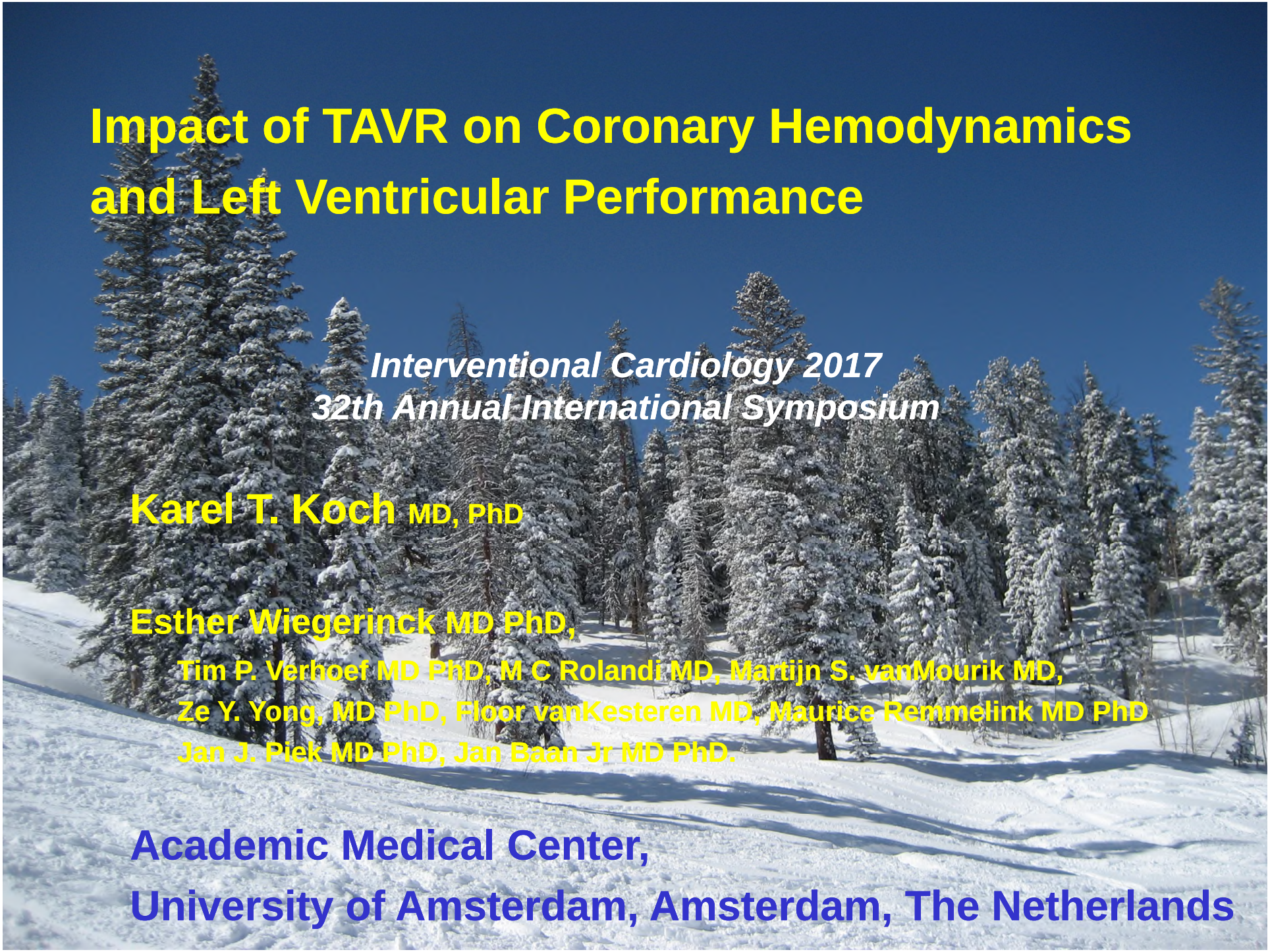

Impact of TAVR on Coronary Hemodynamics and Left Ventricular Performance

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No disclosures

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Relief of AS by transcatheter aortic valve replacement (TAVR) decreases left ventricular afterload and is expected to improve LV dynamics and microvascular function immediately

Objectives

To provide insight in the effects of AS and TAVR on:

- Left ventricular hemodynamics by direct invasive assessment

- Coronary hemodynamics by assessment of the coronary circulation using simultaneous invasive coronary pressure and flow velocity measurements

The effects of TAVR on left ventricular dynamics:
Methods

Invasive intraventricular pressure and volume (PV) were simultaneously assessed in 10 patients directly before and after TAVR by a pressure-conductance catheter positioned in the LV (CD Leycom, Netherlands).

A SG-catheter was placed in the AP for calibration purposes:
Cardiac output was determined by thermodilution and parallel conduction was determined by hypertonic saline injections to calibrate the volume signals of the conduction catheter.

Pressure-volume loop (PV-loop) assessment was performed and parameters for systolic and diastolic LV function as well as afterload were assessed.

After TAVR, the conductance catheter and SG catheter were reinserted, for calibration and repeated PV-loop assessment for off-line analysis.

TAVR was performed under local anesthesia

The effects of TAVR on left ventricular dynamics:
Patient characteristics (n=10)

