University of Helsinki, Faculty of Medicine
Doctoral Programme in Clinical Research
Pediatric Surgery and Pediatric Graduate School

Hospital for Children and Adolescents,
Helsinki University Central Hospital

Anorectal Malformations

- Outcomes up to adulthood

Kristiina Kyrklund

Academic Dissertation

For presentation with the permission of the Faculty of Medicine,
University of Helsinki, for public examination
at the Niilo Hallman Auditorium,
Hospital for Children and Adolescents
29th of April 2016

SUPERVISORS

Professor Risto Rintala
Department of Pediatric Surgery
Hospital for Children and Adolescents
University of Helsinki,
Helsinki, Finland

Associate Professor Mikko Pakarinen
Department of Pediatric Surgery
Hospital for Children and Adolescents
University of Helsinki,
Helsinki, Finland

PRE-EXAMINERS

Professor Marc Levitt
Surgical Director , Center for Colorectal and Pelvic Reconstruction,
Nationwide Children's Hospital
Professor of Surgery, The Ohio State University
Columbus, Ohio
USA

Docent Anna Lepistö
Department of Colorectal Surgery
Helsinki University Central Hospital
Helsinki, Finland

OPPONENT

Professor Tomas Wester
Department of Women's and Children's Health
Karolinska Institute
Stockholm, Sweden

ISBN 978-951-51-1970-4 (paperback)
ISBN 978-951-51-1971-1 (PDF)
http://ethesis.helsinki.fi
Unigrafia Oy 2016
Cover photo: Kristiina Kyrklund

To the Patients

"He is a good surgeon, who possesses courage and presence of mind, a hand free from perspiration, a tremorless grip of sharp and good instruments and who carries his operations to success and the advantage of his patient who has entrusted his life to the surgeon. The surgeon should respect this absolute surrender and treat his patient as his own son."

- Sushrut, father of Indian surgery, 800BC

Abstract

Aims – To perform a detailed evaluation of the bowel functional outcomes of anorectal malformations (ARMs) after standardized treatment and systematic follow-up in relation to matched controls. To study the bowel habits of a large cohort of individuals from the general population to obtain a baseline for comparison to patients.

Methods – A single-institution, cross-sectional study of all patients treated between 1983-2006 for anterior anus (AA, conservative or anal dilatations), perineal fistula (PF) males (anoplasty and/or dilatations) vestibular fistula (VF) or PF females (anterior sagittal anorectoplasty - ASARP) rectourethral fistula (RUF; posterior sagittal anorectoplasty – PSARP). Patients with significant cognitive impairment, total sacral agenesis/caudal regression syndrome, Currarino syndrome, or meningomyelocele were excluded. Participants answered a detailed questionnaire on bowel function by post. Parents of children <16 years assisted in responses. Case details were obtained from records. Patients were matched by age and gender to 3 individuals from the general population who had answered identical questionnaires. Ethical approval was obtained.

Results – Our study of 594 individuals from the general population identified that minor aberrations in bowel function, especially soiling prevail in healthy individuals in an age-dependent manner. A total of 159 patients (72%; median age 12.5 (4-29) years) participated in the study on outcomes for ARMs (79 females: 45 AA and 34 VF/PF and 80 males: 46 PF/low ARM and 34 RUF males (35% bulbar, 53% prostatic, 12% bladder neck fistula). Fecal control in AA females and low ARM males was not significantly different from controls in the long-term (p=NS). In VF/PF in females, 68% of patients attained a functional outcome comparable to controls and 85% were socially continent (vs 100% of controls; p<0.001) Among RUF males, 76% of patients were social continent (vs 95% of controls; p<0.002). Despite some improvement in symptoms with increasing age, both soiling and fecal accidents among patients with VF/PF (65% and 24% respectively) and RUF (59% and 37% respectively) remained significantly higher than in controls in the long-term (18-26% for soiling and 4-6% for fecal accidents; p≤0.006 vs patients).The median BFS, the proportion with voluntary bowel movements and total continence decreased with increasing level of fistula in RUF. Constipation was an important sequel in all types of ARMs, affecting 31-44% of patients vs 2-13% of controls (p≤0.003 vs patients). Social restrictions affected a 15-36% of patients with severe ARMs (vs ≤5% of controls; p≤0.01).

Conclusions - Our results support the appropriateness of sagittal repair methods for the treatment of VF/PF in females and RUF, and minor perineal procedures for mild ARMs. Patients with mild ARMs can generally be expected to develop bowel functional outcomes comparable to matched peers. In females with VF/PF and males with RUF, problems with fecal control persist at higher levels than controls into adulthood. However, the majority can be expected to achieve social continence with appropriate aftercare and effective management of constipation.

Table of Contents

1. Original Publications

This thesis is based on the following publications. In the text, the articles are referred to by their Roman numerals I-V and reprinted here with permission of the publishers.

I Kyrklund K, Koivusalo A, Rintala RJ, Pakarinen MP. Evaluation of bowel function and fecal continence in 594 Finnish individuals aged 4 to 26 years. *Dis Col Rectum* 2012; 55: 671-676.

II Kyrklund K, Pakarinen MP, Taskinen S, Rintala RJ. Bowel function and lower urinary tract symptoms in females with anterior anus treated conservatively: controlled outcomes into adulthood. *J Pediatr Surg* 2015; 50: 97-103.

III Kyrklund K, Pakarinen MP, Taskinen S, Rintala RJ. Bowel function and lower urinary tract symptoms in males with low anorectal malformations: an update of controlled-long-term outcomes. *Int J Colorectal Dis* 2015; 30: 221-228.

IV Kyrklund K, Pakarinen MP, Koivusalo A, Rintala RJ. Bowel functional outcomes in females with perineal or vestibular fistula treated with anterior sagittal anorectoplasty: controlled results into adulthood. *Dis Col Rectum* 2015; 58: 97-103.

V. Kyrklund K, Pakarinen MP, Koivusalo A, Rintala RJ. Long-term bowel functional outcomes in rectourethral fistula treated with PSARP: controlled results after 4-29 years of follow-up: a single-institution, cross-sectional study. *J Pediatr Surg* 2014; 49: 1635-1642.

2. Abbreviations

AA	Anterior Anus
ACE	Antegrade continence enema
AM	Anorectal manometry
ARM(s)	Anorectal malformation(s)
AS	Anal stenosis
ASARP	Anterior sagittal anorectoplasty
BFS	Bowel function score
CM	Cloacal membrane
EAS	External anal sphincter
EUROCAT	European Surveillance of Congenital Anomalies Registry
IAS	Internal anal sphincter
MRI	Magnetic resonance imaging
PF	Perineal fistula
PSARP	Posterior sagittal anorectoplasty
LAARP	Laparoscopic-assisted anorectoplasty
RA	Rectal atresia
RUF	Rectourethral fistula
TAEAPP	Transanal endoscopic assisted proctoplasty
TSA	Total sacral agenesis
VACTERL	Vertebral, Anal, Cardiac, Tracheoesophageal fistula with or without Esophageal atresia, Renal and Limb anomalies
VBM(s)	Voluntary bowel movement(s)
VF	Vestibular fistula

3. Introduction

"The point is to understand."
- Albert Einstein

Anorectal malformations (ARMs) comprise a spectrum of congenital anomalies that continue to present a challenge for pediatric surgeons.[1] ARMs affect around 1:2000-2500 births,[2-4] ranging in severity from mild anterior displacement of the anus to very complex malformations of the hindgut and urogenital tract.[3,4] Advances in modern surgical techniques and neonatal care have greatly improved survival among ARM patients over the last decades, and early mortality is now unusual in the absence of fatal associated cardiac or chromosomal defects.[5] Accordingly, the focus of surgical care has shifted beyond initial survival of the patient towards ensuring that children treated for ARMs to grow up having bowel function that is compatible with a good quality of life.[6] For most, this means being able to actively participate in their social environment without significant limitations from bowel function, for which fecal continence is a major determinant.[7-9]

Posterior sagittal anorectoplasty (PSARP), first introduced in 1982 by De Vries and Peña[10] and followed later by its limited modification anterior sagittal anorectoplasty (ASARP),[11] represents the basis of the modern surgical approach to ARMs with termination of the anal canal outside the voluntary sphincter complex. PSARP, entailing exposure of structures under direct vision and restoration of the normal anatomical relationships between structures has replaced earlier classical operations, including abdominoperineal or sacroabdomino- and sacroperineal pull through[12-15] as the 'gold-standard' approach.[16] Other significant developments have included recommendations for centralisation of surgery for ARMs to specialist tertiary units,[16] increasing understanding of their pathologic anatomy, and improved treatment of major functional complications such as constipation.[16]

Patients treated from the beginning of the 1980's have now reached an age at which evaluation of the long-term functional outcomes is possible. The literature that has accumulated concerning the outcomes in childhood has been more optimistic than preceding the PSARP era,[17] but the results for severe ARMs in particular have varied widely, and there remains limited information on the outcomes of modern treatments up to adulthood.

This study represents an attempt to systematically evaluate the long-term bowel functional outcomes for individual types of ARMs after standardised, modern management at a single institution with comparison to age- and gender-matched controls from the general population. The results are aimed towards providing continued evidence-based practice and optimal standards of care for patients and families affected by ARMs.

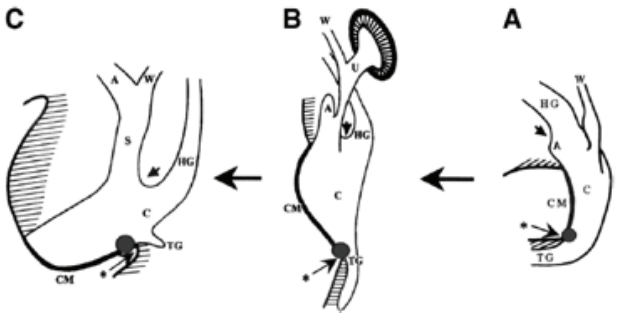
4. Literature Review

4.1 Embryology

4.1.1 Normal development of the hindgut

In early embryology, the hindgut is a tubular endoderm-lined structure that is cranially continuous with the midgut and caudally in contact with the ectoderm over an area termed the cloacal membrane (CM).[18] The caudal region of the undifferentiated hindgut is termed the cloaca, and this is a normal structure during human development. During the 7th week of gestation, the cloaca differentiates to form two separate organ systems – ventrally, the urogenital tract and dorsally, the anorectal tract (**Figure 1**). The urorectal fold divides the cloaca into these ventral and dorsal components, ultimately forming the perineal body between them.[19] Posteriorly, the CM disintegrates where the tip of the urorectal fold meets the CM, forming the anal orifice.[18] Ventrally, the urogenital sinus develops. The anal orifice initially closes with ectoderm and is recanalized 2 weeks later.[19] Aberrations in recanalization during the 9th gestational week could explain some mild "low" abnormalities such as anal membranes.[19]

Figure 1 – Normal cloacal development in the rat model



Schematic drawing of normal cloacal development in rats (drawn after SEM photographs). (A) A 12.5-day old embryo; (B) 14-day embryo; and (C) 15-day embryo. Note the movement of the cloacal membrane (CM) from a vertical to a horizontal position. This movement is caused by the ventral outgrowth of the genital tubercle and the cloaca. Note the descent of the urorectal fold (short arrows). The dorsal part of the cloacal membrane (gray dots) is the area of the future anal opening. Arrows with asterisk (*) point to the tail groove. This area is the fixed point in development of the cloaca. HG, hindgut; CM, cloacal membrane; C, cloaca, TG, tail gut; A, allantois, S, sinus *urogenitalis*; W, Wolffian (mesonephric) duct; U, ureter. (Reprinted from Figure 1 in Kluth D (2010)[18] with kind permission from Elsevier.

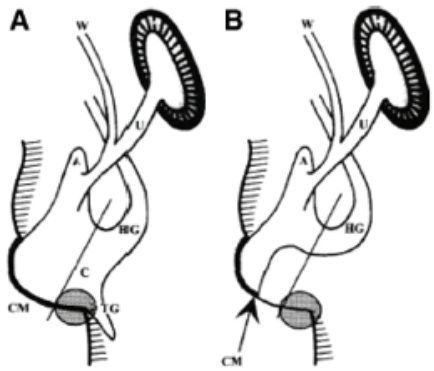
4.1.2 Theories of abnormal development

The recto-urogenital or -perineal communication in ARMs essentially has the characteristics of a normal anal canal, including the distal transitional epithelium, anal glands and the internal anal sphincter.[20-22] The theory of rectal migration[23,24] proposed that the developing rectum descended to the position of the normal anal opening during development, and that the aberrantly placed anal canal in ARMs was resulted from prematurely ceased migration.[18] Van der Putte's (1986)[20] modification of this theory proposed that a downward "shift" of the dorsal cloaca determined the location of the future anal opening. Both theories placed cloacal subdivision as the central determinant of normal hindgut development, but normal formation of the CM may instead be the critical factor.[18,25] Studies of normal mouse embryos have shown that the location of the future anal orifice is already established and identifiable at a fixed point prior to cloacal subdivision.[22] Additionally, embryologic cloacae in the normal mouse model have not been found to pass through a stage that if arrested, would resemble any form of ARM in neonates.[18,25]

4.1.3 Recent advances

Danforth's short tail mice[26,27] are mutants of the house mouse exhibiting a spectrum of anorectal and urogenital abnormalities that have been used as models of ARMs.[18,22,25] Significant features in developing embryos are that the dorsal cloaca is missing, the dorsal part of the CM is abnormally shortened, and the junction between the proximal hindgut and the cloaca is abnormal (**Figure 2**).[18,25] These primary abnormalities could lead to a missing or misplaced anal opening and an abnormal communication between the rectum and urogenital tract during the process of cloacal subdivision.[25] The extent of the anorectal defect could relate to the degree of abnormal development of the posterior aspect of the cloaca, with smaller defects leading to milder "low" presentations, and larger defects leading to more severe anomalies and urogenital connections.[19]

Figure 2 – Model of abnormal cloacal development



Schematic drawings of a normal (A) and an abnormal (B) cloaca. In the abnormal embryo, the cloacal membrane (CM) is too short (arrow). The cloacal membrane does not extend to the region of the tail groove (gray area). The dorsal cloaca is missing. In the normal embryo (A), the cloacal membrane is of normal length and extends to the region of the tail groove (gray area). (Reprinted from Figure 7 in Kluth D (2010)[18], with kind permission from Elsevier.

