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Effect of preservation of Denonvilliers' fascia during laparoscopic resection for mid-low rectal cancer on protection of male urinary and sexual functions

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Abstract

The aim of this study was to investigate the effect of preservation of Denonvilliers' fascia (DF) during laparoscopic resection for mid-low rectal cancer on protection of male urogenital function. Whether preservation of DF during TME is effective for protection of urogenital function is largely elusive.

Seventy-four cases of male mid-low rectal cancer were included. Radical laparoscopic proctectomy was performed, containing 38 cases of preservation of DF (P-group) and 36 cases of resection of DF (R-group) intraoperatively. Intraoperative electrical nerve stimulation (INS) on pelvic autonomic nerve was performed and intravesical pressure was measured manometrically. Urinary function was evaluated by residual urine volume (RUV), International Prostatic Symptom Score (IPSS), and quality of life (QoL). Sexual function was evaluated using the International Index of Erectile Function (IIEF) scale and ejaculation function classification.

Compared with performing INS on the surfaces of prostate and seminal vesicles in the R-group, INS on DF in the P-group exhibited higher increasing intravesical pressure (7.3 ± 1.5 vs 5.9 ± 2.4 cmH_2O, $P = 0.008$). In addtion, the P-group exhibited lower RUV (34.3 ± 27.2 vs 57.1 ± 50.7 mL, $P = 0.020$), lower IPSS and QoL scores (7 days: 6.1 ± 2.4 vs 9.5 ± 5.9, $P = 0.002$ and 2.2 ± 1.1 vs 2.9 ± 1.1, $P = 0.005$; 1 month: 5.1 ± 2.4 vs 6.6 ± 2.2, $P = 0.006$ and 1.6 ± 0.7 vs 2.1 ± 0.6, $P = 0.003$, respectively), higher IIEF score (3 months: 10.7 ± 2.1 vs 8.9 ± 2.0, $P = 0.000$; 6 months: 14.8 ± 2.2 vs 12.9 ± 2.2, $P = 0.001$) and lower incidence of ejaculation dysfunction (3 months: 28.9% vs 52.8%, $P = 0.037$; 6 months: 18.4% vs 44.4%, $P = 0.016$) postoperatively.

Preservation of DF during laparoscopic resection for selective male mid-low rectal cancer is effective for protection of urogenital function.

Abbreviations: DF = Denonvilliers' fascia, IFSF = Index of Female Sexual Function, IIEF = International Index of Erectile Function, INS = intraoperative electrical nerve stimulation, IPSS = International Prostatic Symptom Score, LAPE = laparoscopic abdominoperineal excision, LLAR = laparoscopic low anterior resection, PAN = pelvic autonomic nerve, PANP = preservation of pelvic autonomic nerve, QoL = quality of life, RUV = residual urine volume, TME = total mesorectal excision.

Keywords: Denonvilliers' fascia, rectal cancer, sexual dysfunction, total mesorectal excision, urinary dysfunction

1. Introduction

Postoperative urinary and sexual dysfunctions are frequent complications of rectal resection, even combined with preservation of pelvic autonomic nerve (PANP).[1–4] Heald at al[5] suggest that Denonvilliers' fascia (DF) should be resected during total mesorectal excision (TME). However, it is proved that the bilateral neurovascular bundles and their communicating branches walk closely in front of DF. Thus, resection of DF

Editor: Pedro Silva Vaz.

Authors' contributions: H-BW and J-FF designed the study; H-BW, Z-HZ, J-LH, and YH performed surgery; J-FF and P-RL contributed in acquisition of data; T-FC analyzed the data; J-FF and BW wrote the article.

Category for article: Colorectal/Anal neoplasia

H_BW and J-FF contributed equally to this work.

Funding: The study was supported by grants from the Industry-Academia-Research Major Project of Guangzhou Science and Technology Program (No.2060404), Science and Technology Planning Project of Guangdong Province, China (No.2014A020211009), Natural Science Foundation of Guangdong Province, China (No.2015A030313063) and Medical Scientific Research Foundation of Guangdong Province, China (No.A2015318).

The authors report no conflicts of interest.

