Review Board Guidance for Hypertrophic/Restrictive (HCM/RCM) Cardiomyopathy Exception Requests

Summary and Goals

The OPTN/UNOS Board of Directors recently approved the Thoracic Organ Transplantation Committee's (Committee) Proposal to Modify the Adult Heart Allocation System during its December 2016 meeting.[1] One of the major components of the new allocation system was the creation of three additional medical urgency statuses, for a new total of six. This new six-status system stratifies heart transplant candidates according to waiting list mortality.

During the development of the adult heart allocation policy, the Committee received feedback from the heart transplant community that hypertrophic and restrictive cardiomyopathy (HCM/RCM) candidates may be disadvantaged by the new system, as they are a heterogeneous candidate group and they may not always be optimal candidates for devices or inotropes, and these candidates therefore would not qualify for most of the higher urgency statuses. Specific examples include HCM patients with end-stage diastolic heart failure, but with preserved systolic function. For these patients with small left ventricular cavities, with low cardiac output and high filling pressures, inotropes may provide little benefit and possibly cause harm.[2,3] Similarly, placement of a mechanical circulatory support cannula into a small, stiff left ventricle may not provide adequate unloading, and may precipitate right ventricular failure, suction events, thrombosis and low flow alarms.[4,5,6,7]

The Committee acknowledged that some HCM/RCM candidates may have a higher waiting list mortality, warranting a status but there were insufficient data to create qualifying criteria for these candidates in higher than Tier 4.urgency statuses. The new allocation policy includes hemodynamic criteria in addition to criteria based on levels of support. While these hemodynamic criteria will likely apply to most HCM/RCM candidates with advanced disease, improvements in hemodynamic parameters after initiation of inotropes may not require high doses or dual therapies, and in some instances may not safely provide support while awaiting transplant. Thus strict criteria regarding drug doses may be unnecessary and may precipitate destabilizing arrhythmias. Therefore, HCM/RCM candidates may have difficulty meeting criteria for higher status according to policy, despite potentially having waitlist mortality equivalent to other candidates at higher statuses.[8] Instead, the review board exception and review process will continue to accommodate these candidates, who can apply for an exception at any status as their medical urgency

---

[1] OPTN/UNOS Policy Notice. *Proposal to Modify the Adult Heart Allocation System*. Accessed June 27, 2017. https://optn.transplant.hrsa.gov/media/2028/thoracic_policynotice_201612.pdf .

[2] Rowin, J., Ethan, Maron, J., Barry, Kiernan, S., Michael, Casey, A., Susan, Feldman, S., David, Hryniewicz, M., Katarzyna, Chan, H., Raymond, Harris, M., Kevin, Udelson, E., James, Denofrio, C., David, Roberts, S., William, and Maron, S., Martin. "Advanced Heart Failure With Preserved Systolic Function in Nonobstructive Hypertrophic Cardiomyopathy: Under-Recognized Subset of Candidates for Heart Transplant." *Circulation: Heart Failure* 7, no. 6 (2014): 967-75.

[3] Pasqualucci, Fornaro, Castelli, Rossi, Arretini, Chiriatti, Targetti, Girolami, Corda, Orrù, Matta, Stefàno, Cecchi, Porcu, and Olivotto. "Clinical Spectrum, Therapeutic Options, and Outcome of Advanced Heart Failure in Hypertrophic Cardiomyopathy." *Circulation: Heart Failure* 8, no. 6 (2015): 1014-021.

[4] Topilsky Y, Pereira NL, Shah DK et al. Left ventricular assist device therapy in patients with restrictive and hypertrophic cardiomyopathy. *Circ Heart Fail* 2011;4(3):266-275.

[5] Muthiah K, Phan J, Robson D et al. Centrifugal continuous-flow left ventricular assist therapy for patients with hypertrophic cardiomyopathy: a case series. *American Society for Artificial Internal Organs.* 2013;59:183-187.

[6] Sivathasan, Cumaraswamy, Teing E. E. Tan, David Sim, and Ka Lee Kerk. "Burnt Out" Dilated Hypertrophic Cardiomyopathy Causing Acute LVAD Thrombosis." *Clinical Case Reports* 3, no. 6 (2015): 376-78.

