ORIGINAL

Microsurgical penile revascularization for ischemic erectile dysfunction : Cumulative effective rate over time and factors affecting surgical outcomes.

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Abstract : Objectives : This study aimed to clarify the cumulative effectiveness of microsurgical penile revascularization over time and factors that affect surgical outcomes. Subjects and Methods : This study analyzed 114 men with a median age of 30.5 years. They had localized arterial lesions on the internal pudendal artery by angiography. They underwent the anastomosis of the distal end of the inferior epigastric artery to the dorsal artery of the penis with 11-0 sutures. Results : The final cumulative effectiveness rate calculated by the Kaplan–Meier method was 92.5%. The 1- and 3-year cumulative effectiveness rates were 58.0% and 92.5%, respectively. Twenty-one patients were not cured during the study. Age was a factor significantly affecting the surgical outcomes ($p = 0.018$), and the peak systolic and end-diastolic velocities on Doppler ultrasound, corporal veno-occlusive dysfunction, and venous ligation were less significant ($p = 0.290$, $p = 0.559$, $p = 0.054$, and $p = 0.732$, respectively). Conclusion : The final cumulative effectiveness rate of penile revascularization was 92.5%. Latency was observed until cure, half of the cases were cured in approximately 10 months. Cavernous function appears to be reversible and cavernous dysfunction was not a significant factor in surgical outcome. J. Med. Invest. 71 : 219-224, August, 2024

Keywords **:** *Penile revascularization, erectile dysfunction, ischemic, mixed vasculogenic erectile dysfunction*

INTRODUCTION

Erectile dysfunction (ED) can impair the quality of life. In young men, ED is a serious problem. Moreover, pelvic fractures and perineal trauma, which can cause ED, are common accidents among young men (1). In young men with pelvic or perineal trauma, microsurgical penile revascularization is considered to have a long-term success rate of 60-70% (2). Several techniques are available for penile revascularization ; however, the effectiveness of each surgery or the factors that influence the outcomes of each surgery is unclear.

We performed penile revascularization using the same method, i.e., anastomosis of the inferior epigastric artery to the dorsal penile artery, in patients with ischemic ED diagnosed according to standard procedures. The effectiveness of surgery (primary endpoint) was evaluated using a validated questionnaire, and the cumulative effectiveness was calculated over time. Factors that affect surgical outcomes (secondary endpoint) were investigated by multivariate analysis.

PATIENTS AND METHODS

This cohort study was conducted at a single institution. The indication for penile revascularization was determined according to the standard procedures of the International Society for Sexual Medicine (3). A subjective assessment using the international index of erectile function (IIEF) questionnaire (4), a blood test, and a duplex Doppler ultrasound examination of cavernous arteries using alprostadil alfadex was performed. To evaluate cavernous function, dynamic infusion cavernosometry with alprostadil redosing schedule was performed in all cases. Normal cavernous function was defined as a maintenance flow rate of < 20 mL/min at 90 mmHg of intracavernous pressure. All patients underwent selective internal pudendal artery angiography as a definitive diagnosis. Inclusion criteria : suboptimal response to intracavernous injection of 10 μg of alprostadil alfadex, angiographically confirmed focal lesion of the internal pudendal artery or its distal branches, and inferior epigastric artery to dorsal penile artery anastomosis. Exclusion criteria : patients with diabetes, neurological disease, depression, schizophrenia, Peyronie's disease, and endocrine abnormalities, cases in dispute because of industrial accidents or traffic accidents, and cases in which follow-up was not performed after surgery.

