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Journal Article

Kalle Landerholm, Maie Abdalla, Pär Myrelid and Roland Andersson, Survival of ileal pouch anal anastomosis constructed after colectomy or secondary to a previous ileorectal anastomosis in ulcerative colitis patients: a population-based cohort study, Scandinavian Journal of Gastroenterology, 2017. 52(5), pp.531-535.
Scandinavian Journal of Gastroenterology is available online at informaworldTM:
http://dx.doi.org/10.1080/00365521.2016.1278457

Survival of ileal pouch anal anastomosis constructed after colectomy or secondary to a previous ileorectal anastomosis in ulcerative colitis patients: a population-based cohort study

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Results presented at the European Society of Coloproctology (ESCP) Scientific and Annual Meeting in Milan, Italy 28-30 September 2016

Word count: 2,083

Keywords

- Ulcerative colitis
- Inflammatory bowel disease
- Ileal pouch anal anastomosis
- Ileoanal pouches
- Ileoanal reservoir
- Pelvic pouches
- Ileorectal anastomosis
- Restorative proctocolectomy
- Pouch failure
- Pouch survival

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Abstract

Objectives

Ileorectal anastomosis (IRA) affects bowel function, sexual function and reproduction less negatively than ileal pouch anal anastomosis (IPAA), the standard reconstruction after colectomy for ulcerative colitis (UC). In younger UC patients IRA may have a role postponing pelvic surgery and IPAA. The aim of the present study was to investigate the survival of IPAA secondary to IRA compared to IPAA as primary reconstruction, as this has not previously been studied in UC.

Patients and methods

All patients with UC diagnosis between 1960 and 2010 in Sweden were identified from the National Patient Registry. From this cohort, colectomized patients reconstructed with primary IPAA and patients reconstructed with IPAA secondary to IRA were identified. The survival of the IPAA was followed up until pouch failure, defined as pouchectomy and ileostomy or a diverting ileostomy alone.

Results

Out of 63,796 patients, 1,796 were reconstructed with IPAA, either primarily (n = 1,720) or secondary to a previous IRA (n = 76). There were no demographic differences between the groups, including length of follow up (median 12.6 (IQR 6.7–16.6) years and 10.0 (IQR 3.5–15.9) years, respectively).

Failure of the IPAA occurred in 103 (6.0%) patients with primary and in 6 (8%) patients after secondary IPAA (P = 0.38 logrank). The 10-year pouch survival was 94% (95% CI 93–96) for primary IPAA and 92% (81–97) for secondary.

Conclusion

Patients choosing IRA as primary reconstruction do not have an increased risk of failure of a later secondary IPAA in comparison with patients with primary IPAA.

Introduction

Despite recent medical advances in the treatment of ulcerative colitis (UC) there is still a need for surgical intervention in patients with fulminant or complicated acute colitis as well as in patients with chronic steroid dependency and in patients with dysplasia or cancer of the colon [1]. Colectomy with the rectum left *in situ* and diverted with an ileostomy is standard when operating on the severely ill and malnourished patient, who is often also on anti-inflammatory medical treatment. Later, when conditions for anastomotic healing have improved and the risk also for other complications is lower, reconstruction may be performed at a second operation. Patients with presence of severe dysplasia in biopsies, and in particular patients with proven adenocarcinoma, normally require proctocolectomy. In this more elective setting, reconstructive surgery may be undertaken already during the initial procedure.

The standard method for bowel reconstruction in UC is ileal pouch anal anastomosis (IPAA) at the same time as a completion proctectomy is performed. As an alternative, if the rectum responds to topical medication and patients are otherwise suitable, the rectum can be left *in situ* and a reconstruction performed by an ileorectal anastomosis (IRA). IPAA affects both bowel function and sexual function more negatively than IRA [2]. Surgery with IPAA also severely reduces fecundity in female UC patients [3] and familial adenomatous polyposis (FAP) patients [4]. The impact on fertility by IRA in UC patients is unknown, but IRA did not affect fecundity in women with FAP [4]. For these reasons, IRA may be preferable for younger patients as an interim procedure in order to postpone pelvic surgery with proctectomy and IPAA [1, 2].

