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Abstract:	Purpose: Although lymph node metastases to pancreatic and gastroepiploic lymph node stations in transverse colon cancer have been described, the mode of lymphatic spread in this area remains unclear. This study was undertaken to describe possible pathways of aberrant lymphatic spread in the complex anatomic area of the proximal superior mesenteric artery and vein, the greater omentum, and the lower pancreatic border. Methods: Abdominal specimens obtained from four cadaveric donors were dissected according to the principles of complete mesocolic excision. The vascular architecture of the transverse colon was scrutinized in search of possible pathways of lymphatic spread to the pancreatic and gastroepiploic lymph nodes. Results: Vascular connections between the transverse colon and the greater omentum at the level of both the hepatic and the splenic flexure could be identified. In addition, small vessels running from the transverse mesocolon to the lower pancreatic border in the area between the middle colic artery and the inferior mesenteric vein were demonstrated. Moreover, venous contributaries to the gastrocolic trunk could be exposed to highlight its surgical importance as a guiding structure for complete mesocolic excision. Conclusion: The technical feasibility to clearly separate embryologic compartments by predefined tissue planes in complete mesocolic excision was confirmed. However, the vicinity of all three endodermal intestinal segments (foregut, midgut, and hindgut) obviously gives way to vascular connections that might serve as potential pathways for lymphatic metastatic spread of transverse colon cancer.

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Anatomy of the transverse colon revisited with respect to complete mesocolic excision and possible pathways of aberrant lymphatic tumor spread

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Abstract

Purpose: Although lymph node metastases to pancreatic and gastroepiploic lymph node stations in transverse colon cancer have been described, the mode of lymphatic spread in this area remains unclear. This study was undertaken to describe possible pathways of aberrant lymphatic spread in the complex anatomic area of the proximal superior mesenteric artery and vein, the greater omentum, and the lower pancreatic border.

Methods: Abdominal specimens obtained from four cadaveric donors were dissected according to the principles of complete mesocolic excision. The vascular architecture of the transverse colon was scrutinized in search of possible pathways of lymphatic spread to the pancreatic and gastroepiploic lymph nodes.

Results: Vascular connections between the transverse colon and the greater omentum at the level of both the hepatic and the splenic flexure could be identified. In addition, small vessels running from the transverse mesocolon to the lower pancreatic border in the area between the middle colic artery and the inferior mesenteric vein were demonstrated. Moreover, venous contributaries to the gastrocolic trunk could be exposed to highlight its surgical importance as a guiding structure for complete mesocolic excision.

Conclusion: The technical feasibility to clearly separate embryologic compartments by predefined tissue planes in complete mesocolic excision was confirmed. However, the vicinity of all three endodermal intestinal segments (foregut, midgut, and hindgut) obviously gives way to vascular connections that might serve as potential pathways for lymphatic metastatic spread of transverse colon cancer.

Key words:

Complete mesocolic excision, transverse mesocolon, gastrocolic trunk, superior mesenteric vein, superior mesenteric artery, anatomy

Introduction

Complete mesocolic excision (CME) describes the mobilisation and separation of the colon together with the entire regional mesocolon and supplying vessels as a contiguous and coherent embryologically defined compartment from the surrounding tissues in combination with a central vascular tie [1,2]. It represents the consequent extension of the philosophy of total mesorectal excision (TME) and of cancer-arresting capabilities of both the mesorectal and mesocolic fascia respectively to the entire large bowel [3-5]. Arterial blood supply, venous and lymphatic drainage take place within the boundaries of the mesocolon; and it is presumed that there are no compartment-crossing vessels that could potentially pave the way to cancer spread outwith the main route along the colic arteries [6]. It has been proven that CME results in a higher lymph node yield, a larger area of mesentery removed, a greater distance between the tumor and the central vascular tie and ultimately in better patient outcome [7-10].

The transverse colon, however, exhibits embryologic and anatomic peculiarities that result from its central position between the foregut and midgut. Although its proximal two thirds correspond to the end of the midgut and its distal third to the beginning of the hindgut, it is in an intimate relationship with the proximal superior mesenteric vessels and with foregut structures such as the greater omentum, the pancreas, and the lesser sac. On the one hand, this peculiar topographic relationship gives rise to the possibility of aberrant lymphatic spread; on the other hand, the venous drainage is especially variable and closely related to pancreatic and omental veins. If the surgeon is not aware of the latter, some troublesome bleeding may occur during surgery.

Thus, we performed a macroscopic dissection study in human cadaveric donors to search for possible vascular connections between derivatives of the fore-, mid- and hindgut in order to provide a morphologic basis for cancer spread outside the main drainage routes. Furthermore, we aimed to scrutinize the peculiar anatomical features of the venous drainage

into the superior mesenteric vein at the triangle between the right transverse mesocolon, the pancreas and the greater omentum.

Materials and Methods

Macroscopic studies

Gross anatomical dissections were undertaken on four formalin-fixed specimens obtained from cadaveric donors (body donation programme, Institute of Anatomy, University of Kiel, Germany), which exhibited no evident disease of the intra-abdominal organs. The greater omentum and the colon/mesocolon were released from the parietal fascia along areolar tissue planes as far as possible. Care was taken to preserve even tiny vessels that possibly crossed these areolar planes.

Furthermore, the tributaries to the superior mesenteric vein just below the pancreatic head and neck were meticulously dissected to describe their course in relation to the surgical technique of CME. Dissection then followed the posterior leaf of the lesser sac that was carefully detached from the anterior aspect of the transverse mesocolon to get access to the lower border of the pancreas. The relation of the mesocolon to the pancreas left of the superior mesenteric vessels and to the duodenum was demonstrated. Finally, findings obtained from the dissection studies were verified during surgical operations performed for transverse colon cancer or cancer at either the hepatic or the splenic flexure. All steps of the dissection studies were photographically documented using a high resolution digital colour camera. The dissected specimens were preserved for reference purposes and instructional skills laboratory workshops.

Microscopic studies

Tissues were harvested from sites of the transverse mesocolon where vascular structures could be identified by diaphanoscopy running from the transverse colon towards the lower border of the pancreas. Specimens (approximately 2 cm x 2 cm) were dehydrated in increasing series of alcohol, embedded in paraffin wax and cut perpendicular to the surface of the transverse mesocolon. The mesocolic cross-sections were stained with haematoxylin

& eosin and Masson´s trichrome /orcein to characterize the vascular structures at histological level.

