

OPTN Vascularized Composite Allograft Transplantation Committee

Meeting Summary

January 13, 2021

Conference Call

Bohdan Pomahac, MD, Chair
Sandra Amaral, MD, Vice Chair

Introduction

The Vascularized Composite Allograft (VCA) Transplantation Committee met via Citrix GoTo teleconference on 01/13/2021 to discuss the following agenda items:

1. Update – Policy and Bylaw Language Clarification
2. Update – VCA Membership
3. Update – Genitourinary Membership Requirements Workgroup
4. New Project Ideas

The following is a summary of the Committee’s discussions.

1. Update – Policy and Bylaw Language Clarification

The Chair presented an update on the status of proposed clarifications to VCA policies and bylaws to address concerns from HRSA about Final Rule compliance, and to address questions from members regarding gland transplants.

Summary of discussion:

HRSA staff will meet with FDA staff on February 5th to discuss questions regarding the regulation of gland transplants as well as sentinel flaps. The Chair noted that while policy clarifications can be approved by the Executive Committee, changes to bylaws must be approved by the OPTN Board of Directors. The Chair reviewed interim guidance from HRSA regarding body parts that should not be considered as organs, pending FDA input, including:

- Any flap transplanted solely for the purpose of immunologic monitoring (e.g. “sentinel flap”)
 - NOTE: If a vascularized (blood vessels sutured anastomosis) muscle and/or skin flap is transplanted “for homologous use (the replacement or supplementation of a recipient’s organ with an organ that performs the same basic function or functions in the recipient as in the donor)”, e.g., would or structural cover/protection or movement, then that would appear to meet the criteria for “homologous use” as listed in the OPTN Final Rule¹
- Any body part not vascularized with sutured anastomoses of blood vessels (except “pancreatic islets”), e.g., any sliced, diced, fragmented, minced, or cell separation process
- Any body part (even if intact and not manipulated) not vascularized with sutured anastomoses of blood vessels, e.g., a parathyroid or adrenal whole gland implant

¹ 42 CFR §121.2

The Chair thought it would be less complicated for sentinel flaps to be considered organs under the purview of the OPTN rather than as tissue regulated by the FDA. One possible approach would be for HRSA and FDA to establish an exception to consider sentinel flaps as organs, in the way that extra blood vessels used for organ transplantation are considered organs from a regulatory standpoint. A member agreed that sentinel flaps should be considered organs, since sentinel flaps are always linked to allotransplants but defined as VCA, and none of these flaps would be transplanted without another VCA allotransplant. The Chair said that if sentinel flaps are considered organs, the Committee would have to consider whether to establish reporting structures, like the Transplant Recipient Registration (TRR) and Transplant Recipient Follow-up (TRF), for outcomes of the sentinel flaps. On the one hand, programs are not as concerned about the outcomes of the sentinel flap when it serves a monitoring purpose, but on the other hand, if the sentinel flap fails, the Committee must consider whether that is a transplant failure. This may present additional burden since the primary transplant, most likely a face or hand, will also be subject to reporting. The Committee will probably need to discuss this further down the line, if HRSA and FDA agree that sentinel flaps should be classified as an organ.

The Chair mentioned that some programs have used abdominal wall in conjunction with small bowel transplant to investigate whether the abdominal wall could function as a sentinel flap for immune monitoring of small bowel rejection. It is possible that sentinel flap transplants could be used for monitoring of other organs like hearts, which could alleviate the need for internal biopsies in favor of skin biopsies, but this has not been proven. A member said that if the abdominal wall fails, it does not impact the patient outcome. If the abdominal wall is needed, it is important early on after the transplant, but if the abdominal wall fails later, it is not critical to the survival of the patient. Accordingly, the abdominal wall graft would need to stay linked to the organ that is lifesaving from a data collection standpoint.

Next steps:

The Committee will receive an update following the HRSA-FDA meeting on 02/05/2021.

2. Update – VCA Membership

UNOS staff presented an update on VCA membership.

Summary of discussion:

Three VCA transplant programs have submitted applications; six currently approved VCA transplant programs submitted their intent to opt out from the application process; and the OPTN is still waiting to hear back from 57 transplant programs. Membership staff will be reaching out to those programs within the coming weeks to help answer any questions.

UNOS staff shared the breakdown of the 60 potential VCA transplant programs by VCA type:

- 16 – upper limb
- 16 – head and neck
- 14 – abdominal wall
- 9 – genitourinary organ
- 3 – lower limb
- 2 – musculoskeletal composite graft segment
- 0 – spleen
- 0 – glands

The Chair asked how the Committee should monitor whether the rest of the applications are likely to be submitted on time. UNOS staff said they will know more after they do outreach to all of the centers who have not yet submitted their applications and can reassess at that point whether the original timeline is feasible.

