Transcatheter treatment of severe tricuspid regurgitation with the MitraClip system

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Aim
The aim of this study was to show technical principles and feasibility of transcatheter tricuspid valve repair by use of the MitraClip system.

Methods and results
Three consecutive patients were treated successfully for severe symptomatic Tricuspid regurgitation. Three-dimensional transoesophageal echocardiography confirmed reduction of measured effective regurgitant orifice in all patients [effective regurgitant orifice area-baseline/post-procedure (cm²): 0.7/0.3; 1.5/0.8; 0.4/0.1], which was accompanied by an increase in left ventricular stroke volumes [baseline/post-procedure (mL): 42.8/45.4; 38/45; 35.2/45], decrease of measured levels of N terminal pro brain natriuretic peptide (pg/mL: baseline/post-procedure: 548/440; 2526/1702; 1754/623), and significant relief of clinical symptoms for chronic right heart failure in all patients.

Conclusions
Transcatheter tricuspid valve repair by use of interventional edge-to-edge repair with the MitraClip system was feasible, and safe in three consecutive patients. Reduction of tricuspid insufficiency associates with relief of clinical symptoms for right heart failure. This strategy seems a promising treatment option for patients at prohibitive surgical risk.

Keywords
Edge-to-edge repair • Tricuspid regurgitation • Percutaneous transcatheter valve repair

Introduction
Tricuspid regurgitation (TR) is a common finding in patients with left-sided valvular heart disease, and it is independently associated with increased mortality rates. The prognostic benefit of isolated TR repair is unclear and medical treatment of decompensated right heart failure alone does not prevent progression of disease. Minimal invasive catheter-based techniques might be an option for TR treatment in selected high-risk patients. Recently, Schofer et al. and our group reported the first cases of successful tricuspid valve repair with the Mitralign annuloplasty system. We herein report on the basic principles of interventional edge-to-edge repair by use of the MitraClip system.

Patient selection
Three consecutive patients were treated with significant TR in advanced stages of right heart failure with functional NYHA class III–IV and multigorgan damage. Echocardiography confirmed relevant TR in all patients, with an anatomy, which was judged to be suitable for interventional edge-to-edge repair. In all patients invasive right heart catheterization was performed to exclude TR in the presence of severe pulmonary hypertension defined by a systolic pulmonary pressure > 60 mmHg. After heart team decision open-heart surgery was denied due to each individuals’ extreme surgical risk (Table 1). We opted for interventional tricuspid repair with the MitraClip system, since we gained clinical experiences with its use in patients presenting with atypical anatomical conditions similar to a true tricuspid valve.

Interventional strategy
Our interventional strategy was planned to enable edge-to-edge repair in between all three tricuspid commissures, aiming to achieve a relevant reduction of TR in order to increase of RV stroke volumes, with residual TR of not more than moderate (Figure 1). In patients with large central coaptation defects, we followed a modified zipping technique with the first clip was placed as close as possible to the defect in order to facilitate second clip placement. Acceptable mean tricuspid gradient after clip placement was defined to be less than or equal to 15 mmHg.
<3 mmHg. Owing to the steep angulation of the tricuspid annulus in relation to the inferior caval vein, we chose a trans-jugular access to the tricuspid valve, and owing to this atypical approach the catheter was inserted in the sheath after 90° clockwise rotation.

In a first step, this technique was tested ex vivo in a bench top model (Figure 1A and D) to identify basic steering maneuvers:

- anterior rotation of the steerable sheath directs the clip towards the septal-anterior commissure of the valve;
- the ‘+/-’ knob allows posterior- and septal navigation of the system;
- the ‘ap’-knob and the ‘M-knob’ allow for optimization of the clip orientation towards the tricuspid leaflets.

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In two patients, computed tomography with reconstruction of the tricuspid annular anatomy helped to identify an optimal fluoroscopic view for procedural device orientation (Figure 1B). Three-dimensional transoesophageal echocardiography was used for patient selection and to ensure adequate visualization of valve anatomy and guiding (Figure 1C).

### Procedure

The procedure was performed under general anaesthesia with interventional guidance from transoesophageal echocardiography (2D, 3DTEE) and fluoroscopy. Unfractionated heparin was administered after 24F sheath insertion via the jugular vein aiming for an ACT of 250s throughout the procedure.

In a first step, the clip was inserted in the right atrium and 3DTEE was used to correct the clip orientation towards the tricuspid commissures (see Supplementary material online, Video S1). Leaflet grasping was documented with 2DTEE using predefined transoesophageal and transgastric views (Figure 1E; Supplementary material online, Videos 24). In one patient, 2D-imaging with intracardiac echocardiography was used for procedural guidance.

