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# Short-term Outcomes of Tricuspid Edge-to-Edge Repair in Clinical Practice

**Brief title:** Outcomes of Transcatheter Tricuspid Repair

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**Abstract**

**Background:** Severe tricuspid regurgitation (TR) is known to be associated with substantial morbidity and mortality.

**Objectives:** To study the acute outcomes of subjects treated by tricuspid transcatheter edge-to-edge repair with the TriClip system in a contemporary, real-world setting.

**Methods:** The bRIGHT post-approval study is a prospective, single-arm, open-label, multicenter, post-market registry conducted at 26 sites in Europe. Echocardiographic assessment was performed at a core laboratory.

**Results:** Enrolled subjects were elderly (79 ± 7 years) with significant comorbidities. Eighty-eight percent had baseline massive or torrential TR and 80% percent of subjects were in NYHA class III or IV. Successful device implantation occurred in 99% of subjects and TR was reduced to ≤moderate at 30 days in 77%. Associated significant improvements in NYHA class (20% to 79% I/II, $p < 0.0001$) and KCCQ score (19 ± 23 points improvement, $p < 0.0001$) were observed at 30 days. With baseline TR grade removed as a variable, smaller RAV and smaller tethering distance at baseline were independent predictors of TR reduction to ≤ moderate at discharge (OR:0.679, CI: [0.537, 0.858], $p = 0.0012$; OR: 0.722, CI: [0.564, 0.924], $p=0.0097$). Fourteen (2.5%) subjects experienced a major adverse event at 30 days.

**Conclusions:** Transcatheter tricuspid valve repair was found to be safe and effective in treating significant TR in a diverse, real-world population.

**Condensed Abstract:** The bRIGHT registry is a prospective, single-arm, open-label, multicenter, post-market registry comprising a contemporary unselected cohort of high-risk patients with predominantly massive or torrential tricuspid regurgitation undergoing transcatheter tricuspid valve repair. Transcatheter edge-to-edge repair of tricuspid valve was

found to be safe and effective. Estimates of atrial and ventricular remodeling as a consequence of longstanding tricuspid regurgitation predicted procedural success.

**Keywords:** tricuspid regurgitation, TriClip, tricuspid repair, leaflet repair

**Abbreviations**

KCCQ – Kansas City Cardiomyopathy Questionnaire

NYHA – New York Heart Association

SLDA – Single Leaflet Device Attachment

RVEDD – Right Ventricular End Diastolic Diameter

RAV – Right Atrial Volume

TAPSE –Tricuspid Annular Plane Systolic Excursion

TEE – Transesophageal Echocardiography

TR – Tricuspid Regurgitation

TTE – Transthoracic Echocardiography

T-TEER- Tricuspid Transcatheter Edge-to-Edge Repair

**Clinical trial:** NCT04483089

**Introduction**

Severe tricuspid regurgitation (TR) is a common disease that, when left untreated, is known to be associated with increased morbidity and mortality (1). Since the prevalence of TR increases after the age of 65, patients requiring treatment for TR are often elderly, at increased surgical risk, and have significant relevant comorbidities (2). Today, decades after the introduction of surgical repair as a treatment option for patients with severe TR, high perioperative mortality rates (6 -12%) limit the widespread use of surgical techniques in this elderly and high-risk population (3-5). Medical therapy, which is currently the standard of care for patients with TR, is largely limited to diuretic use and often can require intravenous diuretic administration in hospital or out-patient settings. In recent years, increasing awareness of tricuspid regurgitation and its association with poor clinical outcomes have reinvigorated the need for improved treatment options.

Amongst other interventional approaches (6), tricuspid transcatheter edge-to-edge repair (T-TEER) has been proposed and applied as a non-surgical therapy to reduce TR with promising early results (7). Most recently, the primary endpoint results from the TRILUMINATE™ Pivotal trial, the randomized clinical trial evaluating the safety and effectiveness of the TriClip system (Abbott, Santa Clara, California, USA; hereafter referred to as "transcatheter tricuspid valve repair system") against medical treatment alone in symptomatic patients with severe TR, demonstrated that the T-TEER system was safe, effective in reducing TR, and significantly impacted the quality of life of patients in a selected cohort.

The bRIGHT post-approval study is the first prospective, single-arm, open-label, multicenter, post-market registry to evaluate the safety and performance of the transcatheter tricuspid valve repair system in a contemporary, non-selected real-world cohort. The primary endpoint is acute procedural success (APS) defined as successful implantation of the device

with resulting TR reduction of at least one grade at discharge. Herein we report on the acute outcomes and primary endpoint of the bRIGHT study.

## Methods

### *Study Design and Patient Population*

The bRIGHT EU post-approval study (PAS) is a prospective, single-arm, open-label, multicenter, post-market registry that was designed to confirm the safety and performance of T-TEER with the transcatheter tricuspid valve repair system in a contemporary real-world setting. A total of 511 consecutive subjects were enrolled at 26 sites in Europe, where eligibility for T-TEER was determined through site specific, standard of care procedures in addition to evaluating the patient according to the protocol specified inclusion and exclusion criteria. Briefly, subjects were required to have severe, symptomatic TR despite medical therapy, be at least 18 years of age, be eligible to receive T-TEER per the currently approved intended use and target patient population, and not be a participant in another clinical study that could impact the follow-up or results of the bRIGHT PAS. The study was approved by local ethics committees and the respective health authorities of the participating countries. All subjects provided written informed consent.

### *Echocardiographic Assessment*

All echocardiograms were analyzed by an independent core laboratory that followed the American Society of Echocardiography standards (8). TR was assessed using standard 2D color Doppler methods and graded according to the class grading scheme of none, mild, moderate, severe, massive, and torrential, which enabled a broad and yet differentiated assessment (9). Among others, parameters included were biplane vena contracta width, effective regurgitant orifice area, and regurgitant volume. Single leaflet device attachment

(SLDA) and tricuspid valve gradient were also assessed by the echocardiography core laboratory. Tricuspid stenosis was defined as a mean gradient ≥ 5 mmHg.

