Feasibility of Coronary Alignment in TAVI with Balloon-Expandable Valves: Insights from a COMPARE-TAVI 1 Substudy

Rebekka Vibjerg Jensen[1,2], MD, PhD; Bjarne Linde Nørgaard[1], MD, PhD; Troels Thim[1,2], MD, PhD; Evald Høj Christiansen[1,2], MD, PhD; Jesper Møller Jensen[1], MD, PhD; Christian Juhl Terkelsen[1,2], MD, PhD

[1] *Department of Cardiology, Aarhus University Hospital, Denmark*

[2] *Department of Clinical Medicine, Aarhus University, Denmark*

Short title: Coronary alignment - COMPARE-TAVI 1 substudy

Keywords

TAVI, coronary alignment, valve-to-aorta-distance, balloon expandable valves, redo-TAVI

Wordcount (incl. the title page, abstract, legends, and references): 3519

Corresponding author

Rebekka Vibjerg Jensen

Aarhus University Hospital

Palle-Juul Jensens Blvd 99

8200 Aarhus N

Denmark

Telephone +4530714316

Rebethom@rm.dk

Abstract

Background

Coronary alignment may be an important prerequisite for redo-TAVI and may be achieved with ballon-expandable valves (BEV) by intentional orientation of neo-commissures during crimping.

Aims

To evaluate whether coronary alignment is possible during implantation of BEVs and to assess the risk of coronary obstruction limiting the feasibility of redo-TAVI.

Methods

On post-TAVI CT scans available in 375 patients enrolled in the COMPARE-TAVI 1 study, we assessed coronary alignment defined by neo-commissure-to-coronary-angles and assessed coverage of coronary ostia by the THV frame and valve-to-aorta distance.

Patients were randomized to treatment with Sapien 3 (Group A) or Myval (Group B) with random orientation of neo-commissures during valve crimping (Period 1), or Sapien 3 (Group C) or Myval Octacor (Group D)(Period 2), where intentional orientation of neo-commissures during crimping was attempted according to pre-TAVI CT-scan.

Results

Left main alignment or mild misalignment occurred in 50%, 51%, 47% and 55% of patients in groups A, B, C and D, p=0.33, and right coronary alignment or mild misalignment occurred in 52%, 62%, 54% and 53%, p=0.53. The proportion of patients considered feasible for redo-TAVI defined as a) no coronary coverage by the THV frame, b) coronary coverage but VTA≥2 mm, or c) coronary coverage and VTA<2 mm but coronary alignment optimal or only mild misalignment, was 81%, 78%, 80%, 87% in groups A, B, C and D, p=0.33.

Conclusions

Crimping BEV neo-commissures at predefined angles did not increase coronary alignment, however, the majority of patients treated with BEVs were still considered eligible for redo-TAVI.

Abbreviations and acronyms

BEV: Balloon expandable valve

LM: Left main

MSCT: Multislice computed tomography

RCA: Right coronary artery

TAVI: Transcatheter aortic valve implantation

THV: Transcatheter heart valve

VTA: Valve-to-aorta distance

Introduction

Coronary alignment is defined as the angle between a coronary ostium and the nearest transcatheter heart valve (THV) neo-commissure and categorized into aligned (angle 45-60^{0}), mildly misaligned (angle 30-44^{0}), moderately misaligned (angle 15-29^{0}), and severely misaligned (angle 0-14^{0})(1). The major pitfall of redo-TAVI is the occurrence of coronary obstruction. Accordingly, obtaining coronary alignment during the index procedure might be beneficial to mitigate the risk of coronary obstruction and to perform leaflet modification techniques in high risk anatomies(2, 3). As guidelines expand TAVI treatment to younger patients with longer life expectancy(4-6), coronary alignment becomes increasingly important.

The current evidence regarding the practical feasibility of coronary alignment in TAVI procedures is limited. Commissural alignment has proven feasible for several self-

expandable valves(7-9), but was only recently introduced for ballon-expandable valves (BEV)(10, 11). In theory, coronary alignment can be achieved with attention to neo-commissure orientation during crimping (Figure 1). However, individual differences in coronary eccentricity and iliofemoral and aortic tortuosity may challenge the validity of this theory.

The aim of this study was three-fold: 1. to evaluate coronary alignment after implantation of Sapien 3/Sapien 3 Ultra THV series and Myval/Myval Octacor THV series. 2. to evaluate if patient-specific rotation of a THV neo-commissure during valve crimping facilitates coronary alignment. 3. to assess subsequent coronary coverage by the THV frame and the risk of coronary obstruction that may limit the feasibility of redo-TAV.

Methods

Study population

This is a substudy of the TAVI-COMPARE 1 trial(12), a multicenter all-comers RCT randomizing (n=1031) patients with severe aortic stenosis 1:1 to Sapien 3/Sapien 3 Ultra THV series (Edwards Lifesciences, Irvine, California, USA) and the Myval/Myval Octacor THV series (Meril Life Sciences Pvt. Ltd., Vapi, Gujarat, India) BEV (Figure 2). From June 2020 to August 2021 (study period 1) Sapien and Myval THVs were used in the study. Patent-related issues made Myval unavailable from August 2021. When enrollment was resumed in August 2022 (study period 2) Myval Octacor was introduced instead of Myval, and with this the idea of coronary alignment using the OctaAlign technique(10). Patients enrolled in the COMPARE-TAVI 1 trial at Aarhus University Hospital (n=538) who also had a

one-month post-TAVI MSCT scan performed as part of a MSCT-substudy (n=375) comprised the current study population(13). At Aarhus University hospital LM alignment was prioritized in all patients randomized to Myval Octacor.

Pre-TAVI MSCT measurement of Left Main orientation

Patients had a pre-TAVI MSCT scan as described previously(14). After August 2022, the angle between anterior (12 o'clock) and the left main (LM) take off on the annular plane was measured using 3Mensio imaging software (3mensio Medical Imaging, Utrecht, Netherlands).

Crimping of THV

In theory, coronary alignment can be achieved with attention to neo-commissure orientation during crimping. Provided that the right coronary artery (RCA) ostium is located anterior and the left main (LM) 120^{o} from anterior, the neo-commissure will in theory rotate 180^{o} when passing through the aortic arch, achieving coronary alignment with neo-commissures located 60^{o} from each coronary artery (Figure 1).

Between June 2020 and August 2021 (study period 1) all THVs (Sapien 3: Group A; Myval: Group B) were mounted on the delivery system with random orientation (no particular attention to the orientation) of the neo-commissures during crimping (Figure 2). After the introduction of Myval Octacor in August 2022 (study period 2) all Sapien 3 THVs (Group C) were crimped with a neo-commissure aligned to 12 o´clock when inserted in the crimping device. For Myval Octacor THVs (Group D) patient specific rotation of a neo-

commissure was implemented: the valves were crimped with a neo-commissure oriented 120^0 from the LM take off measured on the pre-TAVI CT scan. If the LM take off was 120^0 from anterior, the Myval Octacor THV was crimped with a neo-commissure aligned to 12 o´clock when inserted in the crimping device, so in theory it would end at 6 o'clock after transversing the aortic arch, and thus 60° from the LM (Figure 1). For every six degrees the LM take off was greater than 120^0, the THV was rotated 1 minute clockwise on the crimping device or rotated accordingly counterclockwise for every six degrees lower than 120^0 (Figure 2).

Multislice Computed tomographic imaging and analysis

One-month post-TAVI MSCT scans were performed using a dual-source CT systems (Siemens Somatom Definition Flash or Force, Siemens Healthcare, Forchheim, Germany) scanner. Scans were obtained with a prospective ECG-gated acquisition protocol, generally timed to 65–75% of the R–R interval. In cases of atrial fibrillation or inability to maintain breath-hold, an ECG-triggered high-pitch spiral acquisition mode was used.

