EDITORIAL

The quest for noninvasive predictors of pulmonary vascular resistance in heart transplant candidates

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by Szczurek et al, see p. 830

Heart transplantation has become the definitive therapy for end-stage heart failure with the median survival reaching 12.5 years. Pulmonary hypertension poses a distinct challenge to graft function and patient survival after heart transplant. In the early years of heart transplant, acute right ventricular failure was identified in patients with pulmonary hypertension; in 1971, Griepp et al[1] published their outcomes linking the early right ventricular failure and deaths of patients with PH prior to transplant.

Detecting patients who have pulmonary vascular resistance (PVR) that is preclusive for heart transplant is crucial to optimize survival but also to identify patients who may benefit from therapies such as the use of left ventricular assist devices that may decrease pulmonary hypertension and restore eligibility for heart transplant.[2]

Right heart catheterization has been established as the gold standard for diagnosing pulmonary hypertension prior to transplant as well as determining responsiveness to therapies and improvement with left ventricular unloading.[3] Right heart catheterization is an invasive procedure (albeit one that is usually low risk and tolerated well) and does have some risk of complications.[4] Alternative methods of detecting pulmonary hypertension such as spectral Doppler imaging have proven to be inaccurate and unreliable.[5,6]

In this issue of *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*), Szczurek et al[7] present a retrospective analysis of patients with end-stage heart failure evaluated for heart transplant at a single center between 2016 and 2018. The authors performed univariable logistic regression to identify potential predictive variables followed by a multivariable logistic regression model. The primary endpoint was determining the association of clinical variables and models associated with increased PVR, defined in this study as a PVR of more than 3 WU.

Out of 341 patients who were undergoing evaluation for heart transplant, the investigators identified 282 patients who met the study inclusion criteria. The patient population was largely male (87.9%) and older (mean age 57). In this group of patients, 30.1% had increased PVR. Of note, patients with irreversible pulmonary hypertension were already excluded by predefined exclusion criteria.

The authors found significant association of lower heart failure survival scores (HFSS) (OR, 0.590; 95% CI, 0.383–0.908; $P = 0.0164$), higher Model for End-Stage Liver Disease excluding INR (MELD-XI) scores (OR, 1.127; 95% CI, 1.024–1.24; $P = 0.0141$), and higher alkaline phosphatase levels (OR, 1.016; 95% CI, 1.007–1.024; $P = 0.0004$) as independently associated with elevated PVR.

In 2013, Miller et al[8] identified a PVR value of more than 3 WU as a marker of increased mortality in a cohort of 463 heart failure patients. The only noninvasive variables that they found to be significantly correlated to high PVR were smaller body size, higher natriuretic peptide levels, and higher left ventricular filling pressure estimated by Doppler. The current analysis by Szczurek et al[7] indeed identifies additional noninvasive variables that were not previously reported to be associated with an increased PVR, all of which are easily obtainable and could help identify this higher risk subset of patients.

The authors also describe their own center-specific approach to managing a high PVR in heart transplant candidates, and specifically mention the use of a phosphodiesterase inhibitor, sildenafil, in those who are found to have a significant precapillary component of pulmonary hypertension on right heart

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catheterization. There is still no large trial demonstrating benefit with the use of these agents in heart failure with reduced ejection fraction and pulmonary vascular remodeling. However, it has been shown that pulmonary artery medial hypertrophy is a probable driver of pulmonary vascular remodeling in chronic heart failure.[9] Sildenafil has antiproliferative effects on the pulmonary artery smooth muscle, therefore the physiologic rationale for targeting a high PVR in heart failure with sildenafil is certainly present.[10]

As identified by the authors,[7] the primary limitations of this study are the small number of patients, single time point of measured variables, as well as the single-center retrospective nature of its design. This study does suggest that not only are these variables associated with increased mortality after transplant, as has been demonstrated in prior studies, but they are also associated with increased PVR.[11,12] Further validation of MELD-XI, HFSS, and alkaline phosphatase in predicting presence of pulmonary hypertension in heart failure patients undergoing evaluation for transplant, such as a prospective study or in a secondary validation cohort, is likely to provide further insights to the predictive power of these variables.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

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REFERENCES

1 Griepp RB, Stinson EB, Dong E, et al. Determinants of operative risk in human heart transplantation. Am J Surg. 1971; 122: 192-197.

2 Biełka A, Kalinowski M, Hawranek M, et al. Mechanical circulatory support restores eligibility for heart transplant in patients with significant pulmonary hypertension. Kardiol Pol. 2020; 78: 1008-1014.

3 Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. J Heart Lung Transplant. 2016; 35: 1-23.

4 Lopes MC, de Cleva R, Zilberstein B, Gama-Rodrigues JJ. Pulmonary artery catheter complications: report on a case of a knot accident and literature review. Rev Hosp Clin Fac Med Sao Paulo. 2004; 59: 77-85.

5 Rich JD, Shah SJ, Swamy RS, et al. Inaccuracy of Doppler echocardiographic estimates of pulmonary artery pressures in patients with pulmonary hypertension: implications for clinical practice. Chest. 2011; 139: 988-93.

6 Fisher MR, Forfia PR, Chamera E, et al. Accuracy of Doppler echocardiography in the hemodynamic assessment of pulmonary hypertension. Am J Respir Crit Care Med. 2009; 179: 615-21.

7 Szczurek W, Gąsior M, Skrzypek M, et al. Factors associated with elevated pulmonary vascular resistance in ambulatory patients with end-stage heart failure accepted for heart transplant. Pol Arch Intern Med. 2020; 130: 830-836.

8 Miller WL, Grill DE, Borlaug BA. Clinical features, hemodynamics, and outcomes of pulmonary hypertension due to chronic heart failure with reduced ejection fraction: pulmonary hypertension and heart failure. JACC Heart Fail. 2013; 1: 290-299.

9 Delgado JF, Conde E, Sánchez V, et al. Pulmonary vascular remodeling in pulmonary hypertension due to chronic heart failure. Eur J Heart Fail. 2005; 7: 1011-1016.

10 Tantini B, Manes A, Fiumana E, et al. Antiproliferative effect of sildenafil on human pulmonary artery smooth muscle cells. Basic Res Cardiol. 2005; 100: 131-138.

11 Sargut TA, Julia S, Pergantis P, Knosalla C, Knierim J, Hummel M, et al. Adjusting preoperative risk models of post heart transplant survival to a European cohort in the age of a new cardiac allocation score in Europe. Heart Surg Forum. 2018; 21: E527-E33.

12 Bobbio M, Dogliani S, Giacomarra G. Superiority of the heart failure survival score to peak exercise oxygen consumption in the prediction of outcomes in an independent population referred for heart transplant evaluation. Ital Heart J. 2004; 5: 899-905.