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# Anorectal malformations - their impact on early phases in life

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2014

Link to publication

*Citation for published version (APA):*
Stenström, P. (2014). *Anorectal malformations - their impact on early phases in life*. [Doctoral Thesis (compilation), Paediatrics (Lund)]. Paediatrics, Faculty of Medicine, Lund University.

*Total number of authors:*
1

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# Anorectal malformations

–their impact on early phases in life

Pernilla Stenström


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DOCTORAL DISSERTATION

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To be defended at Belfragesalen 16/5 2014 at 10.00 am.

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Göteborg, Sweden

| Organization | Document name: Doctoral dissertation |
|---|---|
| LUND UNIVERSITY \| Faculty of Medicine, Department of Clinical Sciences Lund | Date of issue 16/5 2014 |
| Author(s) Pernilla Stenström | Sponsoring organization |


**Title and subtitle:** Anorectal malformations –their impact on early phases in life


Abstract:

**Background:** Anorectal malformations (ARM) occur in 4:10000 newborn children with the gender distribution 1:1.5 females:males. The reconstruction of ARM, posterior sagittal anorectal plasty (PSARP), was implemented worldwide in the late 1980s and therefore the follow-ups are limited.

**Aims:** To assess bowel symptoms in children and adolescents with ARM, operated on with PSARP, and to evaluate the quality of life (QoL) and sexual health among the same adolescents. To evaluate the outcome of appendicostomy in preschool children with ARM. To study the anatomical status of the pelvic floor, and its possible correlation with bowel symptoms, among females with ARM.

**Results:** Fecal incontinence was reported by 45% of the 121 children, and by 75% of the 24 adolescents. Constipation was reported by 50% children and 83% adolescents. Symptoms were more frequent among females than males with the same subtype of ARM. Physically related QoL was lowered for females with ARM, while the mental domains in QoL were higher for the males with ARM compared with healthy controls. Intimate situations were influenced by gas and fecal incontinence for both genders. Appendicostomy in 17 preschool children with ARM improved the fecal continence significantly, but 43% had minor complications. All 17 females with ARM examined with perineal ultrasonography had multiple defects on the anal sphincter, without correlation with the degree of bowel symptoms.

**Conclusion:** Bowel symptoms in children and adolescents with ARM are considerable and gender differences are present. The QoL and sexual health are influenced both by gas and fecal incontinence, and by self-efficacy, so directed psychological support could be valuable. Appendicostomy in preschool children is successful and will be continued. All pregnant females with ARM should preferably be recommended to deliver by cesarian section.



Key words: Anorectal malformation, fecal incontinence, adolescence, quality of life, sexual health, appendicostomy, pelvic floor, cesarian section

Classification system and/or index terms (if any)

| Supplementary bibliographical information | | Language: English |
|---|---|---|
| ISSN and key title 1652-8220 | | ISBN 978-91-87651-71-7 |
| Recipient's notes | Number of pages 154 | Price |
| | Security classification | |



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# Anorectal malformations

– their impact on early phases in life

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Front page: Shells on the beach in summer 2013, Pernilla Stenström

Back page: Bacillakuten, SVT

All photos in this thesis are published after consent received from the children´s parents.

Drawings of anorectal malformations and sphincter anatomy: Mette Hambraeus

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Faculty of Medicine, Department of Clinical Sciences Lund

ISSN 1652-8220
ISBN 978-91-87651-71-7
Lund University, Faculty of Medicine Doctoral Dissertation Series 2014:46

Printed in Sweden by Media-Tryck, Lund University
Lund 2014

If only the strongest trees could take root
how barren the earth would be

If only the bluest sky was blue
how gray would the days pass by

If only the brightest star would shine
how lonely the moon would be

If only the wildest wolfs would howl
If only the most beautiful birds would sing
How silent the forest would be?

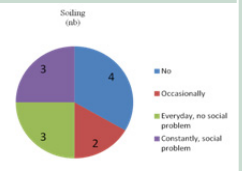
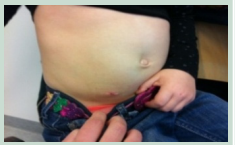
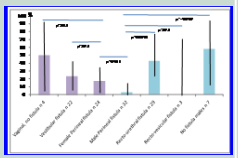
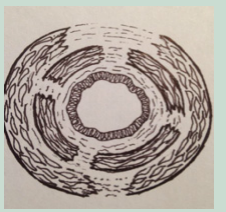
Who would sing?
Who would then sing?

**by Frida Gryndel, my dear cousin**
**From" Tango behind the clouds" 2009**

*To my patients*

# Contents

# Thesis at a glance

| | Main questions | Method | Results | Illustrations | Conclusion |
|---|---|---|---|---|---|
| I | What is the outcome among adolescents with ARM regarding bowel symptoms, QoL and sexual health?<br>Is there any need of transfer to adult care for adolescents with ARM? | A clinical quantitative case control study and qualitative interview study.<br>Correlation analysis between symptoms and QoL. | Studied: 24 adolescents 15-21 years old. Bowel symptoms were common in both genders. 2/3 had fecal incontinence. Compared to controls, mental QoL was high for the males and physical QoL low for the females. Females lacked information about their ARM. Gas and fecal incontinence influenced sexual health. |  | Fecal incontinence is common among adolescents. Strong coping and self-efficacy seem to improve QoL. Sex issues should be raised by the pediatric surgeons in the early adolescence.<br>An organized transfer to adult care should be provided for all adolescents with ARM. |
| II | Does appendicostomy in preschool children with ARM help to reach fecal continence before school start? | A combined prospective and retrospective clinical follow-up. Telephone interviews about the use and satisfaction. | Studied: 17 children 1-6 years old. Fecal incontinence decreased significantly after appendicostomy. High rate (43%) of smaller complications. High satisfaction rate (88%) among the families. |  | Appendicostomy in preschool children is successful. It gives compliance to enema, fecal cleanness and early autonomy. |
| III | Are there any gender differences in bowel symptoms in children with different subtypes of ARM? | Two-center study. A clinical follow-up performed during counseling. | Studied: 121 children 4-12 years old. Fecal incontinence was more common among females than males with perineal fistulas (42% vs 10%). The outcome for females with perineal and vestibular fistulas did not differ. |  | There are gender differences in bowel control, especially in genderwise comparisons between perineal fistulas. This knowledge is suggested to be regarded in the follow-up and expectations on outcome. |
| IV | What are the characteristics of the sphincter anatomy in females with ARM?<br>What mode of delivery should be recommended? | A case–control and descriptive interventional study with perineal ultrasonography.<br>Correlation analysis between sphincter anatomy and bowel symptoms. | Studied: 40 females 4-21 years old. All females had minimum one serious defect in the anatomy. A typical substantial defect and diastasis between the intestinal wall and skin in perineum was seen in 65%. |  | The anatomy of the pelvic floor in ARM is very much influenced by the malformation and the operation.<br>Cesarian section should be recommended to every pregnant female with ARM. |

# Papers included in the thesis

- Stenström P, Kockum CC, Benér DK, Ivarsson C, Arnbjörnsson E. Adolescents with anorectal malformation: physical outcome, sexual health and quality of life. Int J Adolesc Med Health. 2013 May 1:1-11. doi: 10.1515/ijamh-2012-0111. [Epub ahead of print] PubMed PMID: 23633464.
- Stenström P, Granéli C, Salö M, Hagelsteen K, Arnbjörnsson E. Appendicostomy in preschool children with anorectal malformation: successful early bowel management with a high frequency of minor complications. Biomed Res Int. 2013;2013:297084. doi: 10.1155/2013/297084. Epub 2013 Sep 23. PubMed PMID:24175287; PubMed Central PMCID: PMC3794643.
- Stenström P, Kockum CC, Emblem R, Björnland K, Arnbjörnsson E. Bowel symptoms in children with anorectal malformation – a follow-up with a gender and age perspective. Journal of Pediatric Surgery. Accepted for publication. Doi: 10.1016/j.jpedsurg.2013.10.022.
- Stenström P, Hambraeus M, Arnbjörnsson E, Örnö AK. Pelvic floor in females with anorectal malformations – findings on perineal ultrasonography and aspects of delivery mode. Submitted for publication.

# Abbreviations and definitions

| | |
|---|---|
| ARM | Anorectal malformation |
| Autonomy | Self-direction and independence of others, such as a child's independence of its parents. |
| C | Cloaca |
| Currarino triad | A congenital disorder where 1. The sacrum is malformated: 2. There is a mass - a meningocele or a presacral teratoma in the presacral space: 3. There are malformations of the anus or rectum. |
| EAS | External sphincter |
| Giqli | Gastrointestinal quality of life. Questionnaire regarding symptom specific QoL. |
| HAQL | Hirschsprung's disease and anorectal malformation quality of life questionnaire |
| IAS | Internal anal sphincter |
| IM | Intermediate: Previously used entity of some of the ARM-subtypes. |
| MRI | Magnetic Resonance Imaging |
| Perineal groove | A congenital anomaly of perineum: a strip of squamous epithelium, located between vagina and anus, lined by rectal type of mucosa. It may be an embryological remnant such as urorectal septum. |
| PF | Recto-perineal fistula |
| PSARP | Posterior Sagittal Anorectal Plasty |
| PSARVUP | Posterior Sagittal Anorectal Vaginal Urethral Plasty |
| QoL | Quality of life |
| RB | Recto-bulbar fistula |
| RU | Recto-urethral fistula |

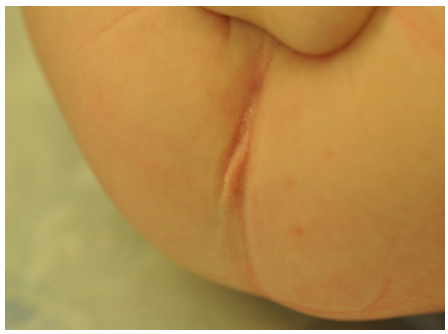
| | |
|---|---|
| RP | Recto-prostatic fistula |
| RV | Recto-vesical fistula |
| Self-efficacy | The extent or strength of one's belief in one's own ability to complete tasks and reach goals. |
| SF-36 | Short Form questionnaire with 36 questions. A generic test measuring health related general QoL. |
| VCUG | Voiding Cysto Urethrography |
| VaF | Recto-vaginal fistula |
| VF | Recto-vestibular fistula |
| VACTERL | A summarizing expression for multiple malformations. It includes at least 3 of the following malformations: **V**ertebral anomalies, **A**no rectal malformation, **C**ongenital heart disease, **T**racheo esophageal fistula, **R**enal anomaly, **L**imb defect |

# Populärvetenskaplig sammanfattning

## Född utan ändtarmsöppning – det finns mer hjälp!

Varje år föds femtio barn i Sverige utan ändtarmsöppning, så kallad analatresi. De sista 2-3 centimetrarna av ändtarmen saknas liksom ändtarmsöppningen och delar av ringmuskeln. Orsaken tros vara plötsligt uppkomna genförändringar tidigt hos fostret. Starten i livet blir svår eftersom det behövs flera operationer. Redan under första levnadsdygnet görs en första operation så att avföring kan komma ut via stomi på magen. Efter någon vecka genomförs en ny operation där en ändtarmsöppning skapas genom att grovtarmen dras ned. Därefter måste ändtarmsöppningen vidgas dagligen under några månader. Missbildningen kommer att prägla barnets uppväxt på grund av avföringsläckage och svår förstoppning. Detta trots att ändtarmsoperationen lyckats och trots att vården gör allt som hittills är känt för barnets bästa.

Avhandlingen syftade till att ta reda på hur vi som barnkirurger kan hjälpa barn och ungdomar som är födda utan ändtarmsöppning att få det fysiskt och psykiskt bättre. Studierna är utförda på Barnkirurgiska kliniken i Lund, som är en av de fyra kliniker i Sverige där analatresi behandlas.

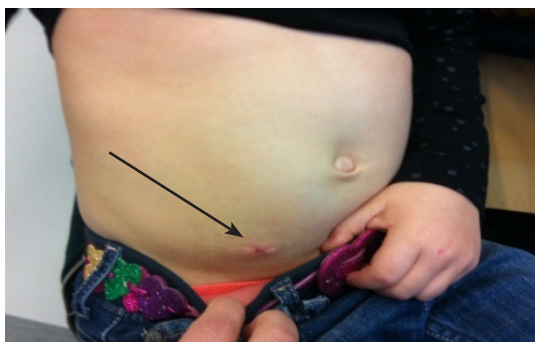


**Nyfödd pojke utan ändtarmsöppning, så kallad analatresi.**

I det första delarbetet kartlades tarmproblem, livskvalitet och sexuell hälsa hos 24 ungdomar i åldern 15-21 år, födda utan ändtarmsöppning. Undersökningen gjordes i samarbete mellan barnkirurger och sexologer med hjälp av enkäter vid patientmöten och djupintervjuer. Friska kontrollpersoner i samma ålder som patienterna ingick i

studien. Två av tre flickor och pojkar med analatresi hade läckage av avföring och gas samt förstoppningsproblem medan endast någon enstaka procent av kontrollpersonerna hade liknande problem. Pojkarna födda med analatresi hade utvecklat metoder till att hantera sina tarmproblem, så kallade copingstrategier, genom att ha förberedda lögner om ljud och lukt vid gas- eller avföringsläckage. De angav högre mental livskvalitet än kontrollpersonerna. Flickorna födda med analatresi undvek vissa situationer, som att sova borta och idrotta med andra, för att inte riskera att bli påkomna om det läckte avföring och gas. De hade, till skillnad från pojkarna, nästan inte fått någon information om sin missbildning och angav sämre livskvalitet. Tonåringarna önskade att vi barnkirurger tog upp ämnet sex, eftersom de själva inte vågade. Undersökningen visar att många ungdomar med analatresi har mycket tarmproblem och att ett riktat stöd för att utveckla copingstrategier och självtillit kan öka deras livskvalitetet. Egen kunskap om missbildningen verkar också bidra till högre livskvalitet. Inom vården och i familjerna bör man därför tänka på att prata med flickorna lika mycket som med pojkarna om missbildningen av ändtarmen och deras problem med detta. I studien framkom tydligt att det behövs en organiserad överföring av tonåringarna med analatresi från barn- till vuxenvård.

I den andra studien undersöktes förskolebarn som behöver lavemang efter analatresioperationen, men har problem med att ta lavemanget i ändtarmen pga rädsla. Det finns en metod där blindtarmen opereras ut på magen i en liten öppning där lavemangsvätskan ges. Lavemanget ges på så sätt direkt i grovtarmen istället för via ändtarmen. Metoden kallas appendikostomi och har hittills bara varit ägnad barn i åldern 9-10 år, men denna studie visade att det fungerar utmärkt även för förskolebarn. Alla de 17 förskolebarn som fått appendikostomi blev av med avföringsläckaget innan de började skolan. Komplikationer efter operationerna var dessutom mindre allvarliga än hos större barn, och familjerna var nöjda vid studiens uppföljning. Betydelsen är att Barnkirurgiska kliniken i Lund kommer att fortsätta att rekommendera appendikostomi även till små barn som fötts utan ändtarmsöppning.



**5 år gammal flicka med blindtarmsöppning som lavemanget ges i.**

Det tredje delarbetet i avhandlingen gjordes i samarbete med Barnkirurgiska kliniken i Oslo. Studien kartlade avföringsläckage och förstoppning hos 121 flickor och pojkar i olika åldrar med olika typer av analatresi. Ungefär hälften av barnen hade avföringsläckage. Flickorna med den lättaste typen av analatresi hade mer avföringsläckage och förstoppning än pojkarna med samma missbildning. Könsskillnaden är aldrig studerad förut, eftersom man alltid studerat en könsblandad grupp. Orsaken till könsskillnaden är okänd, men man kan fundera på om det beror på olika anatomi eller om tarmbehandling ges på olika sätt till flickor och pojkar. Avföringsläckage var lika vanligt hos äldre som hos yngre barn oavsett kön. Detta står i motsats till en del tidigare studier där man i könsblandade grupper anger en förbättring ju äldre barnet blir. Resultaten kan ha betydelse för att ge en mer könsanpassad tarmbehandling till både flickor och pojkar oavsett ålder.

Den fjärde studien utfördes tillsammans med gynekolog för att se hur bäckenbotten och ringmuskeln ter sig på flickor och kvinnor som är födda utan ändtarmsöppning. Totalt 40 flickor och kvinnor undersöktes avseende tarmsymptom. Av dessa undersöktes 17 med ultraljud av bäckenbotten via mellangården. Metoden är en ny teknik, så kallad perinealt 4D/3D ultraljud, och visade att samtliga de undersökta hade betydliga ärr på ringmuskeln och annorlunda anatomi i bäckenbotten. Skadorna på musklerna kunde jämställas med förlossningsskador. De ultraljudsundersökta hade lika mycket tarmproblem som de övriga. Graden av avföringsläckage angav inte hur stora skadorna på ringmuskeln var och kan således inte användas för att avgöra förlossningssätt. Om en kvinna född med analatresi skulle få förlossningsskador skulle dessa vara ytterst svåra att reparera på grund av den missbildade anatomin. Studien talar därför för att kvinnor födda utan ändtarmsöppning bör få rekommendationen att föda med kejsarsnitt.

Sammanfattningsvis tvingas många barn och tonåringar födda med analatresi att klara av att leva med det osynliga handikapp som det innebär att inte kunna kontrollera gaser och avföring. Avhandlingen visar att det finns mer att göra för dessa patienter såsom att underlätta behandlingen med lavemang, rikta det psykologiska stödet, öppna upp för samtal omkring kroppen och närhet samt ge välgrundade råd om framtida förlossningssätt. Eftersom problem kvarstår efter tonåren behövs ett samarbete mellan barn- och vuxensjukvården så att patienterna födda med analatresi får den goda vård som de förtjänar.

# Introduction

## The scope of the problem

To grasp an ARM patient's true outcome regarding bowel control and QoL is difficult. The symptoms are integrated in the child's normal condition and habits already from the first day of life. Failure in compliance to medication and enemas impose guilt upon the child and its guardians, while fecal incontinence may remain untreated. A hidden handicap, such as fecal incontinence, may have a negative impact on QoL and social interaction. Such a handicap is also difficult to illuminate and treat.

This thesis is designed with the intention to increase knowledge of a genderwise outcome for children and adolescents with ARM. The findings can help in the ambition to provide an equal age adjusted care.

The main treatment goal for all patients with ARM must be to help the children to achieve fecal cleanness before school start, and then to be in continuing good physical and mental shape as adolescents. This is of importance since being able to function well in childhood and adolescence, prepares for healthy adulthood.

## Anorectal malformations – a background

### Epidemiology and etiology

The prevalence of ARM is 4/10000 with a gender distribution of around 1:1.5 females:males [1-3]. There are no reports on geographical differences.

The etiology of ARM is, as with many other malformations, a combination of environmental and genetic factors. The environmental factors of importance are paternal smoking, maternal overweight and maternal diabetes, according to a metaanalysis [4]. ARM, as with other malformations, is shown to be more common after in vitro fertilization, but the cause is unknown [5].

The genetics in ARM are complex and the research little developed [6,7]. To date, most ARM cases are reported to be isolated results of sporadic mutations without familial predisposition [6]. Still an analysis of a genetic database of nearly 400 children with ARM indicated a 3% risk for siblings and 2% risk for first degree relatives to be born with vestibular or perineal fistulas [7]. No single gene or chromosomal locus has been identified as the cause of all, or even a majority of ARM, although there are some identified families with autosomal-dominant or autosomal-recessive inheritance of isolated ARM where deletions of specific genes can be identified [7,8]. Some children with ARM have other genetic or inherited conditions. In the mentioned extensive genetic review 15% of all patients with ARM had underlying chromosomal abnormalities of which trisomi 21, 18 and 13 formed the largest group [7]. Of children with ARM 15% are reported to have multiple malformations as in VACTERL [9] or Currarino triad [6,7].

## Embryology

The embryologic development from the hindgut and cloaca into urogenital sinus and rectum takes place between weeks 5-8. Then the rectum forms either through separation of the primary cloaca or by migration of the rectum between week 8-12 [10,11]. During the same time, the gender is established through the development of inner and outer genitals [12]. The sphincter is established in week 12 and grows slowly in weeks 14-19 and more rapidly during week 20-30 [13]. The ARM are suggested to arise between weeks 5-12 [10].

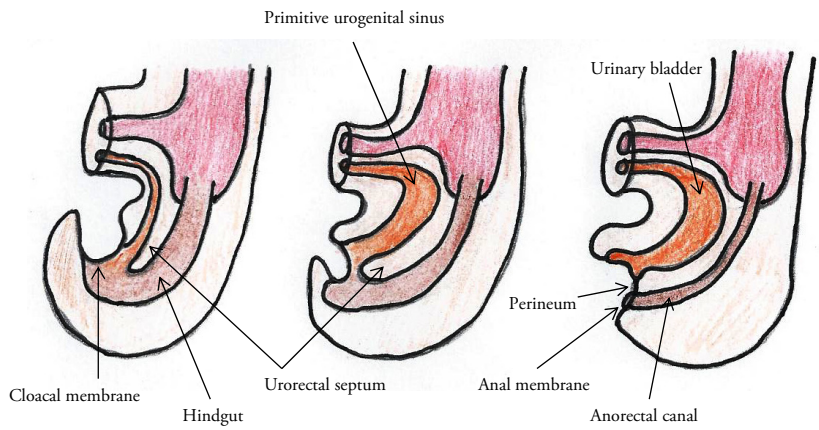



**Figure 1.** The early embryological development from hindgut into anorectal canal and the urorectal septum into perineal body between weeks 5-8.

## Prenatal diagnosis

Efforts to diagnose ARM prenatally are made only infrequently. Prenatal diagnosis of ARM currently occurs in 0-16% [14,15]. Images that cause suspicion of ARM are dilated or calcified bowel or lack of meconium at the expected level. Findings of multiple anomalies such as hydronephrosis, vertebral anomalies, hydrocolpus, cystic abdominal mass increase the index of suspicion of ARM [1,16]. It has been suggested that it would be possible to diagnose ARM before 20 weeks of gestation by ultrasonography of the sphincter and measurements of amnioitic fluid digestive enzymes [13].

The advantage of a prenatal diagnosis of ARM is both psychological and medical. It gives the parents some information about the type of malformation and the treatment that could be expected. A prenatal diagnosis will prepare the family and doctors for immediate interventions and gives the opportunity to arrange the delivery in a specialized center that is familiar with the neonatal management of children born with ARM [1,14,17].

## Subtypes of ARM

In 1982 the different subtypes of ARM were described in detail. The subclassification was based on the anatomical location of the fistula that is present in 95% of ARM [18]. In this original description and in subsequent ones following, the males' perineal fistula, anal stenosis and bucket handle malformation were gathered into "low" subtypes [19,20]. Then "high" and "intermediate" subtypes were added in the literature, gathering different types of ARM into two or three groups [21]. This is suitable for statistical analyses but is not interesting for any evaluation of outcome for the different subtypes [1,22]. The simplified classification with "low" and "high" ARM was frequently used until the early 2000s.

In 2005 the international classification of ARM was established through international collaborative work held in Krickenbeck castle in Germany [23]. The Krickenbeck classification is now recommended to be used always, so that the outcome for each subtype of ARM can be registered separately. Although the classification is detailed, it does not separate female from male perineal fistulas.

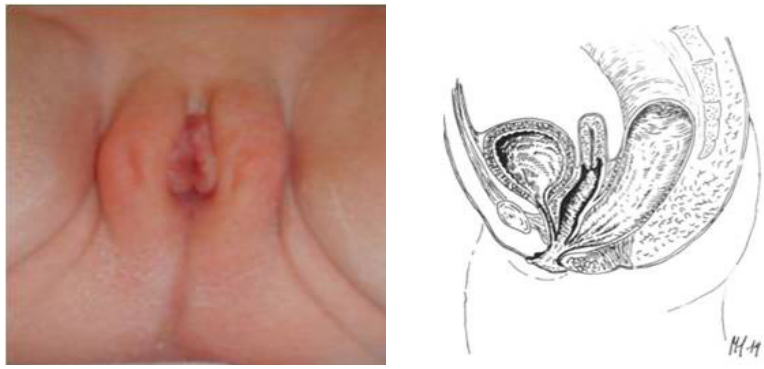


**Figure 2a.** Cloaca: This is a more complex subtype of ARM, where rectum, vagina and urethra enter a common channel. The cloacae are subdivided into >3cm or <3 cm common channel.

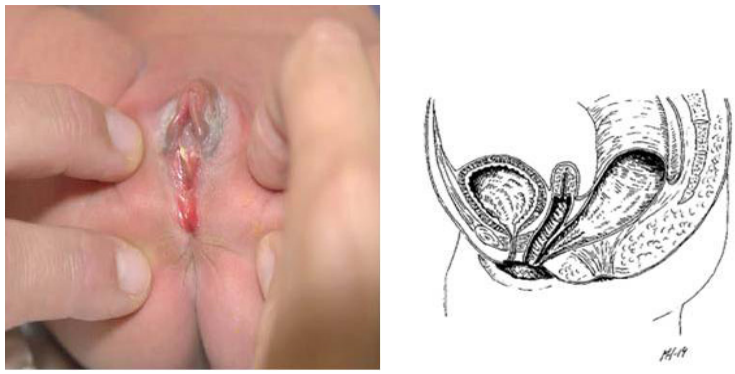


**Figure 2b.** Recto-vestibular fistula with perineal groove.

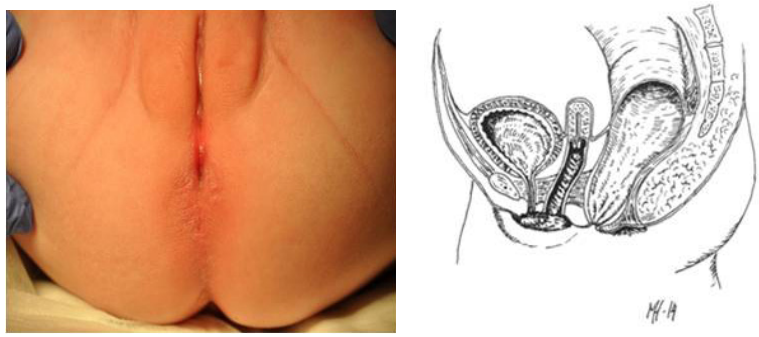


**Figure 2c.** Perineal fistula in female.

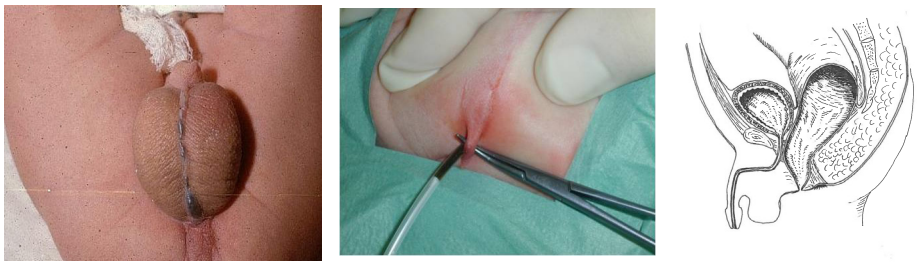


**Figure 2d.** Perineal fistula in male. Left photo: Perineal fistula with scrotal outlet. Right photo: Typical bucket handle could be found in both male and female perineal fistulas.

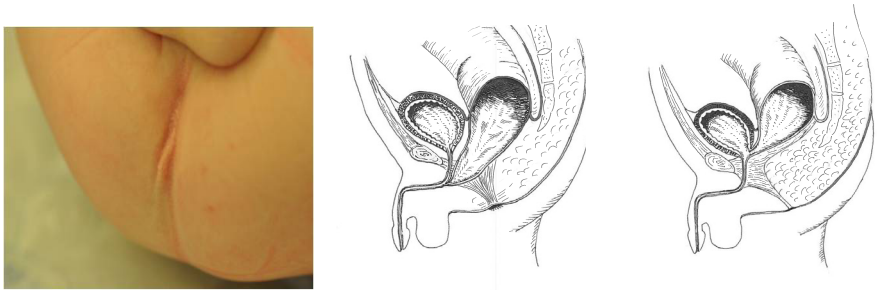


**Figure 2e.** No visible fistula on the outside could be recto-urethral fistula (left), recto-vesicular fistula (right) or no fistula.

**Table 1.** The Krickenbeck international classification of ARM with the reported prevalence of each subtype of ARM [22,24-26].

| Krickenbeck classification | Gender | Reported prevalence in the gender (%) |
|---|---|---|
| Perineal fistulas | Mixed | 25-42 |
| No fistula | Mixed | 3-12 |
| Rectal atresia | Mixed | 1-3 |
| Perineal fistula | Female | 41 |
| Recto-vestibular fistula | Female | 21-29 |
| Recto-vaginal fistula | Female | 1-5 |
| Cloaca | Female | 4-10 |
| Perineal fistula | Male | 43 |
| Recto-urethral fistula: | Male | 19-50 |
| - Recto-bulbar fistula | Male | 5-15 |
| - Recto-prostatic fistula | Male | 12-20 |
| Recto-vesical fistula | Male | 6-12 |

### Associated anomalies

Associated malformations are reported to be present in 58-78% of all children with ARM [2,26,27]. Concomitant urological anomalies are reported in 28-50% [2,24-26,28]. Cardiac anomalies are seen in 20% and both the concomitant urological and cardiac anomalies have the highest rate among cloacae and recto-urethral fistulas [24,26]. Overall gastrointestinal anomalies are reported in 15% including malrotation in 6% [24] and neurological impairness and syndromes in 6-26% [24,26].

The prevalence of spinal dysraphism, defined as imperfect fusion of the midline neural and bony structures, such as spina bifida, low-lying conus, tethered cord, spinal lipoma and sacral meningocele, on MRI has been reported to be 34% overall in ARM children [3]. Patients with cloaca and recto-urethral fistula are reported to be more likely to have spinal dysraphism; 60% and 41%, respectively, but also the frequency among those with perineal fistulas is considerable 10% [3]. Only vertebral anomalies are reported to be present in 17% [24].

Genital malformations in ARM are common. On average in all female subtypes of ARM, vaginal anomalies have been found in 30% and uterine anomalies in 35% [9,29-31]. Half of the patients with cloacae and 5% of females with perineal fistula or vestibular fistula are reported to have vaginal septum [29,32] and 17% of vestibular fistulas have some gynecologic anomaly such as vaginal septa, bicorn uterus or cervix or vaginal aplasia [32]. Hypospadia and undescended testis are the most common concomitant genital malformations in males with reported prevalences of 10-45% [9,33].

## Neonatal management and investigations in ARM

A newborn child with ARM often requires a diverting stoma or a direct reconstruction of anus during the first 24 hours, to give sufficient outlet for meconium. In order to make a correct decision on whether a colostomy is necessary or not, it is important to collect enough information about the subtype of ARM as well as the concomitant anomalies. The condition of the baby and the surgeon's experience must also be taken into account. Definitive indications for a colostomy are a flat bottom without a visible fistula, cloaca, meconium in the urine or gas seen only above the coccyx on a plain X-ray [1,19]. If a colostomy is the choice, it is preferably divided so that intestinal overflow is avoided and a colostogram can be performed in order to diagnose the subtype of fistula [1,20,34].

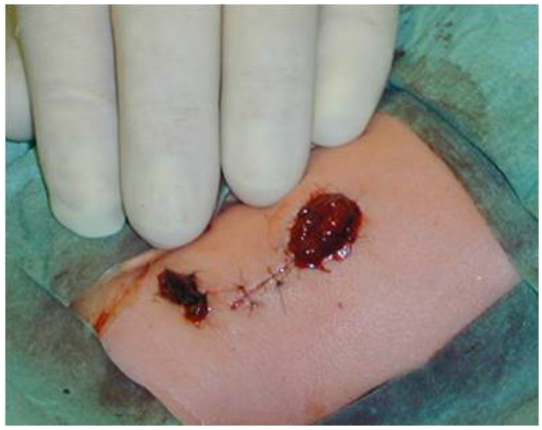


**Figure 3.** Divided colostomy on sigmoideum in a newborn boy without any visible fistula on the skin.

*The following investigations are important in the first management before the first operation:*

**Cardiac:** An evaluation of the heart by a pediatric cardiac specialist and an echo-cardiogram rule out major cardiac failures that may be important per- and postoperatively.

**Esophagus, stomach and colon:** Thoracic and abdominal radiography rule out esophageal atresia, duodenal atresia or other intestinal atresia. An invertogram, a plain X-ray with the child in a leaning-forward position, can help in the decision of stoma or not. Gas >1 cm from skin indicates that the malformation could be more severe and that a stoma is probably needed [1].

**Bladder and kidney:** Ultrasonography of the urinary tract should be performed in order to rule out renal agenesia, severe hydronephrosis or bladder anomaly. Hydrocolpus, in case of cloaca, must be exluded or drained [1,17,31]. If there are no prenatal signs of kidney abnormalities or presence of cloaca, the ultrasonography of the urinary tract could be performed after the primary operation [35]. Bladder function should be checked by controlling the voiding and urine volumes, by a bladder scan or ultrasonography[36]. If bladder dysfunction is suspected, a urethral or suprapubic catheter should be placed.

*The following investigations are important in the second management after diverting colostomy or after reconstruction of a perineal fistula:*

**Sacrum:** The sacrum could be examined with ultrasonography at the same time as the kidneys. A plain X-ray of the sacrum and the vertebra should be performed [1]. If there are signs of anomalies in the sacrum, a MRI should be performed within the first months in order to diagnose or rule out tethered cord and other anomalies on the spinal cord. Spinal cord anomalies might need operations and they are important in the evaluation of the bladder dysfunction and bowel control [1,3,36].

**Bladder, urethra, ureters and vagina**: If VCUG is performed with a high pressure, urethral reflux could be diagnosed, which is of special concern when additional renal anomalies are present. An atypical form of the bladder may be a sign of bladder neurogenicity [35]. A urodynamic investigation is indicated when sacral malformations or atypical patterns of bladder form or emptying are present [36,37]. In case of cloaca a genitogram visualizes the length of the common channel, and could give useful additional information to the colposcopy [17,31].

**Fistula and classification of subtype of ARM:** When a divided colostomy is established, the distal colon allows a high pressure distal colostogram to decide the specific type of ARM and for measuring the length of bowel available for the pull-through. In addition to the colostogram, a VCUG is also performed in order to add information on the fistula anatomy [1,19].

