Original Article

Examining Results of Post-Thelarche Screening Pelvic Ultrasound in Females with Anorectal Malformations

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ABSTRACT

Study Objective: Mullerian duct anomalies are common in females with anorectal malformations (ARMs), although there are no universally recommended screening protocols for identification. Historically, at our institution, we have recommended a screening pelvic ultrasound (PUS) 6 months after thelarche and menarche. We aimed to evaluate outcomes associated with our post-thelarche screening PUS in females with ARMs.

Methods: An institutional review board–approved retrospective chart review was performed for all female patients 8 years old or older with ARMs and documented thelarche. Data were collected on demographic characteristics and clinical course. The primary outcome was adherence to the recommended PUS. Secondary outcomes included imaging correlation with suspected Mullerian anatomy and need for intervention on the basis of imaging findings.

Results: A total of 112 patients met the inclusion criteria. Of them, 87 (77.7%) completed a recommended post-thelarche screening PUS. There were no differences in completion on the basis of age, race, establishment with a primary care provider, insurance status, or type of ARM. Nine patients (10.3%) had findings on their PUS that did not correlate with their suspected Mullerian anatomy; five (5.7%) required intervention, with two requiring menstrual suppression, two requiring surgical intervention, and one requiring further imaging.

Conclusion: Most patients completed the recommended post-thelarche screening PUS. In a small subset of patients, PUS did not correlate with suspected Mullerian anatomy and generated a need for intervention. Post-thelarche PUS can be a useful adjunct in patients with ARMs to identify gynecologic abnormalities.

Key Words: Mullerian anomaly, Adolescent gynecology, Menstrual suppression, Uterine didelphis, Ovarian cyst

Introduction

Anorectal malformations (ARMs) are uncommon congenital abnormalities, affecting approximately 1 in 5000 children.[1,2] In females, the most common ARM is a rectoperineal fistula. Other ARM subtypes include cloaca, imperforate anus without fistula, rectovestibular fistula, and rectovaginal fistula.[3] Screening for associated anomalies is recommended in new diagnoses of ARMs to allow for appropriate identification and management, and ARMs are frequently associated with the VACTERL association, including vertebral, cardiovascular, tracheoesophageal, renal, and limb defects.[4,5] Females with ARMs are specifically at higher risk of anatomic gynecologic anomalies including vaginal agenesis, distal vaginal atresia, presence of a longitudinal vaginal septum, and Mullerian duct anomalies (MDAs) such as uterine didelphys.[6] Upper tract gynecologic abnormalities involving the uterus and adnexa may occur in anywhere from 20% to 50% of patients.[7]

MDAs can be difficult to diagnose before puberty given the small size of these structures before estrogen stimulation, the variation in density of the myometrium, and a wide range of possible gynecologic anatomy.[8,9] After puberty, patients with MDAs may be asymptomatic or may present with primary amenorrhea, abdominal-pelvic pain, and, as adults, infertility or recurrent pregnancy loss.[10] Early identification of MDAs is critical for anticipatory guidance about future reproductive health, including the risk of menstrual outflow obstruction, contraceptive guidance, and pregnancy counseling. Early identification of patients at risk of menstrual outflow obstruction allows for the initiation of menstrual suppression and surgical intervention, which can reduce symptoms and help prevent long-term consequences such as infertility and endometriosis.[11] Given the strong association between MDAs and ARMs, historically, screening pelvic ultrasounds (PUSs) have been recommended for this patient population. However, there are limited data examining the utility of this recommendation.[12]

We sought to determine adherence to recommendations for a screening PUS after thelarche in patients with ARMs. Secondarily, we aimed to understand whether a screening PUS correlates with suspected Mullerian anatomy and to determine if PUS can identify situations requiring further intervention.

Abbreviations: ARM, anorectal malformation; MDA, Mullerian duct anomaly; PUS, pelvic ultrasound.

