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Peripheral perfusion of lower limb after transcatheter aortic valve implantation (TAVI) in patients with peripheral artery disease

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ABSTRACT

Background: In TAVI patients, peripheral arterial disease (PAD) is a common concomitant disease. Given the fact that calcified severe aortic stenosis (AS) limits the blood flow that reaches the periphery, it is conceivable that the treatment of AS may positively influence the peripheral perfusion.
Aim: To evaluate whether, and if so, how the peripheral perfusion changes after TAVI in patients with PAD comparing with patients without PAD.
Methods: On the basis of objective vascular tests, peripheral perfusion in the lower extremities were studied in 108 TAVI patients with or without concomitant PAD.
Results: 108 consecutive patients with a median logistic EuroSCORE of 12.7 (IQR: 8.5 to 22.0) % underwent TAVI with an extensive pre- and post-procedural assessment of the peripheral perfusion. In patients without PAD, the time to peak flow (tPF) did not differ before (6.45 ± 5.24 s) and after (6.45 ± 5.91 s) TAVI ($p = 1.000$). In PAD patients, however, the tPF was significantly shortened following TAVI (9.51 ± 9.45 s vs. 8.33 ± 8.16 s, $p < 0.001$), thereby reflecting an improvement in peripheral blood flow. The resting arterial blood flow before and after TAVI showed the highest level at the beginning (0 s) and constantly decreased afterwards. No improvement in the peak flow was achieved.
Conclusions: In PAD patients, TAVI led to improved peripheral blood flow as reflected by shortened time to peak flow measurements.

1. Introduction

Peripheral arterial disease (PAD) refers to a cluster of conditions that reduces blood flow capacity due to chronic narrowing and hardening of peripheral arteries, particularly in the legs. By now, PAD affects >200 million people worldwide with symptoms ranging from none to critical ischemia [1]. The prevalence of PAD is known to increase with age, especially in the presence of certain predisposing atherosclerotic factors such as high blood pressure, high blood fat (particularly hypercholesterinemia), obesity, diabetes mellitus, and smoking. These vascular risk determinants overlap with other manifestations of systemic atherosclerosis, including coronary artery disease (CAD), cerebrovascular disease (CVD) and calcified aortic valve stenosis [2–5]. Since calcified aortic stenosis (AS) is the most frequent valvular heart disease in the elderly in developed countries, transcatheter aortic valve implantation (TAVI) has emerged as validated treatment option for patients who have been deemed to be inoperable or at intermediate to high surgical risk due to comorbidities [6–8]. In many TAVI candidates, PAD is a common concomitant disease with prevalence rates ranging from 20% up to >40% [9–12]. Given the fact that calcified severe AS limits the blood flow through the valve that reaches the periphery, it is conceivable that the treatment of calcified AS may positively influence the peripheral perfusion in terms of improvement of peripheral blood flow and relative reduction of hemodynamically relevant narrowing of the arteries due to acutely increased cardiac output and reduction of afterload.

The aim of the present study was to evaluate whether, and if so, how the peripheral perfusion changes in patients with PAD after TAVI determined on the basis of objective vascular tests (mercury-in-silastic

Abbreviations: ABI, ankle-brachial-index; AS, aortic stenosis; ATA, anterior tibial artery; CAD, coronary artery disease; CVD, cerebrovascular disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; PAD, peripheral arterial disease; PTA, posterior tibial artery; SGP-RH, strain-gauge plethysmography – reactive hyperemia; STS-PROM, The Society of Thoracic Surgeons' Predicted Risk of Mortality score; TAVI, transcatheter aortic valve implantation; TBI, toe-brachial-index.

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strain-gauge plethysmography during reactive hyperemia (SGP-RH)) comparing with patients without PAD.

2. Methods

2.1. Patient population

From October 2016 to August 2017, a total of 108 patients suffering from severe, symptomatic AS underwent TAVI at the Heart Center Bonn, and were included into this observational study after written informed consent. Ethics approval for the study was obtained from the local ethics committee of the University of Bonn. The TAVI procedure has been described previously [13].

2.2. Categorization into specific study group

Prior TAVI, specific study group (PAD) or control group (no PAD) categorization was generally undertaken in accordance with the calculation of the ankle-brachial pressure index (ABI) in all patients. In case of the existence of media sclerosis with ABI-values ≥1.4, the categorization into PAD- or no PAD-group was further carried out on the basis of additional toe pressure index (TBI) measurements. A precise quantification of the narrowing of the arteries, either by ultrasound or angiography, was not performed.

2.3. Assessment of ABI (ankle pressure measurements)

The assessment of the ankle-brachial pressure index (ABI) is a simple, non-invasive clinical test to diagnose PAD.

