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Understanding Treatment Preferences for Patients with Tricuspid Regurgitation

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Abstract

Background. Tricuspid regurgitation (TR) is a high-prevalence disease associated with poor quality of life and mortality. This quantitative patient preference study aims to identify TR patients' perspectives on risk-benefit tradeoffs. **Methods.** A discrete-choice experiment was developed to explore TR treatment risk-benefit tradeoffs. Attributes (levels) tested were treatment (procedure, medical management), reintervention risk (0%, 1%, 5%, 10%), medications over 2 y (none, reduce, same, increase), shortness of breath (none/mild, moderate, severe), and swelling (never, 3 × per week, daily). A mixed logit regression model estimated preferences and calculated predicted probabilities. Relative attribute importance was calculated. Subgroup analyses were performed. **Results.** An online survey was completed by 150 TR patients. Shortness of breath was the most important attribute and accounted for 65.8% of treatment decision making. The average patients' predicted probability of preferring a "procedure-like" profile over a "medical management-like" profile was 99.7%. This decreased to 78.9% for a level change from severe to moderate in shortness of breath in the "medical management-like" profile. Subgroup analysis confirmed that patients older than 64 y had a stronger preference to avoid severe shortness of breath compared with younger patients ($P < 0.02$), as did severe or worse TR patients relative to moderate. New York Heart Association class I/II patients more strongly preferred to avoid procedural reintervention risk relative to class III/IV patients ($P < 0.03$). **Conclusion.** TR patients are willing to accept higher procedural reintervention risk if shortness of breath is alleviated. This risk tolerance is higher for older and more symptomatic patients. These results emphasize the appropriateness of developing TR therapies and the importance of addressing symptom burden.

Highlights

- This study provides quantitative patient preference data from clinically confirmed tricuspid regurgitation (TR) patients to understand their treatment preferences.
- Using a targeted literature search and patient, physician, and Food and Drug Administration feedback, a cross-sectional survey with a discrete-choice experiment that focused on 5 of the most important attributes to TR patients was developed and administered online.
- TR patients are willing to accept higher procedural reintervention risk if shortness of breath is alleviated, and this risk tolerance is higher for older and more symptomatic patients.

Keywords
discrete choice experiment, patient preference, tricuspid regurgitation, treatment

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Background

Tricuspid regurgitation (TR) is a type of heart valve disease in which the valve leaflets are unable to close correctly, allowing blood to flow backward from the right ventricle to the right atrium.[1] Approximately 1.6 million people in the United States and 3.0 million people in Europe have TR.[2] The prevalence of TR is strongly associated with increased aging and is higher in women than in men.[3] Moderate or severe TR is associated with increased mortality.[4] Patients with TR experience signs and symptoms associated with right-sided heart failure (fatigue, weight gain, abdominal discomfort, ascites, lower-extremity edema, and shortness of breath) that affect quality of life.[5,6] As the US population is aging and the prevalence of TR increases with age, the burden of TR is likely to become a progressively important health issue.[7,8]

The mainstay of treatment for TR is medical therapy with diuretics to manage volume overload and treatment of contributing factors such as left-sided heart disease or pulmonary hypertension. It is unclear whether diuretics affect the disease process or only temporarily treat symptoms.[9] Data on the success of surgical management is conflicted, and relatively few isolated cases are performed.[10–12] There are no class I indications (i.e., strong recommendations where one intervention should be chosen over another) for surgical repair of isolated TR in the American College of Cardiology/American Heart Associated guidelines, even when it is severe and symptomatic.[13] European guidelines do offer a class I indication for isolated TR but only in primary etiologies without right ventricular dysfunction.[14] Both guidelines emphasize the important impact of TR by providing Class II recommendations (is or may be reasonable to consider) for addressing even mild or moderate TR with annuloplasty when a left-sided valve surgery is required.

There is a clear gap in TR treatment options. Recent advances in technology have led to the development of percutaneous interventions for TR.[6] These technologies are actively being studied. The goal is to deliver significant and consistent TR reduction using a transcatheter-based, minimally invasive approach that places patients at less risk than conventional open surgery. No percutaneous interventions for TR had been approved by the US Food and Drug Administration (FDA) at the time of this study.