4.2 Etiology and genetic basis of ARMs

The incidence of an ARM in association with a chromosomal anomaly is approximately 5-10%,[19,28] although ARMs have been observed in association with mutations in almost all chromosomes.[29,30] The most frequent chromosomal mutations are microdeletion of chromosome 22q11.2 (Di George or CATCH-22 syndrome) and Trisomy 21 (Down syndrome), in the latter of which imperforate anus without a fistula is the most common defect.[19] Other genetic syndromes associated with ARMs are Townes-Brocks, Pallister-Hall, Opitz-Kaveggia, Johanson-Blizzard, Kaufman-Mckusick, Lowe and Fragile X syndrome, and Trisomy 8.[6]

Familial occurrence in ARMs has been reported to range between 2.4 and 8%.[32,32] The occurrence in monozygotic twins also supports the role of genetic influences in the development of ARMs.[33,34] The importance of a locus on chromosome 7q39 in ARMs, which includes the genes *SHH, EN2* and *HLXB9* has been previously proposed,[6] of which *HLXB9* is responsible for autosomal dominant Currarino syndrome. However, most ARMs with a genetic basis are likely to result from a complex series of genetic interactions involving multiple genes.[31]

In addition to genetic factors, epidemiologic studies also support the role of environmental agents in the development of ARMs, including prenatal exposure to caffeine, nicotine, alcohol, illicit drugs or occupational hazards, as well as maternal diabetes mellitus or obesity.[31,36,37] There also appears to be an increased risk of an ARM in children born following assisted reproductive techniques.[38] Recently, potential risk factors for complex manifestations of ARMs with additional congenital anomalies and VACTERL (Vertebral, Anal, Cardiac, Tracheoesophageal fistula with or without Esophageal atresia, Renal and Limb) identified in a large European study were maternal epilepsy, fertility treatment, multiple pregnancy, primiparity, pre-eclampsia and maternal fever during the first 4 months of pregnancy.[39]

4.3 Associated malformations

It has been estimated that between 50-67% of all patients with ARMs have at least one other associated congenital malformation,[6,39,40] especially components of the VACTERL sequence.[39] These are more common and more severe in high and intermediate ARMs, occurring in up to 93% of high, 77% of intermediate, and approximately 45% of low anomalies according to one large series.[3] Approximately 15-20% of patients may meet the criteria for VACTERL association, having three or more anomalies from this sequence.[3,41] The cardiac defects in ARMs, mainly atrial septal defect, ventricular septal defect and tetralogy of Fallot, were reported in 13% of all ARM cases in a large report from the European Surveillance of Congenital Anomalies (EUROCAT) registry.[39] In this report, the overall prevalence of other associated malformations in ARMs was 15% for skeletal anomalies, 10% for tracheo-esophageal fistula, 25% for urologic anomalies, 13% for limb defects (of which radial in 5.9%), and 12.8% for genital anomalies.[39] The most common urologic abnormality is vesicoureteric reflux, followed by renal agenesis and dysplastic kidney.[6] Uterine and vaginal anomalies occur most often in association with cloaca and are less common in other types of ARMs.[19]

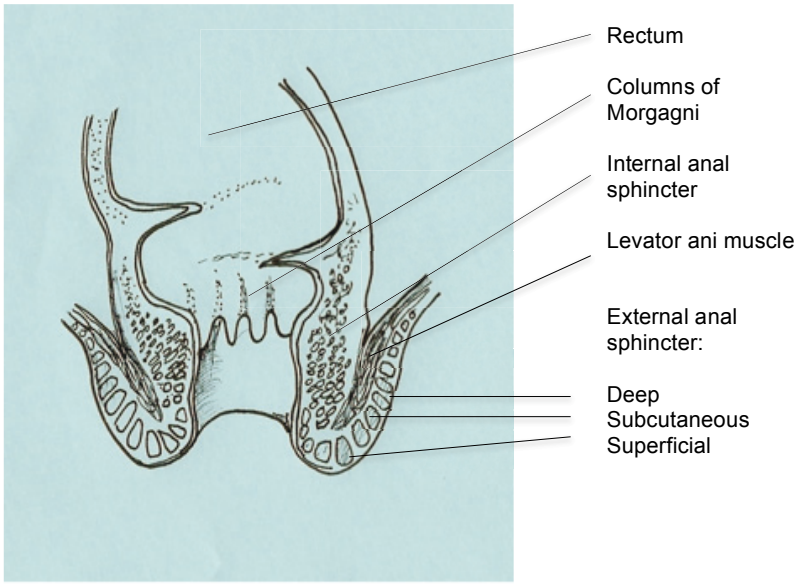
4.4 Normal Anatomy

4.4.1 Basic anatomy of the pelvic floor

The levator ani is the main muscle of the sheet-like hammock of the pelvic floor that holds the abdominal viscera and pelvic organs in place and actively adjusts its contraction in response to changes in intra-abdominal pressure.[42] Its most ventromedial aspect, puboviscerallis (pubococcygeus), runs from the inner surface of the pubis forming a sling around the urethra, vagina and anorectum. Its fibres fuse medially at the perineal body and serve to close the urogenital and anorectal hiatuses by contraction.[42] The puborectalis component of the levator ani takes origin from the pubis and loops posteriorly in a U-shape around the anorectum to create the anorectal junction, dividing the rectum from the surgical anal canal. Puborectalis holds the anorectal junction angled anteriorly at approximately 90 degrees. This anorectal angle contributes to continence by creating a valve mechanism that prevents fecal descent during sudden increases in intra-abdominal pressure.[43]

Some fibres of the puborectalis also merge with the external anal sphincter (EAS), forming the longitudinal coat of the anal canal[44] (**Figure 4)**. The pubococcygeal line, extending from the inferior margin of the os pubis to the os coccyx and corresponding with the attachment of the levator ani muscles to the pelvic wall, has been used in classification systems to define high types of ARMs as those with a rectal termination above the levator muscles.[45]

Figure 4 – Normal anatomy of the anal canal



4.4.2 Anatomy of the Anal Canal

The anal canal itself is composed of external- and internal anal sphincter (IAS) muscles, of which the EAS is a voluntary, striated muscular tube and the IAS is a thickened, inferior continuation of the inner circular (visceral) muscle of the rectum[44] (**Figure 4**). The EAS comprises subcutaneous, superficial and deep components, and its main function is to contract to prevent defecation and the leakage of faeces until an appropriate time.[43] The EAS is also activated during coughing, sneezing or straining and during physical activities such as running.[43] The EAS receives its motor and sensory supply from the inferior rectal branches of the pudendal nerve. These fibres also transmit sensation from the anal skin to approximately 1cm above the dentate line.

The IAS is responsible for approximately 80-85% of the resting anal canal pressure[46] and significantly contributes to fecal continence.[47,48] The efferent (motor) function is provided by sympathetic fibres from the pelvic plexus (contraction), and by parasympathetic fibres from the pelvic splanchnic plexus (relaxation). The afferent (sensory) innervation of the proximal anal canal is both sympathetic and parasympathetic.[44]

Afferent impulses transmit rectal filling and the urge to defecate from the distal bowel to the brain.[43] As previously noted, this functional IAS tissue is present in the rectal termination in ARMs irrespective of the type of malformation, and the fistulous communication in ARMs is actually an ectopic anal canal.[22,49,50] Hence, IAS (fistula)-conserving surgery forms part of the modern approach to the repair of ARMs.

4.3 Classification of ARMs

There have been several available classification systems for ARMs, of which the most recent is the clinically oriented Krickenbeck classification (**Table 1**).[45] The preceding anatomically oriented Wingspread International Classification (**Table 2**)[51] divided ARMs into high, intermediate and low types according to the location of the recto-urogenital communication in relation to the levator plate.[3] The Peña classification (**Table 3**)[52] is based on the surgical approach being determined by the type of ARM. The Wingspread and Peña classifications also divided ARMs by gender into male and female types.

Table 1.Krickenbeck classification (2005)[45]

Major clinical groups	Rare/regional variants
Perineal (cutaneous) fistula Rectourethral fistula Bulbar Prostatic Bladder neck Vestibular fistula Cloaca No fistula Anal stenosis	Pouch colon Rectal atresia/stenosis Rectovaginal fistula H-type fistula Others

Table 2. Wingspread classification (1986)[51]	
Female	Male
High Anorectal agenesis Rectovaginal fistula No fistula Rectal atresia	High Anorectal agenesis Rectoprostatic fistula No fistula Rectal atresia
Intermediate Rectovaginal fistula Rectovestibular fistula Anal agenesis	Intermediate Bulbar fistula Anal agenesis
Low Anovestibular fistula Anocutaneous fistula Anal stenosis	Low Anocutaneous fistula Anal stenosis
Cloaca	
Rare malformations	Rare malformations

Table 3. Peña classification (1995)[52]
Males Perineal fistula Rectourethral fistula Bulbar Prostatic Rectovesical (bladder neck) Imperforate anus without fistula Rectal atresia
Females Perineal fistula Vestibular fistula Persistent cloaca <3cm common channel >3cm common channel Imperforate anus without fistula Rectal atresia

The primary purpose of descriptive classification systems for ARMs has been to enable discussion and assessment of treatment and outcomes according to individual types of malformation and/or surgical procedures. The rare/regional variants of ARMs mentioned in the Krickenbeck classification account for only a small proportion of all ARMs[28] and are not discussed further herein, but the principles of surgical treatment are the same as for other types of ARMs.

4.4 Characteristics of the major clinical groups of ARMs

4.4.1 Malformations in females

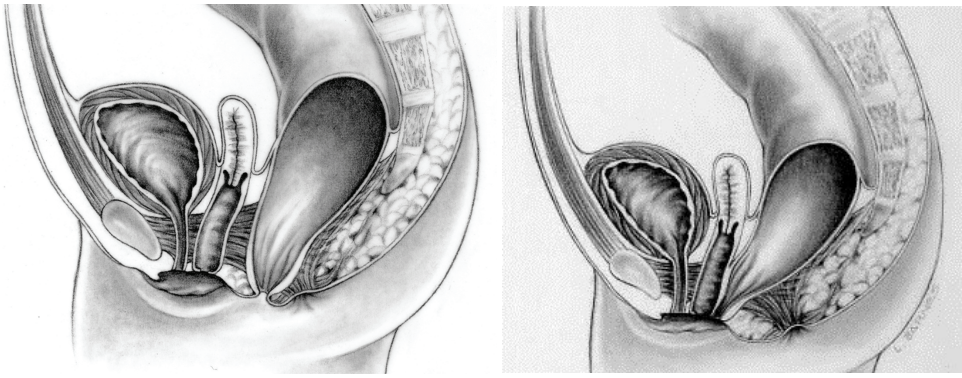
Anterior Anus (AA) with or without anal stenosis (AS)

The mildest form of ARM that occurs almost exclusively in females is AA, which is characterised by an anus that is normal in appearance, but situated in an abnormally anterior position.[53] The anal canal and internal anal sphincter (IAS) are located mostly *within* the voluntary external sphincter funnel. Although approximately 50% of patients have some degree of anal stenosis, this is usually mild only.[54] The diagnosis of AA can usually be made on clinical examination. An ano-genital index of <0.30 in females, measured as the ratio of the anus-fourchette distance over the coccyx-fourchette distance, may be considered abnormal.[55]

Perineal fistula (PF) and vestibular fistula (VF)

In females, PF is characterised by a fistulous opening of the anal canal anteriorly on the perineum (**Figure 5 a**)[56] In vestibular fistula (VF), this opening is located even more anteriorly in the vestibulum or vulva, just posterior to the hymenal ring (**Figure 5 b**).[57] In both cases, the fistula is mostly *outside* the support of the voluntary sphincter complex and contains the components of the anal canal including the internal anal sphincter and anal crypts.[22] Separate and usually normal openings for the urethra and vagina are present.

Figure 5 – Perineal fistula (a), and rectovestibular fistula (b) in females



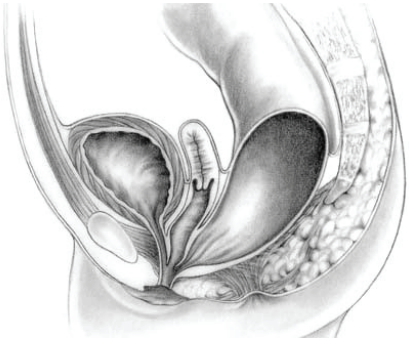
a) Perineal fistula b) Rectovestibular fistula

Reprinted from: Levitt and Peña (2007)[56] Figure 3 (Fig 5 a); and Levitt and Peña (2012)[57] Figure 1 (Fig 5 b), with kind permission from BioMed Central.

Cloaca

In cloaca, there is only a single external opening for a common recto-urogenital channel formed by the rectum, vagina and urethra (**Figure 6**).[57] The channel opening is usually anterior to the normal site of the vagina.[3] Hypoplasia of the vulva and an opening near the base of the clitoris suggest a long common channel.[3] The ARM 'cloaca' is different from the embryologic 'cloaca', which is a normal structure during embryonic development with the same name. The term 'persistent cloaca,' sometimes used to describe this ARM is also a historical misnomer, as it does not arise from prematurely arrested subdivision of the normal embryologic cloaca.[18]

Figure 6 – Cloaca in a female[56]



Reprinted from: Levitt and Peña (2007)[56] Figure 7, with kind permission from BioMed Central.

