ISSN 2305-3127 (Print)•2664-3790 (Online). Кардіохірургія та інтервенційна кардіологія. 2022. № 1–2. С. 18–27.

УДК 616.018.2+616.132-089.843 DOI: http://doi.org/10.31928/2305-3127-2022.1-2.1827

A.Yu. Shkandala [1], B.M. Todurov [1, 2], S.M. Furkalo [2, 3], A.V. Khokhlov [1, 2], O.V. Zelenchuk [1, 2]

[1] Heart Institute, Ministry of Healthcare of Ukraine, Kyiv, Ukraine
[2] Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine
[3] O.O. Shalimov National Institute of Surgery and Transplantology of NAMS of Ukraine, Kyiv, Ukraine

Thoracic endovascular aneurysm repair in patients with connective tissue disorders

The contemporary data regarding the role of the thoracic endovascular aneurysm repair (TEVAR) in patients with connective tissue disorders (CTD) are reviewed. We performed search of the data in electronic databases PubMed, SCOPUS, Embase, Google Scholar OVID, related to the use of TEVAR. Currently, there is a limited amount of large cohort size studies outlining the use of TEVAR in patients with CTD. Endovascular prosthetics of the thoracic aorta in patients with accidents is dangerous because of the progressive dilatation of the aorta and the high probability of further re-interventions in later life. The analysis showed that open reconstruction still remains a gold standard of intervention in young patients with progressive CTDs, especially in acute type of aortic dissection. However, long-term data need to be published to support this practice.

Key words: aorta, thoracic, dilatation, aneurysm, dissecting, aortic diseases, endovascular procedures.

To cite this article: Shkandala A, Todurov BM, Furkalo SM, Khokhlov AV, Zelenchuk OV. Thoracic endovascular aneurysm repair in patients with connective tissue disorders. *Cardiac Surgery and Interventional Cardiology*. 2022. № 1–2. С. 18–27.

Посилання: Шкандала А.Ю., Тодуров Б.М., Фуркало С.М., Хохлов А.В., Зеленчук О.В. Ендоваскулярне протезування грудного відділу аорти в пацієнтів із захворюваннями сполучної тканини. *Кардіохірургія та інтервенційна кардіологія.* 2022;1–2:18–27.

Connective tissue is a supporting structural material found throughout the body. It consists of proteins such as collagen and elastin, providing extracellular binding and support in various tissues and organs [66]. Hereditary genetic abnormalities may lead to the connective tissue disorders (CTDs), tissue degeneration and loss of structural integrity [15].

More than 50 connective tissue diseases are known. The most common CTDs associated with aortic disease are Marfan syndrome (MFS), vascular Ehlers – Danlos syndrome (EDS), and Loeys – Dietz syndrome (LDS) [51]. Aortic disease is the most prevalent cause of high morbidity and mortality in this patient population, and surgical repair is one of the main treatment options available [13]. Aorta, being exposed to a high pressure because of constant blood flow, becomes weakened; therefore, it is at increased risk of developing aneurysm, rupture, and dissection [14]. According to the existing guidelines, open surgical aortic prosthetics is a gold standard of treatment in this cohort of patients. However, most patients with CTD may require several aortic surgeries during their lifetime. Recent studies have shown that endovascular aortic prosthesis has a lower success rate in patients with CTD, and therefore it is not a method of choice in this population.

This article aims to review the current literature data to determine the role of endovascular thoracic aortic prosthetics in patients with CTDs. A comprehensive literature search has been conducted in the main electronic databases (PubMed, SCOPUS, Embase and Google Scholar) to identify articles discussing use of the thoracic endovascular aneuryam repair (TEVAR) in patients with CTDs. Three main diseases affecting aorta are Marfan syndrome, vascular Ehlers – Danlos syndrome and Loeys – Dietz syndrome.

Шкандала Анна Юріївна, лікар-кардіолог відділення хірургічного лікування ішемічної хвороби серця
E-mail: annashkandala@gmail.com

Стаття надійшла до редакції 15 травня 2022 р.

Marfan syndrome

MFS occurs in approximately 2-3 cases in 10,000 people [46] and is diagnosed according to a set of clinical data known as the revised Ghent criteria [61]. The disease is caused by an autosomal dominant mutation in the fibrillin-1 gene (FBN1). The FBN1 gene is located on chromosome 15q21.1 and is responsible for the production of proteins that form the extracellular matrix involved in the attachment of smooth muscle to collagen and elastin fibers [14, 46], increasing structural integrity of the aortic walls *(Fig. 4)*. Transforming growth factor-β (TGFB) becomes overactive in the presence of the defective FBN1 gene and causes inflammation and aortic fibrosis. This results in weakness of the aortic wall, leading to the expansion and formation of aneurysms, appearing in approximately 80 % patients with MFS [46]. The aortic ring, root, and ascending aorta are the sites most often affected by progressive weakening [68] *(Fig. 1)*.

Valsalva sinus dilatation starts already in utero [4]. As the patient grows, increasing the size of the aorta increases the likelihood of rupture [48]. Adults with aortic root diameter > 45 mm are advised to consider surgery. A fixed diameter requiring surgery in children has not been established. However, growth by more than 1 cm per year, problems with valve insufficiency and Z-index > 2-3 in the diameter of the aortic root are considered as unfavorable prognostic factors [66].

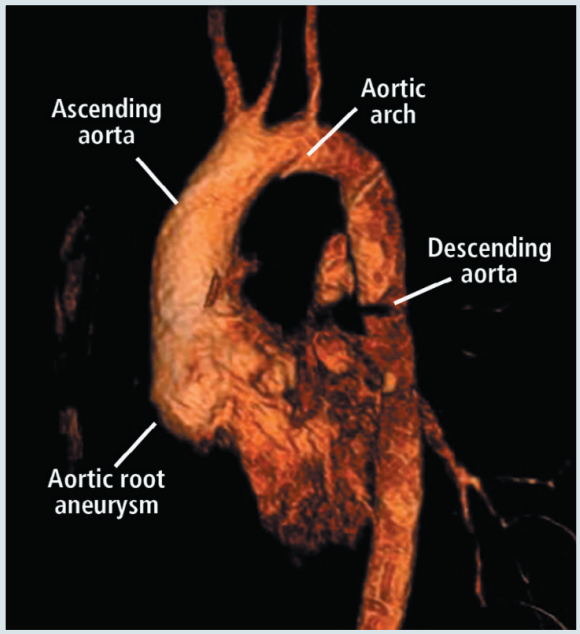

Fig. 1. **A three-dimensional computed tomography of aorta showing aortic root aneurysm in a patient with Marfan syndrome [50]**

The average life expectancy of patients with MFS is about 60 years [22]. *Figures 1* and *2* show examples of aneurysms and descending thoracic dissection, and *Figures 3* and *4* show aortic tissue histology in Marfan patients [2, 3, 56, 60].