MSCT data were analyzed in a blinded fashion by a dedicated core laboratory at Aarhus University Hospital. All MSCT image analyses were performed using 3Mensio imaging software (3mensio Medical Imaging, Utrecht, Netherlands). Neo-commissures were identified and the angles between the LM and the RCA ostium and the nearest neo-commissure were measured. For each coronary, alignment was classified as follows:

aligned if the neo-commissure–to–coronary angle was 45-60^{0}; mildly misaligned at 30-44^{0}; moderately misaligned at 15-29^{0}; and severely misaligned at 0-14^{0} (Figure 3)(15).

In short frame BEV THVs, as Sapien and Myval THVs, the future neoskirt height is close to the height of the index THV frame, but with small variation depending on valve size(16). The THV frame was used as neoskirt plane, and the coronary risk plane was defined as the lowest point of each coronary ostium(17). For each coronary artery it was determined if the neoskirt plane was above coronary risk plane, and if this was the case the narrowest valve-to-aorta distance (VTA) was measured in the area from the top of the coronary ostia to the top of the THV frame(17).

Unfeasible redo-TAVI was defined as moderate or severe misalignment of at least one coronary artery in combination with THV frame coverage and VTA<2 mm.

Statistical analysis

Categorical data as number (per centage). Comparisons of proportions were made using Chi-square test.

Results

In the COMPARE-TAVI 1 trial 538 patients were enrolled at Aarhus University Hospital. 433 of these patients consented to a MSCT-substudy with one-month post-TAVI MSCT-scans, and in 390 (90.1%) the one-month MSCT-scan was available. MSCT image quality allowed for coronary alignment assessment in 375 (96%), who comprise the current study cohort. 40 patients (10.6%) had bicuspid anatomy, and 16 patients (4%) had valve-in-

valve procedure. 170 patients were included during period 1 and treated with Sapien THV series (Group A, n=84) or Myval THV series (Group B, n=86), and 205 patients were included during study period 2 and treated with Sapien THV series (Group C, n=99) or Myval Octacor THV series (Group D, n=106) (Figure 4).

Coronary alignment

During study period 1, when all THVs were crimped with random orientation of the neo-commissures there was no difference in the proportion of Sapien (Group A) and Myval THVs (Group B) that were aligned, mildly misaligned, moderately misaligned or severely misaligned for neither LM (p=0.82) nor RCA (p=0.55) (Figure 4).

During study period 2, when neo-commissures were oriented at 12 o'clock for Sapien (Group C) and LM alignment was attempted for Myval Octacor (Group D) during the crimping process, there were also no differences in the proportion of Sapien and Myval Octacor THVs that were aligned, mildly misaligned, moderately misaligned or severely misaligned for neither LM (p=0.11) nor RCA (p=0.83) (Figure 4).

When comparing all 4 groups (A-D), there were also no differences in the proportion of Sapien and Myval/Myval Octacor THVs that were aligned, mildly misaligned, moderately misaligned or severely misaligned for neither LM (p=0.33) nor RCA (p=0.53) (Figure 4).

Coverage of coronary ostium

LM take-off above the THV frame was more frequent with Myval than with Sapien, 60% vs 46%, (p = 0.006) (Figure 5). In contrast, the proportion of patients with the RCA above the frame did not differ between valves (p=0.11).

To estimate the redo-TAVI feasibility Figure 6 shows the distribution of patients with the following anatomy: a) neoskirt plane below coronary risk plane; b) neoskirt plane above coronary risk plane for one or both coronary arteries but associated VTA≥2 mm; c) high-risk setting: neoskirt plane above coronary risk plane for one or both coronary arteries and VTA<2 mm but associated coronary alignment optimal or only mild misalignment; and d) high-risk setting: neoskirt plane above coronary risk plane combined with VTA<2 mm and moderate or severe misalignment for at least one coronary artery (unfeasible redo-TAVI).

For both the LM and the RCA, there was no difference between how often the neoskirt plane extended beyond the coronary ostium and the VTA was <2 mm (Figure 5). The number of patients in the study who had at least one artery in the neoskirt plane combined with VTA<2mm was 31%, and 18% had at least one artery in the neo-skirt plane and VTA<2mm combined with severe or moderate misalignment (Figure 6).

Discussion

Our study has three main findings. 1. Coronary alignment with the BEV Sapien 3 and Myval THVs is random. 2. Crimping BEV neo-commissures at certain angles did not

improve coronary alignment. 3. In at least 30% of patients with a BEV, coronary alignment may be of importance in redo-TAVI.

As guidelines extend TAVI indication to younger patients with less comorbidity and longer life expectancy(4-6), the need for TAVI-in-TAVI likely increases and coronary alignment of the index THV may be an issue. When the index THV commissure level extends above the coronary ostium, there can be a risk of coronary obstruction by the neoskirt formed by leaflets of the index-THV in a TAVI-in-TAVI procedure. In BEV THVs, the height of the neoskirt is in bench testing close to the height of the THV frame; 2-3 mm lower depending on valve size(16). We approximated THV frame height as the neoskirt plane and the VTA was measured if the neoskirt plane was above the coronary risk plane, i.e. a coronary artery was fully covered by the THV frame. Thereby we may have slightly overestimated the risk of coronary obstruction. The risk of coronary obstruction during TAVI is also influenced by the VTA. When the VTA is less than 2 mm, the likelihood of obstruction is significantly increased, necessitating the implementation of specific management strategies during TAVI-in-TAVI procedures. In certain cases, chimney stenting can be successfully performed even without coronary alignment; however, this approach serves as a bailout rather than a preventive strategy, aimed at mitigating an obstruction once it occurs (18). In contrast, true preventive measures—such as intentional leaflet laceration of the index THV—are unlikely to be effective in the absence of coronary alignment. (19, 20). Our finding of alignment to the left main in only 25% of cases is therefore interesting.

Two earlier studies have evaluated commissural alignment for Myval Octacor. In the research letter by Revaiah et al, it was described for the first time how to implant

Myval with the OctaAlign technique, which theoretically can increase commissural alignment achievability(10). When orientating the Myval to 12 o´clock during crimping commissural alignment was achieved in 38% of cases, while mild, moderate, and severe misalignment was seen in 31%, 19%, and 13%, respectively. Coronary alignment was not evaluated in this study, and the study cohort comprised only 32 patients, implanted in 8 centers so no statistical calculations were relevant.

Sandos-Martinez et al refined the Myval Octacor crimping technique to improve commissural-coronary alignment outcomes(11). The latter study group performed patient-specific rotation of the THV during crimping according to an aortic root biomodel based on pre-TAVI MSCT scan. They found commissural alignment in 50% of the patients and 70% and 60% had coronary alignment to the LM and RCA, respectively. The authors found a higher rate of alignment than our study, but with only 10 patients the study is mainly hypothesis generating.

Our study is in line with the larger studies available(8, 21, 22). All three studies found THV alignment was random with respect to commissures(21, 22), and coronary overlap occurs in 30-50% cases(8). Tang et al also found that initial intentional orientation of the Sapien 3 THV during crimping had no impact on alignment(8).

While the COMPARE-TAVI 1 trial was designed as a multicenter RCT, this specific substudy is based on a single-center cohort representing a potential limitation regarding generalizability. Nevertheless, as described above, our findings are consistent with other studies.

In the COMPARE-TAVI 1 trial Myval THV was non-inferior to Sapien 3 THV at 1-year follow-up. One earlier study has found that coronary alignment may have impact on device performance of the Sapien 3 THV(22). Studies on the impact of commissure or coronary alignment on long-term outcomes are warranted, and 3-, 5- and 10-year follow-up of the current cohort is planned.