Patient preference research is an evolving area of regulatory science.[15] The FDA Center for Devices and Radiological Health recognizes that only patients live with their medical conditions and make daily choices regarding their health care.[16] Patient preference information identifies the unique aspects of patient perspectives on benefits and risks that come with treating their disease. These studies elicit which attributes are important to patients, how important they are, and what risk-benefit tradeoffs patients are willing to make when undergoing treatment.[17] This style of research is timely and well-suited to assess TR patients' preferences as disease burden and treatment options are both expanding.

The objective of the study is to gain an understanding of TR patients' willingness to undergo a transcatheter tricuspid valve replacement or repair procedure versus medical management based on prescribed risk-benefit profiles for each treatment. Improved understanding of this patient population and their treatment preferences can inform decision making in therapy development, trial design, and patient communication for this disease process.

Methods

Study Design

A cross-sectional survey with a discrete-choice experiment (DCE) was developed to elicit patient preferences related to TR treatment. The survey had 3 sections: 1) disease history (clinical and treatment history characteristics, symptom preference rankings), 2) treatment preferences (current number of pills [total pills, not number of different medications, current shortness of breath,

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current swelling, preference rankings of non-DCE treatment characteristics, dominance test and DCE task evaluation questions, frequency of straight-lining, and attribute dominance on choice tasks), and 3) sociodemographic characteristics. DCE is an accepted methodology under the CDHR guidelines for patient preference analysis.[6,7,16,17]

Preference Ranking

Participants were asked to rank up to 5 symptoms that they considered the most important to improve, ranking from 1 (most important) to 5 (least important). The symptoms included abnormal heart rhythms; anxiety; chest pain; depression; fatigue; loss of appetite; poor sleep quality; pulsing in your neck; shortness of breath; swelling of the abdomen; swelling of the hands, legs, and feet; and weight change.

DCE Instrument Development

Targeted literature review. The DCE attributes and levels, as well as symptoms mentioned in other parts of the survey and the treatment-like profiles, were initially based on a targeted literature review and input from TR patients, cardiologists, and medical device manufacturer experts. The following terms were searched in EMBASE and MEDLINE to identify studies that would inform attribute selection: tricuspid valve disease, valve disease, CVD, tricuspid, tricuspid valve disease preference studies, preference studies, CVD preference studies, and surgical valve preference studies. The inclusion criteria were articles in which the sample population consisted of adult patients with valvular disease with a focus on qualitative or quantitative preference methods.

Attribute and level selection. A list of potential attributes as identified through the literature review was assessed by physicians ($n = 4$) and industry experts from a medical device manufacturer ($n = 4$) individually for relevance to the disease state and relationship with other attributes. Qualitative interviews with TR patients ($n = 4$) for 60 min each were conducted to analyze the 8 attributes that were narrowed down from the literature review by the physicians and industry experts (treatment type, need for medications, reintervention, severe adverse events, need for pacemaker, shortness of breath, fatigue, and edema) and determine appropriate levels. Feedback on attribute relevance and importance from these qualitative interviews was used to build a draft survey. The survey was then pretested with additional TR patients ($n = 5$) via a web conference in which both the interviewer and patients could jointly review an online DCE survey. Participants provided thoughts and reactions to wording, formatting, and functionality of the survey. Edwards Lifesciences (www.Edwards.com) presented a Q-Submission to request FDA feedback related to this study in Q4 of 2019. Q-Submissions or Q-Subs are used to track various mechanisms for requesting FDA feedback. Edwards Lifesciences is a global leader in the science of structural heart disease and hemodynamic monitoring. Their technologies address patient populations in which there are significant unmet clinical needs, such as structural heart disease, heart valve disease, and advanced monitoring of the critically ill. The FDA responded with study feedback and input in Q1 of 2020 that included increasing the sample size from 100 to 150 and updating the need for medication attribute to include frequency not just quantity. A revised survey reflected interviewer feedback and FDA recommendations.