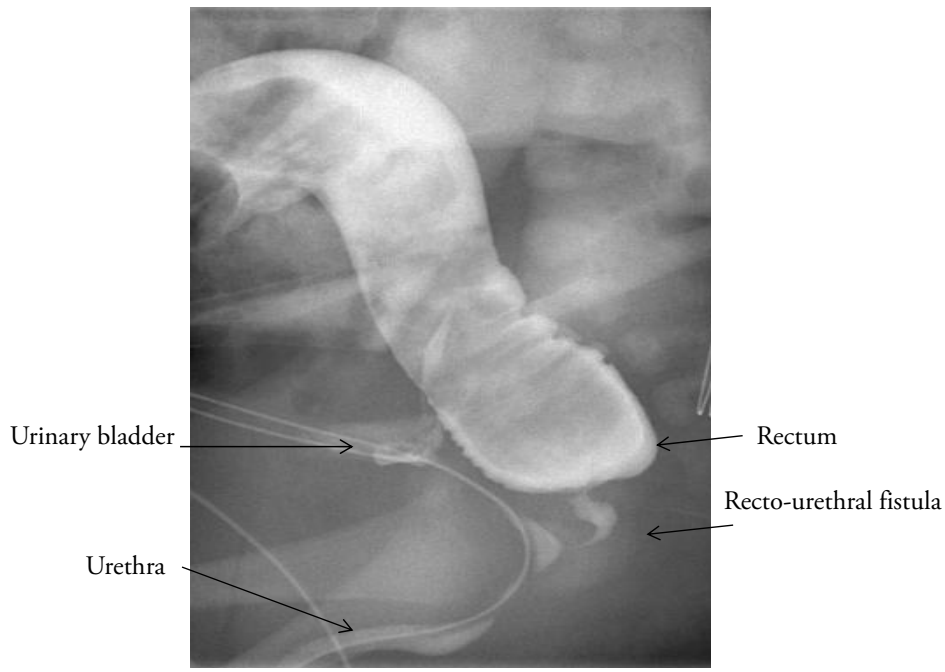



**Figure 4.** The picture illustrates how the recto-urinary fistula could be visualized by a high pressure colostogram through the passive stoma and via contrast in the urinary bladder.

# Operations

In the 80s the PSARP procedure was described by Dr. Pena and implemented worldwide [18].

**PSARP:** The anal sphincter complex is defined by electro-myostimulation, the pelvic floor divided in the midline from the coccygus to perineum, rectum is identified, dissected, opened and the fistula localized. The fistula to urethra or bladderneck in boys is divided and the rectum is mobilized to the center of the sphincter complex. In the original PSARP procedure the rectum is resected 1-2 cm and the fistula is resected as well [1,20]. Since the internal sphincter is suggested to be located in the fistula, fistula saving surgery has been provoked [38,39]. The patients studied in the thesis have been operated on according to the original PSARP description with resection of the fistula based on the initial and latest recommendations [20,40].

**PSARVUP:** In the case of cloaca PSARVUP is performed, which is a more complex operation with mobilization of vagina and urethra [20,31]. The PSARP or PSARVUP is performed within some weeks or months after the colostomy has been established.

**Limited PSARP:** In the case of perineal fistula a limited PSARP is performed. In limited PSARP the pelvic floor is not divided as extended as in PSARP since the rectum ends beneath the puborctalis muscle [20].

**Laparoscopic assistance:** Ten years ago laparoscopic assisted reconstruction was introduced. Some laparoscopic reports present a slightly better outcome than after the open PSARP [21] but there are controversies whether redo-operations because of prolapse and stenosis are more frequent or similar in laparoscopic PSARP compared with open PSARP [41,42]. It is also debated whether the laparoscopic approach for males with recto-urethral fistulas may cause a higher incidence of urethral diverticula [43]. There is no controversy over the indication for the laparoscopic approach, instead of laparotomy, on recto-vesical fistulas [1,21,41,42,44].

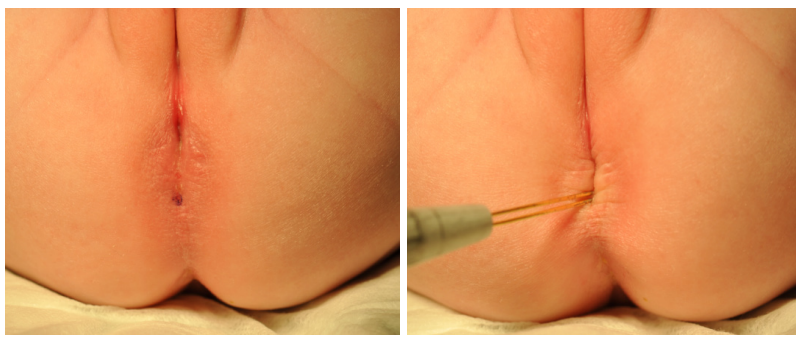


**Figure 5.** The centrum of the sphincter complex is defined with electro-myostimulation before the PSARP, limited PSARP or PSARVUP is performed.

**Serial anal dilatation:** The proportions of the sphinter and rectum are small in newborn children, and the scar after PSARP is circular. Therefore there is a need for calibration and dilatation of the reconstructed anus [1,45]. All children in the thesis, operated on with PSARP, limited PSARP or PSARVUP, routinely entered a dilatation program after the reconstruction. Daily dilatations with Hegar dilators were performed by the parents.

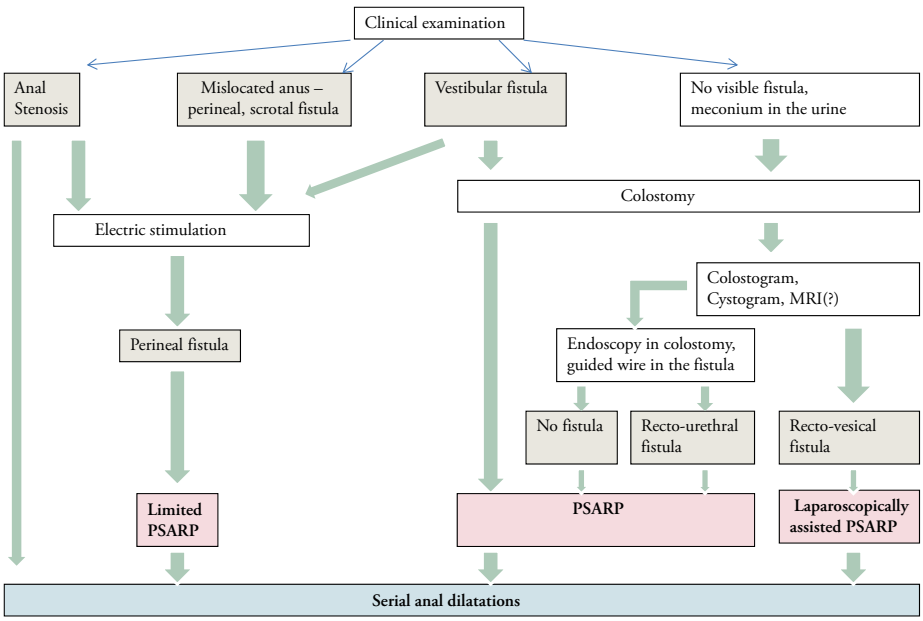



**Figure 6.** Flow chart on diagnosis and subsequent treatment of different ARM subtypes at our institution.

# Pelvic floor and sphincter anatomy

## Normal anatomy

From an anatomical point of view, fecal continence depends on the muscular and sensory capacity in the pelvic floor and the anal sphincter complex. The structures and muscles involved in the continence are, apart from rectum, the perineal body, the levators, the puborectalis, the external sphincter and the internal sphincter. The nerves involved are mainly sympathetic fibers from N Hypogastricus, parasympathetic fibers from sacral nerve rootes and the somatic N Pudendus [46,47].

The IAS comprises thicker circular smooth muscles than those of the rectum wall cranially to IAS, and there are septa in between the muscle bundles. The IAS is the main muscle that keeps an adequate resting anal tone to maintain continence [48]. Upon rectal distension it will relax and is thus involved in the anorectal inhibitory reflex, which is considered crucial both for bowel emptying and for continence [46,47]. The reflex is reported to be absent in Mb Hirschsprung [49].

The EAS has three separate muscle bundles: 1. subcutaneous, 2. superficial and 3. deep. The subcutaneous part is located caudal to the IAS, the superficial part surrounds the IAS and the deep part above IAS. There are controversies about whether the deep part of EAS is a part of the puborectalis muscle or if the puborectalis muscle is a separate muscle as a cranial continuation of EAS [47]. This could be of importance when evaluating different levels of the ending of rectum in ARM.

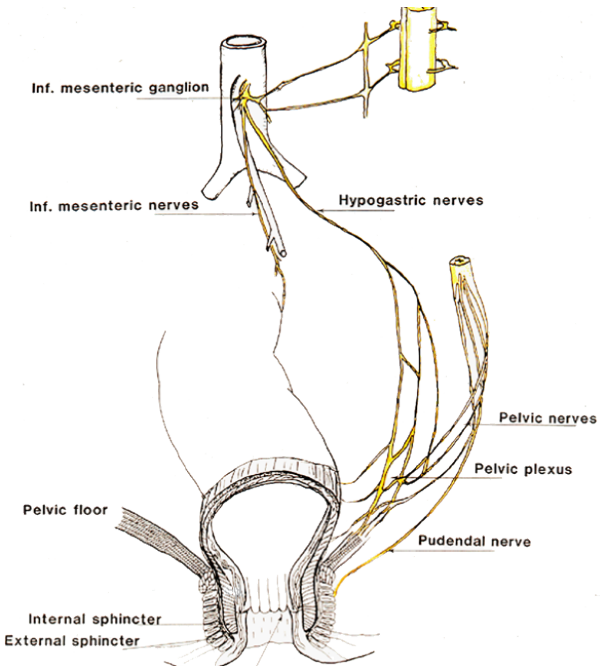



**Figure 7a.** The normal anatomy of the anus, rectum and pelvic floor.

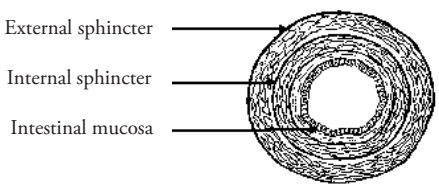



**Figure 7b.** The normal transsectional anatomy of the sphincter complex.

### Anatomy in ARM

In ARM, the anatomy of the pelvic floor, the sphincter complex and the innervation deviates because of the nature of the malformation. In 10-60% of the ARM patients there are additional spinal and sacral anomalies which could have a negative impact on the function because of a lowered rectal sensation and muscle control [3,36,50,51].

Patients born with ARM in most cases lack the normal rectal properties such as a normal volume adaptation, the rectal sensibility might be compromised and a normal recto-anal inhibitory reflex is reported weak or missing [38,52-54]. Therefore bowel control in ARM might depend heavily on the muscle capacity.

Additionally, postoperatively to PSARP, there is scarring from the division of the pelvic floor and EAS. The existence of IAS in ARM, is controversial. Remnants of IAS may be located in the fistula and therefore fistula saving surgery has been recommended [38,39,55]. According to the original description of PSARP, the IAS does not exist [18,20] and according to the most recent recommendations the fistula and 2-3cm of the rectum should be resected because of high presence of anomalies in nerves and connective tissue [19,40]. If a resection of the fistula and rectum is performed, the picture on anal ultrasonography does not show any original IAS, but instead a rectal wall: a neo-IAS. However the difference between original IAS and neo-IAS is seldom mentioned in the literature [52,54].

## Functional outcome

### Physical factors influencing the outcome

The physically functional outcome in ARM is reported as fecal, urinary and gas continence [33,50,56-58]. The outcome is reported to depend mainly on the subtype of ARM [19,22,25]. Early treatment with bowel management has been shown to improve bowel function also later [59,60].

Spinal cord malformation is one important predictor of functional outcome in gender mixed analyses [36,50,51] but also the status of the sacrum alone is reported to be an important factor [1,19,61,62]. Whether the sacral malformation alone predicts for a worse outcome, or if it is the concomitant spinal defect that worsens, is not clarified. The “flat bottom”, a consequence of weak developed muscles, is reported to be another predictor of outcome [50,63].

## Assessing bowel symptoms

Bowel symptoms, such as fecal incontinence and constipation, have been in focus when reporting outcome in ARM. There is great heterogeneity in the reports because of the use of different classifications of ARM subtypes and different assessments and scales of symptoms [61,64,65]. This diversity has made it difficult to understand and compare the outcome after PSARP. In 2005 the International Krickenbeck criteria of outcome of bowel symptoms in ARM was developed. The criteria are descriptive and non-scoring. Their intended use is to describe the patients' bowel symptoms before or without bowel management [23].

**Table 2.** Bowel symptoms according to the Krickenbeck criteria.

| Symptoms | Answer |
|---|---|
| **Voluntary bowel movement**<br>Feeling of urge, capacity to verbalize, hold the bowel movements | Yes |
| | No |
| **Soiling** | No |
| Grade 1 | Occasionally (1-2 times /week) |
| Grade 2 | Every day, no social problem |
| Grade 3 | Constant, social problem |
| **Constipation** | No |
| Grade 1 | Manageable by diet |
| Grade 2 | Requires laxatives |
| Grade 3 | Resistant to diet and laxatives |

This uniform way of reporting bowel symptoms enables comparisons of physical outcome in different subtypes of ARM [22,64,66] and facilitates the evaluation of different operative techniques [21,40,42]. It can also be useful in evaluating different bowel management regimens and in comparisons between different centers [59,60]. A uniform way of following up the patients could also facilitate collaborations between different centers [22,25] which may increase the number of ARM patients included in reports.

### Bowel symptoms in children and adolescents with ARM

Until now the reports using the Krickenbeck criteria on children with ARM have shown bowel control in 0-77%, soiling in 5-100% and constipation in 5-100% (Table 3). The huge variability of outcomes mirrors that the studies report different subtypes of ARM, gender mixed populations and different age groups.

Reports on bowel symptoms during adolescence are scarce. The studies include small numbers of patients, or a mixture of children and adults [33,50,58,67]. To our knowledge there is so far only one report on adolescents using Krickenbeck criteria and this concerns a total of 13 patients [50]. In that study and in studies including both young adolescents and young adults (13-25 years old) with ARM operated on with PSARP fecal incontinence is reported in 38-75%, severe incontinence in 23-25% and constipation in 9%-62% [33,50,58,67].

In some reports the bowel symptoms seem to be less frequent in adolescence than in childhood, others do not show any differences between age groups. In longitudinal studies, excluding perineal fistulas, "good outcome" and "total continence" increased from 5 to 15 years of age for both genders and all types of ARM [50,68]. However, cross sectional comparisons of outcome in different age groups do not show any better outcome in adolescence [22,66,69].

**Table 3.** A summary of the outcome reported in recent studies using Krickenbeck follow-up of bowel symptoms in ARM [21,22,40,42,50,60,64,66,69]. Outcomes are presented according to the ARM subtypes or age groups.

| Author | Operation | Gender | ARM subtypes | Age at follow-up (years) | Number patients | Bowel control (%) | Soiling/ Fecal incontinence (%) | Constipation (%) |
|---|---|---|---|---|---|---|---|---|
| Daher 2007 | PSARP/ Limited PSARP | Mixed | All | 1 day - 4 y | 21 | 66 | 50 | 75 |
| Hassett 2009 | PSARP | F | VF | >10 | 14 | 57 | 14 | 28 |
| | | M | RU | >10 | 18 | 58 | 5 | 42 |
| | Limited PSARP | Mixed | PF | >10 | 19 | 90 | 0 | 21 |
| Maerzhauser 2009 | PSARP+ Limited PSARP | Mixed | All | 10 (4-18) | 30 | 0 | 63 | 33 |
| John 2010 | PSARP | Mixed | VF/RU+RV | 7 (2.5-10) | 2/40 | | 88 | |
| Senel 2010 | PSARP | F | VF | 9 (3-25) | 17 | 100 | 17 | 88 |
| | | M | RU/RV | 9 (3-25) | 26/5 | 88/80 | 38/80 | 46/20 |
| | Limited PSARP | Mixed | PF | 9 (3-25) | 23 | 100 | 0 | 9 |
| Wong 2011 | Lap PSARP | Mixed | High/IM | ? | 18 | 89 | 44 | 17 |
| | PSARP | Mixed | High/IM | ? | 20 | 80 | 55 | 35 |
| England 2012 | Lap PSARP | M | All but PF | 4 (3.5-6) | 7 | 85 | 57 | 57 |
| Schmiedeke 2012 | PSARP | F | VF/C | 10 (4-20) | 21/11 | 81/54 | 76/100 | 56/64 |
| | | M | RB/RP/RV | 10 (4-20) | 6/20/7 | 83/74/57 | 83/95/86 | 50/75/57 |
| | Limited PSARP | Mixed | PF | 10 (4-20) | 25 | 88 | 60 | 64 |
| Borg 2012 | PSARP | F | VF | 5/10/15 | 9/12/7 | 33/58/75 | 80/100/75 | 100/67/57 |
| | | M | RP | 5/10/15 | 8/5/2 | 0/60/100 | 88/20/0 | 100/100/50 |
| Lombard 2013 | PSARP/ Limited PSARP | Mixed | VF/PF | 5(3-8) | 20/22 | 95 | 5 | 5 |

**F=Females M= Males PF=Perineal fistula VF=Vestibular fistula C=Cloaca RU=Recto-urethral fistula RB= Recto-bulbar fistula RP= Recto-prostatic fistula RV=Recto-vesical fistula H/IM = High/Intermediate types Lap=Laparoscopic**

### Soiling or fecal incontinence?

The term soiling is used in the Krickenbeck criteria, although the definition of soiling is an overflow from impacted rectum [70]. This is not always the reason for fecal leaks among patients with ARM. The term fecal incontinence is recommended for functional bowel disturbances according to Rome III criteria [71-73]. Therefore the term fecal incontinence is used, instead of soiling, in Papers II-IV.

## An approach to QoL

QoL has become established as an important endpoint in medical care [74]. The WHO QoL-group has defined QoL as "an individual's perception of his/her position in life in the context of culture and value systems where he/she lives, and in relation to his/her goals, expectations, standards and concerns" [75]. In other words, QoL is a subjective evaluation of a person's functioning in different areas, and refers to satisfaction. It is a multidimensional construct which should reflect the individual's wellness across several domains of life, including at a minimum physical, emotional and social functioning [75,76]. The QoL is considered to be especially important in patients with chronic conditions and, as in ARM, where dysfunction may be lifelong [74].

There are two main approaches to QoL: The general health related generic QoL and the disease/symptom specific QoL, respectively. The generic QoL tests have the advantage of assessing health and well-being independently of the disease, making it possible to compare QoL between patients and disease-free persons. The disease specific QoL has the advantage of focusing on specific issues relevant to the disease under assessment.

**The generic QoL questionnaire** used worldwide is SF-36 [77-82]. It is validated in Sweden from 15 years of age [83,84] and has been used in studies concerning adolescents [79] and adults born with different malformations and colorectal disease [78,80,85] and in follow-ups of adults with ARM [82,86]. Therefore SF-36 was used in Paper I.

There are no validated generic QoL questionnaires for children or adolescents in Sweden. Most reports from other countries on general QoL in ARM use the PedsQL [87-89]. The questionnaire is developed for age groups 2-18 years old and can be used both in self reports and by proxy [90].

**The symptom specific QoL questionnaire** Giqli has been developed for gastrointestinal symptoms and diseases. It is validated in Sweden and used for people >15 years old [91,92]. Therefore this questionnaire was used in Paper I. It has previously been used for assessing QoL in follow-ups of adults with other malformations than ARM [78,81,93].

The disease specific QoL questionnaire developed for ARM and Hirschsprung's disease is HAQL. This is used for children in different age groups and for adolescents and adults >17 years old [94]. HAQL has recently been translated and culturally adapted for Sweden [95] but this was after the investigation in Paper I had been conducted.

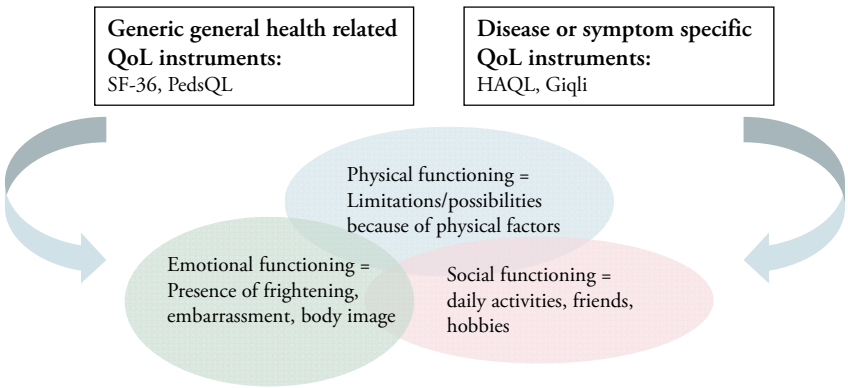



**Figure 8.** The two main types of measurement of QoL: generic and symptom specific. Both should measure the three mandatory dimensions: physical function, emotional function and social function which should reflect a person's subjective experience of her/his situation [75].

## QoL in children and adolescents with ARM

The outcome in the generic QoL results in children with ARM is diverse. In some reports children with ARM have a similar outcome as healthy children [96] while others report both that children and adolescents with ARM experience lower health related QoL than healthy peers [82,97].

The outcome in disease specific QoL, HAQL, among children and adolescents with ARM is consequently low regarding the domains emotional and social functioning [97] and also in other psychosocial aspects [82,98,99].

Reports of the change in QoL over time from childhood to adolescence vary. In some studies the QoL seems to increase with age from child to adolescent [100] but in most reports it decreases in adolescence [82,101,102].

The degree of bowel symptoms does not seem to influence the general health related QoL [96]. Still, more bowel symptoms are reported to lower specific domains such as body image and emotional functioning in disease specific QoL among children and adolescents with ARM [97]. Furthermore, soiling, constipation and abdominal pain have been suggested to be independent risk factors for psychosocial morbidity in both childhood and early adolescence [2,103].

| | Children with ARM | Adolescents with ARM | Adults with ARM |
|---|---|---|---|
| Generic health related QoL compared to healthy |  |  |  |
| Disease/ symptom specific QoL compared to healthy |  |  |  |
| Correlation severe bowel symptoms - lower QoL |  |  |  |
| Improvement of QoL with time |  |  |  |

**Figure 9.** Overview of the reported outcomes on QoL among patients with ARM. The figure shows the sometime diverse outcomes reported [82,87,94,97,99,100,102,104-106]. Arrow up = high, arrow down= low, straight arrow= similar

Psychological morbidity among patients with ARM has been reported among 80% of children and adolescents with ARM who experienced anxiety, depression and very low self esteem [2]. Depression has been reported to be more marked among young adolescents 12-16 years old than among children with ARM [99,103]. Among adolescents with ARM 35-58% fulfilled criteria for psychiatric diagnosis [107-109]. Gas incontinence among adolescents with ARM seems to be closely associated with psychiatric dysfunction [107]. It is suggested that the history of anal dilatations constitutes one important factor with negative impact on the mental health among the group [110].

## Sexual health in ARM

Sexual identity will start to form during adolescence [111,112]. Patients with ARM have a history of living with malformation and operations of the pelvic floor with remaining scars and often fecal and urinary incontinence. In males with ARM, erectile dysfunction and abnormal erection angle have been observed in 17% and 50-60%, respectively [86,113]. Effects on the psychological part of sexual health for adults with ARM have been indicated in the literature [114] and physical impairment is suggested to lower the sexual function for adult women and men with ARM [115]. There are no studies on sexual health in specifically adolescent ARM patients.

Sexual functioning is considered to be an aspect of QoL [74,114]. This does not only include being able to have intercourse but also intimacy, satisfaction and body image [86,116,117]. Adolescents and female adults with ARM are reported to score lower in the domain of body image than others without ARM [87].

Both sexual intercourse and intimacy could be restricted because of poor bowel control. 13-20% of adults with ARM with perineal fistulas and other ARM subtypes have reported avoidance because of poor bowel control [57,86,118]. This is reported to be without any correlation between sexual activity to subtype of ARM or gender [86]. However, urinary incontinence, even more than fecal incontinence, is reported to have a negative influence on sexual functioning [87]. A higher self-efficacy among adult patients with ARM, is shown to correlate with less limitation in sexual activities [114].

# Appendicostomy in anorectal malformations

Antegrade enema through an appendicostomy was introduced in the early 1990s as an alternative to the rectal enema [119]. The main indication is to treat fecal incontinence and constipation avoiding a rectal approach, in patients with MMC, Hirschsprung's disease, ARM and severe chronic constipation of other origin [120-122]. Different methods have been developed for appendicostomy. The appendix could be placed in the lower right quadrant with or without invagination into caecum [119,123]. Or the appendix could be mobilized to the umbilicus which has been promoted in order to reach good cosmetic results as well as giving the appendix an angle counteracting possible leakage [124,125]. Since the late 90s the procedure has been mainly performed laparoscopically [123-126].

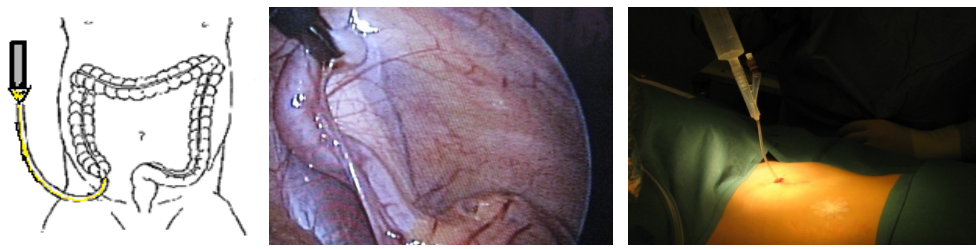


**Figure 10.** Appendicostomy: Left picture: The technique with enema administered through the appendix to the proximal colon ascendance. Middle picture: Laparascopic view with appendix being mobilized up through the abdominal port. Right picture: After stitching the appendix to the skin a peroperative control of the conduit is performed.

It has been taught worldwide that appendicostomy is only to be used in order to increase the child's autonomity. Therefore only children who already have good compliance to rectal enema have been offered appendicostomy [59,124,125,127]. The few studies on

appendicostomy in children with ARM report on patients with a median age of 8.5-10 years. The outcomes seem to be excellent regarding fecal cleaness. The complications reported are mainly backward leakage and stenosis (18-50%) which rarely need surgical revision or dilatations [125,126,128].

In preschool children with ARM 1/5 achieves fecal cleanness only with help of enemas [22]. Rectal manipulation is rarely well tolerated among those children, who have a history of operations and dilatations of anus. The psychological consequences of being subjected to rectal enemas could be difficult both for the child and the families [110,129,130]. Compliance to the rectal enema may fail and therefore fecal incontinence may remain when the child starts school.

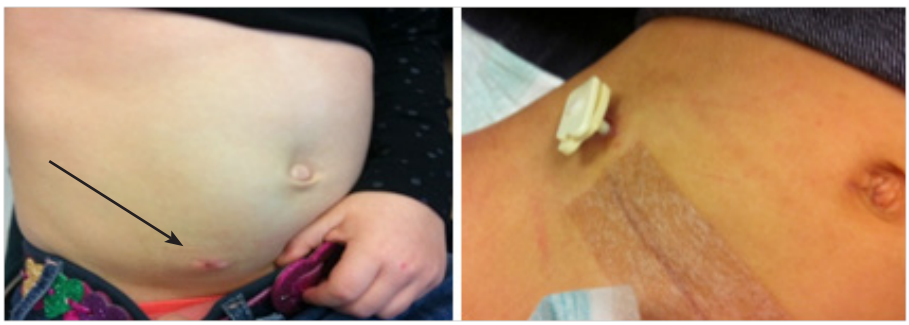


**Figure 11.** What appendicostomy looks like 6-12 months postoperatively. Left picture: 5 year old girl with ARM. Appendicostomy in the lower right quadrant with regular intermittent catheterizing. Right picture: 2 year old girl. Chait button® placed in the appendicostomy, eases the treatment in younger children, and can be used as a stopper during the first 6 months in order to avoid stricturing.

# Aims

## Paper I

To examine the physical, functional and psychological outcomes for adolescents with ARM operated on with PSARP, in order to evaluate any need of a general transfer to adult care.

## Paper II

To evaluate the outcome of an appendicostomy in preschool children with ARM regarding bowel related symptoms and type and frequency of complications. The secondary aim was to describe the use of, and the families' satisfaction with the appendicostomy.

## Paper III

To describe bowel function separately for females and males 4-12 years old with different subtypes of ARM. The secondary aim was to evaluate if fecal incontinence and constipation differed between the age groups.

## Paper IV

To evaluate the pelvic floor muscles involved in the control of fecal continence in females with ARM operated on with PSARP using perineal 4D/3D ultrasonography. The second aim was to correlate the severity of muscle anomalies to the severity of bowel symptoms, in order to evaluate if the patients' history of bowel symptoms can provide information on the status of the sphincter.

# Patients and controls

## Paper I

The study included all adolescents born with ARM and operated on as neonates with PSARP, limited PSARP or PSARVUP 1990-1995 in Lund. The study was conducted 2011-2012. Forty-six patients were included. After exclusion of those who died, emigrated, had severe mental syndromes and malignancy, the study group consisted of 27 adolescents. These were invited to a final medical examination at the Department of Pediatric Surgery in Lund. Together with the invitation they received study-information with the option to participate in the study regarding bowel symptoms, QoL and a study with in-depth interviews about sexual health. Twelve females, median age 18.0 (15-21) years, and 12 males, median age 17.5 (15-21) years, agreed to answer the questionnaires about their symptoms and QoL. Eight females and 7 males agreed to participate in interviews.

The controls were 26 females aged 17.7 (15-21) years and 25 males aged 17.5 (15-21) years. They were recruited from two nearby primary schools, three different high schools and the university. The age and gender adjusted reference population to SF-36 was obtained from 315 healthy adolescents (137 females and 168 males) collected by the health related quality of life (HRQL)-group [83,84].

## Paper II

The study included all 164 children born with ARM and admitted to the Department of Pediatric Surgery in Lund 1990-2012. The study was conducted in 2013. Appendicostomies had been performed since 1998 and all children with ARM operated on with appendicostomy, openly or laparoscopically were registered. In total, 21 children median age 4 (1-12) with ARM had received an appendicostomy. In preschool age there were 6 females and 11 males, median age 4 (1-6) years. All of these participated in the study.

## Paper III

The study included all children referred to two tertiary centers of Pediatric Surgery one in Lund (Sweden) and one in Oslo (Norway). The cohort included those operated on in Lund January 1998-December 2008 and in Oslo January 2000-December

2008. The results were collected during 2010-2012 when the children were between 4 and 12 years of age. 137 children, 56 females and 81 males, fulfilled the criteria for inclusion. After exclusions because of death, emigration, no operation and one who declined participation in the study, the studied group finally consisted of 121 children: 50 females and 71 males, with a median age of 8 (4-12) years in each gender.

## Paper IV

The study included all females born and operated on with ARM 1990-2009 in Lund. The ARM subtypes included were perineal fistula, vestibular fistula and cloaca. The study was conducted 2011-2013. All females 4-21 years old were asked to participate in the study with bowel symptoms follow-up. Those aged 11-21 years were asked if they agreed to be examined with perineal ultrasonography. Those 11-15 years of age were offered to have the ultrasonic examination performed during the regular gynecological control performed under general anesthesia; the older females were awake during the examination. The females 4-10 years old who were planned for general anesthesia for other reasons were asked to participate in the study with perineal ultrasonography. Finally, out of all the 40 females who participated in the follow-up, 17 also participated in the examinations with perineal ultrasonography.

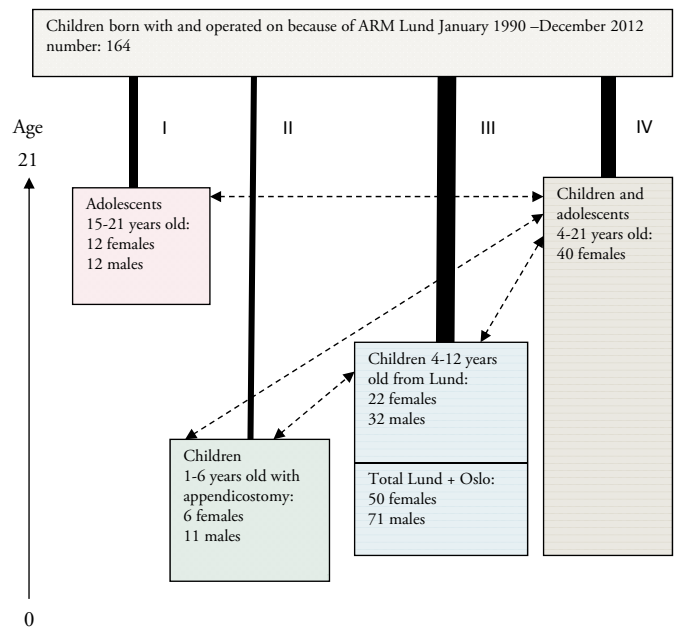



**Figure 12.** A summary of the patients involved in Paper I-IV. The arrows indicate that some of the patients were included in different Papers.

# Methods

## Generalized methods

### Bowel symptoms

In Papers I-IV the Krickenbeck follow-up [23] was used as the main tool for assessing the bowel symptoms (Appendix 1). All the follow-ups were done during the medical counseling in Lund. In Paper III, the majority of patients from Oslo were also followed up during the medical counseling and some were retrospectively registered from medical records. The Krickenbeck postoperative criteria in its original form is descriptive. In order to correlate the symptoms to the scores of QoL in Paper I and to the muscle deviations in Paper IV they were converted into the summary score 0-7 points (7= worst).

| Krickenbeck criteria with scoring | | |
|---|---|---|
| **Symptoms** | **Answer** | **Score** |
| **1. Voluntary bowel movements** Feeling of urge, capacity to verbalize, hold the bowel movements | Yes | 0 |
| | No | 1 |
| **2. Soiling** | No | 0 |
| Grade 1 | Occasionally (1-2 times /week) | 1 |
| Grade 2 | Every day, no social problem | 2 |
| Grade 3 | Constant, social problem | 3 |
| **3. Constipation** | No | 0 |
| Grade 1 | Manageable by diet | 1 |
| Grade 2 | Requires laxatives | 2 |
| Grade 3 | Resistant to diet and laxatives | 3 |

**Table 4.** The bowel symptom assessment with Krickenbeck criteria [23]used in Papers I-IV and an additional scoring 0-7 (7=worst) used in Papers I and IV.

### Concomitant malformations

In Papers II and III the associated malformations are reviewed. All the children born with ARM have been examined with X-ray and ultrasound of the sacrum and ultrasound and VCUG of the urinary tract. With signs of sacral anomalies, tethered cord or neurogenic bladder a MRI and/or urodynamic investigation was performed.

Since 2007, urodynamic investigations have been performed in all children with all subtypes of ARM, except perineal fistulas. Echography of the heart was routinely performed on all patients. The concomitant malformations are collected from the prospectively maintained database or, for patients recruited before 2007, from the medical records. In Paper III the children from Norway had their concomitant malformations retrospectively registered from the medical records.

## Prospectively maintained database

From 2007 a prospectively maintained database was established in Lund, collecting the symptoms in children born with ARM. All children with ARM come to regular counseling during the first year, and then at age of 2, 5, 10 and 14 years. The subtype of ARM is registered, as well as the bowel symptoms assessed by Krickenbeck criteria, concomitant malformations and urinary symptoms. The data base is used in Papers II-IV.