Impact on daily practice

The study shows that it is random if coronary alignment is achieved in the index TAVI procedure with BEV THVs. Furthermore, in one third of TAVI patients treated with BEV THVs future TAVI-in-TAVI procedures may be challenging due to coverage of a coronary ostium combined with a small VTA. Therefore, our study underlines that in patients with a life expectancy greater than expected THV durability, great attention should be given during planning your index procedure to optimize chances for successful future redo-TAVI despite coronary misalignment, i.e. carefully choosing THV type and implantation depth.

Conclusions

In this COMPARE-TAVI 1 substudy we found that patient specific orientation of the BEV during crimping had no impact on coronary alignment. With BEV, 69% are at low risk of coronary obstruction in redo-TAVI.

Funding

Institutional research grants from Meril Life Sciences, the Danish Heart Foundation, Vingmed Denmark, and the Central Denmark Region for the conduct of the COMPARE-TAVI 1 trial.

Data availability statement

Study-related documents can be made available on request. Individual data can be made available for collaborative pooled analyses provided relevant contracts and data sharing agreements are made. Only anonymized data can be shared.

Conflict of interest statement

BLN: Unrestricted research grants from the Novo Nordisk Fonden. TT: lecture fees from Terumo and Chiesi. EHC: institutional research grants from Abbott, proctor fees from Edwards Lifesciences, Meril Life Sciences, Boston Scientific and Abbott, lecture fees from Edwards Life Sciences, Meril Lifesciences, Boston Scientific and Abbott. CJT: proctor and lecture fees and research grants from Edwards, Terumo, Medtronic and Meril. All other authors: none.

References

1. Tang GHL, Amat-Santos IJ, De Backer O, Avvedimento M, Redondo A, Barbanti M, et al. Rationale, Definitions, Techniques, and Outcomes of Commissural Alignment in TAVR: From the ALIGN-TAVR Consortium. JACC Cardiovasc Interv. 2022;15(15):1497-518.
2. Greenbaum AB, Kamioka N, Vavalle JP, Lisko JC, Gleason PT, Paone G, et al. Balloon-Assisted BASILICA to Facilitate Redo TAVR. JACC Cardiovasc Interv. 2021;14(5):578-80.
3. Khan JM, Babaliaros VC, Greenbaum AB, Spies C, Daniels D, Depta JP, et al. Preventing Coronary Obstruction During Transcatheter Aortic Valve Replacement: Results From the Multicenter International BASILICA Registry. JACC Cardiovasc Interv. 2021;14(9):941-8.
4. Avvedimento M, Tang GHL. Transcatheter aortic valve replacement (TAVR): Recent updates. Prog Cardiovasc Dis. 2021;69:73-83.
5. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, 3rd, Gentile F, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021;143(5):e35-e71.
6. Praz F, Borger MA, Lanz J, Marin-Cuartas M, Abreu A, Adamo M, et al. 2025 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2025;46(44):4635-736.
7. Hamid N, Ranard LS, Khalique OK, Hahn RT, Nazif TM, George I, et al. Commissural Alignment After Transfemoral Transcatheter Aortic Valve Replacement With the JenaValve Trilogy System. JACC Cardiovasc Interv. 2021;14(18):2079-81.
8. Tang GHL, Zaid S, Fuchs A, Yamabe T, Yazdchi F, Gupta E, et al. Alignment of Transcatheter Aortic-Valve Neo-Commissures (ALIGN TAVR): Impact on Final Valve Orientation and Coronary Artery Overlap. JACC Cardiovasc Interv. 2020;13(9):1030-42.
9. Tarantini G, Nai Fovino L, Scotti A, Massussi M, Cardaioli F, Rodino G, et al. Coronary Access After Transcatheter Aortic Valve Replacement With Commissural Alignment: The ALIGN-ACCESS Study. Circ Cardiovasc Interv. 2022;15(2):e011045.
10. Revaiah PC, Jose J, Gunasekaran S, Mandalay A, Garg S, Bhatt S, et al. Neocommissural/Coronary Alignment With a Novel Balloon Expandable Transcatheter Aortic Valve: First-in-Human Experience. JACC Cardiovasc Interv. 2023;16(20):2581-3.
11. Santos-Martinez S, Redondo A, Gonzalez-Bartol E, Barrero A, Sanchez-Luna JP, Revilla-Orodea A, et al. Feasibility of precise commissural and coronary alignment with balloon-expandable TAVI. Rev Esp Cardiol (Engl Ed). 2023;76(1):19-24.
12. Terkelsen CJ, Freeman P, Dahl JS, Thim T, Norgaard BL, Mogensen NSB, et al. SAPIEN 3 versus Myval transcatheter heart valves for transcatheter aortic valve implantation (COMPARE-TAVI 1): a multicentre, randomised, non-inferiority trial. Lancet. 2025.
13. Terkelsen CJ, Thim T, Freeman P, Dahl JS, Norgaard BL, Kim WY, et al. Randomized comparison of TAVI valves: The Compare-TAVI trial. Am Heart J. 2024;274:84-94.
14. Hansson NC, Thuesen L, Hjortdal VE, Leipsic J, Andersen HR, Poulsen SH, et al. Three-dimensional multidetector computed tomography versus conventional 2-dimensional transesophageal echocardiography for annular sizing in transcatheter aortic valve replacement: Influence on postprocedural paravalvular aortic regurgitation. Catheter Cardiovasc Interv. 2013;82(6):977-86.
15. Yoon SH, Gabasha S, Dallan LAP, Ukaigwe A, Tang GHL, Rushing G, et al. Commissural and Coronary Alignment After Transcatheter Aortic Valve Replacement Using the New Supra-Annular, Self-Expanding Evolut FX System. Circ Cardiovasc Interv. 2023;16(4):e012657.
16. Ochiai T, Oakley L, Sekhon N, Komatsu I, Flint N, Kaewkes D, et al. Risk of Coronary Obstruction Due to Sinus Sequestration in Redo Transcatheter Aortic Valve Replacement. JACC Cardiovasc Interv. 2020;13(22):2617-27.

17. De Backer O, Tang GHL, Zaid S, Khokhar AA, Fukui M, Bapat VN. Coronary Risk Zone: A Practical Framework to Simplify Redo TAVR Planning. JACC Cardiovasc Interv. 2026;19(3):379-82.
18. Cao D, Albani S, Gall E, Hovasse T, Unterseeh T, Seknadji P, et al. Aortic Valve-in-Valve Procedures: Challenges and Future Directions. J Clin Med. 2024;13(16).
19. Khan JM, Bruce CG, Babaliaros VC, Greenbaum AB, Rogers T, Lederman RJ. TAVR Roulette: Caution Regarding BASILICA Laceration for TAVR-in-TAVR. JACC Cardiovasc Interv. 2020;13(6):787-9.
20. Tagliari AP, Petersen Saadi R, Medronha EF, Keller Saadi E. The Use of BASILICA Technique to Prevent Coronary Obstruction in a TAVI-TAVI Procedure. J Clin Med. 2021;10(23).
21. Fuchs A, Kofoed KF, Yoon SH, Schaffner Y, Bieliauskas G, Thyregod HG, et al. Commissural Alignment of Bioprosthetic Aortic Valve and Native Aortic Valve Following Surgical and Transcatheter Aortic Valve Replacement and its Impact on Valvular Function and Coronary Filling. JACC Cardiovasc Interv. 2018;11(17):1733-43.
22. Raschpichler M, Flint N, Yoon SH, Kaewkes D, Patel C, Singh C, et al. Commissural Alignment After Balloon-Expandable Transcatheter Aortic Valve Replacement Is Associated With Improved Hemodynamic Outcomes. JACC Cardiovasc Interv. 2022;15(11):1126-36.

