Rectal prolapse: enlightenment of the obscure
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Chapter 2

What is the natural history of internal rectal prolapse?

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Background: The nature and clinical significance of internal rectal prolapse is controversial. Its natural history is unclear. Longitudinal cohort studies show rare progression to external prolapse but lack adequate follow-up. We aimed to study the relationship of age to various stages of internal rectal prolapse using the Oxford Rectal Prolapse Grade (ORPG) and evaluate the influence of sex and vaginal delivery on this relationship.

Method: Internal rectal prolapsed (IRP) diagnosed at proctography and external rectal prolapse were graded using the ORPG. Age, sex and obstetric history were documented. Mean age of each prolapse grade (1-5) was analyzed and regression analysis performed for age and prolapse. Subgroup analyses were made for males, and females with (V+) and without (V0) history of vaginal delivery.

Results: Sixty males (11%) and 471 females (89%) were studied. The difference in the mean ages of each group was statistically significant (grade 1, 38.6; grade 2, 52.1; grade 3, 56.0; grade 4, 60.3 and grade 5, 66.5, p<0.0001). On average male (8.7 years) and V0-group (8.0 years) were younger than V+ group (95% CI difference 4.5 - 12.9 years, p<0.0001, and 3.8 - 12.2 years, p<0.0001, respectively). Males and V0-group had weaker correlation between age and prolapse grade (r = 0.16 and r = 0.17, respectively, versus 0.41), and a faster prolapse progression rate than the V+ group.

Conclusion: These data demonstrate a strong relationship between age and prolapse grade, supporting the view of internal rectal prolapse as a precursor to external prolapse in the spectrum of rectal prolapse disease.
Introduction

Rectal intussusception (RI) or internal rectal prolapse (IRP) is defined as a funnel-shaped infolding of the rectal wall that occurs during the act of defaecation. It presents classically with obstructed defaecation, yet there is ongoing debate about its clinical significance.

Several authors have suggested that IRP probably represents the first stage of a progressive anomaly that eventually leads to full thickness external rectal prolapse (ERP)\(^1\)\(^2\)\(^3\). However, two observational studies of rectal prolapse (RP) showed that progression of IRP to ERP was only rarely observed at long-term follow-up\(^4\)\(^5\). In asymptomatic volunteer-studies\(^6\)\(^7\)\(^8\), IRP has been noted to be a common cinedefaecographic finding (in up to 50% of volunteers\(^9\)), thus clouding its clinical significance. The poor surgical results of posterior rectopexy lead to the abandonment of IRP surgery for 15 years and relegated IRP to a mere incidental finding\(^10\).

More recent research has shown that IRP is proctographically significantly different in symptomatic patients compared to symptomatic individuals\(^11\)\(^12\), being deeper (recto-anal) and more commonly full-thickness. These studies suggest that previous normal volunteer studies had incorrectly included clinically insignificant mucosal and low-grade recto-rectal intussusceptions, and had overstated the frequency of true, asymptomatic recto-anal intussusceptions. Excellent functional results of the novel autonomic nerve sparing anterior rectopexy for IRP\(^13\)\(^14\) have been recently achieved. These developments have all lead to a recent reappraisal of the pathophysiology of IRP.

One of the difficulties of evaluating the natural history of IRP is the lack of a widely accepted grading system. This has lead to inflexibilities in the understanding of IRP. We have developed and use a radiological grading system based on the lowest point reached by the intussusceptum in relationship to the rectum, the rectocele and the anal canal that allows sub grading of IRP for clinical and research purposes (figure 2, table 1, pages 12,13). If the natural history of IRP was one of general progression through the various grades until the appearance of ERP, it should be reflected in the different ages seen at each grade, also allowing calculation of the speed of progression thought the grades. We aimed to study the natural history of IRP by exploring any correlation between age and radiological prolapse grade using the Oxford rectal prolapse grade\(^15\).
Method

Defaecating proctography was performed on patients attending at the pelvic floor clinic with external rectal prolapse, obstructed defaecation or faecal incontinence. Patients were included to the study if they had a full thickness rectal prolapse (ERP) or if a rectal intussusception with an intussusceptum greater than 3 mm was found on defaecating proctography. Patients with previous rectal surgery, including surgery for rectocele, enterocoele and IRP, were excluded.

