Association of the rectovestibular fistula with MRKH Syndrome and the paradigm shift in the management in view of the future uterine transplant

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KEYWORDS
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ABSTRACT
Uterine transplantation in Mayer-Rokitansky-Küster-Hauser (MRKH) patients with absolute uterine function infertility have added a new dimension and paradigm shift in the management of females born with rectovestibular fistula coexisting with vaginal agenesis. The author reviewed the relevant literature of this rare association, the popular and practical classifications of genital malformations that the gynecologists use, the different vaginal reconstruction techniques, and try to know what shall serve best in this small cohort of these patients lest they wish to go for uterine transplantation in future.

INTRODUCTION
In a female newborn, a single perineal opening with shorter appearing introitus suggests cloaca. If instead, there are three openings in the introitus with the rectal opening appearing as a fistula in the posterior vestibule, outside of the hymen, it is diagnostic of a rectovestibular fistula (or simply, vestibular fistula as per Krickenbeck classification). [1] However, if two openings are seen in the introitus with an absent anus, then we would have a differential diagnosis of three entities- i) imperforate anus with no fistula [commonly seen in patients with trisomy 21], ii) anorectal agenesis with rectovaginal fistula and iii) rectovestibular fistula with vaginal atresia, cervicovaginal atresia or uterocervicovaginal atresia, popularly known as Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome. [2] The majority of these patients with such anorectal malformations would present in the neonatal period. But, in a developing country like India where there are still home deliveries happen in remote villages, there may be some girls with wide rectovestibular fistula who may be decompressing stools relatively well and may present as late as in early adolescence.

The presence of two openings in the introitus is probably the least common presentation of the anorectal malformation in a female newborn. Traditionally, it has been said that if there are two orifices in the perineum of a girl with an imperforate anus, then the malformation is most likely a rectovaginal fistula with a reported incidence in literature varying widely from 0% to 84%. [3,4] These false high reported incidences have been attributed to the indiscriminate inappropriate labeling of rectovestibular fistula and cloaca as rectovaginal fistula. [5,6] The true incidence of this variant is probably less than 1%. [7]

Though anorectal agenesis without fistula is known to constitute 2-4% of all anorectal malformations, it is much less common in females as compared to their male counterparts. [8,9] Male-female ratio has been quoted around 5:1 in one large series. [8] The associated presence of Down’s Syndrome is a pointer and has been quoted to coexist in 40-95% subjects. [8,9] These neonates would obviously not been able to decompress the meconium and would present as surgical emergencies.

The author of this review article has not encountered a single case of anorectal agenesis with or without rectovaginal fistula in his entire professional career spanning over 3 decades but has treated 14 patients (few unreported) of the third unusual variant of the rectovestibular fistula with vaginal atresia, the major-
ity being MRKH Syndrome; each of them had some or
the other form of bowel vaginoplasty.[2,10,11]

The focus of this review article is on the management
strategies of the rectovestibular fistula with vaginal
atresia. Robert Gross described two cases of vaginal
atresia among 507 patients with anorectal malfor-
mation, but without a description of a surgical re-
pair.[12] The exact frequency of vaginal agenesis in
patients with rectovestibular fistula is unknown. The
reported incidence has been anywhere between 0.5% to
16.3%.[13,14] The incidence seen in tertiary referral
base with high workloads is around 10%.[10,15]

De la Torre et al. in 2016 [14] and Skerritt et al. in
2017 [16] did two historic metanalyses; adding few
more cases from the literature, at least 113 patients
of rectovestibular fistula associated with vaginal atre-
sia could be searched in published literature (Table 1).
So, it will be fair to label it as a rare variant in the
Krickenbeck classification. The 15 patients reported
by Ahmed et al. in 2020 [17] from Cincinnati Chil-
dren’s Hospital Medical Center, Cincinnati enrolled
from 1991 to 2017 have not been included as it was
difficult to find out if there was any overlap of this
cohort with the patients earlier reported by Levitt
from the same institution in 2009.[18]

We, pediatric surgeons, are usually involved in the
management as far as the creation of neovagina and
and the neo-anus, but do not get to follow these children
in their post-pubertal period or when they grow up as
adults, ready to cohabit with a male partner or marry.
The transplant surgeons have added a new dimension
by venturing into uterine transplantation (UTx) in
these subjects. This has led to a paradigm shift in the
management. Earlier, the debate used to resolve
around vaginal replacement using bowel via a vix oth-
er neovagina creation methods (non-surgical as well
as surgical using skin grafts/flaps, peritoneum, buc-
cal mucosa, etc.) and their pros and cons. But in the
futuristic scenario, we have to evaluate the neovagina
creation methods and their potential impact on sub-
sequent UTx.[50] Most importantly, any surgery that
would entail a laparotomy and result in adhesions in
the lower abdomen and pelvis has to be avoided as
this would prohibit future uterine transplantation.
Further, we must equip ourselves to accurately rec-
ord the different components of associated Mullerian/
uterovaginal anomalies as per the classifications de-
vised by the American and European Associations so
that we are on the same page and avoid any mis-
communication with the surgeons who are going to
undertake subsequent surgeries in later adult lives of
these subjects.

**MRKH Syndrome and the various classifications**

The MRKH syndrome is regarded as an inhibitory
malformation of the Mullerian (paramesonephric)
ducts. Clinically, this malformation of the female gen-
ital organs presents as a rudimentary solid bipartite
uterus with a solid vagina. Mayer and Rokitansky
described one case each of the ‘bipartite uterus’ in the
years 1829 and 1838, respectively.[51,52] Küster in
1910, for the first time, summarized and collected
individual cases of ‘rudimentary solid septate uterus
with solid vagina’ from the literature in a review pa-
per.[53] It was only in 1961 that the ‘rudimentary
solid septate uterus with a solid vagina’ was first giv-
en its current name, ‘Mayer–Rokitansky–Küst
s syndrome’ by the gynecologist Hauser,[54] later being
extended to ‘Mayer–Rokitansky–Küster–Hauser’ syn-
drome.

MRKH patients have normal development of the fe-
male phenotype, with normal thelarche and pubar-
che, and a female karyotype (46 XX) with primary
amenorrhea. In its typical form or isolated type, there
is a septate, rudimentary uterus, aplasia of the cervix
and upper 2/3rd of the vagina, and normal or hypo-
plastic bilateral adnexa. The ovarian function is in-
taxt, as evident by development of pubarche and thelarche and the presence of a biphasic basal tem-
perature curve, and also that hormonal secretion
does not differ from that in normal individuals.

Schmid-Tannwald and Hauser in 1977 described an
atypical form of MRKH syndrome associated with var-
ious additional malformations of ovaries and kid-
neys.[55] Two years later, in 1979, Duncan et al. de-
scribed the most severe form of MRKH syndrome, the
MURCS association that comprised of Mullerian duct
aplasia, renal aplasia, and cervicothoracic somite
dysplasia.[56] Some authors describe typical and
atypical MRKH syndrome anomalies as type 1 and
type 2 MRKH and include all patients having associ-
ated extra-genital anomalies, including MURCS asso-
ciation as Type 2.[57]

Oppelt et al. in 2006 reported in their large series of
53 MRKH patients that the typical form, atypical
form, and those with MURCS association existed in
64%, 24%, and 12% patients respectively; or in other
words, associated extra-genital congenital malfor-
mations were present in more than a third of cas-
es.[58] However, the spectrum of types 1 and 2 of the
MRKH syndrome is known to vary across different
races and geographical locations; the incidence of
MURCS association was only 3% in a large cohort of
274 Chinese subjects with MRKH syndrome.[59]

Oppelt et al. recommend sets of essential and desira-
ble investigations that are required for work-up of
MRKH syndrome.[59] Essential investigations includ-
ed chromosomal analysis (to rule out the differential
diagnoses of testicular feminization and adrenogenital
syndrome), MRI of abdomen/pelvis, and hormonal
status (LH, FSH, estradiol) to rule out non-functional
ovaries. The desirable investigations included an ul-
trasound of the vaginal vestibule and rectum, diag-