The ABI was performed by measuring the systolic blood pressure from both brachial arteries and from both the posterior (PTA) or anterior tibial (ATA) and the dorsalis pedis arteries, irrespective of the access site during TAVI. All measurements were performed with the use of appropriately sized pneumatic cuffs for both the ankle and the arm. The systolic ankle pressures were recorded with a handheld 5 MHz bidirectional pocket Doppler instrument by continuous wave (cw) velocity detection (Bidop ES-100V3, HADECO, Kawasaki, Japan). To standardize the measurements, blood pressure was determined first in the right arm, then in the right leg, then in the left leg and finally in the left arm, as the blood pressure might drift during testing. The ABI was calculated for each lower limb as the ratio of the lowest pressure from the right or the left PTA and ATA (dorsalis pedis) over the greatest brachial systolic pressure according to the following formula:

$$\mathrm{ABI} = \frac{\text{Lowest systolic pressure from the right or the left PTA and ATA}}{\text{Greatest systolic pressure from the right or left brachial artery}}$$

For each patient, only the lowest ABI recorded in the two ankles was used for patients' categorization into the specific study group. Ratios of 0.90 to 1.30 are considered normal, and ratios <0.9 indicate that PAD is present [14–17]. For the present study, PAD severity is based on the following ABI values: ABI 0.75–0.90 = mild PAD; ABI 0.50–0.75 = moderate PAD; ABI < 0.50 = severe PAD.

2.4. Assessment of TBI (toe pressure measurements)

In many cases, the toe-brachial-index (TBI) is useful in medical conditions associated with media calcifications (called Mönckeberg's sclerosis) such as advanced age, longstanding diabetes or chronic kidney disease that can lead to not reliable ABIs due to non-compressible vessels [18], because the toe vessels, however, are less susceptible to vessel stiffness [19].

The TBI is determined as the ratio of the pressure from the right and the left big toe by means of a photo plethysmograph (PPG) infrared light sensor (vasolab®320, ECLAT GmbH, Wolfratshausen, Germany) over the greatest brachial systolic pressure, respectively. Ratios <0.70 are considered appropriate to define PAD [15].

$$\mathrm{TBI} = \frac{\text{Systolic pressure from the right or the left big toe}}{\text{Greatest systolic pressure from the right or the left brachial artery}}$$

2.5. Objective clinical assessment of peripheral blood flow

Before (one day prior TAVI) and after TAVI (three to seven days after TAVI), clinical assessment of PAD in the lower extremities were studied by means of objective clinical vascular tests.

2.5.1. Assessment of mercury-in-silastic strain-gauge plethysmography (SGP-RH)

The assessment of mercury-in-silastic strain-gauge plethysmography (SGP-RH) is a simple and reliable non-invasive method for peripheral blood flow measurements that has been in use for >100 years and allows to diagnose und further evaluate PAD. Despite its long history, its current clinical importance for both clinical use and research is rather small and mostly limited to the assessment of venous diseases of the lower legs [20] as the method proved to be prone for errors and artefacts which made result interpretation difficult.

SGP-RH, that is based on the principle of post-occlusive reactive hyperemia (RH), offers the examiner the opportunity to register blood flow and volume changes after a certain period of hyperemia by applying a controlled pressure to a cuff around a segment of the limb. These measurements in turn are designed to provide information on the ability of the arterial inflow to respond to an ischemic stimulus [21], especially in patients who are limited to perform an exercise test (e.g. treadmill exercise) because of an underlying illness such as severe symptomatic AS. Lastly, SGP-RH allows to draw a conclusion as to the level of severity of the arterial perfusion disturbance and the level of compensation in presence of PAD.

2.6. Experimental setup

Before the peripheral blood flow measurements, the patients were invited to rest in a supine position for at least 15 min. The patient's legs were positioned in such a way that the knee should be neither flexed nor hyperextend while lying on the examination couch and the lower legs were placed slightly above the heart level (approximately at an angle of 30°) by supporting the heels by the use of specially tailored foam cushions and pillows. Room temperature was maintained at an average of 20 °C. Peripheral blood flow measurements were conducted in both legs simultaneously. For the testing, both appropriately sized pneumatic occlusion cuffs were wrapped around the patients' thighs and the strain-gauge detectors were circularly placed on the thickest part of the calf and connected to a plethysmography device (vasolab®320, ECLAT GmbH, Wolfratshausen, Germany).

This method enables the evaluation of the following parameters:

1. Resting flow (RF) in $\mathrm{ml \cdot min^{-1} \cdot 100\ ml}$
2. Peak flow (PF) in $\mathrm{ml \cdot min^{-1} \cdot 100\ ml}$
3. Time to peak flow (tPF) in s.

The peripheral blood flow measurements consisted of two stages:

(1) Measurement of resting flow (RF)

For the measurement of the resting flow (RF), the pneumatic occlusion cuffs of the thigh were inflated up to 60 mmHg to guarantee venous occlusion. For the testing, 3 consecutive pressure inflations were performed three times per minute for 5 s each made with a 15 s interval in between each occlusion in which the cuff was instantly deflated. As a result, values of RF were obtained at 0 s, 15 s and 30 s.

The normal RF may reach 3–4 ml·min^{-1}·100 ml. In patients with mild or moderate PAD (Fontaine's stage II/III), the blood flow at rest remains within in the normal range, whereas in patients with severe PAD and pain or discomfort while resting (Fontaine's stage IV), a reduction of the RF becomes apparent [22].

