The Ethics of Penile Transplantation: Preliminary Recommendations

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Background. For men with significant genitourinary injury, penile transplantation is being considered as an option when reconstruction is not feasible or proves unacceptable to the injured patient. Methods. A review of the literature was conducted to assess the current state of penile reconstruction and transplantation options, as well as to evaluate scholarly research addressing the ethical dimensions of penile transplantation. Results. The state of penile transplantation is elementary. If reconstruction is not a possibility, proceeding ethically with research on penile vascularized composite allotransplantation will require the articulation of guidelines. To date, very little has been published in the scholarly literature assessing the ethics of penile transplantation. Conclusions. Guidelines should be developed to address penile transplantation and must cover the donation of tissue, consent, subject selection, qualifications of the surgical team, and management of both failure and patient dissatisfaction. Unless guidelines are established and disseminated, penile transplants should not be undertaken. The preliminary recommendations suggested in this article may help to inform development of guidelines.

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BACKGROUND

Over the last several decades, there has been an increase in injuries caused by improvised explosive devices (IEDs)3,4 and a concurrent improvement in survival of wounded soldiers and civilians sustaining such injuries.4 Although recent advances in protective body armor have decreased mortality rates, many who survive an attack from an explosive device are left with disabling and disfiguring injuries.3,5 In Iraq and Afghanistan, injuries from IED attacks on American and allied forces exceed injuries from guns and remain the leading cause of all combat-related allied casualties.4,5 Although much attention has focused on treating Americans and other allied personnel who have lost limbs or have suffered grievous facial injuries due to explosive weapons and IEDs, injuries to the genitourinary (GU) system have drawn less attention.4,6,7 Despite the fact that they are becoming increasingly common3,5 and more severe.8 According to the Department of Defense Trauma Registry, from 2001 to 2013, 1378 male service members suffered GU injuries, the majority of them caused by IED explosions.9

This article focuses specifically on penile injury and treatment in men. Among men, the sequelae of penile injury are long-term, affecting hormonal, sexual, and urinary function and resulting in psychological consequences.3,5 Damage to the penis may result in major impairment of excretion, sexuality, and fertility. Patients may be left incontinent of urine. Even if they are not fully incontinent, voiding from a standing position may become difficult. The psychosocial impact on those who have suffered severe war-related penile injuries is not clear, because few studies have examined psychosocial outcomes in this population.5,10 Much of what is known comes from studies of older men with urotrauma due to cancer or motor vehicle accidents.11 Victims of combat injuries tend to be younger and are often unpartnered.
Penile defects range in severity, and the goals of reconstructing the phallus include restoration of urinary and reproductive function, as well as aesthetic reconstruction, which is thought to be paramount in optimizing psychological recovery. Although reconstructive approaches continue to evolve, they still fall short of these goals and may result in uncomfortable and debilitating side effects, including infection, scarring, and urinary complications. The need for superior penile reconstructive and genital replacement options for severe penile damage is pressing, and growing interest in VCA procedures is encouraging the pursuit of clinical penile transplantation.

State of Penile Transplantation

For men with significant penile injury, penile transplantation may be considered as an option when reconstruction is not feasible or proves unacceptable to the injured patient. However, the state of penile transplantation is elementary, with very few animal studies completed to date. Three known attempts have been made in human subjects. In 2006, a penile transplant was performed in China, which resulted in amputation of the graft on postoperative day 15 due to extreme psychological distress of the recipient and his wife after the procedure. A second transplant was undertaken in South Africa, resulting in reported technical success and return of erectile function leading to a pregnancy. A third transplant has recently been reported in the United States, with the outcome still to be determined.

To the greatest extent possible, penile transplant should be proven safe before using living humans as research subjects. As of last year, only 1 vascularized penile allogeneic transplantation animal study involving 48 rats was completed. Three transplants on living humans have been attempted, and only 1 has been deemed successful (as of this writing, it is too early to declare success for the third transplant). Accordingly, more animal studies are needed to establish the best techniques for surgical success and long-term maintenance of function with penile transplants. Studies using brain-dead volunteer donors and cadaver recipients who have donated their bodies to scientific research may prove useful in refining surgical technique and team coordination.

Any program considering undertaking penile transplantation should prospectively develop appropriate protocols to prepare, study, investigate, ultimately perform, and follow up recipients long term (treating rejection and/or failure) to ensure patient safety. Only programs with a history of transplantation experience that are capable of providing stable long-term monitoring and psychosocial support should be considered as possible experimental centers for developing the required techniques. Penile transplants should only be performed by teams willing to publish their protocol and results. Publication ensures that research results are transparent and widely disseminated, thus helping to advance the field in an ethical manner.

