Animal Model For Comprehensive Assessment Of Hemodynamic Effects of Differently Oriented Paravalvular Leakage Jets

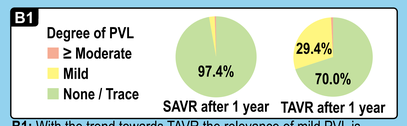
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Background

Mild aortic PVL is of increasing clinical interest

A major complication of Transcatheter Aortic Valve Replacement (TAVR) is paravalvular leakage (PVL) between the prosthetic valve and the native aortic tissue. While most PVL remain clinically silent, even mild PVL may have an impact on long-term outcome. Even newest generation transcatheter valves in low risk TAVR patients have shown a rate of at least mild PVL of around 30%.[1] While severe PVL is covered by clear guidelines, this is not the case for mild to moderate PVL. With the ongoing trend towards usage of TAVR in younger and physically more active patients it is important to better understand mild to moderate PVL.
The influence of the PVL location, the orientation of its jet as well its effect on ventricular flow and function are largely left unconsidered albeit having the potential to explain different symptoms and courses of disease in supposedly similarly classified mild to moderate PVL.



B1: With the trend towards TAVR the relevance of mild PVL is increasing [1]

[1]Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. N Engl J Med. 2019;380(18):1695-705.

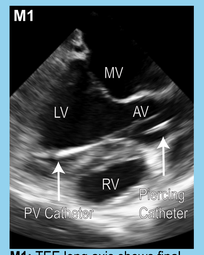
Objective

To develop a translational model to investigate mild to moderate PVL

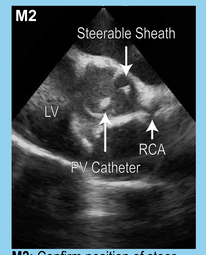
Provide a model to study the impact of differently located mild to moderate paravalvular leakage (PVL) of the aortic valve to study the impact of the resulting regurgitant jet on left ventricular hemodynamics and flow in a clinically relevant, reproducible and cost-effective translational large animal modell to better understand this increasingly relevant condition.

Methods

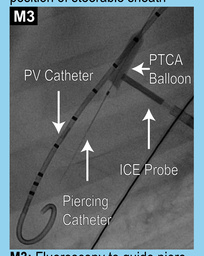
Pierce and dilate aortic leaflets at hinge region to simulate post TAVR PVL



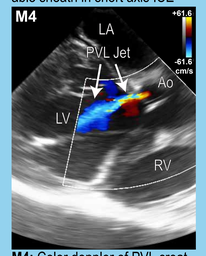
M1: TEE long axis shows final position of steerable sheath



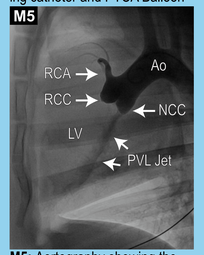
M2: Confirm position of steerable sheath in short axis ICE



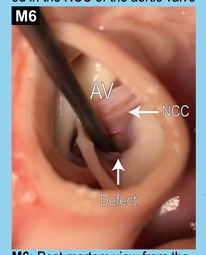
M3: Fluoroscopy to guide piercing catheter and PTCA Balloon



M4: Color doppler of PVL created in the NCC of the aortic valve



M5: Aortography showing the created PVL jet in the NCC



M6: Post mortem view from the aorta ascendens on NCC defect

Initial Pressure Volume (PV) measurements
- Baseline
- Afterload increase with Phenylephrine*
- Baseline
- Heart rate increase with Dobutamine*
- Baseline

* Order randomized

PVL defect creation
M1) Initial positioning of steerable sheath with long axis TEE
M2) Verification of final position with short axis in ICE
M3) Piercing of leaflet with stiff guide wire under fluoroscopy
M3) Positioning and inflation of PTCA balloon under fluoroscopy
M4) Inspecting the resulting PVL jet in TEE

Post defect PV measurements
- Baseline
- Afterload increase with Phenylephrine*
- Baseline
- Heart rate increase with Dobutamine*
- Baseline

