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Aortic aneurysms in patients with atherosclerotic coronary artery disease in the southwestern region of Romania – clinical and histopathological study

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Abstract

An aneurysm is defined as a dilation of the arterial wall with a diameter exceeding 1.5 times the normal diameter of the vessel concerned. Aortic aneurysms (AAs) can develop at any level but are mostly found at the abdominal and infrarenal levels and extend to the iliac arteries. AAs are usually asymptomatic and are most often discovered incidentally during various imaging investigations for other conditions. Rupture of an AA is usually dramatic, being one of the causes of sudden cardiac death. Surgical treatment and, more recently, endovascular treatment are the only effective methods of AA repair. In this study, we screened for the diagnosis of AAs in patients with stable exertional angina who had indications for coronary angiography. The study was carried out in the period 2021–2023 in the Institute of Cardiovascular Diseases Timişoara, Romania. Of the 2458 patients with exertional angina who required coronary angiography, a number of 1844 (75%) patients had at least one stenotic atheromatous plaque, and of these 312 patients had AAs, of which 173 at the level of the abdominal aorta.

Keywords: aortic aneurysms, dilatation, endovascular treatment, rupture of aortic aneurysm.

Introduction

An aneurysm is defined as the dilatation of the arterial wall with a diameter exceeding 1.5 times the standard diameter. Aortic aneurysms (AAs) can develop at any level but are mostly found at the abdominal and infrarenal levels and extend to the iliac arteries [1]. A diameter greater than 3 cm in the abdominal aorta is defined as an abdominal aortic aneurysm (AAA) [2]. A thoracic aortic aneurysm (TAA) is a dilatation of at least 50% of the expected size that includes all three layers of the wall structure [3]. AAs are usually asymptomatic and are discovered during various imaging investigations for other conditions [4–6]. Aneurysm rupture is usually dramatic, being one of the causes of sudden cardiac death [6–8]. Thus, screening for early detection before rupture or other complications is crucial [2, 9, 10]. Preventive treatment for aneurysms involves appropriate screening for diagnosis, follow-up imaging, and surgical repair or endovascular repair (ER) when indicated. Drug treatment of aneurysms is not effective in stopping their progression [11, 12]. Surgical treatment and, more recently, endovascular treatment are the only effective methods of aneurysm repair [12, 13].

Endovascular treatment is a modern, less invasive method for treating thoracic and abdominal aneurysms. The anatomy of the aneurysm plays a very important role in the success of ER procedures. Thus, an appropriate selection based on aneurysm anatomy is essential before surgery [14].

Aim

The aim of paper was the identification of favorable anatomy for ER of AAA and TAA in patients with AAA and/or TAA and coronary artery disease (CAD) [coronary atherosclerosis (ATS) >50% on at least one large epicardial artery] from the southwestern (SW) region of Romania.

Patients, Materials and Methods

In this study, we performed screening for the diagnosis of thoracic and/or abdominal aneurysms in patients with stable exertional angina pectoris (AP) and present cardiovascular risk (CVR) factors who had indications for coronary angiography. The study was carried out between the years 2021–2023 in the Institute of Cardiovascular Diseases Timişoara, Romania, with doctors from the Clinic of Cardiology and the Department of Interventional Cardiology.

In order to publish the results of the study, we obtained the Approval of the Ethics Committee from the Institute of Cardiovascular Diseases Timişoara.

All patients were asymptomatic in terms of AA, having exertional AP. Once coronary angiography was performed, patients who had coronary ATS >50% on at least one large

epicardial coronary vessel, also did a peripheral aortography performed to diagnose AAs (thoracic, thoracoabdominal, or abdominal). Patients who had thoracic aortic dilatation (TAD) >4.5 cm or abdominal aortic dilatation >4 cm had a computed tomography angiography (CTA) of the thorax and/or abdomen performed for better assessment of the aneurysm. A diameter greater than 5 cm was evaluated for ER. The anatomy of aneurysms >5 cm was compared with the standard instructions for use (IFU) recommended for most endovascular prosthesis manufacturers and the extended IFU. The standard IFU was an aortic neck length ≥15 mm, suprarenal angulation ≤45°, infrarenal angulation ≤60°, and a neck diameter between 8 and 32 mm.