4.4.2 Malformations in males

Low/mild malformations

In males, perineal fistula (PF) (**Figure 7**) and anal stenosis (AS) essentially constitute variants of the same type of mild malformation.[58] The only exception is a complete anal membrane, which could also represent the least severe form of imperforate anus without a fistula.[59] In contrast to females with PF, the anal canal in males with low malformations is usually located mostly *within* the voluntary sphincter complex.[3,53,58] A diagnostic feature is meconium tracking for a variable distance superficially the midline scrotal raphe. A low malformation may also be associated with a median bar defect 'covering' the site of the external sphincter, with a tiny opening on one or both sides from which meconium may be seen to extrude.

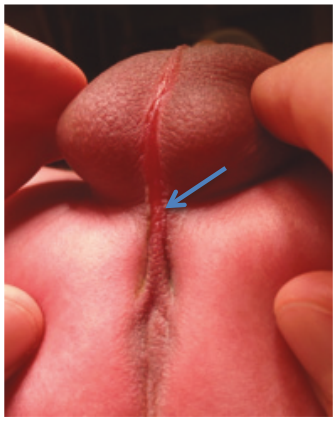


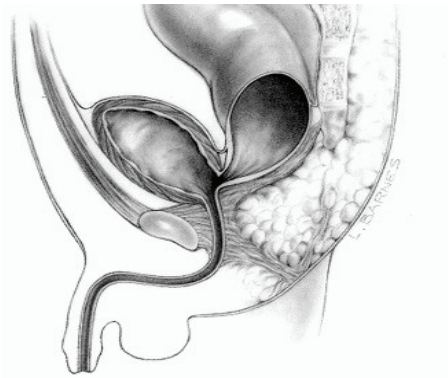
Figure 7 (right) – Perineal fistula in a male with meconium tracking superficially in the scrotal raphe and exiting from a tiny opening (arrowed)

Rectourethral fistula (RUF)

Males with no opening on the perineum usually have a fistulous connection between the terminal anorectum and the urethra, which in most cases is at the level of the prostatic or bulbar urethra.[54] Less commonly, higher termination at the level of the bladder neck is present **(Figure 8**).[56] The passage of meconium-stained urine per urethra in these patients confirms the diagnosis clinically. Recto-bulbar urethral fistula was considered an "intermediate" level of ARM in the Wingspread classification, as the rectal pouch is located within the proximal part of the external sphincter funnel. Prostatic and bladder neck fistulae were both classified as "high" anomalies, as the rectal termination is above the level of the levator plate.[54] The appearance of the perineum is an indicator of the likely degree of voluntary sphincter muscle hypoplasia: a flat, featureless bottom and poorly

developed natal cleft suggest significant underdevelopment, whereas a relatively normally contoured bottom with a pigmented “anal pit” suggests a lesser degree of external sphincter hypoplasia.

Figure 8 – Rectourethral fistula with termination of the fistulous opening at the bladder neck



Reprinted from: Levitt and Peña (2007).[56] Figure 6; with kind permission from BioMed Central

Malformations in males or females

Imperforate anus without a fistula

In imperforate anus without a fistula, there is a variable distance between the blind-ending rectal pouch and the perineum. The anal sphincters are usually well developed. This type of ARM is present in 95% of patients with Down syndrome associated with an ARM.[60,61] A significant proportion of patients with no fistula have anal agenesis, a low and almost membranous defect where the rectal termination lies below the dentate line and immediately subcutaneous to the anal pit.[53] Rectal atresia (1-2% of ARMs) is a higher variant where the distal anus is usually well-formed and normal-looking, but ends blindly at 1-3 cm of depth and the rectal pouch terminates above the pubo-coccygeal line.[62]

4.5 Diagnostic workup and initial treatment

4.5.1 Clinical examination

In a newborn, the severity of an ARM can provisionally be determined with careful clinical examination in the majority of patients.[3] The presence of a fistula or meconium on the perineum is indicative of a “low” or mild ARM in males, and most patients with “low” anomalies will pass at least a small amount of meconium within the first 48 hours.[53] In females, the location of a fistula on the perineum or vestibulum and the presence of separate urethral and vaginal openings must be noted, and the fistula calibrated using Hegars. If it is unclear on clinical examination whether a female has an anteriorly located anus or a perineal fistula, the position of the anal canal in relation to the voluntary sphincter complex can be determined using an electrical muscle stimulator under anaesthesia.

If no fistula is apparent on gentle probing and after 24 hours of observation, it is safest to assume a more severe ARM as the working diagnosis and to perform a double-barrelled colostomy until the level of the anomaly is formally ascertained.[53] Wangsteen-Rice invertography,[63] cross-table lateral radiography[64] or perineal ultrasonography are techniques which have been aimed at identifying those patients with no apparent fistula but with a likely rectal termination close to the perineal skin, where a primary mini-PSARP might be attempted.[65] At our centre, these investigations are not routinely undertaken,[3] opting for an initial colostomy if level of the anomaly is clinically uncertain.

4.5.2 Screening for associated anomalies

Screening for associated anomalies is an essential part of the investigation of all newborns with ARMs. At the minimum, this comprises a thorough clinical examination, echocardiography, ultrasound of the renal tract and spinal cord, cystourethrography and spinal column X-rays during the newborn period.[53] Cystourethrography can give an indication of site of the fistula in RUF patients in addition to imaging the anatomy of the

renal tract for vesicoureteric reflux and other structural abnormalities. A naso-gastric tube may be passed to rule out esophageal atresia. Prior to corrective surgery, patients with a colostomy also undergo distal colonography to demonstrate the anatomy of the distal colon and the rectourogenital connection in RUF from the colon side. In a female with a cloaca, injection of water-soluble contrast medium can be used to determine the anatomy and length of the common channel in addition to endoscopy.[67] Magnetic resonance imaging (MRI) of the spinal cord may be performed at a later date to rule out intraspinal anomalies.

4.6 Principles of surgical treatment

The surgical treatment of ARMs is geared towards restoring the normal anatomical relationships between structures with minimal disturbance to existing fecal continence mechanisms. At our centre, standardized approaches based on these principles, by type of ARM, have been employed since the advent of sagittal repairs in the 1980's. The degree of surgical intervention is dependent on the type and severity of the malformation, and all patients receive systematic outpatient follow-up up to adulthood.

4.6.1 Mild ARMs with anal canal termination mostly within the external sphincter complex

Females with anterior anus (AA)

Anterior anus is managed non-operatively at our centre. Upon diagnosis by an experienced pediatric colorectal surgeon, the anus is calibrated using Hegars, and any stenosis is treated with serial Hegar dilatations gradually up to size 14. The position of the termination of the anal canal may be verified using an electrical muscle stimulator under anaesthesia if necessary.

Males with low/mild ARMs

Perineal fistula (PF) and anal stenosis (AS) in males are managed with minimally invasive perineal procedures that aim to create a functionally and cosmetically satisfactory anal opening that allows for the normal passage of stool.[53] Males with PF receive cutback anoplasty, ideally within the first day of life. Limited posterior sagittal anorectoplasty is an accepted alternative practiced in some centres,[65] but requires more tissue dissection and carries a potential risk of injury to the urethra.[59,68] Standardized cutback anoplasty comprises verification of the limits of the external sphincter using an electrical muscle stimulator, after which the fistula is laid open over a thin probe in the midline up to the centre of the external sphincter complex. The anus is dilated to an appropriate size (Hegar 6-8 in a term neonate), and the rectal mucosa is sutured using interrupted, absorbable 6-0 sutures to the posterior margins of the layed-open fistula. Our treatment of choice for complete anal membranes is a cruciate incision of the membrane under anaesthesia. All patients, including those with isolated AS, undergo an anal dilatation programme over 6-8 weeks. The Hegar size is increased at weekly intervals up to Hegar 14. This is commenced 2 weeks after anoplasty for PF, shortly following incision of a complete membrane, and at diagnosis for AS.

Severe ARMs with fistulous termination of the anal canal outside the external sphincter complex

Vestibular and perineal fistula (VF and PF) in females

Anatomical repair with anterior sagittal anorectoplasty (ASARP), also known as limited PSARP, is a standardized operation for the treatment of females with VF and PF. ASARP, which was first described in the literature in 1992,[11] entails a “squash-racket” incision around the opening of the fistula, extending in the midline up to the centre of the external sphincter complex. Only the anterior aspect of the external sphincter is divided to gain exposure to the terminal anorectum, making this operation a limited modification of

full PSARP. As with perineal fistula in the males, the centre of the external sphincter complex is identified with an electrical muscle stimulator and marked pre-operatively. The anorectum is mobilized from its adjacent structures, including the posterior vaginal wall, until tension-free anastomosis to the centre of the sphincter complex is possible. Fistula-saving (IAS-saving) surgery is practiced at our centre in all sagittal repairs. Reconstruction of the perineal body is performed in layers using absorbable sutures. The procedure may be performed with or without a covering colostomy depending on the age of the patient and the choice of the surgeon. Post-operatively, the perineum is washed with water after defecations and intravenous antibiotics (cephalosporin and metronidazole) are administered for 48 hours post-operatively. Patients undergo a standard anal dilatation programme over 6-8 weeks up to Hegar 14, beginning 2 weeks after surgery. Any colostomies are closed upon completion anal dilatations.

Traditionally, as in males with perineal fistula, cutback anoplasty has been used to treat females with VF and PF. In females, however, this results in a greatly shortened perineal body, which may be cosmetically[69] and hygienically unsatisfactory. It has also been suggested that fecal continence may also decline later in adulthood and following pregnancies.[69] Y-V and X-Z plasties[70] have also been employed to treat these ARMs in females, but have been largely superseded by ASARP. Full PSARP is also performed for VF/PF in females in some centres, suggestion of comparable functional results to ASARP, but better cosmesis after ASARP.[71]

Rectourethral fistula

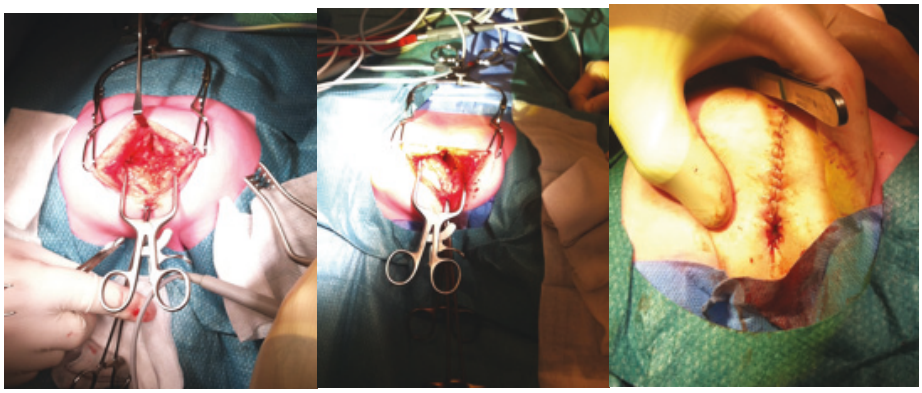
Following primary colostomy, the definitive repair is carried out at approximately 2-3 months of age. Posterior sagittal anorectoplasty (PSARP)[10] has become the 'gold standard" technique of repair for urethral fistula in males.[53] Significantly, the posterior sagittal approach emphasises the importance of the voluntary sphincter complex in the reconstruction, and not just the puborectalis sling as in classical approaches.[49] PSARP involves a midline sagittal incision through the external anal sphincter and levator muscles

with the patient in a prone position (**Figure 9a**). The current practice at our centre involves a modification of PSARP that leaves the most distal part of the muscle complex forming the external sphincter intact.

The posterior sagittal approach permits exposure of the terminal bowel and fistula under direct vision, and ligation of the urethral communication with preservation of the complete fistula. The bowel is mobilised in an easily identifiable and largely avascular plane to allow for tension-free anastomosis to the centre of the voluntary sphincter complex (**Figure 9b)**. The rectal termination and IAS are thus conserved and anatomically repositioned. The incised structures are closed anatomically in layers using absorbable sutures (**Figure 9c**).

Figure 9 – Stages of PSARP: a) exposure and ligation of the fistula under direct vision; b) bowel brought down for anastomosis in centre of sphincter complex; c) anatomical closure in layers after anoplasty.

a) b) c)



Patients undergo an anal dilatation programme as for ASARP followed by colostomy closure. In some bladder neck and vesical fistulas, trans-abdominal ligation of the fistula, either laparoscopically or via a Phannenstiel laparotomy, is required when it cannot be reached via a sagittal incision alone.[72] In these cases, laparoscopic access avoids the need for a laparotomy.[73]

Almost fully laparoscopic methods of repair have also been practiced for urethral fistula.[74,75] In laparoscopy-assisted anorectal pull-through (LAARP), first described by Georgeson,[76] the bowel termination is brought down through a bluntly dissected route from a small perineal incision to the centre of the external sphincter complex.[77,78]

The main technical challenges of this approach relate to ensuring accurate positioning of the pull-through canal and complete ligation of the fistula, especially in bulbar cases.[79] Although LAARP avoids a lengthy sagittal incision, short-term studies have not demonstrated a significant functional benefit over classical PSARP.[73] Recently, a combined laparoscopic and modified posterior sagittal approach (PSAP) conserving the external sphincter was described as a more physiologic technique for the repair of urethral fistula, with encouraging short-term results.[80] This also represents our current approach to recto-bladder neck and vesical fistulas.

Imperforate anus without a fistula

Patients with imperforate anus and no fistula undergo primary colostomy formation in the neonatal period. At the time of definitive repair, our practice has involved initial retrograde endoscopy of the distal rectum to identify those cases where the anal canal terminates just above the overlying skin. Bright translumination at the anal dimple and within the external sphincter is indicative of a low, almost membranous defect that is amenable to treatment by incision alone under direct endoscopic visual control (transanal endoscopic-assisted proctoplasty – TAEAPP).[53,81] The colostomy can usually be closed in the same procedure. Poor or no translumination is indicative of a higher separation between the rectal pouch and the external sphincter, and for these patients our approach consists of standard PSARP with later closure of the colostomy.

