Silent Cerebral Ischemia After Thoracic Endovascular Aortic Repair: A Neuroimaging Study

Philipp Kahlert, MD, FESC, Holger Eggebrecht, MD, FESC, Rolf A. Jáñosi, MD, Heike A. Hildebrandt, MD, Björn Plicht, MD, Konstantinos Tsegakis, MD, Christoph Moenninghoff, MD, Felix Nensa, MD, Petra Mummel, MD, Gerd Heusch, MD, FRCR, Heinz G. Jakob, MD, Michael Forsting, MD, Raimund Erbel, MD, FESC, and Marc Schlamann, MD

Departments of Cardiology and Thoracic and Cardiovascular Surgery, West-German Heart Center Essen; Institute of Diagnostic and Interventional Radiology and Neuroradiology, Department of Neurology, and Institute for Pathophysiology, Essen University Hospital, University Duisburg-Essen, Essen, Germany

Background. The risk of clinically apparent, periprocedural stroke after thoracic endovascular aortic repair (TEVAR) due to dislodgement and embolization of aortic debris from intravascular manipulation of guidewires, catheters, and large-bore delivery systems ranges between 2% and 6% and has been associated with increased postoperative mortality. The rate of clinically silent cerebral ischemia is yet unknown, but may be even higher.

Methods. Nineteen patients (13 male, 6 female) who underwent TEVAR were included into this descriptive study. Periprocedural apparent and silent cerebral ischemia was assessed by daily clinical neurologic assessment and serial cerebral diffusion-weighted magnetic resonance imaging (DW-MRI) at baseline and 5 days (median, interquartile range: 3.5) after the procedure.

Results. The TEVAR was successful in all patients without immediate clinically apparent neurologic deficits. Postinterventional cerebral DW-MRI detected a total of 29 new foci of restricted diffusion in 12 of 19 TEVAR patients (63%). Lesions were usually multiple (1 to 6 lesions per patient) and ranged in size between 15 mm³ and 300 mm³; 16 lesions were found in the left hemisphere, 13 lesions in the right hemisphere. Overstenting of the left subclavian artery was performed in 8 cases, but was not associated with lateralization of lesions. There were no additional apparent neurologic events during the in-hospital period.

Conclusions. Thoracic endovascular aortic repair resulted in a high incidence of new foci of restricted diffusion on cerebral DW-MRI in a pattern suggestive of periprocedural embolization. Although multiple lesions per patients were found, these lesions were not associated with apparent neurologic deficits during the in-hospital period. Further developments in TEVAR should be directed toward reducing the risk of periprocedural cerebral embolization.

Intercranial stroke and paraplegia from spinal cord ischemia are among the most dreaded complications of thoracic endovascular aortic repair (TEVAR). Although there are no randomized studies so far, it is generally believed that the risk of paraplegia after TEVAR compares favorably with open surgery. Periprocedural stroke is more common than spinal cord ischemia and occurs with similar incidence rates compared with conventional surgery of the descending thoracic aorta [1]. Contemporary studies estimate the risk of clinically apparent, periprocedural stroke after TEVAR between 1.9% and 5.8% [2–6]. Importantly, stroke has been associated with significant postoperative mortality [5].

Periprocedural stroke after TEVAR is thought to be related to multiple emboli, which are dislodged during manipulation of guidewires, catheters, and large-bore delivery devices in the diseased aortic arch [2, 7]. In addition to stroke with clinically apparent, disabling neurologic deficits, these device manipulations in the aorta may also result in clinically silent cerebral embolization from aortic atheroma. Such clinically silent emboli are associated with more lingering neurologic impairment and may thus be of less importance for the in-hospital period, but still result in a decline in neurocognitive function and deterioration of dementia during long-term follow-up [8].

The risk of clinically silent cerebral embolism after TEVAR is yet unknown. We therefore sought to evaluate clinically silent cerebral ischemia in patients undergoing TEVAR using serial diffusion-weighted (DW) magnetic resonance imaging (MRI) and neurologic examination before and after the procedure.