### Table 1  Patient characteristics and outcome parameter after edge-to-edge repair

| Patient | Age (years) | Logistic EuroSCORE (%) | CAD | History of stroke | Smoking | Arterial hypertension | History of right heart failure | Pacemaker | AF | Diabetes | Procedure time (min) | Number of clips | Before LVEF (%) | After LVEF (%) | Before sPAP (mmHg) | After sPAP (mmHg) | Before LVESV (mL) | After LVESV (mL) | Before LVEDV (mL) | After LVEDV (mL) | Before LVSV (mL) | After LVSV (mL) | Before TAPSE (mm) | After TAPSE (mm) | Before RVFAC (%) | After RVFAC (%) | Before Creatinine (mmol/L) | After Creatinine (mmol/L) | Before NTproBNP (pg/mL) | After NTproBNP (pg/mL) | TR PISA (mm) | Before TR PISA (mm) | After TR PISA (mm) | VC width (mm) | Before VC width (mm) | After VC width (mm) | EROA (cm²) | Before EROA (cm²) | After EROA (cm²) | ICV (mm) | Before ICV (mm) | After ICV (mm) | Leaflet coaptation mode | Before Leaflet coaptation mode | After Leaflet coaptation mode | Annular diameter (mm) | Before Annular diameter (mm) | After Annular diameter (mm) | TR grade | Before TR grade | After TR grade | Analysis of parameters
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LVEF, left ventricular ejection fraction; sPAP, systolic pulmonary artery pressure; ESV, end-systolic volume; EDV, end-diastolic volume; SV, stroke volume; TAPSE, tricuspid annular systolic elevation; RVFAC, right ventricular fractional area change; PISA, proximal isovelocity surface area; VC, vena contracta; ICV, inferior vaval vein; TR, tricuspid regurgitation; EROA, effective regurgitant orifice area; NTproBNP, N terminal pro brain natriuretic peptide.
After each clip placement, the acute effect of edge-to-edge repair on global TR severity was quantified and procedural steps were repeated when reduction of TR seemed insufficient (see Supplementary material online, Videos 5 and 6).

Finally, the system was retracted in the superior caval vein and the jugular puncture side was closed by use of a ‘Z-suture’.

**Statistical analysis plan**

We present a series of three cases, which does not allow for detailed statistical analysis. Values are presented as mean ± standard deviation from the whole group. Delta of changes was calculated by subtracting follow-up from baseline measurements.

**Results**

**Patient characteristics and acute outcomes**

Table 1 gives detailed information on each patients risk profile and outcome:

In summary, echocardiography confirmed severe, isolated TR in all patients [effective regurgitant orifice area (EROA), patient 1: 0.7 cm², patient 2: 0.3 cm², patient 3: 1.5 cm²] with dilatation of the inferior caval vein (patient 1: 33 mm, patient 2: 22 mm, patient 3: 37 mm). Clinically, all patients presented with functional NYHA class ≥III in advanced stages of chronic right heart failure and with elevated levels of serum NT pro-BNP (patient 1: 548 pg/mL, patient 2: 440 pg/mL, patient 3: 2526 pg/mL).

The procedure was completed successfully in all three patients. No severe complications occurred during the procedures, and mean procedural time was 133.7 ± 42.2 min (87–169 min), without use of contrast dye. The patients were discharged after 5.5 ± 2 days with improved clinical conditions accompanied by decreased levels of N terminal pro brain natriuretic peptide (NTproBNP) (Δ-NTproBNP, 2409 ± 2914 pg/mL).

Echocardiography showed acute reduction of TR in all patients (Δ-EROA, 0.4 ± 0.4 cm²), which was confirmed with TTE before discharge. Along with other TR defining measures, internal vena cava (IVC) width (Δ-IVC width, 3.5 ± 2.1 mm) and TV annular diameters (Δ-TV annular diameters, 14.3 ± 8.9 mm) were reduced.
after the procedure; measures on left heart function and volumes remained unchanged (Table 1). Concerning future directions for patient selection: Patient 2 was treated with massive symptomatic TR (EROA 1.5 cm²). Placement of three clips reduced the TR severity, with residual relevant TR (EROA 0.8 cm²). The patients’ clinical improvement and measurable effect on NT-proBNP levels was less pronounced than in the other two patients, who were treated in less advanced stages of chronic right heart failure.

All patients were contacted by telephone call 30 days after the procedure; they were still alive with stabilized clinical conditions and without need for hospitalization due to left or right heart failure.

**Discussion**

Clinicians are confronted with different types of symptomatic TR affecting patients in varying stages of acute or chronic heart disease.

Group 1 presents with more than-mild TR at time of left-sided valve surgery. Tricuspid regurgitation is a common finding in patients with chronic left heart disease, it has a prevalence of ~50% in patients with severe mitral valve insufficiency. The prognostic impact of TR in such patients is directly related to its severity and current guidelines propose correction of TR at time of surgical correction of left-sided heart disease.