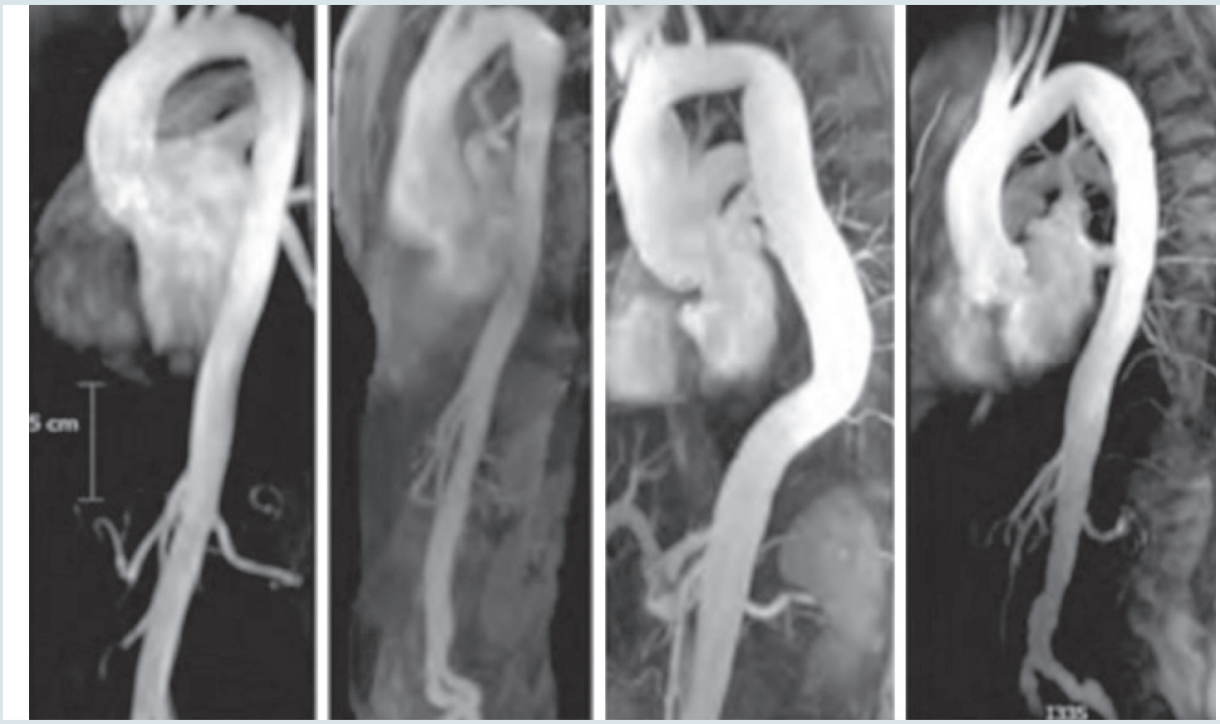

Fig. 2. **Aortic imaging of a patient with Marfan syndrome showing dilatation of the thoracic aorta [38]**

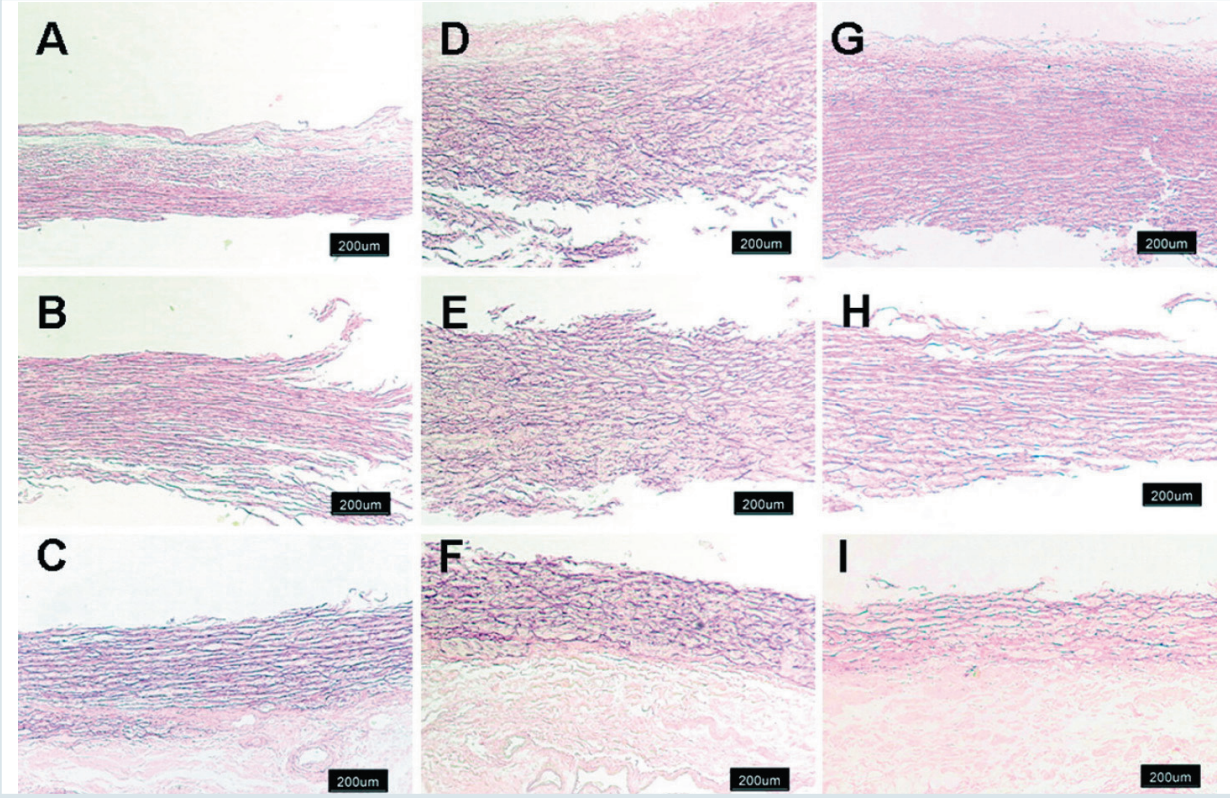

Fig. 3. **Histology and separation of aortic tissue for proteomic analysis. Van Gieson elastic stain of aorta from representative control (A through C) and aneurysmal aorta from Marfan syndrome (MFS) patients (D through F) and bicuspid aortic valve patients (G through I) are shown. Aorta from MFS patients presents fragmentation of elastic fibers and thickened aortic wall (magnification × 4). Intima with media (A, D, and G), separated media (B, E, and H), and media with adventitia (C, F, and I) are shown [42]**

