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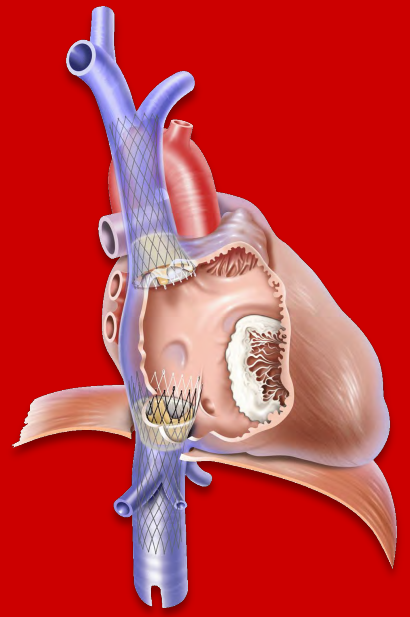
TricValve® Transcatheter Bicaval Valves System



MINIMAL INVASIVE HEART VALVES

BACKGROUND

DEVELOPMENT ON MINIMAL INVASIVE HEART VALVES

In the last 5-10 years tremendous increase in the use of transcatheter minimal invasive heart valves has occured

Primarily Aortic Valve Replacement has initiated the tremendous increase in procedures, with the indication now being widened to medium risk patients due to solid results

Intensive research in Mitral-and Tricuspid disease is continuing, primary severe regurgitation in the course of severe heart failure

Pulmonary Valve disease in congenital heart disease

OVERVIEW HEART SURGERIES IN GERMANY 2016

78 CARDIAC CENTRES

32.000 VALVE Operations

126% INCREASE IN OVER 80-YEAR-OLD PATIENTS

AORTIC VALVE REPLACEMENT

- SAVR (conventional heart surgeries) stayed stable over the last 15 years with a tendency towards getting less.
- TAVR (minimal invasive transcatheter aortic valve implantation) has gone up from 78 in 2006 to almost 20.000 in 2017.
- Initially patients over the age of 80 with very high risk were treated, moving to increasingly younger patients at lower risk.

MITRAL VALVE REPLACEMENT

- 6000 procedures in Germany in 2015
- 1/3 mechanical heart valve
- 2/3 reconstruction
- Increasingly minimal invasive techniques are needed, due to increasing prevalence of left heart failure in elderly multimorbid patients.

TRICUSPID VALVE REPLACEMENT

- App. 0,8% of the overall population suffer from moderate to severe Tricuspid regurgitation (TR), which leads to right heart failure and death. Many cases are seen post left side valve surgery
- Surgical treatment yields bad results in severe TR (high mortality rate).

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ISOLATED AORTIC VALVE IMPLANTATION 2006-2015

Berechnung auf Grundlage der DGTHG-Leistungsstatistik

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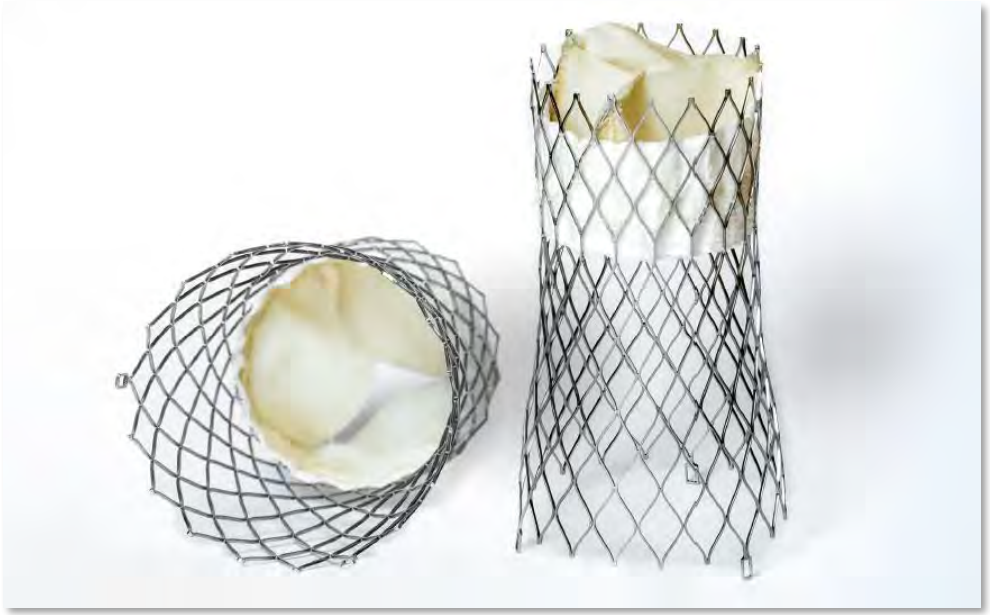
TRICVALVE® TRANSCATHETER BICAVAL VALVES SYSTEM



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BACKGROUND

Tricuspid regurgitation (TR) is mainly caused by right ventricular (RV) enlargement with annular dilatation

The implantation of self-expanding valves into the superior (SVC) and inferior (IVC) vena effectively reduce backward regurgitant flow and increase cardiac output.

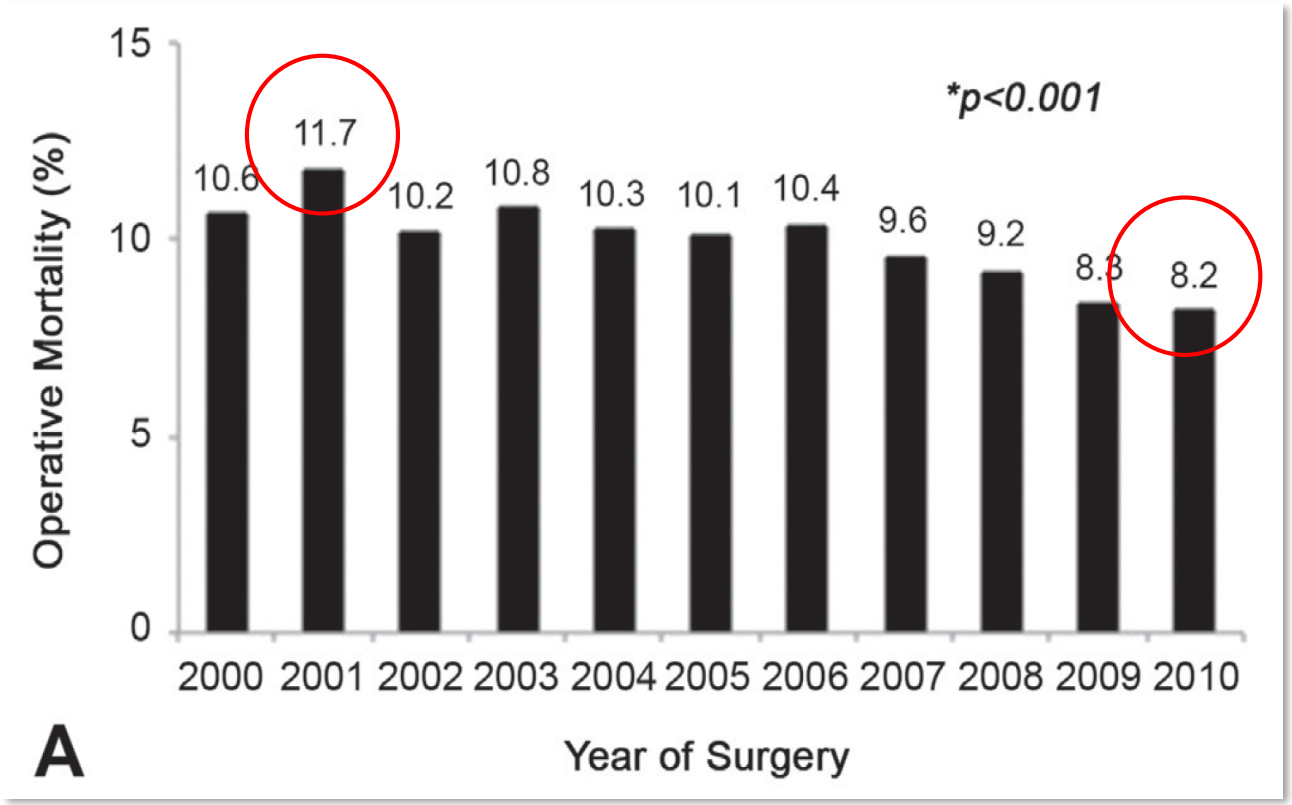
CAVI does not address TR itself but the regurgitation of blood into the caval veins, a condition found often in patients with severe, long-standing TR and RV enlargement. As the RA serves as a reservoir limiting venous backflow hemodynamic proof of caval regurgitation is essential prior to valve implantation

