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Underdiagnosis of Mild Congenital Anorectal Malformations

Jara E. Jonker, BSc^{1,2}, Monika Trzpis, PhD², and Paul M. A. Broens, MD, PhD^{1,2}

Objective To determine whether the frequency and severity of congenital anorectal malformations (CARMs) differs by sex.

Study design We included 129 patients (0-319 weeks old) diagnosed with CARMs, who had been referred to our Department of Pediatric Surgery between 2004 and 2013. Rectoperineal and rectovestibular fistulas were classified as mild CARMs, all others as severe. If a patient was diagnosed with CARM within 48 hours after birth, this was considered an early diagnosis, all others as late.

Results Seventy-five (58%) girls and 54 (42%) boys were diagnosed with different forms of CARM. More patients had mild rather than severe forms of CARM (67% and 33%, respectively, $P < .001$). We found that 89% of girls had a mild form of CARM, whereas 65% of boys had severe forms ($P < .001$). All severe forms were diagnosed early, whereas 54% mild forms were diagnosed early and 46% were diagnosed late.

Conclusions Girls more often have mild forms of CARM, whereas boys more often have severe forms. Overall, the distribution across the sexes is equal. Because chronic constipation can be the only symptom of mild CARMs, it often requires more time to diagnose than severe forms. Many women are, therefore, diagnosed with CARMs at an older age, or they may go undiagnosed altogether. Subsequently, these women have a greater risk of full rupture during vaginal delivery. (*J Pediatr* 2017;186:101-4).

Congenital anorectal malformations (CARMs) occur in between 2 and 4.05 per every 10 000 births.¹ Anorectal malformation comprises a broad spectrum of different abnormalities in which the anus and the anal canal are always involved. Some of the abnormalities are clearly visible, particularly in case of the most severe forms of CARM, such as absent anus. Diagnosing the mild forms, however, often requires additional medical analyses. Experience with this type of patient is essential. In cases where the symptoms are not very obvious, anorectal malformations may be overlooked, leading to a delayed diagnosis.²⁻⁴

Although it has been reported that CARMs are more frequent in men, there are also a number of publications that report an equal distribution between men and women.^{1,5-8} To date, a comparative study of the prevalence of CARMs, which takes into account severity and the time of diagnosis, has not been reported.

In this study, we aimed to determine whether the frequency and severity of CARMs differed by sex. In addition, we investigated whether a patient's sex and the form of CARM had an influence on the time of its diagnosis.

Methods

Retrospectively, we reviewed the medical records of all patients with CARMs who were seen at the Department of Pediatric Surgery of the University Medical Center of Groningen and who were born between January 2004 and December 2013 (N = 155). We excluded 26 patients for the following reasons: echocardiogram not available (n = 20), emigration or adoption (n = 4), or death (n = 2). Finally, 129 patients were included for analysis.

We have used the Krickbeck classification to assess the different types of CARMs in our patient population.⁹ Further, patients with a rectoperineal or a rectovestibular fistula were classified as having a mild form of CARM, whereas all other fistula types were categorized as severe forms.

We noted the patient's sex and age at the time CARMs were diagnosed. In accordance with previous studies, we considered the diagnosis to be early if the patient had been diagnosed with CARMs within 48 hours after birth, all others diagnoses were considered late.²⁻⁴

The study was conducted at University Medical Center Groningen, The Netherlands, in compliance with the requirements of our local medical ethics review board.

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CARM Congenital anorectal malformation

Table I. Patient characteristics

Patients with CARM (N = 129)	Number
Age (wk)	0-319
Girls	75 (58%)
Boys	54 (42%)
Mild CARM	85 (66%)
Severe CARM	44 (34%)
Congenital heart defects	22 (17%)

Statistical Analyses

The data were analyzed with SPSS 22.0 for Windows (IBM SPSS Statistics, IBM Corporation Armonk, New York). Either Fisher exact test or the χ^2 test was used to compare the proportions. The level of statistical significance was set at a probability of <.05.

Results

To investigate whether the exclusion of patients who had not undergone an echocardiogram could have influenced our findings, we compared the severity of CARMs in the included and excluded patient groups. There was no difference in prevalence of mild and severe CARMs between the groups of excluded and included patients ($P = 0.305$). Out of 129 included patients, 75 (58%) girls and 54 (42%) boys were diagnosed with different forms of CARM ($P = .078$). The age of these patients at the time of diagnosis ranged between 0 and 319 weeks. Significantly more patients (85 [66%]) had a mild form of CARM, in comparison with the severe forms, which occurred in 44 (34%) of the cases ($P < .001$, **Table I**).

