# Soluble ST2 Is a Marker for Acute Cardiac Allograft Rejection

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*Background.* **Soluble ST2 (sST2), an interleukin (IL)-1 receptor family member, has a role in immunologic tolerance and has also emerged as a biomarker of cardiac stretch and remodeling. The sST2 role in heart transplantation is still unknown.**

*Methods.* **From the heart transplantation population at our institution (n = 74), we selected a subset of 26 patients who had an acute rejection episode in the first year after transplantation (35%; 52 ± 14 years; 76% men). Endomyocardial biopsy (EMB) results obtained at the time of the first rejection episode represented the rejection cohort (n = 26). Each patient served as a control to himself or herself, with EMB without rejection obtained before and after the rejection episode (n = 52). All laboratory measurements and blood samples were obtained at the time of EMB.**

*Results.* **sST2 concentrations rose significantly in the context of acute rejection (130 [60 to 238] versus 51 ng/mL [28 to 80]; $p = 0.002$). Tertile analyses of sST2 concentrations revealed a graded association with rejection ($p = 0.002$) and repeated measurement analyses showed that sST2 concentrations were significantly modulated by the presence of rejection ($p = 0.001$). In receiver operator characteristic (ROC) analysis, sST2 had an area under the curve (AUC) of 0.72; the optimal cutoff point was 68 ng/mL (positive predictive value of 53%, negative predictive value of 83%), which predicted acute cellular rejection (odds ratio [OR] 4.9; 95% confidence interval [CI], 1.7 to 14.5; $p = 0.004$). The addition of sST2 values to those for the N-terminal pro B-type natriuretic peptide (NT-proBNP) resulted in a significant improvement on the integrated discrimination index (IDI) for rejection (relative improvement of 24%; $p = 0.021$).**

*Conclusions.* **sST2 concentrations are modulated by the presence of acute rejection and provide complementary predictive ability to NT-proBNP for the biochemical identification of rejection.**

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ST2 peptide is a member of the interleukin (IL)-1 receptor family with membrane-bound (ST2L) and soluble forms (sST2). Originally described as playing a role in modulating endogenous immunologic tolerance through interaction of type 2 T-helper cells [1–3], ST2 was also recently found to be highly induced when mechanical strain was applied to cultured rat cardiac myocytes [4]. Subsequently the discovery that IL-33 is the functional ligand of both sST2 and ST2L and that IL-33/ST2L signaling acts as an antiremodeling cardioprotective paracrine system [5–7] led to the examination of sST2 as a cardiac biomarker. sST2 concentrations are elevated and associated with an adverse outcome in patients with acute coronary syndrome and heart failure [8–12] and are predictive of more adverse remodeling on echocardiography [13]. Thus in addition to its putative role in modulating immune tolerance, sST2 is thought to play a pivotal role in the response to cardiac stretch and injury.

Among patients who have undergone orthotopic heart transplantation (OHT), an important clinical issue is acute cellular rejection. Despite the progress in immunosuppressive therapy, 30% to 40% of heart transplant patients experience at least 1 acute cellular rejection episode during the first year after transplantation, and rejection is the cause of 12% of deaths during this period [14]. Currently endomyocardial biopsy (EMB) is the standard procedure for diagnosis of acute rejection despite its known limitations, such as its invasive nature. Thus there is an evident need for new diagnostic tools that are noninvasive, sensitive enough, and integrative with other measures to not only detect acute cellular rejection but also monitor the progress of therapy.

There are no data about the role of sST2 in patients after OHT. Given its dual role in immune tolerance as well as myocardial stretch and response to injury, we

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**Abbreviations and Acronyms**

| | |
|---|---|
| EMB | = endomyocardial biopsy |
| IQR | = interquartile range |
| LVEF | = left ventricular ejection fraction |
| NT-proBNP | = N-terminal pro B-type natriuretic peptide |
| OHT | = orthotopic heart transplantation |
| ROC | = receiver operating characteristic |
| sST2 | = soluble form of ST2 |

hypothesized that measurement of sST2 would be potentially useful to identify acute cellular rejection while simultaneously showing potential utility to monitor the course of rejection treatment.