Results

Macroscopic findings

Separation of embryological planes was proven to be feasible in formalin-fixed specimens. The mesocolic package could easily be mobilized from the parietal fascia on either side, the duodenum and the pancreatic head (Fig. 1). Separation of the greater omentum from the transverse colon was also possible along a preformed embryological plane. The area of the greater omentum attached to the wall of the transverse colon was almost free of adipose tissue and could be released from the bowel wall and the anterior aspect of the transverse mesocolon. Thus, the lesser sac remained initially unopened reflecting its embryological origin from the dorsal mesogastrium. The tissue that could be dissected off the transverse mesocolon represents the two posterior leafs of the dorsal mesogastrium. In the region of both the hepatic and splenic flexures small blood vessels were identified that connected the greater omentum with the bowel wall (Fig. 2).

At the lower border of the pancreatic body and proximal tail, the transverse mesocolon consisted only of a thin tissue sheet that was attached to the retroperitoneum along an insertion line running from the inferior mesenteric vein towards the superior aspect of the duodenojejunal flexure and the tissue bridge over the superior mesenteric vessels. Within this mesocolic sheet, several small vessels could be readily observed by diaphanoscopy extending between the transverse colon and the lower pancreatic border (Fig. 3). Whereas some vessels established direct connections between the transverse colon and the pancreas, other vessels originated either from the pancreatic side or from the bowel side without any obvious communications.

The main arterial blood supply of the transverse colon was provided by a single middle colic artery in all specimens. Further ramifications were variable. In two specimens, the middle colic artery divided into two branches only few centimeters from the origin of the superior mesenteric artery that ran parallel to each other towards the bowel before forming an arcade

close to the bowel wall to supply the transverse colon. An additional branch originated from the proximal part of the middle colic artery to form the right colic artery (Fig. 3, 4). In the other two specimens, the middle colic artery divided in an obtuse angle with a branch running to each of the two flexures without a separate branch for the right colon (Fig. 5).

Venous drainage of the middle and left transverse colon was carried out by the middle colic vein that peripherally followed the middle colic artery but took a different course centrally and drained directly into the superior mesenteric vein in all specimens. On the right side, two veins of about the same diameter, namely the right colic vein and the superior right colic vein, merged in three specimens and received tributaries from the right gastroepiploic and pancreaticoduodenal veins forming the gastrocolic trunk (Fig. 5, 6). This venous trunk entered directly into the superior mesenteric vein. Thus, centrally the course of the veins was completely independent from the course of the arteries (compare Fig. 4, 5, 6). In the fourth specimen, the right colic vein was missing and venous drainage of the right side of the transverse colon was realized by the superior right colic vein only. The connection of the right-sided colic veins to the gastroepiploic and pancreaticoduodenal veins marked the end of the embryologic tissue interfaces. From this confluence point towards the superior mesenteric vein the venous vessels were embedded in adipose tissue.

On the left side, separation of the descending mesocolon from the parietal fascia was as feasible as on the right side, again without any evidence of vessels crossing the embryological interface. This observation could be confirmed intraoperatively during mobilisation of the descending colon and the splenic flexure for CME (Fig. 7). Only around the inferior mesenteric artery, a continuous tissue connection to the para-aortal tissue and similarly, but to a lesser extent, around the inferior mesenteric vein to the retropancreatic tissue was encountered. Between these two connections, the mesocolon medial to the inferior mesenteric vein consisted only of a thin connective tissue layer covered by peritoneum that spread over the lateral aspect of the first jejunal sling and the parietal fascia.

Microscopic findings

Cross-sections of the transverse mesocolon were covered on either side by a serosal mesothelial lining supported by a subserosal connective tissue layer. Embryologically, the serosal layer of the anterior aspect belongs to the posterior leaf of the greater omentum. The mesocolic matrix was primarily composed of lobular adipose tissue and loosely arranged connective tissue septa. Those vascular structures previously identified by diaphanoscopy at the macroscopic level connecting the transverse colon and the pancreatic border could be readily confirmed at the microscopic level. Based on their histological peculiarities, the vascular structures consisted of arteries, veins and lymphatic vessels (Fig. 8, 9a, 9b).

Discussion

The emergence of the superior mesenteric vessels between the pancreas and the duodenum represents the embryological pivot of intestinal rotation. This intestinal rotation shapes the peculiar architecture of colonic anatomy with its frame-like position around the small bowel and its adhesions between the mesocolic parts and the structures sited posterior to it [11]. The transverse colon is situated in the centre of abdominal anatomy; the right and middle third deriving from the midgut, and the left third from the hindgut. Moreover, it is covered by the greater omentum and thus stays in direct connection to the embryological foregut.

The caecum, ascending colon and hepatic flexure including the corresponding mesocolon can easily be separated from the parietal fascia, the duodenum and the pancreatic head within an embryological interface [12]. It is possible to gently open this interface that reveals thin areolar tissue without breaching the fascial layers on either side [13]. In this plane we were not able to demonstrate vascular connections crossing the interface. It is reasonable to presume that an intact covering on the mesocolon, the mesocolic fascia, serves as a tumor-arresting barrier in the same way as it was demonstrated for the mesorectal fascia [3,5]. It is one of the cornerstones of CME to respect the integrity of this embryological envelope [1,7]. If surgical dissection follows this plane, an accidental injury to the ureter is not possible as it belongs to a different embryological compartment.

The only connection of the right mesocolic package to the retroperitoneal structures is represented by the tissue along the superior mesenteric vessels that consists of nerves, lymphatics, and adipose tissue extending from just below the neck of the pancreas proximally towards the ileocolic vessels distally. This part of the superior mesenteric vessels is by some authors called the "surgical trunk" [14-16]. However, the close relationship of the various embryologically defined components of the viscera entails that vascular architecture, especially venous drainage, is complex and variable [14,17,18].

Based on these considerations it is mandatory for right-sided CME to meticulously identify the specific course of the veins in this area, which differ substantially from that of the arteries. Although commonly not mirrored in anatomical textbooks, it has been described by several authors that the colic vein draining the region of the hepatic flexure, called the superior right colic vein, joins with the right gastroepiploic vein to form a short venous trunk that ends in the superior mesenteric vein [13,14, 19,20]. This trunk was first described as the gastrocolic vein by Henle in 1868 [21]. Many variants of this venous confluence have been found. Quite commonly, an anterior pancreaticoduodenal vein contributes to Henle's trunk as does the right colic vein and rarely even the middle colic vein [14,18,19,22]. There is still a debate on whether this pancreaticoduodenal vein belongs to the anterior-inferior or to the anterior-superior arcade [23,24]. We could demonstrate that due to the aforementioned variability, more than one pancreaticoduodenal vein may run into this venous trunk. This peculiar confluence of veins from the foregut and midgut explains the bleeding episodes frequently observed during dissection in this area despite the identification of the confluence of the superior right colic vein and the right gastroepiploic vein. Hohenberger et al. have raised the awareness of this critical region ("bleeding point") in the surgical community and standardized dissection of these veins as guiding structures that lead to the superior mesenteric vein in right-sided CME [1].

