Update of complications and functional outcome of the ileo-pouch anal anastomosis: overview of evidence and meta-analysis of 96 observational studies

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Abstract

Objective The objective of this study is to provide a comprehensive update of the outcome of the ileo-pouch anal anastomosis (IPAA).

Data sources An extensive search in PubMed, EMBASE, and The Cochrane Library was conducted.

Study selection and data extraction All studies published after 2000 reporting on complications or functional outcome after a primary open IPAA procedure for UC or FAP were selected. Study characteristics, functional outcome, and complications were extracted.

Data synthesis A review with similar methodology conducted 10 years earlier was used to evaluate developments in outcome over time. Pooled estimates were compared using a random-effects logistic meta-analyzing technique. Analyses focusing on the effect of time of study conductance, centralization, and variation in surgical techniques were performed.

Results Fifty-three studies including 14,966 patients were included. Pooled rates of pouch failure and pelvic sepsis were 4.3% (95% CI, 3.5–6.3) and 7.5% (95% CI 6.1–9.1), respectively. Compared to studies published before 2000, a reduction of 2.5% was observed in the pouch failure rate (p=0.0038). Analysis on the effect of the time of study conductance confirmed a decline in pouch failure. Functional outcome remained stable over time, with a 24-h defecation frequency of 5.9 (95% CI, 5.0–6.9). Technical surgery aspects did not have an important effect on outcome.

Conclusion This review provides up to date outcome estimates of the IPAA procedure that can be useful as reference values for practice and research. It also shows a reduction in pouch failure over time.

Keywords Functional outcome · Ileo-pouch anal anastomosis · Meta-analysis

Introduction

Restorative proctocolectomy by means of an ileo-pouch anal anastomosis (IPAA) is the procedure of choice for the surgical treatment of ulcerative colitis (UC) and familial adenomatous polyposis (FAP). The IPAA procedure generally results in acceptable long-term functional outcomes and improvement of quality of life. It is, however, associated with substantial morbidity with complications up to 50% of patients [1]. Since its introduction in 1978, the IPAA procedure has continuously been subjected to attempts of improvements in technique [55]. Additionally, much has been achieved in improving the perioperative care. Centralization of complex surgery has been a recent development in many countries. All these developments may have resulted in improved outcomes.
A large number of observational studies have reported outcomes of the IPAA procedure, most commonly from a selected group of patients in one hospital. This review aims to provide an overview of the available evidence and to evaluate the effect of the continuous developments on outcomes. Previously, a systematic review summarizing complications and functional results after an IPAA procedure in studies published until 2000 was conducted. This current systematic review provides an update regarding the outcomes of the IPAA procedure and uses the combined data set of both reviews to analyze changes in the outcomes of the IPAA procedure.

Methods

This systematic review aims to provide an overview regarding the outcomes of the open IPAA procedure. Additionally, it evaluates the effect of development of practice on the most important outcomes over time.

Search strategy

A systematic literature search with predefined search terms was carried out in four electronic databases: Medline (1–1–2000 to 1–1–2010), EMBASE (1–1–2000 to 1–1–2010), and the Cochrane Library (Issue 1, 2010) (Fig. 1). Two authors (SZ and UAA) independently performed the selection of the publications according to inclusion criteria. Disagreements were discussed with a third reviewer (FK). Additional relevant studies were looked for by cross-reference checking of all included studies. Language restrictions were not applied.

Selection of studies

Inclusion criteria

Title and abstract of all identified publications (prospective and retrospective and observational and comparison studies) were screened according to the following inclusion criteria: The study population consists of adult patients with established UC or FAP undergoing a primary IPAA procedure; the intervention is a clearly documented open IPAA procedure in an elective setting with or without a diverting ileostomy and irrespective of the number of stages of the operation; the study reports at least one of the primary outcomes reported below; and the study includes a consecutive series with a minimal sample size of 50 patients.

Exclusion criteria

Studies were excluded from this systematic review if they included children (<18 years) or primarily elderly patients (>65 years). Studies were excluded as well when the IPAA was performed for other indications than UC or FAP (e.g., Morbus Crohn) or when a secondary IPAA was performed (e.g., after ileo-rectal anastomosis). Studies were also excluded when there was selective outcome reporting, i.e., studies focusing on one parameter (e.g., pouchitis) without reporting of any additional outcomes.

