Penile allotransplantation for penis amputation following ritual circumcision: a case report with 24 months of follow-up

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Summary

Introduction Ritual circumcision complicated by gangrene is a leading cause of penile loss in young men in South Africa. This deeply rooted cultural tradition is unlikely to be abolished. Conventional reconstructive techniques using free vascularised tissue flaps with penile implants are undesirable in this often socioeconomically challenged group because donor site morbidity can hinder manual labour and vigorous sexual activity might lead to penile implant extrusion. The psychosociological effects of penile loss in a young man are devastating and replacing it with the same organ is likely to produce the maximum benefit.

Methods We first performed a cadaver-to-cadaver penile transplantation as preparation. After approval from the Human Research Ethics Committee was obtained, we recruited potential recipients. We screened the potential participants for both physical and psychological characteristics, including penile stump length, and emotional suitability for the procedure. A suitable donor became available and the penis was harvested. We surgically prepared the penile stump of the recipient and attached the penile graft. Immunosuppression treatment with antithymocyte globulin, methylprednisolone, tacrolimus, mycophenolate mofetil, and prednisone were commenced. Tadalafil at 5 mg once per day was commenced after 1 week as penile rehabilitation and was continued for 3 months. We collected on quality-of-life scores (Short Form 36 version 2 [SF-36v2] questionnaires) before surgery and during follow-up and measured erectile function (International Index for Erectile Function [IIEF] score) and urine flow rates at 24 months post transplant.

Findings The warm ischaemia time for the graft after removal was 4 min and the cold ischaemia time was 16 h. The surgery lasted 9 h. An arterial thrombus required urgent revision 8 h after the operation. On post operative day 6, an infected haematoma and an area of proximal skin necrosis were surgically treated. The recipient was discharged after 1 month and first reported satisfactory sexual intercourse 1 week later (despite advice to the contrary). The recipient reported regular sexual intercourse from 3 months after the operation. An episode of acute kidney injury at 7 months was reversed by reducing the tacrolimus dose to 14 mg twice per day. At 8 months after surgery, the patient had a skin extrusion. The psychosociological effects of penile loss in a young man are devastating and replacing it with the same organ is likely to produce the maximum benefit.

Interpretation Penile transplantation restored normal physiological functions in this transplant recipient without major complications in the first 24 months.

Introduction Penile loss and injury can have various causes.1–4 A distressing number of healthy young men in South Africa are rendered aphaic because of complications arising from ritual circumcisions.5–9 Ritual circumcision is deeply rooted in cultural practice in South Africa, especially among the Xhosa-speaking people of the Eastern Cape. Circumcision is an integral part of a larger initiation ritual, which is considered a rite of passage to manhood. The initiation ritual serves an educational function, preparing older adolescents for the challenges and responsibilities of adulthood. The ritual is generally an eagerly anticipated event in a young man’s life, symbolising his transition to manhood; failure to comply results in social stigmatisation.2 Groups of young Xhosa men voluntarily enter this month-long camp, colloquially referred to as “going to the bush”, for a period of seclusion. During the ritual process, the circumcisionist removes the foreskin with an assegai (traditional spear). A haemostatic bandage of a strip of buckskin or cloth and herbal leaves is wrapped tightly around the full length of the pendulous penis encroaching the pubic skin. The initiates are then confined to a hut for the first 8 days and the consumption of certain foods and drinks is restricted. During the seclusion period the initiates receive sexual and cultural counselling that prepares them for the responsibilities of adulthood and family life.3
 Articles

Research in context

Evidence before this study
We searched PubMed and MEDLINE up to July, 2016, using the MeSH terms “penile transplantation”, “penis allotransplantation”, “penile gangrene”, “phalloplasty”, “ritual circumcision”, “botched circumcision”, “SF 36” AND “penis/penile”, “gender reassignment”. In South Africa many young men are rendered aphallic as a very serious complication of traditional circumcisions. To date these men who have suffered penile loss have not been optimally managed, thus depriving them of dignity and satisfaction in life. Although prostheses and phalloplasties are available, therapeutic approaches are expensive and fraught with complications. We explored the option of a penile allotransplant as a definitive procedure. The first penile allotransplant was done in Guangzhou, China, in 2005. The allograft was removed 2 weeks later because of psychological rejection by the donor’s wife. In this study, we report the second penile allotransplant, which was done in Cape Town, South Africa. A subsequent transplant was done in Boston, USA, in 2016 and we successfully performed our second allotransplant on April 21, 2017.

