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ORIGINAL ARTICLE

Functional outcome and quality of life after transanal minimal invasive pouch surgery

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Abstract

Purpose To investigate functional outcomes and quality of life (QoL) after restorative proctocolectomy (RPC) using transanal minimal invasive surgery (TAMIS).

Method The study consists of two sub-studies. A cohort study comprised 98 consecutive patients, who underwent TAMIS RPC. These patients were the first at our department to undergo TAMIS RPC. We collected information about surgery, complications, postoperative morbidity and mortality ≤ 30 days, and pouch problems. Patients were also invited to participate in a case–control study in which the patients would respond to three different questionnaires, the Inflammatory Bowel Disease Questionnaire (IBDQ), the Short Form-36 General Health Questionnaire (SF-36), and questions from the Pouch Dysfunction Score. We compared the responding TAMIS RPC patients to a Danish national cohort (0–10 years from RPC, $n = 514$) of patients having RPC between 1980 and 2010. We compared functional outcomes and QoL.

Results Four (4%) of the TAMIS patients had an anastomotic leak; none of these required re-operation with removal of the pouch. Anastomotic leak was treated with antibiotics and drain. Out of the four leaks, only one ended up with a permanent stoma; all others had their stoma reversed successfully. The TAMIS patients had the same number of bowel movements as the patients in the Danish national cohort study. The same was seen with regard to incontinence. We had no conversions in our series of TAMIS procedures.

Conclusion The TAMIS technique shows acceptable outcomes, both in regard to postoperative complications and also functional outcome and QoL.

Keywords Transanal minimal invasive surgery · Quality of life · Functional outcome

Introduction

Since the late 1970s, restorative proctocolectomy (RPC) with ileal-pouch anal anastomosis (IPAA) has been the procedure of choice for patients with medical refractory ulcerative colitis [1]. Different configurations of the pouch have since been described, but today the most commonly used design is a J-configuration [2]. In the initial IPAA procedures, the ileal pouch-anal anastomosis was hand sewn, but later the anastomosis was double-stapled which improved functional outcomes [3, 4]. As with many other surgical procedures, pouch surgery has changed from open to minimal invasive procedures either laparoscopic or robot-assisted [5]. Short-term results are better after a minimal invasive procedure [6], whereas long-term function and quality of life seem identical after the two approaches [7, 8].

In 2013, Brandsborg et al. described pouch function and quality of life (QoL) in more than 1000 Danish pouch patients operated with open technique [9]. The study cohort included all patients operated in Denmark from 1981 until 2010. Pouch function was found to be relatively stable over time and with a high degree of satisfaction in most patients. Lovegrove et al. also found that the main determinants for QoL was stool frequency, urgency, and incontinence [10].

Transanal minimal invasive surgery (TAMIS) is a newer procedure in pouch surgery [11]. A laparoscopic single port is introduced into the anal canal, thus temporarily expanding the anal canal. With the open and laparoscopic methods, the rectum is dissected from above, and the lowermost part

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of the rectum is closed by cross-stapling. Accordingly, the pouch anal anastomosis is double-stapled. With TAMIS, the rectum is transected transanally just above the pelvic floor, and the lower part of the rectum is dissected from below [11]. The top of the anal canal is closed with a purse-string suture enabling double purse-string, single stapled pouch-anal anastomosis. Whether these differences have impact on functional outcome and QoL needs to be investigated with the main concern being that stretching the anal sphincters intraoperatively could lead to later functional impairment. At present, data on functional outcomes and QoL after TAMIS are sparse. The aim of this study was therefore to compare outcomes in patients who underwent TAMIS to the cohort from the study by Brandsborg et al. [9] using identical questionnaires.

Materials and methods

The present study consists of two sub-studies. The first is a cohort study comprising 98 consecutive patients, who underwent TAMIS IPAA; almost all had a colectomy prior to the procedure.

All patients had surgery at Department of Surgery, Aarhus University Hospital, from April 2015 to June 2019. These patients were the first at our department to undergo TAMIS IPAA.

Clinical data

Through their patient records, we identified information about surgery, complications, postoperative morbidity and mortality ≤ 30 days, and pouch problems. We considered visualized anastomotic leak and pelvic collection as two different complications.