The final DCE contained 5 attributes with 2 to 4 levels each (Table 1). The attributes tested were treatment type, risk of reintervention, need for medication, shortness of breath, and experience with swelling. A full description of each attribute was in the survey followed by comprehension questions. Details on the survey are provided (see Supplementary Material). The risk for reintervention attribute levels was based on the Edwards CLASP TR early feasibility study (clinicaltrials.gov ID: NCT04097145), which had a major adverse event rate of 5.9% with no patients experiencing cardiovascular mortality, stroke, myocardial infarction, renal complication, or reintervention within 30 d of the procedure.[15] Improvement in shortness of breath and swelling were among the most valued symptoms from a patient's perspective from Edwards CLASP TR early feasibility study. Since the current standard of care for managing TR patients is medical management, increasing or decreasing medication was an attribute.[18]

Experimental Design

Based on the 5 attributes and levels in the DCE, 288 separate profiles and 82,944 combinations were possible. To narrow down the number of choice tasks, a D-efficient main-effects experimental design was applied using Ngene software (www.choice-metrics.com). An algorithm systematically chose a subset of possible choice tasks that still allowed for independent estimation of each attribute level's effect on choice. The developed

Table 1 Final DCE Attributes and Levels

Attribute	Attribute Level			
	Level 1	**Level 2**	**Level 3**	**Level 4**
Treatment type[a]	Medical procedure	Medical management	—	—
Risk for reintervention[a]	0% (0 in 100 people)	1% (1 in 100 people)	5% (5 in 100 people)	10% (10 in 100 people)
Need for medications[b]	No medication in 2 y	Reduced number of pills in 2 y	Same number of pills in 2 y	Increased number of pills in 2 y
Shortness of breath	None/mild	Moderate	Severe	—
Swelling in hands, ankles, feet, or abdomen	Never	3 times per wk	Every morning	—

[a]The "risk of reintervention" attribute was linked to the "treatment type" attribute such that if treatment type was medical management, risk of reintervention was always 0%; if treatment type was medical procedure, then risk of reintervention was 1%, 5%, or 10%. As the effects of these attributes could not be estimated independently, in the analysis model they were treated as a single composite categorical attribute of "treatment type and risk of reintervention."
[b]Number of pills refers to the actual quantity of pills taken at a certain time. Number of pills is not the number of medications.

design included 24 paired comparisons divided into 3 blocks (8 paired comparisons each). Participants were randomly assigned to 1 of the blocks.

Due to the link between the risk for reintervention attribute and the treatment type attribute (in which medical management was always shown with 0% risk of reintervention and medical procedure was always shown with 1%/5%/10% risk), experimental design properties were not met. The absence of balance between the attributes should not affect estimating parameters.[19,20] In the analysis, the linked attributes were treated as a single composite categorical attribute of "treatment type and risk of reintervention," with each possible combination of the risk for reintervention and treatment type levels (4 in total) treated as an independent attribute level.

In addition to the 8 tasks, a dominance test was included. The dominance test showed 1 treatment profile that was clearly preferable to the other across all attributes. A sensitivity analysis excluded participants who exhibited illogical responses (i.e., selected the inferior treatment in the dominant scenario logic test or straightlined choices on the DCE tasks).

The DCE approach uses random utility theory to model treatment choices and estimate the relative importance of attributes. In this model, the utility (U) a participant obtains from choosing a treatment (i) is dependent on the utility the participant obtains from the characteristics/attributes of this treatment (X) and a random error (ε). The characteristics of treatment were divided into a vector of treatment type and risk of reintervention, need for medications, shortness of breath, and swelling (X). Then,

Equation 1: Random utility model

$$U_i = \alpha X_i + \varepsilon_i$$

where α represents the participant's utility from the treatment attributes. α is the preference estimate. It is assumed that the error term, ε_i, follows an independently and identically distributed type 1 extreme-value distribution.[16]

The assumption of the extreme-value distribution of ε_i results in the following logit model:

Equation 2: Logit model

$$P(\text{choosing alternative } i) = \frac{e^{\alpha X_i}}{\sum_j e^{\alpha X_j}}$$

where option i is one alternative among a set of j alternatives.