Added value of this report
This is the first report of a penis transplant that has resulted in restoration of all physiological functions of the penis. The main value of our report is that of proof of concept, removing the doubt that normal erections could be achieved with an allotransplanted organ and challenges reports of potential major skin necrosis after penile transplantation. An important aspect of the process is the careful screening and selection of the recipients, as well as consideration of the ethical issues pertaining to the procedure. The benefit of a successful transplant must be weighed against the inevitable consequences of lifelong immunosuppression.

Implications of all the available evidence
There are many circumstances under which penile loss occurs and the knowledge that penile allotransplantation is now a feasible option can give hope to affected patients. Vascularised composite allotransplantation is still novel and much about this form of transplantation remains uncertain. We believe that our experience will help to progressively improve the way in which vascularised composite allotransplantation is managed. Penile allotransplants present unique sociocultural and ethical challenges, and the success of the procedure should stimulate societal discourse on dealing with these issues.

Conventional reconstructive techniques, including free vascularised tissue transfer, are imperfect substitutes for a normal penis. Common complications include flap atrophy or necrosis, urethral strictures, extrusion of the prosthesis, and cosmetically unacceptable hair growth.13,14 The radial forearm (fasciocutaneous) flap currently used in our practice can impair functional capacity in patients who rely heavily on manual labour to earn a living. The cost of penile implants after free-flap reconstructive surgery, combined with the potentially high extrusion rate in a young sexually active population, makes this option less desirable in the resource-constrained context of South Africa. The high risk of complications, general scarcity of reconstructive expertise, and high cost of a suitable prosthesis created the need for a more suitable alternative; this alternative had to have few complications, be cosmetically acceptable, restore normal sexual function, and permit normal urination. The first attempt at penile allograft transplantation was reported from Guangzhou, China, in 2006. The surgery was technically successful; the penis was warmed post operatively with an infra-red lamp and had superficial skin necrosis on histology with viable corpora cavernosa and corpus spongiosum. The transplanted penis was removed 14 days after the surgery at the request of the recipient’s partner.16 The current report describes the second penis transplant; the third was done in Boston, MA, USA, in 2016. We can report that we did a subsequent penis transplant on April 21, 2017, which was our second case.

Current ritual circumcision practices in South Africa have raised serious health concerns. Complications of the procedure result in severe penile mutilation or varying degrees of penile amputation in roughly 250 young men per year17 and mortality is unacceptably high (9%) among those admitted to hospital.16 Because of the secrecy of the process, reliable data on complications are scarce.17,20 Ritual circumcision is typically done in a non-clinical setting by a traditional circumcisionist with minimal, if any, formal clinical training. In addition to the surgical risks, if the haemostatic bandage is applied excessively tightly, the penile skin or the whole pendulous penis can undergo necrosis. Furthermore, the initiates are discouraged from fluid intake in the days after the circumcision in an attempt to reduce urine production and voiding, and thus prevent acute urine retention. The resulting dehydration predisposes initiates to thrombosis of the penile blood vessels, increasing the risk of penile necrosis. The constrictive bandage can cause necrosis of the pendulous penis at various levels depending on the extent of pressure applied. Loss of the penis deprives the young man of the ability to urinate standing, to enjoy normal sexual intercourse, or to impregnate a female partner. Of even greater concern, is that infection is common and subsequent septicemia causes an estimated 100 deaths each year. Complications are often not reported to health authorities because this “shames the custom” and might be punished with physical violence by cultural purists.16,17,18
The notion that to be ethical, research must be socially valuable is widely accepted in medical ethics. Research that imposes risks and burdens to participants is only justified when it has sufficient social value. The local social value of penile transplantation in South Africa is shown by the relatively large number of young men rendered aphallic following complications of ritual circumcision. Alternative forms of penile replacements were not considered suitable in this setting. Although not life saving, penile transplantation can be significantly life enhancing, especially for the post-adolescent young men most affected by penile loss, at a stage in their life where they have not yet had the opportunity to partner or father children.

In view of the large number of healthy young men rendered aphallic each year, and the shortage of feasible or affordable reconstructive alternatives for our local population, we investigated the feasibility of penile transplantation within the resource-constrained public health sector in South Africa. We report here the first functionally successful penis allotransplant procedure with 24 months of follow-up.

