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The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS*, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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MINIREVIEWS

From basic to clinical: Anatomy of Denonvilliers' fascia and its application in laparoscopic radical resection of rectal cancer

Zhou Chen, Xiao-Jing Zhang, Hao-Dong Chang, Xiao-Qian Chen, Shan-Shan Liu, Wei Wang, Zhi-Heng Chen, Yu-Bin Ma, Liang Wang

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Abstract

The total mesorectal excision (TME) approach has been established as the gold standard for the surgical treatment of middle and lower rectal cancer. This approach is widely accepted to minimize the risk of local recurrence and increase the long-term survival rate of patients undergoing surgery. However, standardized TME causes urogenital dysfunction in more than half of patients, thus lowering the quality of life of patients. Of note, pelvic autonomic nerve damage during TME is the most pivotal cause of postoperative urogenital dysfunction. The anatomy of the Denonvilliers' fascia (DVF) and its application in surgery have been investigated both nationally and internationally. Nevertheless, controversy exists regarding the basic to clinical anatomy of DVF and its application in surgery. Currently, it is a hotspot of concern and research to improve the postoperative quality of life of patients with rectal cancer through the protection of their urinary and reproductive functions after radical resection. Herein, this study systematically describes the anatomy of DVF and its appli-cation in surgery, thus providing a reference for the selection of surgical treatment modalities and the enhancement of postoperative quality of life in patients with middle and low rectal cancer.

Key Words: Denonvilliers' fascia; Total mesorectal excision; Middle and low rectal cancer; Laparoscopic surgery; Dissect

Core Tip: Denonvilliers' fascia, an influential separating and barrier structure surrounding the rectum, is of paramount significance to the quality of life and the protection of pelvic autonomic nerves following surgery for rectal cancer.

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INTRODUCTION

Rectal cancer, one of the most common cancers worldwide[1], is currently treated with a complete surgical approach. Heald *et al*[2,3] proposed that total mesorectal excision (TME) is the gold standard for the surgical treatment of middle and low rectal cancer and that the integrity of mesorectal specimens can be utilized as an essential criterion for evaluating surgical quality and has the function of predicting tumor recurrence.

As reported[2], the most frequent postoperative complications of rectal cancer are urination disorder and sexual dysfunction caused by intraoperative pelvic autonomic nerve (PAN) damage. These two complications have an incidence rate of 30%-60% and 50%-70%, respectively, and severely affect the postoperative quality of life of patients. The precise separation of planes in front of the rectum was not overemphasized in the early surgical description of Heald. Importantly, recent years have witnessed the constant development of TME technology for rectal cancer and the increasing requirements for PAN preservation, which enables the selection of scope of radical resection for rectal cancer and the better preservation of postoperative urinary, reproductive, and defecation functions of patients to become an important issue that must be solved urgently. It has been extensively demonstrated that the removal of Denonvilliers' fascia (DVF) during TME is a primary contributor to postoperative urogenital dysfunction in patients with rectal cancer [4]. Nonetheless, there is currently a paucity of long-term follow-up results on DVF-preserving TME (iTME), and it is yet to be reported on the results of long-term research on whether DVF preservation affects the long-term survival rate and increased local recurrence rate of patients. At the moment, it is a consensus to free the posterior and lateral anatomical levels of the rectum during TME, that is, freeing along the fascia propria of the rectum. However, the freeing of the anterior rectal wall and DVF-related levels is still debatable[5]. Accordingly, this study explores the anatomy of DVF and its use in surgery in greater detail and analyzes the comprehension of DVF and its preservation or not, thus providing a further reference for the selection of surgical treatment modes for middle and low rectal cancer.

