Editorial

Should Patients With Cardiac Amyloidosis be Prioritized for Heart Transplantation?

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Amyloidosis is caused by the extracellular deposition of misfolding fibrillary protein, resulting in multiorgan system dysfunction. Three types of systemic amyloidosis are reported to involve the heart commonly, including light-chain amyloidosis (AL), hereditary mutated transthyretin amyloidosis (ATTRm) and wild-type transthyretin amyloidosis (ATTRwt).[1] The prognosis of cardiac amyloidosis (CA) is poor, in general, but varies depending on the type of amyloidosis. AL CA has the worst prognosis, with a median survival of 6 months, while ATTRm and ATTRwt CA are less aggressive, with a median survival of 2.5−3.5 years without treatment after initial diagnosis,[2,3] though the clinical identification of both forms of ATTR CA is often delayed.[4]

Treatment of AL CA is limited. Pharmacologic therapy, including angiotensin-converting enzyme inhibitors and β-blockers, often are not well tolerated or are contraindicated due to worsening renal function, hypotension or conduction disease, and they have not been shown to improve survival rates in this population. Furthermore, implantable cardioverter-defibrillator implantation offers no survival benefit in patients with AL CA. Left ventricular assist device implantation is generally not appropriate due to the small left ventricular chamber that is common with CA.[5] Specific therapy with chemotherapy, including bortezomib-based therapy followed by autologous stem cell transplantation (ASCT), has improved overall survival for AL amyloidosis in recent years.[6] However, for patients with Mayo stage III AL CA, the median survival after chemotherapy was only 7 months,[7] though bortezomib-based therapy improved median survival to over 12 months.[8,9]

Heart transplantation (HT), therefore, is a potential option for these patients. However, prior to the ASCT era, many patients were excluded from being listed for HT due to multiple system involvement, and patients with AL CA who received HT had poor long-term survival due to recurrence of AL with deposition in the allograft.[10] Over the past 2 decades, a few centers have reported a small number of carefully selected AL CA patients who underwent HT followed by ASCT and had an improved survival rate that is comparable to that of patients without CA,[11−13] and similar results were reported in selected patients with isolated AL CA treated with chemotherapy and HT.[14] As a consequence, there has been a push to prioritize patients with all forms of CA on the transplant waitlist.

The 2016 International Society for Heart Lung Transplantation Listing Criteria for Heart Transplantation guidelines makes the following recommendations: selected patients with heart failure due to AL amyloidosis who are not candidates for disease-specific therapies due to cardiovascular compromise may be considered for HT in experienced centers with established collaborations between cardiovascular and hematology teams. ASCT should be planned as soon as clinically feasible after recovery from HT (Class IIA).[15]

In the current issue of the Journal, Panhwar et al report that based on the United Network for Organ Sharing registry, patients with CA were less likely to be listed at highest priority status for orthotopic HT and were at increased risk of waitlist mortality and mortality/delisting compared to patients with dilated cardiomyopathy.[16] The limitations of this study are obvious due to the nature of the registry data, which has significant selection bias, and because the specific type of amyloidosis cannot be identified. The time-to-event period seems to be shorter in patients with CA, but the variation is large, and there is significant overlap between the CA and non-CA groups. Nonetheless, the results from this study are in line with previous reports and support the prioritization of patients with CA on the HT waitlist.[13]

On October 18, 2018, the Organ Procurement and Transplantation Network updated its allocation policy of hearts; the prior 3-tier system (statuses 1A, 1B and 2) was upgraded to a 6-tier system (statuses 1−6). CA has now been

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categorized as status 4, with a similar priority to the prior status 1B.[16] It is important to note that the new allocation policy does not specify the subtype of CA. Prioritizing all patients with CA does not seem to be necessary based on our current knowledge, and we are still not sure how much impact early screening and the initiation of new therapies approved for ATTR amyloid would have on the progression of ATTR CA to the advanced stage that would ultimately need an HT. In addition, the studies that support policy changes are derived from some highly selected patients with AL CA in a limited number of experienced centers; thus, these results may not be generalizable beyond these centers. How many patients with AL (and ATTR) CA can benefit from such changes remains to be seen, and the uncertainty about best practice is likely to continue.

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