SURGICAL TECHNIQUES

Microsurgical penile revascularization was performed with the patient under general intubated anesthesia. A curvilinear incision was made at the base of the penis on the side opposite the planned abdominal incision for inferior epigastric artery harvesting. The dissection is advanced deeply, while being careful not to damage the fundiform and suspensory ligament, the dorsal penile artery, accompanying vein, and dorsal nerve bundles. To avoid damage to the dorsal nerve of the penis, in this step, the dorsal artery of the penis is only checked for its appearance. Then, a pararectal incision is made, reaching the surface of the rectus sheath. The anterior sheath is cut, and the rectus muscle is retracted medially. The inferior epigastric artery is exposed and dissected, including its two accompanying veins. The dissection is continued cephalad for 12–13 cm to free two major branches (Figure 1). Clip and divide them, lower them down to the internal inguinal ring, and passed them through the inguinal canal to the base of the penis. Apply diluted papaverine hydrochloride topically to reduce arterial spasm. After that, perform the operation under a microscope (Figure 2). The penile

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dorsal nerve and accompanying veins were detached from the dorsal penile artery. This surgical method restores blood flow to the corpus cavernosum via the communicating branch of the dorsal penile artery. This not only increases the intra-cavernous pressure but also restores the nourishment of the cavernous tissue. Therefore, the communicating branches of the dorsal penile artery and the cavernous artery should be preserved as much as possible. The dorsal artery of the penis is cut and anastomosed end-to-end with the harvested inferior epigastric artery end using an 11-0 polyamide suture (single-armed, 80 μm, 3-mm needle). Basically we perform vascular anastomosis in both the proximal and distal directions of the penile dorsal artery (5). After bidirectional anastomosis, indocyanine green videoangiography is performed to confirm the patency of the anastomosis.

Some patients were diagnosed with cavernous dysfunction. Clinically, cavernous dysfunction manifests as corporal veno-occlusive dysfunction, that is, venous leakage during erection. Therefore, for these patients, we performed both penile revascularization and venous ligation surgery between 2003 and 2018. Venous ligation was completed by the dorsal vein complex bunching technique. Specifically, incise the endopelvic fascia on both sides, and then ligate the dorsal vein complex of the prostate with a non-absorbable suture (6). Alprostadil alfadex (5 μg/h) was administered intravenously for 3 consecutive days after surgery. Aspirin (100 mg/day) was administered for at least 1 year after surgery.

The primary endpoint is the cumulative efficacy of long-term surgical outcomes. Since the period until cure varies from patient to patient and there are censored cases, the effectiveness rate was calculated using the Kaplan-Meier method. Surgical outcomes were assessed using the internationally validated IIEF-6 questionnaire (7). The IIEF-6 is an abbreviated version of the IIEF that consists of 15 questions related to sexual function (4). IIEF-6 is a six-item questionnaire designed to evaluate surgical results. Each question is scored on a 5-point scale, and a total score of 24 or higher was considered cured.

The secondary endpoint is a logistic regression analysis of factors that affect surgical outcomes. Factors examined were age at the time of surgery, peak systolic and end-diastolic velocities on Doppler ultrasound, maintenance flow rate in dynamic infusion cavernosometry, and venous ligation.

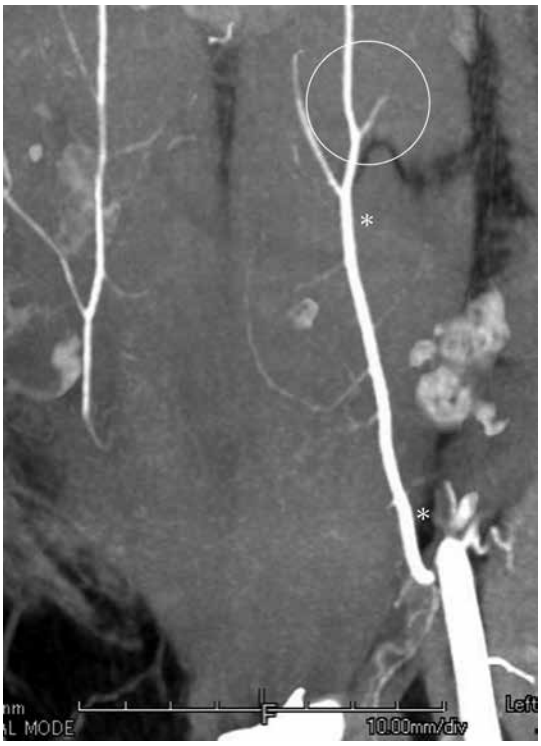

Figure 1. Inferior epigastric artery, donor vessel for penile revascularization surgery
A pararectal incision is made, and the inferior epigastric artery (*) is dissected on the dorsal surface of the rectus abdominis muscle. Cut off the distal branches (white circle) and guide them to the base of the penis.

