PULSATILITY ASSESSMENT IN PATIENTS WITH ABDOMINAL AORTIC ANEURYSMS AND NATIONAL ADVANCEMENTS IN ENDOVASCULAR AORTIC REPAIR

PhD Thesis – short version

Daniele Mariastefano Fontanini MD

Cardiovascular Medicine and Research Program

Semmelweis University

Supervisor:	Csaba Csobay-Novák MD, PhD
Official reviewers:	Bálint Lakatos MD, PhD
	Eszter Végh MD, PhD
Head of the Complex Examination Committee:	Prof. Tivadar Tulassay MD, PhD
Head of the Complex Examination Committee:	Prof. Henriette Farkas MD, PhD
	Prof. Charaf Hassan, PhD

Budapest

2023

1. Introduction

1.1. Aortic Pulsatility and Endovascular Repair Planning

Advancements in CT imaging enable rapid ECG-gated CTA of the entire aorta in a single breath, ushering in new challenges. Determining the optimal cardiac cycle phase for image acquisition and subsequent reconstruction is of utmost importance. Aortic dimensions exhibit considerable variability due to the pulsatile motion of the vessel wall, especially in younger individuals. Our prior research investigated pulsatility along the aortic course in elderly atherosclerotic patients, followed by assessing younger patients' aortic pulsatility, primarily in the descending aorta. However, aneurysmatic patients' aortic pulsatility has not yet been assessed. Significantly differing aortic diameters between systole and diastole may pose a potential risk of undersizing stent grafts. The pulsatile behavior of aortic segments used as landing zones for EVAR, raises concerns about complications like endograft migration or endoleaks. Furthermore, with the increasing number of TEVAR using the ascending aorta as a landing zone, diameter changes within this segment may also be important.

1.2. Endoanchors in Endovascular Aortic Repair

Effective proximal fixation is crucial for the success of EVAR. The term "hostile neck" encompasses anatomical features of the initial segment of the infrarenal aorta that might compromise endograft fixation. Hostile neck configurations include short, thrombotic, calcified, angulated, dilated, and conical shapes. In EVAR with a hostile neck as a proximal landing zone, the use of endoanchors has emerged as a promising technique. This small, corkscrew-shaped metal object is implanted through a dedicated system, screwing into the aortic wall through the endograft's textile material. This process enhances fixation in the proximal landing zone, preventing type Ia endoleaks and endograft migration.

1.3. Endovascular Aortic Repair in Hungary

Aligned with global and European trends, endovascular aortic procedures are progressively establishing themselves as routine in vascular care across Hungary. The analysis of data on aortic procedures performed in Hungarian centres is of great importance. This data analysis stands as a valuable contribution to the enhancement of vascular medicine in Hungary, aligning it with contemporary standards and practices in the field.

2. Objectives

Three studies on the current state of aortic disease management have contributed to this thesis, with the following objectives:

2.1. Aortic Pulsatility in Patients with AAA

Pulsatile changes of aortic diameter between systole and diastole may pose a challenge in endograft sizing. In our first, retrospective study, the primary purpose of our research was to investigate aortic pulsatility in 31 patients with AAA. Our secondary goal was to examine the potential correlation between systolo-diastolic pulsatile changes of the aortic diameter and aneurysm growth rate.

2.3. Use of Endoanchors in EVAR in Hungary

In our second, retrospective study, our purpose was to analyse the perioperative and early risk, as well as the success rate of EVAR with adjunct endoanchors in the Hungarian patient population. 14 cases of the procedure were examined.

2.4. TEVAR in Hungary Between 2012 and 2016

In our third study, our aim was to create a national database with perioperative data and 5-year mortality outcome of 131 TEVAR cases performed in Hungary.

3. Methods

3.1. Aortic Pulsatility Assessment in Patients with AAA

In this retrospective, single-center study, we analyzed readily accessible images of 31 patients who underwent CTA as part of their routine AAA surveillance at the Semmelweis University Heart and Vascular Centre. For our research, we selected a cohort of patients who had undergone a minimum of two aortic CTA scans with a time interval of at least four years between them. The examinations utilized for this study were conducted between 24/11/2005, and 12/06/2020.

CTA scans were performed with retrospective ECG gating, covering the entire aorta and iliofemoral arteries. Employing retrospective ECG-gating with a helical protocol reduced artifacts from aortic motion, enabling acquisition in systolic and diastolic phases. Iterative reconstructions were performed with 1 mm slice thickness, 1 mm increments for every 10% of the R-R cycle, resulting in 10 image series per patient. Acquired data was then analyzed on a dedicated workstation.

