Abstract: Dissection of thoracic aorta is the major detectable complication, given the fact that usually the pathology of this aortic segment is asymptomatic, progressing slowly and represents a life-threatening condition, due to its particular amplitude. In this highly unpredictable event, mostly associated with increasing age, particularly for the descending aorta, the aortic wall strength becomes exceeded and is followed by a dissection or a severe rupture, closely related to sudden death.

All three distinct components of the aortic wall, intima, media and adventitia are affected by the vascular rupture, the vascular smooth muscle cells and the elastic fibers from the media being the most active in reconfiguring the aortic design.

Although the intima and the media were usually incriminated as the major factors responsible for the aortic vulnerability, a new perspective about the adventitial vasa vasorum has to be taken into account - this is in fact not a minor but a redoubtable participant especially in the prevalent with age vascular pathology. Our study was focused on the distribution of thoracic aorta vasa vasorum in normal state at different ages and in aortic dissection in aged people, in order to identify a possible medial ascent, triggering the vascular wall alteration. The transmural extensionion of the aortic vasa vasorum, extremely reduced, was not significant to allow as to correlate the current day profile of thoracic aorta dissection with the adventitial involvement.

Key Words: thoracic aorta, aneurysm, dissection, sudden death, vasa vasorum.
of large arteries is now elucidated, the supplementary vascular perfusion provided by the microvessels ensuring the trophicity of large caliber aorta [3, 4]. Complex debates were concentrated on the determining role of vasa vasorum in vascular patophysiology, in conditions in which growing evidence supports a high frequency of vascular injuries advancing from the adventitia to the internal intima [5]. The structural and functional integrity of the vasa vasorum is usually reflected in a normal aortic state. Extremely various disease-related factors promptly interact with vasa vasorum constituents, which become able to generate through multiple interactions, the development of atheromatous plaques, aortic dissection, aortic aneurysm [6-8]. The involvement of vasa vasorum in these processes is correlated with a transmural extension, branching through the media, close to the intima.

Our morphometric study evaluated the vasa vasorum of the descendent thoracic aorta, in normal state and also in aortic dissection, together with the interpretation of CT images of redoubtable aortic injuries - aneurysm and aortic dissection. The study was designed to reveal and analyse the possible existence of a distinct age related evolutive pattern for its distribution and its parameters and to determine if a medial ascension can be associated with aortic dissection.

**MATERIALS AND METHODS**

Samples were prelevated from descendent thoracic aorta of 5 groups, each of 15 subjects: group 1 newborns (ages ranging from one day to 30 days), group 2 children (ages ranging from 2 to 12 years), group 3 young (age ranging from 18 to 26 years), group 4 adults (age ranging from 39 to 48 years) and group 4 aged persons (60 to 75 years old), without any evident cardiovascular disease causing their death. A separate group 6-12 aged persons with aortic wall dissection was also investigated.

**Histologic exam**

Paraffin embedded samples were processed; thricrome Szekeli stain, H&E and EVG stains was used for thoracic aorta samples.

**Light microscopy, image acquisition**

Histologic samples were examined with a Nikon

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**Figure 1.** Vasa vasorum (Szekeli stain, ob. ×40) - (A - newborns, B - children, C - young, D - adults, E - aged).
After the intravenous injection of 100 ml nonionic contrast material, at a rate of 5 ml/sec. Axial, coronar and sagital 3D-reconstructions and VRT are used for image analysis.

**RESULTS**

The morphometric assessment of vasa vasorum was studied on Szekeli stained samples from the 5 investigated groups: newborns, children, young, adults and aged subjects (Figs. 1a-1e). All the samples were prelevated from the thoracic descendent aorta.

We analyzed the proportion in which vasa vasorum in present in the adventitial layer, in every group, pointing on its specific density, according to age (Fig. 2). The development and representative density follow an ascendant trend from newborns to young subjects, with a consecutive decrease in the adults and aged subjects.

The relevance of the amplitude of vasa vasorum as a distinct structure of the aortic wall was observed by determining the evolution of its principal parameters; because of the great number of data, the resulted values were centralised for each parameter and for each group.

