Laparoscopic Davydov Procedure for the Creation of a Neovagina in Patients with Mayer-Rokitansky-Küster-Hauser Syndrome: Analysis of 7 Cases

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Objective: Several surgical techniques have been described for creating a neovagina in patients with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, however as yet there is no standardized treatment. The aim of this report is to assess anatomic and functional outcomes after the laparoscopic Davydov procedure for the creation of a neovagina in patients with MRKH syndrome.
Methods: Seven patients with MRKH syndrome underwent the laparoscopic Davydov technique from January 2005 to August 2010. The anatomic and functional results were evaluated after 3, 6, 12, 24, 36, 48, and 60 months.
Results: The surgical procedure was performed with no major complications except in one case in which an intraoperative bladder injury occurred and was successfully corrected. The mean duration of surgery was 162.9 minutes (range, 120–230 min). Mean lengths/widths (cm) of the neovagina were 6.4/2.6, 6.5/2.5, 6.5/2.8, 6.4/2.8, 7.1/2.8, and 7.2/2.8 at 3, 6,12, 24, 36, 48, and 60 postoperative months, respectively.
Conclusion: The laparoscopic Davydov procedure seems to be a safe and effective surgical treatment for patients with MRKH syndrome if postoperative intermittent self dilation was done.

Key words: Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, Davydov technique, laparoscopy, neovagina

INTRODUCTION

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome was first described by Mayer in 1829, followed by Rokitansky in 1838, Küster in 1910, and Hauser *et al*. in 1961 [1]. It is characterized vaginal agenesis and rudimentary or absent uterus. It occurs at the rate of 1 in 4,500 newborn girls. Patients with MRKH syndrome have normal development of secondary sex characteristics, normal external genitalia and 46, XX karyotype, typically presenting with amenorrhea or problems with sexual intercourse during adolescence [2–4]. Although patients with this condition are usually unable to carry a pregnancy because the uterus is missing or not functional, but they have normally functioning ovaries and may be able to have children through assisted reproduction techniques (ART) such as gestational surrogacy and uterus transplantation [5, 6]. The syndrome can be classified as either type I or type II. Type I corresponds to isolated uterovaginal aplasia, and type II corresponds to uterovaginal aplasia with concomitant defects, such as renal and skeletal malformations, hearing defects, and rarely cardiac and digital anomalies [7]. MRKH syndrome is also known as müllerian agenesis or müllerian aplasia [8].

Although several surgical and nonsurgical techniques have been described for the treatment of vaginal agenesis with MRKH syndrome, there is not yet a standardized treatment [9–17]. The laparoscopic Davydov procedure is a simple surgical technique with good cosmetic outcome [12]. We report anatomic and functional outcome in 7 patients with MRKH syndrome performed by the laparoscopic Davydov procedure and assess evaluation the surgical feasibility.

MATERIALS AND METHODS

Patients

From January 2005 to August 2010, 7 patients with MRKH syndrome underwent construction of a neovagina by the laparoscopic Davydov procedure. All the patients were referred to our hospital with the chief complaint of primary amenorrhea. Before surgery, all patients underwent pelvic and abdominal ultrasonography, pelvic magnetic resonance imaging (MRI) (Fig. 1), hormonal profile, and karyotyping. All their karyotypes were 46, XX and had normal hormonal levels for their ages. The clinical characteristics of the patients are shown in Fig. 1. We informed the patients and their parents of the objective and possible complications of the laparoscopic Davydov procedure. All patients and/or their parents signed the written consent. The investigation conforms with the principles outlined in the Declaration of Helsinki and approved by the ethics committee of Tokai University School of Medicine.