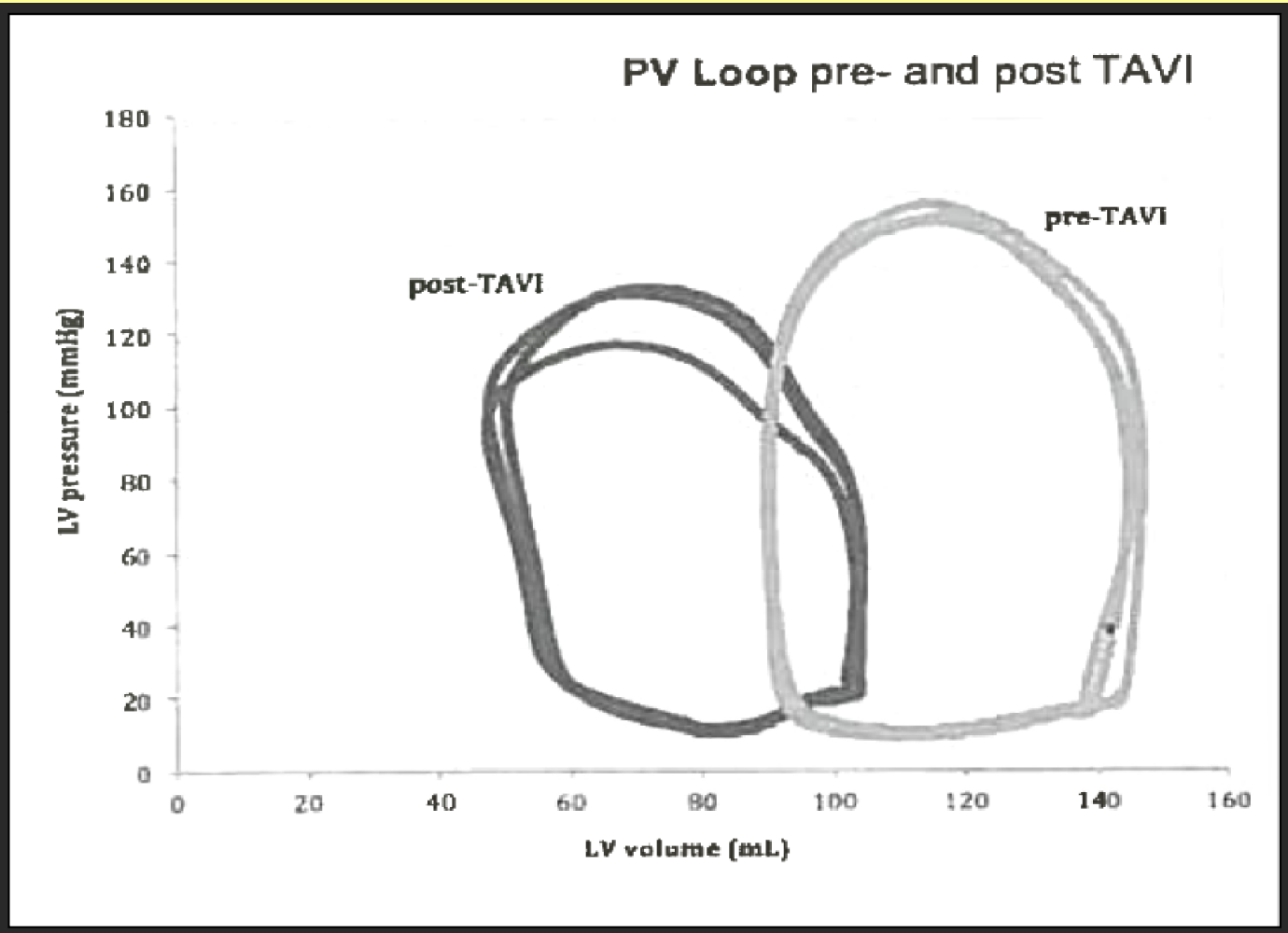
Patient characteristics	Total (n = 10)
Patients	
Age, yrs	77.4 ± 9.1
BMI, kg/m2	30.6 + 3.6
Male gender	5 (50)
NYHA class ≥ 3	5 (50)
History	
Hypertension	7 (70)
Diabetes	6 (60)
Hypercholesterolemia	2 (20)
prior MI	2 (20)
Prior PCI	3 (30)
CABG	1 (10)

Pre- and post TAVR echocardiographic characteristics

	pre-procedure			post- procedure			p-value
Aortic valve area, cm²	0.96	±	0.28	2.29	±	1.07	0.006
EOAI	0.48	±	0.17	1.04	±	0.189	0.002
AVPG max, mmHg	65.4	±	16.8	20.4	±	8.9	<0.001
AVPG mean, mmHg	38..5	±	8.42	11.3	±	5.1	<0.001

Values are mean ± SD. AVPG, aortic valve pressure gradient; EOAI, Effective orifice area index

The effects of TAVR on left ventricular dynamics
Example of Pressure-Volume loop



Schematic example of PV-loop pre- and post TAVR:
Left and downward shift of the curve after TAVR

The effects of TAVR on left ventricular dynamics
Result (1)

Effects of TAVR on global LV-function

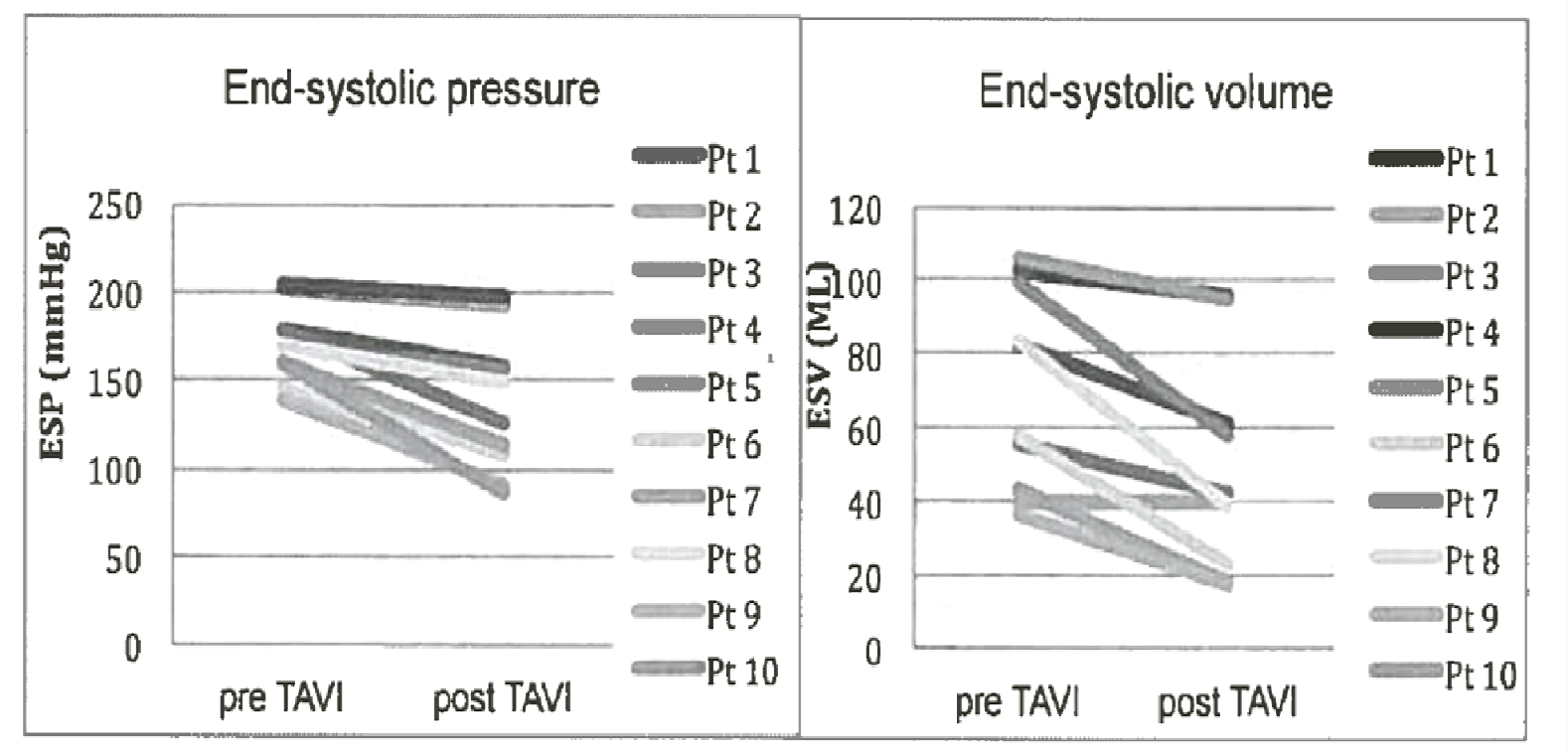
global cardiac function	Pre	(SD)	Post	(SD)	p-value
HR	69	(9.90)	71	(8.50)	0.360
CI	4.24	(5.59)	5.11	(7.29)	0.229
EF	53.8	(10.6)	61.8	(15.7)	0.047
SV	70.1	(19.1)	86.0	(24.9)	0.070
SW	11222	2343	9518	3588	0.022

