# High Transpulmonary Artery Gradient Obtained at the Time of Left Ventricular Assist Device Implantation Negatively Affects Survival After Cardiac Transplantation

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## ABSTRACT

**Aim:** Preoperatively elevated pulmonary vascular resistance (PVR) is a contraindication to heart transplantation (HT). Transpulmonary pressure gradient (TPG) is one of the main variables used in PVR determination (ie, PVR = TPG/cardiac output). Unlike PVR, which is subject to the shortcoming of cardiac output estimation, TPG is directly measured. We aimed to evaluate the relationship of TPG obtained before left ventricular assist device (LVAD) implantation on post-HT survival.

**Methods and Results:** A total of 490 patients were implanted with Heartmate II LVADs in the multicenter Heartmate II Bridge-to-Transplantation clinical trial, and 416/490 had pre-LVAD TPG data available. Outcomes during LVAD support and after HT stratified by both PVR and TPG were studied. The median pre-LVAD TPG was 10 mm Hg. Baseline demographic and clinical characteristics were similar for patients with and without TPG >10 mm Hg. Outcomes during LVAD support (ie, recovery to LVAD explantation, HT, or ongoing device support) for patients below and above the median TPG were similar. However, post-HT 1-year survival rate was significantly higher for patients with TPG ≤10 mm Hg compared with those with TPG >10 mm Hg (91% vs 80%; $P = .016$). Analysis based on the median PVR of 2.68 Wood units did not stratify post-HTx 1-year survival rates between the groups (89% vs 83%; $P = .25$).

**Conclusions:** Elevated TPG, rather than high PVR, before LVAD implantation was associated with increased mortality following HT. Pre-LVAD TPG may be useful to identify a cohort that requires close follow-up with serial hemodynamic monitoring before HT. (*J Cardiac Fail 2019;25:777−784*)

**Key Words:** Pulmonary hypertension, pulmonary vascular resistance, ventricular assist device.

Pulmonary hypertension (PH) is highly prevalent in the advanced heart failure (HF) population and is associated with worse post−heart transplantation (HT) survival, mostly attributable to the development of severe right ventricular failure (RVF).[1−3] Current guidelines have defined severe PH (pulmonary vascular resistance [PVR] >5 Wood units [WU] or transpulmonary pressure gradient [TPG] >15 mm Hg) and a resistance to pulmonary vasodilators as a relative contraindication for cardiac transplantation.[4] Traditionally, the emphasis has been placed on PVR because of early reports documenting an incremental risk of post-transplantation mortality with elevated PVR values.[5] Furthermore, advanced medical and device therapies have targeted PVR lowering when evaluating appropriate timing and candidacy for transplantation. Previous studies have shown that LVAD support in patients with PH can substantially lower PVR and TPG,[6] allowing patients to proceed safely to transplantation. However, PVR remains elevated after LVAD implantation in up to two-thirds of patients with significant PH.[7] Although many of these patients have gone on to HT, studies to date have been underpowered to identify PH as a persistent risk factor for HT in patients bridged with the use of LVADs.[8,9]

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Lack of consensus persists over which of the 2 hemodynamic parameters (TPG or PVR) is superior for predicting post-transplantation mortality:[10] PVR is a flow-dependent measurement, which can vary greatly depending on a patient's cardiac output (CO). Given the inherent limitations and potential inaccuracy of CO measurement by means of either thermodilution or the Fick method,[11] the use of PVR as the prevailing standard has been challenged.[12,13] Proponents of using TPG have argued that because it is directly measured, it better captures the resistance across the pulmonary vasculature.[13] This may be particularly relevant in the population of patients receiving LVAD, who are sicker than other patients being considered for transplantation, and tend to present acutely with profoundly reduced CO, leading to markedly elevated PVR measurements. Therefore, TPG may be a more consistent and relevant parameter to measure in these patients to understand the degree of their pulmonary vasculature disease.

In the current era of advanced HF treatment, device utilization is rapidly becoming the mainstay for inotrope-dependent patients awaiting HT, affording patient improvement in the quality of life and survival to transplantation.[14] The advantage of HT compared with remaining on long-term device support is less clear for some patients, especially those with comorbidities and fixed severe PH, who may experience worse long-term survival after HT.[8,9]

We hypothesized that TPG would provide stronger risk prediction for post-HT outcomes than PVR and may help to guide therapeutic decision making. Therefore, our objective was to assess the prognostic value of pre-LVAD TPG and PVR on post-HT outcomes, with the use of data from the multicenter Heartmate II Bridge-to-Transplantation (BTT) clinical trial.

