

Briefing to the OPTN Board of Directors on

Modify Graft Failure Definition for VCA

OPTN Vascularized Composite Allograft Transplantation Committee

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Modify Graft Failure Definition for VCA

<i>Affected Policies:</i>	<i>1.2: Definitions</i> <i>12.1 Waiting Time</i> <i>18.1 Data Submission Requirements</i>
<i>Data Instruments Affected:</i>	<i>VCA Transplant Recipient Registration (TRR) Form</i> <i>VCA Transplant Recipient Follow-up (TRF) Form</i>
<i>Sponsoring Committee:</i>	<i>Vascularized Composite Allograft Transplantation</i>
<i>Public Comment Period:</i>	<i>January 27, 2022 – March 23, 2022</i>
<i>Board of Directors Meeting:</i>	<i>June 27, 2022</i>

Executive Summary

The OPTN Vascularized Composite Allograft (VCA) Transplantation Committee is proposing changes to the current OPTN definition of graft failure as it does not appropriately characterize graft failure for VCAs. The current OPTN definition states that a graft has failed if "... an organ is removed, a recipient dies, or a recipient is placed on a chronic allograft support system." While the first two criteria can be broadly applied to VCA, chronic allograft support systems are not applicable to VCA transplants. Additionally, the nuance of VCA transplantation includes instances where a candidate may be re-registered for a covered VCA which would denote graft failure as there is no chronic allograft support for VCA. Also, for uterus, the transplanted graft may be removed intentionally when the graft is still functioning, but has fulfilled its intended goal (i.e. following a successful birth), so that the recipient does not require continuous immunosuppression.¹ These graft removals are reported as graft failure under the current policy definition and the associated required data collection, even though the transplant resulted in a successful outcome for the recipient and the transplant program. As more uterus transplants are performed in the U.S. and the overall volume of uterus transplantation continues to grow, it is important to accurately document uterus graft removal when it indicates a successful transplant outcome separately from all current reports of graft failure. Furthermore, this proposal will revise policy and update relevant data collection to more accurately reflect VCA transplant outcomes for all approved covered VCA types.

¹ Jones, BP, Saso, S, Yazbek, J, Thum, M-Y, Quiroga, I, Ghaem-Maghani, S, Smith, JR, on behalf of the Royal College of Obstetricians and Gynaecologists. Uterine Transplantation. Scientific Impact Paper No. 65. *BJOG*. 2021; 128: e51– e66.

Background

Effective in 2014, VCAs were designated by the U.S. Department of Health and Human Services as organs under the purview of the OPTN, this inclusion also calls on OPTN to create a list of “covered VCAs”.^{2,3} Since then, the OPTN Vascularized Composite Allograft Transplantation Committee (Committee) has been working steadily to recommend updates to OPTN policies and data collection as appropriate to reflect unique aspects of VCA transplantation relative to other solid organ transplants.⁴

Information on patient graft failure is used in a number of ways as it is used as a measure of success in transplant. OPTN data regarding graft failures are reported to the Scientific Registry of Transplant Recipients (SRTR) so that they can calculate risk-adjusted graft survival rates and make this information available to the public.⁵ For some organs (kidney, pancreas, and intestine), waiting time is reinstated for transplant candidates following graft failure.⁶ For lung, candidates registered for lung retransplant or graft failure are assigned to a specific diagnosis group that impacts the candidates’ allocation score.⁷ Additionally, hospitals recovering organs from living donors must provide data on transplanted organ survival, as measured by graft function, as part of the informed consent process.⁸

While SRTR does not currently generate program-specific reports (PSRs) for VCA transplant programs due to the low volume of these transplants, the field of uterus transplantation has developed rapidly since the first successful uterus transplant was performed in the U.S. in 2016. As of April 22, 2022, 36 uterus transplants have been performed and at least 21 children have been born to 19 uterus recipients.⁹ Four transplant hospitals in the U.S. have performed these transplants and at least two of these hospitals have moved beyond clinical research trials and are now offering uterus transplantation outside of those clinical trials. Currently, there are 11 approved OPTN VCA Genitourinary transplant programs, which are able to perform uterus transplants, and the Committee is aware of at least four other hospitals interested in starting uterus transplant programs specifically with this number being expected to grow.

The term “covered VCA” is used in reference to the list of covered body parts defined in OPTN Bylaws and Policies.^{10,11} In December 2021, the Board of Directors approved a proposal to split genitourinary organs into three types: uterus, external male genitalia, and other genitourinary organs. The *Establish Membership Requirements for Uterus Transplant Programs* proposal created more specific membership requirements for uterus transplant programs to address needs for the most common type of covered VCA transplant performed.¹²

² U.S. Department of Health and Human Services, Final Rule, “Organ Procurement and Transplantation Network.” 78 *Fed. Reg.* 40,003 (July 3, 2013). <https://www.govinfo.gov/content/pkg/FR-2013-07-03/pdf/2013-15731.pdf> (accessed on November 29, 2021).

³ “Implement the OPTN’s Oversight of Vascularized Composite Allografts (VCAs),” Public Comment Proposal, OPTN, accessed April 1, 2021, https://optn.transplant.hrsa.gov/media/1118/05_vca_implementation.pdf.

⁴ “VCA Committee,” Web Page, OPTN, accessed April 21, 2022, <https://optn.transplant.hrsa.gov/members/committees/vca-committee/>.

⁵ “Data That Drives Development,” Web Page, Scientific Registry of Transplant Recipients, accessed December 2, 2021, <https://www.srtr.org/about-the-data/the-srtr-database/>.

⁶ OPTN Policy 3.6.B, *Waiting Time Reinstatement for Non-Function of a Transplanted Organ* (April 11, 2022).

⁷ OPTN Policy 10.1.F.i, *Lung Disease Diagnosis Groups* (April 11, 2022).

⁸ OPTN Policy 18.5 *Living Donor Data Submission Requirements* (April 11, 2022).

⁹ OPTN data as of April 22, 2022.

¹⁰ *Vascularized Composite Allograft Membership Changes*, Combined Policy Notice, OPTN, accessed December 7, 2021, https://optn.transplant.hrsa.gov/media/3922/20200731_vca_membershipchanges_policynotice.pdf.