Figure legends

Figure 1

Achieving coronary alignment in theory when a balloon-expandable valve is crimped with a neo-commissure at 12 o`clock on the crimping device.

Figure 2

Illustration of crimping methods during the two study periods. Abbreviations: LM: Left main; THV: transcatheter heart valve.

Figure 3

Classification of coronary alignment. Abbreviations: LM: Left main; RCA: Right coronary artery

Figure 4

Coronary alignment during the two study periods for left main (two top panels) and right coronary artery (two bottom panels). Data presented are % of patients who had alignment; mild misalignment, moderate misalignment, and severe misalignment, respectively. Abbreviations: LM: Left main; THV: transcatheter heart valve.

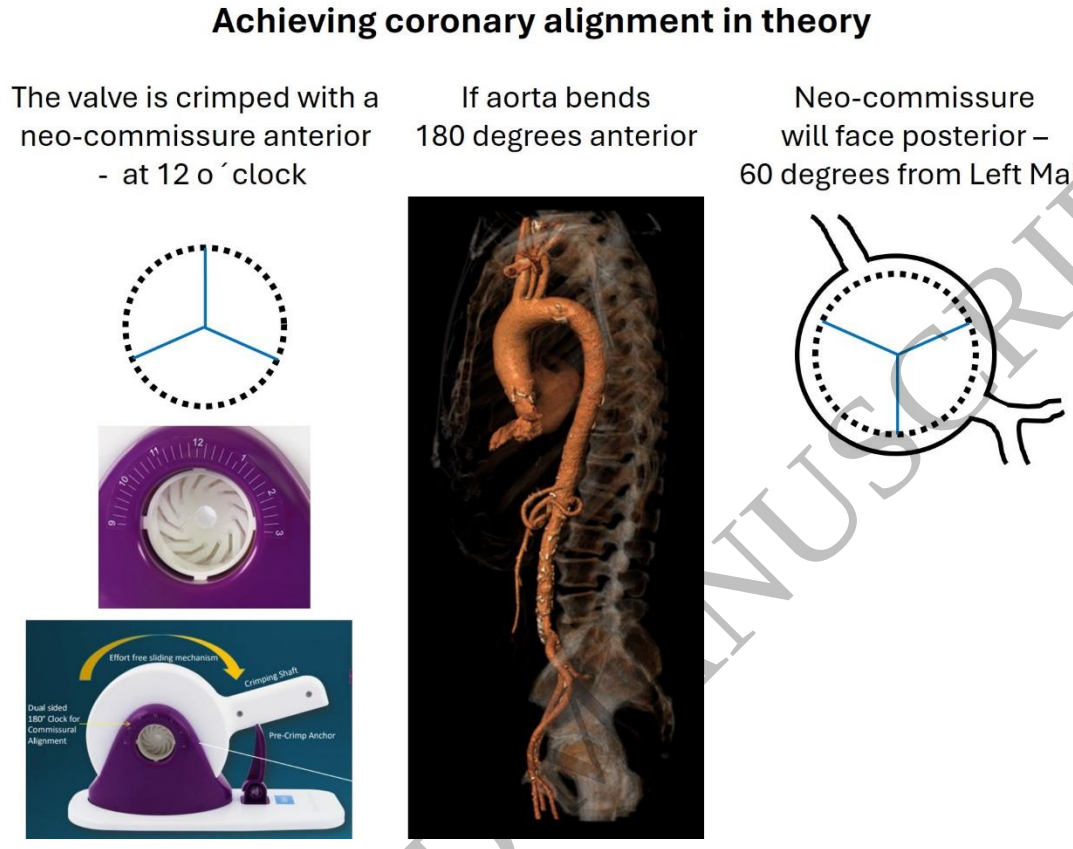
Figure 5

Percentage of patients where the THV is either below the coronary artery ostium, or the frame covers the ostium combined with various VTA distances. These results are presented for the left main (top panel) and the right coronary artery. Abbreviations: LM: Left main; RCA: Right coronary artery; THV: transcatheter heart valve; VTA: valve-to-aorta.

Figure 6

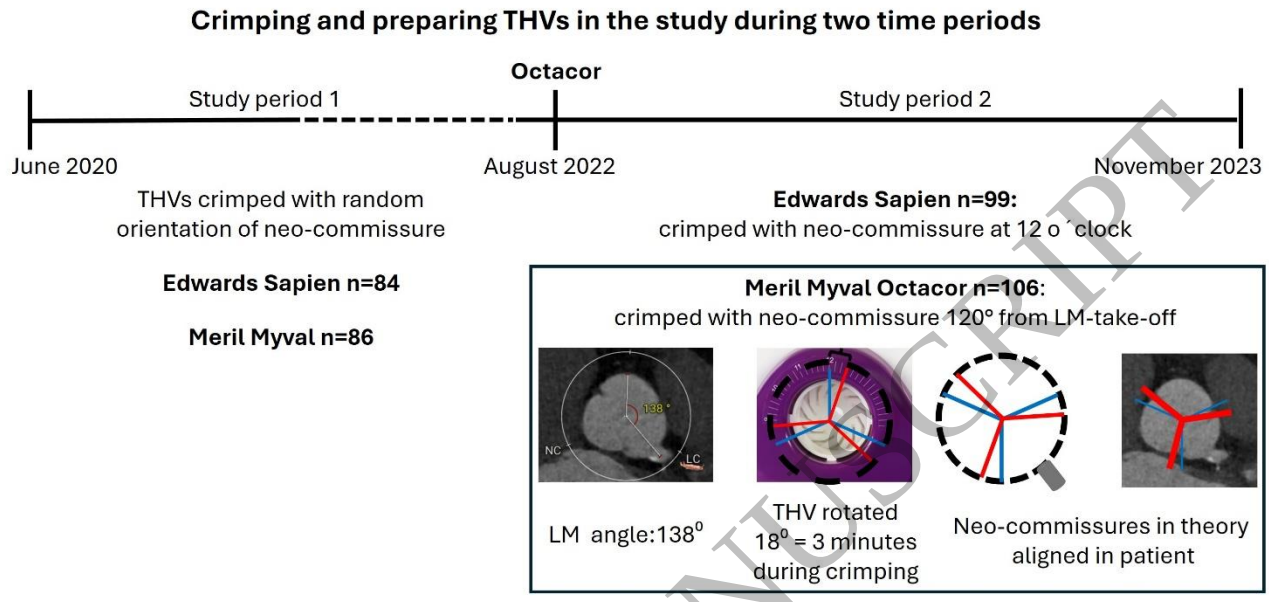
Distribution of patients with neoskirt plane below coronary risk plane; neoskirt plane above coronary risk plane for one or both coronary arteries but associated VTA≥2 mm; patients with neoskirt plane above coronary risk plane for one or both coronary arteries and VTA<2 mm, but associated coronary alignment optimal or only mild misalignment; and lastly patients with neoskirt plane above coronary risk plane for one or both coronary arteries and severe or moderate misalignment i.e. redo TAVI unfeasible. THV frame height was used as the neoskirt plane. Abbreviations: THV: transcatheter heart valve; VTA: valve-to-aorta.