THE ORIGIN, BASIS, AND CLINICAL ANATOMY OF DVF

The anatomical position of DVF and its association with adjacent organs are responsible for its critical role in surgery for rectal cancer and influence the choice of surgical plane in front of the rectum during TME. This structure can be understood to some extent through anatomy and embryology (Figure 1A). At present, three basic hypotheses exist for the embryonic origin of DVF, including peritoneal fusion of embryo dead sac, condensation of embryo mesenchyme, and mechanical pressure. According to certain experts[5], DVF is formed through peritoneal fusion. Another opinion[4] holds that DVF formation is not derived from the occurrence of peritoneal fusion or pelvic dead sac of peritoneum. Moreover, DVF is a tension-induced structure, rather than a fascia fusion. DVF formation, whether caused by peritoneal fusion or tension, is the result of fusion or compression, which certainly results in its thickening structure. Under the light microscope, DVF is observed to have a single-layer, double-layer, multi-layer, or composite single-layer structure. Nevertheless, DVF has not been observed to be stratified to the naked eye in practically all individuals, and individual DVF is partially separated into two layers of vacuolated structures. Nonetheless, such individuals may also be particular. This structure has also been corroborated in the studies by Abdelrahman[6] and Wang *et al*[7].

The DVF structure was first discovered in male cadavers and then accepted by surgeons. However, the structure of DVF in females has not been thoroughly characterized, since physicians seldom find structures identical to DVF in males between the rectum and vagina after surgery. Hence, the presence of DVF in females has been controversial. However, mounting embryological, anatomical, and histological studies show the existence of DVF in females, including the structure of the rectovaginal septum. Despite no agreement on the embryonic origin of DVF, three theories including tension induction, mesenchyme, and peritoneal fusion all support the concept of DVF as a separate structure that neither belongs to the fascia propria of the rectum nor to the urogenital system[8-11]. Frizzell *et al*[12] observed that DVF fused with the anterior mesorectal fascia in imaging such as magnetic resonance imaging and therefore was difficultly differentiated and that the above two types of fascia exhibited a low-signal shadow of a single-layer linear structure after being reflected between the anterior rectal wall of the rectum and vagina, the seminal vesicle and the prostate, and peritoneum (Figure 1B). Another researcher discovered that intraoperative observations (endorectal ultrasound) were completely consistent with the anatomical course of DVF and that DVF divided the rectum and urogenital organs into posterior prostatic space and anterior rectal space, among which the latter existed objectively as the anatomical plane of separation plane during TME. A histological study[13] revealed that DVF was markedly stratified and varied among individuals,