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| Author          | Year | Country         | N  | RVF | Sigmoid | Vagina | Ileum | Skin/mucosa flaps | Dilatation | PC | PP | No vaginal replacement | Functional uterus preserved (Y/N) |
|-----------------|------|-----------------|----|-----|---------|--------|-------|-------------------|------------|----|----|-----------------------|----------------------------------|
| Gross [1]       | 1953 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Wachs [12]      | 1953 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Wang [13]       | 1996 | Canada          | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Cohn [14]       | 1996 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Ein [15]        | 1996 | Canada          | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Fujiwara [16]   | 1996 | Japan           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| King [17]       | 1996 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Toleti-Valchek [18] | 1999 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Digray [19]     | 1999 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Okoye [20]      | 2000 | UK              | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Adejuyigbe [21] | 2000 | Nigeria         | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Sarin [22]      | 2002 | India           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Dhar [23]       | 2002 | India           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Okoye [24]      | 2002 | Nigeria         | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Tei [25]        | 2002 | Japan           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Deshpande [26]  | 2002 | India           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Patankar JZ [27]| 2004 | Singapore       | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Baba [28]       | 2004 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Banu [29]       | 2005 | Bangladesh      | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Wakhlu [30]     | 2005 | India           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Sarin [31]      | 2005 | India           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Wakhlu [32]     | 2006 | Bangladesh      | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Komura [33]     | 2006 | Japan           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Wakhlu [34]     | 2007 | India           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Dhar [35]       | 2007 | India           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Komura [36]     | 2007 | Japan           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Leveque [37]    | 2007 | France          | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Cohn [38]       | 1953 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Ein [39]        | 1953 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Fujiwara [40]   | 1953 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Komura [41]     | 1953 | Japan           | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Wakhlu [42]     | 1953 | USA             | 1  |     |         |        |       |                   |            |    |    |                       | Y                                |
| Name          | Year | Country          | RVF | NM | PF | PC | Notes |
|---------------|------|------------------|-----|----|----|----|-------|
| Jessel        | 2012 | USA              |     |    |    |    |       |
| de Blauuw     | 2013 | Netherland       |     |    |    |    |       |
| Kisku         | 2014 | India            |     |    |    |    |       |
| Kapczuk       | 2014 | Poland           |     |    |    |    |       |
| Pandya        | 2015 | USA, Japan       |     |    |    |    |       |
| Teo           | 2015 | Singapore        |     |    |    |    |       |
| De la Torre   | 2016 | India            |     |    |    |    |       |
| Bjørsum-Meyer | 2016 | Denmark          |     |    |    |    |       |
| Tiwari        | 2017 | India            |     |    |    |    |       |
| Gupta         | 2016 | India            |     |    |    |    |       |
| RVF = Rectovestibular Fistula, NM = Not Mentioned, PF = Peritoneal Flap, PC = Pouch Colon |
The association of the rectovestibular fistula with MRKH Syndrome and the paradigm shift in the management in view of the future uterine transplant

In view of the variability in the genital malformations and the presence of associated anomalies, Oppelt et al. suggested VCUAM (Vagina Cervix Uterus Adnex-associated Malformation) classification in the same year 2005.[60] The external and internal female genital organs were divided into the following subgroups in accordance with the anatomy: vagina (V), cervix (C), uterus (U), and adnexas (A). Associated malformations were assigned to a subgroup (M) relative to each specific organ (Table 2).

So, using VCUAM classification, the different genital anomalies depicted in Fig. 1 (a), (b), and (c) below could be designated as V5b,C2b,U4b,A1b,M#; V5b,C2b,U0,A0,M#; and V+,C0,U0,A0,M#. One of the limitations of this classification is that distal vaginal atresia is not included.

Table 2: VCUAM classification of genital malformations - Description of the individual malformations relative to the organ.

| Organ       | Classification                                                                 |
|-------------|--------------------------------------------------------------------------------|
| Vagina (V)  | 0 Normal                                                                       |
|             | 1a Partial hymenal atresia                                                    |
|             | 1b Complete hymenal atresia                                                   |
|             | 2a Incomplete septate vagina _50%                                               |
|             | 2b Complete septate vagina                                                     |
|             | 3 Stenosis of the introitus                                                    |
|             | 4 Hypoplasia                                                                   |
|             | 5a Unilateral atresia                                                         |
|             | 5b Complete atresia                                                           |
|             | S1 Sinus urogenitalis (deep confluence)                                       |
|             | S2 Sinus urogenitalis (middle confluence)                                     |
|             | S3 Sinus urogenitalis (high confluence)                                       |
|             | C Cloacae                                                                     |
|             | + Other                                                                        |
|             | # Unknown                                                                      |
| Cervix (C)  | 0 Normal                                                                       |
|             | 1 Duplex cervix                                                                |
|             | 2a Unilateral atresia/aplasia                                                  |
|             | 2b Bilateral atresia/aplasia                                                   |
|             | + Other                                                                        |
|             | # Unknown                                                                      |
| Uterus (U)  | 0 Normal                                                                       |
|             | 1a Arcuate                                                                     |
|             | 1b Septate<50% of the uterine cavity                                           |
|             | 1c Septate>50% of the uterine cavity                                           |
|             | 2 Bicornate                                                                    |
|             | 3 Hypoplastic uterus                                                           |
|             | 4a Unilaterally rudimentary or aplastic                                         |
|             | 4b Bilaterally rudimentary or aplastic                                          |
|             | + Other                                                                        |
|             | # Unknown                                                                      |
| Adnexa (A)  | 0 Normal                                                                       |
|             | 1a Unilateral tubal malformation, ovaries normal                               |
|             | 1b Bilateral tubal malformation, ovaries normal                                |
|             | 2a Unilateral hypoplasia/gonadal streak (including tubal malformation if      |
|             | appropriate)                                                                   |
|             | 2b Bilateral hypoplasia/gonadal streak (including tubal malformation if       |
|             | appropriate)                                                                   |
|             | 3a Unilateral aplasia                                                          |
|             | 3b Bilateral aplasia                                                           |
|             | + Other                                                                        |
|             | # Unknown                                                                      |
| Associated Malformation (M) | 0 None               |
|             | R Renal system                                                                |
|             | S Skeleton                                                                    |
|             | C Cardiac                                                                     |
|             | N Neurologic                                                                  |
|             | + Other                                                                        |
|             | # Unknown                                                                      |
There is one more classification that is often used.[62] The new European Society of Human Reproduction and Embryology–European Society of Gastrointestinal Endoscopy (ESHRE/ESGE) classification system incorporates all cases of uterine aplasia under Class U5 or aplastic uterus, defined as a formation defect characterized by the absence of any fully or unilaterally developed uterine cavity (Fig. 2). The further classification includes Class U5a or aplastic uterus with rudimentary (functional) cavity and Class U5b without a rudimentary (functional) cavity. This may come with co-existent subclassification of the cervical and vaginal anomaly, which is C4 (cervical aplasia/dysplasia) and V4 (vagina aplasia). The co-existence of other anomalies of any fully or unilateral form is reported separately.

To explain further, the findings of seven patients of the rectovestibular fistula with vaginal atresia reported by Kisku et al. are tabulated [40] and then the anomalies have been cataloged the two aforesaid classifications (Table 3).[60,62]

Besides the VCUAM classification and ESHRE/ESGE classification, there are two more classifications in vogue these days- American Fertility Society classification and the clinical and embryological classification of the malformations of the female genital tract by Acien et al.[63,64] The limitation of the AFS classification lies in the impossibility of assigning variations of a malformation to precise organ subgroups.

**Treatment of rectovestibular fistula associated with vaginal atresia**

Traditionally, the main goal of treatment of the vaginal atresia was considered to create an appropriate vaginal cavity in order to facilitate sexual intercourse and egress of menstrual blood (in case of vaginal or cervicovaginal atresia, where functional endometrium and uterus is present). Throughout the years, a lot of non-surgical and surgical interventions have been developed. Currently, the best management method remains controversial due to the lack of longitudinal studies and prospective evaluation of the interventions undertaken.[65]

**Non-Surgical treatment**

According to the American Committee of Obstetricians and Gynecologists (ACOG) recommendations, the first-choice treatment should begin with non-surgical methods based on dilation.[66] A recent multicenter study showed that surgery was not superior to non-surgical methods.[67] Non-surgical options are reserved for those patients who are motivated and psychosexually mature because the success rate depends mainly on the patient’s compliance and attitude.[68] Multidisciplinary care involving social workers, trained nurses, psychologists, and physicians plays a key role in the success rate.[69]