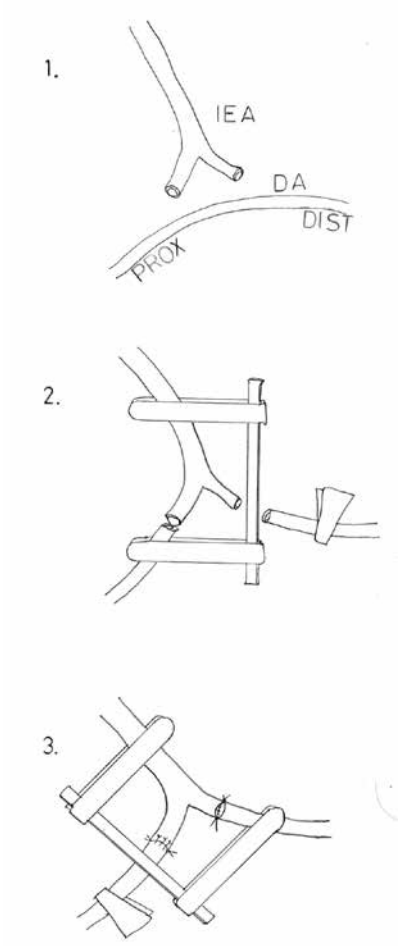

Figure 2. Microvascular anastomosis between the harvested inferior epigastric artery and the penile dorsal artery
To perform vascular anastomosis in both the proximal and distal directions of the penile dorsal artery, the bifurcation of the distal end of the inferior epigastric artery is used for vascular anastomosis (1). After determining the site of the anastomosis with the dorsal penile artery, the dorsal penile artery was cut. Initially, the proximal end of the penile dorsal artery and inferior epigastric artery are anastomosed (2). Then, the distal end of the dorsal penile artery and the other stump of the inferior epigastric artery are anastomosed (3).

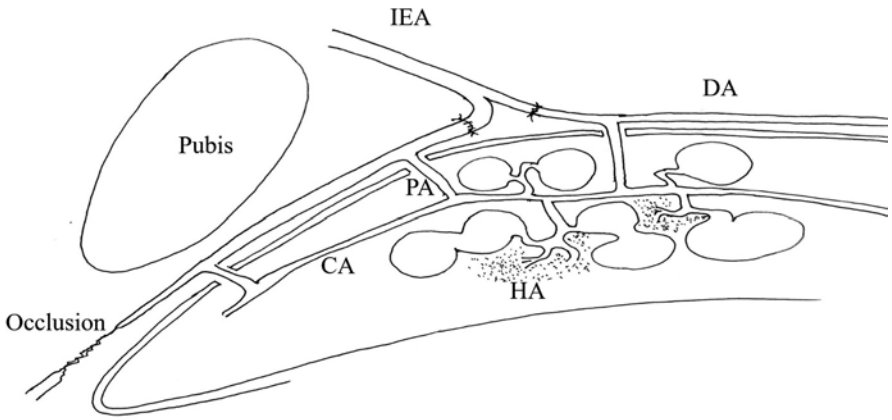

Figure 3. Completion of vascular anastomosis
After vascular anastomosis, blood flow in the inferior epigastric artery reaches the cavernous artery via penetrating branches, and to the helicine arteries, and to the cavernous sinuses and cavernous tissues. The perfusion pressure of the cavernous sinus is restored and the nourishment of the cavernous tissue is restored.