The descriptive statistics for adventitial vasa vasorum areas was distinct and specific for every explored group (Table 1). The variability of this parameter can be observed in different stages of life, especially newborns and aged subjects seems to be poles apart (Fig. 3). The descriptive statistics was also realized for the adventitial vasa vasorum perimeters (Table 2).

![Figure 2](image_url)  
**Figure 2.** Variability of vasa vasorum density in explored groups.

![Figure 3](image_url)  
**Figure 3.** Variation of area values for the adventitial vasa vasorum.

Table 1. Descriptive statistics of adventitial vasa vasorum areas

<table>
<thead>
<tr>
<th>Lot studiu</th>
<th>Medie</th>
<th>Modul</th>
<th>Mediană</th>
<th>Deviație std.</th>
<th>Eroare std.</th>
<th>Varianță</th>
<th>Min</th>
<th>Max</th>
<th>Rang</th>
<th>Skewness</th>
<th>Kurtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=34)</td>
<td>67.77</td>
<td>73.09</td>
<td>66.50</td>
<td>10.54</td>
<td>1.89</td>
<td>111.13</td>
<td>53.73</td>
<td>94.49</td>
<td>40.76</td>
<td>1.047</td>
<td>0.753</td>
</tr>
<tr>
<td>2 (n=34)</td>
<td>218.45</td>
<td>201.79</td>
<td>210.37</td>
<td>38.24</td>
<td>6.46</td>
<td>1462.53</td>
<td>156.53</td>
<td>321.10</td>
<td>164.56</td>
<td>0.958</td>
<td>0.603</td>
</tr>
<tr>
<td>3 (n=34)</td>
<td>377.36</td>
<td>348.80</td>
<td>370.60</td>
<td>88.11</td>
<td>15.11</td>
<td>7763.74</td>
<td>220.53</td>
<td>615.21</td>
<td>394.68</td>
<td>0.417</td>
<td>-0.072</td>
</tr>
<tr>
<td>4 (n=34)</td>
<td>305.78</td>
<td>293.34</td>
<td>292.77</td>
<td>81.06</td>
<td>13.90</td>
<td>6570.18</td>
<td>173.72</td>
<td>492.72</td>
<td>319.00</td>
<td>0.589</td>
<td>0.181</td>
</tr>
<tr>
<td>5 (n=34)</td>
<td>428.80</td>
<td>416.56</td>
<td>427.34</td>
<td>120.78</td>
<td>20.71</td>
<td>14588.84</td>
<td>233.70</td>
<td>663.97</td>
<td>430.27</td>
<td>0.177</td>
<td>-0.724</td>
</tr>
</tbody>
</table>
The perimeters present a moderate degree of variability in the adventitial layer. The descriptive statistics was performed for the diameter of blood vessels from vasa vasorum, too (Table 3). Diameters of the adventitial blood vessels present an ascendant dynamics, reported to the examined groups (Fig. 4).

The short and the long axis of the examined blood vessels were quantified in order to obtain a better understanding of their evolutive pattern. For example, short axis has comparable values in young and in aged

<table>
<thead>
<tr>
<th>Lot studiu</th>
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<th>Rang</th>
<th>Skewness</th>
<th>Kurtosis</th>
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<td>9.26</td>
<td>9.69</td>
<td>9.20</td>
<td>0.70</td>
<td>0.13</td>
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<td>8.27</td>
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<td>2.70</td>
<td>0.862</td>
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</tr>
<tr>
<td>2 (n=34)</td>
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<td>17.32</td>
<td>16.37</td>
<td>1.42</td>
<td>0.24</td>
<td>2.01</td>
<td>14.12</td>
<td>20.22</td>
<td>6.10</td>
<td>0.746</td>
<td>0.226</td>
</tr>
<tr>
<td>3 (n=34)</td>
<td>21.78</td>
<td>20.97</td>
<td>21.72</td>
<td>2.55</td>
<td>0.44</td>
<td>6.50</td>
<td>16.76</td>
<td>27.99</td>
<td>11.23</td>
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<td>-0.401</td>
</tr>
<tr>
<td>4 (n=34)</td>
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<td>19.31</td>
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<td>0.44</td>
<td>6.64</td>
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<td>25.05</td>
<td>10.17</td>
<td>0.297</td>
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</tr>
<tr>
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<td>22.87</td>
<td>23.33</td>
<td>3.33</td>
<td>0.57</td>
<td>11.10</td>
<td>17.25</td>
<td>29.08</td>
<td>11.83</td>
<td>-0.076</td>
<td>-0.898</td>
</tr>
</tbody>
</table>