First described by Frank in 1938, the dilators of increasing sizes are placed inside the vaginal dimple, and intermittent, progressive, manual pressure is applied to deepen it over a period of 6-12 months.[70] In 1981, Ingram modified Frank’s technique to avoid some inconveniences by installing a dilator on a bicycle seat, allowing the patient to perform other activities during the sessions such as doing homework or practicing a musical instrument.[71] It is recommended that the dilators are used 3 times a day for 15-20 min each; some advice dilation for up to 2 hours a day.[69,72] Both methods are cost-effective procedures, with a low complication rate, allowing the creation of a functional neovagina as long as >6 cm in depth.[73,74] Adjuvant treatment, such as estriol cream, lidocaine ointment, paracetamol, naproxen, diazepam, nitrous oxide, and oxygen have been known to improve outcomes of these dilation methods by minimizing discomfort and anxiety during progressive dilation.[75]

But an extensive review of MRKH patients with rectovestibular fistula, including the published case reports/series and even metanalyses, barely revealed a couple of patients who received the dilatation technique (Table 1); the reason could lie in the fact that unlike the MRKH syndrome, subjects without the associated rectovestibular fistula, this cohort of patients does not have a vaginal dimple, reminiscent of the lower 1/3rd-1/5th of vagina derived from the urogenital sinus; instead, there is the anorectal opening of variable size present there. Hypothetically assuming that a particular patient has a wider introitus and even a vaginal dimple anterior to the anorectal opening, it is still hard to believe if the subject or her partner could have sexual gratification, as an inversion of an epithelial lined tissue achieved by these measures would lack

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**Figure 1:** Rectovestibular fistula associated with a) MRKH (vaginal agenesis with varying degrees of uterine agenesis/hypoplasia), b) Cervicovaginal atresia (vaginal and cervical agenesis with the normal functioning uterus), c) Distal vaginal atresia (atresia of the distal vagina, hematocolpos of the proximal vagina)-(Adapted with permission from Kisku et al. Int Urogynecol J. 2015;26:1441-8.[61]}

**Table 1:**| Classification |
|----------------|
| VCUAM         |
| ESHRE/ESGE    |
| American Fertility Society |
| Clinical and embryological classification |

**Table 3:**| Classification |
|----------------|
| U5a            |
| U5b            |
| C4             |
| V4             |
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Lubrication for intercourse. Second, she could have a problematic vaginal prolapse as the apex of the neovagina is not anchored. So, the assertions made by many obstetricians and gynecologists regarding these non-surgical measures do not break the ice with the pediatric surgeons.

**Figure 2**: Scheme for the classification of female genital tract anomalies according to the new ESHRE/ESGE classification system (Reproduced with permission from Grimbizis et al. Hum Reprod. 2013;28:2032-44.)[62]
Table 3: Classification of seven patients of the rectovestibular fistula with vaginal atresia as per the anomalies (adapted with permission from Kisku et al. Pediatr Surg Int. 2014;30:6333-9).[43]

| No. | Vaginal malformation | Associated genital malformations | Associated extra-genital malformations/ anomalies of non-Mullerian origin | MRKH-Typical/ atypical/ assoc. with MURCS | VCUAM classification [56] | ESHRE/ESGE classification [62] |
|-----|----------------------|---------------------------------|-------------------------------------------------|------------------------------------------|--------------------------|-------------------------------|
| 1   | Vaginal atresia      | Left rudimentary uterine horn. Right uterine horn hypoplastic with small cavity and cervical atresia | Absent left kidney, segmental thoracoolumbar spine scoliosis | Typical | V5b,C2b,U4b, A#,M0 | U5a,C4,V4 |
| 2   | Vaginal atresia      | Hypoplastic uterus, chocolate cysts in the sigmoid mesentery, endometriosis noted | VSD closed at 6 years. Bilateral external and middle ear anomalies | Atypical | V5b,C#,U3,A#,M0 | U1c,C4,V4 |
| 3   | Vaginal atresia      | Absent uterus                   | Absent right kidney | Atypical | V5b,C#,U4b, A#,MR | U5b,C4,V4 |
| 4   | Vaginal atresia      | Cervix absent uterus distended with hematometra | Bilateral ectopic ureters. Left poorly functioning kidney | Atypical | V5b,C2b,U0,A#,M+ | U0,C4,V4 |
| 5   | Vaginal atresia      | Bicornuate uterus, cervix hypoplastic with left adnexal chocolate cyst | Bilateral ectopic ureters. Left poorly Functioning kidney | Atypical | V5b,C+,U2,A1a,MR | U3,C3,V4 |
| 6   | Vaginal atresia      | Rudimentary uterus              | Absent left kidney | Atypical | V5b,C#,U4b,A#,MR | U5b,C4,V4 |
| 7   | Vaginal atresia      | Rudimentary hemiuteri           | Absent left kidney | Atypical | V5b,C#,U4b,A#,MR | U5b,C4,V4 |

**Surgical treatment**

Surgical methods should be reserved for patients who refuse the dilation technique as well as for those after unsuccessful non-surgical management. There are a number of surgical techniques used to create an artificial vagina.

**Bowel vaginoplasty**

Sneuguireff in 1892 had utilized rectum for neovaginal reconstruction; while mentioning this, Baldwin had described intestinal vaginoplasty using ileum in 1904.[76] He performed the same 3 years later in 1907. Wallace performed the first sigmoid colon vaginoplasty in 1911. Subsequently, these procedures were abandoned because of a high mortality rate in the pre-antibiotic era, only to be revisited after half of a century or so.[77] Today, the sigmoid colon is favored for vaginoplasty for its larger diameter close proximity to the perineum and easily mobilized vascular pedicle. Ileum, as a vaginal replacement, has been also used, but is known to be associated with a higher risk of stenosis.[78] In addition, ileal segments produce copious mucus, which is not as lubricating as the colonic mucous, leading to dyspareunia. Post-coital bleeding also occurs with the ileum owing to a more fragile mucosal lining.[77] Cecum and jejunum segments have also been used but have never become popular due to associated high morbidity and mortality. A blind duplicated rectum has also been used as a vaginal replacement.[10] An eight-centimeter-long sigmoid colon in a child and a little longer (up to 12 cm) in case of adolescent/adult, with its own blood supply, is mobilized to the introitus. There are a number of advantages of this method, e.g., it provides an epithelial-lined, lubricated passage as a conduit for menstrual flow and coitus, and no dilators are usually required after the surgery.[10,61,79] In a recent study, 43 cases of sigmoid vaginoplasty were reviewed, and the overall success was reported, both anatomical (the mean length of a neovagina was 11.7 ±1.2 cm) and functional (97% of patients rated their sexual intercourse as satisfactory).[80] The most concerning flaws are excessive odoriferous secretions in the beginning, donor site morbidity, defecation problems, postoperative ileus, anastomotic leaks, the development of inflammatory bowel disease, ulcerative colitis, diversion colitis, potential neoplasia and carcinoma in the grafts, neovaginal prolapse, and stenosis.[61,81,82] The laparoscopic modification has been gaining more and more popularity, with fewer postoperative pelvic adhesions, less intraoperative blood loss, a better cosmetic effect, a shorter hospital stay, and faster recovery.[83] Robotic approaches are also evolving, but due to high costs, they still remain limited.[84]
In the presence of vaginal atresia with recto vestibular fistula itself, the latter itself has been often used as neovagina for infants with MRKH, and the rectosigmoid pulled down as the neoanus; Cohn and Murphy were the first to report this surgical correction using this procedure of combined anovaginoplasty in 1956.[19] Ein and Stephens also similarly operated through the abdominal route in 1971.[20] Levitt and Pena (1998) later, however, chose to operate through an incision that they use for the posterior sagittal anorectoplasty.[15] Levitt et al. and Kisku et al. also reported retaining rectovestibular fistula for vaginoplasty in such patients initially,[15] but subsequently advised against it owing to the delay in toilet training.[18,61] Levitt et al. even mentioned the need for further augmentation of the neovagina when the patient became sexually active.[18] However, we had good short-term results with this procedure; the time consumed for surgery was significantly reduced, and the final cosmetic appearance was extra-ordinary.[10] Unfortunately, our patients were not available for follow up, so we don’t know how they fared in their adult lives. Levitt et al. and Kisku et al. felt that it would be better to use the rectovestibular fistula as the neoanus. Stressing at the psychological implications of delaying the genital reconstruction, we propagate that the neovagina and neoanus be created at the same operation in infancy or any time later at the presentation by the procedure shown in Fig.3,[10,61] but Kisku et al. propagated that the neoanus be created in infancy, but the creation of neovagina using sigmoid colon should be deferred till puberty when the uterine structures can be assessed for anastomosis with the bowel segment.[43] In their series of 7 patients, 4 of them had a uterus or its remnants. Delayed surgery allowed them to assess the growth of the rudimentary uterus/hemiuteri. At puberty, the functioning uterus was Anastomosed to allow for menstruation (Fig. 4).[43] Non-functioning ones may be excised. They felt that this distinction might be difficult in the neonatal period. They also pondered if the delayed operation would allow the use of non-operative treatment to create a neovagina![44]

Figure 3: Using the rectovestibular fistula as the neovagina (Reproduced with permission from Kisku et al. Int Uro-gynecol J. 2015;26(10):1441-8.) [61]

The merits of both techniques were debated in a recent paper published in 2015; the data included were that of 15 patients with vaginal anomalies and atresia associated with imperforate anus (5 were rectovestibular fistula)- 10 operated in the USA where it was believed that the distal rectum should be used for neoanus, be created with proximal colon and 5 operated in Japan where the distal rectum was used as neovagina and the proximal colon was pulled through as neoanus. The Japanese technique did not leave a colon anastomosis after reconstruction, while the USA technique used a potentially better-vascularized segment of the colon for the neovagina. This study couldn’t detect a difference in the continence outcomes between the two approaches and concluded that it was difficult to know if there was a long-term continence advantage to pulling through the more distal rectum for the correction of the imperforate anus.

