

Feasibility of laparoscopic total proctocolectomy with ileal pouch–anal anastomosis and total colectomy with ileorectal anastomosis for familial adenomatous polyposis: results of a nationwide multicenter study

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Abstract

Background Data supporting the safety and feasibility of laparoscopic total proctocolectomy with ileal pouch–anal anastomosis (TPC-IPAA) and total colectomy with ileorectal anastomosis (TC-IRA) for patients with familial adenomatous polyposis (FAP) are limited. The aim of this study was to clarify the feasibility and morbidity of laparoscopic TPC-IPAA and TC-IRA for patients with FAP, using a large Japanese multicenter dataset.

Methods Data on 256 patients with FAP who underwent TPC-IPAA ($n = 171$) or TC-IRA ($n = 85$) at 23 institutions between the years 2000 and 2012 were collected. Short- and long-term clinical outcomes were compared between laparoscopic and open approaches for each procedure.

Results Among the 256 patients with FAP, a total of 126 patients underwent laparoscopic surgery, consisting of 74 laparoscopic TPC-IPAA and 52 laparoscopic TC-IRAs.

The proportion of the FAP patients who underwent laparoscopic surgery increased during the study period, reaching 79 % of all TPC-IPAA and 82 % of all TC-IRAs in the final two years covered by the data. In both TPC-IPAA and TC-IRA, the laparoscopic approach was associated with a longer operative duration but a similarly low postoperative morbidity and comparably adequate anal function compared with the open approach. The overall survival and the incidence of desmoid tumor were also comparable between the laparoscopic and open approaches in both procedures.

Conclusions Laparoscopic TPC-IPAA and TC-IRA are both feasible options—with low rates of morbidity, good functional outcomes, and excellent overall survival rates—in patients with FAP. Since the data indicate that laparoscopic TPC-IPAA and TC-IRA are feasible, they also support the recent increase in laparoscopic surgery for patients with FAP in Japan.

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Keywords Familial adenomatous polyposis · Ileal pouch–anal anastomosis · Ileorectal anastomosis · Laparoscopic surgery · Total colectomy · Total proctocolectomy

Introduction

Familial adenomatous polyposis (FAP) is a rare autosomal dominant disease characterized by the development of numerous adenomatous polyps throughout the colon and rectum. This condition can lead to cancer at a young age if untreated. Because of the inevitable spread of this cancer, either total proctocolectomy with ileal pouch–anal anastomosis (TPC-IPAA) or total colectomy with ileorectal anastomosis (TC-IRA) is warranted at a certain point for all patients with FAP.

Since the first article on laparoscopic total proctocolectomy (TPC) was written by Peters in 1992, many authors have reported on this procedure [1–5]. However, data supporting the safety and feasibility of the laparoscopic approach for the two major procedures for patients with FAP, TPC-IPAA and TC-IRA, are limited. In particular, previous studies have shown inconsistent results regarding the advantages of laparoscopic TPC-IPAA. Some studies have failed to show any benefits of laparoscopic TPC-IPAA as compared with open TPC-IPAA [6–10], while others have shown favorable results [11–13]. Also, in those studies, the majority of the population comprised patients with ulcerative colitis (UC), and the number of patients with FAP was less than 100 in each study [9, 12–18]. Given that UC is often associated with high morbidity after surgery due to malnutrition, steroid use, and emergent conditions, such mixed heterogeneity in the population could be the cause of the inconsistent results in the previous studies. Thus, only a few studies have focused on patients with FAP; the feasibility and morbidity of laparoscopic surgery in this rare disease are yet to be determined.

We recently reported that laparoscopic surgery is increasingly being performed for patients with FAP in Japan [19]. Despite this trend towards a wider indication, overall surgical outcomes of laparoscopic surgery for FAP patients have not deteriorated in recent years, suggesting that the adoption of this approach in Japan is acceptable. However, those analyses were limited by pooled datasets of all procedures, including those without pouch reconstruction, and the data lacked detailed complication profiles or a direct comparison of the laparoscopic and open approaches in each specific procedure. Hence, it is yet to be determined whether the laparoscopic approach is truly safe and feasible compared with the open approach in the two procedures TPC-IPAA and TC-IRA. In light of this, the present study aimed to clarify the feasibility and the safety of the

laparoscopic approach compared with the open approach in TPC-IPAA and TC-IRA, using Japanese multicenter data. In the present study, we present short-term surgical outcomes, including detailed complication profiles, long-term outcomes, and functional outcomes for each procedure.