*Clinical outcomes*

APS was defined as successful implantation of the device resulting in TR reduction of at least 1 grade (as assessed by the echocardiography core laboratory) at discharge. All major adverse events (MAE), including cardiovascular mortality, myocardial infarction, stroke, new onset renal failure, endocarditis requiring surgery, and non-elective cardiovascular surgery for tricuspid valve repair system-related adverse events, were adjudicated by an independent events committee. Additional safety endpoints (major bleeding, new onset liver failure, etc.) and heart failure hospitalizations were assessed at each site according to definitions provided in the clinical investigation plan. Clinical status was assessed using New York Heart Association (NYHA) functional class and Kansas City Cardiomyopathy Questionnaire (KCCQ).

*Subject Follow-up*

Per-protocol, follow-up visits are evaluated at 30 days with a follow-up window of -14 to +60 days, while safety events are reported through 30 days of the attempted procedure.

*Statistical analysis*

All subjects who signed and dated an Informed Consent Form and had an attempted procedure were included in the analysis population upon femoral vein puncture with the T-TEER system. Data are presented as mean ± standard deviation (SD) for continuous variables and are presented as counts and percentages for categorical variables. Paired t-test was used to compare the mean of paired continuous variables and McNemar's test was used to compare paired categorical data. An exact binomial test was used to evaluate the primary endpoint. Stepwise model selection was used to identify possible echocardiographic

predictors of TR reduction to moderate or less. A variable was entered if significant at 0.2 level and had to be significant at 0.1 level to stay in the model. All statistical analyses were performed using the SAS version 9 (SAS Institute; Cary, NC, USA).

## Results

### *Baseline Characteristics*

Baseline characteristics of enrolled subjects are summarized in **Table 1**. A total of 511 subjects (56% female) with a mean age of 79 ± 7 years were included. Tricuspid regurgitation was functional in 90% of subjects, and baseline TR severity in most patients was massive and torrential, at 61.3% and 26.7% respectively. Eighty percent of subjects were in NYHA functional class III or IV and on average, subjects had KCCQ scores of 43.1 ± 23.7. Enrolled subjects had significant comorbidities including hypertension (87%), atrial fibrillation (86%), chronic renal disease (40%), diabetes (22%), and prior myocardial infarction (10%). Twenty-seven percent (27%) of subjects had a prior mitral intervention, 23% had a permanent pacemaker/implantable cardioverter defibrillator (ICD), and 40% had a heart failure hospitalization within 1 year prior to the index procedure **(Central Illustration).** On average, left ventricular ejection fractions (LVEF) were normal (55.8 ± 10.6) and subjects had dilated right ventricles (end diastolic basal diameter 4.63 ± 0.92 cm), dilated tricuspid annular diameters (4.54 ± 0.76 cm) and increased right atrial volumes (151.66 ± 70.46 mL). Enrolled subjects had a broad range of tricuspid valve anatomies, including annulus diameters ranging from 2.6 to 5.8 cm, with 23% of annulus diameters above 5 cm. Subjects had coaptation gaps of 6.49 ± 2.7 mm, with approximately 47% of subjects having gaps of 7 mm or greater. The jet location was on various coaptation lines, however the majority of subjects had jets along the anteroseptal line (75%) or a combination of anteroseptal, posteroseptal, and anteroposterior lines (14%). Subjects also had varying degrees of leaflet

restriction (echo core lab assessed), with 30% of subjects experiencing no leaflet restriction, 54% mild, 11% moderate, and 5% severe.

*Procedural Outcomes*

The primary endpoint of APS, evaluated in the primary analysis population of the first 200 subjects, was achieved in 92% of subjects, successfully meeting the primary endpoint performance goal of 75% ($p<0.0001$). The implant success, defined as the successful delivery and deployment of the T-TEER device, was achieved in 504 (99%) of the 511 enrolled subjects and procedural success, defined as implant success with resulting TR reduction of at least 1 grade at discharge (or at 30 days if discharge TR grade was unavailable), was achieved in 451 (91%) of the 496 subjects with readable TR severity. On average, 1.9 ± 0.7 clips were deployed, and the mean device time was 76 ± 39 minutes. Five hundred and forty-seven (56%) of the 978 devices used were XT, 419 (43%) were XTW, 11 (1%) were NT, and 1 (0.1%) was (NTW). The clips were placed on the antero-septal leaflets in 714 (73%) of 978 implants, the septal-posterior leaflets in 219 (22%), and the anterior-posterior leaflets in 45 (5%).

Of the 511 subjects, 479 subjects had evaluable TR severity at both baseline and discharge. Missing data were due to death (n=2), withdrawal (n=2), visit not completed (n = 15), and TR not measurable (n = 13). A paired analysis showed that TR severity at discharge was moderate or less in 80% of subjects treated with the device (compared to only 2% at baseline) (**Figure 1**). The TR reduction was shown to be durable at 30 days for the 389 subjects with evaluable TR severity at both baseline and 30 days follow-up, with 77% of subjects evaluated as moderate or less (**Central Illustration**). Missing pairs between baseline and 30 days follow-up were due to death (n=17, 12 beyond 30 days but within follow-up window. See also **Table 4**), consent withdrawal (n=17), visit not completed (n=57), TR not measurable at baseline (n = 9), and TR not measurable at 30 days follow-up (n = 22). TR

severity at 30 days follow-up stratified by baseline TR severity demonstrates that with increasing baseline severity, there is a decrease in percent reduction to moderate or less TR (**Figure 2**). The percentage of subjects that have no reduction or worse TR severity at 30 days remains fairly consistent across baseline TR severities, at around 6%.