## Statistical methods

In Papers I, III and IV the outcome for the different subtypes of ARM are compared, and therefore statistical corrections for multiple comparisons were performed controlling the number of false positive findings to, at most, the reported p-value. In Paper III confidence intervals were used as a complement to the statistical results, illustrating the range of results in each observation. $p<0.05$ was considered significant.

**Table 5.** A summary of the statistical methods used in Paper I-IV.

| Statistical method | Statistical test | Paper | | | |
|---|---|---|---|---|---|
| | | I | II | III | IV |
| **Non-parametric tests** for dichotomous results and for multiple comparisons | Wilcoxon Mann-Whitney | x | | | |
| | Fisher's generalized test | | | x | x |
| | Fisher's Exact Test with post hoc | | | x | |
| | Fisher's 2-by-2 subtabled test or Fisher's Exact test, two tailed | | x | x | |
| | Chi-square test | | | | x |
| **Non-parametric test** for ranks and multiple comparisons | Kruskal Wallis | x | x | x | x |
| | Kruskal Wallis with post hoc test | x | | x | |
| Correlation test | Spearman's rank correlation | x | | | x |

# Specific methods

## Paper I

*Performance of the study regarding symptoms and QoL*

Patients: During the medical counseling, the patients were followed up regarding their bowel symptoms and gas incontinence. The investigator (P.S.) was not the operating surgeon. The QoL questionnaires were filled in directly after the meeting.

Controls: The control persons got the questionnaires on bowel symptoms, gas incontinence and QoL delivered with information about the aim of the study and consents. They enclosed their answers themselves in envelopes, thus ensuring anonymity.

*Gas incontinence*

The gas incontinence answers were graded similarly to the Krickenbeck criteria: If they had gas incontinence (no=0, yes=1). If they had gas incontinence, how big was the problem (no=0, small: 1-2 times/week=1, moderate: every day, no social problem=2, big: constantly, social problem=3). How much did the gas incontinence restrict their activities (never=0, sometimes: every month=1, often: every week=2, always: every day=3). The score for gas incontinence was 0-7 points (7= worst). Appendix 2.

*QoL Giqli*

The Giqli questionnaire is a symptom oriented instrument for measuring QoL in gastrointestinal disorders [92]. It consists of 36 questions scoring from 0 (worst) to 4 (best) with a total score maximum of 144. (Appendix 3). A score under 105 is usually measured in individuals with clearly symptomatic situations [91]. Five dimensions of QoL can be analyzed: symptoms (19 items), associated physical disease (7 items), emotions (5 items), social integration (4 items), effects of treatment (1 item). Appendix 3.

*QoL SF-36*

The SF-36 is a generic test measuring health related general QoL [83]. The SF-36 includes 8 domains of functioning: physical, role limitation because of physical functioning, bodily pain, general health, vitality, social functioning, emotional role and mental health (Appendix 4). Scores are summed for each domain and then transformed into scores from 0 (worst) to 100 (best). Two higher order summary scores have been shown to well represent the subscales Physical Component Summary (PCS) and Mental Component Summary (MCS) [84]. There is a centrally collected reference population for adolescents >15 years old and adults [83,84].

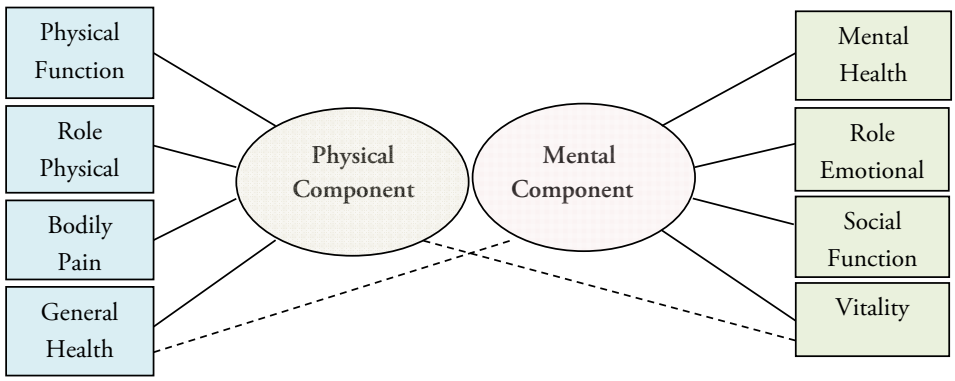



**Figure 13.** SF-36 is a generic QoL questionnaire measuring general health. The questionnaire is based on physical and mental components with eight domains of functioning.

*In-depth interviews on sexual health and body image*

The interviews were semistructured in-depth interviews and carried out by two sexologists: one interviewed the females and the other the males. The interviews focused the influence of ARM on body imaging and sexuality. Each interview, limited to 90 minutes, was recorded and then transcribed.

## Paper II

The outcome and complications after the appendicostomies were registered prospectively 2007-2012 and retrospectively 1998–2006 through regular medical counseling and the patients' files. The bowel symptoms were statistically compared pre- and postoperatively.

*Postoperative complications*

The registered postoperative complications were stenosis, infections, backward leakage, pain and perforations, which was similar to previous reports on appendicostomy in ARM [124,125,128].

*Telephone interviews about the use and satisfaction*

The follow-up regarding the use of and satisfaction with the appendicostomy was registered through telephone interviews according to a questionnaire about the time required, volumes used and parents' and children's satisfaction (Appendix 5). The telephone interviews were carried out by physicians who were unknown to the families.

## Paper IV

*4D/3D perineal ultrasonography*

The ultrasonography examination of the pelvic floor was performed with the patient in the dorsal lithotomic position. The transducers (M6C, RSP6, system Voluson E8 GE) were held to allow a sagittal inspection of the levator ani and the anal sphincter complex [131,132]. If the patients were awake they were instructed to squeeze their pelvic muscles using a 4D/3D mode [132,133]. All scans were saved in 3D and analyzed off-line by a trained sonographer.

*Description of the sphincter and the anal canal*

The description of the sphincter and pelvic floor focused on the deep and subcutaneous parts of the EAS the neo-IAS, the levators and the distal part of the anal canal. The evaluation of the EAS was made based on the diastase between the ends of the circular muscle anteriorly. A diastase >15 degrees was considered as a real defect. The neo-IAS i.e. the inner circular muscle layer, was evaluated as fragmented or not. It was measured above the anastomosis or above the diastase between rectum and skin. The m. levator ani was described as with or without any visible disruptions.

A defect between rectum and the skin may be present in patients with ARM anteriorly in the anal canal. A distance of up to 5 mm was considered as scar, while >5 mm was considered as a defect.

In order to correlate the defects of the muscles with the severity of symptoms (Table 4) a scoring of the muscles was performed with 1 point for every deviation. Diastasis in both the deep and superficial parts of EAS was considered as serious and thus given two points. The score ranged from 0-6 (6=worst).

**Table 6.** Muscle score used in Paper IV: Description and scoring of the muscles and structures in the anal canal, the sphincter and the pelvic floor.

| Structure | Finding | Score (0-6) |
|---|---|---|
| **M. Levator Ani** | Complete<br>Disrupted | 0<br>1 |
| **Neo-internal anal sphincter** (neo-IAS) | Complete<br>Fragmented | 0<br>1 |
| **External anal sphincter** (EAS) | | |
| Deep part | Complete<br>Diastasis > 15 degrees | 0<br>1 |
| Superficial part | Complete<br>Diastasis > 15 degrees | 0<br>1 |
| Both deep and superficial parts | Diastasis >15 degrees | + 1 |
| **Anal canal** | | |
| Rectum to the skin anteriorly | No diastasis<br>Diastasis > 5 mm | 0<br>1 |

# Results

## Bowel symptoms

In all the four papers the bowel symptoms were assessed with Krickenbeck criteria (Table 7). Analyses of the outcome for each ARM subtype were made for females and males separately in Papers I and III, respectively, and for females particularly in Paper IV (Table 8).

**Table 7.** Summary of the bowel symptoms presented in each paper.

| Paper | P1 | | PII | | PIII | | PIV |
|---|---|---|---|---|---|---|---|
| Gender | Females | Males | Females | Males | Females | Males | Females |
| ARM subtypes | PF/VF/C | PF/RU/RV | PF/VF/C | PF/RU/RV/No | PF/VF/VaF/No | PF/RU/RV/No | PF/VF/C |
| Median age (range) | 18(15-21) | 17.5(15-21) | 8(1-19) | | 8(4-12) | 8 (4-12) | 13.5(4-21) |
| Number of patients | 12 | 12 | 17 | | 50 | 71 | 40 |
| Comments | | | Before appendicostomy | | | | |
| Voluntary Bowel Movements (%) | 75 | 33 | 0 | | 70 | 58 | 67.5 |
| Soiling (%) | 67 | 58 | 88 | | 48 | 42 | 75 |
| Grade 1 | 17 | 33 | 0 | | 26 | 11 | 22.5 |
| Grade 2 | 25 | 17 | 12 | | 8 | 6 | 40 |
| Grade 3 | 25 | 8 | 76 | | 14 | 25 | 12.5 |
| Constipation (%) | 92 | 67 | 88 | | 62 | 35 | 92.5 |
| Grade 1 | 33 | 50 | 2 | | 6 | 5 | 12.5 |
| Grade 2 | 59 | 8 | 17 | | 42 | 20 | 42.5 |
| Grade 3 | 0 | 8 | 59 | | 14 | 10 | 37.5 |

**Table 8.** Summary of the outcome of bowel symptoms in each subtype of ARM in Paper I, III and IV.

| Gender | Females | | | | | | | | | Males | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Subtype ARM** | Perineal fistula | | | Vestibular fistula | | | Cloaca | | | Perineal fistula | | Recto-urethral fistula | | Recto-vesical fistula | |
| **Paper** | I | III | IV | I | III | IV | I | III | IV | I | III | I | III | I | III |
| **Number of patients** | 7 | 24 | 21 | 4 | 22 | 15 | 1 | 0 | 4 | 6 | 32 | 5 | 29 | 1 | 3 |
| **Voluntary Bowel Movements** Yes (%) genderwise | 57 | 79 | 29 | 100 | 50 | 67 | 100 | | 50 | 100 | 91 | 40 | 32 | 0 | 0 |
| **Soiling/ Fecal Incontinence** Yes (%) genderwise | 57 | 42 | 67 | 75 | 50 | 80 | 100 | | 75 | 33 | 10 | 80 | 69 | 100 | 33 |
| Grade 1 | 14 | 25 | 24 | 0 | 27 | 27 | 100 | | 0 | 33 | 6 | 40 | 10 | 0 | 33 |
| Grade 2 | 14 | 8 | 33 | 50 | 5 | 33 | 0 | | 75 | 0 | 3 | 20 | 3 | 100 | 0 |
| Grade 3 | 29 | 8 | 10 | 25 | 18 | 20 | 0 | | 0 | 0 | 0 | 20 | 55 | 0 | 0 |
| **Constipation** Yes (%) genderwise | 85 | 62 | 90 | 100 | 55 | 87 | 100 | | 100 | 50 | 25 | 80 | 41 | 100 | 57 |
| Grade 1 | 28 | 8 | 24 | 50 | 5 | 20 | 0 | | 25 | 50 | 9 | 40 | 3 | 100 | 0 |
| Grade 2 | 57 | 46 | 42 | 50 | 32 | 13 | 100 | | 50 | 0 | 13 | 20 | 21 | 0 | 57 |
| Grade 3 | 0 | 8 | 24 | 0 | 18 | 53 | 0 | | 25 | 0 | 3 | 20 | 17 | 0 | 0 |

# Paper I

## Bowel symptoms and gas incontinence

**Bowel symptoms:** Voluntary bowel movements, fecal incontinence and constipation, were significantly more common among the 24 adolescent females and males with ARM compared with the 51 controls ($p<0.0001$ for each gender, Wilcoxon Mann-Whitney exact test). Bowel symptoms were also more common among those with perineal fistulas compared with the controls genderwise ($p<0.0001$ for each gender, Kruskal-Wallis with post hoc test). No differences in the score of bowel symptoms were found between those with perineal fistulas and the other subtypes of ARM ($p=0.942$ for the females and $p=0.3190$ for the males; Kruskal-Wallis with post hoc test).

**Gas incontinence** was reported by 6/12 (50%) of the females with ARM, and 25% reported that gas incontinence restricted their activities. 10/12 (83%) males with ARM reported gas incontinence, and 50% were restricted in their activities due to this. Gas incontinence did not differ significantly between the female ARM subtypes, but among the males those with recto-urethral fistulas scored higher than those with perineal fistulas

(p=0.017, Kruskal-Wallis with post hoc test). Only the ARM males, not the females, reported significantly more gasincontinence than the controls (p=0.005, Wilcoxon Mann-Whitney exact test).

## Quality of life

**Generic QoL:** Total SF-36 scores showed no differences between the females or the males with ARM and the normative reference population. The females scored lower in the physical component summary (PCS), than the controls (Figure 14).

The males with ARM scored higher than both the reference population and the controls in social functioning (p=0.034 and 0.030, respectively, Mann-Whitney Test). Compared with the controls, the males with ARM scored higher in all mental items and in the mental component summary (MCS) (Figure 14).

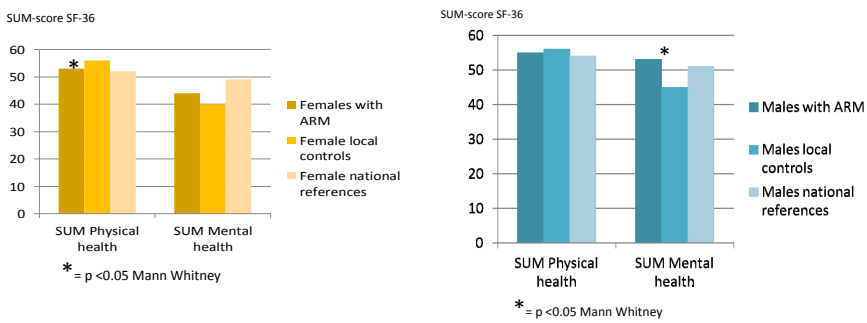



**Figure 14.** The summarizing scores for SF-36 regarding physical health (PCS) and mental health (MCS). The PCS was lower for the females with ARM and the MCS higher for the males with ARM.

**Symptom specific QoL:** In Giqli three females and none of the males had a score under 105 (very low QoL), though four males scored as low as 105-110. The females with ARM scored lower in Giqli total sum compared with the controls (p=0.004, Mann-Whitney Exact test), but there was a wide spread of the results for the ARM females. The females also scored significantly lower than the controls in three of the Giqli subscales: "large bowel function", "upper GI function" and "meteorism" (Table 9). There were no significant differences in QoL between the female ARM subtypes (p>0.3 Kruskal-Wallis with post hoc test).

The males with ARM had similar scores in Giqli total QoL sum as the controls. Only in the physical domain "large bowel function" did the males with ARM score lower than the controls (Table 9). There were no significant differences between the male ARM subtypes (p>0.3 Kruskal-Wallis with post hoc test).

**Table 9.** QoL measured with Giqli. Results for adolescent females and males with ARM compared with age and gender matched controls.

| | ARM females (n 12) | Controls females (n 26) | |
|---|---|---|---|
| **Subscales GIQLI** | Median (Range) | Median (range) | **P-value*** |
| | | | |
| Physical role | 40.0 (17-44) | 43.0 (30-44) | 0.178 |
| Large bowel function | 21.0 (9-22) | 22.0 (18-24) | ***0.013*** |
| Emotional role | 24.5 (9-30) | 26.0 (19-30) | 0.212 |
| Upper GI function | 26.0 (12-31) | 30.0 (22-32) | ***0.004*** |
| Meteroism | 7.5 (3-11) | 10.0 (4-11) | ***0.015*** |
| **TOTAL** | 120.5 (73-134) | 131.5 (115-138) | ***0.004*** |

| | ARM males (n 12) | Control group (n 26) | |
|---|---|---|---|
| **Subscales GIQLI** | Median (range) | Median (range) | **P-value*** |
| | | | |
| Physical role | 41.5 (32-44) | 43 (37-44) | 0.138 |
| Large bowel function | 20 (10-24) | 23 (17-24) | ***0.029*** |
| Emotional role | 27 (20-30) | 27 (17-30) | 0.534 |
| Upper GI function | 30 (21-32) | 29 (27-31) | 0.811 |
| Meteroism | 9 (4-12) | 10 (5-12) | 0.378 |
| TOTAL | 125 (108-132) | 131 (109-142) | 0.217 |

*Wilcoxon- Mann Whitney Exact test

## Correlation between symptoms and quality of life

The only statistically significant correlation between bowel symptoms and QoL was found for the males and the symptom specific Giqli.

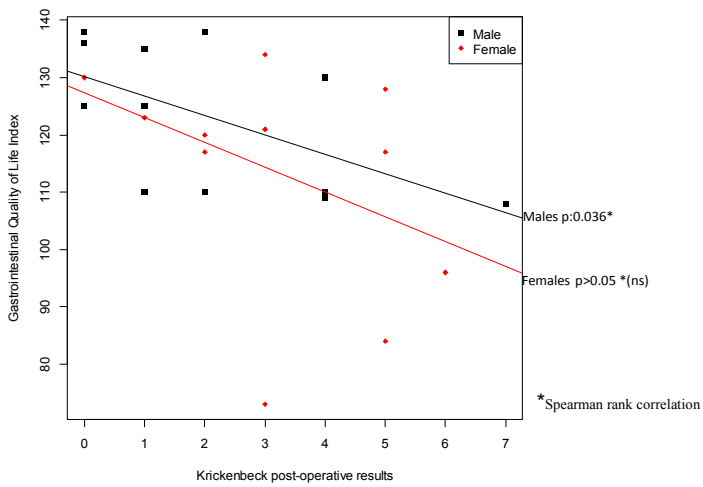



**Figure 15.** Illustration of the significant correlation between more bowel symptoms and lower QoL in symptom specific QoL. The figure also illustrates the wide spread of individual results, especially among the females.

## Sexual health and body image

**Females:** All females had the feeling that there was something different about them. They all remembered that they had been treated with bowel management during childhood but none experienced psychological effects from these treatments.

Among the females, the body images contained elements of embarrassment about their anatomy and abdominal scars. Still, sexuality and body imaging were not associated with their ARM by any of the females.

In summary, the female adolescents with ARM thought they themselves had the same attitude to sexuality and bodies as their peers. All requested that the doctor should mention sexual issues related to ARM since they were too embarrassed to broach the subject themselves.

| |
|---|
| 7/8 adolescent females were uninformed about their malformation and the operations performed.<br>They had not talked about it in their families, and the anus was seldom mentioned |
| They were concerned about the scars on the stomach –<br>they influenced body image |
| 50% had experienced intercourse<br>- adjusted timing of sex to gas leakage<br>- none had pelvic or genital pain |
| They wished that sexual issues had been raised during early adolescence by the pediatric surgeon |

**Figure 16.** The main results for the females with ARM in the in-depth interviews conducted by a sexologist.

**Males:** All males were aware that the rectal leakage could be stigmatizing both in sexual intercourse and in other activities in life. Four of the males had debuted with sexual intercourse and the others had had other kinds of sexual experience such as masturbation.

| |
|---|
| All were informed about the malformation, and it had been openly discussed at home |
| Coping mechanisms to symptoms were developed –<br>hard physical exercise, good lies |
| 4/7 had experience of intercourse<br>- One with impotence, one small size of penis<br>- Treatment with enema when timing the intimacy |
| 6/7 experienced that their body image and sexuality were influenced by the malformation |

**Figure 17.** The main results for the males with ARM in the in-depth interviews conducted by a sexologist.

Six out of the 7 males thought that their body and sexuality in some way was affected by the ARM. The reasons were mainly that the leakage of gas forced them to be controlled, and the need for emptying the intestine before or during sex diminished the good feeling. Six of the males wished that the surgeon would have mentioned possible sexual problems due to ARM.

In summary, the male adolescents were concerned about their sexuality and bodies. They were aware of their malformations, and had active coping mechanisms.

# Paper II

## Bowel symptoms before and after appendicostomy

The postoperative improvements after appendicostomy were significant regarding increased control of bowel movements and decrease of soiling and constipation.

**Table 10.** Bowel symptoms before and after appendicostomy with a median follow-up time of 5 years. *Fisher's Exact Test, two-tailed

| Number of children n= 17 median age 4 (1-6) years old | Answers | Pre-op n 17 | Post-op n 17 | p- value* |
|---|---|---|---|---|
| **1.Voluntary bowel movements** Feeling of urge, capacity to verbalize, hold the bowel movements | **Yes/No** | 0/17 | 16/1 | ***<0.001*** |
| **2. Soiling** | **No** | 2 | 15 | ***<0.001*** |
| Grade 1 | Occasionally (1-2/week) | 0 | 1 | |
| Grade 2 | Every day, no social problem | 2 | 1 | |
| Grade 3 | Constant, social problem | 13 | 0 | |
| **3. Constipation** | **No** | 2 | 14 | ***=0.001*** |
| Grade 1 | Manageable by changes in diet | 2 | 2 | |
| Grade 2 | Requires laxatives | 3 | 1 | |
| Grade 3 | Resistant to laxatives and diet | 10 | 0 | |

**Concomitant malformations:** All of the children who received appendicostomy <6 years of age were shown to have either spinal cord malformation, neurogenic bladder or were born with a neurological syndrome. However these findings were not prescribed for having an appendicostomy.

## Complications

Postoperative complications were present in 7/17 (43%) of the children; 29% had a postoperative subcutaneous infection. The total number of complications were 10/17.

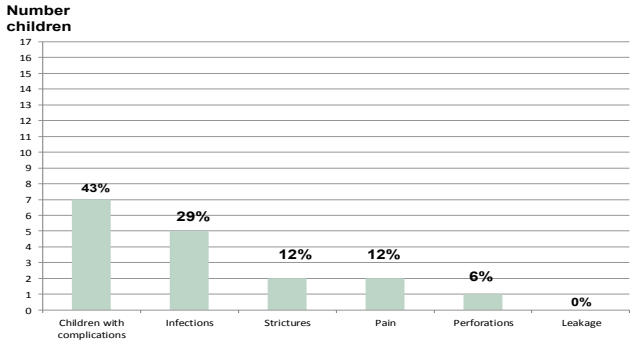



**Figure 18.** Frequency of different postoperative complications after appendicostomy in a gender mixed group of children with ARM <6 years of age.

## The use of and satisfaction with appendicostomy

The range of volumes used in the appendicostomy was wide 11-80 ml/kg. The time consumption was reported to be 15-60 minutes daily. The satisfaction rate reported by the parents was 15/17 (88%).

**Table 11.** During telephone interviews conducted by doctors who were not known to the families, the following use, volume and satisfaction with the appendicostomy was reported:

| Qustionnaire | Answer | Median (range) | Number |
|---|---|---|---|
| Stopped using the appendicostomy (years) | | 5 (1.5-10) | 3 |
| Total volume enema used at each treatment (ml) | | 850 (200 - 3000) | 14 |
| Volume enema used at each treatment (ml/kg) | | 35 (11-80) | 14 |
| Time needed to administer the enema and finish the bowel emptying (min) | | 45 (15-60) | 14 |
| Frequency of the use of the appendicostomy | Once daily | | 10 |
| | Three times daily | | 1 |
| | Every other day | | 2 |
| | Weekly | | 1 |
| Appendicostomy could be recommended to others in same situation | Yes | | 15 |
| | No | | 2* |
| Use of Chait button® | | | 8 |

*comments: 1. too early to evaluate and 2. were satisfied themselves but had heard negative experiences from others.

# Paper III

## Voluntary bowel movements

***Total females/males**:* Voluntary bowel movements were achieved statistically equally in the females (70%) and the males (58%) (p>0.3, Fisher's Exact Test, two-tailed).

***Perineal fistulas:*** Among the children with perineal fistulas, 79% of the females reported voluntary bowel movements as opposed to 91% of the males, however this was not significant (p>0.3, post hoc 2-by-2 Fisher's Exact Test adjusted for multiple comparisons).

***Female perineal/vestibular fistulas:*** The frequency of voluntary bowel movements was not different for the females with perineal fistula (79%) than for those with vestibular fistula (73%) (p>0.3, post hoc 2-by-2 Fisher's Exact Test adjusted for multiple comparisons).

## Fecal incontinence

***Total females/males:*** The frequency of fecal incontinence was similar among the females (48%) and the males (42%) (p>0.3, Fisher's Exact Test, two-tailed).

***Perineal fistulas:*** Females with perineal fistulas reported a higher frequency of incontinence (42%) than the males with perineal fistulas (10%) (p=0.006, Fisher's Exact Test, two-tailed). Also severe incontinence (grade 2 and 3) was significantly more frequent among the females with perineal fistulas than among the males with perineal fistulas (Figure 19).

***Female perineal/vestibular fistulas:*** There were no differences in incontinence between females with perineal fistulas and vestibular fistulas when comparing incontinence overall (p>0.3, Fisher's Exact Test, two-tailed), all grades (0-3) of incontinence (p>0.3, Kruskal-Wallis with post hoc test for rank data) or severe incontinence (grade 2 and 3) (Figure 19).

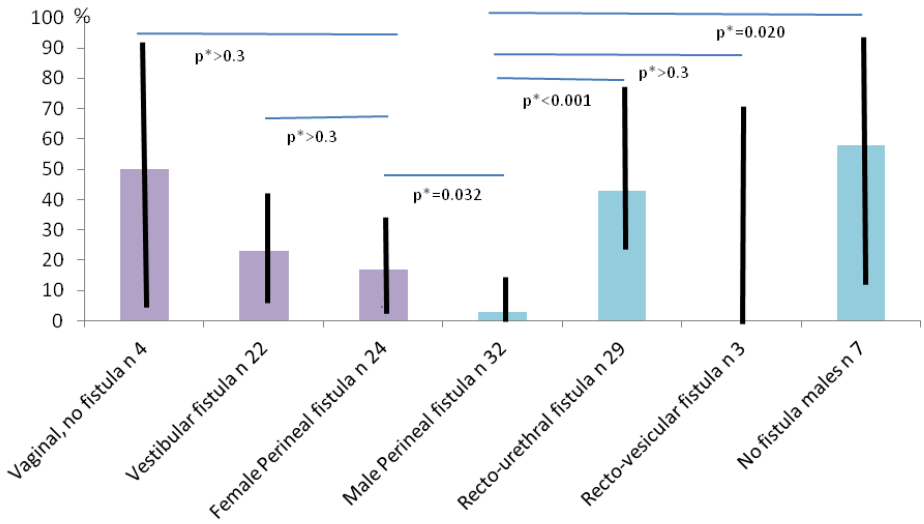



**Figure 19.** Severe fecal incontinence (daily fecal soiling with or without social implications) in comparison between the ARM subtypes. p*=post hoc 2-by -2 Fisher's Exact Test adjusted for multiple comparisons

## Constipation

***Total males/females:*** The frequency of constipation (yes) was statistically higher among the females (62%) than among the males (35%) (p=0.005, Fisher's Exact Test, two-tailed).

***Perineal fistulas:*** Constipation was significantly more frequent among the females than among the males with perineal fistulas (Figure 20) but the prevalence of constipation grade 3 (not manageable with diet or laxatives) did not differ between females and males with perineal fistulas (p>0.3, Fisher's Exact Test with post hoc test).

***Female perineal/vestibular fistulas:*** The frequency of constipation was similar for the females with perineal fistulas and those with vestibular fistulas (Figure 20). Neither were there any significant differences in the rank or grade 3 between the female subypes of ARM (p>0.3 Kruskal-Wallis post hoc test for rank data and p>0.3 Fisher's Exact Test with post hoc test).

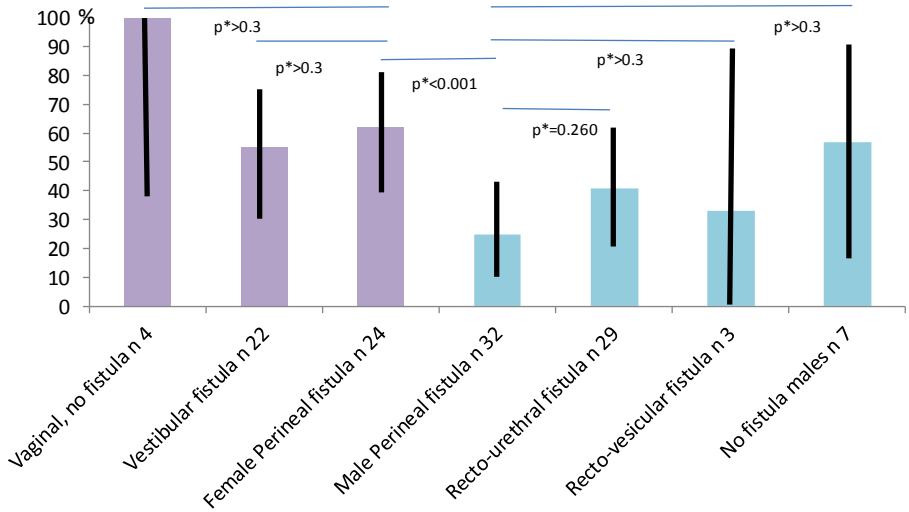



**Figure 20.** Constipation (yes) in comparisons between the different subtypes of ARM.
p*=post hoc 2-by -2 Fisher's Exact Test adjusted for multiple comparisons

## Comparisons of bowel symptoms between the age groups

The loss of voluntary bowel movements, and severe incontinence did not differ significantly between the lower and higher age groups for females nor males with ARM (p>0.3 post hoc 2-by-2 Fisher´s Exact Test adjusted for multiple comparisons).

Constipation was the only symptom with lower frequency in the older age group, at least among the males (Figure 21).

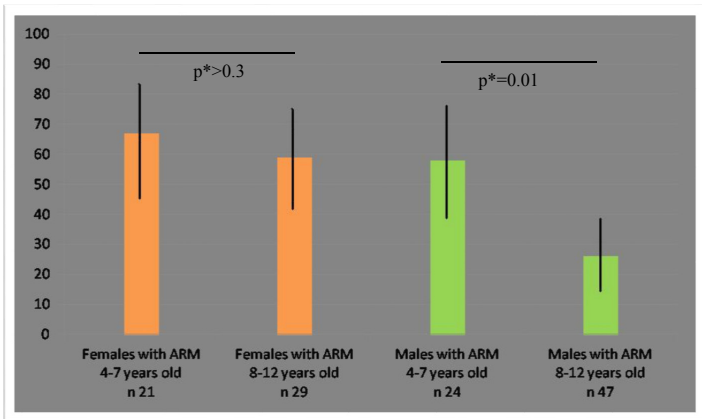



**Figure 21.** Constipation among males with ARM was the only symptom that differed between the age groups. p*=post hoc 2-by-2 Fisher´s Exact test adjusted for multiple comparisons

## Sacral malformation and bowel symptoms

The frequency of sacral malformations did not differ significantly between the females (28%) and males (23%) nor in genderwise comparisons between the perineal fistulas (p>0.05, Fisher's Exact Test, two tailed).

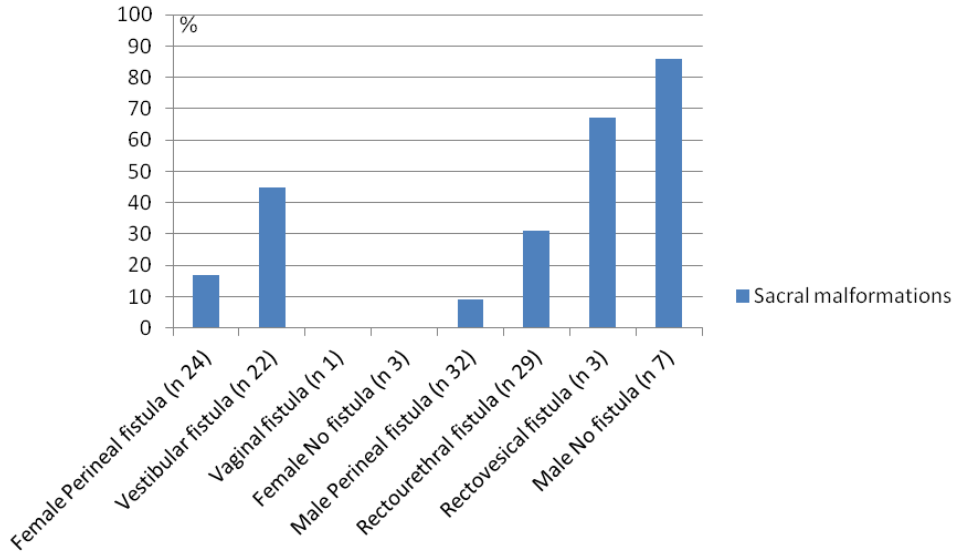



**Figure 22.** Frequency of sacral malformations in the different ARM-subtypes.

The only significant positive correlation between sacral malformation and bowel symptoms was found among males with recto-urethral fistulas, of whom 100% had no voluntary bowel movements and 100% had fecal incontinence compared with 50% and 55% without sacral malformations (p=0.011 and p=0.027, respectively, Fisher's Exact Test, two tailed).

# Paper IV

## Bowel symptoms

In 40 females the bowel symptoms were assessed, and out of those 17 were investigated with 4D/3D ultrasonography. The distribution of bowel symptoms and symptom score did not differ significantly between those examined with or without ultrasonography.

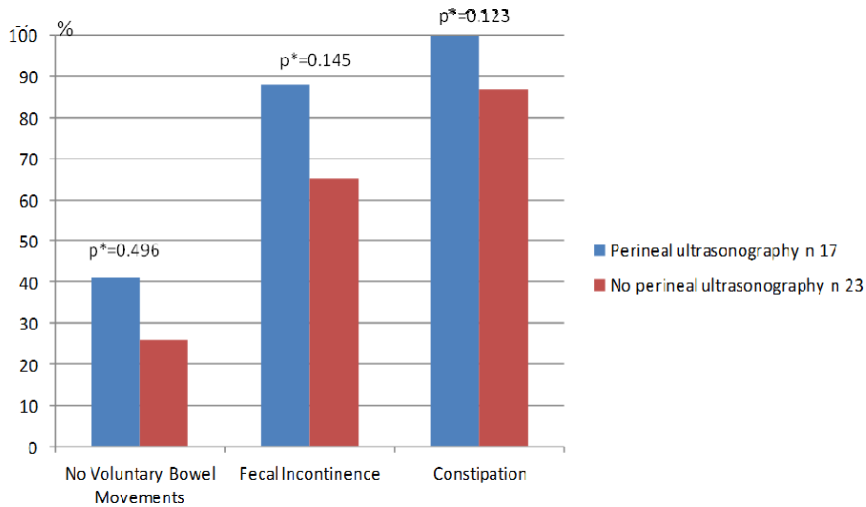



**Figure 23.** The group of females investigated with ultrasonography was considered to be representative for all 40 females in terms of bowel function since there were no significant differences in bowel function between the groups. *Fisher's Exact Test, two-tailed

## Muscle components

All the females had at least one muscle defect. None of the females had any rupture of the m. levator ani. All the females who were awake during the examination had good control of the levators. The most frequent finding was fragmented neo-IAS in 14 females. In 11 females diastasis in both the deep and superficial component of the EAS was identified. A majority of the patients had a gap of > 5 mm from the rectum to the skin anteriorly.