CAVI results in an increase in RV-afterload by exclusion of backward regurgitation into the caval veins, thus potentially leading to impairment of RV-function. Therefore, this approach should be applied in patients with preserved RV-systolic function and normal pulmonary vascular resistance

Lauten et al. Circ Cardiovasc Interv. 2014;7:268-272

RATIONALE FOR INTERVENTIONAL TREATMENT OF TR

Mortality of Tricuspid Regurgitation:
Surgical Reconstruction / Replacement



Surgical mortality of TVR
≈ 3-4x higher compared to other single valve procedures

n = 54375 pt. | *Kilic A et al. Ann Thorac Surg 2013; 96:1546-52

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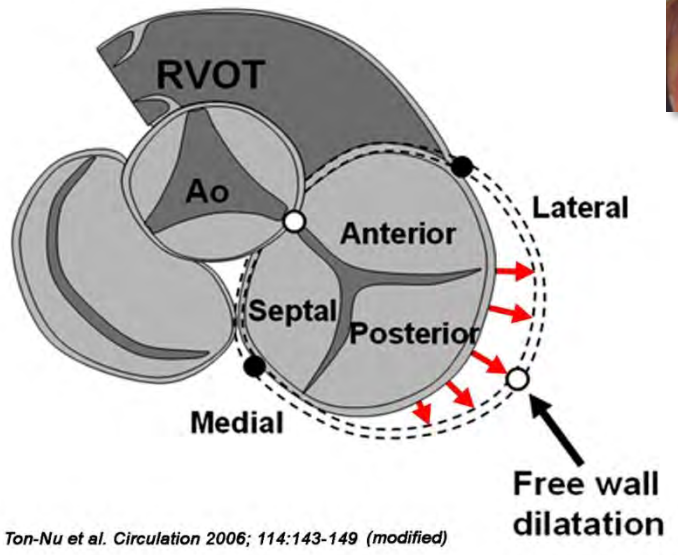
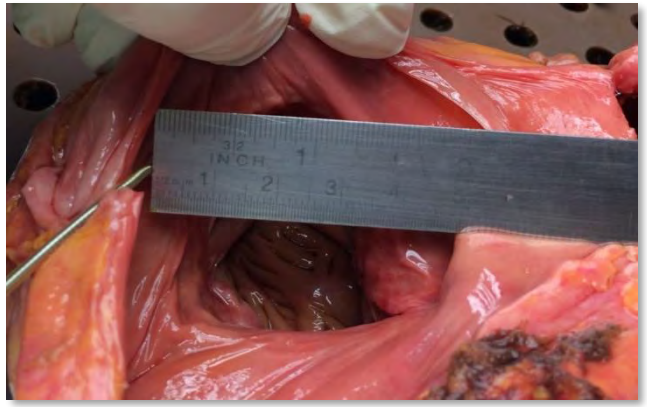
ETIOLOGY AND SURGICAL TREATMENT OF TR

- Tricuspid regurgitation (TR) functional in up to 90% of all patients
- Prevalence US-Population: 1.6 Mio pts.
- Poor prognosis (1-year mortality)
  - mild: 9.7%
  - moderate: 21.1%
  - severe: 36.1%
- Surgical Repair:
  - Operative mortality: 12-26%
  - metaanalysis (1258 pts): 19%



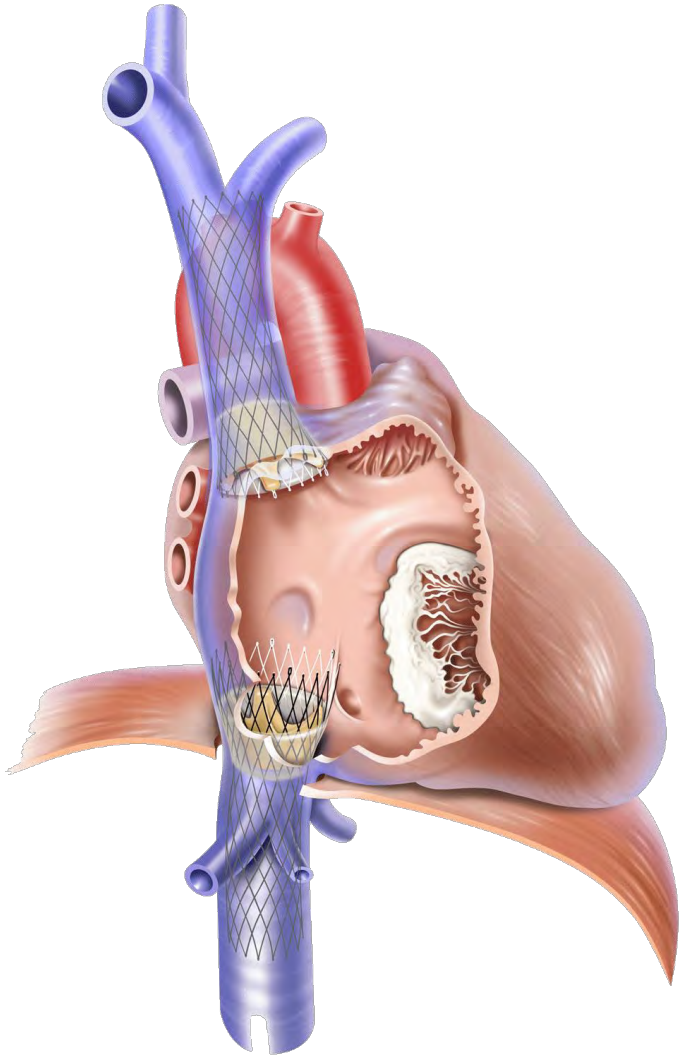
Ton-Nu et al. Circulation 2006; 114:143-149 (modified)



Tricuspid Annulus in Severe TR is huge!!

* Nath J et al. JACC 2004; 43(3) 405-9

TRICVALVE TRANSCATHETER BICAVAL VALVES SYSTEM



- TricValve® Transcatheter Bicaval Valves is a system of two self-expanding biological valves for the treatment of patients with hemodynamically relevant tricuspid insufficiency and cavalreflux.
- The prostheses are implanted percutaneously into the inferior and superior vena cava without disturbing the native tricuspid valve.
- It is especially intended for use for patients at extreme risk or who are inoperable for open surgical therapy.

SIZES:

TRICVALVE® MODEL	VALVE SIZE	PROXIMAL DIAMETER	DISTAL DIAMETER	LENGTH AFTER DEPLOYMENT
SVC 25	25	25	20	66,60
SVC 29	29	29	20	69,10
IVC 31	31	34	38	65
IVC 35	35	38	47	65