Table 1 shows that though there may not be a universal consensus in favor of one approach or the other, creating neovagina using the rectovestibular fistula is the favored technique.

Performing such UTx in the future should be taken into consideration while choosing the method for neovagina creation. Gauthier et al. advised against bowel vaginoplasty fearing the high risk of infections from intestinal flora under immunosuppressive therapy, with potential endometritis or thrombosis and failure of UTx.[85]

Vecchietti vaginoplasty

One of the most popular types of surgery in those patients presenting in adulthood is the laparoscopic Vecchietti vaginoplasty, first described in 1965 as a laparotomy.[86,87] A unique hybrid of surgical and non-surgical techniques, it involves continuous upward traction on a plastic olive placed in the vaginal dimple that is attached to sutures that pass through the vesicorectal space into the abdominal cavity, through then extraperitoneal space, and later traverse the anterior abdominal wall with attachment to a
traction device. Continuous upward pressure on the vaginal vestibule stretches the mucosa, leading to elongation of the cavity to a 7cm to 10cm functional neovagina, after several weeks.[88] This method preserves natural vaginal tissue and avoids stenosis complications and excessive mucus production. The procedure can be accomplished in less than one hour.[73] However, these have never been performed in children.[89] Some alternatives to Vecchietti’s procedure have been proposed, using balloons or a Foley catheter instead of acrylic olives, or applying a different approach, avoiding vesicorectal tunneling. It is considered a safer, shorter, more effective, and less traumatic procedure, with a very low complication rate.[90,91] Kolle et al. from Germany have given the verdict in favor of the laparoscopic-assisted Vecchietti procedure as the most ideal functional vaginoplasty from the point of a later UTx.[50]

Since this procedure requires very careful dissection, so it is done in only surgically naive tissue and is not possible in subjects with rectovestibular fistula and vaginal atresia.

**McIndoe Procedure**

The McIndoe procedure, very popular with gynecologists, involves creating a neovaginal space post-puberty between the rectum and the urethra-bladder through the perineal route by inserting an inlay graft.[92,93] Graft methods require the postoperative use of molds or frequent vaginal dilations in order to prevent possible graft contraction and stenosis. McIndoe modifications with different types of grafts have been proposed, e.g., with split-thickness skin grafts and full-thickness skin grafts, an amnion, autologous vaginal tissue cultured in vitro, and artificial grafts. Injury to the neighboring organs, such as the rectum and bladder, is the most serious complication. Complications include lack of vaginal length, inadequate lubrication, resulting in dyspareunia, a high rate of stenosis, and excessive hair growth.[94] External visible scars from the usual graft harvest sites – the buttock, groin, or thigh – may not be acceptable to the patients. The molds need to be carefully changed to avoid the shearing of the graft, as the secondary healing of lesions is connected with unfavorable long-term results.[95] According to McQuillan and Grover, graft techniques require the longest hospital stay after the surgery.[96] There have been case reports of squamous cell carcinoma and squamous papillomas arising in skin grafts used for vaginal construction.[97-99]

Given the risk of transplant rejection and high infection rates, the McIndoe technique cannot be considered a suitable first-line treatment before UTx, considering the mandatory immunosuppression that UTx involves.[50]

**Williams vaginoplasty**

Williams vulvovaginoplasty and its modification by Creatasas et al. are procedures in which the vulvoperineal flaps are sutured to form a vertically-oriented neovagina that subsequently requires regular dilation or frequent sexual intercourse.[100,101] It would be impossible to raise the vulvar tissues because of the adhesions caused locally due to the prior dissection of the rectovestibular fistula, so probably would not be possible in the cohort of patients that is being discussed. The unnatural axis and the aforementioned complications associated with natural skin grafts render these techniques unsuitable for subsequent UTx, however.

**Wharton–Sheares–George vaginoplasty**

In the Wharton–Sheares–George vaginoplasty procedure,[102,103] the rudimentary Müllerian ducts were dilated incrementally by pushing Hegar dilators in the direction of the pelvic axis, and the resulting median raphe was then intersected using diathermy. Subsequently, a vaginal mold is inserted into the newly created cavity and held in position by two sutures. A mean vaginal length of 8.3 cm and a width of 3.3 cm was achieved. No major Intraoperative and postoperative complications or prolapse were reported to date. Overall, it was concluded that the Wharton–Sheares–George method of vaginoplasty is a minimally invasive, quick, and safe surgical option that does not require allogenic or autologous transplants, nor does it require traction devices or specialized surgical equipment and provides anatomically and functionally successful outcomes.

**Davydov procedure**

In the Davydov procedure, an autologous peritoneal graft is used for vaginoplasty. Laparoscopically, peritoneum graft from the pouch of Douglas is dissected and mobilized. After creating vesicorectal space, the peritoneum is reached and then the mobilized peritoneal sac is opened and fashioned to form the future neovagina.[104] The procedure is known to result in a good anatomic and functional vagina and has low Intra- and postoperative risks.[105] The peritoneal pouch gets laid with vaginal epithelium in 6 months that could be documented by vaginoscopy and biopsy.[106] The complications include bladder or intestinal injury, postoperative infections, vaginal prolapse, postoperative vaginal vault granulation, and vaginal stenosis.[65]

With regard to later UTx, the suitability of the Davydov method is limited. In the case of postoperative failure, reoperations are difficult and are associated with intra-abdominal adhesions.[50] The feasibility of uterus transplantation may be impaired by the altered pelvic anatomical structures.
Acellular porcine small intestinal submucosa (SIS) graft for vaginal reconstruction

Vaginoplasty using SIS graft has been successfully achieved in women with MRKH, and the anatomical and functional outcomes of this procedure are comparable to the laparoscopic Davydov procedure.[107] Combined laparoscopic and Wharton-Sheares George cervicovaginal reconstruction using SIS graft have also been reported in MRKH patients.[108]

Jejunal free graft

Free jejunal graft has also been used for vaginal replacement in one case of vaginal atresia in 2011; 2 years later, she underwent deceased donor UTx.[109]

Vaginoplasty procedures and their potential impact on subsequent UTx

There is as yet no consensus in the medical literature as to which of the surgical options for the creation of a neovagina provides the best UTx results.[51] According to Kolle et al.,[50] the following requirements should be met to ensure successful UTx:

i. Candidates must have normal ovaries with good ovarian reserve

ii. Candidates must not previously have undergone major intra-abdominal surgery or intestinal neovagina creation

iii. Candidates must get a neovagina that has the following features

a. High elasticity
b. Natural anatomical axis
c. Sufficient dimensions - length (≥28 cm) and width (≥2 cm)
d. Lined with natural epithelium, and
e. No need for lifelong dilation.
f. 4 cm wide anastomosis between donor’s uterus and neovagina

They concluded that the Vecchietti-based laparoscopically assisted method of neovagina creation provides ideal functional conditions for later UTx. Frank’s nonsurgical self-dilation method and the Wharton–Sheares–George vaginoplasty appear to provide further suitable options for neovagina creation prior to uterus transplantation. However, these authors had not accounted for the presence of the opening of the rectovestibular fistula in the vulva. For the cohort under discussion, i.e., patients with rectovestibular fistula and vaginal agenesis, it would be appropriate to leave the rectovestibular fistula as neovagina, and the colon should be pulled down to create neonalsa, but it is important to perform through these procedures concurrently either laparoscopically, or through the posterior sagittal route with which we neonatal/pediatric surgeons are well conversant with.

