Chapter 3

PROSPER: A Randomised Comparison of Surgical Treatments for Rectal Prolapse

Senapati A, Gray RG, Middleton LJ, Harding J, Hills RK, Armitage NC, Buckley L, Northover JM. PROSPER Collaborative Group. Colorectal Dis. 15(7):858–868, 2013

Reviewed by Emily Steinhagen

Research Question/Objective Rectal prolapse is a surgical problem that is not well understood or described. There are no reliable estimates regarding its prevalence, and the number of procedures performed for prolapse annually is not known. Many different procedures can be used to address prolapse both from the abdominal approach and through perineal procedures. Limited high-quality data are available to compare the risks and benefits of the various procedures for rectal prolapse. A 2008 Cochrane review had only 380 patients in 12 randomized studies[1] with variations in inclusion criteria and procedures performed. The aim of the PROSPER study was to create high-quality evidence comparing procedures for rectal prolapse that include longer follow-up and patient-related outcomes.

Study Design PROSPER is a multicenter prospective, randomized trial that the authors describe as pragmatic and factorial. Patients could be randomized to either abdominal or perineal surgery and then, within their groups, randomized to either suture rectopexy or resection and rectopexy for the abdominal group and to either the Altemeier or Delorme procedure for the perineal surgery group. Once patients were enrolled, surgeons could opt out at either the first or second randomization and select patients to be in either the abdominal or perineal group but then randomized within that group in the second step of randomization. Randomization was performed electronically, controlling for age, level of incontinence, and preoperative physiologic status. A mentoring system was in place for surgeons who lacked experience with any of the techniques, and a video was provided to assist in training. Abdominal procedures could be performed open or laparoscopically.

The primary outcome was recurrence of prolapse. The other outcomes were inconvenience, bowel function, and quality of life as measured by Vaizey incontinence score[2] and EuroQol Group 5-Dimension Self-Report Questionnaire (EQ-5D).[3] The Vaizey incontinence score ranges from 0 (perfect) to 24 (totally incontinent), and the EQ-5D scores range from −0.59 (worst state) to 1.0 (perfect health). The study design included a follow-up duration of 3 years. The other outcome measures that were collected included morbidity and mortality, overall

DOI: 10.1201/9780429285714-3

bowel function on a 0–100 scale, frequency of bowel motions, straining, incomplete emptying, use of laxatives, suppositories, and enemas, and resource use. The assessments were done by clinicals at 6 weeks, 1 year, and 3 years after surgery. In addition, patients were mailed a modified questionnaire for self-completions. The research team attempted to contact patients by letters and phone if they did not return questionnaires.

The PROSPER study was powered to detect a 5% difference in recurrence, set at 10% versus 5% between the abdominal procedures and perineal procedures; this would have required 950 patients. However, this was later decreased to 300 patients due to slow enrollment. The aim was also revised from comparing recurrences to detecting meaningful difference in quality of life or Vaizey scores. and the new power analysis required 230 patients to detect a 0.37 standard deviation, considered a moderate to small difference with 80% power. The revised recruitment target would only enable detection of large differences in recurrence rates. The analyses were performed on an intention-to-treat basis. Scores on the quality of life measures were analyzed with inclusion of covariant including baseline scores. Recurrence rates were used to create Kaplan–Meier plots that were censored by last follow-up date or form completed or by date of death, withdrawal, or loss of follow-up.

Sample Size The study enrolled 293 patients over 7 years. They were recruited from 30 centers in the UK, and 1 each in India, Serbia, Spain, and Finland.

Follow-Up The authors planned to follow the patients at 6 weeks, 1 year, and 3 years with a clinician but had provisions to mail surveys for other patients who did not come for in-person follow-up.

The research team attempted to contact patients by letters and phone if they did not return questionnaires.

Inclusion/Exclusion Criteria The inclusion criteria for this study was full-thickness rectal prolapse. The protocol states that patients should have a rigid sigmoidoscopy; all other studies are at the discretion of the operating surgeon. No exclusion criteria are noted in the protocol or the manuscript.

Intervention or Treatment Received There were 49 patients who were randomized in step 1, abdominal versus perineal approach. For the remainder, the surgeon selected the approach and then they were randomized within the approach for step 2 only. For those undergoing perineal procedures, 213 patients were randomized between the Altemeier and Delorme procedures; in the group that underwent abdominal procedures, 78 were randomized between suture and resection rectopexy. Of these 293 randomized patients, 270 underwent surgery and 91% underwent the assigned procedure.

Results Patients who underwent perineal procedures were older and were described as having worse physical status and bowel function preoperatively. The average age for patients who were assigned by their surgeons to abdominal versus perineal procedures was 73 years for perineal procedures and 58 for abdominal procedures. Of the patients who were randomized between abdominal and perineal procedures, the median age was 63.