¹¹ *Clarification of Policies and Bylaws Specific to VCAs*, OPTN Policy Notice, accessed December 13, 2021, https://optn.transplant.hrsa.gov/media/4673/policy-notice_vca-clarification_june-2021.pdf.

¹² *Establish Membership Requirements for Uterus Transplant Programs*, Policy and Bylaw Notice, accessed April 18, 2022, https://optn.transplant.hrsa.gov/media/gapkro1m/policy-notice_establish-membership-requirements-for-uterus-transplant-programs_december-2021.pdf.

The current OPTN definition of graft failure does not appropriately characterize graft failure for all VCAs, particularly for uterus. The definition outlines that graft failure occurs when "... an organ is removed, a recipient dies, or a recipient is placed on a chronic allograft support system."¹³ The first two criteria are relevant to VCA broadly, but the last criterion is not applicable, as there are no chronic allograft support systems available for VCAs. Additionally, there may be instances in which a candidate is re-registered for a covered VCA, which is a marker for graft failure because the graft may no longer be suitable. Furthermore, for uterus transplantation, the graft may be removed intentionally following a successful transplant outcome (birth of a child) when the graft is still functioning properly,¹⁴ so that the recipient does not require continuous immunosuppression.¹⁵ Under the current OPTN definition and associated required data collection, these graft removals must be reported as graft failures, even though the transplant resulted in a successful outcome. As more uterus transplants are performed in the U.S. and the overall volume of uterus transplantation continues to grow, it is important to accurately document uterus graft removal when it indicates a successful transplant outcome separately from all current reports of graft failure.

Purpose

The purpose of this proposal is to appropriately tailor the definition of graft failure and associated data collection for covered VCAs to represent VCA transplantation outcomes more accurately. This includes updating the policy definition of graft failure, adding a policy definition for planned removal of a uterus, and revising the associated data collection on VCA Transplant Recipient Registration (TRR) and Transplant Recipient Follow-up (TRF) data collection instruments. It will also revise policy related to waiting time accrual to reflect the most recently approved covered VCA types.

Proposal for Board Consideration

This proposal would update OPTN policies by:

- Defining graft failure for VCA transplantation separately from the current OPTN definition of graft failure as:
 - a recipient re-registers for the same covered VCA
 - the recipient dies
 - or an unplanned removal of a covered VCA
- Modifying policy to reflect the ability to accrue waiting time for the recently approved three covered genitourinary VCA organ types which includes uterus
- Modifying policy to stop the generation of VCA Transplant Recipient Follow-up (TRF) forms after a planned uterus removal

This proposal would revise OPTN data collection by:

- Modifying data collection on graft failure for covered VCAs to improve data quality
- Modifying data collection on hysterectomies performed for uterus transplants to improve data quality
- Modifying data collection on causes of VCA graft failure to eliminate redundancy and add clarity

¹³ OPTN Policy 1.2 *Definitions* (April 11, 2022).

¹⁴ Jones, BP, Saso, S, Yazbek, J, Thum, M-Y, Quiroga, I, Ghaem-Maghami, S, Smith, JR, on behalf of the Royal College of Obstetricians and Gynaecologists. Uterine Transplantation. Scientific Impact Paper No. 65. *BJOG*. 2021; 128: e51– e66.

¹⁵ *Ibid*.

- Modifying “Primary Cause of Death” to eliminate redundancy and add a new option

Defining VCA Graft Failure

The Committee proposes modifying the current OPTN definition of graft failure to more accurately represent graft failure for covered VCAs and collect more accurate data on VCA graft outcomes.¹⁶ The proposed changes would add a separate VCA graft failure definition to include re-registration for the same covered VCA, death, or the unplanned removal of a covered VCA with an accompanying definition for planned removal open to all covered VCA. Based on public comment feedback, the Committee recommends keeping unplanned removal tailored to the uterus, instead of the broader covered VCA, because while the Committee acknowledged the possibility that other VCA grafts, such as abdominal wall, may be transplanted with the intent of temporary coverage in the future, this is not current practice and the Committee felt that it would be appropriate to revisit when the procedures are being performed.¹⁷

Re-registering for a covered VCA indicates that the graft is no longer functioning adequately and the transplant program and recipient have agreed that retransplant is the suitable option.¹⁸ Additionally, the current definition of graft failure includes “a recipient is placed on a chronic allograft support system” which is not applicable to VCA since this technology does not exist for covered VCA transplantation, but instead these recipients may re-register for the same covered VCA and continue to use the failed graft until they receive an offer under the proposed definition.¹⁹ The process for reporting graft failure in the case of re-registration of the same VCA would be as follows:

- The graft failure is reported on the “Interim Report of Graft Failure, Death or Lost Record” within 14 days which then generates the next TRF or on the next TRF if it is within the 14 days from notification of the recipient’s death or graft failure
- The candidate is re-registered for the same VCA in OPTN Waiting List

These two functions are not linked between the OPTN Waiting List and the Data System for the OPTN, so re-registering the candidate will not trigger the graft failure report and the failed graft must be reported separately in the Data System for the OPTN.

The most notable difference in VCA transplantation versus solid organ is the occurrence of planned removal of a graft due to a successful outcome. While this is primarily applicable to uterus, there is opportunity for planned removal to include other VCAs, such as abdominal wall grafts and musculoskeletal composite graft segments when transplanted for purposes of temporary coverage or to allow for the regrowth of the original tissue.²⁰ The Committee also contacted programs who have abdominal wall programs to gain insight on the likelihood of abdominal walls being transplanted for temporary coverage and the feedback was mixed with programs feeling strongly that planned removal would be applicable and others feeling it would not be. The Committee felt that this information was helpful in their discussion to limit planned removal to uterus transplantation only.²¹ With the addition of excluding planned removal of a uterus from graft failure, planned removal of a uterus will also be

¹⁶ Ibid.

¹⁷ VCA Committee Meeting Summary, April 6, 2022, OPTN, accessed May 5, 2022, https://optn.transplant.hrsa.gov/media/tekiukkq/20220406_vca-committee-meeting-summary_final.pdf.