Patients and methods

Original data sources for this study

The original data for this study were compiled from 23 institutions that are members of the Japanese Society for Cancer of the Colon and Rectum (JSCCR), which includes the departments of surgery, internal medicine, pathology, and radiology at hospitals distributed throughout Japan [20, 21]. All patients diagnosed as having FAP and who underwent colorectal resection in each institution between the years 2000 and 2012 were retrospectively collected and registered for the database. Patients with a previous history of colorectal resections were excluded from the database to avoid double registration. The diagnosis of FAP was established if the patients met any of the following three criteria (according to the 2012 JSCCR Clinical Practice Guidelines for Hereditary Colorectal Cancer [22, 23]): (1) patients with 100 or more adenomatous polyps in the colon with or without a family history of FAP, (2) patients with fewer than 100 adenomatous polyps in the colon with a family history of FAP, and (3) patients with germline mutations in the adenomatous polyposis coli gene. We defined FAP patients with ≥ 1001 polyps in the colon and rectum as having a profuse phenotype, those with 100–1000 polyps as having a sparse phenotype, and those with ≤ 99 polyps as having an attenuated phenotype, respectively. This was a retrospective observational cohort study that was approved by the ethical committees of the JSCCR and each participating institution.

Patient selection and data extraction

Data on all patients who underwent TPC-IPAA and TC-IRA were extracted from the database. Clinical variables, incidence of desmoid tumor, and overall survival were compared between patients undergoing laparoscopic and open surgery.

Statistical analysis

Statistical analysis was performed using the JMP software, v.9.0.0 (SAS Institute, Cary, NC, USA). To compare laparoscopic and open surgery, univariate analysis was performed using Pearson's chi-square test or Fisher's exact probability test for categorical variables and the *t* test for

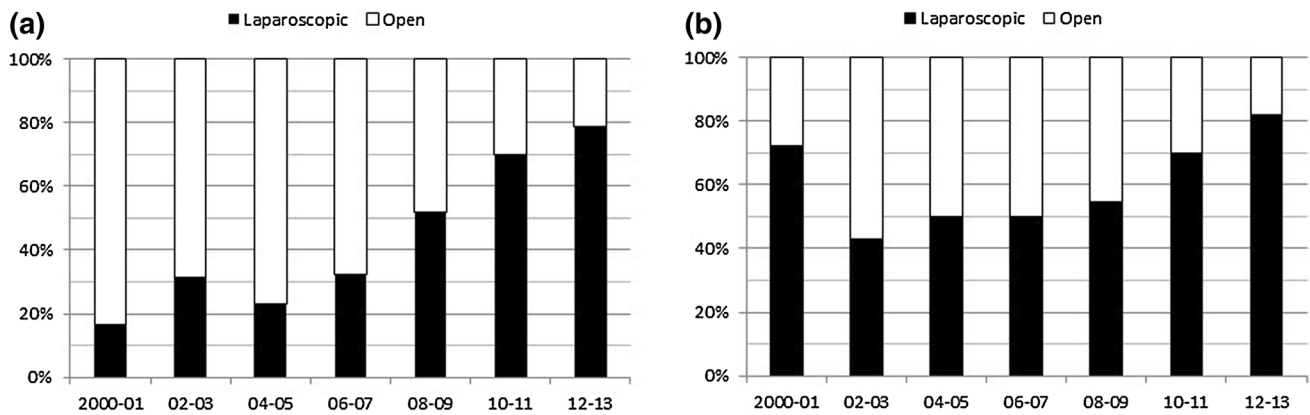


Fig. 1 Proportion of the patients with familial adenomatous polyposis (FAP) who underwent a particular laparoscopic procedure (either TPC-IPAA or TC-IRA). **a** Total proctocolectomy with ileal pouch-

anal anastomosis (TPC-IPAA); **b** total colectomy with ileorectal anastomosis (TC-IRA)

continuous variables. Survival and incidence of desmoid tumor were analyzed using the Kaplan–Meier method. Patients who were alive and did not have a desmoid tumor at the most recent follow-up were treated as censored. *P* values <0.05 were considered to be significant.