## Material and Methods

### *Study Population and Protocol*

We designed a case-crossover study for evaluating the association between sST2 and acute rejection. A total of 74 patients underwent OHT between 2002 and 2007 in our institution. EMB was carried out as part of routine posttransplantation care either as surveillance protocol or for clinical suspicion of rejection based on the new appearance of heart failure signs, arrhythmias or echocardiographic manifestations of graft dysfunction. Acute rejection was defined as either a clinically suspected rejection episode (n = 14) or a biopsy-confirmed acute rejection (n = 12; > International Society of Heart and Lung Transplantation [ISHLT] grade 1R) resulting in the administration of intravenous steroids for resolution. Among the entire OHT population, we selected a subset of 26 patients who had an acute rejection episode in the first year after transplantation (35%), which represents the population included in this study. To avoid potential confounding by recently treated rejection episodes, we selected only patients with first rejection episodes. The biopsy samples obtained at the time of the first rejection episodes represent the rejection cohort in this study (n = 26). Because each patient served as a control to himself or herself, the EMB samples that did not show rejection, obtained before and after the rejection episode, represent the nonrejection cohort (n = 52). All blood samples were obtained by venipuncture at the time of EMB and aliquots of serum were stored at −80°C until analyzed. All patients were treated with standard triple immunosuppression, including cyclosporine (73%) or tacrolimus (27%), mycophenolate mofetil (100%), and prednisone (100%). EMB samples were assessed for cellular rejection using standard methods (formalin-fixed paraffin-embedded tissue with hematoxylin and eosin staining) and graded according to the ISHLT standardized grading system [15]. Right atrial pressure was also recorded. An echocardiogram was obtained in all patients, and standardized measures were used according to the American Society of Echocardiography recommendations. Left ventricular ejection fraction (LVEF) was measured by Simpson's method. The investigation conforms with the principles outlined in the Declaration of Helsinki. The study was approved by the local ethics committee (Ethical Committee of University Hospital Virgen de la Arrixaca), and informed consent was obtained from each patient at study inclusion.

### *Biochemical Analysis*

Concentrations of sST2 were determined using a novel high-sensitivity sandwich immunoassay, Presage ST2 (Critical Diagnostics, San Diego, CA), which has recently been validated [16]. The sST2 assay had within-run and total coefficients of variation of < 2.5% and 4.0%, respectively; the reported 95th percentile of a blood donor population was 31 ng/mL in men and 21 ng/mL in women [16]. The N-terminal pro B-type natriuretic peptide (NT-proBNP) levels were measured by electrochemiluminescence immunoassay using an Elecsys 2010 analyzer (Roche Diagnostics GmbH, Mannheim, Germany) with a total imprecision value lower than 3%. The XE-2100 (Sysmex Corporation, Kobe, Japan) automated hematology analyzer and the Modular Analytics E170 analyzer (Roche Diagnostics GmbH, Mannheim, Germany) were used for all other laboratory measurements.

### *Statistical Analysis*

Continuous variables were tested for normal distribution by use of the Kolmogorov-Smirnov test. Variables not normally distributed are expressed as median (interquartile range [IQR]). Normally distributed continuous variables are expressed as mean ± standard deviation. Frequencies of categorical variables are expressed as numbers (percentage). Univariable Spearman's correlation was used to evaluate the magnitude and significance of relationships between sST2 and other continuous covariates. Multivariable linear regression analysis using log transformed values of sST2 as the dependent variable identified continuous variable predictors of sST2 concentrations. Comparisons between rejection and nonrejection cohorts were performed using the Mann-Whitney *U* test. The comparison of rejection probabilities across tertiles of sST2 was performed using the $\chi^2$ test. The comparison of sST2 concentrations across the histologic grades of rejection was performed using the Kruskal-Wallis test. After log transformation of sST2 levels, the general linear model analysis with repeated measures of analysis of variance was used for studying the significance of sST2 changes within subjects across 3 levels (before rejection, during rejection, and after rejection). The receiver operating characteristic (ROC) curve analysis was constructed to determine the optimal cutoff points of sST2 and NT-proBNP for predicting rejection. The optimal cutoff value was identified as the point on the ROC curve that maximized both sensitivity and specificity. Logistic regression analysis was used for evaluating the predictive values of ST2 and NT-proBNP according to cutoff values. The added predictive ability of sST2 over NT-proBNP was evaluated by using the integrated discrimination improvement (IDI), as described by Pencina and colleagues [17]. A new ordinal variable