Ethical Issues Moving Forward

Very little has been published in the scholarly literature on the ethics of penile transplantation. Like other forms of VCA transplantation, penile transplantation is life enhancing rather than life saving. Accordingly, the risk/benefit ratio is different than would be the case for solid organ transplantation. Current research in VCA transplantation suggests that, at present, the primary risk associated with such procedures is long-term exposure to immunosuppressive regimens. In addition, there is also some acknowledgement that the psychosocial impact of VCA transplantation differs from solid organ transplantation. Unlike solid organ grafts, VCA grafts are visible, with more pronounced implications for the recipient’s sense of self. The process of adapting to a new VCA graft involves integrating the new graft into the recipient’s sense of identity and bodily integrity. Failure to adapt psychologically and emotionally to the graft has been associated with adverse clinical outcomes. Initial findings also suggest that implications for physical intimacy and identity for various forms of VCA procedures may be unique to each procedure, thus requiring differentiated approaches to weighing risks and benefits of these techniques. In the case of penile transplantation, the impact on sexuality and implications for sense of identity and sexual intimacy in the context of intimate partner relationships are specific to this procedure and, thus, warrant careful consideration and study.

In the case of severe injury to or defect of the penis, if reconstruction is suboptimal or impossible to achieve with traditional approaches, making an ethical case for proceeding with research in penile transplantation should require follow-up establishing guidelines to safeguard transplant recipients. While an effort was undertaken in China to recommend guidelines for the ethical conduct of penile transplantation in the wake of the first failed attempt, little else has reached the published literature. To our knowledge, any guidelines that may have been developed for the procedure in South Africa have not been referenced in the literature or made publicly available, and guidelines for the procedure in the United States have not yet been made public.

Current State of Guidelines

In the United States, as of July 2014, VCA transplants are classified as organs and are subject to the policies and bylaws of the Organ Procurement and Transplantation Network (OPTN). At present, these policies address VCA transplants as a general category and do not yet offer guidance on key ethical questions, including selection of donors, recipient screening, consent, or how best to manage approaches to families. The OPTN has acknowledged that VCAs are beyond the scope of usual donation and transplant considerations. In addition to the OPTN’s role in policy development, other professional organizations may play a part in developing and disseminating guidelines. For instance, the American Society of Reconstructive Transplantation should support and uphold guidelines as a model for other countries involved in VCA transplantation or interested in pursuing penile transplantation.

Many members of the general public may have reservations about donation for penile transplants. The media is likely to take a keen interest in surgery in this area, thus requiring extraordinarily careful attention to ethical and policy development, and to donor and recipient selection with respect to coping with public interest.

Attitudes Toward Donation and Transplantation

It is unclear what the attitude of American males may be concerning donating reproductive organs and genitalia upon
their death. Prevailing psychosocial attitudes among the general public in the United States regarding donation of any organs or tissues related to sexual activity or reproduction are poorly understood. Similarly, little is known about the attitude of prospective recipients toward transplantation of such tissues, or what their spouse or partner’s views might be. Considering that victims of combat injuries tend to be young and may be single, further exploration should be a part of any study to shed light on the potential role of penile transplantation in reducing barriers to partnering.

The experience gleaned from other forms of VCA transplantation suggests that VCA transplants raise unique psychosocial and ethical considerations with respect to identity and to physical intimacy, with implications for past or current relationships and future partners. Although little is known about attitudes toward penile donation and transplantation in the general public, it is likely that the concerns around identity and intimacy raised by other forms of VCA transplantation will be present, and perhaps even more pronounced, in penile transplantation.

Currently, a minority of potential donors knows that their reproductive organs and genitalia can be donated. Informal surveys of groups of medical students, professionals, bioethicists, and the general public demonstrate that many registered organ donors are unaware that the face and hands can be donated. After learning this information, several of those surveyed indicated they would consider revoking their donor status. One study of over 1000 patients, family members, and friends in a New Jersey hospital indicated significantly greater willingness to donate and receive solid organs than either hand or face transplants. Because reproductive organs are uniquely personal, it is likely that they may cause registered donors similar concern. Education and public awareness can help to mitigate donor concerns. Ideally, individuals will consider VCA transplantation when making their donor registration decisions. If organs continue to be procured for VCA from individuals who were unaware of this practice during their lives, new potential donors may be deterred from registering.