Cloaca

The primary management of cloaca is a diverting colostomy and drainage of hydrometrocolpos, if present.[65,82] The colostomy should leave enough distal colon available for a pull-through, and also for vaginal replacement, if needed.[82] The later definitive repair via a posterior sagittal approach depends on the length of the common channel and anatomy of the malformation, and should be performed in a specialist unit with experience in the management of cloacas.

4.7 Complications

4.7.1 Mortality

With modern surgical management and intensive care facilities, mortality at our centre has decreased from 23% between 1946-53 to 3% between 1984-1998.[5] Usually, mortality is caused by the presence of severe or uncorrectable associated anomalies, which occur more often in association with severe ARMs.[5]

4.7.2 Operative complications

Serious operative complications such as peritonitis, major wound breakdown or re-fistula to the urogenital tract occurred in approximately 2% of patients in recent literature, mostly after cloacal repair.[5,52] The prevalence of serious operative complications following classical operations was approximately 10-30%.[5] Local anal complications such as rectal prolapse are also less common after PSARP than after laparoscopic-assisted anorectal pull-through (LAARP), although minor mucosal ectopy may affect some patients.[5,52,75] Operative trauma to the genitourinary tract such as urethral stricture, is also less likely after PSARP than classical pull-through operations (0% vs 12% in one series) (Misra 1996).[83] Insignificant or no alterations to urinary tract function have been reported after PSARP for various types of ARMs,[84-86] unless extensive retrovesical dissection or laparotomy has been required. Posterior urethral diverticulum has been reported after laparoscopic approaches and usually relates to incomplete excision of the fistula, mostly in bulbar cases.[75,79]

Colostomy problems, mainly prolapse and/or stricture, are the main potential complications in patients with more severe ARMs, but are less common after proximal sigmoid colostomy than transverse colostomy.[54] In patients with a cloaca, a sigmoid colostomy that has left too little distal colon for later repair and/or vaginal reconstruction can be avoided with a transverse colostomy. Complications following perineal procedures such as cutback anoplasty for males with low anomalies are unusual and mostly minor.[5]

Significant anal stenosis is preventable with close follow-up during the dilatation programme and is uncommon thereafter. Minor perineal procedures for low malformations in males also should not, in theory, risk injury to the genitourinary tract.

4.8 Measurement of outcomes

4.8.1 Scoring systems

Over the years, many different scoring systems have been employed for the evaluation of outcomes following the surgical treatment of ARMs, which has presented challenges for the later comparison of outcomes between series. Fortunately, the major scoring systems have placed fecal continence as the most important endpoint in patients with ARMs[87] and have focused on the evaluation of this from different perspectives. Historically, the Scott method[88] defined outcomes as "good," "fair," or "poor" based only on the presence or absence of stool control, perianal soreness and sphincter tension. The Kelly score[89] introduced more detail and a quantitative scoring system based on otherwise similar functional and objective criteria. Later, Holschneider and Metzer[90] built on the concept of quantitative clinical scoring and added manometric parameters to the evaluation. The Wingspread Score[91] approaches the problem from a slightly different angle by gauging the functional outcome from the degree of therapy required for symptom control. These systems have all contributed to the development of further models of evaluation.

The system of Peña[52] importantly brought in the concept voluntary bowel movements (VBMs) as one of its major criteria of assessment. VBMs, defined as the ability to recognise the urge to defecate, the capacity to verbalise this and the ability to hold the movement, have since established a key role as in the reporting of outcomes for ARM patients.[45,52] The Bowel Function Score (BFS), developed by Rintala and Lindahl[92] in 1995 and used in the current study (Appendix 1), presented an observer-independent system for evaluating fecal continence. It has the advantages of being easy to complete by the child or their parents and requires no physical examination.[93] It also contains an enquiry of

the social effects of bowel function on the individual that has not been featured in other models. Previous evaluation of the BFS, including comparison with control data, has consistently demonstrated a good correlation of scores with functional outcomes.[87]

4.8.2 Objective methods

Anorectal manometry (AM) has represented the mainstay for obtaining objective data on sphincter function.[5] There is general agreement that the presence of the rectoanal inhibitory reflex (RAIR), indicative of the presence of functioning IAS muscle, correlates with better clinical continence.[92,94,95] Conversely, decreased rectal sensitivity to rectal distension has been linked to a poor functional outcome.[95,96] The excellent soft tissue visualisation capacity of magnetic resonance imaging can demonstrate sphincter hypoplasia, misplacement of the bowel and abnormalities in the anorectal angle in ARM patients, although the correlation with clinical outcomes has not been conclusively reported.[5,97] Electromyography and endoanal ultrasound have also been used to assess EAS function and to image the anatomy of the anal sphincters, respectively.[98]

4.9 Functional outcomes following repair of ARMs

4.9.1 Constipation

Constipation has been reported in approximately 42-56% of patients with ARMs, more so after IAS-saving PSARP than classical operations.[53,58,92,99-102] Constipation in ARM patients most likely stems from abnormal development of the muscular or enteric nervous system of the terminal rectum,[103,104] leading to dyssynergic defecation and disordered rectal emptying.[52,102,105] Uncommonly, it may be a consequence of untreated anal stenosis.[5] The mainstay of treatment at our institution involves dietary modification and oral laxatives, short courses of rectal enemas for acute fecal impaction. Improvement of constipation has been reported around adolescence in some series.[106] The main potential

long-term complications of constipations are overflow incontinence and development of a megarectum requiring surgical resection.[107]

4.9.2 Fecal incontinence and soiling

Mild malformations

Traditionally, it has been thought that the continence outcomes for "low" or mild anomalies are good in most cases.[49,53] Severe soiling that is not associated with constipation is unusual after treatment of low ARMs.[5] The functional outcomes of low ARMs during childhood have been deemed "good" in 80-88% of patients in older series,[108-110] and "normal" in 47-53% of patients in others.[100,111,112] In these series, a "good" functional outcome implies sufficient or acceptable continence for social functioning, but this does not equate to having normal bowel function.[5] Recently, more detailed analyses have suggested that minor functional aberrations may be present in a significant proportion of patients in the long-term.[66,113,114]

Severe malformations

Outcomes after classical repair up to the 1980's

The prognosis for fecal continence is thought to be less optimistic from the outset for patients with more severe malformations. Continence issues are particularly likely for in high urogenital connections due to increasingly severe hypoplasia of the sphincter mechanisms with ascending level of anomaly.[5,52,92,115] Prior to the PSARP era, the percentage of patients who achieved a "good" outcome during childhood has varied widely between 6-56%, and conversely "poor" outcomes affected 10-66%.[66,108,110,116-118] These wide variations are unlikely to be due to large differences in operative outcomes.[66] Rather, they are likely to reflect the outcomes as measured by different methods of clinical assessment, which have differed substantially in their index of sensitivity for the effects of social adaptation to abnormal anorectal function.[66,119]

Out of two large series, however,[2,116] only 7.5% of patients were free of soiling and fecal accidents after classical methods of repair.

In adulthood, by which time any residual dysfunction can be considered to be largely permanent, the prevalence of soiling was 81-94% in the few series that are available,[120-122] and 30-68% of these patients had undergone some form of secondary sphincter reconstruction for deficient continence. Twenty-one to 27% had a "poor" outcome, indicating near-total incontinence or a permanent stoma, and up to 85% reported significant social disability due to deficient continence.[66] It is therefore apparent that the continence outcomes preceding the PSARP era were suboptimal in most cases. Iatrogenic sphincter damage, failed primary surgery, mental retardation and severe sacral dysplasia are other major determinants associated with a reduced continence outlook.

Outcomes of severe ARMs in the PSARP era

Classical operations represented the best available treatment until the advent of PSARP in the early 1980's. To date, there remains limited data on the long-term functional outcomes up to adulthood following sagittal repair. The available literature generally supports an improved clinical outcome and better quality of life[52,106,123,124] compared to classical repair, with some exceptions.[125] Rates of total continence following PSARP during childhood and up to adolescence between 35-50% have been found in larger series, but conversely significant soiling in 22-41% of patients.[52,106,124] Effective and timely treatment of constipation, which is common following PSARP, has allowed some patients to gain "normal" or near-normal bowel function and improved soiling in others.[52,92]

Disappearance of constipation around adolescence and subsequent improvement of bowel function has been reported in some series,[106] although the reasons for this are not entirely clear. The effects of modern systematic aftercare following PSARP, including earlier intervention with bowel management programmes to improve continence,[126] and greater attention to the social and psychological aspects of the illness[127,128] may begin to be reflected in the results of current care.

4.10 Other prognostic factors

Other than the level of the anomaly, the presence of severe sacral anomalies has been associated with more markedly hypoplastic sphincters.[5] The sacral ratio, which relates sacral length to the bony parameters of the pelvis, was proposed as a means of correlating sacral dysplasia with the final functional prognosis.[52] However, studies linking sacral dysplasia to fecal incontinence have yielded conflicting results, with some investigators finding an association and others no correlation.[129,130] However, severe sacral defects in association with caudal regression syndrome/total sacral agenesis or hemisacrum with Currarino syndrome are clearly associated with a reduced continence outlook in ARM patients,[43,131] as is meningomyelocele due to neurogenic bowel and bladder from significant spinal dysraphism.[132] The data concerning the influence of intraspinal abnormalities in isolation (e.g. terminal filum lipomas) on the functional prognosis in ARM patients remains unclear and requires further investigation.[16,133-135]

4.11 Secondary measures for the treatment of fecal incontinence

4.11.1 Re-do anorectal surgery

According to Levitt and Peña,[136] the only candidates who may benefit from revisional surgery are patients born with a malformation that is associated with a good prognosis but with a rectum that is completely mislocated, an intact rectosigmoid, normal sacrum, and an intact sphincter mechanism. They concluded therefore that a "well-executed primary repair" therefore represents the best chance for a good functional outcome.[136] Historically, the results of various re-do operations to the anorectum have mostly yielded outcomes equivalent to, or most often inferior than, after the initial surgery in the long-term.[5,136]

Secondary reconstructions such as graciloplasty to improve the muscular tone around the anus,[137-139] or Kottmeier's levatorplasty and its modifications to increase the anorectal

angle,[140,141] have not resulted in significant anal continence improvements in the long-term.[5] Other efforts of secondary sphincter substitution, including gluteus muscle plasty, free- or smooth muscle transplantation,[142,143] and artificial sphincters have not proved convincing.[5]

4.11.2 Malone Antegrade Continence Enema (ACE)

The Malone Antegrade Continence Enema (ACE) conduit, first described in 1990[144] represents the most potent intervention to date for restoring social fecal continence in ARM patients. A catheterisation channel is formed on the anterior abdominal wall or within the umbilicus, usually from an end-appendicostomy. Caecal, ileal and sigmoid conduits have also be used if the appendix is not available.[145,146] Soiling and fecal accidents are alleviated through patient-controlled colonic emptying at regular intervals with washouts via the conduit. Thus, the mechanism for restoring fecal control is principally based on an empty colon, and is thereby largely independent of anal functioning. The majority of patients are able to achieve social continence with the aid of washouts following this procedure.[145,147-149] Although minor leakage, stenosis, or granulation tissue formation at the ACE site are relatively common (13-26%),[145,146,148,150] these can usually be adequately addressed with minor procedures.

4.11.3 Other measures

Biofeedback therapy has been attempted as a measure for reducing fecal incontinence in selected ARM patients. Biofeedback may improve minor anorectal dysfunction and fecal incontinence that is mainly secondary to concomitant chronic constipation, particularly in combination with other dietary and lifestyle modifications.[151-153] Its impact on ARM patients with severe fecal incontinence is therefore likely to be marginal and insufficient.[5]

Sacral nerve stimulation (SNS) is a concept that has been applied to treat fecal incontinence of various etiologies.[154] Whilst a medium- to long-term effect has been

reported in approximately half of cases,[155] including patients with IAS disruption,[156] a clear role for SNS in the treatment of ARM patients has not been established. Sacral anomalies, which occur frequently in association with high ARMs, also present technical challenges for SNS.[157,158] Antidiarrheal medications such as loperamide may benefit patients with loose stool consistency or increased bowel frequency.

5. Aims of the Present Investigation

The aims of the present study were:

- To study the nature and prevalence of functional bowel symptoms in the general Finnish population to gain a baseline estimate of normality at different ages (I)
- To investigate the hypothesis that the fine-tuning of fecal control continues to develop during childhood in the general population (I)
- To define the long-term functional outcomes for individual types of ARMs after standardized treatment and systematic aftercare in relation to matched controls from the general population:
    - Females with anterior anus treated conservatively or with dilatations (II)
    - Males with low anomalies treated with minimally invasive perineal procedures or dilatations only (III)
    - Females with perineal or vestibular fistula treated with anterior sagittal anorectoplasty (IV)
    - Males with intermediate or high anorectal malformations treated with posterior sagittal anorectoplasty (V)
- To evaluate the frequency of operative complications and requirement for further surgery (II-V).
- To study the effects of increasing age on the prevalence of functional bowel symptoms in ARM patients from childhood to adulthood in the PSARP era (II-IV)
- To establish a baseline for the likely long-term functional prognosis in different types of ARMs to guide patient counselling and clinical management

6. Methods

"Everything must be made as simple as possible. But not simpler."
- Albert Einstein

6.1 Patients

After institutional ethical and research board approval for the study, all patients treated at the University of Helsinki, Hospital for Children and Adolescents for anterior anus (AA), perineal fistula (PF) and/or anocutaneous membrane, vestibular fistula (VF) and rectourethral fistula (RUF) between 1983-2006 were identified from hospital records. Patients with major learning difficulties, Currarino syndrome, total sacral agenesis (caudal regression syndrome) or menigomyelocele were excluded. All remaining alive patients residing in Finland were invited to answer a detailed bowel function score (BFS) questionnaire by post. The study was conducted by an independent investigator who had not been involved in the surgical care of the patients. Participation in the study was voluntary and patients and their parents received a written explanation of the aims and purpose of the study. Parents assisted children below the age of 16 years in their responses. Case records were reviewed retrospectively for operative and clinical details.
In this dissertation, ARMs with a termination of the anal canal mostly within the voluntary sphincter complex were considered mild (i.e. AA females and males with PF/low ARMs) and those with anal canal termination outside the voluntary sphincter complex were considered severe types (i.e. VF/PF females and RUF males).