A member said that this topic came up on a national conference call, and people on the call said they were working on the applications but had questions. The member said that a lot of these programs are not familiar with the OPTN application process and some programs may be doing more work than necessary, for example, gathering documentation on cases when not pursuing the alternate pathway. The member said that the sooner the membership team can reach out to those programs, the better, to help members with the process. UNOS staff shared the link to a document designed to help guide VCA programs through the application process, as well as the email address for reaching out to the membership team. The Vice Chair suggested that the membership team use webinars through the American Society of Transplantation (AST) or another organization to get the word out if multiple programs have similar questions. UNOS staff agreed to keep this in mind as they reach out to centers.

UNOS staff requested volunteers from the VCA Committee to assist the Membership and Professional Standards Committee (MPSC) with review of the applications. Members were asked to email UNOS staff to indicate their interest.

Next steps:

The window to submit VCA membership applications for consideration at the June 2021 Board meeting closes on 02/05/2021.

3. Update – Genitourinary Membership Requirements Workgroup

The Co-Chairs of the workgroup shared an update on progress to date.

Summary of discussion:

A Co-Chair presented the roster for the workgroup, and shared that the project was approved by the Executive Committee on 01/13/2021. The workgroup will be discussing primary surgeon requirements at their next meeting on 01/20/2021.

Next steps:

During future meetings, the workgroup will discuss primary physician requirements, requirements for living donor recovery of genitourinary organs, and any other requirements for the transplant team that are not covered under the key transplant personnel requirements.

4. New Project Ideas

The Committee discussed two new project ideas: updating the graft failure definition for VCA, and updating VCA allocation policy.

Summary of discussion:

Graft Failure Definition

The Committee reviewed the definition of graft failure; policies for other organs that refer to graft failure; and OPTN data collection on graft failure. The current definition in policy states:

For all organs except pancreas, graft failure occurs when any of the following occurs:

- A recipient's transplanted organ is removed
- A recipient dies

- A recipient is placed on a chronic allograft support system

The Chair suggested that graft removal should be considered graft failure for most VCA, because it is difficult to quantify or qualify the function of a hand transplant. For example, there have been hand recipients who had almost no function in their hand, but preferred to retain the graft because the small level of function still helped to improve quality of life. However, if the graft is no longer serving its intended function, or the patient requests removal of the hand transplant because it is not improving quality of life, it seems like that should be considered graft failure. A member agreed that it is difficult to identify objective criteria for upper limb functionality, since to an extent it is defined in the way that the patient defines it. Members agreed that it may make sense to define graft failure differently based on the type of VCA. A member said that for face transplant, a certain extent of necrosis could also define failure of the graft, in addition to graft failure as a consequence of insufficient blood flow.

The Chair noted that for uterus transplant, the plan is ultimately to remove the allograft, so failure should probably be related to inability to conceive a child, or to have a pregnancy, or to deliver a child. A member agreed that intentional removal of a uterus following a successful outcome should not be considered a graft failure. Members agreed that the ultimate goal of a uterus transplant is live birth and delivery of a healthy baby, so removing the graft prior to achieving a live birth should be considered graft failure, in addition to insufficient blood flow. A pregnancy alone is not a successful outcome of uterus transplantation. A member suggested that one live birth should be considered a successful outcome, regardless of what happens afterwards, for example, if an attempt to have a second child fails. A pregnancy is considered viable at 23 weeks, and so anything after that is considered a live birth, though uterus transplantation programs aim for better outcomes.

A member asked if the Committee would need to specify a timetable in which a live birth should be achieved to consider the transplant a success. For example, there was a Turkish group that left a uterus graft in place and exposed the patient to immunosuppression for an extended period of time until finally achieving a live birth after a series of lost pregnancies. A member said it will be difficult to determine how long a temporary graft should be in place. The member thought it might be more appropriate to declare any live birth a successful outcome, though it would be preferable to have a timeline. A member suggested that the uterus transplantation field continue to try to define this further, but suggested that the Committee separate the question of graft failure from the criteria for a successful graft, since there is nuance in the spectrum of success for uterus transplantation. It is easier to define failure, which would be removal of a graft prior to a live birth (23 weeks or later).

The Chair confirmed with UNOS staff that making updates to the definition of graft failure for VCA would require public comment.

Updates to VCA Allocation

The Chair noted that the Committee has previously held off on changes to VCA allocation policy due to the limited data on VCA transplants and the small population of candidates. The Committee reviewed current policy on VCA allocation, which does not distinguish candidates based on VCA type. Current policy is silent on how to prioritize candidates who need multiple VCA, and candidates who need at least one VCA as well as another non-VCA organ. The Chair noted that policy also does not indicate how to prioritize candidates within a VCA type, for example, whether bilateral hand amputees should be prioritized over single hand amputees. UNOS staff shared an example showing that if a candidate is registered for upper limb transplant initially, and then registered for a face transplant at a later date after other candidates, there is nothing in policy that says that the candidate should have access to both VCA types from the same deceased donor.

The Chair said he thought it is still appropriate for a candidate's position on the waiting list to be based on when they were registered, and if they need an additional VCA, that should still be based on the initial registration date. The Vice Chair said that for other organs, multi-organ candidates are often prioritized over single-organ candidates, and it makes sense for VCA as well, as long as it is surgically feasible to perform those surgeries at the same time. Members agreed that it generally makes sense to get all needed VCAs from the same donor when possible.