(HR ;heart rate CI: cardiac index EF: ejection fraction, SV: stroke volume, SW: stroke work as the area of the PV-loop SW

Ejectionfraction increased (54% to 62%)
Stroke volume increased (71 ml to 85 ml)
Stroke work decreased (11222 to 9518)

The effects of TAVR on left ventricular dynamics
Results (2)

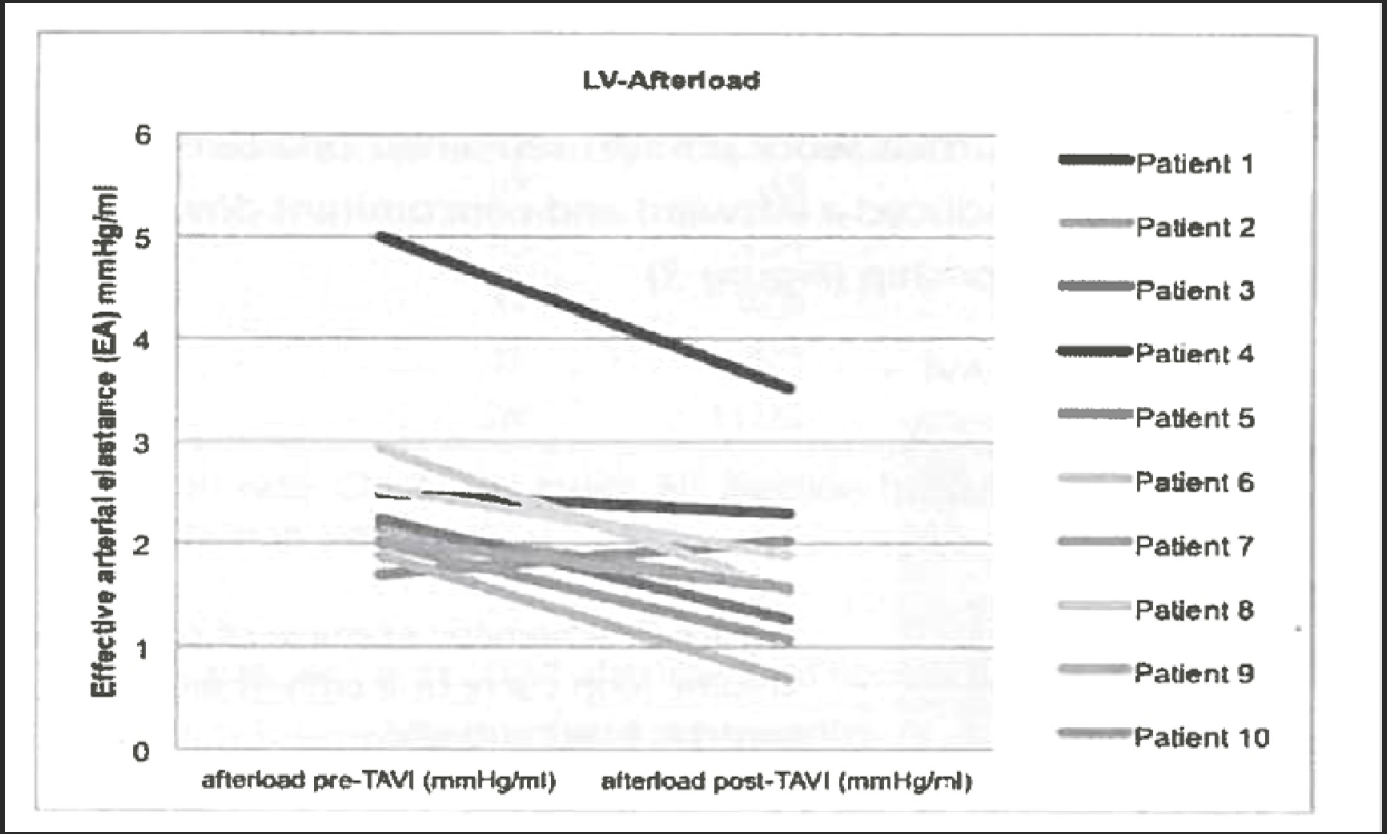
Effects of TAVR on systolic function



Significant decrease of:
LV-endsystolic pressure (171.3±21to138±39mmHg: p=0.001)
LV endsystolic volume (71±27to49±29ml; p=0.001)

The effects of TAVR on left ventricular dynamics
Results (3)

Effects on afterload after TAVR



As an index of afterload, the effective arterial elastance (EA) was used (calculated by endsystolic pressure/stroke volume)

EA decreased significantly (2.61±0.95 to1.75±0.77mmHg/ml; p=0.006)

The effects of TAVR on left ventricular dynamics
Results (4)

Afterload and contractility effects pre- and post TAVR

Afterload and contractility	Pre	(SD)	Post	(SD)	p-value
Effective arterial elastance (EA) (ESP/SV)	2.610	0.953	1.751	0.771	0.003
the valvuloarterial impedance	5.243	1.783	3.587	0.986	0.017
end-systolic volume (ESV)	70.8	27.1	48.9	28.8	0.001
end-systolic pressure (ESP)	170.9	21.1	137.6	39.2	0.001
end-diastolic volume (EDV),	141.5	26.5	134.2	27.0	0.483
end-diastolic pressure (EDP),	17.6	4.7	18.0	7.1	0.872
Max rate pressure change (dP/dtmax)	1.379	392	1.218	329	0.016
relaxation time constant Tau	37.6	6.9	41.8	10.9	0.052
preload recruited stroke work (PRSW)	81.0	18.5	79.6	20.2	0.836