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Address correspondence to Dr Kahlert, West-German Heart Center Essen, Department of Cardiology, Essen University Hospital, University Duisburg-Essen, Hufelandstr. 55, 45122 Essen, NRW, Germany; e-mail: philipp.kahlert@uk-essen.de.

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Patients and Methods

Patient Population

Nineteen clinically stable patients undergoing planned, nonemergent TEVAR procedures were included in this single-center study. Unstable patients and patients undergoing emergent TEVAR, patients with a history of stroke or preexisting neurologic deficits, carotid artery stenoses diagnosed by preinterventional duplex ultrasound, computed tomographic (CT) or MR angiography, known mental disorder, alcoholism, renal failure (creatinine ≥1.5 mg/dL or estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m²), active liver disease, unstable angina, previous cardiac surgery, or contraindications for MRI (eg, claustrophobia, pacemaker) were excluded. The study was approved by the local ethics committee (#06-3026) and oral informed patient consent was obtained.

Stent-Graft Procedure

Stent-graft placement was performed by a team of interventional cardiologists, cardiothoracic surgeons, and anesthetists at a major tertiary referral center with significant expertise in the treatment of patients with acute aortic syndromes. The technique of TEVAR has been previously described in detail [9, 10]. Stent grafts with proximal bare springs (Talent, Medtronic, Minneapolis, MN, n = 4 patients; Valiant, Medtronic, n = 7 patients; Relay, Bolton Medical, Barcelona, Spain, n = 7 patients) were implanted in 18 patients and without bare springs in the remaining case (Gore Tag, W. L. Gore & Associates Inc, Flagstaff, AZ) under systemic hypotension (approximately 65 mm Hg systolic arterial pressure) induced by either intravenous application of sodium nitroprusside (n = 13) or rapid right-ventricular burst pacing with 180 to 200 min⁻¹ (n = 6).

To avoid air emboli, catheters and stent-graft delivery systems were carefully flushed with saline, and the activated clotting time was maintained above 250 seconds to ensure early detection of clinically overt ischemia.

Prior to the TEVAR procedure, surgical revascularization of both the left subclavian and the left carotid artery was performed in 2 and revascularization of the left subclavian artery alone in 1 case in a nonemergent setting, to allow subsequent stent-graft-implantation in a separate procedure. In case of coverage of supraaortic vessels by the proximal bare spring, patients were given acetylsalicylic acid and clopidogrel for 4 weeks.

Cerebral Magnetic Resonance Imaging

Cerebral MRI was performed on a 1.5-T Avanto whole body imaging system (Siemens Medical Systems, Erlangen, Germany). The protocol included the following 2 sequences: (1) transversal fluid-attenuated inversion recovery (FLAIR) (repetition time 9,000 ms, echo time 115 ms, matrix 256 × 208, slice thickness 6 mm); and (2) transversal DW images (DWI) of the whole brain (repetition time 4,600 ms, echo time 137 ms, matrix 128 × 128, slice thickness 5 mm, b values: 0, 500, 1,000 s/mm²).

Patients were imaged preinterventionally and after the procedure when anesthetist-controlled conscious sedation or general anesthesia was completely reversed. Scans were read by 2 experienced neuroradiologists blinded to the data of the patient. For volumetric quantification of new DW-MRI abnormalities on postoperative scans, the lesion area was delineated in each slice and lesion volume calculated using standard scanner software (Syngo, Siemens Medical Systems).

Computed Tomography and Magnetic Resonance Angiography

Computed tomographic or MR angiography was performed before and after the intervention from the level of the cardiac valves to the circle of Willis. The MR angiography was performed by means of repetitive three-dimensional fast flash sequences using gadobutrol (Gadovist® Bayer Healthcare, Leverkusen, Germany) as contrast agent, and CT-angiography by means of a 16-row CT scanner (Siemens Sensation 16, Siemens Medical Systems,) using 80 mL iobitriol (Xenetix 250, Guerbet GmbH, Sulzbach, Germany) infused with a flow rate of 3 mL/s. Slice thickness was 1 mm. Patients were imaged preinterventionally and after the procedure.