Outcomes of interest and definitions

Primary outcomes were pouch failure, pelvic sepsis, and severe day incontinence. Secondary outcomes included other complications (stricture, fistula, small bowel obstruction, pouchitis, and sexual dysfunction) and parameters of functional outcome (defecation frequency and incontinence). Table 1 shows the definitions of all outcomes.

Data extraction

After assessment for eligibility, two authors (SZ and UAA) independently extracted the following data if available: numbers of patients, patient characteristics, dates of start and end of the inclusion period, duration of follow-up,
variations in surgical technique, numbers and type of complications, and parameters of pouch functional outcome. Authors were contacted when data were missing. One author provided updated unpublished information [66]. Double publications describing identical populations were considered as one study.

Data of studies published until 2000

Previously, a systematic review was performed summarizing complications and functional results after an IPAA procedure in studies published until 2000 [39]. For time-frame analyses regarding the development of clinical practice and its effect on outcomes, data from both reviews were combined. Both reviews were conducted with similar methodology, and the full data set from the previous review was available.

Statistical analysis

Relevant study characteristics and outcomes were extracted and presented for each study individually. Outcomes were subsequently pooled, and cumulative probabilities were calculated with 95% confidence intervals (95% CI). Data were pooled using a “random-effects model, based on the restricted maximum likelihood estimator in order to incorporate the heterogeneity between studies. Pooled results of this review (all studies published since 2000) were compared with pooled results of the previously published review (all studies published before 2000) by analyzing the complete set in one random-effects model and incorporating a dummy variable that coded for period. The Knapp and Hartung adjustment was used to obtain estimates and confidence intervals [33]. Additionally, analysis focusing on the effect of time of study conductance, centralization, and variation in techniques were performed using linear regression and one-way ANOVA as appropriate. Data management and statistical analyses were conducted using SPSS (version 15) and R Statistical Software (R Development Core Team, version 2.11.1) with the metafor package [52, 70].

Results

Selection process

The search resulted in a total of 10,301 hits. Initial selections based on titles identified 236 potentially relevant articles. Further selections based on abstracts excluded 142 studies. The full text of the remaining 94 studies was evaluated. Finally, a total of 53 studies with 14,966 patients were included (Fig. 1).

Description of identified studies

The most important characteristics of the included studies are presented in Table 2. Most studies were retrospective cohort studies (70%). The median sample size was 127 (range, 50–2,490) over a median inclusion periods of 12 years (range, 4–30). A diverting ileostomy was used in 79% (range, 5–100%) of all the IPAA procedures. A hand-sewn anastomosis was used in 40% of the procedures (range, 0–100%). Median duration of follow-up was 75 months (range, 6–180). Thirty-one studies mentioned postoperative mortality with a median of 0% (range, 0–2.9%).

Outcomes

Complications

Data on complications were available from all 53 studies. We found a pooled incidence of pouch failure of 4.3% (95% CI, 3.5–6.3; Fig. 2). A sensitivity analysis including only studies with minimal follow-up of 5 years showed a pouch failure rate of 4.7%. The pooled incidence of pelvic sepsis was 7.5% (95% CI, 6.1–9.1; Fig. 3). Pooled incidence rates for other important complications are presented in Table 3.

Functional results

Data on functional results after IPAA were available from 26 studies including 5,321 patients. The pooled incidence of mild and severe fecal incontinence during the day was 14.3% (%CI, 7.3–25.9) and 6.1% (2.9–12.3), respectively (Table 3). Mean defecation frequency was 5.9 (4.9–6.7) per 24 h with a mean nighttime frequency of 1.5 (1.0–2.1).

Comparison with studies published before 2000

The previous review of studies published before 2000 identified 43 studies with a total of 9,317 patients [33]. Median duration of follow-up was 36.7 months (range, 12–99). Detailed discussion of the characteristics of these studies is published elsewhere [33].