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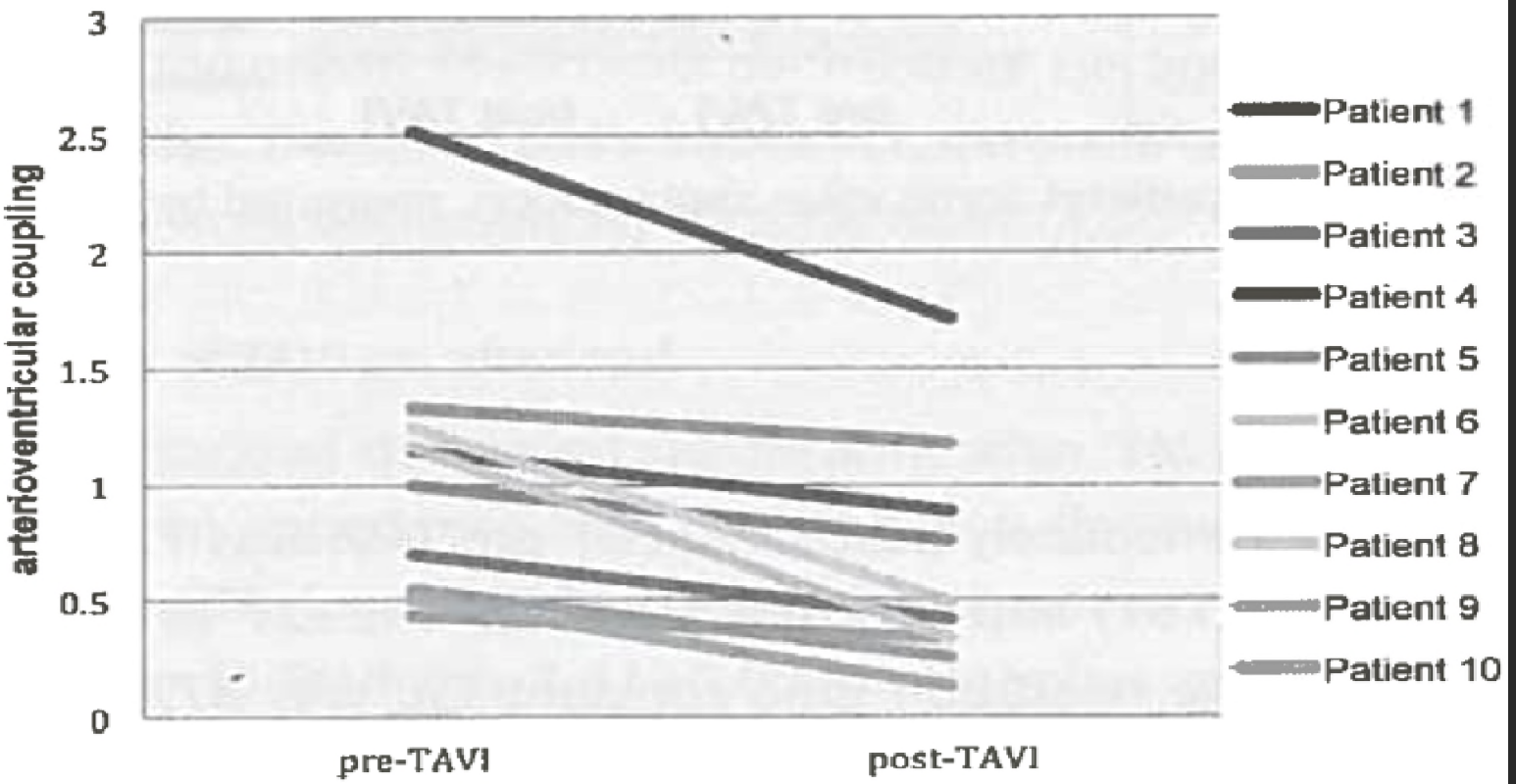
The effects of TAVR on left ventricular dynamics:

Alterations in cardiovascular interaction

Arterio-ventricular coupling (effective arterial elastance/endsystolic elastance)



Arterial-ventricular coupling decreased towards normal(1.13±0.61 to 0.66±0.49 p=.001) indicating that cardiovascular energy efficiency improved after TAVR.

The effects of TAVR on left ventricular dynamics:

Alterations in cardiovascular interaction

Cardiovascular interaction pre- and post TAVR

Cardiovascular interaction	Pre	(SD)	Post	(SD)	p-value
end systolic elastance (Ees),estimated by ESP/ESV	2.767	1.135	3.618	1.659	0.039
end-diastolic stiffness (Eed) by EDP/EDV	0.1256	0.0332	0.1336	0.0429	0.676
The ventricular arterial coupling ratio (Ees/EA)	1.230	0.639	2.628	2.148	0.033

The end-systolic elastance increased significantly, as did the ventricular arterial coupling ratio, indicating an improved interaction of LV performance of the cardiovascular system

The interaction was not improved during diastole, indicated by an unaltered end-diastolic stiffness.

The effects of TAVR on left ventricular dynamics:
Summary

TAVR immediately reduces afterload and markedly improves LV systolic performance and interaction with the vascular system by invasive PV-loop measurements

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Direct PV-loop assessment revealed the first step towards LV-remodeling after TAVR

Limitations: results may be specific for patients with severe AS.

Limited number of patients due to complexity of the measurements

Coronary hemodynamics: methods

A total of 55 patients:
- 27 patients with AS undergoing transfemoral TAVR
- 28 patients as a controls, no AS, elective physiological assessment of an angiografically unobstructed coronary artery.

Dual sensor-equipped guidewire to assess intracoronary pressure and flow velocity (Combo-wire, Volcano Corp. San Diego)

Intracoronary measurements were performed during resting conditions and hyperemia (adenosine)

In TAVR patients: intracoronary measurements immediately before and immediately after valve placement

TAVR under local anesthesia: Edwards Sapien XT and 3, Corevalve.

