210 (120-380)
Intraoperative bleeding	0
Postoperative ileus	3 (17.6)
Anastomotic leak	0
Length of stay	6 (4-20)
T stage	
0 (Adenomatous polyp)	1 (5.9)
Tis	2 (11.8)
II	2 (11.8)
III	7 (41.2)
IV	5 (29.4)
Lymph nodes resected	24 (9-39)
Patients with positive lymph nodes	6 (35.3)
Positive retroperitoneal margin	0
R1 or R2 oncological resection	0
Intra-mesocolic/Intra-muscularis plane	0
Follow-up time, months	28 (16-41)
Postop. Chemotherapy	5 (29.4)
Local recurrence	0
Distal recurrence	0

Figure 1

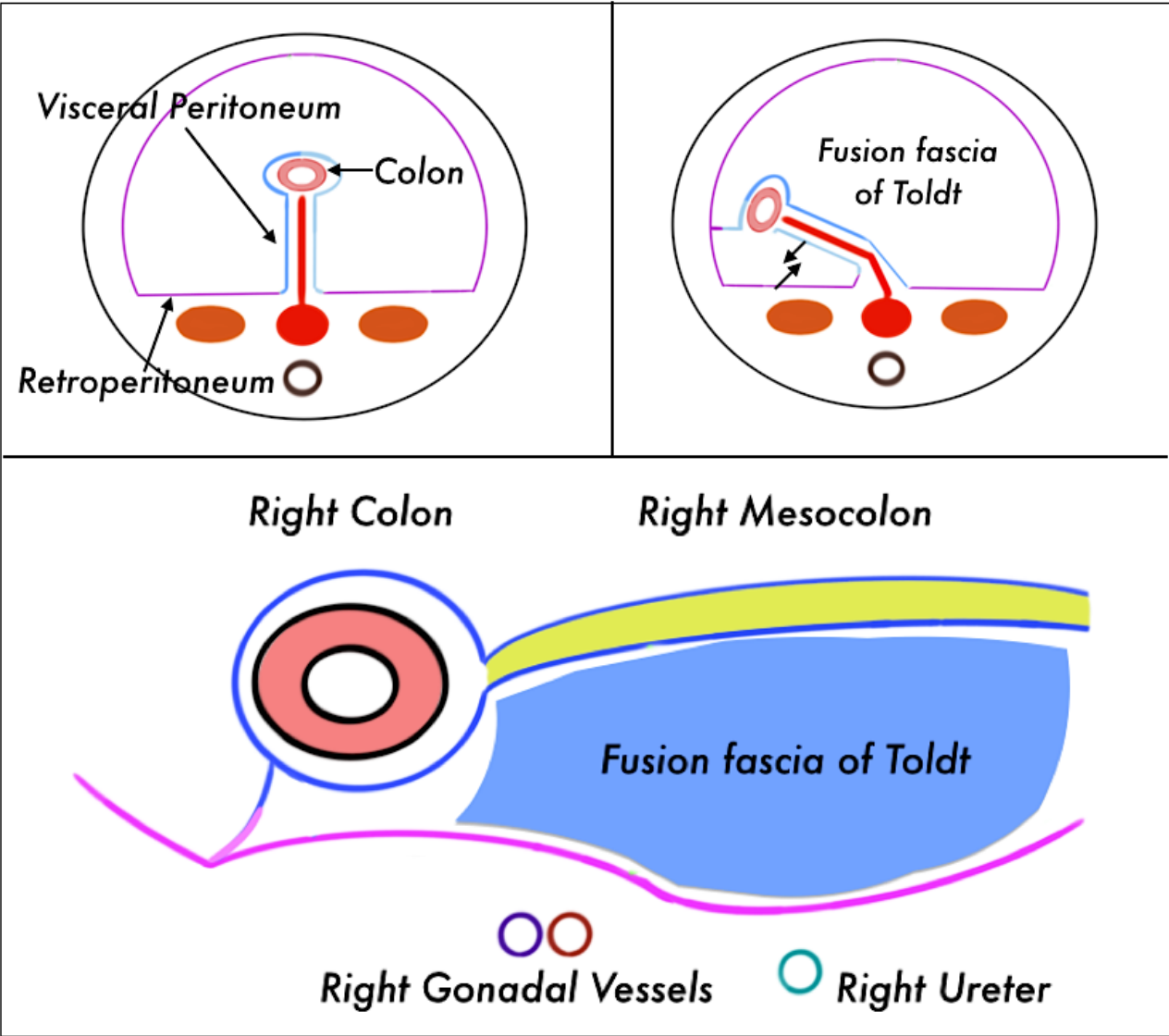


Figure 2

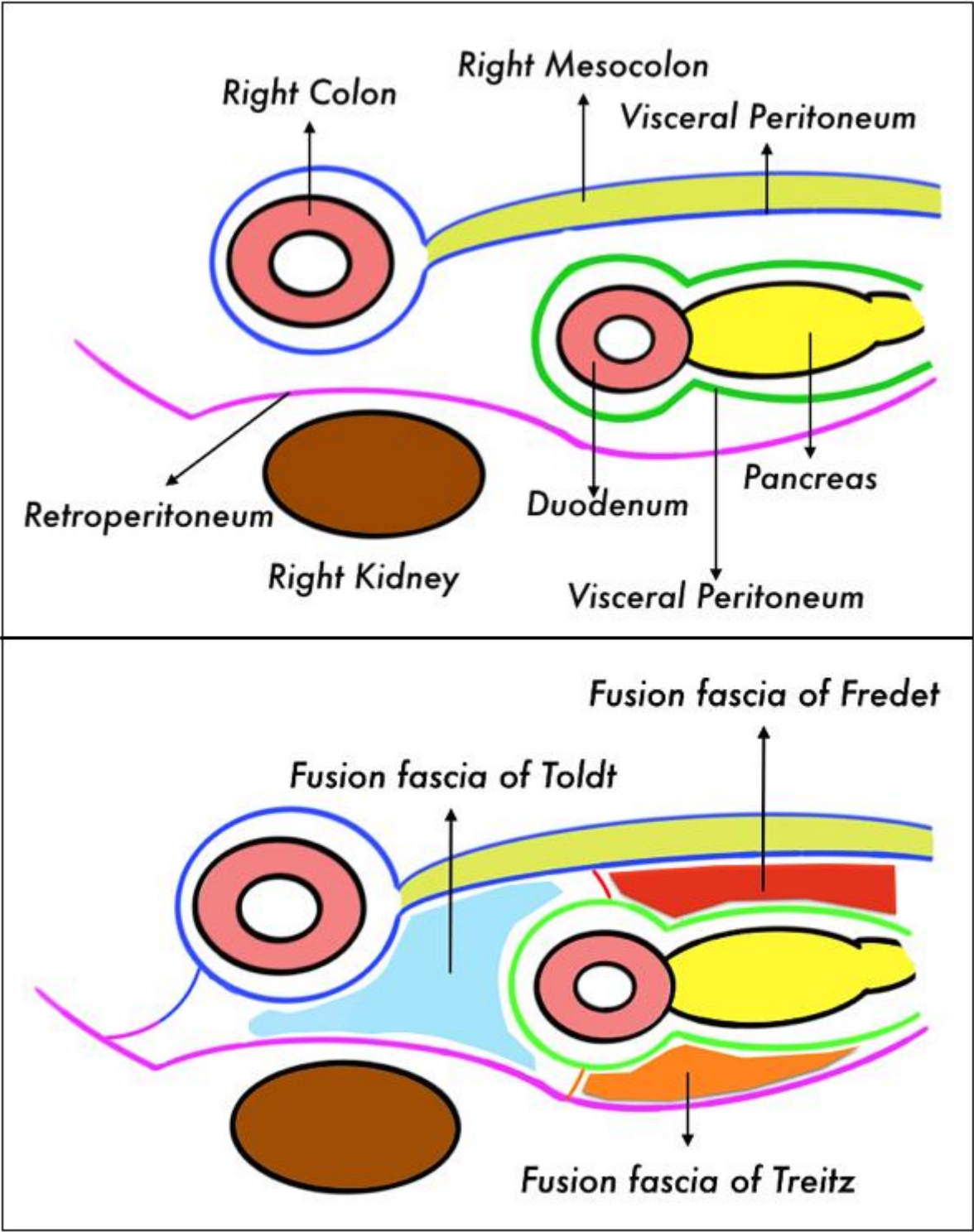


Figure 3A