¹⁸ S.G. Chiverton, J.A. Murie, R.D. Allen, P. J. Morris, “Renal Transplant Nephrectomy,” *Surgery, Gynecology & Obstetrics*, 164.4 (1987): 324-328, <https://pubmed.ncbi.nlm.nih.gov/3551155/>.

¹⁹ OPTN Policy 1.2 *Definitions* (April 11, 2022).

²⁰ VCA Committee Meeting Summary, September 8, 2021, OPTN, accessed November 3, 2021, https://optn.transplant.hrsa.gov/media/gOhlxgy/20210908_vca-committee-meeting-summary.pdf.

²¹ VCA Committee Meeting Summary, April 6, 2022, OPTN, accessed May 5, 2022, https://optn.transplant.hrsa.gov/media/tekiukkq/20220406_vca-committee-meeting-summary_final.pdf.

defined in policy as occurring when the uterus graft is removed with the intent of removal recorded either pre-transplant or at time of transplant to exclude graft removals due to graft failure. For additional clarification, if a program indicates planned removal for a uterus and the graft fails prior to the planned removal, the graft would then be reported as a graft failure.

Revision of VCA TRR and TRF Data Elements

The Committee proposes revising some of the data elements on the VCA TRR and TRF to add clarity and improve data collection for VCA transplants.

In addition to graft status options of “functioning” or “failed,” this proposal would include a new graft status option for “planned removal” to capture removal of uterus transplants that are removed after the graft is no longer needed post-successful live birth(s). Proposed data collection changes include modifying data collection after the removal of a uterus graft to specify whether the removal was due to successful delivery of a neonate or due to graft failure (i.e. complications, reproductive failure). The Committee agreed it would be important to capture “non-traditional” causes for graft failure as it pertains to uterus since there are reproductive reasons for removing these grafts such as failure to conceive.²²

The Committee also proposes revising data collection on causes of graft failure to eliminate redundancy, streamline forms, and use more positive phrasing to remove onus from being strictly on the patient.^{23,24} Current options for causes of VCA graft failure on OPTN forms include “thrombosis” and “ischemia” as distinct options. The Committee proposes combining these options into one field for “vascular complications” as many different types of vascular issues may arise, and these are not limited to thrombosis and ischemia.^{25,26} Currently, there are three causes of graft failure pertaining to non-compliance which include “non-compliance: immunosuppression,” “non-compliance: rehabilitation,” and “non-compliance: level of activity.” The Committee proposes combining these into one more general cause of “non-adherence” to remove some redundancy while also moving away from the negative connotation of “non-compliance”.^{27,28}

The Committee also proposes removing a number of options for cause of death on the VCA TRR/TRF due to redundancy with other existing options. This proposal would also include the addition of an obstetric related cause of death in order to capture those events as they may specifically relate to uterus transplantation. Causes of pregnancy-related deaths in the United States during 2014-2017 included other cardiovascular conditions, infection or sepsis, cardiomyopathy, and hemorrhage.²⁹ The proposed

²² VCA Committee Meeting Summary, October 7, 2021, OPTN, accessed November 5, 2021, https://optn.transplant.hrsa.gov/media/g50hpn0s/optn_vca_summary_20211007_final.pdf.

²³ VCA Committee Meeting Summary, May 12, 2021, OPTN, accessed November 3, 2021, https://optn.transplant.hrsa.gov/media/4661/20210512_vca-committee-meeting-summary_final.pdf.

²⁴ “Adherence To Long-Term Therapies, Evidence for action”, World Health Organization 2003, accessed December 7, 2021, <http://apps.who.int/iris/bitstream/handle/10665/42682/9241545992.pdf;jsessionid=5A7A9CB615699B093818CCFABFBD3D1C?sequence=1>.

²⁵ VCA Committee Meeting Summary, September 8, 2021, OPTN, accessed November 3, 2021, https://optn.transplant.hrsa.gov/media/g0hxcgy/20210908_vca-committee-meeting-summary.pdf.

²⁶ Gavin Low, Ann M. Crockett, Katherine Leung, Anil H. Walji, Vimal H. Patel, A.M. James Shapiro, David J. Lomas, Richard A. Coulden, “Imaging of Vascular Complications and Their Consequences Following Transplantation in the Abdomen,” *RadioGraphics*, 33.3 (2013), <https://pubs.rsna.org/doi/full/10.1148/rg.333125728>.

²⁷ *Ibid.*

²⁸ *Ibid.*

²⁹ “Pregnancy Mortality Surveillance System”, CDC, accessed November 4, 2021, <https://www.cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm>.

changes are outlined in **Table 1** below and the full list of cause of death selection options can be found in **Appendix 3: Patient Status: Primary Cause of Death Selection Options**.

Table 1: Proposed Data Elements to Add and Remove from the VCA TRF³⁰

Section of TRF	Remove	Add
Patient Status: Primary Cause of Death	MISC – acid/base disorder MISC – fluid/electrolyte disorder MISC – multiple system organ failure (MSOF) Trauma: motor vehicle	Maternal and obstetric mortality: other specify

The Committee also discussed whether planned removals of uteri should be reported on the “Interim Report of Graft Failure, Death, or Lost Record”. *Policy 18.1: Data Submission Requirements* requires programs to report recipient graft failures within 14 days of the program’s knowledge of the event.³¹ Currently, these planned removals are reported on an Interim Report since they are reported as graft failures. The Committee determined that planned removal of a uterus does not need to be reported on the Interim Report, as planned removals are not graft failures under the proposed definition and do not indicate an immediate patient safety event which would constitute immediate reporting and would also allow for time between the planned removal and next TRF to report post-hysterectomy complications.^{32,33}

More details on all proposed addition of data elements are located in **Appendix 1: Proposed Modifications to VCA TRR and TRF Data Collection**. Proposed data definitions are also included for all new data elements and are found in **Appendix 2: Proposed Data Definitions**.