TTE assessment was performed prior to and after TAVR

Coronary hemodynamics: data analysis

FFR:
ratio between mean distal coronary and aortic pressure during maximum hyperemia

CFR:
ratio between coronary flow velocity at maximum hyperemia and flow velocity at rest

Microvascular resistance index:
Defined as the ratio of mean distal coronary pressure to average peak flow velocity
At baseline (BMR) and at hyperemia (HMR)

Patient characteristics

	Total (n = 55)	AS-Patients (n = 27)	Control (n = 28)	P-value
Patients				
Age, yrs	72 ± 8	82 ± 8	63 ± 5	<0.001
BMI, kg/m2	27.6 ± 5.6	28.67 ± 4.74	26.62 ± 2.76	0.070
Male gender	30 (54.5)	10 (37.0)	20 (71.4)	0.007
NYHA class ≥ 3	33 (60.0)	13 (48.1)	19 (67.9)	0.093
History				
Hypertension	28 (50.9)	17 (63.0)	11 (39.3)	0.180
Diabetes	10 (18.2)	2 (7.4)	8 (28.6)	0.078
Hypercholesterolemia	22 (40.0)	3 (11.1)	21 (75.0)	<0.001
prior MI	4 (7.3)	2 (7.4)	2 (7.1)	1.00
Prior PCI	49 (89.1)	3 (11.1)	3 (10.7)	1.00
CABG	0 (0)	0 (0)	0 (0)	
Medication				
ACE-inhibitor	14 (25.5)	9 (33.3)	4 (14.3)	0.227
Statines	30 (54.5)	11 (40.7)	19 (67.9)	0.010
B blocker	36 (65.5)	10 (37.0)	26 (92.9)	<0.001

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Echocardiography pre- and postprocedural

Table 2: pre- and postprocedural echocardiographic characteristics

	pre-procedure	post- procedure	p-value
Aortic valve area, cm^2	0.78 ± 0.17	1.86 ± 0.79	<0.001
EOAI	0.42 ± 0.09	1.1 ± 0.35	<0.001
AVPG max, mmHg	67.3 ± 23.9	17.1 ± 8.6	<0.001
AVPG mean, mmHg	42.8 ± 15.3	9.0 ± 5.6	<0.001

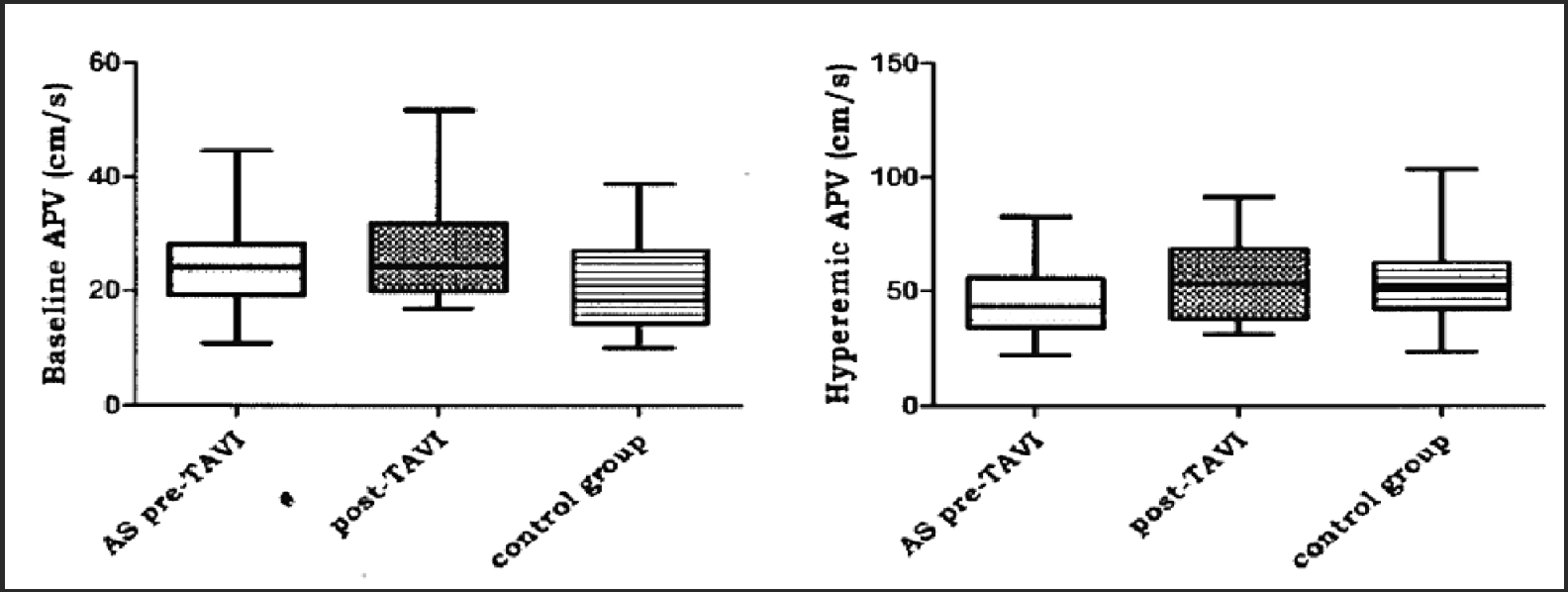
Values are mean ± SD. AVPG, aortic valve pressure gradient; EOAI, Effective orifice area index

