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ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

DOES TEVAR MODIFY THE CARDIAC FUNCTION AND THE AORTIC STIFFNESS?

ΜΕΤΑΠΤ. ΦΟΙΤΗΤΗΣ: **ΕΥΑΓΓΕΛΟΣ ΜΠΟΥΛΤΑΔΑΚΗΣ**

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«Ενδαγγειακές Τεχνικές»

ΠΡΑΚΤΙΚΟ ΚΡΙΣΕΩΣ

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Του Μεταπτυχιακού Φοιτητή Μπουλταδάκη Ευάγγελου.

Εξεταστική Επιτροπή

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- Αν. Καθηγητής Ιωάννης Κακίσης

Η Τριμελής Εξεταστική Επιτροπή η οποία ορίσθηκε απο την ΓΣΕΣ της Ιατρικής Σχολής του Παν. Αθηνών Συνεδρίαση της 13ης Ιανουαρίου 2017 για την αξιολόγηση και εξέταση του υποψηφίου κου Μπουλταδάκη, συνεδρίασε σήμερα 19/05/2017

Η Επιτροπή **διαπίστωσε** ότι η Διπλωματική Εργασία του Κου Μπουλταδάκη Ευάγγελου με τίτλο ***«DOES TEVAR MODIFY THE CARDIAC FUNCTION AND THE AORTIC STIFFNESS?»,*** είναι πρωτότυπη, επιστημονικά και τεχνικά άρτια και η βιβλιογραφική πληροφορία ολοκληρωμένη και εμπεριστατωμένη.

Η εξεταστική επιτροπή αφού έλαβε υπ' όψιν το περιεχόμενο της εργασίας και τη συμβολή της στην επιστήμη, με ψήφους ..... προτείνει την απονομή στον παραπάνω Μεταπτυχιακό Φοιτητή την απονομή του Μεταπτυχιακού Διπλώματος Ειδίκευσης (Master's).

Στην ψηφοφορία για την βαθμολογία ο υποψήφιος έλαβε για τον βαθμό «ΑΡΙΣΤΑ» ψήφους ....., για τον βαθμό «ΛΙΑΝ ΚΑΛΩΣ» ψήφους ....., και για τον βαθμό «ΚΑΛΩΣ» ψήφους ..... Κατά συνέπεια, απονέμεται ο βαθμός «.....».

Τα Μέλη της Εξεταστικής Επιτροπής

- Καθηγητής Γεώργιος Γερουλάκος Επιβλέπων (Υπογραφή) _____
- Καθηγητής Αχιλλέας Χατζηϊωάννου (Υπογραφή) _____
- Αν. Καθηγητής Ιωάννης Κακίσης (Υπογραφή) _____

Στον κόσμο του μόχθου,

με την ελπίδα να φτάσει ο καιρός που

η μελέτη και η πρόοδος της επιστήμης

θα έχει ως άμεσο αποτέλεσμα

την βελτίωση της ζωής τους !!

Στους Γονείς μου,

στη Νικολέτα !!

ΠΕΡΙΕΧΟΜΕΝΑ

DOES TEVAR MODIFY THE CARDIAC FUNCTION AND THE AORTIC STIFFNESS?

Introduction

Endovascular aortic repair is widely performed in patients with thoracic (TAA), thoracoabdominal (TAAA) or abdominal aortic aneurysm (AAA) because it is less invasive than conventional open repair and improves postoperative quality of life. This technique was described first Volodos and his colleagues and is performed by inserting a fabric tube supported by a metal framework through a catheter into a weakened artery (aneurysm) [1, 2].

Later, in early 1990, Parodi and his coworkers conducted the first endovascular abdominal aortic aneurysm repair (EVAR) and since then this process is widely accepted as a safe, effective and less invasive treatment compared to open AAA surgical repair [2]. Thoracic endovascular aortic repair (TEVAR) for descending thoracic aortic aneurysms was first reported by Dake in 1994[3]. Although, EVAR and TEVAR have been widely used into daily clinical practice, recent trials have reported that despite their early survival advantage over conventional open repair[4], the rate of overall survival is similar for both procedures over longer follow-up periods[5, 6]. Yet, cardiovascular mortality remains the main cause of death among AAA patients, even after a successful vascular surgery[7, 8]. The poor outcome of these patients is mainly due to their general bad health condition. For example, in the trial comparing 2-year outcomes of patients receiving treatment for AAAs, a number of deaths from congestive heart failure were documented only in the EVAR group[5]. However, a deleterious effect of the biomechanical changes induced by graftprostheses or stentgrafts is a subject of studying.

Furthermore, the insertion of endovascular prosthesis, such as Dacron, in the descending aorta during the repair of traumatic disruption has been shown to increase characteristic impedance (stiffness) of the ascending aorta[9]. This increase in stiffness can potentially have a negative impact on cardiac and may predispose to the development of left ventricular (LV) hypertrophy[10-12]. The effects of the

endovascular aortic repair on vascular stiffness and LV performance need to be clarified.

The purpose of this article is to review the scientific literature in order to elucidate the relationship of TEVAR with the arterial stiffening and to investigate the effect to the cardiac function and especially to the LV.

Methods

The search strategy and data collection in this study are based on the search strategy and data collection guidelines of the Meta-analysis Of Observational Studies in Epidemiology (MOOSE). Medline was searched for relevant articles. This search on the MEDLINE revealed approximately 500 articles. Titles and abstracts of these articles were independently read and examined. Inclusion criteria were: (1) examination of stiffness of the descending thoracic aorta before or after endovascular aortic aneurysm repair, (2) examination of the cardiac function to the patients with TEVAR, (3) examination of the effect of aortic stiffeness to the left ventricle and in general the cardiac function in patients who had TEVAR. Fifty-two full-text versions of studies that matched the inclusion criteria were obtained.