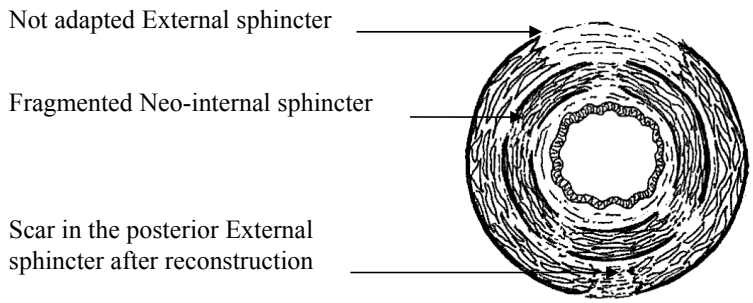



**Figure 24 a**. Illustration of the main anatomical deviations among females with ARM operated on with PSARP a) cross sectional picture of the sphincter.

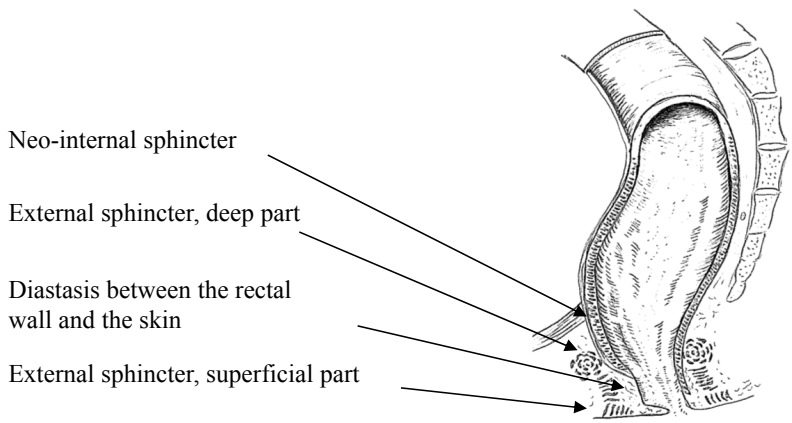



**Figure 24 b.** Illustration of the main anatomical deviations among females with ARM operated on with PSARP b) longitudinal picture the anal canal.

## Correlation of defects and bowel symptoms

The number of defects in the muscles and the severity of bowel symptoms did not correlate significantly (Figure 25). Neither were there any significant correlations between fecal incontinence and the separate type of defects in IAS, EAS or anal canal (p>0.05, Spearman's correlation).

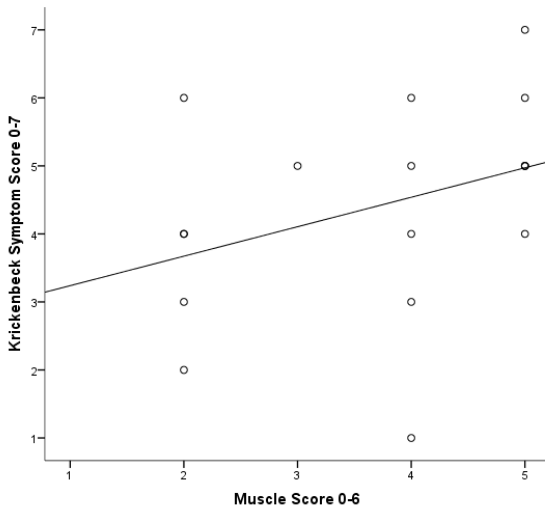



**Figure 25.** Correlation between muscle score (0-6 worst) and Krickenbeck symptom score (0-7 worst). The figure illustrates a trend towards positive correlation between the numbers of defects and the bowel symptoms, but a lack of significance. Correlation coefficient 0.419, p= 0.094 (Spearman correlation test)

# General discussion

The new findings in this thesis are:

1) Adolescent females with ARM lack information about their ARM, while the males are more aware of their ARM and have developed strong coping mechanisms.

2) Appendicostomy already in preschool age improves fecal cleanness with only minor complications.

3) Females with perineal fistulas have more fecal leakage and constipation than males with the same ARM subtype.

4) There are considerable anatomical abnormalities in the anal canal and anal sphincter in females operated on with PSARP.

## General considerations

**Assessing different subtypes of ARM:** ARM is a rare condition, and the number of patients with ARM in childhood and adolescence is limited both in this thesis and in the previous literature. There are 10 different ARM subtypes [23] and it is essential to analyze them separately, since the outcome differs much between them [22,50,60,64]. The downside is that it means an even smaller number of patients in each group. With the aim to make a gender and age analysis, the ARM-groups will become even smaller or can come to include a mix of the subtypes.

In Papers I, III and IV the functional outcome is described separately for each ARM subtype. However, in the comparisons of age groups in Paper III and in the correlation analyses in Papers I and IV, the results are reported on mixed ARM subtypes, which is a limitation.

**Populations:** The strength in this thesis is the assessment of all children and adolescents with ARM operated on with limited PSARP, PSARP or PSARVUP since 1990 at the Department of Pediatric Surgery in Lund. There is no uncontrolled drop-out in any study and the participation rate in follow-ups regarding bowel symptoms is high.

Another strength in the thesis is the prospectively maintained database established with the newborn ARM patients in Lund 2007. The database is used in Papers II, III and IV and has increased the quality and reliability of the follow-up.

**Assessment of bowel symptoms:** The assessment of bowel symptoms was made in Papers I-IV with Krickenbeck criteria. The advantage of this method is that it is internationally recommended which enables gathering of information from different centers [22,25] and comparisons of outcomes [42]. The questionnaire is short and the questions on fecal incontinence and constipation easily understood.

The disadvantages, addressed in Papers I-IV, are: 1. The questions are meant to measure the symptoms before bowel management [23] which can be confusing since many patients use enemas or laxatives at the time for the postoperative evaluation of the appendicostomy; 2. The definition of voluntary bowel movements is somewhat unclear and the answer could depend on if it is the patient or the doctor who is the evaluator (Table 2). Many patients experience that they have voluntary bowel movements even though soiling and constipation are present. Is it possible to have voluntary bowel movements if enemas are needed every day in order to avoid soiling? 3. The Krickenbeck criteria are descriptive, but in order to facilitate correlations in Papers I and IV, they were converted into a score - a score that is not validated (Table 4). The scoring turned out only to weakly reflect the real symptomatology, which could be because of the low scoring of "Voluntary bowel movements".

**Cooperation with other groups:** Paper I was produced together with sexologists, Paper III in collaboration with colleagues in the tertiary center for Pediatric Surgery in Oslo, and Paper IV in cooperation with the Department of Obstetrics and Gynecology in Lund.

The cooperation has many advantages from a scientific perspective. Firstly it contributes to increased knowledge in different areas connected to ARM. Secondly, it increases the insight into the studies, thereby increasing the reliability. Thirdly, the scientific cooperation gives the patients advantages because of the spin-off for clinical cooperation and further studies.

## Bowel symptoms with a gender perspective

The bowel function among children with ARM with perineal fistulas in Paper III, depended on gender with a less favorable outcome among females than males. Among the females with perineal fistula 42% had fecal incontinence and 62% constipation, while the figures for the males were only 10% and 25%, respectively. Perineal fistulas have never been analyzed genderwise before and the findings are new.

Another new finding was that the females with perineal fistulas had a similar outcome as those with vestibular fistulas. Previously the females with vestibular fistulas have been considered to have a better outcome than those with perineal fistulas, but this was only in comparison with gendermixed groups of perineal fistulas [22,60,66].

In the literature there is a lack of genderwise analysis of the outcome after limited PSARP [134] and the patients with perineal fistulas are usually gathered into one gender mixed group [22,23,58]. Since the number of males:females with ARM is 1.5:1 the results can be skewed to a better outcome for the females, and vice versa for the males.

The reasons for gender differences for children with perineal fistulas, are worth speculating on, because they may have implications for an individually designed care program for both females and males with ARM. In both sexes, with perineal fistula, the upper rectum is situated below the sphincter mechanism [20] and according to the result in Paper III there were no gender differences in the frequency of sacral malformations which could explain the gender different outcome. One reason could, speculatively, be embryological since the genitals develop simultaneously with the rectum [10,12,47]. Therefore different innervations or subtypes of connective tissue in the sphincter and pelvic floor, may be related to gender. The size of the pelvis differs between females and males [1,46] already from birth, and maybe the position of the pelvic floor muscles could play a role in bowel function. Further, one could consider that the dissection of the rectum in limited PSARP in females with perineal fistulas could be too limited, because of a fear of perforating the vagina. This could lead to an incomplete rectoplasty or, as shown in Paper IV, to a distance between the rectum and the skin. Another possible reason for gender differences in perineal fistulas is that ARM was less openly discussed with the females in their families according to Paper I. Secondary to this, bowel management may fail, which in the long term could have a negative effect on the bowel control [59,135].

Other gender specific results were found in Paper III. Only the males with recto-urethral fistulas, and no female subtypes, turned out to have a less favorable outcome when concomitant sacral anomalies were present. Further, only the males in the older age group reported less constipation than those in the younger. In line with this a recent study reported that spinal cord malformation did not have any impact on bowel function among the females with vestibular fistulas but among the males [50]. This illustrates the importance of analyzing females and males separately in order to grasp outcomes that can be clinically useful.

## Bowel symptoms and gas leakage among the adolescents

Adolescents operated on for ARM reported high frequencies of fecal leakage; 67%/58% and constipation 78%/92% females/males. These are somewhat higher figures compared with reports on bowel symptoms assessed in or including similar age groups (Table 3). Two small longitudinal studies have suggested that symptoms decrease after childhood [50,67]. In contrast cross sectional comparison between Papers I and III, and between previous reports using Krickenbeck criteria (Table 3) show that bowel symptoms are more frequent in adolescent groups than in childhood groups. A reason for this may be that bowel management was not established during the 90s but later has come into

focus as an important part of the treatment in ARM. Early initiation of potty training and bowel management has resulted in a better outcome maybe because it helps to avoid a dilated rectum and fatigue of the sphincter [1,22,59]. If this theory is correct, future follow-up of adolescents will show a better outcome.

**Gas incontinence** among the adolescents influenced life in 25% of the females and 50% of the males. The in-depth interviews revealed, that gas leakage restricted them in social contexts and in intimate situations.

The reasons for gas incontinence could be the lack of normal sensivity and motor neurons in the anus and sphincter [47]. There are no previous reports on frequencies of only gas incontinence in ARM, although the Rintala scale has the advantage to include gas in the assessment of the total score of bowel symptoms [61]. The gas incontinence questionnaire used in Paper I turned out to be diffuse and difficult to analyze. Therefore it was not used in Paper II-IV, but future studies with improved questionnaires would be valuable.

Gas incontinence among ARM adults has been suggested to be a strong predicting factor for psychiatric problems [107] and our findings indicate that it is important that the doctor broaches the subject. To talk about gas incontinence could be embarrassing, and there is a lack of reliable treatment. A useful tool to approach the topic could be to use specifically prepared in advance questions on gas incontinence as suggested in clinical implications. A gas management plan could be suggested which would include bowel management for constipation, contact with a dietician, gasreducing medication (dimetylpolysiloxan) and information on the anatomy in ARM to help patients cope with the problems.

## Outcome in QoL and sexual health

The adolescent females with ARM scored lower in the total symptom specific QoL sum and the adolescent males with ARM scored higher than the controls in the mental domains. The sexual health and body attitudes among adolescents with ARM were in general similar to those of other adolescents [116,117]. Still, the adolescents with ARM struggled with issues related to ARM, such as adapting intimate situations to their fecal and gas incontinence.

Both females and males scored lower than the controls in the large bowel domain of QoL, which probably reflects their bowel symptoms. However, only the males had a postive correlation between more severe bowel symptoms and lowered total QoL. The absence of correlation for the females, could reflect a wide spread of individual results for the females, which is in line with previous literature [82,87,97,100,104,136]. It could also reflect that other factors influence the QoL more for females. The opinion on a possible correlation between bowel symptoms and QoL differs in the literature

[82,86,87,100,136]. Most studies, although gendermixed, conclude that fecal incontinence and constipation are poor predictors for QoL after childhood [82,136]. Instead the psychosocial functioning and self-efficacy seem to be the most critical factors for QoL in ARM [114,136].

Knowledge of QoL in adolescents with ARM is limited since most reports are on children or adults. Adults with ARM score lower in QoL than children with ARM [86,106,114] and especially two groups are reported to be afflicted by poorer QoL with time; adults with concomitant malformations and females [69,105]. This is in line with the outcome in Giqli for the ARM females in the present study. One could speculate whether a handicap with fecal leakage and gas incontinence is worse to live with for females than males, if it counts that coping strategies differ between the genders as shown in Paper I, or if the design of QoL questionnaires plays a role.

The gender difference in the information given to the patients about ARM was a new finding and may influence QoL. The females had got very little information about their malformation and operations; in their families they did not talk about the incontinence problems. All the males were well-informed and were used to talking about ARM in their families. A majority of the males had developed strong coping strategies such as good lies in case of leakage or smell, and they were keen to exercise hard in order to have a fit body, and to compensate for their invisible handicap. Both the information, and the coping of symptoms, can explain the males' high scoring in mental QoL despite their bowel symptoms and low QoL score in large bowel functioning. It is highly possible that a lack of information about the body, as in the case of the females, could inhibit such development of coping strategies. Good coping strategy has been shown to be followed by self-efficacy, which has been suggested to be closely correlated to good outcome regarding QoL, emotional functioning, body image and sexual functioning [97,114].

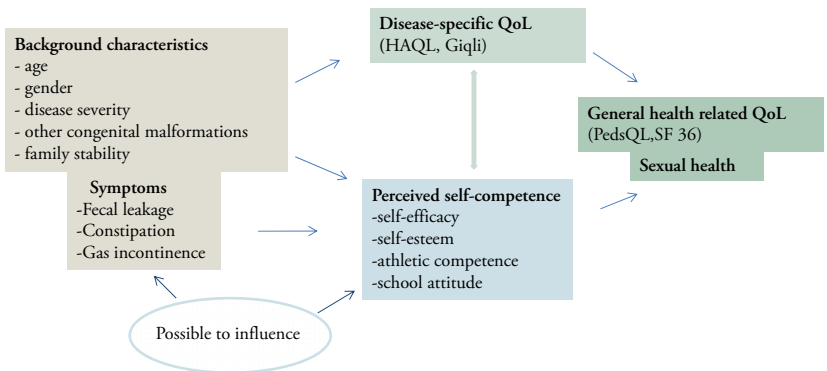



**Figure 26.** The complexity of QoL, bowel symptoms and sexual health. The picture is a synthesis of previous theories [100,114,136] with additional information according to this thesis. Possible areas of enhancement of QoL and sexual health, could be increased by better bowel control and self efficacy.

Follow-ups on sexual functioning among adolescents and adults with ARM are limited, maybe beacause the oldest patients, world wide, operated on with PSARP, just have reached adulthood and the focus has been on anatomical sequelae in the genitals and perineum [115]. However, sexual health and sexual function start before early adolescence, and do not only depend on the genitals, operation technique or bowel symptoms [9,114].

The qualitative method used to approach sexual health must be considered as a strength in Paper I. The in-depth interviews not only contributed to a greater understanding of QoL, but also added the most valuable information. The combination of qualitative and quantitative methods in assessing outcome in ARM is unique. Combinations of qualitative and quantitative studies are difficult to publish because they fall in between scientific fields and the synthesis of results could be perceived as inexact in both psychological and medical contexts.

In conclusion, with emphasis on improving QoL and sexual health among ARM adolescents, both intensified bowel management and information as well as psychological support focusing on self-efficacy, could be valuable.

## Transfer of adolescents with ARM

The particular age group 15-21 years old with ARM has not been described before, but is of interest because this is the time when transition to adulthood takes place. According to the findings, the adolescents will be in need of contact with health care sooner or later. Therefore contact information from colorectal surgeons, gynecologists, urologists and psychologists in adult healthcare, with knowledge about ARM, should be provided. If a transfer to adult health care is urgent a general meeting with the mentioned adult specialists, as well as a pediatric surgeon and the patient should be arranged.

## Appendicostomy

Appendicostomy in preschool children with ARM had an excellent outcome: 88% reached total fecal continence. Postoperative minor complications were frequent, in a total 43% had some kind of complication and subcutaneous infections were most common.

It has been recommended worldwide, without any obvious medical or psychological evidence, that only patients with good compliance and effectiveness on rectal enemas should have appendicostomy [59,63,125]. This stands in contrast to our conclusion as well as to previous studies reporting psychological implications of rectal treatments in children [110,137].

A secondary finding was that all the preschool children with appendicostomy had concomitant spinal deviations, neurogenic bladder or a syndrome. We were not aware of this correlation before the study. This group will probably be users of enemas throughout childhood since no improvement of bowel function can be expected [36,50]. These children's autonomy could be introduced earlier if the appendicostomy is in place at preschool age.

There are only a few previous studies on appendicostomies in ARM [125,126,128] and only one report on postoperative infections (0%) [125]. In the light of this, our 29% is depressing, but true. It is possible that the infections could be caused by insufficient cleaning of the conduit postoperatively, and this could be a challenge in smaller children. It may also be prone to infection because of the Chait button® but this has never been indicated previously [138]. If detected early, a subcutaneous infection is often easy to treat. Stenosis and backward leakage occurred less frequently than previous reports on older children.

**Table 12.** A summary of the available reports on appendicostomy only in ARM

| Reference | Number children | Age | No complications | Stenosis/ Stricture | Leakage | Surgical revision | Bowel obstruction | Infection |
|---|---|---|---|---|---|---|---|---|
| Kim et al 2006 | 8 | 8.5 | 0% | ? | ? | 63% | ? | ? |
| Mattix et al 2007 | 32 | 9 | ? | 50% | ? | 34% | 3% | ? |
| Rangel et al 2011 | 163 | 9.9 | 74% | 18% | 6% | 23% | 0.1% | 0% |
| Present study 2013 | 17 | 4 | 58% | 12% | 0% | 6% | 0 | 29% |

The main strength of the study is that all patients operated on with PSARP and appendicostomy since 1990 were followed up. The study design included a follow-up of the use and satisfaction conducted by non-operating doctors, so that bias of the families' possible dependency on the surgeons was avoided.

One bias could be the awareness of the inclusion in the study, and observations may influence the results. Also the positive attitude to appendicostomies at our department may be a bias, since it is difficult for nurses and doctors to conceal their belief in and positive expectations from this surgical procedure.

The few number of patients limits the possibility to generalize the results and the patients included were not randomized to the appendicostomy. It cannot be excluded that a similar good outcome would have been reached after inset of rectal enemas, and then without postoperative complications. A prospective randomized study evaluating the effectiveness of antegrade contra retrograde enemas regarding functional outcome, time consumption and with a psychological evaluation would be of great value.

## Pelvic floor in females with ARM

Paper IV is the first study to report on perineal ultrasonography in a pediatric and adolescent population. All females with ARM had at least one defect in the sphincter and there were no correlations between the muscular defects and severity of fecal incontinence. A diastasis between rectum and skin anteriorly in the anal canal was common (11/17) and has never been illustrated before.

The neo-IAS was expected to be unharmed, because of the mobilization of full thickness intestinal wall during the PSARP, but in a majority the IAS was multiple fragmented. This could be due to damage during the PSARP or because of repeated dilatation of the neo-anus. The relevance of the findings of neo-IAS is unclear, but original IAS is important for rectal sensitivity which is essential for gas continence [47]. Scarrings in IAS among ARM patients have been reported to correlate to fecal incontinence [52,54], but such correlation could not be shown in Paper IV. The findings in perineal ultrasonography of incomplete adaption of EAS are in line with previous studies, using examinations with rectal ultrasonography [52,54].

We could speculate whether defects in the IAS and EAS change over time secondary to the development of the pelvic floor and to higher hormonal levels after puberty. Paper IV covered a wide range of ages 4-21 years, but since the population examined was limited, no age related comparisons were performed.

Perineal ultrasonography is a non-invasive tool and in the future it could also be valuable for examination of awake children, and maybe with the aim to evaluate if poor results after PSARP are caused by anatomical defects that could benefit from reconstruction. It may also be useful in evaluating the sphincter in other conditions than ARM such as Hirschsprung's disease or traumatic injuries. The perineal ultrasonography has been shown to be good for evaluations of the sphincter complex, but less favorable in visualization of deeper parts of the pelvic floor [131,133]. Therefore, the status of the levator in Paper IV could be doubtful, especially since the patients under anesthesia could not squeeze. Furthermore there are no standardized dimensions for the muscles in the anal canal or pelvic floor for females <18 years of age. However, such references could be gathered with an increased use of perineal ultrasonography.

We should be aware of the fact that bowel function depends on many factors apart from muscles and nerves. There is a large individual variability in regularity of bowel function with different consistences and timing of the bowel movements. These inter-individual differences affect also people with ARM.

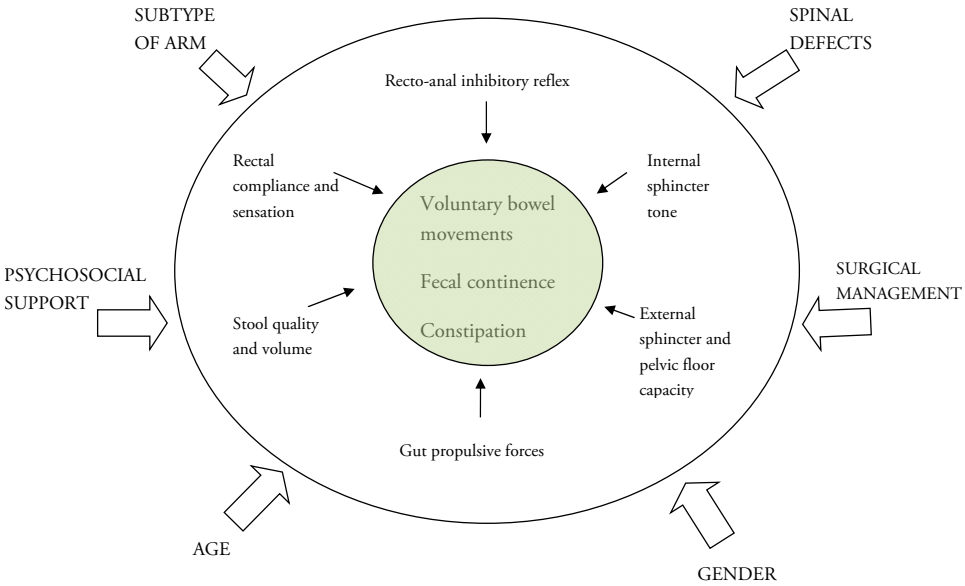



**Figure 27.** Bowel function and fecal continence are multifactorial. All the separate influencing factors can differ because of anatomical differences in the ARM subtypes, age, gender or innervations because of sacral/spinal malformations as is shown in Paper I-IV. Also the surgical management and psychosocial support are shown to have an impact [59,137].

# Summary

The impact of ARM on early phases in life is considerable for a majority of the patients. This thesis indicates different fields where improvements for patients with ARM could be established. Increased self-efficacy through information about the ARM and a psychological guidance to self-efficacy, early autonomy and awareness of gender differences can contribute to such improvements.

It is important to have knowledge about the anatomy in ARM in order to make good reconstructions and to inform the patients about their anatomy, for better coping. Also, knowledge about the anatomical outcome is important for gynecologists in their predelivery consultations.

Lastly, the patients with ARM deserve to be provided with professional care also in adolescence and adulthood by specialists with knowledge of ARM. The pediatric surgeon will always be the one with the greatest knowledge of ARM and continuing cooperation around the patients will give the best outcome also in the long term.

# Conclusions

## Paper I

Adolescents with ARM have considerably more fecal incontinence and constipation compared to their healthy peers. The QoL related to large bowel function, is low for both genders with ARM in adolescence. The males with ARM had developed coping strategies to manage embarrassing situations due to gas and fecal leakage and scored higher in the mental domains in QoL than controls. Females with ARM may lack information on their malformation and scored lower in QoL. Adolescents with ARM adapt the intimate situations to fecal and gas leakage.

## Paper II

Preschool children with ARM, with low compliance to rectal enemas, achieve good bowel control with appendicostomy. The incidence of postoperative infection after appendicostomy was high, while severe complications were infrequent.

## Paper III

Females with perineal fistula have more fecal incontinence and constipation than males with perineal fistula. Females with perineal fistula and vestibular fistula have similar physical outcome. Only constipation among males, and not fecal incontinence for females or males, was less frequent in older age groups prior to adolescence.

## Paper IV

The sphincter anatomy among females with all subtypes of ARM shows considerable defects on 4D/3D ultrasonography. The severity of bowel symptoms does not correlate significantly with the number of anatomical defects. A thorough predelivery consultation concerning a suitable delivery mode is of importance for pregnant females with ARM.

# Clinical implications

## ARM in childhood

**Equal and individual bowel management:** As a consequence of these results we have tried to implement an awareness at our department to think about both subtype and gender in the follow-up. This is in order to give equal, but still individualized, treatment and information to the families and patients.

**Equal follow-up:** All children with ARM, also those with perineal fistulas, enter a regular follow-up program with the following structure:

Before 1 year: Early potty training at 6-8 months. At 1 year: Follow-up of the introduction of early potty training, preparation for start in kindergarten, planning of bowel management. At 2 years: Follow-up of early potty training, support for bowel management, appendicostomy is mentioned. At 5 years: Preparation for school start, psychological issues are raised and independence mentioned. Any need for appendicostomy? At 10-12 years: prepubertal gynecological control, contact with psychologist offered with a focus on support for self-efficacy

**Early appendicostomy:** Among the children who need enemas and have concomitant spinal cord malformations or syndromes, appendicostomy is mentioned already at the age of 1-2 years and provided during preschool age.

## ARM in adolescence

**Consultation before adult health care:** All adolescents with ARM are invited to the Department of Pediatric Surgery before they reach 15 years of age. The aim is to secure that the patient is sufficiently informed about the malformation and the operations performed during the neonatal period, and that he/she knows enough about their present anatomy. The consultation also aims to clarify the patient's need for further contacts in adult care. A team consisting of a colorectal surgeon, gynecologist, urologist, psychologist with knowledge about ARM has been established.

**Referral:** If there is a need and wish for a referral, a meeting with the patient, adult specialists and the pediatric surgeon is arranged. Medical contacts for the future are established.

**Letter:** If the adolescent does not wish for any referral at the time, a letter is sent to the patient with information including the subtype of ARM, medical history and name of a specialist with knowledge of ARM, who could be contacted if need should arise in the future. This has been highly appreciated.

## Approach to sensitive topics

The following useful tips have been recommended by psychologists, social workers and sexologist:

**Gas incontinence:** A useful tool to approach the topic is the pre-prepared questions on gasincontinence: 1. Do you have limitations in life because of gas incontinence? 2. Would your daily life be different if you did not have gas incontinence? If there are problems, a gas management plan is suggested. This includes bowel management for constipation, contact with a dietician, gasreducing medication (dimetylpolysiloxan) and information on the anatomy to help the patients cope with the problems.

**Self-efficacy and psychologist:** The adolescents wished that they had been offered contact with a psychologist in their early adolescence. Therefore, at the routine control when the patient is 10-12 years of age, contact with a psychologist is being provided. This is in order to support improved self-efficacy and coping strategies. Contact information about a specialized psychologist who could be contacted directly when needed during adolescence is provided.

**Sexual health:** According to the adolescents' suggestions, questions on sex in ARM are being raised during medical consultations. The sex issues are approached with standardized questions: 1. Do you feel that you differ from others because of ARM? 2. Is your contact with others influenced by ARM? 3. Have you been thinking about any problems concerning sex, because you have ARM? These questions could be raised already during early adolescence, at 12-14 years of age. Whenever needed, contact with a sexologist, gynecologist or urologist could be established.

# Future perspectives

What more can be done for the patients with ARM?

The classification of ARM and the assessment of bowel symptoms according to Krickenbeck have to be maintained but also further developed. Assessing different symptoms in each ARM subtype, for each gender, becomes very complicated and there is a risk of secondary weaknesses in complex statistical analyses. An international agreement on a suitable scoring system would probably facilitate studies of ARM and thus bring a better understanding of the outcome.

The gender differences in information and coping need to be studied more thoroughly.

Gas incontinence, its impact on life and improved treatment in ARM, should be focused more, both in the clinical meeting and in reports on ARM.

To interpret the results for QoL and to relate them to previous studies, is a challenge. Only a person who is trained in this field can have a deeper understanding of the results, and in coming papers such competence should be involved to enable selection of suitable questionnaires and make a professional analysis.

Studies with non-invasive perineal ultrasonography on children with ARM would probably increase the knowledge of the anatomy and bowel/urinary function in children with ARM or other malformations involving the pelvic floor.

Psychologists with knowledge of coping and self-efficacy related to ARM should be available at centers taking care of ARM patients.

Teams of specialists in adult care, with interest and knowledge of ARM are needed. The number of adult patients with sequelae from ARM may be around 1000 in Sweden. Half of these are women of child-bearing age. It would be preferable if there was one Swedish national pelvic floor center with competence for care of adolescents and adults with ARM.

# Appendix

## Appendix 1 Questionnaire about bowel symptoms

1. Can you/your child control the bowel movements - feel the need to empty the bowel, possibility to wait to empty until there is a toilet Yes/No
2. Do you/ does your child experience fecal leakage? No/Yes seldom 1-3 times/ month/Yes sometimes 1-2 times/week or it is not a problem/ Yes often: every day or it is a social problem
3. Do you/does your child experience constipation? No/Yes, it is manageable with diet/Yes, it is manageable with medications/Yes, it is not manageable with either diet or medications

## Appendix 2 Questionnaire about gas incontinence

1. Do you experience ability to control the farts? Yes/ No
2. How much do the farts trouble you? Never / 1-2 times/week / every day, but it is not a social problem/ constantly, it is a social problem
3. How much do the farts restrict your daily activities?
   Never/ sometimes; every month/ often; every week/ always; every day

# Appendix 3 Gastro intestinal quality of life (Giqli)

1. How often during the past 2 weeks have you had pain in the abdomen? All of the time/ Most of the time/ Some of the time/A little of the time/Never
2. How often during the past 2 weeks have you had a feeling of fullness in the upper abdomen? All of the time/Most of the time/ Some of the time/A little of the time/Never
3. How often during the past 2 weeks have you had sensation of too much gas in the abdomen? All of the time/Most of the time/ Some of the time/A little of the time/Never
4. How often during the past 2 weeks have you been troubled by excessive passage of gas through the anus? All of the time/Most of the time/ Some of the time/A little of the time/Never
5. How often during the past 2 weeks have you been troubled by strong burping or belching? All of the time/Most of the time/ Some of the time/A little of the time/Never
6. How often during the past 2 weeks have you been troubled by noises from the abdomen? All of the time/Most of the time/ Some of the time/A little of the time/Never
7. How often during the past 2 weeks have you been troubled by frequent bowel movements? All of the time/Most of the time/ Some of the time/A little of the time/Never
8. How often during the past 2 weeks have you found eating being a pleasure? All of the time/ Most of the time/ Some of the time/A little of the time/Never
9. Because of your illness, to what extent have you restricted the kinds of the food you eat? Very much/Much/Somewhat/A little/Not at all
10. During the past 2 weeks how well have you been able to cope with everyday stresses? All of the time/Most of the time/ Some of the time/A little of the time/Never
11. How often during the 2 past weeks have you been sad about being ill? All of the time/Most of the time/ Some of the time/A little of the time/Never
12. How often during the 2 past weeks have you been nervous or anxious about being ill? All of the time/Most of the time/ Some of the time/A little of the time/Never
13. How often during the 2 past weeks have you been happy with life in general? All of the time/Most of the time/ Some of the time/A little of the time/Never
14. How often during the past 2 weeks have you been frustrated about your illness? All of the time/Most of the time/ Some of the time/A little of the time/Never
15. How often during the past 2 weeks have you been tired or fatigued? All of the time/Most of the time/ Some of the time/A little of the time/Never
16. How often during the past 2 weeks have you felt unwell? All of the time/Most of the time/ Some of the time/A little of the time/Never
17. Over the past week, have you woken up in the night? Every night/ 5-6 nights/ 3-4 nights/ 1-2 nights/ never
18. Since becoming ill, have you been troubled by changes in your appearance? Much/ Moderate/ Some/ A little/ None
19. Because of your illness, how much physical strength have you lost? Much/ Moderate/ Some/ A little/ None

20. Because of your illness, to what extent have you lost your endurance?A great deal/ A moderate amount/ Somewhat/ A little bit/ Not at all
21. Because of your illness to what extent do you feel unfit? Extremely unfit/ Moderately unfit/ Somewhat unfit/A little unfit/ Fit
22. During the past 2 weeks how often have yu been able to complete your normal daily activities? All of the time/Most of the time/ Some of the time/A little of the time/Never
23. During the past 2 weeks how often have you been able to take part in your usual patterns of leisure or recreational activities? All of the time/Most of the time/ Some of the time/A little of the time/Never
24. During the past two weeks how much have you been troubled by the medical treatment of your illness? Very much/ Much/ Somewhat/A little/ Not at all
25. To what extent have your personal relations with people close to you (family or friend) worsened because of your illness? Very much/ Much/ Somewhat/A little/ Not at all
26. To what extent has your sexual life been impaired or harmed because of your illness? Very much/ Much/ Somewhat/A little/ Not at all
27. How often during the past 2 weeks have you been troubled by fluid or food comin up into your mouth (regurgitation)? All of the time/Most of the time/ Some of the time/A little of the time/Never
28. How often during the past 2 weeks have you felt uncomfortable because slow speed of eating? All of the time/Most of the time/ Some of the time/A little of the time/Never
29. How often during the past 2 weeks have you had trouble with swallowing your food? All of the time/Most of the time/ Some of the time/A little of the time/Never
30. How often during the past 2 weeks have you been troubled by urgent bowel movements? All of the time/Most of the time/ Some of the time/A little of the time/Never
31. How often during the past 2 weeks have you been troubled by diarrhoea? All of the time/ Most of the time/ Some of the time/A little of the time/Never
32. How often during the past 2 weeks have you been troubled by constipation? All of the time/Most of the time/ Some of the time/A little of the time/Never
33. How often during the past 2 weeks have you been troubled by nausea? All of the time/ Most of the time/ Some of the time/A little of the time/Never
34. How often during the past 2 weeks have you been troubled by blood in the stool? All of the time/Most of the time/ Some of the time/A little of the time/Never
35. How often during the past 2 weeks have you been troubled by heartburn? All of the time/ Most of the time/ Some of the time/A little of the time/Never
36. How often during the past 2 weeks have you been troubled by uncontrolled stools? All of the time/Most of the time/ Some of the time/A little of the time/Never

# Appendix 4 SF-36

Instructions for completing the questionnaire: Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

1. In general, would you say your health is: □□Excellent □□Very good □□Good □□Fair □□Poor

2. Compared to one year ago, how would you rate your health in general now? □□Much better now than a year ago □□Somewhat better now than a year ago □□About the same as one year ago □□Somewhat worse now than one year ago □□Much worse now than one year ago

3. The following items are about activities you might do during a typical day. Does your health now limit you in these

activities? If so, how much?

a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf? □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

c. Lifting or carrying groceries. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

d. Climbing several flights of stairs. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

e. Climbing one flight of stairs. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

f. Bending, kneeling or stooping. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

g. Walking more than one mile. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

h. Walking several blocks. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

i. Walking one block. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

j. Bathing or dressing yourself. □□Yes, limited a lot. □□Yes, limited a little. □□No, not limited at all.