Clinical Examination and Neurologic Assessment

An in-depth baseline clinical examination was performed by a specialist in internal medicine and cardiology at baseline and a board-certified neurologist was consulted in case of conspicuous neurologic findings. After each TEVAR procedure, patients were transferred to the intensive care unit for postoperative care and surveillance.

During the intensive care unit stay, clinical examinations were performed once during each shift (ie, 3 times daily) by the attending team of specialists in internal medicine and in neurology, and a comprehensive neurologic examination was performed by a board-certified neurologist once anesthesia was completely reversed, thereby ensuring early detection of clinically overt ischemic cerebral events and spinal cord ischemia [11].

Definitions

Aortic dissection was considered an acute event if it occurred within the first 14 days from the onset of symptoms, whereas it was considered chronic beyond 14 days [12]. The proximal stent-graft landing zone in the aortic arch was characterized using the classification proposed by Ishimaru [13]. Briefly, in this classification zones 0, 1, 2, and 3 are based on lines from the distal side of the branch arteries of the aortic arch and zone 4 is the relatively straight section adjacent to the thoracic and lumbar vertebrae, the border between zone 3 and 4 being the end of the aortic arch curvature.

Statistical Analysis

Continuous variables are presented as median/interquartile range (median/interquartile range), and categorical variables as frequencies and percentages. Comparisons were made with the Wilcoxon signed rank and the χ² test, as appropriate. A p value less than 0.05 was considered statistically significant. All statistical
analyses were performed using the SPSS software pack-
age (version 17.0; SPSS, Chicago, IL).

Results

Patient and Procedural Characteristics

Patient and procedural characteristics are given in Table 1. Mean age of the 19 patients was 59/19 years, and 6 (32%) of them were female. Indications for TEVAR were acute type B dissections in 3 (16%), chronic type B dissections in 9 (47%), thoracic aortic aneurysma in 4 (21%), and penetrating aortic ulcera in 3 (16%) patients. All patients underwent planned, nonemergent TEVAR procedures and were clinically stable. Up to 2 stent grafts (median, 1) with a diameter of 34/0 mm and a length of 170/34 mm were successfully implanted. Procedure time was 165/89 minutes, and 233/88 mL of contrast media were used. In 1 procedure, concomitant abdominal aortic surgery (bypasses on the celiac trunk and the right renal artery) was performed.

During the procedures, the most proximal position the stent-graft delivery system was advanced to was zone 0 in 9 (47%), zone 1 in 7 (37%), and zone 3 in the remaining 3 (16%) patients. The stent graft itself was finally deployed with its proximal end in zone 0 in 2 (11%), zone 1 in 6 (32%), zone 2 in 8 (42%), and zone 3 in the remaining 3 (16%) patients. Active retraction of the endoprosthesis during deployment was necessary in 12 (63%) patients.

In 8 patients, the proximal bare spring of the stent graft was positioned across the left common carotid artery. Coverage of the left subclavian artery was intentionally performed in 8 (42%) patients.

In-Hospital Outcome

In none of the patients, clinically apparent stroke or major complications occurred until discharge after 8.5/6.75 days. During further follow-up, surgical revascularization of both the left subclavian artery and the left carotid artery (n = 1) and of the left subclavian artery alone (n = 1) was performed several months after the initial TEVAR procedure due to a proximal endoleak requiring further intervention.

Cerebral Magnetic Resonance Imaging Findings

Baseline DW-MRI scans showed no signs of prior ischemia in any patient. Postinterventional cerebral DW-MRI was performed 5/3.5 days after TEVAR and detected a total of 29 new foci of restricted diffusion in 12 of 19 (63%) patients. Lesions were usually multiple (1 to 6 lesions per patient) and ranged in size between 15 mm³ and 300 mm³ (Fig 1; Table 2). Sixteen lesions were found in the left hemisphere, 13 lesions in the right hemisphere.