6.2 Controls

A total of 1840 individuals aged 4 to 26 years (40 male and 40 female for each year of age) were randomly selected from the population register of Finland and invited to answer the same BFS questionnaire as patients by post. Participation was voluntary and anonymous. For the study of bowel functional symptoms in the general population (I), the

results were analysed by age group according to developmental stage (pre-school 4-7 years; primary school 8-12 years; secondary school/teenage 13-17 years and young adults 18-26 years) and by gender. For the functional outcomes analysis in ARM patients (II-V), three age- and gender- matched controls were randomly selected for each patient from this pool of respondents, which was the maximum number of controls available per patient. Four patients aged 28-29 years of age had to be matched to 26 year-old controls, as these were the oldest available from our pool.

6.3 Questionnaires

The BFS questionnaire (Appendix 1) is an observer-independent, multivariate qualitative scoring system designed by Rintala and Lindahl in 1995[92] for the assessment bowel function in patients with benign anorectal disorders.[111,159,160] Items are scored from 0-3 according symptom severity, apart from frequency of defecation (scores 0-2). The maximum score is 20. A BFS of ≥17 was taken to indicate a good outcome in the normal range, based on the outcomes of our study on individuals from the general population (I). Parents of respondents ≤12 years of age were asked to give the ages at which diapers for stool were discontinued. Social continence was defined in our studies (II-V) as fecal accidents or soiling <1/week and without requirement for changes of underwear or protective aids.

6.4 Statistics

Data is presented as median (range) or as frequencies. Statistical analysis was performed using Fisher's exact, Chi-squared or Mann-Whitney U-test as appropriate. A *p*-value of <0.05 was considered statistically significant.

7. Results

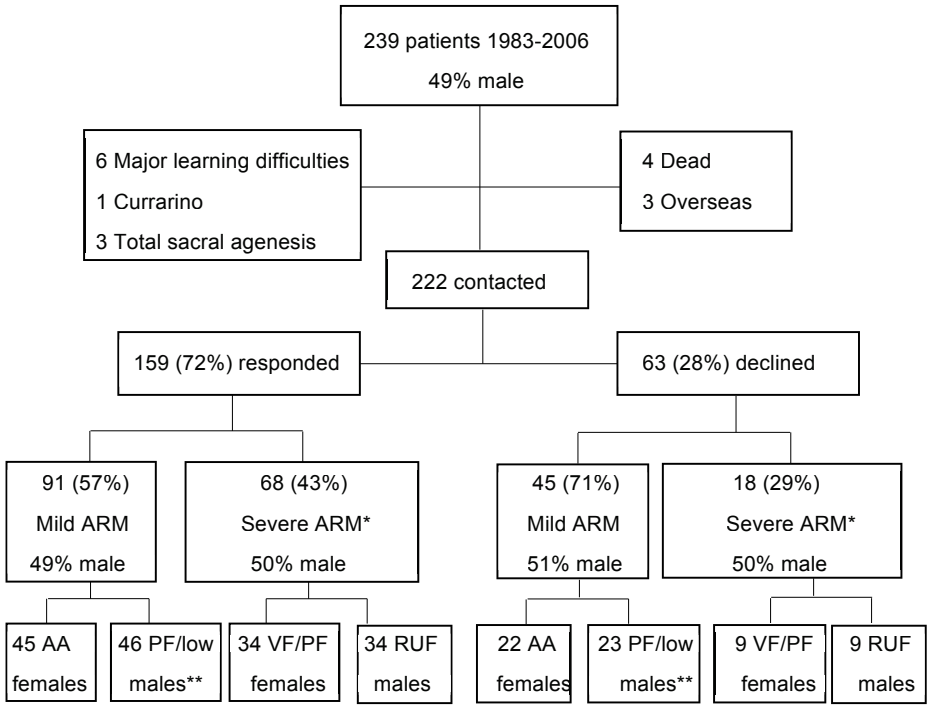
"In theory, theory and practice are the same.
In practice, they are not."
- Albert Einstein

7.1 Patients

7.1.1 Participants

A total of 159 (72%) patients participated in the study (**Figure 10**), including 91 patients (57%) with a mild ARM (II-III), and 68 patients (47%) with more severe malformations (IV-V). The median age of respondents was 12.5 (4-29) years, and all had been followed up regularly since birth. In males with RUF, the fistula was bulbar in 35% (n=12), prostatic in 53% (n=18) and at the bladder neck in 12% (n=4). The sacrum was mildly dysplastic (≥3 segments remaining) in 0% females with AA, in 10% of males a low malformation, in 21% of females with VF or PF, and in 26% of males with RUF. All patients had undergone standardized management according to the same operative principles. All operations had been performed by consultant paediatric surgeons or by younger surgeons trained by them. The 4 deaths in the cohort (1.7%) were unrelated to the surgical repair of the ARM. No patients were lost to follow-up.

Figure 10 – Patient characteristics



*Anomalies with anal canal termination outside the external sphincter complex

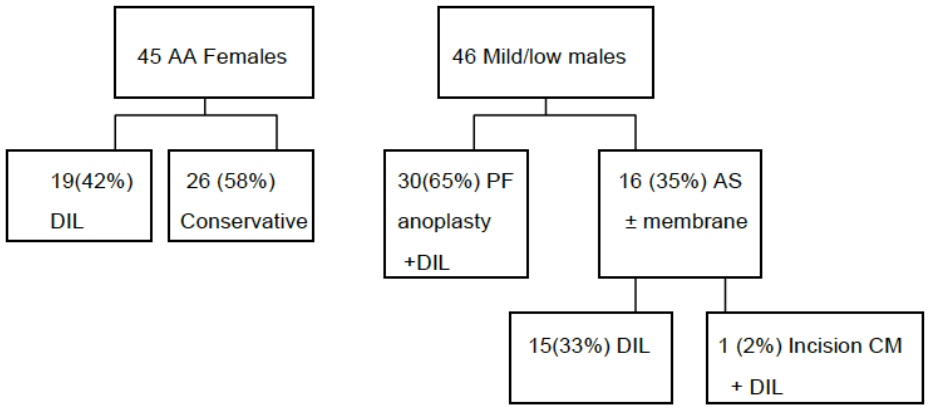
**Includes males with anal stenosis ± anocutaneous membrane

7.1.2 Surgical treatment

Mild ARMs (II-III)

Patients with mild ARMs (n=91), had received conservative treatment or individualized, minimally invasive perineal procedures, as shown in **Figure 11**. For PF in males, the median age at cutback anoplasty had been 1 (0-7) days in all except for 3 cases, where a primary sigmoidostomy had been initially formed due to uncertainty of the level of the ARM. A further 3 males with stenotic defects had also undergone sigmoidostomy formation initially. Anal stenosis (AS) was diagnosed at a median age of 21(0-389) days. Membranous defects had been released by incision in 6 males (13%), and a 'covering' median bar excised in 4 (9%).

Figure 11 – Treatment of mild ARMs



Severe ARMs (IV-V)

All patients with more severe malformations underwent fistula-saving repair via a sagittal approach. Females with PF and VF (n=34) had undergone anterior sagittal anorectoplasty (ASARP) at a median age of 1.0 (0.1-46) months. ASARP had been performed without a covering colostomy in 68% of cases (n=23). In the remainder (n=11), the covering colostomy was closed at a median of 4 (3-5) months after definitive surgery. All males with RUF had undergone sigmoid colostomy formation during the first day of life. Ninety-one per cent had undergone standard PSARP (with laparotomy in one case) and 9% (n=3) had undergone laparoscopic-assisted PSARP at a median age of 3 (1-18) months. The median time from PSARP to stoma closure was 4 (2-7) months.

7.2 Complications

Early post-operative complications

There were 5 colostomy-related complications (4 cases of bowel prolapse, 1 bowel obstruction) among a total 63 respondents with a primary diverting colostomy (8%), all among RUF males. There were 3 cases of perineal wound infection after ASARP (9%), one of which occurred despite a diverting colostomy, and 1 case of perineal wound dehiscence (3%) requiring re-suturing. After PSARP, 1 anal stricture (3%) requiring repeat anoplasty occurred during the dilatation period.

Late complications

Repeat anoplasty was required in two males with PF due to an incomplete primary procedure in one, and due to anal stricture in the second at the ages of 2 months and 1 year, respectively. After ASARP and following severe constipation the perineal body gradually broke down in one patient, requiring several revisional surgeries including re-do ASARP at the age of 5 years. After PSARP, minor mucosal ectopy requiring operative correction on 1-2 occasions occurred in 4 patients (12%). There were 2 cases of rectal stricture in patients who had undergone PSARP with rectal tapering prior to 1991, treated with stricturoplasty in one case and dilatation only in the second. Laparoscopic rectopexy for rectal prolapse was required in 1 RUF patient 3 years after laparoscopic-assisted PSARP. Resection of megarectosigmoid secondary to severe constipation had been performed in 6 patients in the series (4%; 2 patients with mild and 4 patients with severe ARMs). One respondent with RUF had undergone colostomy formation just prior to the time of survey due to intractable diarrhea of unknown etiology. Due to the enterostomy, only the social item of his questionnaire could be analysed, leaving 33 complete responses for other items in RUF patients.

7.3 Non-respondents

The median age of non-respondents (n=63; 28%) was not significantly different from respondents for any type of ARM apart from low anomalies in males, where non-respondents were slightly older (16.8 vs 12.3 years; p=0.04). Other essential patient characteristics, including type of defect and treatment, proportion with a primary colostomy, degree of sacral dysplasia and requirement for ACE conduit were comparable between respondents and non-respondents (p=NS), making significant selection bias unlikely.

7.4 Controls (I)

Of a total of 1840 individuals randomly selected from the general population, 594 (32%; 261 males) returned complete questionnaires (I). There were no significant differences by age or sex between respondents and non-respondents among the controls, apart from a higher percentage of female respondents (71%) in the 18-26 years age group. From this pool of respondents, the randomly selected controls for the comparative study on bowel function in patients were of the same age and gender distribution as patients (*p*=NS).

7.5 Long-term bowel functional outcomes

7.5.1 Functional outcomes in the general population (I)

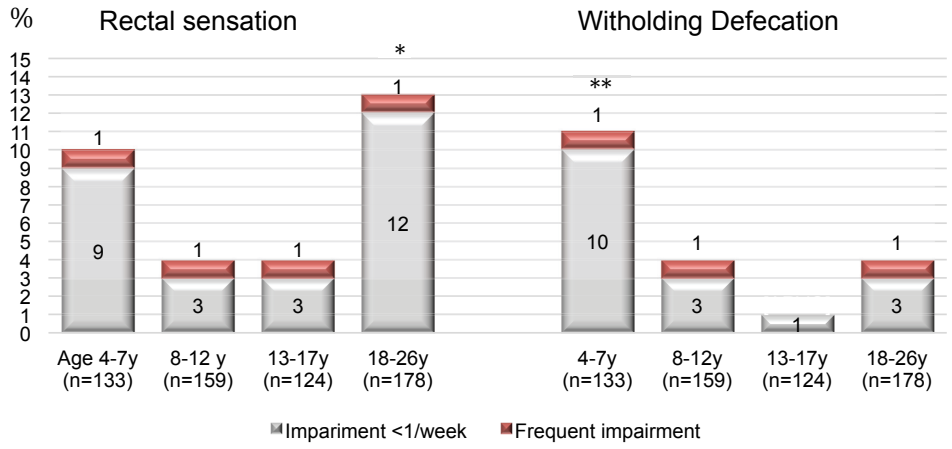
The overall prevalence of impairment in rectal sensation, problems withholding defecation, soiling and fecal accidents in respondents from the general population are shown in **Figure 12.** Soiling, which was mostly occasional (<1/week) was common in the general population. Frequent impairment in any aspect affected between 1-2% overall.

Figure 12 – Prevalence and frequency of functional impairment among 594 controls aged 4-26 years

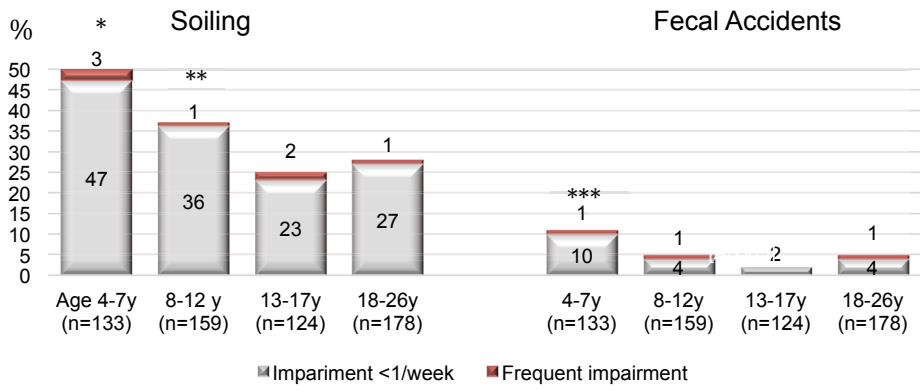
Impairment by age group in controls

Problems with recognition of the need to defecate (rectal sensation) occurred in 8% of controls overall (**Figure 12**) and these were most common in young adults (13%), but there was no significant difference between age groups up to the age of 17 years. Impairment of other aspects of fecal control, including problems withholding defecation, soiling and fecal accidents were significantly more common in patients 4-7 years of age than in other age groups, as shown in **Figure 13**, and decreased significantly with age up to 12 years. Frequent symptoms (>1/week) were uncommon in any age group (≤3%). Occasional soiling continued to prevail in approximately ¼ of respondents in adulthood. There was no significant difference by gender in the prevalence of any of these functional symptoms, except for the overall prevalence of fecal accidents, which were significantly higher in males (8% vs 3% overall, *p*=0.01).