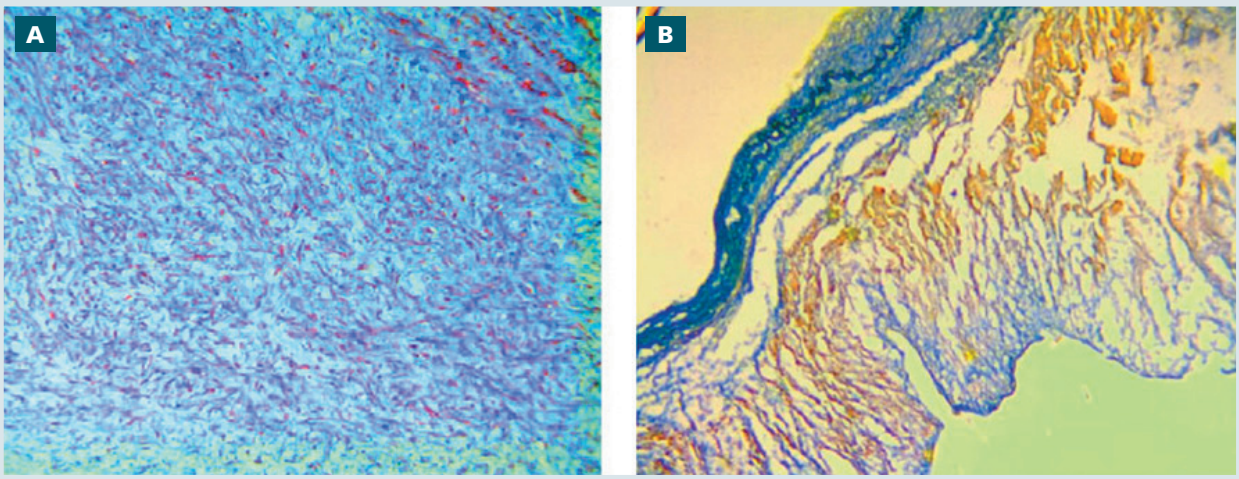

Fig. 4. **Marfan aortic tissue showing cystic medial necrosis with (A) smooth muscle fragmentation and more collagen deposition, Masson ´200; and (B) proliferation and disruption of the intima (blue), and smooth muscle cell fragmentation (yellow) and collagen deposition (red) in the media. VG-Victoria blue bichrome staining ´100 [71]**

Ehlers – Danlos syndrome

EDS refers to a range of genetic disorders affecting collagen production; therefore, it results in joint and skin defects, as well as tissue fragility [13]. There are seven main classifications of EDS, with vascular EDS type IV [3] being most commonly related to cardiovascular complications. In vascular EDS, there is a mutation in the COL3A1 gene which encodes type III procollagen [34, 62]. Type III procollagen makes up the highest proportion of collagen in the aortic wall; therefore, its defect results in severe aortic wall fragility and increased risk of rupture [34, 54]. Vascular EDS usually affects the descending or abdominal aorta [57], and the risk of rupture, unlike MFS, can occur with any diameter [57]. A high incidence of vessel rupture reduces the life expectancy of vascular EDS patients to about 48 years, as opposed to 60 years in MFS patients [57].

Loeys – Dietz syndrome

LDS is caused by a heterozygous mutation in the TGFBR1 and TGFBR2 genes, which encode TGFB receptors I and II, respectively. The mutation triggers an increase in collagen production, while reducing the production of elastin and disrupting the assembly of elastin fibers. LDS is categorized into two main groups, namely, type 1 and type 2. Both conditions can cause vascular diseases in the form of aortic aneurysm, arterial tortuosity, and aortic dissection [34, 54]. Unlike MFS, in LDS, the aortic root is prone to rupture and dissection during childhood and at even smaller diameters. Aneurysms occur less frequently in LDS, at a rate of 9 % [1]. However, the aorta is prone to the increased growth rate and can sometimes be as twice as its normal size in the thoracic region [31]. Close monitoring as well as early surgical intervention are advised to prevent catastrophic outcomes. However, the mean life expectancy for LDS patients remains low, at about 37 years, although sporadic cases have been reported to live as late as 70 years of age [37, 45].

Diagnosis of the aortic aneurysm

Most patients with thoracic aortic aneurysms are asymptomatic at the time of diagnosis, because aneurysms are typically discovered incidentally on imaging studies (chest X-ray, CT scan, or echocardiogram) ordered for other indications *(Fig. 5)*.

A true aortic aneurysm is defined as a localized dilatation involving all three layers of the aorta. The diameter should be at least 1.5 times that

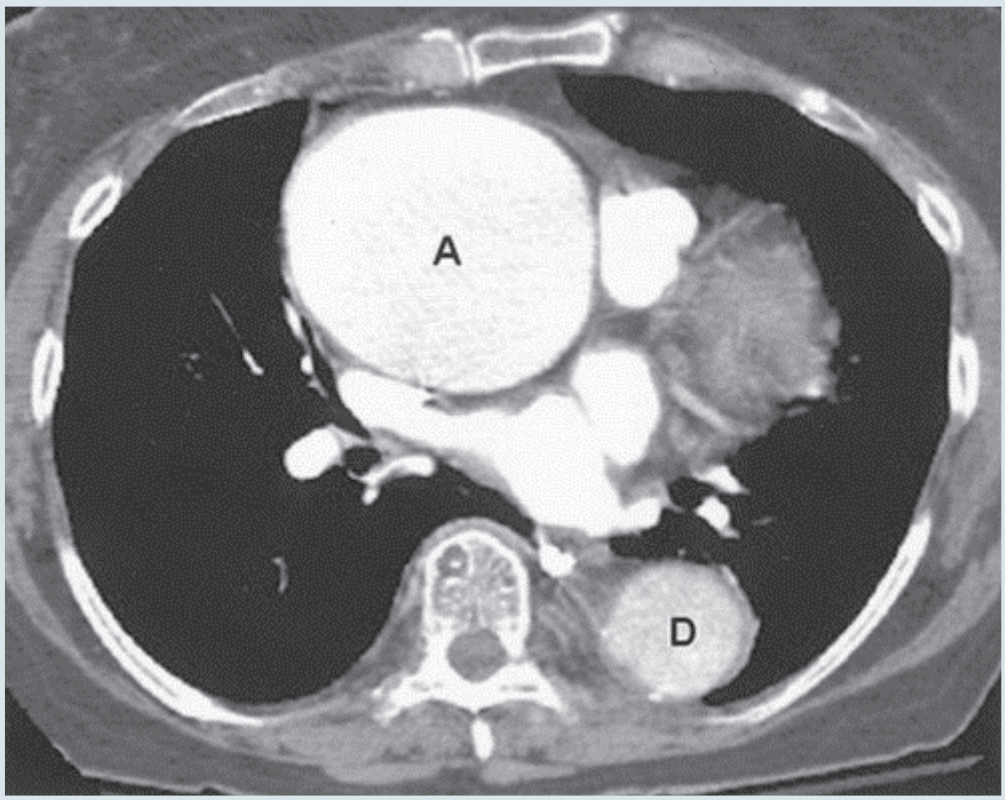

Fig. 5. **Contrast-enhanced CT scan demonstrating a 7.5 × 8.3 cm ascending thoracic aortic aneurysm. A – indicates ascending; D – descending**