When implementing such a strategy, with IRA as a bridging solution, it is crucial that the

outcome of IPAA secondary to IRA is not inferior to that of primary pelvic pouches. The fate of IPAA as a secondary reconstruction has been thoroughly studied in patients with FAP and both pouch survival and function were found to be similar to that of primary pouches [5-8]. By contrast, no previous study to our knowledge compared the outcome of primary and secondary IPAA in UC patients.

The present study aims to assess the long-term risk of failure of secondary versus primary IPAA in UC patients in a population-based cohort.

Methods

Setting

A unique personal identity number is assigned to all permanent Swedish residents allowing follow up in nationwide registers. The National Patient Register in Sweden holds data of diagnoses for diseases at discharge from hospitals or visits at outpatient clinics as well as performed operations.

Cohort

A population-based cohort of all patients in Sweden with a diagnosis of UC registered between January 1 1964 and December 31 2010 was identified from the National Patient Register using the following ICD codes; ICD7 572.20, 572.21, 578.03; ICD8 563.10, 569.02; ICD9 556*; ICD10 K51*.

From this cohort, patients operated with colectomy or proctocolectomy and patients operated with repeated segmental resections ending up with no remaining colon were

identified. Next, patients with a reconstruction in the form of an IRA (operation code 4650, JFH00, JFH01, JFC40, JFC41, JFG26 or JFG29) or an IPAA (operation code 4654, 4823, JFH30, JFH33, JGB50, JGB60 or JGB61) were identified.

Definitions

A primary IPAA was defined as an IPAA with no previous IRA. A secondary IPAA was defined as an IPAA constructed subsequent to a previous IRA.

IRA failure was defined as one or more of the following: occurrence of rectal cancer; proctectomy; formation of ileostomy, continent ileostomy (Kock pouch) or IPAA.

IPAA failure was defined as the removal of the IPAA (*i.e.* pouchectomy) or formation of a diverting ileostomy including continent ileostomy at a later date than the construction of IPAA. Patients with a redo IPAA after a previous IPAA were excluded from the study after their first failure.

Statistical Analysis

Continuous variables are summarized as median with interquartile range (IQR). Differences between groups were assessed using Mann Whitney U test. The Chi squared test and Fisher's exact test were used to test differences in proportions.

The risk for IPAA failure was assessed by survival analytic methods with Kaplan-Meier curves and log rank test. Follow up started on the date of admission for IPAA reconstruction and ended on the date of surgery for IPAA failure. Patients were censored in the survival analyses in the event of death or on 31 December 2010, whichever came first.

The analyses were carried out with Stata/IC 13.1 (StataCorp, College Station, TX, USA). Statistical tests were 2-sided and $P < 0.050$ was considered statistically significant.

Results

A cohort of 63,796 patients with UC diagnosis in Sweden between 1964 and 2010 was identified. IRA was constructed in 1,112 patients. The IRA failed in 265 patients during the study period and 10-year IRA survival was 72.7%. Starting in year 1985 1,796 patients underwent reconstruction with an IPAA, either primarily or secondary to a previous IRA. These patients were followed up for a total of 21,202 person years, with a median of 12.4 (IQR 6.5–16.6) years. The IPAA was the primary reconstruction in 1,720 (95.8%) patients, and secondary to a previous IRA in 76 (4.2%) patients (Fig. 1). There was no statistically significant difference in length of follow up between patients with primary and secondary pouches ($P = 0.12$; Table 1). As expected, the duration from the colectomy to construction of a secondary IPAA was longer (median 1.9 (IQR 0.8–4.8) years) than to construction of a primary IPAA (median 0.4 (IQR 0–1.0) years; $P < 0.001$). The interval between the construction of an IRA and construction of a secondary IPAA was 1.5 years in median (IQR 0.7–4.8 years). Demographic data for the groups are shown in Table 1.

Pouch survival

Failure of the IPAA defined as pouchectomy and ileostomy, or a diverting ileostomy alone, occurred in 103 (6.0%) patients with primary IPAA and in 6 (8%) patients after secondary IPAA (Fig. 1). It was more common to leave the failed pouch behind, only

diverting with an ileostomy, for both primary and secondary IPAA. Only two patients had a redo-IPAA after failure of a primary IPAA.