The probability of choosing alternative i is a function of the attribute levels of alternative i and the attribute levels of all other choice task profiles. The probability of choosing 1 profile from 2 alternatives is 1 minus the probability of choosing the other choice task profile.

Data Collection

A patient survey was fielded via Confirmit, an electronic platform (www.confirmit.com). The full survey has been published (see Supplementary Material). An example

choice task ensured that participants understood each attribute and the choice tasks.

Cardiovascular staff screened patients and referred eligible patients to participate in the electronic online survey. Participants received a postcard with their clinical data and the online survey link from the site staff. Inclusion criteria included adults 21 y or older, clinically confirmed diagnosis of TR (moderate or greater), and untreated or receiving medical management and still symptomatic. Exclusion criteria included previously treated surgically or procedurally for TR. Once a participant completed the survey, each participant received a $25 preloaded gift card. The participating sites include Penn State Milton Hershey, Wake Forest Baptist, Medical College of WI, Buffalo General, Cleveland Clinic, University of Arkansas, Columbia, AZ Cardiovascular, Houston Methodist, USF Health, St Francis, Erlanger, Tallahassee Research Institute, and UT Southwestern. The Western Institutional Review Board determined that the study was exempt from human subject review.

Data Analyses

DCE preferences and tradeoff analysis. A mixed logit (MXL) model was selected as the final primary model, with random effects for all attribute parameters. The MXL accounts for the correlation among repeated choices by the same individual and unobserved preference heterogeneity by assuming that there is a distribution of preference weights for each attribute due to the individual differences among those taking the survey. As a result, the MXL outputs a mean preference weight of each attribute and the corresponding standard deviation (SD). A conditional/multinomial logit (MNL) was used for subgroup analyses. The less complex MNL was chosen for subgroup analysis because of sample size considerations.

The logit model outputs a coefficient for the mean (and SD, if MXL model is used) of the effect (preference estimate) for all but 1 of the attribute levels relative to the omitted level (the reference level) for each categorical attribute. The differences between the coefficients of the attribute levels represent the mean change in utility when a treatment attribute level changes. Each model coefficient (preference estimate) indicates the (mean) preference for the given attribute level compared with the reference level. Positive values indicate the given attribute level is more preferred than the reference level is; negative values indicate it is less preferred.

Primary MXL analyses were conducted on the full analytic sample. "Tricuspid transcatheter–like" treatment (procedure with a 5% risk of reintervention, reduced number of pills in 2 y, no or mild shortness of breath, no swelling) and "medical management–like" treatment profiles (medical management with no risk of reintervention, same number of pills in 2 y, severe shortness of breath, and swelling 3 times per wk) were developed using input from physicians. The predicted probabilities that participants would choose either a tricuspid transcatheter–like treatment or a medical management–like treatment were calculated using equation 2, and the preference estimates (coefficients) derived in the MXL choice model, with 95% confidence intervals (CIs) estimated via the delta method.

Participant characteristics. Descriptions of participants' sociodemographic and clinical characteristics and other variables were provided to understand the study sample, explore preferences of symptoms and treatment characteristics not included as attributes in the DCE, and assess the quality of DCE task data. Data were summarized using descriptive statistics, presenting the mean, SD, median, interquartile range, minimum, and maximum for continuous variables and frequencies and percentages for categorical variables.

Subgroup analyses. Due to sample size constraints, response categories were collapsed into 2 subgroups for subgroup analyses by age (64 y and younger v. 65 y and older), general physical health status (good to excellent health v. fair to poor health), New York Heart Association (NYHA) functional class (I/II v. III/IV, corresponding to no/slight physical activity limitations v. marked and total physical activity limitations, respectively), TR grade (moderate v. severe or worse), heart failure type (heart failure with preserved ejection fraction [HFpEF] v. heart failure with reduced ejection fraction [HFrEF]), and participating site (site 13 v. others). The ranges for the age subgroups were based on the mean age of 64.76 y. Site 13 had a high number of participants compared with other sites because they took an active approach to recruitment and used their electronic health record system to contact eligible patients. Other sites did most recruiting when eligible patients came in for an office visit. A separate MNL model was fit to the data from each subgroup, and differences in preferences between subgroups were identified by Wald tests comparing individual coefficient estimates between the 2 models and likelihood ratio (LR) tests comparing the 2 models overall.