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Methods

Patient Selection

An institutional review board–approved retrospective chart review was performed of female patients evaluated at our institution as part of a multidisciplinary clinic from January 1, 2014, to August 30, 2020. Patients were included if they were natal females aged 8 years old or older with a diagnosis of ARM per the International Classification of Diseases Nine and Ten Codes. Thelarche status was obtained on all patients and categorized as follows: post-thelarche; no thelarche documented before August 30, 2020; or thelarche status unknown. Patients without thelarche or with thelarche status unknown were excluded. Patients with known utero-vaginal agenesis were also excluded from further analysis, as these patients are typically reimaged when symptomatic and do not follow the same recommendations in our clinic for post-thelarche PUS.

Data Collection

Data elements collected included demographic characteristics, ARM subtype, and suspected Mullerian anatomy, as defined by previous imaging, physical examination, and/or operative findings. ARM subtype was defined as mild, moderate, or severe (Supplemental Table 1).[13] Post-thelarche PUS was recommended at 6 months after the beginning of thelarche for all patients with ARMs. Data were then collected surrounding PUS, including evidence of completed screening PUS, findings of completed PUS, and need for gynecologic intervention, which included further imaging, menstrual suppression, and/or surgical intervention.

Statistical Analyses

The cohort was divided into subgroups according to completion of post-thelarche PUS for further analysis. Categorial variables were analyzed with sums and percentages and compared with Fisher's exact and χ^2 tests. Continuous variables were analyzed with medians and interquartile ranges and compared with Wilcoxon rank-sum tests. All statistical analysis was performed with SAS version 9.4 (SAS Institute, Cary, NC).

Results

Demographic and Clinical Characteristics

One hundred and ninety-three natal females were identified, of whom 80 were excluded due to having not undergone thelarche or for unknown thelarche status, and 1 was excluded for uterovaginal agenesis (Fig. 1). Thus, the post-thelarche cohort included 112 patients (Table 1). Of this cohort, 87 patients (77.7%) completed the recommended post-thelarche PUS. One fifth (21.8%) had completed menarche at the time of completing this PUS. There were no differences in completion on the basis of age, race, adoption status, establishment with a primary care provider, insurance, primary language, in-state or out-of-state location, age at

