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Estimating the influence of aortic-stent grafts after endovascular aneurysm repair: Are we missing something?

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ABSTRACT

The implantation of a stiff aortic endograft for endovascular abdominal aneurysm repair (EVAR) has been reported to increase aortic stiffness and pulse wave velocity (PWV), raising potential concern over deterioration of myocardial performance. Yet, additional stiffness indices such as the augmentation index (AIx), reflection magnitude (RM) and changes in augmentation pressure (AP) have not been studied adequately to facilitate and improve our knowledge regarding the ways that EVAR affects central hemodynamics. In this article it is suggested that the implantation of an aortic stent-graft exerts its immediate effects not only by interposing extra stiffness on the infrarenal segment but by also modifying the pulse wave reflection site and changing the aortic flow field without necessarily causing significant alterations in PWV. Hence, further studies on myocardial performance in large patient populations are expected to delineate the precise influence of different designs of EVAR endografts on the cardiovascular hemodynamic which, in turn, can affect the morbidity and survival of these patients.

Introduction

Pulse wave velocity (PWV) is a widely-accepted surrogate of arterial compliance and a robust prognostic marker of cardiovascular morbidity and mortality in older adults and in patients with end-stage renal disease, diabetes, and hypertension [1–4]. It has been also suggested as a useful marker of therapeutic (pharmaceutical or interventional) interventions in the arterial tree [5,6]. Abdominal Aortic Aneurysms (AAA) present higher PWV values compared to age- and gender-individuals [7,8]. Lately, the implantation of a stiff aortic endograft for endovascular abdominal aneurysm repair (EVAR) has been reported to increase aortic stiffness and PWV. Few studies have examined the influence of EVAR on PWV and concluded that this intervention increases the latter, raising potential concern over deterioration of myocardial performance [8–12].

The problem

Before adapting these conclusions, one has to take into consideration certain limitations and drawbacks of the aforementioned conclusions: a) the increases in PWV after EVAR are small, although statistical significant. For example, Kadoglou et al. report an increase from 13.11 ± 3.57 m/s to 16.41 ± 2.33 m/s and Lantelme et al. an increase by 1.0 m/s in carotid-femoral PWV, whereas Takeda et al. document an increase from 19.14 ± 3.89 to 20.96 ± 4.59 m/s in brachial–ankle pulse wave velocity after EVAR [8,12], b) most importantly, these calculations overlook the fact that PWV values depend on gender and age, following an exponential distribution pattern where the normal range of values is determined between +90 and −90% confidence intervals; therefore, a certain PWV measurement may have a totally different meaning for two distinct age-groups, being normal for the one but pathologic for the other [13]. Similarly, a consequent PWV-change postoperatively could have quite different impact and interpretation when it comes to individuals of different age and gender. Besides, additional indices of arterial stiffness such as the augmentation index (AIx), reflection magnitude (RM) and changes in augmentation pressure (AP) could facilitate further our understanding of the modified hemodynamic after EVAR.

The hypothesis

It is suggested that the effects of the implantation of an aortic stent-graft for EVAR are determined not only by the interposition of extra stiffness on the infrarenal segment but also by postoperative geometrical alterations in the AAA flow lumen, namely restoration of a smaller diameter flow lumen and changes of angu-

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lation of the infrarenal segment (flow inlet) and the curvature of flow centerline. These alterations affect the pressure wave reflections in a variant mode and can create a modified flow pattern that may counteract the increased stiffness and decreased compliance of the implanted stent-graft.

Our theory questions the "unidirectional" and linear perception of PWV increase due to endograft's stiffness and underscores that the restoration of a smaller diameter flow lumen does not necessarily coincide with a postoperative increase in aortic stiffness. The hemodynamic consequences vary among the patients and are better approached and described with Aix, RM and AP.

Evaluation of the hypothesis

Pulse wave velocity (PWV) is considered a valid and clinically feasible surrogate of aortic stiffness, correlating with cardiovascular disease. However, despite the independent values of PWV as a measure of post-EVAR increase of arterial stiffness in the aforementioned studies, its use is limited without reliable reference values. Generally, efforts to establish reference and normal values have been conducted only recently, where PWV values were stratified according to patients' age and blood pressure [13]. Therefore, any PWV measurement should be referred with respect to individual's gender and age, where the median values and ±90% confidence intervals are depicted. Otherwise, the comparisons and results could be of limited value, if not misleading. Moreover, the contribution of distal aorta to total arterial compliance is the least compared to central segments of the aorta [14,15].

Wave reflection takes place at all bifurcations and discontinuities of the vascular tree. The major part of the reflections occurs at the arterioles, where numerous bifurcations are present over short distances [16]. The moment that reflected waves return centrally toward the heart depends on a) the distance of the reflection site, b) the wave speed and c) *how* the waves are reflected at the reflection site (i.e., the phase of reflection coefficient). The analysis of arterial pressure and flow waves into their forward and backward reflected components can be used to quantify the importance of wave reflections [17–21].