** Order randomized*

Aortography
M5) Allowing periprocedural densitometric quantification of PVL

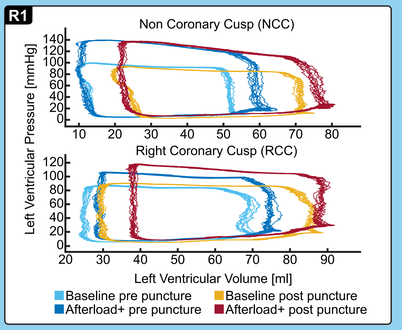
4D Flow MRI
- Baseline
- Afterload increase with Phenylephrine
- Heart rate increase with Dobutamine

Pathology
M6) Optical assessment and documentation of defect size and location as well as inspection for further injury to LVOT or endocardial tissue

Results

Our model allows direct PV-Loop comparison between healthy and PVL as well as correlating the changes to disturbed intraventricular flow patterns

- Targeted isolated Non Coronary Cusp (NCC) and Right Coronary Cusp (RCC) lesions at the hinge point of aortic leaflet and aortic annulus are created in a minimally invasive manner resulting in mild to moderate aortic regurgitation simulating post Transcatheter Aortic Valve Replacement (TAVR) Paravalvular Leakage (PVL)
- Stable PV-Loops were acquired during the entire experiment without intermittent removal of the PV Catheter, thus allowing continuous data acquisition and comparability between baseline and post defect state
- Possibility to precisely titrate the increase of drug induced afterload increase without affecting cardiac contractility
- Possibility to precisely titrate drug induced increase in heart rate
- Changes in PVL severity depending on hemodynamic state detectable and quantifiable in echo and PV-Loops
- Visual representation and additional PVL quantification by video densitometry is possible in pigs
- 4D Flow MRI acquisition without potentially induced artefacts by TAVR implant



R1: Comparing PV-Loops of baseline (light blue / yellow) with an afterload increase (dark blue / red) before/after creating either an NCC or RCC PVL

Discussion

Studying PVL in patients is very challenging

The limited understanding of Paravalvular Leakage (PVL), in particular mild PVL, might have to do with the difficulty of studying this pathology in the affected patients. A healthy baseline prior to the aortic stenosis (AS) and its associated remodelling, which lead to the Transcatheter Aortic Valve Replacement (TAVR), is rarely available, thus only allowing the comparison between this pathological state prior TAVR with the post procedural combination of PVL jet as well as PVL- and AS-induced cardiac remodelling after TAVR. The frequent comorbidities in this patient group, such as heart failure, myocardial ischemia or mitral regurgitation, which also influence left ventricular energetics, hemodynamic and flow, pose additional difficulty. The impact of afterload and heart rate changes is difficult to be isolated and distinguished in patients simultaneously suffering from tachycardia and hypertension. The relatively long acquisition times of 4D Flow MRI might be difficult to endure for these conscious patients, as a general anaesthesia for this purpose probably poses a not justifiable risk. The implanted artificial valve itself may cause considerable MR artefacts, lowering the quality of the acquired data.

Conclusion

New possibilities for the study of PVL

The trend towards the usage of Transcatheter Aortic Valve Replacement (TAVR) in younger and more active patients leads to more patients being treated with TAVR. The considerably higher rate of mild Paravalvular Leakage (PVL) in TAVR compared to Surgical Aortic Valve Replacement (SAVR) leads to larger patient groups being affected by this complication. The limited understanding of these often clinically silent yet still potentially harmful mild to moderate PVL requires further investigation. Since an in-depth study of the hemodynamic effects and ventricular flow pattern as well as their effect on left ventricular performance is not practical in patients an alternative is required. The presented porcine model offers a clinically relevant, reproducible and easy to use platform to study mild to moderate PVL jets originating from different locations under different hemodynamic conditions in an effort to overcome these patient associated limitations and to being able to apply a broad spectrum of diagnostic and measuring tools in the quest for a more precise analysis of PVL severity, prognosis and need for future intervention.

Take Home Message: Piercing and dilating aortic valve leaflets in the porcine model allow the clinically relevant modelling of mild to moderate TAVR PVL and the study of it's hemodynamic and flow