[7] Grupper, Park, Pereira, Schettle, Gerber, Topilsky, Edwards, Daly, Stulak, Joyce, and Kushwaha. "Role of Ventricular Assist Therapy for Patients with Heart Failure and Restrictive Physiology: Improving Outcomes for a Lethal Disease." *Journal of Heart and Lung Transplantation* 34, no. 8 (2015): 1042-049.

[8] OPTN/UNOS Policy Notice. *Proposal to Modify the Adult Heart Allocation System.*

and potential for benefit would warrant, including status 1. The Committee drafted this guidance with the goal of helping review boards standardize decision-making for HCM/RCM exception requests.

Contents

Review Board Guidance for Hypertrophic/Restrictive (HCM/RCM) Cardiomyopathy Exception Requests

Background

Hypertrophic cardiomyopathy (HCM) is a common genetic cardiomyopathy with a prevalence in the general population of 1:500.[9,10] Mutations in genes encoding proteins of the cardiac sarcomere are responsible for HCM and result in a heterogeneous phenotypic expression and clinical course.[11,12] The penetration of a mature sudden death risk stratification algorithm and the implantable cardioverter defibrillator (ICD) have decreased sudden death events and shifted the pendulum toward greater recognition of heart failure, including an increasing subgroup with advanced refractory heart failure symptoms who are candidates for transplantation.

The most common mechanism responsible for heart failure symptoms in HCM is dynamic left ventricular (LV) outflow tract obstruction, due to mitral valve-ventricular septal contact. Obstructive HCM patients with advanced symptoms refractory to medical therapy are candidates for invasive septal reduction therapies (i.e. surgical myectomy or alcohol septal ablation), which are highly effective at substantially improving (or eliminating) heart failure symptoms. Therefore, obstructive HCM patients are not generally candidates for heart transplant listing.

Although relatively uncommon, non-obstructive HCM patients can develop end-stage advanced heart failure. Approximately 50% of these patients demonstrate phenotypic transformation from diastolic dysfunction to LV pump failure with systolic dysfunction (ejection fraction (EF) ≤50%) and adverse LV remodeling involving wall thinning and/or ventricular chamber enlargement due to diffuse myocardial scarring.[13] The remaining non-obstructive HCM patients with refractory heart failure symptoms demonstrate preserved systolic function (ejection fraction (EF) $\geq$ 50%) with a non-dilated LV cavity associated with impaired cardiac output, often associated with impaired LV filling, and pulmonary hypertension. This subset of HCM patients with preserved LV function may progress to New York Heart Association (NYHA) Class IV heart failure with refractory symptoms and poor hemodynamics and are unable to be clinically stabilized on intravenous inotropes and are not candidates for mechanical support devices.[14] Importantly, development of significant pulmonary hypertension, such that hospitalization and attempts at amelioration with continuous inotropes and diuretics are needed, may signal a “fork in the

---

[9] Maron BJ, Gardin JM, Flack JM et al. Prevalence of hypertrophic cardiomyopathy in a general population of young adults: echocardiographic analysis of 4111 subjects in the CARDIA Study Coronary Artery Risk Development in (Young) Adults. *Circ* 1995;92:785-789.

[10] Gersh BJ, Maron BJ, Bonow RO et al. 2011 ACCF/AHA Guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2011;124:37-85. DOI: 10.1161/CIR.0b013e318223e2bd

[11] Maron, Martin S., Maron, Barry J., Harrigan, Caitlin, Buros, Jacki, Gibson, C. Michael, Olivotto, Iacopo, Biller, Leah, Lesser, John R., Udelson, James E., Manning, Warren J., and Appelbaum, Evan. "Hypertrophic Cardiomyopathy Phenotype Revisited After 50 Years With Cardiovascular Magnetic Resonance." *Journal of the American College of Cardiology* 54, no. 3 (2009): 220-28.

