Scandinavian Cardiovascular Journal

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icdv20

Evaluation of cerebrovascular events via retinal angiography during transcatheter aortic valve implantation

Henna Qian, Jarkko Piuhola, Heidi Kiviniemi, Matti Niemelä, Nina Hautala & Juhani Junttila

To cite this article: Henna Qian, Jarkko Piuhola, Heidi Kiviniemi, Matti Niemelä, Nina Hautala & Juhani Junttila (2023) Evaluation of cerebrovascular events via retinal angiography during transcatheter aortic valve implantation, Scandinavian Cardiovascular Journal, 57:1, 2278279, DOI: 10.1080/14017431.2023.2278279

To link to this article: https://doi.org/10.1080/14017431.2023.2278279

Published online: 14 Nov 2023.

SCANDINAVIAN CARDIOVASCULAR JOURNAL
2023, VOL. 57, NO. 1, 2278279
https://doi.org/10.1080/14017431.2023.2278279

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Evaluation of cerebrovascular events via retinal angiography during transcatheter aortic valve implantation

Henna Qian[a], Jarkko Piuhola[a], Heidi Kiviniemi[a,b], Matti Niemelä[a], Nina Hautala[c] and Juhani Junttila[a]

[a]Research Unit of Internal Medicine, Medical Research Center Oulu, University of Oulu and Oulu University Hospital, Oulu, Finland; [b]Turku University Hospital, Turku, Finland; [c]Research Unit of Clinical Medicine, Medical Research Center Oulu, University of Oulu and Oulu University Hospital, Oulu, Finland

ABSTRACT

Objectives: Patients receiving transcatheter aortic valve implantation (TAVI) are elderly with multiple comorbidities and at increased risk of perioperative cerebrovascular events. Retinal vasculature represents a surrogate of central nervous system circulation and is noninvasively achievable by retinal imaging. The aim of this study was to evaluate the applicability of retinal angiography of microvascular complications and association to cerebral ischemic events during TAVI.

Design: One hundred patients (male 54%, age: median 82 years, range 64–95 years) undergoing TAVI were recruited for this study. Imaging of retinal vasculature was evaluated with a handheld fundus camera before, during and 1 month after. Cerebrovascular events were determined as a part of contemporary clinical evaluation with cerebral CT and CTA imaging when symptoms occurred.

Results: Altogether 66/100 patients (66%) were included in the analysis. In-hospital ischemic event (transient ischemic attack, cerebral infarction) was observed in 1/66 patient (1.5%). Retinal vascular abnormalities occurred in 8/66 patients (12.1%); 4/66 patients (6.1%) were detected with a cholesterol plaque in the retinal artery, 2/66 (3%) a capillary leakage, 1/66 (1.5%) and optic disk hemorrhage and 1/66 (1.5%) a macular bleeding. No significant association between retinal vasculature abnormalities and cerebrovascular events was detected mainly due to the low event rate.

Conclusions: Perioperative evaluation of cerebrovascular ischemia with noninvasive imaging of retinal vasculature is possible in most patients undergoing TAVI. More data is needed to evaluate the association of cerebrovascular events and retinal microvascular abnormalities during the procedure.

ARTICLE HISTORY
Received 23 April 2023
Revised 18 October 2023
Accepted 28 October 2023

KEYWORDS
Transcatheter aortic valve replacement; tavi; tavr; cerebrovascular events; retinal angiography; retinal abnormalities

Introduction

Transcatheter aortic valve implantation (TAVI) has become the treatment of choice to treat symptomatic patients with severe aortic stenosis (AS) especially among patients with increased surgical risk [1,2]. The recent European guidelines recommend the use of TAVI in patients older than 75 years characterized by intermediate or high surgical risk or unsuitable for surgical aortic valve replacement (SAVR) [2]. Periprocedural stroke is a rare but serious complication of TAVI and it is associated with high mortality and morbidity rates [3]. However, the pathophysiology of cerebrovascular events remains largely unknown. During the procedure, large and semi-rigid delivery catheters are advanced in the aortic arch and are manipulated in the usually heavily calcified aortic valve [4,5]. It has been reported that many patients undergoing TAVI have cerebral infarction in post-procedural diffusion-weighted magnetic resonance imaging [6,7].

