Postoperative and mid-term hemodynamic changes after replacement of the ascending aorta

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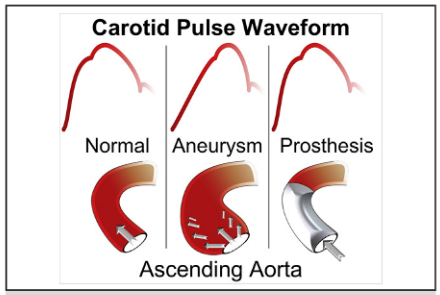
ABSTRACT

Objectives: To evaluate aortic distensibility and pulse waveform patterns associated with the ascending aortic aneurysm, and to analyze the postoperative and mid-term hemodynamic changes induced by prosthetic replacement of the ascending aorta.

Methods: Central blood pressure waves were recorded at the carotid artery level by means of a validated transcutaneous arterial tonometer in 30 patients undergoing prosthetic replacement of ascending aortic aneurysm and in 30 control patients. Measurements were obtained the day before surgery and 5 to 7 days and 16 to 20 months after surgery.

Results: The ascending aortic aneurysm was associated with a less steep slope of early systolic phase of the pressure curve (pulsus tardus) compared with a control group (0.54 ± 0.18 mm Hg/ms vs 0.69 ± 0.26 mm Hg/ms; $P = .011$). Replacing the ascending aorta with a noncompliant vascular prosthesis steepened the pulse pressure slope during the early systolic phase in the postoperative period (0.77 ± .29 mm Hg/ms), providing values comparable with those of the control group in the mid-term (0.67 ± .20 mm Hg/ms). No change in aortic stiffness was found either postoperatively or in the mid-term after ascending aorta surgical replacement (carotid-femoral pulse wave velocity: preoperative, 9.0 ± 2.6 m/s; postoperative, 9.0 ± 2.9 m/s; mid-term postoperative, 9.3 ± 2.8 m/s).

Conclusions: This study does not confirm the assumption that substitution of the viscoelastic ascending aorta with a rigid prosthesis can cause serious hemodynamic alterations downstream, because we did not observe a worsening of global aortic distensibility after insertion of a rigid prosthetic aorta. The ascending aortic aneurysm is associated with a pulsus tardus. (J Thorac Cardiovasc Surg 2022;163:1283-92)



The ascending aortic aneurysm is associated with low slope of the earlier pressure curve.

CENTRAL MESSAGE

Replacement of the ascending aorta with a rigid prosthesis causes significant pulse waveform changes in the postoperative term but does not cause any worsening of aortic distensibility downstream.

PERSPECTIVE

A low systolic maximum upslope of the pressure curve (pulsus tardus) is present in patients with ascending aortic aneurysm and should be considered while interpreting instrumental examinations on peripheral arteries. This study does not confirm the assumption that the substitution of the aneurysmatic ascending aorta with a rigid prosthesis causes serious hemodynamic alterations downstream.

See Commentaries on pages 1293 and 1294.

Replacement of the ascending aorta with a mechanical prosthesis in the presence of a severe aneurysmal dilatation has certainly improved the prognosis of this vascular disorder. However, at present there is little scientific evidence about the systemic hemodynamic effects of this surgical procedure. The ascending aorta and other large elastic arteries play a major role in regulating blood pressure (BP) and peripheral blood flow, damping the pulsatile

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Abbreviations and Acronyms
AIx = augmentation index
BP = blood pressure
PWV = pulse wave velocity

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output of the left ventricle so that the rhythmic, intermittent, and discontinuous activity of the cardiac pump results in a continuous blood flow. This is achieved thanks to the Windkessel effect. In systole, a great quantity of blood remains "stored up" in the aorta and large elastic arteries to be released during diastole. The stored blood stretches the walls of the vessels, generating potential energy, which during the springback of the same walls converts into propulsive kinetic energy, so that proper aortic pressure levels and blood flow are maintained in diastole as well.[1,2] An alteration in the viscoelastic properties of the aorta causes an increase in systolic BP. The resulting increase in cardiac work, together with a reduction in diastolic BP, leads to reduced subendocardial perfusion. Therefore, it can be assumed that replacement of the first part of the aorta (characterized by great viscoelasticity) with prosthetic rigid material may have important repercussions in the systemic circulation.