Uterine transplantation

Though the MRKH cohort represents only ~3% of women with absolute uterine factor infertility (AUIF), the vast majority of UTx attempts have been performed in this cohort only.[110] Women with MRKH syndrome usually have functioning ovaries that can produce viable oocytes. While advances in assisted reproductive technologies are significant, women with AUIF cannot carry a pregnancy, which leaves adoption and the use of in vitro fertilization (IVF) with gestational or surrogate carriers as the only methods for parenting. While many patients find these alternatives to be satisfactory, adoption and surrogacy may be impossible for some patients due to personal, religious, legal, financial, or ethical reasons.[111] Similar is the case of a woman who has undergone a hysterectomy or who has a uterus that is in situ but has been damaged by infection or surgical instrumentation. UTx has added a novel treatment to the existing armamentarium options for all such women.

The first human unsuccessful living-donor UTx procedure was reported in 2002 by physicians in Saudi Arabia and involved a 26-year-old recipient with AUIF due to a prior hysterectomy.[112] There have been no subsequent attempts by this group. The next human uterine transplant did not take place until nine years later, in 2011. The 2011 transplant was performed by a Turkish team and was novel in the first-ever use of a deceased donor. This transplanted uterus showed evidence of menstrual function, but despite several early failed pregnancies, no successful live births have resulted from the graft to date.[113]

During the intervening 9-year period, Brännström and his team in Sweden built many successful animal models in different species, including swine, rodent, and non-human primates.[114] In 2014, they published the results of their first clinical trial of 9 living related donor human UTx, 8 of whom had AUIF due to MRKH.[115] Of the nine transplants performed, seven remaining grafts were successful and recovered menstrual function within months of the transplant without any need for hormonal support. Multiple live births have since been reported from Brännström’s group.[116] All births have been via the planned Cesarean section. This clinical trial is the first that demonstrated that uterine transplantation can achieve the ultimate endpoint of a healthy live birth. This remarkable achievement attracted major attention worldwide and caused many countries to prepare for UTx, including countries in Asia. To date, three groups have performed UTx in humans in Asia, and many others are aiming for the clinical application of
UTx with the accumulation of basic experimental data. Following Sweden, USA, Brazil, and Serbia, India became the 5th country to have a live birth after a successful UTx on October 18th, 2018; the credit goes to a 12-member team headed by surgeon Dr. Shailesh Puntambekar in Galaxy Care Hospital, Pune who had performed UTx in a lady who suffered from AUFi due to Asherman’s Syndrome. Till April 2020, 16 post-UTx live births have taken place worldwide.

![Figure 5: Schematic representation of the major steps of UTx.](Reproduced from Brännström et al. Lancet. 2015;385(9968):607-16.)

The details like recipient factor, donor considerations (live as well deceased), surgical considerations, ischemia times, postoperative management, immunosuppression are beyond the scope of this review article; only a schematic representation of major steps of UTx is given in Fig. 5. The readers are advised to refer to some of the representative articles published in the last 6-7 years. There are three factors that may be worth highlighting here. One is about the short vaginal length of the blind vagina typically found in women with MRKH, especially those who received the non-surgical treatment. Even with patients who report regular intercourse, the vaginal length may be as short as 2–4 cm, and the routine use of dilators prior to surgery or even vaginal augmentation surgical procedures should be considered in such women. The uterine transplanted patients need to have cervical biopsies to monitor the immunosuppressive therapy and the subsequent IVF procedures, so the vagina and the uroepigonal anastomosis should be wide enough to allow instrumentation. Second, the embryo transfer to the transplanted uterus must wait at least for 6 months; most UTx surgeons would rather wait for even a year. Third, UTx is presently the only ephemeral transplant to remain in situ for a limited time in the recipient [109], so every UTx recipient would need to essentially undergo 3 surgeries: the transplant surgery, Cesarean section for delivery, and finally, removal of the uterus after 6 months of successful delivery; some surgeons may allow a second pregnancy before excising the transplanted uterus.

**CONCLUSION**

Rectovestibular associated with vaginal atresia is a rare variant of anorectal malformations in females with little more than 100 cases have been reported globally. The vaginal atresia is usually part of MRKH syndrome. Although a lot of literature is available about non-surgical and surgical treatment of vaginal atresia associated with MRKH syndrome, it is a different scenario when it coexists with rectovestibular fistula. Bowel vaginoplasty has been the favored reconstruction for this association. Of the two philosophies, whether the distal rectovestibular fistula should be retained as neovagina or neoanus, although there is no consensus, the majority of surgeons believe in retaining the distal rectovestibular fistula as the neovagina and performing pull-through of the proximal colon as neoanus via the posterior sagittal route. The advent of uterine transplants in MRKH patients with normal ovarian function has added a new dimension to the surgical management of this association of anomalies. Clearly, all described procedures should be performed by pediatric surgeons with extensive experience in vaginal reconstruction and laparoscopic surgery. Though there is not a single specific mention in the available literature related to uterine transplantation of the association of vaginal atresia and rectovestibular fistula, a review of the various neovagina reconstruction techniques in this context gives a fair idea of the ideal management. The neonatal/pediatric surgeons and gynecologists should work in tandem for such rare cases and learn from each other. The rectovesical space and the lower abdomen/pelvis should be treated as sacrosanct; any gross violation of these areas would lead to adhesions that would preclude any future uterine transplantation. It would be appropriate to leave the distal rectovestibular fistula as neovagina, and the colon be pulled down to create neoanus; it is important to perform these procedures concurrently either laparoscopically or through the posterior sagittal route with a lot of diligence.

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REFERENCES

1. Holschneider A, Hutson J, Peña A, Becket E, Chatterjee S, Coran A, et al. Preliminary report on the International Conference for the Development of Standards for the Treatment of Anorectal Malformations. J Pediatr Surg. 2005;40:1521-6.

2. Sarin YK, Sinha A. Two orifices in the perineum of a girl with imperforate anus: possibility of urogenital agenesis associated with rectovestibular fistula. J Pediatr Surg. 2002; 37:1217-9.

3. Cook RCM. Anorectal malformations. In: Neonatal Surgery. 3rd edition. Edited by Lister J, Irving IM. London, England, Butterworth 1990, p. 547-70.

4. Galífer RB, Chavrier Y, Vialia JS. Principles of the surgical treatment of cloacal malformation. Apropos of 3 cases. Chir Pediatr. 1985; 26:95-103.

5. Peña A. Anorectal malformations. Semin Pediatr Surg. 1995; 4:35-47.

6. Peña A. Imperforate anus and cloacal malformations. In: Pediatric Surgery. 3rd edition. Edited by Ashcraft KW. Saunders, Philadelphia, 2000. p. 473-92.

7. Choudhury SR, Khan NA, Debnath PR, Yadav PS, Shah S, Chadha R. Anorectal agenesis with rectovaginal fistula: a rare/regular variant. J Indian Assoc Pediatr Surg. 2017; 22:79-82.

8. Torres R, Levitt MA, Tovilla JM, Rodriguez G, Peña A. Anorectal malformations and Down’s syndrome. J Pediatr Surg. 1998; 33:194-7.

9. Bischoff A, Frischer J, Dickie BH, Peña A. Anorectal malformation without fistula: a defect with unique characteristics. Pediatr Surg Int. 2014; 30:763-6.

10. Sinha A, Sarin YK. Mayer-Rokitansky Syndrome with imperforate anus - a unique association. J Indian Assoc Pediatr Surg. 2001; 6:30-3.

11. Gross RE. Malformation of the anus and rectum. In: The surgery of infancy and childhood. Edited by Gross RE. Philadelphia, PA: Saunders Company; 1953. p. 348-68.

12. Wakhlu A, Kureel SN, Tandon BK, Wakhlu AK. Long-term results of anterior sagittal anorectoplasty for the treatment of vestibular fistula. J Pediatr Surg. 2009; 44:1913-9.

13. De la Torre L, Cogley K, Calisto JL, Santos K, Ruiz A, Zornoza M. Vaginal agenesis and rectovestibular fistula. Experience utilizing distal ileum for the vaginal replacement in these patients, preserving the natural fecal reservoir. J Pediatr Surg. 2016; 51:1871-6.

14. Levitt MA, Stein DM, Peña A. Rectovestibular fistula with absent vagina: A unique anorectal malformation. J Pediatr Surg. 1998; 33:986-99.