1 Figure 1



2

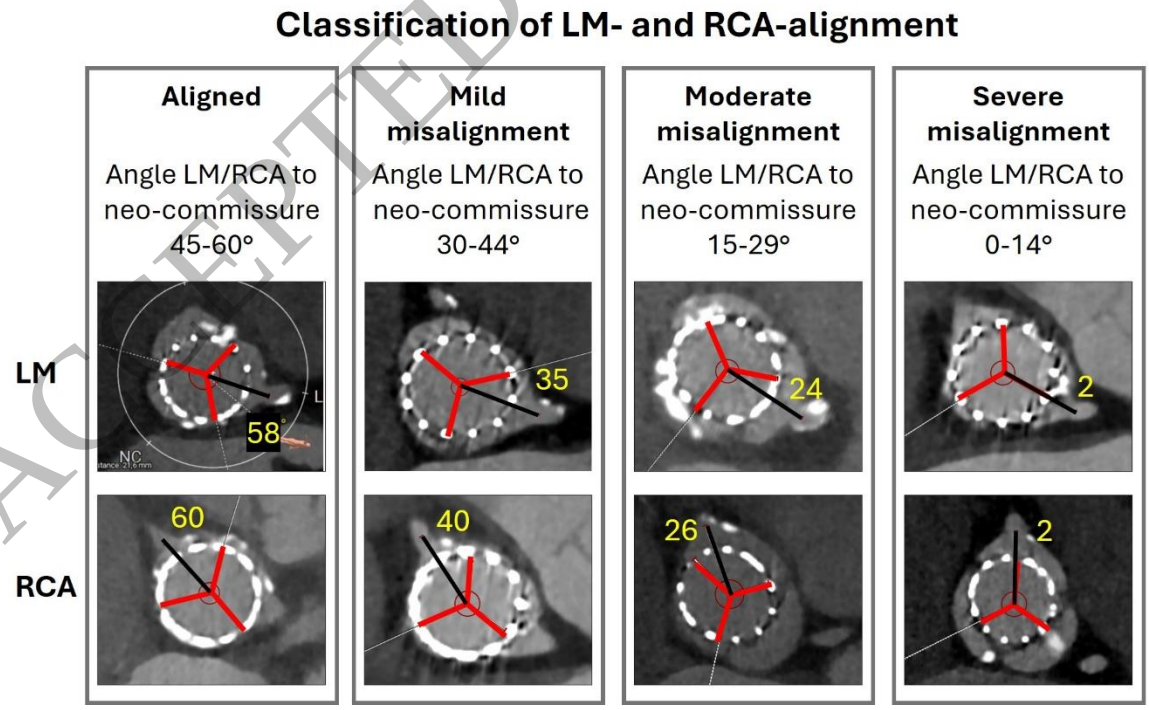
1 Figure 2



2

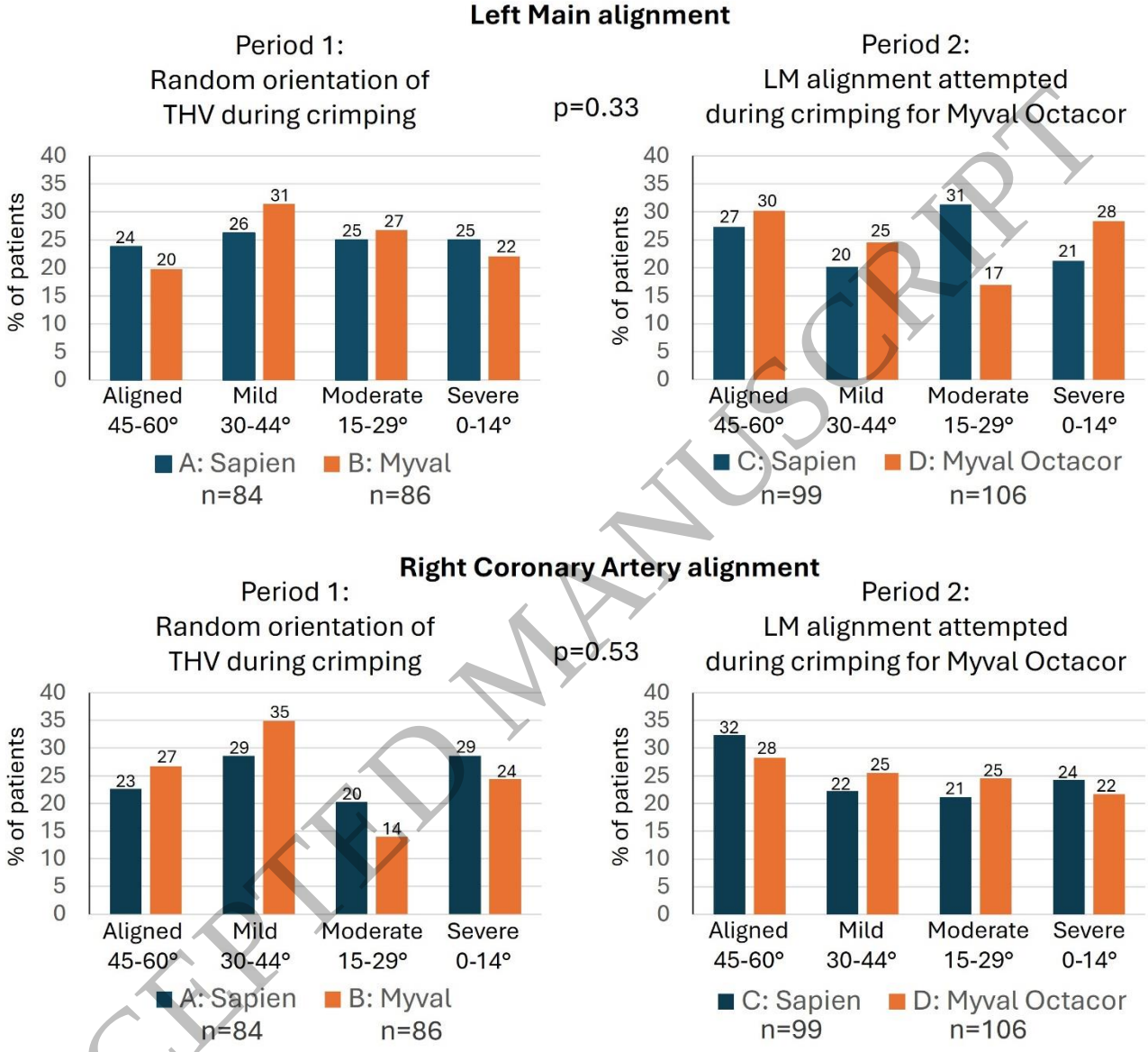
3

4 Figure 3



5

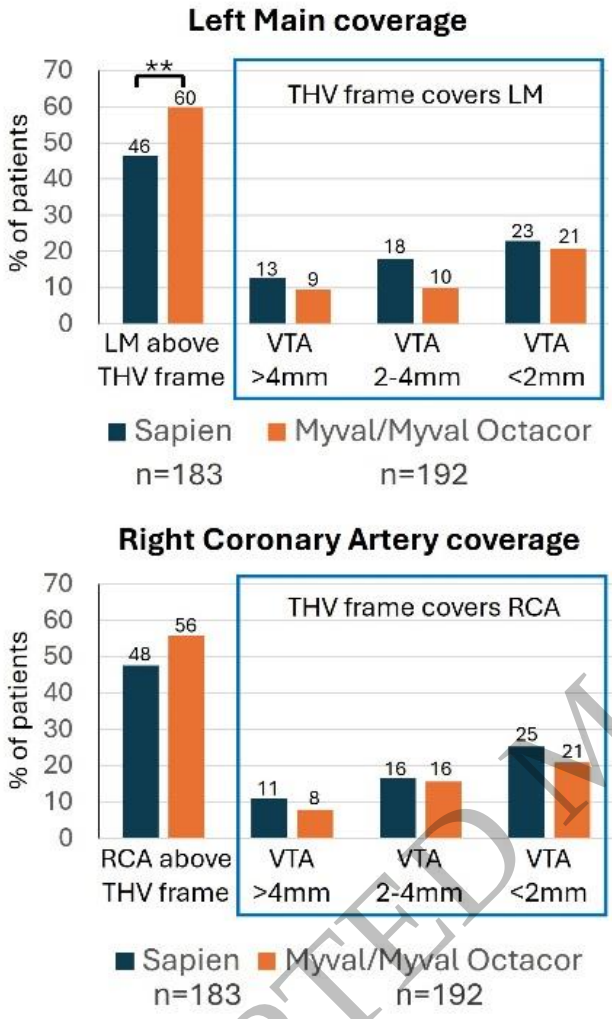
1 Figure 4



2

3

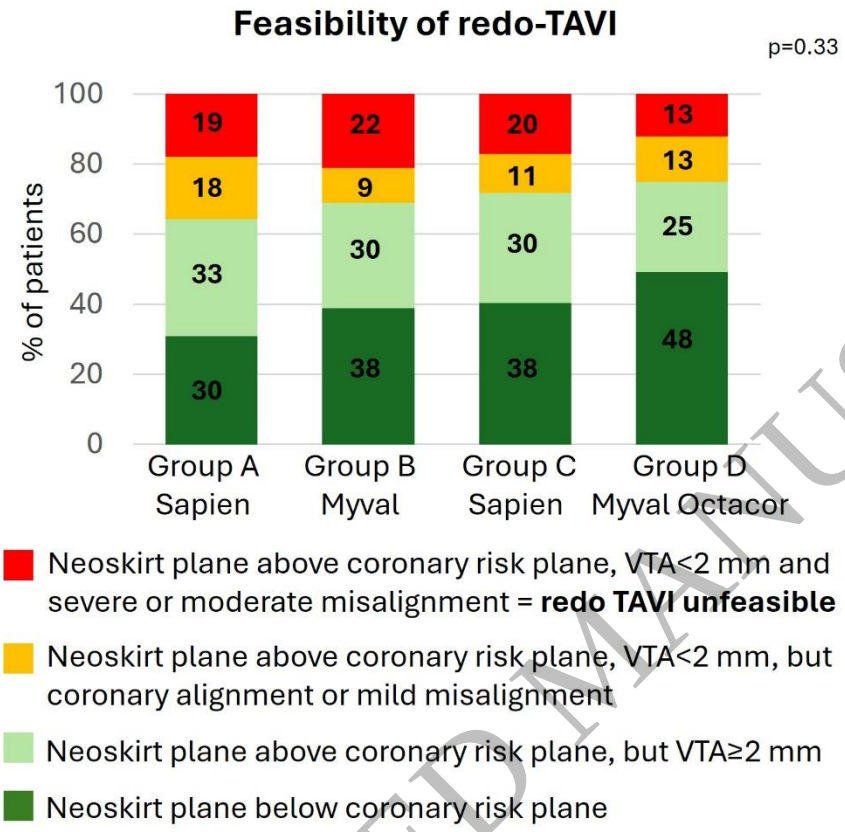
1 Figure 5



2

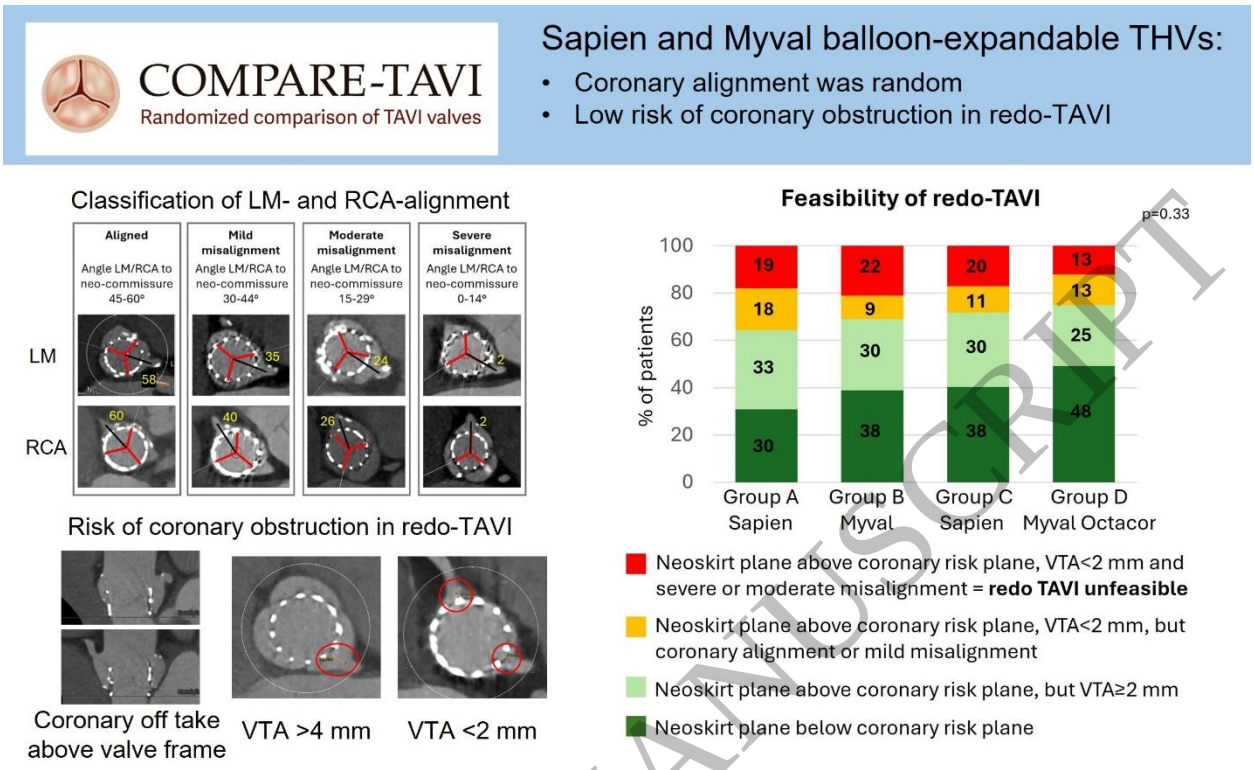
1 Figure 6

2



3

4



Graphical Abstract
165x102 mm (DPI)

Lead Author Biography

2009 - 2012 Aarhus University, Aarhus University Hospital, Skejby, Denmark PhD degree
Main supervisor: Hans Erik Bøtker, MD, Ph.D., FESC, FACC, Professor Department of Cardiology, Aarhus University Hospital Skejby Denmark Research topic: Mechanisms Underlying Resistance to Ischemic Preconditioning in Diabetes Mellitus.

1999 - 2006 Aarhus University, Denmark Doctor of Medicine (MD)

2017-current Aarhus University Hospital, Denmark. Interventional Cardiologist.

Publications

2012 **Jensen RV,** Støttrup NB, Kristiansen SB, Bøtker HE. Release of a humoral circulating cardioprotective factor by remote ischemic preconditioning is dependent on preserved neural pathways in diabetic patients. Basic Res Cardiol. 2012;170(5):285

2012 Michelsen MM, Støttrup NB, Schmidt MR, Løfgren B, **Jensen RV**, Tropak M, St-Michel EJ, Redington AN, Bøtker HE. Exercise-induced cardioprotection is mediated by a bloodborne, transferable factor. Basic Res Cardiol 2012;107(3):260.

2012 **Jensen RV**, Zachara NE, Nielsen PH, Kimose HH, Kristiansen SB, Bøtker HE. Impact of O- GlcNAc on cardioprotection by remote ischaemic preconditioning in non-diabetic and diabetic patients. Cardiovasc Res. 2013 Feb 1;97(2):369-78.