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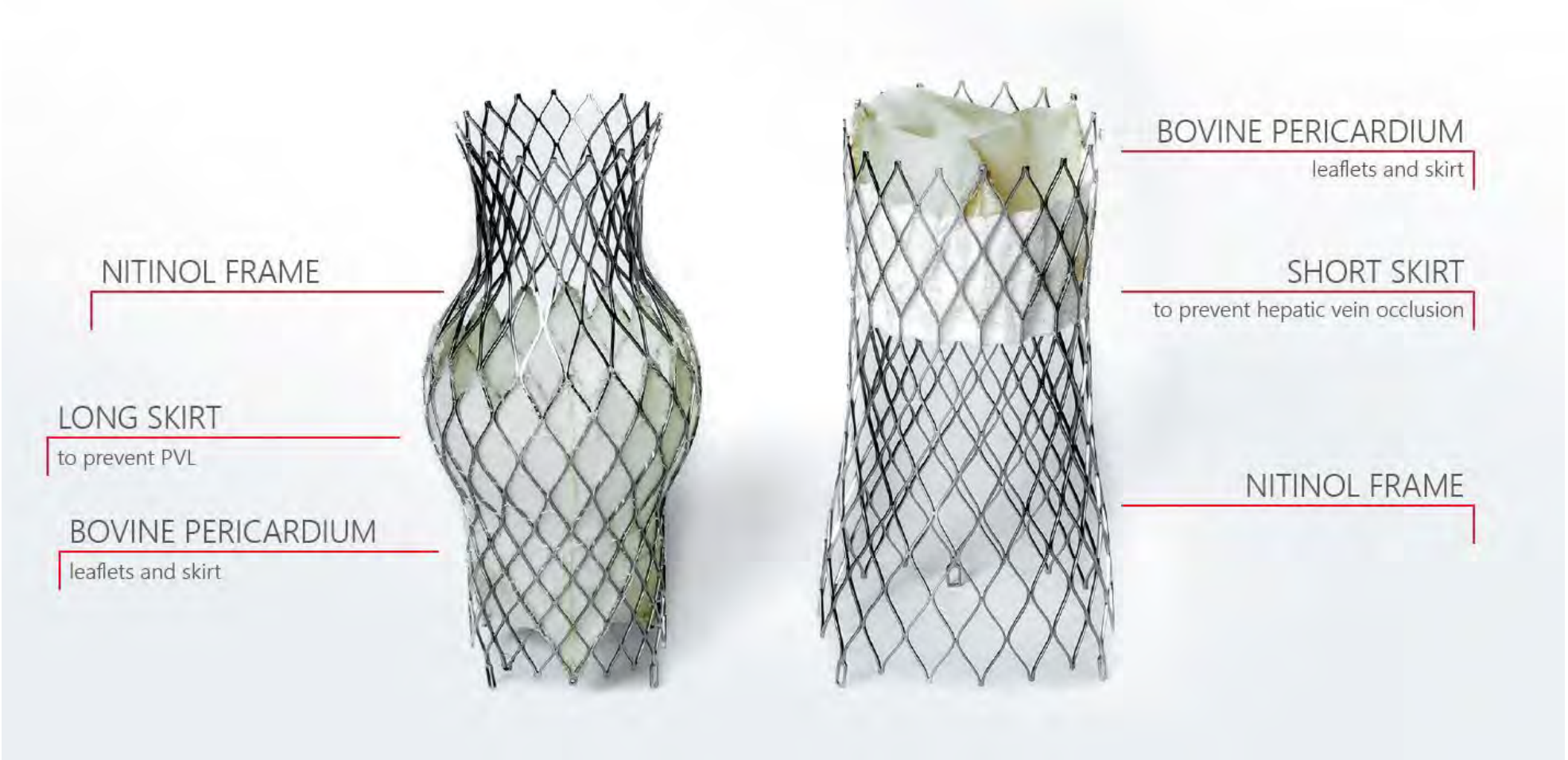
TRICVALVE TRANSCATHETER BICAVAL VALVES SYSTEM



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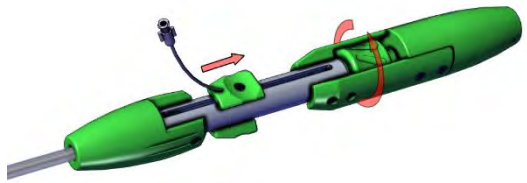
LOADING SYSTEM

The TricValve® Transcatheter Bicaval Valves are supplied already pre-mounted into the Delivery System!

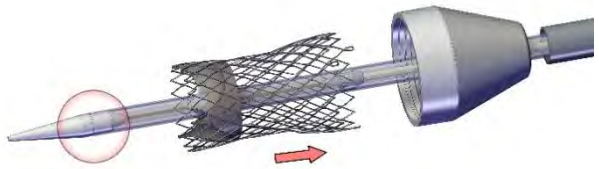
Loading Device
SVC

Loading Device
IVC

Handle
Delivery
Device



Loading
Process IVC



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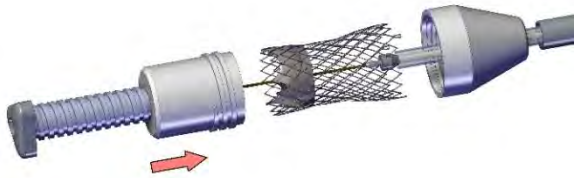
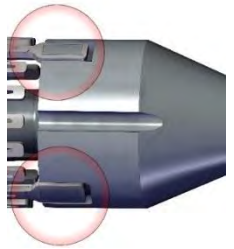


Check
Connectors



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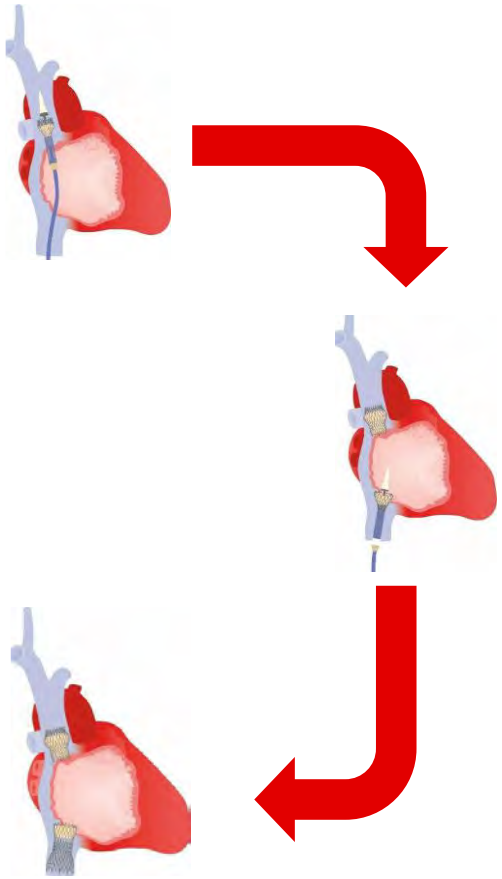
TRICVALVE TRANSCATHETER BICAVAL VALVES SYSTEM

- 2008 Start of Material Research
- 2009/2010 Start of Animal Trials
- 2010 First in Man
- January 2014 First series of clinical trials
- 2015 Design Freeze
- 2017/2018 Start of CE certification
- 2018 Clinical Study TRICUS I in progress
- Beginning of 2019 Start of TRICUS Euro

Process of Placement



Comparison to Tendyne: Tendyne does not offer a Tricuspid Valve, only a Mitral Valve. The development of Tendyne's Mitral Valve is 1 year behind P+F's Tricuspid Valve.

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TRICVALVE TRANSCATHETER BICAVAL VALVES SYSTEM

- CE and ANVISA certification in process. The product is available for compassionate use in selected patients
- current experience with caval valve implantation in 18 compassionate patients undergoing inferior vena cava-only or bicaval valve implantation using either balloon- or dedicated self-expandable valves
- Intact valve function was observed in all implanted devices during follow-up
- Thirty-day mortality was 12%
- In-hospital mortality was 24%
- TRICUS I as clinical trial in process
- TRICUS Euro planned

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PATIENT SELECTION

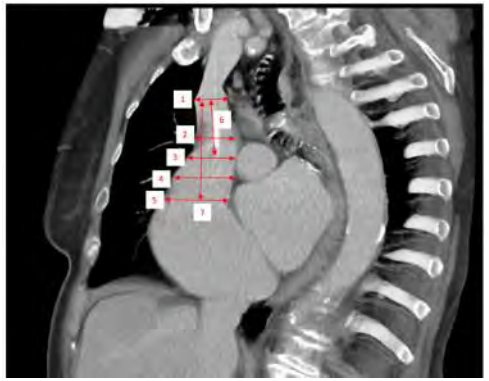
CLINICAL

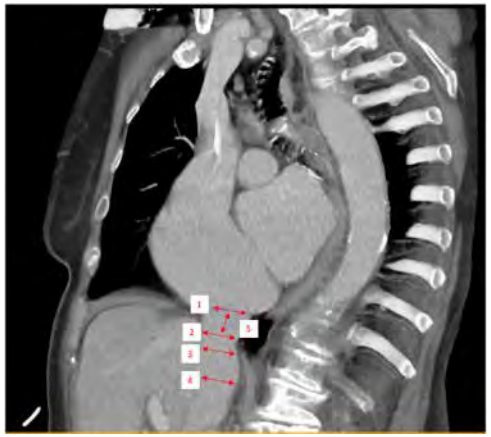
- NYHA ≥ III
- EF ≥ 40%
- 6MWT ≥ 60m
- Life expectancy ≥ 12 month

Absence of:

- Untreated left-sided Valvular heart disease,
- Severe renal failure
- Liver cirrhosis Child C

ANATOMIC





HEMODYNAMIC

- V-Wave in IVC and SVC ≥ 25mmHg
- TAPSE ≥ 14mmHg
- sPAP ≤ 65mmHg

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INCLUSION CRITERIA FOR CLINICAL STUDY

