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CASE AND COMMENTARY

In Experimental Hand Transplantation, Whose Views About Outcomes Should Matter Most?

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Abstract

Consent to any experimental procedure, even when offered as therapeutic, involves extensive discussion between patient-subjects and clinician-researchers. Decision making should be shared with a focus on potential risks and benefits of enrolling in a protocol. Just as patients who underwent nonexperimental interventions might experience regret or reconsider autonomously made choices, patient-subjects who are undergoing or who have undergone experimental therapies should be afforded latitude to reconsider their decisions. Although clinician-researchers tend to be deeply invested in gathering data about patient-subjects' experiences, they are obligated to express respect for patient-subjects' fundamental right to stop being enrolled in research.

Case

After losing his hand in an industrial accident, R sees a television special about a hand transplant recipient who regained the ability to type. He inquires about the experimental surgery, undergoes multiple evaluations, and learns about potential risks and benefits. Although the surgeon stresses limitations of the transplanted hand, which might never regain full strength and sensibility, R hopes his outcome will allow him to return to work.

Two years later, after extensive rehabilitation, R is disappointed with the graft's functioning. His employer does not feel he can safely return to work and advises him to take permanent disability. R is frustrated with other aspects of his posttransplant quality of life: he has dietary restrictions, medications that cause nausea, a directive to avoid crowds, and he does not enjoy many outdoor activities due to the extra care he must take with his graft. He is tired of regular appointments and tests and of his surgeon-researcher's surveillance of his progress.

When he asks about surgical removal of his hand, his surgeon is surprised and says, "Your function is well above what we anticipated and you have had few complications. I don't recommend amputation. You would have to endure another surgery and recovery before being outfitted with a prosthesis. This has been a huge investment for you. What you've got now is probably the best you can get and it

would be unlikely you would get a second chance. However, the side effects and risks of your medications—including kidney damage, infections, and cancers—should be considered."

R says, "I definitely can do things I couldn't do with my prosthetic. But I don't think a hand transplant is right for me in the long run. What I have to do to take care of the hand interferes too much with how I want to live my life. All things considered, I think it was better for me before." The surgeon thanks R for explaining his concerns and suggests they take some time to think things over.

Commentary

Vascular composite allograft (VCA) transplantation is an emerging, still-experimental field in transplantation. VCA transplants can restore function and appearance to patients with severe injuries, disfigurement, and malformations. Most VCAs are upper limb or hand transplants, although craniofacial, uterus, penile, and lower limb transplants have been performed in the United States and worldwide.[1] Since 2014, 39 VCA surgeries have been conducted in the United States,[2,3] with 11 VCA transplants in 2018 alone.[3]

What makes VCA transplantation clinically and ethically different from most types of solid organ transplantation is that VCA transplants are intended to be life enhancing, not lifesaving. In consequence, VCA decision making requires more intense focus on quality of life (QoL) than on extending life. Specifically, as an experimental elective surgery, VCA transplantation requires greater consideration of risks and potential impacts on recipients' QoL because VCA recipients require intensive posttransplant rehabilitation, integration of many self-care tasks into their daily living, and meticulous adherence to lifelong immunosuppression medication regimens that might undermine their QoL. Some transplant recipients, like R in this case, might find requirements like these to be too burdensome or not what they expected. With the exception of craniofacial transplantation, for which graft removal is less feasible, VCA transplants provide unique opportunities in experimental surgery to consider when and which exit strategies should be developed for patients.

Clinical and surgical researchers obviously have a stake in the success of VCA transplantation. Opportunities to improve the functional status and QoL of persons with disabilities drives their desire to explore innovative, cutting-edge advances. However, VCA researchers' early declarations that "functional outcomes exceeded expectations" and that "VCA recipients enjoy a quality of life" unattainable with conventional reconstructive surgery were based on follow-up of fewer than 100 cases[4]; substantial quantitative data on either short or long-term outcomes is lacking.[5] Thus, the spectrum of possible outcomes will not be fully realized until the experimental procedure is well developed.

The uncertainty of outcomes creates important ethical considerations for VCA transplantation. How should clinical researchers maintain equipoise[6] when offering an experimental procedure with an uncertain outcome? How should candidates considering experimental VCA procedures think about their preferences, evaluate unknown risks, and weigh their hopes for improved function and QOL against these risks? Importantly, having participated in an experimental procedure, how should candidates, recipients, and clinical researchers consider exit strategies, including explantation?

Informed Consent to Experimental Surgery

Appropriate expectations for outcomes, such as physical functioning and QoL, begin with thorough explanation and discussion of a proposed procedure, its potential risks and benefits, recovery, and patient-subject responsibilities and self-care. Informed consent requires that a patient-subject have good comprehension of potential risks and benefits and be capable of voluntary decision making. To be informed, a patient-subject also needs time to understand and process complex information and to reflect on risks and benefits relative to his or her personal preferences. To ensure shared decision making, a researcher must not only disclose all information known about the experimental procedure but also consider a patient-subject's unique values, preferences, and expectations when making a recommendation.[7]

The experimental nature of VCA transplantation can complicate informed consent. The elective nature of plastic surgery necessitates disclosure of realistic odds of obtaining desired results[7] and appropriate management of expectations—especially in experimental VCA transplantation, given its substantially heightened high risks and uncertain results. As surgical experience with VCA outcomes grows, however, the risk-benefit ratio will likely change—hopefully in favor of benefits to patient-subjects—which would affect informed consent discussions. Moreover, to fully inform a potential VCA candidate, a clinical researcher should provide information about all currently known outcomes—not just optimal ones[7]—and their likelihood.[7] Because the number of VCAs performed so far is small and each case is unique, the procedure's experimental nature and possible unknown (and potentially undesirable) outcomes should be emphasized.