CTA series were evaluated with 3mensio Vascular software. After manually placing markers into the aortic root, bifurcation and common femoral arteries, automatic lumen segmentation was performed. An ellipsoid contour was manually drawn along the outer wall of the aorta, in the cross-sectional plane. This allowed the effective aortic diameter to be determined. Measurements were taken at various positions, including Z0, Z3, Z5, Z6, Z8, and Z9 (the largest diameter of the AAA).

Taking our previous findings into consideration, each measurement was made in both the systolic series at 30% of the R-R cycle and the diastolic phase at 90%. The positions along the midline remained constant in both phases. A total of 24 measurements were obtained for each patient, resulting in a cumulative total of 744 pulsatility measurements.

Absolute pulsatility refers to the numerical difference in millimeters (mm) between the effective diameters (EDs) of the vessel, measured in systole and diastole (EDsys - EDdia). Relative pulsatility, on the other hand, is expressed as a percentage, calculated as the ratio of absolute pulsatility and the diastolic ED [(EDsys - EDdia) / EDdia].

The assessment of AAA expansion rate was conducted using CTA studies of the patients, which were performed independently from our research. These studies included baseline diagnostic scans as well as follow-up examinations for AAA surveillance.

3.2. Use of Endoanchors in EVAR in Hungary

In our retrospective, single-center study we analyzed data of patients who have undergone EVAR with adjunctive endoanchoring to treat hostile neck AAAs, performed at the Semmelweis University Heart and Vascular Centre.

EVAR procedures utilizing the Heli-FX endoanchor system used for primary prophylactic indication were considered an index intervention. A prophylactic indication is when the procedure is performed because of a hostile neck to minimize the chance of development of a short- or long-term proximal endoleak. The definition of technical and clinical success was determined in concordance with the SVS reporting standards. Technical success was defined as placement of the number of endoanchors deemed necessary by the physician, adequate penetration, no technical complications, and no type I or III endoleak at 30-day follow-up. Clinical success was characterized by the patient's survival without major adverse aorta-related events.

Depending on the results of the routine 30-day follow-up CTA, US or CTA was performed annually or more frequently if complications were suspected. The aneurysmal sac was considered unchanged, if no more than 5 mm change was observed. An increase in aortic diameter of more than 5 mm counted as enlargement, and shrinkage was defined as a decrease in aneurysm diameter of more than 5 mm. We recorded aneurysm sac diameter at baseline and follow-up. Mean follow-up time was 7.0 ± 9.9 month. We describe technical complications during the procedure by describing the success rate and mortality rate assessed on follow-up.

3.3. TEVAR in Hungary Between 2012 and 2016

In our retrospective, multicenter study, we collected perioperative and long-term data from all Hungarian tertiary centers that performed TEVAR between 01/01/2012 and 31/12/2016. Long-term mortality data were collected and verified via official death records of the National Health Insurance Service to ensure data consistency and accuracy. Our data was collected and systematized at the Semmelweis University Heart and Vascular Centre. As a result, we have developed our dataset into a national database, which includes all TEVAR performed in Hungary in the above mentioned 5-year period. Long-term survival analysis was performed using Kaplan-Meier test.

3.4. Statistical Analysis

Continuous variables were presented as either mean ± standard deviation (SD) or median with interquartile ranges, while categorical variables were presented as numbers and percentages. Normality of continuous parameters was assessed using the Kolmogorov-Smirnov test. A paired t-test was used to compare systolic and diastolic measurements. One-way repeated measures analysis of variance (ANOVA) was used to compare absolute and relative pulsatility values along the aorta. Correlation between different continuous variables was assessed using Pearson correlation analysis. Two-sided $p<0.05$ was considered statistically significant for all evaluations. Kaplan-Meier analysis was conducted for mortality assessment. Calculations were performed using SPSS software.

4. Results

4.1. Aortic Pulsatility Assessment in Patients with AAA

806 measurements were conducted for assessing aortic pulsatility and AAA growth rate in a total of 31 patients (25 men) with a median age of 73 years.