[12] Maron, Barry J, Seidman, Christine E, Ackerman, Michael J, Towbin, Jeffrey A, Maron, Martin S, Ommen, Steve R, Nishimura, Rick A, and Gersh, Bernard J. "How Should Hypertrophic Cardiomyopathy Be Classified?: What's in a Name? Dilemmas in Nomenclature Characterizing Hypertrophic Cardiomyopathy and Left Ventricular Hypertrophy." *Circulation. Cardiovascular Genetics* 2, no. 1 (2009): 81-5.

[13] Ho, Carolyn Y., López, Begoña, Coelho-Filho, Otavio R., Lakdawala, Neal K., Cirino, Allison L., Jarolim, Petr, Kwong, Raymond, González, Arantxa, Colan, Steven D., Seidman, J.G., Díez, Javier, and Seidman, Christine E. "Myocardial Fibrosis as an Early Manifestation of Hypertrophic Cardiomyopathy." *The New England Journal of Medicine* 363, no. 6 (2010): 552-63.

[14] Rowin, EJ, et al., “Advanced heart failure with preserved systolic function in nonobstructive hypertrophic cardiomyopathy” *Circulation Heart Failure* no 6, 2014, 967-975, doi: 10.1161/CIRCHEARTFAILURE.114.001435 .

road" where urgent or semi-urgent transplant is required before the patient becomes too high risk for successful transplant because of high pulmonary vascular resistance (PVR).[15]

Restrictive cardiomyopathy (RCM) includes genetic disorders of the sarcomere and cytoskeleton, infiltrative cardiomyopathies secondary to glycogen storages diseases, and amyloid deposition disease from either bone-marrow derived light chains (primary systemic amyloidosis (AL)) or from mutational or wild-type transthyretin protein made in the liver (transthyretin (TTR) cardiac amyloidosis).[16,17,18] Patients may also have an idiopathic RCM (restrictive physiology without any contributing etiology such as atherosclerosis), which may ultimately be genetic-based or secondary to radiation.[19] RCM manifests as dilated atria, non-dilated thickened ventricles, with diastolic dysfunction/restrictive physiology, exhibiting ventricular interdependence, low stroke volumes and often atrial arrhythmias. As with HCM, there is progressive exercise intolerance, end-organ dysfunction, including development of pulmonary hypertension, cardiorenal syndrome, congestive hepatopathy, and ultimately Stage IV heart failure requiring transplant.

While restrictive physiology is a common denominator across the above RCM subtypes, prognoses differ vastly amongst underlying disease categories. Patients with advanced AL amyloidosis have high rates of waitlist mortality, with additional complications related multi-organ involvement.[20] This is in contrast to idiopathic RCM, where there may be a more prolonged decline, similar to TTR amyloid, with the exception of the V122I genotype/phenotype.[21]

In end-stage heart failure, mechanical support options are limited for the vast majority of patients with HCM or RCM and non-dilated ventricles and/or biventricular disease.[22] Total artificial heart surgery is a treatment option, but is limited to few specialized centers, with significant perioperative morbidity and mortality in low volume centers.[23] Given that current allocation schemes give higher transplant priority to patients placed on mechanical support, it is particularly challenging for HCM/RCM patients to advance in priority on the transplant list. This issue has raised concern that HCM/RCM patients who experience progressive biventricular heart failure symptoms are subject to a measure of inequality with respect to pathway to transplant, especially in areas of marked organ shortage where the majority of transplants are

---

[15] Ong, Kevin C., Jeffrey B. Geske, Virginia B. Hebl, Rick A. Nishimura, Hartzell V. Schaff, Michael J. Ackerman, Kyle W. Klarich, Konstantinos C. Siontis, Thais Coutinho, Joseph A. Dearani, Steve R. Ommen, and Bernard J. Gersh. "Pulmonary Hypertension Is Associated with Worse Survival in Hypertrophic Cardiomyopathy." European Heart Journal – Cardiovascular Imaging 17, no. 6 (2016): 604-10.