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Medicine (2016) 95:24(e3925)

Received: 14 December 2015 / Received in final form: 25 April 2016 / Accepted: 14 May 2016

Published online 1 May 2016

http://dx.doi.org/10.1097/MD.0000000000003925

may lead to damage of nerves and urogenital dysfunction. In addition, recent studies reveal that DF is not part of the proper fascia of rectum and should not be resected.[6,7] In brief, whether preservation of DF during TME is effective for protection of urogenital function is still largely elusive. It was the aim of this study to assess the effect of preservation of DF during laparoscopic resection for mid-low rectal cancer on protection of male urinary and sexual functions.

2. Methods

This study was approved by the institutional review board of the Third Affiliated Hospital of Sun Yat-sen University.

2.1. Patients

Between October 2013 and October 2014, 38 consecutive male cases of mid-low rectal cancer undergoing radical laparoscopic proctectomy in the Third Affiliated Hospital of Sun Yat-sen University were included. Diagnosis of rectal cancer was decided by pelvic magnetic resonance imaging, chest x-ray, abdomen CT scan, coloscopy, and biopsy preoperatively. DF was well-preserved during surgery in these patients (P-group). Inclusion criteria were as follows: age between 18 years and 70 years; tumor location $\leq$12 cm from the anal verge; pathologic stage (T_{1-2}, N_0, M_0, AJCC-7th TNM stage); American Society of Anesthesiology function: class I to class III; R_0 resection. Exclusion criteria were as follows: emergency surgery; preoperative urinary or sexual dysfunction; preoperative major pelvic surgery; local excision. The study was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University. Written informed consent was obtained from all patients.

As a control, data of male patients undergoing traditional laparoscopic proctectomy (DF was resected, R-group) between October 2012 and September 2013 were reviewed. Totally, 36 cases met the criteria and were included. The related data were collected and analyzed retrospectively. Assessment of urinary and sexual functions was applied equally in the P-group and R-group.

2.2. Surgery

According to tumor location, either laparoscopic low anterior resection (LLAR) or laparoscopic abdominoperineal excision (LAPE) was performed. TME was carried out by the same team of surgeons with a standardized procedure.

The operation was performed under general anesthesia and the patients were placed in lithotomy position. For the R-group, sharp dissection was performed in front of DF. A U-shaped cut was applied to resect subtotal DF, whereas the lateral edges of DF were identified and preserved. However, in the P-group, transverse dissection of peritoneum was performed 1 cm anterior superior to peritoneal reflection (Fig. 1). Then as we found in the cadaver study (Fig. 2), some loose reticulate structures between DF and proper fascia of rectum would present (Fig. 3), and DF was well-identified as a glistening white surface of the anterior aspect during laparoscopic surgery. The surgical plane behind DF (retrofascial space) was carefully sharp dissected downward to preserve intact DF. Unlike the R-group, the prostate and bilateral seminal vesicles were covered by DF and cannot be observed in the P-group (Fig. 4).

Intraoperative electrical nerve stimulation (INS) was performed during TME as previously described.[8] The stimulating

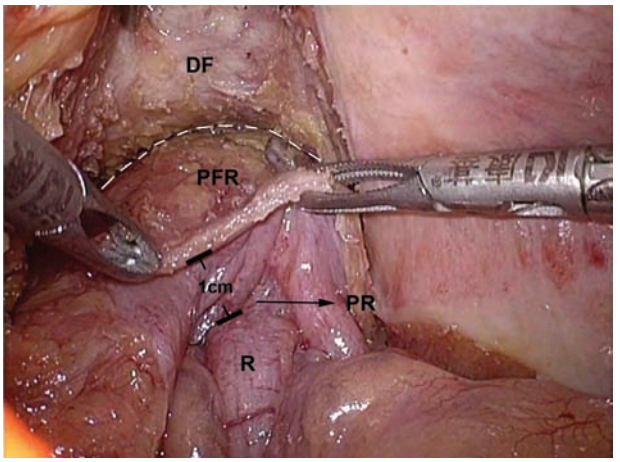

Figure 1. Surgical plane behind Denonvilliers' fascia (DF). In the P-group, dissection of peritoneum is performed 1 cm anterior superior to peritoneal reflection (PR), then the surgical plane (white dotted line) is dissected between DF and proper fascia of rectum (PFR).

electrode was placed into the abdominal cavity through the 12 mm trocar. Monopolar stimulation on the bilateral pelvic splanchnic nerves and DF (or the surfaces of prostate and seminal vesicles in the R-group) was performed, using constant voltage (Stimuplex HNS 12, Braun, Germany) (Fig. 5). The currents applied ranged from 3 to 5 mA, the frequency was 2 Hz, and stimulation lasted 5 to 20 seconds. The urinary bladder was filled with 200 mL of Ringer solution before INS. The intravesical pressure was measured manometrically using a transurethral bladder catheter.