Extended IFU were aortic neck length ≥10 mm, suprarenal angulation ≤60°, infrarenal angulation ≤75°, and a neck diameter between 7–32 mm. The anatomy of the iliac arteries was also assessed regarding a concurrent aneurysm at this level, landing zones of at least 10 mm, and a minimum iliac artery diameter of at least 8 mm (extended IFU ≥7 mm).

Statistical analysis

Statistical analysis was performed using IBM Statistical Package for Social Sciences (SPSS) version 25.0 for Windows. For continuous variables, data are presented as mean ± standard deviation (SD). For those with normal distribution, *t*-test was used for continuous variables, and χ^2 (*chi*-squared) or Fischer's exact tests for categorical variables (if the sample was small). Statistical significance was reached at a value of $p<0.05$.

Histopathological assessment

Patients with atherosclerotic coronary disease and AA, who died or were repaired with classical surgery during the three years of the study, were carefully macroscopically examined. Tissue fragments were collected from the wall of the arterial aneurysm, which were fixed in a 10% neutral buffered formalin solution and included in histological paraffin, according to the histopathological (HP) tissue processing protocol. Using the rotary microtome, 4–5 µm thick sections were obtained, which were stained with Hematoxylin–Eosin (HE), Goldner–Szekely (GS) trichrome, and Orcein.

Results

After performing coronary angiography on 2458 patients with exertional AP addressed to Institute of Cardiovascular Diseases Timişoara, we found that 1844 (75%) patients had at least one >50% stenotic atheromatous plaque in the coronary arteries [*n*=686 (37%) with single-vessel CAD, *n*=623 (34%) with bivascular CAD, *n*=535 (29%) with triple-vessel CAD].

The prevalence of AA in patients with significant coronary ATS was 17.4% (*n*=312). Most of them were AAAs (*n*=173, 9.4%), followed by TADs (*n*=88, 4.8%), TAAs (*n*=38, 2.1%), and thoracoabdominal aneurysms (TAAAs, *n*=13, 0.7%). Out of the AAAs, 59 (34.1%) patients had a diameter between 3.0–3.9 cm, 60 (34.6%) patients had a diameter between 4.0–4.9 mm and 54 (31%) patients had a diameter >5.0 mm.

In our study, 2.4% of patients (*n*=1 with AAA, *n*=1 with TAA, *n*=2 with TAAA) refused CTA of the aorta. Thus, CTA was performed on 213 patients (164 with AAA, 37 with TAA, and 13 with TAAA).

In the anatomical analysis, which aimed to identify the favorable anatomy of aneurysms for ER, TAAAs were also excluded, and only AAAs and TAAs with diameter greater than 5 cm were considered for potential ER.

AAAs with diameters >5 cm were identified in 54 (2.92%) patients, and TAAs with diameters >5.5 cm in five (0.27%) patients.

Due to the small number of TAAs >5.5 cm in patients with CAD (*n*=5 in our study, but with an increased prevalence in the general population – 0.27 per 100 patients *vs* 5 per 100 000 patients), these were not included in the anatomical statistical analysis. The choice of treatment (surgical or endovascular) was determined on a case-by-case basis.

The mean age of patients with AAAs >5 cm was 67.3±6.2 years, and 80.7% (*n*=42) were males. At the initial evaluation, after using the standard criteria, only 19 (36.5%) patients had favorable anatomy for ER, increasing to 55.7% (*n*=29) after applying the extended criteria. In patients without favorable anatomy for ER, the majority had short aortic neck (60%), followed by a wide neck diameter (25%), a greater infrarenal angle (10%), and inadequate iliac artery diameter (5%). Aortic or iliac artery tortuosity assessed by the tortuosity index was not significant.

The anatomical characteristics of patients with AAAs >5 cm is described in Table 1.

Table 1 – ***Anatomical characteristics in AAAs >5 cm***

	Mean ± SD	Male (mean ± SD)	Female (mean ± SD)	*p*-value
Diameter of AAA [mm]	63.5±12.7	65.7±14.2	64.6±11.2	NS
Neck diameter [mm]	25.4±5.8	26.7±6.2	20.2±5.4	NS
Neck length [mm]	21.4±12.5	22.5±13.9	18.2.4±12.7	<0.05
Suprarenal angulation [°]	26.2±22.3	25.3±21.7	29.8±4.6	NS
Infrarenal angulation [°]	47.4±23.1	42.5±24.5	59.4±4.8	<0.05
Small iliac diameter [mm]	7.8±1.9	8.3±1.8	5.4±1.2	<0.05

AAA: Abdominal aortic aneurysm; NS: Not significant; SD: Standard deviation.