Results of univariate analysis of predictors for TR reduction to ≤ moderate are shown in **Figure 3**. A stepwise model selection including all variables from the univariate analysis ( presence of pacemaker lead across the valve, tricuspid regurgitation at baseline and echocardiographic parameters of right ventricular end diastolic diameter (RVEDD), right atrial volume (RAV), tricuspid annular diameter, tethering distance, and gap size) was then used to identify possible echocardiographic predictors of TR reduction to moderate or less at discharge. A variable was entered if significant at 0.2 level and had to be significant at 0.1 level to stay in the model. The multivariate logistic regression shows that smaller RAV at baseline and smaller baseline TR grade are indicated as independent predictors of reducing TR to moderate or less at discharge (Odds Ratio (OR): 0.726, 95% Confidence Interval (CI): [0.572, 0.921], p = 0.0085, OR: 0.371, 95% CI: [0.223, 0.617], p = 0.0001). When baseline TR grade is removed as a variable, smaller RAV and smaller tethering distance at baseline were independent predictors of TR reduction to ≤ moderate at discharge (OR:0.679, CI: [0.537, 0.858], p = 0.0012; OR: 0.722, CI: [0.564, 0.924], p=0.0097).

Significant reductions in effective regurgitation orifice area (0.80 ± 0.51 to 0.42 ± 0.38 $cm^2$, p < 0.0001), regurgitant volume (59.15 ± 28.38 to 31.96 ± 20.89 mL/beat, p < 0.0001), regurgitant jet area (10.41 ± 5.34 to 6.07± 4.74 $cm^2$, p < 0.0001), vena contracta width (0.85 ± 0.36 to 0.50 ± 0.36 cm, p < 0.0001), and PISA radius (0.82 ± 0.22 to 0.56 ± 0.34 cm, p < 0.0001) occurred between baseline and 30 day follow-up (**Table 2**).

Significant improvements in right heart chamber size were observed at 30 days follow-up including decreased RVEDD (4.63 ± 0.92 to 4.28 ± 0.86 cm, $p < 0.0001$), decreased tricuspid annular diameter (4.54 ± 0.76 to 4.27 ± 0.73 cm, $p < 0.0001$), and decreased RAV (151.66 ± 70.46 to 136.25 ± 62.35 mL, $p < 0.0001$) (**Table 2**). No significant changes in RV fractional area change or tricuspid annular plane systolic excursion (TAPSE) were observed.

*Clinical Outcomes*

Significant improvements in functional capacity and quality of life were seen at the 30 day follow-up visit. The percentage of subjects categorized as NYHA functional class I-II increased from 20% at baseline to 79% at 30 days ($p< 0.0001$) (**Figure 4A**). Assessment of quality of life with the Kansas City Cardiomyopathy Questionnaire (KCCQ) showed a mean improvement of 19 ± 23 points from baseline to 30 days post-procedure ($p < 0.0001$) (**Figure 4B**), with 56% of subjects experiencing ≥ 15 points improvement (**Table 3**). The mean increase in KCCQ score as a function of TR severity at 30 days demonstrates that subjects achieving moderate or less TR at 30 days have a higher KCCQ score improvement than those subjects with residual severe or greater TR at 30 days (**Figure 5**).

At 30 days, all-cause mortality was 1% (5/511) (Table 4). Fourteen (2.5%) of 511 subjects experienced a major adverse event, including cardiovascular mortality (n=4), stroke (n=2), new onset renal failure (n=7), and non-elective cardiovascular surgery for device-related AE (n=1) (**Central Illustration**). Other clinical safety events through 30 days included tricuspid valve re-intervention 0.2% (n=1), re-operation 0.4% (n=2), major bleeding 7.2% (defined as BARC 3a, n=37), and single leaflet device attachment 3.8% (SLDA)(n=17). There were no cases of myocardial infarction or embolization.

**Discussion**

We report the acute results from the first prospective, single-arm, open-label, multicenter, bRIGHT post-market registry to evaluate the safety and performance of the transcatheter tricuspid valve repair system in a contemporary, real-world cohort of patients with symptomatic TR. In this first report on the bRIGHT post-approval study, we demonstrate low rates of MAEs and mortality through 30 days, significant TR reduction and significant clinical improvements in KCCQ score and NYHA Class following the T-TEER procedure. This real-world study highlights the acute success in achieving TR reduction and the associated clinical benefit with the transcatheter tricuspid valve repair system in a non-selected cohort.

Overall, subjects treated in the bRIGHT study had fundamental differences when compared to previously published non-randomized T-TEER registries as well as the recently published results of the TRILUMINATE Pivotal trial (7,10-12). Fundamental differences in baseline characteristics include a higher percentage of massive and torrential TR, higher proportion of NYHA class III/IV, lower KCCQ scores, and higher rates of hypertension and diabetes than subjects enrolled into the TEER group of the randomized TRILUMINATE Pivotal trial. Subjects also had a higher rate of existing permanent pacemakers and more subjects had heart failure hospitalizations 1 year pre-index procedure (40% vs. 24%). Most striking is the observation of the very high percentage of patients with massive or torrential TR (88%) in the bRIGHT registry. This exceeds largely the severity of baseline TR reported in the PASTE registry (13), but also contemporary reports of TV replacement technologies(14). Given the fact TR correlates with survival, degrees of baseline TR are of utmost importance when comparing cohorts, especially with regard to hard clinical endpoints. The bRIGHT cohort, representing a realistic reflection of patient profiles currently undergoing T-TEER, comprises more symptomatic patients than several other trials in the field. This is of relevance for interpretation of later outcomes and comparisons between reports. Despite the broad range of anatomies and coexisting conditions of the subjects treated in the real-world population,

major adverse events remained low through 30 days of follow-up. All-cause mortality occurred in only 1% of subjects at 30 days. Other clinical safety endpoints, including re-interventions (0.2%) and re-operations (0.4%) were also rare through 30 days follow-up, demonstrating the excellent safety profile of T-TEER with the transcatheter tricuspid valve repair system.