2013 **Jensen RV**, Johnsen J, Kristiansen SB, Zachara NE, Bøtker HE. Ischemic preconditioning increases myocardial O-GlcNAc glycosylation. Scand Cardiovasc J. 2013;47(3):168-74.

2013 Contractor H, Støttrup NB, Cunnington C, Manlhiot C, Diesch J, Ormerod JO, **Jensen R**, Bøtker HE, Redington A, Schmidt MR, Ashrafian H, Kharbanda RK. Aldehyde dehydrogenase-2 inhibition blocks remote preconditioning in experimental and human models. Basic Res Cardiol. 2013 May;108(3):343.

2017 Holmboe S, Andersen A, **Jensen RV**, Kimose HH, Ilkjær LB, Shen L, Clapp LH, Nielsen- Kudsk JE. Prostacyclins have no direct inotropic effect on isolated atrial strips from the normal and pressureoverloaded human right heart. Pulm Circ. 2017 Apr-Jun;7(2):339-
347.

2017 Pælestik KB, Jespersen NR, **Jensen RV**, Johnsen J, Bøtker HE, Kristiansen SB. Effects of hypoglycemia on myocardial susceptibility to ischemia-reperfusion injury and preconditioning in hearts from rats with and without type 2 diabetes. Cardiovasc Diabetol. 2017 Nov 9;16(1):148.

2018 Hjortbak MV, Hjort J, Povlsen JA, **Jensen RV**, Støttrup NB, Laursen MR, Jespersen NR, Løfgren B, Bøtker HE. Influence of diabetes mellitus duration on the efficacy of ischemic preconditioning in a Zucker diabetic fatty rat model. PLoS One. 2018 Feb
23;13(2):e0192981.

2019 **Jensen RV**, Andreadou I, Hausenloy DJ, Bøtker HE. The Role of O-GlcNAcylation for Protection against Ischemia-Reperfusion Injury. Int J Mol Sci. 2019 Jan 18;20(2):404. doi: 10.3390/ijms20020404.

2019 Kristiansen SB, Pælestik KB, Johnsen J, Jespersen NR, Pryds K, Hjortbak MV, **Jensen RV**, Bøtker HE. Impact of hyperglycemia on myocardial ischemia-reperfusion susceptibility

and ischemic preconditioning in hearts from rats with type 2 diabetes. Cardiovasc Diabetol. 2019 May 31;18(1):66. doi: 10.1186/s12933-019-0872-7.

2020 **Jensen RV**, Hjortbak MV, Bøtker HE. Ischemic Heart Disease: An Update.
Semin Nucl Med. 2020 May;50(3):195-207. doi:
10.1053/j.semnuclmed.2020.02.007. Epub 2020 Mar 2.

2020 Hjortbak MV, Grønnebæk TS, Jespersen NR, Lassen TR, Seefeldt JM, Tonnesen PT, **Jensen RV**, Koch LG, Britton SL, Pedersen M, Jessen N, Bøtker HE. Differences in intrinsic aerobic capacity alters sensitivity to ischemia-reperfusion injury but not cardioprotective capacity by ischemic preconditioning in rats.
PLoS One. 2020 Oct 27;15(10):e0240866. doi:

10.1371/journal.pone.0240866. eCollection 2020.

2021 Hjortbak MV, Jespersen NR, **Jensen RV**, Lassen TR, Hjort J, Povlsen JA, Støttrup NB, Hansen J, Hausenloy DJ, Bøtker HE. Cardioprotective effect of combination therapy by mild hypothermia and local or remote ischemic preconditioning in isolated rat hearts. Sci Rep. 2021 Jan 11;11(1):265. doi: 10.1038/s41598-020-79449-x.

2021 Hjortbak MV, Olesen KKW, Seefeldt JM, Lassen TR, **Jensen RV**, Perkins A, Dodd M, Clayton T, Yellon D, Hausenloy DJ, Bøtker HE; CONDI-2/ERIC-PPCI investigators. Translation of experimental cardioprotective capability of P2Y12 inhibitors into clinical outcome in patients with ST-elevation myocardial infarction. Basic Res Cardiol. 2021 May 26;116(1):36. doi: 10.1007/s00395-021-00870-y.

2021 Lassen TR, Hjortbak MV, Hauerslev M, Tonnesen PT, Kristiansen SB, **Jensen RV**, Bøtker HE. Influence of strain, age, origin, and anesthesia on the cardioprotective efficacy by local and remote ischemic conditioning in an ex vivo rat model. Physiol Rep. 2021 Apr;9(7):e14810. doi: 10.14814/phy2.14810.

2021 Jakobsen L, Christiansen EH, Freeman P, Kahlert J, Veien K, Maeng M, Raungaard B, Ellert J, Villadsen AB, Kristensen SD, Ahlehoff O, Christensen MK, Terkelsen CJ, Erik Bøtker H, Aaroe J, Thim T, Thuesen L, Aziz A, Eftekhari A, **Jensen RV**, Støttrup NB, Rasmussen JG, Junker A, Jensen SE, Hansen HS, Jensen LO.
Randomized Clinical Comparison of the Dual-Therapy CD34 Antibody-Covered Sirolimus- Eluting Combo Stent With the Sirolimus-Eluting Orsiro Stent in Patients Treated With Percutaneous Coronary Intervention: The SORT OUT X Trial. Circulation. 2021 Jun;143(22):2155-2165. doi: 10.1161/CIRCULATIONAHA.120.052766. Epub 2021 Apr 7.

2022 Mortensen MB, Gaur S, Frimmer A, Bøtker HE, Sørensen HT, Kragholm KH, Niels Peter SR, Steffensen FH, **Jensen RV**, Mæng M, Kanstrup H, Blaha MJ, Shaw LJ, Dzaye O, Leipsic J, Nørgaard BL, Jensen JM . Association of Age With the Diagnostic Value of Coronary Artery Calcium Score for Ruling Out Coronary Stenosis in Symptomatic Patients. JAMA Cardiol. 2022 Jan 1;7(1):36-44. doi: 10.1001/jamacardio.2021.4406.

2022 **Jensen RV**, Jensen JK, Christiansen EH, Tang M, Nielsen JC, Terkelsen CJ.
Two case reports of transcatheter valve-in-valve implantation of Sapien 3 and MyVal in degenerated biological tricuspid prosthesis valves. Eur Heart J Case Rep. 2022 Mar 23;6(4):ytac131. doi: 10.1093/ehjcr/ytac131. eCollection 2022 Apr.

2022 Jakobsen L, Christiansen EH, Freeman P, Kahlert J, Veien K, Maeng M, Raungaard B, Ellert J, Kristensen SD, Christensen MK, Terkelsen CJ, Thim T, Eftekhari A, **Jensen RV**, Støttrup NB, Junker A, Hansen HS, Jensen LO. Impact of diabetes on clinical outcomes
after revascularization with the dual therapy CD34 antibody-covered sirolimus-eluting Combo stent and the sirolimus-eluting Orsiro stent.
Catheter Cardiovasc Interv. 2022 Jun;99(7):1965-1975. doi: 10.1002/ccd.30175.

Epub
2022 Apr 6.

2022 **Jensen RV**, Kristensen SD. Kronisk lukkede kranspulsårer – en terapeutisk udfordring.
Ugeskr Laeger. 2022 Nov 14;184(46):V205125.

