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ORIGINAL ARTICLE

Functional outcome after pouch-anal reconstruction with primary and secondary mucosectomy for patients with familial adenomatous polyposis (FAP)

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Abstract

Introduction Restorative proctocolectomy and ileal pouch-anal reconstruction is the surgical standard for the majority of patients with familial adenomatous polyposis (FAP). The pouch-anal anastomosis may be performed handsewn after primary mucosectomy or by double stapling. Better functional results favour the latter; however, higher rates of remaining rectal mucosa with adenomas often necessitate secondary mucosectomy. Data on functional outcome after secondary mucosectomy is scarce. The aim of the study was to analyse whether patients who undergo secondary mucosectomy maintain their functional benefits compared to patients with primary mucosectomy.

Patients and methods Twenty patients after secondary mucosectomy and 31 patients after primary mucosectomy were compared with respect to their functional outcome, using the MSKCC score, the Wexner score and ano-rectal physiology testing.

Results The MSKCC global score and the Wexner score showed a non-significant trend towards slightly better results after secondary mucosectomy (63.1 vs. 56.6, $p = 0.0188$ and 9.5 vs. 11, $p = 0.3780$). Patients after secondary mucosectomy also showed a tendency towards less bowel movements per 24 h (7 (range 4–11) vs. 8.5 (range 3–20), $p = 0.1518$). Resting pressures were slightly higher after secondary (44 vs. 39.6 mmHg, $p = 0.4545$) and squeeze pressures slightly higher after primary mucosectomy (87.6 vs. 81.2 mmHg, $p = 0.6126$). However, the results did not reach statistical significance.

Conclusion The results of this study cannot ultimately resolve the controversy concerning handsewn versus stapled ileal pouch-anal anastomosis. Our results suggest a trend towards better functional results after stapled anastomosis with secondary mucosectomy.

Keywords FAP · IPAA · Primary versus secondary mucosectomy

Introduction

Restorative proctocolectomy with ileal pouch-anal reconstruction has become accepted as standard for most patients with familial adenomatous polyposis coli (FAP). Preventive surgery has reduced the risk for colorectal cancer and has increased life expectancy, at the same time restoring a good long-term quality of life [1–6]. Two different techniques for achieving the ileal pouch-anal anastomosis (IPAA) have been described, including handsewn anastomosis after transanal mucosectomy or double-stapled anastomosis without prior mucosectomy [7, 8]. The main advantages of a stapled anastomosis are better functional results, such as better night-time continence, less seepage and less need for pad use [3, 9–14].

In recent years, a controversial discussion on the two techniques has evolved as a result of reported higher rates of remaining rectal mucosa (RRM), adenomas and even dysplasia after a stapled pouch-anal anastomosis [9, 14–17]. A meta-analysis by Lovegrove and co-workers revealed high rates of dysplasia in the anal transition zone (ATZ) in FAP and ulcerative colitis (UC) patients [3]. Von Roon and colleagues detected adenomas earlier during follow-up after a stapled IPAA

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as compared to a handsewn control group [18]. Furthermore, they estimated a significantly higher cumulative risk for neoplastic transformation within the ATZ after a stapled (51.1%) than after a handsewn (22.6%) anastomosis. These findings are underlined by an earlier study that analysed mucosa strippings from FAP patients and found dysplasia in 12 out of 14 cases [19]. In our own FAP patient population, we found remaining rectal mucosa, mainly small islets, in 42% of patients after primary mucosectomy and handsewn anastomosis compared to 84% in patients after a stapled IPAA. In the latter group, predominantly wide mucosa seams were detected [20]. The amount of RRM is concerning and may result in the need for secondary mucosectomy during follow-up, as RRM indicates a persisting risk for adenoma development and malignant transformation among FAP patients [3, 18, 19]. However, actual rates for rectal cancer in RRM seem to be low. Wide seams of RRM as found after stapled IPAA indicate a better possibility for endoscopic surveillance as compared to small mucosal islets [16, 18, 20, 21].

