Comorbidities and the decision to undergo or forego destination therapy left ventricular assist device implantation: An analysis from the Trial of a Shared Decision Support Intervention for Patients and their Caregivers Offered Destination Therapy for End-Stage Heart Failure (DECIDE-LVAD) study

Haider J. Warraich, MD,[a,b] Larry A. Allen, MD, MHS,[c] Laura J. Blue, NP,[a] Erin L. Chaussee, MS,[c,d] Jocelyn S. Thompson, MA,[c] Colleen K. McIlvennan, DNP, ANP,[c] Kelsey M. Flint, MD,[c] Daniel D. Matlock, MD, MPH,[c] and Chetan B. Patel, MD[a,b] *Durham, NC; and Aurora, CO*

Background Patients considering destination therapy left ventricular assist devices (DT LVAD) often have high comorbid burden but the association between these comorbidities and post-decision outcomes is unknown.

Methods We included subjects in DECIDE-LVAD (NCT02344576), a stepped-wedge multicenter trial of patients considering LVADs, recording comorbidities per INTERMACS protocol. We compared decisional conflict, regret, perceived stress, quality of life (EQ-VAS), depression (PHQ-2), struggle with- and acceptance of illness by comorbid burden and amongst the most common comorbidities.

Results Of 239 patients, LVAD recipients (n = 164) and non-recipients (n = 75) had a similar proportion with ≥1 comorbidity (70% v. 80%, $P = .09$). Patients with comorbidities were younger regardless of LVAD implantation status. After adjusting for age, overall and amongst LVAD recipients, patients with ≥1 comorbidity had higher mean decision conflict at baseline (23.2 ± 1.5 vs. 17.4 ± 2.2), and at 6 months, higher stress (13.0 ± 0.6 vs. 10.4 ± 1.0) and struggle with illness (13.3 ± 0.4 vs. 11.1 ± 0.6) than those without comorbidities ($P < .05$). No difference was noted in decision regret, PHQ-2, EQ-VAS, acceptance of illness and survival overall and amongst LVAD recipients. Of the three most common comorbidities, while patients with pulmonary hypertension had worse decision regret, depression, stress and acceptance of illness at 6-month follow-up than those who did not have pulmonary hypertension, no difference was noted in patients with chronic renal disease or high body mass index.

Conclusion Patients considering LVAD implantation with comorbidities experience increased decision conflict, stress and struggle with illness. These findings provide insights in the role comorbidities play in patient decision-making and decisional outcomes. (Am Heart J 2019;213:91-6.)

From the [a]Department of Medicine, Cardiology Division, Duke University Medical Center, Durham, NC, [b]Duke Clinical Research Institute, Durham, NC, [c]Department of Medicine, University of Colorado, Aurora, CO, and [d]Department of Biostatistics and Informatics, Colorado School of Public Health, Aurora, CO.

Jeroen J. Bax, MD, PhD served as guest editor for this article.

Journal Subject Terms: *left ventricular assist device, heart failure, shared decision-making, decision aids, quality of life, comorbidity*

Funding Source: This work was supported through a Patient-Centered Outcomes Research Institute (PCORI) Program Award (CDR-1310-06998).

Submitted January 3, 2019; accepted April 16, 2019.

Reprint requests: Chetan B Patel, MD, 2301 Erwin Road, Duke University Medical Center, Durham, NC 27710.

E-mail: chetan.patel@duke.edu

0002-8703

https://doi.org/10.1016/j.ahj.2019.04.008

Patients with heart failure (HF) considering destination therapy (DT) left ventricular assist device (LVAD) have a high burden of non-cardiac comorbidities, which are associated increased mortality and poor quality of life (QoL) after DT LVAD implantation.[1] However, it remains unknown if comorbidities affect decisional quality, conflict and regret amongst patients with advanced HF who receive or do not receive DT LVADs. In this study, we analyzed the multicenter DECIDE-LVAD study to assess differences in decision quality amongst DT LVAD recipients and non-recipients with or without high comorbid burden.