Significant AR present in 6/27 patients 22%

Coronary flow velocity

Baseline flow velocity

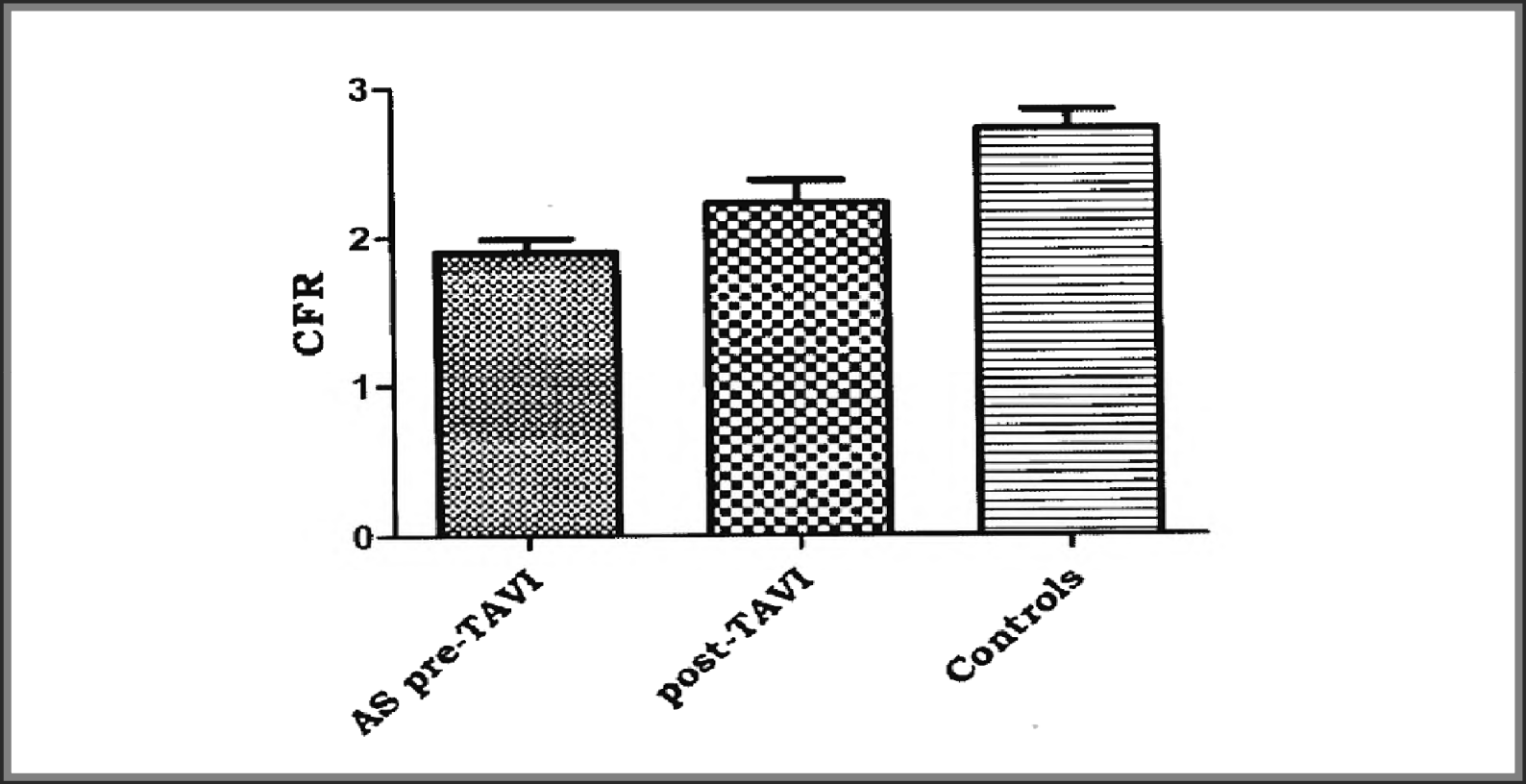
Hyperemic flow velocity



Baseline flow velocity pre TAVR
was higher than controls and did not change significantly after TAVR

Hyperemic flow velocity
increased after TAVR and reached values equivalent to controls

Coronary flow reserve (CFR)

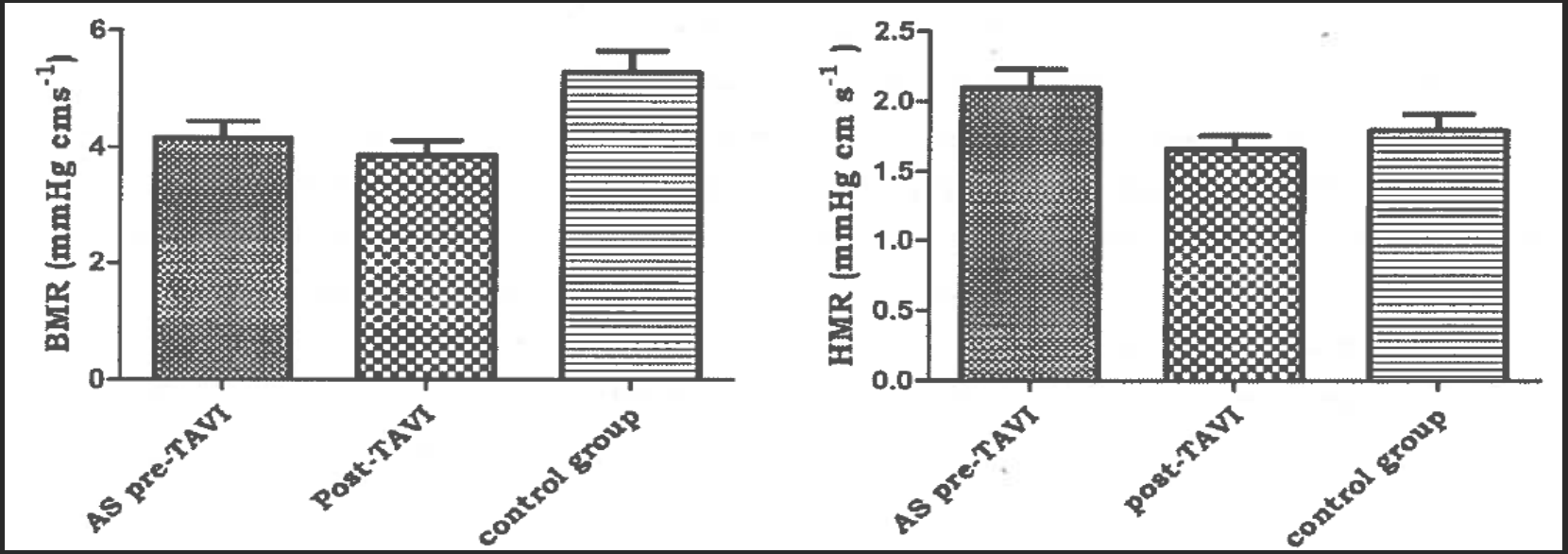


- AS patients had a significantly lower CFR than controls ($p<0.001$)
- TAVR yielded a significant increase in CFR ($p=0.009$)
- CFR increased towards reference values after TAVR, but remained lower than controls

Microvascular resistance

Baseline microvascular resistance index

Hyperemic microvascular resistance index



Baseline microvascular resistance pre-TAVR was significantly lower (p=0.02) than controls, and did not increase significantly after TAVR (p=0.41)

Hyperemic microvascular resistance decreased significantly(p=0.05) post TAVR

Results

Fractional Flow Reserve (FFR)

FFR (mean distal coronary to mean aortic pressure ratio during hyperemia) decreased from 0.97±0.05 prior to TAVR to 0.95±0.06 post TAVR (p=0.042)

FFR is determined by the magnitude of transstenotic flow during hyperemia, which in turn depends on hyperemic microvascular resistance

We demonstrated that TAVR decreases microvascular resistance and thereby increases hyperemic flow.
Thus, TAVR is likely to influence stenosis assessment using FFR

FFR decreased significantly after TAVR, even in angiographically normal arteries

Therefore, these results suggest that FFR assessment may underestimate functional stenosis severity in AS patients

Coronary hemodynamics in AS and TAVR summarized:

In aortic valve stenosis, microvascular dysfunction originates from a combination of physiological compensatory vasodilatation of the autoregulated microvasculature and a pathological increase in microvascular resistance.