The arterial blood supply of the transverse colon is also variable when compared to a highly constant ileocolic artery for the right-sided colon and a similarly constant left colic artery for the left-sided colon [25]. The right colic artery originates directly from the superior mesenteric artery in only 15 to 40 % [26,27]. In about 45 %, it derives from the middle colic artery as a distinct branch (as observed in our cases), or the right branch of the middle colic artery directly supplies the right colon. Rarely, the right colic artery originates from the ileocolic artery [27]. The middle colic artery divides into a right and a left branch in approximately 60 %. In the remaining 40 %, an independent left branch is described. Very rarely it originates from the inferior mesenteric artery or from a dorsal pancreatic artery [27]. These variants

may then give way to aberrant lymphatic tumor spread. Of note is that surgical dissection of the left-sided embryological planes has been part of total mesorectal excision and therefore more widely practiced compared to the complete mobilization of the right-sided embryological planes. This observation may partly explain the better outcomes for left-sided colon cancer when compared to right-sided tumors [28-30].

The transverse colon is in close topographic contact to foregut structures, e.g. to the greater omentum including the gastrocolic ligament, and the pancreas. Although separation of the greater omentum from the transverse colon and mesocolon was possible, we found small vessels in the region of both the hepatic and splenic flexure that crossed between these fore- and midgut derivates. These vascular connections could serve as tracks for blood vessel and lymphatic tumor spread to lymph nodes within the greater omentum and along the gastroepiploic vessels. Perrakis et al. gave clinical proof of this hypothesis in a recent series of 45 patients with carcinoma of the transverse colon or the colonic flexures. They encountered lymph node metastases in four (9 %) of these patients at the gastroepiloic arcade [31]. In another series of 98 patients including cancers of the distal ascending colon, four patients (4 %) with gastroepiploic or infrapyloric lymph node metastases could be identified [32]. Apart from vascular tumor spread, direct infiltration of the greater omentum ("per continuitatem") encompasses an additional possibility of metastatic omental and gastroepiploic lymph node disease. These observations provide the rationale to resect the greater omentum if it is in direct anatomical contact with the cancer-bearing segment of the colon. Omentectomy must include the corresponding gastrocolic ligament and the feeding gastroepiploic vessels. The safety margins should parallel the extent of colonic resection.

Furthermore, we found small vascular structures within the transverse mesocolon composed of arteries, veins and lymphatic vessels running between the transverse colon and the lower pancreatic border. These vessels crossed the transverse mesocolon in the region between the middle colic artery and the inferior mesenteric vein, and established connections between the transverse colon and foregut derivatives (pancreas). Again, this anatomical peculiarity

may explain the clinical observation by Perrakis et al. who demonstrated lymph node metastases in infrapancreatic lymph nodes in five (11%) out of the aforementioned 45 patients [31]. Based on these considerations, mobilisation and dissection of the transverse mesocolon for transverse colon cancer should therefore follow the lower border of the pancreatic compartment and meticulously separate the entire transverse mesocolon in order not to leave behind residual mesocolic tissue. This step of dissection routinely includes lymph nodes at the lower pancreatic border that may accompany the described small vessels in the transverse mesocolon towards the pancreas but are often hardly recognizable. For pathologic work-up, this region of the specimen needs to be marked in order to allow the identification of the topographic localization in case of lymph node metastases.

Studies that have analyzed putative lymphatic connections of the transverse mesocolon to the pancreatic lymph nodes are rare. Hirono et al. used the indocyanine green fluorescence imaging method to describe the lymphatic drainage of the pancreas. They could identify a connection to lymphatic tissue around the middle colic artery via the superior mesenteric artery [33]. Toyota et al. found metastatic infrapyloric lymph nodes in four of 53 (7.5 %) right-sided transverse and in one of 188 (0.5 %) ascending colon cancers [15]. Morikawa et al. could demonstrate that involvement of central lymph nodes along the main vascular trunk only occurred in pT3 and pT4 tumors [34]. From these reports it can be deduced that involved lymph nodes in the pancreatic area occur in up to 10 % of transverse colon carcinoma, are more common in advanced cases and may rarely be found even without any other lymph node stations involved.

Conclusion

We have been able to generate evidence to support the concept of CME by gross anatomic dissection studies highlighting the embryologically distinct colonic/mesocolonic compartment similar to the descriptions of the mesorectal compartment. Anatomic peculiarities of the veins draining the right colon into the superior mesenteric vein, together with veins from the

stomach and pancreas, were described and must be respected during surgical dissection. Finally, small blood and lymphatic vessels between the transverse colon/mesocolon and the greater omentum as well as the pancreas could be identified as possible routes of additional lymphatic tumor spread, emphasizing complete removal of omental and mesocolic tissues.

Disclosures

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Figures legends

Figure 1:

Separation of the right-sided mesocolic package from the parietal fascia and duodenum with mobilisation of the hepatic flexure. Note the smooth surface of both the ascending mesocolon and the underlying parietal fascia. GB – gall bladder.

Figure 2:

Small vessel (red indicator) crossing from the left transverse colon to the greater omentum at the level of the gastrocolic ligament.

Figure 3:

Diaphanoscopy of the transverse mesocolon reveals small vessels (arrow heads) between the bowel wall and the inferior pancreatic border. SMV – superior mesenteric vein; MCA – middle colic artery (right and left branch); RCA – right colic artery (deriving from the middle colic artery).

Figure 4:

Proximal superior mesenteric artery (SMA) and its branches comprising the middle colic artery (MCA, red vessel loop), right colic artery (RCA) deriving from the middle colic artery, inferior pancreaticodurdenal artery (IPDA), and jejunal arteries (JA). RGEA – right gastroepiploic artery (red indicator). Tributaries of the gastrocolic trunk are highlighted by the blue indicator (for details see figure 6).