Table 3. Descriptive statistics of adventitial vasa vasorum diameter

<table>
<thead>
<tr>
<th>Lot studiu</th>
<th>Medie</th>
<th>Modul</th>
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<th>Kurtosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=34)</td>
<td>210</td>
<td>217</td>
<td>211</td>
<td>13.27</td>
<td>2.97</td>
<td>210</td>
<td>196</td>
<td>225</td>
<td>17.10</td>
<td>1.778</td>
<td>3.327</td>
</tr>
<tr>
<td>2 (n=34)</td>
<td>413</td>
<td>420</td>
<td>416</td>
<td>14.78</td>
<td>3.15</td>
<td>413</td>
<td>399</td>
<td>429</td>
<td>15.28</td>
<td>1.778</td>
<td>3.327</td>
</tr>
<tr>
<td>3 (n=34)</td>
<td>317</td>
<td>324</td>
<td>320</td>
<td>12.13</td>
<td>2.48</td>
<td>317</td>
<td>303</td>
<td>331</td>
<td>17.10</td>
<td>1.778</td>
<td>3.327</td>
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<tr>
<td>4 (n=34)</td>
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<td>222</td>
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<td>215</td>
<td>196</td>
<td>225</td>
<td>17.10</td>
<td>1.778</td>
<td>3.327</td>
</tr>
<tr>
<td>5 (n=34)</td>
<td>230</td>
<td>237</td>
<td>234</td>
<td>14.78</td>
<td>3.15</td>
<td>230</td>
<td>216</td>
<td>244</td>
<td>15.28</td>
<td>1.778</td>
<td>3.327</td>
</tr>
</tbody>
</table>

Table 2. Descriptive statistics of adventitial vasa vasorum perimeter

Figure 4. Variation of perimeter values for the adventitial vasa vasorum.

Figure 5. Variation of diameter values for the adventitial vasa vasorum.

Figure 6. Variation of diameter (short axis) values for the adventitial vasa vasorum.

Figure 7. Variation of diameter (long axis) values for the adventitial vasa vasorum.
subjects (Fig. 5); long axis revealed comparable values in young and adults (Fig. 6). The perimeters and the areas of vasa vasorum have different evolutive trends (Figs. 7, 8). All these measurements were realized on normal configured aorta and respect the particularities of the explored tissue. The variability of these two parameters suggest that microvessels of vasa vasorum are adapted to the haemodynamic demands regarding different stages of life, providing evidence that vasa vasorum has its own dynamics.

The analysis of aortic samples revealing aortic aneurysms and aortic dissection didn’t evidentiate, with one exception, the presence of a medial vasa vasorum, but a well defined adventitial one (Figs. 9a-9b).

The number of CT investigated patients has to be correlated with a low frequency of thoracic descendent aorta aneurysms and dissection and to the real time of SOMATOM diagnostic use in the Institute of Cardiovascular Diseases "Prof. Dr. George I. M. Georgescu". The analysis of CT images confirmed the alteration of the aortic wall in aneurysm (Figs. 10a-10c, Figs. 11a-11b) as well as in aortic dissection (Figs. 12a-12c, Figs. 13a-13b).

**DISCUSSION**

Considering adventitia, the external aortic layer, as a passive compartment, which serves only to connect the aorta to the subjacent tissues, seems to be in accord with previous inconstant and inexhaustive findings, but in contrast with the present available evidence that suggests its complex involvement in aortic normal and pathologic status. Fully integrated into the dynamic evolution of the vascular wall, adventitia is still an incomplete elucidated structure, especially when evaluating the pathogenesis of the aortic diseases [9,10]. The particular disposal and functions of adventitial cells, fibers and vasa vasorum represent essential features which trigger some distinct events in aortic injuries, especially in those age dependent diseases.