Females were older than males (74.6±11.2 *vs* 65.7± 14.2 years, $p<0.01$), with a smaller neck length (18.2.4±12.7 *vs* 22.5±13.9 mm, $p<0.05$), larger infrarenal angle (59.4±4.8 *vs* 42.5±24.5°, $p<0.05$) and smaller iliac artery diameter (5.4±1.2 *vs* 8.3±1.8 mm, $p<0.05$). These anatomical differences might explain why women have a less favorable anatomy for the ER compared to men (for standard criteria IFU 21% *vs* 37%, $p<0.001$, and for extended criteria IFU 28% *vs* 55%, $p<0.001$).

The HP examination showed an uneven thickening of the arterial wall, by increasing the amount of collagen fibers, mainly at the level of the internal and middle tunics.

Thus, at the level of the internal tunic, especially in the subintimal area, thick collagen fibers were identified, organized in bundles, with an orderly arrangement, in the long axis of the aorta (Figure 1). The limit between the internal tunic and the middle tunic, respectively "the internal elastic limit" was invaded and disorganized by the increase in the amount of fibrillar collagen (Figure 2). This increase in the amount of collagen may be an adaptive process and was accompanied by an increase in the number of fibroblasts,

the main cells that are responsible for the modification of the connective matrix. In the middle tunic, the elastic fibers were quantitatively reduced by increasing the amount of collagen, the elastic lamellae appeared thinned and sometimes disorganized (Figure 3).

In the wall of some aneurysms, deposits of calcium salts have been identified in the form of punctate calcifications or extended calcifications in the form of plaques, often broken (Figures 4 and 5).

At the periphery of the tunica media and in the *tunica externa* in some aneurysms, microhemorrhage areas were identified (Figures 6 and 7), excessive deposits of amorphous matrix (Figure 8) or inflammatory infiltrates formed mainly by lymphocytes (Figure 9).

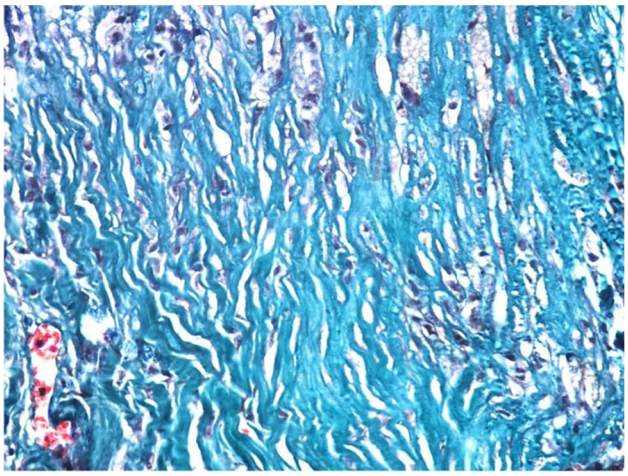

Figure 1 – ***Thick collagen fibers, organized into bundles. Goldner–Szekely (GS) trichrome staining, ×100.***

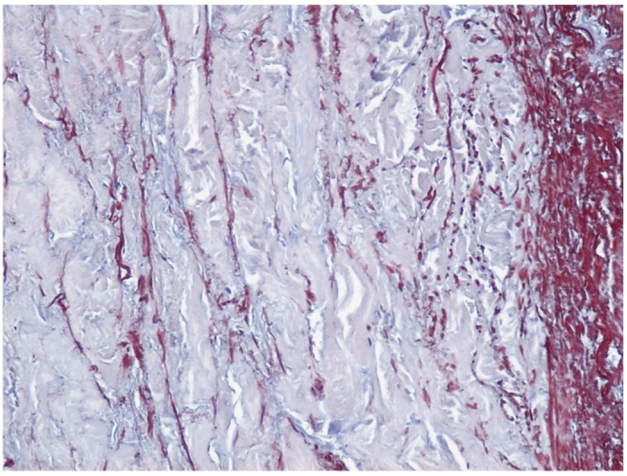

Figure 2 – ***Intense development of collagen fibers at the level of the inner and middle tunics, with the disorganization of the "internal elastic limit". Orcein staining, ×200.***