**Methods**

**Setting**

Our renal transplant unit, which also serves as a composite tissue transplant unit, is situated in Tygerberg Academic Hospital, a tertiary academic, public-sector hospital in Cape Town, South Africa. The renal transplant unit is serviced by a team of nephrologists and urologists. The urologists provide support in terms of vascular access and are responsible for all kidney transplants. The nephrologists are responsible for the postoperative care of patients receiving renal transplants, including immunosuppression. The urology team also routinely manages complications from ritual circumcision and, together with the nephrologists, were therefore well placed to perform the penile transplant. Our proof-of-concept study fits with stage 1 (“Idea”) of the IDEAL framework for new surgical procedures.

**Preparation and patient selection**

Before attempting the penile transplant with a live patient, we did a cadaver-to-cadaver penile transplant to familiarise ourselves with the anatomy and potential sources of blood supply to match the diameter of penile graft neurovasculature. We then identified young men with complete pendulous penile amputations resulting from ritual circumcision. Some patients were referred to us from other hospitals for management of complications arising from ritual circumcisions, because we are the tertiary centre serving the affected region. Men aged 18 years or older with total or partial penile loss as a complication of ritual circumcision, who were willing to provide written, informed consent were included in the study and placed on a waiting list similar to that for potential kidney recipients. We screened all potential participants physically and psychologically. We assessed 16 patients, of whom 12 were placed on the waiting list; of the four patients excluded, two had residual phallices that were deemed adequate for all penile functions, making risk–benefit ratios unfavourable, and two had psychiatric diseases that precluded safe transplantation. Those men deemed unsuitable for transplantation were referred for assistance to a plastic surgeon and a psychologist as appropriate. Suitable participants underwent tissue typing, blood grouping, and screens for hepatitis B virus, cytomegalovirus, and HIV. In our renal transplantation practice, we do not routinely screen for Epstein-Barr virus or any of the other viruses associated with malignancies; we extrapolated this practice to the management of the penile transplantation. Patients with HIV or hepatitis B virus infections who failed to develop immunity to the hepatitis B virus were excluded. Other exclusion criteria were any active bacterial infection (including tuberculosis), any evidence of psychiatric disease or history of substance abuse; urological criteria for exclusion were sufficient for vaginal penetration or for urination standing. We did not do imaging studies of the recipient vasculature because we felt that these would be of little benefit in planning the surgery and add unnecessary expense.

The transplant recipient was chosen from a waiting list of 12 candidates on the basis of immunological parameters that would minimise risk and complications of long-term immunosuppression and on psychological status. He was selected as the first research participant over other potential recipients based on his lower risk profile. This patient was a 21-year-old man who had been rendered aphallic 3 years previous to the transplantation following a ritual circumcision complicated by gangrene of the pendulous penis, depriving him of all the normal functions of a penis. The loss left him psychologically and emotionally bereft. He was fully assessed for penis allotransplantation and deemed to be a suitable candidate.

Once the recipient had been selected, we administered the Medical Outcomes Study Questionnaire Short Form 36 Health Survey version 2 (SF-36v2) preoperatively and at 6 months and 24 months after surgery; the average score for each section in the population in the USA is 50. The whole form was administered to allow electronic validation by Optum Health software. The International Index for Erectile Function (IIEF) score was recorded at 24 months. Stellenbosch University’s Health Research Ethics Committee approved this project in 2011 (N11/07/243).

**Ethics**

The ethical issues surrounding penile transplantation are complex, and similar in some respects to those inherent to facial transplantation. The full range of ethical issues will be discussed in detail in a separate publication, but we briefly address selected pertinent ethical considerations here.
We identified and minimised the potential risks to individual participants to move towards a favourable risk–benefit ratio. In addition to the physical risks of long-term immunosuppression after transplantation, these patients face potential risks of social and psychological harm. The prevailing South African sociocultural environment requires that this experimental treatment be managed with extreme sensitivity. We considered protecting the privacy of our transplant recipient to be paramount to preventing any potential stigmatisation or discrimination. Another important consideration was adherence to treatment. Emerging adulthood, defined as 18–25 years is a high risk period for non-adherence to immunosuppression regimens in renal transplantation. The reason for this behaviour is postulated to be that the brain continues to mature until the age of 25 years.26,27 Additionally, the psychological effect of penile transplantation cannot be underestimated and could induce psychosis or renunciation of the organ.28 Extrapolating from this possibility, we took particular care in selecting candidates for the waiting list who were proven to be compliant with treatment and clinic attendance and considered physically and psychologically suitable for penile transplantation.