Overstenting of the left subclavian artery was not associated with lateralization of lesions, and calcification of the aortic arch was not associated with lesion count. The landing zone of the stent and the most proximal localization of the deployment system were also not associated with lesion load or lateralization. In our small patient population there was, further, no difference in the occurrence of new DW-MRI lesions between type B dissections, thoracic aortic aneurysma, and penetrating aortic ulcer, and also not between acute and chronic dissections. In addition, there was no influence of previous or later surgical revascularization of the supraaortic branches and of concomitant abdominal aortic surgery on the occurrence of new cerebral DW-MRI lesions.

Computed Tomography and Magnetic Resonance Angiography

An anomalous origin of the left vertebral artery was ruled out in all patients by preinterventional CT or MR angiography as was left vertebral artery dominance in cases with intended overstenting of the left subclavian artery.

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<th>Table 1. Patient and Procedural Characteristics</th>
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<tr>
<td>Characteristic</td>
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<tr>
<td>Age, years, median/IQR</td>
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<tr>
<td>Female gender, n (%)</td>
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<tr>
<td>Arterial hypertension, n (%)</td>
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<td>Diabetes mellitus, n (%)</td>
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<td>Smoking, n (%)</td>
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<td>X-ray time, min, median/IQR</td>
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<td>Procedure time, min, median/IQR</td>
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<td>Atrial fibrillation, n (%)</td>
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<tr>
<td>Zone stent (n)</td>
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<td>Zone introducer (n)</td>
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<td>Overstenting of the LSA, n (%)</td>
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IQR = interquartile range; LSA = left subclavian artery; min = minutes; MRI = magnetic resonance imaging.
Comment

This descriptive study is the first to use serial cerebral DW-MRI to provide insights into the risk of clinically silent cerebral ischemia in patients undergoing TEVAR. In almost two thirds of patients undergoing TEVAR for various indications, up to 6 new foci of restricted diffusion were observed after the procedure as a surrogate for procedural embolization. These new embolic lesions were, however, not associated with acute neurologic deficits.

Previous investigators have speculated that stroke after TEVAR is mainly caused by embolization of atherosclerotic debris during manipulations of guidewires, catheters, and delivery devices in a diseased aortic arch [2, 7]. In our study, the distribution of the foci of restricted diffusion in both hemispheres as well as in both the anterior and the posterior circulation corroborates such an embolic hypothesis of stroke after TEVAR. Other potential etiologic factors for stroke include air embolism, extracranial carotid disease, and vertebrobasilar disease [2, 7, 14]. The latter may gain particular importance in patients in whom the left subclavian artery is covered by the stent graft, and Fattori and colleagues [14] and Rehders and colleagues [15] have already found a significant correlation of stent-graft-induced left subclavian artery occlusion without revascularization with the risk of postoperative stroke. This observation, however, was not confirmed in our study. Overstenting of the left subclavian was performed in 8 of the 19 (42%) patients. Nevertheless, the incidence of new DW-MRI lesions postoperatively was not different from that in patients in whom the left subclavian artery was not overstented. This discrepancy may be explained by our rigorous preoperative screening protocol using MR angiography of the supraaortic vessels to exclude patients with left dominant vertebral arteries from intentional left subclavian artery coverage.

Previous investigators have also sought to identify risk factors for stroke after TEVAR. Gutsche and colleagues [5] identified a history of previous stroke, significant atheroma of the aortic arch or proximal descending aorta, and stent-graft placement into the proximal descending aorta and distal arch as risk factors for postprocedural stroke. In none of our patients were severe atheromata greater than 5 mm observed on preoperative computed tomography. We therefore evaluated the presence of aortic arch calcifications as a semiquantitative parameter for atheromatous disease. However, the incidence of new DW-MRI lesions after TEVAR was not different between patients with and without arch calcifications. Similarly, we found no correlation of a more proximal stent-graft position or more proximal introduction of the delivery system with the incidence of postprocedural DW-MRI lesions.