Table I. Baseline characteristics between patients by comorbid burden and LVAD implantation status

		No LVAD/No CMB (n = 15)	No LVAD/≥1 CMB (n = 60)	LVAD/No CMB (n = 50)	LVAD/≥1 CMB (n = 114)	*P*	Missing
Age (years)		67.1 (7.7)	62.6 (10.5)	67.7 (7.7)	61.3 (9.8)	<0.01*	0
Gender	Male	12 (80%)	49 (82%)	44 (88%)	98 (86%)	0.74	0
Race/Ethnicity	NH-White	11 (79%)	44 (79%)	42 (88%)	90 (79%)	0.30	7
	Black	2 (14%)	6 (11%)	3 (6%)	20 (18%)		
	Other	1 (7%)	6 (11%)	3 (6%)	4 (4%)		
Years since doctor told about heart failure	Within 2 years	3 (21%)	11 (21%)	6 (13%)	7 (7%)	0.03*	17
	2–4 years	0 (0%)	10 (19%)	6 (13%)	11 (10%)		
	≥4 years	11 (79%)	31 (60%)	36 (75%)	90 (83%)		
Patient status at enrollment	Outpatient	5 (33%)	13 (22%)	16 (32%)	21 (18%)	0.31	0
	Inpatient	9 (60%)	31 (52%)	25 (50%)	62 (54%)		
	ICU	1 (7%)	16 (27%)	9 (18%)	31 (27%)		
Sodium (mmol/L)		136.2 (3.9)	134.8 (4.8)	135.8 (4.6)	135.9 (4.4)	0.49	5
Creatinine (mg/dL)		1.4 (0.5)	1.6 (0.6)	1.6 (0.5)	1.5 (0.6)	0.50	5
Albumin (g/dL)		3.8 (0.5)	3.6 (0.5)	3.4 (0.5)	3.6 (0.6)	0.05	26
Hemoglobin (g/dL)		13.1 (2.4)	12.1 (2.5)	11.7 (2.5)	12.0 (2.1)	0.21	6
INTERMACS Profile at Enrollment	1	0	3 (5%)	5 (10%)	5 (4%)	0.007*	0
	2	3 (20%)	6 (10%)	8 (6%)	36 (32%)		
	3	4 (27%)	20 (33%)	19 (38%)	37 (33%)		
	4	2 (13%)	12 (20%)	13 (26%)	16 (14%)		
	5	0	3 (5%)	1 (2%)	1 (1%)		
	6	0	2 (3%)	1 (2%)	2 (2%)		
	7	3 (20%)	3 (5%)	2 (4%)	1 (1%)		
	Unknown	3 (20%)	11 (18%)	1 (2%)	16 (14%)		

Results are mean (standard deviation) or number (percentage). Abbreviations: CMB, comorbidity; ICU, intensive care unit; NH, non-Hispanic. *P*: ANOVA for continuous variables, χ^2 for categorical variables. * represents $P < .05$ when the N = 15 patients without LVAD or comorbidities were excluded.

Methods

Design

The DECIDE-LVAD (NCT02344576) trial tested the effectiveness of a shared decision support intervention consisting of a pamphlet and video decision aid and clinician-directed support training. DECIDE-LVAD used a hospital-level, randomized phased roll out in six medical centers implanting DT LVADs in the United States. Details about the trial methodology have been previously published and this trial was approved by institutional review boards at all sites.[2] The authors are solely responsible for the design and conduct of this study, all study analyses and drafting and editing of the paper. This work was supported through a Patient-Centered Outcomes Research Institute (PCORI) Program Award (CDR-1310-06998).

Patients

Eligible patients were ≥18 years old with advanced HF actively who were actively considering primary first implantation of a DT LVAD. Non-recipients included patients who chose not to get an LVAD or were deemed ineligible for LVAD.

Comorbidities

We recorded non-cardiac comorbidities based on the 28 standardized "comorbidities/contraindications/concerns" listed as potential contraindications to transplantation in the INTERMACS registry. (Online Table I) We excluded "history of smoking" and only included active smoking as a comorbidity. We dichotomized our population into patients with low comorbid burden (< median comorbidities) and high comorbid burden (≥ median comorbidities).

Outcomes

Our primary outcomes of interest were decision regret[3] and decisional conflict.[4] Secondary outcomes included Patient Health Questionnaire-2 (PHQ-2), EuroQol Visual Analog Scale (EQ-VAS), PEACE Struggle with Illness subscale[5] and PEACE Acceptance of Illness subscale,[5] Perceived Stress, and mortality. Enrolled patients were surveyed twice at baseline in person and follow-up surveys were conducted at 1 and 6 months.