The subjects enrolled in the bRIGHT real-world study also had increasingly complex anatomies, including larger gaps and a higher percentage of pacemaker leads. The increased proportion of subjects achieving moderate or less TR in the bRIGHT study compared to the selected cohort of the early TRILUMINATE feasibility study can be attributed to both implanter experience and clip selection. In the TRILUMINATE feasibility study, quite complex anatomies were approached with the NT device, as no other clip size was available at the time of this trial. The availability of XT and XTW clips in the bRIGHT study may have contributed to the success in implantation among increasingly complex anatomies, since the majority of clips used in the bRIGHT study were XT or XTW. XT/XTW use in the bRIGHT study was also increased compared to the TRILUMINATE Pivotal trial. Additionally, it is important to note that the TRILUMINATE™ Pivotal trial results to date are exclusively from the randomized cohort. It is expected that, based on the design of the TRILUMINATE Pivotal trial, the more anatomically complex subjects would have been included into the single arm cohort. The bRIGHT study, as the real world experience, represents patients from both the randomized and single-arm cohorts.

The percentage of subjects that achieved TR of moderate or less at 30 days appears to be improved compared to the previously reported TRILUMINATE feasibility study yet decreased in comparison to subjects in the TRICLASP study and the TEER group of the TRILUMINATE Pivotal trial (7, 10-12). These differences are likely to be related to the increased number of subjects with massive or torrential baseline TR who were treated with T-TEER in the real-world setting that had more clip sizes available. Given the fact that baseline

TR independently predicts discharge TR, detailed attention to baseline characteristics is required when comparing TR reduction to outcomes of other trials.

These differences are all important factors to consider when evaluating the procedural and clinical outcomes of this non-selected real-world cohort. Even with the diverse anatomies and progressed disease state treated within a real-world setting, clinical outcomes including average KCCQ score increase, and NYHA class were improved compared to previous studies of T-TEER in registries with more carefully selected cohorts (10-12). A KCCQ increase of ≥ 15 points was realized in 56.2% of subjects, which is increased even compared to the 49.7% of subjects with at least a 15-point increase in the TEER group of the TRILUMINATE Pivotal trial. KCCQ score improvement was increased in subjects with moderate or less residual TR at 30 days when compared to subjects with residual TR of severe or more. The increase in KCCQ score for subjects with residual TR of severe or more at 30 days is substantially higher in subjects in the bRIGHT study than in TRILUMINATE Pivotal, though this result is not unexpected given the proportion of subjects with baseline massive or torrential TR was higher in bRIGHT and there were no control subjects that did not undergo the procedure. Some of the subjects with residual severe (or higher) TR at 30 days still had a 1 or even 2 grade improvement from baseline and this improvement, even while not achieving moderate or less residual TR, could still lead to a significant KCCQ increase at 30 days. The finding that 50% of bRIGHT subjects had KCCQ Improvement of ≥ 20 points at 30 days is also very encouraging.

Signals of early right heart remodelling were observed at 30 days follow-up including decreased RVEDD, tricuspid annular diameter, and RAV. While no significant changes in RV fractional area change or TAPSE were found, we must recall from the early TRILUMINATE feasibility study that positive ventricular remodelling may not occur until later follow-up (11). Variables of right heart size and function were included in a multivariate

predictor analysis to determine which, if any, baseline characteristics would be predictive of TR reduction to moderate or less at discharge. Not surprisingly, baseline TR was found to be predictive of TR reduction to ≤ moderate in addition to RAV. When baseline TR was removed as a possible variable, the resulting model included RAV and tethering distance. Smaller right atrial volumes and tethering distances at baseline suggest that in patients with less advanced physical markers of atrial remodelling, TEER is more likely to result in satisfactory TR reduction than in patients with more severe markers of atrial remodelling. Since baseline TR was also predictive of resulting TR, it may be beneficial for patients with massive/severe TR to be evaluated for T-TEER candidacy separately from patients presenting with torrential TR in the future.

**Limitations**

The bRIGHT study is a single arm registry and with no comparison to a conservative treatment group. Results are limited to acute 30-day outcomes and longer term outcomes are unknown. Core lab echocardiographic analysis of TR grades were not available at baseline and/or post-procedurally.

**Conclusions**

Transcatheter tricuspid valve edge-to-edge repair was found to be safe and effective in treating significant TR in a diverse, real-world population. The reduction in TR was associated with improvements in quality of life. Both atrial and ventricular remodelling predict procedural results.

## Clinical Perspectives

**Competency in Patient Care and Procedural Skills:** In an unselected cohort of high-risk patients with severe tricuspid regurgitation, transcatheter edge-to-edge repair was safe, effective, and associated with substantial clinical improvement.

**Translational Outlook:** Future studies should focus on both anatomical and clinical outcomes to help guide selection of patients for transcatheter tricuspid valve repair.

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**Figure Legends:**

**Figure 1: Comparison of TR Severity at Discharge**

At discharge, TR severity was significantly reduced from baseline, with 80% of subjects achieving moderate or less TR. The p values indicate significance from McNemar's test.

**Figure 2: 30 Day TR Reduction Stratified by Baseline TR Severity**

At 30 days, TR reduction to moderate or less was greatest in subjects with baseline severe TR (95%), and decreased in subjects with baseline massive TR (82%), and baseline torrential TR (59%). The percentage of subjects that have no reduction or worse TR severity remained consistent among baseline TR groups.

**Figure 3: Univariate Predictors of Achieving Moderate or Less TR at Discharge**

In a univariate predictors analysis, tricuspid regurgitation at baseline and echocardiographic parameters of gap size, tethering distance, right ventricular end diastolic diameter (RVEDD), right atrial volume (RAV), and tricuspid annular diameter were found to be predictors of TR reduction to moderate or less at discharge. The p values indicate significance from Wald Test.