As evident from Fig. 2, the risk of IPAA failure was similar after primary and secondary reconstruction (P = 0.38 logrank). The 10-year pouch survival was 94% (95% CI 93–96) for primary IPAA and 92% (95% CI 81–97) for secondary (Table 2). The risk of pouch failure did not differ between men and women (P = 0.73 logrank).

Discussion

The frequency of colectomy in IBD patients has remained unaltered in Sweden despite the introduction of biological treatment [9]. Following colectomy, Nordenvall *et al* found that in recent years 43.4% of Swedish IBD patients in general and 44.7% of UC patients underwent reconstruction at some point during the study follow up [10]. IRA was the first available method for reconstruction but IPAA became the gold standard when it was introduced during the 1980s. Recently, IRA has regained lost ground in parts of the world as an alternative for UC patients [2]. In Sweden for instance, IRA has been performed as frequently as IPAA during the 2000s according to a previous study, both when performed concomitant to the resection and as a staged operation [10]. Continent ileostomy (Kock pouch) was far less frequently constructed. The present study confirms a steep increase in the use of IRA in recent years, but IPAA was still slightly more common for UC patients in Sweden between 2001 and 2010. The overall survival of IPAA in this nationwide study was high with 96, 94, and 92% of IPAAs remaining functioning after 5, 10, and 20 years of follow up, respectively. This is comparable to or even better than previous studies on UC patients from highly specialized referral centers

[11-14]. A recent population-based study of reconstructive surgery from Sweden defined failure differently and reported worse pouch survival [15]. The failure rate of IRA has been similar or somewhat higher than that of IPAA in non-randomized studies [14, 15]. The time between colectomy and secondary IPAA was found to be quite short in the present study (median 1.9 (IQR 0.8–4.8) years) indicating many early failures of IRA, most probably due to recurrent proctitis. In all, the risk of failure would therefore not seem a reason to opt for an IRA instead.

However, there may be other advantages to an IRA, for instance that construction of an IPAA is technically more demanding with more complications and usually requires a temporary, protective loop-ileostomy that must later be reversed [2]. Based on this, IRA can be a safer, possibly permanent reconstruction for elderly patients, as long as they are aware of the need for topical therapy and surveillance. IRA may also be preferable in younger patients in order to postpone an IPAA and pelvic surgery that may affect sex life and fecundity, particularly in women [3, 16-18]. Completion proctectomy may later be called for due to refractory proctitis, presence of dysplasia or cancer during surveillance or as a prophylactic measure. It is then important that the outcome of an IPAA constructed after a previous IRA is no worse than a *de novo* IPAA. As a main finding, this study found that the survival between primary and secondary IPAA did not differ when it comes to survival. Thus, in a selected cohort of patients another step can be added in the therapeutic ladder, possibly postponing the need for an indefinite ileostomy after IPAA failure. Despite the possibility to perform a redo pouch, the function and survival of a redo IPAA is worse than that of an IPAA performed at the same time as the completion proctectomy [19]. Another option is to do a Kock pouch, either re-using the failed IPAA or creating a *de novo* Kock pouch [20], but this procedure also has its

limitations [21]. For patients with early IPAA failure (4% during the first 5 years), and especially among the young, an interim solution with an IRA could still have been of value. Apart from postponing pelvic surgery, IRA may also delay the need for a permanent end ileostomy and add valuable time without a permanent stoma, but at the cost of an extra surgical procedure.

Using a population-based cohort from nationwide registries has the advantages of a large sample and the elimination of referral bias. The National Patient Registry was recently evaluated and found to have a positive predictive value between 85 and 95 % regarding the reliability of diagnoses and procedures [22]. However, registry studies also bear certain limitations such as the restricted amount of data available for each patient. Although no obvious differences were identified between patients with a primary and a secondary IPAA, we cannot rule out selection bias when deciding which patient was suitable for a secondary reconstruction. This could mean that for a few patients IPAA would have been feasible as a first reconstruction but was no longer an option after the IRA. Furthermore, there was no data on the type of pouch construction. In a previous study on FAP patients, W pouches were more common as a primary reconstruction whereas J pouches were preferred as a secondary reconstruction [6]. This could be due to altered preferences of the technique between different time periods, but could also have implications for the function of the IPAA. A comparison of function and quality of life between primary and secondary IPAA in UC mandates future studies.