[16] Kostareva, Anna, Kiselev, Artem, Gudkova, Alexandra, Frishman, Goar, Ruepp, Andreas, Frishman, Dmitrij, Smolina, Natalia, Tarnovskaya, Svetlana, Nilsson, Daniel, Zlotina, Anna, Khodyuchenko, Tatiana, Vershinina, Tatiana, Pervunina, Tatiana, Klyushina, Alexandra, Kozlenok, Andrey, Sjoberg, Gunnar, Golovljova, Irina, Sejersen, Thomas, and Shlyakhto, Eugeniy. "Genetic Spectrum of Idiopathic Restrictive Cardiomyopathy Uncovered by Next-Generation Sequencing." *PloS One* 11, no. 9 (2016): E0163362.

[17] Gray Gilstrap, Niehaus, Malhotra, Ton, Watts, Seldin, Madsen, and Semigran. "Predictors of Survival to Orthotopic Heart Transplant in Patients with Light Chain Amyloidosis." *Journal of Heart and Lung Transplantation* 33, no. 2 (2014): 149-56.

[18] Castaño, Adam, Brian Drachman, M. Judge, and Daniel Maurer. "Natural History and Therapy of TTR-cardiac Amyloidosis: Emerging Disease-modifying Therapies from Organ Transplantation to Stabilizer and Silencer Drugs." *Heart Failure Reviews* 20, no. 2 (2015): 163-78.

[19] Saxena, Joyce, Daly, Kushwaha, Schirger, Rosedahl, Dearani, Kara, and Edwards. "Cardiac Transplantation for Radiation-Induced Cardiomyopathy: The Mayo Clinic Experience." *The Annals of Thoracic Surgery* 98, no. 6 (2014): 2115-121.

[20] Gilstrap, 2014.

[21] Ruberg, Maurer, Judge, Zeldenrust, Skinner, Kim, Falk, Cheung, Patel, Pano, Packman, and Grogan. "Prospective Evaluation of the Morbidity and Mortality of Wild-type and V122I Mutant Transthyretin Amyloid Cardiomyopathy: The Transthyretin Amyloidosis Cardiac Study (TRACS)." *American Heart Journal* 164, no. 2 (2012): 222-28.e1.

[22] Topilsky et al., 2011.

[23] Arabia, Gregoric, Kasirajan, Moriguchi, Naftel, Myers, and Kirklin. "(237) - Total Artificial Heart (TAH): Survival Outcomes, Risk Factors, Adverse Events in Intermacs." *Journal of Heart and Lung Transplantation* 35, no. 4 (2016): S95.

for patients who are listed at the highest urgency statuses. Upgrade on the heart transplant waiting list typically requires application for exception status and use of inotropes at specified doses that may not improve cardiac output in this unique subgroup of cardiomyopathy patients and may expose patients to significant arrhythmias. Lastly, recent data has suggested that transplant list mortality for HCM patients may not be low as previously considered.[24]

Data on heart transplantation in these populations yield the following insights:

- Patients with HCM are typically younger with fewer co-morbidities as compared to non-HCM candidates and have equal or superior long-term survival.[25,26,27]
- A subset of HCM patients with preserved LV function may progress to NYHA Class IV heart failure with refractory symptoms and poor hemodynamics and are unable to be clinically stabilized on intravenous inotropes and are not candidates for mechanical support devices.[28]
- Data extrapolated from children with RCM indicate that high waitlist mortality is associated with need for inotrope use, along with need for intra-aortic balloon pump (IABP), ventricular assist devices (VAD) or extracorporeal membraneous oxygenator therapies (ECMO).[29] Other data in adults with RCM indicate that the RCM diagnosis alone is a marker for worse waitlist outcomes.[30]
- Based on an analysis of the OPTN database from 2009-2016, patients with RCM are less likely to receive a VAD as bridge to transplant by 28.2%, with a multivariate risk score for poor waitlist survival including frailty, renal dysfunction, elevated pulmonary capillary wedge pressure > 20 mmHg and need for inotrope at listing.[31]
- Successful heart transplant in patients with cardiac amyloidosis (or heart-liver transplant for patients with mutational TTR) depends on experienced amyloid centers making timely referrals to transplant centers with appropriate comprehensive diagnostic capabilities for assessment of systemic involvement timely organ availability and experience with chemotherapy prior to and shortly after

---

[24] Rowin EJ, Maron BJ, Abt P et al. The impact of advanced therapies in improving survival to heart transplant in hypertrophic cardiomyopathy. Unpublished manuscript (2017).