15. Skerritt C, Vilanova Sánchez A, Lane VA, Wood RJ, Hewitt GD, Breech LL, et al. Menstrual, sexual, and obstetric outcomes after vaginal replacement for vaginal atresia associated with anorectal malformation. Eur J Pediatr Surg. 2017; 27:495-502.

16. Ahmed H, Almomani M, Strine AC, Reddy PP, Sheldon C, Frischer J, et al. Clinical urologic and urodynamic outcomes in patients with anorectal malformation and absent vagina after vaginal replacement [published online ahead of print, 2020 Feb 4]. J Pediatr Surg. 2020;50:22-34.

17. Levitt MA, Bischoff A, Breech L, Peña A. Rectovestibular fistula rarely recognized associated gynecologic anomalies. J Pediatr Surg. 2009; 44:1261-7.

18. Cohn BD, Murphy DR. Imperforate anus with agenesis of the vagina. Ann Surg. 1956; 143:430-2.

19. Ein SH, Stephens CA. Vaginal construction in children with absent vagina and imperforate anus. J Pediatr Surg. 1971; 6:435-9.

20. Fujiwara Y, Oizumi T, Sasahara M, Kato E, Kakizaki G. A case of congenital imperforate anus and absent vagina with a functioning uterus. Tohoku J Exp Med. 1974; 113:283-9.

21. King SL, Ladd RL, Shochat SJ. Monozygotic twins concordant for tracheoesophageal fistula and discordant for the VATER association. Acta Paediatr Scand. 1977; 66:783-5.

22. Toitele-Velcek F, Hansbrough F, Kugaczewski J, Coren CV, Klotz DH, Price AF, et al. Utero vaginal malformations: a trap for the unsuspecting surgeon. J Pediatr Surg. 1989; 24:736-40.

23. Digray NC, Mengi Y, Goswamy HL, Thappa DR. Rectovaginoplasty for vaginal atresia with anorectal malformation. J Urol. 1999; 162:514-5.

24. Okoye BO, Parikh DH, Buick RG, Lander AD. Pyloric atresia: five new cases, a new association, and a review of the literature with guidelines. J Pediatr Surg. 2000; 35:1242-5.

25. Adejuyigbe O, Sowande OA, Olayinka OS, Fasubaa OB. Rectovaginal fistula with absent distal vagina in an adolescent Nigerian girl. J Pediatr Surg. 2002; 37:1479-80.

26. Güngör C, Genç A, Sencan A, Dağlar Z, Alparslan O, Mir E. MURCS association and rectovestibular fistula: case report of a patient treated with one-stage posterior sagittal anorectoplasty and sigmoid loop vaginoplasty. J Pediatr Surg. 2003; 38:262-4.

27. Tei E, Yamataka A, Segawa O, Kobayashi H, Lane GJ, Tobayama S, et al. Mayer-Rokitansky syndrome and anorectal malformation. J Pediatr Surg. 2003; 38:1770-4.

28. Deshpande AV, Sanghani HH, Sanghavi BV, Borwankar SS. Delayed presentation of vaginal agenesis with anorectal malformation—a unique problem. Ind J Ped Surg. 2003; 8:242-7.

29. Patankar JZ, Mali VP, Yashpal R, Neo GTH, Prabhakaran K. Anorectal malformation with congenital absence of vagina: a case report and review of the literature. Pediatr Surg Int. 2004; 20:295-7.

30. Patankar SR, Kalrao V, Patankar SS. Mayer-Rokitansky syndrome and anorectal malformation. Indian J Pediatr. 2004; 71:1133-5.

31. Banu T, Hannan MJ, Aziz MA, Hoque M, Laila K. Rectovestibular fistula with vaginal malformations. Pediatr Int. 2006; 22:263-6.

32. Wester T, Läckgren G, Christofferson R, Rintala RJ. The congenital pouch colon can be used for vaginal reconstruction by longitudinal splitting. J Pediatr Surg. 2006; 41:e25-e28.

33. Komura M, Kanamori Y, Sugiyama M, Tomonaga T, Suzuki K, Hashizume K, et al. A female infant who had both complete VACTERL association and MURCS association: report of a case. Surg Today. 2007; 37:878-80.

34. Matignas ALA, Delos Reyes RH. Rectovestibular fistula as neovagina in congenital cervico-vaginal agenesis associated with imperforate anus. J Obstet Gynaecol Res. 2008; 34:428-35.
36. Chatterjee SK. Rare/regional variants. In: Anorectal malformations in children. Edited by Holschneider AM, Hutson JM. Berlin Heidelberg New York: Springer; 2008:p. 251-62.

37. Wang S, Lang JH, Zhu L. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome with rectovestibular fistula and imperforate anus. Eur J Obstet Gynecol Reprod Biol. 2010; 153:77-80.

38. Mane SB, Shastry P, Dhende NP, Obaidah A, Acharya H, Reddy S, et al. Our 10-year experience of variable Mullerian anomalies and its management. Pediatr Surg Int. 2010; 26:795-800.

39. Wester T, Tovar JA, Rintala R. Vaginal agenesis or distal vaginal atresia associated with anorectal malformations. J Pediatr Surg. 2012; 47:571-6.

40. Yamataka A, Goto S, Kato Y, Koga H, Lane GJ, Okazaki T. Fecal and urinary continence after scope-assisted anorectovaginoplasty for female anorectal malformation. J Pediatr Surg Int. 2012; 28:907-12.

41. Jessel RH, Laufer MR. Management of lower vaginal agenesis in a patient with unicorneurate uterus. J Pediatr Adolesc Gynecol. 2015; 28:e23.

42. de Blauuw I, Midrio P, Breech L, Bischoff A, Dickie B, Versteegh HP, et al. Treatment of adults with unrecognized or inadequately repaired anorectal malformations: 17 cases of rectovestibular and rectoperineal fistulas. J Pediatr Adolesc Gynecol. 2013; 26:156-60.

43. Kisku S, Barla RK, Sen S, Karl S, Mathai J, Varghese L. Rectovestibular fistula with vaginal atresia: our experience and a proposed course of management. Pediatr Surg Int. 2014; 30:6333-9.

44. Kapczuk K, Frieze Z, Iwaniec K, Kędzia W. Creation of a neovagina in a patient with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome and previously corrected rectovestibular fistula concomitant with imperforate anus. J Pediatr Adolesc Gynecol. 2015; 28:e17-9.

45. Pandya KA, Koga H, Okawada M, Coran AG, Yamataka A, Teitelbaum DH. Vaginal anomalies and atresia associated with imperforate anus: diagnosis and surgical management. J Pediatr Surg. 2015; 50:431-7.

46. Teo XL, Narasimhan KL, Chua JH. Mullerian agenesis in the presence of anorectal malformations in female newborn: a diagnostic challenge. Singapore Med J. 2015; 56:e82-e84.

47. Gupta R, Gupta A, Gupta A, Singh A, Mayer- Rokitansky- Küster-Hauser Syndrome with Imperforate Anus: A Rare Association and an Innovative Surgical Management. IJSS Case Rep Reviews. 2016; 2:1-3.

48. Bjersum-Meyer T, Herlin M, Qvist N, Petersen MB. Vertebral defect, anal atresia, cardiac defect, tracheoesophageal fistula/esophageal atresia, renal defect, and limb defect association with Mayer-Rokitansky-Küster-Hauser syndrome in co-occurrence: two case reports and a review of the literature. J Med Case Rep. 2016; 10:374.

49. Tiwari C, Shah H, Bothra J, Sandias G. Congenital rectovaginal fistula with anorectal agenesis: A rare anorectal malformation. Int J Pediatr Adolesc Med. 2017; 4:138-40.

50. Kölle A, Taran FA, Rall K, Schöller D, Wallwiener D, Brucker SY. Neovagina creation methods and their potential impact on subsequent uterus transplantation: a review. BJOG. 2019; 126:1328-35.