(2) Measurement of reactive hyperemia (RH)

For the measurement of reactive hyperemia (RH), the pneumatic occlusion cuffs of the thigh were inflated to a suprasystolic pressure to exclude peripheral circulation (standard: 180 mmHg, in hypertensives: 30–40 mmHg above systolic blood pressure). After 3 min, the arterial occlusion was released. Hereafter, 5 consecutive pressure inflations up to 60 mmHg (to guarantee venous occlusion) were performed for 5 s each made with a 15 s interval in between each occlusion in which the cuff was instantly deflated. As a result, values of RH were obtained at 5 s, 15 s, 25 s, 35 s and 45 s.

After a three-minute period of interruption of blood flow, the normal arterial blood inflow may reach 20–40 ml·min^{-1}·100 ml in healthy adults. It correlates with disease severity, and decreases steadily depending upon the stage of PAD: in patients with Fontaine's stage II PAD, the arterial blood inflow ranges between 4 and 10 ml·min^{-1}·100 ml, whereas in patients with advanced stage PAD (Fontaine's stage III or IV), the arterial blood inflow is considerably reduced (1–5 ml·min^{-1}·100 ml) [22].

The subsequent computer-assisted analysis factored in first flow, peak flow (PF), and time to peak flow (tPF). The first flow was defined as the first arterial blood inflow during hyperemia after 3 min of circulatory arrest (in ml·min^{-1}·100 ml). The PF was recorded as the maximal arterial inflow during hyperemia after 3 min of circulatory arrest (in ml·min^{-1}·100 ml). The tPF specified the time in seconds until the PF has been reached.

The PF and the tPF are normal if the greatest arterial inflow occurs after the first occlusion maneuver and is constantly decreasing afterwards. If the arterial inflow behaves differently, the PF is pathological. The same applies to the tPF; a healthy, no PAD-patient has reached the maximum within 5 up to 15 s. Any discrepancies thereof (PF happens with delay or not at all) are considered pathological. In conclusion, a PF > 12%/min, a tPF within 15 s and a fast decrease afterwards indicates a good peripheral arterial perfusion reserve. Deviations therefrom indicate the presence of PAD [22].

2.7. Statistical analysis

Data are given as mean ± standard deviation if normally distributed or as median and interquartile range (IQR: quartile 1 to 3) if not normally distributed. Continuous variables were tested for normal distribution with the use of the Kolmogorov-Smirnov test. For comparison between two groups, a Student's *t*-test was performed for continuous variables if normally distributed and a Mann-Whitney *U* test was performed for continuous variables if not normally distributed. For the statistical analysis of the objective vascular tests, an “index leg” was selected and a student's paired *t*-test was performed to compare pre- and postprocedural values. Categorical variables are given as frequencies and percentages. For categorical variables, the χ^2-test was used for further analysis. Statistical significance was assumed when the null hypothesis could be rejected at $p < 0.05$. Statistical analyses were conducted with SPSS Statistics Version 22.0 (IBM Corporation, Somer, NY).

The investigators initiated the study, had full access to the data, and wrote the manuscript. All authors vouch for the accuracy and completeness of the data and all analyses and confirm that the study was conducted according to the protocol.

3. Results

3.1. Baseline characteristics

Baseline characteristics according to vascular status are summarized in Supplemental Table 1. 108 consecutive patients suffering from severe, symptomatic AS with a median logistic EuroSCORE of 12.7 (IQR: 8.5 to 22.0) % underwent TAVI at the Heart Center in Bonn, Germany. Patients were subdivided into two groups according to the presence or absence of peripheral arterial disease (PAD) which was defined by ABI or TBI measurement. Baseline characteristics were well balanced between groups, and the clinical profile of the study cohort was representative for the target population.

Patients with PAD ($n = 52$, 48.1%) suffered more frequently from concomitant carotid artery disease (34.6% vs. 14.3%, $p = 0.014$), which was defined as the presence of a sonographic atherosclerotic lesion correlating to diameter stenosis of ≥50%. Patients without PAD had more often a history of previous myocardial infarction (12.5% vs. 1.9%, $p = 0.036$), even though the proportion of patients with coronary artery disease (CAD) was higher in PAD patients than in patients without PAD (71.2% vs. 62.5%, $p = 0.340$).

3.2. Periprocedural characteristics

Periprocedural characteristics according to vascular status are shown in Supplemental Table 2. Statistical analysis did not reveal any differences between the two groups.

3.3. Objective clinical assessment of peripheral blood flow by means of mercury-in-silastic strain-gauge plethysmography (SGP-RH)

(1) Resting flow (RF)

In patients with and without PAD, the resting blood flow showed both before and after TAVI the highest level after 0 s and constantly decreased afterwards. At 0 s, the RF was within the normal ranges before and after TAVI and reached 3–4 ml·min^{-1}·100 ml, irrespective of PAD. At the remaining two measuring dates (15 and 30 s), a significant decrease below standard RF-values was observed in patients without PAD who had undergone TAVI, whereas PAD-patients showed a trend to an increase after TAVI (Fig. 1).