IEA : inferior epigastric artery
DA : dorsal artery of the penis
PA : penetrating artery : communicating branch between dorsal artery and cavernous artery
CA : cavernous artery
HA : helicine artery

STATISTICAL ANALYSIS

The log-rank test and logistic regression analysis were performed using IBM SPSS Statistics version 28.0.1.0. (USA). Multivariate logistic regression was used to calculate odds ratio and 95% confidence intervals after controlling simultaneously for potential confounders. Variables considered in the models were age (quantitative variable, continuous), end-diastolic velocity of the cavernous artery (quantitative variable, continuous), peak systolic velocity of the cavernous artery (quantitative variable, continuous), peak systolic velocity, flow rate to maintain 90 mmHg of intracavernous pressure (quantitative variable, continuous), and venous ligation surgery (qualitative variable, reference : no surgery). The significance was set at $p < 0.05$.

RESULTS

Characteristics of the patients

Between 2003 and 2020, 140 patients were identified as candidates for microscopic penile revascularization. Of the 140 patients, 26 were excluded from the analysis (Table 1). Consequently, 114 patients were included in the study. Table 2 shows the characteristics of the 114 patients. Of these 114 patients, 72 had pure arterial ED and 42 had mixed vascular ED. Of the 42 patients with mixed vascular ED, 22 underwent both penile revascularization and venous ligation surgery, and 20 underwent penile revascularization only.

Primary endpoint

The median follow-up period was 24.7 months with a range of 0.6 to 43.5 months. During the study period, 93/114 cases (81.6%) were cured, while 21 cases (18.4%) were not cured. IIEF-6 of cured patients was 25.1 ± 0.6, while that of non-cured patients was 6.0 ± 4.1. The Kaplan–Meier method, which considered censored cases, showed a final cumulative effectiveness of 92.5% (Figure 3). It took 3.3 ± 0.5 months to reach a cumulative effectiveness of 25%, 10.0 ± 1.5 months to reach 50%, and 22.0 ± 22.0 months to reach 75%. The 1-, 2-, and 3-year cumulative effectiveness rates were 58.0%, 77.2%, and 92.5%, respectively.

Table 1. Patients excluded from the analysis (n = 26)

Another surgical procedure was inevitably performed	8
Penile revascularization was not chosen and another treatment was selected	7
Receiving accident insurance compensation	6
After surgery, hospitalized for depression	2
Never seen after surgery	2
After surgery, diagnosed with juvenile Parkinson's disease	1

Table 2. Characteristics of the patients

Number of case		114 cases
Median age at surgery (range), years		30.5 (16–47)
Preoperative IIEF-6, (range), points		8.7 ± 6.3 (1–23)
Mean peak systolic velocity of cavernous arteries, (range), cm/s		23.5 ± 7.8 (0–38.1)
Mean end-diastolic velocity of cavernous arteries, (range), cm/s		3.7 ± 4.1 (–2.1–22.7)
Flow rate to maintain intracavernous pressure of 90 mmHg at dynamic infusion cavernosometry, mL/min	<20	72 cases
	20≤ <30	17 cases
	30≤ <60	6 cases
	60≤ <100	7 cases
	100≤	12 cases