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

a. Cut down the amount of time you spent on work or other activities? □Yes □No

b. Accomplished less than you would like? □Yes □No

c. Were limited in the kind of work or other activities?□□Yes □No

d. Had difficulty performing the work or other activities? (for example, it took extra time) □Yes □No

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

a. Cut down the amount of time you spent on work or other activities? □Yes □No

b. Accomplished less than you would like? □Yes □No

c. Did not do work or other activities as carefully as usual? □Yes □No

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? □□Not at all □□Slightly □□Moderately □□Quite a bit □□Extremely

7. How much bodily pain have you had during the past 4 weeks? □□Not at all □□Slightly □□Moderately □□Quite a bit □□Extremely

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? □□Not at all □□Slightly □□Moderately □□Quite a bit □□Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks.

a. did you feel full of pep? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

b. have you been a very nervous person? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

c. have you felt so down in the dumps nothing could cheer you up?□□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

d. have you felt calm and peaceful? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

e. did you have a lot of energy? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

f. have you felt downhearted and blue? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

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g. did you feel worn out? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

h. have you been a happy person? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

i. did you feel tired? □□All of the time □□Most of the time □□A good bit of the time □□Some of the time □□A little of the time □□None of the time

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

□□All of the time □□Most of the time □□Some of the time □□A little of the time □□None of the time

11. How TRUE or FALSE is each of the following statements for you?

a. I seem to get sick a little easier than other people □□Definitely true □□Mostly true □□Don't know □□Mostly false □□Definitely false

b. I am as healthy as anybody I know □□Definitely true □□Mostly true □□Don't know □□Mostly false □□Definitely false

c. I expect my health to get worse □□Definitely true □□Mostly true □□Don't know □□Mostly false □□Definitely false

d. My health is excellent □□Definitely true □□Mostly true □□Don't know □□Mostly false □□Definitely false

# Appendix 5 Questionnaire about the use and satisfaction with appendicostomy

1. What is the weight of your child?_____
2. Does your child use the appendicostomy? Yes/No
3. If you do not use the appendicostomy:
   a. Why did you stop?
   b. When did you stop or how old was your child when stop using it?
4. If you use the appendicostomy:
5. How often do you use the appendicostomy?
   >1 times a day/once daily/ every second day/3 times/week/ once week/ monthly
6. How do you use the appendicostomy?
   Chait button/ Intermittent catheterizing/ Other
7. What liquid do you use in the appendicostomy?
   Saline/Klyx/Oil Other_____
   A combination:_____.
8. What volumes do you use?_____
   —
9. Are you satisfied with the appendicostomy? Yes/ Moderate/No
   If you are not totally satisfied, what is the problem?_____
10. Would you recommend appendicostomy to another in the same situation as your child? Yes/No
    Comment_____

# Acknowledgements

My grateful thanks go to

All children and adolescents born with anorectal malformations, my patients. You and your families fill me with admiration.

Einar Arnbjörnsson, my tutor. You convert unsolvable problems into exciting challenges: how is that possible? From you I have learnt that thinking "this is easy" really makes thing easier. You strengthen my self-efficacy in the operating room as well in the process of writing articles. Thank you so much!

Christina Clementson Kockum, my second tutor and head of the Department of Pediatric Surgery in Lund. Thank you for being so supportive and wise when going through the papers. You are a brilliant mediator and I am greatful for your guidance into self-development during the process of writing this thesis.

Gerhard Malmfors, my former head of the Department, who directly believed in me and offered me employment. Thank you for encouraging me to become a pediatric colorectal surgeon and introducing me to the area of anorectal malformations.

Associate Professor Kristin Björnland and Professor Ragnhild Emblem, my Norwegian colleagues and co-authors. We struggled together and finally reached the goal! I am looking forward to continuing with our next article.

Camilla Ivarsson, Despina Katsianikou, Sven-Axel Månsson and Sara Johnsdotter, sexologists and co-authors from Malmö University. The cooperation with you revealed to me that qualitative methods add important information to quantitative results. Thanks to you the study became possible!

Ann-Kristin Örnö, gynecologist and co-author. Thank you for sharing your knowledge about the anatomy of the pelvic floor. This is a good start for future cooperative projects.

Gillian Sjödahl, the excellent and quick proof reader. Thank you so much for every single word.

Fredrik Nilsson and Håkan Lövkvist, the statisticians. You taught me all, and I learnt some. Thank you for all the time you spent on my results.

Carl-Magnus Kullendorff, my former co-worker. Thank you for your constructive criticism of my initial papers and for your excellent teaching of surgery.

Anna, Gunnar, Lars, Magnus and Tobbe, my fantastic colleagues in Pediatric Surgery since I started. Our confidence in each other is unique and invaluable. Every day at work together with you brings with it a gift of laughs and support.

Hans, Kristine, Christina G, Ann, Mette, Martin and Erik, my newest colleagues. You are all such good and reliable doctors, and I am looking forward to working together with you also in the future. The introduction is written with you in mind!

Eva F, Gun, Billis, Åsa and Sandra, the secretaries who have helped me by bringing trolleys loaded with patient charts to my room, searching in databases, booking journeys and venues, arranging suitable operation times and not least: maintaining friendly contact with the patients and arranging this dissertation.

Birgitta, Marianne, Anna S, Helene och Malin, the nurses at the outpatient clinic. Thank you for taking physical and psychological care of the patients with anorectal malformations and for assisting me so well in the counselings.

The staff at "65:an", the ward of Pediatric Surgery in Lund. Pediatric surgery is only feasible within a team - and you are the most well-skilled team.

The staff at the operation theater, with special thanks to the surgery nurses who have been helpful, interested and patient while my skills in colorectal surgery have improved.

Maggi, Anna and Lotta and all my other friends. Thank you for giving me energy and for being fantastic listeners and supporters.

Maria Bjurberg, my friend, medical colleague and wonderful godmother of Filippa. Your attitude to work and life in general inspires me and has made me complete this dissertation.

Frida och Anne, my cousin and aunt. Thank you for the music!

Kjell, my dear kjäreste. Since we met in the heat in the bar life has become so easy and happy. Thank you for your loving respect and for the beautiful time we have together.

My mother Monica who has always believed in me and always helps me whenever I need it. Thank you so much. You have constantly advised me not to take life so seriously. Maybe now, when the dissertation is finished…..

Filippa, my daughter and dearest love. You are the best daughter I could ever have had. Your fantasy and dreams open my mind and you make me laugh and enjoy. And I am looking forward to reading your own dissertation, the one you told me of, about birds, and your article about blackbirds.

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# Papers I-IV

# Paper I

DOI 10.1515/ijamh-2012-0111 — Int J Adolesc Med Health 2013; aop

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# Adolescents with anorectal malformation: physical outcome, sexual health and quality of life

**Abstract**

**Background:** The necessity of referring adolescents with anorectal malformation (ARM) from pediatric units to adult care is unclear. The issue requires knowledge about the health of the adolescent.
**Objective:** To examine the physical outcome, sexual health and quality of life (QoL) in adolescents with ARM.
**Methods:** At medical counseling, 24 adolescents with ARM, 15–21 years of age, answered questionnaires about physical outcome according to the Krickenbeck follow-up and QoL according to SF 36 and gastrointestinal quality of life (Giqli). Matched control groups were used; 15 adolescents participated in deep interviews about sexual health and body imaging.
**Results:** Fecal soiling, constipation and gas incontinence were much higher for ARM patients compared with controls ($p<0.05$). QoL regarding large bowel function was lower for both genders compared with controls ($p<0.05$). Females scored lower in physically related QoL ($p<0.05$). Social and sexual adaption to the symptoms was obvious in the deep interviews.
**Conclusion:** Adolescents with ARM have considerable intestinal symptoms, which influence QoL and require adaption in intimate situations. A referral to adult care seems to be important, and continuous cooperation between the pediatric surgeon and adult care is suggested.

**Keywords:** adolescents; anorectal malformation; constipation; fecal incontinence; posterior sagittal anorectal plasty; quality of life; sexual health.

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## Introduction

During the period of late adolescence, ages 15–21 years (1), patients with anorectal malformation (ARM) usually have to leave pediatric surgical units. There is a lack of reports on whether adolescents with ARM need special care and if a general transfer to adult care is necessary.

Children born with ARM undergo reconstructive surgery of the anus with posterior sagittal anorectoplasty (PSARP) within their first days or months of life, depending on the subtype of ARM. A temporary stoma may be needed. During the 1980s, the PSARP was implemented worldwide (2). This was followed by a better outcome for the patients with ARM (3). However, frequent treatment sessions at hospitals during childhood are needed because of constipation in 21%–67% and soiling in 10%–73% (4–7). Early treatment has been shown to diminish the risk of developing pseudo-incontinence later (6).

The few long-term postoperative follow-ups after PSARP during adolescence and adulthood conclude that, beyond childhood, half of the PSARP-operated patients still experienced symptoms such as incontinence and severe constipation (3, 7, 8), but the adolescents' symptomatology has not been described.

Quality of life (QoL), social life and psychological morbidity among children with ARM is reported to be affected by the degree of the symptoms (9, 10), and adults with ARM score low in symptom-specific QoL (11, 12). However, the QoL among adolescents with ARM could be important to map separately.

Sexual identity will form during adolescence. Patients with ARM have a history of both malformation of and operations on the pelvic floor with remaining scars and often sustained fecal and urinary incontinence. Effects on the psychological part of sexual health for adults with ARM have been indicated in the literature (13), and physical impairment is suggested to lower the sexual ability for adult women and men with ARM (14). This could also be true for adolescents.

When adolescents with ARM grow up, they may need to contact adult healthcare where ARM is a fairly uncommon diagnosis. Increased knowledge about the physical, psychological and sexual health of adolescents with ARM

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would probably help patients, physicians and psychologists in the transfer from pediatric to adult care.

The aim of the study was to examine the physical, functional and psychological outcomes for adolescents with ARM operated on with PSARP.

# Methods

## Patients

The study included all adolescents born with ARM and operated on as neonates with PSARP during 1990–1995 at our Department of Pediatric Surgery, which is a tertiary center covering an area with 1.8 million inhabitants.

Forty-six patients were included. After exclusion of those who died, emigrated, had severe mental syndromes or malignancy, the study group consisted of 27 adolescents. These were invited to a medical examination and given the option to participate in the study.

Twelve females, median age 18.0 (15–21) years, and 12 males, median age 17.5 (15–21) years, all with ARM, agreed to answer the questionnaires about their symptoms and QoL. The answers were gathered at clinical counseling sessions (21) and over the telephone (3).

Of the participants, eight females and seven males agreed to participate in interviews about their sexual health and body imaging (Figure 1). Reasons given for not participating in the interviews were: unable to communicate in the interviews because of autism (1 female and 1 male); subject too sensitive (2 females and 3 males); and failed to turn up for the interview (1 female and 1 male).

## Controls

### Control group

An age- and gender-matched control group of 51 healthy adolescents, 26 girls aged 17.7 (15–21) years and 25 boys aged 17.5 (15–21) years, was recruited from two nearby primary schools, three different high schools and the university. The exclusion criterion for the controls was a history of any operation on the anus or rectum.

### Reference population

See method for SF 36.

## Methodology

The patients were invited to a medical check-up at the Department of Pediatric Surgery, together with separate invitations to participate in the studies based on questionnaires and interviews. All the patients were examined by the same investigator (PS) and not by the operating surgeon. The interviews about sexuality were conducted by two sexologists. The females were interviewed by one sexologist and the males by the other.

The questionnaires were delivered to the controls with information about the aim of the study. The controls sealed their answers in envelopes themselves, thus ensuring anonymity.

The following instruments were used.

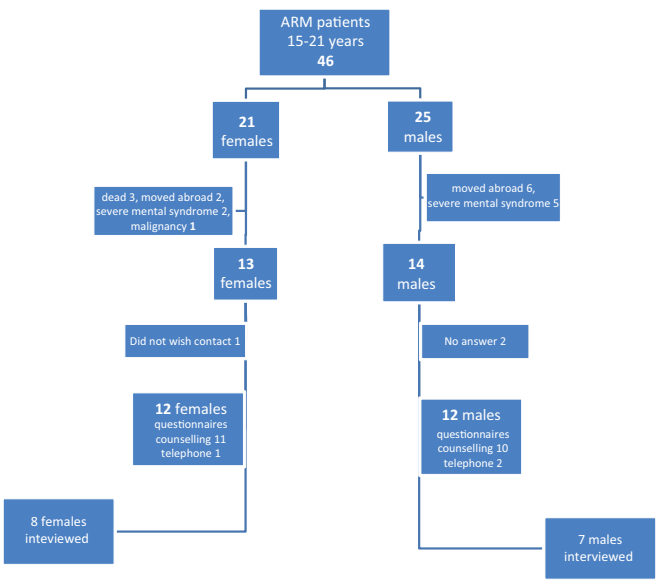


**Figure 1** Consort table of the material: adolescents with anorectal malformation (ARM) in the studies.

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### Krickenbeck classification and postoperative scale

The Krickenbeck classification and postoperative scale is internationally recommended for symptoms in follow-ups of ARM patients (15). The Krickenbeck postoperative scale is descriptive, and, to compare the patients with the controls, it was converted into a binary score with 0–7 points (7 points being the worst) (Table 1).

### Gas incontinence scale

During the medical check-up, the patients were asked whether they were troubled by gas incontinence. The answers were graded as for the Krickenbeck postoperative results. If they had gas incontinence (no=0, yes=1) and if so, how big a problem it was [no=0, small (1–2 times/week)=1, moderate (every day, no social problem)=2; big (constantly, social problem)=3] and how much it restricted their activities (never=0; sometimes, every month=1; often, every week=2; always, every day=3). The score for gas incontinence was 0–7 points.

### Giqli

The Gastro Intestinal Quality of Life Index (Giqli) questionnaire was developed in 1995 and is a symptom-oriented instrument for measuring QoL in gastrointestinal disorders (16). It consists of 36 questions scored from 0 (worst) to 4 (best) with a total maximum of 144. A score under 105 is usually measured in individuals with clearly symptomatic situations. Five dimensions of QoL can be analyzed: symptoms (19 items); associated physical disease (7 items); emotions (5 items); social integration (4 items); and effects of treatment (1 item). The Giqli questionnaire is validated in the country where this study was conducted (17) and is mainly used from 18 years and in adults but can be used from 15 years. It has been used in QoL reports for colorectal diseases (18), Hirschsprung's disease (19) and as a tool in the follow-up of adults treated for malformations other than ARM (20, 21).

### SF-36

The Short-Form Questionnaire (SF-36) is a generic test measuring health-related general QoL and has been validated in many different countries. The age- and gender-djusted reference population (normative) for the population in the country of origin of the study was obtained from 315 healthy adolescents (137 females and 168 males) collected by the Health-Related Quality of Life (HRQL) group (22). The SF-36 includes eight domains of functioning: physical; role limitation because of physical functioning; bodily pain; general health; vitality; social functioning; emotional role; and mental health. Scores are summed for each domain and then transformed into scores from 0 (worst) to 100 (best). Two higher order summary scores have been shown to well represent the subscales Physical Component Summary

**Table 1** The international classification of anorectal malformations (upper panel) with the distribution of subtypes in this report.

| International classification of anorectal malformations according to Krickenbeck | Females questionnaire study (n=12) interview study (n=8) n/n | Males questionnaire study (n=12) interview study (n=7) n/n |
|---|---|---|
| Perineal fistulas females | 7/5 | |
| Rectovestibular fistula | 4/2 | |
| Rectal atresia females | 0/0 | |
| Rectovaginal fistula | 0/0 | |
| Cloaca | 1/1 | |
| Perineal fistula males | | 6/4 |
| Recto urethral fistula (recto bulbar and prostatic) | | 5/2 |
| Rectovesicular fistula | | 1/1 |
| None fistula males | | 0/0 |
| Rectal atresia males | | 0/0 |
| **Krickenbeck postoperative results for anorectal malformation** | **Answer** | **Score** |
| 1. Voluntary bowel movements<br>Feeling of urge, capacity to verbalize, hold the bowel movements | Yes/No | 0/1 |
| 2. Soiling | No | 0 |
| Grade 1 | Occasionally (1–2 times /week) | 1 |
| Grade 2 | Every day, no social problem | 2 |
| Grade 3 | Constant, social problem | 3 |
| 3. Constipation | No | 0 |
| Grade 1 | Manageable by diet | 1 |
| Grade 2 | Requires laxatives | 2 |
| Grade 3 | Resistant to diet and laxatives | 3 |

The lower panel shows the Krickenbeck grading of postoperative results with the assigned arbitrary score points we used for the correlation analysis.

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(PCS) and Mental Component Summary (MCS) (23). SF-36 has been used for adolescents (24), adults born with Hirschsprung's disease (19), colorectal diseases (18) and ARM (25).

#### Interviews on sexual health and body imaging

Semi-structured deep interviews were performed by two sexologists participating in a Master's program in sexology. The interviews focused on the influence of ARM on body imaging and sexuality. Each interview, limited to 90 min, was recorded and then transcribed.

### Statistical analysis

As there were relatively few patients, and it could be foreseen that the data would be skewed, non-parametric statistics were used. These statistics included the Mann-Whitney exact test, the Kruskal-Wallis with post hoc test and Spearman's rank correlation test.

Correlation analysis was performed for the ARM patients, correlating the Krickenbeck symptom score (0–7) and Giqli and subgroups PSC and MCS in SF36, respectively. A p-value <0.05 was considered significant.

### Ethical considerations

This study was performed in according to the Declaration of Helsinki. The adolescents were informed that medical counseling would be based upon their individual needs for medical care planning for adulthood, apart from the studies.

The protocol was designed to meet the legislative documentation required in the country of origin. The regional research ethics committee approved the study (registration number 2010/49). The data are presented in such a way that it is impossible to identify any single patient. Approval for publishing was signed by both patients and controls.

## Results

### Krickenbeck classification

The distribution of the different subtypes of ARM is shown in Table 1. The distribution of the ARM subtypes was similar for the group who answered the questionnaires and those who were interviewed.

#### Krickenbeck postoperative symptoms

Krickenbeck postoperative data for females and males are presented separately in Figure 2A and B, respectively. The Krickenbeck score for female participants was median 3.0 (0–6) and 1.5 (0–7) for male participants. Voluntary control of bowel movements was reported by 75% of females and 33% of males. Soiling was reported by 67% of both females and males, and constipation was experienced to any degree by 92% of females and 67% of males. Female controls reported no symptoms at all, and male controls 12% (3/25) reported constipation; the remainder were symptom-free.

The total number of symptoms was greater among the ARM patients for both females and males ($p<0.0001$, Wilcoxon Mann-Whitney exact test), and for all the subgroups of ARM when compared separately with the controls ($p<0.0001$, Kruskal-Wallis with post hoc test). When comparing the total symptom score between perineal fistula *versus* the rest of the subtypes of ARM, no difference was found for the females ($p=0.942$) nor for the males ($p=0.3190$) (Kruskal-Wallis with post hoc test).

#### Gas incontinence

Symptoms of flatulence were experienced by both patients and controls. Among the females. Three of 12 (25%) experienced frequent gas incontinence that restricted their activities, whereas six of 12 (50%) reported no problems at all with gas incontinence. For the females, no difference in gas incontinence was found compared with the controls ($p=0.240$, Wilcoxon Mann-Whitney exact test) or between the ARM subgroups ($p=0.089$, Kruskal-Wallis with post hoc test). However, a significantly higher gas incontinence with subsequent restrictions in daily life was reported by the male ARM patients compared with the controls, and this was highest among those with recto-urethral fistula ($p=0.005$, Wilcoxon Mann-Whitney exact test). Ten males (83%) with ARM reported a large number of symptoms; 50% were unable to hold the flatus and were restricted in their activities. Those with no perineal fistulas scored higher than those with perineal fistulas ($p=0.017$, Kruskal-Wallis with post hoc test)

### Giqli

Female participants with ARM reported a general lower QoL in Giqli compared with the controls, but there was a wide spread in the results (Figure 3). The females with ARM also scored significantly lower than the controls in three of the Giqli subscales: "large bowel function", "upper GI function" and "meteorism" (Table 2).

No differences in QoL were found between the subgroups of ARM ($p>0.05$) but between those with perineal fistulas/controls ($p=0.024$) and those with vestibular fistulas/controls ($p=0.019$) (Kruskal-Wallis post hoc test).

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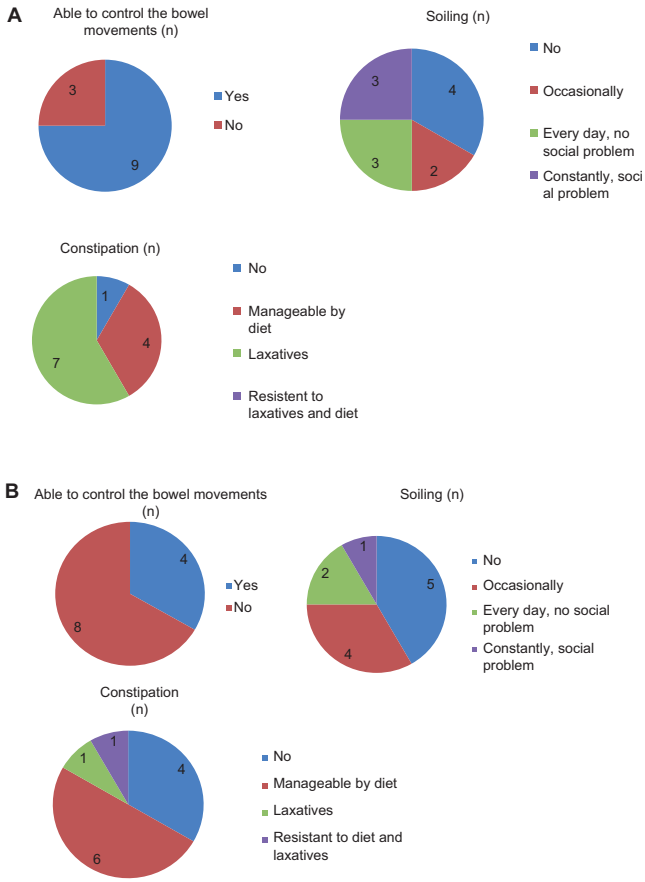


**Figure 2** (A) Descriptive data of the postoperative symptoms according to the international classification of Krickenbeck; 12 females with anorectal malformation. n=number. (B) Descriptive data of postoperative symptoms according to the international classification of Krickenbeck; 12 males with anorectal malformation. n=number.

Males with ARM had no statistically significant differences in QoL according to Giqli, nor in comparison with the controls or between the ARM subgroups ($p>0.05$) (Kruskal-Wallis with post hoc test). Only in the Giqli subscale "large bowel function" did males with ARM score lower than the controls (Table 2). Three females and no males had a score under 105, though four males scored 105–110.

## SF-36

Summarized SF-36 scores showed no differences between the females or males with ARM and the normative reference population, respectively. The females scored lower in the summarizing PCS than the controls (Table 3).

The males with ARM scored higher than both the reference population and controls in social functioning. Compared with the controls, the males scored lower in physical functioning but higher in all mental items and in the summarizing MCS (Table 3).

## Analysis of symptoms correlated with QoL

The only significant correlation between higher degrees of symptoms and lower QoL was found in the Krickenbeck score for males and Giqli measures (Table 4). The spread

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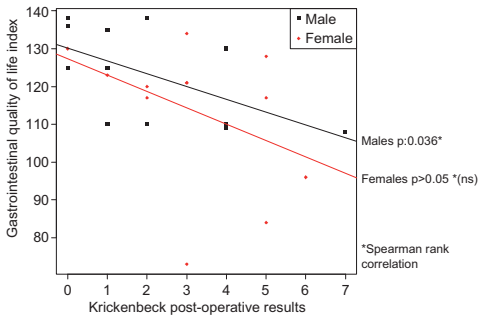


**Figure 3** The association between gastrointestinal quality of life (Giqli) and symptoms according to Krickenbeck is shown in lines. A low Giqli equals a low quality of life, and a high Krickenbeck score equals more symptoms. The Spearman correlation was significantly different from zero for boys (r=−0.62, p=0.036) but not for girls (r=−0.42, p=0.17).

of the Krickenbeck postoperative score correlated with the Giqli for each individual is shown in Figure 3.

## Interviews regarding sexual health

### Females

One of the eight females had not received any information from her parents about her malformation until she was invited to take part in the study. Six of the females were given incomplete information by their parents, who talked generally about the malformation without using the word anus and instead talked about problems with intestines and constipation. Only one female said that she could talk frankly about the ARM in her family with her mother. All females had the feeling that there was something different about them, but in some contexts they felt they were no different from their peers. They all remembered that they had been treated with laxatives and bowel management during childhood because of intestinal problems; none of them experienced psychological effects from these treatments.

Four females had sexual experience with penetrating intercourse. None of these, nor the others, had abstained from intercourse because of scars, pain or leakages. Narrowness of the vagina or genital pain were not mentioned by any female.

Because of their body images, which contained elements of embarrassment about their anatomy and abdominal scars, they used different strategies. One girl with a perineal fistula said that she was always drunk when she had sex so as to avoid embarrassment about her weight and gas leakage. Changing position during intercourse was another strategy used by some females to avoid gas leakage. Two females had sex only in the dark so that no scars could be seen. Two females abstained from anal sex because of fear of harming the anus. Sexuality, body imaging and ARM were not spontaneously associated by any of the eight females. Scars on the abdominal wall, genitals and on other parts of the body from reconstruction

**Table 2** Gastrointestinal quality of life (Gigli) subscales for adolescent femalesand males with anorectal malformation (ARM) compared to matched controls.

| Subscales GIQLI | Median (range) | | p-Value[a] |
|---|---|---|---|
| | ARM females (n=12) | Control females (n=26) | |
| Physical role | 40.0 (17–44) | 43.0 (30–44) | 0.178 |
| Large bowel function | 21.0 (9–22) | 22.0 (18–24) | 0.013 |
| Emotional role | 24.5 (9–30) | 26.0 (19–30) | 0.212 |
| Upper GI function | 26.0 (12–31) | 30.0 (22–32) | 0.004 |
| Meteroism | 7.5 (3–11) | 10.0 (4–11) | 0.015 |
| Total | 120.5 (73–134) | 131.5 (115–138) | 0.004 |
| **Subscales GIQLI** | **Median (range)** | | **p-Value[a]** |
| | **ARM males (n=12)** | **Control group (n=26)** | |
| Physical role | 41.5 (32–44) | 43 (37–44) | 0.138 |
| Large bowel function | 20 (10–24) | 23 (17–24) | 0.029 |
| Emotional role | 27 (20–30) | 27 (17–30) | 0.534 |
| Upper GI function | 30 (21–32) | 29 (27–31) | 0.811 |
| Meteroism | 9 (4–12) | 10 (5–12) | 0.378 |
| Total | 125 (108–132) | 131 (109–142) | 0.217 |

[a]Wilcoxon Mann-Whitney exact test.

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**Table 3** SF-36 mean scores for adolescent females and males with anorectal malformation (ARM) compared to controls and a reference population.

| SF-36 scales | ARM-females | Mean | | p-Value[a] | |
|---|---|---|---|---|---|
| | Mean (range) | Controls | References | Patient control | Patient norm |
| Physical functioning | 95.8 (92–99) | 95.8 | 93.9 | 0.596 | 0.757 |
| Role-physical | 87.5 (74–100) | 93.3 | 88.7 | 0.200 | 0.513 |
| Bodily Pain | 77.5 (65–90) | 79.2 | 77.0 | 0.798 | 0.912 |
| General health | 74.7 (61–88) | 78.5 | 80.3 | 0.161 | 0.300 |
| SUM Physical health (PSC) | 53.4 (51–56) | 56.0 | 52.7 | 0.046 | 0.740 |
| Vitality | 56.7 (42–71) | 51.1 | 66.7 | 0.693 | 0.074 |
| Social functioning | 90.7 (82–99) | 85.8 | 91.1 | 0.552 | 0.732 |
| Role emotional | 75.0 (49–100) | 57.7 | 87.6 | 0.296 | 0.380 |
| Mental health | 75.0 (63–86) | 74.3 | 79.3 | 0.937 | 0.288 |
| SUM Mental health (MSC) | 44.5 (37–51) | 40.1 | 48.8 | 0.323 | 0.144 |
| **SF-36 scales** | **ARM-males** | **Mean** | | **p-Value[a]** | |
| | Mean (range) | Controls | References | Patient control | Patient norm |
| Physical functioning | 97.9 (96–100) | 99.6 | 93.5 | 0.048 | 0.872 |
| Role-physical | 95.8 (90–102) | 97.0 | 94.5 | 0.701 | 0.984 |
| Bodily Pain | 90.9 (81–101) | 85.6 | 85.0 | 0.319 | 0.349 |
| General health | 84.3 (79–91) | 76.2 | 83.5 | 0.102 | 0.592 |
| SUM Physical health (PSC) | 54.8 (53–57) | 55.7 | 53.7 | 0.592 | 0.758 |
| Vitality | 70.4 (58–82) | 56.2 | 75.3 | 0.017 | 0.349 |
| Social functioning | 100.0 (max) | 93.6 | 92.4 | 0.030 | 0.034 |
| Role emotional | 97.2 (91–103) | 82.7 | 90.7 | 0.073 | 0.333 |
| Mental health | 87.3 (82–92) | 77.6 | 84.0 | 0.012 | 0.818 |
| SUM Mental health (MSC) | 52.6 (50–55) | 45.5 | 51.0 | 0.001 | 0.849 |

[a]Mann-Whitney test $p<0.05$=significant.

**Table 4** The table shows the statistical correlation between higher degree of symptoms according to the Krickenbeck scale correlated to lower scores in quality of life (QoL) in Giqli and subscales physical component summary (PCS) and mental component summary (MCS) in SF 36.

| | Correlation to Krickenbeck scale |
|---|---|
| Females | |
| Giqli | 0.175 |
| SF36 PCS | 0.786 |
| SF36 MCS | 0.081 |
| Males | |
| Giqli | 0.036[a] |
| SF36 PCS | 0.081 |
| SF36 MCS | 0.670 |

[a]$p<0.05$ Spearman rank correlation.

operations of other malformations influenced occasions of intimacy. None of the females wished to have contact with a psychologist, but they all thought it would be a good idea if this was offered at the medical consultation. All females wished that the pediatric surgeon raised these topics during medical consultation, as they would like to talk about it but were too embarrassed to ask themselves.

In summary, the female adolescents with ARM themselves thought they had the same attitude to sexuality and their bodies as their peers. None said they were in need of a psychologist. All requested that the doctor should mention sexual issues related to ARM.

### Males

All males had been informed by their parents about their malformation and its consequences. They were all aware that the rectal leakage could be stigmatizing, both in sexual intercourse and in other activities in life. Physical training was used partly as a coping strategy by six of the patients. All defined themselves as heterosexual. Four of the males had debuted with sexual intercourse, and the others had had other types of sexual experience such as masturbation. One had problems with impotence, and one was very concerned about the size of his penis.

Six out of the seven males thought that their body and sexuality in some way was affected by the ARM. The reasons given were mainly that the leakage of gas forced them to be controlled and that the need to empty

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the intestine before or during sex diminished the good feeling. The need for lies was mentioned by one as limiting as well as the lowered self-confidence following leakages. All of them would have appreciated an offer to meet with a psychologist earlier in their adolescence, and they thought that every patient with ARM should be offered such contact. Six of the males wished that the surgeon would mention possible sexual problems due to ARM at the medical consultation.

In summary, the male adolescents were considered to be concerned about their sexuality and bodies. They differed from the female adolescents with ARM in that they were more aware of their malformations and had more active coping mechanisms.

## Discussion

Our results show that adolescents with ARM have much greater loss of control of bowel movements, soiling and constipation compared with adolescents without ARM. Gas incontinence was of special concern, especially for the males. Symptom-specific QoL was negatively influenced for both females and males regarding large bowel function. Sexual health and body image were not identified as problems by the adolescents themselves, but they had to manage social and intimate situations due to fecal and gas leakages. The adolescents in general wished that the pediatric surgeon would raise the issue of ARM related to sexuality during the medical counseling.

The period of adolescence for these patients is of special interest, providing a background to their preparation for good physical, mental and sexual health in adulthood. To our knowledge, this is one of the first reports focusing only on adolescents born with ARM and operated on with PSARP. Thus, it is not easy to make comparisons with the same age group in earlier studies.

The response rate in the study was 89%, which reduces the selection bias, despite the few patients participating. The reasons why adolescents could not or chose not to participate in the interviews about sexuality were such that there is no cause to suspect that these had answered differently. The deep interviews contributed to a greater understanding and put the rest of the results into perspective. The questionnaires about symptoms and QoL were answered during the medical consultations, where help was provided to the adolescents in completing them. This method of conducting a study with personal contact may improve results compared with those from questionnaires answered by post (24).

The control group in our study originated from the same area as the patients, and therefore we consider the group to be representative, although it showed fewer intestinal symptoms compared with other populations reported (26, 27). The SF-36 has been criticized for the geographical selection of a reference population in adolescent ages (24). Both mentioned facts may explain some of the results in our study—high differences compared with the controls and low compared with the reference population.

The prevalence of constipation and soiling for females and males was similar to the reports using Krickenbeck follow-up in children (4, 5). It has been suggested that the physical symptoms, such as constipation and soiling, diminish from childhood to adulthood (8), although this was not mapped in our study.

In our study, the frequency of lack of control of bowel movements, constipation and soiling was found to be the same in all subgroups of ARM. This result differs from earlier studies of postoperative PSARP beyond childhood, where those born with ARM with perineal fistulas have a better outcome than other subgroups (3). However, as different protocols are used for assessing postoperative results in ARM (26, 28), reliable comparison with earlier studies is difficult. We chose to follow the international agreement from 2005 of using Krickenbeck postoperative results (15) to contribute to a common base of knowledge.