In terms of recurrences, in the perineal group, the rate of recurrence after Altemeier was 24% compared with 31% for Delorme, but this was not statistically significant (HR 0.81; 95% CI 0.47–1.38, $p = 0.4$). In the abdominal group, recurrence after resection rectopexy was 13% compared with 26% after resection rectopexy; again, this was not statistically significant (HR 0.45; 95% CI 0.14–1.45, $p = 0.2$). When comparing between abdominal and perineal procedures, there were no differences in recurrence between the group; 19% after abdominal procedures compared with 28% after perineal procedures ($p = 0.2$).

For patients who underwent perineal procedures, there were improvements in Vaizey incontinence, bowel function, and EQ-5D scores from baseline to 6 weeks, and this was maintained at 1 and 3 years. The two perineal procedures, Altemeier and Delorme, did not differ in the degree of improvement. The only measure that differed between the two groups was the number of outpatient hospital visits at 6 weeks and 3 years.

Similarly, patients who underwent abdominal procedures had improvements in Vaizey incontinence, bowel function, and EQ-5D scores from baseline to 6 weeks, and this was maintained at 1 and 3 years. No differences were detected between the suture rectopexy and the resection rectopexy groups. The only measure that had a difference between the groups during follow-up was more laxative use in the suture rectopexy group.

When comparing the abdominal procedures to perineal procedures, there were no differences between the groups with all having improvement from baseline in the primary end points. There were a few differences in the secondary end points, with more patients in the abdominal group reporting straining at 1 and 3 years follow-up), more visits by a social worker at 6 weeks, and patients spending more time in a hospital and visiting their general practitioner at 1 year.

Patients who experienced recurrence had much lower EQ-5D scores at 1 year than those who did not (0.23 points; 95% CI 0.10–0.37, $p = 0.0009$).

There were 5 treatment-related deaths in the study; the 4 who died following a perineal procedure (1 each) died of myocardial infarction, chest infection/renal failure, sepsis due to anastomotic leak, and a ruptured aortic aneurysm on postoperative day 2. There was 1 death in the abdominal group; a patient

randomized to resection rectopexy who received suture rectopexy had peritonitis and died.

Anastomotic leaks occurred in 4 patients who underwent Altemeier, including 1 who had been randomized to Delorme. Three of the 4 were men from a single center.

Study Limitations There were significant difficulties in accruing patients to this study, and the initial aims and enrollment targets were modified. Ultimately, while they were able to accrue enough patients to meet the revised target and aims, this limitation prevented the authors from creating the type of high-quality evidence they had hoped to produce that would enable guidance for surgeons who treat rectal prolapse.

Surgical technique was not standardized, and there was no minimum experience required of participating surgeons for each operation. It is possible that surgeons could have performed a procedure that they either never or rarely performed in the context of this trial. This is of particular importance with Altemeier procedure. Though the study initially aimed to compare abdominal to perineal procedures, the design of the study made it possible for the surgeon to select the approach and randomize within it. The groups were different in terms of age and functional status, but other important differences leading to patient selection for each are likely not captured in this dataset.

Recurrence after rectal prolapse surgery was a primary end point in this study but was not well-defined. It could be that mucosal prolapse was considered by some participating clinicians and that self-reporting may have been inaccurate in some cases.

The design of this study was complex and aimed to answer several questions within the same study: recurrence rates and quality-of-life measures were both assessed, and comparisons between and within procedure types were also made. This created a difficult setup for analysis for the study authors.

Relevant Studies PROSPER was an ambitious study that aimed to provide important clinical guidance in an area with equipoise after many lower-quality studies. Four procedures were included, and the study aimed to randomize patients. However, surgeons were able to specify abdominal or perineal procedures, and their level of comfort with each procedure was not equal. This introduced a significant amount of bias in procedure assignment and potential confounding. However, it does give us more evidence that perhaps there are no clear clinical differences between the many procedures for rectal prolapse.

It is important to recognize that the PROSPER study has high recurrence rates, 24–31% for perineal procedures and 13–26% for abdominal procedures. This

is higher than most other studies but may be due to diligent follow-up that is a more accurate assessment than other retrospective studies. On the other hand, it could be due to surgeons performing procedures that are relatively rare for them and that this impacted success. In general, retrospective studies have demonstrated that abdominal approaches have one-fourth the recurrence rates as perineal surgeries, but multiple Cochrane reviews have not found differences when meta-analysis was used.[1,4,5]

Concurrent to the PROSPER study, the Swedish Rectal Prolapse Trial was conducted from 2000 to 2009.[6] Overall, there are striking similarities between the trials both in study design and outcomes. In this randomized, multicenter trial, participants were similarly assigned to either abdominal or perineal surgery and then, within those randomizations, to Delorme or Altemeier or to suture or resection rectopexy. As in PROSPER, the first randomization step was not required to participate; surgeon discretion could be used to assign procedure type. In this study, 134 patients were randomized, and the median follow-up was 2.6 years. The authors noted improvements in Wexner and RAND-36 incontinence scores in all patients but no significant differences between the groups. Recurrence rates between the groups were different between the approaches, but none achieved statistical significance. Similarly, this study had difficulty recruiting their target sample size of 220 patients and was therefore somewhat underpowered. Both these studies underscore the fact that surgeons often have a preference for abdominal or perineal operations for individual patients, even in the absence of evidence to support patient selection.