Approximately, half of them were excluded because were irrelevant with our subject. After inclusion and exclusion, 26 relevant articles reporting on aortic stiffening and its effect to cardiovascular system remained, and the effect of TEVAR to this situation, allowing for further study.

Results

The study of the literature was organized in two subdivided areas:

1. First was studied the effect of aortic stiffness to the cardiac function, and secondly,

2. The role of endograft in arterial stiffness, and as a consequence the aortic stiffness to the heart.

Thus, the analysis of the results was divided into two sections.

A. Arterial stiffness and Cardiac impact

The cardiovascular system is designed to supply with the appropriate blood pressure and flow the human body. Because blood flow does not follow a straight line, changes in the cardiac output bring alterations in the arterial pulse wave and pressure. Widening of the arterial pulse is common in the older people and is an index of arterial stiffness. Age together with other degenerative processes are responsible for progressive large arterial stiffening, a process known as arteriosclerosis [13, 14], and this aged – related vascular stiffness is usually followed by end systolic chamber stiffness of the left ventricle[15]. Arterial stiffness has been recognized as a measure of target organ damage [16, 17], and its clinical implications should be considered together with the cardiac function, as it is known that the interaction between the ventricular – arterial coupling is the key determinant of the cardiovascular function[18-20].

I. Ventricular/Vascular Coupling

The function of the heart is to send enough blood supplies (cardiac output) through the arteries to the organs and tissues, in order to meet their metabolic requirements[21]. If the heart is ideally matched to its afterload, then ventricular/vascular coupling and cardiac efficiency are optimal and myocardial oxygen consumption is minimal[22]. Moreover, the amount of oxygen that left ventricle is using in order to produce the cardiac output is dependent from both myocardium and arterial system. The flow inside the arteries consists from the static (nonpulsatile) and dynamic (pulsatile) components. These two parameters generally referred to elastance, pulse wave reflectance (dynamic) and peripheral vascular resistance (static) and can be obtained in the frequency domain from the aortic input impedance spectrum (**Fig. 1.)[**22-24].

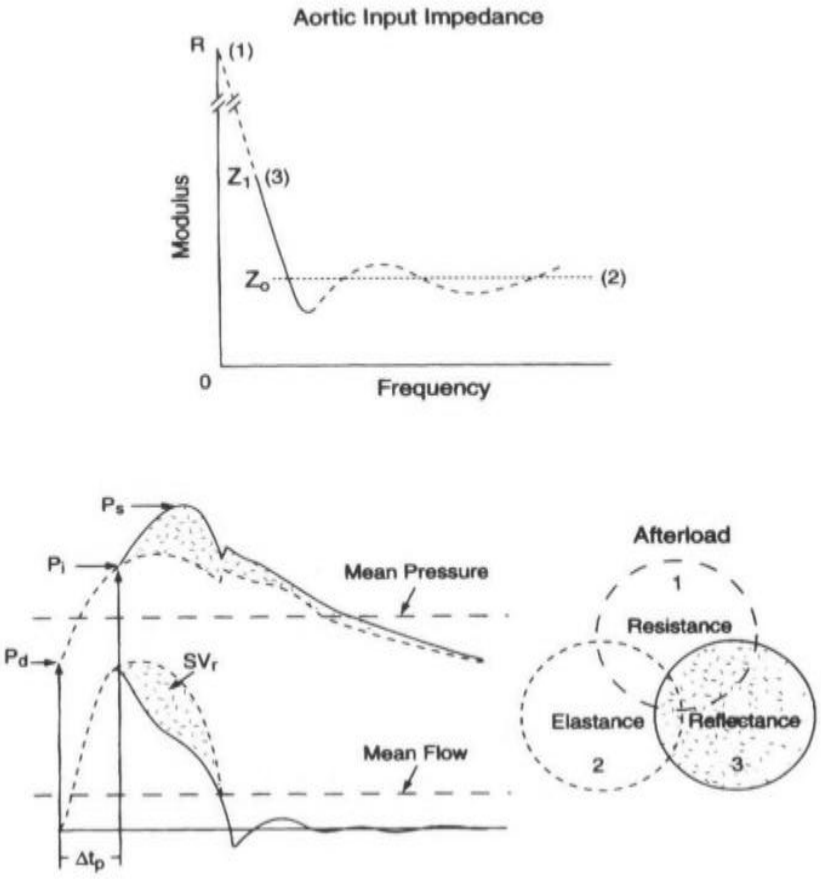

Fig. 1. (Top) Schematic diagram illustrating the different components of the ascending aortic input impedance moduli spectrum. (*1*) Input impedance alt zero frequency or peripheral resistance (*R*). (*2*) Mean value of impedance moduli > 2 Hz or characteristic impedance (Z_0). Z_0 is an index of aortic elastance. (3) Fundamental impedance moduli (Z_1) is an index of wave reflection amplitude ($Ps-P_i$); reflectance. Impedance minimum is related to pulse wave velocity and distance to the major reflection site. **(Lower left)** High-fidelity pressure and flow velocity waveforms measured in the ascending aorta of a middle-aged patient. P_s is peak systolic pressure. P_i is an inflection point that indicates the beginning upstroke of the reflected pressure wave, and P_d is minimum diastolic pressure. Δt_p is the roundtrip travel time of the forward (or initial) wave from the ascending aorta to the major reflecting site and back (backward traveling or reflected wave). The reflected pressure wave adds to the forward traveling wave while the reflected flow wave subtracts from the forward wave. The stippled areas (pressure and flow) represent that part of the respective wave that is reflected. SV_r is that part of stroke volume that is associated with the reflected flow wave, that is, the part of stroke volume that would be ejected in a reflection less system. **(Lower right)** Venn diagram illustrating the three components of afterload. ***1.*** The nonpulsatile or static component is resistance, and the pulsatile or dynamic components; ***2.*** elastance; and ***3.*** reflectance. Changes in any (or all) of this afterload components can alter ventricular function ***(From Wilmer W. Nichols et al)***