2.3. Urinary function

Urinary function was evaluated by the following methods: residual urine volume (RUV, tested by ultrasonic examination; values $\geq$100 mL were diagnosed as pathological urination disorder); international prostatic symptom score (IPSS, containing 7 items of incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia, rated on a scale

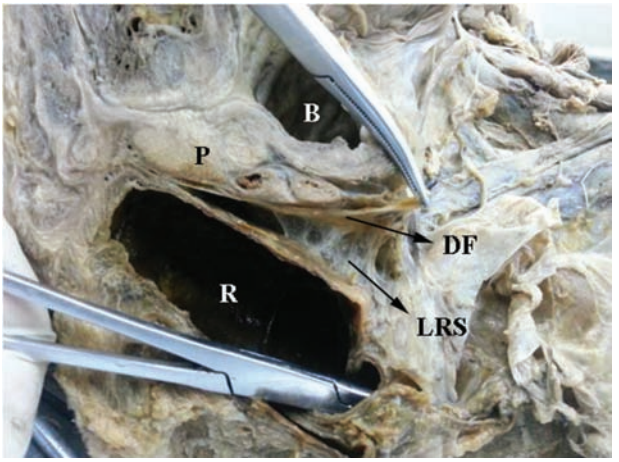

Figure 2. Cadaver study on Denonvilliers' fascia (DF). DF is located between the prostate (P) and rectum (R). DF is more closely adherent to the prostate than to the rectum. There are some loose reticulate structures (LRS) between DF and rectum. B, bladder.

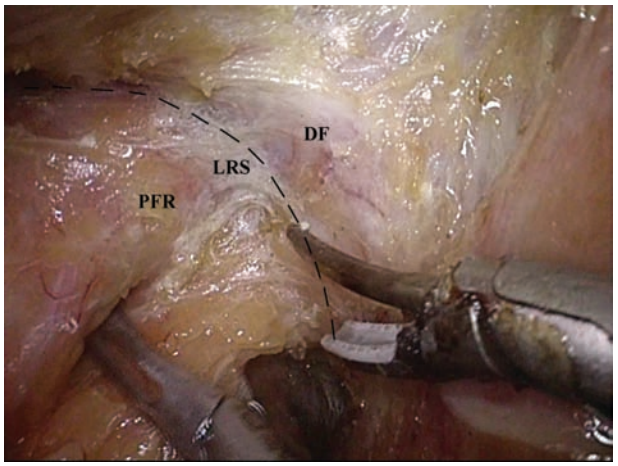

Figure 3. Anatomy of Denonvilliers' fascia (DF) during surgery. There are some loose reticulate structures (LRSs) between DF and proper fascia of rectum (PFR). The black dotted line presents the dissection plane.

from 0 "not at all" to 5 "almost always"). Deterioration of urinary function was categorized into 3 groups: mildly symptomatic (IPSS 0–7 points), moderately symptomatic (IPSS 8–19 points), and severely symptomatic (IPSS 20–35 points); the quality of life (QoL) for urinary function, graded on a scale from 0 "very satisfied" to 6 "very upset."