1. 18 years and older

2. Patient with severe symptomatic tricuspid regurgitation demonstrated by echocardiography with significant backflow in the lower (IVC) and/or upper (SVC) vena cava and with a v-wave ≥ 25 mmHg as demonstrated by right heart catheterization (measured in the IVC and/or SVC 2-4 cm above/ below RA inflow) within 8 weeks prior to the implantation

3. Suitable for TricValve® implantation according to anatomic criteria by computed tomography

4. The patient must have severe, tricuspid regurgitation leading to NYHA class III or IV

5. The patient has LVEF ≥ 40%

6. Distance covert in 6-minute walk test (6MWT) ≥ 60m

7. The patient shall be screened by a "Heart Team" – including an interventional cardiologist, cardiothoracic surgeon, and agreed as a candidate for the TricValve® Transcatheter Bicaval Valve System implantation

8. Patient/authorized legal guardian understands the nature of the procedure, is willing to comply with associated follow-up evaluations, and provides written informed consent

9. Patient/patient's authorized legal guardian is geographically stable (or willing to return for required study follow-up) and understands and is willing to fulfill all of the expected requirements of the clinical protocol

10. Optimal medical treatment of patient

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EXCLUSION CRITERIA FOR CLINICAL STUDY

1. Known significant intracardiac shunt (e.g. ventricular septal defect) or congenital structural heart disease based on heart teams decision

2. Requirement for other elective cardiac procedures e.g. PCI (percutaneous treatment of coronary artery) or CABG (coronary artery bypass surgery) up to 90 days after the procedure or 30 days before the procedure

3. Right ventricular failure (TAPSE ≤13mmHg)

4. Systolic pulmonary arterial pressure > 65 mmHg as assessed by Doppler echocardiography

5. Presence of any known life threatening (non-cardiac major or progressive disease), non-cardiac disease that will limit the subject's life expectancy to less than one year

6. Cerebro-vascular event within the past 3 months

7. History of mitral/tricuspid endocarditis within the last 12 months

8. The patient has untreated, >moderate, left sided valvular heart disease (e.g. mitral regurgitation or stenosis, and aortic regurgitation or stenosis)

9. Documented primary coagulopathy or platelet disorder, including thrombo-cytopenia (absolute platelet count <90k)

10. Documented evidence of significant renal dysfunction (serum creatinine > 3.0mg/dl) or on any form of dialysis at time of screening within the last 4 weeks

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EXCLUSION CRITERIA FOR CLINICAL STUDY

11. Contraindication or known allergy to device's components, anti-coagulation therapy with vitamin K antagonists or contrast media that cannot be adequately premeditated

12. Patients unsuitable for implantation because of thrombosis of the lower venous system or vena cava filter

13. The patient has contraindication against a transesophageal echo (TEE) during the procedure

14. Evidence of an acute myocardial infarction (AMI) ≤ 1 month (30 days)

15. Liver cirrhosis Child C (see appendix)

16. Female patient of child-bearing potential

17. Psychiatric or behavioral disease including known alcohol or drug abuser that is likely to impair compliance with protocol

18. Currently participating in another study of an investigational drug or device that would directly impact the treatment or outcome of the current study

19. Requirement for Antibiotic Treatment within the last 48 hours

CAVI: CLINICAL EXPERIENCE

Patient Population (n=25)

- FIM CAVI 08/2010 -Inclusion08/2010 –02/2017
- 100% compassionate cases („last resort“, non-randomized treatment with ethical consent)

Inclusion criteria:

SevereTR

- Hemodynamic proof of caval backflow (confirmed by doppler and v-wave in IVC and SVC)
- Ethical consent and heart team decision

Exclusion criteria

- *Clinical*: (sPAP) >60mmHg, TAPSE <10mm
- *Anatomic*: (ESXT) SVC & IVC at landing zone > 30mm, TricValve >35mm
- Life expectancy <3month

CAVI: CLINICAL EXPERIENCE

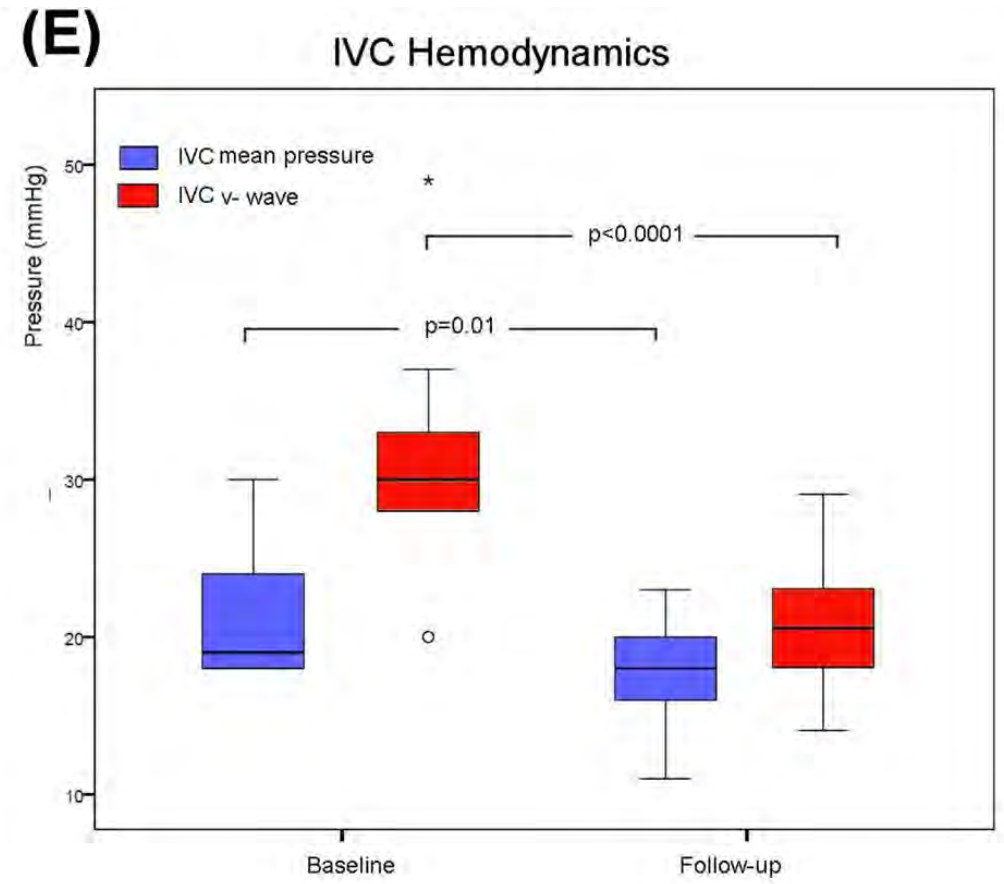
Patient demographics	MW±SD and range or n (%)
Age (mean±SD)	73.9 ±7.6
Female n (%)	13 (52)
EuroScore II	18.2 ±12.9; (5.1 –54.2)
STS Score (MVR)	14.0 ±12.7; (1.6 –42.3)
NYHA IV	18 (72)
NT-proBNPo. BNP	7344±7100pg o. 912±645
LVEF (%)	51±15 (15-74)