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TAVR induces an immediate decrease in hyperemic microvascular resistance and an immediate increase in hyperemic flow velocity while resting hemodynamics remain unaltered

TAVR is thereby associated with an immediate improvement in the reserve vasodilatory capacity of the coronary microcirculation and CFR, in particular in patients without AR after TAVR

In conclusion:

TAVR immediately reduces LV-afterload and improves LV systolic performance as assessed by intraventricular PV-loop measurements. Diastolic function remains unaltered immediately after TAVR.

The vasodilatory reserve capacity of the coronary circulation is reduced in AS. TAVR induces an immediate decrease in hyperemic microvascular resistance and concomittant increase in hyperemic flow velocity, resulting in immediate improvement in coronary vasodilatory reserve.


Thank you for your kind attention

The effects of TAVR on left ventricular dynamics

Background and objectives

In patients with aortic stenosis (AS) the afterload and the enddiastolic volume increases

These alterations are associated with a compensatory increase in end-diastolic volume and pressure, and may eventually induce LV-dysfunction

Treatment of AS by transcatheter valve replacement (TAVR) decreases ventricular afterload and is expected to improve LV hemodynamics

Coronary hemodynamics: data analysis

FFR: ratio between mean distal coronary and aortic pressure during maximum hyperemia

CFR: ratio between coronary flow velocity at maximum hyperemia and flow velocity at rest

Microvascular resistance index:
Defined as the ratio of mean distal coronary pressure to average peak flow velocity
At baseline (BMR) and at hyperemia (HMR)

The ability of the resistance vessels to dilate under maximal hyperemic conditions (variable arteriolar resistance – VAR) was defined as the difference between baseline (BMR) and hyperemic microvascular resistance (HMR), and was expressed both in absolute terms, as in a percentage of baseline

Results (1):
Aortic valve stenosis vs reference vessel

Baseline	pre TAVI			Reference			p-value
HR	68	±	11	65	±	10	0.196
Pd	91	±	14	96	±	16	0.226
Pa	93	±	14	99	±	17	0.158
PdPa	0.99	±	0.03	0.98	±	0.04	0.487
bMR	4.16	±	1.48	5.28	±	2.02	0.023
APV	24.3	±	8.6	20.7	±	7.8	0.100

Hyperemia	pre TAVI			Reference			p-value
HR	70	±	12	66	±	10	0.132
Pd	86	±	12	88	±	13	0.433
Pa	88	±	13	94	±	14	0.170
PdPa	0.97	±	0.05	0.94	±	0.04	0.043
hMR	2.10	±	0.69	1.80	±	0.60	0.096
APV	44.5	±	14.5	54.3	±	18.6	0.035
CFR	1.90	±	0.46	2.73	±	0.66	<0.001
VAR	2.06	±	1.22	3.48	±	1.70	0.001
VAR%	47.0	±	15.5	64.0	±	9.4	<0.001

Values are mean ± SD. HR: heart rate(bpm) Pd: distal coronary pressure (mmHg) Pa: aortic pressure (mmHg) bMR: baseline microvascular resistance (mmHg·cm·s^{-1}) APV: Flow Velocity (cm/s), hMR: hyperemic microvascu ar resistance (mmHg·cm·s^{-1}) CFR: Coronary flow reserve VAR: variable arteriolar resistance VAR%: percentage variable arteriolar resistance.

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Pd	91	±	14	96	±	16	0.226
Pa	93	±	14	99	±	17	0.158
PdPa	0.99	±	0.03	0.98	±	0.04	0.487
bMR	4.16	±	1.48	5.28	±	2.02	0.023
APV	24.3	±	8.6	20.7	±	7.8	0.100

Hyperemia	pre TAVI			Reference			p-value
HR	70	±	12	66	±	10	0.132
Pd	86	±	12	88	±	13	0.433
Pa	88	±	13	94	±	14	0.170
PdPa	0.97	±	0.05	0.94	±	0.04	0.043
hMR	2.10	±	0.69	1.80	±	0.60	0.096
APV	44.5	±	14.5	54.3	±	18.6	0.035

CFR	1.90	±	0.46	2.73	±	0.66	<0.001
VAR	2.06	±	1.22	3.48	±	1.70	0.001
VAR%	47.0	±	15.5	64.0	±	9.4	<0.001

hyperemic microvascu ar resistance (mmHg·cm·s⁻¹) CFR: Coronary flow reserve VAR: variable arteriolar resistance VAR%: percentage variable arteriolar resistance.

Results: preTAVR vs post TAVR (n=27)

Baseline	pre-TAVI			post-TAVI			p-value
HR	68	±	11	72	±	11	0.001
Pd	91	±	14	91	±	14	0.914
Pa	93	±	14	94	±	15	0.768
Pd/Pa	0.99	±	0.03	0.97	±	0.04	0.103
bMR	4.16	±	1.48	3.96	±	1.79	0.413
APV	24.4	±	8.6	25.5	±	9.0	0.401

Hyperemia	pre-TAVI			post-TAVI			p-value
HR	70	±	12	75	±	15	0.006
Pd	86	±	12	85	±	15	0.915
Pa	88	±	13	90	±	15	0.471
Pd/Pa	0.97	±	0.05	0.95	±	0.06	0.042
hMR	2.10	±	0.69	1.83	±	0.58	0.072
APV	44.5	±	14.5	51.1	±	18.1	0.027
CFR	1.90	±	0.46	2.10	±	0.65	0.113
VAR	2.06	±	1.22	2.13	±	1.05	0.768
VAR%	47.0	±	15.5	51.1	±	15.0	0.241

Values are mean ± SD. HR: heart rate (bpm) Pd: distal coronary pressure (mmHg) Pa: aortic pressure (mmHg) bMR: baseline microvascular resistance (mmHg·cm·s $^{-1}$) APV: Flow Velocity (cm/s), hMR: hyperemic microvascular resistance (mmHg·cm·s $^{-1}$) CFR: Coronary flow reserve VAR: variable arteriolar resistance VAR%: percentage variable arteriolar resistance.