![Figure 8](image8.png)

**Figure 8.** Age related evolution of areas and perimeters of adventitial vasa vasorum.

![Figure 9](image9.png)

**Figure 9.** Aortic dissection. A - Vasa vasorum in the aortic media (HE, ob.x40); B - Massive aortic dissection (EVG, ob.x40).

![Figure 10](image10.png)

**Figure 10.** CT features of descendent thoracic aorta aneurysm. A - Axial image of aortic dilatation beyond subclavicular artery; B - Sagital image-fusiform aneurysmal aspect; C - Axial image-aortic intraluminal thrombosis.
Aortic vasa vasorum contains a notable network of microvessels, displaying a precocious development during intrauterine life. Because of its peripheric localization in the aortic wall, for a long time vasa vasorum was regarded only as a supplementary source of oxygen and nutrients, without any significance in the complex aortic performance [11,12]. Recent evidence suggests the particular sensitivity of vasa vasorum to a wide spectrum of disease-related agents; through complex intractions, the microvessels triggering a redoubtable associated vascular pathology [13].

All the classical theories about aortic pathology mechanisms describe an exclusive modality for injury progression, from the lumen to the periphery. Consistent with these data, intimal layer is the main subject of this process, being considered the most vulnerable component in the aortic structure, with a great exposure to factors with a different aggressivity directed toward aortic lumen [14, 15].

A change in perception of vasa vasorum as a particularly dynamic structure, which is able to moderate and also to induce aortic injuries despite its peripheral position in the aortic wall, was the result of many recent laborious studies originateing a new concept regarding the particular role of microvessels network [16]. Intervention of vasa vasorum can change the classic direction of advancement for the aortic injuries, from the lumen to the periphery, with a new sense of progression, from the adventitia to the intimal layer. To detect and to monitor age –related changes of vasa vasorum means not only to perceive the quantitative profile of microvessels evolution, but also to reveal the presence of transmural extension, as a form of creating an area of aortic vulnerability [17].

Although much progress was realized in recent years in deciphering the complex response of vasa vasorum in the aortic aggression, many questions still remain .

There are some opinions that sustain the fact that the complex response of vasa vasorum is following an independent reactive pathway compared to that of the host vessel. The vascular reactivity of vasa vasorum is depending on its own tone, but also has to be correlated with the whole aortic wall response. Disease-related factors are incriminating to interact in different manner with the intimal and adventicial components, the progression of the aortic injury being often determined by their synchronic activation [18]. The connection

Figure 11. VRT of thoracic aorta aneurysm; A.Thoracic aorta dilatation inducing antero-superior displacement of left supraclavicular artery; B.Intraluminal thrombosis.

Figure 12. CT features of descending thoracic aorta dissection; A - Axial section of aortic wall dissection; B - Coronar section-parietal dissection and fluid extension through left pleural space; C - Axial section-diffuse extraluminal hemorrhage.

Figure 13. VRT. A - True and false lumen in the aortic wall; B - dissection flap extending from the distal emergence of left supraclavian artery to descending and abdominal aorta.
between atherosclerosis and vasa vasorum involvement is sustained by its sensitivity to atherogenic factors such as hypercholesterolemia or hypertension. The association of microvessels neovascularization process with the increase in the atherosclerotic plaque progress was frequently mentioned as an inductive pathway of the aortic injury. On the other hand, the direct inhibition of vasa vasorum angiogenesis is fully correlated with a constant decrease of local atherosclerosis [19,20].

A significant cellular influx of cells is allowed by vasa vasorum to enter the aortic wall, together with numerous factors which facilitate atherogenetic process.

The thoracic aorta aneurysms, occurring equally among men and women, especially increasing with age, with a complex nature, despite their reduced frequency, have a high risk of rupture which can be life-threatening. Descending aortic aneurysms usually begin beyond the left subclavicular artery, in this context, the possible vasa vasorum involvement in aneurysms pathogenesis due to its critical role in inflammatory process and alteration of aortic wall stability, followed by the sudden rupture of host vessel.