Results

A total of 303 patients with FAP who underwent colorectal resection were registered in the database. After excluding patients who underwent partial colectomy ($n = 20$), TPC without reconstruction ($n = 8$), TPC with straight ileoanal anastomosis without pouch creation ($n = 13$), and TPC without information on reconstruction ($n = 4$), 256 patients were eligible for the study, consisting of 171 patients who underwent TPC-IPAA and 85 patients who underwent TC-IRA. A total of 126 patients underwent laparoscopic surgeries (49 %): 74 laparoscopic TPC-IPAA and 52 laparoscopic TC-IRAs. The proportion of laparoscopic surgery was significantly higher in the TC-IRA than in the TPC-IPAA group (61 vs. 43 %, $p = 0.0070$). Figure 1 shows the proportion of FAP patients who underwent laparoscopic surgery for each procedure during the study period. This proportion increased over the years for both procedures. The proportion of TPC-IPAA that were laparoscopic increased prominently from 17 to 79 %.

Patient characteristics and surgical background

Patient characteristics and surgical procedures are shown in Table 1. In TPC-IPAA, there were no differences in sex, age, and phenotype between the laparoscopic and open groups. The majority of the patients were of the profuse

or sparse phenotype, and nearly half of the indications for surgery were cancer in both groups. The proportion of the patients for whom a stapled anastomosis was performed tended to be higher in the laparoscopic TPC-IPAA group than in the open TPC-IPAA group, although the majority of the anastomoses in both groups were made using transanal hand-sewn techniques. A covering ileostomy was more frequently created in laparoscopic TPC-IPAA. Laparoscopic TPC-IPAA had a longer operative duration, but the bleeding volume was not significantly different between the groups.

In TC-IRA, there were no differences in sex, age, and phenotype of FAP between the two groups. Almost 65 % of the patients in both groups had the sparse phenotype. The most frequent indication for open TC-IRA surgery was cancer. Nearly 95 % of the anastomoses were stapled anastomosis without covering ileostomy in both groups. Patients that underwent laparoscopic TC-IRA had significantly less bleeding volume despite the longer operative duration.

Postoperative morbidity

Table 2 shows the postoperative complications according to the Clavien–Dindo classification. In both TPC-IPAA and TC-IRA, there were no differences in the incidence of grade III–IV complications between laparoscopic and open surgery. In both procedures, the most frequent grade III complication was ileus. There was no mortality in the study population.

Overall survival

Figure 2 shows the overall survival after surgery excluding the patients with stage IV cancer. The median

Table 1 Baseline characteristics and surgical background of patients

	TPC with IPAA (<i>n</i> = 171)			TC-IRA (<i>n</i> = 85)		
	Laparoscopic	Open	<i>p</i> value	Laparoscopic	Open	<i>p</i> value
Gender			0.7073			0.3047
Male	38 (51)	47 (48)		28 (54)	14 (42)	
Female	36 (49)	50 (52)		24 (46)	19 (58)	
Median age	29 (12–68)	33 (14–66)	0.7329	31.5 (13–65)	34 (18–65)	0.4202
Phenotype			0.1309			0.9431
Profuse (polyps ≥ 1001)	31 (44)	29 (30)		10 (19)	6 (18)	
Sparse (polyps 100–1000)	35 (50)	58 (60)		34 (65)	21 (64)	
Attenuated (polyps ≤ 99)	4 (5.7)	10 (10)		8 (15)	6 (18)	
Number of polyps in the remnant rectum						0.4907
≥100				3 (6.3)	2 (6.9)	
20–99				16 (33)	6 (21)	
≤19				29 (60)	21 (72)	
Indication for surgery			0.7583			0.0087
Prophylactic	37 (50)	49 (52)		28 (55)	10 (30)	
Symptomatic	3 (4.1)	2 (2.1)		4 (7.8)	0 (0)	
Cancer	34 (46)	43 (46)		19 (37)	23 (70)	
Stage 0	6 (20)	5 (14)		3 (17)	1 (4.5)	
Stage I	11 (37)	6 (16)		13 (72)	5 (23)	
Stage II	2 (6.7)	11 (30)		1 (5.5)	2 (9.1)	
Stage III	11 (37)	11 (30)		1 (5.5)	5 (23)	
Stage IV	0 (0)	4 (1.1)		0 (0)	9 (41)	
Anastomosis			0.0617			1.0000
Stapled	22 (31)	16 (18)		45 (96)	29 (94)	
Hand-sewn	50 (69)	73 (82)		2 (4.3)	2 (6.5)	
Covering ileostomy			<0.0001			1.0000
Present	56 (78)	37 (38)		5 (10)	3 (9.4)	
Absent	16 (22)	60 (62)		43 (90)	29 (91)	
Median duration of operation (min)	482 (170–790)	275 (158–972)	<0.0001	313 (175–682)	215 (95–838)	0.0005
Median bleeding (ml)	247 (10–2930)	300 (0–2700)	0.1943	65 (0–920)	186 (0–4700)	0.0209
Median follow-up (months) ^a	44 (0.7–156)	61 (0.5–159)	0.1251	66 (0.8–169)	80 (11–156)	0.2883