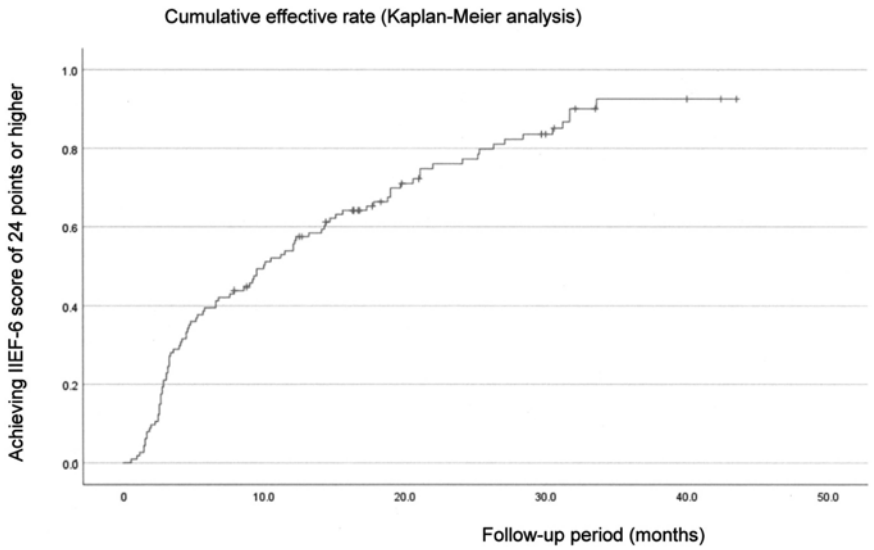

Figure 4. Cumulative rate of efficacy of microvascular penile revascularization
The Y-axis refers to the percentage of patients who achieved an IIEF6 score of ≥ 24, calculated by the Kaplan–Meier method. The X-axis indicates the postoperative follow-up period in months.

Secondary endpoint

In this study, 21 were not cured. The age distribution of these patients ranged from 17 to 45 (median, 34.0) years, and the follow-up period ranged from 7.9 to 199.8 (median, 18.3) months. Of these 21 patients, 5 had anastomosis occlusion. Occlusion occurred 3.6 to 187.0 (median, 10.3) months after surgery. We diagnosed these 21 cases as failure, and the factors that affect surgical outcomes were examined by logistic regression analysis. As a result, age was a significant factor for success ($p = 0.018$), and peak systolic and end-diastolic velocities on Doppler ultrasound, maintenance flow rate on dynamic infusion cavernosometry (cavernous function), and implementation of venous ligation were less significant ($p = 0.290$, $p = 0.559$, $p = 0.054$, and $p = 0.732$, respectively).

Table 3. Results of the logistic regression analysis against cure and odds ratio for each parameter

Parameters	p value	odds ratio	95% CI
Age (1 year increments)	0.018	1.105	1.018–1.200
End-diastolic velocity of the cavernous artery (1 cm/sec increments)	0.559	0.955	0.818–1.115
Peak systolic velocity of the cavernous artery (1 cm/sec increments)	0.290	0.964	0.900–1.032
Flow rate to maintain 90 mmHg of intracavernous pressure (1 mL/min increments)	0.054	1.002	1.000–1.004
Venous ligation surgery (reference : not performed)	0.732	0.772	0.175–3.403

Complications

Adverse events were classified according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0 (8). Adverse events occurred in 9 cases (7.9%). Most of the adverse events were minor, transient, and grade 1. They included penile edema, discomfort, and perineal pain (Table 4). No cases of penile shortening were noted. One patient had retinal hemorrhage, which was judged to be a grade 2 adverse event. One patient had an anastomotic rupture 5 weeks postoperatively due to trauma requiring emergency surgery, which was judged to be a grade 3 adverse event.

DISCUSSION

Endovascular therapy is becoming prevalent in the treatment of vascular ED (9) ; however, microsurgical penile revascularization remains the standard treatment (10). Several surgical methods have been used (11-13) ; however, which one provides the best results is unclear. Our standard method is to anastomose the inferior epigastric artery and dorsal penile artery. Our surgical results were approximately 10% better than previous reports (2). This may be related to our calculation of cumulative effectiveness over time using the Kaplan–Meier method. Furthermore, improvements in the performance of microscopy and new technologies such as infrared videoangiography may be contributing factors. However, the most important difference may be the surgical method chosen. We believe that important things are not only an increase in the amount of blood flow into the cavernous sinus, but also an improvement in the nourishment of the cavernous tissue.

After microsurgical penile revascularization, a relatively long latent period was observed until a cure was obtained. Functional recovery of ischemic organs does not occur immediately after revascularization (14). The mechanism is thought to be tissue degeneration and adaptation to an ischemic environment (15). Similar degeneration was in the tissue of the corpus cavernosum (16). Given this latent period before recovery, both doctors and patients should not rush to judge the effectiveness of surgery.