Litzendorf and colleagues described secondary transanal mucosectomy for completion after stapled IPAA [22]. No study to date has systematically evaluated the functional outcome after this additional procedure involving the pouch-anal anastomosis. We compared pouch function after stapled IPAA and secondary mucosectomy with pouch function after primary mucosectomy and handsewn anastomosis in order to analyse whether patients maintain their functional benefit after stapled anastomosis in case of secondary mucosectomy.

Materials, methods and patients

Ethical approval was obtained from the local review board at Heidelberg University. Patients were included in the study between June 2012 and May 2013. Informed consent of the patients included in the study was obtained during follow-up consultations in our outpatient clinic. Clinical data was retrieved from the Heidelberg Polyposis Register and clinical charts.

The study examinations contained a proctoscopy with standardised biopsies, ano-rectal physiology testing as well as acquisition of the MSKCC and Wexner score additionally to regular yearly follow-up examinations [23, 24]. The latter include clinical examinations, ano-digital examinations and standardised flexible pouchoscopy, carried out in our interdisciplinary endoscopy department.

Endpoints

Primary endpoint was the functional outcome according to the MSKCC incontinence score.

As secondary endpoints, we defined continence according to the Wexner score, sphincter function as indicated by ano-rectal physiology testing and rate of remaining rectal mucosa after secondary mucosectomy.

Polyposis register

The Heidelberg Polyposis Register, which was established in 1992, was used for patient identification. The register is a prospectively maintained database, including all FAP patients having been operated on and/or being followed up at our institution.

Surgical procedures

Pouch procedure

All pouch procedures were performed by senior surgeons of the Department of General, Visceral and Transplantation Surgery at Heidelberg University Hospital. The pouch was constructed with an approximate length of 10–12 cm regardless of the anastomotic technique.

In 2001, there was a major procedural change regarding construction of the pouch-anal anastomosis. Before 2001, IPAA was transanally handsewn after primary mucosectomy. Mucosectomy was performed in the remaining muscular cuff from the dentate line to the end of the cuff. The pouch was then pulled inside the cuff and transanally handsewn with absorbable suture material.

Since 2001, IPAA has been transanally double stapled without prior mucosectomy.

Secondary mucosectomy

Secondary mucosectomy was indicated due to large seams of RRM and adenomas. Details on indications for secondary mucosectomy are listed in Table 1.

For mucosectomy, physiological saline solution or saline diluted suprarenin solution was injected in the submucosal layer. The mucosa was then resected transanally from the dentate line to the anastomosis. Subsequently, the mucosa of the ileal pouch was adapted to the anal canal using single stitches with absorbable suture material.

Regular retractors such as the Lone Star Retractor were used if necessary.

Patient population

We identified 160 patients who underwent restorative proctocolectomy with a stapled IPAA between 2001 and 2011 from the Heidelberg Polyposis Register. Out of this group, 33 patients (20.6%) had undergone secondary mucosectomy.

Table 1 Indications for secondary mucosectomy and histological findings

Parameter	*n*
Preoperative findings	
Wide RRM seam	7
Adenoma	13
Tubular	11
Tubular-villous	1
Villous	1
Histological results	
Rectal mucosa without adenoma and dysplasia	6
Adenomas	13
Tubular with LGIEN	11
Tubular with HGIEN	2
Tubular-villous	0
Villous	0

LGIEN low-grade intraepithelial neoplasia, *HGIEN* high-grade intraepithelial neoplasia, *RRM* remaining rectal mucosa

As a comparison group, we chose 50 FAP patients who had undergone primary mucosectomy and handsewn anastomosis before 2001.

All identified patients were asked for participation in the current study between June 2012 and June 2013.