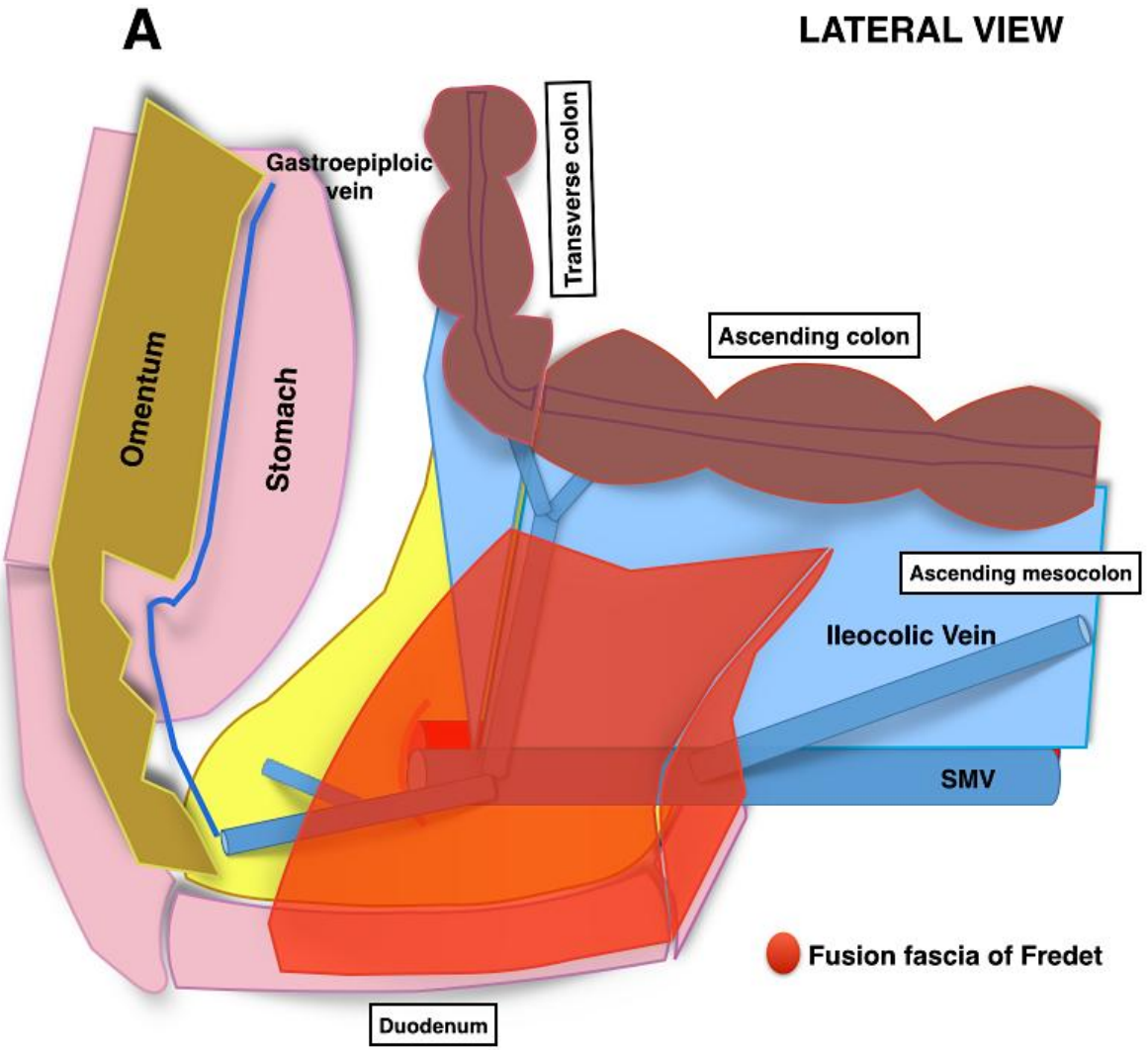


Figure 3B

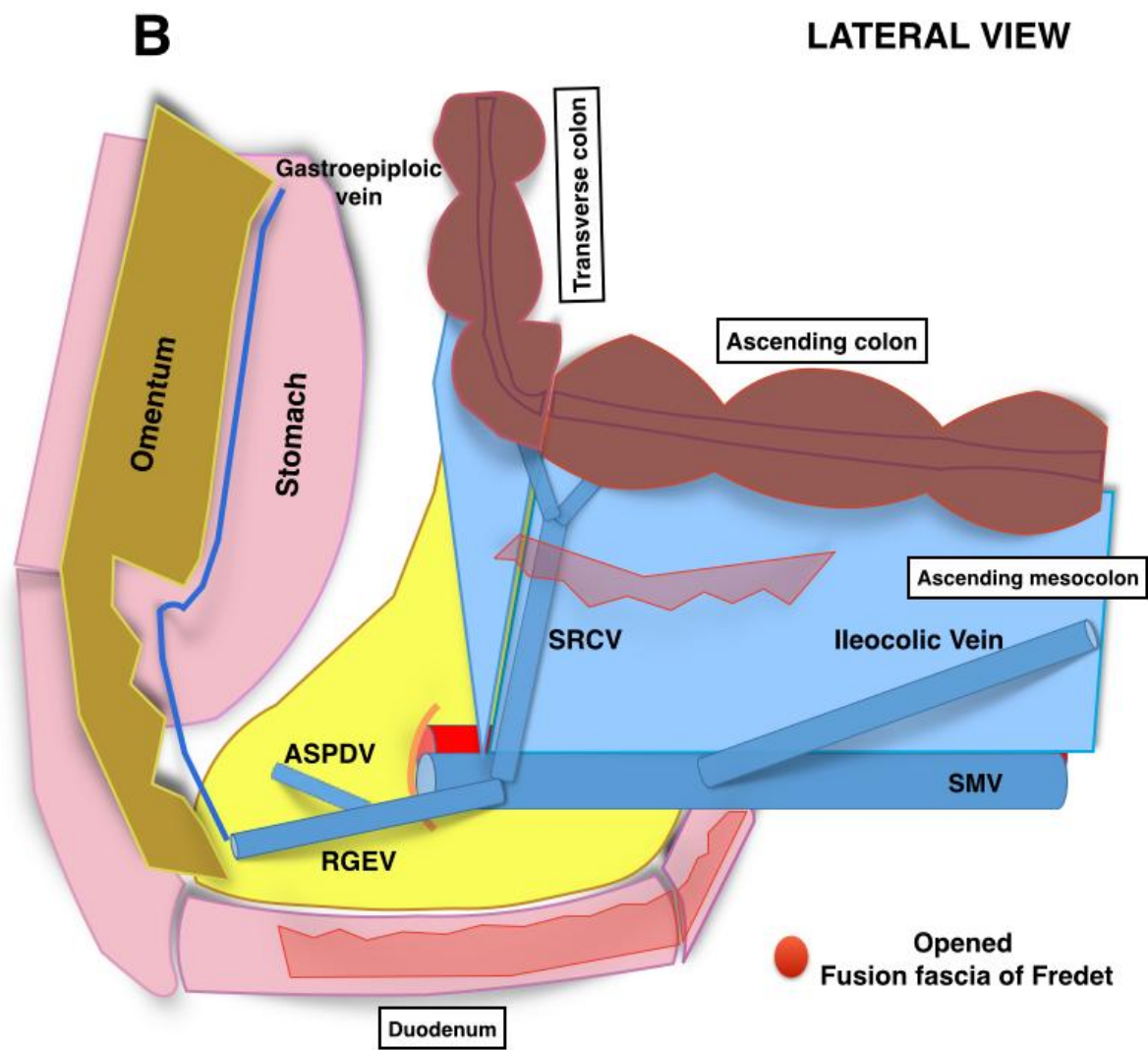


Figure 4

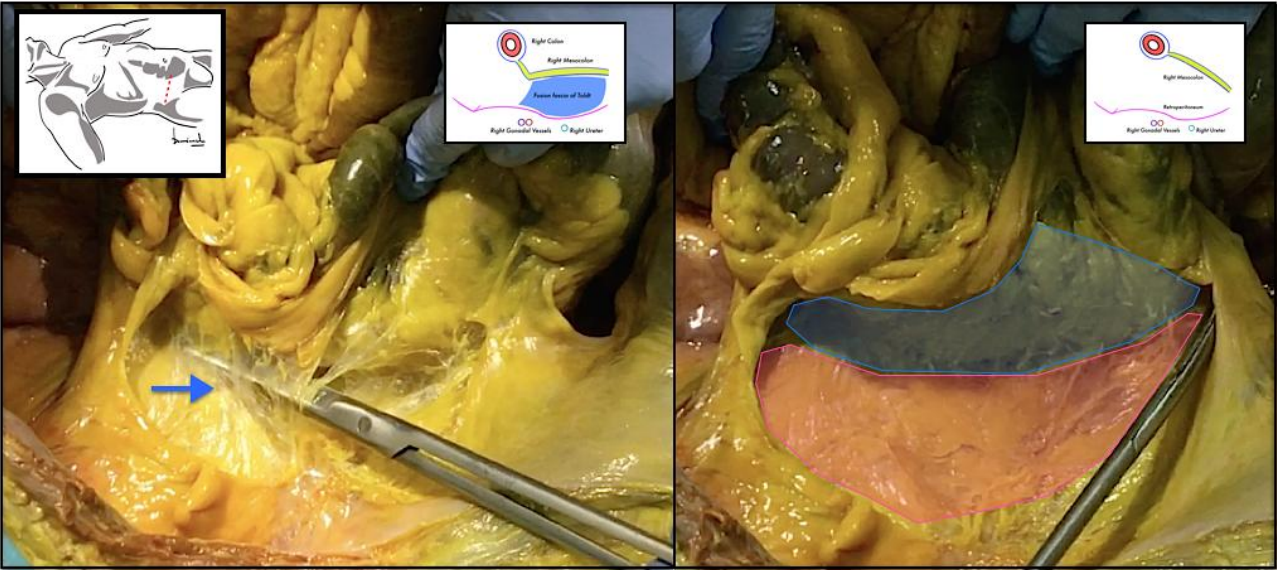


Figure 5