Functional assessment and QoL

The observation time for functional assessment and QoL was from stoma closure. The TAMIS patients were invited to participate in a case–control study in which the patients would respond to three different questionnaires. We compared the responding TAMIS IPAA patients (cases) to a Danish national cohort (0–10 years from IPAA, $n = 514$) of patients previously investigated, having had IPAA between 2000 and 2010 (controls) [9]. In the Danish cohort study (the Brandsborg cohort), three different groups (0–10 years, 11–20 years, and 21–30 years after IPAA) were studied, but we only included the group investigated 0–10 years after IPAA.

Please note that patients in the control cohort did not receive questionnaires again. Instead, we used information gathered in 2010, to achieve the best possible foundation for comparing results. We compared functional outcomes and QoL. The three questionnaires were the Inflammatory Bowel Disease Questionnaire (IBDQ), the Short Form-36 General Health Questionnaire (SF-36), and questions from the Pouch Dysfunction Score. The IBDQ is designed to evaluate quality of life (QoL) in patients with inflammatory bowel disease, but it has also been validated for patients with IPAA and ulcerative colitis [12]. The IBDQ consists of 32 items in four different groups: bowel symptoms, systemic symptoms, emotional function, and social function. The total score is used and ranges between 32 and 224; a high score indicates better QoL. For evaluation of pouch function, we used the initial 13 questions designed by Brandsborg when creating the Pouch Dysfunction Score [13]. The SF-36 questionnaire was used to evaluate general health. The SF-36 is a validated and widely used questionnaire [14]. It consists of 36 items addressing eight health concepts and there are two summary measures: physical component score and mental component score. All participants gave written informed consent to participate in the study.

Surgical technique for the TAMIS IPAA

Almost all patients (97%) had undergone laparoscopic total colectomy with ileostomy at least 3 months prior to IPAA. In the TAMIS IPAA, we started the procedure by mobilizing the stoma completely, and the distal part of the ileum was brought out through the stoma hole. A mini-Alexis port® (Applied Medical) was placed in the stoma hole, and an ileal pouch measuring 15–20 cm in length was constructed using 2–3 firings with a GIA linear stapler (80 mm; Medtronic). A purse-string suture was placed at the apex of the reservoir, the anvil of the circular stapler (Frankemann; 32 mm) was introduced, and the purse string was tied. The pouch was then returned to the abdomen. The abdominal access was obtained through a balloon port (Applied Medical) at the ileostomy site and two to three additional 5-mm ports. First, the small bowel mesentery was mobilized to the origin of the mesenteric root. The proximal part of the rectum was dissected from above following the mesorectal plane posteriorly, whereas close rectal dissection was performed anteriorly and anterolaterally. The dissection was carried out as far distally as convenient. A small gauze compress was placed around the dissection plane to facilitate later connection with the plane created from below. After this, exposure of the anus was achieved by a Lone Star retractor, then a Gel Point single port (Applied Medical) was inserted into the anus and pneumorectum was created using the AirSeal® insufflation platform (Conmed). The rectum was closed with a purse string suture proximal to the site of rectotomy. After this, the rectum was transected approximately 2 cm above the dentate line and the dissection of the rectum was now continued along the mesorectal fascia until reaching

the dissection level from above. The rectum was extracted transanally. In women, care was taken to bluntly mobilize the anterior part of the anal canal/lower rectum from the vagina. The reservoir was then stapled to the top of the anal canal/lower rectum under direct vision and typically with the mesentery located anteriorly to obtain maximal reach. Care was taken not to include the posterior wall of the vagina in the stapling. In cases of gas leak from the anastomotic line, reinforcing stitches of Monocryl 2–0 or 4–0 were placed to seal the leaks. A 25F Foley catheter was placed in the reservoir for passive drainage, and it was left for 2–3 days. A pelvic drain was placed in case of slight oozing from the pelvic sidewalls. In all cases, a protecting loop-ileostomy was created through the previous stoma hole.

Ethical considerations

The study was approved by Aarhus University Hospital, and according to Danish law the study is to be regarded as quality assurance activity. All patients gave written consent.