TPC-IPAA total proctocolectomy with ileal pouch–anal anastomosis, TC-IRA total colectomy with ileorectal anastomosis

^a The analysis was performed excluding patients with Stage IV cancer

follow-up period was 44 and 61 months in laparoscopic and open TPC-IPAA, respectively ($p = 0.1251$), and 66 and 80 months in laparoscopic and open TC-IRA, respectively ($p = 0.2883$). In both TPC-IPAA and TC-IRA, the overall survival was not significantly different between laparoscopic and open surgeries (TPC-IPAA: 98 vs. 98 % at 5 years, $p = 0.1447$; TC-IRA: 100 vs. 96 % at 5 years, $p = 0.1886$). The survival was also similar between the groups after excluding the patients with cancer (TPC-IPAA: 97 vs. 100 % at 5 years, $p = 0.3096$; TC-IRA: 100 vs. 89 % at 5 years, $p = 0.3254$) or upon comparing cancer-associated patients without stage IV disease (TPC-IPAA: 100 vs. 96 % at 5 years, $p = 0.3113$; TC-IRA: 100 vs. 100 % at 5 years, $p = 0.1914$).

Incidence of desmoid tumor

Figure 3 shows the cumulative incidence of desmoid tumor after surgery. In both TPC-IPAA and TC-IRA, the incidence of desmoid tumor was not significantly different between laparoscopic and open surgery (TPC-IPAA: 22 vs. 19 % at 5 years, $p = 0.5892$, TC-IRA: 13 vs. 4.8 % at 5 years, $p = 0.0816$).

Anal, urinary, and sexual function

Table 3 shows anal, urinary, and sexual function after surgery. Among the patients who underwent TPC-IPAA, 99 and 98 % were ostomy-free at the last follow-up in the

Table 2 Postoperative complications (Clavien–Dindo classification grade III–IV)

	TPC-IPAA (<i>n</i> = 171)			TC-IRA (<i>n</i> = 85)		
	Laparoscopic	Open	<i>p</i> value	Laparoscopic	Open	<i>p</i> value
Ileus			0.6517			0.5158
Present	6 (8.3)	5 (6.4)		8 (17)	3 (10)	
Absent	66 (92)	73 (94)		40 (83)	27 (90)	
Anastomotic leakage			0.4800			1.0000
Present	1 (1.4)	0 (0)		1 (2.1)	1 (3.3)	
Absent	71 (99)	78 (100)		47 (98)	29 (97)	
Anastomotic stricture			0.4276			1.0000
Present	4 (5.6)	2 (2.6)		1 (2.1)	0 (0)	
Absent	68 (94)	76 (97)		47 (98)	30 (100)	
Intraperitoneal abscess			1.0000			–
Present	2 (3.0)	2 (2.7)		0 (0)	0 (0)	
Absent	64 (97)	72 (97)		47 (100)	29 (100)	
Wound infection			0.3462			1.0000
Present	3 (4.5)	1 (1.4)		1 (2.1)	1 (3.3)	
Absent	64 (96)	73 (99)		47 (98)	29 (97)	
Female vaginal fistula			0.4219			–
Present	1 (3.7)	0 (0)		–	–	
Absent	26 (96)	37 (100)				