Furthermore, a number of studies have shown accelerated arterial stiffening associated with aneurysmal dilatation of the ascending aorta, especially when this is associated with altered fibrillin-1 synthesis.[3-6] Thus, replacement of a pathological ascending aorta, characterized by compromised viscoelastic properties, might have a deleterious impact on systemic hemodynamics.

The main aim of the present study was to investigate the early postoperative and mid-term hemodynamic changes induced by prosthetic replacement of the dilated ascending aorta in patients with an aneurysmatic dilation of the ascending aorta. The secondary aim was to evaluate aortic distensibility and pulse waveform patterns in patients with an aneurysmatic dilation of the ascending aorta compared with control subjects.

METHODS

Surgical Patients

This study involved the Cardiac Surgery Unit at the S Orsola Hospital, University of Bologna, the Rare Disease Centre "Marfan Clinic" at the Luigi Sacco University Hospital of Milan, and the Cardiovascular Research Laboratory of the Istituto Auxologico Italiano, Milan, Italy. The study protocol was approved by the local Ethics Committees and conformed with the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained from patients before enrollment in the study.

Consecutive patients undergoing surgery for prosthetic replacement of an ascending aortic aneurysm were evaluated for participation in this study. The exclusion criteria were age <18 years, unavailability to participate in the study, presence of atrial fibrillation, and emergency surgery due to dissection or rupture of aneurysm.

Measurements were obtained at 3 different time points: (1) the day before surgery (presurgery), (2) 1 week after surgery (postop), and (3) approximately 18 months from surgery (mid-term). The mid-term postsurgery measurements were performed within 20 days of a computed tomography scan or magnetic resonance imaging check done to evaluate the draft and valve function.

Control Group

The control group was selected from a large database of individuals followed at the Cardiovascular Preventive Medicine Center of the Istituto Auxologico Italiano, Milan. These patients were selected to match enrolled surgical patients for systolic BP and sex, according to age decade.

Central Pressure Wave Analysis

BP waveforms recorded at the common carotid artery were taken as a surrogate for ascending aortic pressure waveforms. Direct application of tonometry to the carotid artery is considered an easy and reliable approach for recording the central BP waveform.[7-10] Indeed, the carotid artery is generally easy to find and superficial, and good-quality carotid waveforms can be easily obtained by experienced operators (ie, A.G., L.S., and P.S.).

Carotid pulse waves were recorded with a validated PulsePen arterial applanation tonometer (DiaTecne, Milan, Italy).[9,11] The main parameters derived from the analysis of pulse waveform were assessed, especially by separately analyzing data obtained during the systolic and diastolic phases of the cardiac cycle. The slope of the early systolic phase was defined by the change in pressure over time, expressed in mm Hg/ms, and was measured for both carotid and femoral arteries. The forward and backward components of central pulse waveform were evaluated separately,[2,12] providing the following parameters: forward wave amplitude (fP), backward wave amplitude (bP), global reflection coefficient (GRC = bP/fP, ie, the backward and forward wave amplitude ratio), the ratio between backward wave area and total pulse wave area, and the time to peak of forward and backward waves. The augmentation index (AIx) was defined as the difference between the second and first systolic peak and expressed as a percentage of central pulse pressure: AIx = augmented pressure × 100/pulse pressure.[13] Because AIx is strongly affected by heart rate, AIx values were normalized for a theoretical heart rate of 75 beats/min, according to the following formula[14]: $AIx_{@75} = AIx - 0.39\ (75 - \text{heart rate})$.

Assessment of Aortic Stiffness

Carotid–femoral pulse wave velocity (PWV) is considered the gold standard noninvasive method for assessing aortic distensibility,[15] and it has the benefit of good repeatability.[16] PWV was measured as the time delay between the foot of the central (carotid) arterial waveform and the foot of the simultaneously recorded peripheral pulse waveform. An arterial tonometer was placed on the common carotid artery, considered the central detection site, while the second transducer recorded the pulse wave curve simultaneously in the femoral artery. Carotid and femoral pulse waves were recorded with a validated transcutaneous PulsePen-ETT tonometer (DiaTecne).[9,11,17] The distance between the carotid and femoral arteries was measured with a steel tape measure, and the PWV was determined automatically, dividing 80% of the carotid-to-femoral distance by the pulse transit time.[18] In each patient, at each step, PWV measurements were repeated 3 times, with the mean values used in our analysis. Examinations

were usually completed in 10 to 15 minutes. In each condition, brachial BP was measured simultaneously with tonometric acquisitions with a validated oscillometric device (Omron 705IT; Omron Healthcare, Tokyo, Japan).

