Functional and anatomic results of amnion vaginoplasty in young women with Mayer-Rokitansky-Küster-Hauser syndrome

Christina Fotopoulou, M.D.,[a] *Jalid Sehouli, Ph.D.,*[a] *Nicole Gehrmann, M.D.,*[a] *Ines Schoenborn, Ph.D.,*[b] *and Werner Lichtenegger, Ph.D.*[b]

[a] Department of Gynecology and Obstetrics, and [b] Department of Obstetrics, Charité, Campus Virchow Clinic, University Hospital, Berlin, Germany

Objective: To evaluate the surgical outcome and the long-term anatomic and functional results in young women with Mayer-Rokitansky-Küster-Hauser Syndrome (MRKH) undergoing neovaginal creation with amniotic membranes.
Design: Evaluation of surgical and functional outcome according to clinical records and validated questionnaires about sexuality (Female Sexual Function Index [FSFI]) over a 1.5-year follow-up period.
Setting: University hospital and referral center for pediatric and adolescent gynecology.
Patient(s): Seven patients with congenital vaginal aplasia with a mean age of 20.86 ± 3.56 years (range 17–26 years).
Intervention(s): McIndoe procedure modified by the application of human freeze-dried amniotic membranes.
Main Outcome Measure(s): Anatomic success was defined by a vaginal length ≥8 cm, and a width allowing the easy introduction of two fingers. FSFI scores were applied to define functional results.
Result(s): Mean neovaginal length was 9.3 cm (range 4–12 cm). The mean FSFI score was 30.0 ± 6.9. Major operative complications occurred in one patient. In six out of seven patients satisfactory anatomic and functional results were achieved.
Conclusion(s): The surgical dissection of the vesicorectal space and the application of human amnion over a vaginal mold to create a neovagina results in satisfying anatomic and functional outcome with low perioperative morbidity in MRKH patients. (Fertil Steril® 2010;94:317–23. ©2010 by American Society for Reproductive Medicine.)

Key Words: Mayer-Rokitansky-Küster-Hauser syndrome, vaginal reconstruction, amnion, vesicorectal space

Mayer-Rokitansky-Küster-Hauser Syndrome (MRKH) refers to a condition of mullerian agenesis where the mullerian ducts fail to develop resulting in the absence of a normal uterus and vagina in the presence of a normal 46,XX karyotype. A shallow vaginal pouch is present, and the fallopian tubes, ovaries, and secondary sex characteristics are normal (1, 2). The MRKH syndrome is the second most common cause of primary amenorrhea in young women. The estimated prevalence is 1 in 4,000–5,000 women (3, 4). It has been considered to be a sporadic anomaly, but recent reports suggest a genetic defect that is transmitted as an autosomal dominant trait with incomplete penetrance and variable expressivity. Nevertheless, the etiology of MRKH syndrome remains unclear (5). Associated congenital anomalies of the upper urinary tract, such as unilateral renal agenesis and pelvic or horseshoe kidneys, are reported to occur in 30%–40% of all cases of MRKH syndrome, and 10%–15% have skeletal anomalies involving the spine, ribs, and extremities (6).

Although numerous methods for creating a neovagina have been proposed, there is no consensus about which procedure should be considered to be the ideal standard. The major differences between the various procedures are access (i.e., laparoscopic, open transabdominal, or vaginal) and type of tissue used to cover the neovaginal cavity (amniotic membranes, peritoneal layers, recombinant artificial dermis, skin graft, intestinal tissue, etc.) (7).

The data regarding the anatomic and functional success of the technique based on the use of amniotic membranes to cover the vaginally dissected vesicorectal space in MRKH patients are very limited (8). The aim of the present study was to assess the perioperative, clinical, and functional course of all consecutive MRKH patients surgically treated in our institution by the creation of an "amnion" neovagina. Systematic anatomic, surgical, and functional data regarding sexuality are presented.