## Methods

### Study Design

The study was conducted at 36 centers in the United States from March 2005 to April 2008 and was supervised by the study sponsor, Thoratec Corporation, now Abbott Corporation. Details of the prospective multicenter study design and trial results have been previously published for the initial 133 patients[14] and the subsequent 148 continued access patients (NCT00121472),[15] all of whom were urgently listed for transplantation (United Network of Organ Sharing status 1A or 1B) and underwent implantation of Heartmate II LVADs. Post-transplantation outcomes from this trial also have been published previously.[16] Data were analyzed for a total of 490 patients enrolled over the study period. A complete list of study and inclusion and exclusion criteria has been reported from the initial study.[14] The principal outcomes assessed from these 2 Heartmate II clinical trials for BTT included survival to transplantation, actual survival, functional status, quality of life, and adverse events throughout the study.

### Evaluated Baseline Variables

Baseline preoperative data, including patient demographics, New York Heart Association (NYHA) functional class, quality of life questionnaire data, and medications, were obtained at enrollment. Hemodynamic data before LVAD implantation was recorded. TPG was defined by the mean pulmonary arterial pressure minus the pulmonary capillary wedge pressure (PCWP). PVR in WU was derived from TPG divided by the CO, which was calculated by means of the indirect Fick method.

### Evaluated Clinical Outcomes

Patients were divided into 2 groups based on the median TPG as well as the median PVR. The effect of the TPG and PVR on outcomes with LVAD support were evaluated (ie, the proportions of patients who reached transplantation, explantation of the device for cardiac recovery, continuation on device therapy, dying on support, or RVF). RVF was defined as either the need for extended inotropic support for $\geq$14 days after implantation, late inotropic support starting 14 days after implantation, or need for additional right ventricular assist device support.[14]

Patients were followed until they met the principal outcomes of transplantation, recovery to LVAD explantation, death, or ongoing device support as of October 2011. Post-transplantation survival rates at 30 days and 1 year were also evaluated.

### Statistical Analysis

The continuous parameters of TPG and PVR were dichotomized at the 25th (Q1), 50th (median), and 75th (Q3) percentiles. The median and Q3 were chosen as the thresholds for analysis. The correlation between TPG and PVR was tested with the use of Pearson correlation coefficients. The impact of TPG and PVR as continuous variables on post-transplantation mortality at 30 days and at 1 year was analyzed with the use of logistic regression analyses. Differences between dichotomized variables, according to the median and Q3 values of TPG and PVR were analyzed with the use of an unpaired *t* test or Mann-Whitney *U* test as appropriate. Fisher exact test was used for comparison between categoric variables. The level of significance was set at $P < .05$. Adverse events, including RVF, were presented as the percentage of patients who had the events, stratified by TPG and PVR. All studies were done with the use of SPSS Statistics 22 (SPSS, Chicago, Illinois).

## Results

### Baseline Characteristics

Of the 490 patients, 416 had pre-LVAD TPG and PVR data and were the subject of this analysis (Fig. 1). Baseline characteristics before LVAD implantation are summarized in Table 1. Most subjects were men, the overall average age was 51.5 years, and the primary etiology of HF for the

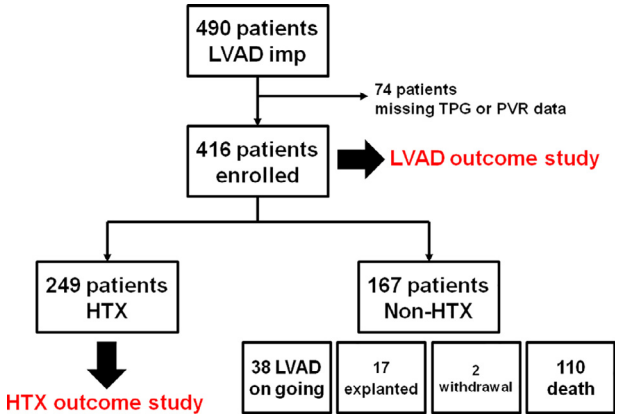



**Fig. 1.** Overview of this study. LVAD, left ventricular assist device; HTX, heart transplantation; TPG, transpulmonary pressure gradient; PVR, pulmonary vascular resistance

majority of patients was nonischemic cardiomyopathy. All patients had NYHA functional class IV HF, and 90% required inotropes.