Data analysis

Patients were analyzed according to the surgical approach, i.e., open or laparoscopic (Brandsborg et al.) or TAMIS. For continuous variables, results are presented as median (range), whereas categorical variables are expressed as numbers (percentage). Continuous variables were compared using the Mann–Whitney *U* test and categorical variables were tested using χ^2 or Fischer exact test. A p value of < 0.05 was considered statistically significant. All analysis was made using STATA 12 (StataCorp LP, College Station, TX).

Results

Cohort study

Patients

From April 2015 to June 2019, 98 patients had TAMIS IPAA at our department. The patients had a median age of 35 years (range 14–67), and 61% of all patients were male. The median BMI was 23.3 (range 17–38.6). In 97% of cases, the previous colectomy was laparoscopic (Table 1).

Surgery, complications, and postoperative morbidity

Table 1 also presents data on intraoperative data, such as conversion rate, cuff length, formation of a stoma, and pouch drain. There were no conversions in the TAMIS procedures.

Table 1 Demographics and intraoperative factors of TAMIS pouch patients, median (range) and number (%) as appropriate

	TAMIS pouch
Number	98
Gender (M/F)	60 (61%)/38 (39%)
Age (years)	35 (14–67)
BMI (kg/m^2)	23.3 (17–38.6)
ASA	
I	16 (16%)
II	81 (83%)
III	1 (1%)
Smoking (yes/no/unknown)	10 (10%)/88 (90%)/0 (0%)
Previous colectomy (laparoscopic/open)	95 (97%)/3 (3%)
Conversions (yes/no)	0 (0%)/98 (100%)
Length of the cuff (mm)	10 (5–20)
Pouch drain (yes/no)	97 (99%)/1 (1%)
Temporary ileostomy (yes/no)	90 (92%)/8 (8%)

Out of the 98 patients, 90 (92%) had a temporary loop ileostomy (Table 1).

Details on 30 days postoperative morbidity and complications are listed in Table 2. In total, 4 (4%) patients had an anastomotic leak, and none of these required re-operation with removal of the pouch.

Two of the leaks were visualized at CT scan with contrast enema; none of the patients had a pelvic collection. Both patients kept their pouch drain for longer than usual and both received antibiotics. The stoma was later reversed in both patients, one of these patients had a bad functional outcome, and later had the pouch defunctionalized with an end ileostomy. In regard to the two last leaks, one was found by endoscopy and had a pelvic collection; the leak was treated with antibiotics and endosponge. The other leak was found by CT scan with contrast enema and a pelvic collection was demonstrated. It was treated with a transgluteal drain and antibiotics. In the last two patients, the stomas were reversed after 4 months and 8 months, and they both ended up having a satisfactory pouch function.

The median time until closure of the stoma was 3 months (range 0–12). In the entire study population, the 30-day mortality was 0 (0%).

Pouch function

Table 3 shows data for pouch-related problems. The median observation time was 44.5 months (range 7–55). In four (4%) patients, pouch problems resulted in the formation of a new stoma; the median time until this was 10 months (range 5–10). In addition, two (2%) patients had their pouch removed; the median time to pouch removal was 32 (range 20–44) months. Thus, in total six patients had serious pouch

Table 2 Postoperative morbidity and complications ≤ 30 days, median (range) and number (%) as appropriate

	TAMIS pouch
Hospital stay (days)	7 (3–28)
Anastomotic leak (yes/no)	4 (4%)/94 (96%)
Treatment of anastomotic leak	
• Reoperation with removal of the pouch (yes/no)	0 (0%)/4 (100%)
• Pouch drain (yes/no)	4 (100%)/0 (0%)
• Endosponge (yes/no)	1 (25%)/3 (75%)
• Transgluteal drain (yes/no)	1 (25%)/3 (75%)
• Antibiotics (yes/no)	4 (100%)/0 (0%)
Intraabdominal abscess without anastomotic leak (yes/no)	2 (2%)/96 (98%)
• Treatment of intraabdominal abscess (reoperation/drain/antibiotics)	0 (0%)/2 (100%)/2 (100%)
Wound infection (yes/no)	1 (1%)/97 (99%)
• Treatment of wound infection (reoperation/antibiotics)	1 (100%)/0 (0%)
Compromised bowel function (yes/no)	10 (10%)/88 (90%)
• Treatment of compromised bowel function (reoperation/conservative)	2 (20%)/8 (80%)
Time until closure of the ileostomy (months)	3 (0–12)
30-day mortality	0 (0%)

problems and had the pouch defunctionalized and ended up with an end ileostomy. Two of these patients also had their pouch removed. All six patients had chronic pouchitis. Anal stenosis after closure of the stoma was seen in four (4%) patients, in all cases, this was treated with anal dilatation, and none of these four patients had their pouch defunctionalized.