An increase in the pulsatile components (elastance and reflectance) of afterload causes an undesirable mismatch between the ventricle and the arterial system which increases myocardial oxygen consumption and decreases cardiac efficiency [10]. These changes in ventricular/vascular coupling promote the development of left ventricular hypertrophy and coronary artery disease, which often lead to myocardial infarction, heart failure, and cardiac arrest.

Furthermore, the influence of ventricular and vascular stiffness on cardiovascular function most easily appreciated by the pressure-volume plane[25]. Ventricular systolic stiffness (contractility) is expressed as end systolic elastance (Ees; Fig. 2), the slope of the end-systolic pressure volume relationship[26]. However, the gold standard method for the calculation of cardiac afterload is through the aortic impedance, in addition, with Fourier analysis of aortic pressure and waves[23, 27]. Sunagawa and his colleagues suggest an alternative index of arterial stiffness and they call it effective arterial elastance (Ea), which although is measured in the same units as Ees, it is easier to calculate it[28]. It also combines both mean and pulsatile loading and in the graph is presented as the negative slope of the line through the end systolic and end diastolic volume (P=0)[25].

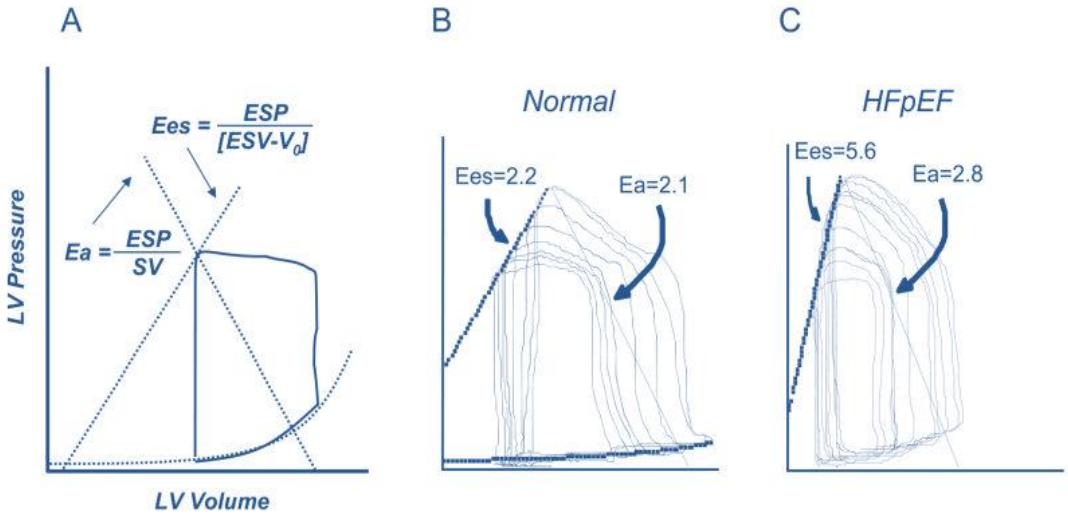

Figure 2. [A] Left ventricular end systolic elastance (Ees) is described by the slope and intercept of the end-systolic pressure-volume relationship, while arterial elastance (Ea) is defined by the negative slope between the end-systolic pressure volume point and end diastolic volume. **[B]** A normal adult has relatively low Ees and Ea, with a coupling ratio around unity, while older aged, hypertensive and HFpEF subjects [C] display marked increases in ventricular and arterial elastance. *(From Borlaug BA[1], Kass DA. Ventricular-vascular interaction in heart failure Heart Fail Clin. 2008 Jan.)*

Experimental and clinical studies tend to suggest that the effective cardiac and artery coupling has to combine the external work or efficiency. Good prediction of these two parameters can easily be found form the ratio Ea/Ees between 0.6 – 1.2[28]. This range can be disrupted and this situation, known as afterload mismatch, is presented in pathological circumstances [29] and with aging and exercise, explaining its age – dependency [30].

II. Mechanism and Pathophysiology

As it is mentioned, Ees is responsible for the arterial and ventricular stiffness. It is determined by either contracting or passive activity of the muscle. In general, it is related to properties of myocyte size, chamber geometry, intra-sarcomeric protein composition, cytosolic and membrane distensibility, and extracellular matrix composition, fibrillar crosslinking, and biophysical properties. Systolic ventricular elastance is related to the same determinants, as well as activated myofilament properties, changes in structural protein behavior shortened to smaller lengths, and interactions of the activated myocytes with the matrix. Smooth muscle tone plays an important role, as does the geometry of the vessel (e.g. dilation), elastin and collagen content, cross-linking of matrix components, and other factors[25, 31].