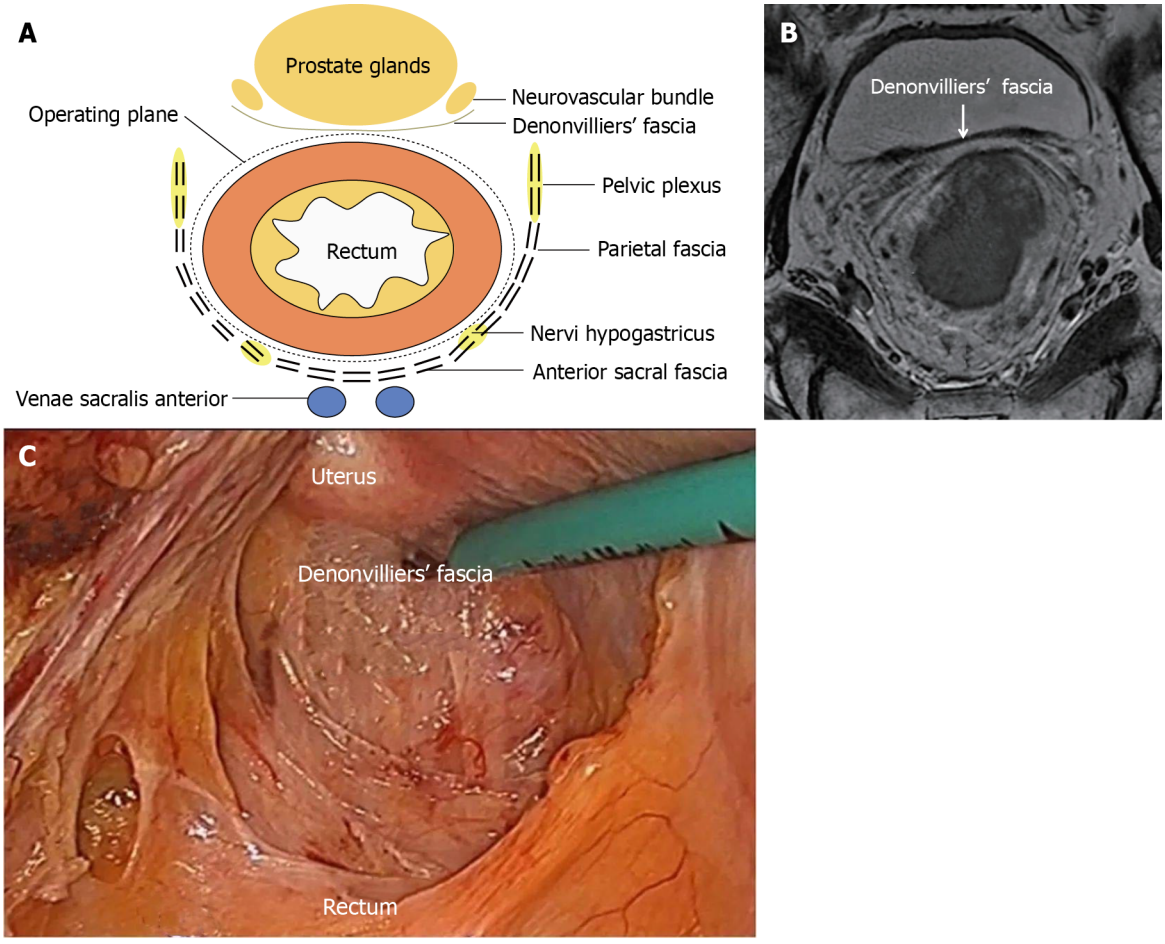

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Figure 1 The anatomical location of the Denonvilliers' fascia is shown in hand-drawn diagrams, images and surgical photographs. A: Diagram of the anatomical pattern of Denonvilliers' fascia (DVF); B: Magnetic resonance imaging-weighted image with DVF shown by arrow; C: Anatomical location and adjacency of DVF during laparoscopy.

manifesting as a variety of distinct configurations. Retrospective studies of laparoscopic surgery videos[14,15] demonstrated the obvious stratification of DVF (Figure 1C). A prior study[11] unraveled that the original structure of DVF was easily disrupted by intraoperative exploration. In addition, the loose porous tissue between the seminal vesicle and the DVF has been questioned as an artificial structure formed by the drawing tension generated by the surgical procedure[16]. As a result, further multi-center fundamental and clinical studies are warranted to identify whether the anatomical structure of DVF is stratified. Although the embryonic origin of DVF remains undetermined, the differences in the anatomical structure of DVF between males and females are recognized by most experts.

THE RELATIONSHIP BETWEEN DVF AND SURROUNDING TISSUES

The association of DVF with perirectal fascia and ligaments is barely reported in both domestic and foreign literature at present. Perirectal fascia and ligaments include the fascia propria of the rectum and the perirectal fat, nerves, and blood vessels, the presacral fascia and sacrococcygeal ligament behind the rectum, the DVF in front of the rectum, the rectal ligament on the side of the rectum, and some unclear fascia. Scholars at home and abroad have individually detailed the aforementioned structures in the past. Nevertheless, the relationship among these structures has been rarely described. This issue has been described by Zhang *et al*[17] in some detail: under peritoneal reflection, the anterior layer of DVF merges to both sides with the presacral fascia behind the rectum, forming the second cyclic structure of the rectum; the posterior layer of DVF directly merges with the rectum to generate the fascia propria of the rectum, constituting the first cyclic structure of the rectum; the pelvic parietal peritoneum and piriformis fascia form the third cyclic structure. The above discussion creatively provides a systematic overview of the overall association of perirectal mesentery. However, additional research on anatomy and histology is still currently necessary to further understand this topic.