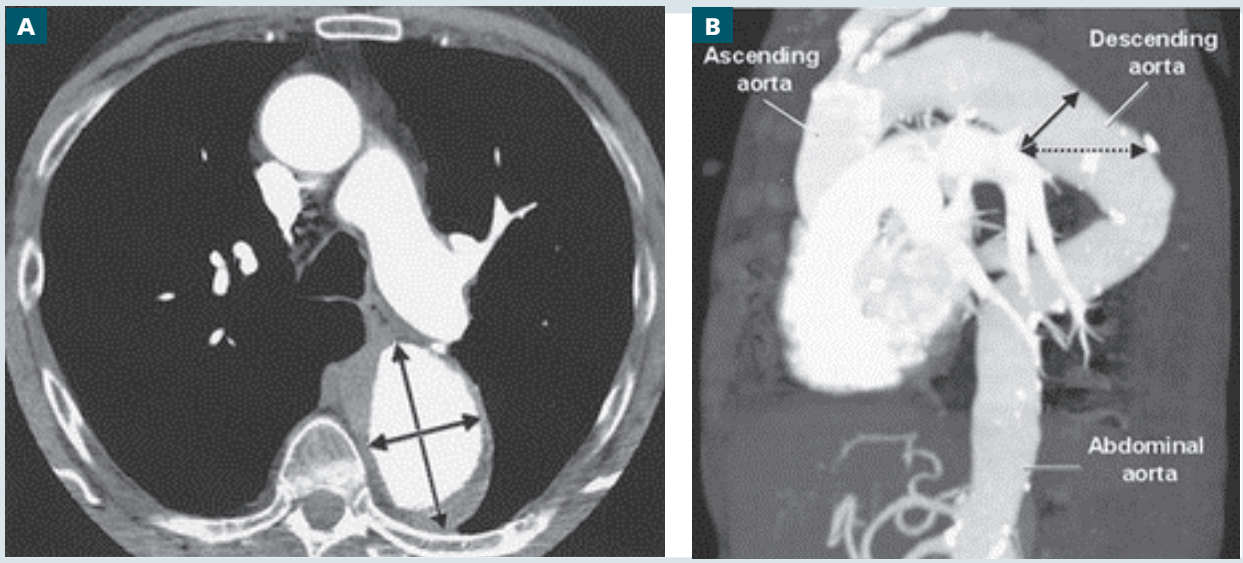

Fig. 6. **A – standard axial image from a contrast-enhanced CT scan showing what appears to be an oval-shaped descending thoracic aortic aneurysm, appearing to measure as much as 8.0 × 5.2 cm in diameter (arrows). B – three-dimensional reconstruction in a left anterior oblique view of same CT scan demonstrating that the descending aorta is tortuous and was consequently cut off-axis (dotted arrow) on axial CT image. The true maximal diameter of this aortic segment was only 5.6 cm (solid arrow)**

of the normal diameter to be considered as true aneurysm. Thoracic aortic aneurysm (TAA) may occur in the aortic root/ascending aorta (60 %), aortic arch (40 %), and the descending aorta including the thoracoabdominal aorta (10 %) [7]. The normal aortic diameter varies with age, gender, as well as ranges in population. *E.g.*, a diameter > 4.5 cm is considered aneurysmal in the United States of America, whereas a diameter > 4 cm is defined as aneurysmal in South Korea, > 4.2 cm – in Ukraine [20].

TAAs are associated with CTD and can lead to aortic incompetence, rupture, and acute dissection. This is the leading cause of premature death in patients with MFS. The pathological hallmark of aneurysmal disease in CTD is cystic medial necrosis, which results from degenerative disruption of collagen, elastin, or smooth muscle, leading to weakening of the arterial wall [35].

Early diagnosis and treatment before the development of life-threatening complications is a key to managing TAAs. Useful imaging modalities include chest X-rays, transthoracic and transoesophageal echocardiography, multidetector computed tomography (CT) of aorta, and magnetic resonance (MR) angiography *(Fig. 5)*. Clinically, contrast-enhanced CT of aorta is a standard imaging technique to diagnose aortic pathology with sensitivity up to 100 % and specificity up to 99 % [28].

A better understanding of genetics and inheritance patterns has allowed to improve screening for aortic disease. Consensus guidelines were developed in 2010 by the American College of Cardiology and the American Heart Association; the key recommendations include [16]:

- First-degree relatives of patients with aortic dissection or TAAs should be screened with aortic imaging to identify asymptomatic disease.
- MFS patients should have an immediate echocardiogram to assess the aorta and followed up in six months to check for enlargement.
- Patients with LDS should have complete aortic imaging immediately and six months later to check for enlargement and annual MR imaging from cerebrovascular circulation to the pelvis.

Once a diagnosis of TAA is established in a patient with underlying connective tissue disease, the primary treatment option is open surgical repair. Another important aspect in the management of patients developing aortic pathology is hypertensive control. Hypertension increases risk and accelerates the rate that pathology develops, therefore antihypertensive therapy is important in the management of aortic aneurysms [59].

The European Association of Cardiothoracic Surgery (EACTS), the European Association of Cardiologists and the European Association of Percutaneous Coronary Intervention in 2012 didn't recommend endovascular treatment in this group of patients. They emphasized that TEVAR is not recommended for patients with connective tissue disease unless the technique is considered as a rescue procedure or bridge before final open surgery or as a procedure after preoperative aortic surgery when

both landing areas lie within previously placed synthetic grafts [69].

The risk of intervention should be considered while deciding upon the treatment of TAA. That is why it must be balanced with the risk of rupture or dissection. Patients with a 6 cm aneurysm have a risk of annual rupture or dissection of 6.9 % and a mortality risk of 11.8 %. Risks increase significantly with aneurysms > 6 cm [69]. Current guidelines address the following factors [43] when considering an intervention:

- Aortic dilatation > 5 cm in patients with MFS, which is a lower threshold compared to the general population (> 5.5 cm) (IC level). Patients with a family history of acute exfoliation, severe aortic or mitral regurgitation, and a rate of increase of 3 mm / year have a lower surgical threshold, still with a diameter > 4.5 cm (IIC level) *(Fig. 7)*.
- Women with MFS contemplating pregnancy may undergo aortic root and ascending aorta replacement at a diameter of 4 cm as per American and Asian guidelines (level IIC), while European guidelines recommend a diameter > 4.5 cm.

In patients with LDS, an aortic diameter > 4 cm for the aortic root, > 5 cm for the descending thoracic aorta, and rate of increase > 0.5 cm/year are considered an indication for surgery, regardless of location [16].

TEVAR compared to the open repair

Today, among the leading specialists, open surgery is preferred for the restoration of thoracic aneurysms in patients with connective tissue diseases [23]. In such patients, the aortic wall is particularly fragile, and the radial force arising from stent graft placement may increase the circumferential load. Long-term radial force is a prerequisite for adequate fixation and sealing during stent graft deployment.

Nowadays, there are limited studies confirming the appropriateness of TEVAR in patients with FTA. A total of 81 % of the procedures were technically successful, with the stent transplant landed proximally. The rate of immediate complications is usually low: 1.9 % risk of death, 1.9 % risk of stroke, < 2 % risk of spinal ischemia, and 3.7 % risk of open surgery. However, long-term results have not yet been fully reported and need further evaluation with an appropriate follow-up period [36].

The re-intervention rate due to primary and secondary endoleaks is high and retrograde dissection can occur in patients undergoing TEVAR. The incidence of stent graft-induced re-entry tears is also significantly high, with 33 % reported in Marfan patients compared to 3 % in the general population and a mortality of nearly 30 % [26].

