Hand transplant surgery

M Nassimizadeh, AK Nassimizadeh, D Power

University Hospitals Birmingham NHS Foundation Trust, UK

ABSTRACT

In September 1998 the world's first hand transplant was performed in Lyon, France. A new era in reconstructive surgery had begun. This case highlighted the potential for composite tissue allotransplantation (CTA). While CTA is not a new technique, it unifies the principles of reconstructive microsurgery and transplant surgery, achieving the goals of absolute correction of a defect with anatomically and physiologically identical tissue with none of the issues of donor site morbidity associated with autologous tissue transfer.

The adoption of this technique for non-life threatening conditions to improve quality of life has generated a number of new ethical considerations. Additionally, the prominence of transplanted hands has led to much discussion around the issue of body identity and psychological assessment of potential recipients. This is fundamental to any hand transplantation programme. With the advent of hand transplantation dawning in the UK, we review the many ethical considerations that contribute to this new frontier.

KEYWORDS

Hand – Transplant – Ethics

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CORRESPONDENCE TO

Mohammad Nassimizadeh, E: m.nassimizadeh@gmail.com

History

The roots of limb transplantation date back to the fourth century when twin saints Cosmas and Damian described the transplantation of a cadaveric leg, replacing a cancerous one. It highlighted early human longing for successful limb transplantation.

In 1964 the first hand transplant was attempted by surgeons in Ecuador, without the benefit of modern immunosuppression. The allograft was rejected within several weeks. Attempts continued subsequently in laboratories but a human hand transplant would not be attempted again for another 34 years, until 23 September 1998 in Lyon.¹ The recipient was a 48-year-old man who had lost his right arm in a saw accident four years earlier. The operation was initially successful but the patient suffered multiple episodes of rejection, became disassociated with the grafts, non-compliant with immunosuppression and ultimately requested graft removal in 2001.

Despite such failures, a new era in reconstructive surgery began with composite tissue allotransplantation (CTA). While CTA is not a new technique, it unifies the principles of reconstructive microsurgery and transplant surgery, achieving the goals of absolute correction of a defect with anatomically and physiologically identical tissue, with none of the issues of donor site morbidity associated with autologous tissue transfer. Nevertheless, the adoption of this technique for non-life threatening conditions to improve quality of life has generated new ethical considerations.

Potential benefits

In solid organ transplantation (SOT), such as liver or heart, transplantation is essential for life. Function is defined by the physiological and biochemical properties of the organ. Surgeons rarely hesitate when discussing these operations. However, in the case of hand transplantation, the patient will survive without the transplant and so the operation is not lifesaving. In fact, undergoing the operation has risks associated with it, which can increase mortality.

While the procedure does not increase quantity, there is a potential increase in quality of life. As a result, hand transplantation has been noted as a life giving/improving procedure.² This perceived improvement in quality is a highly subjective measure and a new hand can mean different things to different people. Since the only measure is quality, many doctors argue that the risks of the operation are not justified by unquantifiable benefits.³ Proponents identify that other transplants, such as kidney, may not be lifesaving, owing to the option of dialysis. The concept of risk exchange for quality of life is one that is easily transferable to hand transplantation.

Risks

The main risk of hand transplantation is long-term immunosuppression, which indiscriminately downgrades the host's immunity, predisposing recipients to infections, malignancy and specific transplant related issues, like post-transplant

lymphoproliferative disease.⁴ In fact, the International Registry on Hand and Composite Tissue Transplantation reports 87% of patients suffer from opportunistic infections.⁵ Required medications also have side effects including diabetes, Cushing's syndrome and nephrotoxicity.⁶ Critics argue that these drugs likely shorten life span after transplantation.⁷ Benatar and Hudsons' case report illustrated this concept.⁸ Two children aged three and four years, who both lost a hand, did not receive a hand transplant as impact to quantity of life posed too great a risk to merit the functional benefits of the operation.