Case–control study

Demographics

Data for the TAMIS cohort are shown in Table 4. One had died and one had an unknown home address at the time of the questionnaire survey. We therefore sent out questionnaires regarding functional outcomes and QoL to 90 patients of which 65 (72%) patients responded. A reminder about the questionnaire was send out twice. Time from stoma closure to return of questionnaire was 44.5 months (range 7–55) in the TAMIS cohort. In the TAMIS cohort, we compared responders to non-responders in regard to years from RPC, gender, and age. We found a significant difference in age showing more young people in the non-responder group.

Patients in the Brandsborg cohort have been described earlier [9]. Notice that we only included patients from the Brandsborg cohort with a follow-up of less than 10 years at the time they were sent questionnaires. These patients had returned their questionnaires in 2011, and it was the data from these that were used for the comparisons. In the Brandsborg cohort, a response rate of 85% was obtained.

The median age in the TAMIS cohort (based on patients responding to the questionnaire) was 32 years (range 14–67) and in the Brandsborg cohort 41 years (14–84).

Table 3 Long-term pouch-related problems (median observation time was 44.5 months (range 7–55)), median (range) and number (%) as appropriate

	TAMIS pouch
Formation of a new stoma due to pouch problems (yes/no)	4 (4%)/94 (96%)
Time to formation of a new stoma due to pouch problems (months)	10 (5–10)
Removal of the pouch due to pouch problems (yes/no)	2 (2%)/96 (98%)
The reason for continuous pouch problems	
Fistulas	0 (0%)
Emptying problems	0 (0%)
Pouchitis	0 (0%)
Repeated emptying of the pouch/poor function	1 (50%)
Others	1 (50%)
Anal stenosis after closure of the stoma (yes/no)	4 (4%)/94 (96%)
Treatment of anal stenosis (anal dilatation/reoperation)	4 (100%)/0 (0%)

Table 4 Patients are grouped as Brandsborg pouch cohort 0–10 years from RPC and the TAMIS pouch cohort 0–10 years from RPC. Only showing patients who has answered the pouch questionnaire, median (range) and number (%) as appropriate

	Pouch cohort–Brandsborg	Pouch cohort–TAMIS
Patients (*n*)	514	65
Age (years)	41 (14–84)	32 (14–67)
Gender		
Male (*n*)	269 (52%)	41 (63%)
Female (*n*)	245 (48%)	24 (37%)

Bowel function

Table 5 lists data regarding bowel function: bowel movements day and night, stool consistency, urge to defecate, ability to suppress the urge to defecate, minor and major incontinence, incomplete evacuation, use of pads, use of antidiarrheal medicine, and use of antibiotics for bowel problems. For all these different items, there was no significant difference between the two groups (all p values > 0.05).

IBDQ

The total IBDQ score (Fig. 1) was the same when comparing males in the two groups 192 (74–224) vs. 181 (85–220) ($p = 0.08$) and the same was seen when comparing females in the two groups 177 (69–220) vs. 161 (97–216) ($p = 0.22$).

SF-36

The SF-36 dimensions for males are shown in Fig. 2, and the dimensions for females are shown in Fig. 3. For only one domain (SF), male TAMIS patients scored significantly lower than males in the Brandsborg cohort, 100 (0–100) vs. 87.5 (0–100) ($p = 0.04$). For all other domains both in males and females, there was no significant difference (all p values > 0.05).

Discussion

One of the major concerns with the TAMIS technique for dissection of the lower rectum in IPAA is that per operative stretching of the anal sphincters might result in impaired pouch function, and as a consequence, be associated with impaired QoL. In the present study, we were able to demonstrate that patients operated with the TAMIS approach had a functional outcome that was similar to a large cohort of Danish pouch patients, operated with abdominal approach (the Brandsborg cohort). In addition, there was no difference in QoL when comparing patients operated with the different approaches.