Several researchers have cited similar theories. Menon et al studied the hemodynamic, endothelial and protein expression changes that occur in patients with aortic coartacion before and after repair[32]. They described the vascular remodeling which is the response to physiological or pathological stimuli wherein blood vessels undergo compensatory changes in lumen diameter and wall thickness to maintain wall tensile stress or wall share stress (WSS)[32-34]. The vascular endothelium is dynamic and impaired vasorelaxation through endothelial nitric oxide (NO) release, known as “endothelial dysfunction”, is a characteristic effect of hypertension in human and animal models including prior CoA models [35]. Similar findings happen also during the arterial constriction during the response of them to hypertension. Smooth muscles, who mediated to this action, as alterations in the resting and active contractile force of elastic conduit arteries, such as the thoracic aorta and carotid arteries, may indicate atherogenic changes in stiffness[36]. Other evidences suggest that these vascular

behavior between vasoconstriction and vasorelaxation may be the major factor in coronary artery disease (CAD)[37].

In general, as central arterial elastance and wave reflection amplitude increase, systolic pressure rises, arterial pulse pressure widens, and ventricular wall stress and myocardial oxygen demand increase while aortic diastolic pressure decreases[21]. Since the main coronary flow occurs during diastole, it is obvious that such unbalance in their blood supplies affects negative the heart and promote myocardial ischemia and contractile dysfunction[22]. In addition, in the studies s by Watanabe and associates [38] and Ohtsuka and co-workers [39], when the heart ejected into a stiff or noncompliant aorta, systolic pressure and myocardial oxygen demand increased and diastolic pressure decreased but coronary blood flow also increased in response to the increased demand. It is obvious that myocardial contractile function was maintained at rest. **Table 1** summarizes the effects of ventricular/arterial stiffening.

Framingham publication that investigated the various blood pressure components as predictors of risk for coronary heart disease showed that in middle-aged and elderly individuals, coronary heart disease risk was significantly increased with lower diastolic pressure [40]. Others have also shown an inverse (or negative) relationship between diastolic blood pressure and both myocardial infarction [41, 42] and cardiovascular mortality [43, 44].

Moreover, as large artery stiffness is related with cardiovascular mortality Bronwyn et al tried to find a threshold point in patients with CAD[45]. Factors as Systemic Arterial Compliance (SAC), Distensibility Index (DI), PWV, and Augmentation Index (AI) were used to assess different aspects of large artery stiffness at rest in relation to ischemic threshold. All of them correlated in various ways with time to ischemia. Therefore, the new finding of this study is that large artery stiffness is an important independent determinant of myocardial ischemic threshold during exercise in patients with CAD. It also can be used the factors that the researchers studied as alternative indexes of the large artery stiffness.

Underlying Abnormality	Hemodynamic Consequences	Clinical Relevance
Increased Ventricular Systolic Stiffness	1. Exaggerated change in blood pressure for a given change in preload or afterload 2. Lower contractile reserve 3. Lower stroke volume reserve 4. Greater energetic cost to eject a given stroke volume	1. Hypotension and oliguria with slight over-diuresis or the addition of a new vasodilator agent 2. Modest volume infusion leads to hypertension and/or acute pulmonary edema 3. Impaired exercise tolerance and functional disability 4. Increased myocardial oxygen demand and ischemia
Increased Arterial Stiffness	1. Exaggerated change in blood pressure for a given change in preload or contractility 2. Increased total afterload, wave reflections and late systolic load 3. Greater dependence upon systolic pressure for coronary flow 4. Abnormal endothelial mechanotransduction	1. Same as #1 and #2 above 2. Impaired relaxation and decreased LV diastolic compliance, prolonged systole, abbreviated diastole 3. Increased ischemia and infarct size for a given drop in systolic blood pressure 4. Endothelial dysfunction, abnormal vasodilation response to stress

Table 1. Pathophysiology of Ventricular-Vascular Stiffening.
(From Borlaug BA et al, Ventricular-vascular interaction in heart failure Heart Fail Clin. 2008)

As further investigations and clinically-based pathophysiologic research continues to identify mechanisms whereby ventricular-arterial stiffening impairs cardiovascular function, and basic research defines the key cellular players involved in promoting ventriculoarterial stiffness, remodeling, and hypertrophy, we will increasingly be able to better treat patients with ventricular/arterial stiffness risk by targeting these pathophysiologic pathways.

B. Arterial Stiffness after TEVAR and their effect to the LV

Open surgical aneurysm repair remains the preferred treatment. However, endovascular aortic repair is a widely performed method nowadays. Although, they considered as an effective alternative treatment to the conventional open repair, few data are available about the connection of endovascular grafts and the mechanical aortic and cardiac changes. Experimental studies show that aortic endografts increased arterial stiffness in animal models [46]. In addition, it can be assumed that the alterations of aortic mechanical properties can have a direct impact on heart output.

Increased central aortic stiffness has potentially important prognostic implications and it has been associated with increased cardiovascular morbidity and mortality in follow-up studies [47, 48]. Several indexes have been studied as prognostic factors of cardiac function. Most of them have been correlated with the aortic stiffness. However, there is indicated a link between the levels of PWV and the risk of late cardiovascular events[49, 50]. Thus, PWV is accepted as the most simple, robust, and reproducible method to determine the regional arterial stiffness. There is a linear correlation between the speed of travel of pulse along an arterial segment and arterial stiffness[46, 51].

Supporting this theory, Takeda and his colleagues studied the early and the long-term outcomes of consecutive patients who had endovascular aortic repair and their effect to the cardiac function, cardiac geometry and exercise tolerance[52]. They enrolled 40 patients who underwent endovascular aortic repair (8 TAA cases, 2 TAAA cases, 30 AAA cases). Echocardiography and brachial–ankle pulse wave velocity (baPWV) data were collected before, 1 week, and 1 year after the procedure.

The results of this study demonstrate for first time that endovascular procedure increases vascular stiffness and induces LV hypertrophy and Left Atrium (LA) enlargement without elevating blood pressure (BP) in the short-term postoperative period. As result of this phenomenon, these patients have limited performance and generated clinical symptoms.