MATERIALS AND METHODS

From January 2005 to April 2008, we surgically treated seven MRKH patients. All of the patients presented to our

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Reprint requests: Christina Fotopoulou, M.D., Department of Gynecology and Obstetrics, Charité, Campus Virchow Clinic, University Hospital, Augustenburger Platz 1, 13353 Berlin, Germany (FAX: 0049-30-450564900; E-mail: christina.fotopoulou@charite.de).

Department of Pediatric and Adolescent Gynecology for further evaluation of primary amenorrhea. Diagnostic criteria for the MRKH syndrome were normal physical development according to the Tanner stages (9), blind-ending vagina, the finding of a fibrous remnant in place of the uterus at rectal examination and no signs of hematocolpos or hematometra due to hymenal atresia. Each patient underwent a transrectal or transabdominal sonography, which confirmed the absence of a normal developed uterus as well as ultrasonographic examination of the urinary system and karyotyping to exclude other differential diagnoses such as testicular feminization.

All patients underwent a vaginoplasty using chemically processed and sterilized freeze-dried human amniotic membranes. The human amnion was readily harvested from the amniotic sac of term infants delivered from healthy women. Split-thickness skin grafts are categorized as thin (0.005–0.012 in), intermediate (0.012–0.018 in), or thick (0.018–0.030 in), based on the thickness of the harvested graft. The thickness of the used amnion was similar to a classic thin split-thickness skin graft. The freeze-dried amniotic membranes we used, were specially processed, tested, and sterilized by the blood bank of our institution. Therefore, no additional testing was required to be performed on the donor amnion tissue before insertion into the neovaginal cavity.

A transverse incision was made at the vaginal dimple, and a vesicorectal cavity of approximately 12 cm was dissected to the level of the peritoneum. After thorough bipolar hemostasis a mold of glass covered by sofratyl and moisturized amniotic membranes was then inserted and the labia minora were secured around the stent to prevent expulsion. The freeze-dried amnion was soaked in sterile saline solution for approximately 10 minutes before insertion into the vaginal space, to form a soft and moisturized thin-layer tissue to easily cover the whole surface of a mold of glass covered by sofratyl. The different steps of the preparation of the vaginal mold are presented in Fig. 1. In that way, difficulties with the thin amnion shearing off the form were avoided.

Vaginal tamponade was then the method of filling the neovaginal cavity, by introducing a sterile gauze with estriol creme (1%) to promote epithelialization. The gauze was changed twice daily for the first 5 days. The patient remained on bedrest during this period, after which the mold was removed and replaced by a soft silicon vaginal dilator lubricated with estriol creme (1%) to induce epithelialization of the newly created surface. The patients were advised to continue using the dilator for the first 3–5 postoperative months to prevent contraction of the neovagina. The patients were also encouraged to engage in sexual activities to induce their motivation and comply with the required postoperative measures necessary to guarantee a successful procedure. Once the patients started engaging in sexual activities, the use of dilators was recommended for shorter periods of time.

All patients could be discharged within an average 10 days after surgery and were instructed how to use and apply the vaginal dilator and the estriol creme by adolescent gynecologists. All patients received a special vaginal dilator 12 cm long with an adjustable diameter, achieved by insufflation, to fit the individual proportions. Care of the dilators includes simple flush with water and soap after each use. Vaginal intercourse was allowed no earlier than 6–8 weeks after vaginoplasty, and this varied depending on the wound healing process and the grade of epithelialization of the neovagina. Patients were followed-up in the initial postoperative period once every 4 weeks for the first 3 months and then twice a year. The clinical evaluation included vaginal and rectal examinations as well as vaginoscopy. Functional results were additionally assessed by the Rosen Female Sexual Function Index (FSFI) questionnaire (10), validated for the German-speaking population (11). This short 19-item quiz is validated for assessment of female quality of life and detection of sexual dysfunction in adults. It has demonstrated its validity in earlier studies (11, 12), and its score is unbiased regarding age, education, and economic status of the patients. The 19 items are assigned to six separate domains of female sexual function; the first four relate to the four major categories of sexual dysfunction: desire, arousal, orgasmic, and sexual pain disorder. The fifth domain describes the quality of vaginal lubrication, and the sixth the global sexual and relationship satisfaction.