### Stratification by TPG in Pre-LVAD Data

The median TPG was 10 mm Hg, and baseline characteristics and clinical outcomes were analyzed for subgroups above (n = 188) and equal to or below (n = 228) that value. The patient characteristics were similar concerning age, sex, and duration of LVAD support ($P > .05$ for all). In the higher TPG group, more patients had systemic hypertension compared with the lower TPG group (55% vs 45%; $P = .039$). A larger percentage of patients in the higher TPG group required inotropes (96% vs 85%; $P < 0.001$), but conversely had lower rates of intra-aortic balloon pump support than the lower TPG group (34% vs 48%; $P = .005$).

**Table 1.** Baseline Characteristics

| Characteristic | Result (n = 416) |
|---|---|
| Age, y | 51.5 ± 13.3 |
| Male sex | 324 (78%) |
| Nonischemic etiology | 233 (56%) |
| Hypertension | 206 (50%) |
| Diabetes mellitus | 116 (28%) |
| History of stroke | 41 (10%) |
| COPD | 43 (10%) |
| LVAD duration, d | 419 ± 498 |
| NYHA IV | 416 (100%) |
| Inotrope support | 373 (90%) |
| IABP support | 173 (42%) |
| CRT | 210 (50%) |
| LVEF, % | 16.7 ± 6.5 |
| LVEDD, mm | 69.7 ± 11.5 |
| TPG, mm Hg | 10.8 ± 6.0 (Q1, 7; median, 10; Q3, 14) |
| PVR, WU | 2.92 ± 1.59 (Q1, 1.80; median, 2.68; Q3, 3.80) |

COPD, chronic obstructive pulmonary disease; LVAD, left ventricular assist device; NYHA, New York Heart Association functional class; IABP, intra-aortic balloon pump; CRT, cardiac resynchronization therapy; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; TPG, transpulmonary arterial pressure gradient; PVR, pulmonary vascular resistance.

Pre-LVAD hemodynamics stratified by median TPG are presented in Table 2. The difference in PVR between the 2 groups was largely driven by the TPG (15.8 ± 4.8 mm Hg vs 6.6 ± 2.8 mm Hg; $P < .001$) and not by the CO (3.96 ± 1.36 vs 4.06 ± 1.24 $L \cdot min^{-1} \cdot m^{-2}$; $P = .34$). Because PVR is a product of TPG, we evaluated the degree of correlation between these 2 variables and found only a modest correlation ($R^2 = 0.400$; Appendix Fig. 1), suggesting that TPG only weakly predicted PVR.

Given that PCWP was similar in both groups before device implantation ($P = .14$), the elevation in TPG in the TPG >10 mm Hg group would be a result of higher systolic, diastolic, and mean pulmonary arterial pressures (Table 2). Patients with TPG >10 mm Hg had a higher right ventricular stroke work index compared with the TPG ≤10 mm Hg group (646 ± 311 vs 464 ± 265 mm $Hg \cdot mL \cdot m^{-2}$; $P < .001$), possibly indicating better priming of the native right ventricle to chronically elevated pulmonary arterial pressures without a coupled rise in central venous pressure.

### Overall Clinical Outcomes

The overall follow-up duration was a median of 198 days (range 0−2291 days). Of the 416 patients studied, 249 (60%) received HT after a median duration of 172 days (range 7−1248 days) with device support. Of the remaining 167 LVAD patients who were not transplanted within the study period, 38/167 (23%) remained on device support as of trial completion, 17/167 (10%) were explanted for either myocardial recovery or other reasons, 2/167 (1%) withdrew from study, and 110/167 (66%) died (Fig. 1).