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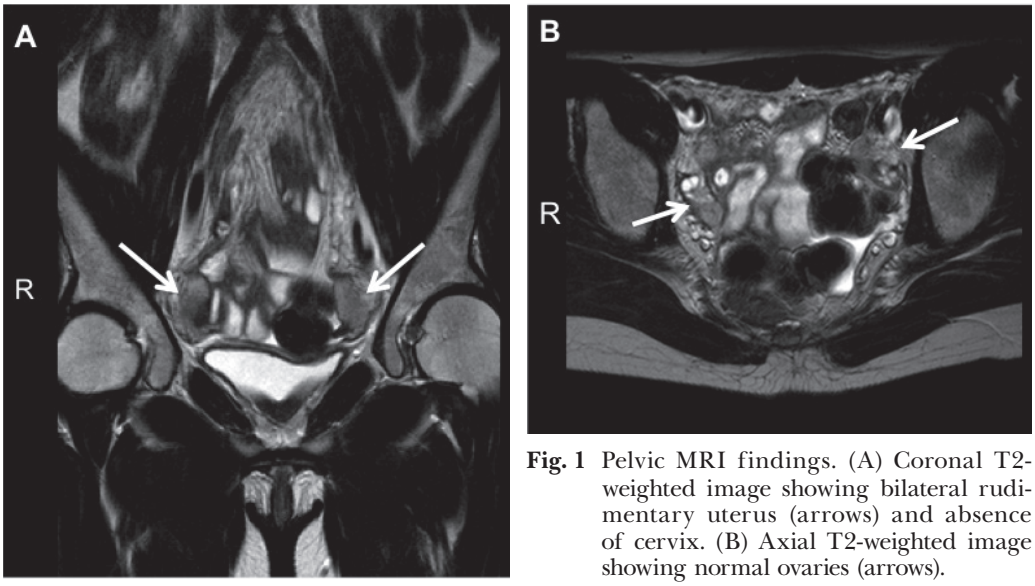

Fig. 1 Pelvic MRI findings. (A) Coronal T2-weighted image showing bilateral rudimentary uterus (arrows) and absence of cervix. (B) Axial T2-weighted image showing normal ovaries (arrows).