Administrative Changes

In December 2021, the OPTN Board of Directors approved *Establish Membership Requirements for Uterus Transplant Programs*,³⁴ which splits the current genitourinary organ VCA type into uterus, external male genitalia, and other genitourinary organs. The Committee proposes updating *Policy 12.1: Waiting Time* to align with those changes.³⁵ This will enable waiting time accrual by genitourinary organ type upon implementation of the approved changes.

The Committee also proposes modifying *Policy 18.1: Data Submission Requirements* to include the cessation of TRF generation should the recipient have a planned removal of a uterus.

Overall Sentiment from Public Comment

The proposal was released for public comment from January 27, 2022 through March 23, 2022. During that time, it received 201 responses, eight of which also had substantive written comments. Following is

³⁰ Ibid.

³¹ OPTN Policy 18.1 *Data Submission Requirements* (April 11, 2022)

³² Ibid.

³³ VCA Committee Meeting Summary, April 6, 2022, OPTN, accessed May 5, 2022, https://optn.transplant.hrsa.gov/media/tekiukkq/20220406_vca-committee-meeting-summary_final.pdf.

³⁴ *Establish Membership Requirements for Uterus Transplant Programs*, Policy and Bylaw Notice, accessed April 18, 2022, https://optn.transplant.hrsa.gov/media/gapkro1m/policy-notice_establish-membership-requirements-for-uterus-transplant-programs_december-2021.pdf.

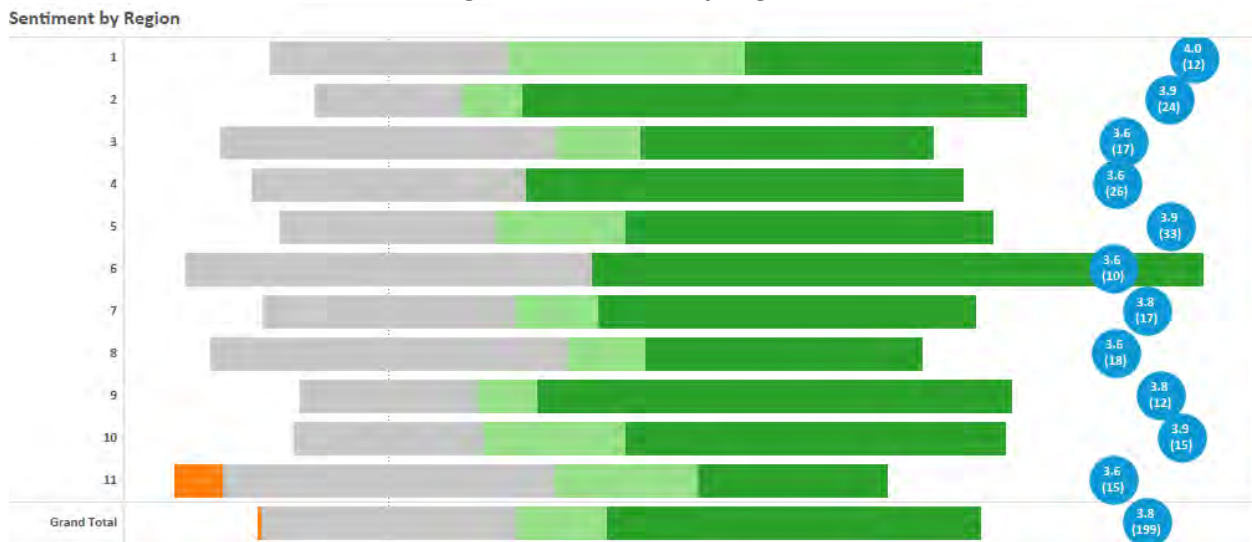
³⁵ *Programming VCA Allocation in UNet*, Policy Notice, OPTN, accessed December 7, 2021, https://optn.transplant.hrsa.gov/media/3922/20200731_vca_membershipchanges_policynotice.pdf.

a summary of the overall sentiment for the proposal, as well as a summary of feedback on certain themes throughout the sentiment. The major areas that the OPTN received feedback on were:

- Planned Removal
- Multiple Uterus Transplants
- Re-registration for the Same VCA
- Data Clarification and Questions
- Suggestions for Future Proposals

Generally, public comment sentiment was supportive of this proposal with pockets of concern. **Figure 1** shows the sentiment by Region.

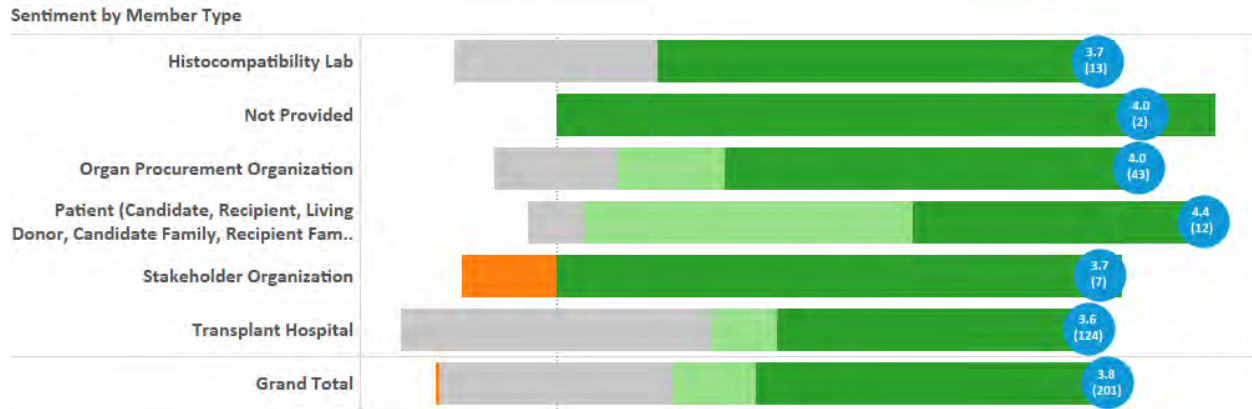
Figure 1: Sentiment by Region³⁶



The next graphic, Figure 2, shows the sentiment received at regional meetings and through the OPTN Public Comment website by member type, with the highest support coming from patient representatives. Overall, the proposal was generally supported with one sentiment of opposition submitted. The feedback of opposition was not supportive of the open-ended nature of planned removal due to the possibility that graft failure could be under-reported and recommended limiting planned removal to uterus only which has since been incorporated.

