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Evolving ethics, policy and reimbursement issues of vascularized composite allotransplantation: Symposium summary

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Abstract

In this article, we present a report from a national meeting titled, "Evolving Issues of Vascularized Composite Allotransplantation—A Symposium on Ethics, Policy, and Reimbursement Issues," which convened in September 2017. We discuss the maturation of vascularized composite allotransplantation from an emerging technology to becoming an extension of clinical practice for select patients with complex reconstructive needs. Viewpoints and action items were presented by and discussed among the 70+ clinicians, researchers, policymakers, ethicists, healthcare administrators, and third-party payers who attended the symposium with the goals of implementing a collaborative roadmap for vascularized composite allotransplantation growth, evaluation, and sustainability by establishing a unified plan to help address concerns of the public, policymakers, and healthcare finance. We review the current status of vascularized composite allotransplantation in clinical practice and summarize symposium discussions regarding ethical considerations, reimbursement, payer strategies, and standardization of data collection.

Keywords

Vascularized composite allotransplantation, reconstructive surgery, ethics, policy

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Background

Vascularized composite allotransplantation (VCA) is gaining recognition as a reconstructive treatment following extensive injury to complex structural units, such as the face and upper extremities, in adults and children.[1,2] More recently, penis and uterus transplantation have expanded the scope of VCA.[3–5] Published clinical case series, a journal documenting technical and immunological progress, and dedicated professional societies such as the American Society for Reconstructive Transplantation (ASRT) and the International Society of Vascularized Composite Allotransplantation (ISVCA) attest to the early maturation of this field.[6] The number of sites interested in performing VCA has increased, from 17 United Network for Organ Sharing (UNOS)–registered programs in 2014 to 61 in 2017.[1,2,7,8] While debate continues regarding best clinical practices, challenges encountered at the policy level are complicating and limiting VCA expansion.

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In September 2017, clinicians, researchers, policymakers, ethicists, healthcare administrators, and third-party payers convened at a symposium in Baltimore, Maryland, to discuss opportunities and barriers related to VCA. The symposium, "*Evolving Issues of Vascularized Composite Allo-transplantation: A Symposium on Ethics, Policy, and Reimbursement Issues,"* aimed to prepare a collaborative roadmap for VCA growth, evaluation, and sustainability by establishing a unified plan to help address concerns of the public, policymakers, and healthcare finance. In this article, we review the current status of VCA and summarize symposium discussions regarding regulatory oversight, ethical considerations, reimbursement, payer strategies, and standardization of data collection. This summary does not reflect the authors' personal opinions, but rather the content of the symposium discussion.

Regulatory oversight

In 1999, when the first successful hand transplant was performed in the United States, VCA was regulated by the Food and Drug Administration (FDA) as a human cell and tissue product (HCT/P) (21 CFR 1271).[9] These rules, which govern human cells and tissue such as corneas, skin, and bone, did not accurately reflect the similarities of VCA to solid organ transplantation (SOT) nor support the expanding implementation of VCA. Like solid organs, VCAs are vascularized, prone to ischemia-induced damage, and unable to survive significant delays between procurement and transplantation.[8] Careful donor and recipient matching is based on physical characteristics as well as immunologic factors. Under FDA HCT/P regulation, teams interested in performing VCA needed to work with individual organ procurement organizations (OPOs) to establish candidate wait-listing and allograft procurement processes. Effective 3 July 2014, VCAs were designated as "organs" under the US Department of Health and Human Services (DHHS) Organ Procurement and Transplantation Network (OPTN) Final Rule (42 CFR part 121),[9,10] leveraging the UNOS's well-established SOT infrastructure. Under UNOS, VCA programs must meet specific requirements based on the SOT experience.[11] These requirements establish universal expectations in terms of (1) quality control of the performing facilities and personnel, (2) protocols for candidate wait-listing and organ allocation, and (3) collection of standardized data elements. These conditions are expected to evolve to address the changing characteristics and challenges unique to VCA.