*Table 1. Characteristics of Rejection and Non-Rejection Samples*

| Variable | Rejection n = 26 | No Rejection n = 52 | *p* |
|---|---|---|---|
| Time from OHT, months | 3.0 (1.2–7.0) | 3.1 (1.0–7.9) | 0.81 |
| Body mass index, kg/m$^2$ | 28 ± 10 | 29 ± 11 | 0.90 |
| ISHLT grade | | | <0.001 |
| 0R | 0 | 17 | |
| 1R[a] | 14 | 35 | |
| 2R | 8 | 0 | |
| 3R | 4 | 0 | |
| Cyclosporine level, ng/mL | 253 ± 102 | 242 ± 98 | 0.78 |
| Tacrolimus level, ng/mL | 12.1 ± 4 | 14.8 ± 7 | 0.51 |
| Mycophenolic acid level, μg/mL | 2.6 ± 1.7 | 2.5 ± 1.6 | 0.82 |
| Left ventricular ejection fraction, % | 57 ± 8 | 62 ± 5 | 0.010 |
| NT-proBNP, pg/mL | 6,111 (1033–14,948) | 1,703 (778–4,355) | 0.012 |
| Right atrial pressure, mm Hg | 8 (5–13) | 8 (5–13) | 0.161 |
| Creatinine, mg/dL | 1.4 ± 0.6 | 1.3 ± 0.4 | 0.191 |
| Blood urea nitrogen, mg/dL | 68 ± 41 | 57 ± 30 | 0.183 |
| Uric acid, mg/dL | 6.7 ± 2.7 | 6.4 ± 2.0 | 0.650 |
| C-reactive protein, mg/dL | 1.2 (0.3–2.8) | 0.8 (0.1–2.2) | 0.162 |
| Hemoglobin, g/dL | 11.2 ± 1.7 | 11.7 ± 1.6 | 0.176 |
| White blood cell count, × 10$^3$/μL | 8.3 (5.6–8.5) | 7.6 (5.6–8.5) | 0.203 |
| Lymphocytes, × 10$^3$/μL | 1.1 ± 0.5 | 1.3 ± 0.5 | 0.116 |
| sST2, ng/mL | 130 (60–238) | 51 (28–80) | 0.002 |

[a] Clinically suspected rejection episode included heart failure signs and depressed LVEF < 50% in 12 patients and heart failure signs and atrial arrhythmias in 2 patients.

Data are expressed as mean ± SD and median (interquartile range).

ISHLT = International Society of Heart and Lung Transplantation; NT-proBNP = N-terminal pro B-type natriuretic peptide; OHT = orthotopic heart transplant; sST2 = soluble ST2.

was built on the basis of the presence of none, 1, or 2 of these 2 biomarkers above the ROC-derived cutoff points. The predictive ability of this multimarker model was quantified using the C-index (ROC curve) and Hosmer-Lemeshow statistic for goodness of fit. To validate internally the ability of the multimarker model to discriminate, the ROC curves of 1000 samples (using bootstrap method) were calculated. All tests were 2-sided, and a $p$ value < 0.05 was considered statistically significant. All data analyses were performed with SPSS software, version 18.0 (SPSS Inc, Chicago, IL).

## Results

We studied 78 biopsy specimens obtained from 26 heart transplant recipients (52 ± 14 years; 76% men) at a median of 3.0 months (IQR, 1.0 to 7.8) after transplantation. The baseline characteristics in the rejection and nonrejection cohorts are shown in Table 1. In the entire population, sST2 concentration had a nonnormal distribution, with a median value of 63 ng/mL (IQR, 29 to 138 ng/mL).