³⁶ Sentiment is reported by the participant using a 5-point Likert scale (1-5 representing Strongly Oppose to Strongly Support). Dark green indicates strongly support, light green indicates support, grey indicates neutral/abstain, and orange indicates oppose. Sentiment for regional meetings only includes attendees at that regional meeting. Region 6 uses the average score for each institution. The circles after each bar indicate the average sentiment score and the number of participants is in the parentheses.

Figure 2: Sentiment by Member Type³⁷



Planned Removal

Feedback on the proposed definition of graft failure for VCA included concern over leaving the planned removal definition open to all VCA transplants. Both the American Society of Transplant Surgeons (ASTS) and the American Society of Transplantation (AST) recommended limiting planned removal to uterus since this is the only VCA transplant currently performed with the intent of being temporary. AST also suggested that a planned removal after a successful live birth should be documented as a defined success. AST also was in support of adding a timeframe for planned removal with the intent to monitor if “planned removal” is being utilized appropriately.

After reviewing the feedback and extensive discussion among the Committee, a majority of the members agreed that the planned removal definition be limited to uterus. The Committee also discussed that timeframes for planned removal are still nuanced and should be at the discretion of the program. The discussion did note that it is likely that planned removals of abdominal walls will be utilized in the future due to their use in providing temporary coverage in the event of considerable swelling when done with other organ transplant. However, this has not been documented to date. With this in mind, a majority of the Committee supported waiting until that was in practice before opening the definition of planned removal to more VCA types as part of a future project.³⁸

ASTS noted concern over under-reporting of graft failures for uterus and other VCAs due to the planned removal designation. To address this, the OPTN will collect data on planned removals and program records can be requested to be reviewed during an OPTN contractor site survey. ASTS also recommended that reproductive failure in a uterus transplant be recorded separately from graft failure. While reproductive failure would be considered as a graft failure, specific reporting of reproductive failure and complications as a cause of graft failure is included in the proposed data collection outlined in **Appendix 1** in order to be able to distinguish from other types of graft failure.

Other feedback included that a uterus that is menstruating at the time of removal, but does not result in a successful live birth, should be reported as a graft failure. This scenario would also fall under reproductive failure and would be captured with the proposed data collection outlined in **Appendix 1**. The transplant program would be required to report the graft failure in accordance with OPTN Policy 18.1 *Data Submission Requirements* and report “reproductive failure” as the reason for hysterectomy on the uterus TRF.

³⁷ Ibid.

³⁸ VCA Committee Meeting Summary, April 6, 2022, OPTN, accessed May 6, 2022, https://optn.transplant.hrsa.gov/media/tekiukkq/20220406_vca-committee-meeting-summary_final.pdf.

Multiple Uterus Transplants

The Committee also discussed the scenario in which a uterus recipient has one successful uterus transplant and planned removal, but then later wants to pursue a second uterus transplant. Based on current OPTN data reporting, registering for a second uterus transplant would not cause the first uterus transplant to be reported as a graft failure. The process for this scenario would be that the removal of the initial graft would be documented on the recipient's next TRF, the data collection for that graft would cease due to the proposed changes to *Policy 18.1*, and then the patient would go through the regular transplant registration process for the second uterus.³⁹

Re-registration for the Same VCA

As previously outlined, re-registering for the same covered VCA indicates that the graft is no longer functioning adequately and the transplant program and recipient have agreed that retransplant is the suitable option.⁴⁰ AST commented that the proposal should include “definitions of, and mechanisms of determining at what point decreased or limited function is no longer acceptable” to avoid under-reporting of graft failures and consider graft-specific functional expectations similar to pancreas.⁴¹ The VCA Committee had extensive discussion on this topic for purposes of this proposal and agreed that these areas should be captured by the outcomes data collection, but not as part of the graft failure data collection. The Committee noted that the VCA field is still growing and as more information is available, more specific metrics may be able to be developed as part of future projects.^{42,43}

Feedback from both the OPTN Membership and Professional Standards Committee (MPSC) and AST stated that the proposal should ensure that it is not considered a re-registration graft failure if a recipient of one laterality VCA who then registers for the opposite laterality VCA does not have the first graft flagged as graft failure (ex: a left hand recipient who then registers for a right hand). Currently, when a candidate is registered for upper limb, the laterality is specified so the registration of the separate right and left upper limbs would not indicate the possibility of graft failure for either transplant unless re-registering for the same laterality. Re-registering for the same VCA would also not be what reports the graft as failed, which would be reported separately by the transplant program.

Another possible scenario pertaining to re-registration was how graft failure would be captured if the graft is not removed and the patient does not re-register for the same VCA. In this scenario, the graft would not be reported as graft failure and the approved but not yet implemented data collection on functional outcomes would provide more insight on these grafts.⁴⁴

Data Clarification and Questions

There was overall support for the clarifications being made to the VCA data collection on graft failure, ensuring that successful uterus transplants are not counted as failed grafts, and reporting patient requested removal due to inadequate function as graft failure. AST also noted that a wider array of

³⁹ Ibid.

⁴⁰ S.G. Chiverton, J.A. Murie, R.D. Allen, P. J. Morris, “Renal Transplant Nephrectomy,” *Surgery, Gynecology & Obstetrics*, 164.4 (1987): 324-328, <https://pubmed.ncbi.nlm.nih.gov/3551155/>.

⁴¹ OPTN Policy 1.2 *Definitions* (April 11, 2022).

⁴² VCA Committee Meeting Summary, April 6, 2022, OPTN, accessed May 6, 2022, https://optn.transplant.hrsa.gov/media/tekiukka/20220406_vca-committee-meeting-summary_final.pdf.

⁴³ *Update to VCA Transplant Outcomes Data Collection*, Policy Notice, accessed April 19, 2022, <https://optn.transplant.hrsa.gov/media/3889/update-to-vca-transplant-outcomes-data-collection.pdf>.