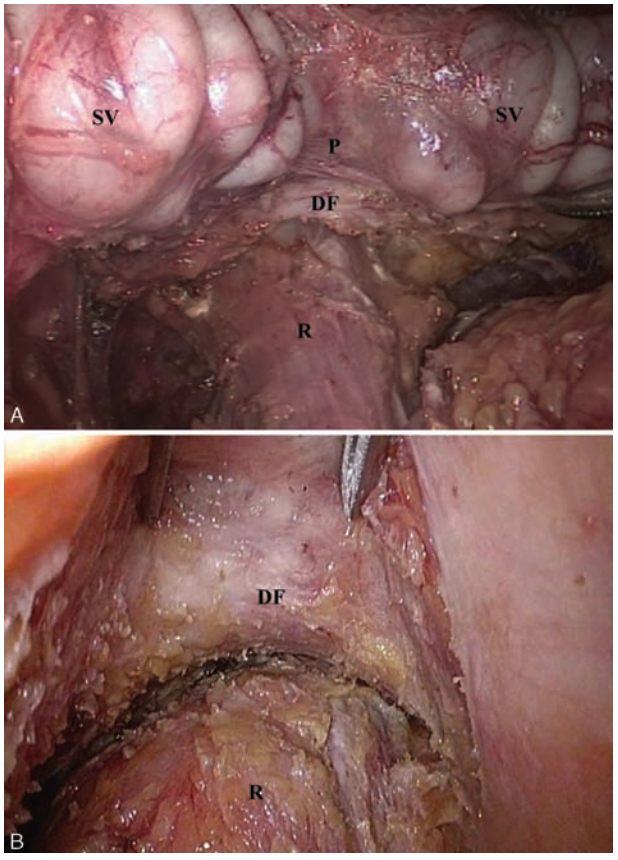

Figure 4. Comparison of the 2 surgical planes during TME surgery. (A) Sharp dissection is performed in front of Denonvilliers' fascia (DF). Subtotal DF is resected, and the prostate (P) and bilateral seminal vesicles (SV) are visible. (B) Sharp dissection is performed behind DF. DF is well-preserved; the prostate and bilateral seminal vesicles are covered by DF and cannot be observed.

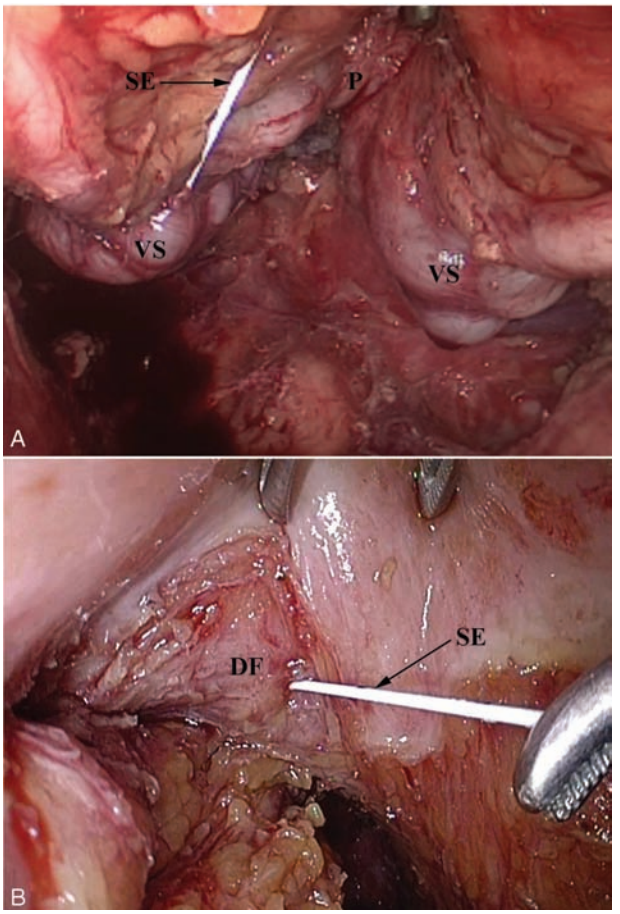

Figure 5. Application of intraoperative electrical nerve stimulation (INS). The stimulating electrode (SE) is placed into the abdominal cavity through the 12 mm trocar. Monopolar stimulation is performed using constant voltage (Stimuplex HNS 12, Braun, Germany). Application of the currents ranges from 3 to 5 mA, frequencies 2 Hz, and lasted 5 to 20 seconds. (A) In the R-group, INS is performed on the surfaces of prostate (P) and bilateral seminal vesicles (SV). (B) In the P-group, INS is performed on Denonvilliers' fascia.