Results: preTAVR vs post TAVR (without AR n=20)

Baseline	pre-TAVI			post-TAVI			p-value
HR	70	±	11	75	±	10	0.002
Pd	92	±	15	94	±	13	0.404
Pa	94	±	15	97	±	13	0.220
PdPa	0.99	±	0.04	0.97	±	0.05	0.186
bMR	3.90	±	1.23	3.86	±	1.18	0.886
APV	25.6	±	8.9	26.8	±	9.6	0.454

Hyperemia	pre-TAVI			post-TAVI			p-value
HR	72	±	12	78	±	16	0.004
Pd	86	±	13	87	±	14	0.437
Pa	89	±	14	93	±	14	0.123
PdPa	0.96	±	0.06	0.94	±	0.07	0.122
hMR	2.03	±	0.71	1.66	±	0.45	0.050
APV	46.2	±	15.5	56.6	±	17.4	0.003
CFR	1.86	±	0.39	2.23	±	0.64	0.009
VAR	1.82	±	1.01	2.20	±	1.02	0.122
VAR%	46.2	±	14.9	54.1	±	14.5	0.021

Values are mean ± SD. HR: Heart rate (bpm) Pd: distal coronary pressure (mmHg) Pa: aortic pressure (mmHg) bMR: baseline microvascular resistance (mmHg·cm s^{-1}) APV: Flow Velocity (cm/s), hMR: hyperemic microvascular resistance (mmHg·cm s^{-1}) CFR: Coronary flow reserve VAR: variable arteriolar resistance VAR%: percentage variable arteriolar resistance.

Results: preTAVR vs post TAVR (without AR n=20)

Baseline	pre-TAVI			post-TAVI			p-value
HR	70	±	11	75	±	10	0.002
Pd	92	±	15	94	±	13	0.404
Pa	94	±	15	97	±	13	0.220
PdPa	0.99	±	0.04	0.97	±	0.05	0.186
bMR	3.90	±	1.23	3.86	±	1.18	0.886
APV	25.6	±	8.9	26.8	±	9.6	0.454

Hyperemia	pre-TAVI			post-TAVI			p-value
HR	77	±	12	78	±	16	0.604
Pd	86	±	13	87	±	14	0.437
Pa	89	±	14	93	±	14	0.123
PdPa	0.96	±	0.06	0.94	±	0.07	0.122
hMR	2.03	±	0.71	1.66	±	0.45	0.050
APV	46.2	±	15.5	56.6	±	17.4	0.003
CFR	1.85	±	0.39	2.23	±	0.64	0.009
VAR	1.82	±	1.01	2.20	±	1.02	0.122
VAR%	46.2	±	14.9	54.1	±	14.9	0.021

Values are mean ± SD. HR: Heart rate (bpm) Pd: distal coronary pressure (mmHg) Pa: aortic pressure (mmHg) bMR: baseline microvascular resistance (mmHg·cm s^{-1}) APV: Flow Velocity (cm/s), hMR: hyperemic microvascular resistance (mmHg·cm s^{-1}) CFR: Coronary flow reserve VAR: variable arteriolar resistance VAR%: percentage variable arteriolar resistance.

Results: preTAVR vs post TAVR (without AR n=20)

Baseline	pre-TAVI			post-TAVI			p-value
HR	70	±	11	75	±	10	0.002
Pd	92	±	15	94	±	13	0.404
Pa	94	±	15	97	±	13	0.220
Pd/Pa	0.99	±	0.04	0.97	±	0.05	0.186
bMR	3.90	±	1.23	3.86	±	1.18	0.886
APV	25.6	±	8.9	26.8	±	9.6	0.454

Hyperemia	pre-TAVI			post-TAVI			p-value
HR	77	±	12	78	±	16	0.604
Pd	86	±	13	87	±	14	0.437
Pa	89	±	14	93	±	14	0.123
Pd/Pa	0.96	±	0.06	0.94	±	0.07	0.122
hMR	2.03	±	0.71	1.66	±	0.45	0.050
APV	46.2	±	15.5	56.6	±	17.4	0.003
CFR	1.86	±	0.39	2.23	±	0.64	0.009
VAR	1.82	±	1.01	2.20	±	1.07	0.122
VAR%	46.2	±	14.9	54.1	±	14.5	0.021

hyperemic microvascular resistance (mm Hg·cm·s⁻¹)/CFR: coronary flow reserve; VAR: variable arteriolar resistance; VAR%: percentage variable arteriolar resistance.

Results: post TAVR vs reference vessel

Baseline	post TAVI			Reference			p-value
HR	72	±	11	65	±	10	0.009
Pd	91	±	14	96	±	16	0.206
Pa	94	±	15	99	±	17	0.221
PdPa	0.97	±	0.04	0.98	±	0,04	0.478
bMR	3.96	±	1.29	5.28	±	2.02	0.006
APV	25.5	±	9.0	20.7	±	7.8	0.039
Hyperemia	**post TAVI**			**Reference**			**p-value**
HR	75	±	15	66	±	10	0.012
Pd	85	±	15	88	±	13	0.437
Pa	90	±	15	94	±	14	0.366
PdPa	0.95	±	0.06	0.94	±	0,04	0.575
hMR	1.83	±	0.58	1,80	±	0.60	0.871
APV	51.1	±	18.1	54.3	±	18.6	0.524
CFR	2.10	±	0.65	2.73	±	0.66	0.001
VAR	2.13	±	1.05	3.48	±	1.70	0.001
VAR%	51.0	±	15.0	64.0	±	9.4	<0,001

Values are mean ± SD. HR: heart rate(bpm) Pd: distal coronary pressure (mmHg) Pa: aortic pressure (mmHg) bMR: baseline microvascular resistance (mmHg·cm·s^{-1}) APV: Flow Velocity (cm/s), hMR: hyperemic microvascular resistance (mmHg·cm·s^{-1}) CFR: Coronary flow reserve VAR: variable arteriolar resistance VAR%: percentage variable arteriolar resistance.

Results: post TAVR vs reference vessel

Baseline	post TAVI			Reference			p-value
HR	72	±	11	65	±	10	0.009
Pd	91	±	14	96	±	16	0.206
Pa	94	±	15	99	±	17	0.221
PdPa	0.97	±	0.04	0.98	±	0,04	0.478
bMR	3.96	±	1.29	5.28	±	2.02	0.006
APV	25.5	±	9.0	20.7	±	7.8	0.039

Hyperemia	post TAVI			Reference			p-value
HR	75	±	15	66	±	10	0.012
Pd	85	±	15	88	±	13	0.437
Pa	90	±	15	94	±	14	0.366
PdPa	0.95	±	0.06	0.94	±	0,04	0.575
hMR	1.83	±	0.58	1,80	±	0.60	0.871
APV	51.1	±	18.1	54.3	±	18.6	0.524

APV	51.1	±	18.1	54.3	±	18.6	0.524
CFR	2.10	±	0.65	2.73	±	0.66	0.001
VAR	2.13	±	1.05	3.48	±	1.70	0.001
VAR%	51.0	±	15.0	64.0	±	9.4	<0,001

resistance VAR%: percentage variable arteriolar resistance.