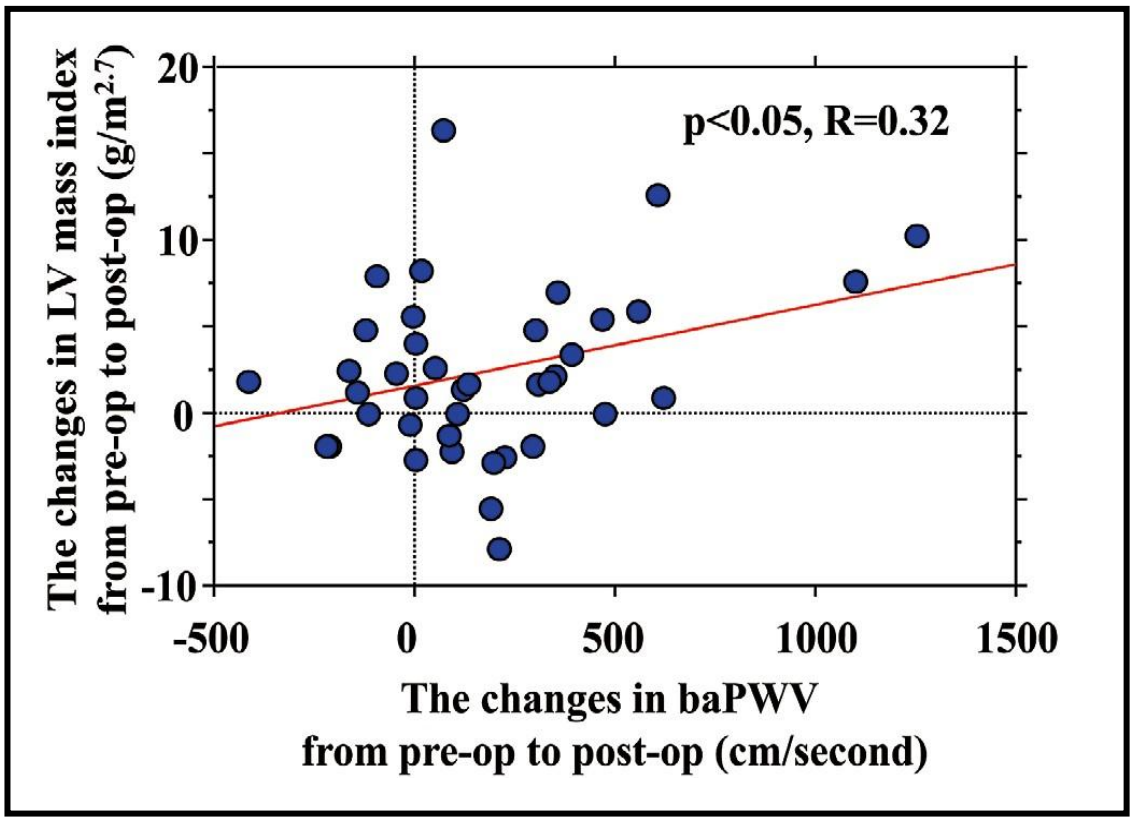

Figure 3. Relationship between changes in left ventricular (LV) mass index from pre-op to post-op and those in brachial–ankle pulse wave velocity (baPWV). As shown by the trendline, the changes in LV mass index positively correlated with those in baPWV (From Takeda Y et al, Circ J. 2014)

The same author few years earlier in collaboration with Yamashina and his partners, had suggested the baPWV as a simple, noninvasive method, suitable for screening vascular damages in a large population[53]. How important is this index for the evaluation of vascular disease was confirmed by the results of this study. More specific, baPWV were higher in non-Coronary Artery Disease (CAD) patients with risk factors than in healthy subjects without risk factors. Therefore, this factor could help in the outcome of these patients.

However, these patients are characterized by high comorbidity because of their various health problems and especially cardiovascular diseases. In the meantime, several studies correlate the levels of the blood pressure with the age and the role of PWV as a prognostic factor for cardiovascular problems. Meaume S. and his partners showed that aortic PWV was a major independent predictor of Cardiovascular (CV) mortality and that this marker was extremely powerful over the cut-off point of 17.7 m/sec[54]. Thus, the validity and reproducibility of baPWV measurements are considerably high, and this method seems to be an acceptable marker reflecting vascular damages.

In addition, Tzilalis et al made a clinical study with 11 patients who underwent TEVAR because of thoracic aortic transection. They observed that nine of these patients presented arterial hypertension postoperatively and four had hypertension during the follow – up. The authors supported that endografts produce a discontinuation of pulsaltile waves, which increases the aortic PWV. Tzilalis and co-authors concluded that this is a significant risk factor to develop cardiovascular disease these type of patients[55].

The results of the arterial stiffening especially after intervention to the aorta can also be observed in patients with aortic coarctation (CoA) repair. There have been raised many concerns about the outcome of these patients whose aorta have been corrected. Several studies have dealt with their life expectancy, because of the complications that they present late. A high proportion of asymptomatic young adults who survived the aortic repair, develop significant hypertension either at rest[56] or during exercise[57]. Nowadays, stent implantation to these patients, has become the treatment of choice for adolescents and adults[58]. Despite its wide preference, there are only few articles, which studied the long-term effects of stents to these patients. Maschietto and colleagues performed an experimental protocol to growing animal models[59]. Their results showed that stent does not alter the overall hemodynamics of the aorta, results which agree with Pihkala et al[60]. Nonetheless, alterations of the normal laminar blood flow at the level of the interface between the stent and the native artery induced oxidative stress (OS), endothelial dysfunction (ED) and increased protein turn over in the ascending aorta (ASAO) above the stent. The researchers try to correlate the endothelial aortic damage with gene expression, such

as NOS3, SOD1 and MMP9 in ASAO. Although, the present results cannot predict any clinical relevance of the grafts with the aorta, they concluded that having implanted a stent in it of otherwise normal animals, it can induce OS, ED, and increased stiffness in ASAO but not hypertension[59].