The vaginoplasty method using freeze- dried amniotic membranes has extensively been used in our institution inclusively in the field of pediatric surgery (i.e. burns), since more than 15 years, so no institutional review board approval was required. An informed written consent was obtained by every patient who was operated on this procedure prior to surgery.

RESULTS

Between July 2005 and August 2008, seven patients with a mean age of 20.86 $\pm$ 3.56 years (range 17–26 years) underwent vaginoplasty by human amniotic membranes. Median follow-up for the whole group of patients was 16.43 months (range 4–41 months).

Only one patient was identified to have a urinary tract abnormality, specifically horseshoe kidney. No skeletal anomalies were described. Mullerian remnants were seen in four of the seven patients (57%), presenting as a noncavitary streak of fibrous tissue. All patients presented initially to our clinic an average 1.2 years (range 0–3) before reconstructive surgery owing to primary amenorrhea carrying already the diagnosis of a MRKH syndrome. Two patients underwent at initial presentation a diagnostic laparoscopy to confirm the diagnosis. No routine laparoscopy was otherwise performed, because clinical examination and sonographic findings were considered to be sufficient to establish the diagnosis. All patients were counseled that the individual's readiness for vaginal manipulation and/or intercourse is critical for the timing of the surgery and so the operative procedure was planned when the young woman stated she was willing to become

sexually active. Three of the patients had a stable partner at the time of surgery.

The mean operative time was 24.7 ± 2.09 minutes (range 20–33 minutes) with only minimal blood loss in all cases. The mean length of hospital stay was 10.8 ± 0.97 days (range 8–14 days). Six of the seven patients had a rather uncomplicated hospital course; one patient developed a urinary tract infection within the first postoperative week, requiring oral antibiotic treatment. One patient developed extensive infection with ulceration of the rima ani and vulva 7 days after surgery. Speculum examination revealed a rectovaginal fistula, for which she required surgical repair with fistula excision and diverting loop ileostomy. The infection resulted in a stricture and shortening of the newly created vagina, so that the patient expressed the desire of a new neovagina 4 months after the initial procedure. She underwent neovaginal reconstruction using a sigmoid loop. This was further complicated by anastomotic leak and sepsis, and multiple reoperations were performed to control the peritonitis. Five weeks later she was discharged in very good condition and with satisfying functional and anatomic results of the neovagina.

In all of the other patients a satisfactory neovaginal length of at least 9 cm could be obtained (mean vaginal length 9.8 ± 1.7 cm, range 9–12 cm), and the neovaginal cavity was easily passable for two fingers already at the time of discharge. The follow-up examinations 1, 3, and 6 months after surgery revealed a well epithelialized neovaginal cavity, without stricture formation or shortening, because all of the patients successfully applied the vaginal phantom or had regular vaginal intercourse. The anatomic and functional results as well as the data regarding the operative complications are presented in Table 1. Six of the seven patients (85.7%) experienced regular or less regular vaginal intercourse in an average 5.28 ± 1.25 months after surgery; the range expanded from 2 to 7 months mainly depending on the psychologic ability of each woman. None of the patients stated having dyspareunia or contact bleeding during intercourse; however, five of the patients (71.4%) used lubricants, more in a prophylactic matter than owing to insufficient lubrification of the neovagina, according to their statements. The mean postoperative period the patients used almost permanently a vaginal phantom to prevent constriction of the neovaginal cavity was 5 ± 2.5 months (range 2–8 months).

When evaluating the functional success according to the FSFI, the mean full FSFI score of all five sexually active patients was 30.0 ± 6.9, thus corresponding to the equivalent score of 30.2 ± 6.1 reached by healthy women (10). Detailed values of the FSFI of our five sexually active MRKH patients after amnion vaginoplasty compared with the equivalent mean FSFI values of MRKH patients after sigmoid vaginoplasty and with healthy individuals are presented in Table 2.