Retinal vasculature presents a surrogate of the circulation of the central nervous system and is noninvasively achievable by retinal imaging [8]. It has been shown that greater retinal arteriolar tortuosity is associated with higher systolic blood pressure and higher mean arterial pressure and in addition narrower arterioles were associated with higher systolic blood pressure, mean arterial pressure, and arterial stiffness index [9]. Long-term risk of mortality, ischemic stroke in both sexes and coronary heart disease in female has been associated with wider retinal venules and narrower retinal arterioles [10].

The aim of this study was to evaluate the applicability of retinal angiography of microvascular complications and its association to cerebral ischemic events during TAVI.

Materials and methods

One hundred symptomatic patients with severe AS undergoing TAVI in Oulu University Hospital between February 2020 and March 2021 were recruited for this study. Written informed consent to participate in the study and for the processing of personal data was obtained from each participant prior to the study. The study was approved by the ethical committee of the Northern Ostrobothnian Hospital

CONTACT Henna Qian henna.qian@pohde.fi Research Unit of Internal Medicine, Medical Research Center Oulu, University of Oulu and Oulu University Hospital, Oulu, Finland.

District (approval number 23/2017) and follows the guidelines of The Declaration of Helsinki.

Imaging of retinal vasculature was evaluated with an Optomed Smartscope FA handheld fundus camera in all patients before and during the procedure. Additionally, long-term changes in retinal vasculature were imaged after 1 month in most of the patients. Patients received tropicamide eye drops 30 min preoperatively for pupil dilatation and both eyes were imaged. Both digital black and white and color fundus images were taken. The right retinal image was selected in most of the cases but the fundus image of the left eye was selected when the quality of the image was better. In addition, fluorescent angiography (FAG) was performed; sodium fluorescein 2.5 ml was admitted intravenously and the transit phase fundus images were taken from the selected eye every 10–20 s up to 1 min, and then the control image of the opposite eye was taken. After 5 min from the sodium fluorescein i.v. bolus the late FAG image was taken. At the end of the TAVI procedure, black and white and color images were taken from the previously selected eye, and also FAG was conducted. In one month of control, only digital fundus images were taken except a couple of cases when FAG imaging was also conducted.

The retinal images were evaluated blinded by an ophthalmologist to detect potential abnormalities in the retinal vasculature. The outcome of the study was cerebrovascular events and they were determined as a part of contemporary clinical evaluation with cerebral CT and CTA imaging when symptoms occurred.

Table 1. Baseline characteristics.

Characteristic	Study Group ($n = 100$)
Median age (range)—yr	82 (64–95)
Male sex—n (%)	54 (54)
Body-mass index (mean value)	27.8
Current smoker—n (%)	2 (2)
Hypertension—*n* (%)	66 (66)
Diabetes mellitus—*n* (%)	43 (43)
Type 1	1 (1)
Type 2	42 (42)
Previous cardiovascular disease—*n* (%)	68 (68)
CABG	20 (20)
Atrial fibrillation—*n* (%)	47 (47)
Paroxysmal	16 (16)
Chronic	31 (31)
Peripheral arterial disease—*n* (%)	13 (13)
Hypercholesterolemia—*n* (%)	51 (51)
Previous stroke—*n* (%)	11 (11)
transient ischemic attack	3 (3)
amaruosis fugax	1 (1)
cerebral infarctation	7 (7)
Left ventricular ejection fraction	
mean value	55
value of ≤40%—*n* (%)	15 (15)
Reduced eGFR (<60ml/min/1,73 m2) —*n* (%)	38 (38)
Previous antiplatelet therapy—*n* (%)	53 (53)
Aspirin	50 (50)
Clopidogrel	4 (4)
Ticagrelor	1 (1)
aspirin + dipyridamole	1 (1)
DAPT	3 (3)
Previous anticoagulation—*n* (%)	48 (48)
NOAC	29 (29)
Warfarin	19 (19)
Previous antiplatelet therapy + anticoagulation—*n* (%)	3 (3)
No previous antiplatelet therapy or anticoagulation—*n* (%)	2 (2)

CABG: coronary artery bypass graft surgery; eGFR: estimated glomerular filtration rate (Pt-GFReEPI); DAPT: dual antiplatelet therapy; NOAC: non-vitamin K antagonist oral anticoagulant.