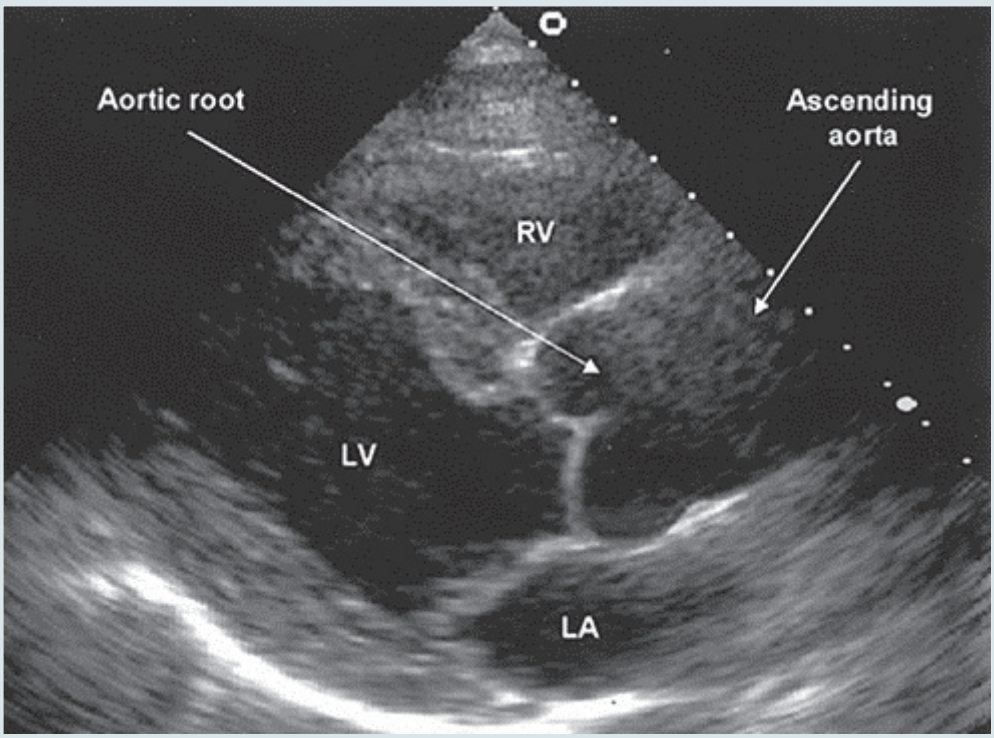

Fig. 7. **A transthoracic echocardiogram, in a parasternal long-axis view, demonstrating a dilated aortic root (4.4 cm) and ascending aorta (4.2 cm). Whereas the aortic root is well visualized, the ascending aorta is less so, as is often the case with transthoracic imaging. RV – indicates right ventricle; LV – left ventricle; LA – left atrium**

Endovascular repair is also not recommended for vascular EDS. In this cohort, even invasive angiography, unless absolute necessary, is to be avoided due to the high risk of vessel rupture, with one study showing a 67 % complication rate and 12 % mortality rate for digital subtraction angiography [9].

Future of the open repair

There have been no large studies directly comparing open surgical repair and endovascular repair in CTD patients. However, open surgery for aneurysm repair is a well-established technique with a low complication rate as it has a 100 % technical success rate. The perioperative mortality has been shown to range from 0 to 11.5 %, with an overall survival rate of 53–96 % [67]. The morbidity includes a risk of up to 6.5 % for paraplegia, risk of up to 13 % for permanent renal failure, and risk of up to 11 % for re-exploration for bleeding [4].

The complication rate in open surgery can be reduced by using extracorporeal partial left heart bypass, intraoperative cold renal perfusion, and cerebrospinal fluid drainage. It is also important to use branched grafts rather than visceral patches. In one review, visceral patches were used in 107 patients including 17 CTD patients [33, 41]. Visceral patch aneurysm expansion occurred in eight patients, among them three had CTD, which is a predisposing factor to patch aneurysm formation. The morbidity rate for open repair of patch aneurysm is 20–30 %, which is high compared to the primary operation and endovascular repair [10].

Endovascular surgery has a technical success rate ranging from 38 % to 100 % with a primary treatment failure rate of up to 44 %. Treatment failure may occur due to type I or type II endoleak, retrograde dissection, and ongoing dilatation of the false lumen in chronic dissection. The aorta distal to the stent graft fails and patients may develop recurrent aneurysms and acute dissections. The mortality rate ranges from 0 to 25 % with an overall survival of 75 to 100 %, which is comparable to open surgery, although only few studies have been done on small cohorts [39, 63]. This is encouraging as it shows endovascular therapy may safely be done in the short term, although concerns exist regarding longer-term outcomes and effectiveness. The perioperative morbidity includes a risk of paraplegia up to 3.3 %, risk of permanent renal failure up to 6.7 %, and risk of re-exploration for bleeding in up to 14 % of patients [41].

In view of the lower morbidity, endovascular therapy is possibly an option in patients who have an especially high risk of open surgery, such as elderly patients with multiple comorbidities [12]. However, patients with connective tissue diseases do not fall into this category as they tend to be younger and otherwise healthier. As it is a simpler and quicker technique, TEVAR is also recommended in emergency situations, such as aortic rupture, where it can be life-saving [12]. Endovascular repair is especially useful when the proximal and distal landing zones exist and is recommended in such situations (e.g., focal intercostal patch aneurysm, as part of the frozen elephant trunk procedure or hybrid procedures where a synthetic graft has been inserted previously via open surgery). The complication rate from endovascular therapy can be reduced further by using ultrasound guidance to obtain vascular access.

TEVAR does have a limited role in the management and treatment of aortic disease in patients with CTD, however due to the tissue and vasculature of these patients causing technical difficulties, open surgical repair is still a preferred treatment option. TEVAR also does not have better outcomes than open surgical repair, which still means open repair is the preferred treatment option. TEVAR may be the preferred treatment in selective patient groups who are at high risk of mortality or increased morbidity from open surgery; with further advances and improving outcomes over time, TEVAR could offer an alternative to open surgery in patients with multiple comorbidities.

In the period from 2008 to 2022, 42 patients with descending aortic aneurysm underwent TEVAR surgery at the Heart Institute. Among them, no patients with FTA were identified by genetic testing, however, phenotypically 6 of the patients had signs of connective tissue disease. They all received endovascular aortic prosthetics. In the remote period (after 6 months), there were no cases of reimplantation. These data may suggest that this technique should be considered for this cohort of patients, but the selection of patients should be personalized.

Conclusion

Open repair remains a gold standard method of intervention in young patients with progressive CTD, especially in the setting of acute type A aortic dissection. However, TEVAR can be sought as a reliable alternative in emergency setting of diseases involving the descending thoracic aorta; yet the long-term data needs to be published to support such practice.