### *Correlates of sST2 Concentrations*

sST2 concentrations correlated positively with NT-proBNP levels, right atrial pressure, serum creatinine and C-reactive protein concentrations, and total white blood cell count, whereas they correlated inversely with time after transplantation, blood levels of immunosuppressive agents, total lymphocyte count, albumin and hemoglobin levels, and LVEF (Table 2). sST2 concentra-

*Table 2. Univariable Correlates of sST2 Concentrations in the Entire Population of Samples (n = 78)*

| | sST2 | | |
|---|---|---|---|
| Variable | $R^2$ | r | p |
| NT-proBNP, ng/L | 0.38 | 0.62 | < 0.001 |
| C-reactive protein, mg/dL | 0.11 | 0.46 | < 0.001 |
| Lymphocyte count, × 10$^3$/μL | 0.22 | −0.47 | < 0.001 |
| Time from transplant, months | 0.11 | −0.47 | < 0.001 |
| Blood urea nitrogen, mg/dL | 0.21 | 0.43 | < 0.001 |
| Uric acid, mg/dL | 0.19 | 0.42 | < 0.001 |
| Creatinine, mg/dL | 0.18 | 0.36 | 0.001 |
| Hemoglobin, g/dL | 0.10 | −0.35 | 0.002 |
| Right atrial pressure, mm Hg | 0.22 | 0.34 | 0.003 |
| White blood cell count, × 10$^3$/μL | 0.14 | 0.32 | 0.005 |
| Mycophenolic acid level, μg/mL | 0.06 | −0.27 | 0.022 |
| Left ventricular ejection fraction, % | 0.04 | −0.26 | 0.023 |
| Cyclosporine level, ng/mL | 0.03 | −0.23 | 0.066 |
| Tacrolimus level, ng/mL | 0.04 | 0.33 | 0.230 |
| Body mass index, kg/m$^2$ | 0.03 | 0.11 | 0.352 |

NT-proBNP = N-terminal pro B-type natriuretic peptide; sST2 = soluble ST2.

tions were significantly higher in samples from biopsies performed during the first 30 days after OHT (n = 19; median, 228 ng/mL; IQR, 97 to 249 ng/mL) than from those performed thereafter (n = 59; median, 45 ng/mL; IQR, 27 to 78 ng/mL) ($p < 0.001$). When all these variables were entered together into a multiple linear regression model, NT-proBNP ($p = 0.001$), C-reactive protein ($p = 0.009$) and lymphocyte count ($p = 0.001$) were the only independent correlates of ST2 concentrations ($R^2 = 0.48$).

### *sST2 and Acute Rejection*

sST2 concentrations were significantly higher in the context of acute rejection than in the context of no rejection (130 ng/mL; IQR, 60 to 238 ng/mL versus 51 ng/mL; IQR, 28 to 80 ng/mL; $p = 0.002$). Moreover tertile analyses of sST2 concentrations examined as a function of rejection rates revealed that there was a graded increase in rejection rates with rising concentrations of sST2 (15% in first tertile, 27% in second tertile, 58% in third tertile; $p$ for trend = 0.002). Considered as a function of histologic findings (Fig 1), sST2 also showed a significant linear association with severity of acute rejection as a function of ISHLT grade, particularly by existing sST2 differences between grade 3 rejection and the other grades ($p$ for trend = 0.02). In a general linear model for repeated measures of analysis of variance, we found sST2 concentrations to be significantly modulated by the presence of rejection ($p = 0.001$); this is reflected in Figure 2A, which demonstrates a significant increase in sST2 values associated with acute rejection; after successful rejection therapy there was a significant decline. The dynamic behavior of sST2 in association with rejection was also observed when the analysis was performed separately for patients with biopsy-proven rejection (Fig 2B).

Among laboratory variables, beside sST2 only NT-proBNP concentrations were higher in the presence of rejection (6,111 pg/mL [IQR, 1,033 to 14,948 pg/mL] versus 1,703 pg/mL [IQR, 778 to 4,355 pg/mL]; $p = 0.012$). ROC analysis, including the entire population (n = 78), showed an area under the ROC curve of 0.72 (95% CI, 0.61 to 0.82) for sST2 and 0.68 (95% CI, 0.57 to 0.78) for NT-proBNP ($p = 0.543$ for pair-wise comparison). The optimal values derived from ROC analysis were 68 ng/mL for sST2 and 5,100 pg/mL for NT-proBNP, which maximized sensitivity and specificity. Table 3 shows the predictive performance and the risk of rejection associated with sST2 and NT-proBNP concentrations greater than the respective cutoff values, adjusted for time after transplantation, LVEF, right atrial pressure, C-reactive protein and creatinine levels, and lymphocyte count. The addition of sST2 over NT-proBNP was associated with a significant improvement in the IDI (absolute IDI of 0.042; relative IDI of 24%; $p = 0.021$) and the combination of sST2 and NT-proBNP was considerably more powerful than either marker alone. The model containing both biomarkers had a good discrimination power (C index = 0.762; 95% CI, 0.647 to 0.877) and was well calibrated (Hosmer-Lemeshow goodness of fit; $p = 0.610$). As shown in Table 3, at less than their respective cutoff values, both