Analysis

We compared baseline characteristics by comorbidity burden and DT LVAD status using chi square test for categorical variables and Analysis of Variance (ANOVA) for continuous variables. We compared characteristics of participant comorbidities by DT LVAD status using chi-square tests and Wilcoxon rank sum tests. To estimate outcome scores over time by comorbidity burden group, we fit linear mixed models, which included a random effect for center, a fixed effect for time period, and

Table II. Distribution of major comorbidities by LVAD implantation status

	LVAD recipients (n = 164)	LVAD non-recipients (n = 75)	Total (n = 239)	*P*
Any comorbidity	114 (70%)	60 (80%)	174 (73%)	.09
Median comorbidity	1 (0,2)	1 (1,2)	1 (0,2)	.08
Chronic renal disease	31 (19%)	23 (31%)	54 (23%)	.04
Large body mass index	36 (22%)	18 (24%)	54 (23%)	.73
Pulmonary hypertension	24 (15%)	11 (15%)	35 (15%)	.90
Severe diabetes	17 (10%)	6 (8%)	23 (10%)	.56
Currently smoking	12 (7%)	9 (12%)	21 (9%)	.24
Frailty	9 (6%)	11 (15%)	20 (8%)	.02
Pulmonary disease	11 (7%)	5 (7%)	16 (7%)	.99

Results are presented as number (percentage) or as median (interquartile range). Significant *P* values are bolded. Abbreviations: LVAD, left ventricular assist device.

Table III. Adjusted decision outcomes in the overall population by comorbid burden and in DT LVAD recipients by comorbid burden

		No CMB (n = 65)	≥1 CMB (n = 174)	*P*	LVAD/No CMB (n = 50)	LVAD/≥1 CMB (n = 114)	*P*
Decisional conflict	BL	17.4 (2.2)	23.2 (1.5)	.02	14.7 (2.4)	21.4 (1.7)	.02
(0–100)*	6MFU	13.5 (2.1)	15.7 (1.4)	.33	12.7 (2.3)	15.3 (1.6)	.31
Decision regret	1MFU	16.5 (2.9)	16.1 (2.1)	.90	17.5 (2.9)	14.1 (2.1)	.28
(0–100)*	6MFU	15.1 (3.2)	15.7 (2.2)	.86	14.7 (3.2)	15.3 (2.3)	.87
Patient health Questionnaire 2 (0–6)*	BL	1.8 (0.3)	1.7 (0.2)	.52	1.8 (0.3)	1.8 (0.2)	.88
	6MFU	0.7 (0.2)	1.1 (0.2)	.17	0.7 (0.3)	1.1 (0.2)	.17
Euro QoL Visual	BL	47.4 (3.1)	45.7 (1.9)	.64	43.6 (3.4)	41.8 (2.3)	.65
Analog Scale (0–100)^	6MFU	73.5 (2.8)	68.1 (1.8)	.11	73.6 (3.0)	69.0 (2.1)	.20
PEACE acceptance of illness (5–20)^	BL	17.7 (0.3)	17.2 (0.2)	.11	17.7 (0.4)	17.2 (0.2)	.26
	6MFU	18.2 (0.3)	17.6 (0.2)	.12	18.2 (0.4)	17.3 (0.3)	.06
PEACE struggle with	BL	13.4 (0.5)	13.8 (0.3)	.50	13.6 (0.6)	14.1 (0.4)	.48
illness (7–28)*	6MFU	11.1 (0.6)	13.3 (0.4)	<.01	10.9 (0.7)	13.3 (0.5)	<.01
Perceived stress	BL	15.1 (0.8)	15.4 (0.5)	.72	15.4 (0.9)	16.3 (0.6)	.4
(0–40)*	6MFU	10.4 (1.0)	13.0 (0.6)	.02	10.1 (1.1)	13.4 (0.7)	.01

Adjusted mean (standard error) from linear mixed models. *Higher score is worse; ^Lower score is worse. Abbreviations: *1, 6MFU*, 1, 6-month follow-up; BL, baseline; CMB, comorbidity; LVAD, left ventricular assist device.

accounted for within-subject correlation using an unstructured covariance matrix. We also adjusted for patient age. We fit these models on the entire group, and then in the subset of LVAD recipients. In an additional sensitivity analysis, we removed the participants in the low comorbidity burden group who did not receive an LVAD and compared outcome scores by a 3-level categorical variable: (1) low comorbidity burden LVAD recipients, high comorbidity burden non recipients, and high comorbidity burden LVAD recipients. In LVAD recipients, we compared patient time to event (death) by comorbidity burden using a log-rank test. To assess the validity of comorbidity categories, e.g. "high body mass index" (BMI) and "chronic renal disease," we assessed the relationship between measured BMI and serum creatinine values with the dichotomous categories. We also compared outcomes between patients who did or did not have the most commonly occurring comorbidities. All analyses were performed using SAS version 9.4 (Cary, NC).