The duration of LVAD support in the nontransplanted group (n = 167) was a median of 380 days. The nontransplanted patient population was more likely to be female

**Table 2.** Comparison of Pre-LVAD Hemodynamics Stratified by the Median of TPG

| Characteristic | TPG >10 mm Hg(n = 188) | TPG ≤10 mm Hg(n = 228) | *P* Value |
|---|---|---|---|
| TPG, mm Hg | 15.8 ± 4.8 | 6.6 ± 2.8 | <.001* |
| PVR, WU | 4.00 ± 1.50 | 2.05 ± 1.02 | <.001* |
| Central venous pressure, mm Hg | 12.9 ± 6.5 | 12.3 ± 6.4 | .35 |
| Systolic PAP, mm Hg | 58.6 ± 12.0 | 46.3 ± 11.8 | <.001* |
| Diastolic PAP, mm Hg | 29.6 ± 8.0 | 24.4 ± 7.7 | <.001* |
| Mean PAP, mm Hg | 40.4 ± 8.0 | 32.4 ± 8.6 | <.001* |
| PCWP, mm Hg | 24.5 ± 7.3 | 25.8 ± 8.0 | .14 |
| Cardiac output, L/min | 4.06 ± 1.24 | 3.96 ± 1.36 | .34 |
| Cardiac index, $L \cdot min^{-1} \cdot m^{-2}$ | 2.08 ± 0.67 | 2.01 ± 0.60 | .38 |
| Heart rate, beats/min | 92 ± 19 | 90 ± 18 | .26 |
| RVSWI, mm $Hg \cdot mL/m^2$ | 646 ± 311 | 464 ± 265 | <.001* |

LVAD, left ventricular assist device; TPG, transpulmonary artery pressure gradient; PVR, pulmonary vascular resistance; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; RVSWI, right ventricular stroke work index.

*$P < .05$ by unpaired *t* test or Mann-Whitney *U* test as appropriate.

($P = .01$), to be older ($P = .008$), and to have comorbid chronic obstructive pulmonary disease ($P = .03$). There was no evidence for significant differences in the hemodynamic indices of PVR ($P = .50$), TPG ($P = .66$), and CO ($P = .22$) between transplanted patients and nontransplanted patients.

### Outcomes While on LVAD Support

Outcomes with LVAD support for the entire cohort (n = 416) were assessed according to the medians and Q3s of TPG values (median 10 mm Hg, Q3 14 mm Hg) and PVR values (median 2.68 WU, Q3 3.80 WU; Table 3).

For either hemodynamic parameter, there were no significant differences in the number of patients who were transplanted, remained alive with ongoing device support, were explanted, withdrew from the study, or died while awaiting transplantation. Notably, the incidence of RVF and the associated number of deaths were statistically similar between the TPG >10 mm Hg and the TPG ≤10 mm Hg groups. There was a trend toward higher rates of RVF in the Q3 TPG >14 mm Hg group (27% vs 19%; $P = .12$).

There were more deaths related to RVF in the TPG >14 mm Hg group (8/96 [8%] vs 4/320 [1%]; $P = .027$), suggesting that RVF may have been of greater severity and responsible for worse post-LVAD outcomes in this group, although all-cause mortality on the device was not adversely affected for this higher-TPG population. There was no difference in deaths related to RVF in the PVR >3.8 group (5/100 [5%] vs 7/316 [7.2%]; $P = .17$).

Survival over 1 year during Heartmate II LVAD support was statistically similar for all patients stratified according to the medians and Q3s of TPG and PVR values ($P > .05$ for all; Fig. 2).