**Figure 4: NYHA functional class improvement and KCCQ-OS change through 30 Days**

The proportion of subjects classified as NYHA function class I/II increased from 20% at baseline to 79% at 30 days follow-up. The p value indicates significance from McNemar's test. Self-assessed heart failure symptoms measured by KCCQ showed a significant improvement at 30 days follow-up, with an average point increase of 19. The p value indicates significance from the paired t-test. KCCQ-OS = Kansas City Cardiomyopathy Questionnaire overall summary score.

**Figure 5: KCCQ-OS Improvement Stratified According to the Severity of Residual TR**

Subjects achieving moderate or less TR at 30 days have an average KCCQ score improvement of 20 points compared to 12 points improvement for subjects with residual severe or greater TR at 30 days.

**Central Illustration: Transcatheter tricuspid valve repair safe and effective in real-world population**

Transcatheter tricuspid valve repair using the transcatheter tricuspid valve repair system was found to be safe and effective in treating significant TR in a symptomatic, real-world population. Significant reduction of TR to moderate or less at 30 days was achieved in 77% of subjects, and a low major adverse event rate of 2.5% was observed in this real-world study.

## Tables

### Table 1 – Baseline Characteristics

| VARIABLE | n=511 |
|---|---|
| Age, mean (years) | 78.9 ± 7.1 |
| Male/Female | 44 %/56 % |
| NYHA Class III/IV | 80 % |
| KCCQ score | 44.52 ± 22.56 |
| Left Ventricular Ejection Fraction | 55.8 ± 10.6 |
| Functional Tricuspid Regurgitation | 90 % |
| Baseline TR Severity[1] | |
| Moderate | 2.0 % |
| Severe | 10.0 % |
| Massive | 61.3% |
| Torrential | 26.7 % |
| Atrial TR/Ventricular TR | 76%/24% |
| Hypertension | 86.7% |
| Atrial Fibrillation | 86.3 % |
| Mitral Regurgitation (≥ Moderate) | 6.0% |
| Prior Aortic Intervention | 9.2% |
| Prior Mitral Intervention | 26.8% |

| | |
|---|---|
| Prior CABG | 11.5% |
| Diabetes | 22.3% |
| Chronic Renal Disease | 39.5% |
| Chronic Obstructive Pulmonary Disease | 13.1% |
| Peripheral Vascular Disease | 11.0% |
| Prior Stroke | 8.0% |
| Permanent Pacemaker/ICD | 22.5% |
| Prior Myocardial Infarction | 10.4% |
| Prior Heart Failure Hospitalization (1 Year Pre-Index Procedure) | 40.3% |

**Table 2**

| Summary of Echocardiographic Endpoints | Baseline | Discharge | 30 Days | P-Value* Baseline vs 30 Days |
|---|---|---|---|---|
| **Tricuspid Regurgitation** | | | | |
| Effective Regurgitant Orifice Area, $cm^2$ | 0.80 ± 0.51 | 0.44 ± 0.47 | 0.42 ± 0.38 | <0.0001 |
| Regurgitant Volume, mL/beat | 59.15 ± 28.38 | 32.27 ± 26.23 | 31.96 ± 20.89 | <0.0001 |
| Regurgitant Jet Area, $cm^2$ | 10.41 ± 5.34 | 5.69 ± 5.15 | 6.07 ± 4.74 | <0.0001 |
| Vena Contracta Width, cm | 0.85 ± 0.36 | 0.47 ± 0.37 | 0.50 ± 0.36 | <0.0001 |
| PISA Radius, cm | 0.82 ± 0.22 | 0.56 ± 0.29 | 0.56 ± 0.34 | <0.0001 |
| IVC Diameter, cm | 2.31 ± 0.66 | 2.09 ± 0.75 | 2.09 ± 0.71 | 0.0059 |
| **Right Heart Remodeling** | | | | |
| RV End Diastolic Dimension, cm | 4.63 ± 0.92 | 4.39 ± 0.81 | 4.28 ± 0.86 | <0.0001 |
| Tricuspid Annular Diameter, cm | 4.54 ± 0.76 | 4.36 ± 0.73 | 4.27 ± 0.73 | <0.0001 |
| Right Atrial Volume, mL | 151.66 ± 70.46 | 141.47 ± 64.81 | 136.25 ± 62.35 | 0.0023 |
| RV fractional area change, % | 39.4 ± 8.4 | 37.4 ± 9.2 | 38.9 ± 8.6 | 0.5929 |
| TAPSE, cm | 1.70 ± 0.44 | 1.65 ± 0.45 | 1.69 ± 0.48 | 0.2035 |
| Left Ventricular Ejection Fraction | 55.79 ± 10.58 | 57.25 ± 11.66 | 57.73 ± 10.13 | 0.0114 |