Group 2 presents with late occurring TR after mitral valve surgery. It affects up to 37% of patients and is associated with worse clinical outcomes. Treatment options are limited since operative mortality rates are described with 10–20%.

Group 3 are patients with isolated ‘true TR’. In this group, reduction of TR seems directly related with relief of heart failure symptoms. However, current guidelines are reluctant to advice isolated TR surgery for this group because the prognostic benefit of surgery is unclear and operative mortality is high. Treatment options for patients in group 2 or 3 are limited and medical therapy alone does not prevent progression of global heart failure.

**Available treatment strategies**

The tricuspid valve apparatus has a complex anatomy and minimal invasive approaches for the treatment of severe, symptomatic TR predominantly aimed for placement of transcatheter valves either in the position of the native tricuspid valve or the caval veins. More recently, Schofer and our group reported the potential benefits of direct tricuspid valve annuloplasty by use of the Mitralign system.

In line with interventional techniques for mitral valve therapies the modified interventional edge-to-edge repair offers certain advantages:

1. Interventional cardiologists are familiar with the MitraClip system and its use in atypical valve anatomies. This technique can be adopted for TR repair in selected patients.
2. The direct approach on the tricuspid valve leaflets enables treatment of degenerative valve disease or functional and/or mixed aetiology of TR.
3. The combination of edge-to-edge repair with an annuloplasty system might maximize TR reduction in a subset of patients with advanced stages of disease.

**Therapeutical considerations**

Future direction of interventional TR treatment must aim for refinement in patient selection focused on haemodynamic, clinical and anatomical measures, which must be addressed with future studies.

In contrast to current guidelines, we opt for a more precise definition of PH based on measures of vascular resistance and not estimates of systolic pulmonary pressures. Clinical response and procedural success rates seem relevantly influenced by severity of chronic right heart failure, which directly impacts on patient selection. The tricuspid apparatus has its own complexity, which must be taken into account when approaching severe or massive TR with large central coaptation defects. Finally, refinements in procedural strategy and modification of the device for dedicated use in tricuspid valve disease will be necessary to expand the applicability of this technique. In this study, we cannot report on the durability of the results, but according to ‘mitral experiences’, TV leaflet detachment is not more likely to occur in a low-pressure system with reduced mechanical strain on the device.

In conclusion, we were able to show that transcatheter tricuspid valve repair by use of interventional edge-to-edge repair with the MitraClip system was feasible, and safe in three consecutive patients. Intervventional reduction of TR was associated with relief of symptoms for right heart failure.

Future research will have to confirm feasibility and durability of interventional TR repair in larger subset of patients and to optimize patient selection.

**Supplementary material**

Supplementary material is available at European Heart Journal online.

**Authors’ contributions**

C.H. and R. S. performed statistical analysis. G.N. and N.W. handled funding and supervision. C.H., R.S. and M.M. acquired the data. C.H. and R.S. conceived and designed the research. C.H. and R.S. drafted the manuscript. G.N. and N.W. made critical revision of the manuscript for key intellectual content.

**Conflict of interest:** none declared.

**References**


**CARDIOVASCULAR FLASHLIGHT**

**Triple transcatheter and surgical valve replacement: a ‘hybrid’ approach to valvular heart disease**

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An 85-year-old patient presented with global heart failure from mitral and tricuspid valve disease. In 1990, he had undergone aortic valve replacement with a tilting-disc mechanical prosthetic valve (Björk-Shiley) which was still functioning flawlessly. At the time of admission, echocardiography and invasive diagnostics confirmed moderate-to-severe mitral stenosis and severe tricuspid regurgitation causing chronic right heart failure. Due to his fragile condition and previous heart surgery, a surgical treatment was prohibitive and an interventional strategy was pursued.

As tricuspid regurgitation was considered to be the leading cause of the clinical problem, caval valve implantation (CAVI) was performed using custom-made self-expandable bioprosthetic valves. Rational and details of the CAVI-procedure as well as devices have been reported previously. In a second procedure, the patient underwent transcatheter mitral valve replacement. After surgical access through a right anterior thoracotomy, a balloon-expandable 26 mm Sapien XT-Valve (Edwards Lifesciences Inc.) was implanted. In a transatrial approach, the valve was deployed during rapid pacing into the native, severely calcified annulus. Initial echocardiography and invasive haemodynamics confirmed excellent function of all implants (Panels A and C; Supplementary material online). However, the post-operative course of the patient was complicated by sepsis and multiorgan failure leading to death of the patient 20 days after the final procedure.

Autopsy confirmed an excellent function of the caval valves (Panel B) and the mitral prosthesis (Panel D) with all devices securely anchored in their anatomic location. No obstruction of the left ventricular outflow tract by the anterior mitral leaflet was observed (Panel E).

Supplementary material is available at European Heart Journal online.

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