51. Mayer CA. [About doubling of the uterus and its types, along with remarks about rabbits and wolf throats] J Chir Augen. 1829; 13:525-64. [Article in German]

52. Rokitansky KE. [About the so-called doubling of the uterus]. Med Jahrb Österr Staat. 1838; 26:39-77. [Article in German]

53. Kuester H. [Rudimentary solid bipartite uterus with solid vagina]. Z Geburtshilfe Gynäkol. 1910; 67:692-718. [Article in Latin]

54. Hauser GA, Schreiner WE. [Das Mayer-Rokitansky- Küster-Syndrome]. Schweiz Med Wochenschr. 1961; 91:381-4. [Article in German]

55. Schmid-Tannwald I, Hauser GA. [Atypical forms of the Mayer-Rokitansky-Küster syndrome]. Geburtshilfe Frauenheilkd. 1977; 37:386-92. [Article in German]

56. Duncan PA, Shapiro LR, Stangel JJ, Klein RM, Addonizio JC. The MURCS association: Mullerian duct aplasia, renal aplasia, and cervicothoracic somite dysplasia. J Pediatr. 1979; 95:399-402.

57. Lisewskas-Kaplon M, Strzoń M, Kotarski L, Baglaj M, Hirnle L. Mayer-Rokitansky-Küster-Hauser syndrome as an interdisciplinary problem. Adv Clin Exp Med. 2020; 29:505-11.

58. Oppelt P, Renner SP, Kellemann A, Brucker S, Hauser GA, Ludwig KS, et al. Clinical aspects of Mayer-Rokitansky-Küster-Hauser syndrome: recommendations for clinical diagnosis and staging. Hum Reprod. 2006; 21:792-7.

59. Deng S, He Y, Chen N, Zhu L. Spectrum of type I and type II syndromes and associated malformations in Chinese patients with Mayer-Rokitansky-Küster-Hauser syndrome: A retrospective analysis of 274 cases. J Pediatr Adolesc Gynecol. 2019; 32:284-7.

60. Oppelt P, Renner SP, Brucker S, Strissel PL, Strick R, Oppelt PG, et al. The VCUAM (Vagina Cervix Uterus Adnex-associated Malformation) classification: a new classification for genital malformations. Fertil Steril. 2005; 84:1493-7.

61. Kisku S, Verghese L, Kekre A, Sen S, Karl S, Mathai J, et al. Bowel vaginoplasty in children and young women: an institutional experience with 55 patients. Int Urogynecol J. 2015; 26:1441-8.

62. Grimbizis GF, Gordts S, Di Spiezo Sardo A, Brucker S, De Angelis C, Gerogeto M, et al. The ESHRE/ ESGE consensus on the classification of female genital tract congenital anomalies. Hum Reprod. 2013; 28:2032-44.

63. Buttram VC Jr, Gomel V, Siegler A, DeCherney A, Gibbons W, March C. American Fertility Society. The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion secondary due to tubal ligation, tubal pregnancies, mullerian anomalies and intrauterine adhesions. Fertil Steril. 1988; 49:944-55.

64. Acién P, Acién M, Sánchez-Ferrer M. Complex malformations of the female genital tract. New types and revision of classification. Hum Reprod. 2004; 19:2377-84.

65. Callens N, De Cuyperge D, De Sutter P, Monstrey S, Weyers S, Hoebeke P, et al. An update on surgical and nonsurgical treatments for vaginal hypoplasia. Hum Reprod Update. 2014; 20:775-801.

66. Committee on Adolescent Health Care. ACOG Committee opinion No. 728: Mullerian agenesis: Diagnosis, management, and treatment. Obstet Gynecol. 2018; 131:e35-e42.

67. Cheikhelard A, Bidet M, Baptiste A, Vuaud M, Pagot C, Khen-Dunlop N, et al. Surgery is not superior to dilation for the management of vaginal agenesis in Mayer-Rokitansky-Küster-Hauser syndrome: A multicenter comparative observational study in 131 patients. Am J Obstet Gynecol. 2018; 219:281.e1-281.e9.

68. Adeyemi-Fowode OA, Dietrich JE. Assessing the experience of vaginal dilator use and potential barriers to
ongoing use among a focus group of women with Mayer-Rokitansky-Küster-Hauser syndrome. J Pediatr Adolesc Gynecol. 2017; 30:491-4.

69. Liszewska-Kaplon M, Strózak M, Kotarski L, Baglaj M, Hrynle L. Mayer-Rokitansky-Küster-Hauser syndrome as an interdisciplinary problem. Adv Clin Exp Med. 2020; 29:505-11.

70. Frank RT. The formation of an artificial vagina without operation. Am J Obstet Gynecol. 1938; 35:1053-5.

71. Ingram JM. The bicycle seat stool in the treatment of vaginal agenesis and stenosis: A preliminary report. Am J Obstet Gynecol. 1981; 140:867-73.

72. Williams JK, Lake M, Ingram JM. The bicycle seat stool in the treatment of vaginal agenesis and stenosis. J Obstet Gynecol Neonatal Nurs. 1985; 14:147-50.

73. McQuillan SK, Grover SR. Dilation and surgical management in vaginal agenesis: A systematic review. Int Urogynecol J. 2014; 25:299-311.

74. Edmonds DK, Rose GL, Lipton MG, Quek J. Mayer-Rokitansky-Küster-Hauser syndrome: A review of 245 consecutive cases managed by a multidisciplinary approach with vaginal dilators. Fertil Steril. 2012; 97:686-90.

75. Ketheeswaran A, Morrissey J, Abbott J, Bennett M, Dudley J, Deans R. Intensive vaginal dilation using adjuvant treatments in women with Mayer-Rokitansky-Küster-Hauser syndrome: Retrospective cohort study. Aust N Z J Obstet Gynaecol. 2018; 58:108-13.

76. Baldwin JF. The formation of an artificial vagina by intestinal transplantation. Ann Surg. 1904; 40:398-403.

77. Lima M, Ruggeri G, Randi B, Domini M, Gargano T, Pergola EL, et al. Vaginal reconstruction with the modified Creatsas operation for its relief. J Obstet Gynaecol Commonw. 1964; 71:511-18.

78. Hensle TW, Reiley EA. Vaginal replacement in children and young adults. J Urol. 1998; 159:1035-40.

79. Georgas K, Belgrano V, Andréasson M, Elander A, Selvaggi G. Bowel vaginoplasty: A systematic review. J Plast Surg Hand Surg. 2018; 52:265-73.

80. Özkcan Ö, Özkcan Ö, Çinpolat A, Dogan NU, Bektas U, Doley K, et al. Vaginal reconstruction with the modified rectosigmoid colon: Surgical technique, long-term results and sexual outcomes. J Plast Surg Hand Surg. 2018; 52:210-6.

81. van der Shuis WB, Bouman MB, Meijerink WJHJ, Elfering L, Mullender MG, de Boer NKH, et al. Diversification of neovaginitis after sigmoid vaginoplasty: Endoscopic and clinical characteristics. Fertil Steril. 2016; 105:834.e1-839.e1.

82. Djordjevic ML, Stanojevic DS, Bizic MR. Rectosigmoid vaginoplasty: clinical experience and outcomes in 86 cases. J Sex Med. 2011; 8:3487-94.

83. Zhang M, Li S, Huang X, Du H, Wang C, Zhang L, et al. Transumbilical single-incision laparoscopic vaginoplasty hybrid transperineal approach using a sigmoid colon segment: Initial twenty-five cases. Int Urol Nephrol. 2016; 48:1401-6.

84. Boztosun A, Olgan S. Robotic sigmoid vaginoplasty in an adolescent girl with Mayer-Rokitansky-Küster-Hauser syndrome. Female Pelvic Med Reconstr Surg. 2016; 22:e32-e35.

85. Gauthier T, Lavoue V, Prer P, Aubard Y, Ayoubi JM, Garbin O, et al. Which neovagina reconstruction procedure for women with Mayer-Rokitansky-Küster-Hauser syndrome in the uterus transplantation era? Editorial from the French Uterus Transplantation Committee (CETUP) of CNGOF. J Gynecol Obstet Hum Reprod. 2018; 47:175-6.

86. Vecchiotti G. [Neovagina in the syndrome of in Rokitansky-Küster-Hauser]. Attualita Obstet Ginecol. 1965; 11:131-47. [Article in Italian]

87. Vecchiotti G. [The neo-vagina in Rokitansky syndrome-Küster-Hauser]. Rev Med Suisse Romande. 1979; 99:593. [Article in French]

88. Fedele L, Bianchi S, Frontino G, Fontana E, Restelli E, Bruni V. The laparoscopic Vecchietti’s modified technique in Rokitansky syndrome: anatomic, functional, and sexual long-term results. Am J Obstet Gynecol. 2008; 198:377.e1-377.e6.

89. Borruto F, Camoglio FS, Zampieri N, Fedele L. The laparoscopic Vecchietti technique for vaginal agenesis. Int J Gynaecol Obstet. 2007; 98:15-9.