Functional results

The MSKCC incontinence score was used to obtain functional results, consisting of 18 questions referring to continence, factors influencing continence and number of bowel movements [23]. Questions are summed up into a global score and three subscales including frequency, dietary and urgency/soilage. Four questions are evaluated as single items and are included in the global score. The single items refer to complete defecation and discrimination between gas and stool. A higher score corresponds to a better functional result. The questionnaire was translated into German and handed out to the patients during follow-up consultations. An internal validation study of the German translation proved adequate validity. In addition, the Wexner score was used, consisting of five questions, four concerning continence for different qualities of stool and one on quality of life [24]. A lower score corresponds to a better function. Ano-rectal physiology testing was performed, evaluating resting and squeeze pressures.

Proctoscopy

Proctoscopies, including standardised biopsy sampling, were performed by a single surgeon with endoscopy experience of > 5 years.

Biopsies were taken from all four quadrants of the anastomosis and from macroscopically suspicious lesions. Specimens were analysed histologically for rectal mucosa, adenomas and dysplasia.

Standard proctoscopes with a diameter of 20, 15 and 10 mm and a length of 8 cm and standard 5-mm biopsy forceps were used. Sedation or anaesthesia was not required.

Statistics

Statistical analysis was carried out by SAS software (Release 9.1; SAS Institute, Inc., Cary, NC, USA). The character of the distributions of the quantitative parameters was determined by using the Shapiro–Wilk test and a normal probability plot. A normal distribution of the MSKCC incontinence score and of the Wexener score could be assumed in both groups. Therefore, the score values were presented as mean with standard deviation. Additionally, the results of the MSKCC incontinence score were presented graphically as box-and-whisker plots. To compare the two groups with respect to the incontinence scores, the *T* test for two independent groups was used. The parameters resting and squeeze pressure, age and time interval after pouch surgery as well as after secondary mucosectomy were presented as median with interquartile range (IQR). The Mann–Whitney *U* test was used to compare resting and squeeze pressure values, age and time interval between both groups. Fisher's exact test was used to compare the rate of colorectal carcinoma at time of IPAA between both groups. All tests were used two-sided. P values ≤ 0.05 were considered statistically significant.

Results

Out of 33 patients after secondary mucosectomy, 20 (60.6%) were included in the present study. Six patients were excluded due to appointment conflicts and another seven patients because they were currently followed up outside our institution.

Out of 50 patients defined as comparison group, 31 (62%) patients were included in the study. Of the remaining 19 patients, three patients denied participation, one patient had meanwhile died of a metastasised neuroendocrine CUP syndrome and one patient had an ileostomy at the time of the study. Seven patients could not be included due to appointment conflicts and another seven patients were currently followed up outside our hospital.

Patient characteristics are summarised in Table 2. The median age at the time of IPAA did not differ significantly between the two groups ($p = 0.2843$). However, the median follow-up interval between pouch surgery and the time of the study was significantly longer in the patient group undergoing primary mucosectomy than in the group requiring

Table 2 Characteristics of study population

	Stapled IPAA with secondary mucosectomy	Handsewn IPAA with primary mucosectomy	*p* value
Male ($n = 25$)	10 (50.0%)	15 (48.4%)	ns
Female ($n = 26$)	10 (50.0%)	16 (51.6%)	ns
Median age at time of IPAA in years (IQR)	24.7 (17.2–38.2)	31.5 (24.3–37.7)	0.2843
Colorectal cancer at time of IPAA	1 (5%)	6 (19.4%)	0.2232
Median follow-up interval after IPAA in years (IQR)	7.3 (5.5–9.3)	15.3 (13.0–17.3)	< 0.0001
Median interval between IPAA and mucosectomy in years (IQR)	2.5 (1.4–4.1)		
Median follow-up interval after mucosectomy in years (IQR)	4.0 (2.8–5.1)		