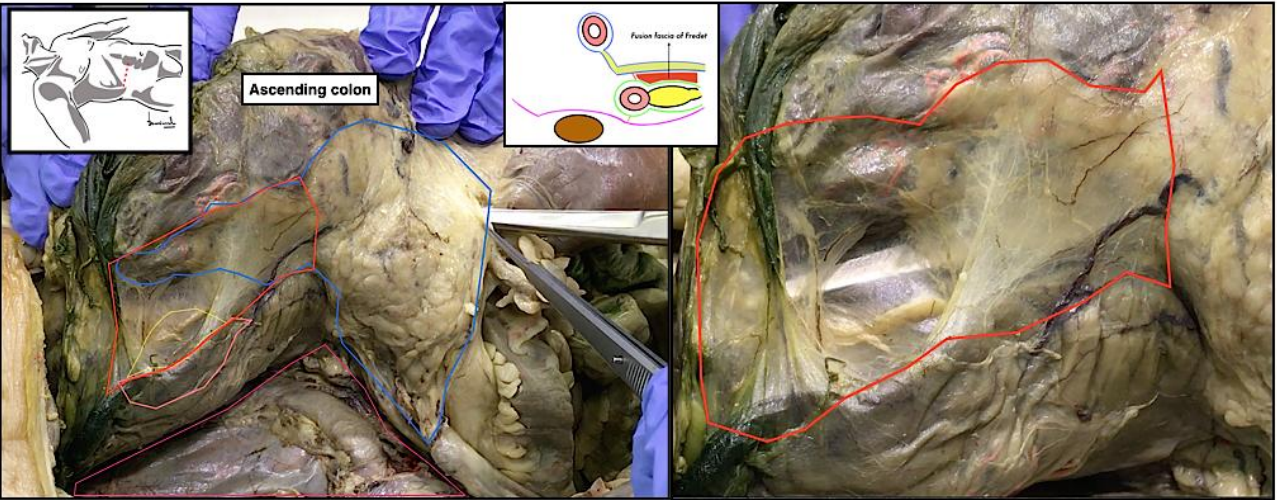


Figure 6

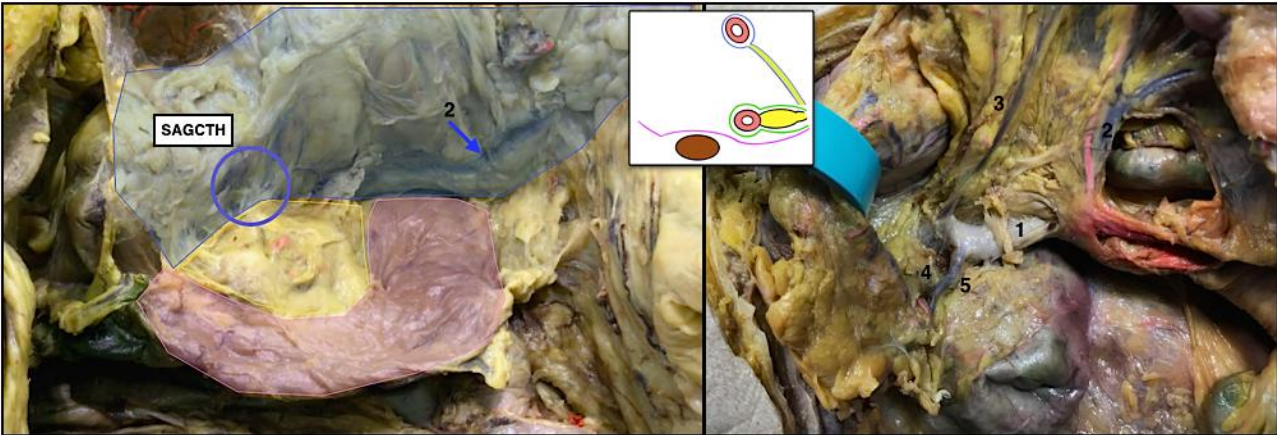


Figure 7

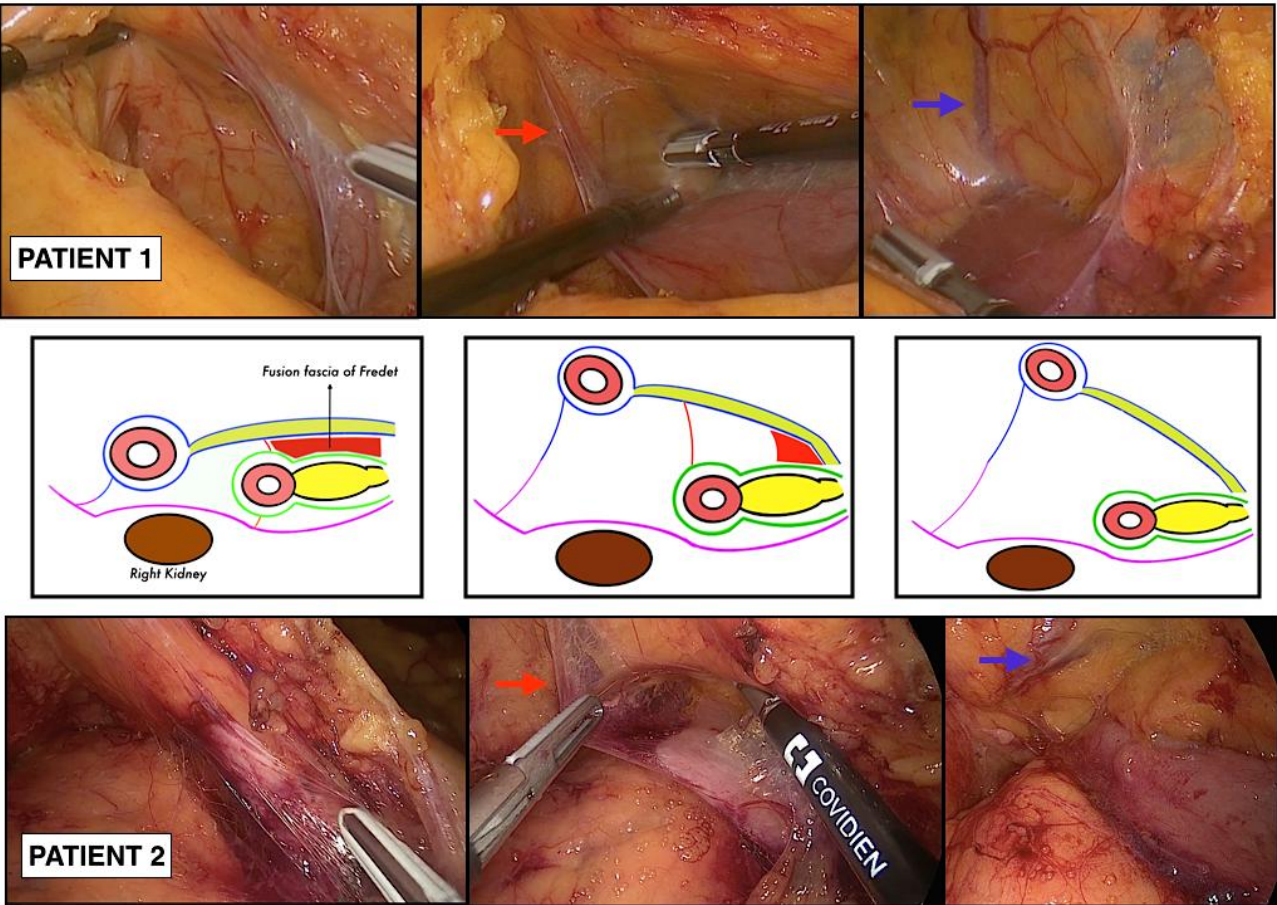


Figure 8