Due to meteorism, the adolescent females in the study reported a lower QoL. The male patients with rectourethral fistula proved to have the significantly highest degree of gas incontinence. Gas incontinence among ARM patients has previously been shown to be the strongest correlating factor with psychiatric illness among adults with ARM (29). Also, in the interviews and medical counseling in this study, gas incontinence was frequently mentioned as the most difficult and socially limiting handicap to live with. In the deep interviews and at the medical consultations, the adolescents told how, in intimate situations, they adapted to the gas leakages as well as to the soiling. With this knowledge, it seems important to pay attention to gas incontinence to provide both medical and psychological help.

The only correlation between symptoms and QoL was found for the males in Giqli. One reason for the low correlation, despite the multiple symptoms and lowered symptom-specific QoL, could be the spread of results. This was especially true for the females and is illustrated with individual scores in Figure 3.

The high degree of symptoms was transparent for females in the Giqli total score, in three of the Giqli subscales as well as in the sum of physical health (PSC) in

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SF 36. QoL was reported to be low regarding large bowel function for both females and males. Similar lower scoring of QoL in symptom-specific questionnaires, such as Giqli, has earlier been shown for adults with Hirschsprung's disease (19).

One reason why QoL is not much affected in general QoL as measured in SF 36 could be an accommodation to a lifelong handicap. This has been suggested before, regarding both ARM and other congenital malformations (25, 30). This theory is supported by our deep interviews, where both the females and males spoke of how symptoms restricted their lives socially and sexually, but they had no personal feeling of generally lowered QoL due to the symptoms.

Another reason why QoL may be difficult to measure is that the questionnaires may not be adapted to the ages of the adolescents or may not be sensitive enough to ARM. During the counseling, when the adolescents answered the questionnaires, they frequently had to ask about the meaning of different words and expressions in both Giqli and SF36. For example, the word "illness" made answering difficult as the adolescents with ARM did not consider themselves as "ill". We think that the deep interview was a better tool for the adolescents for reaching an understanding of the type and degree of their problems. However, Hartman et al. have developed a disease-specific instrument "Hirschsprung's disease and anorectal malformation quality of life questionnaires"(HAQL), which have been successfully used in children and young adolescents up to 17 years and adults (12). The instrument has not yet been validated in our language and was therefore not used, but it may be a good tool in the future.

The ARM females in our study reported a lower physical health status compared with the controls, but had good mental statuses (MCS). The males in the study scored higher in all mental parameters in SF 36 compared with the controls. This is in line with earlier studies where male adolescents with lifelong handicap scores low on physical parameters without negatively influencing mental scores (31) and for adults in general with ARM vis-à-vis normal populations (11).

There was a clear gender difference in how much information the female and male adolescents had received from their parents about their malformation. One can speculate that the more open attitude toward the males contributes to the better mental wellbeing and social functioning reflected by the questionnaires. In the interviews, it was clear that the males had developed coping strategies, such as physical training, and tactics, such as lies in leaking situations. The coping strategies may contribute to their feeling of having a high mental status.

In this study, the psychiatric problems were not mapped. Psychiatric illness and lowered social ability among children, young teenagers and adults with ARM have been illuminated before (10, 29, 32). It has been suggested that the degree of symptoms in adults with ARM does not correlate with QoL as much as with psychosocial problems (33), which shows that QoL should be interpreted with caution.

In summary, the authors' experience is that QoL measured in questionnaires is difficult to interpret for adolescent individuals with ARM. To detect psychiatric problems or low QoL, contact with a psychologist could be offered early in adolescence. This is supported by the fact that males with ARM expressed a wish to be offered such a contact at an earlier period in their adolescence.

In the study about sexual health, none of the females reported problems during sexual intercourse, although they had to manage leakages and scars in such situations. There are no earlier studies about sexual problems for adolescent females with ARM. The reported prevalence of gynecological malformations, such as vaginal septum, absent vagina and bicorn uterus, in females with ARM is 5%–38%, and this could contribute to physically related lower sexual health. Also, perineal scarring could restrict sexual possibilities by stenosis of the vagina (14) or lower self-esteem (34, 35). However, among the adolescents in the study, the scars in the pelvic floor were no bother as were the abdominal scars from the stomas and thoracic scars from cardiac operations.

Among the males, only one had intermittent erectile problems, which is less than the previously described study among adults with ARM (14). Genital abnormalities in males with ARM are reported to be 26% (36), and this must be taken into consideration when counseling the adolescents. In the transfer of ARM patients to adult care, sexual issues are important, and sexual experience will often develop, especially after the adolescent has left the pediatric unit.

## Conclusion

Adolescents, 15–21 years old, with all subtypes of ARM report a lot of symptoms and express a need for information about their malformation, especially the sex-related issues. This could be offered at a personal meeting with the adolescent patient. A transfer from the units of pediatric surgery to adult care is mandatory and should involve the gynecologist, urologist, colorectal surgeon, psychologist and perhaps a sexologist working at a pelvic floor

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center or similar organization. Pediatric surgeons will still have the most profound knowledge about ARM, and we suggest continued cooperation with them after referral.

**Acknowledgements:** Gillian Sjödahl, Lexis English for Writers, Lund, Sweden, for linguistic revision of the manuscript. Fredrik Nilsson, biostatistician at the Competence Centre for Clinical Research, Skåne University Hospital, Lund, Sweden, for statistical advice.Sara Johnsdotter, Professor, and Sven-Axel Månsson, Professor, both at the Faculty of Health and Society, Malmö University, Sweden, for their cooperation. Mette Hambreus, MD at the Department of Pediatric Surgery, Skåne University Hospital, Lund, Sweden for her help with the figures.

Received October 25, 2012; accepted January 6, 2013

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# Paper II

Hindawi Publishing Corporation
BioMed Research International
Volume 2013, Article ID 297084, 8 pages
http://dx.doi.org/10.1155/2013/297084

*Clinical Study*

# Appendicostomy in Preschool Children with Anorectal Malformation: Successful Early Bowel Management with a High Frequency of Minor Complications

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Received 29 April 2013; Accepted 21 August 2013

Academic Editor: Giuseppe Rubini

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*Aim*. The aim of this study is to evaluate postoperatively bowel symptoms of antegrade colon enema through appendicostomies in preschool children with anorectal malformation (ARM). *Method*. 164 children with ARM operated on with posterior sagittal anorectal plasty were included. The malformations were classified according to Krickenbeck classification. Seventeen children in preschool age had an appendicostomy. The bowel symptoms according to the Krickenbeck follow-up were analysed pre- and postoperatively. All complications were registered. A questionnaire on the use of the appendicostomy was answered. *Results*. The median age (range) at the time of the appendicostomy was 4 (1–6) years. The observation time was 5 (0.5–14) years. The main indications for appendicostomy were incontinence and noncompliance to rectal enemas. Postoperatively there was a significant decrease in soiling and constipation ($P < 0.001$). The total complication rate was 43% with infections (29%), stenosis (12%), and retrograde leakage (0). The median time required for giving enema in the appendicostomy was 45 minutes (range: 15–120) once a day varying from 2 times/week to 3 times/day. And: complications are less frequent than in older children. *Conclusion*. Appendicostomy in preschool children with ARM is a way to achieve fecal cleanness before school start. The infection rate was high, but other complications are less frequent than in older children.

## 1. Introduction

The background to the study is the different approach to appendicostomy practiced at our institution compared with that described in the literature. In order to reach a good bowel management early on in life and with respect to the psychological aspects, we operate appendicostomies with the indication of poor compliance to rectal enemas, in young preschool children with ARM. The question is whether this can be supported by medical evidence.

Children with anorectal malformation (ARM) should be fecally clean when starting school, at the age of 5-6 years, in order to be socially accepted. The prevalence of fecal incontinence according to the Krickenbeck follow-up is reported to be 57–78% among the children with ARM [1–3]. Therefore many of these children are in need of organized bowel management, and this involves rectal enemas [4, 5]. However, compliance to rectal enemas is questionable since rectal manipulation is not well tolerated by the children who have a history of anus operations and dilatations. The psychological consequences of being subjected to rectal enemas could be difficult both for the child and the families [6, 7].

Antegrade enema through an appendicostomy was introduced in the early 1990s as an alternative to the rectal enema [8]. The main indication, besides fecal incontinence, has been to increase the child's autonomy in children who already have a good compliance to rectal enemas [9, 10]. Problems with compliance in young children with incontinence have never been described as an indication for operation. The median age

in the few reports on appendicostomy in children with ARM has been 9 years [10, 11], and there are no studies about the outcome only for children at preschool ages.

The reports on the symptomatic outcome after an appendicostomy in children with ARM are few, and these describe full relief from incontinence in 96% and 72%, respectively [10, 12]. The few reports on the complications to appendicostomy in children with ARM present a relatively high complication rate of 26%–63% with strictures and fecal retrograde leakages [10, 11, 13]. The complications are reported to be more frequent among children with ARM than among other children and with more complications among younger children [13].

## 2. Aim

The primary aim of the study was to evaluate the outcome of an appendicostomy in preschool children with ARM regarding bowel related symptoms and type and frequency of complications. The secondary aim was to describe the use of and the families' satisfaction with the appendicostomy in order to prepare relevant preoperative information for the guardians.

## 3. Material and Methods

Since 1990, 164 children born with ARM have been admitted and initially treated at our tertiary centre for paediatric surgery with a catchment area of 2 million inhabitants. After falling off, mainly due to death or migration, the reconstructive posterior anorectal sagittal rectoplasty (PSARP) or posterior sagittal anorectal vaginal urethroplasty (PSARVUP) has been performed on 55 females and 77 males who have all been followed up at the institution (Figure 1). The type of ARM was classified according to Krickenbeck's classification, and the bowel symptoms were classified according to Krickenbeck's postoperative symptom scale [3]. The distribution of appendicostomies among the different types of ARM was statistically analysed.

The outcome and complications after the appendicostomies were registered prospectively in 2007–2012 and retrospectively in 1998–2006 through regular medical counselling and the patients' files. The bowel symptoms were statistically compared pre- and postoperatively while the complications were registered and described.

The follow-up regarding the use of and satisfaction with the appendicostomy was registered through telephone interviews according to a questionnaire about the time required, volumes used, and parents' and children's satisfaction. The telephone interviews were carried out by doctors who were unknown to the families.

The postoperative infections were diagnosed through bacterial culturing, controlled after clinical suspicion of infection.

## 4. The Method of Operation

Appendicostomy was introduced at our centre in 1998 and has been performed with laparoscopy assistance since 2000. The procedure has been carried out or supervised by two paediatric surgeons. The laparoscopic procedure involves an open minimal laparotomy at the umbilicus with 2, 3 or 5mm 0 or 30 grade laparoscopic optic. At the site chosen for the appendicostomy, as low as possible in the right inguinal fossa, a 5 mm laparoscopy port is introduced. Through this a grasper is used to catch the appendix and pull it out through the hole of the working port. The appendix is then opened at the tip, removing 5–10 mm of the appendix. The appendiceal wall is sutured only to the skin with resorbable stiches. Until 2009, a 6- or 8-French urinary catheter was left in the stoma, and later a Chait button has been placed in the stoma. The catheter or Chait button is removed not earlier than six weeks postoperatively and in the youngest children or children with syndromes left for at least 6 months or more due to problems with accepting regular catheterising. The perioperative antibiotic prophylaxis constitutes one dose of the combination metronidazole and trimethoprim sulfa.

## 5. Statistical Analysis

As the patients were few and data could be skewed, nonparametric statistics were used. Fisher's exact Probability test, two tailed, was used for the comparisons of symptoms pre- and postoperatively and for the distribution of appendicostomy in the children with different Krickenbeck subtypes of ARM. $P$ value $< 0.05$ was considered significant.

## 6. Ethical Considerations

The study protocol was designed to meet the legislative documentation required in the country of origin. The regional research ethics committee approved the study, registration no. 2010/49. All data are presented in such a way that it is impossible to identify any single patient.

## 7. Results

During the period from 1990 through 2012, a total of 139 children were operated on with reconstruction of the anorectal malformation at our department, and three of the children were operated on at other centres and migrated to the region. Out of these, 21 children, 1–12 years old, underwent surgery for appendicostomy (Figure 1). The distribution of appendicostomies was uneven between the different subtypes of ARM according to Krickenbeck, with the highest number of appendicostomies among the boys with rectourethral fistula (8) and the females with vestibular fistula (5). The highest rate was among the girls with cloacae (50%). In Table 1 the age of the children and the follow-up time are presented. The median age was the same in the whole group of patients 1–12 years, as in the studied group of the preschool aged children.

The preschool children's comorbidity to ARM is summarized in Table 2. None of the children were without any comorbidity, and all of them either had spinal cord malformation, neurogenic bladder or were born with a neurological syndrome.

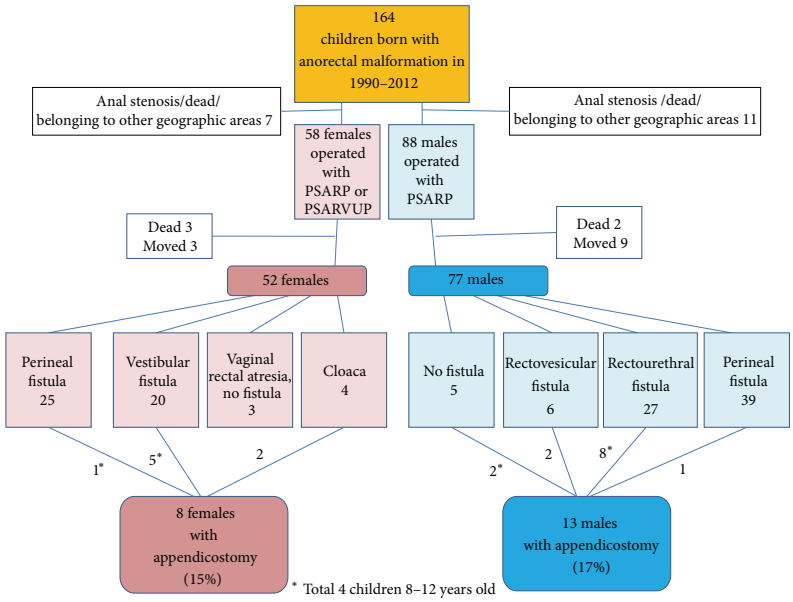


Figure 1: The children with anorectal malformation (ARM) operated on with posterior sagittal anorectal plasty (PSARP) and posterior sagittal anorectal vaginourethral plasty (PSARVUP) in 1990–2012 and those operated on with appendicostomies in 1998–2012. The appendicostomies among the different subtypes of ARM according to the Krickenbeck classification were unevenly distributed ($P < 0.05$, Fisher's exact test).

Table 1: Description of all the children (1–12 years) and the studied group (1–6 years) with appendicostomy.

| | Number | Years median (range) |
|---|---|---|
| Children operated on with appendicostomy 0–12 years old | 21 | |
| Age at the appendicostomy operation | | 4 (1–12) |
| Children operated on with appendicostomy 1–6 years old | 17<br>6 females, 11 males | |
| Age at the appendicostomy operation | | 4 (1–6) |
| Observation time after the operation | 17 | 5 (0.5–14) |
| Age at the follow-up | 17 | 8 (1–19) |
| Method used | | |
| Laparotomy | 4 | |
| Laparoscopy | 13 | |

Postoperative complications were present in 7/17 (43%) of the children. The total number of complications was 10. The type and time lapse from the appendicostomy to the complication are presented in Table 3. One patient with Mb Down had an iatrogenic subcutaneous perforation 4 months postoperatively, which had to be reoperated on. Eight out of the 17 children started with a Chait button at the time of the operation, and another two had it because of stricture. At the follow-up 8 children were still using the Chait button because of the convenience of not needing intermittent catheterising.

The pre- and postoperative symptoms according to the Krickenbeck postoperative follow-up scheme are summarized in Table 4. The results demonstrate a significant improvement of voluntary bowel movements or the ability to decide when to pass stools, as well as a significant decrease of soiling and constipation.

In three of the children the appendicostomy was allowed to close spontaneously when it is no longer needed. None had stopped using it because they did not like it, or due to any complication (Table 5).

The use of the appendicostomy is described in Table 5. As shown, the range of volumes used in the appendicostomy is wide. The volume and frequency of enema have to be tried out over a long period of time, and the results here presented are only the findings at the point of the follow-up and can change over time. Also the enemas used differed and constituted of a saline, Klyx, oil, movicol, and mixtures of these products.

Table 2: The comorbidity among the 17 children 1–6 years old who were operated on with appendicostomy.

| Type of comorbidity | Number of children (17) |
|---|---|
| Without comorbidity | 0 |
| Spinal cord malformation, neurogenic urinary bladder, or syndromes | 17 |
| Syndrome or neurological impairment<br>Mb Down 2, autism 1, or mitochondrial disease 1 | 4 |
| Spinal cord malformation<br>Tethered cord 4, caudal regression 5, or skeletal anomalies 10 | 10 |
| Neurogenic urinary bladder | 15 |
| Urinary tract anomalies<br>Single kidney 2, VUR 5 | 5 |
| Cardiac malformations | 5 |
| Gynecological malformations<br>Bicorn uterus 3, cloaca 2 | 3 |
| Male genital anomalies<br>Hypospadia 1, undescended testicle 2 | 3 |
| Tracheal stenosis | 1 |
| Skeletal anomalies | 3 |
| Gastrointestinal anomaly<br>Esophageal atresia 1, duodenal atresia 1, or duodenal stenosis 1 | 3 |
| VACTERL | 8 |

Table 3: Description of frequency and types of complications after appendicostomy in the children 1–6 years with anorectal malformation.

| | Number | Time at the diagnosis in weeks median (range) | Treatment |
|---|---|---|---|
| Peroperative complications | 0 | | |
| Children with postoperative complications | 7 (43%) | | |
| Incidents | 10 | | |
| Types of complications | | | |
| Leakage | 0 | | |
| Stricture | 2 (12%) | 16 (13–19) | Dilatation, Chait button |
| Pain | 2 (12%) | 14 (12–16) | Chait button |
| Infections | 5 (29%) | 3 (2–4) | Antibiotics |
| Iatrogenic perforation | 1 | 18 | Reoperation, Chait button |

Table 4: Krickenbeck postoperative follow-up scheme: postoperative outcome in the 17 children with anorectal malformation operated on with appendicostomy at 1–6 years old.

| Number of children<br>$n = 17$<br>median aged 4 (1–6) years old | | Preop.<br>$n$ 17 | Postop.<br>$n$ 17 | $P$ value* |
|---|---|---|---|---|
| (1) Voluntary bowel movements, feeling of urge, capacity to verbalize, and holding the bowel movements | Yes/no | 0/17 | 16/1 | <0.001 |
| (2) Soiling | No | 2 | 15 | <0.001 |
| Grade 1 | Occasionally (1-2/week) | 0 | 1 | |
| Grade 2 | Every day, no social problem | 2 | 1 | |
| Grade 3 | Constant, social problem | 13 | 0 | |
| (3) Constipation | No | 2 | 14 | =0.001 |
| Grade 1 | Manageable by changes in diet | 2 | 2 | |
| Grade 2 | Requires laxative | 3 | 1 | |
| Grade 3 | Resistant to laxative and diet | 10 | 0 | |

*Fishers' exact two-tailed test.

Table 5: The use of the appendicostomy among the children with anorectal malformation operated on with appendicostomy at 1–6 years of age, with a median follow-up time of 5 (0.5–14) years.

| Questionnaires | Answer | Median (range) | Number |
|---|---|---|---|
| Stopped using the appendicostomy (years) | | 5 (1.5–10) | 3 |
| Total volume enema used at each treatment (mL) | | 850 (200–3000) | 14 |
| Volume enema used at each treatment (mL/kg) | | 35 (11–80) | 14 |
| Time needed to administer the enema and finish the bowel emptying (min) | | 45 (15–60) | 14 |
| Frequency of the use of the appendicostomy | Once daily | | 10 |
| | Three times daily | | 1 |
| | Every other day | | 2 |
| | Weekly | | 1 |
| Appendicostomy could be recommended to others in the same situation | Yes | | 15 |
| | No | | 2* |
| Use of Chait button | | | 8 |

*Comments: (1) too early to evaluate and (2) were satisfied but had heard negative experiences from others.

## 8. Discussion

This is the first study to report the outcome of appendicostomy and its use among preschool children with ARM. The results support the approach to operate appendicostomies early, before school start. The study also shows that weak compliance to rectal enemas strengthens the indication for appendicostomy since compliance to bowel management was obtained.

Since bowel management is essential to achieve fecal cleanness both at school start and for the future bowel function [4, 14], even the psychological aspects must be respected when considering appendicostomy.

It can be pointed out that a high proportion of normal babies between the ages of 2 and three are still using diapers, passing stools 1–3 times daily. However, their use of diapers does not lead to that they are defined as incontinent and cannot be compared with the incontinent children born with ARM that are passing several stools daily and seldom are clean in between. Besides, the children here reported have a prevalence of 100% of associated malformations, especially spinal malformations, which may predict a need of appendicostomy in the near future anyway. Thus, it is justified to perform the appendicostomy operation even in one- or two-year-old babies.

The population of children with ARM belonging to the catchment area of our single institution is well controlled thanks to the national new-born register, diagnosis register, operation registers, and the national ID number. The frequency of appendicostomies was similar for the genders: 11/77 (14%) males and 6/52 (12%) females had an appendicostomy. This distribution could be questionable since the faecal incontinence among females with ARM in general is more frequent than among the males [1, 2]. One reason for the gender difference could be that the problems arising from anorectal malformation are not discussed as much with females as much as with males [15], and therefore the females may not be offered the same treatment, as appendicostomy.

The children undergoing appendicostomy are described according to Krickenbeck's classification, and this has been done once previously [10]. In comparison to that study the distribution of appendicostomies among the subtypes of ARM was similar for rectovestibular fistulas and perineal fistulas but differed for rectourethral fistulas and cloacae: 47%, 12%, respectively, in this study versus 25%, 20%, respectively, in the other study. The children with rectourethral bulbar fistulae, rectovestibular fistulae, and rectoperineal fistulae usually have an excellent functional prognosis when they receive a technically correct reconstructive procedure. However, there are exceptions to this, especially when the child has an associated malformation as spinal cord malformation or is neurologically impaired. Those children have a weaker prognosis and could therefore benefit from an appendicostomy.

In the present study, the prevalence of associated malformations with the ARM in those who underwent an appendicostomy was 100%. Spinal cord abnormalities were present in 70% and neurogenic bladder in 88%. These figures are higher than those reported among all children with ARM, where associated anomalies were present in 78% and spinal cord abnormalities in 26% [16]. Therefore it seems that anomalies in the spinal cord and urinary bladder could be predictors of a future need of appendicostomy in a new-born child with ARM.

The complication rate in this study was 43% which must be considered as high. The families with preschool children undergoing appendicostomy must be preoperatively informed about this. However, the complication rate with strictures and leakage was lower than among the previously reported older children with ARM [10, 11, 13] (Table 6). Maybe the young age could be an advantage in avoiding strictures since it seems that hypertrophic scars are less common among younger children [17]. The difference in success rate compared with what is reported before can be addressed by pointing out the young age of the children, the prospective character of the study with frequent and regular visits to the centre of pediatric surgery involved, and the difference in the duration of observations time compared with other reports. Long term results, more than 10 years, are missing.

Table 6: Discussion table: the types and frequency of complications with appendicostomy reported exclusively among children with anorectal malformation (ARM).

| Reference | Number children | Age | No complications | Stenosis/stricture | Leakage | Surgical revision | Bowel obstruction | Infection |
|---|---|---|---|---|---|---|---|---|
| Kim et al. 2006 [13] | 8 | 8.5 | 0% | ? | ? | 63% | ? | ? |
| Mattix et al. 2007 [11] | 32 | 9 | ? | 50% | ? | 34% | 3% | ? |
| Rangel et al. 2011 [10] | 163 | 9.9 | 74% | 18% | 6% | 23% | 0.1% | 0% |
| Present study 2013 | 17 | 4 | 58% | 12% | 0% | 6% | 0 | 29% |

Further, we do not use any stopper described as effective in preventing stoma stenosis in older children [18]. Instead the Chait button, earlier described for appendicostomy [19], is used for the very young children who do not accept the catheterising. The Chait button could be useful for long periods, months, or years, probably works as a stopper, and prevents stenosis. On the other hand the Chait button may be a reason for infections. A continent appendicostomy may achieve the same or better results than those obtained by us, without the use of a Chait button. However, the reason to use the Chait button is partly to avoid a stricture formation in the stoma and partly because the possible difficulties to perform catheterising in small children.

Postoperative infection was the most common complication and required antibiotic treatment in 1/3 of the patients after a median of 2-3 weeks postoperatively. Only few other studies have presented postoperative infection following appendicostomy. The reported figures are 0% in 163 patients with ARM [10] and 12–43% among children with different diagnoses, including ARM [20, 21]. The infection rate in our group of children is extremely high. This may be explained by a very close follow-up of our patients and tendency to react on minor wound problems, defining these as a treatable wound infection. On the other hand the reported figure of 0% infections in 163 patients with ARM [10] is unbelievably low in comparison to our results. At our institution the routine has been changed to an early medical control after 7–10 days postoperatively in order to start early treatment of a possible infection.

The most unexpected result was that there was no backward faecal leakage at all among the preschool children, compared to the previously reported leakage rates of 6% among ARM [10] and 21–43% among different diagnoses with a median age of 8 years [20, 21]. The reasons for the lack of retrograde leakage in young children could only be speculated on. Maybe the valve of the appendix is more continent in younger children which could explain the low incidence of leakage among the preschool children. Also the good compliance to the daily colonic wash, that was reported, could bring about low resistance in the colon, which may minimize the backward pressure and secondary leakage.

Another reason could be the operation technique. The technique used in this study is very simple without any cecal wraps or mobilization of caecum, only stitches of the appendix to the skin. In contrast to our results, the only previous study comparing complications in younger children (5.5 years) with older ones (9.1 years) used a slightly different operation technique and found that the leakage and need of manual evacuation were higher among the younger children [13]. In some studies a cecal wrap is shown to be essential to avoid a high frequency of leakage [10]; in other studies the cecal wrap is shown to be unnecessary [22].

One weakness in the study is that the symptoms were retrospectively registered in 1/3 of the patients. The information still is reliable since it was collected through contact with the parents and from the documentation of frequent notes in the files. A further weakness is that the Krickenbeck symptom scale is more suitable for the preoperative measurement and weak for the postoperative measurement, since the primary paper recommends the registration to be based on "what would the symptoms be if you/your child had no bowel management" [3]. In order to reach a balance, the postoperative questions in the study were based on the situation: "if your child only had the appendicostomy."

Furthermore, one must consider the risk of bias when the operating surgeon is involved in a study like this one, since the result could tend to favour the operation. We are aware of this and tried to minimize the bias by delegating the follow-up to two doctors who had never met the patients and had not been the operating doctors.

The results of the questionnaires show that the time consumption for the antegrade enema is considerable and similar to earlier studies. This is a very important point in the preoperative information, especially for families who have only a little experience from rectal enemas. A good bowel management program implemented correctly takes one week. This may be true if the child and his/her guardians accept the necessary regime and stick to it. If not, a longer period of trying out the frequency and type of enema is needed. Sometimes a delayed acceptance of the duration of the enema procedure in daily life delays the compliance and the fecal cleanness. Therefore it is necessary to inform the families that it can take months until the colonic wash is well functioning because the individual amount and type of enema must be tried out, even if this has been done before with rectal enema.

The preoperative information should also include the risk of the high frequency of postoperative complications already

discussed, and the fact that a Chait button is useful for a long period, sometimes years, especially in the smaller children where catheterisation could be troublesome because of their physical activity.

The results of this study could not support the long term failure of the appendicostomies discussed in previous literature, where 40% of children have stopped using the appendicostomy after 5 years mainly because of problems [23]. Even though the follow-up time in our study was long enough: median 5 years, only 3/17 (18%) stopped using the appendicostomy. These children developed bowel control later in life after a period of being fecally clean due to the use of the appendicostomy. This does not mean that the operation was not indicated to those patients during a period of their life when they had severe incontinence problems. The reasons to why those three patients stopped using the appendicostomies were that they managed without enemas. All of them would recommend appendicostomy to others.

Earlier long term follow-ups have shown that the stenosis and reoperations will come later postoperatively, with a mean time of around 8 months [10, 24]. In our study the complications came earlier. Maybe the reasons, also to these findings, could be related to the young age.

## 9. Conclusion

The benefit of appendicostomy early on in life is that fecal cleanness could be achieved before school start and also in children who refuse rectal enemas. The complications are frequent, but stenosis and leakage less than in older children with ARM. The preoperative information about expected time and enema volumes is very important for gaining a good psychological outcome. In the end the families report a high level of satisfaction with having appendicostomy to their preschool children, and the children's autonomy could be introduced early because the appendicostomy is already in place.

## Acknowledgments

The authors thank: Gillian Sjödahl, Lexis English for Writers, Lund, Sweden, for linguistic revision of the paper and Fredrik Nilsson biostatistician at the Competence Centre for Clinical Research, Skåne University Hospital, Lund, Sweden, for statistical advice.

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# Paper III

YJPSU-56562; No of Pages 9

Journal of Pediatric Surgery xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

# Bowel symptoms in children with anorectal malformation — a follow-up with a gender and age perspective

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ARTICLE INFO

*Article history:*
Received 16 July 2013
Received in revised form 6 October 2013
Accepted 28 October 2013
Available online xxxx

*Key words:*
Anorectal malformation
Krickenbeck
Sacral malformation
Fecal incontinence
Gender
Age

ABSTRACT

*Background:* Gender specific outcome for children with anorectal malformations (ARM) is rarely reported although it is important for medical care and in parent counseling.
*Purpose:* To assess bowel function according to the Krickenbeck system in relation to ARM-subtype, gender and age.
*Method:* All children born with ARM in 1998–2008 and referred to two centers in two different countries were followed up. The bowel function in 50 girls and 71 boys, median age 8 years, was analyzed.
*Results:* Among those with a perineal fistula, incontinence occurred in 42% of the females and in 10% of the males ($p = 0.005$) whereas constipation occurred in 62% of the females and 35% of the males ($p < 0.001$). No bowel symptoms differed between the females with perineal and vestibular fistulas ($p > 0.3$ for every symptom). Sacral malformations were associated with incontinence only in males with rectourethral fistulas. Constipation among the males differed between the age groups: 58% versus 26% ($p = 0.013$). Bowel symptoms did not change with age among the females.
*Conclusion:* Gender differences in outcome for children with ARM must be considered. Males with perineal fistulas had less incontinence and constipation than the females with perineal fistulas. The females with perineal and vestibular fistulas had similar outcomes.

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Knowledge about the prognosis for bowel control in a newborn child with an anorectal malformation (ARM) is of great concern for the parents and important for planning the child's future medical care. Bowel function in children with ARM operated on with posterior sagittal anorectal plasty (PSARP) [1] has been described in many ways using different classification and follow-up systems [2]. This diversity has made it difficult to report the true outcome after PSARP and to compare results in different patient populations. Therefore, in 2005 the Krickenbeck classification system of ARM sub-groups and postoperative results was established [3]. This way of classifying the subtypes and outcome in children with ARM has been used in some recent reports [4–10], and facilitated prediction of the outcome and comparisons between groups. So far the subtype of ARM according to the Krickenbeck classification seems to be one of the most important factors for predicting outcome after PSARP for a single child [4,7,9,10,6]. Interestingly, none of the previous reports have analyzed gender-specific outcome.

## 1. Aim

The main aim of the study was to describe bowel function according to the Krickenbeck follow-up system separately for females and males 4–12 years old with ARM. The secondary aim was to evaluate if fecal incontinence and constipation were less frequent in the older age group.

## 2. Materials and method

### 2.1. Children with anorectal malformation

All newborn children with ARM referred to two tertiary centers for pediatric surgery in two countries during the periods from January 1998 and January 2000, respectively, until December 2008 were included in the study. The eligible populations in the two countries have similar socio-economic conditions with free health care for the inhabitants. There were always two surgeons performing the operations, and at least one of them was an experienced pediatric

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http://dx.doi.org/10.1016/j.jpedsurg.2013.10.022

Please cite this article as: Stenström P, et al, Bowel symptoms in children with anorectal malformation — a follow-up with a gender and age perspective, J Pediatr Surg (2013), http://dx.doi.org/10.1016/j.jpedsurg.2013.10.022

**Table 1**
International classification Krickenbeck postoperative results for anorectal malformation.

| | |
|---|---|
| 1. Voluntary bowel movements | Yes/No |
| Feeling of urge, capacity to verbalize, hold the bowel movements | |
| 2. Soiling | No |
| Grade 1 | Occasionally (1–2/week) |
| Grade 2 | Every day, no social problem |
| Grade 3 | Constant, social problem |
| 3. Constipation | No |
| Grade 1 | Manageable by changes in diet |
| Grade 2 | Requires laxative |
| Grade 3 | Resistant to laxative and diet |

colorectal surgeon. In total, six colorectal pediatric surgeons were responsible for the operations included here.

The results were collected when the children were between 4 and 12 years of age. Excluded from the study were those with anal stenosis, rectal atresia and cloaca. Those operated on at other centers and those who had migrated were excluded. The studied group finally consisted of 60 and 77 children, respectively, from the two centers. These 137 children, 56 females and 81 males, fulfilled the criteria for inclusion. The children with ARM were subtyped according to the Krickenbeck classification suggested by the International Conference for the Development of Standards for the treatment of Anorectal Malformations in 2005 [3].

### 2.2. Operation methods and follow-up

Both centers operate according to the PSARP-procedure, described by Dr. Pena [1]. The anal sphincter complex is defined by electromyostimulation and the mobilized rectum is placed in the center of the sphincter complex. A diverting colostomy is used for males with rectourinary fistulas or no fistula, and for some of the females with vestibular fistulas and those with no fistula.

In two females and three males with perineal fistulas the skin incision was performed as a Y-V-plasty. Another two males with perineal fistulas were operated on with cut back where the centre of the anal channel was reached by an incision through the fistula without dividing the sphincter, followed by dilatations of the fistula.

All the children were examined under general anesthesia approximately two weeks after the operation, and then a dilatation program was started if needed. The majority of the children underwent regular dilatations.

The children were examined for associated anomalies with x-ray and ultrasound of the sacrum, and the urinary tract was examined with ultrasound and voiding cystourethrography. If there were signs of tethered cord or neurogenic bladder a MRI and/or urodynamic investigation was performed. Echocardiography of the heart was routinely performed.

### 2.3. Method

The study is a clinical follow-up and is both descriptive and comparative. Information about the subtypes of ARM, concomitant malformations and symptoms was collected from the regular annual follow-up of the patients. The registration of the bowel symptoms includes consequent registration in the medical records and in a prospectively maintained database, using the Krickenbeck postoperative follow-up scheme [3] (Table 1). As suggested in the original article the outcome was measured before bowel management was introduced. Severe incontinence was defined as Krickenbeck grade 2 and 3.