References

1. Albornoz G, Coady MA, Roberts M, Davies RR, Tranquilli M, Rizzo JA, et al. Familial thoracic aortic aneurysms and dissections-incidence, modes of inheritance, and phenotypic patterns. *Ann Thorac Surg.* 2006;82(4):1400–5. doi:10.1016/j.athoracsur.2006.04.098.
2. Arslan-Kirchner M, von Kodolitsch Y, Schmidtke J. The importance of genetic testing in the clinical management of patients with Marfan syndrome and related disorders. *Dtsch Arztebl Int.* 2008;105(27):483-91. doi:10.3238/arztebl.2008.0483.
3. Black JH III. Aneurysms caused by connective tissue abnormalities. In: Cronenwett JL, Johnson KW, editors. Rutherford's vascular surgers. 7. Philadelphia: Saunders Elsevier; 2010. pp. 2168-85.
4. Böckler D, Meisenbacher K, Peters AS, Grond-Ginsbach C, Bischoff MS. Endovascular treatment of genetically linked aortic diseases. *Gefasschirurgie*. 2017;22(Suppl 1):1–7. doi:10.1007/s00772-016-0221-z.
5. Botta L, Russo V, La Palombara C, Rosati M, Di Bartolomeo R, Fattori R. Stent graft repair of descending aortic dissection in patients with Marfan syndrome: an effective alternative to open reoperation? *J Thorac Cardiovasc Surg.* 2009;138(5):1108-14. doi:10.1016/j.jtcvs.2009.03.014.
6. Cannavale A, Santoni M, Fanelli F, O'Sullivan G. Aortic dissection: novel surgical hybrid procedures. *Interv Cardiol.* 2017;12(1):56–60. doi:10.15420/icr.2016:16:3.
7. Cho IJ, Jang SY, Chang HJ, Shin S, Shim CY, Hong GR, et al. Aortic aneurysm screening in a high-risk population: a non-contrast computed tomography study in korean males with hypertension. *Korean Circ J.* 2014;44(3):162–9. doi:10.4070/kcj.2014.44.3.162.
8. Cikach F, Desai MY, Roselli EE, Kalahasti V. Thoracic aortic aneurysm: how to counsel, when to refer. *Cleve Clin J Med.* 2018;85(6):481-92. doi:10.3949/ccjm.85a.17039.
9. Cikrit DF, Miles JH, Silver D. Spontaneous arterial perforation: the Ehlers-Danlos specter. *J Vasc Surg.* 1987;5(2):248–55. doi:10.1016/0741-5214(87)90133-9.
10. Clough RE, Martin-Gonzalez T, Van Calster K, Hertault A, Spear R, Azzaoui R, et al. Endovascular repair of thoracoabdominal and arch aneurysms in patients with connective tissue disease using branched and fenestrated devices. *Ann Vasc Surg.* 2017;44:158–63. doi:10.1016/j.avsg.2017.05.013.
11. Cooper M, Black J. Aortic surgery for patients with connective tissue disorders. *Indian J Vasc Endovasc Surg.* 2015;(2):60–5. doi:10.4103/0972-0820.161943.
12. Coselli JS, Green SY, Price MD, Hash JA, Ouyang Y, Volguina IV, et al. Results of open surgical repair in patients with Marfan syndrome and distal aortic dissection. *Ann Thorac Surg.* 2016;101(6):2193–201. doi:10.1016/j.athoracsur.2015.11.008.
13. Cury M, Zeidan F, Lobato AC. Aortic disease in the young: genetic aneurysm syndromes, connective tissue disorders, and familial aortic aneurysms and dissections. *Int J Vasc Med.* 2013;2013:267215. doi:10.1155/2013/267215.
14. Dake MD, Kato N, Mitchell RS, Semba CP, Razavi MK, Shimono T, et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. *N Engl J Med.* 1999;340:1546–52.
15. Dake MD, Miller DC, Semba CP, Mitchell RS, Walker PJ, Liddell RP. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. *N Engl J Med.* 1994;331:1729–34.
16. Davies RR, Goldstein LJ, Coady MA, Tittle SL, Rizzo JA, Kopf GS, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg.* 2002;73(1):17–27; discussion 27-8. doi:10.1016/s0003-4975(01)03236-2.
17. den Hartog AW, Franken R, Zwinderman AH, Timmermans J, Scholte AJ, van den Berg MP, et al. The risk for type B aortic dissection in Marfan syndrome. *J Am Coll Cardiol.* 2015;63(3):246–54. doi:10.1016/j.jacc.2014.10.050.
18. Di Bartolomeo R, Leone A, Di Marco L, Pacini D. When and how to replace the aortic arch for type A dissection. Ann *Cardiothorac Surg.* 2016;5(4):383-8. doi:10.21037/acs.2016.07.07.
19. Di Bartolomeo R, Murana G, Di Marco L, Pantaleo A, Alfonsi J, Leone A, et al. Frozen versus conventional elephant trunk technique: application in clinical practice. *Eur J Cardiothorac Surg.* 2017;51(suppl 1):i20-8. doi:10.1093/ejcts/ezw335.
20. Di Cesare E, Splendiani A, Barile A, Squillaci E, Di Cesare A, Brunese L, et al. CT and MR imaging of the thoracic aorta. *Open Med (Wars).* 2016;11(1):143–51. doi:10.1515/med-2016-0028.
21. Di Eusanio M, Trimarchi S, Peterson MD, Myrmel T, Hughes GC, Korach A, et al. Root replacement surgery versus more conservative management during type A acute aortic dissection repair. *Ann Thorac Surg.* 2014;98(6):2078-84. doi:10.1016/j.athoracsur.2014.06.070.
22. Dietz HC, Cutting GR, Pyeritz RE, Maslen CL, Sakai LY, Corson GM, et al. Marfan syndrome caused by a recurrent de novo missense mutation in the fibrillin gene. *Nature.* 1991;352(6333):337–9. doi:10.1038/352337a0.
23. Dong Z, Fu W, Wang Y, Wang C, Yan Z, Guo D, et al. Stent graft-induced new entry after endovascular repair for Stanford type B aortic dissection. *J Vasc Surg.* 2010;52(6):1450–7. doi:10.1016/j.jvs.2010.05.121.
24. Eid-Lidt G, Gaspar J, Meléndez-Ramírez G, Cervantes SJ, González-Pacheco H, Dámas de Los Santos F, et al. Endovascular treatment of type B dissection in patients with Marfan syndrome: mid-term outcomes and aortic remodeling. *Catheter Cardiovasc Interv.* 2013;82(7):E898–905. doi:10.1002/ccd.24725.
25. Esposito G, Cappabianca G, Bichi S, Cricco A, Albano G, Anzuini A. Hybrid repair of type A acute aortic dissections with the Lupiae technique: ten-year results. *J Thorac Cardiovasc Surg.* 2015;149(2 Suppl):S99–104. doi:10.1016/j.jtcvs.2014.07.099.
26. Geisbüsch P, Kotelis D, von Tengg-Kobligk H, Hyhlik-Dürr A, Allenberg JR, Böckler D. Thoracic aortic endografting in patients with connective tissue diseases. *J Endovasc Ther.* 2008;15(2):144–9. doi:10.1583/07-2286.1.
27. Ghanta RK, Green SY, Price MD, Arredondo CC, Wainwright D, Preventza O, et al. Midterm survival and quality of life after extent II thoracoabdominal aortic repair in Marfan syndrome. *Ann Thorac Surg.* 2016;101(4):1402–9; discussion 1409. doi:10.1016/j.athoracsur.2015.10.018.
28. Grabenwöger M, Alfonso F, Bachet J, Bonser R, Czerny M, Eggebrecht H, et al. Thoracic endovascular aortic repair (TEVAR) for the treatment of aortic diseases: a position statement from the European association for cardio-thoracic surgery (EACTS) and the European society of cardiology (ESC), in collaboration with the European association of percutaneous cardiovascular interventions (EAPCI). *Eur Heart J.* 2012;33(13):1558–63. doi:10.1093/eurheartj/ehs074.
29. Harky A, Chan J, MacCarthy-Ofosu B. The future of stenting in patients with type A aortic dissection: a systematic review. *J Int Med Res.* 2020;48(1):300060519871372. doi:10.1177/0300060519871372.
30. Harky A, Chan JSK, Wong CHM, Francis N, Grafton-Clarke C, Bashir M. Systematic review and meta-analysis of acute type B thoracic aortic dissection, open, or endovascular repair. *J Vasc Surg.* 2019;69(5):1599–1609.e2. doi:10.1016/j.jvs.2018.08.187.
31. Harky A, Garner M, Roberts N. A late presentation of Loeys-Dietz syndrome associated with an aortic root aneurysm. *Ann R Coll Surg Engl.* 2017;99(3):e114–5. doi:10.1308/rcsann.2017.0018.
32. Harky A, Iqbal R, Giordano V, Al-Adhami A. Aortic endovascular stenting in patients with systemic connective tissue disorders: does the prohibitive dogma still stand tall? [(published online ahead of print, 2019 Jul 29)]. *J Int Med Res.* 2019;300060519863963. doi:10.1177/0300060519863963.
33. Harky A, Kai Chan JS, Ming Wong CH, Bashir M. Open versus Endovascular Repair of Descending Thoracic