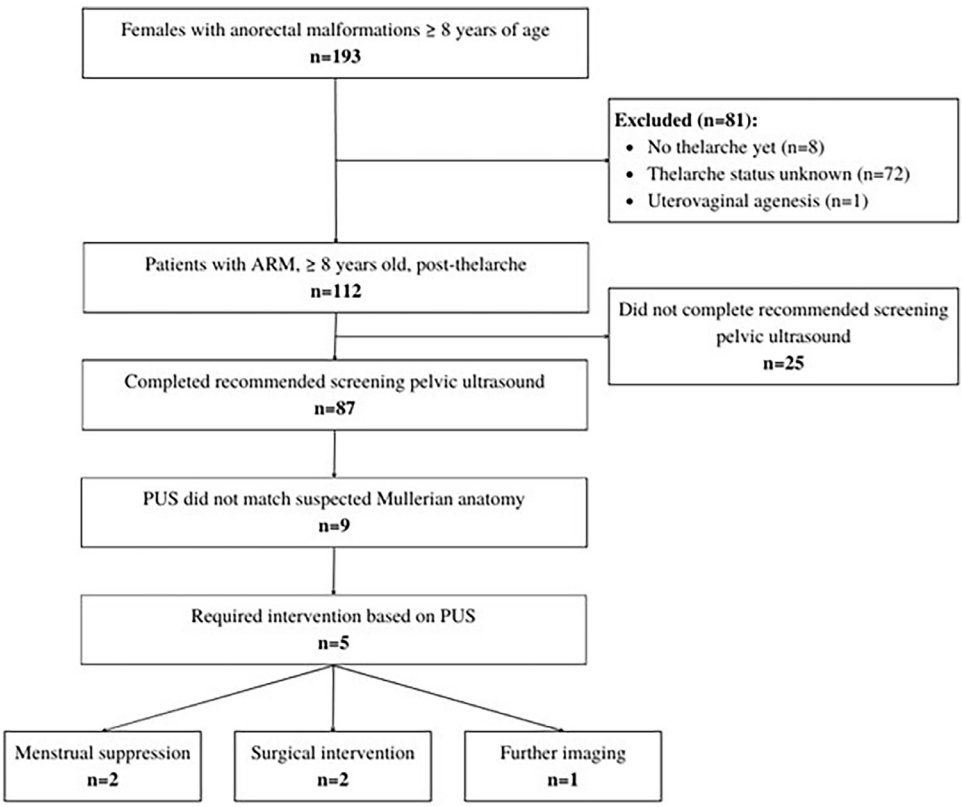

Fig. 1. Patients were included if they had a diagnosis of anorectal malformation, were ≥ 8 years old, and had documented thelarche. Most (77.7%) completed the recommended screening pelvic ultrasound (PUS). Of this cohort, a subset (10.3%) did not match suspected anatomy, and a further subset (55.6%) required intervention of some kind.

Table 1
Patient Characteristics

	Completion of post-thelarche screening ultrasound (PUS)		*P* value
	Yes n = 87 (77.7%)	No n = 25 (22.3%)	
Demographic characteristics			
Race			.570
White	53 (60.9)	18 (72.0)	
Black	17 (19.5)	3 (12.0)	
Other/unknown	17 (19.5)	4 (16.0)	
Adopted	20 (23.0)	2 (8.0)	.096
Has a primary care provider	74 (85.1)	21 (84.0)	.897
Insured	82 (94.3)	22 (88.0)	.285
English as primary language	83 (95.4)	24 (96.0)	.899
Lives in state	35 (40.2)	11 (44.0)	.736
Behavioral/developmental disorder	26 (29.9)	11 (44.0)	.186
Clinical characteristics			
Age at thelarche, y	10 [9–11]	9 [9–11]	.143
Has undergone menarche	59 (67.8)	11 (44.0)	.025
Timing of ultrasound			-
Post-thelarche	62 (71.7)	-	
Within 1 year after menarche	6 (6.9)	-	
Post-menarche	19 (21.8)	-	
Anorectal malformation severity*			.807
Mild	35 (40.2)	8 (32.0)	
Moderate	13 (14.9)	5 (20.0)	
Severe	29 (33.3)	8 (32.0)	
Unknown	10 (11.5)	4 (16.0)	

* See Supplementary Table 1 for details.

Table 2
Patients with Unexpected Findings or Findings Necessitating Action

	Type of anorectal malformation	Suspected Mullerian anatomy	Pelvic ultrasound findings	Change in clinical course?	Risk of obstruction	Intervention performed
1	Cloaca	Normal uterus	Normal uterus with 2.3 cm simple right ovarian cyst	No	No	None*
2	Cloaca	Normal uterus	Normal uterus with possible complex left ovarian cyst	No	No	None†
3	Rectovaginal fistula	Normal uterus	Normal uterus with left para-tubal cyst	Yes	No	Open left para-tubal cystectomy
4	Perineal fistula	Vaginal agenesis with obstructed mullerian horns	Obstructed Mullerian horns, normal ovaries	Yes	Yes	Menstrual suppression
5	Cloaca	Didelphic uterus	Didelphic uterus with left adnexal mass including left hemorrhagic cyst and left hydrosalpinx	Yes	No	Left salpingectomy and left ovarian cystectomy
6	Perineal fistula	Normal uterus	Bicornuate uterus, normal ovaries	No	No	None
7	Unknown	Right hemi-uterus with cervical anastomosis to neovagina	Uterine horns separated, normal ovaries	No	No	None‡
8	Rectovestibular fistula	Noncommunicating left Mullerian structure	Incompletely visualized left Fallopian tube with small left Mullerian structure, normal ovaries, surgically absent right Fallopian tube	No	Yes	MRI to confirm diagnosis menstrual suppression
9	Cloaca	Mullerian structures not meeting in midline	Right unicornuate uterus	Yes	No	Pelvic MRI

* Patient had planned exam under anesthesia, excision of R labial cyst, introitoplasty, and labioplasty after pelvic ultrasound.
† Of note, this patient was incidentally evaluated in the operating room for a nongynecologic concern and was found to have normal appearing ovaries without a left ovarian cyst.
‡ Vaginal dilators.

thelarche, or ARM severity. Patients who completed their post-thelarche PUS have since undergone menarche more commonly (67.8% vs 44.0%, $P = .025$).