TPC-IPAA total proctocolectomy with ileal pouch–anal anastomosis, TC-IRA total colectomy with ileorectal anastomosis

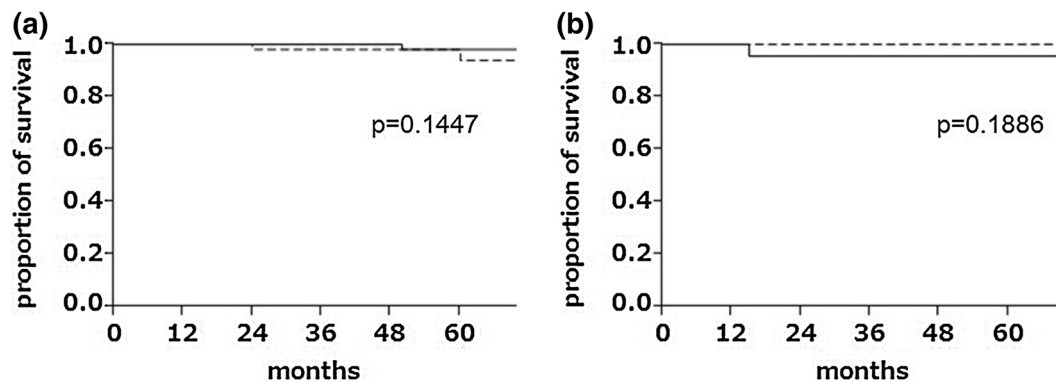


Fig. 2 Overall survival after laparoscopic (*dotted line*) and open (*solid line*) surgery for patients with FAP. **a** TPC-IPAA; **b** TC-IRA. Patients with stage IV cancer were excluded from the analysis

laparoscopic and open groups, respectively. The mean duration from sphincter-preserving TPC-IPAA to ileostomy closure was 4 months in both groups. The mean Wexner score after TPC-IPAA showed that both groups achieved adequate anal function. None of the patients that underwent TPC-IPAA presented with urinary dysfunction. Although the data on sexual function were limited given the small number of patients available for the analysis, there was no significant difference in the incidence of sexual dysfunction between laparoscopic and open TPC-IPAA. All patients that underwent TC-TRA were ostomy free at the last follow-up, with preservation of adequate

anal function. None of the patients had urinary dysfunction after TC-IRA.

Discussion

The present multicenter retrospective study analyzed short- and long-term outcomes of a total of 256 patients with FAP in Japan, including 126 laparoscopic and 130 open TPC-IPAA and TC-IRAs. Although there have been multiple studies of laparoscopic surgery for patients with FAP, previous studies included only 8–70 patients who underwent

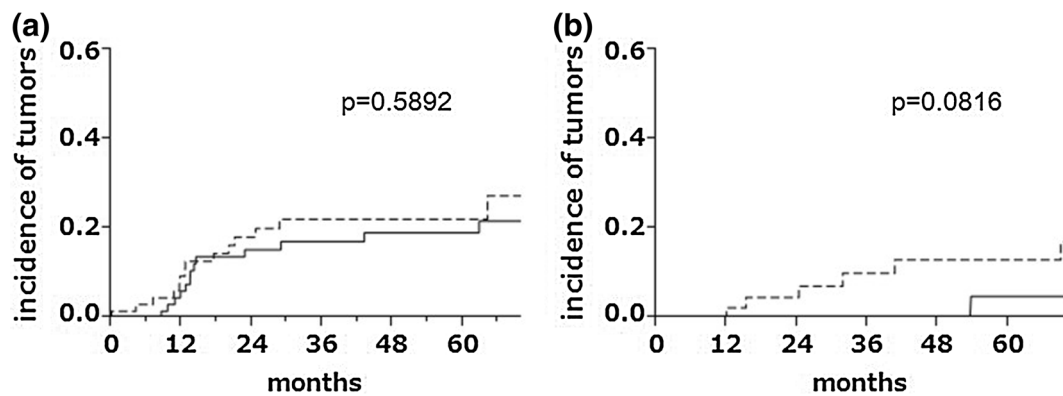


Fig. 3 Incidence of desmoid tumor after laparoscopic (*dotted line*) and open (*solid line*) surgery for patients with FAP: **a** TPC-IPAA, **b** TC-IRA