Informed consent to experimental VCA can also be complicated by how VCA transplantation is covered by the media. Perhaps unsurprisingly, amazing and courageous stories of VCA recipients and their surgical teams tend to attract media coverage,[8] which can influence the public's and potential VCA patient-subjects' perceptions of the procedure. As with many new interventions, positive media coverage has potential to benefit researchers' careers and their institutions and should be recognized as a possible conflict of interest. Additionally, positive coverage focusing on VCA recipients with the best outcomes may lead to VCA candidates' misunderstanding of surgical risks and outcomes, thereby compromising informed consent and respect for autonomy.[7]

In experimental VCA transplantation, patient-subjects' motives can powerfully influence their decision to proceed; this power should not be underestimated. Some patient-subjects harbor undisclosed fantasies about complete restoration of functioning or cosmesis or expect that, among possible outcomes, theirs will be optimal. Despite some patient-subjects' apparent willingness to accept a less-than-optimal outcome, they really might only be prepared to accept an optimal outcome. Furthermore, it can be difficult for some to fully comprehend and evaluate future demands of postoperative care, rehabilitation, medication regimens, laboratory and procedure monitoring, restrictions and limitations, and daily self-care tasks. When faced with daily realities of these activities and demands, patient-subjects—such as the one in the case—might find them unacceptable over time and feel that their prior QoL, while not optimal, was preferable to their QoL with a VCA transplant. In the case, for example, R continued to hope unrealistically for complete restoration of function and found the demands of postsurgical care too burdensome. Ultimately, his expectations of benefit were not realized and his QoL diminished.

Respect for Autonomy

VCA researchers and subjects must accept that when actual outcomes are not satisfactory to VCA recipients and accommodations cannot be made to improve them, then VCA recipients should be able to terminate postsurgical interventions and request graft explantation. Discussion of such exit strategies and their possible risks and benefits should be part of informed consent prior to surgery or informed refusal after surgery. Prior to experimental VCA transplantation, patient-subjects should be made aware that graft removal could be recommended by the research team. Circumstances that would possibly or definitely require graft explantation should therefore be discussed. Likewise, circumstances for which explantation is not possible should be considered by the research team and discussed with a VCA candidate.

In the case, a clinical researcher should inform R that explantation risks could include those related to the surgery itself, extended recovery, difficulty in fitting a new prosthetic, compromised functionality relative to presurgery functionality, and inability to be considered for retransplantation. Importantly, the researcher in the case reviewed possible benefits of explantation, including termination of chronic immunosuppression medications with their significant risks.[9] Providing time for R or any VCA recipient to process and reflect on this information should be allowed to ensure that the patient-subject's ultimate decision is not impulsive. The patient-subject's perceived QoL and perceived deviations from expected QoL after surgery are individual, subjective, and worthy of respect.

It might seem intuitive and self-evident that VCA candidates' and recipients' QoL and autonomy should be priorities in decisions about engaging in or disengaging from experimental surgery. Patient-subjects might decide that their outcomes did

not meet their expectations, or they might change their minds about how acceptable specific outcomes are after they experience them. However, a researcher might believe that explantation would introduce new risks and harms and be inclined to strongly recommend against it. The researcher must weigh this potential recommendation against potential conflicts of interest when he or she is highly invested in developing a novel surgical technology or has concerns about the impact of a poor outcome on a study. Would such an outcome negatively affect the continuation of the research, cause early termination of a research protocol, or lead to greater oversight? Given the substantial individual and institutional investment of time and resources in experimental VCA, it can be difficult—though it is essential—for clinical researchers to be mindful of their own hopes when discussing risks and benefits with VCA candidates or recipients.

Future Considerations

There are several ways to better prepare VCA candidates and to reduce the likelihood of their being dissatisfied with their outcome. Importantly, the risks and benefits of explantation should be emphasized during the informed consent process. Additionally, psychological counseling—conducted independently of the VCA team to allow candidates to reflect on their decision and prepare for and adapt to the demands of VCA transplantation—might improve satisfaction and acceptance of outcomes. Opportunities for VCA candidates to speak with VCA recipients who have had a range of positive and negative outcomes could also help inform their decision. Additionally, similar to policy for living donor transplantation programs,[10] independent advocates could help evaluate VCA candidates' understanding of the procedure's risks and benefits and help temper clinician-researchers' influence on candidates' decisions. As VCA experimental surgery evolves, inclusive approaches will be needed to safeguard candidates' and recipients' autonomy and optimize their QoL outcomes.

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