DVF is a thin fascial layer that connects the rectum and its mesentery to the posterior wall of the seminal vesicle or prostate of males or the vagina of females, which originates upward from the peritoneal reflection to the prostate apex and the perineal central tendon, with some fibers forming the intramuscular fibers of the anal sphincter. DVF progressively thins to the sides and extends with the posterior pelvic fascia, separating the anterior rectal space into two

independent fascia spaces: the anterior rectal space and the posterior prostatic space[18]. The incision is conducted along the Denonvilliers line (the inverted thickening line of the pelvic floor peritoneum, that is, the projection of DVF on the peritoneal surface) from the lowest point of the pelvic floor peritoneum directly into the large anterior rectal space behind DVF. The Denonvilliers line extends laterally as a yellow-white borderline between the mesorectum and the pelvic fascia, which is a crucial anatomical landmark during TME[19]. During the surgery, DVF is closely connected with the seminal vesicle or prostate in males or the posterior wall of vagina in females, with numerous blood vessels in the space, which is difficult to separate during the surgery, particularly for patients who had underwent neoadjuvant chemotherapy.

Posteriorly to the rectum, the superior hypogastric plexus and hypogastric nerve of the PAN branch course between the inside (also named the anterior fascia of the hypogastric nerve) and outside of the pelvic fascia. In most individuals, the fascia propria of the rectum exhibits a complete columnar surface contour on the lateral side, from which the smooth interface may be separated. Some nerves and blood vessels course to the fascia propria of the rectum only at the "lateral ligament" position. The neurovascular bundle (NVB) in males is located below the seminal vesicle in the front and travels through DVF tissues *via* the anterolateral side, whose branches are distributed in the prostate and seminal vesicle[18]. Liang *et al*[20] investigated the association between autonomic nerves and the prerenal fascia-presacral fascia in 7 cadaveric specimens and 52 patients with rectal cancer who underwent laparoscopic excision and observed that the abdominal aortic plexus, superior hypogastric plexus, hypogastric nerve, and inferior hypogastric were located in the posterolateral side of the presacral fascia-presacral fascia. Histological examination unveiled that nerve fibers were located behind fascia, with some thinner fibers in the fascia. Hence, when the tissues behind the descending mesocolon and mesorectum are separated during the surgery for rectal cancer, the basic skills to protect nerves are as follows: maintaining the integrity of the prerenal fascia-presacral fascia (Gerota fascia) and dissection in the fusion space between it and mesentery. Accordingly, the maintenance of the fascia integrity is the anatomical basis and fundamental strategy for protecting the autonomic nerve in surgery for rectal cancer surgery.