2023 Jakobsen L, Christiansen EH, Freeman P, Kahlert J, Veien K, Maeng M, Raungaard B, Ellert J, Villadsen AB, Kristensen SD, Christensen MK, Terkelsen CJ, Aaroe J, Thim T, Lassen JF, Hougaard M, Eftekhari A, **Jensen RV**, Støttrup NB, Rasmussen JG, Junker A, Jensen SE, Hansen HS, Jensen LO. Dual-therapy CD34 antibody-covered sirolimus- eluting COMBO stents versus sirolimus-eluting Orsiro stents in patients treated with percutaneous coronary intervention: the three-year outcomes of the SORT OUT X randomised clinical trial. EuroIntervention. 2023 Oct 23;19(8):676-683. doi: 10.4244/EIJ-D-23-00330.

2023 Thim T, Jakobsen L, **Jensen RV**, Støttrup N, Eftekhari A, Grove EL, Larsen SB, Sørensen JT, Carstensen S, Amiri S, Veien KT, Christiansen EH, Terkelsen CJ, Maeng M, Kristensen SD. Real-World Experience with Cangrelor as Adjuvant to Percutaneous Coronary Intervention: A Single-Centre Observational Study. Cardiol Res Pract. 2023 Jun 16;2023:3197512. doi: 10.1155/2023/3197512. eCollection 2023.

2023 Jakobsen L, Christiansen EH, Freeman P, Kahlert J, Veien K, Maeng M, Raungaard B, Ellert J, Kristensen SD, Christensen MK, Terkelsen CJ, Thim T, Eftekhari A, **Jensen RV**, Støttrup NB, Junker A, Hansen HS, Jensen LO. Impact of acute coronary syndrome on clinical outcomes after revascularization with the dual-therapy CD34 antibody-covered sirolimus-eluting Combo stent and the sirolimus-eluting Orsiro stent. Catheter Cardiovasc Interv. 2023 Jan;101(1):13-21. doi: 10.1002/ccd.30480. Epub 2022 Nov 15.

2024 Seefeldt J, Homilius C, Hansen J, Lassen T, Jespersen N, **Jensen RV**, Boedtkjer E, Bøtker HE, Nielsen R.
The short-chain fatty acid butyrate is an inotropic agent with vasorelaxant and cardioprotective properties. Journal of the American Heart Association. J Am Heart Assoc. 2024 May 7;13(9):e033744. doi: 10.1161/JAHA.123.033744.

2024 Trøan J, Christiansen EH, Hansen KN, Eftekhari A, Jakobsen L, Mæng M, Freeman P, **Jensen RV**, Christensen MK, Noori M, Ellert-Gregersen J, Støttrup NB, Kahlert J, Veien KT, Jensen LO. Five-year outcomes of patients with diabetes mellitus treated with a sirolimus-eluting or a biolimus-eluting stents with biodegradable polymer. From the SORT OUT VII trial. Diab Vasc Dis Res. 2024 Sep- oct;21(5): 14791641241283939. doi: 10.1177/14791641241283939

2025 **Jensen RV**, Jense JM, Iraqi N, Grove EL, Mathiassen ON, Pedersen KB, Partner E, Leipsic J, Terkelse CJ, Nørgaard BJ. Coronary CT angiography instead of invasive angiography before TAVI: Feasibility and outcomes. Int J Cardiol. 2025 Jan 15:419:132694. doi: 10.1016/j.ijcard.2024.132694.

2025 Nielsen CGA, Rasmussen MB, Rohde PT, Bagner DV, **Jensen RV**, Jakobensen L, Støttrup NB, Veien KT, Larsen EN, Charlot MG, Boesgaard AE, Terkelsen CJ. Randomized comparison of rapid versus oximetry guided deflation of the transradial-band after coronary angiography or angioplasty. Int J Cardiol. 2025 Jan 15:419:132708. doi: 10.1016/j.ijcard.2024.132708

2025 Christensen LJ, Larsen AM, Homilius C, Gopalasingam N, Moeslund N, Berg-Hansen K, Boedtkjer E, **Jensen RV**, Johannsen M, Hansen J, Seefeldt J, Bøtker HE, Schütz J, Hørsdal OK, Nielsen BRR. Butyrate increases cardiac output and causes vasorelaxation in a healthy porcine model. Life Sci.
2025 Feb 15:363:123407. doi: 10.1016/j.lfs.2025.123407. Epub 2025 Jan 17

2025 Winther S, Rasmussen LD, Karim SR, Westra J, Dahl JN, Søby JH, Nissen L, Lomstein FB, Würtz M, Sundøll JM, Ejlersen JA, Hansson NCL, Nyegaard M, **Jensen RV**, Madsen MA, Christiansen EH, Gormsen LC, Böttcher M. Myocardial Perfusion Imaging With PET; A Head-to-Head Comparison of 82Rubidium Versus 15O-water Tracers Using Invasive Coronary Measurements as Reference. Circ Cardiovasc Imaging. 2025 Apr 3:e017479. doi: 10.1161/CIRCIMAGING.124.017479.

2025 Nielsen CGA, Rasmussen MB, Rohde PT, **Jensen RV**, Jakobensen L, Støttrup NB, Veien KT, Larsen EN, Charlot MG, Terkelsen CJ. Randomized comparison of sheath size for coronary intervention: time to hemostasis and risk of radial artery occlusion. Cardiovasc Revasc Med. 2025 May 1:S1553-8389(25)00222-2. doi: 10.1016/j.carrev.2025.04.042

2025 Eftekhari A, Jensen LO, Veien K, Raugaard B, Rasmussen JG, Mæng M, Terkelsen CJ, Ellert-Gregersen J, Støttrup NB, Lassen JF, Hansen HS, Thim T, **Jensen RV**, Nielsen
Roni, Jensen SV, Kristensen SD, Hougaard M, Junker A, Christensen MK, Aarøe J, Frøslev
T, Jakobsen L, Christiansen EH. Biolimus-Eluting Biomatrix Stent Versus a Dual-Therapy
Sirolimus-Eluting Stent in PCI: SORT OUT XI Randomized Trial. J Am Coll Cardiol. 2025
May 16:S0735-1097(25)06485-X. doi: 10.1016/j.jacc.2025.05.012

2025 Støttrup NB, Christiansen EH, Raungaard B, Kahlert J, Terkelsen CJ, Kristansen SD, Thim T, Jakobsen L, **Jensen RV**, Eftekhari A, Freeman P, Jensen SE, Veien KT, Jensen LO, Maeng M, Everolimus-eluting versus biolimus-eluting stents with biodegradable polymers in unselected patients undergoing percutaneous coronary intervention: five-year results of the randomised, non-inferiority SORT OUT VIII trial. EuroIntervention. 2025 Jun
2;21(11):e629-e638. doi: 10.4244/EIJ-D-24-00763.

2025 Jensen LO, Jakobsen L, Eftekhari A, Ellert-Gregersen J, Støttrup NB, Engstrøm T, Kahlert J, Freeman P, Veien KT, **Jensen RV**, Lassen JF, Junker A, Christiansen EH. Five-year outcomes of a drug-coated polymer-free biolimus-eluting stent versus an ultrathin-strut biodegradable-polymer sirolimus-eluting stent. EuroIntervention. 2025 Jun

2;21(11):e617-e628. doi: 10.4244/EIJ-D-24-00586

2025 Hansen KN, Christiansen EH, Ellert-Gregersen J, Eftekhari A, Jakobsen L, Veien KT, Freeman P, **Jensen RV**, Noori M, Støttrup NB, Lassen JF, Trøan J, Maeng M, Terkelsen CT, Raungaard B, Kahlert J, Junker A, Jensen LO. Impact of Diabetes Mellitus on 5-year Outcomes After PCI with a Polymer-Free Drug-Coated Stent or a Biodegradable Polymer Ultra-Thin Strut Stent. Am J Cardiol. 2025 Dec 15:257:159-167. doi: 10.1016/j.amjcard.2025.09.048.