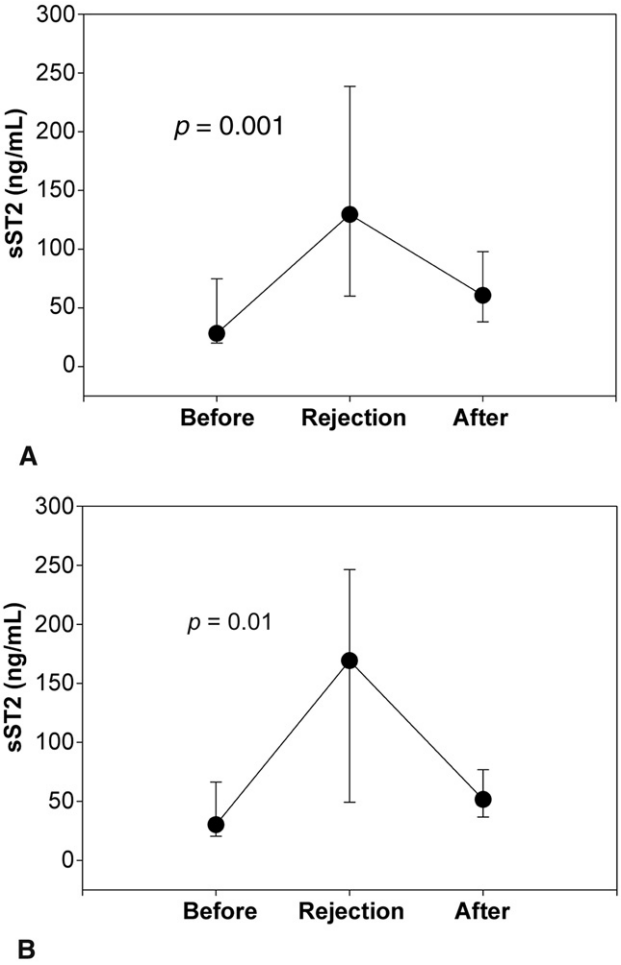


*Fig 2. Serial changes of sST2 concentrations (before, during, and after rejection) in all patients (n = 26). (A) Patients with biopsy-proven rejection (n = 12). (B) Data shown are median and interquartile ranges. The p value refers to changes within subjects across the 3 measurements. (sST2 = soluble ST2.)*

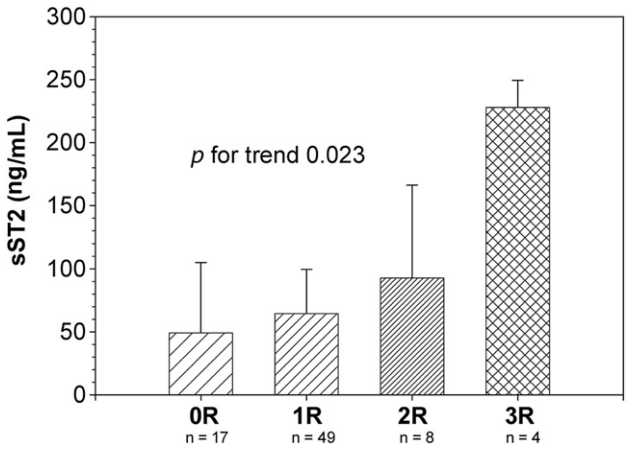


*Fig 1. sST2 concentrations as a function of histologic grade of rejection severity (International Society of Heart and Lung Transplantation grading system; sST2 = soluble ST2).*