To avoid jeopardizing the existing supply of deceased donor organs, it is ethically important to increase awareness of this form of donation, and equally important that those responsible for procuring organs for VCA, including GU tissues, do so only from registered donors. As regulation now requires that additional consent be sought from family members, further research is needed to clarify whether the public views this level of consent as adequate and appropriate.

Selection of Donors

Donors will be individuals who have been declared deceased while on organ-perfusion support, according to determination of death by neurological criteria. As in solid organ transplantation, this means that donor families will need to have a thorough understanding of the process for determining death. They also must receive comprehensive counseling to ensure that they understand the experimental nature of the donation they are being asked to make and the fact that the transplant involves urinary, sexual, and aesthetic considerations.

The law in every state prevents the procurement of organs from individuals who explicitly refused consent, regardless of family wishes. For individuals who did not explicitly provide or refuse consent, the law requires that family members provide consent before organs can be procured. Increasing public awareness and education regarding organ donation and transplantation has been cited in the literature as a critical step toward boosting consent rates to organ donation. Efforts to boost public education about novel forms of organ donation are imperative, lest requests to families trigger a loss of overall support on the part of the public for all forms of organ and tissue donation.

Selection of First Recipients

In selecting the first human subjects, close attention must be paid to their psychosocial status. The initial procedures will challenge accepted cultural norms about reproductive organs, and grafts may not function exactly as healthy, native tissue. The transplant will raise many issues for partners and other family members around intimacy and identity. Although these issues are present in other forms of VCA transplantation, they may be especially acute for penile transplantation, given the intensely personal and sensitive nature of the procedure.

Despite (or perhaps because of) the highly personal dimensions of penile transplantation, the media is likely to take an active interest in penile transplant procedures. This was evident in the media’s coverage of the first face, hand and uterine transplants, as well as the first publicized penile transplants in South Africa and the United States. Having a recipient capable of enduring publicity, comment, and scrutiny is important, because it will be difficult to keep the surgery private or confidential, and especially as transplant teams may not wish to do so. By extension, media exposure also may impact the recipient’s partner or family members, and they should be prepared for the possibility.

The following factors should be weighed in selecting the first subjects, in addition to the usual considerations for eligibility for VCA and/or solid organ transplantation:

- Sexually active or wishes to be
- Spouse/partner attitude toward the transplant
- Mental health status, including posttraumatic stress disorder
- Social support—standing in the community, attitudes of friends and family
- Ability to cope with “humor,” stigma, scorn
- Economic resources to cover long-term medical needs
- Ability to relocate should the transplant team move
- Tolerance for publicity

Transplant programs will need to establish a transparent policy for identifying subjects, as well as a “compassionate use” policy. Such a policy would enable a fledgling program to anticipate emergency requests for priority of access that may be made before the program has publicly announced interest in undertaking this form of transplantation and recruiting subjects. Demand for surgery may be substantial, but a highly selective process is warranted initially, in order to ensure subject safety, the chance for benefit, the ability to learn, and the opportunity to follow recipients long-term.

Informed Consent

Informed consent must be obtained from each subject. Because the transplant will have implications for the recipient’s
sexual and reproductive future, the prospective subject’s mate or partner, if there is one, should be informed and given the opportunity to ask questions and express opinions. Consent should involve quizzes for comprehension with taped responses to ensure full understanding of the highly risky and experimental nature of this form of transplantation. With respect to the risk of graft failure, given that subjects are likely to be young, it is possible, perhaps even probable, that subjects may outlive the function of their grafts. Subjects should be aware of the possibility of acute rejection or chronic rejection of the transplanted graft, the need for lifelong immunosuppression, toxicity of immunosuppressive drugs, increased risk of malignancy, psychosocial distress, and all options in the event of short- or long-term graft failure.

Full consent will require exploration of aesthetic expectations, urinary function, sexual function, and, in some cases, reproductive function. There should be an understanding that public curiosity around the procedure, media coverage, and provider involvement will be extensive. Privacy almost certainly will not be possible for donor families, early subjects or for those close to them.

Consent should also be a process, providing the subject and his family time to consider the full ramifications of the decision and to ask questions about the procedure. Studies show an increase in patient satisfaction with increased time spent discussing treatment effects. Documentation of consent should include responses to key questions so as to demonstrate comprehension. Consent should be not only for the surgery, but also for follow-up care and the right to publish results, and it should cover all aspects of financial liability and assistance, both short- and long-term. Decisions about how to manage failure, including acute rejection or disappointment with the graft, must be fully reviewed and understood.

