Isolated puborectalis muscle contraction is a common cause of dyssynergic defecation in constipated adolescents and adults with anorectal malformations

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Abstract

Background We aimed to evaluate the etiologies of constipation in adolescents and adult patients with anorectal malformations with colon transit time and high resolution anorectal manometry.

Methods We included twenty-five patients from the Odense University hospital in Denmark. Written and verbal informed consent was obtained. Patients were subjected to colon transit time examination and high resolution anorectal manometry. Presence of constipation was diagnosed based on the Rome IV criteria. Questionnaires regarding functional bowel outcome and severity of constipation were filled in.

Results The median age was 18 (14-24) and 48% (12/25) were females. Fifty-two % (13/25) of patients were diagnosed with constipation. Most frequent type of anorectal malformation was anocutaneous fistula (9/25), vestibular fistula (8/25) and urethral bulbar fistula (4/25). No difference in either total colon transit time nor segmental colon transit times were found based on the presence of constipation. Constipated patients and patients without constipation were equal on manometric parameters. Only four of the constipated patients fulfilled criteria for dyssynergic defecation with dyssynergic defecation pattern and prolonged colon transit time. A Type I dyssynergic pattern was dominant in constipated patients as it was detected in 54% (7/13). Dyssynergic defecation pattern was due to isolated contraction of puborectalis muscle in 69% (9/13) of constipated patients.

Conclusions We found a dyssynergic defecation pattern during attempted defecation in patients with anorectal malformations disregarded the presence of constipation. In the majority of constipated patients an isolated contraction of the puborectalis muscle was visualized with high resolution anorectal manometry. Trial registration: ClinicalTrials.gov. (NCT02624232).

1. Background

Anorectal malformation (ARM) is an inborn anomaly affecting approximately one out of 2500 newborns. Constipation is a common finding in patients operated for ARM with a reported incidence ranging from 22 to 87 % at the age above 10 years. In the general population constipation is reported in up to 30 % and dyssynergic defecation (DD) found in 25 to 50% of these. Chronic constipation affects daily life including education and ability to work and has been associated to increased psychological distress. DD is an acquired condition whereby an involuntary contraction of the external anal sphincter and puborectalis muscle may lead to fecal obstruction during defecation and in some instances overflow incontinence. The pathophysiology of constipation has been associated to prolonged recto-sigmoid transit time and the presence of DD in early childhood after operation for ARM but remains unclear in adolescence among adults. High Resolution Anorectal Manometry (HRAM) is a recently developed technique offering spatiotemporal plots with three-dimensional pressurization which have been used to investigate functional defecation disorders but the value compared to other diagnostic modalities is still unclear.

We aimed to describe findings from colonic transit time (CTT) and HRAM in patients > 10 years of age operated for anorectal malformations and to compare the results in ARM-patients with constipation and ARM-patients without signs of constipation with special regard to the incidence of dyssynergic defecation.

2. Methods

2.1. Patients

We recruited patients from a tertiary pediatric surgical center at Odense University Hospital (OUH), Denmark with a catchment area of 3.5 million people. Patients with ARM were identified through local databases using the ICD-9 codes: 725.1, 725.2 (1985-1994) and ICD-10 codes: Q42 (all included) and Q438K (1995-2004). Inclusion criteria were primary surgery for anorectal malformations from 1985 to 2004 at OUH. Exclusion criteria were cognitive disability to an extent that the patient could not properly understand purpose and consequences of the study and the presence of an enterostoma.

An invitational letter was sent to each subject and if no response was registered, another letter was sent 14 days later. A total of 25 subjects fulfilled inclusion criteria and consented to participate (fig.1). We were unable to perform HRAM in two patients due to anal stenosis and one patient refrained from HRAM leaving 22 patients for further analyses on HRAM.

Data obtained from patient charts were: Age, comorbidity, type of malformation, type of primary surgery for anorectal malformation, other known congenital abnormalities or malformations and, in women childbirth.

2.2. Statistics

A non-normal distribution of data was assumed. Data were presented as medians and interquartile ranges (IQR) if not otherwise indicated. Discrete data were compared with Fisher exacttest and for cont ∈ wosdata the Ma ∩ − Whit ≠ yU/testwasapplied. Level of sign if iancewasrep or edwithtwo − sdp − s rank order correlation and reported with a correlation coefficient rho (p) and two-sided p-value.