The exact numeric values for flow rates are set out in Table 1.

(2) Assessment of reactive hyperemia

(2.1) Assessment of peak flow (PF)

Regardless whether PAD was present or not, the peak flow (PF) showed the highest level after 5 s and constantly decreased afterwards (all results as follows: before vs. after TAVI: no PAD: 12.60 ± 5.73 ml·min^{-1}·100 ml vs. 11.29 ± 5.69 ml·min^{-1}·100 ml, $p = 0.044$; PAD: 10.77 ± 8.32 ml·min^{-1}·100 ml vs. 8.53 ± 5.25 ml·min^{-1}·100 ml, $p = 0.047$). All measured values were below standard. Both, in patients with and without PAD, no improvement in PF after TAVI was noted (Table 1, Fig. 2).

(2.2) Assessment of time to peak flow (tPF)

In patients without PAD, the time to peak flow (tPF) did not change before (6.45 ± 5.24 s) and after (6.45 ± 5.91 s) TAVI ($p = 1.000$). In patients with PAD, however, the tPF has drastically shortened following TAVI (9.51 ± 9.45 s vs. 8.33 ± 8.16 s, $p < 0.001$) (Table 1, Fig. 3).

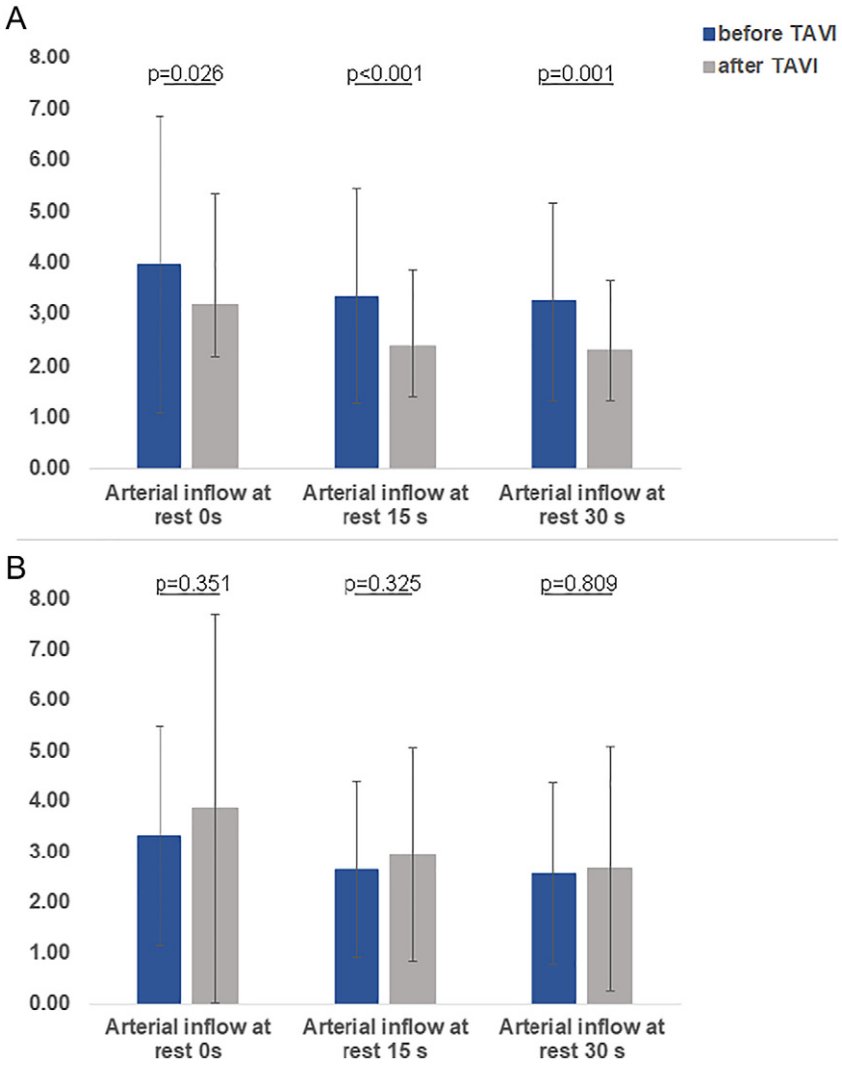

Fig. 1. Resting flow measurements before and after TAVI in patients without PAD (A) and with PAD (B). In patients with and without PAD, the resting arterial blood flow showed both before and after TAVI the highest level after 0 s and constantly decreased afterwards. At 0 s, the RF was within the normal ranges before and after TAVI and reached 3–4 ml·min^{-1}·100 ml, irrespective of PAD was present or not. At the remaining two measuring dates (15 and 30 s), a significant decrease below standard RF-values was observed in patients without PAD who had undergone TAVI, whereas PAD-patients showed a trend indicating an increase after TAVI.