APPLICATION OF DVF IN SURGERY FOR RECTAL CANCER

The anterior separation of DVF needs to be performed during the dissection of the anterior rectal space in laparoscopic surgery for rectal cancer, which is in accordance with the surgical protocol for rectal cancer optimized by Heald *et al*[21] and fulfills the standards of TME. Moszkowicz *et al*[22] proposed that anus-preserving surgery for rectal cancer primarily aims to improve the quality of life of patients and diminish the risk of local tumor recurrence, with the second goal of minimizing nerve damage and preserving organ function. As a result, DVF should not be separated in patients with tumor infiltration in the mesentery if the bottom of the seminal vesicle is not completely exposed but should be separated in front of the DVF. For patients with serious tumor infiltration, a portion of the seminal vesicle (male) or posterior vaginal wall (female) should be excised. Overall, the scope of alternative resection should be selected based on the extent of infiltration and specific location for patients with tumor-infiltrating anterior mesorectum. The resection scope is 1 cm above the peritoneal reflection and down to 0.5 cm from the seminal vesicle (male) or 5 cm below the peritoneal reflection (female) to ensure the integrity of the anterior mesentery. After excision, the anterior lobe of the DVF is shaped in an inverted "U" from both sides to the inner side of the NVB. When invaded by a tumor, the fascia should be separated downward in front of it. If the condition is severe, a portion of the seminal vesicle (male) or the posterior vaginal wall (female) should be excised. After the separation of the anterior and posterior rectal spaces, the lateral rectal space should be separated from the anterosuperior side toward the posteroinferior side, and the sacred plane should be found to ensure complete mesorectum wrapping, which can prevent damage to the pelvic plexus or the NVB. Specifically, the membrane bridge is first incised in an arc 1 cm above the peritoneal reflection and directly to the anterior space of the DVF. A free space is observed in front of the thick anterior lobe of DVF under the magnifying effect of laparoscopy or robot, which is similar to the structure of "hairs of the angel". Then, it is facile to enter the anterior space of DVF through this space. Because of the dense anterior lobe of DVF, it is simple to maintain the integrity of the anterior lobe and mesentery of DVF. Furthermore, the 1 cm of peritoneum on the peritoneal reflection can be used for intraoperative retraction, which facilitates the exposure of the loose connective tissues in the anterior rectal space and the expansion of the surgical operation space and causes difficulty in fogging the laparoscopic mirror. In this way, it is extremely beneficial for pelvic floor operation in male patients with contracted pelvis. The hypogastric nerve, hypogastric nerve plexus, and subabdominal fascia are all covered by the first layer of fascia (DVF) and the anterior abdominal fascia. Importantly, the anterolateral side of this layer is the most key anatomical site. NVB can be found but is not always visible after the anterior lobe of DVF is transected. This phenomenon can be explained by the fact that NVB cannot be found when the incision line is located before the stratification of the anterior lobe of DVF, since NVB is covered by the middle layer of the anterior lobe of DVF after stratification; however, NVB is obviously exposed and has a sponge-like structure when the incision line is located after the stratification of the anterior lobe of DVF because its surface is not covered by membranous tissues. Accordingly, the NVB is not ensured to be undamaged if the surgical plane is selected between the first and second layers at the semi-prostate angle level. The third layer originates from the posterior bladder neck and then courses upward to attach to the second layer while crossing the upper surface of the bladder to form a common layer. This layer is separated by loose connective tissues from the lower bladder fascia and the upper peritoneum. Meanwhile, it receives some NVB branches from both sides, similar to the second layer. Some researchers consider that this layer is the third layer of DVF, not the bladder-related fascia, because it is completely isolated from the bladder that is covered by the adventitia. Additionally, this layer extends upward and connects to the second layer, which is considered one of the mentioned DVF complexes. Furthermore, at 2 and 10 o'clock directions, NVB specifies the location of the second and third layers with a highly complicated neural network, where there was no evident dissociative innervation,

thus enabling us to believe that this layer is one of the multi-layer DVF complexes. According to Lu *et al*[23], the surgery should be performed with an approach above the peritoneal reflection. Next, separation should be conducted in close proximity to the DVF during the surgery. The DVF should be severed near the bottom of the seminal vesicle for male patients and 5 cm below the peritoneal reflection for female patients. The separation is subsequently continued by entering the space between the fascia propria of the rectum and the DVF. This surgery not only maintains the integrity of the local fascia propria of the rectum during excision, but also protects the autonomic nerve and prevents seminal vesicle damage. This surgery method should be widely used in clinical practice since it not only is beneficial for reducing mesangial injury but also elevates the complete rate of anterior mesangial resection. Meanwhile, it is useful for preventing or avoiding bleeding and peripheral nerve injury during pelvic free surgery to understand the interaction between DVF and surrounding tissues. Finding and dissecting DVF and elaborating on the surgical approach and technology for the anterior rectal space provide essential surgical experience in addressing this challenging and critical issue.

Dissection anterior to the DVF is not recommended when the tumor does not invade the fascia propria of the rectum or DVF[24], since the NVB coursing from the tail of the seminal vesicle to the bladder, seminal vesicle, prostate, and urethra in males is easily damaged during this surgery, therefore resulting in the occurrence of postoperative urogenital dysfunction. DVF should be removed when the tumor is located in the anterior wall of the rectum or invades the fascia propria or DVF, the local tumor is at the late stage, or edema and fibrosis changes occur in the focus due to preoperative neoadjuvant chemoradiotherapy. A prior study[25] demonstrated that DVF was directly connected to the fascia propria anterior to the rectum, contributing to difficulty in its dissection. Hence, the anatomy should be conducted in front of the DVF during the surgery, and attention should be paid to NVB protection when it reaches the anterior side of the mesorectum. The author recommends that the region in front of the DVF and spaces of the seminal vesicle, the vas deferens, and the fascia propria of prostate should be dissected for males with tumors in the anterior rectal wall or a tumor at > T2 stage who receive preoperative neoadjuvant radiotherapy and chemotherapy. For female patients, the region in the front of the DVF and the space of the fascia of the posterior vaginal wall should be dissected. When it reaches the anterior side of the rectum, the DVF can be cut off and dissected along the fascia propria surface outside the mesentery of the anterior side of the rectum, preserving as much as possible the integrity and continuity of the anatomical plane and preventing fascia plane distortion due to insufficient or excessive traction tension.