2.3. Constipation diagnosis

Patients were verbally screened for constipation according to the Rome IV criteria when verbal and written informed consent was obtained for study inclusion.

2.4. Questionnaires

2.4.1. Krickenbeck classification
The Krickenbeck classification of postoperative functional results in patients with ARM was used to evaluate bowel outcome.18

Krickenbeck classification of postoperative results:

Voluntary bowel movements (Feeling of urge, capacity to verbalize and able to hold bowel movements): yes/no

Soiling

Grade 1: Occasionally (once or twice per week), grade 2: Every day, no social problem, grade 3: Constant, social problem.

Constipation

Grade 1: Manageable by changes in diet, grade 2: Requires laxatives, grade 3: Resistant to laxatives and diet.

2.4.2. Cleveland Clinic Constipation Score (CCCS)

The severity of constipation was evaluated with CCCS.19 Scores ranged from 0 (best) to 30 (worst). The CCCS was correlated to findings from colonic transit time (CTT) and HRAM.

2.5. Clinical examinations

2.5.1. High resolution anorectal manometry

We used a Manoscan™ anorectal High Resolution Manometry system (Medtronic, MN, USA) mounted with a 3D probe. The rigid probe had 256 pressure sensors circumferentially aligned over the length of 64 mm and a circumference of 10 mm. The probe was calibrated before use in each participant. A disposable sheath with a rectal balloon was applied and lubricated before introducing the probe into the anus. Neither enema or colonic preparation nor sedatives were used before examination. Participants were placed in the left decubitus position with hips and knees flexed 90 degrees during the procedure. Before introducing the probe, a rectal examination was done to ensure the rectum was empty. The same clinician (TBM) with experience in performing anorectal manometries performed all examinations.

After introducing the probe, a resting period of one minute was awaited before measurements. The resting pressure was measured continuously during a period for 20 seconds and repeated three times. The mean value for these three measurements was used for the calculation. Squeeze pressure and push maneuvers were then performed three times with 30 seconds intervals and mean value was used for the calculation. The presence of a lambda pattern was registered on the 2D opening of the 3D pressure cylinder during the squeeze maneuver indicating normal function of the puborectalis muscle and external anal sphincter (fig.2). This is observed as maximal pressures in the posterior part of the proximal high-pressure zone (HPZ) which is corresponding to the puborectalis muscle and the anterior part of the distal HPZ which is corresponding to the external anal sphincter. In order to elicit the recto-anal inhibitory reflex (RAIR) the rectal balloon was forcefully inflated with increasing volumes of air in 10 ml aliquots stopping at 60 ml if the reflex was not elicited. Rectal sensitivity was examined by consecutively inflating aliquots of 10 ml of air until first sensation, urge to defecate and discomfort was registered. The procedure was stopped at a volume of 400 ml. The HPZ area was calculated as (rectal pressure + (anal resting pressure – rectal pressure)) x 0.25). Pressure measurements were all referenced to actual atmospheric pressure.

Dyssynergic defecation pattern was identified on tracings during attempted defecation. They were divided in to either type I, II, III or IV (fig.3). If one of the three attempted defecations were without signs of dyssynergic defecation pattern it was considered normal.

In patients fulfilling the diagnostic criteria for functional chronic constipation, dyssynergic defecation (DD) was defined according to the following diagnostic criteria which have shown to be in line with the London Classification.20,21

1. Patients must demonstrate an obstructive pattern of defecation during high resolution anorectal manometry at more than one attempt
2. A prolonged colonic transit time

Moreover we assessed the individual muscle activation during attempted defecation on three-dimensional cylindrical pressure-distribution plots as a localized pressure increment (fig.4). If the pressure increment was localized to the posterior and proximal part of the anal canal it was attributed to the puborectalis muscle. Pressure increment in the distal part of the anal canal was attributed to the external anal sphincter.

Each manometry data set was assessed by the same author (TBM) with more than five year experience in interpreting data from HRAM. Data was assessed with an interval of 2 weeks and if discrepancies appeared, data was assessed again after another 2 weeks at which intra-observer agreement on all data was achieved.