One major drawback of the present study is that it was not randomized. When introducing the TAMIS technique in our department, we realized that performing a randomized, single-center study would not be feasible due to the fairly low annual number of patients. Instead, we decided to rely on comparisons to an earlier national study examining all Danish patients who had undergone IPAA up to year 2010. These patients had all received questionnaires identical to those that were sent to patients in the TAMIS group. Importantly, the historical group had returned these questionnaires years ago, so that we could select those patients with a short (< 10 years) interval from surgery to the functional scoring. We acknowledge that there still was some difference in median time from surgery to assessment between the groups, but according to previous studies pouch function is known to be fairly stable over the first 10 years [15, 16]. On that background, we find it justified to compare the two groups.

TAMIS patients reported the same number of bowel movements both during day and night as did patients in the Brandsborg cohort. The same was seen with regard to both minor and major incontinence. Chandrasinghe and colleagues have recently reported similar data from a multicenter study [17] and found that the TAMIS and abdominal approaches yield comparable results regarding functional outcome and QoL.

Complications after restorative proctocolectomy are not uncommon. Mostly feared is a leaking ileoanal anastomosis, because it may be associated with long-term pouch failure [18]. Anastomotic leak occurred in 4% of our TAMIS patients as compared to 6–15% reported in the literature [17, 19]. Hence, our results are indeed comparable to other studies. Chandrasinghe et al. [17] found a leak rate of 6%, in TAMIS patients and the 15% was reported in a three-center study investigating patients operated with open, laparoscopic-assisted and laparoscopic techniques [19]. In a Danish study from 2016, no anastomotic leaks were found in 170 patients after open pouch surgery [5]. When looking at the TAMIS procedure, we suggest that anastomotic leak and pelvic collection should be considered as two different complications. In fact, one downside to the TAMIS procedure is a greater risk of pelvic collections due to higher degree of contamination in the pelvis after the procedure [20]. Therefore, if a CT scan shows a pelvic collection, it should only be considered an anastomotic leak if a leak can be demonstrated with an enema or by endoscopy. Among our 4 anastomotic leaks, only two had a pelvic collection, and we found two patients with a pelvic collection where no leak was visualized. These two patients had both an endoscopic examination of the pouch and contrast enema with CT scan, and no leak was found.

Table 5 Function comparing Brandsborg pouch cohort 0–10 years from RPC with the TAMIS pouch cohort 0–10 years from RPC

	Pouch cohort–Brandsborg *n* (%)	Pouch cohort–TAMIS *n* (%)	*p*
Variable			
Bowel movements during the day			0.55
< 1	1 (0.2)	0 (0)	
1–3	82 (16.2)	7 (11.1)	
4–7	302 (59.7)	44 (69.8)	
8–10	89 (17.6)	10 (15.9)	
> 10	32 (6.3)	2 (3.2)	
Bowel movements at night			0.36
0 (i.e., never)	75 (14.8)	6 (9.4)	
< 1	154 (30.4)	17 (26.6)	
1–2	196 (38.7)	32 (50.0)	
> 2	82 (16.2)	9 (14.1)	
Stool consistency			1.00
Solid	18 (3.5)	2 (3.2)	
Semisolid	421 (82.6)	52 (82.5)	
Watery	71 (13.9)	9 (14.3)	
Episodes of sudden and severe urge to defecate			0.20
Yes	246 (48.3)	25 (39.7)	
No	263 (51.7)	38 (60.3)	
Number of episodes per 24 h of a sudden and severe urge to defecate			0.92
< 1 (i.e., not every day)	98 (40.2)	11 (44.0)	
1–3	87 (35.7)	9 (36.0)	
4–7	40 (16.4)	5 (20.0)	
8–10	8 (3.3)	0 (0.0)	
> 10	11 (4.5)	0 (0.0)	
Ability to suppress the sudden and severe urge to defecate			0.31
Longer than 1 h	50 (20.3)	4 (16.0)	
No more than 1 h	69 (28.1)	4 (16.0)	
No more than 30 min	71 (28.9)	7 (28.0)	
No more than 15 min	39 (15.9)	8 (32.0)	
No more than 5 min	17 (6.9)	2 (8.0)	
Episodes of seepage (minor incontinence) per 24 h			0.28
0 (i.e., never)	187 (36.7)	21 (33.9)	
< 1 (i.e., not every day)	205 (40.2)	22 (35.5)	
1–2	57 (11.2)	13 (21.0)	
3–4	30 (5.9)	4 (6.5)	
> 4	31 (6.1)	2 (3.1)	
Episodes where unable to hold the stool (major incontinence) per 24 h			0.25
0 (i.e., never)	373 (73.0)	38 (61.3)	
< 1 (i.e., not every day)	97 (19.0)	18 (29.0)	
1–2	29 (5.7)	4 (6.5)	
3–4	10 (1.9)	2 (3.2)	
> 4	2 (0.4)	0 (0.0)	
Episodes of incomplete evacuation per 24 h			0.67
0 (i.e., never)	112 (22.0)	11 (17.7)	
< 1 (i.e., not every day)	182 (35.7)	25 (40.3)	
1–2	115 (22.6)	11 (17.7)	
3–4	52 (10.2)	9 (14.5)	