The proctogram technique was standardized. Small bowel was opacified with a 310-ml mixture containing 100-ml Baritop (Barium sulphate 94.6% w/w; Sanochemia Ltd, UK) and 10-ml Gastrograffin (Schering Health Care Ltd, UK), ingested 30 min prior to the procedure. The rectum was prepared with 100 ml of E-Z-Paste (Barium sulphate cream, 60% w/w; E-Z-EM, Canada), injected per anum using a 50-ml bladder catheter-tip syringe. Lateral X-ray images were taken with the Siemens Sireskop SD image intensifier at 3 pulses/s, with the patient seated on a perspex commode. Images were taken at rest, squeeze and evacuation (for at least 30 seconds).

IRP seen on a defaecating proctogram was graded according to the Oxford rectal prolapse grade (figure 2, table 1, page 12,13), a radiological grading system. The patients’ sex and age at presentation were documented. Obstetric history was documented: nullips and females with children delivered by caesarian section only were placed in the no vaginal delivery group (V0), females with 1 or more vaginal deliveries were placed in the vaginal delivery group (V+).

The following analyses were made. The mean ages of each prolapse grade (1-5) were calculated and the differences compared with each other. A regression analysis was made for age and prolapse grade for all patients, using a simple linear regression model (the equation for a simple linear regression is \( y = a + bx \), where \( b \) is the slope). The regression slope was used to calculate the “progression gradient” (years/prolapse grade). The flatter the slope, the faster the progression. (For example; a progression gradient of 2.5 means that it will take 2.5 years to progress to the next prolapse grade). Finally we calculated the mean rate of progression from early recto-anal intussusception (grade 3) to external prolapse (grade 5) to allow a rough form of prognostication.

Subgroup analyses were made for males, V0 and V+ females to examine the influence on sex and parity on prolapse grade. The mean ages of each prolapse grade (1-5) were calculated and the differences compared with each other across the 3 subgroups. A regression analysis was made for age and prolapse grade for subgroups. The mean rate of progression from grade 3 to 5 was calculated to allow subgroup prognostication.
We have chosen to calculate the progression from grade 3 to grade 5 because this is in our view of clinical importance. When patients present with a recto-anal intussusceptions (grade 3), depending on the severity of symptoms, a surgical procedure could be offered (compared to patients with a recto-rectal intussusception (grade 1 or 2) who in our view should be treated conservatively). Information regarding the average progression rate to a possible ERP (grade 5), of the investigated group of patients, may be very informative in the discussion about the procedure with the patient.

Statistical analysis
For categorical data, results were analysed in contingency table format, using the Chi-square test. The student's t test was used for parametric continuous data. The age of the patients was correlated with prolapse grade using Pearson's correlation coefficient. Analysis of variance in mean age between different grades, using the Oxford rectal prolapse grade, was calculated using the one-way ANOVA test. Difference in mean age between different grades was calculated using the Tukey's HSD test. A p-value of 0.05 (2-sided) was considered as the limit of significance.

Results

Patients' demographics
531 patients were included, 471 females (89%) and 60 males (11%). The mean age (s.d) was 59 years (15) (figure 2, table 2). Of 471 females, the obstetric history was available in 401 (85%). Sixty-eight females (17%) were in group V0 and 333 (83%) in V+.

Proctographic prolapse grade
Eleven patients (2%) had a grade 1 rectal prolapse on defaecating proctogram, 66 patients (12%) grade 2, 145 patients (27%) grade 3, 161 (30%) patients grade 4 and 148 patients (28%) with grade 5 or ERP (table 2). Sex (p = 0.23) and obstetric history (p = 0.14) were reasonably evenly distributed across each rectal prolapse grade.

Age and prolapse grade (all patients)
For all patients, the mean age (s.d.) was 59 years (15). The mean age increased with each increase in rectal prolapse grade (figure 2). The mean age (s.d.) of patients in the grade 1 group was 38.6 (7.9); grade 2, 52.1 (11.0); grade 3, 56.0 (13.7); grade 4, 60.3 (13.4) and grade 5, 66.5 (16.1) (table 2).
Figure 2, All patients: mean age vs. prolapse grade. Red, Box-and-Whisker plots; green lines, average age per prolapse grade; grey line, overall average age.

Table 2, Results.

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</tr>
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<td>(7.9)</td>
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<td>56</td>
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<td>4</td>
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The measured difference (variance) in the average ages of the group (grade 1-5) was statistically significant ($p<0.0001$, ANOVA test). When each average age of each grade is compared individually to each other using the Tukey’s HSD test, the average age in grade 1 and grade 5 are significantly different compared to the average age in all other groups, the average age of grade 2 is significantly different compared to the average age in all other groups except to grade 3, the average age in grade 3 is significantly different compared to the average age in all other groups except to grade 2 and 4, and the average age in grade 4 is significantly different compared to the average age in all other groups except to grade 3.