The one patient with sigmoid neovagina after rectovaginal fistula formation was not included in the FSFI evaluation, because she no longer had an amnion neovagina.

DISCUSSION

Various studies have evaluated the functional and anatomic evaluation of several operative (7, 8, 12–30) and nonoperative (31, 32) vaginoplasty methods in patients with vaginal agenesis due to MRKH syndrome. However, no "ideal"

TABLE 1

Data of perioperative morbidity, anatomic, and functional characteristics related to vaginal reconstruction with human amniotic membranes in seven Rokitansky patients at least 4 months after vaginoplasty.

	Mean ± SD (range)	Patients, n (%)
Patient age (y)	20.86 ± 3.58 (17–26)	
Vaginal length (cm)	9.3 ± 2.3 (4–12)	
Operation time (min)	24.7 ± 2.09 (20–33)	
Length of hospital stay (d)	10.8 ± 0.97 (8–14)	
Time of vaginal phantom using after surgery (mo)	4.1 ± 1.07 (3–5)	
Start of regular vaginal sexual intercourse (mo after surgery)	5.28 ± 1.25 (2–7)	
Early operative complications:		
Infection and rectovaginal fistula formation		1 (14.3)
Urinary tract infection		1 (14.3)
Dyspareunia		0
Contact bleeding		0
Vaginal stenosis		0
Prophylactic use of lubricants during vaginal intercourse		5 (71.4)

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TABLE 2

Female Sexual Function Index (FSFI) values of the five sexually active Mayer-Rokitansky-Küster-Hausen (MRKH) syndrome patients after amnion vaginoplasty compared with the equivalent mean FSFI values of MRKH syndrome patients after sigmoid vaginoplasty and with healthy individuals.

	MRKH syndrome patients		
Domain	After amnion vaginoplasty (n = 5)	After sigmoid vaginoplasty (n = 11; ref. 12)	Healthy women (n = 131; ref. 10)
Desire	4.9 ± 1.2	4.7 ± 0.9	4.1 ± 1.1
Arousability	5.0 ± 0.8	4.9 ± 0.6	5.0 ± 1.0
Lubrication	4.0 ± 0.7	5.0 ± 0.9	5.5 ± 0.9
Orgasm	5.5 ± 1.0	5.3 ± 0.8	5.0 ± 1.2
Satisfaction	5.3 ± 1.4	4.7 ± 1.6	5.1 ± 1.2
Pain	5.3 ± 1.8	3.5 ± 2	5.5 ± 1
Total score	30.0 ± 6.9	28.1 ± 6.8	30.2 ± 6.1

Note: The patient after rectovaginal fistula formation and subsequent sigmoid neovagina and the patient without sexual intercourse were not included in this FSFI evaluation. Full FSFI score is 36 points. Values are given as mean ± SD.

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method is yet established which can be universally recommended. The choice of vaginoplasty depends on numerous factors, including patient preparedness, preference, and expectations and certainly the surgeon's experience. Regardless of the surgeon's personal preference, the patient should be thoroughly informed about treatment alternatives, including description of potential complications, long-term durability, and results on long-term sexual function. Thomas and Brock (33), in a review of nonoperative and operative alternatives for vaginal replacement, concluded that the most popular

TABLE 3

Relevant series and case reports in the literature concerning the treatment of Rokitansky (MRKH) syndrome by human amniotic membranes.

Author, y (ref.)	No. of MRKH patients	Anatomic success	Complete epithelialization/ metaplasia of the amnion into squamous cells	No. of major complications
Tancer et al., 1979 (36)	1	100%	yes	0
Karjalainen et al., 1980 (38)	3	100%	yes	0
Morton and Dewhurst, 1986 (30)	27	92.6%	yes	1 (rectal injury)
Ashworth et al., 1986 (21)	15	100%	NR	NR
Mac, 1988 (37)	9	100%	yes	0
Nisolle and Donnez, 1992 (35)	—	"good"	NR	NR
Bleggi-Torres et al., 1997 (16)	10	100%	yes	0
Sharma et al., 2008 (14)	17	88.23%	yes	2 (1 rectal injury and 1 rectovaginal fistula)
Tözüm, 1976 (20)	1	100%	yes	0

Note: NR = not reported.