Table 3 Anal, urinary, and sexual function

	TPC-IPAA (<i>n</i> = 171)		<i>p</i> value	TC-IRA (<i>n</i> = 85)		<i>p</i> value
	Laparoscopic	Open		Laparoscopic	Open	
Ostomy at the last follow-up			1.0000			1.0000
Present	1 (1.4)	2 (2.1)		0 (0)	0 (0)	
Absent	69 (99)	94 (98)		45 (100)	29 (100)	
Median days before ostomy closure ^a	119 (35–835)	119 (49–1001)	0.6962	–	–	–
Mean Wexner score	1.3	1.9	0.4507	0.3	0	0.5161
Urinary disorder			1.0000			1.0000
Present	0 (0)	0 (0)		0 (0)	0 (0)	
Absent	57 (100)	69 (100)		30 (100)	20 (100)	
Male erection disorder			1.0000			–
Present	1 (3.3)	0 (0)		–	–	
Absent	29 (97)	16 (100)		–	–	
Male ejaculation disorder			0.6019			–
Present	2 (6.7)	2 (12)		–	–	
Absent	28 (93)	14 (88)		–	–	

TPC-IPAA total proctocolectomy with ileal pouch–anal anastomosis, TC-IRA total colectomy with ileorectal anastomosis

^a The analysis was performed in patients with covering ileostomy

laparoscopic surgery [24–27]; the present work focused on a considerably larger series.

Many authors have disagreed about the advantages of laparoscopic TPC-IPAA over open TPC-IPAA. Although some authors observed favorable results with laparoscopic TPC-IPAA [11–13], others reported that it had no benefit over open TPC-IPAA [6–10]. A recent systematic review evaluated 607 patients with FAP who underwent TPC-IPAA from 11 trials, and reported an increase in operative time but no differences between laparoscopic and open TPC-IPAA in terms of mortality, complications, reoperation and readmission rates, as well as postoperative recovery [6]. Another meta-analysis of 329 patients from 10 studies reported a longer operative time but similar

adverse events with laparoscopic TPC-IPAA as compared with open TPC-IPAA [10]. In accordance with these studies, the present study showed equivalent postoperative complications and bleeding volumes for laparoscopic and open TPC-IPAA, although the operative time was longer in laparoscopic TPC-IPAA. Of note, the present study showed very low incidences of IPAA-related complications in laparoscopic TPC-IPAA, with 1.4 % anastomotic leakage, 5.6 % anastomotic stricture, and 3.0 % pelvic abscess. Furthermore, laparoscopic TPC-IPAA had 99 % ostomy closure with good preservation of anal function and excellent overall survival compared with open TPC-IPAA. In light of these findings, laparoscopic TPC-IPAA seems to be a feasible option for patients with FAP. The present study also

showed that the proportion of TPC-IPAA that are laparoscopic has increased to 79 % in Japan. This active adoption of a laparoscopic approach in Japan appears to be justified by the outcomes shown in the present study. On the other hand, laparoscopic TPC-IPAA had a significantly higher proportion of covering ileostomy and a greater tendency for stapled anastomosis compared with open TPC-IPAA. The data suggest that many Japanese surgeons are rather reluctant to adopt one-stage IPAA without diversion in a laparoscopic approach to minimize the risk of anastomotic complications, and prefer to use stapled anastomosis in laparoscopic IPAA, probably due to technical convenience.