Results

Of 248 patients enrolled, we excluded 9 (4%) who withdrew from all study assessments. Of the remaining 239 patients, most (n = 164, 69%) opted to receive an LVAD; all LVADs received were rotary pumps and the primary first implant for the patient. (Online Figure 1) The median number of INTERMACS comorbidities was 1 (inter-quartile range 0,2) for both LVAD recipients and non-recipients, so our low comorbid burden group was defined as the group with no comorbidities and the high comorbid burden group was defined as those who had at least one comorbidity. (Online Figure 2) Patients listed as having "high BMI" had greater BMI than those not listed (mean BMI 38.0 kg/m^2 [standard deviation 6.3 kg/m^2] vs. mean BMI 27.3 kg/m^2 [standard deviation 6.2 kg/m^2], $P < .01$), and patients with "chronic renal disease" had higher serum creatinine than those not listed (mean serum creatinine 1.8 mg/dL [standard deviation 0.6 mg/dL] vs. mean serum creatinine 1.5 mg/dL [standard deviation 0.6 mg/dL], P < .01). Patients without comorbidities were older compared to patients with comorbidities. (Table I) Numerically fewer LVAD recipients had comorbidities than non-recipients (70% vs. 80%, $P = .09$). (Table II) The most common comorbidities in our population were chronic renal disease (23%), high BMI (23%), pulmonary hypertension (15%), severe diabetes (10%), current smoking (9%) and frailty (8%). LVAD recipients were

Table IV. Differences in adjusted primary and secondary outcomes over time by major comorbidity status in patients in the DECIDE-LVAD study

		Chronic renal disease			Large body mass index			Pulmonary hypertension		
Measure	**Visit**	**No**	**Yes**	***P***	**No**	**Yes**	***P***	**No**	**Yes**	***P***
Decisional Conflict (0–100)*	BL	20.3 (1.50)	26.4 (2.45)	.020	22.8 (1.57)	17.8 (2.58)	.067	21.5 (1.41)	22.5 (2.93)	.728
	6MFU	14.8 (1.44)	16.6 (2.40)	.463	16.0 (1.53)	12.7 (2.42)	.203	14.4 (1.35)	19.3 (2.69)	.078
Decision Regret (0–100)*	1MFU	16.5 (2.07)	15.1 (3.15)	.664	17.0 (2.14)	13.6 (3.18)	.289	15.0 (1.89)	21.6 (3.27)	.049
	6MFU	15.4 (2.21)	16.2 (3.50)	.815	16.3 (2.27)	13.1 (3.47)	.387	14.4 (2.03)	20.4 (3.67)	.117
Euro QOL Visual Analog Scale (0–100)^	BL	46.5 (1.81)	44.9 (3.39)	.663	46.9 (1.85)	43.6 (3.49)	.407	46.2 (1.72)	46.1 (4.09)	.992
	6MFU	70.6 (1.71)	66.3 (3.33)	.241	70.0 (1.79)	68.6 (3.28)	.699	70.6 (1.64)	65.0 (3.73)	.164
PEACE Acceptance of Illness (5–20)^	BL	17.4 (0.19)	17.1 (0.35)	.416	17.2 (0.19)	17.5 (0.36)	.514	17.3 (0.18)	17.3 (0.42)	.952
	6MFU	17.9 (0.20)	17.4 (0.40)	.240	17.8 (0.21)	17.8 (0.39)	.984	17.9 (0.19)	16.8 (0.45)	.027
PEACE Struggle With Illness (7–28)*	BL	13.9 (0.30)	13.3 (0.56)	.396	13.6 (0.30)	14.1 (0.59)	.491	14.0 (0.28)	12.6 (0.67)	.055
	6MFU	12.5 (0.37)	13.2 (0.74)	.400	12.6 (0.38)	12.6 (0.71)	.973	12.5 (0.36)	13.1 (0.85)	.498
Patient Health Questionnaire 2 (0–6)*	BL	1.71 (0.17)	1.64 (0.26)	.798	1.67 (0.17)	1.80 (0.27)	.644	1.69 (0.16)	1.71 (0.30)	.958
	6MFU	0.89 (0.17)	1.29 (0.27)	.148	0.91 (0.17)	1.18 (0.27)	.343	0.87 (0.16)	1.51 (0.30)	.038
Perceived Stress (0–40)*	BL	15.4 (0.47)	15.1 (0.90)	.742	15.3 (0.48)	15.4 (0.94)	.962	15.5 (0.45)	14.3 (1.08)	.309
	6MFU	11.8 (0.59)	14.0 (1.17)	.105	11.9 (0.61)	13.4 (1.13)	.242	11.8 (0.57)	14.8 (1.34)	.038