DCE analytic modeling was conducted in R version 3.6.2. Calculations of descriptive statistics, group comparisons of participant characteristics, DCE data quality metrics, and DCE task evaluation were conducted using SAS version 9.4.

Relative attribute importance. The relative attribute importance (RAI) was calculated to identify the relative value of each of the 5 attributes included in the DCE. The absolute value of the difference in the model coefficients between the minimum and maximum levels for each attribute reflected the utility associated with each attribute. The RAI for each attribute was expressed as a percentage weight, calculated by dividing the difference/range in coefficients (for that attribute) by the sum of the differences/ranges in coefficients for all attributes. The 95% CIs for each RAI percentage from the MXL model were generated via the delta method. Attributes with a greater RAI are more important in the decision-making process, on average.

Results

The survey was completed by 150 patients with clinically confirmed moderate or greater TR across 14 US sites. Twelve participants were excluded from the final analytic sample: 9 participants did not have untreated TR, 1 had mild TR, and 2 claimed they were unable to view the DCE. Patients with treated TR and or mild TR could have differing preferences from the eligible population in this study. The median time to complete the survey was 33.83 min. The final sample included 138 participants, since 12 of the 150 respondents did not meet eligibility criteria.

Fourteen participants (10.1%) failed the dominance (logic) test as they chose the clearly less preferable treatment option on the dominance choice task. Twelve participants (8.7%) straight-lined their answers on all choice tasks, either always choosing the treatment option on the left or always choosing the treatment option on the right. A total of 19 participants either failed the dominance test and/or straight-lined all the choice tasks. These participants were included in the final sample but excluded from the sensitivity analyses. Results from this MXL sensitivity analysis model did not vary significantly.

Sociodemographic Characteristics

The sample had a mean age of 65 y (range, 23–91 y), and 55.8% of participants were women. Most participants identified as white Caucasian (81.9%), and 37.0% of the participants reported having a bachelor's degree or higher. Participants reported seeing a doctor for their heart problems for approximately 15 y on average (8 y was the median). Of the sample, 25.2% received their diagnosis less than 1 y ago, 28.3% of the sample were diagnosed 1 to 5 y ago, and 20.3% received their diagnosis more than 5 y ago; 20.3% of participants did not remember being told about their diagnosis, and 5.8% were unsure about the time of diagnosis. Based on the clinically reported data collected within the survey, 54.4% of participants had a NYHA classification of class I/II, and 45.7% had a NYHA classification of class III/IV. Most of the sample (61.6%) had preserved ejection fraction (HFpEF), 31.2% had reduced ejection fraction (HFrEF), whereas 7.2% reported no heart failure. With regard to the participants' TR grade, 60.1% reported having moderate TR, 35.5% reported having severe TR, and 4.4% reported having massive or torrential TR (see the Supplementary Material).

The top 5 symptoms participants experienced in relation to their heart problems were shortness of breath (76.1%), heart arrhythmia (75.4%), edema (64.5%), poor-quality sleep (54.3%), and swelling of the abdomen (41.3%). A large proportion (72.5%) of participants reported experiencing shortness of breath in the 2 wk before taking the survey. Two participants (1.4%) ranked no symptoms.

Preference Rankings

Overall, the most highly ranked (most important) symptom to improve was shortness of breath, with a mean (SD) of 1.9 (1.0), followed by fatigue with a mean (SD) of 2.2 (1.2), then chest pain with a mean (SD) of 2.4 (1.3), and then abnormal heart rhythms with a mean (SD) of 2.4 (1.4) (see Supplementary Material).