Figure 5:

Proximal superior mesenteric artery (SMA) and vein (SMV) with the transverse mesocolon flipped upwards. The middle colic artery (MCA) divides into two main branches which run along the transverse colon on either side. The gastrocolic trunk (white star) is formed by the tripod of the right gastroepiploic vein (RGEV), the superior right colic vein (SRCV) and a pancreaticoduodenal vein (PCV) and receives the right colic vein only shortly before it drains

into the SMV. The middle colic vein (MCV) drains directly into the SMV forming a trunk with two jejunal veins (JV).

Figure 6:

Tributaries of the gastrocolic trunk (white star) comprise the right colic vein (RCV), superior right colic vein (SRCV), pancreaticoduodenal veins (PDV), and right gastroepiploic vein (RGEV) highlighted by blue indicators. The middle colic vein (MCV) directly drains into the superior mesenteric vein (SMV).

Figure 7:

Intraoperative view of the left upper abdominal quadrant during CME for transverse colon cancer. The splenic flexure has been mobilised following the embryological planes. The greater omentum was removed from the greater curvature. The jejunum is seen at the duodenojejunal flexure. Note the smooth surface of the parietal fascia after complete removal of the left-sided mesocolic package.

Figure 8:

Transverse mesocolon with serosal coverings. The upper serosal layer is elevated by forceps to expose the adipose tissue harbored within the transverse mesocolon. The histologic section displayed in figure 8 corresponds to the interrupted black line. MCA – middle colic artery

Figure 9:

Histological cross-section of the transverse mesocolon. Overview magnification (a) and higher magnification of insert (b). Between the two continuous serosal layers (arrowheads) extends adipose tissue and connective tissue septa with embedded vascular structures. The insert displays the characteristic features of arteries (A), veins (V) and lymphatic (L) vessels. Masson´s trichrome /orcein. Magnification 40x (a), 200x (b).

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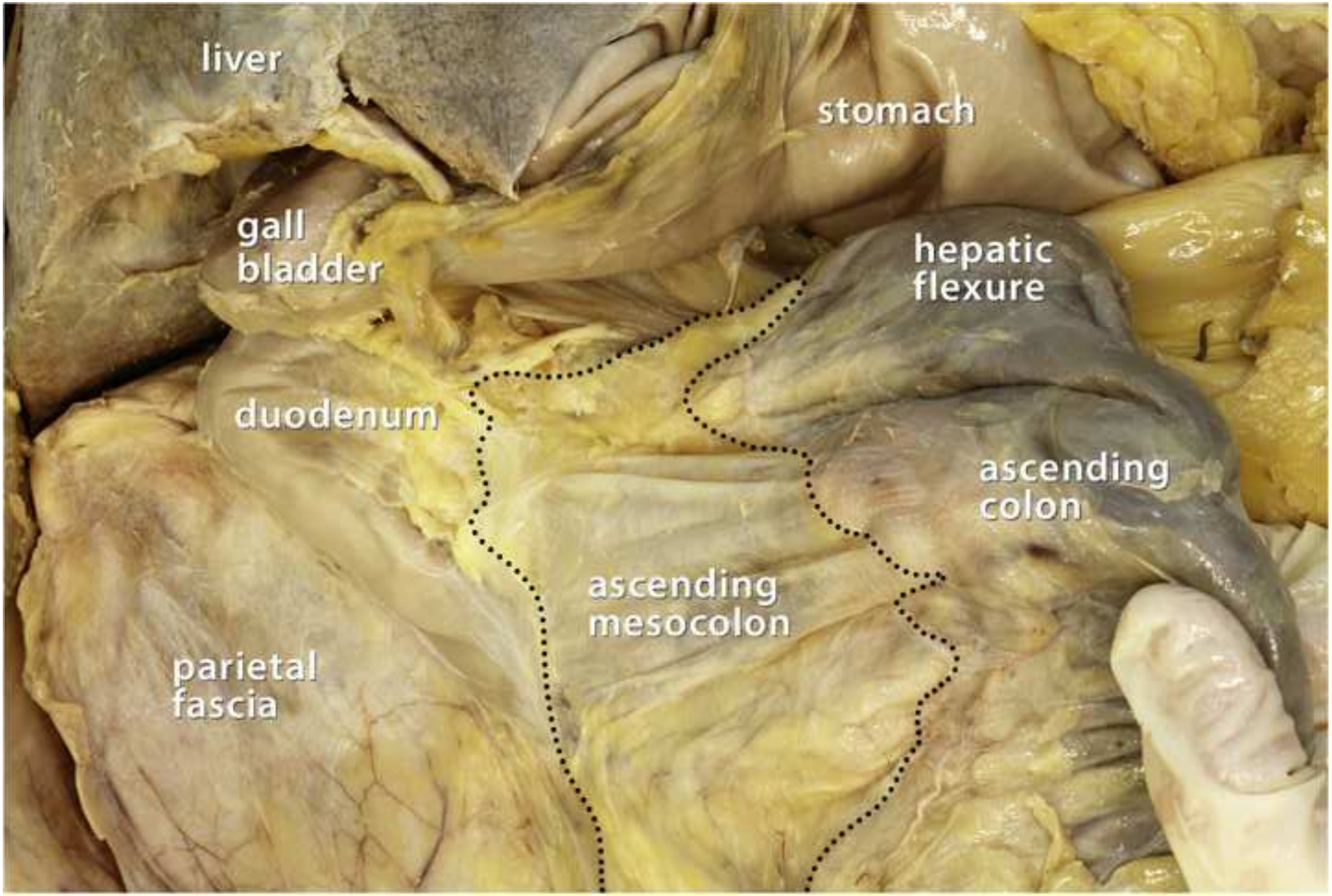