Screening PUS Findings

Of the 87 patients who completed a post-thelarche PUS, there were nine patients (10.3%) in whom the findings on PUS did not match their suspected Mullerian anatomy (Table 2). All patients had completed PUS post thelarche and within the first year of menarche. Anatomical abnormalities diagnosed on PUS in this cohort by direct report included "obstructed Mullerian horns," "didelphic uterus with adnexal mass (hemorrhagic cyst of the left ovary and left hydrosalpinx)," "bicornuate uterus," "separated uterine horns," "atretic left Mullerian structure," and a "unicornuate uterus." Additionally, two ovarian cysts and a para-tubal cyst were incidentally noted. Five of the nine patients (5.7% of those who completed PUS, 55.6% of those with abnormal PUS) required further intervention on the basis of

PUS findings. One patient had a suspected but undiagnosed anomaly and was found to have a right unicornuate uterus on pelvic ultrasound. She was expected to have two Mullerian structures before imaging, and, therefore, she underwent MRI to clarify anatomy; after MRI, she did not require further intervention. Two patients, one with a suspected normal uterus and the second with a suspected didelphic uterus, were found to have ovarian and tubal cysts and underwent an open left para-tubal cystectomy due to extensive adhesive burden and a left salpingectomy with left ovarian cystectomy, respectively. Finally, in two patients with discordance between suspected Mullerian anatomy and post-thelarche screening PUS, a menstrual outflow obstruction was identified before menarche. In both cases, noncommunicating Mullerian horns were seen on imaging. Both patients were placed on menstrual suppression, although 1 required further MRI imaging as well. Patient 4 had a diagnosis of vaginal agenesis, but it was unclear whether she had functional endometrium. If her PUS had confirmed no functional endometrium, she would not have required menstrual suppression; however, in identifying functioning tissue, her clinical course changed. In the patient requiring MRI imaging (patient 8), it was unclear before imaging whether she had a communicating or obstructed left Fallopian tube. PUS was inconclusive, necessitating further imaging, which identified a noncommunicating left horn requiring menstrual suppression in the setting of abdominal distension and pain. Both patients undergoing menstrual suppression were suppressed before menarche, as they did not have patent outflow tracts and were symptomatic. In total, screening PUS identified discordant anatomy in 8.0% of all patients and prompted intervention in 4.5% of all patients recommended to undergo PUS and 5.7% of patients adherent to this recommendation.

Did Not Complete Post-thelarche PUS

There were 25 patients (22.3%) in whom a post-thelarche PUS was recommended but not completed. The reasoning was predominately unknown (n = 18, 72.0%). Review of records suggested cancelled or not showing up to the imaging appointment (n = 3, 9.5%), pregnancy (n = 2, 6.3%), plans for local completion with no follow-up (n = 2, 6.3%), started thelarche less than 6 months before data analysis (n = 1, 3.1%), and lack of gynecologic consultation (n = 1, 3.1%) as potential contributing factors. Two patients (6.3%) were noted to have a subsequent ultrasound performed in the setting of pregnancy but no other post-thelarche PUS.

Discussion

In our patients with ARMs for whom a 6-month post-thelarche ultrasound was recommended, we found that most patients (77.7%) were adherent to the recommendation, with no differences in demographic characteristics or ARM subtype between subgroups. In those who underwent PUS, there was a small number (10.3%) in whom radiographic anatomy regarding the Mullerian system was discordant with suspected anatomy and a smaller subset (5.7%) in whom medical or surgical intervention was required.