*Table 3. Measures of Predictive Performance According to Cutoff Values Derived From ROC Analyses (n = 78)*

| Variable | AUC | Odds Ratio[a] | *p* | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|
| sST2 | 0.72 (0.61–0.82) | | | | | | |
| > 68 ng/mL | | 4.8 (1.7–14.2) | 0.004 | 73% | 67% | 53% | 83% |
| NT-proBNP | 0.68 (0.57–0.78) | | | | | | |
| > 5100 ng/L | | 5.6 (1.9–16.2) | 0.002 | 62% | 80% | 59% | 81% |
| sST2 and NT-proBNP | 0.76 (0.65–0.88) | | | | | | |
| One above | | 4.6 (1.3–17.6) | 0.031 | 81% | 65% | 54% | 87% |
| Both above | | 10.2 (2.9–40) | 0.005 | 54% | 85% | 65% | 79% |

[a] Also adjusted for time after transplantation, left ventricular ejection fraction, right atrial pressure, C-reactive protein, creatinine, and lymphocyte count.

AUC = area under curve; NPV = negative predictive value; NT-proBNP = N-terminal proB-type natriuretic peptide; PPV = positive predictive value; ROC = receiver operator characteristic; sST2 = soluble ST2.

biomarkers were associated with 87% of negative predictive value, whereas at greater than their cutoff values, both biomarkers determined 65% of positive predictive value. Using the bootstrap method, with an average ROC curve of 0.761 and standard deviation of 0.056, it was demonstrated that estimates were stable and the multimarker approach had a good ability to discriminate between biopsy specimens with and those without rejection markers.

## Comment

In this first exploratory study of sST2 after OHT, we found that concentrations of sST2 are predictive of the presence of acute cellular rejection. Although the study population was small, this finding is mechanistically plausible given the associations between sST2 and immunologic tolerance as well as myocardial stretch and injury.

The transplanted heart is exposed to several insults after transplantation. First, the heart suffers acute ischemic damage at explantation, which is aggravated by the surgical and hemodynamic compromise at implantation. After this acute stress, the next important source of injury to the allograft is immunologic rejection. We found that sST2 concentrations are high during the first 30 days after transplantation, most likely reflecting the damage incurred in the perioperative period; however after the first month sST2 concentrations also remain above the 95th percentile recently described in a population of blood donors [16]. These elevated concentrations of sST2 are presumably determined by both immunologic processes related to allograft acceptance and subclinical myocardial injury and dysfunction. Such behavior is similar to that found for NT-proBNP concentrations, which are higher during the first month after transplantation but do not normalize thereafter despite the presence of normal heart function [18, 19]. Not surprisingly therefore NT-proBNP was one of the independent correlates of sST2 concentrations together with lymphocyte count and C-reactive protein. These factors were repeatedly described as correlates of sST2 in previous studies [8–13] and seem to reflect the proposed physiologic features of the ST2 system: mechanical stress (NT-proBNP), inflammation (C-reactive protein), and immune response (lymphocyte count).

In our population, sST2 concentrations at the time of rejection episodes were higher and showed a dynamic behavior in response to rejection (increase) and antirejection therapy (decrease), which suggests that sST2 concentrations are modulated by the appearance of acute rejection. This finding could be explained by the myocardial injury caused by the acute rejection episode, similar to the increase of sST2 observed in acute myocardial infarction or acutely decompensated heart failure [8, 9, 11, 12]. However it is important to remember that IL-33/ST2 signaling also modulates immune responses mediated by type 2 T-helper cells [6, 20, 21] and favors immune deviation toward T-helper 2 function, which is associated with induction of tolerance after transplantation [1–3]. In fact upregulation of ST2L in dendritic cells has been found to be associated with immunosuppression and allograft tolerance processes [22]. Therefore IL33/ST2 signaling could have an additional cardioprotective role in the implanted heart by favoring immune tolerance and decreasing the risk of rejection. Thus dysregulation of sST2 could also be associated with a higher risk of rejection by acting as a "decoy" receptor and blocking the IL33/ST2L union. Supporting a maladaptive role of sST2, an inverse bivariate correlation was found between blood levels of immunosuppressive agents and concentrations of sST2.