The participant selected to receive the transplant was counselled on the potential risks and benefits of the procedure for 2 years before transplantation. During this period, we addressed ethical issues surrounding penile transplantation including the risk of therapeutic misconception, innovative alliance between the eager patient and surgeon, and selective hearing by the participant not attending to potential side-effects of immunosuppression.22,29

Procedures
A suitable donor (36 years old, brain-dead, beating heart) became available on Dec 10, 2014, and consent for multi-organ recovery was obtained from the donor’s family, including the heart, liver, kidneys, and penis, with the recovery occurring in that order. The donor and recipient shared blood group A+ and the T-cell cross-match was negative. The recipient only shared HLA-B7 with the donor (donor: HLA-A1–32, HLA-B7–44, and HLA-DR7–16; recipient: HLA-A24–24, HLA-B7–7, and HLA-DR 3–15). The recipient had 8% HLA class I antibodies, but no HLA class II antibodies. The HLA class I antibody was specific for HLA-B35. No donor-specific antibodies were detected in the recipient’s serum. Both donor and recipient tested negative for the HIV, hepatitis B virus, and hepatitis C virus. The donor and recipient were both positive for cytomegalovirus immunoglobulin G.

The donor penis was harvested at the level of the inferior pubic rami. The cold ischaemia time was 16 h. The prolonged cold ischaemia was enforced by our need to prioritise the kidney transplant done by the same team, as well as other logistical issues, including competition for access to operating theatres in a busy academic hospital. The dorsal penile neurovascular structures were identified and dissected as far proximal as possible before the penis was transplanted. The warm ischaemic time was 4 min. The penis was cooled by irrigating ice cold Custodial HTK solution (Essential Pharmaceuticals, Ewing, NJ, USA) directly into the corpora cavernosa; we resorted to this technique when we found that intra-arterial perfusion via the dorsal penile arteries was not possible because of excessive cannula size (figure 1). We prepared the corpora, nerve, and vascular structures on the bench. We fashioned an abdominal skin flap phallus to resemble a penis for the donor; this procedure took about 30 min to complete and was done for cosmetic reasons as agreed beforehand with the donor’s family and was crucial in obtaining their consent.

The penile stump of the anaesthetised recipient was prepared by excising the distal approximately 0·5 cm of the corpora cavernosa and isolating the urethra and spongiosal stump (figure 2). We found that the dorsal penile vascular structures of the recipient had been obliterated by the infective and ischaemic processes that initially led to the penile loss. The left inferior epigastric artery was therefore mobilised via a paramedian skin incision, distally transected once adequate length and a matching diameter to the donor vessels was achieved, and re-routed subcutaneously. The inferior epigastric artery was anastomosed to the right dorsal penile artery under microscope magnification by use of a 9-0 nylon suture. The contralateral dorsal penile artery was similarly anastomosed to the left superficial external pudendal artery (figure 3). We used a 2 mm GEM Microvascular Anastomotic COUPLER ring (Synovis Micro Companies Alliance, Birmingham, AL, USA) for
the anastomosis of the deep dorsal vein of the penis to one of the deep inferior epigastric veins. The vascular clamps were released before we made the cavernosal and spongiosal anastomoses. On release of the clamps the penis perfused well with immediate pinking of the glans penis and with blood flowing freely from the corporeal and spongiosal tissue. Both dorsal nerves were repaired under loupe magnification with a 9-0 nylon epineural suture. The urethra was spatulated and anastomosed with interrupted 3-0 polyglycolic acid sutures. The tunica albuginea of the cavernosal bodies and urethra were sutured in a watertight fashion with interrupted 2-0 polyglycolic acid sutures (figure 4). Skin was closed subcutaneously with 4-0 poliglecaprone sutures.