Figure2

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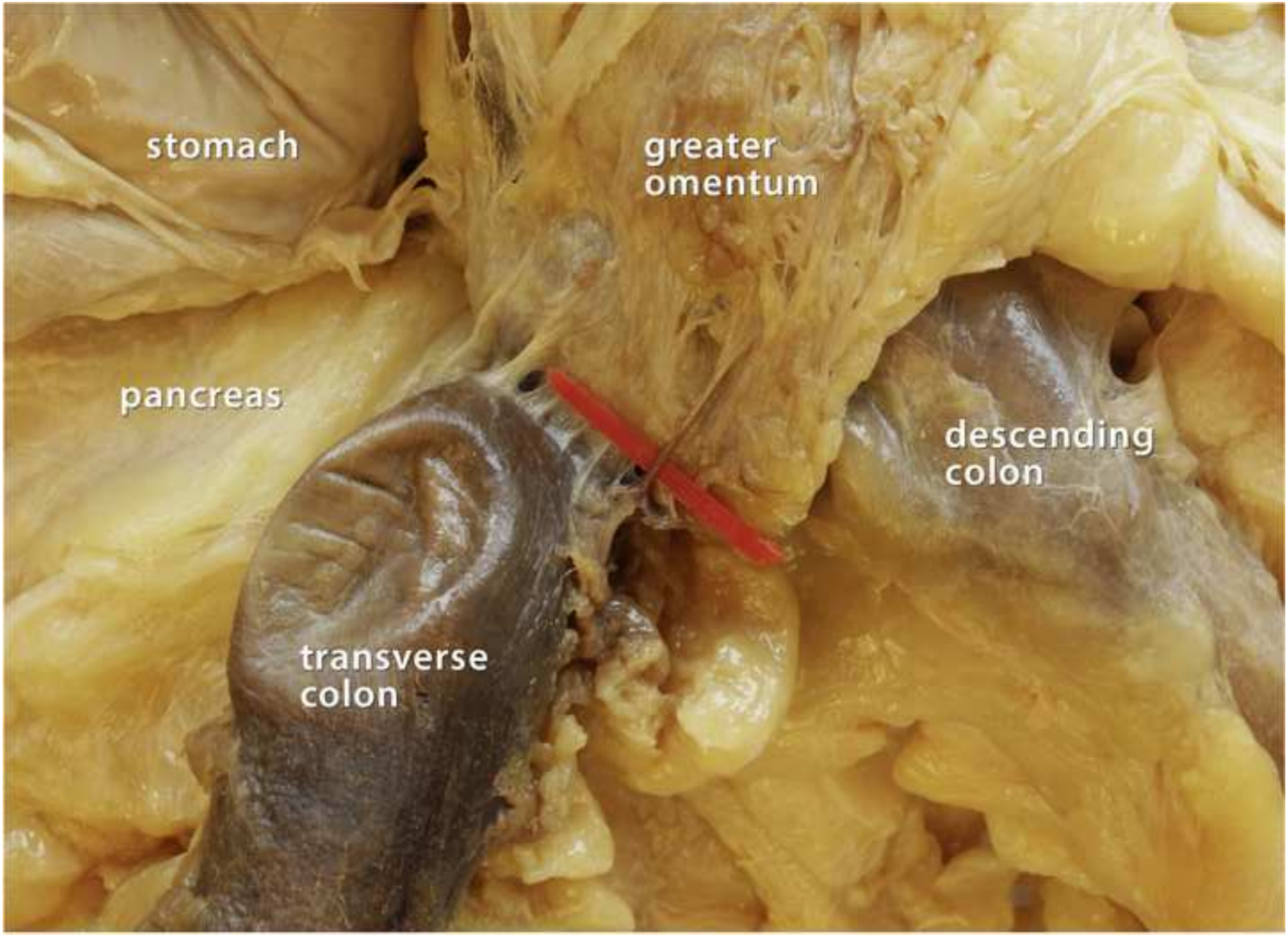

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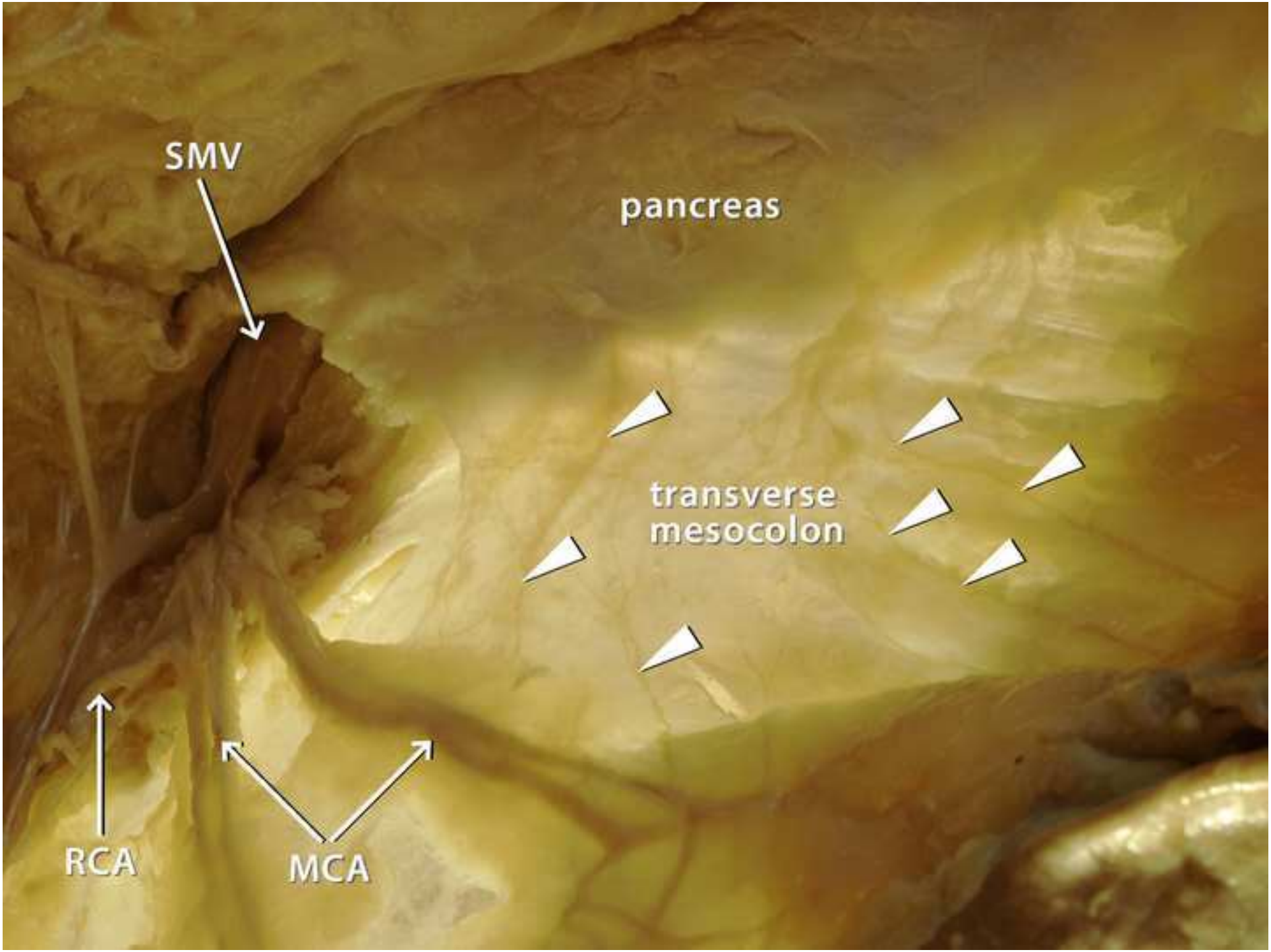