Immunosuppression has progressed dramatically and with careful monitoring, risks to the recipient can be reduced. In conjunction with this, combining immunosuppressants has led to reduced concentrations of any individual drug, resulting in reduced toxicity and side effects without significantly increasing the rate of rejection.⁴ The risk–benefit balance of immunosuppression is shifting with explorations into bone marrow cell-based treatment.⁹ Transplant patients receive an infusion of donor bone marrow cells isolated from 9 vertebral bodies 14 days following surgery. This allows patients to be maintained on a low dose tacrolimus monotherapy, potentially reducing side effects (achieving maximal suppression with minimal toxicity).

Ethical concerns

At this point, two key ethical issues in medicine, beneficence and non-maleficence are considered. Non-maleficence requires that one does not intentionally harm patients, either through acts of omission or commission. Beneficence is action that is done to benefit, the principle being to act in the best interest of the patient. Hand transplants can potentially provide improved functionality, self-image and a possible return to work for the patient, thereby fulfilling the obligation of beneficence. However, unlike SOT, which is unquestionably lifesaving, the variable benefits rest with the individual. Considering the risks of immunosuppression and wide variety of prosthetics, it is difficult to demonstrate that benefits outweigh risk. Furthermore, the delay from operation to functional outcomes must be appreciated, with a latency of up to 18 months before benefits are seen, owing to neural regeneration.

The advancement of sophisticated myoelectric prostheses also weigh against CTA.¹⁰ Future biointegrated prostheses will assume the benefits of CTA without the risk. Sceptics believe that these have many years before their functional outcomes can be comparable and emphasise that they are expensive as the development costs will not be offset by the relatively few patients requiring them.

Given the current financial climate, the cost effectiveness of healthcare is in the spotlight. Hand transplantation involves lifelong high level follow-up from a multidisciplinary service. One study by Chung *et al* suggests 62% of the estimated \$530,000 cost for a single hand transplant relates to postoperative management and lifelong immunosuppression.¹¹ This cost needs to be offset by the benefit of returning a patient to work and compared with the cost of a lifelong prosthesis, which are estimated at \$21,000 and

\$41,000 respectively.¹¹ When assessing quality adjusted life years (a measure of disease burden taking into account quality and quantity of life lived), those for a prosthesis have been suggested to outweigh those for a hand transplant.¹¹

The Carroll test measures patients' ability to perform tasks requiring a combination of motor function, mobility and sensation. At the 8 and 6-year follow-up review of the first 2 American hand transplant recipients, their scores were considered fair at 72/99 and 55/99, both exceeding expected results for a prosthesis of 20–30/99.¹² Furthermore, while prostheses aim to return some functionality, they fall short on many fronts. One hand transplant recipient stated that prior to the transplant, the inability to hold his family led to his feeling of loss.¹⁵ This indicates that the transplant aids functionally while simultaneously alleviating feelings of loss and grief.

If the principles of beneficence and non-maleficence are our only ethical guides, hand transplantation would be denied simply on the basis of doing the least amount of harm. Instead, we ask the question: Who determines benefit? In essence, only a surgeon with bilateral hand amputations could provide adequate insight. Were society or surgeons to reject all patients for CTA, this might be regarded as paternalistic, a less favourable view as increasing respect is given to patient autonomy.

Patients with capacity have the right to determine what happens to their bodies; an individual has the right to make an informed decision. Supporters of hand transplantation argue that this is the pivotal ethical argument. The literature suggests that hand transplantation restores both motor and sensory function as well as self-image.^{12,14–19} In fact, the degree of function is comparable with and potentially better than hand reimplantation after amputation, which is more favourable than prostheses.²⁰ In this specific cohort, quality of life outweighs quantity.