4. Discussion

To the best of our knowledge, this is the first study to evaluate whether, and if so, how the peripheral perfusion changes after TAVI. Our study shows that TAVI induced an improvement in peripheral blood flow reflected by a significantly shortened time to peak flow in patients with PAD. Peak flow was not altered by the TAVI procedure.

Table 1
Objective clinical assessment of peripheral blood flow.

	No PAD ($n = 56$)		*p*-Value	PAD (n = 52)		*p*-Value
	Before TAVI	After TAVI		Before TAVI	After TAVI	
Resting flow						
At 0 s	3.98 ± 2.88	3.18 ± 2.19	**0.026**	3.31 ± 2.18	3.99 ± 3.84	0.351
At 15 s	3.36 ± 2.09	2.39 ± 1.48	<**0.001**	2.65 ± 1.75	2.95 ± 2.11	0.325
At 30s	3.25 ± 1.92	2.33 ± 1.34	**0.001**	2.57 ± 1.79	2.67 ± 2.42	0.809
Reactive hyperemia:						
1. Peak flow						
At 5 s	12.60 ± 5.73	11.29 ± 5.69	**0.044**	10.77 ± 8.32	8.53 ± 5.25	**0.047**
At 15 s	8.59 ± 4.41	7.71 ± 4.53	0.105	7.45 ± 5.61	6.63 ± 4.66	0.355
At 25 s	7.13 ± 4.11	5.65 ± 3.42	**0.002**	5.85 ± 4.34	4.72 ± 3.43	0.122
At 35 s	5.92 ± 3.68	5.06 ± 3.31	**0.042**	5.35 ± 3.80	4.30 ± 3.35	0.119
At 45 s	5.90 ± 3.61	4.81 ± 3.36	**0.005**	5.07 ± 3.91	4.40 ± 3.24	0.303
2. Time to peak flow	6.45 ± 5.24	6.45 ± 5.91	1.000	9.51 ± 9.45	8.33 ± 8.16	<**0.001**

Values are given mean ± SD.

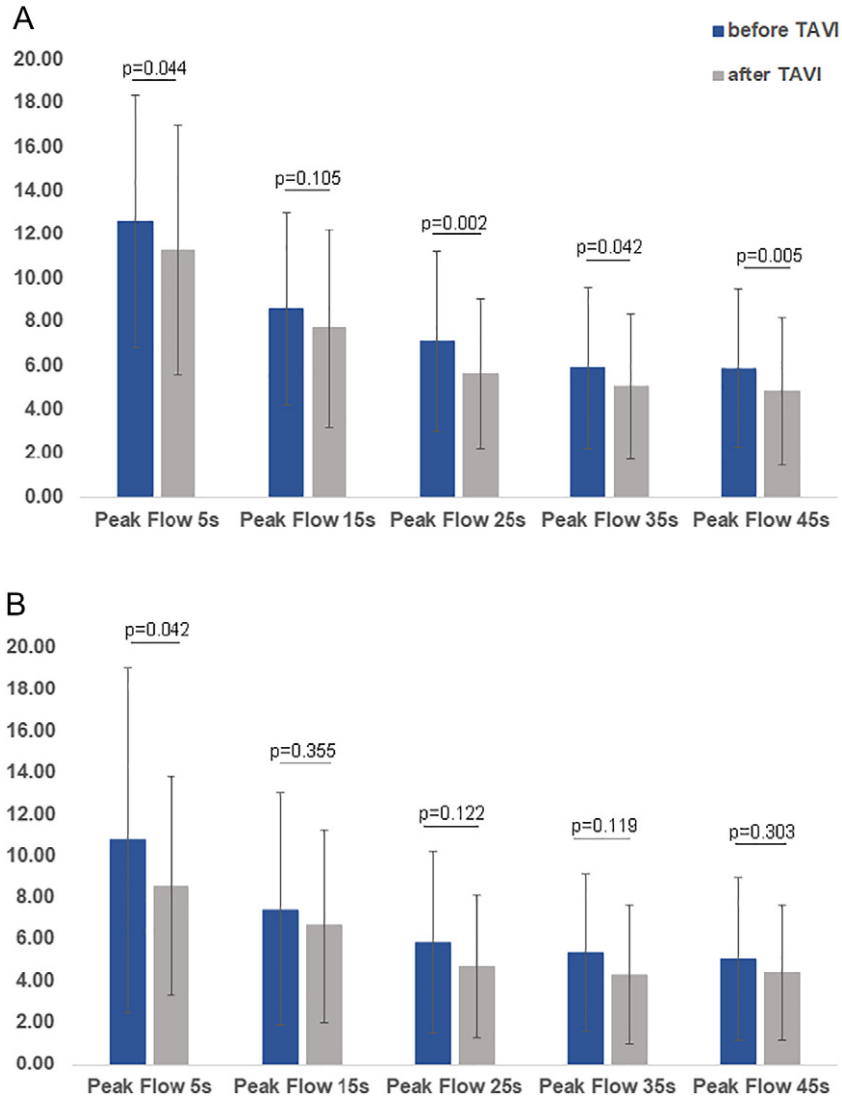

Fig. 2. Peak flow before and after TAVI in patients without PAD (A) and with PAD (B). Regardless whether PAD was present or not, the peak flow showed the highest level after 5 s and constantly decreased afterwards. All measured values were below standard. Both, in patients with and without PAD, no improvement in peak flow after reactive hyperemia has been noted.