Figure 13 – Functional impairment reported by controls by age group



Above: *p=0.01 compared to 8-12y and 13-17y age groups. *P*-values refer to overall prevalence of any impairment; **p<0.05 compared to all other groups, p=NS between other age groups.

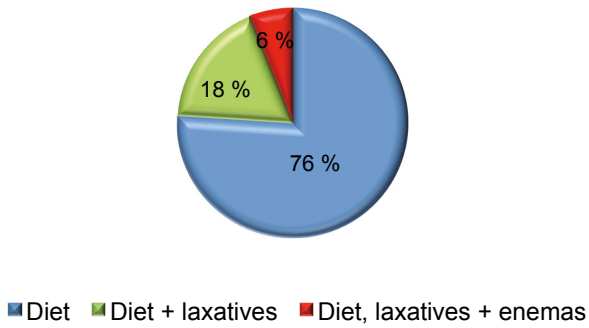


Above: *p<0.05 compared with all other age groups; **p=0.005 compared to 13-17y age group; ***p=0.02 compared to 13-17y and 18-26y groups. *P*-values refer to overall prevalence of any impairment.

Constipation among controls

The overall prevalence of constipation among controls was 8%, and it was more frequent among females (13% vs 3% in males; p<0.0001). Most constipation was diet-controlled (**Figure 14**). In males, constipation occurred in 2-4% by age group, but in females a bimodal distribution was observed, with peaks between 4-7 years (19%) and 18-26 years (18%) which was significantly higher than in males of these age groups (p≤0.008) and in females aged 13-17 (3%; p<0.05).

Figure 14 – Treatment of constipation among controls (8% prevalence overall)



Social problems in relation to bowel function

Social problems relating to bowel function were uncommon and usually mild. They were reported by 5% of the control population overall: 0% between 4-7years of age, 3.5% thereafter up to age 17, and 10% in young adults with no significant gender differences. Major social restriction or psychological problems due to bowel function were rare (0.8%).

Bowel function score (BFS) and age at completion of diapers for stool

By age group, the 10^{th} percentile of the BFS was 17 in 4-7 year-olds, 19 in 13-17 year-olds and 18 in the other age groups. There were no significant gender differences. Diapers for stool had been completed at a mean of 2.2±0.6 years (2.1±0.6 years in girls and 2.3±0.6 years in boys; *p*=NS).

7.5.2 Bowel Functional Outcomes in ARM Patients (II-V)

Voluntary bowel movements (VBMs)

All patients with mild ARMs and all females treated for PF/VF with ASARP had voluntary bowel control. Only 1 female in the VF/PF group had previously undergone ACE formation, which had since been closed. Among RUF patients, 74% had developed VBMs and the remaining 26% (n=9) only emptied their bowels using ACE washouts.

Total and social continence

The overall rates of total- and social continence are shown in **Table 4**. There were no significant differences compared to controls for the rates of total- or social continence in mild ARMs after this follow-up period (median 12.5 years). In severe ARMs, the rates of both total- and social continence were significantly inferior to controls, being lowest in RUF males. Of controls, only 64-76% reported total continence, but almost all reported social continence (≥98%).

Table 4 – Continence rates among patients and matched controls

ARM type (n)	Total continence, n (%)			Social continence, n (%)		
	Patients	Controls	*p**	Patients	Controls	*p**
AA females (45)	31 (69)	88 (65)	NS	44 (98)	135 (100)	NS
Low males (46)	31 (67)	88 (64)	NS	45 (98)	97 (134)	NS
VF/PF females (34)	14 (41)	78 (76)	0.0003	29 (85)	102 (100)	0.001
RUF males (33)	10 (30)	69 (70)	<0.0001	25 (76)**	95 (96)	0.002

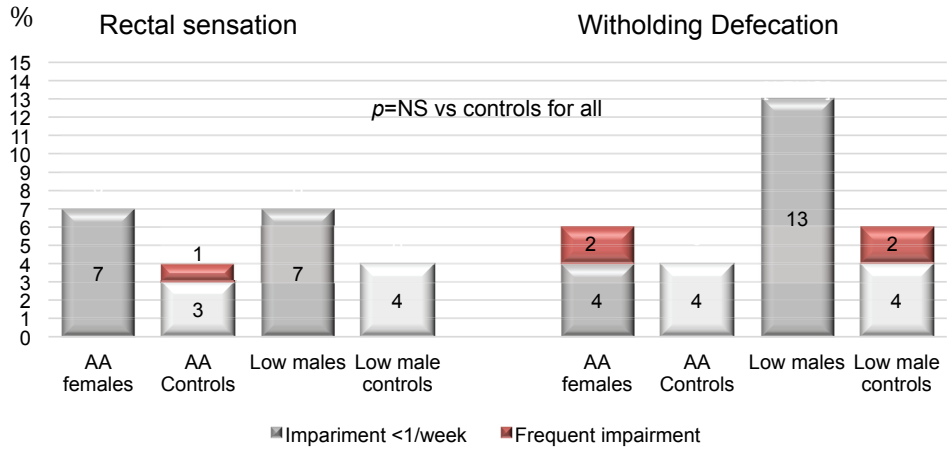
* *p* vs respective controls; ** includes 6 patients with ACE who were socially continent by artificial means

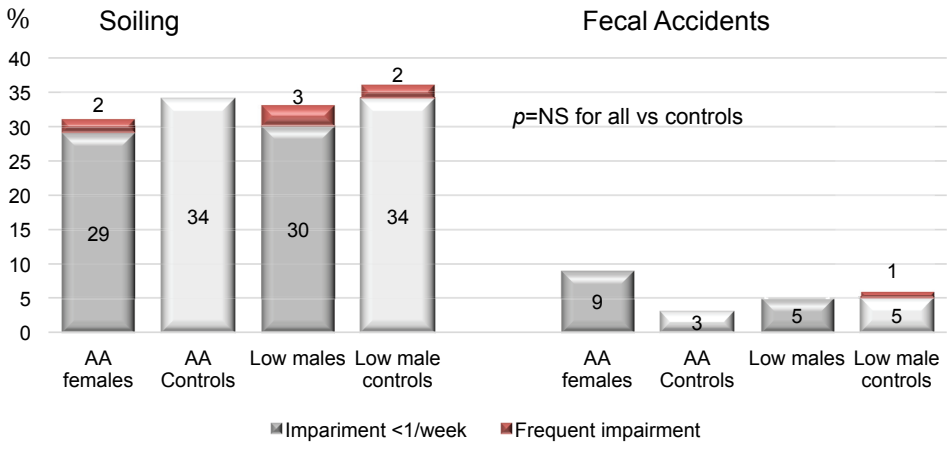
Prevalence of impairment of fecal control

Mild ARMs (II-III)

In patients with mild ARMs, the overall prevalence of impairment of any aspect of fecal control was not significantly different to controls, as shown in **Figure 15.** Problems withholding defecation were twice as common in males with low ARMs compared to controls, but the difference was not statistically significant (p=0.11). Minor soiling was comparably common among both patients and controls.

Figure 15 – Impairment of fecal control in patients with mild ARMs vs controls

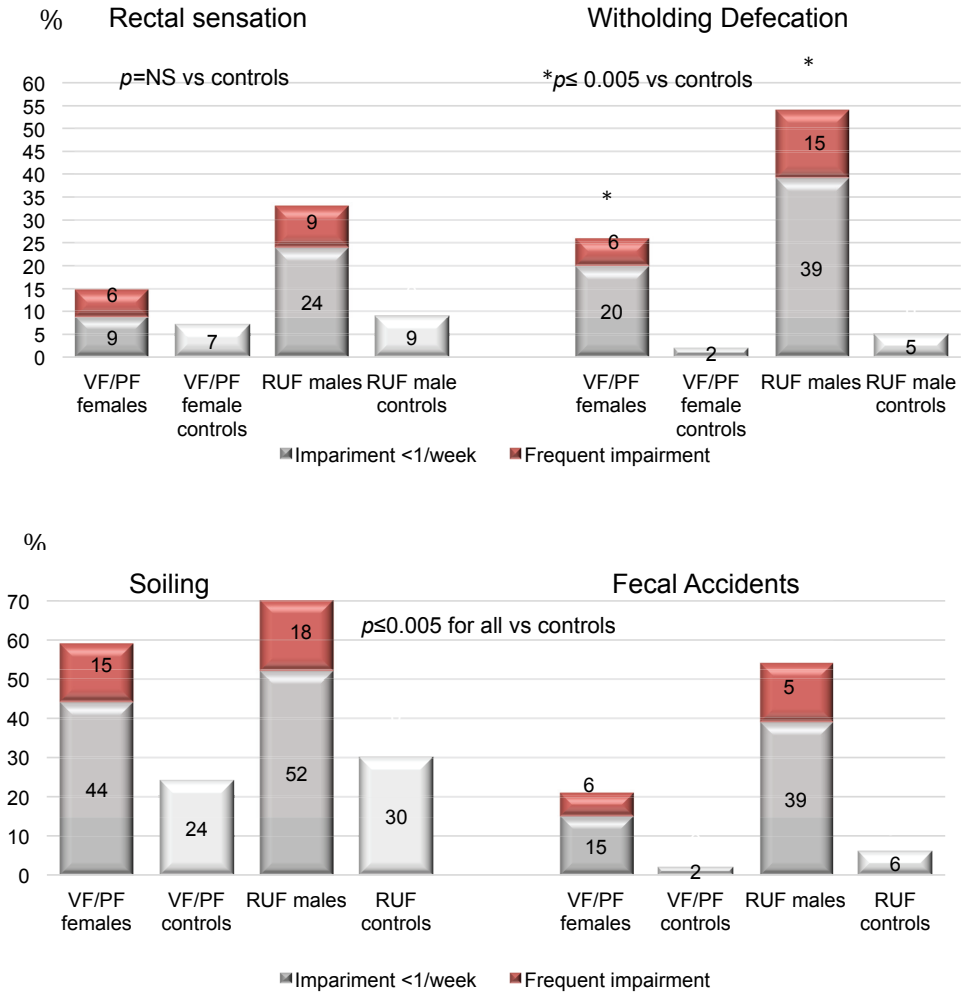




Severe ARMs (IV-V)

As shown in **Figure 16,** all aspects of fecal control apart from rectal sensation were significantly impaired in comparison to controls, and the differences were greatest in RUF males.

Figure 16 – Impairment of bowel function in patients with severe ARMs

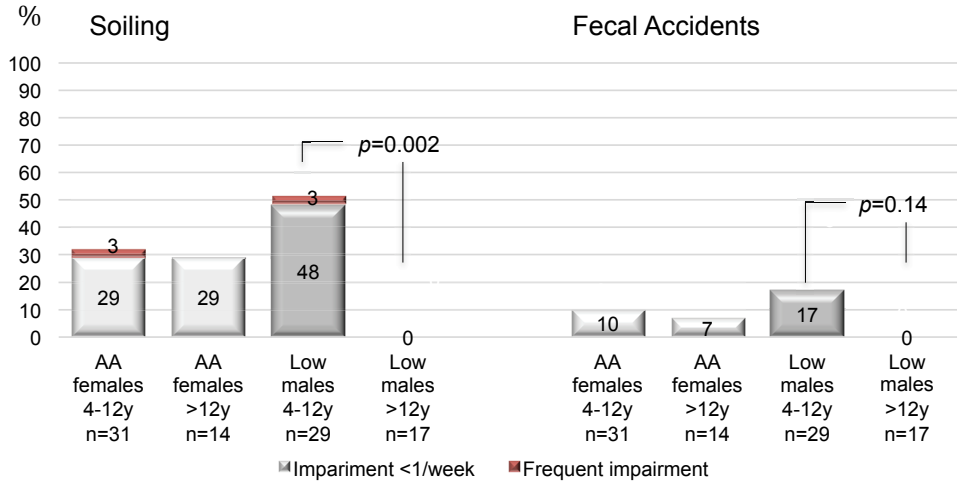


Effects of age on soiling and fecal accidents

Mild ARMs (II-III)

As shown in **Figure 17,** soiling in males with low ARMs declined significantly with age (*p*=0.002*)* and less fecal accidents were reported (*p*=0.14). Symptom prevalence by age group was not significantly different from controls, except for lower soiling in males with low ARMs, where the prevalence in respondents >12 years of age was lower than controls (0% vs 30% in controls; *p*=0.01). No age-related differences were apparent in our cohort of in females with AA.

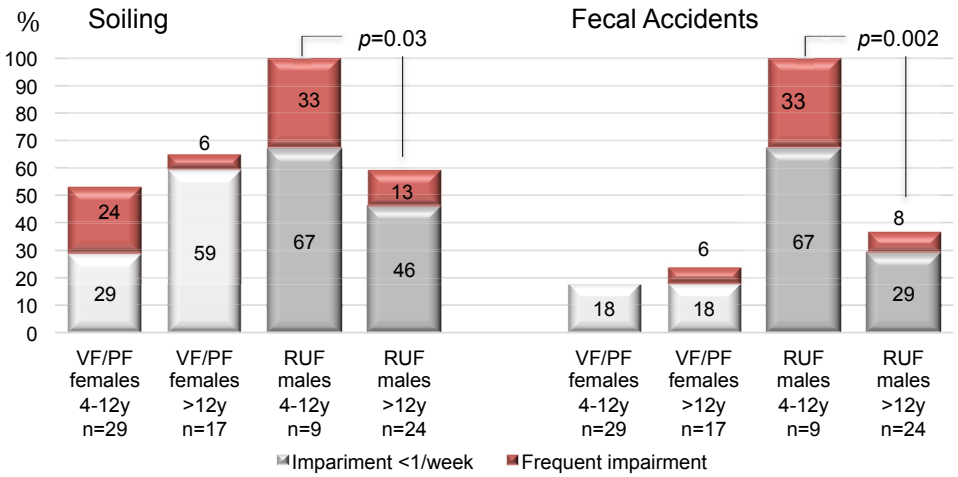
Figure 17 –Soiling and fecal accidents by age group in mild ARMs



Severe ARMs (IV-V)

The assessment of fecal control by age group in severe ARMs is shown in **Figure 18.**

Figure 18 – Soiling and fecal accidents by age group in severe ARMs



In females with VF/PF, no significant age-related decline in the prevalence of soiling or fecal accidents was apparent (*p*=NS). The prevalence of soiling was higher in patients than in controls in the long-term (29% in controls aged 4-12 years; *p*=0.08, and 18% in controls over 12 years of age, *p*=0.0005 vs respective patients by age group). Frequent soiling (>1/week) was also significantly higher in patients <12 years of age (24% vs 0% respectively; *p*=0.003). Fecal accidents were higher in female patients in both age groups (0% in controls aged ≤12 years, and 4% in older controls; *p*≤0.03 vs patients).