90. Brucker SY, Geygusch M, Zubke W, Rall K, Gauwerky JF, Wallwiener D. Neovagina creation in vaginal agenesis: Development of a new laparoscopic Vecchietti-based procedure and optimized instruments in a prospective comparative interventional study in 101 patients. Fertil Steril. 2008; 89:1940-52.

91. Rall K, Schickner MC, Barresi G, Schonfisch B, Wallwiener M, Wallwiener CW, et al. Laparoscopically assisted neovaginoplasty in vaginal agenesis: A long-term outcome study in 240 patients. J Pediatr Adolesc Gynecol. 2014; 27:379-85.

92. McIndoe AH, Bannister JB. An operation for the cure of congenital absence of the vagina. J Obstet Gynecol Brit Emp. 1938; 45:490-4.

93. McIndoe A. The treatment of congenital absence and obliterative conditions of the vagina. Br J Plast Surg. 1950; 2:254-67.

94. Cali RW, Pratt JH. Congenital absence of the vagina. Long-term results of vaginal reconstruction in 175 cases. Am J Obstet Gynecol. 1968; 100:752-63.

95. Han SE, Go JY, Choi DS, Seo GH, Lim SY. Experience with specially designed porcine polyacetal mold dressing method used in McIndoe-style vaginoplasty. J Pediatr Urol. 2017; 13:621.e1-621.e6.

96. McQuillan SK, Grover SR. Dilation and surgical management in vaginal agenesis: A systematic review. Int Urogynecol J. 2014; 25:299-311.

97. Hopkins MP, Morley GW. Squamous cell carcinoma of the neovagina. Obstet Gynecol. 1987; 69:525-7.

98. Baltzer J, Zander J. Primary squamous cell carcinoma of the neovagina. Gynecol Oncol 1989; 35:99-103.

99. Idrees MT, Deligdisch L, Altchek A. Squamous papilloma with hyperpigmentation in the skin graft of the neovagina in Rokitansky syndrome: Literature review of benign and malignant lesions of the neovagina. J Pediatr Adolesc Gynecol. 2009; 22:e148-e155.

100. Williams EA. Congenital absence of the vagina; a simple operation for its relief. J Obstet Gynaecol Commonw. 1964; 71:511-4.

101. Creatsas G, Deligioroglou E, Makrakis E, Kontoravdis A, Papadimitriou L. Creation of a neovagina following Williams vaginoplasty and the Creatsas modification in 111 patients with Mayer-Rokitansky-Küster-Hauser syndrome. Fertil Steril. 2001; 76:1036-40.

102. Sheares BH. Congenital atresia of the vagina—a technique for tunneling the space between the bladder and rectum and construction of a new vagina by a modified Wharton-technique. J Obstet Gynecol Br Emp. 1960; 67:24-31.
103. Kuessel L, Wenzl R, Marschalek ML, Slavka G, Doerfler D, Husslein H. Using the Wharton-Sheares-George method to create a neovagina in patients with Mayer-Rokitansky-Küster-Hauser syndrome: a step-by-step video tutorial. Fertil Steril. 2016; 106:e20-e21.

104. Kriplani A, Karthik SD, Kriplani I, Kachhawa G. Laparoscopic peritoneal vaginoplasty for Mayer-Rokitansky-Küster-Hauser syndrome: an experience at a tertiary care center. J Gynecol Surg. 2018; 34:63-7.

105. Bianchi S, Frontino G, Ciappina N, Restelli E, Fedele L. Creation of a neovagina in Rokitansky syndrome: comparison between two laparoscopic techniques. Fertil Steril. 2011; 95:1098-100.e1-3.

106. Fedele L, Frontino G, Restelli E, Ciappina N, Motta F, Bianchi S. Creation of a neovagina by Davydov’s laparoscopic modified technique in patients with Rokitansky syndrome. Am J Obstet Gynecol. 2010; 202:33.e1-e6.

107. Ding JX, Chen LM, Zhang XY, Zhang Y, Hua KQ. Sexual and functional outcomes of vaginoplasty using acellular porcine small intestinal submucosa graft or laparoscopic peritoneal vaginoplasty: a comparative study. Hum Reprod. 2015; 30:581-9.

108. Zhang X, Ding Y, Hua K, Liu S, Jia N. Combined Laparoscopic and Vaginal Cervicovaginal Reconstruction Using Acellular Porcine Small Intestinal Submucosa Graft in a Patient with Mayer-Rokitansky-Küster-Hauser Syndrome (UsaC4V4). J Minim Invasive Gynecol. 2019; 26:396-7.

109. Ozkan O, Akar ME, Ozkan O, Erdogan O, Hadimioğlu N, Yılmaz M, et al. Preliminary results of the first human uterine transplantation from a multiorgan donor. Fertil Steril. 2013; 99:470-6.

110. Brännström M, Dahm-Kähler P. Uterus transplantation and fertility preservation. Best Pract Res Clin Obstet Gynaecol. 2019; 56:109-16.

111. Flyckt R, Falcone T, Eghtesad B, Fung J, Tzakis A. Uterus transplantation: medical considerations. Curr Transpl Rep. 2016; 3:380-4.

112. Fageeh WRH, Jabbad H, Marzouki A. Transplantation of the human uterus. Int J Gynecol Obstet. 2002; 76:245-51.

113. Erman A, Ozkan O, Aydinuraz B, Dirican K, Cincik M, Mendicinoğlu I, et al. Clinical pregnancy after uterus transplantation. Fertil Steril. 2013; 100:1358-63.

114. Brännström M, Diaz-Garcia C, Hanafi A, Olausson M, Tzakis A. Uterus transplantation: animal research and human possibilities. Fertil Steril. 2012; 97:1269-76.

115. Brännström M, Johannesson L, Dahm-Kähler P, Enskog A, Molne J, Kvarnstrom N, et al. First clinical uterus transplantation trial: a six month report. Fertil Steril. 2014; 101:1228-36.

116. Johannesson L, Jarvholt S. Uterus transplantation: current progress and future prospects. Int J Womens Health. 2016; 8:43-51.

117. Kisu I, Liu Y, Chen G, Song MJ, Chang CY, Koon TH, et al. Current progress in uterus transplantation research in Asia. J Clin Med. 2019; 8:245.

118. Daolio J, Palomba S, Paganelli S, Falbo A, Aguzzoli L. Uterine transplantation and IVF for congenital or acquired uterine factor infertility: A systematic review of safety and efficacy outcomes in the first 52 recipients. PLoS ONE. 2020; 15:e0232323.

119. Gautheir T, Piver P, Pichon N, Bipes R, Guillaudeau A, Piccardo A, et al. Uterus retrieval process from brain dead donors. Fertil Steril. 2014; 102:476-82.

120. Johannesson L, Kvarnström N, Mölne J, Dahm-Kähler P, Enskog A, Diaz-Garcia C, et al. Uterus transplantation trial: 1-year outcome. Fertil Steril. 2015; 103:199-204.

121. Flyckt R, Davis A, Farrell R, Zimberg S, Tzakis A, Falcone T. Uterine Transplantation: Surgical Innovation in the Treatment of Uterine Factor Infertility. J Obstet Gynaecol Can. 2018; 40:86-93.

122. Punjabekar S, Telang M, Kulkarni P, Jadhav S, Sathe R, Warty N, et al. Laparoscopic-assisted uterus retrieval from live organ donors for uterine transplantation. J Minim Invasive Gynecol. 2018; 25:571-2.

123. Georgopapadakos N, Manoli A, Passia G, Skandalakis PN, Filipou D. Uterus transplantation as a therapy method in Mayer-Rokitansky-Küster-Hauser Syndrome. Cureus. 2019; 11:e6333.

124. Ejzenberg D, Andraus W, Baratelli Carelli Mendes LR, Ducatti L, Song A, Tanigawa R, et al. Livebirth after uterus transplantation from a deceased donor in a recipient with uterine infertility. Lancet. 2019; 392:2697-704.

125. Pluta D, Lemm M, Franik G, Kowalczyk K, Blucakz L, Tekieli-Balon A, et al. Mayer-Rokitansky-Küster-Hauser syndrome - case studies, methods of treatment and the future prospects of human uterus transplantation. Eur Rev Med Pharmacol Sci. 2020; 24:549-63.

126. Brännström M, Johannesson L, Bokström H, Kvarnström N, Mölne J, Dahm-Kähle P, et al. Livebirth after uterus transplantation. Lancet. 2015; 385:607-16.