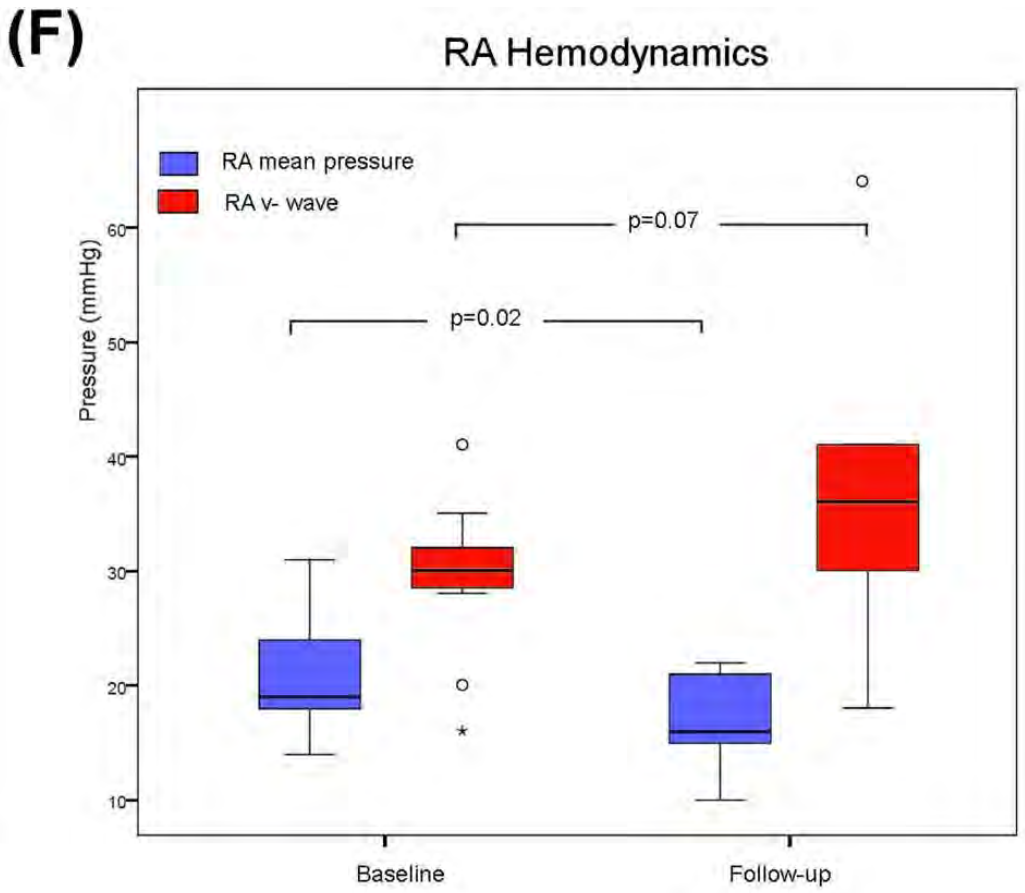
CAVI: CLINICAL EXPERIENCE

Procedural, Safety and in-hospital data	N (%)
Immediate Procedural Success	24/25 (92)
Device Embolisation	2/25 (8)
Conversion to surgery	2/25 (8)
Vascular Complications	0 (0)
New permanent pacemaker	0 (0)
Stroke	0/25 (0)
„New onset“ renal failure (requiring dialysis)	0/14 (0)

CAVI: CLINICAL EXPERIENCE

IVC and RA Pressure before versus after CAVI





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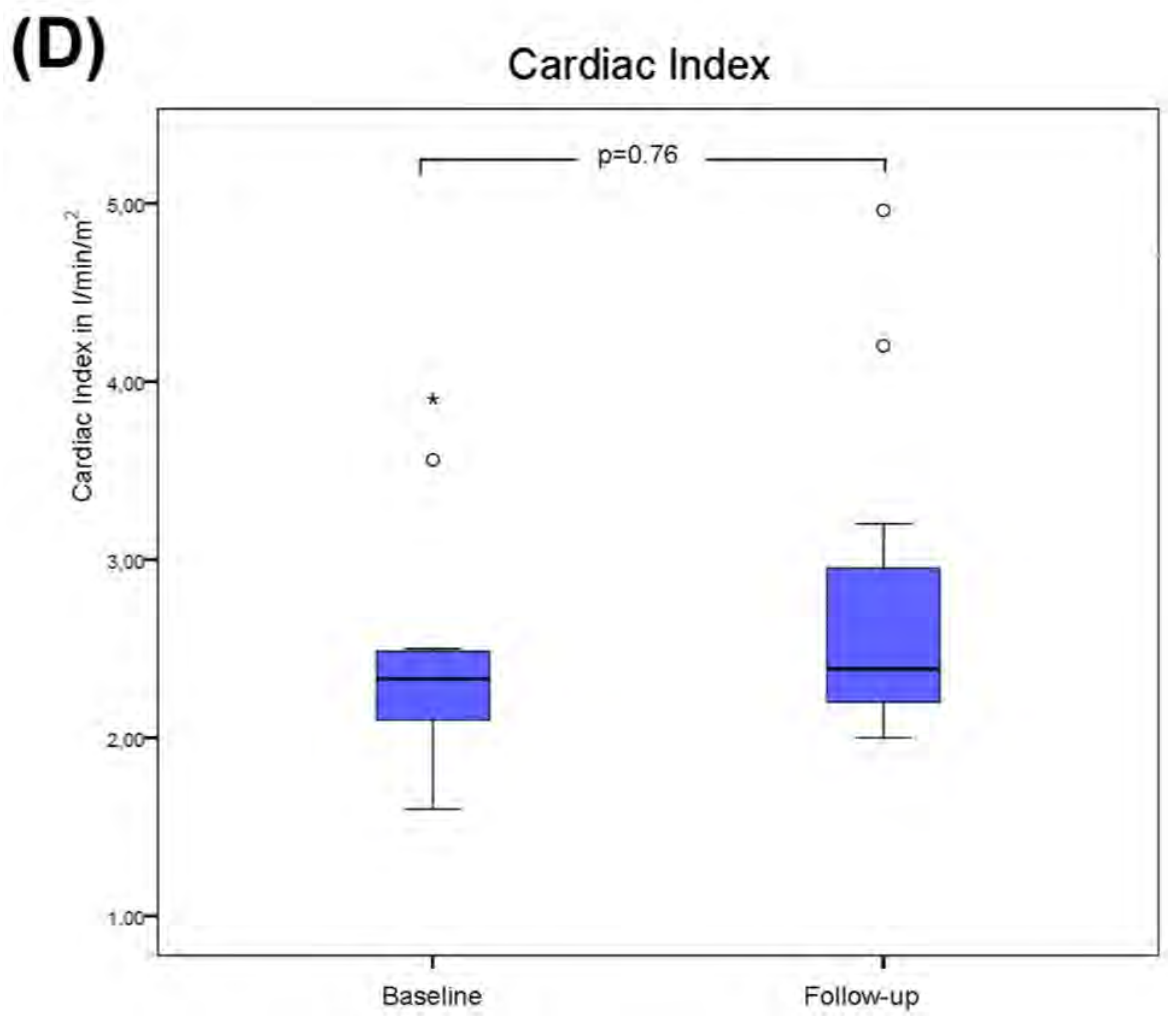
CAVI: CLINICAL EXPERIENCE

Cardiac Index before versus after CAVI



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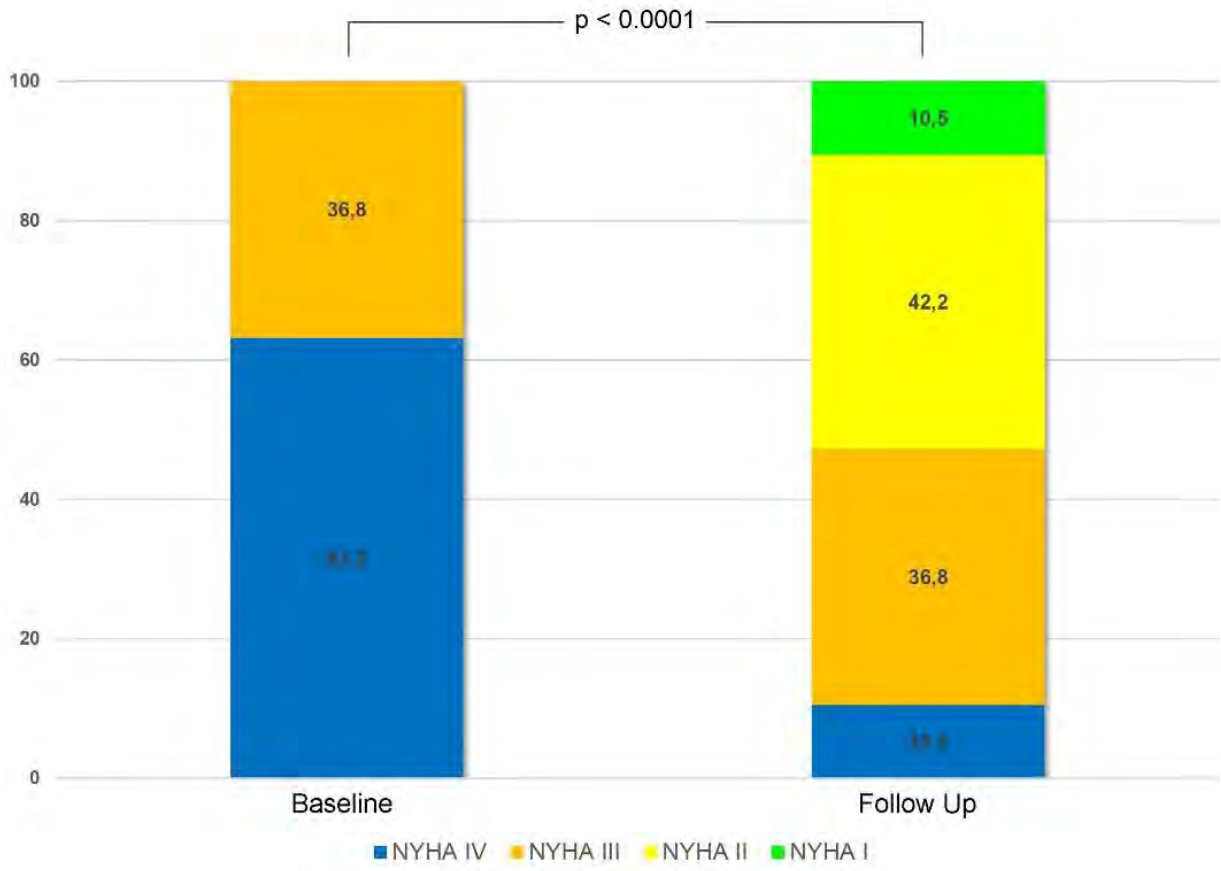
CAVI: CLINICAL EXPERIENCE