DCE Results

Preference estimates were statistically different from zero for at least 1 level of every attribute when choosing between treatments. All attributes in the DCE were considered important. Preference estimates for all attributes were in the expected directions, whereby treatments involving increased severity or risk were less preferred than treatments with less severity/less risk (Table 2). The greater the severity/risk, the less preferred was that option. A procedure with 0% risk of reintervention was preferred over a procedure with more risk of reintervention at a 5% (95% CI: −1.55, −0.25; $P = 0.006$) or 10% (95% CI: −2.03, −0.48; $P = 0.002$) level. No medication in 2 y was preferred over an increase in medications over 2 y (95% CI: −1.54, −0.22; $P = 0.009$). No

Table 2 Mixed Logit (MXL) Model Main Effects ($N = 138$)

Attribute Level	Mean Estimate			SD Estimate		
	Coefficient	95% CI	*P* Value	Coefficient	95% CI	*P* Value
Treatment type and risk of reintervention						
Medical management with 0% risk of reintervention (reference)	0.00			0.00		
Medical procedure with 1% risk of reintervention	−0.46	(−1.01, 0.08)	0.096	0.03	(−1.09, 1.15)	0.96
Medical procedure with 5% risk of reintervention	−0.90	(−1.55, −0.25)	0.006	1.23	(0.18, 2.29)	0.022
Medical procedure with 10% risk of reintervention	−1.25	(−2.03, −0.48)	0.002	1.62	(0.53, 2.72)	0.003
Need for medications[a]						
No medication in 2 y (reference)	0.00			0.00		
Reduced number of pills in 2 y	−0.17	(−0.77, 0.42)	0.57	0.13	(−0.78, 1.04)	0.78
Same number of pills in 2 y	−0.57	(−1.18, 0.04)	0.065	0.05	(−1.17, 1.28)	0.93
Increased number of pills in 2 y	−0.88	(−1.54, −0.22)	0.009	1.29	(0.35, 2.23)	0.007
Shortness of breath						
None/mild (reference)	0.00			0.00		
Moderate	−1.33	(−1.96, −0.70)	<0.001	1.16	(0.34, 1.98)	0.006
Severe	−5.96	(−8.37, −3.55)	<0.001	4.48	(2.53, 6.43)	<0.001
Swelling in hands, ankles, feet, or abdomen						
Never (reference)	0.00			0.00		
3 times per wk	−0.49	(−1.01, 0.03)	0.064	1.20	(0.22, 2.19)	0.017
Every morning	−0.97	(−1.55, −0.38)	0.001	1.29	(0.43, 2.15)	0.003
Model fit statistics						
Log likelihood			−462.56			
AIC			965.12			
BIC			1,065.25			

AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; CI, confidence interval; SD, standard deviation.
[a]Number of pills refers to the actual quantity of pills taken at a certain time. Number of pills is not the number of medications.

or mild shortness of breath was preferred over moderate (95% CI: −1.96, −0.70; $P \leq 0.001$) or severe (95% CI: −8.37, −3.55; $P < 0.001$) shortness of breath. No swelling was preferred over swelling every morning (95% CI: −1.55, −0.35; $P = 0.001$). Statistically significant SD estimates indicate heterogeneity in attribute-level preferences and suggest the MXL is appropriate for the data. Severe shortness of breath demonstrated the greatest preference heterogeneity (SD: 4.48; $P < 0.001$), and medical procedure with 1% risk of reintervention showed the least, albeit statistically insignificant, variability in preferences (SD: 0.03; $P = 0.96$).

Choice Probabilities

The predicted probability that the average participant would choose the tricuspid transcatheter–like treatment profile over the medical management–like treatment profile was 99.7% (95% CI: 99.1%, 100.0%). This predicted probability could be driven by the difference in levels for the dominating shortness of breath attribute, whereby the tricuspid transcatheter–like profile had a shortness of breath level of none/mild compared with the medical management–like profile that had a severe shortness of breath level (Table 3).

In a sensitivity analysis, the medical management–like treatment profile had a redefined shortness of breath level from severe to moderate, which found a 78.9% predicted probability that the average participant would choose a transcatheter tricuspid repair or replacement device–like profile over a medical management–like profile. This suggests that a transcatheter tricuspid repair or replacement device–like profile would be preferred over a medical management–like profile, even when the shortness of breath level was estimated as moderate in the medical management–like profile.