We investigated whether the prevalence of the mild and severe forms of CARM differed between boys and girls (**Table II**). Out of the total of 75 girls, 89% suffered from a mild form of CARM, whereas out of the total of 54 boys, 67% suffered from a severe form of CARM ($P < .001$). Furthermore, we analyzed the distribution of the different forms of CARM in boys and girls, as shown in **Table II**. We found that rectoperineal fistulas were the most frequent form of CARM in both sexes, but this form was present 3 times more often in girls than in

Table II. Distribution of the different forms of CARM among boys and girls

	Forms of CARM	Boys (%)	Girls (%)
Mild CARM	Rectoperineal fistula	18 (33.3%)	54 (72.0%)
	Rectovestibular fistula	0	13 (17.3%)
	Total mild forms of CARM	18 (33.3%)	67 (89.3%)
Severe CARM	Rectoscolotal fistula	4 (7.4%)	0
	Rectobulbar fistula	17 (31.5%)	0
	Rectoprostatic fistula	9 (16.7%)	0
	Rectovesical fistula	1 (1.9%)	0
	Membrane CARM	4 (7.4%)	0
	Complex CARM	1 (1.9%)	1 (1.3%)
	Cloaca	0	7 (9.3%)
	Total severe forms of CARM	36 (66.7%)	8 (10.6%)

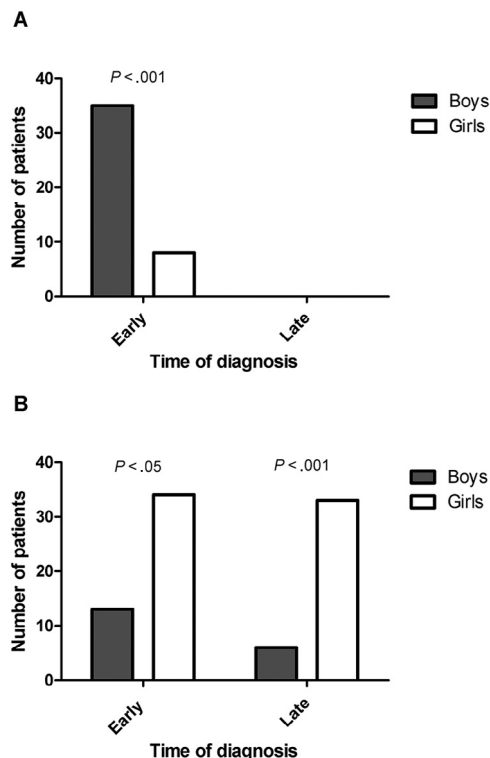


Figure 1. Association between form of CARM, sex, and the time of diagnosis between **A**, severe forms of CARM and **B**, mild forms of CARM. Early diagnosis within 48 hours after birth, late all others.

boys (n = 54 [72.0%] vs n = 18 [33.3%], respectively). The severe forms of CARM were present 4.5 times more often in boys than in girls (n = 36 [66.7%] vs n = 8 [10.6%], respectively).

The range of the time required for the late diagnosis was between 2 and 2233 days (**Table III**; available at www.jpeds.com). All patients suffering from a severe form of CARM were diagnosed within 48 hours after birth. In case of mild CARMs, 54% of the patients were diagnosed early and 46% were diagnosed late (**Figure 1**). Within the group of mild patients, 50% of the patients with a rectoperineal fistula were diagnosed early, whereas the other 50% were diagnosed late. In girls with a rectovestibular fistula, 77% were diagnosed early and 23% were diagnosed late (**Table III**).

Discussion

We found that in general the distribution of CARMs is equal across the sexes, but that the distribution between boys and girls differs when the severity of CARMs is taken into account.

In the past, it has been reported that men suffer from CARMs more often than women; however, there are also a number of publications that report an equal distribution between men and women.^{1,5-8} Based on our daily practice, we had the impression that there might actually be differences in the distribution of different forms of CARM among men and women. This study confirmed our impression.