Table 5 (continued)

	Pouch cohort–Brandsborg *n* (%)	Pouch cohort–TAMIS *n* (%)	*p*
> 4	49 (9.6)	6 (9.7)	
Pads, panty liners, or similar			0.10
Yes	132 (25.8)	22 (35.5)	
No	380 (74.2)	40 (64.5)	
Antidiarrheal medicine			0.10
Yes	175 (34.4)	28 (45.2)	
No	333 (65.6)	34 (54.8)	
Antibiotics for bowel problems			0.22
Yes	49 (9.6)	9 (14.5)	
No	463 (90.4)	53 (85.5)	

Chi-square test and Fischer's exact

Park and colleagues [21] have recently reported a higher anastomotic leak rate after TAMIS IPAA than after transabdominal (open or hybrid) IPAA. A leak rate of 12% (9 leaks in total) was reported in the TAMIS group, and it is noteworthy that most of the leaks (8 out of 9 in the TAMIS group) occurred after hand-sewn anastomosis. Hand-sewn anastomoses were used far more frequently in the TAMIS group than in the transabdominal group, which may explain the different outcomes.

Of similar interest is the long-term failure rate, which amounts to about 12% at 20 years in high-volume departments [22]. A low pouch failure rate in the first years after surgery seems to predict a low long-term failure rate [22], and as such, it is reassuring that the early failure rate both in the present study and in the study by Chandrasinghe was low.

In our experience, the TAMIS technique may have advantages for an IPAA procedure. The accessibility to the dissection of the lower rectum is easier, and in our opinion, it is easier to get the correct length of the cuff than with abdominal approaches. The cuff is the remnant of rectal mucosa, and the length of the cuff has significant importance, since a too long cuff may result in pour pouch function [23].

When using a laparoscopic or robotic approach for pouch surgery, it seems inevitable to convert to open approach in a number of cases [5]. The most common cause is inability to