In a sensitivity analysis, the medical management–like treatment profile had a redefined shortness of breath level from severe to none/mild; the predicted probability that participants would choose a transcatheter tricuspid repair or replacement device–like profile or a medical management–like profile was approximately equal (49.6% and 50.4%, respectively). This suggests that the preference is similar for a transcatheter tricuspid repair

Table 3 Comparison of Predicted Choice Probabilities ($N = 138$)

Attribute	Transcatheter Tricuspid Repair or Replacement Device–like Profile	Medical Management–like Profile
Treatment type	Medical procedure	Medical management
Risk of reintervention	5% risk	0% risk
Need for medications	Reduced number of pills in 2 y	Same number of pills in 2 y
Shortness of breath	None/mild	Severe
Swelling	Never	3 times per wk
Predicted choice probability, %	99.7%	0.3%
95% CI	(99.1%, 100.0%)	(0.0%, 0.9%)

CI, confidence interval.

or replacement device–like treatment and a medical management–like profile with shortness of breath as none/mild.

Subgroup Analyses Results

A large proportion (38%; $n = 52$) of the study sample was recruited from a single clinic (site 13). Site 13 was compared with the other sites to assess the generalizability of the results. Sociodemographic characteristics, clinical characteristics, and treatment preferences for site 13 were analyzed, and the preferences of these patients did not differ from other sites.

For the 2 age groups of 64 y or younger ($n = 56$) and 65 y or older ($n = 82$), there were differences for certain attribute levels, such as older participants wanting to more strongly avoid severe shortness of breath compared with the younger participants ($P = 0.011$). For the NYHA subgroups of NYHA class I or II ($n = 75$) and NYHA class III or IV ($n = 63$), there were differences in preferences for certain attribute levels, such as NYHA class I/II wanted more strongly to avoid a medical procedure with 10% risk of reintervention (v. medical management with 0% risk; $P = 0.025$) and avoid severe shortness of breath (v. none/mild; $P = 0.017$), compared with the NYHA class III/IV subgroup. For the TR grade subgroups of moderate TR ($n = 83$) and severe or worse TR ($n = 55$), participants with severe or worse TR wanted to more strongly avoid shortness of breath ($P < 0.02$) compared with participants with moderate TR. For the heart failure type subgroups of preserved ejection fraction ($n = 85$) and reduced ejection fraction ($n = 43$), participants with HFpEF more strongly wanted to avoid a medical procedure with 10% risk of reintervention (v. medical management with 0% risk; $P < 0.03$) compared with participants with HFrEF.

DCE Task Evaluation

Overall, 81.9% of participants strongly agreed or agreed that the choice tasks were easy to understand, 76.1% strongly agreed or agreed that they were easy to answer, 92.8% strongly agreed or agreed they answered questions according to their preferences, and 85.5% strongly agreed or agreed that the questions were relevant to them.

Of the participants who failed the dominance test, 22% strongly disagreed or disagreed that the questions were easy to answer, and 78% strongly agreed or agreed that the questions were easy to answer.

RAI

Shortness of breath was the most important attribute, accounting for 66% of patient utility. The rest of the treatment attributes accounted for 9% to 13% of relative importance and did not statistically differ from each other. Results of the subgroup analyses were similar. Shortness of breath was the most important attribute across all subgroups, with estimates ranging from 56% to 68% of patient utility.

Discussion

Transcatheter structural heart disease interventions have transformed the care of patients with valvular heart disease, particularly those with advanced severity.[21] Patient selection and procedural planning rely on a multidisciplinary heart team collaboration and discussion with the patient regarding the risks and benefits of such interventions, especially if performed in the context of a clinical trial. Given the novel nature of transcatheter TR interventions, patient preference is of paramount importance in facilitating shared decision making.[22] Currently, the only treatment option for patients with TR in the United