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methods of vaginal substitution include passive dilation, inlay skin grafts, rotational myocutaneous flaps, and bowel substitute vaginoplasty. The American College of Obstetricians and Gynecologists committee opinion on adolescent health care (34) published that the condition can usually be successfully managed in a conservative way by the use of vaginal dilators as long as the patient is sufficiently motivated. If a surgical option is considered, a number of approaches are available; with the Abbè-McIndoe operation being the most common.

The Abbè-McIndoe technique (29) is indeed considered to be a valid treatment option for vaginoplasty, but no consensus has been reached on what material should be used for the neovagina canal wall lining (27). Various authors have reported on the use of several artificial or biologic materials to cover the neovaginal cavity and induce epithelialization. Autologous human amniotic membranes (14, 16, 21, 30), homologous amniotic membranes (20), peritoneal layers of the pouch of Douglas (13), artificial dermis and recombinant basic fibroblast growth factor (7), split-thickness skin graft from the buttocks (29), oxidized cellulose (18), acellular human dermal allograft (26) and autologous in vitro–cultured vaginal tissue (27) are some of the applied tissues that have been named.

Limited and rather older reports are available on the anatomic and functional success of vaginoplasty with human amnion (14, 16, 20, 21, 30, 35, 36). The most relevant series are presented in Table 3. One of the first attempts of vaginal reconstruction from amniotic membranes was in 1934 in the French-language literature, where Brindeau used amnion to construct a neovagina for a patient with mullerian agenesis (39).

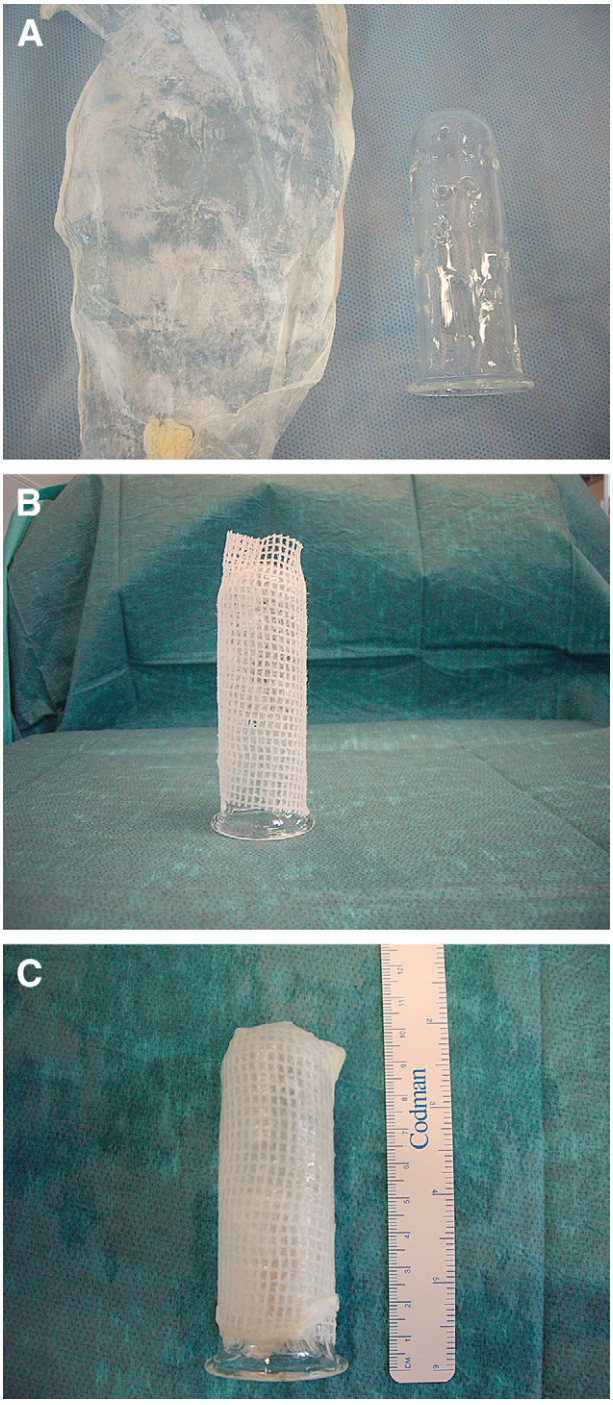
In the present analysis, we report very good anatomic and functional results of amnion vaginoplasty similar to results from previous reports. These findings confirm those obtained by many previous authors applying the same method (Table 3). In a total of 68 reported patients (14, 16, 20, 30, 36, 38), all major complications were related to rectal injury (3 cases, 4.4%) with otherwise very satisfying anatomic results.