Results

We successfully examined 79/100 patients (79%) before, 67/100 (67%) during and 63/100 (63%) one month after the TAVI. Altogether 66/100 patients (66%) were included in the analysis. 34/100 patients were excluded because of undiagnostic retinal images (lack of cooperation, lack of imaging experience, poor quality of the fundus images) or lack of control images (no images because of patient's poor condition during procedure, patient withdrawal of consent, no control visit in the study center, undiagnostic previous images, malfunction of the camera). If the images before or during the procedure were undiagnostic, the patients were directly excluded.

Median age of the patients was 82 years (range 64–95 years) and 54% of the patients were male. In-hospital ischemic event (transient ischemic attack, cerebral infarction) was observed in 3/100 patients (3%). In the analysis group, 1/66 patient (1.5%)

Table 2. Baseline characteristics.

Characteristic	Patients with retinal abnormalities ($n = 8$)	Other patients ($n = 58$)
Previous cardiovascular disease—*n* (%)	3 (37.5)	42 (72.4)
Atrial fibrillation—*n* (%)	4 (50)	34 (58.6)
Diabetes mellitus—*n* (%)	3 (37.5)	24 (41.4)
Hypertension—*n* (%)	5 (62.5)	40 (69)
Peripheral arterial disease—*n* (%)	0 (0)	8 (13.8)
Hypercholesterolemia—*n* (%)	5 (62.5)	31 (53.4)
Previous stroke—*n* (%)	1 (12.5)	10 (17.2)
Current smoker—*n* (%)	0 (0)	2 (3.4)
Previous antiplatelet therapy—*n* (%)	4 (50)	25 (43.1)
DAPT	0 (0)	1 (1.7)
Previous anticoagulation—*n* (%)	4 (50)	33 (56.9)
NOAC	2 (0.25)	19 (32.8)
Warfarin	2 (0.25)	14 (24.1)
Previous antiplatelet therapy + anticoagulation—*n* (%)	0 (0)	2 (3.4)
No previous antiplatelet therapy or anticoagulation—*n* (%)	0 (0)	2 (3.4)

DAPT: dual antiplatelet therapy; NOAC: non-vitamin K antagonist oral anticoagulant.
66 patients included in the analysis. Statistical analysis was not performed due to the low number of subjects with retinal abnormalities.

had a symptomatic stroke and multiple cerebral infarctions detected in CT scan. [Table 1 near here]

Retinal vascular abnormalities occurred in 8/66 patients (12.1%); 4/66 patients (6.1%) were detected with a cholesterol plaque in the retinal artery, 2/66 (3%) a capillary leakage, 1/66 (1.5%) and optic disk hemorrhage and 1/66 (1.5%) a macular bleeding (Figure 1). Most of the retinal vascular abnormalities (7/8, 87.5%) were detected during the TAVI procedure, but one of the patients was diagnosed with retinal abnormality in one month control. Most of the patients with retinal vascular abnormalities (6/8, 75%) received self-expanding bioprosthesis. [Table 2 near here]