2.5.2. Colonic transit time test

Patients were asked to take a break with laxatives one week before the first day of capsule ingestion. One gelatin capsule was digested on six consecutive days at nine a.m. Each capsule contained 10 radio-opaque poly-urethrane markers containing 40% barium sulphate (PA. Mauch, Münchenstein, Switzerland). Shape of the markers varied from day one to day six containing; rods, spheres, large rings, cubes, small rings and rods respectively. A plain X-ray of the abdomen was performed on day seven without any preparation. 22
For interpretation of the X-rays three imagine lines were placed from the center of the fifth lumbar vertebrae. One line was placed cranially along the vertebrae, one line to the right pelvic outlet and one line towards the left iliac crest (fig.5).

Total numbers of radio-opaque markers were counted by a radiologist and by the first author of this manuscript (TBM). If discrepancies between numbers of counted markers occurred, an agreement on number of markers between radiologist and TBM was achieved. In addition to the total number of markers the number of markers was registered in the right colon, the left colon and the recto-sigmoid colon. With 10 markers per day each marker is equivalent to 0.1 days=2.4 hours. Therefore the formula M x 2.4 where M is sum of markers can be used on both the total and segmental colonic transit times providing transit times in hours.

Normal upper limit for total colon transit time was set to </= 70 hours for women and </=60 hours for men. Segmental colon transit times were used for comparison between groups.

3. Results

3.1. Demographics

Data are presented in table 1. All patients were Caucasians, born and raised in Denmark. None of the patients were diagnosed with diabetes mellitus or other acquired metabolic or neurologic diseases known to have a possible effect on the gastrointestinal function. Cardiac anomalies were atrial septal defect (n = 9), persistent ductus arteriosus (n = 5) and ventricular septal defect (n = 3). In four patients more than one cardiac anomaly was present at birth. None of the cardiac anomalies required treatment. Renal anomaly was diagnosed in four patients with unilateral renal agenesis in three, neurogenic overactive bladder (n = 1) and hydronephrosis in one. One patient (a male) who later was diagnosed with a neurogenic bladder had undergone a cystoenterocutaneostomí and used clean intermittent catheterization. In three patients a spinal anomaly was found. One with spinal a filum terminal lipoma, closed spina bifida at level C6 and T12 and sacral agenesis, one patient had a tethered cord which was surgical released and one patient with an untreated syringomyelia at spinal level C7/T1. Möbius syndrome was diagnosed in one patient with facial palsy as the clinical presentation.

3.3. Colon transit time test

Data on colon transit time is presented in table 2. Total colon transit time and segmental transit times were all longer in patients with constipation but not at a level of statistical significance. The recto-sigmoid transit time was twice as long in patients with constipation.

3.4. HRAM

We were not able to show any differences on HRAM parameters between groups based on the presence constipation. A type I dyssynergic pattern was present in 50% (7/14) of patients with constipation and in 37% (3/8) of patients without constipation. For type IV dyssynergic pattern it was observed in 14% (2/14) of constipated patients and in 50% (4/8) with no constipation.

3.5. Correlation analysis

CCCS was correlated to the following HRAM parameters: mean anal resting pressure (ρ = 0.145, p = 0.733), mean anal squeeze pressure (ρ = -0.338, p = 0.414), recto-anal pressure gradient (ρ = 0.229, p = 0.586), first sensation (ρ = -0.280, p = 0.503), desire to defecate (ρ = -0.442, 0.272), discomfort (ρ = -0.467, p = 0.244) and length of high pressure zone (ρ = -0.358, p = 0.384).

CCCS was correlated to the following colonic transit time (CTT) parameters: total colon transit time (ρ = 0.128, p = 0.763), right colon transit time (ρ = -0.108, p = 0.798), left colon transit time (ρ = 0.188, p = 0.656) and recto-sigmoid transit time (ρ = -0.006, p = 0.989).

4. Discussion

In the present study all patients fulfilling the diagnostic criteria for constipation had a dyssynergic defecation pattern, and 79% (9/13) of these patients had a colon transit time within the normal range. Surprisingly a dyssynergic defecation pattern was also observed in patients with no signs of constipation (8/8).