Statistical Analysis

Continuous variables are reported as mean ± standard deviation for variables with normal distribution (evaluated with Shapiro's test) and as median and interquartile range in cases of nonnormal data. Categorical data are shown as frequencies and proportions. Differences in anthropometric and clinical variables between patients and controls were tested, the unpaired *t* test (Mann–Whitney *U* test in cases of nonnormal distribution) for continuous variables and the χ^2 (Fisher's test in cases of an expected frequency <5) for categorical variables. Two-way repeated-measures analysis of variance was applied to investigate differences in hemodynamic and pulse wave variables between presurgery and postop and between presurgery and mid-term. The comparisons of hemodynamic and pulse wave variables between presurgery and controls and between mid-term and controls were done using the *t* test or Wilcoxon's test.

For both repeated-measures analysis of variance and the *t* test/Wilcoxon's test for unpaired groups performed on hemodynamic and pulse wave variables, the false discovery rate approach[19] was applied to control the problem of inflated type I error due to test multiplicity. Separate univariate and multivariate linear regression analyses were fitted to estimate the differences of the carotid systolic upslope and carotid-femoral PWV between presurgery vs control and between mid-term vs control. We applied a logarithmic transformation of the variables of interest in cases of nonnormal distribution. Along with the variable of interest (surgery patient or control), the multivariate models included some variables defined a priori based on their clinical significance (ie, heart rate and central systolic BP). Finally, a sensitivity analysis including as covariates the 3 matching variables (age, sex, and systolic BP)[20] in addition to heart rate and central systolic BP was carried out.

The sample size was evaluated as follows. Based on the available literature on this topic,[18] we calculated that a sample size of 30 subjects was needed to detect a mean paired difference in PWV of 0.6 m/s (between preoperative and mid-term) with an estimate standard deviation of differences of 1.08 m/s and with a significant level of 0.05 and a power of 0.8 using a 2-sided paired *t* test.

RESULTS

Study Population

This study cohort comprised 30 patients undergoing surgery for prosthetic replacement of an ascending aortic aneurysm and 30 control patients. Table 1 summarizes anthropometric and clinical parameters of the enrolled patients and controls. Twelve patients (40%) had a bicuspid aortic valve, and 5 (16.7%) had a diagnosis of Marfan syndrome. Three patients (10%) already had an implanted mechanical aortic valve prosthesis. In our cohort, the prosthetic replacement of the ascending aorta and aortic root was performed according to the David procedure in 6 patients (20%) and according to the Bentall procedure in 24 patients (80%), with insertion of biological aortic valve in 9 patients (30%) and mechanical valve in 15 (50%). In all patients, the native aneurysmatic aorta was replaced from the aortic annulus to the distal ascending aorta just before the

TABLE 1. Preoperative anthropometric and clinical characteristics of the enrolled patients and controls

Characteristic	aTTA presurgery	Controls	*P* value
Sex, male/female, n	26/4	26/4	1.000*
Age, y, mean ± SD	55.7 ± 13.7	56.1 ± 13.5	.918†
Weight, kg, mean ± SD	81.9 ± 13.2	79.1 ± 12.3	.406†
Height, cm, mean ± SD	174.4 ± 10.0	173.1 ± 6.8	.547†
BMI, kg/m^2, mean ± SD	27.0 ± 4.2	26.3 ± 3.4	.526†
Ejection fraction, %, median (IQR)	61.0 (58-64)	61.5 (58-66)	.664‡
Ascending aorta, mm, median (IQR)	50.0 (46-51)	33.0 (29-35)	<.001‡
Valsalva sinus, mm, median (IQR)	45.7 (40-51)	34.5 (32-37)	<.001‡
Smoking, n (%)	8 (26.7)	7 (23.3)	.766§
Hypertension, n (%)	19 (63.3)	15 (50.0)	.297§
Beta-blockers, n (%)	20 (66.7)	5 (16.7)	<.001§
RAAS antagonists, n (%)	20 (66.7)	13 (40.0)	.069§
Calcium channel blockers, n (%)	6 (20.0)	3 (10.0)	.472*
Diabetes, n (%)	3 (10.0)	2 (6.7)	1.000*
Dyslipidemia, n (%)	8 (26.7)	5 (16.7)	.347§
Thyreopathy, n (%)	3 (10.0)	2 (6.7)	1.000*
Carotid artery atheroma, n (%)	3 (10.0)	6 (20.0)	.472*
Coronary artery disease, n (%)	5 (16.7)	0 (0.0)	.052*
Pacemaker, n (%)	1 (3.3)	0 (0.0)	1.000*