NYHA Class before versus after CAVI (pts discharged from hospital n=19)



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CLINICAL EXPERIENCE PATIENT No 3

Compassionate use, female patient 83 yrs., final stage right heart failure

EXCELLENT DEVICE FUNCTION after 3 and 12 months

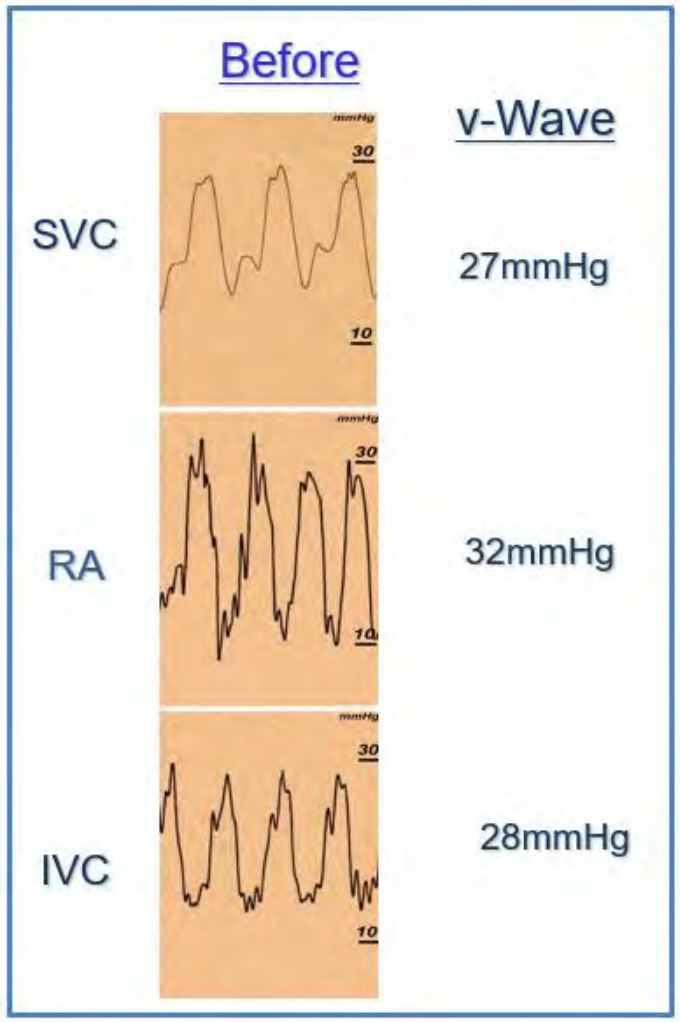
- IVC: 28/19 mmHg → 16/14 mmHg
- SVC: 27/14/19 mmHg → 21/13/18 mmHg
- RA: 32/7 mmHg → 37/11 mmHg

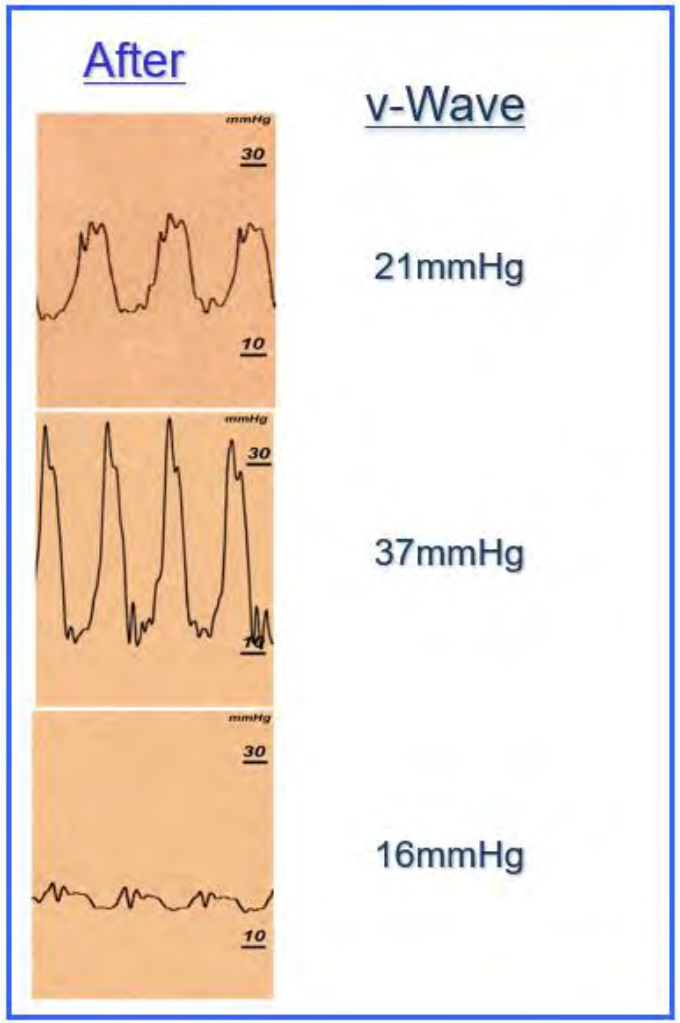
NYHA IV → NYHA I

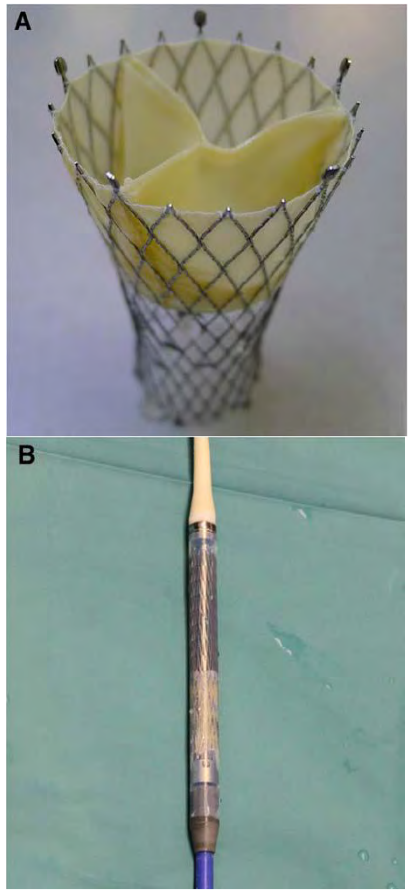
MEDICAL HISTORY

- severe, long-standing functional and structural TR
- chronic right heart failure with peripheral edema, ascites, and orthopnea
- right ventricle enlargement with preserved systolic function
- severe TR with a ventricular wave (v-wave) in the right atrium (RA), the SVC, and the IVC of 32, 27, and 28 mm Hg