Table 1 Definition of outcomes

| Outcome               | Definition                                                                 |
|-----------------------|---------------------------------------------------------------------------|
| Pouch failure         | Pouch excision or a nonfunctioning pouch at 12 months after IPAA           |
| Pelvic sepsis         | Pelvic abscess, anastomotic leakage or dehiscence, pelvic/perineal wound infection |
| Fistula               | Any pouch-related fistula                                                 |
| Stricture             | Anastomotic fibrosis necessitating dilatation                              |
| Mild fecal incontinence| Soiling, spotting in underwear                                            |
| Severe fecal incontinence| Regularly severe leakage or fecal loss passive fecal incontinence        |
### Table 2 Characteristics of studies and selected outcomes following IPAA in the 53 included studies published since 2000

| Author | Year of publication | Inclusion period | Number of patients | FU (months) | Age Gender (% female) | Type of disease | Handsewn anastomosis (%) | With diverting ileostoma (%) |
|--------|---------------------|------------------|--------------------|-------------|-----------------------|----------------|--------------------------|-----------------------------|
| Fonkalsrud et al. [20] | 2000 | 1993–1997 | 77 | 34.5 | 50 | UC | 57.1 | 100 |
| Karlbom et al. [36] | 2000 | 1983–1996 | 168 | 32 | 39.3 | UC | 58.9 | 70.8 |
| Seidel et al. [60] | 2000 | 1985–1996 | 55 | 31.2 | 45.5 | Both | | |
| Simchuk [61] | 2000 | 1987–1996 | 114 | 38 | 43.9 | UC | 58.9 | 70.8 |
| Gullberg and Lüjeqvist [25] | 2001 | 1990–1995 | 86 | 34.1 | 45.3 | Both | | |
| Barton et al. [5] | 2001 | 1983–2000 | 110 | 30 | 36.8 | UC | 100 | 66.7 |
| Heuschen et al. [29] | 2001 | 1991–2000 | 171 | 30 | 36.7 | UC | 100 | 66.7 |
| Regimbeau et al. [53] | 2001 | 1984–1998 | 172 | 36 | 47.1 | Both | 100 | 100 |
| Blumberg et al. [12] | 2001 | 1982–1995 | 154 | 151 | 34 | Both | 64 | |
| Dayton et al. [16] | 2002 | 1987–1996 | 114 | 38 | 43.9 | UC | 100 | 100 |
| Rossi et al. [56] | 2002 | 1989–2000 | 75 | 40 | 33.3 | Both | 54.7 | 100 |
| Bullard et al. [13] | 2002 | 1980–1992 | 154 | 151 | 34 | Both | 64 | |
| Gullberg and Liljeqvist [25] | 2001 | 1990–1995 | 86 | 34.1 | 45.3 | Both | 2.3 | |
| Barton et al. [5] | 2001 | 1983–2000 | 110 | 30 | 36.8 | UC | 100 | 66.7 |
| Heuschen et al. [29] | 2001 | 1991–2000 | 171 | 30 | 36.7 | UC | 100 | 66.7 |
| Regimbeau et al. [53] | 2001 | 1984–1998 | 172 | 36 | 47.1 | Both | 100 | 100 |
| Blumberg et al. [12] | 2001 | 1982–1995 | 154 | 151 | 34 | Both | 64 | |
| Dayton et al. [16] | 2002 | 1987–1996 | 114 | 38 | 43.9 | UC | 100 | 100 |
| Rossi et al. [56] | 2002 | 1989–2000 | 75 | 40 | 33.3 | Both | 54.7 | 100 |
| Bullard et al. [13] | 2002 | 1980–1992 | 154 | 151 | 34 | Both | 64 | |
| Gullberg and Liljeqvist [25] | 2001 | 1990–1995 | 86 | 34.1 | 45.3 | Both | 2.3 | |
| Barton et al. [5] | 2001 | 1983–2000 | 110 | 30 | 36.8 | UC | 100 | 66.7 |
| Heuschen et al. [29] | 2001 | 1991–2000 | 171 | 30 | 36.7 | UC | 100 | 66.7 |
| Regimbeau et al. [53] | 2001 | 1984–1998 | 172 | 36 | 47.1 | Both | 100 | 100 |
| Blumberg et al. [12] | 2001 | 1982–1995 | 154 | 151 | 34 | Both | 64 | |
| Dayton et al. [16] | 2002 | 1987–1996 | 114 | 38 | 43.9 | UC | 100 | 100 |
| Rossi et al. [56] | 2002 | 1989–2000 | 75 | 40 | 33.3 | Both | 54.7 | 100 |
| Bullard et al. [13] | 2002 | 1980–1992 | 154 | 151 | 34 | Both | 64 | |
| Gullberg and Liljeqvist [25] | 2001 | 1990–1995 | 86 | 34.1 | 45.3 | Both | 2.3 | |
| Barton et al. [5] | 2001 | 1983–2000 | 110 | 30 | 36.8 | UC | 100 | 66.7 |
| Heuschen et al. [29] | 2001 | 1991–2000 | 171 | 30 | 36.7 | UC | 100 | 66.7 |
| Regimbeau et al. [53] | 2001 | 1984–1998 | 172 | 36 | 47.1 | Both | 100 | 100 |
| Blumberg et al. [12] | 2001 | 1982–1995 | 154 | 151 | 34 | Both | 64 | |
We compared incidences of the most important complications reported in studies published prior to 2000 versus the incidences reported in studies published since 2000 (Table 3). Pouch failure decreased between the two time periods from 6.8% to 4.3% \((p=0.0038)\). Pelvic sepsis showed a decrease from 9.5 to 7.4% \((p=0.1284)\). Other complications and the functional results showed no significant differences between the two groups of studies.