The patient made an uncomplicated recovery from anaesthesia and was subsequently transferred to the Renal Transplant Intensive Care Unit. Pain was treated with intravenous morphine sulphate at 5–10 mg every 6–8 h as required. Prophylactic anticoagulation was commenced with unfractionated heparin 5000 IU twice per day subcutaneously for 3 weeks. Immunosuppression was initiated postoperatively with induction therapy consisting of intravenous antithymocyte globulin (ATG, Fresenius Kabi, Bad Homburg vor der Höhe, Germany) at 100 mg per day for 10 days (figure 5). The patient received intravenous methylprednisolone at 500 mg preoperatively and at 250 mg per day for 3 days postoperatively, followed by oral prednisone at 30 mg per day. The dose of prednisone was maintained for almost 3 months, then tapered to 10 mg per day over 8 weeks. The recipient was also commenced on tacrolimus at 5 mg twice per day on the basis of his bodyweight. The dose of tacrolimus was monitored and adjusted to maintain serum residual levels 10–15 ng/mL. Mycophenolate mofetil was commenced at 500 mg twice per day for 3 days, then increased to 1 g twice per day. Additionally, the patient received 160 mg trimethoprim and 800 mg sulfamethoxazole per day as prophylaxis against Pneumocystis jirovecii and isoniazid at 300 mg per day as prophylaxis against tuberculosis. Both agents were prescribed for 1 year. Full blood count and serum urea and creatinine were monitored daily for the first 10 days. The serum glucose and creatinine concentrations of the recipient were also monitored weekly or more frequently in the first month after discharge, and monthly thereafter; then 3 monthly after 6 months or as determined by the caring physician. Tadalafil at 5 mg once per day was commenced 1 week after the operation as penile rehabilitation and was continued for 3 months. The use of tadalafil was extrapolated from its use in penile rehabilitation after surgery for prostate cancer.30 We monitored acute rejection of the graft by visual examination of the skin, which is the most immunogenic component of the allotransplant. Any clinical signs of rejection would have triggered a skin biopsy. We opted not to use routine skin biopsies of the actual graft to detect acute rejection, as done in vascularised composite allotransplants, because of concerns about infection in a sexually active, immunosuppressed young man and the limited skin area available for biopsy. We did not use a satellite donor skin transplant because of the relatively poor predictive value of this technique for diagnosing rejection in the actual graft;31 this approach is often taken in vascularised composite allotransplants because it removes the need to biopsy the vascularised composite allotransplant itself to diagnose rejection.31,32

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The surgery and immunosuppression were
funded as a one-off concession with no further conditions, and future cases would require motivation on a case-by-case basis. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results
The recipient was observed postoperatively in the Postoperative Acute Care Unit for 24 h and then transferred to the Renal Transplant Intensive Care Unit to be cared for by experienced transplant nursing staff. The arterial anastomosis to the external superficial pudendal artery required urgent revision 8 h after surgery because of thrombosis of the right dorsal penile artery anastomosis. This thrombosis was possibly caused by a slight decline in blood pressure following opioid administration. Urgent thrombectomy and successful reanastomosis were performed; thereafter blood pressure was carefully maintained and the dosing interval of heparin was increased to three times per day. Thrombosis did not recur.

The patient expressed delight on day 3 at the first sight of the transplanted organ when the dressings were removed for the first time, declaring “I want to see my penis”. Because of an infected haematoma and skin oedema, combined with a small amount of proximal skin necrosis, the patient was returned to theatre on day 6 for evacuation of the haematoma and minor skin debridement; a suprapubic catheter was placed to divert the urine flow away from the urethra and to reduce the risk of infection. The suprapubic catheter became obstructed by a blood clot on day 8 causing the patient to pass urine through the transplanted urethra. This resulted in disruption of the urethral anastomosis and the development of a urethrocutaneous fistula. The fistula failed to close spontaneously and required surgical repair at 3 months. Throughout the early and late postoperative periods the penis remained warm and well perfused, as evidenced by the pink colour of the skin and glans penis. Penile rehabilitation consisted of maintenance tadalafil for 3 months after surgery. Erections were first reported by the recipient 3 weeks after surgery and he confirmed this with photographs he had taken himself. The recipient reported satisfactory penetrative sexual intercourse at 5 weeks after the operation, despite our advice to abstain for at least 3 months; on examination at this time however there were no signs of corporeal anastomotic leak or haematoma of the penis.

Up to 3 months after the transplant, all erections had been self-reported, but we witnessed a normal erection on the operating table on induction of anaesthesia at the time of his urethrocutaneous fistula repair. At the time of this operation the patient was still receiving tadalafil penile rehabilitation treatment, but it was discontinued shortly thereafter. The patient was carefully monitored and the immunosuppressive medication was well tolerated throughout, with no clinical signs of rejection.

