Treatment of vaginal agenesis in Mayer-Rokitansky-Küster-Hauser syndrome in Denmark: a nationwide comparative study of anatomical outcome and complications

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Objective: To compare the long-term anatomical outcome and complications in treatments of vaginal agenesis in Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome.
Design: A historical comparative follow-up study using medical chart reviews.
Setting: Public hospitals.
Patient(s): A nationwide cohort of patients diagnosed with MRKH syndrome (n = 168).
Intervention(s): McIndoe vaginoplasty (n = 54), self-dilation (n = 60), coital dilation (n = 20), Baldwin vaginoplasty (n = 4), Williams vaginoplasty (n = 3), Davydov vaginoplasty (n = 2), or no treatment (n = 29).
Main outcome measures(s): Mean vaginal depth at follow-up, anatomical treatment success rates at levels of ≥6 cm, ≥7 cm, and ≥8 cm, complications, and resurgery.
Result(s): Mean vaginal depths were 7.4 cm (95% confidence interval [CI] 6.8–8.1 cm), 7.3 cm (95% CI 6.7–7.9 cm), and 8.7 cm (95% CI 7.9–9.5 cm) at follow-up in patients treated by McIndoe vaginoplasty, self-dilation, and coital dilation, respectively. Overall complication rates in the three groups were 35/54 (65%), 21/52 (35%), and 1/20 (5%), respectively. Eighteen (33%) of the patients who underwent McIndoe vaginoplasty needed resurgery.
Conclusion(s): Our findings support the current recommendations of dilation therapy as the first-line treatment of vaginal agenesis and emphasize the relevance of coital dilation in patients able to regularly engage in coital activity. However, further studies of functional outcome and patient satisfaction are needed. (Fertil Steril® 2018;110:746–53. ©2018 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Dilation, Mayer-Rokitansky-Küster-Hauser syndrome, müllerian aplasia, vaginal agenesis, vaginoplasty

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a congenital anomaly characterized by agenesis of the uterus and upper two-thirds of the vagina. The patients are characterized by having a normal female karyotype (46,XX) and normal development of secondary sex characteristics (1). The anomaly results in absolute uterine factor infertility and coital difficulties. The prevalence of MRKH syndrome has been reported to be 1 in 5,000 live female births (2, 3). The diagnosis is typically established during adolescence when patients present with primary amenorrhea. The etiology of MRKH syndrome remains unknown. However, reports of familial occurrence have suggested a genetic cause (4).

The hallmarks in the management of patients with MRKH syndrome are psychological counseling and support upon diagnosis and onward, as well as creating a functional vagina, enabling the patients to have normal penile–vaginal coitus (5). Historically, different surgical approaches using

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allografts have dominated the field. The most commonly used procedure has been the McIndoe vaginoplasty using a split-skin allograft (6, 7). Other procedures include intestinal vaginoplasty (Baldwin), peritoneal vaginoplasty (Davydov), and vulvavaginoplasty (Williams) (8–10). An alternative surgical approach to allografting uses forced surgical traction (Vecchietti) (11), which has been modified to a laparoscopic procedure with promising results (6, 12). In contrast, the use of nonsurgical correction by dilation has increased. The most common method involves self-application of successive dilators of increasing length and width (Frank) (13). Other dilation methods described in the literature involve dilators attached to a bicycle stool (Ingram) and dilation by coitus (d'Alberton) (14, 15). Since 2002, the American College of Obstetricians and Gynecologists (ACOG) recommended dilation as first-line treatment owing to the overall good results and low risk of complications (5, 16–18). Most of the literature, however, consists of noncomparative single-center case series with poor standardization and follow-up. Thus, the best treatment of vaginal agenesis in regard to outcome and complication rate remains controversial (6, 19).

The aim of this study was to compare anatomical outcome and complications in treatments of vaginal agenesis in Denmark using data from medical chart reviews.

MATERIALS AND METHODS

Study Design and Patients

This study was a historical cohort study investigating a nationwide cohort of patients diagnosed with MRKH syndrome in Denmark using prospectively recorded data in medical charts. The Danish National Health Service provides universal tax-funded health care with free access to hospital and primary medical care for all Danish residents. The patients were identified through a search of hospitalizations and outpatient visits at public hospitals Denmark from January 1, 1994 to April 10, 2015. We searched the Danish National Patient Registry using diagnosis codes from the *International Statistical Classification of Diseases and Related Health Problems*, *Tenth Revision*. The following diagnosis codes were used: Q51.0 "Congenital absence of uterus," Q51.5 "Congenital absence of cervix," Q51.8C "Atresia of uterus," Q51.8H "Hypoplasia of uterus," and Q52.0 "Congenital absence of vagina." Subsequently we validated the diagnoses through a review of karyotype data and patient medical charts. The charts were retrieved from June 2015 to October 2015. The validation process and patient characteristics have previously been described in detail (2).

Medical Charts Data Abstraction

In patients with a confirmed diagnosis of MRKH syndrome, we performed a systematic review of the patients' medical charts. We obtained information on the following categorical variables: method to establish diagnosis, choice of treatment for vaginal agenesis, complications related to treatment, need of resurgery, and psychosexual support. Continuous variables included vaginal depths at referral, after surgery, and the last day of follow-up. We registered dates of dilation start, surgery, resurgery, and of last follow-up. Dates of referral were given in the Danish National Patient Registry data.

With patient medical charts as the main data source in this study, we could not measure the functional outcome or patient satisfaction in any objective way.

To ensure the accuracy and reliability of the data abstraction, we made a standardized digital abstraction form using EpiData Software (v2.0.3.15; EpiData Association). All data abstraction was performed by M.H.

Statistical Methods

Basic descriptive statistics, including frequency distributions, medians, and interquartile ranges, were used to describe choices of examination and treatment, age at start of treatment, and days from referral to start of treatment. We grouped the patients by date of referral (before and after January 1, 2004) to look for differences in management during the study period.

To compare the anatomical effectiveness of the different treatments, we calculated mean vaginal depths with 95% confidence intervals (CIs) at the last day of follow-up, constituting the main outcome of the study. For patients treated by surgery, mean vaginal depth after operation was also calculated. Patients treated by surgery after failure of dilation therapy were placed in both groups, with vaginal depths at last day of follow-up during dilation and after surgery. As a subanalysis we measured rates of anatomical treatment success by dichotomizing the anatomical outcome data (success/failure). With no consensual vaginal length defining treatment success, success rates were calculated at levels of ≥ 6 cm, ≥ 7 cm, and ≥ 8 cm.

Group differences in mean vaginal depths at follow-up were tested using one-way analysis of variance after normality testing by the Shapiro-Wilk's test. In the case of a statistically significant difference, post hoc analysis by Bonferroni's multiple comparison test was performed. Group differences in categorical variables were tested using Pearson's χ^2 test. Finally, we performed a correlation analysis of age at treatment start and the anatomical outcome by calculation of Spearman's correlation coefficients, r_s. We used an α level of 0.05 in all analyses to define statistical significance.

All statistical analyses were performed using Stata Statistical Software (v14.2; StataCorp).

Ethics

The study was approved by the Danish Data Protection Agency (journal no. 2008-58-0028) and the Danish Health Authority (journal no. 3-3013-873), waiving the need of institutional review board approval.

RESULTS

A cohort of 168 patients with a confirmed diagnosis of MRKH syndrome was established. Table 1 lists the diagnostic methods used before and after January 1, 2004.