Dyssynergic defecation (DD) pattern as detected with anorectal manometry was observed in all patients subjected to HRAM in our study without regard to the presence of constipation. Only 38% (4/13) of patients with constipation were diagnosed with dyssynergic defecation. A type 1 DD pattern was present in all four patients.

In a retrospective study of mainly pediatric ARM-patients with constipation, DD pattern type 1 was observed in 27/28 and type IV in the last patient. Information on colon transit time was not included in this study but 69% (20/28) of the patients were able to perform balloon expulsion within one minute (defecometry) and thus not fulfilling diagnostic criteria for DD. The etiology of DD is unclear. The condition may be regarded as an acquired behavioral disorder and a study found that in 2/3 of cases it was acquired during adulthood.9 In symptomatic patients, DD is important to diagnose and treat, owing to the fact that DD is associated with impaired disease-related quality of life.23. Dyssynergic defecation has been reported to occur in nearly 90 % of asymptomatic controls and in patients with chronic proctalgia without constipation, with high inter-observer agreement rates for type I and IV DD.24,25 This can partly be explained by a non-physiologic position during anorectal manometry as in our setting in which the patient was placed in the left decubitus position with an empty rectum. Optimal the patients should be placed on a commode for HRAM to mimic the natural defecation position but the placement of the rigid 3D-probe in the anal canal is expected to be inconvenient for examiner and elicit discomfort for the patient. Moreover the left lateral decubitus position is recommended by The International Anorectal Physiology Working Group.21
When it comes to treatment for DD, coaching has in one study revealed a normalization of manometric results in 12 out of 39 patients. Type I DD was dominant in our patients with constipation, found in eight out of 13 cases. In a study including 40 females with constipation, a dyssynergic defecation pattern was found with HRAM in 28 (70%) with Type I in 17 (43%), Type III in 9 (23%), Type IV in 2 (5%) and none with Type II. The patients were older than our population (median age 53 vs. 23 years) and previous anorectal surgery was registered in 12 (29%), not otherwise specified.

We did not find any significant differences in total or segmental colonic transit times between patients with constipation and patients without constipation. None the less the recto-sigmoidal transit time was twice as long in patients reporting constipation compared to patients with no constipation. In our study the recto-anal inhibitor reflex (RAIR) was only present in 36% (5/14) of patients with constipation compared to 63% (5/8) of patients with no constipation. RAIR is characterized by transient relaxation of the internal anal sphincter in response to distension of the rectum and is an indication of functioning internal anal sphincter. Many patients with ARM lack the recto-anal inhibitory reflex probably as a consequence of corrective surgery or the inborn atresia of the anal channel. An absence of RAIR is proposed to contribute to the development of constipation as it increases anal resting pressure. In our patients with constipation RAIR was absent in 62% (8/13) suggesting that the contribution to constipation is questionable.

We found isolated paradoxical activation of the puborectalis muscle in ten out of thirteen constipated patients indicative of puborectalis syndrome. None of the patients without constipation presented isolated paradoxical puborectal activation during straining. Relaxation of the puborectalis muscle is important during attempted defecation in order to straighten the anorectal angle and facilitate the passage of stool.

Knowledge about the pathophysiology in constipated ARM-patients is important to target the treatment. An isolated slow-transit constipation benefits from treatment with laxatives but biofeedback treatment is the mainstay in constipated patients with dyssynergic defecation or absence of RAIR. However, the evidence behind these treatments is inadequate and randomized controlled studies is needed. The strength of our study is that it was protocolized and all examination performed systematically under standardized conditions. The study also had limitations. The cohort was relative small and therefore the comparisons between even smaller groups based on the presence of constipation have limited statistical value. The unnatural left decubitus position during HRAM as mentioned previously may have overestimated the true incidence of dyssynergic defecation. We did not perform endoscopy in our population to rule out stenosis as a cause of constipation which normally is part of a diagnostic work-up.

5. Conclusions

We found a dyssynergic defecation pattern with HRAM during attempted defecation to be common in patients operated for ARM irrespective of functional bowel outcome. The clinical relevance is questionable in that only 31% of patients diagnosed with constipation fulfilled the conventional criteria for DD including the presence of functional constipation, dyssynergic defecation pattern on HRAM and prolonged CTT. In constipated patients puborectalis syndrome was a common finding. The use of HRAM in the diagnosis of patients with constipation after surgery for ARM has yet to be proven.