However, endovascular repair of the aorta does not always bring negative impact to the cardiac function and especially LV. Toshihiro Yamaguchi and his coauthors suggest that Aortic structure or pathology may affect afterload to various extents[61]. They presented one of their patients, a 78-year-old man with severe heart failure who made a dramatic recovery from cardiac decompensation following endovascular thoracic aortic aneurysm surgery. His severe depressed cardiac function and heart failure dramatically improved following stent grafting. Furthermore, the left ventricular ejection fraction improved from 13% pre-surgery to 55% post-surgery and the serum brain natriuretic peptide (BNP) level had significantly decreased to 70– 240 pg/mL. This case suggests that other hemodynamic modulating factors derived from an aortic aneurismal lesion can affect cardiac function and modify the conditions of heart failure.

Several hypotheses and theories have been introduced. Sughimoto et al suggested a new model of blood flow dynamic and its energy loss and how grafting of the dilated aorta may ameliorate these hemodynamic disturbances, contributing to the alleviation of the energy efficiency of blood flow delivery[62]. Similar protocols have been proposed in the past, although, needs more studies to be determined[63].

Moreover, the exact association between heart failure and aortic disease is not completely clear. Until this point, we presented various theories who suggest that TEVAR probably affect negatively the LV. However, Cuypers, et al reported that hemodynamic parameters, including cardiac index and stroke volume, were improved after aortic aneurysm repair with both open and endovascular surgery[64]. To verify this hypothesis, Sughimoto and colleagues investigated changes in cardiac function in patients who underwent aortic aneurysm repair by comparing cardiac function before and after the intervention[62]. The results showed Left Ventricle Ejection Fraction (LVEF) improvement on echocardiography after aortic aneurysm repair and the mean value of LVEF significantly increased from 64.9 ± 5.8% to 72.3 ± 5.6% perioperatively ($P < 0.05$). In conclusion, the presence of an aortic aneurysm may

magnify the favorable effects of aortic aneurysm repair on patients with aortic aneurysm and exacerbating heart failure. However, most of these cases refer to abdominal aortic aneurysm and so further investigation is needed.

Finally, reviewing the literature, a very interesting article analyzes the dynamics of the aorta before and after endovascular aneurysm repair[65]. This review article presents, among others, three studies that were concerned of the dynamic changes on the thoracic aorta. However, only one of these observed the changes of the thoracic aorta before and after TEVAR procedure[66].

Furthermore, Van Prehn and his colleagues studied the changes in patients with TAA who were evaluated for TEVAR to their institute, were scanned pre- and postoperatively using dynamic cine-Computed Tomographic Angiography (CTA). There were selected five positions along the thoracic aorta t measure aortic distention during cardiac cycle. The results showed significant distention of the thoracic aortic arch and descending thoracic aorta during the cardiac cycle before and after TEVAR. Distention ranged 3-12% in diameter and 2-20% in area. In addition, this distention was preserved after TEVAR [66]. The mean differences between the minimum and maximum aortic area per heartbeat in this study group, reported from proximal to distal, were 6.3%, 6.2% and 6.3%. Postoperatively, there was significant distension at several levels

The next two studies measured the aortic distension at different levels of the thoracic aorta. Van Prehn et al. and Muhs et al. observed the distension of the thoracic aorta in patients with AAA. The researchers use the same method as in the previous article. Maximum diameter and area change per cardiac cycle was measured at surgically relevant anatomic thoracic landmarks. There is impressive change in both maximum diameter and area in the thoracic aorta during the cardiac cycle. Mean area changes of the ascending aorta, reported from proximal to distal, were 12.7%, 7.5% and 5.6%[67]. However, only the mean distension most proximal to the heart was significant. Respectively, in the second study, mean area changes of the aortic arch and descending thoracic aorta, reported from proximal to distal, were 4.8%, 5.0%, 5.5% and 7.0%[68]. Again, none of those values was significant.

Regarding the results of TAA dynamics, it is shown that the thoracic aorta expands significantly at relevant levels per heartbeat too. Since the diameter of the thoracic aorta is larger than the diameter of the abdominal aorta, equal relative changes will result in larger absolute changes[65]. In addition, aortic distention varies among those patients and it might be possible those people who have more pronounced distention to be the one with more probably compromised graft durability.

These results suggest that the native thoracic aorta in patients with TAA exhibits various importance distention throughout the cardiac cycle, and this phenomenon is reported that is preserved even after endograft implantation [66]. This statement seems to be in contrast with the arterial stiffness and needs further study.

Discussion

In this systematic review, an overview of the current knowledge of aortic stiffness before and after TEVAR and its effect to the cardiac function is given. As it was presented the arterial stiffness is related with age and other degenerative processes which together are known as arteriosclerosis [13, 14]. This aged – related vascular stiffness is usually followed by end systolic chamber stiffness of the left ventricle [15]. In addition, it is repeated that arterial stiffness has been recognized as a measure of target organ damage [16, 17], and its clinical implications should be considered together with the cardiac function, as it is known that the interaction between the ventricular – arterial coupling is the key determinant of the cardiovascular function[18-20].