Of great importance is the fact that following diagnosing of vaginal agenesis in adolescent girls, it is important to wait until the patient is ready to engage in sexual activity before initiating any kind of treatment. For those patients who have a 2–3-cm hymenal fossa, Frank's method of progressive vaginal dilation should be always offered (8), but the patient should be informed that success has proven to be variable and unpredictable and that the patient needs to be highly motivated and willing to continue long-term dilations (21, 41). Effective management should, moreover, include a careful comprehensive psychologic preparation and support of the patient.

We believe that vaginal construction from amniotic membranes carries the following advantages over other operative reconstructive methods. The human amnion appears to have

FIGURE 1

Pictures of the freeze-dried human amniotic membranes and the vaginal mold that is inserted for vaginoplasty in Mayer-Rokitansky-Küster-Hauser syndrome patients. (**A**) Freeze-dried amnion and vaginal mold. (**B**) Vaginal mold covered with sofratyl. (**C**) Vaginal mold wrapped in sofratyl and moisturized amniotic membranes just before insertion into the neovaginal cavity.



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great advantages over the split skin graft previously used in the original Abbè-McIndoe technique (29). Amnion is readily available, and there is no need for additional incisions as at the donor site in the split skin graft technique. Furthermore, there have been no problems with immune rejection, because human amniotic epithelial cells do not express on their surfaces histocompatibility antigens such as HLA-A, -B, -C, and -DR or ®2- microglobulin. Akle et al. (40) found no evidence of tissue rejection after implanting amnion subcutaneously in volunteers.

Compared with the laparoscopic approach of the Vecchietti method, where the creation of the neovagina is achieved by invagination using an acrylic "olive" that is laparoscopically placed against the vaginal dimple (8), the present method requires no abdominal incision. Furthermore, the Vecchietti straight thread-bearing cutting needle, which subperitoneally reaches the space between the bladder and rectum, can also cause injuries of the neighboring organs, such as the bladder (8). Rectal injuries and local infections are the major risk factors predisposing rectovaginal fistulas. During dissection of the vesicorectal space, the surgeon should always avoid any contamination of the amnion graft with bacteria from the rectal flora. He/she can, for additional help, insert an index finger into the rectum, during rectovesical dissection, so that the anatomic borders are more easily recognized and sharp injury of the rectal mucosa is avoided. If, nevertheless, a rectal injury occurs, a temporary diverting loop ileostomy could be considered after rectal repair, to promote local wound healing and prevent future fistula formation.

Despite the lack of evidence from randomized trials comparing the various vaginoplasty operative methods, we conclude, based on our results, that the neovaginal reconstruction using freeze-dried amniotic membranes is a safe and easy technique, without induction of scar at the donor site, and should be the preferred surgical technique, as a modification of the McIndoe procedure, for patients with Rokitansky syndrome.

Still, in the absence of an "ideal" treatment strategy, patients should be objectively and professionaly informed also about the nonsurgical alternatives, so that an individual ideal method, addressed to each patient́s preference, is then selected.

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