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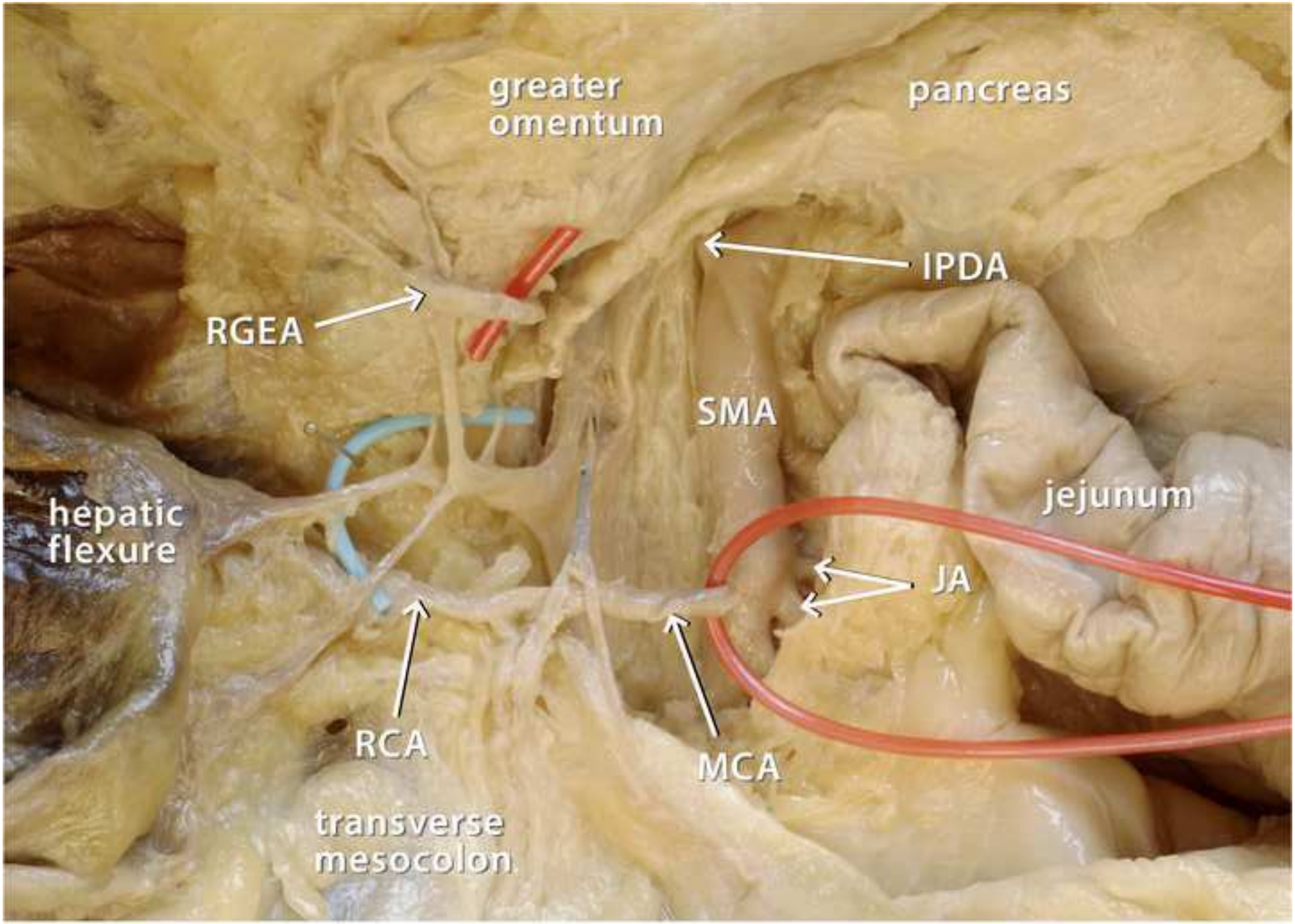

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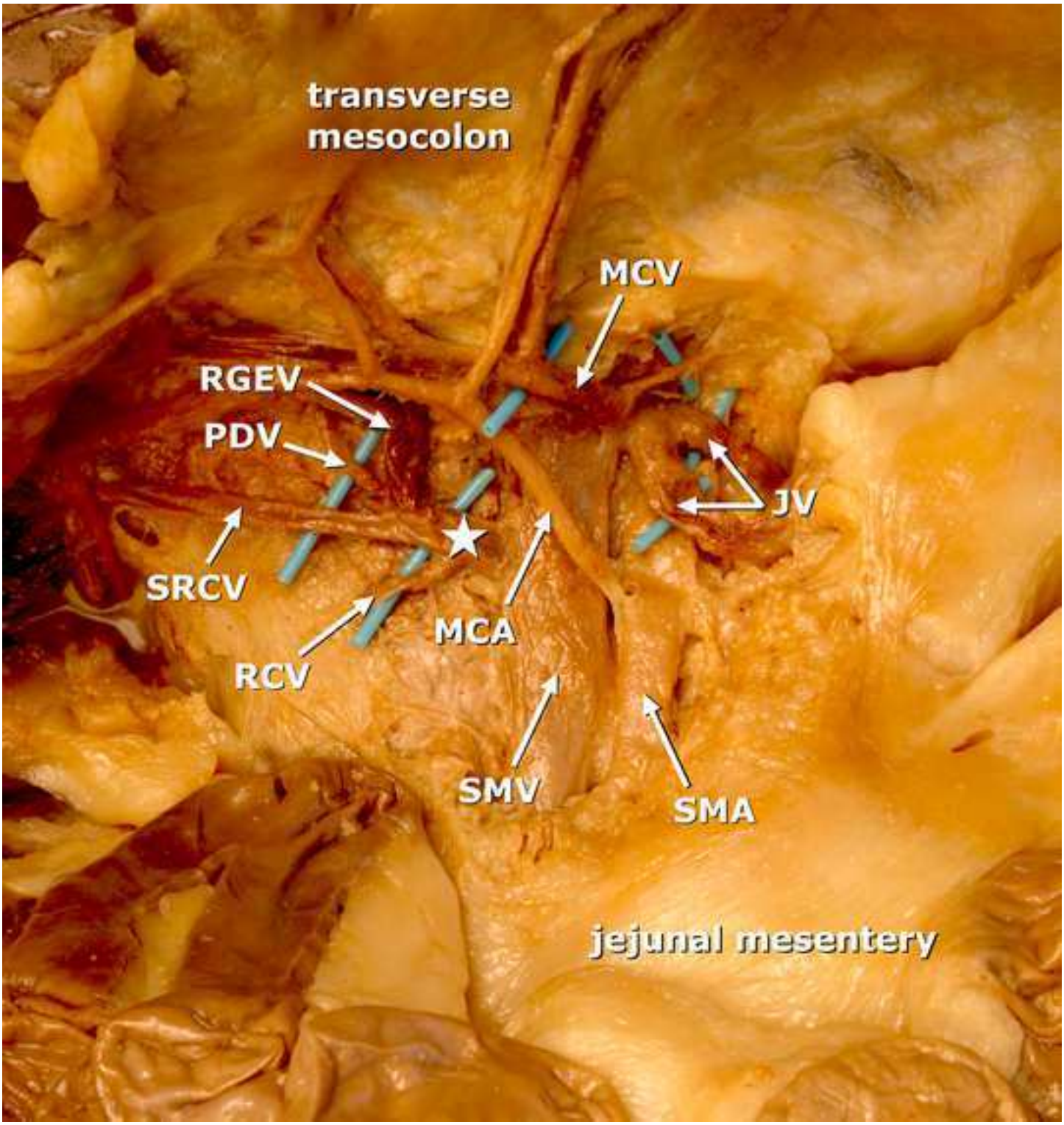