Ethical considerations and transparency

As with all emerging medical interventions, VCA has been and continues to be a subject of ethical debate. One such point is weighing the benefits of a life-enhancing or function-restoring (as opposed to life-saving) procedure against the risks of lifelong immunosuppression[12–14] and ensuring patients grasp those risks during the informed consent process. This is not insignificant as being chronically immunocompromised can be considered a disease state.[15] One argument favoring VCA is that it greatly impacts the quality of life (QOL) of patients for whom there is no other satisfactory conventional, function-restoring reconstructive option.[16,17] The NYU/Johns Hopkins Working Group on Ethics and VCA addressed this issue, emphasizing the need to establish allograft-specific lists of standardized functional outcomes.[14]

Other concerns relate to how the public, and thereby potential organ donors and their legally authorized representatives, view such a highly personal type of organ donation. While the Uniform Anatomical Gift Act (2006, amended in 2009) does not contain language excluding VCA donation, neither does it specifically address it.[18,19] If the public perceives VCA donation as morally problematic, this could result in decreased solid organ donation rates. This may apply to penis or uterus transplantation, particularly if these grafts were requested as a part of gender affirmation surgery. In order to preserve valued relationships with solid organ transplant surgeons and care teams, and to maintain public trust and investment in non-directed/altruistic organ donation, OPOs have thus far elected to keep VCA donor requests separate. Although VCA wait listing processes, matching criteria, and organ distribution policies have been established by the UNOS VCA Committee, sharing this information more broadly with the public may enhance graft donation. Public education should include information about how traits uniquely associated with vascularized composite allografts, such as identity, are handled and how VCA can benefit recipients. An example of such an outreach is a 2018 VCA Organ Transplantation Web Video of a bilateral upper extremity transplant recipient, created through a partnership between the patient, the transplant program, and DHHS.[20]

Regardless, explicitly considering broadly established principles of bioethics (autonomy, beneficence, non-maleficence, and justice) should facilitate determination of the appropriateness of performing VCA in particular patients as well as formulating policies related to doing so. The principle of *autonomy* underscores the requirement to engage in informed and voluntary decision-making and obtaining consent. This process should include setting expectations for function based on the extent of the original injury, the subsequent graft, and potential graft longevity within the context of medication adherence. *Beneficence* includes ensuring that a candidate is appropriate, both physically and psychologically, for VCA, which will involve conducting a comprehensive battery of tests and evaluations. *Non-maleficence* necessitates prescribing an immunosuppression regimen that is as safe as possible and imparts the fewest side effects and complications. *Justice* requires treating patients fairly and ensuring responsible stewardship of health care resources. The latter would be facilitated in two ways: (1) by reporting, assessing, and reassessing adverse events associated with the

different types of VCA based on patient and donor characteristics, and (2) by developing procedures to ensure fair access to all suitable candidates and minimize financial barriers to VCA and follow-up care. Using longitudinal outcomes data to conduct cost-benefit and valuation analyses is critical to determining the potential return-on-investment for candidate recipients. As a related matter, there is a lack of consensus on appropriate indications for VCA, such as blindness, past-history of attempted suicide or suicidal ideation, age extremes (e.g. children or senior citizens), and, for upper extremity transplantation, the level of amputation,[21] which makes it difficult to assess equitable access to VCA. This is especially true since this lack of consensus has been used by third-party payers as a reason to decline coverage in initial requests for payment.

Reimbursement and third-party payers

From the first successfully performed transplant in the United States, VCA has been generally considered an experimental procedure. As such, its costs have been absorbed primarily by grants (e.g. from the Department of Defense), cost-sharing by participating hospitals, and philanthropic gifts. Efforts to obtain reimbursement from third-party payers have met with limited success: while some programs have secured payment for long-term immunosuppression as early as 3–6 months post-transplant, no US program has yet reported obtaining third-party payment for the allograft procurement, surgical procedure, or acute post-operative care (hospitalization). In addition, the physical therapy critical to obtaining the best possible outcomes following upper extremity and face transplantation is costly and infrequently covered by third-party payers.