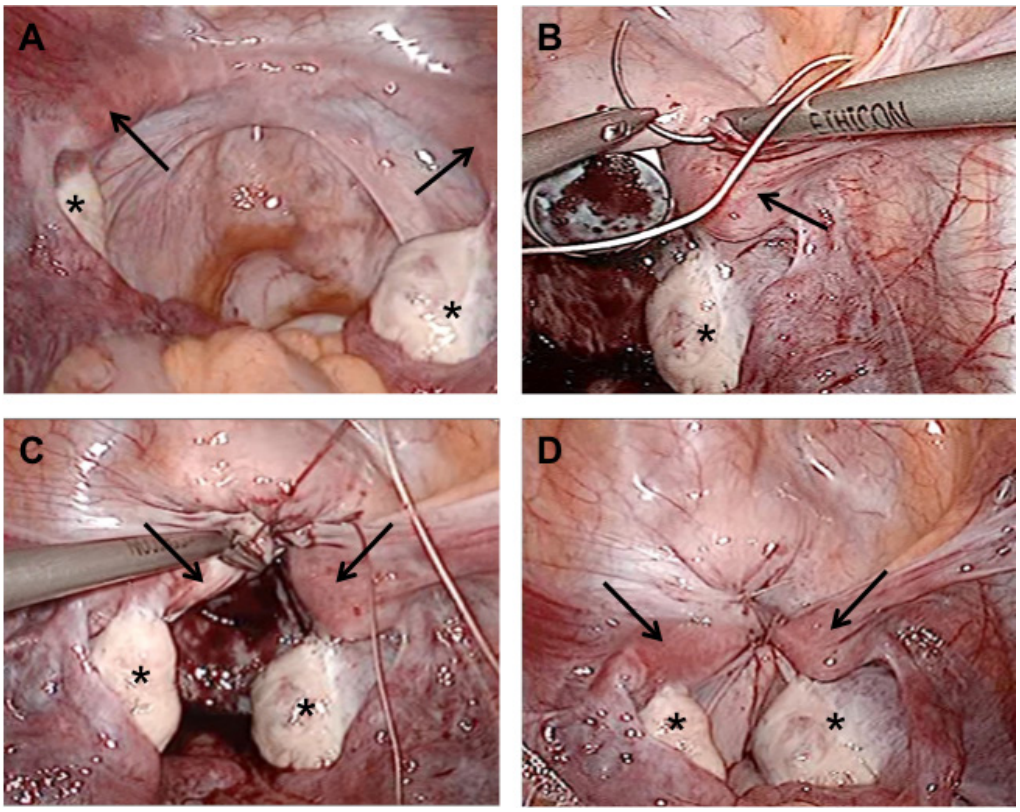

Fig. 2 Laparoscopic findings. (A) Laparoscopy confirmed bilateral rudimentary uterus (arrow) and normal ovaries (asterisk). (B) Transfixion of the round ligament. (C) Creation of a left purse-string suture by consecutively transfixing the round ligament, the utero-ovarian ligament, the lateral peritoneal leaf, and the rectal serosa. (D) Final laparoscopic vision.

Operation techniques

Operation techniques and postoperative management were performed according to the methods described by Fedele *et al.* [15]. The outline is as follows.

First, the diagnosis of MRKH syndrome is confirmed (Fig. 2A). A 2-cm transverse incision is made on the vaginal vestibulum. To create a vaginal space between the bladder and the rectum, the surgeon works forward with blunt dissection to the peritoneal margins (Fig. 3). Laparoscopically, the strand that connects the bilateral rudimental uterine horns is lifted, and the peritoneum immediately below is incised transversely for a 5-cm section (Fig. 2A). Peritoneal margins are pulled down to the edge of the incised vaginal vestibulum, and 8 points were sutured with 2–0 Vicryl. Laparoscopic creation of the purse-string suture is done by consecutively transfixing the round ligament (Fig. 2B), the tubal isthmus, the utero-ovarian ligament, the lateral peritoneal leaf, and the rectal serosa (Fig. 2C, D). This laparoscopic creation procedure

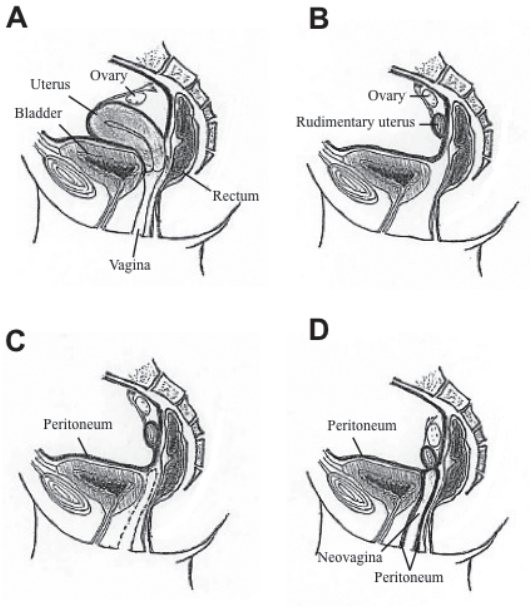

Fig. 3 Diagrams of the operation method. (A) Female reproductive organs (normal). (B) Reproductive organs of patients with MRKH syndrome: rudimentary uterus, absence of vagina, and normal ovaries. (C) Creation of a vaginal space between the bladder and the rectum (dotted line). (D) Final vision of the neovagina, which is covered by the peritoneum.