The quantification of pulse wave reflections focuses on measurements of central aortic systolic pressure and its augmentation through reflections, as calculated with pulse wave analysis (PWA). Additionally, the wave separation analysis (WSA) quantifies the total amount of arterial wave reflection considering both aortic pulse and flow waves, whereas PWV is estimated from the time difference between the forward and reflected waves [22].

The most commonly used surrogates of wave reflections and arterial stiffness are the AIx which reflects the increase of aortic systolic pressure due to wave reflections, the RM defined as the ratio of the amplitude of the backward wave to the forward wave and the augmentation pressure (AP) determined by the difference of the pressure at second inflection point minus the pressure at first inflection point of the systolic part of pressure wave (Fig. 1). The first inflection point is indicative of the arrival of reflected waves at ascending aorta.

PWA can be easily performed currently with validated software (ARCSolver algorithm, as implemented in Mobil-O-Graph 24 h PWA Monitor ambulatory device) using frequency-domain based calculations to derive the amplitudes of the forward and backward traveling waves, based on brachial non-invasive recorded pressure and flow waves (oscillometric method) [19,23,24].

Murgo et al. estimated the aortic pressure waveform and the arterial impedance using invasive catheterization techniques and concluded that the differences in pressure and flow waves are due to differences in reflections in the arterial tree [25]. By occluding manually the iliac arteries of animals, the reflection coefficient increased in magnitude with subsequent increases in backward wave resulting also in an increased Aix. Although reflections occur from many sites in the arterial tree, all these hemodynamic changes are more pronounced in the distal and terminal aorta. Accordingly, the Aix should be corrected to 75 bears-per-minute (Alx@75) and interpreted with respect to median values and reference range (confidence intervals) with respect to patient's age and gender, since a significant difference for the average Alx@75 between men and women has been reported [26].

Exemplifying the hypothesis

The following cases demonstrate the PWA of three patients (A; male, B; female and C; male) with AAA of none (A) or minimal intraluminal thrombus (B) compared to large (C) amount of intraluminal thrombus (Fig. 2), preoperatively and 6-months after the implantation of the same type of aortic nitinol-based endograft for EVAR. None patient had a history of current or past smoking, diabetes mellitus, renal insufficiency nor received medication for hypertension. All patients had no sign of peripheral arterial disease and presented palpable peripheral pulses with ankle-brachial-index of 1.1.

Patient A (male, 73 years-old) had an AAA of 7.5 cm whereas Patient B (female, 75 years-old) had an AAA of 6.7 cm and Patient C (male, 71-years old) a 6.1 cm AAA. Patients B experienced a marked increase of central systolic while it was kept constant in patients A and C. As can be seen in Table 1, PWV was increased only slightly in Patients A and B and kept constant in C. The AP and AI@75 decreased in patient A with excessively large lumen and disturbed flow due to minimal thrombus deposition (AI@75 28 to 17 and AP 15 to 10 mmHg) but increased in patients B with the moderate thrombus and excessive centerline angulation (AI@75 from 32 to 46 and AP from 23 to 43 mmHg) and in patient C with the straight, restricted AAA lumen (AI@75 16 to 30 and AP 1 to 4 mmHg). RM increased postoperatively in patients B after restoration of a narrow flow field (71–80%) compared to the AAA lumen preoperatively, as well as in patient C (51–73%) after implantation of the endograft in the already previously narrow AAA lumen. Interestingly, while the PWV was abnormally high preoperatively in A and B, the implantation of the endograft returned these values toward the upper reference limits with respect to patients' age and gender.

Discussion

Current interpretation theories of the hemodynamic effects of endovascular grafts focus on the increase of stiffness in the infrarenal aortic segment. On the contrary, our theory brings into play the role of AAA-intraluminal flow field and focuses on describing the postoperative changes by means of AI@75 and RM.

The deceleration of the reflected wave is also mirrored in the magnitude of the AP which is declined by more than half. It has been shown that AAA present higher PWV and AI than normal individuals (as accordingly adjusted) [7]. Beckmann et al. have recently investigated the AIx in patients with peripheral arterial disease and/or AAA and showed that AIx differs according to the pattern of the disease [27]. AIx was significantly lower in patients with AAA, higher in patients with both AAA and peripheral arterial disease and highest in sole peripheral disease. These findings not only show that the AIx depends on the pattern of the disease (i.e., obstructive, aneurismal or both) but also underscore the importance of wave reflection on central hemodynamic and, consequently cardiac pathology [27]. Although AAA are not associated with a flow obstacle, alteration in wave reflection is generated via decreased compliance.