Aortic Aneurysm Disease: A Systematic Review and Meta-analysis. *Ann Vasc Surg.* 2019;54:304–315.e5. doi:10.1016/j.avsg.2018.05.043.
34. Harky A, Fan K, Fan K. The genetics and biomechanics of thoracic aortic diseases. *Vascular Biology.* 2019;1(1):R13-R25. https://doi.org/10.1530/VB-19-0027.
35. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American college of cardiology foundation/American heart association task force on practice guidelines, American association for thoracic surgery, American college of radiology, American stroke association, society of cardiovascular anesthesiologists, society for cardiovascular angiography and interventions, society of interventional radiology, society of thoracic surgeons, and society for vascular medicine. *Circulation.* 2010;121(13):e266–369. Erratum in: *Circulation.* 2010;122(4):e410. doi:10.1161/CIR.0b013e3181d4739e.
36. Ince H, Rehders TC, Petzsch M, Kische S, Nienaber CA. Stent-grafts in patients with marfan syndrome. *J Endovasc Ther.* 2005;12(1):82–8. doi:10.1583/04-1415MR.1.
37. Isselbacher EM. Thoracic and abdominal aortic aneurysms. *Circulation.* 2005;111(6):816–28. doi:10.1161/01.CIR.0000154569.08857.7A.
38. Kalkat MS, Rahman I, Kotidis K, Davies B, Bonser RS. Presentation and outcome of Marfan's syndrome patients with dissection and thoraco-abdominal aortic aneurysm. *Eur J Cardiothorac Surg.* 2007;32(2):250-4. doi:10.1016/j.ejcts.2007.04.013.
39. Kalra A, Harris KM, Kische S, Alden P, Schumacher C, Nienaber CA. Endovascular repair of descending thoracic aorta in Loeys-Dietz II syndrome. *Ann Vasc Surg.* 2015;29(7):1452.e17-21. doi: 10.1016/j.avsg.2015.04.071.
40. Kazui T, Inoue N, Yamada O, Komatsu S. Selective cerebral perfusion during operation for aneurysms of the aortic arch: a reassessment. *Ann Thorac Surg.* 1992;53(1):109–14. doi:10.1016/0003-4975(92)90767-x.
41. Keschenau PR, Kotelis D, Bisschop J, Barbati ME, Grommes J, Mees B, et al. Editor's choice-open thoracic and thoraco-abdominal aortic repair in patients with connective tissue disease. *Eur J Vasc Endovasc Surg.* 2017;54(5):588–96. doi:10.1016/j.ejvs.2017.07.026.
42. LeMaire SA, Carter SA, Volguina IV, Laux AT, Milewicz DM, Borsato GW, et al. Spectrum of aortic operations in 300 patients with confirmed or suspected Marfan syndrome. *Ann Thorac Surg.* 2006;81(6):2063-78; discussion 2078. doi:10.1016/j.athoracsur.2006.01.070.
43. Leshnower BG, Chen EP. When and how to replace the aortic root in type A aortic dissection. *Ann Cardiothorac Surg.* 2016;5(4):377-82. doi:10.21037/acs.2016.03.15.
44. Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, et al. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. *Nat Genet.* 2005;37(3):275–81. doi:10.1038/ng1511.
45. Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, et al. Aneurysm syndromes caused by mutations in the TGF-beta receptor. *N Engl J Med.* 2006;355(8):788–98. doi:10.1056/NEJMoa055695.
46. Majumder PP, St Jean PL, Ferrell RE, Webster MW, Steed DL. On the inheritance of abdominal aortic aneurysm. *Am J Hum Genet.* 1991;48(1):164–70.
47. Marcheix B, Rousseau H, Bongard V, Heijmen RH, Nienaber CA, Ehrlich M, et al. Stent grafting of dissected descending aorta in patients with Marfan's syndrome: mid-term results. *JACC Cardiovasc Interv. 2*008;1(6):673-80. doi:10.1016/j.jcin.2008.10.005.
48. Marfan ABJ. Un cas de déformation congénitale des quatre membres, plus prononcée aux extrémités, caractérisée par l'allongement des os avec un certain degré d'amincissement. Paris: Impr. Maretheux, 1896.
49. Milewicz DM, Dietz HC, Miller DC. Treatment of aortic disease in patients with Marfan syndrome. *Circulation.* 2005;111(11):e150-7. doi:10.1161/01.CIR.0000155243.70456.F4.
50. Mommertz F, Sigala S, Langer TA, Koeppel WH, Mess GW, Schurink MJ, et al. Thoracoabdominal aortic aneurysm repair in patients with marfan syndrome. *Eur J Vasc Endovasc Surg.* 2008;35(2):181-6. doi:10.1016/j.ejvs.2007.10.013.
51. Nienaber CA, Fattori R, Lund G, Dieckmann C, Wolf W, von Kodolitsch Y, et al. Nonsurgical reconstruction of thoracic aortic dissection by stent-graft placement. *N Engl J Med.* 1999;340:1539–45.
52. Nienaber CA, Rousseau H, Eggebrecht H, Kische S, Fattori R, Rehders TC, et al. Randomized comparison of strategies for type B aortic dissection: the INvestigation of STEnt grafts in aortic dissection (INSTEAD) trial. *Circulation.* 2009;120(25):2519–28. doi:10.1161/CIRCULATIONAHA.109.886408.
53. Nordon IM, Hinchliffe RJ, Holt PJ, Morgan R, Jahangiri M, Loftus IM, et al. Endovascular management of chronic aortic dissection in patients with Marfan syndrome. *J Vasc Surg.* 2009;50(5):987-91. doi:10.1016/j.jvs.2009.05.056.
54. Oderich GS, Panneton JM, Bower TC, Lindor NM, Cherry KJ, Noel AA, et al. The spectrum, management and clinical outcome of Ehlers-Danlos syndrome type IV: a 30-year experience. *J Vasc Surg.* 2005;42(1):98–106. doi:10.1016/j.jvs.2005.03.053.
55. Omura A, Tanaka A, Miyahara S, Sakamoto T, Nomura Y, Inoue T, et al. Early and late results of graft replacement for dissecting aneurysm of thoracoabdominal aorta in patients with Marfan syndrome. *Ann Thorac Surg.* 2012;94(3):759–65. doi:10.1016/j.athoracsur.2012.04.061.
56. Ouriel K, Greenberg RK, Clair DG, O'hara PJ, Srivastava SD, Lyden SP, et al. Endovascular aneurysm repair: gender-specific results. *J Vasc Surg.* 2003;38(1):93–8. doi:10.1016/s0741-5214(03)00127-7.
57. Pepin M, Schwarze U, Superti-Furga A, Byers PH. Clinical and genetic features of Ehlers-Danlos syndrome type IV, the vascular type. *N Engl J Med.* 2000;342(10):673–80. Erratum in: *N Engl J Med.* 2001;344(5):392. doi:10.1056/NEJM200003093421001.
58. Pilop C, Aregger F, Gorman RC, Brunisholz R, Gerrits B, Schaffner T, et al. Proteomic analysis in aortic media of patients with Marfan syndrome reveals increased activity of calpain 2 in aortic aneurysms. *Circulation.* 2009;120(11):983–91. Erratum in: Circulation. 2010;121(6):e38. doi:10.1161/CIRCULATIONAHA.108.843516.
59. Rozado J, Martin M, Pascual I, Hernandez-Vaquero D, Moris C. Comparing American, European and Asian practice guidelines for aortic diseases. *J Thorac Dis.* 2017;9(Suppl 6):S551–60. doi:10.21037/jtd.2017.03.97.
60. Sandford RM, Bown MJ, London NJ, Sayers RD. The genetic basis of abdominal aortic aneurysms: a review. *Eur J Vasc Endovasc Surg.* 2007;33(4):381-90. doi:10.1016/j.ejvs.2006.10.025.
61. Sun JCJ. Genetic disorders of the thoracic aorta and indications for surgery. *Cardiol Clin.* 2017;35(3):317–20. doi:10.1016/j.ccl.2017.03.003.
62. Superti-Furga A, Steinmann B, Byers PH. Type III collagen deficiency. *Lancet.* 1989;1(8643):903-4. doi:10.1016/s0140-6736(89)92899-7.
63. Svensson LG, Kouchoukos NT, Miller DC, Bavaria JE, Coselli JS, Curi MA, et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. *Ann Thorac Surg.* 2008;85(1):S1–41. doi:10.1016/j.athoracsur.2007.10.099.
64. Tjaden B, Azizzadeh A. Endovascular therapy in Marfan syndrome: PRO. *Ann Cardiothorac Surg.* 2017;6(6):672–6. doi:10.21037/acs.2017.10.06.
65. Volodos NL, Shekhanin VE, Karpovich IP, Troian VI, Gur'ev I. A self-fixing synthetic blood vessel endoprosthesis. *Vestn Khir Im I I Grek.* 1986;137:123–5.
66. von Kodolitsch Y, De Backer J, Schüler H, Bannas P, Behzadi C, Bernhardt AM, et al. Perspectives on the revised Ghent criteria for the diagnosis of Marfan syndrome. *Appl Clin Genet.* 2015;8:137–55. doi:10.2147/TACG.S60472.