ns not significant

secondary mucosectomy (15.3 (IQR 13.0–17.3) vs. 7.3 (IQR 5.5–9.3) years, $p < 0.0001$). The median interval between IPAA and secondary mucosectomy among patients with stapled IPAA was 2.5 years (IQR 1.4–4.1). The median follow-up period after secondary mucosectomy was 4 years (IQR 2.8–5.1). One patient after secondary mucosectomy and six patients after primary mucosectomy were diagnosed with colorectal cancer at the time of IPAA. Of the comparison group, two patients (6.5%) had anastomotic complications after IPAA, one a leak and one a fistula. Among patients with primarily stapled IPAA, three developed anastomotic complications (15%), two leaks and one bleeding from the pouch. All but one patient after stapled IPAA had a diverting ileostomy for 3 months after IPAA. None of the patients developed complications after secondary mucosectomy.

Proctoscopies as part of this study were performed in 16 patients (51.6%) after primary and 13 patients (65%) after secondary mucosectomy. All other patients refused this examination. RRM was histologically confirmed in two patients (15.4%) after secondary mucosectomy and was not detected in any patient after primary mucosectomy.

Functional results

The MSKCC global score was significantly higher after secondary mucosectomy (63.1) than after primary mucosectomy (56.6), $p = 0.0188$, when the single items were included in the analysis (Fig. 1a). Evaluation of the global score excluding the single items, however, did not show a significant difference between the two groups, yet there was still a tendency towards a better score after secondary mucosectomy (Fig. 1b). All subscale analysis revealed only marginally better scores after secondary mucosectomy, without statistical significance (Fig. 1c–e).

The mean number of bowel movements per 24 h was slightly lower after secondary mucosectomy (7 (range 4–11) vs. 8.5 (range 3–20), $p = 0.1518$). Analysing the percentage of patients with six or less and seven or more bowel movements per 24 h in both groups showed that significantly more patients after secondary mucosectomy had six or less bowel movements per 24 h (58.8% vs. 26.9%, $p = 0.0365$) (Fig. 1f).

Regarding the Wexner score, patients after secondary mucosectomy showed a non-significant trend towards better functional results (8.8 vs. 11.5, $p = 0.3780$). Concerning the subscale analysis, the same non-significant tendency was detected, except for the subscale ‘incontinence for gas’ which showed a statistically significant larger proportion of patients not or only marginally being affected. Details are shown in Table 3 and Fig. 2.

Ano-rectal physiology testing demonstrated higher mean resting pressures after secondary mucosectomy than after primary mucosectomy (44.0 vs. 39.6 mmHg, $p = 0.4545$). The mean squeeze pressures were higher in the handsewn group (87.6 vs. 81.2 mmHg, $p = 0.6126$). Moreover, the high-pressure zone was longer in this group (20.1 vs. 17.4 mm, $p = 0.2472$). None of the differences reached statistical significance.

Discussion

Restorative proctocolectomy and IPAA represent the gold standard for the operative treatment of FAP patients. However, there is an ongoing controversy concerning the pouch-anal reconstruction. Several authors favour a double-stapled anastomosis due to better functional results [2, 3, 9–14, 19]. However, as adenomas arising from RRM stand for a persisting risk for FAP patients, recurrent endoscopic removal or surgical resection of RRM will likely become necessary. Whether the functional advantage after stapled IPAA over handsewn anastomosis persists after secondary mucosectomy is unclear. The presented study—to our knowledge—is the first one addressing the problem of functional outcome after secondary mucosectomy.