At every measuring point, significantly larger maximum systolic diameters were observed compared to diastolic measurements: Z0: 34.82±2.96 mm versus 34.62±2.78 mm, Z3: 30.73±4.40 mm versus

30.31±3.27 mm, Z5: 28.53±2.97 mm versus 28.31±4.07 mm, Z6: 27.02±3.76 mm versus 27.00±3.22 mm, Z8: 23.97±4.61 mm versus 23.43±4.47 mm, Z9: 40.55±7.33 mm versus 39.90±7.33 mm, all with $p<0.001$.

The mean values for absolute and relative pulsatility were determined based on the dual measurements. There were no significant differences in the absolute pulsatility values between the measured positions, with the following mean values: Z0: 0.7±0.8 mm, Z3: 1.0±0.6 mm, Z5: 1.0±0.6 mm, Z6: 0.8±0.7 mm, Z8: 0.7±1.0 mm, Z9: 0.9±0.9 mm ($p=0.62$) [Figure 1].

While relative pulsatility values showed a tendency to decrease along the course of the aorta, the difference in these values was not statistically significant. The calculated relative pulsatility values were as follows Z0: 2.3%±2.3%, Z3: 3.6%±2.1%, Z5: 3.6%±2.5%, Z6: 3.2%±2.5%, Z8: 2.9%±4.4%, Z9: 2.2%±2.2% [Figure 2]. Both absolute and relative aortic pulsatility peaked at Z3, with values of 1.0 mm and 3.6% respectively.

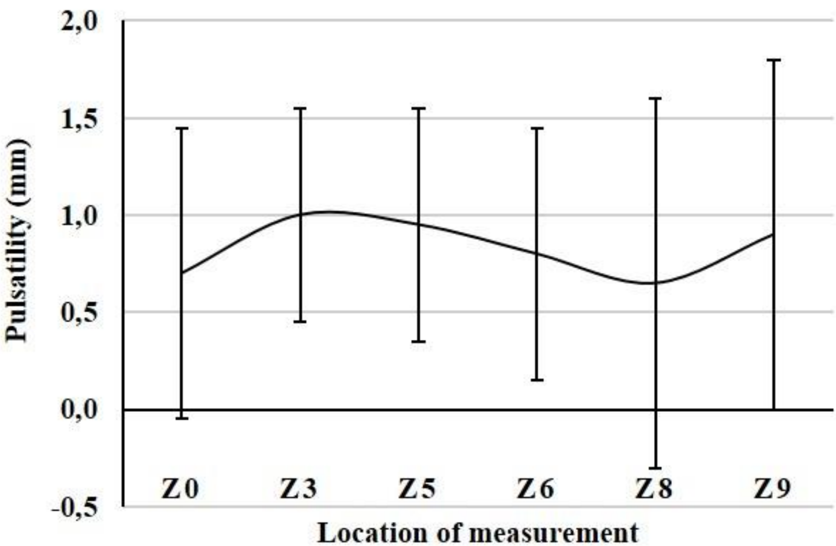

Figure 1: Absolute pulsatility values.

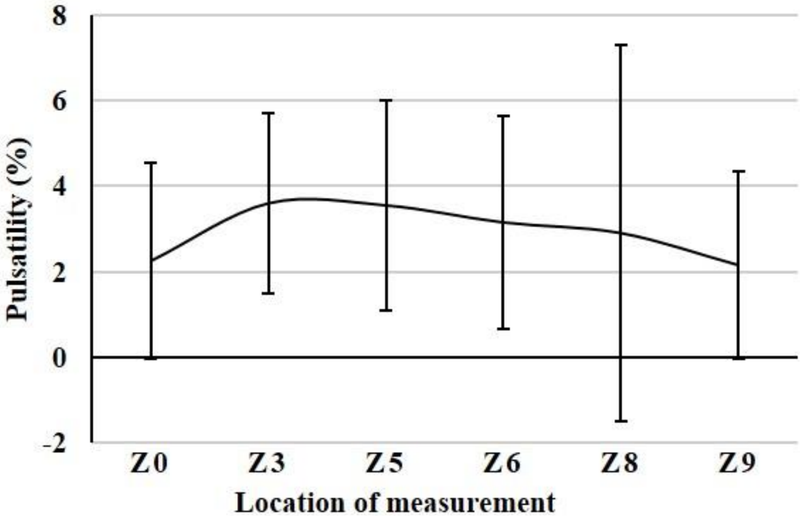

Figure 2: Relative pulsatility values.