Table 1 Clinical characteristics of 7 patients

Case number	1	2	3	4	5	6	7	Average
Phenotype	Type II	Type I	Type I	Type I	Type I	Type I	Type I	
Height (cm)	161	165	161	158	164	161	149.4	159.9
Weight (kg)	48.5	57	55	41.7	54.8	50	42.7	49.9
BMI (kg/m2)	18.7	20.9	21.2	16.7	20.3	19.2	19.1	19.4
Genital sys.	RU	RU	RU	RU	RU	RU	RU	
	VA	VA	VA	VA	VA	VA	VA	
Renal sys.	Rt. nephrop	Norm	Norm	Norm	Norm	Norm	Norm	
Musculo. sys.	Norm	Norm	Norm	Norm	Norm	Norm	Norm	
Heart	Norm	Norm	Norm	Norm	Norm	Norm	Norm	
Hearing	Norm	Norm	Norm	Norm	Norm	Norm	Norm	
Others	None	None	None	None	None	None	BIH	

Abbreviations: BMI; body mass index, sys.; system, RU; rudimentary uterus (bilateral), VA; vaginal agenesis, Rt. nephrop; right nephroptosis, Norm; normal, Musculo.; musculoskeletal, BIH; biaterall inguinal hernia

helps to establish the desired length of the neovagina. Compared with the peritoneal approach alone, laparoscopic closure that sutures the top of the neovagina more efficiently achieves adequate length of the neovagina. Finally, the dilator is inserted into the neovagina. The dilator is made of polystyrene. Before use, the dilator is washed and covered with 2 condoms and lidocaine hydrocholoride and povidone iodine cream is applied to the dilators so as to cause less pain and to help prevent infections.

Postoperative management

The dilator was removed 48 hours after surgery. All the patients practiced how to insert the dilator themselves. Patients were discharged after they properly learned how to insert the dilator themselves. The patients were instructed to insert it approximately 6–8 hours every day for 3 months after being discharged; and, thereafter, the dilator may be inserted as needed. Sexual intercourse is allowed after the neovagina is epithelialized almost 3–6 months after the operation.

Clinical follow-up was at 2 weeks, 1, 3, 6, 12, 24, 36, 48, and 60 months after surgery. Vaginal examinations were performed and symptoms and the quality of sexual intercourse were evaluated at each visit. Anatomic success was defined as a neovagina of ≥ 6 cm in length that allows the easy introduction of 2 fingers within 6 months after surgery. Functional success was considered when the patient reported satisfactory sexual intercourse [17]. Some of the patients did not complete the follow-up examinations because they moved or dropped out of the study; therefore, that data is not available (Table 1).

RESULTS

The laparoscopic Davydov procedure was performed in 7 patients with MRKH syndrome. The anatomic and functional outcomes are shown in Table 2. At the first hospital visit, the mean age of the patients was 19.5 (range, 16–27) years. At the definitive diagnosis, the mean age of the patients was 20.2 (range, 16–27) years and 21.4 (range, 18–27) years at the operation. In 3 of the 7 patients, diagnosis was made intraoperatively. The mean operation time was 162.9 minutes

Table 2 Anatomic and functional outcomes

Case number	1	2	3	4	5	6	7	Average
Initial consultation	17 y, 3 m	27 y, 9 m	16 y, 11 m	16 y, 2 m	18 y, 7 m	23 y, 9 m	16 y, 3 m	19.5 ± 4.5
Laparoscopic examination	19 y, 8 m	27 y, 11 m	17 y, 1 m	16 y, 9 m	18 y, 9 m	24 y, 3 m	16 y, 9 m	20.2 ± 4.3
LDP	19 y, 8 m	27 y, 11 m	18 y, 0 m	21 y, 2 m	18 y, 9 m	25 y, 4 m	19 y, 1 m	21.4 ± 3.8
Surgery duration (min)	200	190	230	120	135	130	135	162.9 ± 43.0
Total blood loss (ml)	120	108	439	136	28	84	117	147.4 ± 133.3
Intraoperative complications	None	None	Bladder	None	None	None	None	
Hospital stay (days)	15	11	17	9	7	8	10	11.0 ± 3.7
Self dilaton	+	+	+	−	+	+	−	
Neovagina length/width (cm)								
3 months	7/2.5	7/3	6.5/2.5	3/2.5	7/2.5	7/3	7/2	6.4/2.6
6 months	7/2.5	8/3	7/2.5	6/2.5	5/2.5	8/3*	4.5/1.5	6.5/2.5
12 months	7/2.5	8/3	7/2.5	NA	6/2.5	8/3	3/3	6.5/2.8
24 months	7/2.6	8/3	NA	NA	6/2.5	8/3	3/3	6.4/2.8
36 months	7/2.6	8/3	NA	NA	5.5/2.5	8/3	NA	7.1/2.8
48 months	NA	8/3	NA	NA	5.5/2.5	8/3	NA	7.2/2.8
60 months	NA	8/3	NA	NA	NA	8/3	4.5/3	6.8/3