**Table 3.** Comparison in Clinical Outcomes During LVAD Support Stratified by TPG or PVR

| Cutoff median TPG | TPG >10 mm Hg(n = 188) | TPG ≤10 mm Hg(n = 228) | *P* Value |
|---|---|---|---|
| Clinical outcomes | | | .45 |
| Transplanted | 115 (61%) | 134 (59%) | |
| Ongoing | 14 (7%) | 24 (11%) | |
| Explanted | 7 (4%) | 10 (4%) | |
| Expired | 50 (27%) | 60 (26%) | |
| Withdrawn | 2 (1%) | 0 (0%) | |
| Incidence of RVF | 45 (24%) | 43 (19%) | .23 |
| **Cutoff: Q3 TPG** | **TPG >14 mm Hg(n = 96)** | **TPG ≤14 mm Hg(n = 320)** | |
| Clinical outcomes | | | .089 |
| Transplanted | 54 (56%) | 195 (61%) | |
| Ongoing | 7 (7%) | 31 (10%) | |
| Explanted | 4 (4%) | 13 (4%) | |
| Expired | 29 (30%) | 81 (25%) | |
| Withdrawn | 2 (2%) | 0 (0%) | |
| Incidence of RVF | 26 (27%) | 62 (19%) | .12 |
| **Cutoff: median PVR** | **PVR >2.68 WU(n = 202)** | **PVR ≤2.68 WU (n = 214)** | |
| Clinical outcomes | | | .64 |
| Transplanted | 122 (60%) | 127 (59%) | |
| Ongoing | 18 (9%) | 20 (9%) | |
| Explanted | 7 (3%) | 10 (5%) | |
| Expired | 53 (26%) | 57 (27%) | |
| Withdrawn | 2 (1%) | 0 (0%) | |
| Incidence of RVF | 46 (23%) | 42 (20%) | .47 |
| **Cutoff: Q3 PVR** | **PVR >3.80 WU(n = 100)** | **PVR ≤3.80 WU (n = 316)** | |
| Clinical outcomes | | | .12 |
| Transplanted | 55 (55%) | 194 (61%) | |
| Ongoing | 9 (9%) | 29 (9%) | |
| Explanted | 5 (5%) | 12 (4%) | |
| Expired | 29 (29%) | 81 (26%) | |
| Withdrawn | 2 (2%) | 0 (0%) | |
| Incidence of RVF | 27 (27%) | 61 (19%) | .12 |

TPG, transpulmonary arterial pressure gradient; RVF, right ventricular failure; PVR, pulmonary vascular resistance.

### Outcomes After Cardiac Transplantation

Among 249 patients who received HT, survival data was missing on a total of 8/249 patients (3%) at 30 days and 20/249 patients (8%) at 1 year. Missing data were equally distributed between the high and low TPG groups.

*Stratification by TPG.* In contrast to survival during LVAD support, survival after HT was significantly affected by TPG (and not by PVR). When TPG was modeled as a continuous variable, there was no association with 30-day post-transplantation survival (odds ratio 1.04, 95% CI 0.92−1.16; $P = .54$), but there was a significant association with 1-year post-transplantation survival (odds ratio 1.08, 95% CI 1.02−1.15; $P = .011$).

At 30 days, survival between the TPG >10 and ≤10 mm Hg groups were similar, at 96% vs 97%, respectively ($P = .82$); whereas 1-year post-HT survival rate in the TPG >10 mm Hg was substantially lower (80% vs 91%; $P = 0.016$; Fig. 3A). TPG quartiles did not stratify 30-day survival rate ($P = .54$; Fig. 3B); whereas looking at 1-year survival per TPG quartiles demonstrated a trend of reduced survival rate in the higher-TPG groups ($P = .081$; Fig. 3C).

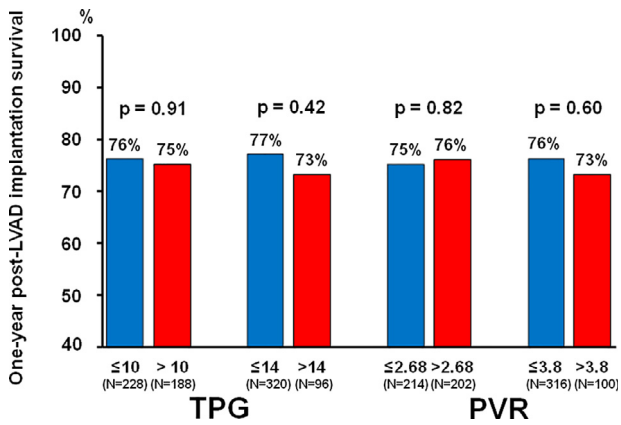



**Fig. 2.** One-year post-LVAD survival rate stratified by the median (10 mm Hg) or third quartile (14 mm Hg) of TPG and the median (2.68 WU) or third quartile (3.80 WU) of PVR. Variables were compared by means of unpaired *t* test. Abbreviations as in Fig. 1.