This is the reason why researchers as Bronwyn et [45] suggested factors as Systemic Arterial Compliance (SAC), Distensibility Index (DI), PWV, and Augmentation Index (AI) to assess different aspects of large artery stiffness at rest in relation to ischemic threshold. However, the new finding of this study is that large artery stiffness is an important independent determinant of myocardial ischemic threshold during exercise in patients with CAD.

However, the innovation to this subject came from Takeda and his colleagues who demonstrated for the first time that endovascular techniques increase vascular stiffness and induces LV hypertrophy and LA enlargement without elevating BP in the short-term postoperative period [52] situation that leaded to limited clinical symptoms. And for the best screening of vascular damages in a large population the same author few years earlier in collaboration with Yamashina and his partners, had suggested the baPWV as a simple, noninvasive method, suitable for [53].

Although, Takeda suggested that hypertension is not always connected to patients with TEVAR and arterial stiffness, this is a topic with a lot of controversies. Tzilalis et al found that nine of their patients had postoperative arterial hypertension after TEVAR, and four had durable hypertension during the follow-up period [55]. In addition, they suggested that aortic endografts could produce a discontinuation of the pulsatile waves with a subsequent increase of aortic PWV. Thus, Increased PWV is an

important risk factor for future cardiovascular events and should be evaluated in all patients after TEVAR.

However, the most interesting findings were presented by Toshihiro Yamaguchi et al who presented the positive effect that TEVAR offered to an 78 year old patient with severe cardiac failure. They suggested a possible beneficial effect of aortic aneurysm repair for improving cardiac function and heart failure and a new concept of another extrinsic factor that can affect cardiac function through modulation of afterload [62]. Despite all the observations presented in this article, the clinical relevance of TEVAR with aortic stiffeness and cardiac function has not yet been proven. All the presented studies are observational studies, and none of them confirms a relationship between them. Future studies and clinical trials are necessary to study the influence of TEVAR on clinical outcome to either aortic stiffness or heart function. The value of dynamic preoperative or postoperative number of PWV for the evaluation of patient's outcome need to be studied.

Conclusion

To conclude, cardiovascular mortality remains the main cause of death among patients with aortic aneurysm, even after a successful vascular surgery. This brief review was made to present the significant effect of arterial stiffness to the heart function. In addition, it wants to present the most recent studies who studied the correlation of aortic endografts, especially TEVAR, to the arterial stiffness and to the LV function. The results of this study show that endovascular techniques have controversial effect to cardiac function. However, it can be concluded that blood pressure is a matter of study because in either elevated (hypertension) or small levels (small diastolic pressure) can affect the coronary arteries. In addition, PWV is an important index for the evaluation of patients with TEVAR. Also, a cut off point of 17.7 m/sec can be used as a major independent predictor of Cardiovascular (CV) mortality. It is obvious that small research has been done to this particular subject. However, as endovascular surgery is becoming the gold standard for the vascular disease and especially aneurysm repairs, these patients require more and deeper investigation.

Περίληψη

Εισαγωγή: Αναφέρεται στη βιβλιογραφία ότι η ενδαγγειακή αποκατάσταση ανευρυσμάτων της κατιούσας θωρακικής αορτής επηρεάζει την ελαστικότητα της αορτής μετρέποντάς την σε άκαμπτο αγγείο. Γεγονός που συσχετίζεται με αυξημένη καρδιαγγειακή θνησιμότητα.
Σκοπός της παρούσας μελέτης είναι να μελετήσει τη βιβλιογραφία και να ερευνήσει την επίδραση που έχουν τα ενδομοσχεύματα της κατιούσας θωρακικής αορτής στην ελαστικότητα της αορτής αλλά και στην καρδιακή λειουργία.

Μέθοδος: Ως βάση δεδομένων χρησιμοποιήθηκε το Medline όπου χρησιμοποιήθηκαν παρεμφερείς εκφράσεις για τον έλεγχο της βιβλιογραφίας. Αφού οριοθετήθηκαν τα κριτήρια με τα οποία θα επιλέγονταν τα άρθρα για μελέτη πραγματοποιήθηκε η μελέτη της βιβλιογραφίας. Αφαιρέθηκαν όσα θεωρήθηκαν πως δεν πληρούσαν τα κριτήρια και τελικά καταλήξαμε σε 26 άρθρα τα οποία μελετήθηκαν διεξοδικά.

Αποτελέσματα: Λόγω του περιεχομένου της μελέτης διαπιστώθηκε πως δεν υπάρχουν πολλά άρθρα και μεγάλες μελέτες πάνω στο συγκεκριμένο αντικείμενο. Ωστόσο, η ακαμψία των αγγείων και δη των αρτηριών αποτελεί βλάβη των οργάνων στόχων και οι οποιεσδήποτε βλάβες αυτών συσχετίζονται άμεσα με την καρδιακή λειτουργία. Αυξημένη αορτική ακαμψία ή μειωμένη ελαστικότητα της αορτής έχει κακή προγνωστική αξία καθώς συσχετίζεται με αυξημένη καρδιαγγειακή νόσο. Ο δείκτης ταχύτητας μετάδοσης του παλμικού κύματος (Pulse Wave Velocity, PWV) θεωρείται ως ο πλέον απλός, ανεξάρτητος, αξιόπιστος και ανακυκλώσιμος δείκτης για της εκτίμηση της περιοχικής ελαστικότητας μίας αρτηρίας. Επίσης, αποτελεί προγνωστικό παράγοντα της καρδιαγγειακής θνησιμότητας με ισχυρή προγνωστική ικανότητα από τη τιμή των 17.7 m/sec και πάνω. Ανάλογα αποτελέσματα μπορούν να παρατηρηθούν στους ασθενείς με συγγενή στένωση αορτής (Aortic coartation, CoA). Μελέτες υποστηρίζουν πως σε αυτούς τους ασθενείς η ενδοπρόθεση δεν προκαλεί αιμοδυναμικές μεταβολές στο αγγείο. Ωστόσο,αύξηση της ροής του αγγείου στο σημείο της μετάπτωσής του στην ενδοπρόθεση επάγει το οξειδωτικό στρες (Oxidative Stress, OS) και την ενδοθηλιακή δυσλειτουργία (Endothelial Dysfunction, ED) καθώς και την αυξημένη εναπόθεση πρωτεϊνών στην ανιούσα θωρακική αορτή (Ascending