In RUF males, the prevalence of soiling and fecal accidents (**Figure 18**) were significantly higher than in controls up to age 12 (100% for both symptoms in patients vs 41% for soiling and 7% for fecal accidents among controls; *p*≤0.002), and remained higher in the long-term (59% for soiling and 37% for fecal accidents among patients vs 26% soiling and 6% fecal accidents among controls; *p*≤0.006). Both soiling and fecal accidents showed significant decline with age in patients (**Figure 18**; p≤0.03). Frequent impairment tended to be less common among older patients, but the difference by age group was not statistically significant.

RUF patients with VBMs followed up for >12 years

Of the 24 RUF patients followed up for >12 years, 20 (83%) had developed VBMs. Of these, 50% (n=10) were free of both soiling and fecal accidents (vs 73% of their controls; *p*=0.10) and 85% were socially continent. Five patients (20%) had no bowel symptoms at all (BFS 20/20). However, problems withholding defecation up to an appropriate time were reported by a significantly higher proportion of patients than controls (35% vs 5% of controls), and fecal accidents still occurred in a higher proportion of patients (35%, of which 5% >1/week vs 7% occasional accidents in controls; $p \leq 0.005$ for both). Soiling was reported by 50% of patients (vs 27% of controls; *p*=NS) of which 15% occurred >1/week (vs 2% in controls; *p*=0.04).

Outcomes by level of fistula in RUF males

In males with RUF, the median BFS, the proportion with VBMs and total continence decreased with increasing level of the fistula (**Table 5**). Although no patient with a bladder neck fistula was totally continent, 2/4 patients (50%) were socially continent (1 of whom had voluntary bowel control and the other with the aid of ACE washouts).

Table 5 – Continence outcomes by level of fistula in RUF

Fistula level	n	Median BFS (range)*	%VBMs	% Totally continent
Bulbar	12	18 (6-20)	92	42
Prostatic	17	16 (17-20)	76	29
Bladder neck	4	15 (15)	25	0

*BFS of patients with VBMs

Constipation in ARM patients

The overall prevalence of constipation (**Table 6**) was significantly higher in all types of ARMs than in controls ($p \leq 0.002$ vs patients). Above age 12, the prevalence had declined to a level that was no longer significantly different from the control population for any group. Bowel frequency was comparable to controls in all groups of patients ($p \geq 0.07$).

Table 6 – Prevalence of constipation among ARM patients by type of ARM

ARM type	Constipation, %*			*p for reduction in prevalence by age group*	Normal bowel frequency, %**
	Overall*	Age 4-12 y	Age >12 y		
AA females	36	45	14	0.09	91
Low males	33	45	12	0.02	87
VF/PF females	44	59	25	0.16	88
RUF males[¶]	31	44	13	0.01	67

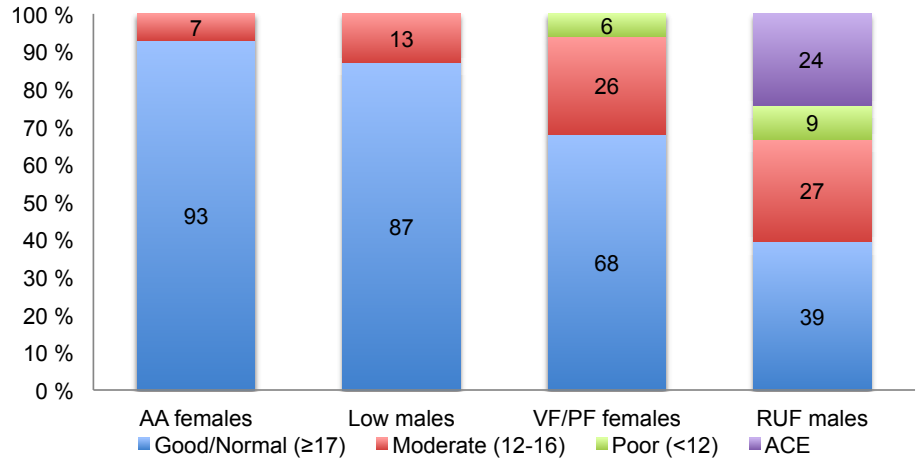
* Prevalence 2-13% in controls; $p \leq 0.002$ vs patients; ** motions 1-2 times per day to once every 2 days, $p \geq 0.07$ vs controls; [¶] includes 25 patients with VBMs; additionally 8 patients only opened their bowels with ACE washouts.

Most constipation was diet- or laxative- controlled; rectal enemas were in use by 6% ≤12 year-old males with low ARMs, and 7% of ≤12 year-old females with VF/PF. Among RUF males, there were additionally 8 patients who were reliant on ACE washouts for opening their bowels and staying clean. They comprised 44% (4/9) of 4-12 year-olds, and 17% (4/24) of older patients. The median age at ACE formation had been 5(4-5) years in patients aged ≤12 years, and 12 (7-22) years in patients >12 years. If all 33 RUF males (including patients with ACE) are considered together, the percentage requiring some form of bowel intervention (entailing dietary, oral laxatives or ACE washouts) was 48% overall. By age group, this was 89% of patients ≤12 years, and 30% of patients >12 years (p=0.005 for reduction with age).

Outcomes by Bowel Function Score (BFS)

The outcomes by BFS, by type of ARM are shown below in **Figure 19.** No patient with a mild ARM reported a poor outcome by BFS. Constipation was the main reason for a reduced score in mild ARMs.

Figure 19 – Outcomes by BFS by type of ARM



The median BFS (range) and proportion of patients and controls with a completely normal BFS (20/20) are shown in **Table 7.** In terms of BFS, patients with mild ARMs achieved scores comparable to controls, whereas in patients with severe ARMs both the median BFS and proportion with a total score of 20 were significantly lower than in controls (p<0.001).

Table 7 – Median BFS and proportion of respondents with an optimal score

ARM type	Median BFS (range)			BFS 20/20, %		
	Patients	Controls	*p*	Patients	Controls	*p*
AA females	19 (14-20)	19 (15-20)	NS	44	48	NS
Low males	19 (13-20)	20 (10-20)	0.05	48	56	NS
PF/VF females	18 (10-20)	20 (16-20)	<0.001	24	57	<0.001
RUF males	17 (6-20)*	19 (11-20)	<0.001	15	59	<0.001

* In 25 patients with VBMs; BFS for 8 patients with ACE cannot be calculated

Completion of toilet training for stool

Completion of toilet training had occurred in all patients with mild ARMs and VF/PF females at an age that was comparable to controls, as shown in **Table 8**. Seven out of the 9 patients aged 4-12 years with RUF had successfully completed toilet training for stool, but the age at completion had been significantly delayed in relation to controls (p<0.0001). In 5/7 cases, discontinuation of diapers had only been possible following formation of an ACE conduit. One patient still in diapers underwent ACE channel formation shortly after completing this survey and became toilet trained.

Table 8 – Stage of toilet training in respondents 4-12 years of age vs controls

ARM type	Toilet training, n (%)		Median age at completion, years (range)		*p*
	Completed	Incomplete	Patients	Controls	
AA females (n=31)	31 (100)	0	2.5 (1.1-3.0)	2.0 (1.1-5.5)	NS
Low males (n=29)	29 (100)	0	2.5 (1.1-3.5)	2.3 (1.3-4.0)	NS
VF/PF females (n= 17)	17 (100)	0	2.2 (1.1-4.0)	2.0 (1.1-2.8)	NS
RUF males (n=9)	7 (77)	2 (23)	5 (2.5-7.3)	2.3 (1.4-4.0)	<0.0001

Social problems in relation to bowel function

In patients with mild ARMs, social problems were reported by ≤3% of patients and ≤3% of the controls (p=NS). The prevalence of social problems in patients with VF/PF was 15% (vs 2% of controls; p=0.01), and 36% among RUF patients (vs 5% of controls; p<0.0001). Moderate to severe social impairment was reported by 9% of both VF/PF and RUF patients. In RUF patients, further sub-analysis of the distribution of social problems found that they occurred in 38% of patients with VBMs and in 36% of patients with an ACE conduit (p=NS). They occurred in 33% of RUF patients ≤12 years of age and 37% of older patients (p=NS).

8. Discussion

"*There is nothing either good or bad, but thinking makes it so.*"

-William Shakespeare

8.1 Normal bowel habits of the general population (I)

This study has aimed to systematically define the long-term bowel functional outcomes that may be expected in patients with different types of ARMs treated with modern methods. The study commenced with a detailed enquiry of these symptoms in the general population (I) to gain a baseline for 'normality' against which results of patients with ARMs and other benign anorectal disorders can be compared. To date, there has been very limited information on what constitutes normal bowel function and fecal continence in children, and only a few series that have attempted to describe these in larger populations.[161-165] The current study (I) has outlined the defecation patterns of a large cohort of children and young adults, and shows for the first time, that the fine-tuning of fecal control continues to mature during childhood (I). The results suggest that minor imperfections in bowel function prevail in healthy individuals in an age-dependent manner, and may not completely disappear even in adulthood (I).

With increasing age, a significant decline in the prevalence of both soiling and fecal accidents was observed, alongside a concurrent reduction in problems withholding defecation that continued up to adolescence. Minor soiling was surprisingly common in the general population, affecting 50% of children age 4-7 years of age, and continuing to be reported by just over a quarter of young adults (I). However, frequent impairment >1/week in any domain of fecal continence was uncommon (≤3% beyond age ≥4 years) and could serve as an indicator of abnormal function in patients. The low rates of social problems due to bowel function in controls (5% overall; of which 0.8% serious) suggests that the kind of occasional soiling reported is not usually perceived to be socially disturbing. Our data on the prevalence of soiling is supported by our previous work using the same questionnaire and a number of other studies,[92,111,159,165] although lower prevalences have also been described.[163,166,167]

Some differences may relate to methodological variations between studies. For instance, the parents of young children may fail to disclose minor symptoms or regard them as normal-for-age unless specifically asked,[3] and other occasional events may be missed if the follow-up period has been short.

Constipation was the only symptom for which our data suggested a gender difference (13% in females vs 3% in males; $p<0.0001$), but this has not been found in other series.[92,111,162,164,165] As most constipation in our series was diet-controlled only (75%), the higher rate reported by females may relate to the sensitivity of our questionnaire to pick up even very mild cases. A limitation of the study (I) was a lack of enquiry into comorbidities and/or pregnancy, which might explain the findings. Also, the possibility of drop-out selection bias affecting the results must be acknowledged due to the overall response rate of 32%. Our results for bowel frequency (92% 1-2 times/day to once every 2 days) and for age at discontinuation of diapers for stool (26±7.2 months) were, however, entirely in keeping with other investigators,[161,165,170] in support of the reliability of our findings.

8.2 Outcomes in ARM patients (II-V)

Evaluation of the bowel functional outcomes following repair of ARMs has been previously challenged by considerable variation in the methods of clinical evaluation,[16,104] and by the inclusion of multiple types of ARMs and/or treatments within the same series.[16,171-173] In the current studies (II-V), we have aimed to overcome this by using a standardized questionnaire, the BFS,[92] applied to patients according to the type of ARM and after standardized management. Patients have been approached by an independent investigator who has not been involved in their surgical care to avoid the potential unwillingness of patients or their parents to disclose poor results to the surgeon who has cared for them.[53,66] Patients with major learning difficulties, total sacral agenesis or hemisacrum with Currarino syndrome, or meningomyelocele were excluded to avoid the effects of major confounding factors on results.

The drop-out analyses showed that the essential characteristics of responders and non-responders including age, gender and treatment were comparable, making significant selection bias unlikely. The age limit of ≥4 years was taken as the lower cut-off in all our work to enable reliable evaluation of bowel functional outcomes in patients, which is possible beyond the age by which toilet training is normally complete.[66,170]

8.3 Fecal continence outcomes in mild ARMs (II-III)

Patients with mild ARMs (II-III) have been treated at our centre with individualized, minimally invasive perineal procedures depending on the exact phenotype of the defect. Females with AA were treated entirely non-operatively with dilatations (42%) or conservative (58%) follow-up only (II) and most males (65%) had undergone minor cutback anoplasty and serial dilatations (III). These methods are aimed towards conserving the existing continence mechanisms as far as possible. Overall, our data on long-term outcomes for continence strongly supports the effectiveness and appropriateness of these treatments for mild ARMs (III).

All patients with mild ARMs achieved voluntary bowel control, consistent with other large series.[52,174] Our data supports the consensus that the outcomes for mild ARMs are generally good, and that bowel function comparable to matched peers can be expected to develop in the vast majority. A BFS within the normal range (≥17) indicative of a good outcome was achieved by 9/10 patients (87% of AA and 93% of low males) with systematic aftercare, and no patient had a poor outcome by BFS (II-III). Patients did exhibit minor symptoms such as soiling, but only at similar levels to their peers. Soiling and fecal accidents by age group did not depart significantly from peers even between 4-12 years, and soiling was incidentally even lower in males patients >12 years of age than in controls. It is possible that the controls were more willing to report minor symptoms than our patient cohort, or this may be a chance finding due to the relatively small numbers of patients.