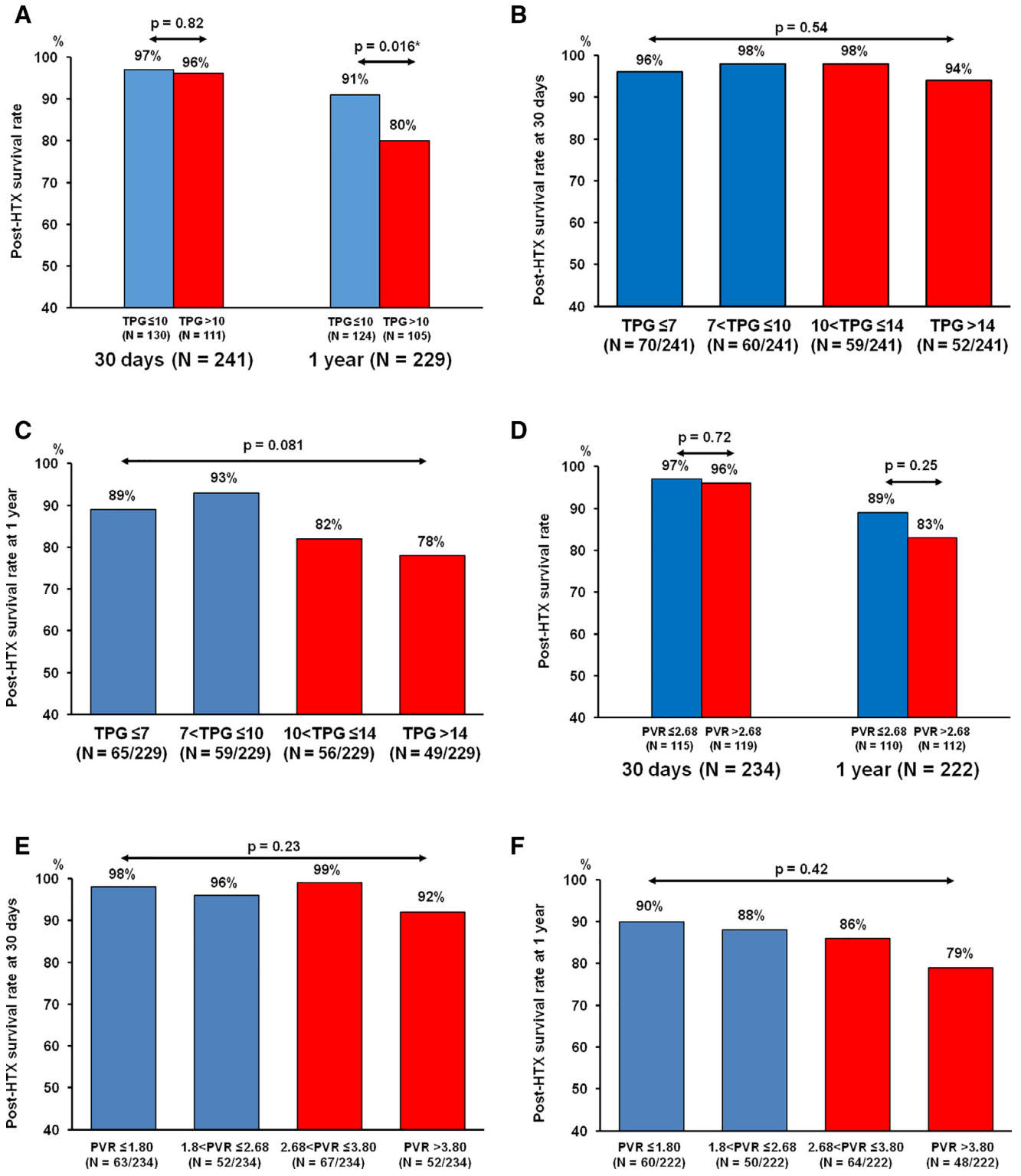



**Fig. 3.** Post-HT survival rates at 30 days and 1 year stratified by (A) median TPG, (B and C) TPG quartiles (ie, Q1, median, and Q3), and those stratified by (D) median PVR, and (E and F) PVR quartiles (ie, Q1, median, and Q3). *$P < .05$. Variables were compared by means of (A and D) unpaired *t* test or (B, C, E, and F) analysis of variance. Abbreviations as in Fig. 1.

*Stratification by PVR.* In contrast to TPG, a median value (Fig. 3D) or quartiles of PVR did not identify patients at risk for worse 30-day (Fig. 3E) or 1-year (Fig. 3F) post-HT survival ($P > .05$ for both). As a continuous variable, PVR was not associated with either 30-day post-transplantation survival (odds ratio 1.21, 95% CI 0.88−1.67;

$P = .24$) or 1-year post-transplantation survival (odds ratio 1.14, 95% CI 0.91−1.41; $P = .26$).

