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Review Article

The Effects of the Thoracoabdominal Aortic Metabolism on the Endovascular Procedures Outcomes

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Abstract: Aortic metabolism is a merge of complex processes. Atherosclerotic infiltration of the aortic wall is a crucial factor when choosing an appropriate endovascular treatment modality for anatomically suitable patients. Due to the rise of endovascular treatments and placement of endovascular devices in younger patients, many physicians are starting to take a more considerable interest in this complex process. Many experimental animal models are used for elucidation of individual aspects in this area. This led to an in-depth explanation of many metabolic processes of the aortic wall. However, only a few papers are reporting on the assessment of these pathological processes in human tissues. This paper outlines some of the crucial aspects of the thoracoabdominal aortic metabolism. Final results of endovascular treatments are believed to be significantly affected by the quality of the aortic wall and the ability to predict its further changes. This includes the pathological changes and their effects on the symbiotic metabolic changes. "Patient-tailored" endovascular aortic treatments based on the aortic metabolic assessment may be able to optimise the cases outcomes. Due to the rise of endovascular treatments and placement of endovascular devices in younger patients, further research is needed to understand better aortic metabolic processes in various patient groups, including groups of patients suffering from chronic metabolic diseases. Aortic wall metabolism should be assessed with the aim to optimise the endovascular treatment outcomes.

Keywords: Abdominal Aorta, Thoracic Aorta, Metabolism, Oxygen Consumption, Differences

1. Introduction and History

Atherosclerotic infiltrations of the aorta are a key factor when choosing an appropriate endovascular treatment modality in anatomically suitable patients [1]. The difference in metabolisms of the thoracic and abdominal aorta are becoming more significant due to the present trends towards the use of extensive endovascular treatments vs surgical repair [2].

The predisposition to atherosclerotic infiltration of the abdominal aorta and the thoracic aorta had been observed and compared by pathologists since 1947 [3]. The difference was attributed to the different metabolism of arterial tissue. Lazovskaya et al. wrote the very first paper dealing with the metabolism of vessels. In early 1943 [4]. Other early papers such as Briggs et al. "The metabolism of arterial tissue" published in 1949 and Henderson et al. ''The respiration of arterial tissue'' suggested that arterial tissue might have a specific metabolism when compared to the other tissues in the human body [5-6]. The major observed difference was a greater consumption of oxygen by the abdominal and thoracic aorta when compared to other vessels. This was experimentally demonstrated using a rat model in the late 1940's [3-4]. Although abdominal and thoracic aorta oxygen consumptions were similar, abdominal aorta had shown lower metabolic activity compared to the thoracic segment [5-6].

Early papers also documented that atherosclerosis in humans develops in anatomically specific regions [7-9]. In 1970 Dayton S. et al. published data on the fact that most of the cholesterol in atherosclerotic plaques in aortas is acquired from plasma lipoproteins. Furthermore, it was suggested that arterial lipoproteins play an essential role in atherosclerosis [10].

2. Clinical Science & Pathology

2.1. Low-Density-Cholesterol

The association of low-density-cholesterol (LDL) with arterial extracellular matrix increases both aortic concentrations of ungraded LDL and increased LDL retention within the atherosclerotic lesions [11]. Studies by Schwenke D. C. et al. and Tozer E. C. et al. using a rat model demonstrated that aortic LDL retention did not differ between the branch and uniform abdominal aorta [12-13]. However, none of these studies considered the aspect that LDL might be metabolically sequestered in the atherosclerotic free aorta. In another study, Schwenke D. C. demonstrated the metabolic evidence of LDL being sequestered in a form that does not readily undergo cellular degradation in the abdominal aorta [14]. Furthermore, it was shown that LDL is steadily exchanged with plasma LDL [14]. These studies had also described an association between LDL with extracellular arterial matrix and increased metabolism of LDL by macrophages. Furthermore, prolonged intra-arterial LDL retention can promote intra-arterial oxidation of LDL leading to the build-up of cholesterol in arteries [15].

2.2. 18F-Fluorodeoxyglucose

The 18F-fluorodeoxyglucose (^{18}FDG) is one of the most frequently used tracer in clinical practice. ^{18}FDG is taken up into the cell by endothelial glucose transport. Afterwards, it is converted to ^{18}FDG -6-phosphate. Unlike glucose, which is metabolised further, the phosphorylated ^{18}FDG -6-phosphate cannot undergo further metabolism and is therefore trapped in the cell. Increased cellular uptake of ^{18}FDG and a higher rate of intracellular phosphorylation are the underlying signs for the cells with higher metabolism [16].