Our overall rates of soiling in patients with low ARMs compare well with other recent series.[4,100,111,160] The proportion of patients and controls that were totally continent (69% of AA patients and 67% of low males vs 64-65% of controls; *p*=NS) and socially continent (98% of both AA and low males vs 97-100% of controls; *p*=NS) were comparable, in support of our overall conclusions.

8.4 Continence outcomes in severe ARMs after modern repair (IV-V)

The patients with more severe ARMs (IV-V), entailing VF/PF in females and RUF in males, have been treated with standardized anatomical repair by sagittal or limited sagittal approach to restore the normal anatomical relationships between the ectopic anal canal (and IAS) and the external sphincter apparatus. We did not specifically distinguish between females with VF and PF in our series (IV), as our management is the same for both. Although approximately 1/3 of females had a covering colostomy, single-stage repair without colostomy has been shown to be safe and feasible[70,174-178] and also represents our current practice (IV).

Overall, our data supports the safety of modern techniques for the repair of severe ARMs. After ASARP, the main complications relate to the perineal wound (12%) and are mostly minor. Similar complication rates (5-13%) have been reported in the literature.[70,175] After PSARP, one case of anal stricture occurred during the dilatation period, and the remaining early complications were stoma-related (15%), entailing mostly prolapse. This compares favourably with the 10-30% rates of serious operative complications reported following classical repair.[5] Like others,[75] we observed rectal prolapse as a late complication of LAARP in 1 patient.

In terms of fecal continence, all patients with VF/PF reported VBMs, which is in accordance with the 93-100% found in other large series after the same treatment.[70,174-176] However, our evaluation identified that the fine-tuning of fecal control continues to be impaired at a level that is higher than in controls in a substantial proportion of patients with

VF/PF, even in the long-term. After >12 years of follow-up, both soiling and fecal accidents remained more prevalent in patients (65% and 24% respectively vs 18% and 4% in controls; $p \leq 0.03$), although most symptoms were infrequent (<1/week). Interestingly, much lower rates (2%) or no soiling at all have been reported following ASARP for VF/PF in other series.[70,175,176] However, as our work (I) has previously suggested that minor soiling is quite common even among healthy individuals, it is possible that these series have only documented major events or that the investigator has been the surgeon in charge of the patient's care. By BFS, 68% of our female cohort achieved an overall score of ≥17, and 85% reported social continence (IV). Therefore, despite experiencing minor functional aberrations more often than their matched peers, our results suggest that the majority of female patients with VF/PF do well after ASARP. In children, discontinuation of diapers for stool can be expected to be complete within the normal time.

Among RUF patients who represent the most severe type of ARM studied herein, a much lower proportion had achieved VBMs a (74%), consistent with the 64-79% reported in other major series.[52,180] In relation to controls, all aspects of fecal control were significantly impaired in the cohort. Soiling was much more common than in controls, affecting 70% of patients overall (and 30% of controls; $p<0.001$), but this was frequent (>1/week) in only 18% (vs 0% of controls; $p=0.0002$). Our findings on soiling are similar to other series after PSARP of 77-82%,[92,180] although our work contributes greater detail on the likely frequency of symptoms. A quarter of respondents were reliant on ACE washouts to produce bowel actions. By level of fistula, patients with higher urethral fistulae tended to have a reduced prognosis, consistent with more significant hypoplasia of continence structures and in keeping with the conclusions of other reports.[43,52,180] A limitation of this study was the very small number of patients with bladder neck fistulas (n=4), which limits the ability to analyse and draw conclusions on outcomes by level of fistula.

RUF patients with voluntary bowel control, who technically represent those patients with the best outcomes, still reported significantly higher rates of fecal accidents (35%) and problems withholding defecation (35%) than controls (7% and 5% respectively; $p \leq 0.004$) even after >12 years of follow-up. Fortunately, most symptoms were infrequent (<1/week), although moderate soiling (>1/week) still occurred in 15% of patients with VBMs in the long-term (vs 2% of controls; $p=0.04$). On the other hand, half of this subset (n=10/20 patients with VBMs followed up for >12 years) also reported total continence. This reflects the degree of variation of outcomes within the cohort itself. By BFS, 39% of all 33 patients with RUF reported clearly "good" or normal outcomes, and 27% had a "moderate" outcome (BFS 12-16) (V). Nine per cent (3 patients) had a clearly poor score, but these comprised two patients aged 5 and one adult who was among the first to undergo PSARP at our institution. One of these younger patients has since undergone an ACE procedure, and is now socially continent.

Approximately one quarter of our RUF patients were reliant on ACE washouts at the time of the study. They comprised 44% of patients ≤12 years of age, and 17% of those older than this, reflecting the current trend towards earlier intervention with ACE. Their functional outcome is more difficult to define. On one hand, they represent those patients who would otherwise have very deficient fecal control. However, with ACE bowel management, 75% (6/8) were socially continent and no patient reported daily impairment. Social problems did not specifically cluster amongst those patients with ACE either (38% vs 36% in RUF patients with VBMs; *p*=NS). Completion of diapers had also been possible in 2/3 of the younger patients after the ACE procedure. In the literature, 2/3-96% of patients are able to stay socially clean using an ACE conduit.[16,148] With increasing experience of the effectiveness of this procedure, the practice at our centre has become to offer an ACE conduit to all ARM patients with deficient continence from the age of 4 onwards, prior to starting elementary school.

With modern treatment and systematic aftercare, 76% of patients with RUF in our series (V) were socially continent, with or without artificial means in the form of ACE washouts. Toilet training for stool is likely to be significantly delayed, in contrast to less severe ARMs. Our data supports the notion of some improvement in function over time, as reflected in the declining prevalence of soiling and fecal accidents with age, from 100% below age ≤12 years to 59% and 37% respectively beyond this age ($p \leq 0.03$). Other studies have made similar observations in patients with high ARMs, both after PSARP[5,43,92] but also after classical operations.[2,109,181] For the most part, this is likely to represent adaptation to residual dysfunction rather than actual improvement of anorectal function (V). However, the benefits of vigorous and timely treatment of functional complications, of which the most important in ARM patients is constipation, are well established (Rintala & Lindahl 1995, Rintala and Pakarinen 2008, Pena 1995, Grano 2012, Levitt & Pena 2010). Our data also unequivocally supports the superiority of PSARP over classical operations, after which only 5-7.5% of children were reported to achieve complete continence.[2,5,92,116,]

8.5 Constipation in patients with ARMs

Constipation was a major functional sequel in ARM patients in our studies (II-V), affecting between 31-44% of patients. The functional outcomes achieved in these series (II-V) represent the results after sustained surgical follow-up and timely management of functional complications including constipation. The prevalence of constipation in all types of ARMs declined with age to a level that was no longer significantly different from controls beyond 12 years of age, which is in accordance with other studies of subsiding constipation around puberty.[2,43,106] The proportion of patients and controls in all our ARM study groups (II-V) had comparable frequency of bowel motions, however, suggesting that most constipation was well controlled. The high prevalence of constipation even amongst patients with mild ARMs is a strong indication for maintaining patients under regular, long-

term follow-up. Over the years, isolated patients (n=6; 1-2 from each type of ARM in this series) had required resection of a megarectum following severe, prolonged constipation. Fortunately, these patients represent only a small minority of our ARM patient population where medical treatment has failed, but they underpin the potential seriousness of constipation in these patients.

8.6 Social disability due to bowel function

Our data suggests that with modern treatment, social problems due to bowel function in patients with mild ARMs may not be significantly more common than in matched peers. Patients with more severe ARMs, however, may continue to experience these at higher levels than the general population (15% of VF/PF and 36% of RUF patients in studies IV-V vs 2.5% of controls; $p \leq 0.01$), although the proportion that were moderate-severely restricted was fortunately smaller (6 patients in total; 3 VF/PF and 3 RUF). The negative consequences of deficient fecal control on patients' personal relationships, social activities, education and employment and ultimately quality of life are becoming increasingly recognised,[182,183] and minimising social disability in these patients should be one of the central goals of their management.

Conclusions

"All generalizations are false, including this one."
- Albert Einstein

This study has aimed to investigate the bowel functional outcomes up to adulthood for patients with different types of ARMs treated during the PSARP era, in relation to matched peers. The results from our large series of 159 respondents adds considerable information to what is known so far about the effectiveness of modern treatments. Our study of the general population has attempted to describe 'normality' for the bowel habits of a large cohort of healthy individuals as a background for comparison of outcomes in patients with benign anorectal disorders. From this, it is apparent that minor imperfections in bowel function, particularly minor soiling, also affect healthy individuals and not just patients in an age-dependent manner. In our cohort of mild ARMs (II-III), we showed that functional outcomes comparable to matched peers are achieved in the majority after minimally invasive, individualized perineal procedures or conservative management and regular surgical follow-up.

For more severe ARMs, our data (IV-V) supports the safety and efficacy of modern sagittal repair methods over classical procedures. In females with VF/PF, good functional outcomes were achieved by 2/3 after ASARP, despite a higher prevalence of minor aberrations than controls (IV). For RUF patients, who represent the most severe end of the spectrum, social continence was achieved in the majority after PSARP, although approximately one quarter required ACE bowel management. The effective and timely management of constipation, which affects all groups of patients with ARMs, is central to achieving optimal outcomes.

It is clear that ARM patients represent a complex spectrum of congenital abnormalities of which bowel function is just one important facet. After surgical repair of the defect, the functional outcomes do not develop spontaneously in most - rather they represent the results of years of hard work by medical professionals, patients and their families.

Each patient is also an individual – and increasing severity of the ARM introduces greater variation into the possible outcomes as we have shown here, even after the best available treatments. Ideally, ARM patients should receive care from a multidisciplinary team that is experienced in their management and can provide a holistic, individualized approach to their care – both medical and psychosocial. Appropriate contacts and transitional arrangements into adult surgical practice should be created for those ARM patients with an on-going requirement for surgical input.

Acknowledgments

This work was conducted at the Hospital for Children and Adolescents, University of Helsinki between 2010-2015. I wish to thank the Director of the hospital Jari Petäjä, Head of the Department of Pediatric Surgery Pentti Kallio, Professors Risto Rintala, Markku Heikinheimo and Mikael Knip and Docent Jussi Merenmies and the Paediatric Graduate School for their continued commitment to supporting excellence in clinical research at our institution.

I gratefully acknowledge the financial support received from the Finnish Foundation for Paediatric Research, the Finnish Medical Foundation, the Päivikki and Sakari Sohlberg Foundation, Helsinki University Central Hospitals Research Fund, Sigrid Juselius Foundation and the Finnish Association of Pediatric Surgeons - Sulamaa Society.

I am deeply grateful to the patients who participated in this study. Your contribution serves towards advancing the surgical care standards for patients with anorectal malformations.

I would also like to express my gratitude to the Finnish general population who so willingly took the time to respond to our survey.

To my exceptional supervisors Professor Risto Rintala and Associate Professor Mikko Pakarinen, thank you for always taking the time to patiently answer all my questions and for your expert guidance and advice. Your dedication to research is inspirational. I hope the work I have produced reflects the high quality and standards that you have always set for your own.

To my wonderful research nurse Eerika Tenhovuori, thank you for being my right hand lady in this project and for your many organizational talents. I am also grateful to nurses Elina Sallinen, Leila Uusimaa and Anita Juslén for stepping in to help out whenever necessary.

To my excellent pre-examiners Dr Marc Levitt and Docent Anna Lepistö, it is an honor to have had you to review this work.

Thank you to my co-authors Docents Seppo Taskinen and Antti Koivusalo for your valuable input, and to paediatric radiologist Dr Reetta Kivisaari and Docent Ilkka Helenius

for our on-going collaboration. A special thank you to Dr Riitta Fagerholm for being my academic sparring partner and for helping me survive statistics.

To my paediatric surgical research colleagues Malla Neuvonen, Hanna Lampela, Silja Kosola, Annika Mutanen, Janne Suominen, Saara Sistonen, Elina Laitakari, Topi Luoto, Valtter Virtanen, Anna Kerola, and Silja Voutilainen, I am thankful for our continued friendship. I have greatly enjoyed our many travels and conversations. I am grateful also to Päivi Salminen and Sari Pyörälä for running the department whilst we have been away at meetings and for taking our (many) annoying phone calls.

To my research follow-up team Kaija-Leena Kolho and Anna Lepistö – thank you for your valuable guidance during this project.

To David Drake, Clinical Lead at the Evelina Children's Hospital in London, thank you for all your encouragement over the years.

I am immensely grateful to my wonderful parents Raija and Jouko and to my dear sister Katariina for their unconditional love and for always believing that I can do anything.

To both my parents Raija and Jouko and my parents-in-law Ulla-Maija and Kid, I am grateful for the countless hours of childcare you have provided that enabled the completion of this research. Thank you to auntie Aino for helping with this too.

To my children, I will always be more thankful than words can describe to have you in my life. May you continue to teach me on the joys of motherhood and on the wonders of childhood, and may I continue to see the beauty in this world through your eyes.

Finally, to my dearest husband Niklas, thank you for sharing your life with me. This project has been yours as much as it has been mine. I love you so.

Kristiina Kyrklund

Helsinki, February 2016

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12. Appendix

The Bowel Function Score (BFS) Questionnaire of Rintala and Lindahl[92]

Feels/reports the urge to defecate	Score
Always	3
Most of the time	2
Uncertain	1
Absent	0
Ability to hold back defecation	
Always	3
Problems <1/week	2
Weekly problems	1
No voluntary control	0
Frequency of defecation	
Every other day to twice a day	2
More often	1
Less often	1
Soiling	
Never	3
Staining <1/week, no change of underwear required	2
Frequent (>1/wk) change of underwear often required	1
Daily, requires protective aids	0
Accidents	
Never	3
Fewer than 1/week	2
Weekly, requires protective aids	1
Daily, requires protective aids day and night	0
Constipation	
No constipation	3
Managed with diet	2
Managed with laxatives	1
Managed with enemas	0
Social problems	
None	3
Sometimes (foul odours) 2	
Problems restricting social life	1
Major social/psychological problems	0

13. Articles