During the evaluation of aneurysm growth rate, maximum diameters of the AAAs were recorded from baseline and latest preoperative follow-up images. The average time interval between the two examinations was 5.5±2.2 years. The mean absolute diameter of the aneurysms changed from 41.6±7.3 mm to 52.8±11.3 mm during the observed time frame. The average extent of aneurysm growth was 13.4±9.1 mm over the observed period, equivalent to an average yearly growth rate of 2.5±1.6 mm, assuming that the growth rate of the AAAs was constant.

When examining the correlation between absolute or relative aortic pulsatility values at each position and the growth rate of the aneurysms, no significant associations were found.

4.2. Use of Endoanchors in EVAR in Hungary

Between 01/01/2019, and 30/09/2021, a total of 14 EVAR were performed with adjunct endoanchors with prophylactic indication (11 men, mean age: 70.4 ± 8.1 years) [Figure 3].

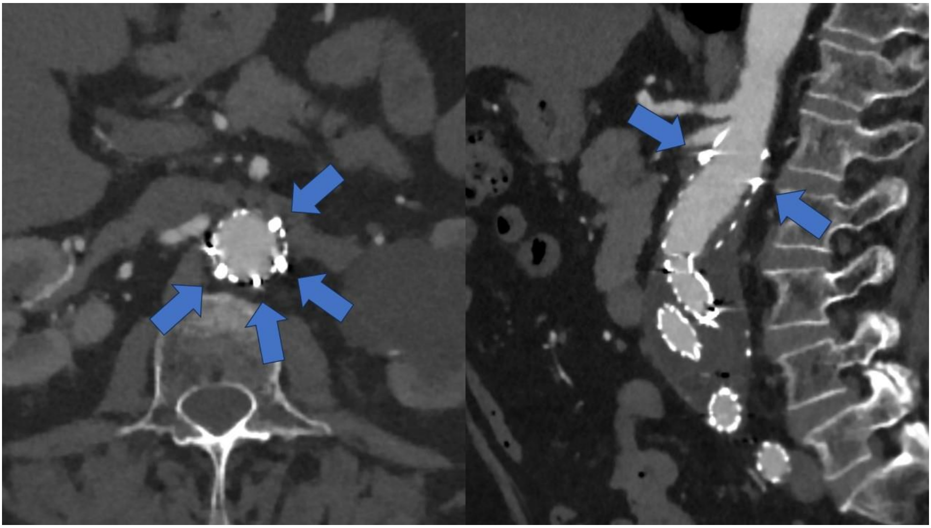

Figure 9: Postoperative follow-up CTA scan after EVAR supplemented with endoanchors. Oblique planar reconstructions show endoanchors (arrows) screwed into the endograft in order to seal the proximal neck used as landing zone. (Image by the author)

During the interventions, no technical complications occurred. In one case in which endoanchors were used to treat an intraoperative type Ia endoleak, a smaller persisting type Ia endoleak was confirmed during the 30-day imaging control. Therefore, the technical success rate was 92.9% (13/14).

The average initial aneurysm sac diameter of 64.9 ± 10.8 mm decreased to 60.6 ± 11.8 mm by the end of the 7.0 ± 9.9-month follow-up period, representing no significant change in the average diameter. Significant shrinkage was observed in 21.4% of the cases (3/14). In the remaining cases, the AAA was stable (11/14, 78.6%). Aneurysm sac growth was not shown in any of the cases (0/14, 0%). No mechanical complications were detected (endoanchor breakage or migration) during the follow-up period. We detected type II endoleaks in nearly half of the cases (6/14, 42.9%) during follow-up. Since none of these cases were associated with sac growth, conservative treatment was chosen. No reintervention took place (0/14, 0%). During follow-up, we lost one patient due to a complication unrelated to the aorta, hence our mortality rate is 7% (1/14), and our clinical success rate is 92.9% (13/14).

4.3. TEVAR in Hungary Between 2012 and 2016

In Hungary, between 01/01/2012 and 31/12/2016, a total of 131 TEVAR procedures were performed at the Semmelweis University Heart and Vascular Centre and 5 other major vascular centres.

The mean age of the patients undergoing the procedure was 62.80 ± 15.3 years. 67.18% of the patients were male. The percentage of diabetic patients was 13.74%. The TEVAR was performed in an acute setting in 25.19% of cases, while it was elective in 74.81% of cases. Regarding the indications, TAA was the most common among the conditions requiring TEVAR, accounting for 64.89% of the procedures. TAA rupture was present in 16.47% of cases. TBAD was the second most common disease, which indicated 17.56% of TEVAR surgeries. Within the TBAD repairs, the proportion of acute interventions was 73.91%. In 6.87% of all cases, the indication for implantation was blunt thoracic aortic injury, while in the remaining 10.69%, TEVAR was required for other reasons (postoperative endoleak, IMH, PAU). Debranching surgery on the supra-aortic branches was performed in 26.72% of the endograft implantations.