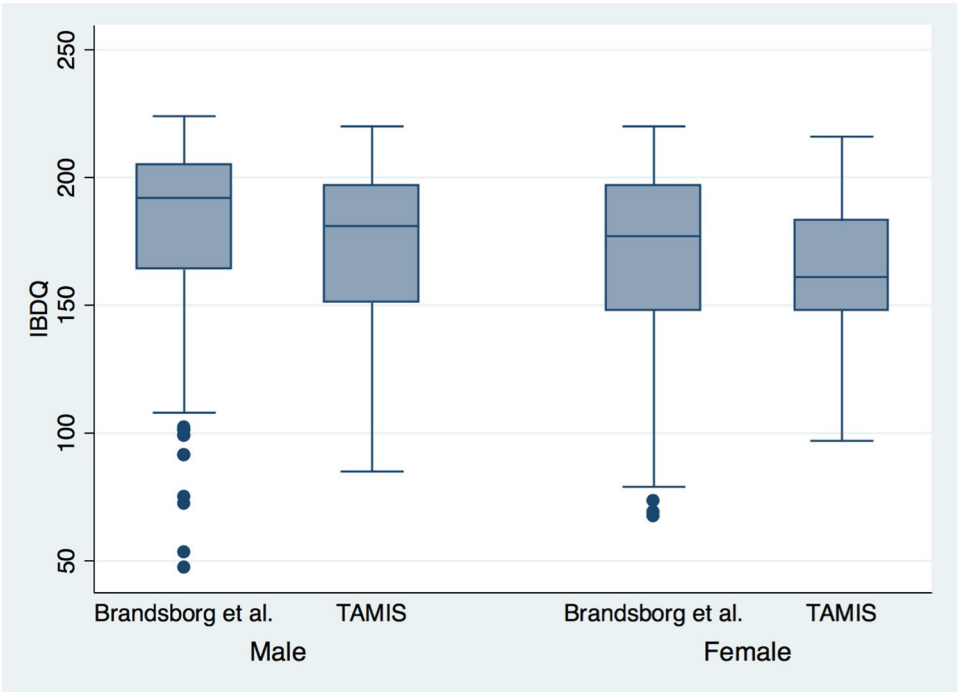

Fig. 1 Differences in the IBDQ score, Brandsborg cohort vs. TAMIS for males and females. There was no significant difference between males ($p = 0.08$), or between females ($p = 0.22$)

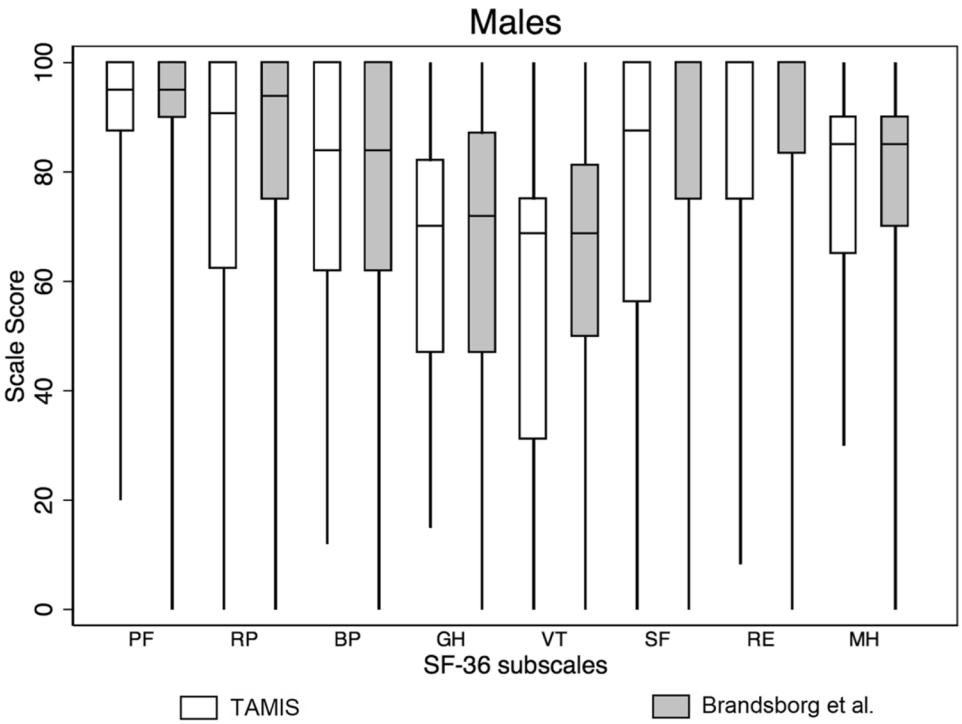

Fig. 2 The SF-36 dimensions for males, Brandsborg cohort vs. TAMIS. For only one domain (SF), male TAMIS patients scored significantly lower than males in the Brandsborg cohort ($p = 0.04$). For all other domains, there was no significant difference (all p-values > 0.05)

staple the rectum at the appropriate level using a laparoscopic stapler and thereby requiring conversion to either a pfannenstiel or a midline incision to be able to place an open stapler. This is particularly an issue in male patients [5], where open stapling was required in up to 50%. In comparison, we had no conversions in our series of TAMIS procedures, which may in fact constitute the single most important difference between laparoscopic/robotic and TAMIS approaches.