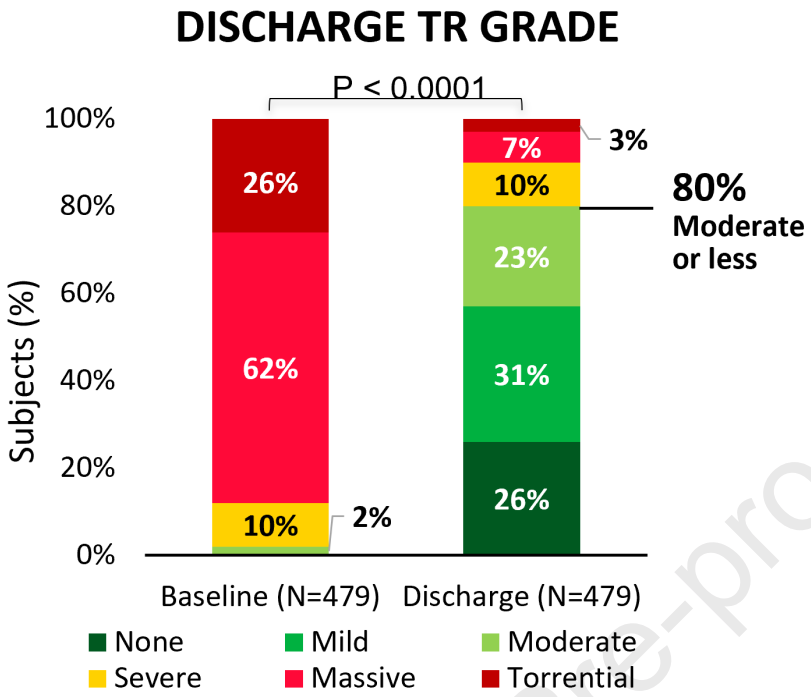
**Table 3**

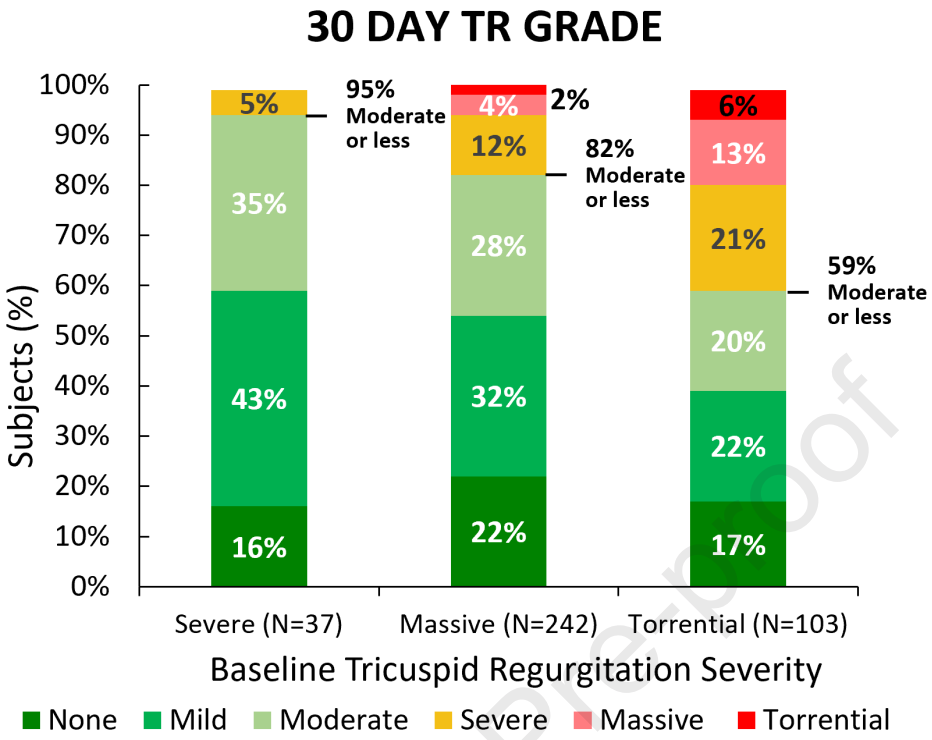
| KCCQ Score Improvement from Baseline to 30 Days (points) | n = 420 |
|---|---|
| **< 5** | 26.4% (111/420) |
| **[5, 10)** | 7.9%% (33/420) |
| **[10, 15)** | 9.5% (40/420) |
| **[15, 20)** | 7.9% (33/420) |
| **≥ 20 pts** | 48.3% (203/420) |

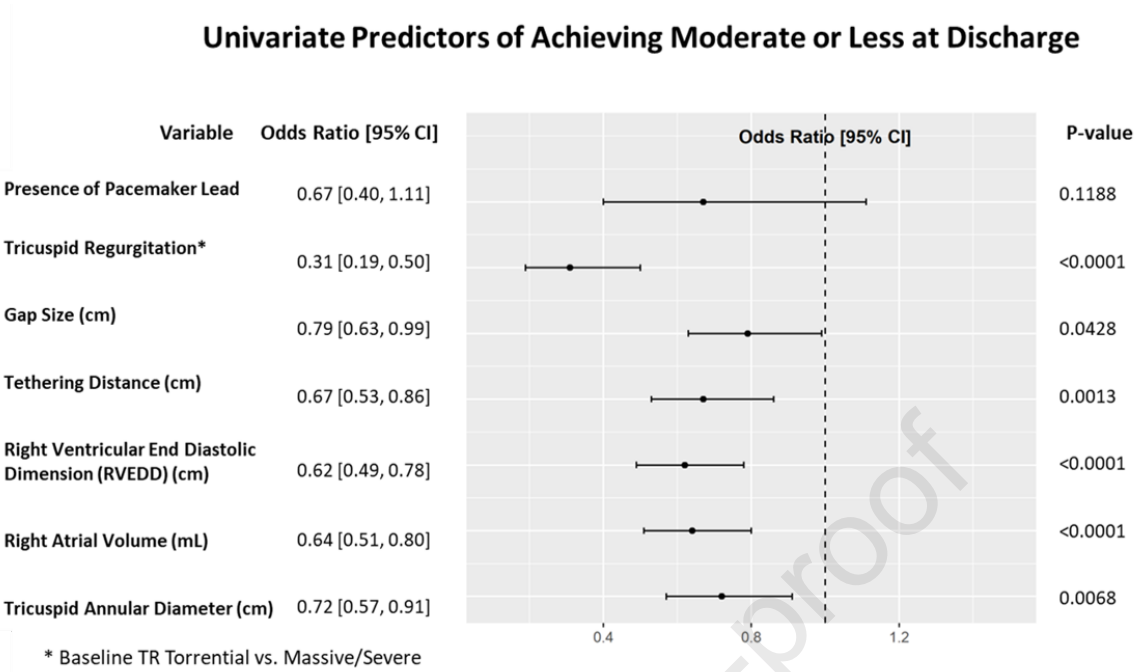
**Table 4**

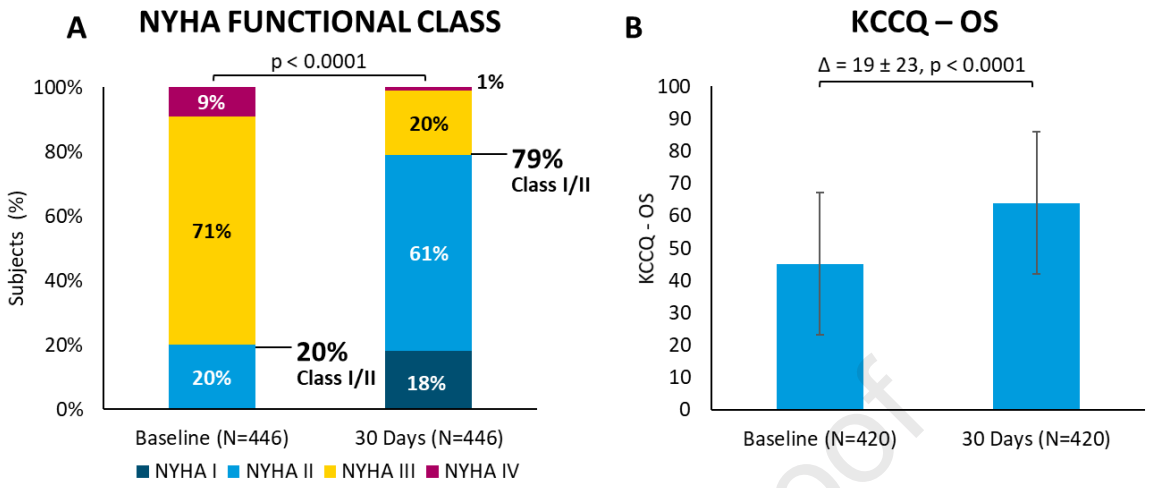
| EVENT (up to 30 days) | n=511 |
|---|---|
| **MAEs** | 2.5% (14) |
| Cardiovascular Mortality | 0.8% (4) |
| Myocardial Infarction | 0.0% (0) |
| Stroke | 0.4% (2) |
| New Onset Renal Failure | 1.4% (7) |
| Endocarditis Requiring Surgery | 0.0% (0) |
| Non-Elective Cardiovascular Surgery for Device-Related AE | 0.2% (1) |
| **Other Clinical Safety Endpoints** | |
| All-cause Mortality | 1.0% (5) |
| TV Re-intervention | 0.2% (1) |
| TV Re-Operation | 0.4% (2) |
| Major Bleeding* | 7.2% (37) |
| Device Embolization | 0.0% (0) |
| Device Thrombosis | 0.0% (0) |
| New Pacemaker Implantation | 0.0% (0) |
| Single Leaflet Device Attachment (SLDA) | 3.8% (17) |

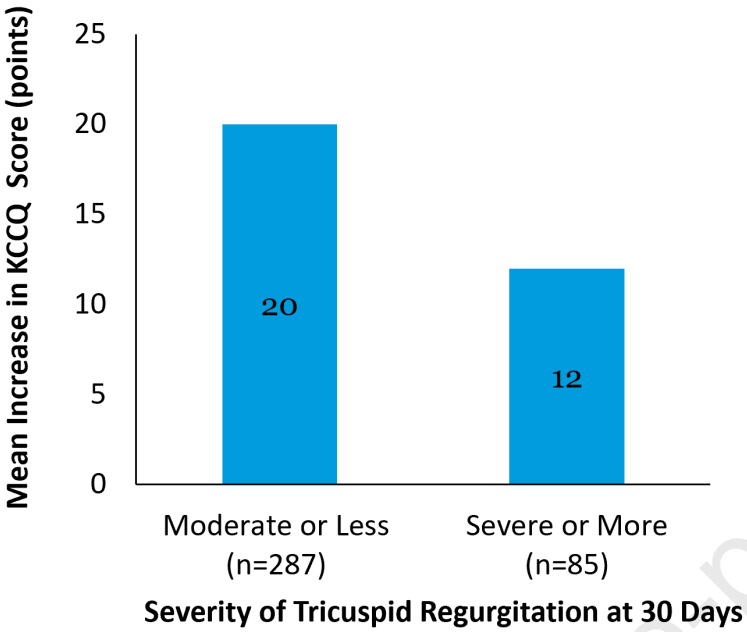
* Major defined as bleeding BARC Type 3A











**CENTRAL ILLUSTRATION** **Transcatheter tricuspid valve repair safe and effective in real-world population**

## REAL-WORLD POPULATION

**Mean age**: 78.9 years

**Mean LVEF:** 55.8

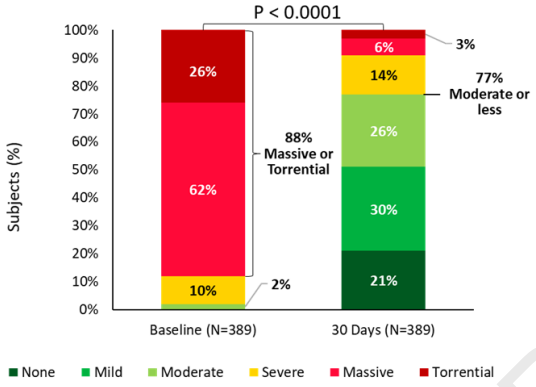
**NYHA Class III/IV**: 88%

**Male:** 44%

**Prior heart failure hospitalization:** 40.3%

**Baseline KCCQ score:** 44.52

## REDUCTION IN TR AT 30 DAYS



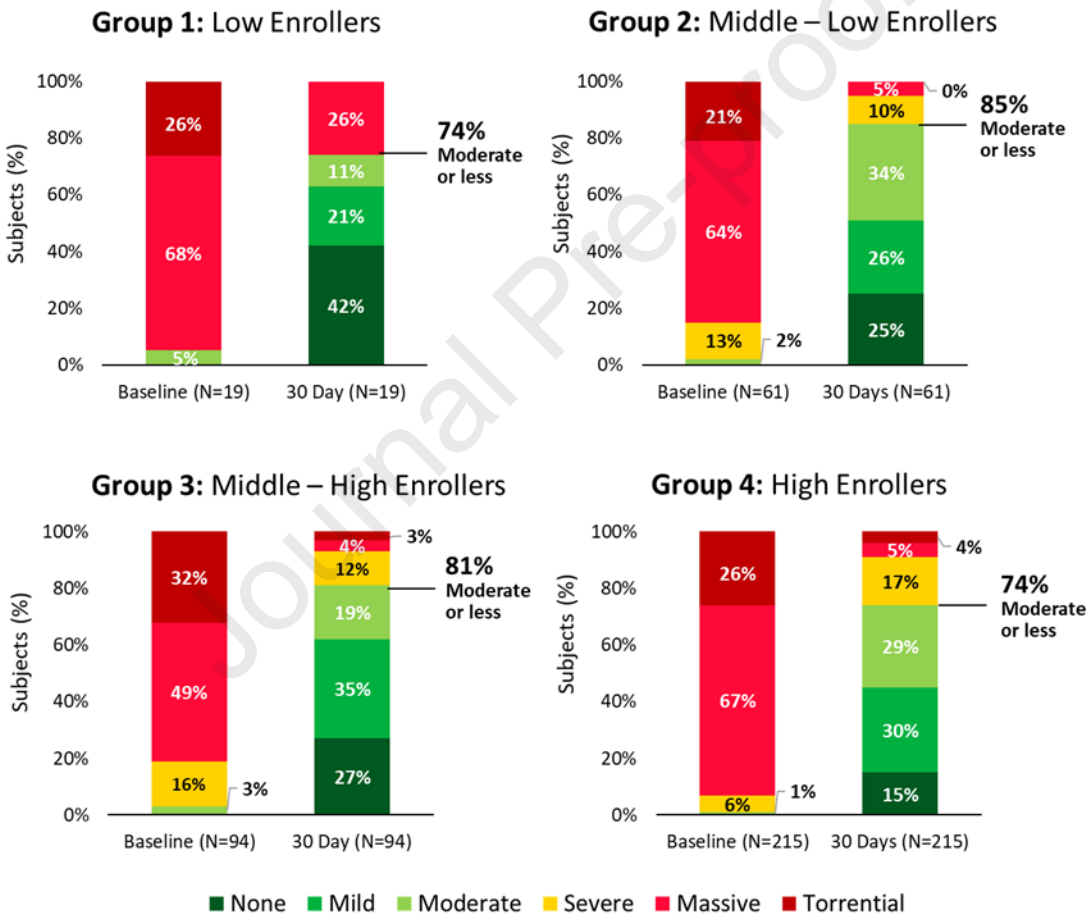

## SAFETY PROFILE AT 30 DAYS

| Major Adverse Event | % of Patients (N=511) |
|---|---|
| Cardiovascular mortality | 0.8% |
| Myocardial infarction | 0.0% |
| Stroke | 0.4% |
| New onset renal failure | 1.4% |
| Endocarditis requiring surgery | 0.0% |
| Non-Elective CV Surgery for Device-Related AE | 0.2% |

MAEs adjudicated by independent clinical events committee

## Supplementary Figure 1: Comparison of 30 Day TR Reduction as a Function of Center Enrollment

Study centers were split into quartiles by number of enrolled subjects. TR reduction to moderate or less at 30 Days ranged between 74% and 85%, and did not appear to change with enrollment number. Middle-low and middle-high enrollers had an increased number of subjects with baseline severe TR compared to the low and high enrolling groups, which had higher rates of Massive/torrential TR at baseline.



## Appendix A: bRIGHT PAS principal investigators and institutions

| Site Name | PI Name |
|---|---|
| Az. Osp. Spedali Civili di Brescia | Marianna Adamo |
| Azienda Ospedaliera Monaldi | Paolo Golino |
| Centro Hospitalar Vila Nova Gaia | Bruno Melica |
| DRK Kliniken Berlin Köpenick | Iskandar Atmowihardjo |
| Elisabeth-Krankenhaus Essen GmbH | Thomas Schmitz |
| Herz-und Diabetes Zentrum NRW | Volker Rudolph |
| Herzklinik Hirslanden | Roberto Corti |
| Herzzentrum Leipzig GmbH | Philipp Lurz |
| Hospital Alvaro Cunqueiro, Dept of Interventional Cardiology | Rodrigo Estevez-Loureiro |
| Hospital Clínic de Barcelona | Xavier Freixa |
| Hospital de la Santa Creu I Sant Pau | Dabit Arzamendi |
| Inselspital - University Hospital of Bern | Fabien Praz |
| Katholisches Marienkrankenhaus GmbH | Edith Lubos |
| Maria Cecilia Hospital | Fausto Castriota |
| Odense University Hospital | Karsten Veien |
| Otto-von-Guericke-Universität Magdeburg | Alexander Schmeisser |
| Robert-Bosch-Krankenhaus | Raffi Bekeredjian |
| Schüchtermann-Schiller´sche Kliniken GmbH & Co. KG | Marek Kowalski |
| St. Antonius Ziekenhuis | Bernard Rensing |
| St.-Johannes-Hospital | Helge Möllmann |
| UKE Hamburg (Universitatsklinik Eppendorf) | Niklas Schofer |
| Universitatsmedizin der Johannes Gutenberg-Universitat Mainz | Ralph Stephan von Bardeleben |
| Universitätsklinik Graz | Andreas Zirlik |
| Universitätsklinikum Bonn AdöR | Georg Nickenig |
| Universitätsklinikum Ulm | Wolfgang Rottbauer |
| Zentralklinik Bad Berka GmbH | Harald Lapp |