aTAA, Ascending thoracic aortic aneurysm; *BMI*, body mass index; *SD*, standard deviation; *IQR*, interquartile range; *RAAS*, renin-angiotensin-aldosterone system. *Fisher's test. †*t* test. ‡Wilcoxon's test. §χ^2 test.

emergency of the brachiocephalic trunk. No patient underwent hemiarch or arch replacement under circulatory arrest; aortic clamping was performed in all operations. All grafts were polyester. Prosthesis diameter was 32 mm in 7 patients, 30 mm in 15 patients, 28 mm in 7 patients, and 26 mm in 1 patient. Noninvasive hemodynamic measurements were repeated at 3 time points: presurgery (the day before surgery), postop (mean 7.0 ± 0.3 days after surgery), and mid-term (mean 16.6 ± 1.4 months) after surgery.

Hemodynamic Features in the Ascending Aortic Aneurysm

The slope of the early systolic phase of the carotid pressure curves was significantly steeper in the control group than in patients with ascending aortic aneurysm before surgery (0.69 ± 0.26 mm Hg/ms vs 0.54 ± 0.18 mm Hg/ms; $P = .011$). Table 2 shows the preop and mid-term changes in hemodynamic parameters after ascending aorta replacement and comparisons with data recorded in the control group. A multivariate analysis was also performed also including age, sex, and mean arterial pressure as covariates with no change in the results. The ascending aorta aneurysm was associated with a less steep slope of the early systolic phase of the pressure curves (pulsus tardus) compared with the control group (Table 3). Figure 1 shows the average of pulse pressure waveforms in the controls and patients undergoing surgery before and after surgery and highlights the differences in slope of the early systolic phase of the pressure curves. The mean maximum slope of the pressure waveform in the early systolic phase recorded in the carotid artery was similar to that recorded in the femoral artery in all enrolled patients and in different phase of the study: 0.63 ± 0.23 mm Hg/ms in the control group and 0.55 ± 0.18 mm Hg/ms in patients before surgery.

Postoperative Changes

Aortic surgery caused a major loss of blood, as evidenced by the drop in mean hemoglobin (from 14.3 ± 1.3 g/dL to 10.7 ± 1.3 g/dL) and red blood cells (from 4.9 ± 0.5 × 10^{12}/L to 3.7 ± 0.5 × 10^{12}/L) (Table 4). Only 1 patient required blood transfusion. All hemodynamic parameters except PWV and BP values changed significantly in the postop period. Mean heart rate increased significantly in the days following surgery, from 60.6 ± 10.8 bpm to 83.7 ± 14.9 bpm. Increased forward and decreased backward wave amplitude were associated with reduced augmentation index values normalized for heart rate (from 10.3 ± 15.0% to 0.6 ± 15.0%) and global reflection coefficient (from 41.4 ± 9.1 to 29.5 ± 10.3). Replacement of the ascending aorta with noncompliant vascular prosthesis steepened the pulse pressure slope during the early systolic phase in the carotid artery (from 0.54 ± 0.18 mm Hg/ms to 0.77 ± 0.29 mm Hg/ms) and the femoral artery (from 0.55 ± 0.18 mm Hg/ms to 0.78 ± 0.30 mm Hg/ms).

Mid-Term Changes After Aortic Surgery

The computed tomography scan or magnetic resonance imaging check showed the absence of surgical complications and aortic valve alteration or failure in the 18 months following surgery. Heart rate and BP values were higher at 15 to 18 months after aortic surgery compared with before surgery. The mean slopes of the early systolic phase of the carotid and femoral pressure curves remained higher compared with values recorded presurgery (0.67 ± 0.20 mm Hg/ms vs 0.68 ± 0.26 mm Hg/ms), reaching values similar to the upslope measured in the control group ($P = .853$).