All values are adjusted mean (standard error) from linear mixed models. *Higher score is worse. ^Lower score is worse. Abbreviations: *1, 6MFU*, 1, 6-month follow-up; *BL*, baseline.

less likely to have chronic renal disease (19% vs. 31%, $P = .04$) and frailty (6% vs. 15%, $P = .02$).

Patients with ≥1 comorbidities regardless of LVAD implantation status were noted to have worse mean decisional conflict score at baseline but the difference was not significant at 6-month follow-up (Table III, Online Figure 3) No difference was noted in decision regret, PHQ-2, EQ-VAS and PEACE acceptance of illness score at any time point in the study. At 6-month follow-up, patients with comorbidities had worse mean PEACE struggle with illness score and mean perceived stress score than those without comorbidities. (Table III, Online Figure 3)

Compared to LVAD recipients without comorbidities, LVAD recipients with comorbidities had higher decisional conflict score at baseline but not at 6-month follow-up. (Table III) At 6-month follow-up, compared to LVAD recipients without comorbidities, LVAD recipients with comorbidities had worse PEACE struggle with illness scores and increased perceived stress scores even though there were no differences at baseline. No differences at any time point throughout study were noted in decision regret, PHQ2, EQ-VAS and PEACE acceptance of illness scores between these two groups. Results of our sensitivity analysis are shown in Online Table II. At 6-month follow-up, survival was similar between LVAD recipients with no comorbidities and those with ≥1 comorbidities (88% (n = 44) vs. 86% (n = 98), $P = .72$). (Online Figure 4)

While there were no differences at baseline, patients with pulmonary hypertension had worse decision regret, depression, stress and acceptance of illness compared to patients who did not have pulmonary hypertension. (Table IV) While patients with chronic renal disease had greater decision conflict at baseline than patients without chronic renal disease, no other differences at baseline or at follow-up met statistical significance. Lastly, there were no significant differences at baseline or follow-up for patients with large BMI.

Discussion

Our study provides novel findings with regards to how comorbidities influence the decision experience of patients considering DT LVAD implantation. Compared to patients without comorbidities, patients with comorbidities were younger, had greater stress and demonstrated greater struggle with illness at 6 months, both overall and amongst LVAD recipients. Patients with comorbidities also had greater decisional conflict at baseline, although this difference was reduced at 6 months, both overall and amongst LVAD recipients. Finally, while patients with pulmonary hypertension had worse decision regret, depression, stress and acceptance of illness at 6-month follow-up than those who did not have pulmonary hypertension, no difference was noted in patients with chronic renal disease or high body mass index. These results illuminate the role comorbidities play in patient decision-making.

Comorbidities have a significant impact in clinical decision-making. In a qualitative study assessing clinical decision-making in end-stage renal disease, comorbidities frequently affected physicians' decision to offer or withhold therapies.[6] It is quite likely that some patients were excluded from DT LVAD consideration given medical comorbidities that may have prevented a successful outcome. This might explain why comorbidities were fewer amongst our patients than in other studies.[7]

Prior analyses have demonstrated that patients with comorbidities sometimes make different decisions than

patients without comorbidities. Prostate cancer patients with comorbidities are more likely to defer aggressive management compared to similar patients without comorbidities, and are more likely to experience greater regret if they elected aggressive management.[8,9] Comorbidities attenuate the benefits without mitigating the inherent risk of interventions, therefore justifying the decision by patients in this study to opt for less invasive management.[10] These data support our findings that patients with comorbidities faced greater decisional conflict at baseline when considering LVAD implantation. Furthermore, this might help explain why in our study, older patients with comorbidities might have been reluctant to consider or be referred by their physicians for LVAD therapy.