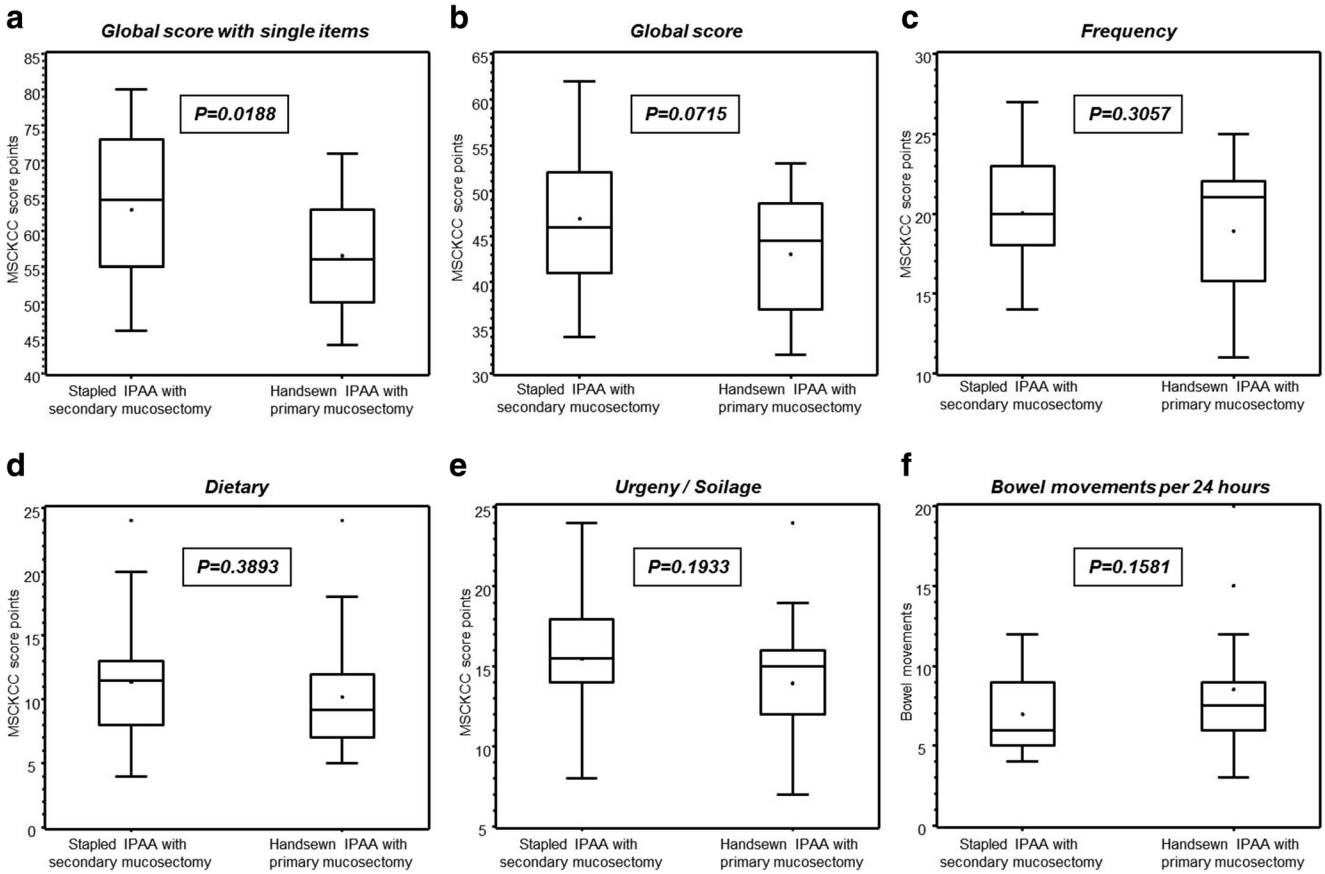

Fig. 1 Results of the MSKCC questionnaire showing the global score with single items, the global sore alone and results for the subscales and number of bowel movements. Frequency refers to factors influencing the number of bowel movements. Dietary refers to food and beverages influencing bowel function. Urgency/soilage refers to continence