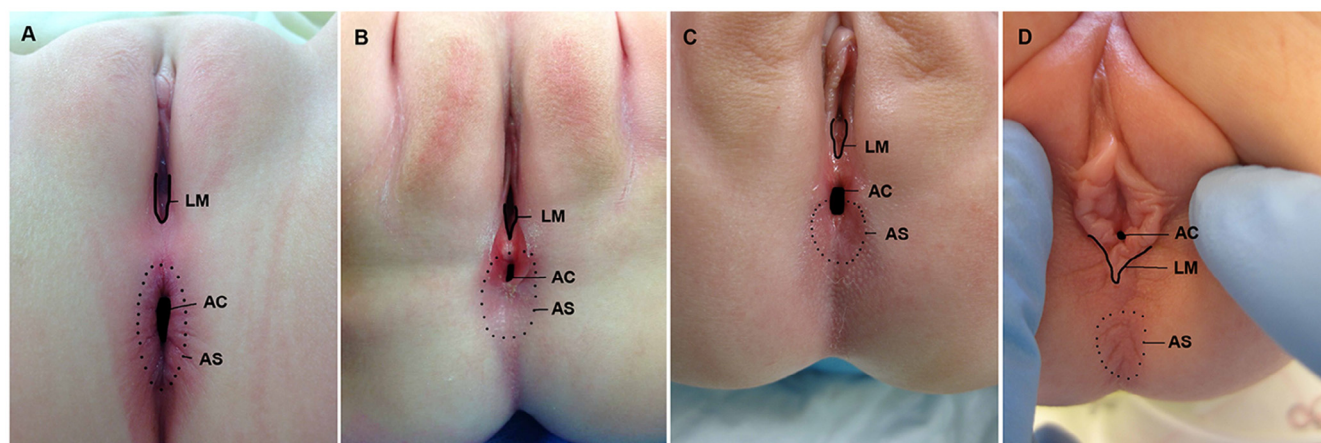


Figure 2. Clinical view of mild CARM in female babies. **A**, A girl without CARM, normal anatomy with the anal canal in the center of the anal sphincter. **B**, Perineal fistula, with the anal canal just within the border of the anal sphincter. **C**, Perineal fistula, with the anal canal outside the anal sphincter. **D**, Vestibular fistula, with the anal canal within the labia minus, far away from the anal sphincter. The anal orifice in children with CARM can be smaller but not always. Even when the size of the anal orifice is not smaller compared with healthy babies, they still do suffer from (mild) constipation. The mechanism behind this clinical observation has not yet been clarified. For boys, the position of the anal canal in relation to the sphincter complex is comparable with the girls presented in A, B, and C. Also in their case, the main point of recognition is identifying the place of the anal sphincter in relation to the position of the anal orifice. AC, anal canal; AS, border of the anal sphincter, as can be recognized by change of the color and surface of the perineal skin; LM, labium minus.

As a rule, a severe form of CARM is evident. For example, a completely absent or delocalized anus will be readily found during a physical examination. A mild form of CARM, on the other hand, may be difficult to diagnose for any midwife or doctor lacking in experience in diagnosing this condition. In case of a mild form of CARM, the anus may be only slightly deviated to anterior, which may be easily overlooked. Because the severe forms of CARM are more readily diagnosed than the mild forms, it is possible that fewer women are diagnosed with this condition, which leads to an apparent fewer prevalence of CARMs. We found that almost one-half of the mild forms of CARM were diagnosed late, whereas none of the severe forms were diagnosed late. It appears that in girls the prevalence of CARMs has been underestimated because of late diagnosis, or lack of diagnosis.

Because mild forms of CARM can be difficult to diagnose, one may assume that we actually overestimated the prevalence of rectoperineal fistulas and that the mild group contained incorrectly diagnosed patients. The fact that these patients were indeed correctly diagnosed is supported by the 17% prevalence of congenital heart disease in these patients. This prevalence of congenital heart disease did not differ between the mild and the severe forms of CARM.¹⁰ In a normal population, the prevalence of congenital heart disease is 0.8%.¹¹ Thus, in this study these patients are correctly diagnosed with CARMs.

Our study not only explains the lack of consensus in the prevalence of CARMs among boys and girls, it has clinical implications as well. We recommend that women who experience chronic constipation should also be examined for CARMs. For example, we refer to the case of a 6-year-old girl. She suffered from constipation, but the medical specialist could not

find any underlying reasons of her condition. The child was referred to a psychiatrist who noticed a very small abnormality of the anus. The girl was subsequently referred to a pediatric surgeon. Examination of the girl resulted in the diagnosis of a rectoperineal fistula, a mild form of a CARM. In addition, Tareen et al² reported an unusual case of a 7-year-old girl who was diagnosed with CARM.

It is important to emphasize that the main point of recognition of the less severe forms of CARMs, where the anatomy is only slightly altered, is to observe the position of the anal orifice in relation to the anal sphincter (Figure 2). The place of the anal sphincter can be recognized by altered skin texture and color. Thus, the distance between the anal orifice and the labia minus is unfortunately an unreliable approach to identify a mild version of CARM because of the natural variation of the location of the anal sphincter among different children.

Even though CARMs are rare, it is possible that there are more chronically constipated patients whose condition results from mild forms of CARM but that have not been recognized as such. Therefore, we aim to encourage physicians who see patients with chronic constipation to consider the possibility of CARMs. Constipation, provided it is treated conservatively, is not a life-threatening disease, and mild forms of CARM do not always require surgery. Nevertheless, there is another aspect of CARMs that does need to be taken into consideration in case of adult female patients, which is vaginal deliveries. Vaginal deliveries are not recommended in patients with CARMs because of the increased risk of total rupture. When a woman is aware of having CARMs, a cesarean delivery should be planned to prevent postdelivery complications.

Currently, the number of women with CARM is probably underestimated. As a consequence, they are at a higher risk of a full rupture during vaginal delivery. It would be wise to consider the possibility of CARMs in patients with chronic constipation, especially in the case of women. ■

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Table III. Prevalence of early and late diagnosis in boys and girls with mild and severe forms of CARM

Forms of CARM		Boys		Girls	
		Early diagnosis (n = 48)	Late diagnosis (n = 6) (range in d after birth)	Early diagnosis (n = 42)	Late diagnosis (n = 33) (range in d after birth)
Mild CARM	Rectoperineal fistula	12	6 (2-907 d)	24	30 (3-2233 d)
	Rectovestibular fistula	n.a.	n.a.	10	3 (10-587 d)
	Total mild forms of CARM	12	6 (2-907 d)	34	33 (3-2233 d)
Severe CARM	Total severe forms of CARM	36	0	8	0

n.a., not applicable.

Early diagnosis is within 48 hours after birth, late all others.