Third-party payers typically exclude coverage of "experimental/investigational" treatments compared with what is considered "standard of care (SOC)."[22] Many innovative procedures are categorized as experimental until sufficient data are accumulated to warrant acceptance as part of the SOC, though how much and what type of data constitutes "enough" is not clearly defined. Data are generally collected and reported under institutional review board (IRB)–approved protocols; however, performing a procedure under IRB oversight can trigger third-party payers to deem the intervention experimental and ineligible for reimbursement. Acquiring a "qualifying clinical trial" designation may help but does not guarantee coverage for all study-related procedures or a path to acceptance as the SOC.[23]

In order to avoid the clinical trial label altogether, certain VCA centers in the United States have obtained approval to perform VCA as extensions of clinical practice through their Institutional/Hospital Ethics Committees (IECs). This determination can then be used when seeking reimbursement from third-party payers. However, this strategy entails challenges including establishing medical necessity, qualifying the type of VCA as treatment for a life-threatening condition, establishing graft survival rates, and comparing return-on-investment of VCA to established alternative treatments.

Further complicating the reimbursement scenario is the idea that randomized controlled trials (RCTs) are the primary route through which to test treatments. Currently, RCTs are not feasible or generally appropriate for studying VCA. Rigorous inclusion and exclusion criteria limit the number of potential candidates, leading to small sample sizes. Randomization of patients into control treatment (if available) versus treatment intervention groups is inappropriate and potentially unethical. Variability between the different applications of VCA (e.g. face, upper extremity), extent of reconstruction, and degree of long-term follow-up needed add to the heterogeneity of available patient data. Instead, in the absence of RCT-established evidence, other forms of systematic evidence and consensus statements by recognized authorities can be used.[24] Such statements will require a clear and unified message from multiple VCA experts and stakeholders and represent the most likely path toward SOC designations and third-party reimbursement.

One route to coverage may be available for Medicare beneficiaries: requesting Local Coverage Determinations (LCDs; Section 1869(f)(2)(B), Social Security Act) from one's regional Medicare Administrative Contractor (MAC).[25] This path may be pursued in the absence of a Medicare National Coverage Determination (NCD).[25] Currently, it would be imprudent for any particular type of VCA to be put forth for consideration of an NCD as it is a one-time approval request that, if rejected, may not be requested again. Instead, LCDs may cover a broad range of a given beneficiary's VCA and/or follow-up care, help accumulate needed data demonstrating the utility of VCA, and encourage private insurers that often follow payment precedents set by the Centers for Medicare & Medicaid Services (CMS). When seeking a LCD, programs should enlist resources at their institution as it is highly likely that (1) certain administrators have existing relationships with the LCD director, and (2) leveraging institutional resources and experience in applying for an LCD will help prevent the request from being rejected. However, LCDs only apply to Medicare beneficiaries, can be time-intensive since each case must be submitted individually, require significant institutional support, and are often not approved outright but instead are returned with a "wait and see" designation. This means that no guarantee of payment is made preoperatively; instead, institutions are to submit bills to Medicare following the procedure and track incoming or rejected payments.

Finally, comprehensive lifelong coverage is crucial for adherence to immunosuppressive therapies and post-transplant rehabilitation as well as facilitating necessary surgical revisions to help prevent gaps in care that can result in catastrophic consequences for transplant recipients. Despite the challenges facing VCA, they are not unlike those affecting the solid organ transplant community where insurance coverage has been secured.[26–28] Collaboration, universal data

collection using common outcomes measures as well as consensus statements will be essential to obtaining coverage.

Standardization

Establishing standardized methods to assess VCA outcomes and requirements for VCA Centers of Excellence will be critical to securing third-party reimbursement. VCA transplantation is an extension of surgical and microsurgical techniques used by plastic and reconstructive surgeons, orthopedic surgeons, otolaryngologists, general surgeons, urologists, and gynecologic oncologists to treat or repair the anatomical area of each VCA type. As a result, several VCA-related professional societies (e.g. ASRT, American Society for Surgery of the Hand (ASSH), American Association for Hand Surgery (AAHS), American Society for Reconstructive Microsurgery (ASRM), and American Society for Reproductive Medicine (ASRM)) offer guidance regarding acceptable practice. These organizations maintain active dialogues between provider institutions serving as a collective voice through which programs may lobby for recognition of the field and set appropriate regulation.