Dislodgement of atherosclerotic plaque debris by catheters has been observed with a variety of intravascular catheterization procedures [16, 17] but has not, so far, been systemically studied in patients undergoing TEVAR. While we used DW-MRI to detect silent cerebral lesions as hidden fingerprints of the TEVAR procedure [8], other groups have performed real-time intraoperative monitoring using transcranial Doppler sonography focusing on cerebral perfusion during induced hypotension [18] and on the occurrence of microembolic...
signals [19]. Bismuth and colleagues [19] found that the highest amount of microembolic signals was generated by pigtail catheter placement during the diagnostic phase and by device placement during the treatment phase in 20 patients undergoing TEVAR for aneurysm treatment. Interestingly, embolic count was equal between the left and the right side [19]. These results support the notion that most emboli occur during direct manipulation of the diseased aortic arch. During transcatheter aortic valve implantation, in contrast, most embolic signals are observed during manipulation of the usually heavily calcified aortic valve during positioning and implantation of the stent valve [20, 21].

**Limitations**

First, our study is limited by the small number of patients, precluding reliable identification of patient- or procedure-related risk factors for silent cerebral embolism and affecting the robustness of our statistical analysis. Our findings should thus be considered as hypothesis generating and have to be validated in future larger scale studies that should also focus on a more detailed assessment of neurocognitive function. Second, this was not a consecutive series of patients, which might have further biased the results of our study. Nevertheless, we still believe that our patient cohort reflects a representative sample of patients currently treated by TEVAR.

**Conclusions**

Our data indicate that TEVAR, which is increasingly used for the treatment of patients with aortic aneurysmata and type B dissections, is associated with a high incidence of new foci of restricted diffusion on cerebral DW-MRI in a pattern suggestive of periprocedural embolization. These cerebral lesions, although multiple in most cases, were not associated with clinically apparent neurologic deficits during the in-hospital period. Further research should be aimed at identifying patient- and procedure-related risk factors for cerebral embolism during TEVAR, and technical developments in the field of TEVAR should be directed toward reducing the risk of periprocedural cerebral embolization by introduction of smaller and less traumatic delivery systems.

**References**

ABTS Requirements for the 10-Year Milestone for Maintenance of Certification

Diplomates of the American Board of Thoracic Surgery (ABTS) who plan to participate in the 10-Year Milestone for the Maintenance of Certification (MOC) process as Certified-Active must hold an unrestricted medical license in the locale of their practice and privileges in a hospital accredited by the JCAHO (or other organization recognized by the ABTS). In addition, a valid ABTS certificate is an absolute requirement for entrance into the MOC process. If your certificate has expired, the only pathway for renewal of a certificate is to take and pass the Part I (written) and the Part II (oral) certifying examinations.

The CME requirements are 150 Category I credits over a five-year period. At least half of these CME hours need to be in the broad area of thoracic surgery. Category II credits are not accepted. Interested individuals should refer to the Board’s website (www.abts.org) for a complete description of acceptable CME credits.

Diplomates will be required to take and pass a secured exam after their application has been approved. Taking SESATS in lieu of the secured exam is not an option. The secured exam is administered over a two-week period in September of every year at Pearson Vue Testing Centers, which are located nationwide. Diplomates will have the opportunity to select the day and location of their exam. For the dates of the next MOC exam, visit the Board’s website at www.abts.org.

The ABTS has voted to replace the requirement for mandatory database participation with Performance Improvement. The Board is considering the appropriate start date for the Performance Improvement process, but it will not be earlier than January 2016. For those who do not participate in a Board approved database/registry, the Board will continue to require participation in the Professional Portfolio until the Performance Improvement process starts.

Diplomates may apply for MOC in the year their certificate expires or, if they wish to do so, they may apply up to two years before it expires. However, the new certificate will be dated 10 years from the date of expiration of their original certificate or most recent MOC certificate. In other words, going through the MOC process early does not alter the 10-year validation. Diplomates certified prior to 1976 (the year that time-limited certificates were initiated) are also required to participate in MOC if they wish to maintain valid certificates.

Information outlining the rules, requirements, and application deadline for the 10-year Milestone of MOC in thoracic surgery is available on the Board’s website at www.abts.org. For additional information, please contact the American Board of Thoracic Surgery, 633 N Saint Clair St, Ste 2320, Chicago, IL 60611; telephone (312) 202-5900; fax (312) 202-5960; e-mail: sesats@abts.org.