The recipient was diagnosed with acne soon after commencement of steroids but this resolved by 7 months as the dose of the steroids was progressively tapered. At 5 months, the patient was noted to have elevated blood pressure, which resolved when the prednisone dose was reduced. At 8 months, he complained of a painful right foot and knee; on examination he was found to have an infected supra-patellar bursa. This was drained and a biopsy of the foot lesion confirmed infection with phaeohyphomycosis due to Alternaria alternata. Fungal blood cultures were negative and the patient remained systemically well. Treatment was commenced with topical broad spectrum clotrimazole antifungal cream, leading to the slow but steady resolution of the lesion.

24 months after the operation, the patient is doing well with no episodes of rejection. He reports regular satisfactory sexual intercourse in a stable relationship with normal ejaculation and orgasm. He accepted the penis as his own, despite a small tuft of donor pubic hair growing at the dorsal base of the graft. 6 months after the transplant, the patient reported that his partner was about 3 months pregnant; sadly, she delivered a stillborn baby at term in another province. The patient has been adherent to his medication as evidenced by blood drug concentrations. Biochemical and haematological parameters were regularly monitored. Renal function deteriorated transiently at 7 months, but improved on adjustment of the tacrolimus dose. Other laboratory tests remained within normal limits. Specifically, with reference to tacrolimus use, blood sugar concentrations remained normal. Routine ultrasonography of the kidneys and bladder were normal throughout. Superficial skin sensation improved progressively, from being patchy to
becoming fully established with normal touch sensation over the whole penis by 7 months. We did a cost analysis including surgical and anaesthetic services and the first month cost US$18 653 while immunosuppression and clinic visits in the subsequent 2 months cost $1184 per month. The cost of treatment continues to be carried by the Western Cape Government.

The slight colour discrepancy, tuft of donor hair, and scarring at the suture line were acceptable to the patient. His SF-36v2 mental health scores improved from 25 before the transplant, to 57 at 6 months and 46 at 24 months post transplant; physical health scores improved from 37 at baseline to 60 at 6 months and 59 at 24 months post surgery. At 24 months the maximum urine flow rate ($Q_{\text{max}}$) was 16·3 mL/s from a volume voided of 109 mL, with a normal flow-time curve. The IIEF showed an overall satisfaction score (domain E) of 8 from a maximum score of 10. The scores for the specific domains were 26 from a maximum of 30 for erectile function (domain A), 8 from a maximum of 10 for orgasmic function (domain B), 9 from a maximum of 10 for sexual desire (domain C), and 12 from a maximum of 15 for intercourse satisfaction (domain D). However, at the 24 month interview, the recipient admitted that he struggled to have a second erection per night should he wish. He reported that when the second erection did occur, he could have normal intercourse. He declared that this finding remained unchanged from sexual activity soon after the operation. No types of assistance to achieve erections were provided after 3 months post surgery. At a visit 18 months after the transplant, the recipient declared that the most valuable result of his penis transplant was that he is “happy” again; this he ascribed to the complete restoration of all the individual components of penile function and not to any single one of them such as the cosmetic result (figure 6).

**Discussion**

This study is the first to report a functionally successful penile allotransplant; we deemed the transplant to be successful because the patient is able to urinate normally, achieve erections suitable for vaginal penetration, and experience normal orgasm and ejaculation.
There is an unmet, unquantified need for penile transplantation because of wartime and industrial genital injuries, penile malignancies, and severe congenital penile abnormalities. In South Africa, the need for this type of transplant arose because of the relatively large number of post-adolescent young men rendered aphallic following ritual circumcision.3

Composite tissue transplantation is complex and technically challenging. Key to the technical success of the surgery is adequacy of the vascular supply to the allograft; although the importance of the arterial supply is obvious, venous drainage is also paramount; establishing sufficient venous drainage for our patient allowed us to reduce the swelling. During the surgery on this patient we mobilised the inferior epigastric artery for anastomosis to the right dorsal artery of the penis as previously described in penile replantation. The dorsal arteries of the penis in our patient were obliterated by the previous injury and fibrosis at the time of penile loss. On release of the vascular pedicles, the skin, corpora cavernosa, and corpus spongiosum had visibly good blood supply. We deliberately avoided warming the graft because we were concerned that this might increase the metabolic requirements of the graft and compromise its viability. In our patient the dorsal arteries were clearly supplying the corpora cavernosa and the corpus spongiosum, as shown by cavernosal backflow after release of the vascular clamps. We did not anastomose the very small and contracted cavernosal arteries and this does not seem to have affected the outcome, contrary to a report suggesting that the corpora cavernosa cannot be supplied by the dorsal arteries of the penis. We were concerned about the position of the neo-vasculature that ran across the pubic symphysis (as opposed to emerging from underneath the pubic arch as occurs normally) becoming compressed during sexual intercourse, causing sudden detumescence of the erect penis, but this concern seems to have been unfounded. Full sensory recovery occurs in penile replantation and also occurred for our patient; nerves, once approximated grow into nerve sheaths at about the rate of 1 mm per day.