The mean carotid-femoral PWV did not significantly change at mid-term (from 9.0 ± 2.6 m/s to 9.3 ± 2.8 m/s). A similar change was observed for the carotid-radial PWV (from 7.8 ± 1.9 m/s to 7.4 ± 1.6 m/s). The control group had comparable carotid-femoral PWV and carotid-radial PWV values (8.6 ± 2.1 m/s and 7.6 ± 1.2 m/s, respectively). Figure 2 illustrates the changes in PWV at the 3 time points of the study, highlighting the changes in patients with Marfan syndrome and in patients who underwent surgery with the David procedure and those who did so with the Bentall procedure.

DISCUSSION

The present study provides some new and important results. No change in aortic stiffness was observed at either the postop or mid-term assessment after ascending aorta surgical replacement. The ascending aortic thoracic aneurysm is associated with pulsus tardus, supported by a less steep slope of the early systolic phase of the pressure curve compared with the control group. Replacing the ascending aorta with a noncompliant vascular prosthesis produced significant postop changes in the pressure waveform. In particular, there was a marked steepening of the pulse pressure slope during the early systolic phase. At 16 to 20 months from surgery, our cohort showed a reduction in the early systolic pulse pressure slope, with values comparable to those of the control group.

To our knowledge, this is the first study designed to evaluate the mid-term hemodynamic effects in patients undergoing prosthetic replacement of the ascending aorta. Some previous studies have explored the hemodynamic changes induced by simulating prosthetic aortic replacement in mathematical models.[21-23] The simulated replacement of the aorta resulted in increased pressure amplitude and increased characteristic impedance, suggesting partial impairment of the aortic Windkessel function. In physiological conditions, during the systolic phase, the aorta is stretched by the blood ejected from the left ventricle, transforming the kinetic energy generated

TABLE 2. Preoperative hemodynamic parameters and short- and mid-term changes after replacement of the ascending aorta: comparison with a control population

Parameter	Presurgery (A)	Postop (B)	Mid-term (C)	*P* value, B vs A*	*P* value, C vs A*	Controls (Ctr)	*P* value, Ctr vs A	*P* value, Ctr vs C
Brachial systolic BP, mm Hg	119.3 ± 18.5	116.4 ± 15.0	128.5 ± 18.8	.447	.037	123.3 ± 14.5	.532†	.536†
Central systolic BP, mm Hg	110.4 ± 16.9	111.7 ± 14.7	119.3 ± 17.9	.682	.031	114.2 ± 12.9	.517†	.513†
Diastolic BP, mm Hg	70.4 ± 11.3	68.6 ± 8.2	76.9 ± 11.5	.401	.017	75.3 ± 9.3	.219†	.783†
Brachial pulse pressure, mm Hg	49.1 ± 11.9	47.8 ± 11.6	51.7 ± 11.2	.668	.340	47.9 ± 10.6	.785‡	.910‡
Central pulse pressure, mm Hg	39.9 ± 10.0	43.2 ± 12.3	41.7 ± 9.9	.277	.332	38.8 ± 10.6	.726‡	.513‡
Mean BP, mm Hg	86.7 ± 13.0	84.5 ± 9.4	94.1 ± 13.4	.388	.017	91.3 ± 10.1	.300†	.718†
Heart rate, bpm	60.6 ± 10.8	83.7 ± 14.9	65.0 ± 8.5	<.001	.050	64.0 ± 9.3	.294‡	.783‡
End systolic BP, mm Hg	92.5 ± 14.6	82.7 ± 11.5	97.0 ± 15.7	.001	.198	95.8 ± 100	.517†	.791†
AIx, %	11.6 ± 13.7	-2.1 ± 18.1	12.6 ± 14.1	.001	.720	2.9 ± 13.8	.051†	.125†
$AIx_{@75}$	6.0 ± 14.6	1.3 ± 17.4	8.7 ± 14.5	.198	.333	-1.3 ± 13.7	.175†	.125†
Global reflection coefficient, %	41.4 ± 9.1	29.5 ± 10.3	40.6 ± 9.5	<.001	.659	35.3 ± 10.2	.110†	.235†
Pulse pressure amplification, %	23.1 ± 7.7	12.7 ± 11.3	22.9 ± 100	.001	.953	25.0 ± 11.1	.596†	.718†
Left ventricular ejection time, ms	316 ± 23	245 ± 21	298 ± 27	<.001	.017	303 ± 23	.175†	.718†
Diastolic time, ms	702 ± 146	495 ± 114	641 ± 108	<.001	.037	654 ± 125	.318†	.783†
Peak time, ms	181 ± 39	107 ± 32	165 ± 33	<.001	.087	146 ± 51	.051†	.354†
Reflected wave delay (Ti), ms	123 ± 35	108 ± 27	105 ± 37	.061	.037	128 ± 43	.959‡	.235‡
BP at Ti, mm Hg	104.0 ± 15.6	105.6 ± 14.6	112.4 ± 15.7	.668	.017	109.6 ± 12.8	.300†	.718†
Time to forward wave peak, ms	132 ± 25	84 ± 19	116 ± 28	<.001	.017	113 ± 30	.092†	.783†
Forward wave amplitude, mm Hg	34.9 ± 8.3	41.2 ± 12.8	37.1 ± 9.4	.020	.332	36.5 ± 10.8	.914‡	.718‡
Time to backward wave peak, ms	279 ± 39	259 ± 53	269 ± 56	.060	.332	288 ± 50	.785‡	.338‡
Backward wave amplitude, mm Hg	14.2 ± 4.3	11.4 ± 3.6	14.6 ± 3.7	.001	.738	12.4 ± 3.4	.318‡	.235‡
Carotid systolic upslope, mm Hg/ms	0.54 ± 0.18	0.77 ± 0.29	0.67 ± 0.20	.003	.017	0.69 ± 0.26	.017‡	.783‡
Femoral systolic upslope, mm Hg/ms	0.55 ± 0.18	0.78 ± 0.30	0.68 ± 0.26	.001	.037	0.63 ± 0.23	.318‡	.718‡
Carotid-femoral PWV, m/s	8.95 ± 2.63	9.01 ± 2.87	9.34 ± 2.84	.841	.302	8.59 ± 2.06	.875‡	.705‡
Carotid-radial PWV, m/s	7.78 ± 1.94	7.17 ± 1.28	7.39 ± 1.60	.106	.332	7.60 ± 1.23	.785‡	.783‡