## Discussion

We examined whether high TPG at the time of LVAD implantation negatively affects outcomes after HT, and compared it with elevated PVR in a BTT population. Our principal findings are as follows:

(1) Post-transplantation outcomes at 1 year are worse in patients with higher TPG values prior to LVAD implantation.
(2) In contrast, baseline PVR before LVAD implantation, which is substantially influenced by CO estimation and therefore may be less reliable, did not predict post-transplantation outcomes.
(3) TPG and PVR did not differentially affect survival during LVAD support, although patients with TPG >14 mm Hg (in the 4th quartile) were predisposed to a higher incidence of RVF.

Although transplant centers have traditionally relied on PVR cutoffs for determining eligibility of transplantation, we think that TPG may represent a more clinically essential and accurate determinant of PH disease severity and prognosis. Indeed, previous studies have confirmed an increase in late post-transplantation mortality in a non-VAD population with elevated TPG levels >12 or 15 mm Hg, regardless of PVR.[12,13] The present study is the largest to date in a BTT cohort analyzing the predictive role of preoperative TPG compared with PVR for post-transplantation mortality.

Improved outcomes with mechanical circulatory support have led to increased utilization of this technology for advanced HF patients as a means of effective hemodynamic support and optimization of pre-transplantation condition. A previous study by Alba et al assessed the impact of LVAD therapy on post-transplantation survival for patients with and without fixed PH before device implantation.[8] The authors concluded that once LVAD support successfully reversed the fixed PH, post-transplantation survivals at 1 and 6 years were as high as those of non-PH groups. However, it is of note that the study population was small and that there were numerically large differences in 1- and 6-year survival rates in patients with and without fixed PH (88% vs 78% and 70% vs 52%, respectively).

TPG directly measures the pressure drop across the pulmonary system, and may ultimately be a superior clinical and prognostic marker for following BTT patients over time. Previous studies have not thoroughly tested this in a large LVAD population because all hemodynamic measures of PH response have uniformly centered on systolic pulmonary arterial pressure or PVR,[8,17,18] and the recommended frequency of post-VAD hemodynamic assessment, especially with longer waiting times for transplantation, is not established.

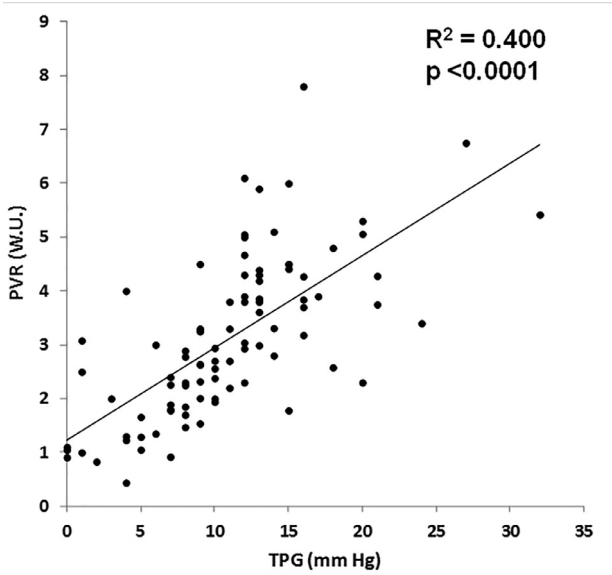
Data from the current INTERMACS report,[19] with more than 20,000 implants, highlights the favorable results of a primary destination therapy (DT) strategy with the use of continuous-flow pumps, with 1-year survival approaching 75%. Survival with DT remains somewhat lower compared with a BTT strategy, where the current 1-year LVAD survival is ∼85% and 1-year post-transplantation survival >90%. In an older DT population with more prevalent comorbidities and risk of device complications without "rescue" therapy, lower survival is to be expected. Note that data from this study from the Heartmate II clinical trial are >10 years old, and 1-year post-LVAD survival results have improved about 10 absolute percentage points.