As in other studies (17, 18), age was a significant factor that affects surgical outcomes. The mechanism by which age affects surgical outcomes is unclear ; however, deterioration of the tunica albuginea and corpus cavernosum may be involved. Basic

Table 4. Adverse events

CTCAE v5.0 code	CTCAE v5.0 Term	Grade	Clinical course
10018146	Genital edema	Grade 1	Disappeared within 3 days.
10038604	Reproductive system — Other	Grade 1	Deformity of the penis at the flaccid state continued for > 3 months, subjective complaints only, no objective findings.
10034310	Penile pain	Grade 1	Disappeared within 1 month.
10055322	Postoperative hemorrhage	Grade 1	Resolved within 3 days.
10033474	Pain of skin	Grade 1	Resolved within < 1 month.
10038923	Retinopathy	Grade 2	Occurred 1 month after surgery, and healed by 2 months of outpatient ophthalmology treatment.
10061339	Perineal pain	Grade 2	Continued for > 3 months, no medication needed after the second month.
10038604	Reproductive system — Other	Grade 2	Discomfort of glans at erection, resolved within than 3 months.
10055322	Postoperative hemorrhage	Grade 3	Accidental rupture of the anastomosis 5 weeks after surgery due to a collision with a boy. Reparative surgery was performed at our hospital within 24 h.

studies have reported that the structure of the albuginea and cavernous function begin to deteriorate in men aged 30–40 years (19). The age of candidates for this surgery is the age at which penile structures begin to deteriorate.

Chronic ischemia of the corpus cavernosum can lead to cavernous dysfunction and subsequent abnormal venous leakage from the corpus cavernosum (16). Some reports have denied the indication for surgery in patients with vasculogenic ED having cavernous dysfunction (2). However, some studies have also reported that concurrent cavernous dysfunction does not affect surgical outcomes (17, 18). Our results were similar to those of the latter studies. This is an important fact. The idea that surgery is not indicated in cases with cavernous dysfunction is based on the premise that cavernous dysfunction is irreversible. However, there are cases in which erectile function normalizes after penile revascularization even in ischemic ED patients with cavernous dysfunction, and the presence of cavernous dysfunction is not a significant factor in postoperative cure. This indicates that the cavernous dysfunction has been resolved after penile revascularization surgery. Moreover, Judging from the recovery over time, cavernous dysfunction will recover to normal soon after revascularization.

Some of the adverse events were considered caused by damage to the dorsal nerve of the penis. Since the dorsal penile nerve may run around the dorsal penile artery, even if it is dissected with great care under a microscope, a small nerve injury may occur, exposing the anastomosis site. We experienced a case in which the vascular anastomosis was severed because of trauma 5 weeks after the operation. Goldstein (13) recommended avoiding sexual intercourse or masturbation for 6 weeks after revascularization to prevent the rupture of the anastomosis. We should have instructed our patients more strongly about protecting the anastomosis.

As limitations, this study was a cohort study performed at a single institution. The number of patients analyzed was small because of the rarity of the disease. For the same reason, the research period was long, and the surgeon's technique may have changed in the meantime.

CONCLUSION

This study showed that the effectiveness of microsurgical penile revascularization was sufficiently high at 92.5%. A certain latency was observed until cure in penile revascularization. Half of the patients were cured in approximately 10 months, whereas others took longer. In addition, age was a significant factor for surgical outcomes, although cavernous dysfunction or Doppler parameters were less significant. This result indicates the reversibility of cavernous dysfunction in patients who are candidates for revascularization. In addition, research on the effectiveness of surgical treatment in young ischemic ED with cavernous dysfunction is warranted.

CONFLICT OF INTEREST STATEMENT

All authors declare no conflict of interest.

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None.

APPROVAL OF THE LOCAL ETHICAL COMMITTEE

Written informed consent for this clinical study was obtained from all cases (Approval nos. 1020 and 13011).

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