67. Waterman AL, Feezor RJ, Lee WA, Hess PJ, Beaver TM, Martin TD, et al. Endovascular treatment of acute and chronic aortic pathology in patients with Marfan syndrome. *J Vasc Surg.* 2012;55(5):1234-40; discussion 1240-1. doi:10.1016/j.jvs.2011.11.089.
68. Webster MW, St Jean PL, Steed DL, Ferrell RE, Majumder PP. Abdominal aortic aneurysm: results of a family study. *J Vasc Surg.* 1991;13(3):366–72. doi:10.1067/mva.1991.26359.
69. Williams JA, Loeys BL, Nwakanma LU, Dietz HC, Spevak PJ, Patel ND, et al. Early surgical experience with Loeys-Dietz: a new syndrome of aggressive thoracic aortic aneurysm disease. *Ann Thorac Surg.* 2007;83(2):S757-63; discussion S785-90. doi:10.1016/j.athoracsur.2006.10.091.
70. Yokoi Y, Azuma T, Yamazaki K. Advantage of a precurved fenestrated endograft for aortic arch disease: simplified arch aneurysm treatment in Japan 2010 and 2011. *J Thorac Cardiovasc Surg.* 2013;145(3):S103–9. doi:10.1016/j.jtcvs.2012.11.058.
71. Yuan SM, Jing H. Cystic medial necrosis: pathological findings and clinical implications. *Rev Bras Cir Cardiovasc.* 2011;26(1):107-15. Erratum in: *Rev Bras Cir Cardiovasc.* 2012;27(1):173. doi:10.1590/s0102-76382011000100019.
72. Zhang H, Qiao T. Aortic remodeling in type B aortic dissection after thoracic endovascular aortic repair with an aortic extender cuff implantation. *Clin Interv Aging.* 2018;13:2359–66. doi:10.2147/CIA.S179526.

А.Ю. Шкандала [1], **Б.М. Тодуров** [1, 2], **С.М. Фуркало** [2, 3], **А.В. Хохлов** [1, 2], **О.В. Зеленчук** [1, 2]

[1] ДУ «Інститут серця МОЗ України», Київ
[2] Національний університет охорони здоров'я України імені П.Л. Шупика, Київ
[3] ДУ «Національний інститут хірургії та трансплантології імені О.О. Шалімова НАМН України», Київ

Ендоваскулярне протезування грудного відділу аорти в пацієнтів із захворюваннями сполучної тканини

У статті проаналізовано сучасні наукові погляди на визначення ролі ендоваскулярного протезування грудного відділу аорти (TEVAR) у сучасних наукових публікаціях у пацієнтів із захворюваннями сполучної тканини (ЗСТ). Використано загальний пошук статистики в електронних базах даних: PubMed, SCOPUS, Embase, Google Scholar OVID, а також підтверджено результатами власних спостережень використання TEVAR у невідповідні години надання медичної допомоги. Результати досліджень проаналізовано в оглядовому форматі. Роль TEVAR оцінено відповідно до кожного дослідження. Наразі існує обмежена кількість великих когортних досліджень, які описують використання TEVAR у пацієнтів із ЗСТ. Протезування грудного відділу аорти ендоваскулярним протезом у пацієнтів із ЗСТ небезпечне дилатацією аорти, яка прогресує, та високою ймовірністю подальших повторних втручань у старшому віці. Встановлено, що відкрита реконструкція досі залишається золотим стандартом втручання в молодих пацієнтів із ЗСТ, які прогресують, особливо при гострому типі розшарування аорти. Однак для підтвердження цієї практики необхідно опублікувати довгострокові дані.

Ключові слова: аорта, грудна клітка, дилатація, аневризма, розшарування, захворювання аорти, ендоваскулярні процедури.