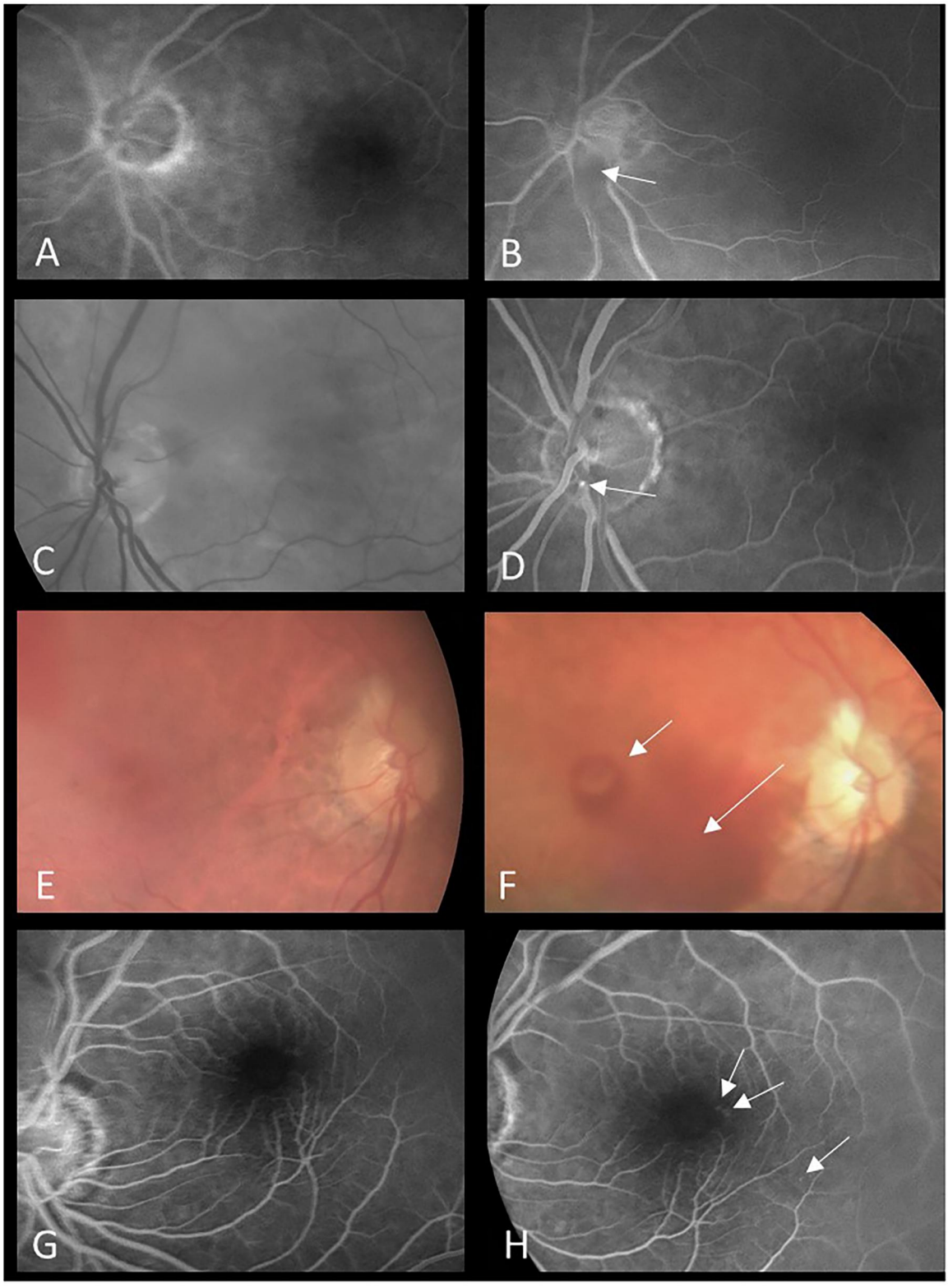

Figure 1. Ocular findings in retinal fluorescein angiography and fundus images before and after transcatheter aortic valve replacement. *Notes*: Ophthalmic changes were not detected in preoperative images (A, C, E, G). Postoperative retinal abnormalities included an optic disc hemorrhage (B), cholesterol plaque in the central retinal artery (D), retinal macroaneurysm with vitreous bleeding (F), and a leakage of microaneurysms in macular vasculature (H).

Because of the low event rate statistical analysis had not been meaningful. No significant association between retinal vasculature abnormalities and cerebrovascular events was detected due to the low event rate.

Discussion

In this study, we evaluated the retinal vasculature abnormalities potentially associated with cerebral ischemic events by visualizing retinal vasculature during TAVI. We also evaluated the applicability of retinal angiography imaging of microvascular complications during TAVI. Retinal vasculature abnormalities occurred in 8/66 patients (12.1%). Most of them (4/66 patients, 6.1%) were detected with a cholesterol plaque in the retinal artery potentially originated from the valve itself or calcified aorta. A capillary leakage was seen in 2/66 patients (3%), an optic disk hemorrhage in 1/66 patient (1.5%) and a macular bleeding in 1/66 patients (1.5%). Bleeding can be caused by ischemia, mechanical damage of retinal artery or thrombotic, cholesterol or air emboli.