The second ethical principle that overrides paternalism is double effect. It balances the principles of gain and harm, concluding that as long as the primary intention is good/beneficial, then one can proceed. As the ultimate aim of both the operation and the surgeon is benefit for the patient, the harm of immunosuppression is not intentional. The weight of the benefit rests with each patient, however, as one patient may be happy with limited motor function but another may decide that the benefit is not sufficient to justify the operation.² Owing to lack of follow-up information, this balance is not a realistic possibility.⁷ The longest current follow-up duration is 12 years and as the reservoir of literature improves internationally, we can provide more accurate information to patients, facilitating autonomy and informed consent.

Interestingly, although the accumulated hand transplant literature on immunosuppression does not suggest any differences, the risks of immunosuppression are well documented in SOT so patients do have access to an estimate of risks. Two studies investigated individuals' perceived risk assessment with immunosuppression. One analysed the general public and those who have undergone transplants²¹ while the other study considered the general public, organ

transplant recipients and amputees.²² In both studies, all groups accepted the same amount of risk for double hand transplantation irrespective of previous experience with immunosuppression.^{21,22}

The developers of the Louisville Instrument for Transplantation have looked at patients' perception of risk. One study enquired about facial transplantation in three study populations²³ but the results are transferable. When the authors provided details of 20 immunosuppression side effects, 77% of those with facial disfigurement, 93% of those with kidney transplants and 86% of healthy control individuals were willing to still have a face transplant.²³ Conversely, when the authors gave a 50% failure rate, 71% of those with facial disfigurement, 88% of those with kidney transplants and 87% of controls were still willing. All groups therefore demonstrated the capability for informed decision making.

It is here we introduce a new ethical consideration that has emerged with the advent of CTA: the concept of identity. SOTs are intrinsically not on public display and so do not become the subject of public opinion or stigma. However, our hands play an important role in personal identity and body image. A hand transplant is subject to constant visualisation by both the recipient and the public, raising potentially serious psychological issues.

The greatest fear may be that if individuals cannot assimilate the hand as their own, they could face psychological rejection of the transplant.⁷ This was demonstrated by the first recipient of a hand transplant in Lyon, who became disassociated with the grafts, and had the transplant removed.¹ This has led many centres like Louisville in the US²⁴ to have stringent psychological evaluations of recipients. In a paper by Klapheke *et al*, screening data of 213 potential recipients were presented, of whom 9 were identified as suitable candidates who stated they would feel physical and psychological ownership of the transplanted hand.²⁵ The patient must incorporate the transplant to the concept of self.^{26,27}

Opponents of hand transplantation question whether a recipient can ever cope with the idea of having someone else's hands as their own. Would they consider them to be their own hands or see someone else's hands touching their body? Would skin colour or tattoos affect their perception of it?^{28,29}

Who is hand transplantation for?

The prime indication is in an individual who is already on immunosuppression and has an amputation. This has not been met to date. The most widely agreed international indication is therefore bilateral mid-forearm amputations with good stumps, in a motivated patient. More controversial is the debate over unilateral amputation of a dominant hand³⁰ and congenital amputations. However, all centres agree that patient selection is the key proponent for success.^{1,31–34}

Summary

Publicity and reaction to the UK's first hand transplant in 2012 is reminiscent of that after the first cardiac transplant

by Christian Barnard in South Africa in 1967. At the time, the general consensus of the medical community was that the world was not ready. The only thing that is clear is what was once considered an experimental exercise is now a clinical reality, with over 65 hand transplants having been performed by 2015.

The future of hand transplantation is finely balanced. While there are functional and psychological benefits of the operation, there are the potential hazards of immunosuppression and unknown long-term outcomes.

With a follow-up survival rate of 90% and favourable functional outcomes superior to prosthetics, hand transplantation may become the gold standard treatment for bilateral amputees. However, ethical debates will continue, splitting both the professional and public community over the risks versus benefits of this life improving procedure. The future of CTA is vast and the balancing scales are moving constantly with new developments. The only certainty we face is that we must understand this new development to enable optimisation of function and choice for the most important person: the patient.

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