### 2.4. Statistical considerations

The exact Kruskal–Wallis test was used for ranks and the generalized Fisher's exact test was used for dichotomous outcomes between all groups. If statistical difference was found, the results were

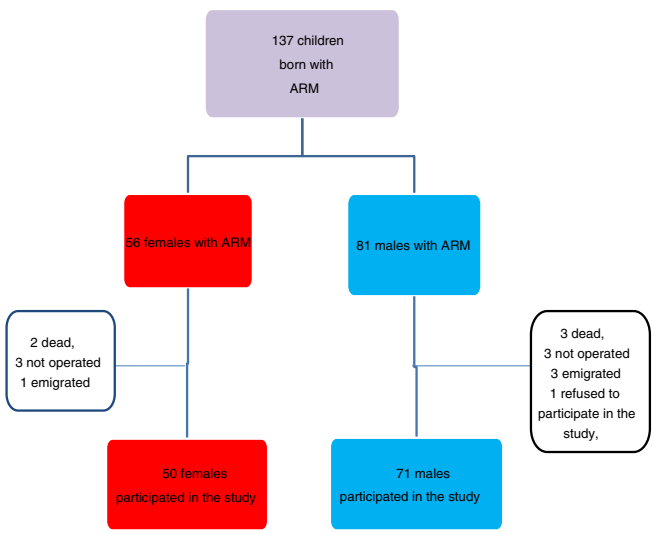


**Fig. 1.** Consort table illustrating the included children with anorectal malformation (ARM) and the reasons for drop out. n = number.

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**Table 2**
Number (n) and per cent (%) of the children with anorectal malformation (ARM) and the distribution in the age groups 4–7 and 8–12 years, respectively.

| Krickenbeck classification of the subtypes of ARM studied in this report | Females n 50 | | | Males n 71 | | | The distribution of the ARM-subtypes n 121 (%) |
|---|---|---|---|---|---|---|---|
| | All females | 4–7 years old n 21 | 8–12 years old n 29 | All males | 4–7 years old n 24 | 8–12 years old n 47 | |
| Perineal fistula females | 24 | 10 | 14 | | | | 20% |
| Vestibular fistula | 22 | 9 | 13 | | | | 18% |
| No fistula females | 3 | 1 | 2 | | | | 2.5% |
| Vaginal fistula | 1 | 1 | 0 | | | | 1% |
| Perineal fistula males | | | | 32 | 11 | 21 | 26% |
| Recto-urethral fistula (recto-bulbar and prostatic fistula) | | | | 29 | 11 | 18 | 24% |
| Recto-vesicular fistula | | | | 3 | 0 | 3 | 2.5% |
| No fistula males | | | | 7 | 2 | 5 | 6% |

The distribution of the different subtypes of ARM in both age groups in both gender was similar ($p > 0.3$ for each group, Fisher's Exact Probability Test, two tailed).

**Table 3**
Number (n) and (%) associated anomalies in the cohort of 121 children with anorectal malformation.

| Associated malformations, anomalies and disability | Females Total | Females Perineal fistula | Females Vestibular fistula | Females Vaginal fistula | Females No fistula | Males Total | Males Perineal fistula | Males Recto-uretheral fistula | Males Recto-vesicular fistula | Males No fistula |
|---|---|---|---|---|---|---|---|---|---|---|
| n | **50** | **24** | **22** | **1** | **3** | **71** | **32** | **29** | **3** | **7** |
| No concomitant malformation or disability | 23 (46) | 16 (67) | 7 (32) | 0 | 0 | 22 (31) | 15 (47) | 7 (24) | 0 | 0 |
| Syndrome, neurological disability | 8 (16) | 2 (8) | 2 (9) | 1 | 3 (100) | 5 (7) | 2 (6) | 2 (7) | 0 | 1 |
| Sacral malformation | 14 (28) | 4 (17) | 10 (45) | 0 | 0 | 16 (23) | 3 (9) | 9 (31) | 2 (67) | 6 (86) |
| Cardiac malformation | 12 (24) | 4 (17) | 5 (23) | 1 | 2 (67) | 10 (14) | 1 (3) | 8 (28) | 0 | 1 |
| Urinary tract anomaly, vesicourethral reflux, neurogenic bladder | 20 (40) | 4 (17) | 13 (60) | 1 | 2 | 27 (38) | 8 (25) | 14 (48) | 3 (33) | 2 (21) |
| Other malformations (genital, hypospadia, coloboma, ear-anomaly, cleft-lip-palate, esophageal atresia, tracheoesophageal fistula, skeletal malformation) | 11 | 4 | 6 | 0 | 1 | 18 | 12 | 6 | 0 | 0 |

analyzed with post hoc tests of joint ranks for ranks of symptoms or with the relevant 2-by-2 subtabled Fisher's exact test when comparing binary symptoms. P-values are described between <0.3 and >0.001. A p-value < 0.05 was considered significant. All statistical computations were performed by a statistician using the computer program R version 2.15.2 [11]. Multiple comparisons were adjusted using the false discovery rate procedure.

### 2.5. Ethical considerations

The regional research ethics committee approved the study (registration number 2010/49) for one center and the institutional board at the hospital approved it at the other center. The data are presented in such a way that it is impossible to identify any single patient.

## 3. Results

Six females and 10 males dropped out from the study (Fig. 1). The studied group finally consisted of 121 children: 50 females and 71 males, each group with a median age of 8 years (4–12) (Fig. 1). The distribution between the different subgroups of ARM according to the Krickenbeck classification, gender and age group is shown in Table 2. The distribution of the ARM subtypes in the young and old age groups did not differ significantly ($p > 0.3$) for any of the largest subgroups (Table 2).

In total reoperations were performed in three females and two males. All had perineal fistulas.

The outcomes for the children with perineal fistulas operated on with Y-V-plasty (2 females and 3 males) and cut back (2 males) were gender-wise statistically compared with those operated on with PSARP. No statistical differences were found between the

**Table 4**
The frequency of voluntary bowel movements (feeling of urge, ability to verbalize and hold back) in 121children with anorectal malformation (ARM). n = number (%).

| Voluntary Bowel Movements | Females Total | Females Perineal fistula | Females Vestibular fistula | Females Vaginal fistula | Females No fistula | Males Total | Males Perineal fistula | Males Recto-uretheral fistula | Males Recto-vesicular fistula | Males No fistula |
|---|---|---|---|---|---|---|---|---|---|---|
| n | 50 | 24 | 22 | 1 | 3 | 71 | 32 | 29 | 3 | 7 |
| Yes | 35 (70) | 19 (79) | 16 (73) | 0 | 0 | 41 (58) | 29 (91) | 10 (34) | 0 | 2 (29) |
| No | 15 (30) | 5 (21) | 6 (87) | 1 | 3 | 30 (42) | 3 (9) | 19 (66) | 3 | 5 (71) |

Statistical analyses: Comparisons of the frequency of voluntary bowel movements between.
a) the total group of females and males, respectively ($p = 0.1864$).*
b) the females with perineal fistula and the rest of the females ($p = 0.224$).*
c) the males with perineal fistula and the rest of the males ($p < 0.0001$).*
Gender specific statistical analyses regarding the ARM-subtypes are illustrated in Fig. 3.
* Fisher's Exact Probability Test, two-tailed.

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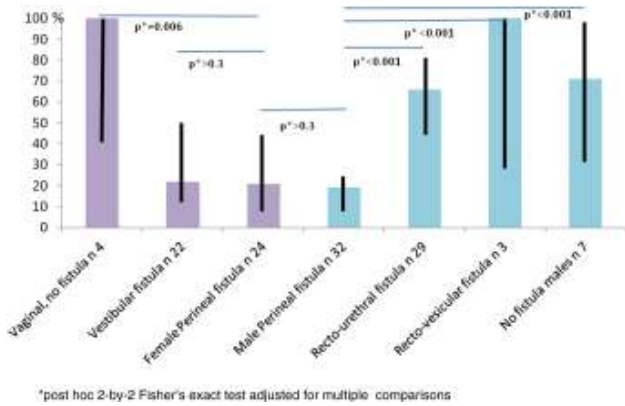


**Fig. 2.** Absent voluntary bowel movements among children with anorectal malformation (ARM). Comparison gender-wise between the perineal fistulas and the rest of the subtypes of ARM with 95% confidence interval. n = number.

groups concerning voluntary bowel movements ($p > 0.3$), fecal incontinence (>0.3) or constipation (>0.3) (Fisher's exact probability test, two tailed).Therefore all the patients with perineal fistulas were analyzed.

The frequency of associated anomalies in each gender and ARM-subtype is summarized in Table 3.

### 3.1. Voluntary bowel movements

Voluntary bowel movements were achieved statistically equally in the females (70%) and the males (58%). Among the children with perineal fistulas, 79% of the females reported voluntary bowel movements as opposed to 91% of the males. Almost 75% of the females with vestibular fistula had voluntary bowel movements, but only 33% of the males with rectourethral fistula (Table 4). The frequency of absent voluntary bowel movements was similar for the females with perineal fistula and for those with vestibular fistula, while among the males with rectourethral fistula significantly more reported absent voluntary bowel movements than those with perineal fistulas (Fig. 2).

The loss of voluntary bowel movements did not differ between the lower and higher age groups for the females or for the males (Fig. 3).

### 3.2. Incontinence

The frequency of fecal incontinence was equal among the females (48%) and the males (42%). Females with perineal fistulas reported a higher frequency of incontinence than the males with perineal fistulas (42% and 10%, respectively) and similar to that of the females with vestibular fistulas (50%). The males with perineal fistulas had significantly less incontinence compared to the rest of the males with other subtypes of ARM (Table 5).

When comparing all grades (0–3) of incontinence in the females, there was no significant difference in the distribution of ranks of

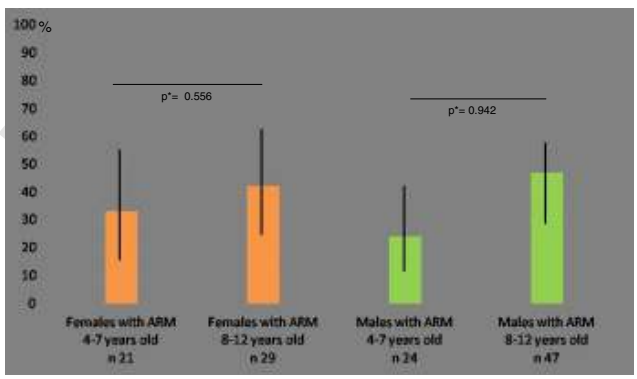


**Fig. 3.** Absent voluntary bowel movements among the children with anorectal malformation (ARM) in the age groups 4–7 and 8–12 years. Comparisons between the age groups for females and males, respectively, with all subtypes of ARM with 95% confidence interval. n = number.

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**Table 5**
Fecal incontinence of different degrees according to the Krickenbeck follow-up in 121 children with anorectal malformations (ARM) n = number (%).

| Fecal Incontinence | Females Total | Females Perineal fistula | Females Vestibular fistula | Females Vaginal fistula | Females No fistula | Males Total | Males Perineal fistula | Males Recto-uretheral fistula | Males Recto-vesicular fistula | Males No fistula |
|---|---|---|---|---|---|---|---|---|---|---|
| **n** | 50 | 24 | 22 | 1 | 3 | 71 | 32 | 29 | 3 | 7 |
| **No** | 26 (52) | 14 (58) | 11 (50) | 0 | 1 (33) | 41 (58) | 29 (90) | 9 (31) | 2 (67) | 1 (14) |
| **Yes** | 24 (48) | 10 (42) | 11 (50) | 1 | 2 (67) | 30 (42) | 3 (10) | 20 (69) | 1 (33) | 6 (86) |
| Grade 1 (occasionally 1–2/week) | 13 (26) | 6 (25) | 6 (27) | 1 | 0 | 8 (11) | 2 (6) | 3 (10) | 1 | 2 (29) |
| Grade 2 (every day, no social problem) | 4 (8) | 2 (8) | 1 (5) | 0 | 1 | 4 (6) | 1 (3) | 1 (3) | 0 | 2 (29) |
| Grade 3 (constant, social problem) | 7 (14) | 2 (8) | 4 (18) | 0 | 1 | 18 (25) | 0 | 16 (55) | 0 | 2 (29) |

Statistical analyses: Comparing fecal incontinence (yes/no) between.
a) the total group of females and the total group of males ($p > 0.3$).*
b) the females with perineal fistula and the rest of the females respectively females with vestibular fistula ($p = 0.282$ respectively $p > 0.3$).*
c) the males with perineal fistula with the rest of the males respectively with rectourethral fistula ($p < 0.0001$ respectively $p < 0.0001$).*
d) the females with perineal fistula with the males with perineal fistula ($p = 0.006$)*.
* Fisher's Exact Probability Test, two-tailed.

incontinence when comparing perineal and vestibular fistula ($p > 0.3$, Kruskal–Wallis with post hoc test for rank data). Also severe incontinence (Krickenbeck grade 2 and 3) was equally reported in females with perineal and vestibular fistula (Fig. 4).

Comparison of all grades (0–3) of incontinence in males showed that those with perineal fistulas had a rank profile with less incontinence than the other male subtypes of ARM ($p < 0.001$, Kruskal–Wallis with post hoc test for rank data). In line with this, severe incontinence was significantly more common in the subgroups with recto-urethral fistula and no fistula compared with the males with perineal fistula (Fig. 4).

Among those with perineal fistula, severe incontinence was significantly more frequent among the females than among the males (Fig. 4).

The prevalence of severe incontinence did not differ between the lower and higher age groups, either for females or males with ARM (Fig. 5).

### 3.3. Constipation

The frequency of constipation (yes/no) was statistically higher among the females (62%) than among the males (35%). The frequency did not differ between the children with perineal fistulas and the rest of the subtypes of ARM, either for females or males (Table 6). For those with perineal fistulas, constipation was more frequent among the females than among the males. The frequency of constipation was similar for the females with perineal fistulas and those with vestibular fistulas (Fig. 6).

The rank of the different degrees of constipation (Krickenbeck grades 0–3) did not differ between the perineal fistulas and the rest of the subtypes of ARM in either gender ($p > 0.3$ Kruskal–Wallis post hoc test for rank data). The prevalence of constipation grade 3 (not manageable with diet or laxatives) did not differ between females and males with perineal fistulas ($p > 0.3$, Fisher's exact post hoc test) or between those with perineal fistulas and the rest of the subgroups in each gender ($p > 0.3$ in each comparison, Fisher's exact post hoc test).

The frequency of constipation did not differ significantly between the younger and older females with ARM. However, among the males constipation was less frequent in the higher than in the lower age group (Fig. 7).

### 3.4. Sacral malformation correlated to bowel symptoms

The frequency of sacral malformations did not differ between the females (28%) and males (23%), between the females and males with perineal fistula (17% and 9%, respectively) or between the females

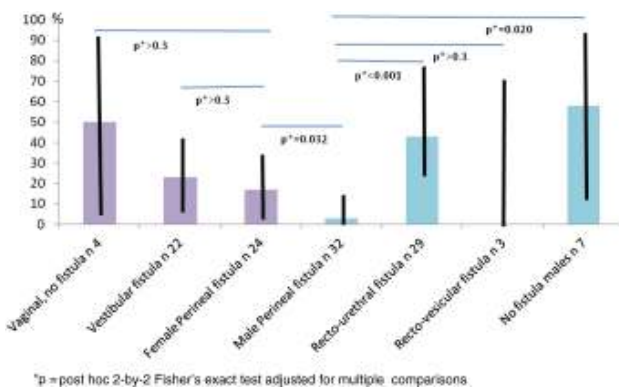


**Fig. 4.** Severe incontinence according to Krickenbeck grade 2 and 3 among children with anorectal malformation (ARM). Comparisons gender-wise between perineal fistulas and the rest of the subtypes of ARM with 95% confidence interval. n = number.

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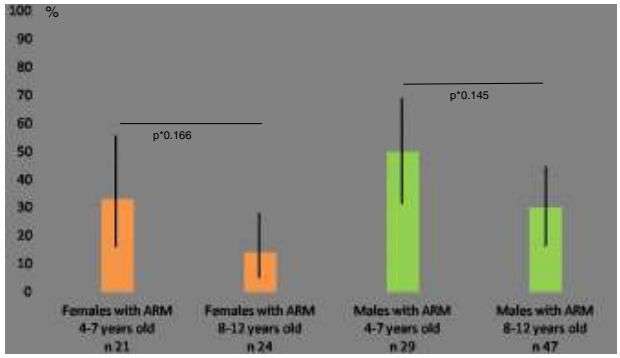


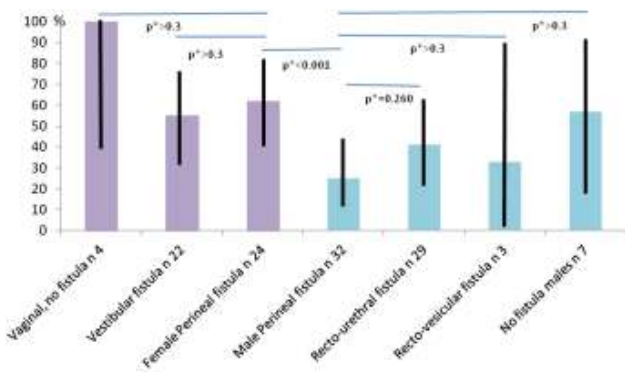

p*=post hoc tested 2-by-2 Fisher´s exact testadjusted for multiple comparisons

**Fig. 5.** Severe incontinence according to Krickenbeck grade 2 and 3 in the age groups 4–7 and 8–12 years. Comparison between the age groups for females and males with all subtypes of anorectal malformation (ARM) with 95% confidence interval. n = number.

**Table 6**
Constipation of different degrees according to the Krickenbeck follow-up in 121 children with anorectal malformations (ARM). n = number, (%).

| Constipation | Females Total | Females Perineal fistula | Females Vestibular fistula | Females Vaginal fistula | Females No fistula | Males Total | Males Perineal fistula | Males Recto-uretheral fistula | Males Recto-vesicular fistula | Males No fistula |
|---|---|---|---|---|---|---|---|---|---|---|
| **n** | 50 | 24 | 22 | 1 | 3 | 71 | 32 | 29 | 3 | 7 |
| **No** | 19 (38) | 9 (38) | 10 (45) | 0 | 0 | 46 (65) | 24 (75) | 17 (59) | 2 (67) | 3 (43) |
| **Grade 1 (diet)** | 3 (6) | 2 (8) | 1 (5) | 0 | 0 | 4 (5) | 3 (9) | 1 (3) | 0 | 0 |
| **Grade 2 (laxatives)** | 21 (42) | 11 (46) | 7 (32) | 1 | 2 (67) | 14 (20) | 4 (13) | 6 (21) | 1 (33) | 4 (57) |
| **Grade 3 (diet or laxatives are not enough)** | 7 (14) | 2 (8) | 4 (18) | 0 | 1 (33) | 7 (10) | 1 (3) | 5 (17) | (0) | (0) |

Statistical analysis: Comparison of the frequency of constipation (yes/no) between.
a) the total group of females and males, respectively, with ARM (p = 0.005).
b) the females with perineal fistula and the rest of the females (p > 0.3.)*
c) the males with perineal fistula and the rest of the males (p = 0.136).*
Gender specific statistical analyses regarding the ARM-subtypes are illustrated in Fig. 8.
* Fisher's Exact Probability Test, two-tailed.




*p = post hoc 2-by-2 Fisher's exact test adjusted for multiple comparisons

**Fig. 6.** Frequency of any grade of constipation (grades 1–3) according to Krickenbeck follow-up in children with anorectal malformation (ARM). Comparison between the perineal fistulas and the rest of the subtypes of ARM, gender-wise, with 95% confidence interval. n = number.

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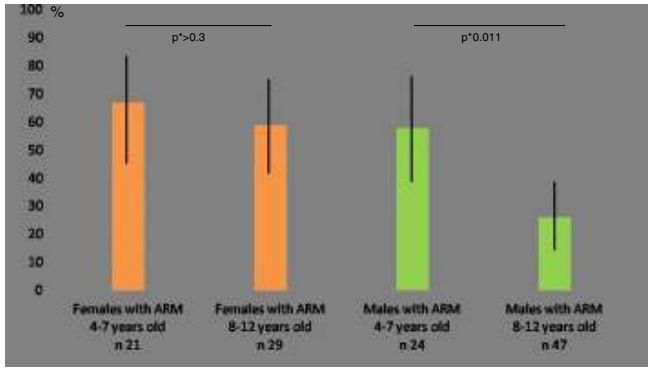


**Fig. 7.** Frequency of any grade of constipation (grades 1–3) according to Krickenbeck follow-up in the age groups 4–7 and 8–12 years for children with all types of anorectal malformation (ARM). Comparisons between the age groups, gender-wise, with 95% confidence interval. n = number.

with vestibular fistula (45%) and males with rectourethral fistula (31%) (Fig. 8).

Tables 7 and 8 show the correlation between bowel symptoms and sacral malformations in the gender specific subgroups of ARM. The only significant positive correlation found was that males with rectourethral fistulas and concomitant sacral malformations, had significantly less voluntary bowel movements (100%) and a higher frequency of fecal incontinence compared to those without sacral malformations (100% and 55%, respectively).

### 3.5. Discussion

The most important and new finding in this study is that females with perineal fistula seem to have a less favorable outcome than males

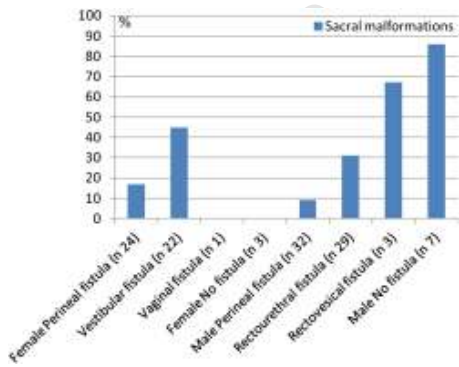


**Fig. 8.** Frequency (%) of sacral malformations in the different subgroups of anorectal malformations (ARM). n = number. Statistical analyses with comparison of the frequency of sacral malformations between: a) The total groups of females and males ($p = 0.672$)*. b) The females and males with perineal fistulas ($p = 0.686$)*. c) The females with perineal fistulas and vestibular fistulas ($p = 0.035$)*. d) The males with perineal fistulas and rectourethral fistulas ($p = 0.052$)*. d) The females with vestibular fistulas and males with rectourethral fistulas ($p = 0.384$)*. *Fisher's Exact Probability Test, two-tailed.

with the same malformation. In this patient population, females with perineal fistulas have the same outcome as those with vestibular fistulas. Consequently, the gender of a child with perineal fistula seems to be a factor that has to be taken into consideration when the prognosis for post operative bowel function is assessed.

There is a lack in the literature of gender specific analysis of the outcome after PSARP for perineal fistulas. Perineal fistulas are gathered into one gender mixed group, also in the Krickenbeck classification [3]. Contrary to our study, none of the other reports using Krickenbeck system [4,7,6] have evaluated females and males with perineal fistulas separately. As far as we are aware, similar gender specified results have not been demonstrated before.

Sacral anomalies have in some studies been associated with the outcome for bowel control in ARM-patients [12,13]. Interestingly, in the present study sacral malformation did not correlate with the outcome in the female ARM subtypes, the total group of females/males with ARM or perineal fistulas. The prevalence of syndromes was also the same for both genders with perineal fistulas. Therefore, the gender differences in functional outcome for perineal fistulas cannot be referred to either sacral malformations or an unequal frequency of syndromes.

It is difficult to speculate on the reasons for the gender different outcome. Anatomically there should not be any difference in the anorectal malformation. It would be unfortunate if the operation technique differed between the genders, but one could consider that a limited dissection of the rectum in females because of a fear of perforating the vagina, could lead to an incomplete rectoplasty. Another speculative reason for gender differences in bowel symptoms is that the anorectal malformation is less openly discussed with the females in their families [14]. Secondary to this, bowel management may fail, which in the long term could have a negative effect on the bowel control [15]. Other studies focusing on the gender differences in order to confirm or oppose our findings would be of value.

Since there are no previous studies separating females and males with perineal fistulas, it is not possible to make comparisons regarding the similar outcome for female perineal fistulas and vestibular fistulas. In the present study the frequency of concomitant malformations and sacral malformations was higher among the females with vestibular fistulas compared to the females with perineal fistulas. In spite of this, and that the anatomical features are supposed to differ between the subtypes, the outcome regarding incontinence and constipation was similar for those females. Since the numbers of

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**Table 7**
Correlation between sacral malformations and symptoms, in females with.

| Krickenbeck follow-up | | Female Perineal fistula n 24 | | | Vestibular fistula n 22 | | |
|---|---|---|---|---|---|---|---|
| | | Sacral malformations | | p-value[a] | Sacral malformations | | p-value[a] |
| | | Without n 20 | With n 4 | | Without n 12 | With n 12 | |
| **Voluntary Bowel Movements** | **Yes** | **17 (85)** | **2 (50)** | p = 0.179 | **9 (75)** | **7 (70)** | p > 0.3 |
| | **No** | **3 (15)** | **2 (50)** | | **3 (25)** | **3 (30)** | |
| **Fecal incontinence** | **No** | **13 (65)** | **1 (25)** | p = 0.272 | **8 (67)** | **3 (30)** | p = 0.198 |
| | **Yes** | **7 (35)** | **3 (75)** | | **4 (33)** | **7 (70)** | |
| Occasionally | Grade 1 | 5 | 1 | | 1 | 5 | |
| Every day, not a social problem | Grade 2 | 1 | 1 | | 0 | 1 | |
| Constantly, social problem | Grade 3 | 1 | 1 | | 3 | 1 | |
| **Constipation** | **No** | **9 (45)** | **0** | p = 0.259 | **6 (50)** | **4 (40)** | p > 0.3 |
| | **Yes** | **11 (55)** | **4 (100)** | | **6 (50)** | **6 (60)** | |
| Diet controlled | Grade 1 | 2 | 0 | | 1 | 0 | |
| Laxative | Grade 2 | 8 | 3 | | 4 | 3 | |
| Diet or laxative is not enough | Grade 3 | 1 | 1 | | 1 | 3 | |

[a] Fisher's Exact Probability Test, two-tailed.

patients in the various subgroups are relatively small, further studies are needed to assess gender specific outcome.

Without separation of female and male perineal fistulas, there are some earlier published studies of the outcome after PSARP where the Krickenbeck postoperative follow-up system has been used. One is a multicenter study [4] and there are also some comparable single center studies [7,9,6]. A similar distribution of the subtypes of ARM, as in this study, was found in two of those reports [4,7]. However the subtypes recto-bulbar and recto-prostatic fistulas had to be gathered into "recto-urethral fistula" in the present report since the Krickenbeck subtyping was not used in the early years of the study, and a retrospective interpretation was considered as unreliable.

The results from this study demonstrate a considerably poorer outcome compared with results from the single center studies [7,6] but in line with those from the multicenter study [4]. Severe incontinence (Krickenbeck grade 2 and 3) was reported by 24% in the present study and by 30% in the multicenter study. The frequency of severe constipation (Krickenbeck grade 3) was similar in the multicentre and our study, 15% and 12% respectively [4]. An even worse outcome regarding voluntary bowel movements was found in the present study where 37% did not have any voluntary bowel control compared with 24% in the multicenter study [4]. In contrast, better results were reported in our study than in the multicenter study [4] regarding "no incontinence" and "no constipation". The similarities and differences could be true or reflect the difficulties in interpreting the outcome according to the Krickenbeck follow-up and definitions of soiling and incontinence. The results could also reflect that the answers in our study were based only on those of the families and not on any objective examination of constipation as in the multicenter study [4].

Regarding evaluation of the outcome for the small groups of males with recto-vesicular fistula and females with no/vaginal fistula, we have too few patients to make any conclusion.

The outcome of the males with perineal fistulas in this report differed from a follow-up study of males with perineal fistulas, median age 9 years, where all the patients had voluntary bowel movements and mainly suffered from light soiling and light constipation [16,17]. Since the follow-up schedules were different, it is difficult to make a trustworthy comparison, especially regarding the severity of symptoms. One reason for the difference may be that the age of the males in the two studies differs. As the result in the present study suggests, constipation becomes less frequent as males with ARM grow older.

One potential bias in the present study was the perineal fistulas operated with cut-back and Y-V-plasty. However, in comparison of outcome there were no statistical differences in either gender.

**Table 8**
Correlation between sacral malformations and symptoms in 71 males with anorectal malformation (ARM).

| Krickenbeck Follow-up | | Male Perineal fistula n 32 | | | Rectourethral fistula n 29 | | | Rectovesical fistula n 3 | | Male No fistula n 7 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Sacral malformations | | | Sacral malformations | | | Sacral malformations | | Sacral malformations | | |
| | | Without n 29 | With n 3 | p-value[a] | Without n 20 | With n 9 | p-value[a] | Without n 1 | With n 2 | Without n 1 | With n 6 | p- value[a] |
| **Voluntary Bowel Movements** | **Yes** | **26 (90)** | **3 (100)** | >0.3 | **10 (50)** | **0** | **=0.011** | **0** | **2** | **1** | **1** | =0.287 |
| | **No** | **3 (10)** | **0** | | **10 (50)** | **9 (100)** | | **1** | **0** | **0** | **5 (83)** | |
| **Fecal incontinence** | **No** | **26 (90)** | **3 (100)** | >0.3 | **9 (45)** | **0** | **=0.027** | **1** | **1** | **0** | **1** | >0.3 |
| | **Yes** | **3 (10)** | **0** | | **11 (55)** | **9 (100)** | | **0** | **1** | **1** | **5 (83)** | |
| Occasionally | Grade 1 | 2 | 0 | | 3 | 0 | | 0 | 1 | 1 | 1 | |
| Every day, not a social problem | Grade 2 | 1 | 0 | | 0 | 1 | | 0 | 0 | 0 | 2 | |
| Constant, social problem | Grade 3 | 0 | 0 | | 8 | 8 | | 0 | 0 | 0 | 2 | |
| **Constipation** | **No** | **21 (72)** | **3 (100)** | >0.3 | **11 (55)** | **6 (67)** | >0.3 | **1** | **1** | **0** | **3 (50)** | >0.3 |
| | **Yes** | **8 (28)** | **0** | | **9 (45)** | **3 (33)** | | **0** | **1** | **1** | **3 (50)** | |
| Diet-controlled | Grade 1 | 3 | 0 | | 1 | 0 | | 0 | 0 | 0 | 0 | |
| Laxative | Grade 2 | 4 | 0 | | 5 | 1 | | 0 | 0 | 1 | 3 | |
| Diet or laxatives is not enough | Grade 3 | 1 | 0 | | 3 | 2 | | 0 | 1 | 0 | 0 | |

The number of males with rectovesical fistulas was too small for statistical comparison. n = number (%).
[a] Fisher's Exact Probability test, two tailed.

Please cite this article as: Stenström P, et al, Bowel symptoms in children with anorectal malformation — a follow-up with a gender and age perspective, J Pediatr Surg (2013), http://dx.doi.org/10.1016/j.jpedsurg.2013.10.022

Bowel function reported by the ARM patients in this study was compared with bowel symptoms reported in a Finnish population of normal children aged 4–12 years assessed by the Rintala scale [18]. Since the evaluation differed from the Krickenbeck follow-up scheme, the comparisons of the severity of symptoms had to be approximated. In the present study fecal incontinence occurred in 48%/42% of all females/males with ARM and severe incontinence in 36%/37%. In the normal population 43% had some incontinence but only 1% had severe problems. Thus, children with ARM suffer significantly more from severe incontinence than healthy children. Also constipation was reported more frequently among the patients than the normal population. 11% of the healthy children reported constipation compared to 62% females and 35% males with ARM in this study. The lowest prevalence of constipation was found among the males with perineal fistulas (25%), but still this figure was twice that of the normal population. The information that light soiling and constipation are normal phenomena among children in general is important when initiating bowel management for patients with ARM. The goals should not be set too high but instead aimed to reach "social continence" [19].

The secondary aim of the study was to map if bowel symptoms differed between the younger and older age group. Improvement of bowel related symptoms over time among children with ARM has been suggested [20] and also shown in some few patients in a longitudinal follow-up until 15 years of age [10]. The result from this study did not show less incontinence in the older age group or less constipation for older females with ARM. Still the oldest children in the study were only 12 years old, and there may be improvements later on in adolescence [14].

Weaknesses with the present age-related comparisons are that this was not a longitudinal study and that all subtypes of ARM were gathered together. Caution is therefore advisable when drawing conclusions about the symptom development over time in the different ARM-subtypes.

In conclusion, the results from this study suggest that bowel symptoms in a child with ARM depend on both gender and subtype of ARM. Females and males with perineal fistulas should not be expected to have a similar prognosis, while females with perineal and vestibular fistulas have a similar outcome.

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Please cite this article as: Stenström P, et al, Bowel symptoms in children with anorectal malformation — a follow-up with a gender and age perspective, J Pediatr Surg (2013), http://dx.doi.org/10.1016/j.jpedsurg.2013.10.022

# Paper IV

# Pelvic floor in females with anorectal malformations – findings on perineal ultrasonography and aspects of delivery mode

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Running title: Pelvic floor in females with anorectal malformations
Key words: Anorectal malformation, Pelvic floor, Sphincter anatomy, Ultrasonography, Delivery

## Abstract

Background: Advice on the mode of delivery to females born with anorectal malformation (ARM) is needed. The primary aim was to evaluate the anatomy of the pelvic floor muscles in females with ARM operated with posterior sagittal anorectal plasty (PSARP). The second aim was to correlate the extent of muscle defects to the bowel symptoms.

Methods: This interventional study with perineal 4D/3D ultrasonography describes the smooth muscles in the intestinal wall (neo-IAS), external sphincter, levators and anal canal using a muscle score (0-6 worst). The bowel symptoms were prospectively registered with Krickenbeck criteria score (0-7 worst).

Results: Forty females with different subtypes of ARM, median age 13 (4-21), were followed up regarding bowel symptoms. Seventeen were examined with ultrasonography. Bowel symptoms were similar for those examined with ultrasonography and those not, median score 5 and 3 (1-7) respectively, (p=0.223, Fisher's exact test). All the females had at least one muscular defect. There was no significant correlation between muscle defects and bowel symptoms (p=0.094, Spearman's correlation).

Conclusion: Females with ARM have considerable defects in the pelvic floor without any significant correlation to bowel symptoms. Caesarian section seems to be the safest delivery mode for this patient group.

# Introduction

The prevalence of anorectal malformations (ARM) among females is 15/100000 live births. ARM includes a spectrum of anomalies in the pelvic floor with different subtypes of ARM [1]. All children born with ARM need a reconstructive operation in order to have the rectum located in the center of the sphincter complex. The reconstruction is mainly Posterior Sagittal Anorectal Plasty (PSARP), implemented worldwide in the late 80s [2] .

The long term outcome after PSARP is reported to depend especially on the ARM-subtype [3-5]. Among adolescent and adult females with different types of ARM, fecal incontinence is reported by 40-67% and lack of voluntary bowel control by 15-30 % [3,6,7].

The length of follow up time of adult females with ARM operated on with PSARP is limited since the oldest PSARP-operated patients are 20-25 years old. Therefore few are of child bearing age and reports on deliveries are scarce. In view of this it is of interest to evaluate the anatomy of the pelvic floor among females with ARM.