In laparoscopic TC-IRA, the present study showed one-third less blood loss than open TC-IRA and equivalent postoperative morbidity. The proportion of patients in which a covering ileostomy was performed was equivalently low in both laparoscopic and open TC-IRA, and both groups showed excellent preservation of anal function. These data are compatible with the results of a previous case-matched study [28]. Although a decrease in blood loss from a median of 186 ml to 65 ml might not be clinically important, the data clearly reflect the minimal invasiveness of laparoscopic TC-IRA. This reduced intraoperative bleeding without causing postoperative morbidity make laparoscopic TC-IRA a favorable option for patients with FAP despite the longer duration of the procedure versus the open approach.

In the present study, ileus was among the most frequent of the postoperative complications of both TPC-IPAA and TC-IRA. The incidence of ileus in the present study was comparable to that (11.4–31 %) reported in previous studies [29–32]. Generally, laparoscopic colorectal surgery is associated with decreased ileus [33, 34]. Indeed, there is evidence that performing TPC-IPAA using the laparoscopic approach results in decreased adhesions [35, 36]. However, a recent case-matched study that focused on laparoscopic and open TPC-IPAA failed to show a decrease in the incidence of ileus with the laparoscopic approach [37]. In accordance with that study, the present data failed to show a decrease in the incidence of ileus with either laparoscopic TPC-IPAA or laparoscopic TC-IRA. Although our data confirmed the feasibility of the laparoscopic approach, we did not find any evidence of it leading to a decreased incidence of ileus.

Another concern after surgery for patients with FAP is the development of a desmoid tumor, because it is the second or third leading cause of death in patients with FAP [38]. Previous studies have reported preliminary results that laparoscopic surgery may reduce the incidence of desmoid tumor in patients with FAP [39–41]. In contrast to these reports, the present study failed to show a decrease in the incidence of desmoid tumor after laparoscopic TPC-IPAA or TC-IRA. The 5-year incidence of desmoid tumor in the

present study was 17 % in open TPC-IPAA and 21 % in laparoscopic TPC-IPAA, which were comparable to those previously reported [41, 42]. As our study lacked data on some important risk factors for desmoid tumors, such as a family history of desmoid tumor and any specific mutations 3' to codon 1444 on the APC gene, the baseline risk for desmoid tumor may differ between the laparoscopic and open groups. A larger study with these required variables and a longer follow-up period is needed to clarify the contribution of the laparoscopic approach to decreasing desmoid tumor incidence in patients with FAP.

It is commonly suggested that patients with FAP are ideal candidates for minimally invasive approaches, as the disease usually affects young and cosmesis-conscious patients. Indeed, the median age in the present study was 29–34 years in each group. Additionally, surgeons should bear in mind that young patients are socially active, so great efforts should be made to preserve postoperative sexual, urinary, and anal function. However, previous studies have reported that impaired function after TPC-IPAA, mainly due to autonomic nerve injury and poor pouch function, is not uncommon [43–45]. The present study demonstrated 99 % sphincter preservation with an excellent Wexner score after laparoscopic TPC-IPAA. Urinary and sexual function were also rarely impaired after laparoscopic TPC-IPAA. These data on functional outcome provide evidence in support of the use of the laparoscopic approach in TPC-IPAA, particularly in young patients.

Although the present work was a nationwide multicenter study that included a large number of patients with FAP, it has several limitations. First, this study is retrospective in nature and has the limitations inherent to this type of design. Additionally, a comparison was made without a case-matched design. Second, the proportion of patients who underwent laparoscopic surgery increased due to technical advances during the study period, which could have resulted in a heterogeneous population in the laparoscopic group. Finally, data on some important parameters relating to the benefits and disadvantages of laparoscopic surgery were not available in the database, including data on postoperative recovery of bowel function, postoperative pain, time to resume oral intake, duration of hospital stay, and open conversion rate. Due to the rare incidence of the disease and the small number of cases available from a single institution, well-planned multi-institutional trials are needed to address these issues and to clarify the clinical advantage of laparoscopic surgery in patients with FAP. Despite these limitations, we believe that this study reflects the actual outcomes and feasibility of laparoscopic TPC-IPAA and TC-IRA in this study setting.

In conclusion, laparoscopic TPC-IPAA and TC-IRA are feasible options with low rates of morbidity, good functional outcomes, and excellent overall survival in

patients with FAP. The data provides support for the recent increase in laparoscopic surgery for patients with FAP in Japan.

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Compliance with ethical standards

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