Subsequent to PROSPER, another Cochrane review in 2015 was published that included three trial types: abdominal compared to perineal approaches (43 patients), rectopexy compared to resection rectopexy (115 patients), and Delorme compared with Altemeier procedure (201 patients).[5] The pooled analysis did not show significant differences in recurrence rates between abdominal and perineal approaches. Others have assessed complication rates after perineal and abdominal procedures for prolapse. Although these rates may be that due to the randomization scheme in PROSPER, surgeon bias about assigning less healthy patients to perineal procedures confirmed the same findings in the retrospective studies that have previously been utilized to draw conclusions on this topic. For example, a study of the National Surgical Quality Improvement Project suggested that the morbidity and mortality of the perineal approach is underestimated and may in fact be higher than abdominal approaches, likely due to patient selection for each approach.[7]

Since PROSPER was designed, the ventral mesh rectopexy (VMR) procedure has become increasingly popular for rectal prolapse. Some prospective trials, such as one with 120 patients that compared VMR with pelvic organ suspension, only followed patients for 6 months but showed no significant differences in function or complications[8] and another comparing suture rectopexy to VMR

with 75 patients, again showing no major differences in functional outcomes.[9] There was also a study of 75 patients comparing Delorme, which was the most common perineal procedure in the PROSPER study, to VMR and again was unable to demonstrate superiority of either procedure (Emile). There are even fewer studies that include long-term follow-up to assess recurrence, but again it is difficult to detect differences between techniques.[10] A systematic review that compared posterior rectal dissection and rectopexy to VMR suggested a recurrence rate of 3.4% and a weighted decrease in postoperative constipation rate estimated to be 23% among VMR patients.[11]

While PROSPER was ultimately not successful in achieving its aims in definitively answering the questions about procedure selection for patients with rectal prolapse, it helps create space for the next set of questions about how surgeons and patients decide on a specific procedure.

REFERENCES

1. Tou S, Brown SR, Malik AI, et al. Surgery for complete rectal prolapse in adults. *Cochrane Database of Systematic Reviews*. Epub ahead of print 2008. DOI: 10.1002/14651858.CD001758.pub2.
2. Vaizey CJ, Carapeti E, Cahill JA, et al. Prospective comparison of faecal incontinence grading systems. *Gut*. 1999;44. DOI: 10.1136/gut.44.1.77.
3. EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy (New York)*. 1990;16. DOI: 10.1016/0168-8510(90)90421-9.
4. Bordeianou L, Paquette I, Johnson E, et al. Clinical practice guidelines for the treatment of rectal prolapse. *Diseases of the Colon & Rectum*. 2017;60:1121–1131.
5. Tou S, Brown SR, Nelson RL. Surgery for complete (full-thickness) rectal prolapse in adults. *Cochrane Database of Systematic Reviews*. Epub ahead of print 2015. DOI: 10.1002/14651858.CD001758.pub3.
6. Smedberg J, Graf W, Pekkari K, et al. Comparison of four surgical approaches for rectal prolapse: multicentre randomized clinical trial. *BJS Open*. 2022;6. DOI: 10.1093/bjsopen/zrab140.
7. Fang SH, Cromwell JW, Wilkins KB, et al. Is the abdominal repair of rectal prolapse safer than perineal repair in the highest risk patients? An NSQIP analysis. *Diseases of the Colon & Rectum*. 2012;55:1167–1172.
8. Farag A, Mashhour AN, Raslan M, et al. Laparoscopic pelvic organ prolapse suspension (Pops) versus laparoscopic ventral mesh rectopexy for treatment of rectal prolapse: prospective cohort study. *World Journal of Surgery*. 2020;44:3158–3166.
9. Lundby L, Iversen LH, Buntzen S, et al. Bowel function after laparoscopic posterior sutured rectopexy versus ventral mesh rectopexy for rectal prolapse: a double-blind, randomised single-centre study. *The Lancet Gastroenterology and Hepatology*. 2016;1:291–297.
10. Madbouly KM, Mohii AD. Laparoscopic ventral rectopexy versus stapled transanal rectal resection for treatment of obstructed defecation in the elderly: long-term results of a prospective randomized study. *Diseases of the Colon & Rectum*. 2019;62:47–55.
11. Samaranayake CB, Luo C, Plank AW, et al. Systematic review on ventral rectopexy for rectal prolapse and intussusception. *Colorectal Disease*. 2010;12:504–512.