[25] Maron, Martin S., Benjamin M. Kalsmith, James E. Udelson, Wenjun Li, and David DeNofrio. "Survival after Cardiac Transplantation in Patients with Hypertrophic Cardiomyopathy." *Circulation: Heart Failure* 3, no. 5 (2010): 574-79.

[26] Kato, Takayama, Yoshizawa, Marboe, Schulze, Farr, Naka, Mancini, and Maurer. "Cardiac Transplantation in Patients with Hypertrophic Cardiomyopathy." *The American Journal of Cardiology* 110, no. 4 (2012): 568-74.

[27] Rowin et al. The impact of advanced therapies in improving survival to heart transplant in hypertrophic cardiomyopathy, 2017.

[28] Rowin et al. Advanced heart failure with preserved systolic function in nonobstructive hypertrophic cardiomyopathy, 2014.

[29] Zangwill, Steven D., Naftel, David, L&Amp;Apos, Ecuyer, Thomas, Rosenthal, David, Robinson, Blair, Kirklin, James K., Stendahl, Gail, and Dipchand, Anne I. "Outcomes of Children With Restrictive Cardiomyopathy Listed for Heart Transplant: A Multi-institutional Study." *Journal of Heart and Lung Transplantation* 28, no. 12 (2009): 1335-340.

[30] Hsich, Rogers, Mcnamara, Taylor, Starling, Blackstone, and Schold. "Does Survival on the Heart Transplant Waiting List Depend on the Underlying Heart Disease?" *JACC: Heart Failure* 4, no. 9 (2016): 689-97.

[31] Sridharan L, Givens R, Takeda K et al. The new heart allocation system: Implications on patients with restrictive cardiomyopathy in the UNOS registry. *J Heart Lung Transplant* 36 (2017): S129

organ transplant.[32,33,34] A key variable in survival of patients with amyloidosis is organ transplant based on progressive heart failure *in the context* of a progressive systemic medical illness.

- There is sparse literature on the outcomes of patients with radiation induced cardiomyopathy, especially as patients with restrictive/non-dilated cardiomyopathy were combined with systolic dysfunction.[35,36,37] Overall, post-transplant outcomes in patients with prior radiation appear to be worse than those without prior radiation, mostly related to post-transplant lung cancer and other complications, irrespective of prior restrictive physiology.
- In end-stage heart failure, mechanical support options are limited for the vast majority of patients with HCM or RCM and non-dilated ventricles and/or biventricular disease.[38] Total artificial heart (TAH) surgery is a treatment option, but is limited to few specialized centers, with significant perioperative morbidity and mortality in low volume centers.[39]

Given that the current allocation policy prioritizes patients in cardiogenic shock requiring mechanical support, it is particularly challenging for HCM/RCM patients to advance in priority on the transplant list. This issue has raised concern that HCM/RCM patients who experience progressive heart failure symptoms, and who may be on the precipice of cardiogenic shock, may be subject to a measure of inequality with respect to pathway to transplant. Upgrade on the heart transplant waiting list typically requires application for exception status and use of inotropes at specified doses that may modestly improve cardiac output in these unique subgroup of cardiomyopathy patients, but may precipitate destabilizing arrhythmias without an adequate back up mechanical support option.

Within the diverse spectrum of cardiovascular diseases, which can progress to advanced heart failure, patients with HCM, RCM and amyloid represent a subgroup with unique considerations with respect to priority for transplant listing. Many of these patients develop low output heart failure, often in the setting of normal (or near normal) systolic function. Unfortunately, the opportunity to improve end-stage heart failure clinical symptoms and/or hemodynamics is limited compared to other cardiovascular diseases since intravenous inotropes are often ineffective (or not well tolerated) in these patients and mechanical support as a bridge to transplant can be technically challenging with higher complication rates and may provide inadequate unloading.[40,41] Taken together, these considerations, as well as the recent observation that transplant list mortality may not be as low as previously considered for HCM, raise important considerations to providing alternative organ allocation schemes which address more specifically these considerations.