The effect of time of study conductance on IPAA outcomes

Results of both reviews were combined to analyze the effect of time of study conductance on the outcomes of the IPAA procedure. For this, the relationship between the median year of inclusion of each study and the outcomes observed in that study was evaluated. Regression analysis showed that studies with an earlier median year of inclusion have a higher rate of pouch failure than studies with a more recent median year of inclusion \((p<0.001)\). Figure 4 is a scatter plot depicting this relationship. In a sensitivity analysis excluding the five studies with a pouch failure rate of >12.5%, the relationship remained statistically significant \((p=0.009)\). Additionally, we categorized the median year of inclusion of all studies (published before and after 2000) into four interquartile ranges in order to evaluate the median rate of pouch failure over these four time periods. Figure 5 shows a consecutive decline in the pouch failure rate over these time periods \((p=0.005\), one-way ANOVA analysis).
Centralization: trends over time

The median inclusion rate for all studies was 14 patients per year (range from 2.9 to 105). We evaluated the effect of time of study conductance (median year of inclusion) on the inclusion rate (Fig. 6). The figure shows that between 1991 and 2000, an increase was seen in studies from centers including less than one patient per month, from eight studies

**Table 3** Pooled incidences of complications and functional outcome following an IPAA procedures in studies published since 2000 compared to studies published before 2000