Aorta, ASAO) κεντρικότερα της ενδοπρόθεσης. Ωστόσο, οι παραπάνω μεταβολές φαίνεται να προκαλούν σχετική ανελαστικότητα της αορτής, χωρίς όμως να προκαλούν αύξηση της αρτηριακής πίεσης. Η υπέρταση αποτελέι διφορούμενο ζήτημα, καθώς στη βιβλιογραφία ένας μεγάλος αριθμός μελετών παρουσιάζουν αυξημένα ποσοστά υπέρτασης στους προαναφερόμενους ασθενείς. Τέλος, μικρός αριθμός μελετών αναφέρουν βελτίωση παραμέτρων όπως καρδιακός δείκτης και όγκος παλμού μετά από διόρθωση ανευρύσματος αορτής είτε με ανοικτή είτε με ενδαγγειακή αποκατάσταση. Χαρακτηριστικά, το κλάσμα εξώθησης (ejection fraction,EF) βελτιώθηκε από 13% προεγχειρητικά σε 55% μετεγχειρητικά, ενώ και οι τιμές του νατριουρητικού πεπτιδίου (Brain Natriuretic Peptide, BNP) μειώθηκαν χαρακτηριστικά στα επίπεδα του 70 – 240 pg/mL.

Συμπέρασμα: Η παρούσα μελέτη καταλήγει πως οι επιπτώσεις της ενδαγγειακής αποκατάστασης στην καρδιακή λειτουργεία έχουν αντικρουόμενα αποτελέσματα. Ωστόσο, η συστηματική αρτηριακή πίεση μπορεί και πρέπει να αποτελέσει αντικείμενο μελέτης καθώς έχει άμεση επίδραση στην καρδιακή λειτουργεία και συχετίζεται και άμεσα με την καρδιαγγειακή νόσο (επηρεάζεται η διαστολική λειτουργεία της καρδιάς). Επίσης, προτείνει το δείκτη ταχύτητας μετάδοσης του παλμικού κύματος μέσα από το αρτηριακό δίκτυο ως δείκτη εκτίμησης των ασθενών με ενδαγγειακή αποκατάσταση της κατιούσας θωαρκικής αορτής καθως και της καρδιαγγειακής νόσου αυτών των ασθενών. Τέλος, προτείνει την τιμή 17.7 m/sec ως το όριο για τους ασθενείς αυτούς να εμφανίσουν στεφανιαία νόσο.

Abstract

Introduction: It has been reported that TEVAR affects aortic stiffness which is a factor associated with increased cardiovascular morbidity. The purpose of this report is to review the literature and investigate the effect on TEVAR on the aortic stiffness and the cardiac function.

Methods: Medline was searched for relevant articles. After inclusion and exclusion, 26 relevant articles reporting on aortic stiffening and its effect to cardiovascular system remained, and the effect of TEVAR to this situation, allowing for further study.

Results: The sample size of studies upon this subject is limited and translational studies are missing. However, arterial stiffness has been recognized as a measure of target organ damage and its clinical implications should be considered together with the cardiac function. Increased central aortic stiffness has potentially important prognostic implications and it has been associated with increased cardiovascular morbidity and mortality. Pulse Wave Velocity (PWV) is accepted as the most simple, robust, and reproducible method to determine the regional arterial stiffness. In addition, PWV was a major independent predictor of Cardiovascular (CV) mortality and was extremely powerful over the cut-off point of 17.7 m/sec. The results of the arterial stiffening especially after intervention to the aorta can also be observed in patients with aortic coarctation. In these kind of patients, several studies supported that stent does not alter the overall hemodynamics of the aorta. However, alterations of the normal laminar blood flow at the level of the interface between the stent and the native artery induced oxidative stress (OS), endothelial dysfunction (ED) and increased protein turn over in the ascending aorta (ASAO) above the stent. The conclusion is that having implanted a stent in it of otherwise normal animals, it can induce OS, ED, and increased stiffness in ASAO but not hypertension. The issue of hypertension is controversial because different studies suggest that is a usual result after TEVAR procedures. Finally, it is reported that hemodynamic parameters, including cardiac index and stroke volume, were improved after aortic aneurysm repair with both open and endovascular surgery. The left ventricular ejection fraction improved from 13% pre-surgery to 55% post-surgery and the serum brain natriuretic peptide (BNP) level had significantly decreased to 70 – 240 pg/mL.

Conclusions: The results of this study show that endovascular techniques have controversial effect to cardiac function. However, it can be concluded that blood pressure is a matter of study because in either elevated (hypertension) or small levels (small diastolic pressure) can affect the coronary arteries. Inn addition, PWV is an important index for the evaluation of patients with TEVAR. Also, a cut off point of of 17.7 m/sec can be used as a major independent predictor of Cardiovascular (CV) mortality. It is obvious that small research has been done to this particular subject

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