PAD is highly prevalent in elderly populations and is a common concomitant disease in TAVI candidates with AS as both diseases share the same predisposing atherosclerotic factors. PAD often coexists with CAD, CVD and calcified AS which could also be verified in our cohort [2–5,9–12].

Physiological changes in pressure and flow within the arteries show that in presence of a "healthy" aortic valve and with increasing distance from the heart, the maximum pressure impulse increases slightly at the detriment of the flow pulse [23]. In cases of pre-existing high-degree AS, the respective values are markedly reduced and may become hemodynamically relevant in cases of a pre-existing PAD. Once the AS becomes resolved, so will reduced perfusion, as a result of the improved peripheral perfusions pressure due to an acutely increased cardiac output and reduction of afterload. Given these facts, it is conceivable that the treatment of calcified AS may improve peripheral blood perfusion and reduction of hemodynamically relevant narrowing of the arteries.

Clinical assessment of peripheral hemodynamic status was mainly achieved by mercury-in-silastic strain-gauge plethysmography.

With regard to our resting flow (RF) measurements, it should be noted that the RF appears to be a quite unspecific parameter that does not provide any substantial information. At 0 s, the RF was within the normal ranges before TAVI, did not change substantially afterwards and reached 3–4 $ml \cdot min^{-1} \cdot 100$ ml, independent whether PAD was present or not. These values are considered normal and are consistent with previous findings: Bossaert et al. has established that the blood circulation of the lower extremity is rather low in contrast to the cerebral or renal perfusion under resting conditions; the human organism makes use of merely 15% of the entire cardiac output to guarantee proper blood flow in both the upper and lower extremities. In healthy individuals, scintigraphic measurements with xenon radionuclides resulted in values around 3–4 ml $ml \cdot min^{-1} \cdot 100$ ml [24]. Under physical stress, however, an increase of muscle blood circulation by up to 80 $ml \cdot min^{-1} \cdot 100$ ml can be obtained by reactive hyperemia as a physiological response to stress or following short-term ischemia [25]. In vascular patients, however, a reduction in RF would have been reasonably expected because of the narrowing of the arteries. The fact that expectations were not met might be due to the fact that our patients had only mild forms of PAD or that PAD-patients may compensate disturbed and/or impaired blood circulation in small vessels by reducing peripheral vascular resistance. Reasons for this will amongst others originate from local regulatory processes and metabolic pathways that were in fact not yet known. Finally, at this time, it is not possible to give a reliable statement on the importance of RF in terms of the peripheral perfusion. Therefore, the decisive diagnostic technique appears to be the

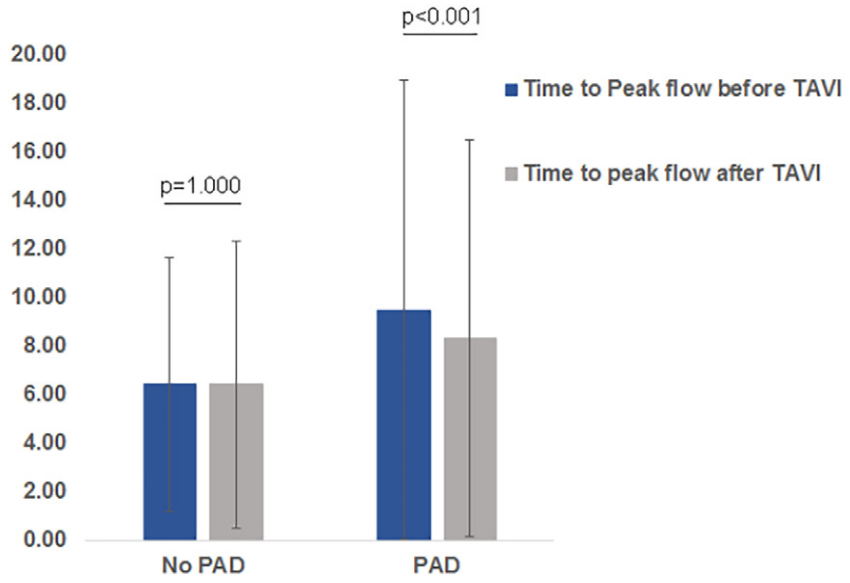

Fig. 3. Time to peak flow before and after TAVI. In patients without PAD, the time to peak flow did not change before (6.45 ± 5.24 s) and after (6.45 ± 5.91 s) TAVI ($p = 1.000$). In patients with PAD, however, the tPF has drastically shortened following TAVI (9.51 ± 9.45 vs. 8.33 ± 8.16 s, $p < 0.001$).