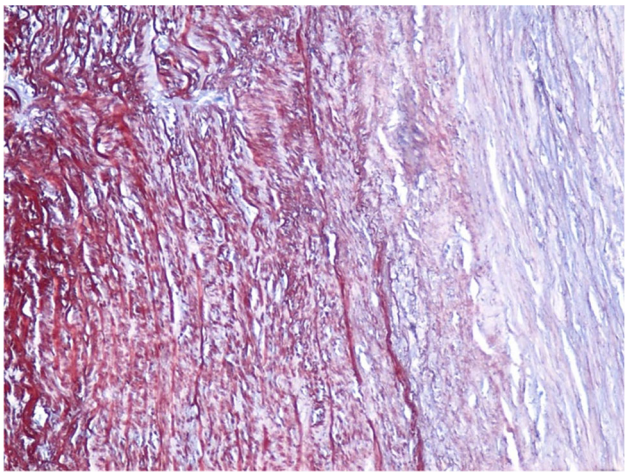

Figure 3 – ***Medium tunic with few elastic fibers, with thinned and disorganized elastic lamellae. Orcein staining, ×100.***

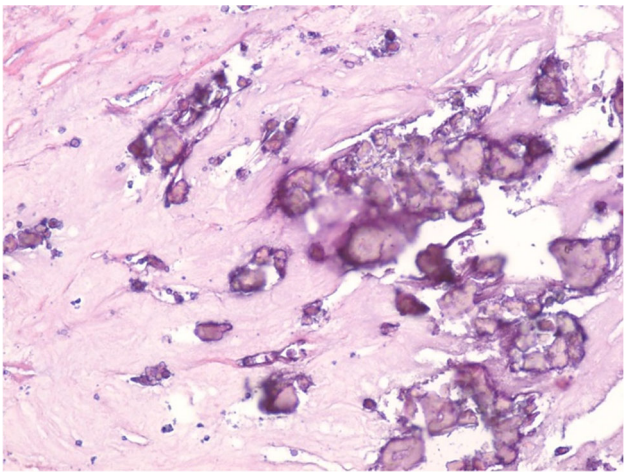

Figure 4 – ***Aneurysm area with "punctate calcifications". Hematoxylin–Eosin (HE) staining, ×200.***

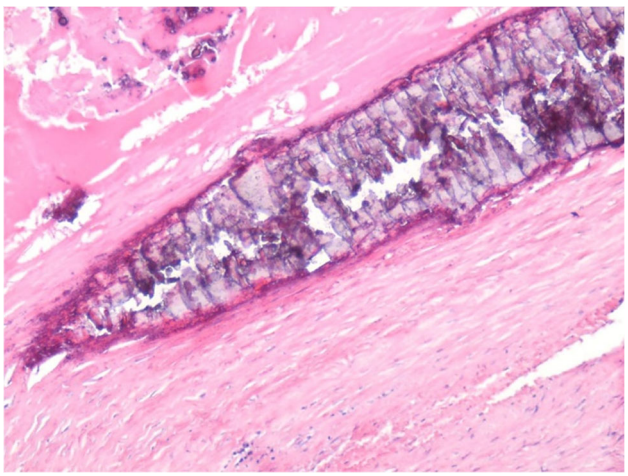

Figure 5 – ***Extensive parietal calcification in the form of a broken calcareous plaque. HE staining, ×200.***

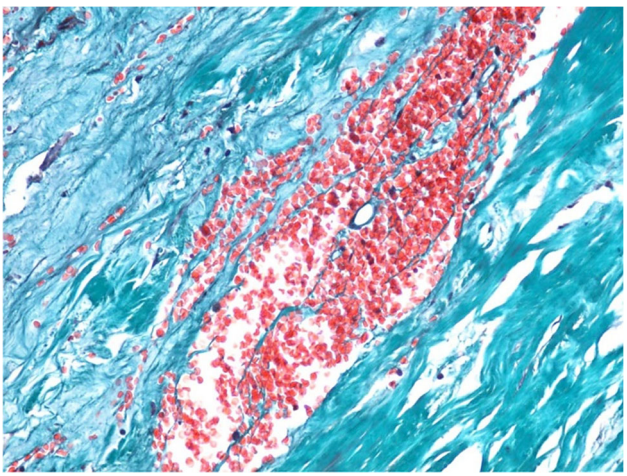

Figure 6 – ***Microhemorrhage in the middle tunic. GS trichrome staining, ×200.***