List Of Abbreviations

ARM: AnoRectal Malformations.
DD: Dyssynergic Defecation.
HRAM: High Resolution Anorectal Manometry.
CTT: Colonic Transit Time.
CCCS: Cleveland Clinic Constipation Score.
HPZ: High-Pressure Zone.
RAIR: Recto-Anal Inhibitory Reflex.

6. Declarations

Ethics approval and consent to participate: The study was conducted according to the 7th revision of the Helsinki declaration (2013). Verbal and written informed consent was obtained from adult participants and in participants below 18 year of age, from parent(s) or guardian(s). The study was approved by the National Committee of Health Research Ethics (S–20140017) and the Danish Data Protection Agency. It was registered in Clinical.Trials.gov (NCT02624232).

Consent for publication: not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors’ contributions: All authors contributed equally to this work. TBM and NQ conceived the ideas and designed the study. TBM performed High resolution Anorectal manometry. Acquisition and analysis of data was carried out by TBM. TBM, NQ and PC did interpretation and presentation of data. MSJ, GB and JA were involved in critical revision of the manuscript.

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**Tables**

Table 1 – Demographics and functional outcome, n=25
| Parameter                        | 18(14-24) | 48(12/25) |
|---------------------------------|-----------|-----------|
| Age, years                      |           |           |
| Female sex                      |           |           |
| Type of ARM                     |           |           |
| Anocutaneous fistula            | 9         |           |
| Vestibular fistula              | 8         |           |
| Urethral(bulbar) fistula        | 4         |           |
| Anal stenosis                   | 2         |           |
| No fistula                      | 1         |           |
| Urethral (prostatic) fistula    | 1         |           |
| Associated anomalies            | 52(13/25) |           |
| Cardiac                         | 11        |           |
| Urologic                        | 4         |           |
| Spine                           | 4         |           |
| Limb                            | 2         |           |
| Eyes                            | 1         |           |
| Fascial                         | 1         |           |
| Syndromes                       | 1         |           |
| Type of repair                  |           |           |
| PSARP                           | 15        |           |
| Perineal                        | 5         |           |
| Dilatations                     | 4         |           |
| Cutback                         | 1         |           |
| Functional outcome              |           |           |
| Normal bowel function           | 12(3/25)  |           |
| Constipation^                  | 52(13/25) |           |
| Grade 1                         | 9         |           |
| Grade 2                         | 4         |           |
| Voluntary bowel movements       | 100(25/25)|           |
| Soiling                         | 48(12/25) |           |
| Grade 1                         | 7         |           |
| Grade 2                         | 4         |           |
| Grade 3                         | 1         |           |
| Constipation and soiling        | 46(6/13)  |           |

^Rome III criteria for constipation. Data are presented as % (ratio) or in numbers.

Table 2 - Results from Colon Transit Time and High Resolution Anorectal Manometry
| Parameter                              | Constipation | No constipation | P-value |
|---------------------------------------|--------------|-----------------|---------|
| **n=13**                              | **n=12**     |                 |         |
| Age                                   | 18(14-24)    | 23(20-24)       | 0.327   |
| Female sex                            | 6            | 6               | 1.000   |
| BMI                                   | 20(19-23)    | 22(22-29)       | 0.342   |
| Vaginal delivery                      | 0            | 1               | 1.000   |
| Soiling                               | 4            | 8               | 0.115   |
| **Colon transit time examination**    |              |                 |         |
| CCT (hours)                           | 49.2(40.8-108.0) | 44.4(25.2-61.2) | 0.358   |
| RCT (hours)                           | 18.6(9.6-45.6)  | 18.5(25.2-30.0)  | 0.704   |
| LCT (hours)                           | 8.4(4.8-38.4)   | 6(0-41.4)       | 0.129   |
| RST (hours)                           | 16.8(12.0-21.6) | 8.4(4.2-19.2)   | 0.342   |