assessment of a transient increase in blood flow that occurs following a brief period of ischemia (reactive hyperemia, RH). It is to be anticipated that an upstream stenosis of an artery may limit the blood flow into the periphery which in turn may lead to a reduction and delay of the intensity of RH. As far as the measurement of peak flow after RH is concerned, it might be indeed expected that an improvement has taken place after TAVI. However, contrary to our expectations, the values of peak flow have deteriorated after removal of severe ventricular afterload. We can only speculate that the diagnostic method is insufficiently sensitive to detect relevant changes, even though we observed a pronounced variability that may have excluded a statistical significance based on the low sample size. This might be due to the fact that for one thing our cohort predominantly consists of patients with mild PAD forms and that, apart from that, our timing of the investigation was maybe unfortunate. We believe that in patients with Fontaine's stage III or IV PAD, a trend towards a steady increase after hyperemia should have been clearly identifiable.

4.1. Study limitations

Our study has several limitations. This study was designed to examine the peripheral perfusion in the early post-TAVI period. Due to the short clinical follow-up period which took seven days at maximum, the collection of surrogates in representing health-related quality of life (HRQL) such as long-term reduction of symptoms or improvement in functional performance including pain-free and maximal walking distances has been ignored while attention has focused on hemodynamic changes. In addition, this is a single-center experience that started in 2017. As such, the clinical assessment of PAD was limited to only a small number of patients. Given the small sample size and proportion of PAD-patients, the majority of PAD-patients had only mild forms of peripheral arterial disease and were not well balanced in terms of PAD severity. Moreover, the lack of sensitivity of the used methods and the manifold error source was a further limitation. In the case of SGP-RH, artefacts, which made result interpretation difficult, can be due to patients that do not tolerate the suprasystolic pressure of the pneumatic occlusion cuffs of the thigh and the resulting pain-triggered contractions of the lower legs musculature. Other causes include the wrong fitting of the strain-gauge detectors or movements of the patients during the measurements.

5. Conclusions

In PAD patients, TAVI led to improved peripheral blood flow as reflected by shortened time to peak flow measurements.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.09.008.

Declaration of competing interest

Drs. Sinning, Werner, Grube and Nickenig receive research grants and speaker honoraria from Medtronic, Edwards Lifesciences, and Boston Scientific. Dr. Grube works as proctor for Medtronic and Boston Scientific. The other authors report no conflicts.

References

[1] F.G. Fowkes, D. Rudan, I. Rudan, V. Aboyans, J.O. Denenberg, M.M. McDermott, P.E. Norman, U.K. Sampson, L.J. Williams, G.A. Mensah, M.H. Criqui, Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis, Lancet 382 (2013) 1329–1340.
[2] W.S. Aronow, Peripheral arterial disease in the elderly, Clin. Interv. Aging 2 (2007) 645–654.
[3] S. M de Ferranti, J.P. Després, H.J. Fullerton, V.J. Howard, M.D. Huffman, S.E. Judd, B.M. Kissela, D.T. Lackland, J.H. Lichtman, L.D. Lisabeth, S. Liu, R.H. Mackey, D.B. Matchar, D.K. McGuire, E.R. Mohler 3rd, C.S. Moy, P. Muntner, M.E. Mussolino, K. Nasir, R.W. Neumar, G. Nichol, L. Palaniappan, D.K. Pandey, M.J. Reeves, C.J. Rodriguez, P.D. Sorlie, J. Stein, A. Towfighi, T.N. Turan, S.S. Virani, J.Z. Willey, D. Woo, R.W. Yeh, M.B. Turner, American Heart Association Statistics Committee and Stroke Statistics Subcommittee, Heart disease and stroke statistics—2015 update: a report from the American Heart Association, Circulation 131 (2015) e29–e322.
[4] G.W. Eveborn, H. Schirmer, G. Heggelund, P. Lunde, K. Rasmussen, The evolving epidemiology of valvular aortic stenosis. The Tromsø study, Heart 99 (2013) 396–400.
[5] Fanaroff AC, Manandhar P, Holmes DR, Cohen DJ, Harrison JK, Hughes GC, Thourani VH, Mack MJ, Sherwood MW, Jones WS, Vemulapalli S. Peripheral artery disease and transcatheter aortic valve replacement outcomes: a report from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Therapy Registry. Circ Cardiovasc Interv. 2017 Oct;10(10). pii: e005456. doi: https://doi.org/10.1161/CIRCINTERVENTIONS.117.005456.
[6] M.B. Leon, C.R. Smith, M. Mack, et al., Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery, N. Engl. J. Med. 363 (2010) 1597–1607.
[7] M.B. Leon, C.R. Smith, M.J. Mack, et al., Transcatheter or surgical aortic-valve replacement in intermediate-risk patients, N. Engl. J. Med. 374 (2016) 1609–1620.
[8] C.R. Smith, M.B. Leon, M.J. Mack, et al., Transcatheter versus surgical aortic-valve replacement in high-risk patients, N. Engl. J. Med. 364 (2011) 2187–2198.
[9] L. Fusini, O. Mirea, G. Tamborini, M. Muratori, P. Gripari, C. Cefalù, S. Ghulam Ali, F. Maffessanti, D. Andreini, G. Pontone, A.L. Bartorelli, F. Alamanni, M. Agrifoglio, M. Pepi, Incidence and severity of atherosclerotic cardiovascular artery disease in patients undergoing TAVI, Int J Cardiovasc Imaging 31 (2015) 975–985.