CLINICAL EXPERIENCE PATIENT No 3







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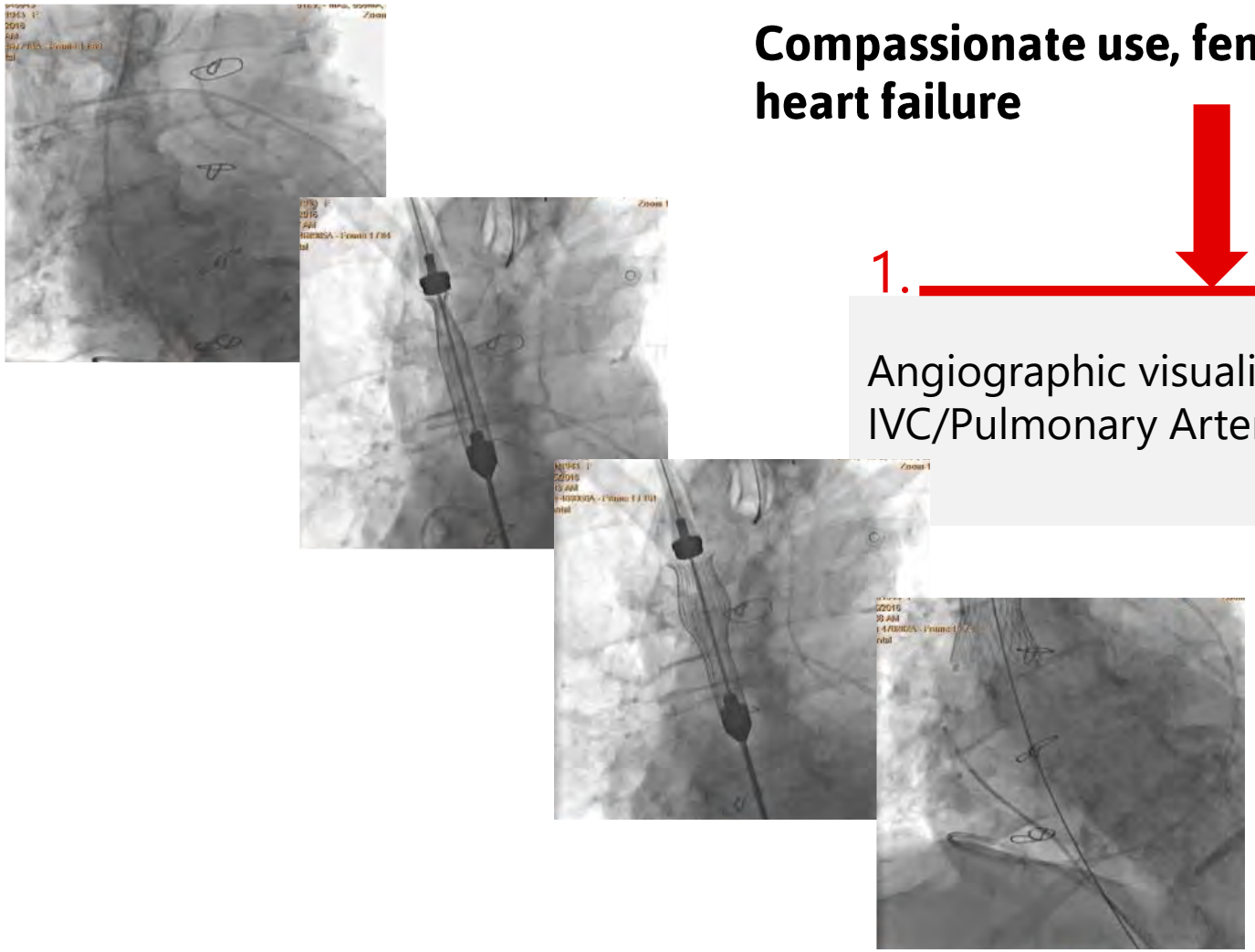
CLINICAL EXPERIENCE PATIENT No 9



Compassionate use, female patient 80 yrs., final stage right heart failure

1. Angiographic visualization of IVC/Pulmonary Artery

2. Introduction of 27F-Catheter from right femoral vein and valve deployment in SVC and IVC

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CLINICAL EXPERIENCE PATIENT No 9

HEMODYNAMICS AND CLINICAL CONDITION 3 AND 24 MONTHS AFTER CAVI

EXCELLENT DEVICE FUNCTION after 3 and 24 months

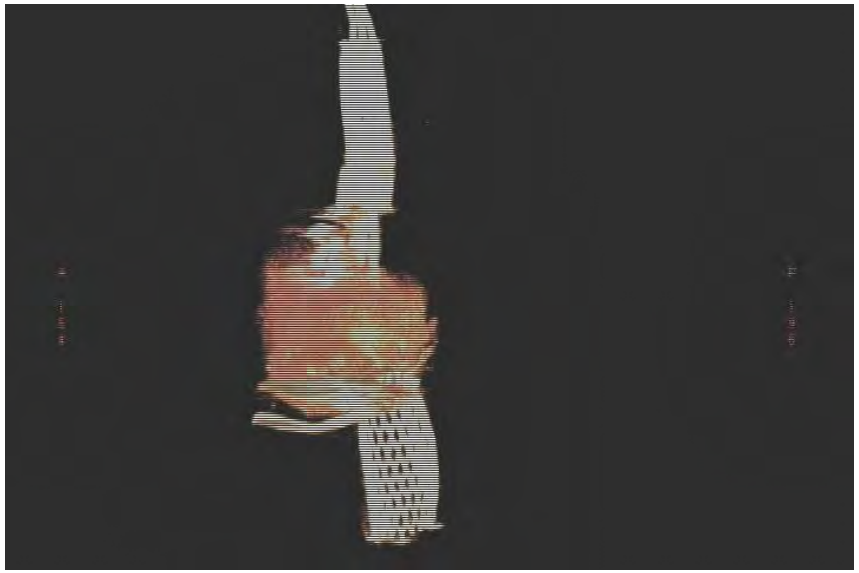
- IVC: 28/15/19 mmHg → 13/6/9 mmHg
- SVC: 27/14/19 mmHg → 21/7/11 mmHg
- RA: 32/7/20 mmHg → 36/3/16 mmHg