The risk for cancer with IRA in UC patients means weighing pros and cons for each patient with the information at hand. We recently described that the risk for rectal cancer with an IRA in UC patients is associated with a significant increase in the relative

risk for rectal cancer compared to IPAA, but that in absolute numbers only 2.2% of patients with IRA develop cancer with adequate surveillance [23]. This, together with the present finding that patients choosing IRA as primary reconstruction do not risk worse outcome of a later secondary IPAA compared to a primary, lends support to IRA as an alternative to IPAA for reconstruction after colectomy in UC patients.

Ethical considerations

The study was approved by the Regional Ethical Review Board at Linköping University, Sweden.

Disclosure of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

Funding

This work was supported by grants from Bengt Ihre's Fund; Medical Research Council of Southeast Sweden; and Futurum – Academy for Health and Care, Region Jönköping County, Sweden. In addition, Kalle Landerholm is a fellow in Bengt Ihre Research Fellowship during 2016 and 2017.

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	IRA	IPAA			*P**
		Total	**Primary**	**Secondary**	
No. patients	1,112	1,796	1,720	76	
No. per period (%)					
1964-1979	90 (100)	0	0	0	
1980-1989	222 (53.0)	197 (47.0)	187	10	
1990-1999	208 (18.8)	897 (81.2)	868	29	
2000-2010	592 (45.7)	702 (54.3)	665	37	
Age at reconstruction	39.3 (28.0–51.9)	36.9 (28.2–45.8)	36.8 (28.2–45.8)	38.6 (28.8–48.0)	0.31
Duration of IBD at reconstruction	3.0 (0.7–8.7)	3.2 (1.2–8.2)	3.1 (1.2–8.1)	6.1 (2.2–11.7)	0.002
Time from colectomy to reconstruction	0.0 (0.0–0.5)	0.4 (0.0–1.0)	0.4 (0.0–1.0)	1.9 (0.8–4.8)	< 0.001
Male sex, %	57.3	62.3	62.6	54.0	0.13
Failure (%)	265 (23.8)	109 (6.1)	103 (6.0)	6 (8)	0.50
Follow up	5.2 (1.6–11.6)	12.4 (6.5–16.6)	12.6 (6.7–16.6)	10.0 (3.5–15.9)	0.12

Table 1 Patient characteristics. Age, duration of IBD, time from colectomy and follow up given as years in median (IQR) at time of reconstructive surgery.