Values of the variables are presented as mean ± standard deviation. The false discovery rate approach was applied to control the problem of inflation of type I error due to test multiplicity. *Ctr*, Control group; *BP*, blood pressure; *AIx*, augmentation index; $AIx_{@75}$, augmentation index normalized for a theoretical heart rate of 75 bpm; *Ti*, travel time of the reflected wave; *PWV*, pulse wave velocity. *Repeated-measure analysis of variance. †*t* test. ‡Wilcoxon's test.

TABLE 3. Presurgery hemodynamic parameters and mid-term changes after ascending aorta replacement: comparison with a control population

Parameter	Univariable analysis		Multivariable analysis	
	β (SE)	*P* value	β (SE)	*P* value
Presurgery vs controls				
Carotid systolic upslope				
Controls	Reference		Reference	
Presurgery	-0.230 (0.087)	.011	-0.166 (0.071)	.023
Heart rate			0.005 (0.004)	.214
Central SBP			0.013 (0.002)	<.001
Carotid-femoral PWV				
Controls	Reference		Reference	
Presurgery	0.029 (0.064)	.650	0.076 (0.057)	.185
Heart rate			0.008 (0.003)	.007
Central SBP			0.005 (0.002)	.010
Mid-term vs controls				
Carotid systolic upslope				
Controls	Reference		Reference	
Presurgery	−0.016 (0.086)	.853	−0.083 (0.070)	.240
Heart rate			0.004 (0.004)	.362
Central SBP			0.012 (0.002)	<.001
Carotid-femoral PWV				
Controls	Reference		Reference	
Presurgery	0.070 (0.065)	.285	0.033 (0.058)	.575
Heart rate			0.007 (0.003)	.030
Central SBP			0.006 (0.002)	.004

The dependent variables are log-transformed. β indicates regression coefficients. *SE*, Standard error; *SBP*, systolic blood pressure; *PWV*, pulse wave velocity.

by the left ventricle into potential energy stored in the aortic wall. During the recoil of the aortic wall, this potential energy stored in the aortic wall in systole turns into kinetic energy in the diastolic phase of the cardiac cycle, pushing stored blood forward. In this way, the aorta behaves like a sort of pump in diastole.[2] Those previous studies supported the usefulness of developing aortic prostheses using more elastic materials. Semaan and colleagues[24] found in humans that replacing the ascending aorta with graft material resulted in increased peak velocities and flow acceleration throughout the thoracic aorta.