The involvement of the vasa vasorum in aortic pathology is conditioned by its huge disponibility to promptly respond to any kind of aggression of the vascular wall, through its main disponible components: the endothelial cells, the smooth muscle cells and the connective tissue fibers. Endothelium is susceptible in case of inflammation or incipient fibrosis, when its functions become altered and affect the blood flow through the aortic media [21].

Our study explored the vasa vasorum distributed in descendent thoracic aorta in normal conditions, based on the hypothesis of a considerable impact of an aortic injury at this level and its subsequent critical evolution [22]. Aortic dissection, aneurysms or atheromatous plaques can be easier explained in conditions of a direct monitorisation of this microvessels network. In normal state, vasa vasorum is distributed only in the adventitia. The complet and well defined disposal of vasa vasorum provides an extensive vascular supply for the aorta; numerous experimental studies revealed that any disruption of this supply is associated with medial necrosis. These observations confirm and sustain that the delivering of nutrients and oxygen through vasa vasorum maintains aortic physiologic status, supplementing the medial blood flow.

This study was realized in terms of a better understanding of vasa vasorum distribution based on different stages of life and with regard to a possible age dependent evolution and also a particular distribution in associated pathology. The investigated groups are extremely large: newborns, children, young subjects, adults and aged subjects, without any evident cardiovascular disease, in order to explore vasa vasorum at different ages and to obtain a correct and complete assessment of its evolution [25].

The first step of the study was to determine the age correlated microvessels density in the thoracic aorta adventitia. The complet and well defined disposal of vasa vasorum in the newborns aorta is pleading for its early time development in the aortic wall, at the beginning of the intrauterine life [26, 27]. The difference of vasa vasorum density in the newborns and children’ aorta is minor, being followed by a precipitously increase in the young subjects, as a result of a change in the hemodynamic new local conditions. Vasa vasorum also presents a progressive and distinctive decrease in the adults and finally in the aged persons.

The second step of this study was to evaluate the evolution of some distinct aortic vasa vasorum parameters: area, diameter (with its short and long axis), perimeter, all of these elements regarded as relevant for the microvessels configuration in different groups of age.

The hyperactivity of vasa vasorum gives rise to a well defined microvessel segment directed to the internal layers of the aorta, creating the circumstances in the aged persons to be confronted with a transmural extensive pathology [28-30].

The area of thoracic vasa vasorum presents an ascendant trend from the newborns to aged people, with significant increase particularly in the young and in the aged subjects.

The vascular perimeter is also reflecting an increase with age, the most relevant values being observed in the same young and aged subjects, with a clear evolution in the newborns.

The diameter of thoracic vasa vasorum raised from the newborns to the aged persons, the short and long axis of the blood vessels delimiting large vascular structures.

The analysed aortic parameters of vasa vasorum revealed the changes in the microvessels depending on age-in fact, it can be described an evolutive pattern, suggesting a progressive conformation to the major changes in the rest of the aortic wall.

The exam of samples with aortic dissection revealed the same adventitial distribution of vasa vasorum, a single case presenting a medial network of vessels, despite the severity of investigated cases of dissection.

CONCLUSIONS

Although our study did not evidentiate a transmural extension pattern of vasa vasorum in case of aortic dissection, it has to be continued, directed
to a possible correlation between the induction of an inflammatory process in the adventitia and the development of the aortic aneurysm and dissection.

Our study demonstrates that it is conceivable an age dependent evolutive pattern of aortic vasa vasorum, which becomes a dynamic structure, able to respond in a specific manner to different aggressions, operating in concert with other components of the aortic wall. The diversity of investigated subjects allowed this conclusions to be drawn, pointing especially to the changing profile of aortic vasa vasorum, involving a reevaluation of its structure and functions in the aortic general configuration. A better vasa vasorum approach may improve both the diagnosis and the clinical management of the aortic dissection.

References
24. Khan IA, Nair CH, Clinical, Diagnostic and Management Perspectives of Aortic Dissection, Chest 2002, 122: