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TRILUMINATE Pivotal Trial: A New Dawn for Tricuspid Regurgitation Management?

Hesham Aggour, MBBCh, MSc, MRCP(UK).

Cardiology Registrar

Buckinghamshire Healthcare NHS Trust, High Wycombe, UK.

Take Home Messages

- Tricuspid regurgitation is prevalent, but isolated surgical interventions have been limited due to unsatisfactory outcomes.
- The TRILUMINATE Pivotal trial is the first randomised trial comparing percutaneous tricuspid intervention against medical therapy.
- The TRILUMINATE Pivotal trial showcases tricuspid TEER repair as a promising, effective and safe alternative.
- Whilst promising, TRILUMINATE's open-label nature and QoL driven results merit cautious interpretation.

Background

In recent years, tricuspid valve (TV) disease has been under the spotlight.(1) The prevalence of tricuspid regurgitation (TR), primary and secondary, in the community increases with age, representing between 0.55% and 4% in the general population.(2) Despite the high prevalence of severe TR and its association with poor prognosis, independent of biventricular function, (3) there are limited options with regards to TV interventions and surgeries. (2, 4) Current TR treatment guidelines indicate use of medical therapy to treat symptoms of systemic venous congestion.(5)

In part, this likely stems from previous studies which showed suboptimal outcomes with isolated TV surgeries and an associated 8% in-hospital mortality which increased to 37% for redo-surgeries.(6)

With the recent developments in transcatheter valve interventions and evolution of new devices, percutaneous TV intervention has become an attractive alternative to surgery but there is no evidence regarding its clinical efficacy at reducing mortality or heart failure (HF) hospitalisations in patients with severe symptomatic TR.

The TRILUMINATE PIVOTAL is the first randomised controlled trial (RCT) to evaluate the effectiveness and safety of tricuspid transcatheter edge-to-edge repair (TEER) in patients with symptomatic severe TR. (7)

Trial design

The **TRI**al to Eva**LU**ate Cardiovascular Outco**M**es **IN** P**A**tients Treated with the **T**ricuspid Valv**E** Repair System Pivotal (TRILUMINATE Pivotal) is an international, RCT of tricuspid TEER performed with the TriClip™ (Abbott Structural Heart). It included patients with symptomatic, severe or more, primary and secondary TR on echocardiography with no, or stable guideline-directed therapy left sided heart disease who were deemed at an intermediate or higher surgical risk as determined by the local surgical team (**table 1 and 2).**

Table 1: Key inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Age ≥ 18 years.	Systolic PAp > 70 mmHg.
Severe or more TR despite OMT.	Severe uncontrolled HTN.
NYHA class II, III or IV.	Any prior TV procedure or anatomy that would interfere with placement of the TriClip™ device.
≥ Intermediate risk for mortality or morbidity with TV surgery.	Indication for left-sided or PV correction in the prior 60 days.
	CIED leads that would prevent appropriate placement of the TriClip™ device.

CIED = Cardiac implantable electronic device; HTN = Hypertension; NYHA = New York Heart Association; OMT = Optimum medical therapy; PAp = Pulmonary artery pressure; PV = Pulmonary valve; TR = Tricuspid regurgitation; TV = Tricuspid valve

Table 2: Tricuspid regurgitation grading scale

	Trace/Mild	Moderate	Severe	Massive	Torrential
Vena contracta (biplane, mm)	<3	3-6.9	7-13	14-20	≥21
EROA (mm^2)	<20	20-39	40-59	60-79	≥80
Regurgitant volume (mL)	<15	15-44	45-59	60-74	≥75

3D VCA or quantitative EROA (mm^2)		75-94	95-114	≥115

EROA = Effective regurgitant orifice area; VCA = Vena contracta area

Randomisation was performed with assignment to TEER group or medical therapy alone in a 1:1 ratio. Clinical follow up consisted of symptoms assessment, 6-minute walk test and Kansas City Cardiomyopathy Questionnaire (KCCQ), where a higher score represents better health status. An increase of at least 10 to 15 points was considered a significant improvement in health status. The primary end point was the hierarchical composite death from any cause or tricuspid-valve surgery, hospitalisation for HF, and an improvement of ≥15 points in KCCQ at 1 year. The secondary end points are summarised in box 1.

Box 1: Summary of secondary endpoints
1. Freedom from MAE at 30 days after procedure. 2. Change in KCCQ score from baseline at 12 months. 3. TR reduction to moderate or less at 30 days after procedure. 4. Change in 6MWT distance at 12 months.
6MWT = 6-minute walk test; KCCQ = Kansas City Cardiomyopathy Questionnaire; MAE = Major adverse events; TR = Tricuspid regurgitation

Results

A total of 350 patients from centres in the United States, Europe and Canada were enrolled and randomised. The baseline characteristics were well matched between both groups (table 2).

Table 2: Baseline characteristics

	TEER N=175 # (%)	Medical treatment N=175 # (%)
Age, Mean (Years)	78.0 ± 7.4	77.8 ± 7.2
Sex (Female)	98 (56.0)	94 (53.7)
NYHA class III or IV	104 (59.4)	97 (55.4)
KCCQ Score, mean	56.0 ± 23.4	54.1 ± 24.2
Hypertension	142 (81.1)	141 (80.6)
Renal disease	62 (35.4)	62 (35.4)
Liver disease	11 (6.3)	16 (9.1)
Atrial fibrillation	153 (87.4)	162 (92.6)
Atrial Flutter	20 (11.4)	22 (12.5)
Diabetes Mellitus	28 (16.0)	27 (15.4)
COPD	19 (10.9)	24 (13.7)
CRT/CRT-D/ICD/PPM	28 (16.0)	24 (13.7)
TR severity		
Moderate	4 (2.3)	2 (1.2)
Severe	44 (25.4)	49 (29.7)

Massive	37 (31.4)	30 (18.2)
Torrential	88 (50.9)	84 (50.9)
Coaptation gap, Mean	5.5 ± 1.8	5.2 ± 1.7
Heart size/function, Mean		
LVEF (%)	59.3 ± 9.3	58.7 ± 10.5
RV TAPSE (cm)	1.7 ± 0.4	1.6 ± 0.4
RVEDD (base, cm)	5.0 ± 0.8	5.2 ± 0.8
TV annulus diameter (cm)	4.3 ± 0.7	4.5 ± 0.8

COPD = Chronic obstructive pulmonary disease; CRT = Cardiac resynchronisation therapy; CRT-D = Cardiac resynchronisation therapy with defibrillator; ICD = Intracardiac defibrillator; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PPM = Permanent pacemaker; RV = Right ventricle; RVEDD = Right ventricular end-diastolic diameter; TAPSE = Tricuspid annular plane systolic excursion; TR = Tricuspid regurgitation; TV = Tricuspid valve

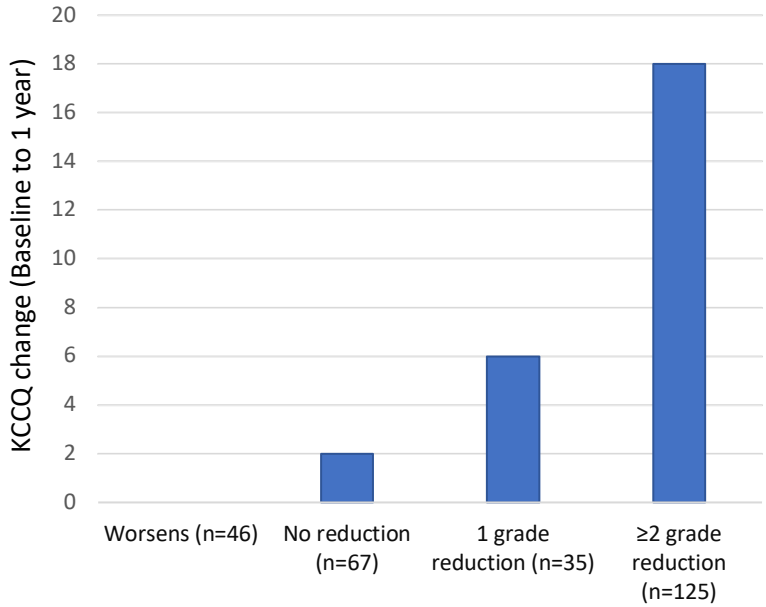
Among the TEER group, successful device implantation was achieved in 98.8% of patients. No deaths occurred during the hospital stay. One patient died within 30 days after the procedure, however it was adjudicated as not device or procedure related.

For the primary endpoint, the investigators chose the "win ratio". This estimated the likelihood that one treatment or the other is better, and the more serious events are analysed first and given higher priority. The win ratio was 1.48 which signifies a 48% advantage of TEER (95% CI, 1.06 to 2.13; P=0.02). The results were almost entirely driven by the KCCQ which improved by ≥15 points in 49.7% in the TEER group and 26.5% in the control group. It changed by a mean (±SD) of 12.3±1.8 points in the TEER group versus 0.6±1.8 points in the control group. There was no significant difference in death, HF hospitalisation and/or TV surgery between groups. Three major adverse events occurred within 30 days. 87% of the TEER group had TR of no more than moderate at 30 days compared to 4.8% in the control group (P<0.001). There was no significant 6MWT change between the TEER and control groups, by a mean of –8.1±10.5 minutes and –25.2±10.3 minutes respectively (P=0.25).

The trial has been criticised being an open label trial, with the results being primarily driven by QoL measures with the lack of benefit in harder clinical endpoints. Also, the patients

enrolled in the trial had a higher baseline KCCQ scores than those in tricuspid registry studies, which might not reflect the more common patient group that we see in our day-to-day practice. Interestingly, when assessed independent of treatment, KCCQ benefits at 1 year increased in a stepwise fashion as severity of regurgitation was reduced (Figure 1).

Figure 1: Change in KCCQ vs change in TR severity



What have we learned?

Observational studies have shown that a reduction in TR led to improvement in QoL (8) which raises questions regarding appropriate timing of TR intervention in our current practice. TRILUMINATE is the first in providing randomized data in the domain of TV percutaneous interventions and it might have set the stage to include more complex anatomies, provide insight into the procedure's durability.

The results affirm that TEER is safe, highly effective in substantially reducing TR and enhances QoL, a benefit directly correlated with the achieved TR reduction.

Disclosures

None.

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