The Chair asked whether there should be any preference for those that need multiple VCAs because they are more debilitated, for example, whether someone in need of bilateral hand transplants should be prioritized over someone who only needs one hand transplant. A member said that in general, one can make an argument that one candidate is more in need of a transplant than another, based on limited access or comorbidities, but it is difficult to capture that objectively. That is why waiting time plays a large role in allocation for some organs, including kidneys. A member noted that other organs like liver have scores for assessing disease severity, but VCA is not at the point where that can be done. The member suggested that it would be easier to update other aspects of allocation at this time, like multi-organ listings, rather than disease severity. There is precedent in OPTN policy for other organs to prioritize multi-organ candidates over single-organ candidates. The member said that a candidate who needs a lifesaving organ should be able to "pull" the VCA from the same donor, and that there is precedent in OPTN policy for similar circumstances. The Vice Chair pointed out that the disease severity score for liver is not without issues and has created gender disparities, so it is difficult to objectively determine disease severity. The member agreed but said that the liver system is better than most organs. A member said that attempts to make the kidney allocation system better have taken a decade and it still is not perfect.

The Vice Chair suggested that the Committee focus on bigger principles, like whether a candidate who needs multiple VCA should have priority; how sensitization should factor into allocation; and how pediatric candidates are prioritized. For some candidates, the donor pool will be more restrictive, based on size or skin or other factors. A member suggested that medical necessity could be considered for urgent transplant in the event of a failed face transplant that requires removal, or the Committee could also consider creating a review board for VCA if a candidate needs higher priority. However, the member noted that a review board would require more resources and there are probably only a few people who could participate without a conflict of interest.

Members agreed that allocation should be organized by VCA type, since not all candidate listings will apply to each VCA donor. UNOS staff explained that current VCA allocation policy groups all VCA types together. While UNOS initially considered programming VCA in UNetSM based on eight match runs, after receiving more feedback from the committee and reviewing policy, UNOS staff believes the best approach is to register candidates based on the eight VCA types, but the default for organ procurement organizations (OPOs) would be to see the full list of VCA candidates. This is why UNOS staff were interested in committee feedback as to whether VCA allocation policy should be updated to break out VCA allocation by the eight types of VCA.

A member asked if it is possible to inactivate VCA candidates based on current policy so that they can still accrue waiting time, and suggested including this in policy if it is not already covered. Other members said that they have inactivated their candidates. UNOS staff noted that the Board-approved proposal for *Programming VCA Allocation in UNet*² included a policy change to *Policy 3.6.A Waiting Time for Inactive Candidates* allowing VCA candidates to accrue unlimited waiting time while inactive.

² Policy Notice, OPTN, accessed February 4, 2021, https://optn.transplant.hrsa.gov/media/4246/policy-notice_vca-in-unet_december-2020.pdf

A member suggested that the Committee start with a white paper to document all these considerations regarding VCA allocation before making it a regulatory framework. A member supported this approach. A member asked how other organs established their principles for allocation, since kidney allocation focuses a lot on waiting time, but heart and lung focus more on disease severity. UNOS staff agreed to look into this but explained that as other organs shift to continuous distribution, that will help to increase consistency across organs in allocation policy and will also help to provide a framework that the VCA Committee could build upon. The VCA Committee is not scheduled to work on continuous distribution until 2023, but if the Committee feels that there are changes to VCA allocation that should be made in the interim, the Committee could look to the continuous distribution model as a guide for the future.

A member said that the numbers in terms of volume of VCA transplants are still very low, and recommended caution in investing a lot of time on changing allocation when there still is not a lot of data. The Chair agreed that the Committee does not want to create policies that are not evidence-based, and said the Committee could develop a basic structure that could be refined over time as more data are available for candidate factors like sensitization. The Vice Chair noted that there may be smaller groups within the VCA types that need to be considered separately, like pediatric candidates. Additionally, allocation for uterus should perhaps consider age based on the time-limited nature of fertility.

Next steps:

The Committee will continue discussing new project ideas in upcoming meetings.

Upcoming Meetings

- February 10, 2021
- March 10, 2021

Attendance

- **Committee Members**
 - Bohdan Pomahac, Chair
 - Sandra Amaral, Vice Chair
 - Linda Cendales
 - Lori Ewoldt
 - Robert Goodman, Visiting Board Member
 - Darla Granger
 - Liza Johannesson
 - Nicole Johnson
 - Deborah McRann
 - Paige Porrett
 - Debra Priebe
 - Patrick Smith
 - Simon Talbot
 - Stefan Tullius
 - Mark Wakefield
- **HRSA Representatives**
 - Jim Bowman
 - Raelene Skerda
- **SRTR Staff**
 - Bryn Thompson
- **UNOS Staff**
 - Elizabeth Miller
 - Leah Slife
 - Kaitlin Swanner
 - Roger Vacovsky
 - Jennifer Wainwright
 - Marta Waris
 - Karen Williams