*means reoperation because of gulanulation.
Abbreviations: LDP; Laparoscopic Davydov procedure, NA; Not available, Bladder; Bladder injury

(range, 120–230 min) with the mean blood loss of 147.4 ml (range, 28–439 ml), and the mean length of hospital stay was 11.0 days (range, 7–17 days). In case 3, intraoperative bladder injury occurred. It was immediately detected and repaired transvaginally without any recurrence; on the other hand, operating time was lengthened, blood loss increased, and hospitalization was lengthy.

The anatomical results were assessed by uterine cervical dilators (Hegar type) without unduly pressure. After the operation at 3, 6, 12, 24, 36, 48, and 60 months, the mean lengths of the neovaginas were 6.4, 6.5, 6.5, 6.4, 7.1, 7.2, and 6.8 cm, respectively. The mean widths of the neovaginas were 2.6, 2.5, 2.8, 2.8, 2.8, 2.8, and 3.0 cm, respectively. Three patients could have sexual intercourse without any difficulties. For 2 patients, who could not insert the dilator by themselves after discharge, the length and width of their neovaginas were reduced. Particularly, in case 4, the patient could not properly care for her neovagina after discharge; and, thus, the length of the neovagina shortened to 3 cm after 3 months. Subsequently, she took better care of her neovagina; so that at 6 months, it had lengthened to 6 cm. In case 7, the width of the neovagina became narrower because of the stricture of the neovaginal orifice. As a result, the patient was unable to insert the dilator herself, and the length of the neovagina became shorter. She was retrained as to how to take care of her neovagina, but it was still only 4.5 cm in length and very narrow.

DISCUSSION

MRKH syndrome is a disorder that occurs in females and mainly affects the reproductive system. This condition causes the vagina and the uterus to be underdeveloped or even absent at birth. Patients typically present with primary amenorrhea in adolescence with normal growth and development. Sexual intercourse and infertility are also problematic [1–4]. Given an incidence of 1 per 4,500 females, most general gynecologists will only encounter MRKH syndrome once or twice during their whole careers [18]. Most cases occur randomly, but some cases run in families [1].

For the diagnosis of MRKH syndrome, transabdominal ultrasonography is a useful and noninvasive technique. It must be the first investigation in evaluating patients suspected of having the syndrome. Magnetic resonance imaging (MRI) is a non-invasive method that provides a more accurate diagnosis than does ultrasonography and should be performed when ultrasonographic findings are unclear. MRI allows an accurate evaluation of MRKH syndrome. Even if the diagnosis remains doubtful after ultrasonography, MRI and/or laparoscopy should be done. Laparoscopy is an invasive technique; however, it defines precise anatomical locations and abnormalities [3].

The karyotype of the patient in the present study is 46, XX, and the endocrine balance was normal. Once MRKH syndrome is diagnosed, a complete checkup must be undertaken to evaluate the associated malformations such as renal and skeletal anomalies [19]. The differential diagnosis of MRKH syndrome includes congenital absence of vagina (with or without uterine structures), a low transverse vaginal septum, an imperforate hymen, as well as 46, XY disorders of sex development, including androgen insensitivity and 17α − hydroxylase deficiency [20].