Previously noninvasive evaluations of cerebrovascular microembolisms have been determined from retinal images during cardiac surgery. It was shown that in patients undergoing coronary artery bypass graft surgery retinal microembolization detected by fluorescein angiography was decreased when using minimized cardiopulmonary bypass (MCPB) compared to conventional extracorporeal circulation that suggests a decreased load of emboli to the brain after MCPB [11]. In addition, retinal embolic events have been studied earlier by running a full ophthalmic examination to TAVI patients perioperatively. A study of 20 TAVI patients who underwent full ophthalmic examination to assess retinal embolic events prior to TAVI and at 48 h and 1 month resulted in an overall incidence of retinal embolic events of 15–20% without any significant visual problems or retinal damage [12]. In another study, retinal abnormalities were evaluated with optical coherence tomography angiography (OCTA) after TAVI showing that capillary dropout lesions could often be found in patients after TAVI [13]. Noninvasive retinal evaluation has been used in TAVI patients and there is some reference that retinal abnormalities occur after the procedure. This study is the first study to evaluate the retinal vasculature changes during the TAVI procedure. This method might be a feasible assessment tool in future studies of cerebral embolic protection devices in TAVI procedures.

In studies with cerebral embolic protection device (Sentinel ®) it has been found that in almost all cases some debris can be captured [14]. This has been proved to result in a diminished number of small asymptomatic cerebral lesions detectable in MRI after the procedure [15]. However, in a large randomized trial there was no significant difference in the total stroke number [16]. The inability of the device to reduce stroke numbers can be due to numerous factors. As seen in the current study, embolic debris is not the only driver of changes in the target vasculature, but also capillary leakage and bleeding were seen.

The study population was small and the event rate was low, thus, there was no significant association with retinal abnormalities and cerebrovascular events. This was an observational study assessing the feasibility of periprocedural retinal imaging and was not designed necessarily to determine outcome association. We used CT imaging only when neurological symptoms occurred because the aim of the study was not to show cerebral imaging differences related to retinal imaging. In addition, among TAVI patients clinical signs of stroke would be more meaningful outcomes than imaging results due to the comorbidities and age of the patients. The quality of many retinal images was not optimal but we observed a beneficial learning curve in the procedure resulting in better quality at the end of the enrollment.

Neuropsychological tests to assess procedure-related neurological abnormalities have been performed previously in CABG related studies [17]. We opted to use clinical endpoints such as stroke due to the age and comorbidities of the patients. After all TAVI patients might have neuropsychological abnormalities unrelated to the vascular complications related to the procedure mostly due to the previously mentioned reasons.

Our study adds understanding of the possible mechanisms of vasculature damage during the TAVI procedure. This study shows that it is possible to evaluate the perioperative cerebrovascular ischemia by visualizing central nervous vasculature with mildly sedated patients undergoing TAVI when the neurological symptoms normally are clinically difficult to evaluate.

Conclusion

Perioperative evaluation of cerebrovascular ischemia with noninvasive imaging of retinal vasculature is possible in most patients undergoing TAVI. More data is needed to evaluate the association of cerebrovascular events and retinal microvascular abnormalities during the procedure.

Disclosure statement

No potential conflict of interest was reported by the author(s)

Funding

This study received funding from Finnish Foundation for Cardiovascular Research and Sigrid Juselius Foundation.

ORCID

Heidi Kiviniemi http://orcid.org/0000-0002-6178-8781
Juhani Junttila http://orcid.org/0000-0002-8896-1281

References

[1] Otto CM, Nishimura RA, Bonow RO, 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. J Am Coll Cardiol. 2021;77(4):450–500. doi: 10.1016/j.jacc.2020.11.035.

[2] Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2022;43(7):561–632. doi: 10.1093/eurheartj/ehab395.