If patients are divided into three groups (recto-rectal intussusceptions, grade 1 and 2; recto-anal intussusceptions, grade 3 and 4; and external rectal prolapse, grade 5), the differences between different groups are even more clear. All three groups significantly differ from each other ($p<0.0001$). The correlation between age and prolapse grade was 0.37 ($p<0.0001$). The mean progression rate from grade 3 to grade 5 prolapse was 10.49 years.
Age and prolapse grade (subgroup analysis)

Males
There were 60 males (11%). The mean age (s.d.) of males was 51.7 years (15.2). There was a weak correlation between age and prolapse grade for males ($r = 0.16, p = 0.24$) (figures 3 & 4). The progression gradient for males was 2.5 years/prolapse grade (figure 4). Therefore the calculated mean progression rate from grade 3 to 5 was 5.0 years.

V0 females
Of 471 females, 70 (15%) had unavailable obstetric history. Of the remaining 401 females, 68 (17%) were in the V0 group. The mean age (s.d.) of V0 females was 52.4 years (16.4). There was a weak correlation between age and prolapse grade for V0 females ($r = 0.17, p = 0.16$) (figures 4 & 5). The progression gradient for V0 females was 2.6 years/prolapse grade (figure 4). Therefore the calculated mean progression rate from grade 3 to 5 was 5.2 years.

V+ females
Of the evaluable 401 females, 333 (83%) were in the V0 group. The mean age (s.d.) of V+ females was 60.4 years (14.6). There was a correlation between age and prolapse grade for V+ females with a correlation coefficient of 0.41 ($p<0.0001$) (figures 4 & 6). The progression gradient for V+ females was 5.4 years/prolapse grade (figure 4). Therefore the calculated mean progression rate from grade 3 to 5 was 10.8 years.

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**Figure 3**, Males.
Average age vs prolapse grade.
Red: Box-and-Whisker plots; green lines, average age per prolapse grade; grey line, overall average age.

**Figure 4**, Regression lines.
Green: V+ group, $r = 0.41$,
slope regression line 5.4;
Blue: V0 group, $r = 0.17$,
slope regression line 2.6;
Red: Males, $r = 0.16$,
slope regression line = 2.5.
Influence of vaginal delivery on age/prolapse
The V0 group was significantly younger than the V+ group (mean age 52.4 versus 60.4 years, \( p<0.0001 \); difference between means 8.0 years, 95% CI 3.8 – 12.2 years). The correlation between age and prolapse grade for was stronger for V+ females \( (r = 0.41) \) compared to V0 females \( (r = 0.17) \). The progression gradient for V0 versus V+ females was lower \( (2.6 \text{ vs. } 5.4 \text{ years/prolapse grade}) \) and the calculated mean progression rate from grade 3 to 5 was faster \( (5.2 \text{ vs. } 10.8 \text{ years}) \) (table 3).

Influence of sex on age/prolapse
Males were significantly younger than V+ females (mean age 51.7 versus 60.4 years, \( p<0.0001 \); difference between means 8.7 years, 95% CI 4.5 – 12.9 years) but not compared with V0 females (mean age 51.7 versus 52.4 years, \( p = 0.80 \); difference between means 0.7 years, 95% CI -4.7 – 6.1 years). There was a similar correlation between age and prolapse grade for males \( (r = 0.16) \) and V0 females \( (r = 0.17) \), both weaker than that for V+ females \( (r = 0.41) \). Males and V0 females demonstrated a similar progression gradient \( (2.5 \text{ vs. } 2.6 \text{ years/prolapse grade}) \) and therefore a calculated mean progression rate from grade 3 to 5 \( (5.0 \text{ vs. } 5.2 \text{ years}) \) (table 3).
<table>
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<tr>
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<td>Mean progress grade 3-5 (yrs)</td>
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<td>10.8</td>
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Table 3, Subgroup analyses.

Discussion

In this study a significant increase of the average age is measured with the increase of rectal prolapse (grade 1-5). There are two possible explanations. Either the groups are different, representing different pathologies, or one group precedes the other group reflecting different evolving stages of the same pathological spectrum, the group with a lower mean age precedes the group with a higher mean age. In the case of rectal prolapse, both internal and external, it is unlikely that the different stages, captured by defaecating proctography, represent different pathologies. This would imply that an external rectal prolapse would appear very suddenly without being preceded by a lower prolapse grade.