**HRAM**

| Parameter                              | Constipation | No constipation | P-value |
|---------------------------------------|--------------|-----------------|---------|
| **n=13**                              | **n=8**      |                 |         |
| Mean anal resting pressure (mmHg)     | 35(29-73)    | 38(33-48)       | 0.889   |
| Maximal anal resting pressure (mmHg)  | 43(36-88)    | 50(42-62)       | 0.976   |
| Maximal anal squeeze pressure (mmHg)  | 124(93-207)  | 96(56-137)      | 0.741   |
| Lambda configuration                  | 6            | 3               |         |
| Recto-anal pressure difference        | -11(-16-28)  | -11(-16-28)     | 0.423   |
| Recto-anal inhibitory reflex          | 5            | 5               | 0.788   |
| Anal high pressure zone (cm)          | 2.6(2.5-3.2) | 3.4(3.3-7.7)    | 0.203   |
| First Sensation (ml)                  | 40(30-60)    | 40(30-45)       | 0.667   |
| Desire to defecate (ml)               | 60(53-100)   | 50(48-75)       | 0.638   |
| Discomfort (ml)                       | 100(65-163)  | 90(58-165)      | 0.433   |
| Perineal descent                      | 3            | 0               | 0.535   |
| Dyssynergic pattern                  |              |                 |         |
| Type I                                | 7            | 3               | 0.660   |
| Type II                               | 3            | 0               | 0.505   |
| Type III                              | 1            | 1               | 1.000   |
| Type IV                               | 2            | 4               | 0.146   |
| Dyssynergic defecation                | 4            | 0               | 0.131   |

**Involved muscles in dyssynergic defecation pattern**

| PB          |          |
|-------------|----------|
| EAS         | 0        |
| PB + EAS    |          |
|             | 0        |
|             | 6        |
| **P-value** |          |
|             | 0.001*   |
|             | 1.000    |
|             | 0.001*   |

Data are presented as medians (interquartile ranges) or in numbers. CCT = colonic transit time. RCT = right colonic transit times. LFT = left colonic transit time. RST = rectosigmoid colonic transit time. HRAM = high resolution anorectal manometry. PB = puborectal muscle. EAS = external anal sphincter.*statistical significant.

Figures
Figure 1
Patient inclusion

Figure 2
Pressure profile obtained by HRAM showing a lambda pattern during squeeze maneuver Fig.2. On the right a normal characteristic \(\lambda\)-pattern after 2D opening of the 3D pressure cylinder on the left. Numbers indicates distance in length from anal verge in centimeters. Ant=anterior. Post=posterior. L=left. H=right. Numbers indicates length in centimeters.
Figure 3

Dyssynergic patterns from HRAM during attempted defecation. Tracings from high resolution anorectal manometry, revealing four different patterns during attempted defecation in study patients. In type I dyssynergia the patient generates an adequate propulsive force (rise in intra-rectal pressure > 40 mm Hg) accompanied by a paradoxical increase in the anal sphincter pressure. In type II dyssynergia the patient is unable to generate an adequate compulsion force with a paradoxical small increase in anal sphincter pressure. In type III dyssynergia the propulsive rectal force is adequate but no relaxation of the anal sphincter. In type IV dyssynergia generated propulsive force is insufficient with inadequate relaxation of the anal sphincter.

Figure 4

Individual muscle involvement during attempted defecation. High resolution anorectal manometry results in two constipated patient during attempted defecation. High pressure areas are seen with "warm" colors (red/purple) and low pressure areas with "cold" color (blue/green/yellow). On the left is presented a three-dimensional cylindrical pressure-distribution during attempted defecation. A two-dimensional landscape plot of the cylindrical presentation is presented on the right. In the upper picture a high pressure area is located in the posterior and proximal part of the anal canal indicative of paradoxical activation of the puborectalis muscle. In the lower picture a high pressure zone is observed in lower part of the anal canal interpreted as external anal sphincter contraction. Numbers indicates length in centimeters. Ant=anterior. Post=posterior. L=left. H=right.
Abdominal frontal x-ray with colonic segments. In this frontal x-ray containing radio-opaque markers, the imaginary white lines mark the areas for segmental colon transit times. From the center of vertebrae L5, one line runs cranially along the vertebrae. The two other strait lines run towards the left iliac crest and the right pelvic outlet. The formed upper right area, the upper left and the lower left areas represents the right colon, the left colon and the recto-sigmoid colon respectively.