Concentrations of the B-type natriuretic peptides, BNP and NT-proBNP, have been found to be elevated when acute cellular rejection episodes occur [23–26]. However the overlap between measurements in specimens showing rejection and specimens not showing rejection determines a low discriminatory capacity of NT-proBNP for detecting a rejection episode [27], which is only partially improved when using within-individual changes [26, 27]. In our study, sST2 and NT-proBNP showed a complementary value for prediction of rejection, similar to that in patients with acute myocardial infarction and acutely decompensated heart failure [9–12]. Gene expression profiling of peripheral mononuclear cells has recently been introduced as a new noninvasive modality for allograft rejection monitoring [28]. This test uses a multigenic algorithm for generating a score ranging from 0 to

4 and, similar to sST2/NT-proBNP, has a time dependence that determines an AUC of 0.72 that increases to 0.80 after 6 months and 0.86 after 1 year [29, 30]. The median time in our population was 3 months, and we found an AUC of 0.72 for sST2 that increases to 0.76 when both sST2 and NT-proBNP are taken into account; this AUC compares favorably with that obtained for gene expression testing for the same period. The strength and main clinical utility of genetic testing derives from its high negative predictive value, ranging from 98% to 100%, which may guide clinicians in ruling out rejection and partially replace the need for EMB [29, 30]. In contrast, the main weakness of genetic testing is a low positive predictive value ranging from 8% to 15%, which greatly limits its ability to rule in rejection [29, 30]. In our population, we found a lower negative predictive value (83% for sST2, which increases to 89% when both biomarkers were low), limiting its ability to replace EMB when compared with genetic testing. Nevertheless the positive predictive value was higher (54% for sST2, which increases to 65% when both biomarkers elevated) and it opens up the possibility of a complementary use of these biomarkers over gene expression profiling to increase the ability to identify allograft rejection. Further studies are needed to evaluate if a combined approach could replace the use of EMB by guiding clinicians in confidently excluding or identifying allograft rejection with a noninvasive approach. Furthermore the use of this approach to serve as guidance for assessing rejection treatment as well as minimizing immunosuppression therapies is theoretically attractive.

The main limitations of the study are its small size, the use of each patient as an internal control for themselves, and the observational design. OHT is a treatment restricted to a very small number of patients, and it was the reason that an observational and retrospective design was chosen to explore the usefulness of a new biomarker in the detection of acute rejection. We did not examine associations between sST2 and antibody-mediated rejection or coronary allograft vasculopathy, both important sources of morbidity after OHT. The use of a definition including any presumed clinical rejection resulting in treatment, besides high-grade biopsy-proven rejection, is supported by previous works and the fact that molecular changes of rejection are more strongly related to the clinical features (LVEF and biopsy indication) than to the histologic lesions [31]. Furthermore the study cohort was selected according to the appearance of a rejection episode; thus the time from transplant as well as the time between measurements of sST2 diverged among patients. In sum, despite its limitations this study provides original and new data about the role of a promising marker that reflects myocardial performance and immune processes. If confirmed in other larger populations of patients after OHT, the findings could be useful as a foundation for developing new studies focusing on the role of sST2 as a noninvasive marker for monitoring the progress of OHT patients. We present this study as hypothesis generating; larger studies are necessary to investigate the role of ST2/IL33 signaling in cellular rejection and allograft dysfunction in this population.

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# The Society of Thoracic Surgeons: Forty-Eighth Annual Meeting

Mark your calendars for the Forty-Eighth Annual Meeting of The Society of Thoracic Surgeons (STS) to be held at the Greater Fort Lauderdale/Broward County Convention Center, Fort Lauderdale, Florida, from January 30–February 1, 2012. Come to Fort Lauderdale to learn from the experts, network with colleagues from around the world, and prepare for whatever the future may hold. This pre-eminent educational event in cardiothoracic surgery is open to all physicians, residents, fellows, engineers, perfusionists, physician assistants, nurses, or other interested individuals who work with cardiothoracic surgeons. Meeting attendees will be provided with the latest scientific information for practicing cardiothoracic surgeons. Attendees will benefit from traditional Abstract Presentations, as well as Surgical Forums, Breakfast Sessions, Surgical Motion Pictures, and Procedural Hands-On Courses. Parallel sessions on Monday and Tuesday will focus on specific subspecialty interests.

An advance program with a registration form, hotel reservation information, and details regarding spouse/guest activities was mailed to STS members this fall. Nonmembers may contact the Society's secretary, David A. Fullerton, MD, to receive a copy of the advanced program; however, detailed meeting information will be available on the STS website at www.sts.org.

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