Costs

The financial cost of this form of transplantation is unknown but can be expected to correlate with other forms of VCA. Vascularized composite allotransplantation procedures are expensive, as much as several million dollars per procedure, because they involve large medical teams, intensive care, psychosocial services, immunosuppression and rehabilitation. Additional costs include long-term support, psychological counseling, costs of adverse events, and incidental expenses for travel related to follow-up care. It must be feasible for the hospital to absorb these costs because insurance does not cover experimental procedures. Currently, there is a lack of standardization regarding who is responsible for cost coverage. Institutions should avoid undertaking a penile transplant until they can explain the coverage, costs, and the ultimate financial burden to the patient long term.

Psychosocial Screening and Postoperative Support

The psychosocial impact of penile injuries cannot be overstated. Feelings of emasculation, compromised sense of manhood, fear of infertility and suicidality, in combination with posttraumatic stress disorder, are common in those who have sustained serious penile injuries. Psychosocial assessment and support are critical elements of the pretransplant and posttransplant process. Although many, if not most, recipients of hand and face transplants have adjusted well, there are a few cases of recipients who experienced emotional distress posttransplant related to personal identity, with some resulting in operation reversal and attempted suicide. Severe psychosocial distress was cited as the primary reason for postoperative amputation of the first reported penile transplant graft. To help prevent such outcomes, screening processes for all VCAs must be detailed with examination of the potential recipient’s social, psychological, and emotional status.

In addition to pretransplant assessment, patients, their significant others and families should receive extensive, long-term psychosocial support after penile transplantation to ensure psychological and emotional adjustment to the transplant. Given that the impact of penile injury and transplantation extends to the sensitive realm of intimacy, both emotional and physical, it is imperative that significant others express support for the patient’s desire to undergo transplantation and receive supportive counseling posttransplant. Postoperative psychosocial support is likely to be as critical to long-term transplant success as technical factors, such as histocompatibility. Accordingly, the willingness of the potential recipient and partner to receive such support should be assessed before transplant, and a plan should be established for care-giving and covering related costs.

Institutional Review Board Involvement

Since the procedure is highly experimental, all of the consent materials must be reviewed by an institutional review board (IRB). It is useful and appropriate for the IRB review to include experts from backgrounds relevant to assessing an experimental VCA transplant procedure. The IRB should ensure that all persons involved in the experiment are fully prepared, including students, information technology, security, public relations, social services, chaplains and business administration staff. The IRB should appoint an advocate for the subject if there is concern that the transplant team’s desire to attempt the procedure may unduly influence the potential recipient’s ability to make an autonomous, informed decision.

The IRB must ensure that a policy is in place prospectively for managing experimental failure and/or adverse events. The desire of the subject to end the experiment, demand removal of transplanted tissue, or even to end his own life if the transplanted tissue is rejected acutely or fails to function must be fully anticipated and addressed in this policy as a part of the IRB approval process and written in the subject consent form.

In addition, the IRB should ensure that a clearly articulated process is in place for assessing and monitoring clinical and psychosocial outcomes following the transplant procedure. The IRB should request clarity about how metrics of “success” will be defined; physiological, immunological, functional, behavioral, and subject satisfaction measures should be used to assess the risk/benefit ratio of the transplant. Both short-term and long-term measures should be developed, with clear lines of responsibility for monitoring them postoperatively and for intervening on behalf of the subject if necessary. The IRB must also ensure that the team has the capacity and intent to publish the results.
of its work, regardless of whether the outcomes are positive or negative.

The IRB ought to attend to the possibility that members of the transplant team may move or become unavailable over time and how this could impact recipient care and publication plans. Similarly, the transplant team must consider how they will manage the situation if recipients move, lose their caregiver(s) or have other medical problems.

CONCLUSIONS

As penile injuries become increasingly common in the era of modern warfare, penile transplantation may play an important role in helping patients recover physically and emotionally from their devastating and life-changing injuries. Penile transplantation may lead to dramatic improvements in quality of life for individuals suffering from penile absence or severe deformity. As an alternative to currently available reconstructive techniques, which may sometimes fall short in their ability to address the myriad issues these individuals face, penile transplantation offers the possibility of significant benefit. However, given the highly experimental nature of this form of transplantation, great care must be taken to assess known and potential risks to ensure that recipients are not subjected to undue harm. The emotionally sensitive nature of this form of transplantation must be kept at the forefront of donation policy. Carefully reasoned, patient-oriented guidelines are paramount to ensuring that such an experimental procedure be carried out in an ethical manner.

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