|                      | Since 2000 | Before 2000 | P value |
|----------------------|------------|-------------|---------|
|                      | Number of studies | Number of patients | Pooled incidences | Number of studies | No. of patients | Pooled incidences |
| Complications        |            |             | % (95% CI) |            |             | % (95% CI) |
| Pouch failure        | 43         | 13,249      | 4.3 (3.5–5.3) | 39         | 8,877       | 6.8 (5.8–8.4) | 0.0038    |
| Pouch failure: FU>5 years | 22       | 9,873       | 4.7 (3.4–6.4) | 11         | 3,198       | 8.5 (5.4–13.2) |
| Pelvic sepsis        | 46         | 13,450      | 7.5 (6.1–9.1) | 41         | 9,082       | 9.5 (8.2–10.9) |
| Fistula              | 38         | 12,398      | 4.5 (3.5–5.7) | 30         | 5,120       | 5.5 (4.3–7.0)  | NS        |
| Stricture            | 35         | 12,219      | 10.7 (8.2–13.8)| 28         | 5,185       | 9.2 (6.8–12.4) | NS        |
| Pouchitis            | 39         | 12,685      | 26.8 (21.0–33.5) | 33         | 7,289       | 18.8 (15.7–22.4) | NS        |
| Sexual dysfunction   | 13         | 6,131       | 3.0 (1.7–5.2)  | 21         | 5,112       | 3.6 (2.7–4.7)  | NS        |
| Small bowel obstruction | 34     | 11,895      | 11.4 (9.1–14.1)| 27         | 5,853       | 13.1 (11.0–15.7) | NS        |
| Fecal incontinence   |            |             | % (95% CI) |            |             | % (95% CI) |
| Mild day incontinence| 21         | 6,988       | 14.3 (7.3–25.9) | 31         | 4,313       | 17.0 (12.8–22.2) | NS        |
| Severe day incontinence | 13    | 3,718       | 6.1 (2.9–12.3) | 27         | 3,914       | 3.7 (2.8–4.8)  | NS        |
| Mild night incontinence | 9       | 5,423       | 17.3 (4.7–46.8) | 17         | 2,582       | 13.1 (9.5–17.9) | NS        |
| Severe night incontinence | 10    | 3,614       | 7.6 (2.5–21.3) | 9          | 1,271       | 4.5 (3.0–6.7)  | NS        |
| Frequency             |            |             | Mean (95% CI) |            |             | Mean (95% CI) |
| Frequency day         | 26         | 5,321       | 5.7 (4.9–6.7)  | 13         | 2,277       | 5.2 (4.0–6.7)  | NS        |
| Frequency night       | 22         | 7,117       | 1.5 (1.0–2.1)  | 20         | 2,950       | 1.0 (0.6–1.6)  | NS        |
| Frequency 24 h        | 26         | 5,132       | 5.9 (5.0–6.9)  | 20         | 3,547       | 5.2 (4.4–6.1)  | NS        |

CI confidence interval, FU follow-up period

**Fig. 4** Scatter plot depicting the median year of inclusion and the rate of pouch failure of studies included in both reviews.
(30%) before 1991 to 23 studies (46%) between 1991 and 2000. It also shows that there are not yet enough studies available that have been conducted after 2000 to draw conclusions about the current situation. Analysis of the effect of the inclusion rate on the outcomes of the IPAA did not show any benefit on the outcomes of the IPAA.

Technical aspects of the IPAA

Overall, 43 out of 78 studies (55%) used a protective ileostomy as a routine part of the IPAA procedure (routine use defined as ileostomy performed in more than 80% of patients). The percentage has decreased from almost 70% (16 out of 23) in studies conducted between 1980 and 1990 to 47% (21 out of 44) in studies conducted after 1990. The number of studies performing an ileostomy in <50% of patients increased from 11% to 32% over the same periods. The rate of ileostomy was not associated with any of the outcomes of the IPAA. Type of anastomosis (hand-sewn vs. stapled) was only available from 31 studies published since 2000 (the previous review did not register this characteristic). Fifteen studies (48%) still performed a hand-sewn anastomosis in more than 50% of
patients. There were no differences in functional outcome or complications between studies performing different types of anastomosis.

Discussion

The open IPAA operation is the most common surgical reconstruction procedure in patients with UC and FAP. Randomized trials on IPAA are rare [1] due to low incidences as well as the complexity of patient selection and the intervention. Therefore, most studies are retrospective case series. Estimates of the outcomes of the IPAA procedure vary considerably. Acceptable complication and functional outcome rates are, therefore, difficult to set. This systematic review provides up to date and reliable incidences of important outcomes of the IPAA procedure, which could provide a reference values for these outcomes. Additionally, this review may provide insights in changes of practice over time and their effects on outcomes.

Several important finding are provided. First, it shows that the rate of pouch failure after an IPAA procedure has declined continuously over time. This decline was larger in the earlier period of the IPAA but seems to continue over time. Secondly, a large proportion of studies with this complex type of surgery are conducted in centers that include less than one patient per month. Thirdly, the functional outcome of the IPAA seems not to improve over time, despite several developments in surgical technique and perioperative care. This may represent an intrinsic limitation of the IPAA technique regarding functional outcome.