In the present study, results indicate that patients will maintain a functional benefit after secondary mucosectomy indicated by a better MSKCC score, a better Wexner score and a higher percentage of patients with six or less bowel movements per 24 h after secondary mucosectomy. Previous studies on long-term quality of life (QoL) have shown that the number of bowel movements, especially nocturnal bowel movements, is a crucial factor influencing QoL [4, 13, 25, 26]. In an earlier study, we could show a relevant cut-off point of six bowel movements per 24 h as a determinant of QoL. In the present study, significantly more patients had less than six bowel movements per 24 h after secondary mucosectomy than in the control group. In addition, remaining higher resting pressures in the stapler group after secondary mucosectomy may indicate better nocturnal continence. This is supported by the results in the MSKCC subscale urgency and soilage. Results of the Wexner score underline these findings as well, as patients after secondary showed better results in the global score and all subscales. Concerning incontinence for gas, the percentage of patients not being affected was significantly higher after secondary mucosectomy. Therefore, patients after secondary mucosectomy may experience a better QoL on the basis of their lower stool frequency and a better sphincter function.

RRM after secondary mucosectomy was analysed as a secondary endpoint. It was histologically confirmed in two patients. As a large number of patients did not agree to a follow-up proctoscopy in this study, results are limited. But these findings indicate that secondary mucosectomy does not resolve the problem of RRM satisfactorily and suggests that patients will require recurrent mucosectomies, possibly altering pouch function more.

Table 3 Results of Wexner score subscales

	Stapled IPAA with secondary mucosectomy $n = 25$	Handsewn IPAA with primary mucosectomy $n = 13$	p value
Incontinence for			
Formed stool	4 (4.2)	9 (3.3)	0.6846
Liquid stool	5.2 (2.5)	14 (5.6)	0.3843
Gas	5.6 (5.7)	13.6 (7.7)	0.0403
Need for pad use	3.2 (4)	11.2 (7.7)	0.1330
Reduction of QoL	5.2 (4.3)	12.2 (5.1)	0.9420