Anal continence is dependent on the internal anal sphincter (IAS), the striated external anal sphincter (EAS) and M. levator ani [8,9]. In females with ARM the muscles and innervation deviate due to the malformation. The original IAS is suggested to be rudimentary in the distal fistula [10,11] and can be resected during the PSARP [2,12]. Furthermore, during the PSARP, the EAS is divided both anteriorly and posteriorly, and M. levator ani is involved in the reconstruction [2,13].

Patients born with ARM in most cases lack the normal rectal properties such as a normal volume adaptation, the rectal sensibility might be compromised and a normal recto anal inhibitory reflex is often missing [14-17]. Sacral and spinal anomalies may influence the bowel control [3,5,18]. Therefore bowel control might depend heavily on the muscle capacity.

When females with ARM become pregnant the question of mode of delivery may be an overlooked topic for some reason. Some females with ARM may have not been given enough information to be able to speak about their malformation or reconstruction [7]. The midwife or obstetrician may be unfamiliar with the diagnosis ARM [19]. Their life-long adaption to the symptoms may lead to young females perceiving their fecal, urinary or gas incontinence as a “normal” condition and therefore this is not mentioned, unless specific questions are asked [7,20]. Furthermore, the scars after the PSARP reconstruction may not be obvious or thoroughly understood by those who are not familiar with ARM.

This study aims at contributing to the knowledge of the anatomy of the pelvic floor among young females with ARM operated on with PSARP. The primary aim of the study was to evaluate the pelvic floor muscles involved in the control of fecal continence in females with ARM operated on with PSARP using perineal ultrasonography. With this knowledge, better guidance with respect

to mode of delivery could be given. The second aim was to correlate the severity of muscle anomalies to the severity of bowel symptoms, in order to evaluate if the patients' history of bowel symptoms could provide information enough to support the decision of the mode of delivery.

## Patients

The study included all females born with ARM between January 1990 until March 2009 who had been admitted to the Department of Pediatric surgery, a tertiary center which covers an area with 2 million inhabitants with free health care. ARM is divided into different subtypes according to the Krickenbeck classification which is based on the entry of the fistula from rectum [1]. Since we intended to describe the pelvic floor only after reconstruction with PSARP, limited PSARP or Posterior Sagittal Ano Rectal Vaginal Urethro Plasty (PSARVUP) [13] those with other treatments, as anal stenosis and rectal atresia, were excluded. In the end 54 females born with the subtypes rectoperineal fistulas, rectovestibular fistulas and cloacas remained (Figure 1a-c). Of these, 14 could not be included in the follow up because of death, severe syndromes or migration (Figure 2).
All of the remaining 40 females were followed up regularly at the department and 30 of these were invited to take part in the study which included perineal ultrasonography and registration of bowel symptoms. They belonged to the following groups:
1. Sixteen females, 14-21 years old, had their last medical consultation at the Department of Pediatric Surgery before transfer to adult medical care
2. Ten females, 10-13 years old, were planned for the regular pre-pubertal follow-up
3. Four females, 4-9 years old, were planned for general anesthesia for other reasons
The remaining 10 females were too young, 4-9 years old, and not planned for other general anesthesia for other reasons. Therefore they were not asked to participate in the examination with ultrasonography, but asked and agreed to being controls regarding bowel symptoms (Figure 2).

## Method

This is a prospective and descriptive interventional study. The study was conducted from July 2011 until May 2013. The patients were collected from the prospectively maintained database with all children with ARM in the region. The invitation to the study was made during the regular follow-ups at the Department of Pediatric Surgery.

**Classification:** The ARM were classified according to international standard of Krickenbeck classification [1] (Figure 1a-c and Table 1).

**Operation method:** The reconstruction of anus was performed within the first months of life, and the standard procedure was PSARP [2]. During PSARP there is a incision performed in the midline of the pelvic floor, all the way from coccygus to vagina. The

fistula and additionally 2 cm of rectum is resected. Rectum is mobilized to the center of the sphincter complex. The posterior rectum is fixed to the adapted posterior levators, the perineal body is built up and the external sphincter adapted both posteriorly and anteriorly. An anastomosis is established between full thickness rectum and the skin. Limited PSARP, used for perineal fistulas, is similar to PSARP but the incision in the midline is shorter and the operation more shallow. PSARVUP, used for cloacas, is a more complicated and extensive variant of PSARP, adding a separation and mobilization of urethra and vagina [2,13]. All the operations were performed or supervised by three pediatric surgeons with a colorectal profile. Diverting colostomy was used in the neonatal period for the females with cloaca and vestibular fistulas [21].

**4D/3D perineal ultrasonography:** The ultrasonography examination of the pelvic floor was performed with the patient in the dorsal lithotomic position. The transducers (M6C, RSP6, system Voluson E8 GE) were held to allow a sagittal inspection of the levator ani and the anal sphincter complex [22,23]. All scans were saved in 3D. If the subjects were awake they were instructed to squeeze their pelvic muscles using a 3D/4D mode [22,24]. The scans were saved on a computer and analyzed off-line by a trained sonographer (AÖ).

**The description of muscles and anal canal:** Descriptions focused on the deep and subcutaneous parts of the EAS, the neo-IAS, the levators and the distal part of the anal canal where the rectum is supposed to meet the skin. The evaluation of the EAS was made based on the possible diastase between the ends of the circular muscle anteriorly (Figure 3b). Up to 15 degrees was considered to represent only scars after the PSARP, while a diastase >15 degrees was determined as a real defect in the muscle [15]. The neo-IAS i.e. the inner circular muscle layer, was measured and evaluated as fragmented or not. It was measured above the anastomosis or above the diastase between rectum and skin, described below (Figure 3b).

The M. levator ani was described as with or without any visible disruptions. When the subjects were awake they were asked to squeeze and push.

The anal canal in some females with ARM clinically often diverts from others. A defect between rectum and the skin may be present, with a secondary "pocket" beneath the perineal skin. This discontinuation of both the intestinal wall and subcutaneous tissue was measured in mm. A distance of 5 mm was considered as scar, while >5 mm was considered as a defect (Figure 3c).

In order to correlate the defects of the muscles to the severity of symptoms, a scoring of the muscles was performed with 1 point for every deviation (Table 3). Diastases in both the deep and superficial parts of EAS were considered as serious and thus given two points. The score ranged from 0-6 (6=worst).

**Bowel symptoms**: The bowel symptoms were registered according to the Krickenbeck functional criteria [1] (Table 2). The registration of bowel symptoms

with the criteria is done routinely in the medical records and in the prospectively maintained database. The bowel symptoms were converted to a scoring system that had been used in a previous report [5]. The score ranged from 0-7(7= worst) (Table 2).

**Anesthesia**: All the females under 15 years of age were examined during general anesthesia performed with Propofol®, Sevoran gas® and Ultiva®. The older females were awake during the examination.

### Statistical considerations

A statistician performed the statistical analyses. The comparisons of bowel symptoms were analyzed with Fisher's two tailed exact test for dichotomous results and with the exact Kruskal-Wallis test for ordinal or numeric test variables. Spearman's rank correlation was used for assessing the correlation between the non-parametric muscle score (0-6) and Krickenbeck symptom score (0-7) and between the defect distance in the anal canal and the severity of fecal incontinence. Possible associations between fecal incontinence (Yes/No) and anatomical defects in neo-IAS or the whole EAS were analyzed by using Chi square tests. P-values below 0.05 were considered significant. Statistical computations were performed by using SPSS statistics software (PASW/SPSS software, version 18, IBM Corporation, Armonk, NY, USA).

### Ethical consideration:

The regional research ethics committee approved the study (registration number 2010/49). Every patient <18 years old had a written consent by their parents.

## Results

**Patients:** All 40 females were followed up regarding their bowel symptoms. Out of the 30 who were asked to be examined with transperineal ultrasound, 17 (57%) agreed (Figure 2). Five were awake during the examination.

The median age of all the females was 13.5 (4-21). The median age among those examined with ultrasonography and registration of bowel symptoms was 15 (4-21) and among those followed up without ultrasonography 11 (4-20). All the anorectal reconstructions were performed within the patients' first 6 months of life, and the median time of follow -up postoperatively among all the females was 13 years (4 – 21). The frequency of the different subtypes of ARM among the females was similar to previously reported frequencies (Table 1).

**Muscle components:** The muscle defects in each patient and the total frequencies of the defects are presented in Table 5. None of the females had any rupture of the M. levator ani. All the females who were awake during the examination had a good control of the levators. The most frequent finding was fragmented IAS. In 11 females diastases in both the deep and superficial component of the EAS were identified (Figure 3b and 4a). A majority

of the patients had a gap of >5 mm from the rectum to the skin anteriorly where also a lack of tissue under the superficial EAS and the skin was found (Figure 3c and 4b).

**Bowel symptoms:** The distribution of patients with voluntary bowel movements, fecal incontinence or constipation did not differ between the subtypes of ARM among those examined with or without ultrasonography. Neither were there any statistically significant differences found for the score between the groups (Table 4 and Figure 5). Thus the group investigated with ultrasonography can be considered to be representative for all 40 females in terms of bowel function.

**Correlations** The number of defects in the muscles and the severity of bowel symptoms did not correlate significantly even though the correlation coefficient was positive (Figure 6). No significant correlation was shown between the diastase distance between rectum and skin and more severe (grade 2-3) fecal incontinence (p=0.031, Spearman´s correlation), fecal incontinence (Yes) and fragmentation of neo-IAS (p=0.331, Chi-square test) respectively, to defects >15 degrees in the whole EAS (p=0.549, Chi-square test).

# Discussion

This is the first study to report the pelvic floor anatomy with focus only on females with ARM. It is also the first report using 4D/3D perineal ultrasonography as a method to describe the sphincter anatomy in females with ARM.

The main findings were that all females with ARM had at least one deviation from normal anatomy. There was no correlation between the number or types of defects and the severity of fecal incontinence. The diastase between rectum and skin anteriorly in the anal canal has never been illustrated before.

In 11/17 of the examined females the rectum did not reach the skin and a subsequent pocket under the skin and superficial EAS was found (Figure 3c and 4b). One reason for this could be an insufficient mobilization of the rectum with a subsequent tension and diastase. Another reason could be a postoperative infection, with a secondary rupture or substantial defect. However, the clinical relevance of this finding remains unclear.

Fragmentation of neo-IAS was, surprisingly enough, noted in a majority of the females. We expected the neo-IAS to be unharmed, because of the mobilization of full thickness intestinal wall during the PSARP. The fragmentation may be due to accidental damage during the PSARP or because of repeated dilatation of the neo-anus during the postoperative course. The relevance of the findings is unclear since the function of neo-IAS in ARM is unknown. Since there is some evidence that the original IAS may be located in the fistula, fistula saving surgery in ARM has been provoked [10,11]. In our cohort of patients the PSARP procedure was carried out according to the original PSARP and the latest recommendations, with resection of the fistula [2,12]. In the present study no correlation was found between fragmented neo-IAS

and fecal incontinence. In contrast, previous studies on rectal sonography in children with ARM, have shown a positive correlation between the number of scars in IAS and incontinence [14,15]. However these studies do not clarify whether the original IAS or neo-IAS has been measured. The same studies report EAS as incompletely adapted in a majority of the patients [14,15]. Those findings on EAS are similar to ours.

The levators in all females in this study were complete, even though some were separated. The role of the levators in healthy women is thought to contribute to fecal- and especially urinary continence [25]. Maybe the females with ARM and extensive scars in EAS, but acceptable continence, have managed to compensate the harmed neo-IAS and EAS with increased control of the intact levators. If so, the levators in women with ARM may play a very important role for continence.

The bowel symptoms among the females with ARM did not correlate to the status of the sphincter anatomy, even though there was a trend (Figure 6). Only weak correlations between EAS disruptions and fecal incontinence have been shown previously [15,26]. We therefore conclude that only the medical history of a patient with ARM, is not enough to decide the status of the sphincter complex. Secondary to this, the mode of delivery cannot be based on the patients' history.

A possible bias in the study may be the selection of females who agreed to be examined with ultrasonography. However in the material analysis, there were no significant differences in bowel symptoms. The number of patients examined with ultrasonography is low and the three variants of ARM in the study may limit the general conclusions. The pelvic floor architecture may change over life time [27] and the heterougenous age group in the present study, may be a limitation. Another factor to consider is that perineal ultrasound is new and not a technique usually reported, so comparisons with previous results from MRI and rectal ultrasound are difficult. Furthermore there are no standardized dimensions for the muscles in the anal channel or pelvic floor for females <18 years of age. Therefore the score of the muscles in this study was basic and broad. Besides, the measurement of the sphincter was performed in 5 awake females and during anesthesia in 12 females. It is known that general anesthesia may influence the tonus of the sphincter muscles. However, the results for neo-IAS, EAS and the anal canal are not likely be influenced by the anesthesia. From this experience we think that 4D/3D perineal ultrasound in the future could be useful in clinical practice, also for children <12 years of age, without anesthesia, since it is non-invasive.

The physical outcome regarding bowel control and urinary leakage in gender mixed groups of patients with ARM and in males, has been reported to depend on concomitant spinal or sacral defects [3,5,18,28]. The focus in the present study was only the muscular status, but in a predelivery consultation it would be of importance also to consider possible sacral anomalies.

During vaginal delivery in primiparas without ARM 93% experience obstetrical tears and 0.9-17.8% sustain a sphincter rupture [29-31]. If such ruptures were to occur during a vaginal delivery in a female with ARM, the reconstruction would be difficult since the anatomy already from before deviates from normal, as described in the present study. Additionally, 20-35% of the patients with ARM may have sacral and spinal cord deviations [3,5,32] which may make the patient with ARM even more vulnerable for secondary incontinence. After vaginal delivery 30% have avulsions in the levators and another 30% lack control of the levators [24,33]. Then, if a levator injury were to occur in a patient with ARM, whose fecal continence may depend on the levators, the risk of incontinence would probably be high. Further, in obstetric sphincter injuries the incontinence scores increase after a second vaginal delivery [34]. The usual recommendation to females with a previous sphincter rupture and anal incontinence is to deliver through caesarian section [35,36] although there are no good predictors on those with functional deficits and who will be worse after a vaginal delivery [37]. According to our results, the status of the EAS and neo-IAS in females with ARM is comparable to a previous sphincter rupture. Consequently vaginal delivery in females with all types of ARM, not only cloacas [19], is not to be recommended.

In conclusion the sphincter structures responsible for fecal continence in females with ARM divert considerably from a normal anatomy. The patients' bowel symptoms do not indicate the status of the pelvic floor, and could not be the only information to rely on in the pre-delivery consultation. All women with ARM would likely benefit from individualized evaluations, but according to this study the pelvic floor in females with ARM does not seem to allow a vaginal delivery.

## Acknowledgements to:

Gillian Sjödahl, Lexis English for Writers, Lund Sweden, for linguistic revision of the manuscript.

Håkan Lövkvist, biostatistician at the Competence Centre for Clinical Research, Skåne University Hospital, LUND, Sweden, for statistical advice

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**Table 1** Standards for the International Krickenbeck Classfication of Anorectal malformation (ARM) [1]. The table illustrates the different subtypes of ARM, the previously reported distribution [2,3] and the prevalence of the subtypes among the females included in the present study.

| **Subtypes of ARM among females** | Reported prevalence among females with ARM | Distribution among the 40 females with ARM in the present study |
|---|---|---|
| **Recto-perineal fistula** | 48% | 50% |
| **Recto-vestibular fistula** | 37-44% | 40% |
| **No fistula** | 1-6% | 0% |
| **Recto-vaginal fistula** | 1-2% | 0% |
| **Cloaca** | 3%-13% | 10% |
| **Rectal atresia** | 1-3% | Excluded |
| **Anal stensois** | 1-5% | Excluded |

**Table 2** Krickenbeck criteria of bowel symptoms in patients with anorectal malformations (ARM) [1] and a conversion to a scoring system 0-7 (7=worst).

| **Krickenbeck postoperative follow -up for ARM** | | |
|---|---|---|
| **Symptoms** | **Answer** | **Score** |
| **1. Voluntary bowel movements** Feeling of urge, capacity to verbalize, hold the bowel movements | Yes | 0 |
| | No | 1 |
| **2. Soiling** | No | 0 |
| Grade 1 | Occasionally (1-2 times /week) | 1 |
| Grade 2 | Every day, no social problem | 2 |
| Grade 3 | Constant, social problem | 3 |
| **3. Constipation** | No | 0 |
| Grade 1 | Manageable by diet | 1 |
| Grade 2 | Requires laxatives | 2 |
| Grade 3 | Resistant to diet and laxatives | 3 |

**Table 3** Description of defects in the pelvic floor and sphincter registered with 4D/3D perineal ultrasonography with a scoring of 0-6 (0= no defects, 6= defects in every components). The diastase in the external sphincter (EAS) is measured anteriorly.

| **Structure** | **Finding** | **Score (0-6)** |
|---|---|---|
| M. Levator Ani | Complete | 0 |
| | Disrupted | 1 |
| Neo-internal anal sphincter (neo-IAS) | Complete | 0 |
| | Fragmented | 1 |
| External anal sphincter (EAS) | Complete | 0 |
| Deep part | Diastasis > 15 degrees | 1 |
| Superficial part | Complete | 0 |
| Both deep and superficial parts | Diastasis > 15 degrees | 1 |
| | Diastasis >15 degrees | + 1 |
| Anal canal | No diastasis | 0 |
| Rectum to the skin anteriorly | Diastasis > 5 mm | 1 |

**Table 4** The distribution of the subtypes of anorectal malformation (ARM) and the bowel symptoms in each sybtype. The table illustrates those followed up with ultrasonography (US) and those without.

| Krickenbeck follow-up | | Females attending the study with perineal ultrasound | | | | Females followed up without perineal ultrasound | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Total n 17 | Perineal Fistula n 9 | Vestibular Fistula n 5 | Cloaca n 3 | Total n 23 | Perineal Fistula n 12 | Vestibular Fistula n 10 | Cloaca n 1 |
| Voluntary Bowel Movements | Yes | 10 | 5 | 4 | 1 | 17 | 10 | 6 | 1 |
| | No | 7 | 4(a) | 1(a) | 2(a) | 6 | 2(d) | 4(d) | 0(d) |
| Fecal incontinence | No | 2 | 2 | 1 | 0 | 7 | 5 | 2 | 1 |
| | Yes | 15 | 7(b) | 4(b) | 3(b) | 15 | 7(e) | 8(e) | 0(e) |
| Occasionally | Grade 1 | 3 | 2 | 1 | 0 | 5 | 3 | 3 | |
| Every day, not a social problem | Grade 2 | 10 | 4 | 2 | 3 | 6 | 3 | 3 | |
| Constantly, social problem | Grade 3 | 2 | 1 | 1 | 0 | 5 | 1 | 2 | |
| Constipation | No | 0 | 0 | 0 | 0 | 3 | 2 | 1 | 0 |
| | Yes | 17 | 9(c) | 5(c) | 3(c) | 20 | 10(f) | 9(f) | 1(f) |
| Diet controlled | Grade 1 | 2 | 1 | 1 | 0 | 3 | 4 | 2 | 1 |
| Laxative | Grade 2 | 9 | 5 | 2 | 2 | 8 | 4 | 1 | 0 |
| Diet or laxative is not enough | Grade 3 | 6 | 3 | 2 | 1 | 9 | 2 | 6 | 0 |
| Median Krickenbeck score 0-7 (7=worst) | | 5 (1-7) | 5(1-6) | 4(3-7) | 5(4-6) | 3(0-7) | 2(0-6) | 4(0-7) | 1 |

**Total symptom score** among those examined with US compared to without US p= 0.223 (Kruskal-Wallis)

**Total symptom score compared between the different ARM-subtypes** among those examined with US p=0.767 respectively without US p=0.120, respectively for all patients p= 0.485 (Kruskal Wallis)

**Comparison of bowel symptoms between those examined with US and without US regarding:**

Voluntary Bowel Movements: (a) with US p=0.197 and (d) without US p=0.178 and for all patients p=0.701 (Pearson Chi-square)

Fecal incontinence: (b) with US p= 0.461 (e) without US p= 0.276 and for all 40 patients p=0.378 (Kruskal-Wallis)

Constipation (c) with US p=0.978 and (f) without US 0.085 and for all 40 patients p=0.343 (Kruskal-Wallis)

**Table 5** Females with anorectal malformation (ARM) 4-21 years old examined with perineal ultrasonography. Evaluation of the muscles responsible for fecal continence and bowel symptoms.

| | | M. Levator Ani | Neo-Internal sphincter (neo-IAS) | External sphincter (EAS) | | | Anal canal | Muscle score | Krickenbeck score |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Deep part anteriorly | Subcutaneus Part anteriorly | Both components | Distal anterior rectum to skin | 0-6 (worst 6) | 0-7 (worst 7) |
| | Subtype of ARM | Disrupted | Fragmented | Diastase >15 degree | Diastase >15 degree | Diastase | Diastas >5 mm | Definition of muscle scoring (Table 3) | Definitions of symptom scoring (Table 2) |
| 1. | Perineal | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 4 |
| 2. | Perineal | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 2 |
| 3. | Perineal | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 6 |
| 4. | Perineal | 0 | 1 | 1 | 1 | 1 | 0 | 4 | 1 |
| 5. | Perineal | 0 | 1 | 1 | 1 | 1 | 0 | 4 | 4 |
| 6. | Perineal | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 5 |
| 7. | Perineal | 0 | 0 | 1 | 1 | 1 | 0 | 3 | 5 |
| 8 | Perineal | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 6 |
| 9. | Perineal | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 7 |
| 10. | Vestibular | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 7 |
| 11 | Vestibular | 0 | 1 | 1 | 0 | 0 | 0 | 2 | 3 |
| 12 | Vestibular | 0 | 1 | 1 | 1 | 0 | 1 | 4 | 3 |
| 13. | Vestibular | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 4 |
| 14. | Vestibular | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 7 |
| 15 | Cloaca | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 4 |
| 16. | Cloaca | 0 | 1 | 1 | 1 | 1 | 0 | 4 | 6 |
| 17. | Cloaca | 0 | 0 | 1 | 1 | 1 | 1 | 4 | 5 |
| | | | | | | | | | |
| | **Total** | 0 | 14 | 13 | 12 | 11 | 11 | Median 4 (2-5) | Median 5 (1-7) |

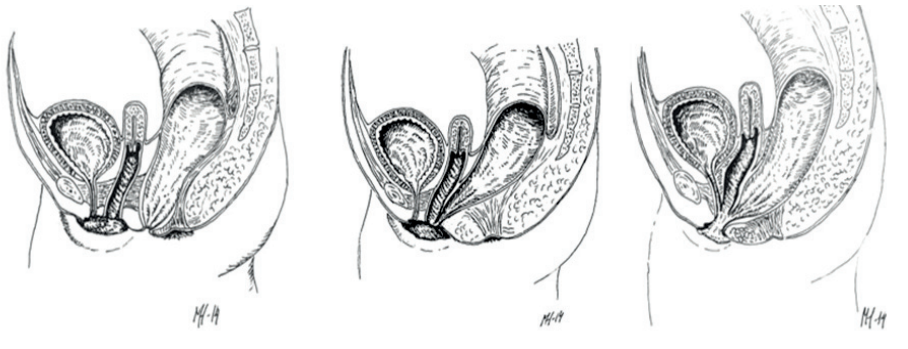

**Figure 1 a-c** Illustration of female types of anorectal malformation (ARM): Anatomical features of the three different subtypes of ARM in the present study a) Recto-perineal fistula b) Recto-vestibular fistula c) Cloaca.

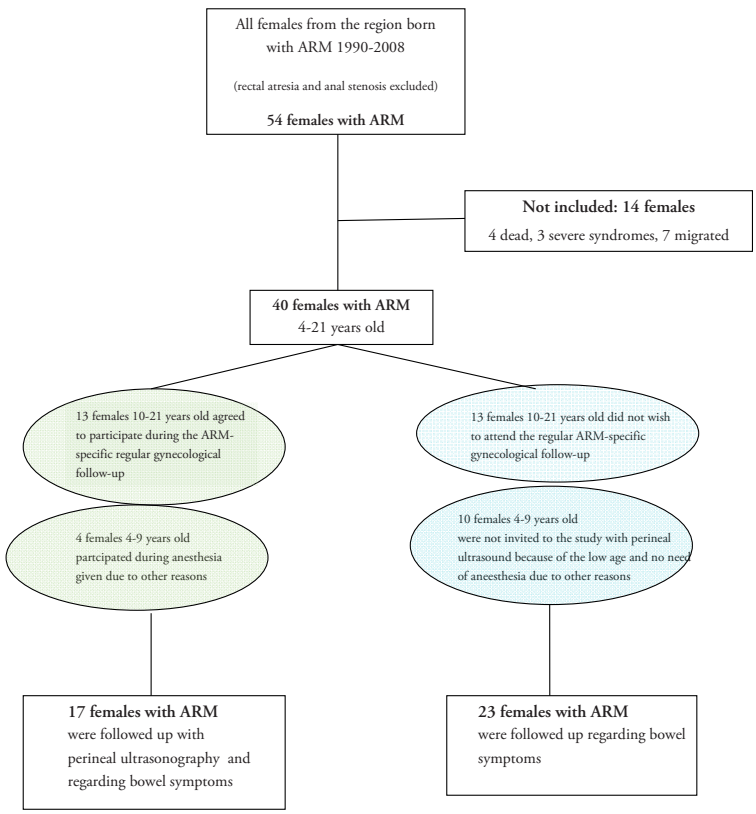


**Figure 2** Flow diagram: Females with anorectal malformation (ARM) born in the region, exluding anal stenosis and rectal atresias.

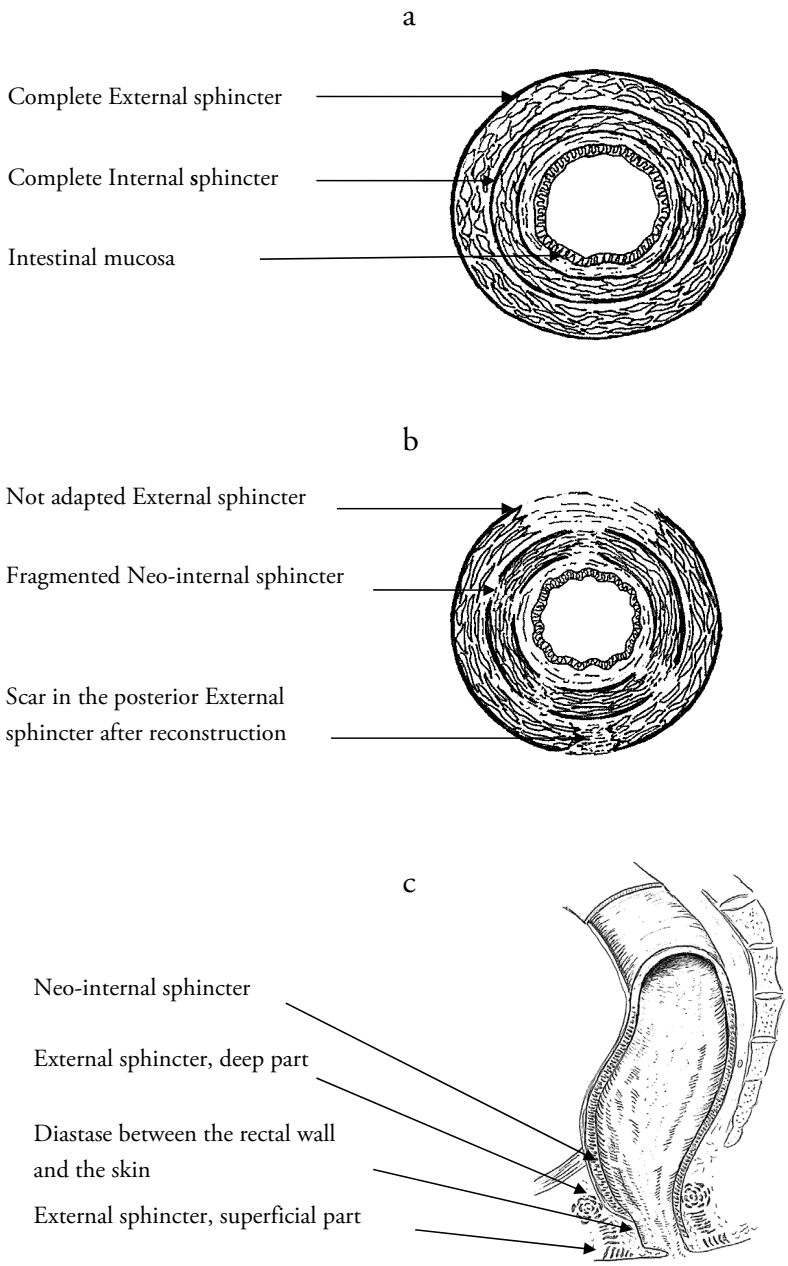


**Figure 3 a-c** Illustrations of sphincter anatomy: a) Cross section illustration of the normal anatomy of rectum. b) Cross section illustration of the rectum in ARM. c) Longitudinal illustration of the rectum and sphincter with findings in the anal canal in a majority of the females with ARM.

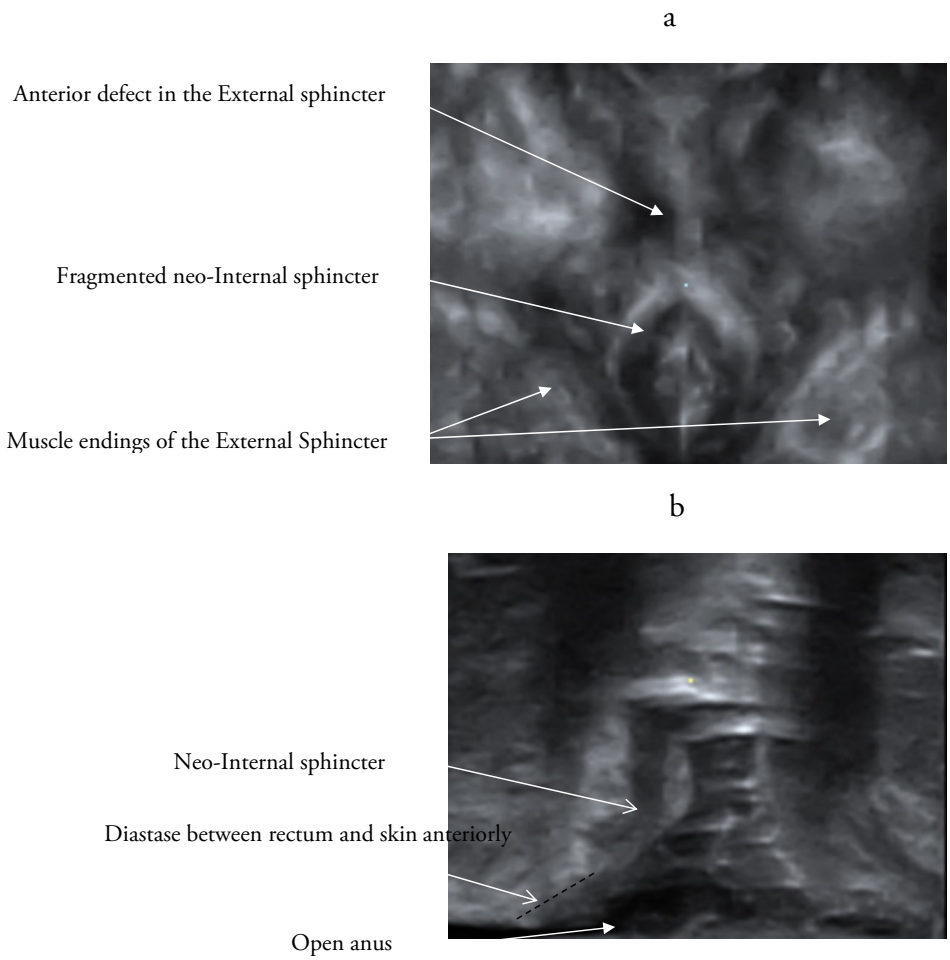


**Figure 4 a-b** Perineal ultrasonography: Pictures of typical findings in females with anorectal malformation. a) Cross sectional picture b) Longitudinal picture.

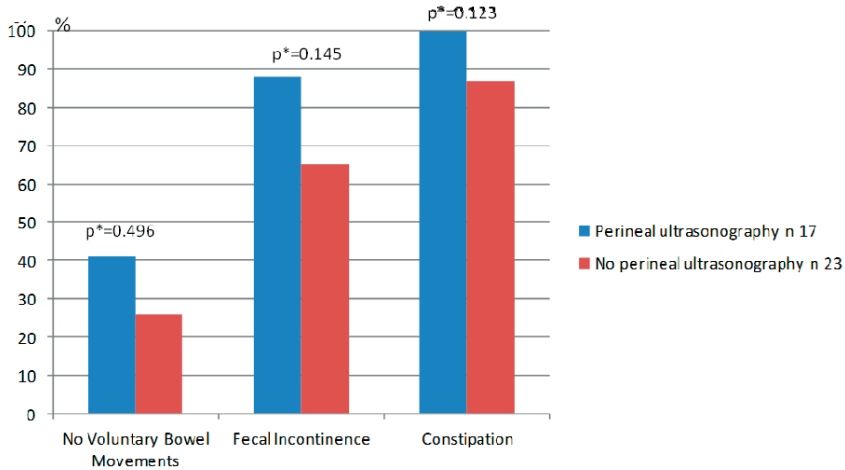


**Figure 5** Prevalence and comparison of bowel symptoms: Bowel symptoms (Yes/No) among females with anorectal malformation (ARM) followed up with perineal ultrasound and without. n= number patients *=Fisher's 2-sided exact test.

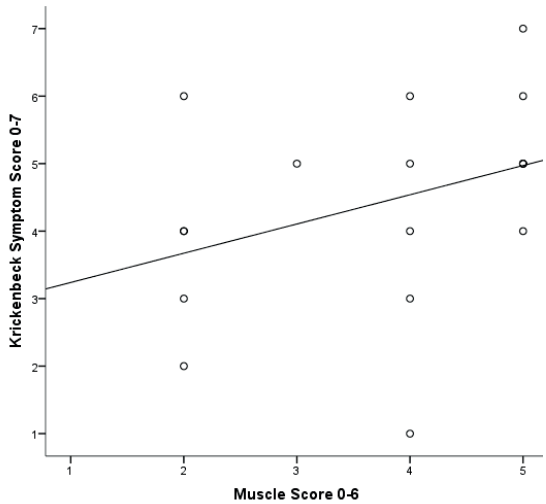


**Figure 6.** Correlation between pelvic floor anomalies and bowel symptoms: Correlation between muscle score (0-6 worst) and Krickenbeck symptom score (0-7 worst). The figure illustrates a lack of significant correlation between the numbers of muscle defects and the bowel symptoms in females with anorectal malformation (ARM). Correlation coefficient 0.419, p= 0.094 (Spearman's correlation test).