States is medical management. This study suggests that if transcatheter treatments for TR are more effective for improving shortness of breath, patients would likely prefer the novel transcatheter treatment, even if the risk of reintervention over a 2-y period is approximately 5%. This study also shows that adults older than 64 y are significantly more likely to choose a therapy that addresses shortness of breath symptoms. Lastly, patient preferences from this study indicate that patients with a lower symptom burden (NYHA class I/II) prefer to avoid reintervention risk compared with those with a high symptom burden (NYHA class III/IV). This result matches previous patient preference findings in which patients with a high symptom burden from heart valve disease are more willing to take on risk after a therapy if it leads to improved symptom management.[23]

These findings may inform regulatory and reimbursement approval processes and clinical trial development. Patient preferences are earning consideration from regulators, payers, and health technology assessment organizations, but consensus is needed on how much weight to give patient preferences in the approval process.[24] When considering future clinical trial design, subjective or objective assessments of shortness of breath would be useful for understanding future patient decision making in accepting a novel invasive therapy. Also, given the results of reintervention risk, it will be useful to engage more symptomatic patients in early intervention testing until data on therapy durability is more robust.

The current evidence related to patient preference in structural heart disease remains limited.[23,25] Patient preference has been studied in patients with severe aortic stenosis, for which transcatheter aortic valve replacement is nowadays standard of care in elderly patients and those at a higher surgical risk.[26,27] A systematic review examining 8 studies addressing preference of patients with aortic stenosis revealed that the patients' willingness to accept risk was highly variable. Most patients had a desire for symptom relief and improved functional capacity.[25] These findings are similar to the results of this study, in which patients' symptoms were a driving factor in their decision making. In contrast to this study, the 8 studies included in this review did not address the possible need for reintervention.

Patient preference information has been used previously to help guide the FDA in determining acceptable risk relative to benefit for key clinical outcomes.[24,26] Going forward, patient preference data will be useful for regulatory and reimbursement decision making. This study is the first to provide quantitative patient preference data from patients with clinically confirmed TR to understand what matters to patients and to what degree and their risk-benefit tradeoffs. As more data emerge on the attributes and levels associated with new TR technologies, it may be helpful to update this study. However, in the interim, our analysis provides initial insight into the key drivers that patients value for treatment of TR.

Limitations

The limitations of this study should be considered in the interpretation of the results. The recruitment sample was subject to biases, including self-selection and nonresponse. The online survey might have limited access or increased completion difficulty for some respondents who did not have internet access or sufficient computer literacy (e.g., those who were older or with lower income). The sample size could be considered small for a DCE study; however, a larger sample size was not possible due to time and resource constraints. Subgroup analyses were only exploratory, because the sample size was not powered for subgroup analyses.

A limitation of any DCE study is that only a subset of all possible attributes distinguishing different treatments can be assessed. The DCE treatment profiles only approximate real-world transcatheter tricuspid repair or replacement device and medical management treatment. Results need to be interpreted within the context of the attributes and levels included in the DCE survey.

The survey included clinical and treatment history questions and practice exercises for each attribute before participants completed the DCE choice tasks. This could have led to fatigue for respondents and lower-quality DCE data. Another potential factor in the data quality is that the DCE itself might have been too complex/difficult for some participants. However, 81.9% of participants agreed or strongly agreed that the DCE was easy to understand, and 76.1% agreed the choice tasks were easy to answer, suggesting that response burden was reasonable.

Only patients with untreated, clinically confirmed moderate or greater TR were included in this study, as this is the patient population most likely to be in the position to decide between medical therapy and a tricuspid transcatheter repair or replacement procedure. It should be noted that individuals who have undergone a surgical or procedural TR treatment were not included in this study; this patient population may have different treatment preferences than those who have not received prior treatment for TR, and surgical procedures are associated with a risk for further reintervention. It may be valuable to include a separate study in the future to assess the treatment preferences of previously treated patients with TR.

Conclusion

Using a discrete-choice experiment to explore TR treatment risk-benefit tradeoffs, this study finds that TR patients are willing to accept higher procedural reintervention risk if shortness of breath is alleviated. This risk tolerance is higher for older and more symptomatic patients. These results emphasize the appropriateness of developing TR therapies and the importance of addressing symptom burden.

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Availability of Data and Material

The data are confidential.

Supplemental Material

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