In the early postoperative period, stroke occurred in 4.58% of cases, temporary renal replacement therapy was required in 1.53% of cases during postoperative intensive therapy, and bowel ischemia developed in 2.29%. Within 30 days after TEVAR, reoperation was needed in 5.34% of patients. Mortality within 30 days was 9.92% [Figure 4]. In the examined 5-year follow-up period, long-term mortality was 16.03%.

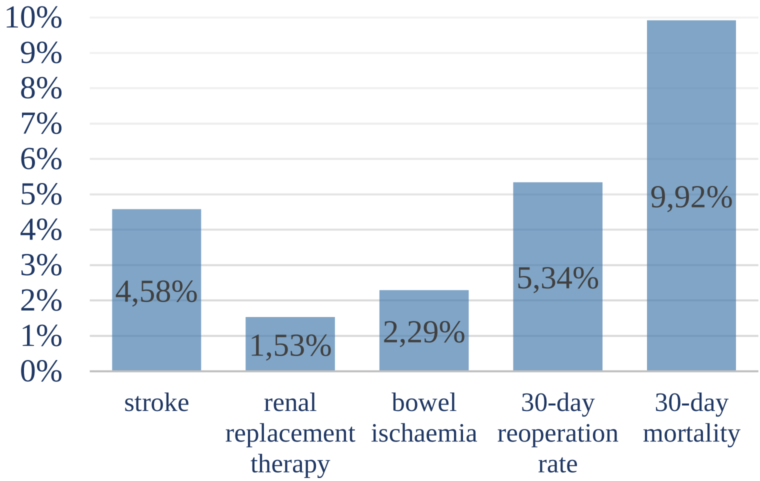

Figure 4: Rate of postoperative complications after TEVAR in Hungary between 2012 and 2016.

5. Conclusions

Our research has provided important insights into the state-of-the-art planning of endovascular aortic interventions and the current status quo of this field in Hungary.

Aortic pulsatility is generally less than 1 mm (5%). Therefore, the commonly used 10-20% oversizing in EVAR planning may be sufficient and the use of systolic phase images instead of diastolic phase images for stent graft sizing is likely not necessary. The need for further oversizing for a landing zone on the ascending aorta is questionable. There is no apparent correlation between aortic pulsatility and the long-term expansion rate of aneurysms, suggesting that this parameter is unlikely to serve as a predictor of AAA growth.

We also confirmed the effectiveness of the national use of endoanchors during EVAR performed on patients with a hostile neck. We found high technical and clinical success rate during the early follow-up, and a low complication rate, without mortality related to the aorta. The method can be used successfully and safely for the endovascular treatment of juxtarenal aneurysms.

TEVAR is a reliable and successful method for the modern treatment of thoracic aortic diseases. National data support the advantages of endovascular intervention over open surgery. Multidisciplinary collaboration is needed to ensure that our patients can receive the highest level of care currently available.

6. Bibliography of the Candidate's Publications

6.1. Publications related to the present thesis

1. Fontanini DM, Huber M, Vecsey-Nagy M, Borzsák S, Csőre J, Sótonyi P, et al. Pulsatile Changes of the Aortic Diameter May Be Irrelevant Regarding Endograft Sizing in Patients With Aortic Disease. J Endovasc Ther. 2023:15266028231172368. **IF: 2.6**

2. Fontanini DM, Borzsák S, Vecsey-Nagy M, Jokkel Z, Szeberin Z, Szentiványi A, et al. [Endoanchoring may be effective in the endovascular aortic repair of juxtarenal aneurysms]. Orv Hetil. 2022;163(16):631-6. **IF: 0.6**

3. Fontanini DM, Fazekas G, Vallus G, Juhász G, Váradi R, Kövesi Z, et al. [Thoracic aortic stentgraft implantations in Hungary from 2012 to 2016]. Orv Hetil. 2018;159(2):53-7. **IF: 0.564**

6.2. Publications not related to the present thesis

1. Borbély K, Balogh H, Kardos IB, Fontanini DM, Oláh L, Berényi E, et al. Cadasil syndrome: Long-term follow-up on MRI. Imaging. 2022;14(2):109–12. doi:10.1556/1647.2022.00059

2. Juhász G, Csőre J, Suhai FI, Gyánó M, Pataki Á, Vecsey-Nagy M, et al. [Diagnostic performance of non-contrast magnetic resonance angiography in patients with lower extremity arterial disease]. Orv Hetil. 2022;163(45):1782-8.