Currently, most VCA patient data are collected independently by individual centers, which have only recently been compiled into centralized, structured databases. This can lead to disjointed and confusing messages regarding the benefits and efficacy of these procedures. Roughly, half of centers contribute data to the International Registry on Hand and Composite Tissue Transplantation (IRHCTA), but this is not regulated, enforced, or standardized in the United States. Since 2014, UNOS/OPTN has required VCA centers to provide data regarding graft and patient survival and other basic measures (e.g. function, rejection episodes). While this serves as a start for monitoring long-term outcomes, it presents several discrete problems. First, no single objective measure of VCA function exists. Second, different centers use a variety of instruments with little agreement between batteries because no tool fully assesses any type of VCA.[26] When establishing their protocols, VCA centers often struggle to identify preexisting, validated assessments that could be used, in full or in part, for VCA patients.[29] Examples include the Innsbruck functional indices and the Action Research Arm Test (ARAT) designed to assess upper extremity function in other populations.[29,30] A paucity of validated VCA-specific assessments is partly due to small patient numbers, which is contradictory to the proper procedures needed to develop validated instruments.[29]

VCA also faces the challenge of validating objective measures of success that go beyond patient and graft survival. Assessing patient-level variables including motor and sensory function, patient satisfaction, QOL, cost/benefit analyses comparing VCA to other acceptable therapies, and return on investment is essential. These measures need to be specific to each type of VCA and allow some flexibility to accommodate the inter-patient variability inherent to these transplants. Novel functional outcomes should be emphasized such as the recovery of protective sensation, proprioception, and the ability to perform activities of daily living; all of which are not currently assessable using conventional measures. This will require a focused effort by VCA teams, representative professional societies (e.g. working groups within ASRT and ISVCA), and the involvement of experts and therapists in psychology, measurement, and physical and occupational therapy. Fortunately, there are tools that the field of VCA may leverage such as the Patient-Reported Outcomes Measurement Information System (PROMIS), developed in partnership with the National Institutes of Health to monitor the physical, mental, and social health of patients of all ages.[31] Implementing PROMIS measures will facilitate persuasive cost-benefit analyses of VCA compared with more traditional treatments, ultimately impacting coverage decisions.

Finally, the VCA community should continue to build on its current foundation to establish criteria to further encourage safe practices and exemplary care for centers performing these procedures.[32] By determining these criteria within the VCA field, firsthand expertise can be used to properly frame system-wide care requirements and outcome expectations.

Conclusion

In his opening remarks for the symposium, US Congressman Dutch Ruppersberger stated, “The effect of VCA is tremendous in our Veteran population.” While its benefits have been clearly demonstrated, it is also clear that the future of VCA now rests on a tipping point. In order to continue advancing, unified strategies must be adopted during the next decade. The symposium consensus was to focus on actionable recommendations, including the following:

- Establish standardized indications and contraindications for VCA;
- Endorse a common dashboard of quantitative *and* qualitative metrics of patient outcomes across centers;
- Maintain transparency regarding outcomes and ethical concerns;
- With emerging data, promote specific forms of VCA as extensions of clinical practice to address severe tissue loss of complex functional units;
- Pursue Current Procedural Terminology (CPT) codes for VCA to enable tracking and establish a universal language with third-party payers;
- Collaborate with third-party payers to develop reimbursement plans;
- Pursue local coverage determinations for CMS beneficiaries;
- Advocate for lifelong insurance coverage for patients to encourage continuity of care.

- Encourage cost/benefit and return-on-investment analyses comparing VCA to existing standards of care.

In order to maximize the future impact of VCA for patients, it is essential to create a unified voice to the public, third-party payers, and policymakers. This symposium established action items for the ASRT to spearhead and to which field experts can contribute.

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