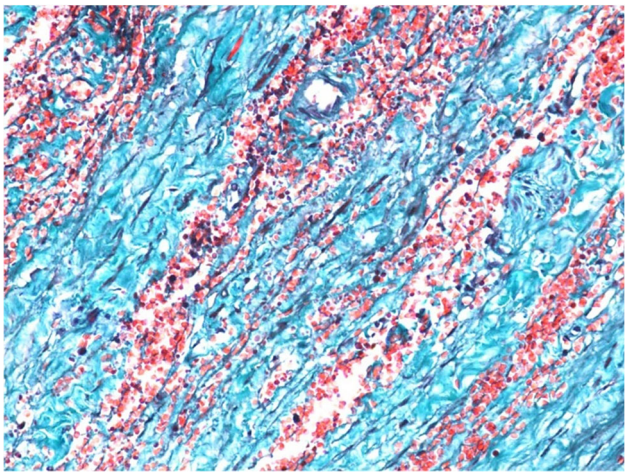

Figure 7 – *Diffuse and extensive hemorrhage in the tunica externa. GS trichrome staining, ×100.*

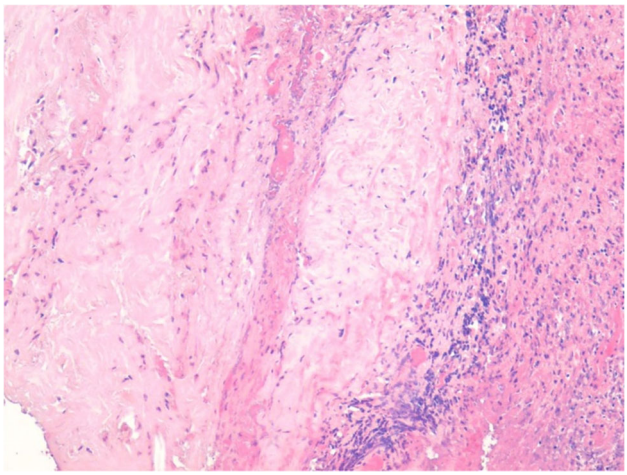

Figure 8 – *Aneurysm area with deposition of amorphous material, infiltrated with inflammatory cells. HE staining, ×100.*

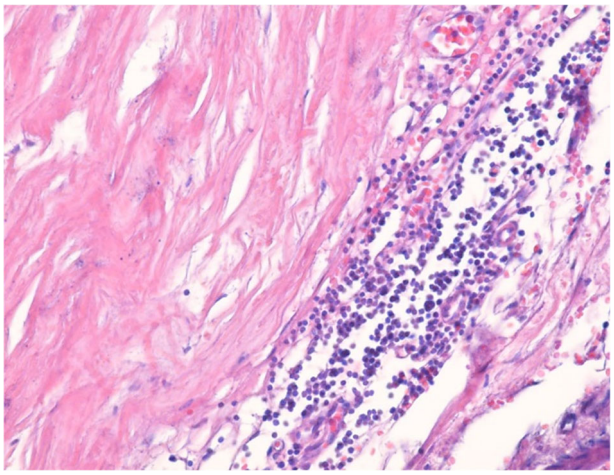

Figure 9 – *Aneurysm wall infiltrated with inflammatory cells. HE staining, ×200.*

Discussions

Our study included patients with AP and CVR factors who were indicated coronary angiography. None of the patients included had previously experienced symptoms suggestive of AA. Patients with already known AA were excluded from this study. The prevalence of AA was 17.4%, and most of them were AAAs (*n*=173, 9.4%), TADs (*n*=88, 4.8%), TAAs (*n*=38, 2.1%), and TAAAs (*n*=13, 0.7%). Most AAAs had a diameter between 3–4.9 cm (*n*=119, 6.45%), and these patients were introduced into a surveillance program according to the *American College of Cardiology* (ACC) 2022 guidelines recommendations [15]. The same screening protocol was applied for TAAs and TAAAs with a diameter less than 5.5 cm. Upon initial inspection, the number of AAAs larger than 5 cm seems small, but the prevalence in our group (with high and very high CVR) was 2.81%, much higher than in the general population (0.6%) [16].