The etiology of this syndrome remains unclear; however, genetic involvement has been confirmed by several investigators, showing autosomal dominant inheritance with incomplete penetrance, variable expressivity of a single mutant gene, or limited chromosomal imbalance undetectable in standard karyotypes [21–24]. Between 2014 and 2015, we tried to detect mutations of the candidate genes, LHX1 and HNF1B, in 9 patients with MRKH syndrome using the PCR (poly-

Table 3 Comparison of laparoscopic procedures.

Laparosopic procedure	Davydov	Vecchietti
Type of vaginal covering tissue	Peritoneum	None/Oxide cellulose
Technical remarks	A portion of the pelvic peritoneum is used to create the vaginal canal. The vaginal apex is formed by the approximation of the fibro-muscular streaks.	A dilatation olive is placed in the vagina and a connected traction device is attached to the external pelvic wall, for 7–9 days.
Postsurgical use of dilator	Yes	Yes
Advantage	Good lubrication that allows satisfactory intercourse. Intercourse is allowed after 3–6 month.	Normal vaginal mucosa. Intercourse is allowed after 6month.
Disadvantage	Discomfort with the dilator device (mild).	Discomfort with the dilator and traction devices (severe).
Complication	Ascending infection	Bladder injury

Modified from Torres-de la Roche LA. *Et. al.* [26]

merase chain reaction)-Sangar method but could not determine the pathological variants (data not shown). However, in a report of 58 women with MRKH syndrome undergoing infertility treatment with gestational surrogates, none of the 17 female infants born exhibited the same syndrome [25]. In that study, the syndrome might not have adequately or generally been explained by single-gene mutation, and the genetic background of the syndrome remained undetermined.

The most common treatment for this syndrome is the construction of a neovagina and follow-up infertility treatment, as needed. The aim of the creation of a functional neovagina is so that the patient can still have sexual intercourse [15]. It is also important that patients feel free from the inferiority that they do not have a vagina. The assisted reproductive technology (ART) for having genetic offspring is important as well. Studies have reported on the emotional hardship associated with the realization of an inability to bear children [26, 27]. Although significant progress has been made in ART, uterine factor infertility (UFI) remains unsolved. Absolute UFI is an incurable cause of infertility that can either be congenital or acquired. In absolute UFI, the major cause is MRKH syndrome [7, 28].

Currently gestational surrogacy remains the standard for women with UFI to have a genetic offspring. Gestational surrogacy is undertaken in some countries, but in Japan it is prohibited, not by law but by a rule of the Japan Society of Obstetrics and Gynecology. Uterus transplantation is currently under trial. Brännström, *et al.* reported the first livebirth after uterus transplantation from a postmenopausal donor to a patient with MRKH syndrome in 2014 [5]. Including that case, to our knowledge, there have only been 4 babies in the world who were born to patients who had successfully undergone uterus transplantation. Those 4 cases were in Sweden. Although, in Japan, we are far from being able to offer uterus transplantation as a therapy for patients with MRKH syndrome, further research may hopefully provide novel therapies in the not too distant future.

The aim of the creation of a functional neovagina is that it enables the patient to have sexual intercourse and provides adequate cosmetics [20]. Several surgical techniques have been described for creating a neovagina in patients with MRKH syndrome [9–17], however, there is not yet a consensual standardized treatment. The choice of techniques differs depending on the patients, the country, and especially on the surgeon. The most important thing is that the surgeon has to be familiar with the technique. The success rate depends on the appropriate first operation and proper postoperative management.

Among the several surgical techniques available, the laparoscopic Davydov procedure, in which the vesicorectal space is coated by the peritoneum, is by far the simplest, safest, and quickest operative method for this type of case. And intraoperative and postoperative complications are rare compared with other surgical techniques [14–16]. Fedele *et al.* [15] compared the Vecchietti and the Davydov laparoscopic techniques for creation of a neovagina in patients with MRKH syndrome. Fifteen patients underwent surgical creation of a neovagina by the Vecchietti procedure and 30 patients by the Davydov procedure. They reported that the only significant difference seemed to be in greater length of the neovagina achieved by the Davydov procedure [15]. And both the Davydov and the Vecchietti laparoscopic techniques seemed to be effective in the treatment of vaginal agenesis in MRKH syndrome (Table 3) [16]. Therefore, we decided to use the laparoscopic Davydov procedure.