Our study shows that comorbidities attenuate the benefit patients might experience from LVAD implantation. Patients without comorbidities had lower perceived stress and struggle with illness over time compared to patients with comorbidities regardless of decision for LVAD implantation. While LVADs are effective therapy for HF-related morbidity and mortality, they are unable to overcome the burden of non-cardiac comorbidities. Analyses from the INTERMACS registry, which assessed comorbidities using similar methodology to ours, showed that comorbidities were associated both with more adverse outcomes and a lesser likelihood of patients not undergoing cardiac transplantation after LVAD implantation.[11,12]

Our analysis suggests that patients with pulmonary hypertension appeared to have many adverse outcomes, though no significant differences were noted in patients with chronic renal disease or large BMI. These results could suggest that of these comorbidities, pulmonary hypertension appears to have the greatest negative impact on patient experience, although further research would be necessary to substantiate this finding.

Our study has several limitations. Data collection of comorbidities followed that used in the INTERMACS registry; the DECIDE-LVAD trial was not primarily designed to be an exhaustive epidemiologic analysis of comorbidities in LVAD recipients and non-recipients. Furthermore, the number of LVAD non-recipients without comorbidities was small (n = 15), limiting the strength of analysis for that particular group. Finally, while patients in trial populations are not always representative of those in the general population, we enrolled 248 of 385 eligible patients (64.4%) across 6 diverse sites, which suggests that our populations is fairly representative of the larger DT LVAD population.

Conclusion

Compared to patients without comorbidities, patients considering DT LVAD implantation with comorbidities were younger, experienced increased decisional conflict at baseline and experienced increased stress and struggle with illness at 6 months, whether or not they chose LVAD implantation. These data can help clinicians counsel patients as they consider DT LVAD implantation and have implications about the role of comorbidities in patient decision-making and decisional outcomes, beyond LVADs.

Acknowledgements

None.

Disclosures

Dr Allen reports consulting for Novartis, Boston Scientific, Janssen, Amgen and Grants from the Patient-Centered Outcomes Research Institute, National Institutes of Health, National Heart, Lung, and Blood Institute, and the American Heart Association. Dr Patel reports consulting for Abbott and Medtronic. Dr Matlock reports funding from the American College of Cardiology Foundation.

Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2019.04.008.

References

1. Arnold SV, Jones PG, Allen LA, et al. Frequency of poor outcome (death or poor quality of life) after left ventricular assist device for destination therapy: results from the INTERMACS Registry. Circ Heart Fail 2016;9.
2. McIlvennan CK, Thompson JS, Matlock DD, et al. A multicenter trial of a shared decision support intervention for patients and their caregivers offered destination therapy for advanced heart failure: DECIDE-LVAD: Rationale, Design, and Pilot Data. J Cardiovasc Nurs 2016;31:E8-E20.
3. Brehaut JC, O'Connor AM, Wood TJ, et al. Validation of a decision regret scale. Med Decis Making 2003;23:281-92.
4. O'Connor AM. Validation of a decisional conflict scale. Med Decis Making 1995;15:25-30.
5. Mack JW, Nilsson M, Balboni T, et al. Peace, Equanimity, and Acceptance in the Cancer Experience (PEACE): validation of a scale to assess acceptance and struggle with terminal illness. Cancer 2008;112:2509-17.
6. Noble H, Brazil K, Burns A, et al. Clinician views of patient decisional conflict when deciding between dialysis and conservative management: Qualitative findings from the PAlliative Care in chronic Kidney diSease (PACKS) study. Palliat Med 2017;31(10), 269216317704625. 921–931.
7. Saczynski JS, Go AS, Magid DJ, et al. Patterns of comorbidity in older adults with heart failure: the Cardiovascular Research Network PRESERVE study. J Am Geriatr Soc 2013;61:26-33.
8. Kattan MW, Cowen ME, Miles BJ. A decision analysis for treatment of clinically localized prostate cancer. J Gen Intern Med 1997;12:299-305.

9. Nguyen PL, Chen MH, Hoffman KE, et al. Cardiovascular comorbidity and treatment regret in men with recurrent prostate cancer. BJU Int 2012;110:201-5.
10. Fitzgerald SP, Bean NG, Ruberu RP. A method of decision analysis quantifying the effects of age and comorbidities on the probability of deriving significant benefit from medical treatments. J Comorb 2017;7:50-63.
11. Kirklin JK, Pagani FD, Kormos RL, et al. Eighth annual INTERMACS report: Special focus on framing the impact of adverse events. J Heart Lung Transplant 2017;36:1080-6.
12. Teuteberg JJ, Stewart GC, Jessup M, et al. Implant strategies change over time and impact outcomes: insights from the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support). JACC Heart Fail 2013;1:369-78.