[10] M.B. Leon, C.R. Smith, M. Mack, D.C. Miller, J.W. Moses, L.G. Svensson, E.M. Tuzcu, J.G. Webb, G.P. Fontana, R.R. Makkar, D.L. Brown, P.C. Block, R.A. Guyton, A.D. Pichard, J.E. Bavaria, H.C. Herrmann, P.S. Douglas, J.L. Petersen, J.J. Akin, W.N. Anderson, D. Wang, S. Pocock, PARTNER Trial Investigators, Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery, N. Engl. J. Med. 363 (2010) 1597–1607.

[11] C. Tamburino, D. Capodanno, A. Ramondo, et al., Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis, Circulation 123 (2011) 299–308.

[12] D.H. Adams, J.J. Popma, M.J. Reardon, S.J. Yakubov, J.S. Coselli, G.M. Deeb, T.G. Gleason, M. Buchbinder, J. Hermiller Jr., N.S. Kleiman, S. Chetcuti, J. Heiser, W. Merhi, G. Zorn, P. Tadros, N. Robinson, G. Petrossian, G.C. Hughes, J.K. Harrison, J. Conte, B. Maini, M. Mumtaz, S. Chenoweth, J.K. Oh, U.S. CoreValve Clinical Investigators, Transcatheter aortic-valve replacement with a self-expanding prosthesis, N. Engl. J. Med. 370 (2014) 1790–1798.

[13] J.M. Sinning, C. Hammerstingl, M. Vasa-Nicotera, et al., Aortic regurgitation index defines severity of peri-prosthetic regurgitation and predicts outcome in patients after transcatheter aortic valve implantation, JACC 59 (2012) 1134–1141.

[14] F. Crawford, K. Welch, A. Andras, F.M. Chappell, Ankle brachial index for the diagnosis of lower limb peripheral arterial disease, Cochrane Database Syst. Rev. 9 (2016), CD010680 Sep 14.

[15] A.T. Hirsch, Z.J. Haskal, N.R. Hertzer, C.W. Bakal, M.A. Creager, J.L. Halperin, et al., ACC/AHA, 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; Trans-Atlantic Inter-Society Consensus; and Vascular Disease Foundation, Circulation 113 (2006) e463–e654.

[16] J.I. Weitz, J. Byrne, G.P. Clagett, et al., Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review, Circulation 94 (1996) 3026–3499.

[17] W.R. Hiatt, Medical treatment of peripheral arterial disease and claudication, N. Engl. J. Med. 344 (2001) 1608–1621.

[18] L. Potier, M. Halbron, F. Bouilloud, M. Dadon, D.J. Le, V.G. Ha, et al., Ankle-to-brachial ratio index underestimates the prevalence of peripheral occlusive disease in diabetic patients at high risk for arterial disease, Diabetes Care 32 (2009) e44.

[19] M.J. Young, J.E. Adams, G.F. Anderson, A.J. Boulton, P.R. Cavanagh, Medial arterial calcification in the feet of diabetic patients and matched non-diabetic control subjects, Diabetologia 36 (1993) 615–621.

[20] S. Keymel, J. Sichwardt, J. Balzer, E. Stegemann, T. Rassaf, P. Kleinbongard, M. Kelm, C. Heiss, T. Lauer, Characterization of the non-invasive assessment of the cutaneous microcirculation by laser Doppler perfusion scanner, Microcirculation 17 (2010) 358–366.

[21] P.J. Breslau, H.B. Slot, J.M. Greep, Comparative study of strain gauge plethysmography and Doppler ultrasound patients with occlusive arterial disease of the lower extremities, Angiology 32 (12) (1981) 840–845 Dec.

[22] K. Kröger, E. Gröchenig, F. Santosa, Nicht invasive Diagnostik angiologischer Krankheitsbilder, ABW Wissenschaftsverlag GmbH, 2012 130–141 Kapitel 12.

[23] K. Kröger, E. Gröchenig, F. Santosa, Nicht invasive Diagnostik angiologischer Krankheitsbilder, ABW Wissenschaftsverlag GmbH, 2012 55–70 Kapitel 6.

[24] H. Bossaert, A. Amery, M. Verstraete, G. Stalpaert, The hyperaemia after reconstructive arterial surgery evaluated by xenon, Angiologica 5 (4) (1968) 263–270.

[25] P.G. Snell, W.H. Martin, J.C. Buckey, C.G. Blomqvist, Maximal vascular leg conductance in trained and untrained men, J Appl Physiol (1985) 62 (2) (1987) 606–610.