2.4. Sexual function

The 5-item version of the International Index of Erectile Function (IIEF) scale, which comprised 4 questions about erectile function and 1 question about intercourse satisfaction, was used for evaluating male erectile function. The IIEF total score ranged from 1 to 25, with a lower score indicating more severe erectile dysfunction. Ejaculation function classification was divided into 3 grades: I (normal ejaculation), II, and III (retrograde ejaculation or ejaculation disorder).

2.5. Statistical analysis

Statistical analysis was performed with SPSS (version 15.0, Chicago, IL). The patients' clinical and demographic characteristics were compared with a Student t test for continuous variables and a χ^2 test for categorical variables. The intravesical pressure, RUV, IPSS, QoL, and IIEF scores were compared between the 2 groups using a Student t test, whereas the

ejaculation function was compared using a χ^2 test. $P<0.05$ was considered statistically significant.

3. Results

3.1. General data

All cases of surgery were performed uneventfully, with no conversion to laparotomy. There were no significant differences in age, BMI, tumor location and size, operation type, operative time, and intraoperative blood loss between the P-group and R-group (Table 1). There was no case of positive circumferential resection margin. All patients complied with regular follow-up, and no local recurrence occurred in 1-year follow-up.

3.2. Urinary function

INS was first performed on the bilateral pelvic splanchnic nerves intraoperatively, and there was no difference in the increasing intravesical pressure between the P-group and R-group. However, INS on DF in the P-group revealed higher increasing intravesical pressure than on the surfaces of prostate and seminal vesicles in the R-group (7.3±1.5 vs 5.9±2.4 cmH_2O, $P=0.008$) (Table 2).

The urinary function was further evaluated by RUV, IPSS, and QoL score. As shown in Table 3, there were no significant differences in preoperative RUV, IPSS, and QoL score between the P-group and R-group. Compared with the R-group, the P-group revealed less deterioration of RUV at 7 days postoperatively (34.3±27.2 vs 57.1±50.7 mL, $P=0.020$). The incidence of urination disorder was lower in the P-group than in the R-group (5.3% vs 22.2%, $P=0.044$).

Both IPSS and QoL score were normal preoperatively, increased at 7 days, and decreased gradually at 1 month and 6 months postoperatively. Compared with the R-group, the P-group presented with lower IPSS and QoL score at 7 days (6.1±2.4 vs 9.5±5.9, $P=0.002$ and 2.2±1.1 vs 2.9±1.1, $P=0.005$) and 1 month postoperatively (5.1±2.4 vs 6.6±2.2, $P=0.006$ and 1.6±0.7 vs 2.1±0.6, $P=0.003$), whereas there was no difference at 6 months postoperatively.

Table 1

Comparisons of patient demographic, clinical and pathologic characteristics, and surgical data between the P-group and R-group.

Variable	P-group (n=38)	R-group (n=36)	P
Age, y	55.6±9.5	55.7±6.8	0.930
BMI, kg/m^2	21.9±1.8	22.5±1.6	0.146
Tumor location (distance)			0.972
Intraperitoneal (8–12 cm)	26	25	
Extraperitoneal (4–8 cm)	6	5	
Extraperitoneal (<4 cm)	6	6	
Tumor location			0.725
Anterior	7	6	
Posterior	10	7	
Lateral	21	23	
Tumor size, cm^2	2.9±1.0	3.0±1.0	0.620
Type of operation			
LLAR	32	30	0.919
LAPE	6	6	
T stage			0.670
I	2	3	
II	36	33	
Operative time, min	130.3±21.1	130.8±21.9	0.910
Blood loss, mL	30.0±13.8	27.1±10.0	0.303

BMI = body mass index, LAPE = laparoscopic abdominoperineal excision, LLAR = laparoscopic low anterior resection.

Table 2

Comparison of increasing intravesical pressure intraoperatively between the P-group and R-group.

	Increasing intravesical pressure, cmH_2O		
Position of INS	P-group (n=38)	R-group (n=36)	P
Left pelvic splanchnic nerve	5.1±1.6	4.9±2.3	0.606
Right pelvic splanchnic nerve	5.2±1.2	4.9±2.2	0.522
Denonvilliers' fascia	7.3±1.5		0.008
Surfaces of prostate and seminal vesicles		5.9±2.4	

INS = intraoperative electrical nerve stimulation.