A clinical trial by Kotze CW et al. had demonstrated a significant increase of ^{18}FDG uptake in an aortic aneurysm wall in a majority of tested patients. This may advocate that increase in ^{18}FDG uptake directly reflects the increased metabolic rate of the aortic wall. This can be caused by chronic inflammatory processes, aortic dilatation, or atherosclerosis [17]. This increase in an aortic tissue metabolism plays undoubtedly major role in further dilatation and the development of aortic aneurysms [18]. On the other hand, Morel O. et al. proved that patients with small aortic aneurysms do not exhibit growth show by low levels of ^{18}FDG uptake due to small numbers of cells present in the aortic wall [19]. Furthermore, low levels of ^{18}FDG also represent the metabolic activity of cells in the aneurysm wall. These cells include not only inflammatory cells but also smooth muscle cells [20]. An interesting finding by Kotze et al. also documented even levels of ^{18}FDG found in aneurysms that were in a state just before maximising their diameter. Despite ^{18}FDG metabolism predicting capabilities, its clinical use is not widespread because the aortic wall covered by thrombus will be influenced by in-blood circulating ^{18}FDG very scarcely [16]. It should be kept in mind that thrombus covering the wall of aorta is also metabolically active and is affecting the metabolism of aorta by its physical presence and metabolism [21]. Cyclic changes in ^{18}FDG uptake reflect cyclic inflammatory processes of atherosclerosis and the transient nature of ^{18}FDG uptake in atherosclerotic lesions [22-13]. No correlation between calcification and increased metabolism of an aortic wall was found as shown by Tatsumi M. et al. [23]. They documented that FDG uptake sites are well-defined and distinct from calcifications. The uptake sites were most likely positioned in metabolically active atherosclerotic areas [24].

2.3. Renin-Angiotensin System

The renin-angiotensin system (RAS) is treated as a circulatory hormonal system that regulates electrolyte balance, blood pressure, blood flow, and fluid volume [25]. Recent findings had shown that RAS is activated locally in the heart, the vessel wall, the kidney, and the brain [26-28].

Vascular inflammation is involved in the initiation and progression of atherosclerosis. RAS plays a critical role in the regulation of vessel wall homeostasis as an anti-inflammatory agent [29-30]. Campbell et al. used an experimental model in 1986 for establishing quantitative data regarding the aortic wall angiotensin activity [26]. Campbell and his team showed that the aortic wall has roughly 70% lower levels of angiotensin when compared to liver [31].

Another aspect of RAS function regarding the aortic metabolism is activation of mesenchymal cells in the tunica media and adventitia. This results in their fibrinogenic remodelation [32]. Experimental work by Bujak-Gizycka et al. identified a new metabolite of angiotensinogen using a rat model [28]. By applying liquid chromatography-mass spectrometry method (LC-MS), they detected significant amounts of pro-angiotensin-12 (proAng-12), the primary product of angiotensinogen metabolism in rat aortic tissue [33]. This contradicts findings by Nagata S. et al. who studied the aorta using radioimmunoassay [34]. The difference in findings was mostly attributed to the short half-life time of proAng-12. They had also shown data showing the proAng-12 playing a crucial role as a substrate for generating angiotensin-1 and subsequently angiotensin-2. This is important for a quick release of these substances that are used in the instant production of RAS components. This process circumvents slower cellular production of these precursors [21, 35]. Despite all of these data, the enzyme for proAng-12 production had not been found yet [20]. Wolkow P. P. et al. investigated exogenous angiotensin-1 role in the metabolism of the aorta in diabetic rats [36]. The obtained data indicate that aortic concentration of angiotensin- 2 is not modified by

diabetes. Additionally, the effect of angiotensin-2 on the contractility of the aorta in diabetes is also uncertain. Despite that, some authors, i.e. Head J. R. et al. suggest that contractility of the aorta does not change with diabetes [37]. The conflicting findings can probably be attributed to the use of different and evolving experimental techniques and different experimental design used by the two research groups [31-32].

3. Clinical Perspective

Aortic stent grafts had become a safe and effective treatment modality in the treatment of various aortic diseases [38-39]. No comparison study had been performed up-to-date to demonstrate what is the optimal stent graft for treating aortic disease. Several devices have undergone FDA trials but had never made it to the emerging market for various technical or structural failures: the Edwards Lifepath balloon-expandable modular bifurcated stent graft suffered from stent fractures of the main body, the Trivascular Enovus device was deliverable through a small-diameter sheath [40-41].

Despite the widespread of aortic stent grafts use, there is almost no evidence documenting the effects of aortic metabolism; hence the progression of atherosclerosis or inflammatory processes of the aortic wall on the intermediate and long-term results of these devices. One may speculate that the progression of atherosclerotic disease or other inflammatory processes can in the future affect the once "suitable" proximal and distal landing zone, compromising the stent graft seal, thus increasing the chance of device failure and endoleak formation. Furthermore, future stent graft dislocation or migration can be affected by these metabolic processes.

In the future clinical studies examining the stent graft behavior over time have to be performed to understand and find an optimal device that can deal with changes occurring in the aortic wall with time.

4. Conclusion

Aortic metabolism is a merge of complex processes. Many physicians are starting to take a more considerable interest in this complex process as there are ever more endovascular treatment modalities available for patients today. Long term results of these endovascular treatments are believed to be greatly affected by the quality of the aortic wall and our ability to predict its further changes. Thoracoabdominal aortic metabolic assessment influence the endovascular device selection for patients, thus prolonging and affecting endovascular devices long-term outcomes. Therefore, due to the rise of endovascular treatments and placement of endovascular devices in younger patients, further research is needed to understand better aortic metabolic processes in various patient groups, including groups of patients suffering from chronic metabolic diseases.

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