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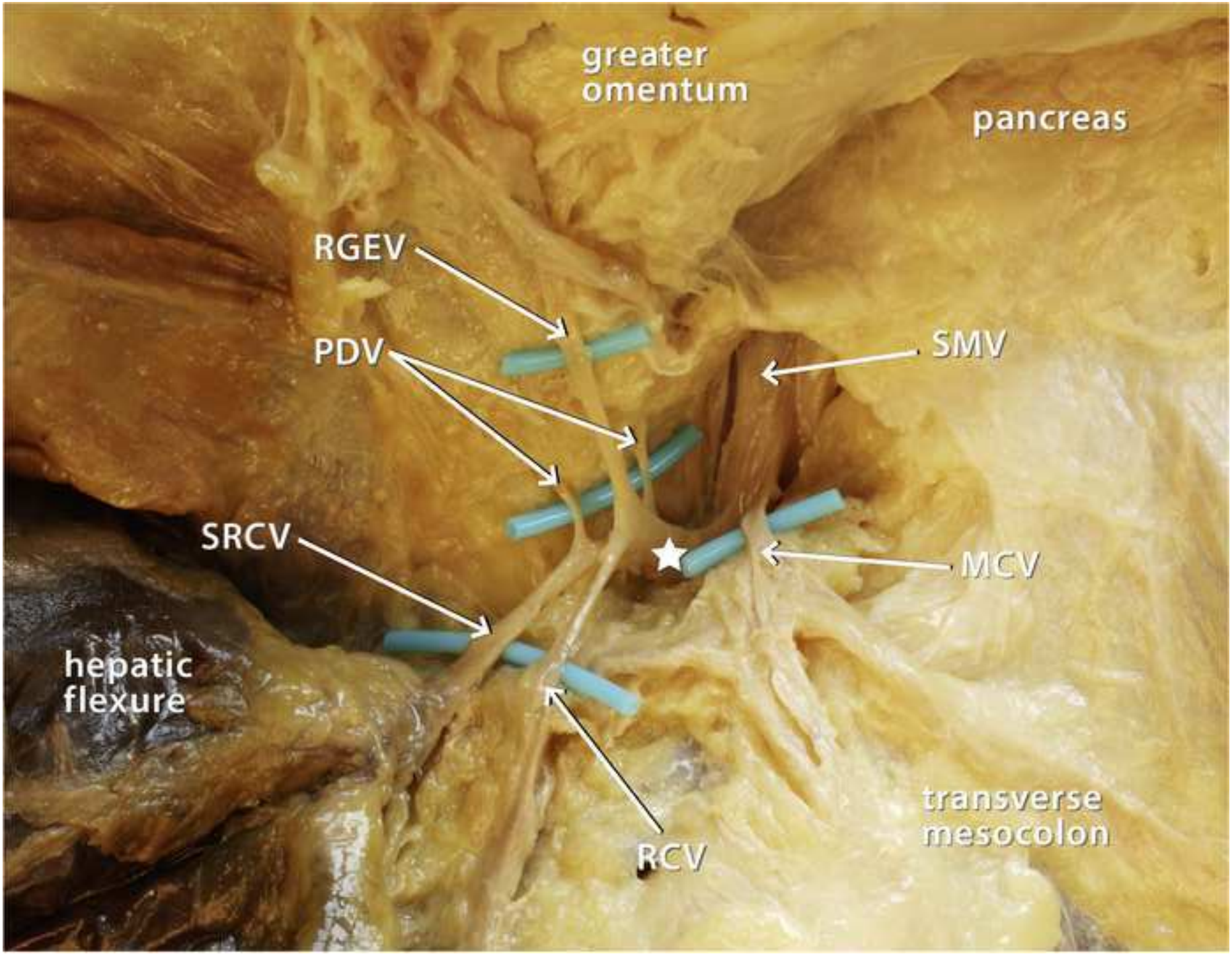

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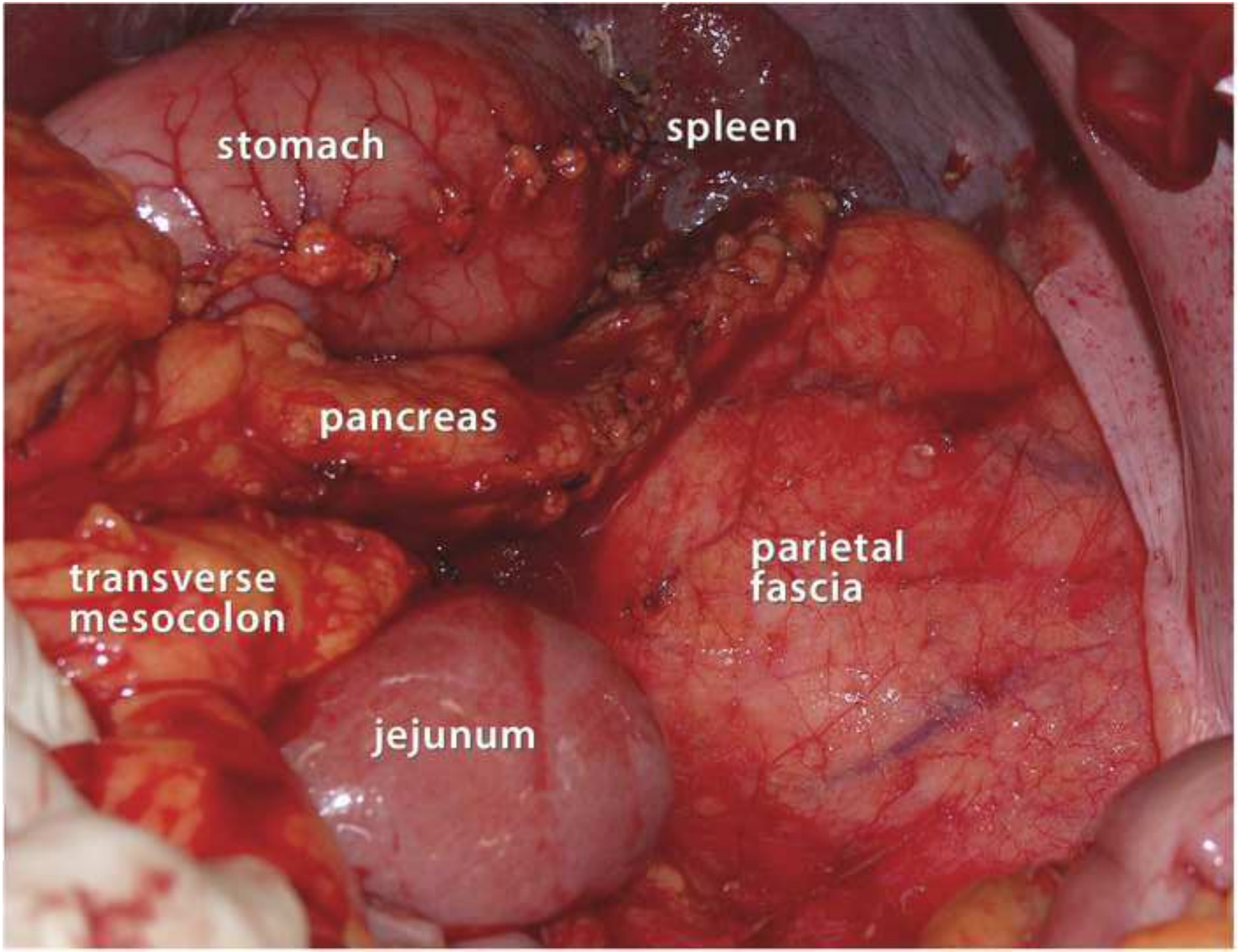

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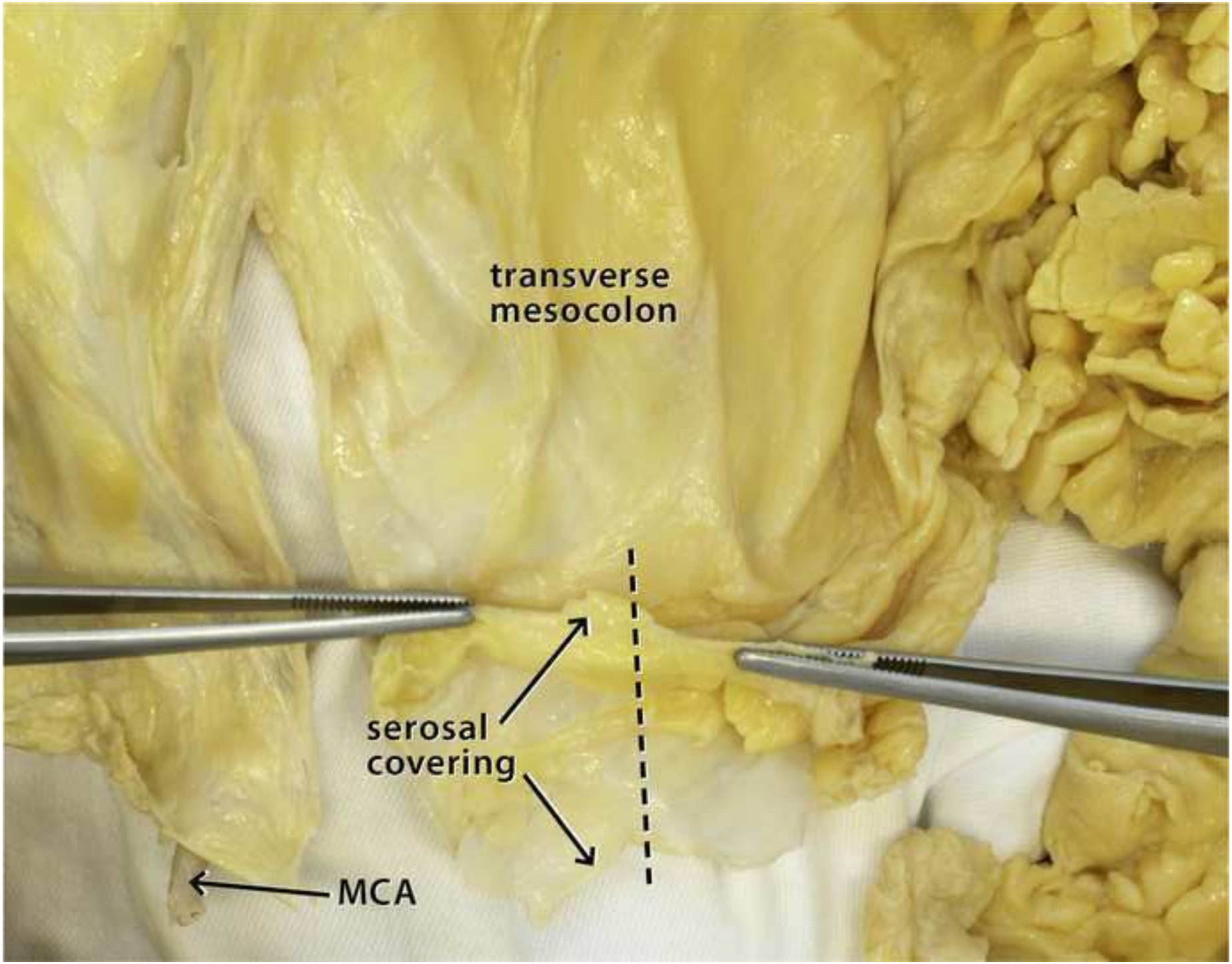

Figure9

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