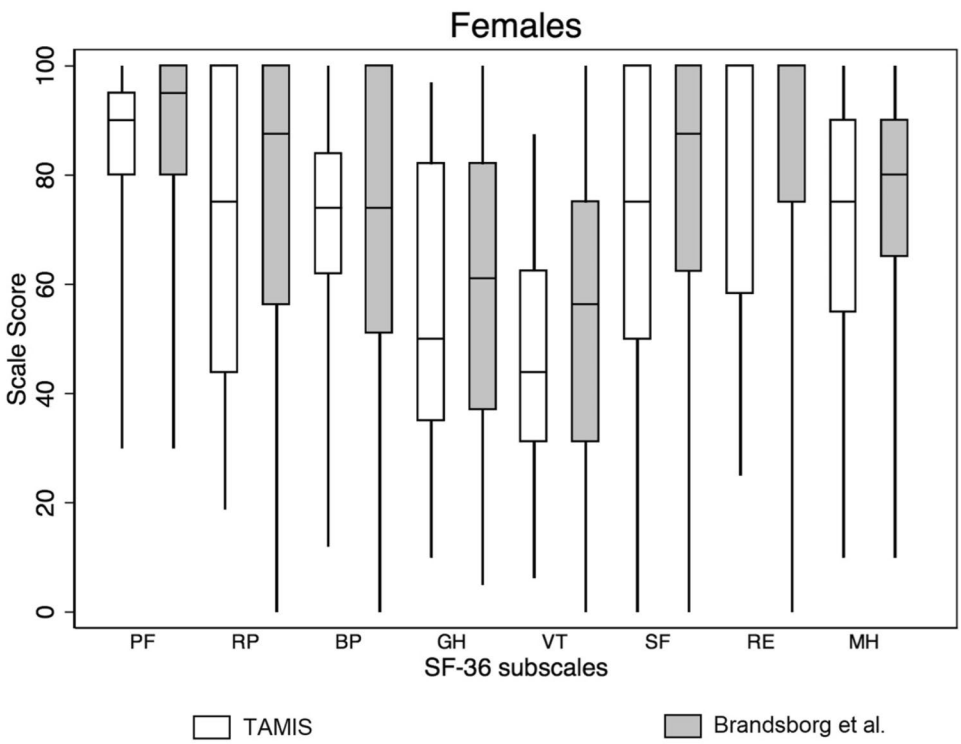

Fig. 3 The SF-36 dimensions for females, Brandsborg cohort vs. TAMIS. For all domains, there was no significant difference (all p-values > 0.05)

The limitations of this study include the small sample size and the relatively short-term follow-up. The small sample size may give some uncertainty about the results. Another limitation is the time gap, since we compare two cohorts that are sampled at different time points, simply because the two surgical methods have not been used simultaneously at our department. There may also be changes in the medical approach to these patients over time along with other unknown confounding factors. A final limitation is the lack of a randomized design.

Conclusions

In conclusion, the TAMIS technique shows acceptable outcomes, both in regard to the immediate postoperative complications and also functional outcome and QoL.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00384-022-04158-y.

Author contribution Sanne Harsløf has contributed sufficiently to the design of the work, the data collection, the statistical analysis, and the interpretation of data and she has made the initial drafting of the manuscript. She has approved the version to be published, and she is in agreement to be accountable for all aspects of the work. Frederik Rønne Pachler has contributed sufficiently to the data collection, the statistical analysis, the interpretation of data, and critical revision of the manuscript. He has approved the version to be published, and he is in agreement to be accountable for all aspects of the work. Henriette Vind Thaysen has contributed sufficiently to the design of the work, the data collection, the interpretation of data, and critical revision of the manuscript. She has approved the version to be published, and she is in agreement to be accountable for all aspects of the work. Marie Drejer has contributed sufficiently to the design of the work, the data collection, and critical revision of the manuscript. She has approved the version to be published, and she is in agreement to be accountable for all aspects of the work. Søren Brandsborg has contributed sufficiently to the design of the work, the statistical analysis, the interpretation of data, and critical revision of the manuscript. He has approved the version to be published, and he is in agreement to be accountable for all aspects of the work. Charlotte Buchard Nørager has contributed sufficiently to the design of the work, the data collection, and critical revision of the manuscript. She has approved the version to be published, and she is in agreement to be accountable for all aspects of the work. Anders Tøttrup has contributed sufficiently to the design of the work, the data collection, the statistical analysis, the interpretation of data, and critical revision of the manuscript. He has approved the version to be published, and he is in agreement to be accountable for all aspects of the work.

Declarations

Conflict of interest The authors declare no competing interests.

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