In our view this is hard to imagine. Anecdotally, our experience of laparoscopic assessment of the pelvic anatomy in over 250 patients with both external and high-grade (recto-anal) internal rectal prolapse undergoing anterior rectopexy consistently demonstrates very similar markers of prolapse disease between the two groups (exaggerated pouch of Douglas, anteriorly excavated pelvis, narrow rectum meandering on the pelvic floor, sigmoid redundancy).

We think that these data support the more likely explanation, that rectal prolapse is a gradually evolving process that passes through various radiologically identifiable stages, from high and low recto-rectal intussusception (grade 1 and 2), through high and low recto-anal intussusception (grade 3 and 4), to eventual ERP. However the rate of progression through these stages is variable, and must depend on other aetiological cofactors other than just being associated with ageing.

This conclusion contradicts the established understanding of the natural history of rectal prolapse. Mellgren et al\(^4\) reported that, after operating on 41 of 79 patients with IRP, 2 out of 30 patients (8 patients lost to follow-up) developed an ERP (6.7%) after mean follow-up of 5.8 years. Choi et al\(^5\), after operating on 10 out of 36 patients, report that 1 out of 26 (3.8%) patients developed an external rectal prolapse after mean follow-up of 3.8 years. This development of IRP to ERP of 6.7% and 3.8% respectively is low but widely
accepted. It is possible that this rate might be higher if follow-up was longer. In our study the time between the mean ages of stages 3 and 5 was 10.5 years. Secondly a selection bias may play a role in these two observational studies. A total of 51 out of 115 patients (44.3%) were operated upon for IRP. Patients were not selected by randomization and therefore the possibility that the more advanced and symptomatic patients were operated on cannot be excluded and is likely.

Our study is not a longitudinal observational study and therefore no firm conclusions can be drawn regarding actual progression rates through different grades of IRP to ERP. Our conclusion is that the data support the view that an ERP is preceded by lower IRP grades. Our data are not inconsistent with these longitudinal observational studies of Mellgren et al and Choi et al. although we do think that the progression rate to ERP might be higher than reported. Mellgren et al and Choi et al stated that the results of their studies do not justify operating on patients with IRP only for the purpose to prevent a progression to ERP. Our study does not provide conclusive evidence to disagree with this statement.

Our regression graph results show a steady gradient with an incremental increase in mean age with increasing RP grade. This graph, demonstrating a correlation between age and RP grade, represents the progression of the average age of a group of patients and describes the average rate of progression for this group of patients. There clearly are other aetiological co-factors involved other than ageing, explaining the variance around this group: some patients will progress faster (flatter graph), some slower (steeper graph) and some not at all.

ERP is generally thought of as a condition of pelvic floor weakness in parous women, yet about 25% of our patients were male or nulliparous. We therefore performed subgroup analyses to examine the influence of sex and vaginal delivery on the age-prolapse relationship. When the mean ages and regression graphs of males and V0 females are compared with V+ females, an intriguing pattern is noticeable (figure 4 and table 3). Firstly, the regression slopes of males and V0 females are remarkably similar and both flatter than that of V+ females (figure 4). Secondly the mean age of males and the V0 groups is significantly different to the mean age of the V+ group. It appears that when males and females without vaginal deliveries develop IRP, the progress is faster (on average about 5 years versus 10 years to progress from grade 3 to 5). This suggests both a similar pathophysiology between males and V0 females on one hand, and different from that for the V+ females on the other.

We are aware however of the limitations of our study. The correlation, between age and prolapse grade, found in the subgroup analysis for males and V0 group was not very strong. The regression lines in these two subgroups are rough estimations. Therefore no firm conclusion can be drawn on the calculated progression rates. The number of patients in these subgroups is probably insufficient to find a strong correlation especially
when keeping in mind that correlation is harder to prove in a flatter regression line, which represents faster regression rate in our study. The significant difference found in mean age between males and V0 group compared with the V+ however is undeniable, expressing a true difference between the males and V0 group on the one hand and the V+ group on the other. Looking at the regression lines we think that this difference is caused by a faster progression in the development in rectal prolapse. If they reach the higher grades sooner the overall average age will be lower.

Various factors that weaken the pelvic floor are believed to contribute to pelvic floor prolapse and rectal prolapse. These include ageing, obstetric trauma associated with vaginal deliveries and connective tissue changes associated with the menopause. Why should males and V0 females develop IRP and ERP with faster progression than V+ females? Karasick et al. found a higher incidence of nulliparous females in a group of patients with ERP than in a control group without ERP (30% versus 15%), suggesting another cause in the development of rectal prolapse. A possible explanation might be a difference in collagen distribution or a connective tissue disorder. An interesting study done by Marshman et al. who found a significant difference in joint mobility between patient operated for ERP and an age- and sex-matched control group, suggesting a connective tissue disorder may play a role in the development in RP. Keane et al found an abnormal ratio of type 1 to type 3 collagen in nulliparous patients compared to parous females with genuine stress urinary incontinence. Our data support further enquiry into the role of abnormal connective tissue in the development of RP.