The results of these studies were related to the reduced compliance of the aortic graft and thus to the absence of the normal Windkessel phenomenon in the initial part of the aorta. Our present data do not support these hypotheses based on mathematical or pathophysiological models: in fact, in our study we found no worsening of distensibility in the remaining portion of the aorta after insertion of the prosthetic ascending aorta, as evidenced by the unchanged carotid-femoral PWV in the post-op and mid-term periods after surgery. The substitution of the ascending aorta (ie, of an arterial segment characterized by high viscoelasticity) with a rigid prosthesis does not result in serious hemodynamic alterations downstream. Actually, the ascending aorta is not directly involved in carotid-femoral PWV measurement, and thus reliable evaluation of aortic PWV is feasible even in patients with an ascending aortic prosthesis.

In patients with ascending aorta dilatation, the central pulse pressure waveform was characterized by a slower rise of the early systolic phase compared with the control group. This reduced maximum systolic upslope, associated with a delayed peak of the forward pressure wave, defined an aspect of pulsus tardus, which was not associated with significant changes in pulse pressure. Figure 3 shows the likely mechanism underlying this particular hemodynamic behavior. Aneurysmal dilatation of the aortic root and ascending aorta significantly increases the surface against which the cardiac output is addressed. The pressure in the ascending aorta is damped and reaches the maximum pressure peak later.

A larger group (40%) of patients included in this study had a bicuspid aortic valve. Goudot and colleagues[25] showed that bicuspid aortic valve function influences aortic dilatation without significant changes in stiffness. Although bicuspid aortic valve with aortopathy was characterized by progressive aortic dilatation, the sinus of Valsalva was the only segment presenting with specifically increased stiffness independent of aortic dilatation compared with healthy relatives.[25] Our findings are consistent with magnetic resonance imaging findings in patients with bicuspid aortic valve reported by Donato Aguaro and colleagues.[26] These authors showed that compared with control subjects, patients with bicuspid valve had a faster flow wave propagation velocity and a slower maximum rate of systolic