The following recommendations are intended to provide objective criteria to guide decision-making in granting access to higher urgency statuses for those HCM, RCM or amyloid patients who meet specific clinical and/or hemodynamic variables, and in the process provide an aspect of greater equality in transplant priority listing.

---

[32] Castano, 2015.

[33] Gray Gilstrap, 2014.

[34] Varr, Liedtke, Arai, Lafayette, Schrier, and Witteles. "Heart Transplantation and Cardiac Amyloidosis: Approach to Screening and Novel Management Strategies." *Journal of Heart and Lung Transplantation* 31, no. 3 (2012): 325-31.

[35] Uriel, Vainrib, Jorde, Cotarlan, Farr, Cheema, Naka, Mancini, and Colombo. "Mediastinal Radiation and Adverse Outcomes after Heart Transplantation." *Journal of Heart and Lung Transplantation* 29, no. 3 (2010): 378-81.

[36] Saxena, 2014.

[37] Depasquale, Nasir, and Jacoby. "Outcomes of Adults with Restrictive Cardiomyopathy after Heart Transplantation." *Journal of Heart and Lung Transplantation* 31, no. 12 (2012): 1269-275.

[38] Topilsky, 2011.

[39] Arabia, Gregoric, Kasirajan, Moriguchi, Naftel, Myers, and Kirklin. "(237) - Total Artificial Heart (TAH): Survival Outcomes, Risk Factors, and Adverse Events in Intermacs." *Journal of Heart and Lung Transplantation* 35, no. 4 (2016): S95.

[40] Topilsky, 2011.

[41] Grupper et al., 2015.

Recommendations

In all cases, candidates must be admitted to the transplant hospital that registered the candidate on the waiting list to be eligible for exceptions to statuses 1-3.

Diagnoses Included within this Guidance

The criteria described herein is appropriate for the following diagnoses groups:

- HCM diagnosis based on 2011 American College of Cardiology Foundation/American Heart Association Hypertrophic Cardiomyopathy Guidelines:[42]

  "…a disease state characterized by unexplained LV hypertrophy associated with nondilated ventricular chambers in the absence of another cardiac or systemic disease that itself would be capable of producing the magnitude of hypertrophy evident in a given patient, with the caveat that patients who are genotype positive may be phenotypically negative without overt hypertrophy. Clinically, HCM is usually recognized by maximal LV wall thickness _15 mm, with wall thickness of 13 to 14 mm considered borderline, particularly in the presence of other compelling information (e.g., family history of HCM), based on echocardiograph".

- Primary restrictive cardiomyopathy, of idiopathic or genetic origin, or secondary to radiation
- Infiltrative cardiomyopathy (e.g. cardiac amyloidosis (TTR or AL)), based on American Heart Association criteria 2006/International Society of Heart and Lung Transplantation 2016 guidelines[43]

Diagnoses Not Included Within This Guidance

While all patients are potentially eligible for exception status based on individual circumstances, this guidance document is intended to apply only to patients with primary HCM/RCM and small ventricular chamber size. Application of these criteria to candidates with the following clinical conditions is therefore not warranted:

- Patients with restrictive physiology as a secondary consequence of other cardiac disease. Therefore, coronary artery disease or transplant coronary artery vasculopathy or chronic rejection, for example, do not fall under this guidance.
- Review boards should use caution in applying these criteria to patients with a primary diagnosis of HCM, but who are otherwise candidates for mechanical support. The guidance is intended for candidates with restricted ventricular chamber size (non-dilated left ventricular end-diastolic dimension indexed to body surface area [BSA]) and normal systolic function (eg. EF > 45%) who are therefore poor candidates for ventricular assist devices.

Criteria

Most candidates, in the absence of the conditions below, are appropriately categorized in status 4. Table 1 provides useful guidance for review boards asked to approve registration in a higher urgency status by exception for hypertrophic, primary or infiltrative or radiation-induced restrictive cardiomyopathy.