⁴⁴ Ibid.

patient causes of death should be included (i.e. cancer, cardiovascular, and infectious death) and are available in the full list outlined in **Appendix 3**.

The question of how the OPTN will evaluate compliance with this proposal was raised throughout discussion and the proposed changes will not alter the routine monitoring of OPTN members; however, the OPTN may review any data entered in the OPTN Computer System and OPTN members must provide any supporting documentation as requested.

Suggestions for Future Proposals

AST suggested that a future Committee project include allowing for VCA programs to set individualized goals for their transplant candidates prior to transplant to allow for future assessment of whether the VCA graft met the patient's goals. The Committee agreed that this is a priority for the VCA community but felt that it would need to be considered whether this is an OPTN role or the role of professional societies in which the OPTN would be included.

Compliance Analysis

NOTA and OPTN Final Rule

The VCA Committee submits this proposal under the authority of NOTA, which requires the OPTN to “collect, analyze, and publish data concerning organ donation and transplants,”⁴⁵ and the OPTN Final Rule, which requires the OPTN to “maintain and operate an automated system for managing information about transplant candidates, transplant recipients, and organ donors...”,⁴⁶ “maintain records of all transplant candidates, all organ donors and all transplant recipients”,⁴⁷ and “operate, maintain, receive, publish, and transmit such records and information electronically”⁴⁸ and requires transplant hospitals “as specified from time to time by the Secretary, to submit to the OPTN...information regarding transplantation candidates, transplant recipients, [and] donors of organs...”⁴⁹ This proposal would collect data on transplant recipients, specifically data regarding their graft status, and if applicable, data on their primary cause of death and functional status of their uterus graft.

Furthermore, per the OPTN Final Rule, “the OPTN shall provide to the Secretary data to assist the Secretary in assessing organ procurement and allocation, access to transplantation, the effect of allocation policies on programs performing different volumes of transplants, and the performance of [organ procurement organizations] and the OPTN contractor... Such data shall include... risk-adjusted patient and graft survival rates following transplantation...”⁵⁰ The OPTN and the Scientific Registry (SRTR) must also “make available to the public timely and accurate program-specific information on the performance of transplant programs,” including “risk-adjusted graft and patient survival following the transplant.”⁵¹

⁴⁵ 42 U.S.C. §274(b)(2)(I).

⁴⁶ 42 CFR §121.11(a)(1)(i).

⁴⁷ 42 CFR §121.11(a)(1)(ii).

⁴⁸ 42 CFR §121.11(a)(1)(iii).

⁴⁹ 42 CFR §121.11(b)(2).

⁵⁰ 42 CFR §121.8(c)(3).

⁵¹ 42 CFR §121.11(b)(1)(iv).

This proposal affects information and records pertaining to transplant recipients as it would modify the data required to be submitted to the OPTN by transplant programs on graft failure for covered VCA transplant recipients, particularly uterus recipients.

OPTN Strategic Plan

Improve waitlisted patient, living donor, and transplant recipient outcomes:

This policy and data collection proposal intends to improve the data collected on VCA recipients to reflect graft failure more accurately as it pertains to VCA. This proposal will also revise and update relevant data collection to more accurately collect data as it pertains to VCA recipient outcomes.

Implementation Considerations

Member and OPTN Operations

The OPTN and transplant hospitals that perform covered VCA transplants would need to modify data collection and reporting practices to implement this proposal, but this proposal is not anticipated to affect the operations of organ procurement organizations or histocompatibility laboratories.

Operations affecting the OPTN

This proposal would require the submission of official OPTN data that are not presently collected by the OPTN via membership application forms. The OPTN Contractor has agreed that data collected pursuant to the OPTN's regulatory requirements in the OPTN Final Rule will be collected through the Office of Management and Budget (OMB) approved data collection forms.⁵² Therefore, after OPTN Board approval, the proposed data collection changes will be submitted for OMB approval under the Paperwork Reduction Act of 1995. This will require a revision of the OMB-approved data collection instruments, which may impact the implementation timeline.

Operations affecting Transplant Programs

Transplant programs performing covered VCA transplants will need to become familiar with the changes to policy and data collection regarding VCA graft failure and how to properly report graft failure for their patients.

Projected Fiscal Impact

This proposal is projected to have a fiscal impact on the OPTN, but no impact on organ procurement organizations and histocompatibility laboratories. There will be an impact for transplant programs regarding data entry.

Projected Impact on the OPTN

This project would require implementing changes to the VCA TRR and TRF forms. The OPTN will incorporate changes approved as part of this proposal into planned implementation for VCA into the OPTN Computer System including the OPTN Waiting List, the OPTN Donor Data and Matching System,

⁵² 34 CFR §121.3(b)(2) "To apply for membership in the OPTN: A transplant hospital shall provide to the OPTN the name and address of the hospital, a list of its transplant programs by type of organ..."; and §121.9(b) "To apply to be a designated transplant program, transplant programs shall provide to the OPTN such documents as the OPTN may require which show that they meet the requirements of §121.9(a) (1), (2), or (3)."

and associated data collection instruments, along with updating to the ten types of covered VCA as outlined in the proposal *Establish Membership Requirements for Uterus Transplant Programs*.⁵³

The OPTN Contractor estimates 1,780 hours for implementation. Implementation will involve updates to the Data System for the OPTN and education on the changes. The OPTN Contractor estimates 125 hours for ongoing support. Ongoing support will involve answering member questions and monitoring graft failure reports at one year and two years post-implementation.

Projected Impact on Transplant Programs

This proposal will only impact transplant programs that perform VCA transplants. This proposal will not have a significant fiscal impact, and no significant resources will be required to implement. There will be initial training required, with costs associated with training data users on the new definitions. That one-time, upfront training will help to streamline consistent data entry for future data analysis. It should take programs less than one month to implement this proposal.

Post-implementation Monitoring

Member Compliance

This proposal will not change current routine monitoring of OPTN members. The OPTN may review any data entered in the OPTN Computer System, and members must provide documentation as requested.