3.3. Sexual function

The erectile function was evaluated by IIEF, as shown in Table 4. There was no difference in preoperative IIEF score between the P-group and R-group. The IIEF score was normal preoperatively, decreased at 3 months, and was ameliorated at 6 months postoperatively. Compared with the R-group, the P-group showed higher IIEF score at either 3 months (10.7±2.1 vs 8.9±2.0, $P=0.000$) or 6 months (14.8±2.2 vs 12.9±2.2, $P=0.001$) postoperatively.

In addition, as shown in Table 4, the ejaculation function was evaluated by ejaculation function classification. Similarly with the IIEF score, the ratio of normal ejaculation function decreased at 3 months, whereas it was ameliorated at 6 months postoperatively. Compared with the R-group, the P-group revealed higher ratios of normal ejaculation function at both 3 months (28.9% vs 52.8%, $P=0.037$) and 6 months (18.4% vs 44.4%, $P=0.016$) postoperatively.

4. Discussion

TME has been proved to highly decrease the incidence of local recurrence and increase the long-term survival rate.[9] However, the incidence of urogenital dysfunction is extremely high if the pelvic autonomic nerve (PAN) is not well-protected during TME. PANP in rectal cancer surgery is widely performed to maintain

Table 3

Comparison of urinary function between the P-group and R-group.

Variable	P-group (n=38)	R-group (n=36)	P
RUV			
Preoperative, mL	12.0±4.1	11.9±3.5	0.876
7 days postoperative, mL	34.3±27.2	57.1±50.7	0.020
Urination disorder	2 (5.3%)	8 (22.2%)	0.044
IPSS			
Preoperative	2.5±1.5	2.6±1.1	0.850
7 days postoperative	6.1±2.4	9.5±5.9	0.002
1 month postoperative	5.1±2.4	6.6±2.2	0.006
6 months postoperative	4.2±1.9	4.7±1.5	0.210
QoL score			
Preoperative	1.1±0.4	1.1±0.5	0.953
7 days postoperative	2.2±1.1	2.9±1.1	0.005
1 month postoperative	1.6±0.7	2.1±0.6	0.003
6 months postoperative	1.4±0.6	1.5±0.6	0.855

IPSS = International prostatic symptom score, QoL = quality of life, RUV = residual urine volume.

Table 4

Comparison of male sexual function between the P-group and R-group.

Variable	P-group (n = 38)	R-group (n = 36)	P
IIEF score			
Preoperative	19.9 ± 1.3	19.6 ± 1.6	0.254
3 months postoperative	10.7 ± 2.1	8.9 ± 2.0	0.000
6 months postoperative	14.8 ± 2.2	12.9 ± 2.2	0.001
Ejaculation function classification			
3 months postoperative			0.037
Grade I	27 (71.1%)	17 (47.2%)	
Grade II + III	11 (28.9%)	19 (52.8%)	
6 months postoperative			0.016
Grade I	31 (81.6%)	20 (55.6%)	
Grade II + III	7 (18.4%)	16 (44.4%)	

IIEF = the International Index of Erectile Function.

urogenital function. Even though, the incidence of urogenital dysfunction still reaches 8.0% to 42.9% after PANP surgery.[1–4] Thus, additional methods should be quested to protect the urogenital function.

DF was first described in 1838.[10] This structure is present between the prostate or vagina and the mesorectum, and it is considered as a tension-induced structure or a peritoneal fusion fascia.[6,11,12] Some experts consider that DF forms the surface of the anterior aspect of the mesorectum and the optimal TME for rectal cancer is by dissection in front of DF.[5,13] However, some studies reveal that DF does not belong to proper fascia of rectum.[6,7,14] There were bilateral neurovascular bundles and their communicating branches crossing within DF closely.[15] Resection of DF may lead to damage of neurovascular bundles and urogenital dysfunction. Thus, Lindsey et al[16] recommend that DF lies anterior to the rectal dissection plane in TME and should be preserved. In brief, selection of surgical plane in TME and role of DF still remain controversial.

In this study, we first performed a clinical study on effect of preservation of DF during laparoscopic resection for mid-low rectal cancer on protection of male urogenital function. Similarly with the previous studies, RUV, IPSS, and QoL score increased, whereas IIEF score decreased postoperatively, demonstrating that RUV, IPSS, QoL, and IIEF score are objective methods for evaluating male urogenital function.[17,18] Our results revealed that compared with traditional dissection in front of DF (R-group), preservation of DF showed less deteriorations on postoperative RUV, IPSS, QoL, IIEF score, and ejaculation function. The results suggested that preservation of DF during rectal cancer resection was effective in urogenital function protection.

In addition, we applied INS to monitor the effect of nerve preservation intraoperatively in this study. Lue et al[19] first reported the successful application of INS to monitor function of cavernous nerves in prostatectomy. After that, INS has been increasingly applied in pelvic surgeries containing TME surgery for rectal cancer, and it has been proved to be effective and sensitive in identification and preservation of the PAN.[20,21,22] In this study, INS on DF revealed more obvious increasing intravesical pressure compared to performance of INS on the surfaces of prostate and seminal vesicles. The real-time monitoring result suggested that resection of DF might cause damage of PAN and thus lead to urogenital dysfunction.

Heald et al considers that the surgical plane in front of DF is natural and bloodless, although there is usually no surgical plane behind DF as it is intimately adherent to the anterior mesorectal fat.[5,23] To avert damage to the neurovascular bundles, the lateral edges of DF should be identified and preserved by a U-shaped cut. However, in accordance with some experts,[16,24,25] we believe that DF is more closely adherent to the prostate than to the rectum. In our experience, dissection of peritoneum should be performed 1 cm anterior superior to peritoneal reflection. After that, some loose reticulate structures between DF and proper fascia of rectum will present, that is, optimal surgical plane behind DF. DF is well identified as a glistening white surface of the anterior aspect during laparoscopic surgery. In this plane, the neurovascular bundles will be well-protected, accompanied with better protection of urinary and sexual functions.

Another controversy on surgical plane in TME is about the oncologic outcome. We included patients of TNM stage I rectal cancer in this study, and no positive circumferential resection margin or local recurrence was found in 1-year follow-up in the 2 groups. It was reported that although there were no major differences in outcome for most patients, those with TNM stage III disease had a local recurrence of 21% in one series (dissection behind DF), compared with 6.5% when the plane of dissection was in front.[26,27] Thus, whether dissection behind DF is suitable for patients with advanced rectal cancer still remains to be confirmed.

5. Limitations

To our knowledge, it is the first clinical study on evaluating the effect of preservation of DF during laparoscopic resection for mid-low rectal cancer on protection of male urinary and sexual functions. However, some limitations should be acknowledged in this study. First, a retrospective study may lead to bias. To control bias, we set strict inclusion and exclusion criteria in this study. Data of the 2 groups, containing patient demographic, clinical and pathologic characteristics, and surgical data, were equal in this study. To confirm our conclusion, we have designed a multiple-center RCT study (ClinicalTrial.gov ID: NCT02435758) and now the RCT study is in progress. Second, oncologic outcome of patients in this study was based on 1-year follow-up. We still need continue follow-up of these patients to get 3- and 5-year oncologic outcomes. Third, female patients were not included in this study because assessment of sexual function is more difficult for female than male. Some questionnaires, such as the Index of Female Sexual Function (IFSF), have been applied to assess female sexual function. However, most of female patients are not willing and feel embarrassed to do questionnaire survey on sexual function, especially in China. In addition, female sexual function is more easily influenced by other factors, such as psychological and social factors. Maybe similar research for female population can be designed in further prospective study. Last, patients of advanced rectal cancer ($T_{3–4}N_{1–2}$) were not included in this study. Thus, whether preservation of DF will lead to local recurrence of advanced rectal cancer is not clear. A prospective study may be designed to discuss the difference of oncologic outcome between the P-group and R-group for advanced rectal cancer.

6. Conclusion

DF has closed relationship with neurovascular bundles. Preservation of DF during laparoscopic resection for selective male mid-low rectal cancer ($T_{1–2}$, N_0, M_0) is effective for preservation of pelvic autonomic nerve, as well as protection of male urinary and

sexual functions. The short-term oncologic outcome is comparable. However, whether dissection behind DF is suitable for patients with advanced rectal cancer still remains to be confirmed.

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