---

[42] Gersh et al., 2011.

[43] Mehra, Canter, Hannan, Semigran, Uber, Baran, Danziger-Isakov, Kirklin, Kirk, Kushwaha, Lund, Potena, Ross, Taylor, Verschuuren, and Zuckermann. "The 2016 International Society for Heart Lung Transplantation Listing Criteria for Heart Transplantation: A 10-year Update." *Journal of Heart and Lung Transplantation* 35, no. 1 (2016): 1-23.

Table 1: Recommended criteria for HCM/RCM status exceptions

If the candidate meets this criteria:	Then the candidate may be eligible for:
Is admitted to the transplant hospital that registered the candidate on the waiting list, has ongoing symptoms of NYHA class IV heart failure symptoms, and meets *all* of the following: 1. Continuous monitoring of hemodynamic data, including cardiac output, with a pulmonary artery catheter 2. Within 24 hours prior to submitting the exception request, *all* of the following are true: a. Candidate reached maximally-tolerated inotropic dosages, as evidenced by documented intolerance at higher dosages (e.g. hypotension, vasodilation, hemodynamically unstable atrial or ventricular arrhythmias) b. Candidate has *either* of the following on maximally tolerated inotropes: • *At least 2* indicators of hemodynamic instability as shown below • One indicator of hemodynamic instability *and* at least one indicator of end-organ dysfunction as shown below **Hemodynamic instability indicators:** • Systolic blood pressure < 90 mmHg • Left or right atrial pressure, left or right ventricular end-diastolic pressure, or pulmonary capillary wedge pressure greater than 20 mmHg • Persistently low cardiac index ≤ 2.2 L/min/m2 • $Sv0_2$ < 50% • Persistent transpulmonary gradient (TPG) ≥ 15 mmHg • Persistent pulmonary vascular resistance (PVR) ≥ 2.5 Wood units **End organ dysfunction indicators:** • Elevated arterial lactate to 2.5 mmol/L • Increase in serum creatinine > 50% above baseline • Increase in total bilirubin > 50% above baseline • AST or ALT > 2x upper limit of normal	**Status 2 exception**
Is admitted to the transplant hospital that registered the candidate on the waiting list, has ongoing symptoms of NYHA class IV heart failure symptoms, and meets *all* of the following: 1. Has *one* of the following: • Invasive pulmonary artery catheter • Daily hemodynamic monitoring to measure cardiac output and left ventricular filling pressures 2. Is supported by continuous inotropic infusion to improve end-organ perfusion/function 3. Prior to initiation of inotropes, demonstrated evidence of decompensated heart failure, as evidenced by *at least two* of the following: • Systolic blood pressure < 90 mmHg • Left or right atrial pressure, left or right ventricular end-diastolic pressure, or pulmonary capillary wedge pressure greater than 20 mmHg • Transpulmonary gradient (TPG) ≥ 15 mmHg • Pulmonary vascular resistance (PVR) ≥ 2.5 Woods units • Cardiac index < 1.8 L/min	**Status 3 exception**

Extensions

According to policy, candidates at higher statuses due to temporary support modalities must generally demonstrate a failure to wean the temporary support in order to extend the status beyond specified periods. Because of the complexity of managing patients with HCM/RCM, a failure to wean should not be required in all patients. However, it is recommended that the requesting center demonstrate a failed attempt to wean inotrope support.

Conclusion

In summary, patients with HCM/RCM represent a small, but perhaps growing cohort of patients who advance to end-stage heart failure and require heart transplantation. The new heart allocation policy was created on the basis of thoracic simulation allocation modeling (TSAM) which indicated that these patients should be prioritized as Status or Tier 4.[44] However, there is great heterogeneity within these disease categories. Some candidates may have urgency comparable to higher status candidates with other etiologies without meeting standard policy criteria for those statuses. This guidance document provides a more standardized approach to the evaluation of exception requests in such candidates. It should minimize variability in access to transplantation and limit the extent to which some candidates with HCM/RCM might be disadvantaged under the current allocation scheme.

#

[44] Scientific Registry of Transplant Recipients. "*HR2015_01.*"