3. Borzsák S, Süvegh A, Szentiványi A, Fontanini DM, Vecsey-Nagy M, Banga P, et al. Midterm Results of Iliac Branch Devices in a Newly Established Aortic Center. Life (Basel). 2022;12(8).

4. Csőre J, Suhai FI, Gyánó M, Pataki Á A, Juhász G, Vecsey-Nagy M, et al. Quiescent-Interval Single-Shot Magnetic Resonance Angiography May Outperform Carbon-Dioxide Digital Subtraction Angiography in Chronic Lower Extremity Peripheral Arterial Disease. J Clin Med. 2022;11(15).

5. Vecsey-Nagy M, Jermendy Á L, Kolossváry M, Vattay B, Boussoussou M, Suhai FI, et al. Heart Rate-Dependent Degree of Motion Artifacts in Coronary CT Angiography Acquired by a Novel Purpose-Built Cardiac CT Scanner. J Clin Med. 2022;11(15).

6. Csobay-Novák C, Pataki Á, Fontanini DM, Borzsák S, Banga P, Sótonyi P. [Branched endovascular aortic repair of a contained rupture in chronic aortic dissection]. Orv Hetil. 2022;163(22):886-90.

7. Borzsák S, Szentiványi A, Süvegh A, Fontanini DM, Vecsey-Nagy M, Banga P, et al. Complex Aortic Interventions Can Be Safely Introduced to the Clinical Practice by Physicians Skilled in Basic Endovascular Techniques. Life (Basel). 2022;12(6).

8. Csobay-Novák C, Fontanini DM. Angiológia a háziorvosi gyakorlatban: Műszeres vizsgálatok: CT- és MR-diagnosztika az angiológiában. Farkas K, Kolossváry E. SpringMed, Budapest, Hungary, 2021. 57-67 p.

9. Vecsey-Nagy M, Jermendy ÁL, Suhai FI, Panajotu A, Csőre J, Borzsák S, et al. Model-based adaptive filter for a dedicated cardiovascular CT scanner: Assessment of image noise, sharpness and quality. Eur J Radiol. 2021;145:110032.

10. Csobay-Novák C, Entz L, Banga P, Pólos M, Szabolcs Z, Csikós G, et al. [Fenestrated endovascular repair of a thoracoabdominal aortic aneurysm in chronic dissection]. Orv Hetil. 2021;162(31):1260-4.

11. Mihály Z, Fontanini DM, Sándor Á D, Dósa E, Lovas G, Kolossváry E, et al. [Differences in guidelines for patients with carotid artery stenosis in some European countries]. Orv Hetil. 2020;161(51):2139-45.

12. Ferencz AB Bárczi G, Heltai K, Zima E, Kovács A, Molnár L, Fontanini DM, Szűcs A, Kiss AR, Gyánó M, Benke K, Németh E, Fazekas L, Szigyártó I, Becker D, Merkely B. An exceptional case of myocarditis: from non-specific symptoms to the ECMO. Cardiologia Hungarica. 2019;49: Suppl. B pp. B68-B68.

13. Csobay-Novák C, Fontanini DM. Vaszkuláris Medicína: Vaszkuláris CT és MR diagnosztika. Sótonyi P, Szeberin Z. Semmelweis; Budapest, Hungary, 2018. 25-8 p.

14. Mihály Z, Banga P, Szatai L, Simonffy Á, Fontanini DM, Bélteki J, et al. [Endovascular treatment of blunt thoracic aortic injuries]. Magy Seb. 2017;70(1):13-7.

15. Csobay-Novák C, Fontanini DM, Szilágyi B, Szeberin Z, Kolossváry M, Maurovich-Horvat P, et al. Thoracic Aortic Strain is Irrelevant Regarding Endograft Sizing in Most Young Patients. Ann Vasc Surg. 2017;38:227-32.

16. Csobay-Novák C, Fontanini DM, Szilágyi BR, Szeberin Z, Szilveszter BA, Maurovich-Horvat P, et al. Thoracic aortic strain can affect endograft sizing in young patients. J Vasc Surg. 2015;62(6):1479-84.