[3] Werner N, Zeymer U, Schneider S, et al. Incidence and clinical impact of stroke complicating transcatheter aortic valve implantation: results from the German TAVI registry. Catheter Cardiovasc Interv. 2016;88(4):644–653. doi: 10.1002/ccd.26612.

[4] Kahlert P, Knipp SC, Schlamann M, et al. Silent and apparent cerebral ischemia after percutaneous transfemoral aortic valve implantation. Circulation. 2010;121(7):870–878. doi: 10.1161/CIRCULATIONAHA.109.855866.

[5] Van Mieghem NM, Schipper ME, Ladich E, et al. Histopathology of embolic debris captured during transcatheter aortic valve replacement. Circulation. 2013;127(22):2194–2201. doi: 10.1161/CIRCULATIONAHA.112.001091.

[6] Arslan U, Erdoğan G, Yenerçağ M, et al. Direct transcatheter aortic valve implantation (TAVI) decreases silent cerebral infarctation when compared to routine balloon valvuloplasty. Int J Cardiovasc Imaging. 2023;39. (10):2029–2039. doi: 10.1007/s10554-023-02895-x.

[7] Suhai FI, Varga A, Szilveszter B, et al. Predictors and neurological consequences of periprocedural cerebrovascular events following transcatheter aortic valve implantation with self-expanding valves. Front Cardiovasc Med. 2022;9:951943. doi: 10.3389/fcvm.2022.951943.

[8] Liew G, Wang JJ, Mitchell P, et al. Retinal vascular imaging: a new tool in microvascular disease research. Circ Cardiovasc Imaging. 2008;1(2):156–161. Sepdoi: 10.1161/CIRCIMAGING.108.784876.

[9] Robyn JT, Owen GO, Barman SA, et al. Associations of retinal microvascular diameters and tortuosity with blood pressure and arterial stiffness: United Kingdom biobank. Hypertension. 2019;74(6):1383–1390. doi: 10.1161/HYPERTENSIONAHA.119.13752.

[10] Seidelmann SB, Claggett B, Bravo PE, et al. Retinal vessel calibers in predicting long-term cardiovascular outcomes, the atherosclerosis risk in communities study. Circulation. 2016;134(18):1328–1338. doi: 10.1161/CIRCULATIONAHA.116.023425.

[11] Rimpiläinen R, Hautala N, Koskenkari JK, et al. Minimized cardiopulmonary bypass reduces retinal microembolization: a randomized clinical study using fluorescein angiography. Ann Thorac Surg. 2011;91(1):16–22. doi: 10.1016/j.athoracsur.2010.08.049.

[12] Fusi-Rubiano WJ, Yang YC, Smallwood AF, et al. Retinal embolic events: frequency and impact following transcatheter aortic valve implantation (TAVI) for aortic stenosis. BMJ Open Ophthalmol. 2017;1(1):e000033. doi: 10.1136/bmjophth-2016-000033.

[13] Gunzinger JM, Ibrahimi B, Baur J, et al. Assessment of retinal capillary dropout after transcatheter aortic valve implantation by optical coherence tomography angiography. Diagnostics. 2021;11(12):2399. doi: 10.3390/diagnostics11122399.

[14] Kroon H, von der Thusen JH, Ziviello F, et al. Heterogeneity of debris captured by cerebral embolic protection filters during TAVI. EuroIntervention. 2021;16(14):1141–1147. doi: 10.4244/EIJ-D-20-00744.

[15] Van Mieghem NM, van Gils L, Ahmad H, et al. Filter-based cerebral embolic protection with transcatheter aortic valve implantation: the randomized MISTRAL-C trial. EuroIntervention. 2016;12(4):499–507. sdoi: 10.4244/EIJV12I4A84.

[16] Kapadia SR, Makkar R, Leon M, et al. Cerebral embolic protection during transcatheter aortic-valve replacement. N Engl J Med. 2022;387(14):1253–1263. doi: 10.1056/NEJMoa2204961.

[17] Kennedy ED, Choy KC, Alston RP, et al. Cognitive outcome after on- and off-pump coronary artery bypass grafting surgery: a systematic review and meta-analysis. J Cardiothorac Vasc Anesth. 2013;27(2):253–265. doi: 10.1053/j.jvca.2012.11.008.