Because several normal volunteer studies showed that IRP is frequently seen in asymptomatic patients, the concept of IRP as a precursor of ERP has been controversial. Pomerri et al. and Dvorkin et al. have both shown that IRP is significantly different in morphology in symptomatic compared with asymptomatic patients. Pomerri et al. showed that intussusception thickness and the ratio between the intussuscipiens diameter and the intussusceptum lumen was significantly greater in symptomatic subjects than in asymptomatic controls. However the group was heterogeneous, containing patients with multiple pelvic floor symptoms and morphological abnormalities. Dvorkin et al. on the other hand studied a more homogeneous group of patients in which the only abnormality found on evacuation proctography was rectal intussusception. They found that patients with symptoms of obstructed defaecation (as defined by the Rome II criteria) had a significantly thicker intussusceptum and that the presence of an occluding intussusception was significantly higher compared to asymptomatic patients. The intussusception was predominantly full thickness in symptomatic patients and mucosal in asymptomatic patients. Patients with symptoms of obstructed defaecation will have in about 40% an IRP identified on proctography. The studies of Pomerri et al. and Dvorkin et al. show an association between severity/degree of rectal prolapse and symptoms. Fleschman et al. showed in 1989 that in high-grade IRP manometric findings were similar to patients with ERP,
suggesting a similar pathophysiology. Our data support the concept of IRP as a precursor of ERP. It is now apparent that IRP seen on a defaecating proctogram in a small number of asymptomatic volunteers is quite different from IRP seen proctographically in symptomatic patients. Patients need to be interviewed very thoroughly to pick up symptoms most sensitive for IRP.\textsuperscript{23} Defaecography should be analysed together by a trained team of colorectal surgeons and radiologists.

We are aware that our study does not give a clear definite answer on the debate whether the more severe rectal prolapse (high-grade internal or external) will cause more severe symptoms. Unfortunately we did not collect data on the severity of symptoms per grade, the duration of symptoms per patient and finally the progression of symptoms in time. Collecting these data would be very interesting in future research. In this study we have only investigated the association between age and degree of rectal prolapse. But from our collected data we do conclude that IRP seems to be a precursor of ERP. If our results are combined with those from the studies of Dvorkin and Pomerri\textsuperscript{10,11} a more clearer view on the natural history of internal rectal prolapse seems to arise. Rectal prolapse might begin as a trivial probably asymptomatic “low grade” rectal prolapse which can be an epidemiologically very large group. This group of asymptomatic patients in our view might be patients with an IRP seen on proctography described in the normal volunteer studies. At least some of these patients will develop a morphologically and anatomically more progressed “high-grade” (internal) rectal prolapse which is then more likely to give symptoms of obstructed defaecation and faecal incontinence\textsuperscript{15}. Finally ERP might be an end stage in elderly patients (or earlier in patients with a certain connective tissue disorder) where at this stage symptoms of discomfort of the prolapsed rectum itself, consisting of pain, bleeding and mucous discharge, are often combined with pre-existing functional symptoms. Interestingly we know that in about 80 percent of all patients with ERP will have functional symptoms at time of presentation (unpublished data of cohort of patients with ERP at John Radcliffe Hospital). This leaves 20 percent of patients with ERP without symptoms. In those cases the ERP will appear very suddenly as a lump without any functional symptoms in the past. To draw a parallel to IRP, assuming that ERP is preceded by IRP, it is likely that not all patients with (high-grade) IRP will be symptomatic. Again these asymptomatic patients with (high-grade) IRP might have been picked-up with the normal volunteer studies. The debate about whether IRP is causing symptoms or not is in our view becoming more and more obsolete. With the possibility that IRP might be either symptomatic or asymptomatic, the more interesting question would be “what is the ratio of symptomatic and asymptomatic patients in patients with IRP as seen on proctography” and “is this ratio influenced by the severity or grade of rectal prolapse (internal and external)”.\textsuperscript{23}
Conclusion

These data demonstrate a strong relationship between age and prolapse grade, supporting the view of internal rectal prolapse as a precursor to external prolapse in the spectrum of rectal prolapse disease. Since the subgroups males and females without a history of vaginal delivery seem to develop prolapse faster another cause in the development of rectal prolapse needs to be postulated. A collagen disorder, implicated in previous work, warrants closer scrutiny.
References