Our data suggest that patients with elevated TPG are at risk for lower-than-expected 1-year post-transplantation survival (80% for TPG >10 mm Hg and 78% for TPG >14 mm Hg; odds ratio 1.08 per mm Hg) and this finding may provide a rationale for supporting a DT strategy in these patients, with ultimately similar outcomes. Of note, patients with elevated TPG may benefit from vasodilator testing to assess reversibility as well as repeated hemodynamic assessments after LVAD implantation to measure change in TPG over time.[20] In addition, we demonstrated that TPG elevation did not have to approach 15 mm Hg, the current threshold for excluding transplantation, to negatively affect survival. We found that even TPG levels in excess of 10 mm Hg, arguably the upper limit of normal, led to a drop-off in 1-year survival (Fig. 3C). Currently, we are expanding the indication of the DT patient, and with the continued donor shortage and significant improvements of outcome during LVAD support with contemporary devices including HVAD[21] and HeartMate 3,[22] studies such as this will help to enhance decision making for patients in whom there is clinical equipoise about the best long-term strategy.

Improved understanding of the risks associated with these different PH measures may ultimately help to improve overall post-transplantation outcomes. Our study emphasizes the predictive power of pre-VAD TPG over PVR in a BTT population, and the significant post-transplantation mortality associated with elevated TPG highlights the need for serial hemodynamic assessments in these patients before proceeding with HT. Furthermore, patients with elevated TPG may benefit from targeted pulmonary vasodilator therapies following LVAD implantation. Our findings may also impact donor heart selection during HT. As patients with elevated TPG represent a high-risk group, it may be prudent to incorporate this variable when considering donor factors such as size matching, ischemia time, and donor age.[23]

## Study Limitations

Several limitations should be noted. Data were collected >10 years ago and survival results with the Heartmate II have since improved substantially which may have an impact on conclusions drawn for the contemporary era. The study was a post hoc analysis of the multicenter Heartmate II BTT clinical trial, and hemodynamic variables were assessed only at baseline before LVAD implantation. We could not analyze TPG and PVR measurements at any time after LVAD placement or in the immediate period preceding HT, owing to




**Appendix Fig. 1.** Correlation between transpulmonary arterial pressure gradient (TPG) and pulmonary vascular resistance (PVR). $P < .05$ by Pearson's correlation coefficient.

lack of consistent hemodynamic assessment during the follow-up period. We also did not have any data on the results of vasodilator testing or pulmonary vasodilator therapy. Therefore, our analysis was unable to assess TPG change during device therapy and that impact on post-HT outcomes. Also, we did not have accurate dates of each event and could not perform time-to-event analyses. Nevertheless, it may be plausible to hypothesize that some of the pre-LVAD PH remains after LVAD implantation and even after cardiac transplantation. Many cases of PH related to left heart disease can be normalized following LVAD implantation owing to the strong unloading of the left ventricle. In the remaining patients, PH may remain despite cardiac unloading owing to refractory damage of the pulmonary vasculature. Furthermore, our group has recently demonstrated that the phenomenon of decoupling during LVAD support (persistence or development of a gradient between the diastolic pulmonary arterial pressure and the pulmonary capillary wedge pressure) is associated with worse prognosis. Pre-LVAD TPG may be useful in identifying the group of patients in which decoupling is most likely to occur. Laboratory, hemodynamic, and echocardiographic data after LVAD implantation would strengthen our hypothesis and clarify the mechanism underlying our findings. In this study, more than half (53%) of the patients who were transplanted received their transplant before 6 months, which may have been an inadequate time on support to successfully reverse their pulmonary vascular disease.

Whether the Fick method or the thermodilution method is better to measure CO remains controversial.[24] Thermodilution is known to be particularly inaccurate in the setting of significant tricuspid regurgitation, which is relatively common in the advanced HF population. Therefore, we chose to use the Fick method for calculation of CO to maintain consistency.

Although we assessed the risks of baseline TPG during LVAD support and elucidated the causes of death for these subgroups, we could not provide a similar analysis for the post-HT patients to understand why the high TPG groups suffered greater post-HT mortality. Also, data on LVAD speed and the use of medications for RV support, such as prolonged inotropes and phosphodiesterase-5 inhibitors, for the higher TPG or PVR group at risk of post-LVAD RVF was not fully reported. We do not deny at all the influence of these clinical parameters other than TPG on the clinical outcomes. The focus of future studies should be directed toward understanding the potential mechanisms responsible for worsened survival in the higher TPG group.

## Conclusion

Elevated TPG, rather than elevated PVR, before LVAD implantation was associated with worse 1-year post-transplantation survival in a BTT population. Elevated pre-LVAD TPG may be an essential risk factor for post-HT mortality, and may be considered when deciding between HT or LVAD DT strategy in patients with advanced HF.

## Disclosures

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