Thelarche generally precedes the onset of menarche by 1-3 years, making this window an ideal time to evaluate reproductive anatomy, as estrogen stimulation makes the reproductive structures larger and more easily visualized, leading to better interpretation of anatomy.[7] The average age at thelarche is 9.7 years, whereas the average age at menarche is 12.3 years, which allows for education, including preparation and anticipatory guidance, before menarche in anyone in whom an abnormality is found.[14] At our institution and many others, patients with ARM are recommended to undergo PUS six months after beginning thelarche to evaluate the Mullerian anatomy, which aids in assessing risk of menstrual outflow obstruction.[15] In this cohort, two patients were identified with obstruction, which facilitated early menstrual suppression, decreasing the risk of symptoms or serious complications such as dysmenorrhea, chronic pelvic pain, endometriosis, and pelvic adhesive disease.[16] In our multidisciplinary clinic, Mullerian anatomy is initially defined by a comprehensive review of available imaging, followed by gynecological involvement in exams under anesthesia or laparoscopic or open assessment of Mullerian structures for direct confirmation. When operative interventions are not necessary, PUS helps piece together the anatomical puzzle. For these patients, use of a screening PUS may help avoid suffering and need for increased healthcare utilization. Overall, the findings on PUS were confirmatory of the suspected Mullerian anatomy, which can help providers continue reproductive health conversations surrounding menstruation, sexual function, and pregnancy (potential and expected outcomes).[17] In 4 patients, ovarian or para-tubal cysts were identified, necessitating procedural intervention in 2 patients.

Most of our patients adhered to recommendation for PUS, with almost 78% of patients completing the study. This adherence may reflect patient and family familiarity with the hospital system and demands for medical needs, patient age, or our institution's counseling and appropriate disclosure of risks and benefits. Ultrasound is the recommended first-line tool used to screen for Mullerian anomalies, as it is cost effective, quickly completed, widely available, and well tolerated by patients. The fact that most of our patients were able to complete the screening PUS supports it as a screening modality without significant barriers. In two patients, further imaging with MRI was recommended following completion of screening PUS to further clarify the anatomy. MRI can be used as an adjunct but is considerably more time-, labor-, and cost-intensive, so is typically reserved for confirmation or clarification of PUS findings rather than a first-line study.[18,19] By starting our screening with a PUS, we are able to more appropriately utilize healthcare resources, saving MRI for those for whom more detailed information is necessary.

Before this study, we recommended screening PUS after thelarche and again after menarche for all patients with ARMs. Given the generally strong congruency between PUS findings and suspected Mullerian anatomy, we have changed our practice pattern. Although we continue

to recommend post-thelarche PUS, we limit post-menarche screening PUSs to patients deemed at high risk for menstrual outflow obstruction, if their Mullerian anatomy has not been assessed at the time of thelarche, or in patients with known Mullerian anatomy who become symptomatic (ie, dysmenorrhea, pelvic pain, or primary amenorrhea without another etiology). On the basis of the encouraging findings in this study of congruence with suspected anatomy, we hope to demonstrate similarly in future work that post-menarche ultrasounds can be avoided in asymptomatic patients.

This is the first work to describe the use of routine screening PUS in patients with any form of ARM. Despite this, there are some limitations. First, our center is a major tertiary referral center with a gynecology service integrated into the care of colorectal patients. This means that more patients with ARMs are seen by gynecology, which ultimately may increase the number of patients to whom a post-thelarche PUS is recommended. The patients referred to our center are often those with more complicated malformations and those with sociodemographic advantages that allow them to seek care at a specialized site. This may contribute to an artificially elevated adherence rate. Second, given our institution's familiarity with ARMs and experienced ultrasound technicians, we may be more able to detect small differences on ultrasound compared with care centers inexperienced in this field. This may have influenced our ability to detect meaningful differences in suspected Mullerian anatomy and findings on post-thelarche PUS. Finally, there are several patients in whom thelarche status was unknown who were not included in further analysis. This represents an important area for future engagement both in accurate medical documentation and in access to gynecologic care.

Conclusion

MDAs are common in patients with ARMs. PUS is a useful tool for evaluating Mullerian anatomy and is generally well accepted by patients. For patients in whom their Mullerian anatomy is known, screening PUS findings are typically congruent with the suspected anatomy. For a minority of patients, screening PUS may identify anatomy incongruent with suspected Mullerian anatomy, leading to improved counseling for patients regarding their anatomy and their contraception choices, pregnancy outcomes, and more. PUS is a useful, easy, and cost-effective modality for screening patients with ARMs after thelarche.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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Author Contributions

GH and **KM** conceived of the idea. **SS, AS, HA, JT**, and **LW** performed the data collection. **SS** performed the statistical analysis. **SS, AS, HA, RW, GH**, and **KM** wrote and revised the manuscript.

Presentation

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jpag.2024.05.001.

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