We have performed the laparoscopic Davydov procedure in 7 patients with MRKH syndrome. The mean operation time was 162.9 minutes (range, 120–230 min) with the mean blood loss of 147.4 ml (range, 28–439 ml). This was relatively long because we used laparoscopy in combination with the vaginal approach, and an intraoperative bladder injury occurred in case 3. In that case, the complication was immediately detected and repaired transvaginally without any recurrence. In the other cases, no remarkable complications were observed. With the laparoscopic Davydov procedure, the operating time and hospital stay tended to be shorter as we gained experience. We assessed anatomical results at 3, 6, 12, 24, 36, 48, and 60 months after the operations. The mean lengths and widths of the neovaginas were all ≥ 6.0 cm and ≥ 2.5 cm, respectively. Three of the 7 patients had sexual intercourse

without any difficulties. Four of the 7 patients did not have sexual partners at that time. However, we did not assess the functional results with the use of a Female Sexual Function Index (e.g., Rosen's Female Sexual Function Index) [27]. This should have been done and compared with age-matched normal control subjects.

Timing for the surgical creation of a neovagina is elective and depends on each individual patient and the circumstances of each case. When the patient is emotionally mature and ready to start sexual activity is the best time to plan the construction of the neovagina [28, 29]. In these cases, 2 patients, who were younger than the others, could not adequately care for their neovaginas after being discharged, and thus, the lengths and widths became reduced. If patients are too young, they may lack the motivation to go through with this procedure and provide themselves with the requisite follow-up care. It is also sometimes difficult for patients who work to visit the clinic as often as is necessary until their treatments are completed. Therefore, we surgeons need to plan the operations at the most opportune time for our patients.

MRKH syndrome is commonly diagnosed in adolescent females due to amenorrhea and has a considerable impact on their lives [24]. Counseling and support are not always easy but of great importance for the patients and their families. While the exact age at diagnosis often differs, from infancy to early adulthood, it is essential to provide accurate information with possible treatment options according to the patients' degree of acceptance [2, 30]. Especially in the event of surgery of the neovagina, the pivotal point is taking account of patients' maturity, carefully considering to deal with any precluded feelings of inferiority or solitude, both on the part of the patients as well as of their families. Genetic counseling can be beneficial in familial cases. Hence, in the counseling sessions, we usually try to focus on the prognoses of the disease more than discussions about the probable causes.

Based on our experience, the laparoscopic Davydov procedure has numerous advantages. First, the procedure is quick and has a low risk of complications. Second, it is excellent esthetically because there are no surgical scars. Third, the length of the neovagina is long enough, and intercourse is allowed 3 to 6 months after the operation. The one disadvantage of these cases is that the patients required intermittent postoperative dilation. We need more data on MRKH syndrome among Japanese patients because their required treatment is different than that for patients of other races, in the context of their physical and sexual lives. Moreover, the care of patients with MRKH syndrome requires the co-ordinated efforts of gynecologists, pediatricians, surgeons, psychologists, and other medical experts. Centers that focus on congenital anomalies of the reproductive tract should be developed in Japan. Those centers should then promote long-term follow-up studies to improve patient care and evidence based medical options.

CONCLUSIONS

The laparoscopic Davydov procedure seems to be a safe and effective surgical treatment for patients with MRKH syndrome, if postoperative self dilation is properly done. While MRKH syndrome is not a life-threatening disease, the diagnosis in adolescence has a significant influence on a patient's life. For such patients, with adequate treatment, sexual relations are possible, and fertility options are available.

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COMPETING INTERESTS

The authors declare no conflicts of interest.

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