AAAs with a diameter >5 cm have an increased risk of rupture [17], which correlates with a higher mortality [18]. Thus, in selected cases, rupture prevention by aneurysm repair is mandatory (surgical or endovascular). In the short term, ER has certain advantages over surgery [19]: lower intra- and perioperative mortality [20, 21], a faster recovery time [22], and a lower risk of infection [23]). However, the use of this technique is dependent on a favorable anatomy to increase the procedural success rate [24].

In this study, we identified the anatomical characteristics of a selected population with high and very high CVR (CAD patients with >50% atherosclerotic lesions in at least one large epicardial coronary vessel). The number of studies assessing favorable AAA anatomy for ER based on the standard criteria is limited. To our knowledge, this current study would be the first to evaluate the anatomy of patients with CAD and AAA >5 cm. In this high CVR population, the favorable anatomy for ER initially had a low prevalence (37.5%) when standard IFU criteria were used. However, this improved to 56% when extended IFU criteria were used.

The results of our study were like those of a recent meta-analysis by Ulug *et al.* that reported a prevalence between 46–64% for men and between 25–47% for women [25]. The difference could be explained by the fact that this meta-analysis also included studies with AAAs >4 cm (we included AAAs >5 cm). At smaller AAAs sizes, the percentage of aneurysms suitable for ER using standard IFU criteria increases. Like our study, the primary anatomical obstacle, especially in women, was the length of the aneurysmal neck, followed in their case by the infrarenal angle, while in our study, the second cause was an increased aneurysmal neck width.

A study conducted in Korea considered only the aneurysmal neck anatomy as a criterion for ER. However, this criterion corresponded to only 32% of AAA patients suited for ER. The most encountered anatomical incompatibility in this study is the increased value of the infrarenal angle, while in our study a shorter aneurysmal neck [26]. In their study, women and those with ruptured aneurysms are most likely not to meet the standard IFU criteria for ER. We did not include patients with ruptured AAAs in our analysis.

Another study by Panthofer *et al.* reported an 85% eligibility rate (lower in women than men) for ER in patients with AAA (diameters ranging from 3.5–5 cm) that is maintained even two years after the diagnosis [27]. This again shows that smaller AAA sizes increase anatomic eligibility for ER. A possible explanation for the higher

percentage of eligible patients (leaving aside the small size) would be the broad spectrum of endovascular prostheses included in the study. Some indicated in anatomies with short AAA necks, even less than 10 mm.

A study evaluating only two endovascular stent graft prostheses concluded that most patients with an AAAs >5 cm do not have a favorable anatomy for ER when using the standard IFU anatomical criteria. The main anatomical problem of incompatibility would be the AAA neck, especially its large diameter and short length. New generations of endovascular prostheses for AAA repair have tried to take these issues into account by improving anatomical compatibility.

The 2021 EXTREME study [28] included patients who would typically have been excluded using conventional anatomical selection criteria (90% had too short aneurysmal neck, and 10% had inadequate vascular access). The success rate of endovascular intervention was 98%, using a particular type of stent graft that provides a seal of the neck using a polymer [28]. Given that in our study, a short AAA neck was the leading cause of anatomical incompatibility, the use of this type of stent graft would increase the number of patients who would benefit from ER, improving anatomical eligibility.

Conversely, some studies have reported an increase in complications after ER when anatomical selection by standard IFU criteria is not followed [29–31].

Conclusions

In patients with atherosclerotic coronary disease from the SW region of Romania, the incidence of AAAs >5 cm is 2.8%, much higher than the general population. Of these, only 36.5% had favorable anatomy for ER when standard IFU criteria were used. This percentage increased to 55.7% when the extended IFU criteria were used. The main anatomical factors that do not favor endovascular intervention were a short aortic neck (60%), followed by a wide neck diameter (25%), a greater infrarenal angle (10%), and inadequate iliac artery diameter (5%).

Conflict of interests

The authors declare that they have no conflict of interests. All authors have read, reviewed, and agreed to the published version of the manuscript.

Availability of data and materials

All data and materials supporting the present study's results are available on request from the corresponding author. The data are not publicly available to limit the amount of publicly available personal information, as classified by the European Union General Data Protection Regulation.

Ethics approval and consent to participate

The participant institutions granted the study ethical approval.

Patient consent for publication

Written informed consent was obtained from patients before enrollment.

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