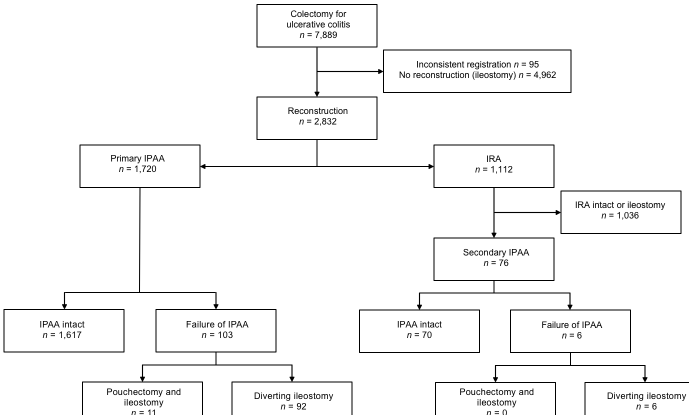
* Primary versus secondary IPAA

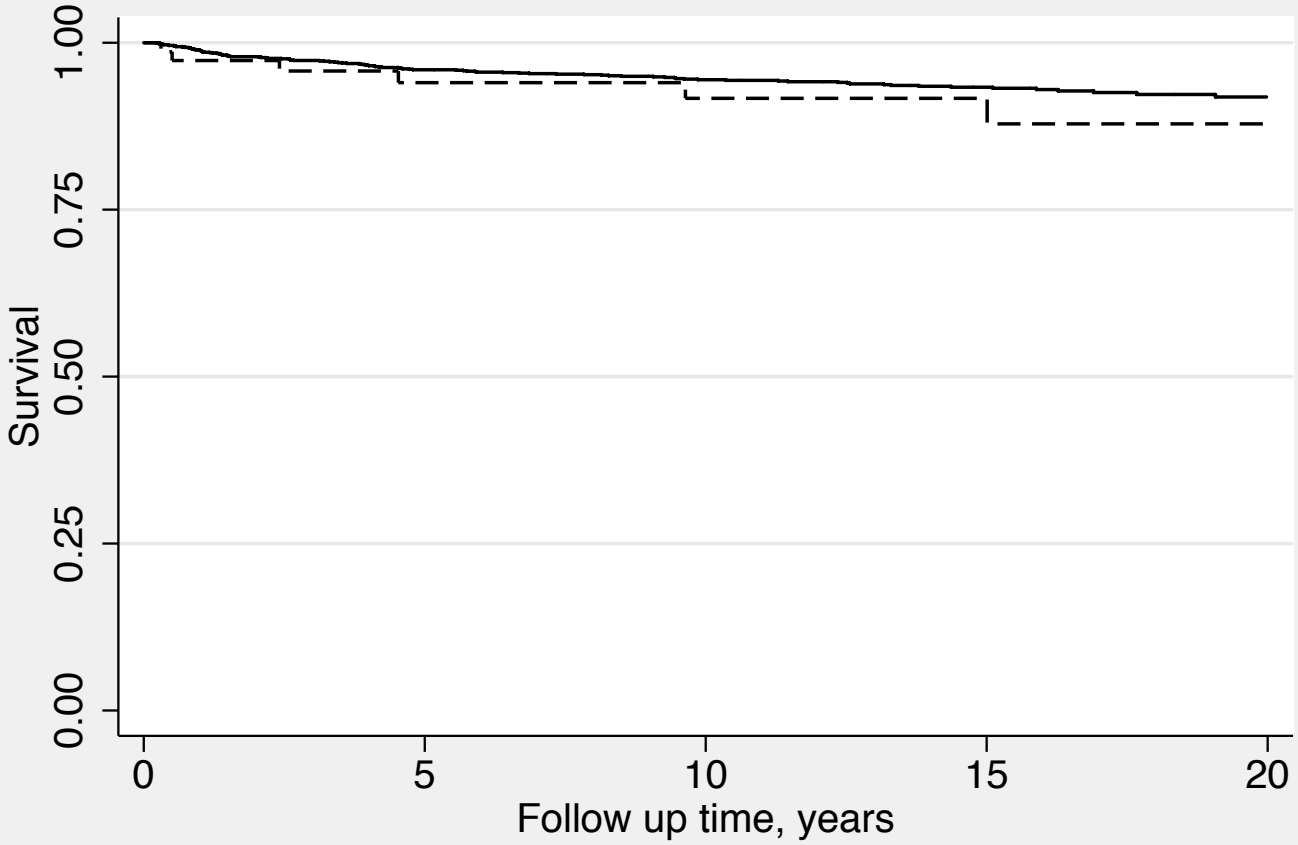
Patency, % (95% CI)	All	Primary	Secondary
5 year	96 (95–97)	96 (95–97)	94 (85–98)
10 year	94 (93–95)	94 (93–96)	92 (81–97)
20 year	92 (90–93)	92 (90–93)	88 (73–95)

Table 2 Cumulative survival of primary and secondary IPAA

Figure 1 Overview of patients with reconstructive surgery for ulcerative colitis in Sweden. Ileostomy includes continent ileostomy (kock pouch).

Figure 2 Long-term survival of primary and secondary IPAA shown as Kaplan-Meier survival curves (P = 0.38 logrank).


Colectomy for ulcerative colitis
n = 7,889
Inconsistent registration n = 95
No reconstruction (ileostomy) n = 4,962
Reconstruction
n = 2,832
Primary IPAA
n = 1,720
IRA
n = 1,112
IRA intact or ileostomy
n = 1,036
Secondary IPAA
n = 76
IPAA intact
n = 1,617
Failure of IPAA
n = 103
IPAA intact
n = 70
Failure of IPAA
n = 6
Pouchectomy and ileostomy
n = 11
Diverting ileostomy
n = 92
Pouchectomy and ileostomy
n = 0
Diverting ileostomy
n = 6



Number at risk

Primary	1720	1386	1063	600	194
Secondary	76	53	38	24	9

Primary Secondary