Policy Evaluation

This policy will be formally evaluated approximately 1 year and 2 years post-implementation. The following metrics, and any others subsequently requested by the Committee, will be evaluated as data become available, and as sample size permits, to compare before and after the implementation of this policy:

- Number of VCA transplants, overall and by organ
- Number and percent of VCA graft failures by organ: overall and by reason(s) for graft failure
- Number of uterus planned removals
- Number of hysterectomies reported for uterus recipients on the TRF, overall and by reason for hysterectomy
- Number of VCA recipient deaths by organ and cause of death

Conclusion

This proposal would define graft failure for VCA transplantation separately from the current OPTN definition of graft failure. The proposed definition would define graft failure for VCA as:

- the recipient re-registers for the same covered VCA
- a recipient dies
- or an unplanned removal of a covered VCA

These proposed changes would capture the planned removal of certain types of VCA transplants, most notably uterus, as a success of the graft rather than inaccurately recording the removal as a graft failure.

⁵³ *Establish Membership Requirements for Uterus Transplant Programs*, Policy and Bylaw Notice, accessed April 18, 2022, https://optn.transplant.hrsa.gov/media/gapkr01m/policy-notice_establish-membership-requirements-for-uterus-transplant-programs_december-2021.pdf.

In addition to the proposed definition of VCA graft failure, planned removal of a uterus would also be defined. This proposal will also revise and update relevant data collection to more accurately collect data as it pertains to VCA recipient outcomes as well as further inform the Committee on future projects.

Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary. The [...] signifies language in the current Policy that is not presented here for the purposes of brevity and will not be affected by the proposal.

1 1.2 Definitions

2 The definitions that follow are used to define terms specific to the OPTN Policies.

3 [...]

4 **G**

5 **Graft failure**

6 For all organs except pancreas and covered VCAs, graft failure occurs when *any* of the following occurs:

7

- 8 • A recipient's transplanted organ is removed
- 9 • A recipient dies
- 10 • A recipient is placed on a chronic allograft support system

11

12 Pancreas graft failure occurs when any of the following occurs:

13

- 14 • A recipient's transplanted pancreas is removed
- 15 • A recipient re-registers for a pancreas
- 16 • A recipient registers for an islet transplant after receiving a pancreas transplant
- 17 • A recipient's total insulin use is greater than or equal to 0.5 units/kg/day for a consecutive 90 days
- 18 • A recipient dies

19

20 Covered VCA graft failure occurs when any of the following occurs:

21

- 22 • A recipient re-registers for the same covered VCA
- 23 • A recipient dies
- 24 • An unplanned removal of a covered VCA

25

26 [...]

27 **P**

28 [...]

29 **Planned Removal of a Uterus**

30 A planned removal of a uterus occurs when the graft is removed with the intent of removal recorded
31 either pre-transplant or at time of transplant.

32

33 12.1 Waiting Time

34
 35 Waiting time for candidates registered for a covered VCA begins when the candidate is registered on the
 36 waiting list. Candidates are registered by covered VCA type: upper limb, head and neck, abdominal wall,
 37 ~~genitourinary organ-uterus, external male genitalia, other genitourinary organ~~, vascularized gland, lower
 38 limb, musculoskeletal composite graft segment, or spleen.

40 18.1 Data Submission Requirements

41
 42 **Table 18-1: Data Submission Requirements**

<i>The following member:</i>	<i>Must submit the following instruments to the OPTN:</i>	<i>Within:</i>	<i>For:</i>
Transplant hospitals	<i>Organ Specific Transplant Recipient Follow-up (TRF)</i>	<i>Either of the following:</i> <ul style="list-style-type: none"> • 90 days after the six-month and annual anniversary of the transplant date until the recipient's death, or <u>graft failure, or planned graft removal of a uterus</u> • 14 days from notification of the recipient's death or graft failure 	Each recipient followed by the hospital

43
 44 #
 45

Appendix 1: Proposed Modifications to VCA TRR and TRF Data Collection

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

Data Element	Form	Current Data Collection	Proposed Removal(s) and Proposed Addition(s)
Graft Status	VCA TRR	Functioning Failed Causes of graft failure Acute rejection (Yes/No) If Yes, Banff score (0, I, II, III, IV) If Yes, Visual skin changes (Yes/No) Chronic rejection (Yes/No) If Yes, Visual skin changes (Yes/No) Sepsis/infection (Yes/No) Trauma (Yes/No) Patient requested removal (Yes/No) Other, Specify	Functioning Failed <u>Planned removal</u> <u>Date of removal</u> Causes of graft failure Thrombosis (Yes/No) Acute rejection (Yes/No) If Yes, Banff score (0, I, II, III, IV) If Yes, Visual skin changes (Yes/No) Chronic rejection (Yes/No) If Yes, Visual skin changes (Yes/No) Ischemia (Yes/No) <u>Vascular complications (Yes/No)</u> Sepsis/infection (Yes/No) Trauma (Yes/No) Patient requested removal (Yes/No) Non-compliance: immunosuppression (Yes/No) Non-compliance: rehabilitation (Yes/No) Non-compliance: level of activity (Yes/No) <u>Non-adherence (Yes/No)</u> Other, Specify
Graft status	VCA TRF	Functioning Failed Causes of graft failure Acute rejection (Yes/No) If Yes, Banff score (0, I, II, III, IV) If Yes, Visual skin changes (Yes/No) Chronic rejection (Yes/No) If Yes, Visual skin changes (Yes/No) Sepsis/infection (Yes/No) Trauma (Yes/No) Patient requested removal (Yes/No) Other, Specify	Functioning Failed <u>Planned removal</u> <u>Date of removal</u> Causes of graft failure Thrombosis (Yes/No) Acute rejection (Yes/No) If Yes, Banff score (0, I, II, III, IV) If Yes, Visual skin changes (Yes/No) Chronic rejection (Yes/No) If Yes, Visual skin changes (Yes/No) Ischemia (Yes/No) <u>Vascular complications (Yes/No)</u> Sepsis/infection (Yes/No) Trauma (Yes/No) Patient requested removal (Yes/No) Non-compliance: immunosuppression (Yes/No) Non-compliance: rehabilitation (Yes/No) Non-compliance: level of activity (Yes/No)