This review has some limitations. First, many of the included studies are retrospective cohort series, which may limit the reliability of the results. However, the overwhelming majority of the evidence in this field consists of this type of studies. This review provides an overview of this evidence, thereby increases its utility for clinicians and researchers. Moreover, the statistical techniques used are rather conservative to allow for incorporation of the heterogeneity of the studies.

Second, publication bias is a factor that should be taken into consideration. For this purpose, we excluded series with <50 patients. Studies with a small sample size do not only increase heterogeneity of results but are also more subject to publication bias; i.e., small studies with “unfavorable” results are less likely to get published. By introducing a threshold, we aimed to prevent including small studies with overestimated intervention effects.

Finally, the lack of individual patient data limits the analyses that could be performed. For example, many studies report a cohort in which several types of operative techniques have been used (e.g., several types of anastomoses). This prohibits analyzing the effect of variations in technique on a patient level, since only aggregate outcomes of the complete cohorts are available. Collecting individual patient data of these large numbers of studies, especially considering the dated studies, is not feasible. We, therefore, limited our analyses to factors that could be analyzed reliably on an aggregate level.

Many factors may have contributed to the reduction of the rate of pouch failure observed. The additional analyses in this review were unable to pinpoint factors responsible for the observed reduction in pouch failure. This is probably caused by the lack of individual patient data (as discussed above), and we believe that general improvements in care over the past decades and the increased experience of surgeons with this approach are the most important factors contributing to this finding.

Another explanation that could be considered is the variation in the surgical techniques that have been introduced and sometimes largely employed over the last decades. Such variations include the various types of pouches used and the use of the double-stapled anastomosis. The routinely constructed deviating ileostoma does not seem to improve the frequency of postoperative complications but only their severity. Despite comparative studies and several large meta-analyses published previously, none of these variations in technique could be identified as factors associated with the reduction of postoperative complications, including pouch failure. [45, 69] This is in line with the findings in this review.

Fewer studies reported on other outcomes, which decreased the power of the analyses concerning these other outcomes. Secondly, it could be that the observed decrease in the rate of pouch failure may be, at least in part, a result of smaller decreases in various other postoperative complications. Complications like pelvic sepsis, fistulae, and strictures could all result in pouch failure, provided they were severe enough. Smaller decreases in these outcomes can be difficult to show statistically. Overall, however, they may have caused the observed substantial decrease in pouch failure rate.

Recently, discussions on the relation between volume of complex surgical interventions and outcomes have gained wide attention [7, 17, 27, 37]. Certain complex surgical interventions have been centralized in high-volume hospitals with improved outcomes [9–11, 31]. Centralization still has to be reflected in the data in the years to come. Therefore, this review was unable to evaluate the potential influence of this development on current practice. However, in the period from 1991 to 2000, nearly 50% of studies were performed in “low inclusion rate” centers (including less than one patient per month). This is a substantial increase from the 30% observed in the period from 1980 to 1990. Taking into account that we only included series of 50 patients or more (Fig. 1) may mean that the true proportion...
of studies conducted in such “low inclusion rate” centers may be much higher. With the repeatedly established relationship between volume and outcome in several fields of surgery, this is a troublesome observation. Centralization of the complex IPAA procedure may offer a way to further improve outcomes in future.

Finally, we found no statistically significant differences in pooled estimates of the functional outcome over time. There were also no differences in functional outcomes between various surgical factors studied in this review. This is in agreement with findings in literature showing no benefits in terms of functional outcome of technical developments of the IPAA procedure, like type of anastomosis [59] or laparoscopic approach [1]. In most patients, however, functional outcome of the IPAA is considered to be highly satisfactorily, allowing for an acceptable quality of life and social functioning [28, 65]. Therefore, reducing complications, especially severe complications like pelvic sepsis and pouch failure, seems to be a more important goal for future surgical developments.

Conclusions

This systematic review and meta-analysis summarizes the available evidence and provides up to date estimates for complications and functional outcome after an IPAA procedure that can be useful as reference values for practice and research. It also shows a reduction in pouch failure over time in patients operated on using the IPAA procedure. The functional results remain unchanged over time and between various operative factors.

Acknowledgment  We did not receive any financial or material support for the research and the work. The first two authors have full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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