6-MIN WALK TEST: 20m → 360m

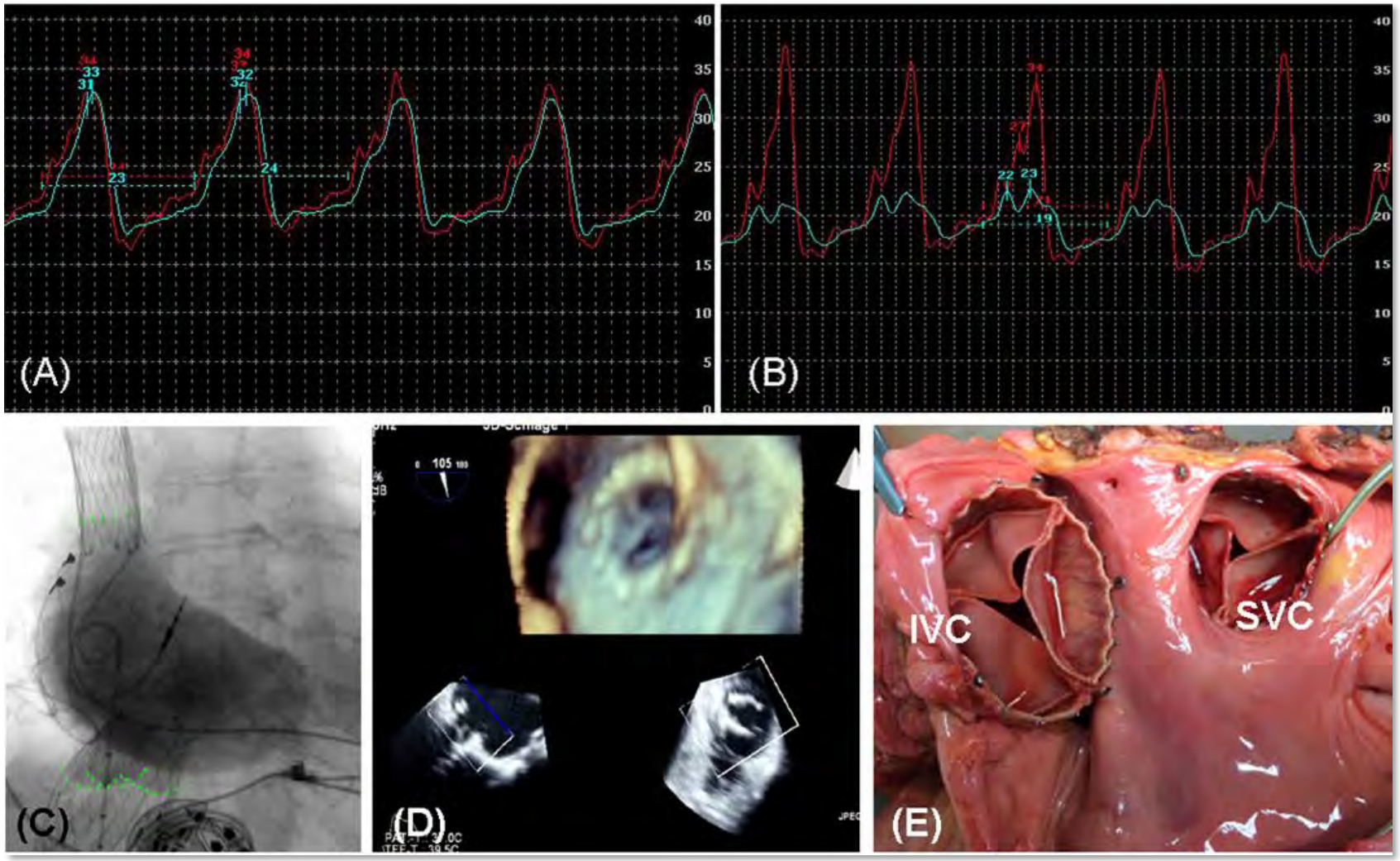
NORMALIZATION OF LIVER FUNCTION

- albumin 36g/l (31-45g/l)
- cholinesterase 89 µmol/l*s (65 -180 µmol/l*s)

NYHA IV → NYHA II



CLINICAL EXPERIENCE PATIENT No 9



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CLINICAL EXPERIENCE PATIENT No 20

Compassionate use, male patient 81 yrs.

Medical History

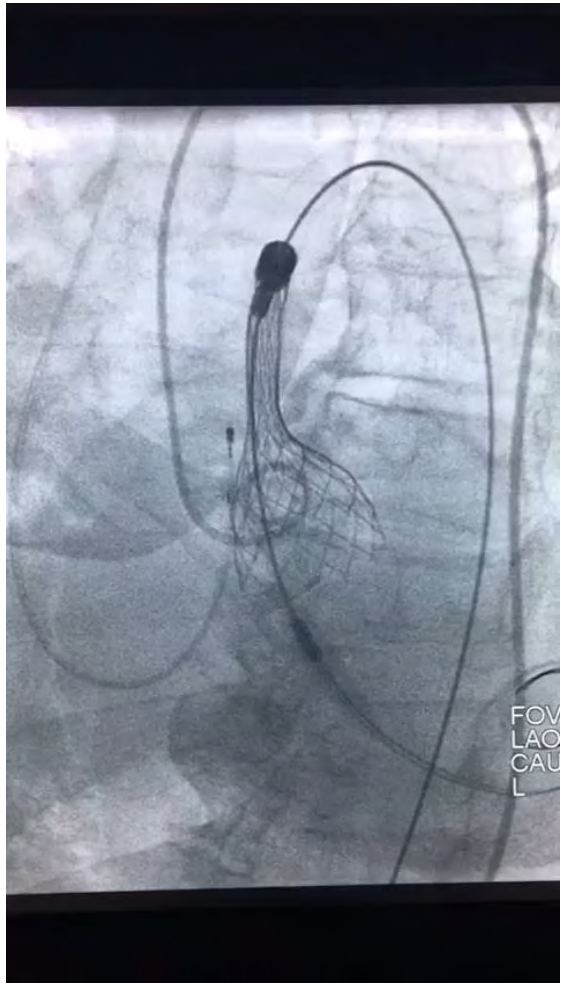
- permanent atrial fibrillation. Multiple hospitalization for right heart failure
- funtionnal isolated severe tricuspid regurgitation diagnosed in april 2018
- Euroscore 2> 9%, STS MVR=14%; Chronic kidney disease; frailty; carotid atherosclerosis. The case has been discussed in Heart team including echocardiologists, heart failure specialists, surgeons and interventionnalists
- None (no indication)

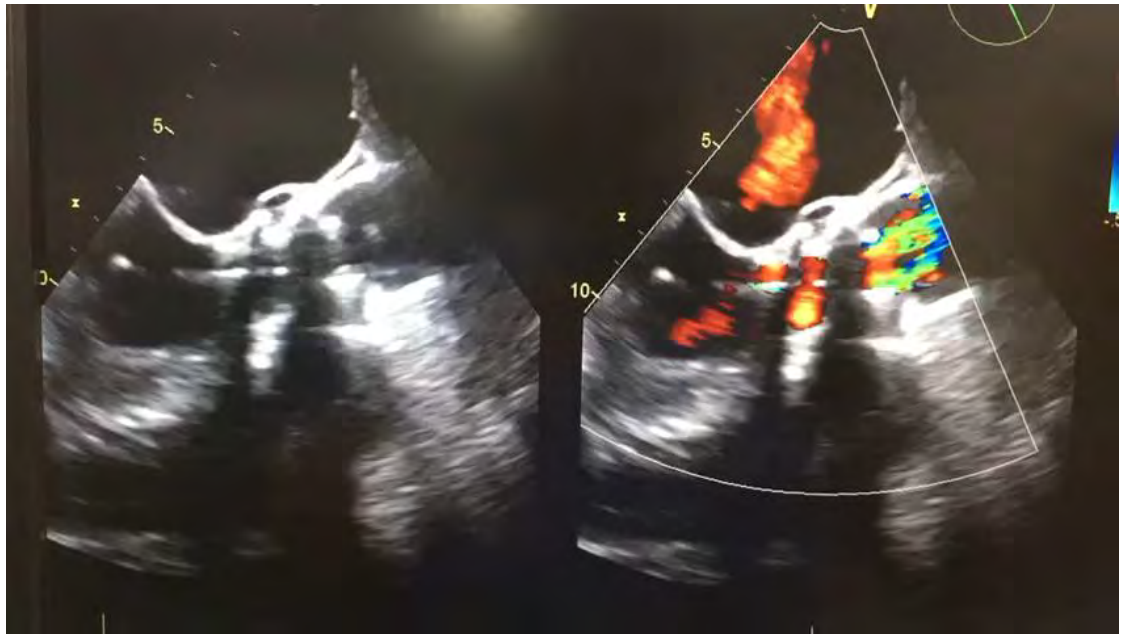
CLINICAL EXPERIENCE PATIENT No 20

NYHA Functional Class (I, II, III or IV)	III-IV
EUROSCORE II STS MVR	9.2% 14%

PASP (Systolic pulmonary arterial pressure)	32mmHg (right heart catheterization)	> 65 mmHg
MR Severity	1-2/4	
LV Ejection Fraction	50	≥ 40%
V-wave (as demonstrated by right heart catheterization; measured in the IVC and/or SVC 2-4 cm above/below RA inflow)	26mmHg	≥ 25 mmHg

Implantation Videos





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CONCLUSIONS

- There is a large unmet clinical need for interventional TV procedures due to the unfavourable surgical risk profile of these patients, not a forgotten valve!
- Orthotopic and heterotopic procedures are in the early stage of clinical investigation
- CAVI is a simple interventional procedure with a straightforward implantation technique when using designated, self-expandable valves
- Clinical benefit and functional improvement have been demonstrated in individual compassionate patients, evolution of the technology is ongoing.
- clinical trials are on an early stage

PUBLICATIONS

[1] Lauten et al., 2018. Caval Valve Implantation for Treatment of Severe Tricuspid Regurgitation. Journal of the American College of Cardiology 2018, Vol. 71, No. 10

[2] B. P. O. Neill, 2018. Caval Valve Implantation. Are 2 Valves Better Than 1? Circulation Cardiovascular Interventions 2018; 11:e006334, Editorial pp. 1–3

[3] Lauten et al., 2018. Interventional Treatment of Severe Tricuspid Regurgitation. Early Clinical Experience in a Multicenter, Observational, First-in-Man Study. Circulation Cardiovascular Interventions 2018; 11:e006061

[4] Figulla, Kiss, Lauten, 2016. Transcatheter interventions for tricuspid regurgitation – heterotopic technology: TricValve®. EuroIntervention 2016; 12:Y1-Y3

[5] Lauten et al., 2014. Percutaneous bicaval valve implantation for transcatheter treatment of tricuspid regurgitation: clinical observations and 12-month follow-up. Circulation Cardiovascular Interventions 2014; 7:268-272

[6] Lauten et al., 2011. Heterotopic transcatheter tricuspid valve implantation: first-in-man application of a novel approach to tricuspid regurgitation. European Heart Journal 2011, 32, 1207-1213

THANK YOU FOR YOUR ATTENTION