Data Element	Form	Current Data Collection	Proposed Removal(s) and Proposed Addition(s)
			<u>Non-adherence (Yes/No)</u> Other, Specify
Patient Status: Primary Cause of Death	VCA TRF	MISC – acid/base disorder MISC – fluid/electrolyte disorder MISC – multiple system organ failure (MSOF) Trauma: motor vehicle	MISC – acid/base disorder MISC – fluid/electrolyte disorder MISC – multiple system organ failure (MSOF) Trauma: motor vehicle <u>Maternal and obstetric mortality: other specify</u>
Hysterectomy	Uterus TRF	Functional Status – Uterus Hysterectomy performed following successful delivery or due to complications: has the recipient received a hysterectomy since transplant of uterus, either performed following successful delivery of neonate or due to complication(s). This field is required. Yes/No/Other – specify	Functional Status – Uterus Hysterectomy performed following successful delivery or due to complications: has the recipient received a hysterectomy since transplant of uterus, either performed following successful delivery of neonate or due to complication(s). This field is required. Yes/No/Other – specify <u>If yes then specify reason:</u> <u>Successful delivery of neonate</u> <u>Complication of graft</u> <u>Reproductive Failure</u> <u>Other: _____</u>

Appendix 2: Proposed Data Definitions

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

VCA TRR

Planned removal: has the recipient had a planned removal of a uterus with the intent of removal recorded either pre-transplant or at time of transplant.

Date of removal: If the recipient's graft status is "Planned removal", enter the date of removal using the standard 8-digit format of MM/DD/YYYY.

Vascular complications (Yes/No): has the graft failed due to vascular complication (not limited to thrombosis or ischemia).⁵⁴

Non-adherence (Yes/No): has the graft failed due to recipient non-adherence to post-transplant treatment (i.e. immunosuppression, rehabilitation, level of activity).⁵⁵

VCA TRF

Planned removal: has the recipient had a planned removal of a uterus with the intent of removal recorded either pre-transplant or at time of transplant.

Date of removal: If the recipient's graft status is "Planned removal", enter the date of removal using the standard 8-digit format of MM/DD/YYYY.

Vascular complications (Yes/No): has the graft failed due to vascular complication (not limited to thrombosis or ischemia).⁵⁶

Non-adherence (Yes/No): has the graft failed due to recipient non-adherence to post-transplant treatment (i.e. immunosuppression, rehabilitation, level of activity).⁵⁷

VCA TRF (Patient Status): Primary Cause of Death

Maternal and obstetric mortality: other specify: was the recipient's death related to pregnancy or obstetric causes. Specify the cause of death in the "Specify" field.

Uterus TRF

Hysterectomy (y/n) and date, performed following successful delivery or due to complication: has the recipient received a hysterectomy since transplant of uterus, either performed following successful delivery of neonate or due to complication(s). This field is required.

⁵⁴ VCA Committee Meeting Summary, September 8, 2021, OPTN, accessed November 3, 2021, https://optn.transplant.hrsa.gov/media/g0hlxcgy/20210908_vca-committee-meeting-summary.pdf.

⁵⁵ VCA Committee Meeting Summary, May 12, 2021, OPTN, accessed November 3, 2021, https://optn.transplant.hrsa.gov/media/4661/20210512_vca-committee-meeting-summary_final.pdf.

⁵⁶ Ibid.

⁵⁷ Ibid.

Yes/ No/ Other—specify

_____ If Other, specify the reason for the hysterectomy in the Specify field

If yes then specify reason:

Successful delivery of neonate

Due to complication(s)

Reproductive Failure⁵⁸

Other: _____

⁵⁸ VCA Committee Meeting Summary, October 7, 2021, OPTN, accessed December 2, 2021, https://optn.transplant.hrsa.gov/media/g50hpn0s/optn_vca_summary_20211007_final.pdf.

Appendix 3: Patient Status: Primary Cause of Death Selection Options

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

Acid/base disorder
 Graft failure: non-specific
 Acute pancreatitis
 Graft failure: recurrent disease
 AIDS
 Graft failure: technical
 Brain dead: never recovered from surgery
 Graft failure: other specify
 Cardiac arrest
 Graft failure: primary
 Cerebrovascular: brain anoxia
 Graft failure: rejection
 Cerebrovascular: degenerative brain disease
 Graft failure: vascular thrombosis
 Cerebrovascular: embolic stroke
 Graft vs. host disease
 Cerebrovascular: hemorrhage (non-stroke)
 Hematologic other specify
 Cerebrovascular: hemorrhagic stroke
 Hemorrhage
 Diabetes mellitus
 Hemorrhage: disseminated intravas coagulation
 Fluid/electrolyte disorder
 Immunosuppressive drug related - hematologic
 Graft failure: graft infection
 Immunosuppressive drug related – non-hematologic
 Infection: bacterial – other specify
 Malignancy
 Infection: bacterial pneumonia
 Malig: lymphoma
 Infection: bacterial septicemia
 Malignancy: metastatic other specify
 Infection: fungal
 Malignancy: other specify
 Infection: mixed other specify
 Malignancy: post-tx lymphoproliferative
 Infection: other specify
 Malignancy: primary other specify
 Infection: protozoal
~~MISC – acid/base disorder~~
 Infection: urinary tract
~~MISC – fluid/electrolyte disorder~~

Infection: viral
MISC—multiple system organ failure (MSOF)
Infection: viral – cytomegalovirus (CMV)
Motor vehicle accident
Infection: viral – hepatitis
Multiple organ failure
Intraop: not hemorrhage – other specify
Multiple organ system failure
Non-compliance
Non-immuno – non-hematologic, specify drug
Non-immuno drug related – hematologic
Non-immune drug related – non-hematologic, specify drug
Other specify
Pulm insuff or edema (exc pneumonia) (ARDS)
Renal failure
Reperfusion syndrome
Respiratory failure: other specify cause
Suicide
Suicide: attempted suicide – died later
Trauma other specify
~~Trauma: motor vehicle~~
Maternal and obstetric mortality: other specify
Unknown