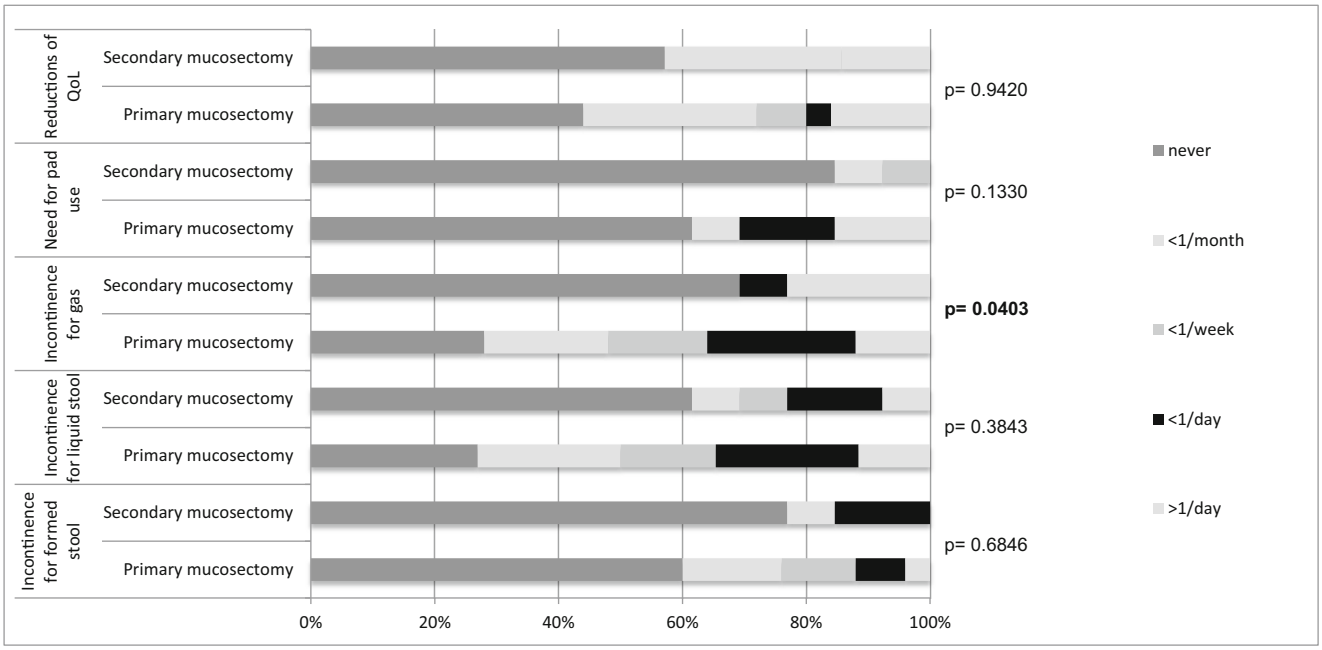

Fig. 2 Percent distribution of how many patients are affected severely by incontinence according to the Wexner score subscales

Although results of this study indicate a remaining functional benefit after secondary mucosectomy, there are some limitations. The study was carried out in a retrospective setting with only a small patient population. The small number of patients, especially after secondary mucosectomy, may affect the results and, therefore, leaves some question as to whether differences would be clearer with a larger number of patients being explored. Data on ano-rectal physiology testing was only available within this study and unfortunately not before secondary mucosectomy. Owed to the retrospective character of this study, the follow-up interval between pouch surgery and data collection was significantly longer after primary mucosectomy (15.3 years) than after stapled IPAA (7.3 years). The median follow-up interval since secondary mucosectomy, being the last surgical procedure with a possible impact on pouch function, was only 4.0 years. Age at time of IPAA and surgical interventions have an effect on functional results after IPAA, so that the respective differences between the monitored patient groups might limit the findings [27]. In a recent finish study, however, Helavirta and co-workers showed that time since surgery did not affect pouch function in a long-term follow-up [27]. Emmertsen and colleagues found that the proportion of patients being affected by symptoms of low anterior resection syndrome (LARS) decreased within 1 year after sphincter-preserving surgery for rectal cancer [28]. However, strong data on development, improvement or worsening of pouch function over time is not available. Therefore, an effect due to different follow-up intervals on the results of the presented study cannot be ruled out entirely. Yet, we believe that the available data mentioned suggest that the presented results of pouch function are reliable.

High rates of RRM with the potential risk of adenoma and carcinoma development after stapled anastomosis are worrying. But large seams of rectal mucosa are accessible for endoscopic surveillance more easily. And primary mucosectomy does not resolve the problem of RRM completely. Small islets of rectal mucosa may prevail within the ATZ and also within the muscular cuff with the same potential of neoplastic transformation, the latter not even being detectable with standard endoscopies. The smaller amount of remaining rectal mucosa and the only marginal reduction in pouch function may justify a primary mucosectomy and handsewn anastomosis for FAP patients. In contrast, an endoscopically accessible seam of rectal mucosa after stapled IPAA offers a good and safe option for surveillance with a preserved functional benefit in case of secondary mucosectomy.

Conclusion

The results of this study cannot ultimately resolve the controversial discussion concerning handsewn versus stapled ileal pouch-anal anastomosis for FAP patients. Easier endoscopic surveillance after stapled IPAA and better functional results after secondary mucosectomy may favour this approach. A prospective analysis including multiple high-volume centres on pouch function after either approach would be favourable to clarify further on this topic.

Author contribution P.G.: primary author of manuscript, conceptual development of study, acquisition of data, analysis and interpretation of results. I.T.: acquisition of data, analysis and interpretation of results.

U.H.: critical review of study design, statistical analysis of data, interpretation of data, interpretation of results, statistical counselling of study. M.K.: conceptual development of study, analysis and interpretation of results, critical review of manuscript and possible impact on clinical management.

Compliance with ethical standards

Conflict of interest All authors declare that they had no conflict of interest concerning the presented study.

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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