The penis seems to be a resilient organ and tolerated the cold ischaemia time of 16 h well. A successful penis replantation was described after a patient with psychosis swallowed his self-amputated penis, which was retrieved on gastroscopy 2 h later and reimplemented. He had minimal sensation loss in the otherwise normal functioning penis after surgery.

The dual psychological impacts on a young man of first losing his penis and then having it replaced, were of concern to us. The self-image, which normally has a fairly solid state, becomes fluid again when adding or removing an organ during transplantation. The loss or gain of an organ can have a devastating effect on the ego; it is described as causing a ripple effect on self-image and might induce psychosis, depression, or even renunciation of the transplanted organ. The addition of something as benign as a cardiac pacemaker can induce serious psychological disturbances. Our recipient remained emotionally stable throughout the ordeal of the penile loss and the subsequent penile transplant, emphasising the need for careful psychological screening of potential recipients. The patient showed indications of his acceptance and ownership of the graft in his early remark “I want to see my penis”, underscoring his eagerness to accept and integrate the penis as part of himself. His comfort with his penis during follow-up suggests that he is unlikely to be suffering from any of the primitive guilt that is sometimes induced by the transplant. The recipient’s quality of life improved substantially as measured by SF-36v2 scores, which are often used in transplantation and were chosen in this case for ease of interpretation. The decline in the mental component of the score at 24 months compared with 6 months is concerning, especially in the context of the normal IIEF score. This decline might be related to personal stressors at the time of the SF-36v2 survey or because the novelty of having a penis again had declined. The patient works in a stressful environment and lives in an area with high rates of violence and crime, which might be reflected in the survey and could be normal for someone living in this environment. The IIEF scores and Qmax are reassuringly more objective measures of normal penile function.

The patient has tolerated the immunosuppression well, likely because of his good physical health before the
transplant. The most serious infective complication he had was a fungal infection resulting from the immunosuppression. Phaeohyphomycoses, such as Alternaria spp., are rare opportunistic fungal infections that predominantly affect the skin in immunocompromised patients, particularly those being treated with mycopropholite mofetil. Systemic dissemination can occur and has a high mortality rate. Treatment regimens however have not been standardised.4,56 The preferred treatment is with triazoles, such as itraconazole, which inhibits CYP3A4/5. This substantially enhances the levels of drugs that are metabolised by the liver such as steroids and calcineurin inhibitors.57 Local antifungal treatment followed by oral terbinafine seems to be safe and has been reported as being successful in a patient who received a heart transplant.58 Our patient responded well to topical broad spectrum antifungal treatment alone.

Our findings show that penile allotransplantation is feasible and can result in restoration of sexual function, penile sensation, and normal urination. We also emphasise the importance of careful patient selection in terms of physical health, emotional and psychological stability, and adherence to treatment. Although the results of the transplant have been rewarding, we are aware that the potential long-term consequences of sustained immunosuppression remain a risk and will be monitored for carefully. This case might also be hypothesis generating in that female-to-male gender confirmation surgery might benefit in selected cases, revascularisation in vasculogenic impotence might be revisited, and other causes of complete loss of the pendulous penis might be addressed in this manner in future. We are now recruiting for a trial of penile transplantation, which is registered on ClinicalTrials.gov, number NCT03149692. This case report gives hope to those with severe genital injuries or loss, who must often suffer in silence as they are too embarrassed to speak out.

Contributors
AvdM conceived the research question, did the literature search, got the software and contributed to the preoperative data collection and authored the manuscript. JTV obtained the software and contributed to the preoperative data collection, particularly the preoperative assessment, and contributed to the data collection, particularly the preoperative data, and editing of the manuscript, particularly the introduction and background sections. KB contributed to the data collection, particularly the immunosuppression data, drafted the graphics, and reviewed the manuscript. JDN contributed to the drafting of the protocol and contributed to the data collection, particularly the preoperative data, and contributed to the preoperative data collection and drafting of the manuscript.

Declaration of interests
We declare no competing interests.

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References