CONTROVERSY ON DVF PRESERVATION

Patients are pursuing radical surgery with increasing concern for postoperative prognosis and quality of life as their requirements for postoperative quality of life increase[26]. Previous research[27] revealed that after laparoscopic radical resection for rectal cancer, approximately 70% of patients might develop dysuria, approximately 45%-55% experienced erectile dysfunction, and 40% suffered from ejaculatory dysfunction and that the above adverse outcomes were related to the damage to the rectum, abdominal cavity, and pelvic cavity during the surgery. It has been reported that intraoperative fascia preservation could substantially improve the quality of life of patients after surgery. DVF is a critical pelvic floor fascia that is positioned anterior to the rectum. DVF may be regarded as a part of the mesorectum in the classic radical resection for rectal cancer and must be entirely excised to assure the radical resection of tumors. Meanwhile, DVF has a complex anatomical structure, whose intraoperative preservation elevates the complexity of the surgery. Hence, DVF preservation during radical resection for rectal cancer is now disputed in the clinic. Abroad, some researchers[28] discovered that the excised DVF tissues had many nerve fibers, including NOS-positive nerve fibers associated with erectile function, which were distributed more broadly and not limited to the previously described NVB region. Therefore, even in the "inverted U-shaped" resection of DVF, NVB preservation is futile, as the efferent branch of inferior hypogastric plexus may be injured, then compromising postoperative urine and sexual functions, particularly erectile function[29]. A prior study[30] utilized intraoperative nerve stimulation to identify PANs and unraveled that after DVF excision, nerve stimulation cannot elicit active bladder contraction, objectively validating the intimate association between DVF and PAN. Li *et al*[31] conducted a retrospective comparison study on the issue of DVF preservation or not in laparoscopic radical resection for low rectal cancer. The use of DVF in laparoscopic radical resection of low rectal cancer not only minimizes the amount of intraoperative bleeding, but also promotes the postoperative recovery of urine and sexual functions in patients and improves their quality of life. In addition, the research by Fang *et al*[32] exhibited that compared to standardized TME surgery, iTME can successfully minimize the incidence of postoperative urinary and sexual disorders in male patients with low rectal cancer without affecting the short-term radical outcome.

CONCLUSION

Conclusively, DVF, an influential separating and barrier structure surrounding the rectum, is of paramount significance to the quality of life and the protection of PANs following surgery for rectal cancer. Previously, the PUF-01 multicenter prospective study was performed on the impact of partial and complete preservation of DVF on the postoperative sexual and urinary function of patients with rectal cancer[24], which unraveled that the complete preservation of DVF exerted a protective effect on postoperative urogenital function as compared to the partial resection of DVF during laparoscopic TME. Nevertheless, long-term follow-up data are lacking for postoperative urogenital function in this group of patients both at home and abroad, precluding a more precise and detailed dynamic evaluation. In China, a tentative agreement has been achieved on the surgical treatment of DVF. According to the China Expert Consensus of iTME[4], iTME surgery can deliver short-term overall survival rates comparable to those of traditional TME surgery for male patients with

middle and low rectal cancer at preoperative clinical stages of T1-4 (T1-2 for anterior wall tumor), N0-2, and M0 (7th editions of AJCC staging). According to this study, iTME can lower the incidence of postoperative micturition and sexual dysfunction in patients with rectum cancer at T1-4, N0-2, and M0 stages. However, existing evidence only supports individuals with tumors in the rectal anterior wall at T1-2, N0-2, and M0 stages. More importantly, PAN protection in radical resection for rectal cancer is a multi-step process that cannot be achieved by focusing only on a few important elements. As a result, further analysis of the entire pelvic structure is warranted to further optimize the membrane-guided PAN protection technology and maximize the benefits to patients from therapy.

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