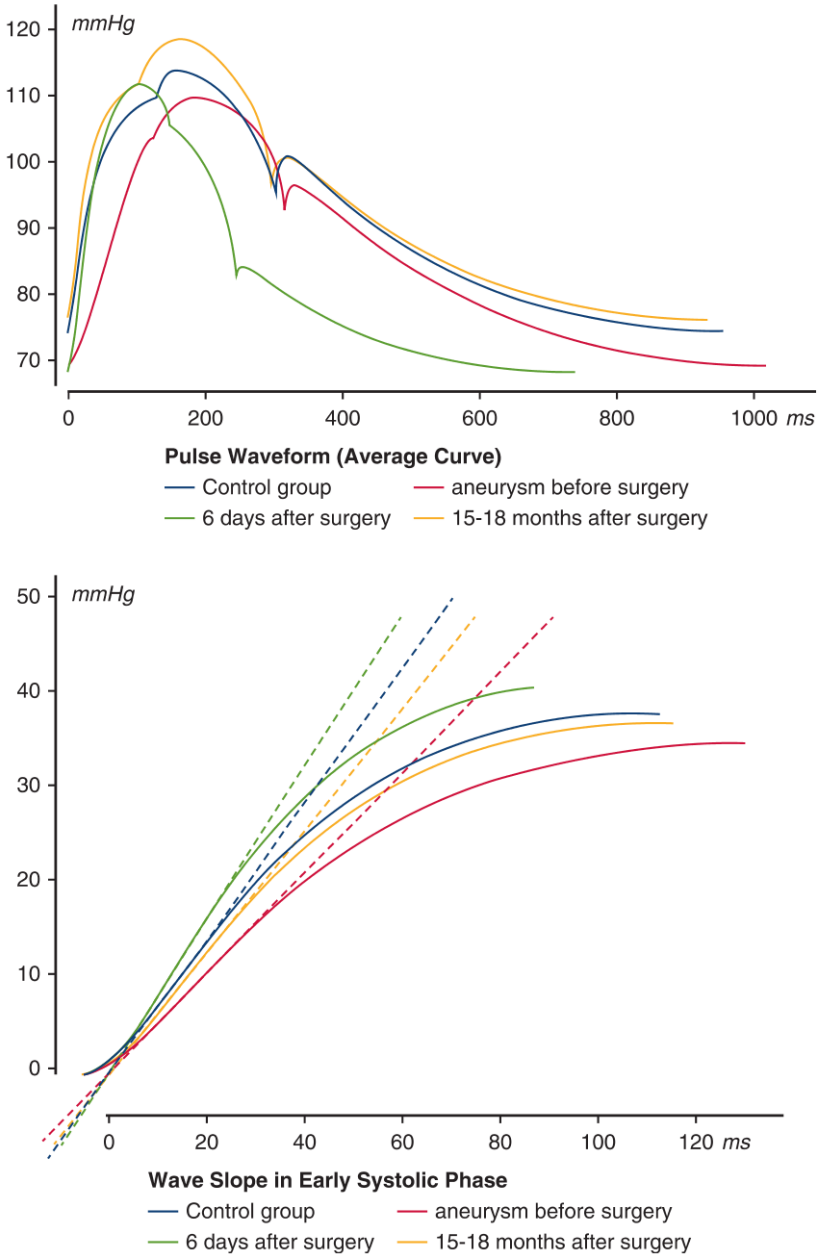

FIGURE 1. *Upper panel*: Average of pulse pressure waveforms in the control group (*blue line*) and in patients with aneurysm of the ascending aorta, before prosthetic replacement (*red line*), postop (*green line*), and mid-term changes (*yellow line*) after surgery. *Lower panel*: Slope of the early systolic phase of the pressure wave in control group and in patients undergoing to surgery.

distension of the ascending aorta cross-sectional area (measured as the maximum systolic upslope).[26]

This particular morphological aspect of the arterial pressure wave in the early systolic phase is not just a didactic curiosity, but could be useful in interpreting vascular examinations of peripheral arteries. The morphological aspects of the pressure curve in the early systolic phase do not change along the entire arterial tree up to the peripheral arteries, as also documented in this study. Thus, the pulse pressure wave in low-resistance districts is analogous to the wave in the ascending aorta, as occurs in cerebral and renal afferent arteries. This peculiarity of transmission of the central pressure wave assumes considerable value in the study of renal circulation, as in the diagnostic process of renovascular hypertension by Doppler ultrasound; morphological aspects such as a pulsus tardus et parvus may lead to pseudopositivity, similar to what was recorded in patients with aortic stenosis. Further studies are needed to confirm this important clinical diagnostic implication.

TABLE 4. Preoperative clinical parameters, and changes at postop (6 to 8 days) and mid-term (15 to 18 months) after ascending aorta replacement

Characteristic	Presurgery	Postop	Mid-term
Blood test assays, mg/dL			
Glucose	92.9 ± 17.0	98.3 ± 17.6	96.5 ± 17.1
Creatinine	1.1 ± 0.3	0.9 ± 0.3	1.1 ± 0.2
Uric acid	6.3 ± 1.5	5.3 ± 1.9	6.2 ± 1.2
Total cholesterol	184.3 ± 36.7	ND	181.8 ± 42.1
HDL cholesterol	50.4 ± 12.8	ND	49.3 ± 11.6
Triglycerides	132.3 ± 71.0	137.0 ± 51.1	136.5 ± 68.8
Hemochromocytometric			
Hemoglobin, g/dL	14.3 ± 1.3	10.7 ± 1.3	14.2 ± 1.5
Hematocrit, %	42.9 ± 3.5	32.6 ± 4.9	43.0 ± 4.4
Red blood cells, $\times 10^{12}$/L	4.9 ± 0.5	3.7 ± 0.5	4.9 ± 0.6
Platelets, $\times 10^{9}$/L	227.3 ± 92.7	195.5 ± 100.8	223.4 ± 81.1
Medications, n (%)			
Diuretic	7 (23.3)	25 (83.3)	7 (23.3)
Beta-blocker	20 (66.7)	26 (86.7)	24 (80.0)
ACE inhibitor	6 (20.0)	3 (10.0)	6 (20.0)
Angiotensin II receptor blocker	14 (46.7)	2 (6.7)	11 (36.7)
Aldosterone antagonist	1 (3.3)	14 (46.7)	3 (10.0)
Calcium channel blocker	6 (20.0)	1 (3.3)	3 (10.0)
Alpha-blocker	3 (10.0)	1 (3.3)	4 (13.3)
Statin	9 (30.0)	3 (10.0)	10 (33.3)
Heparin (low molecular weight)	2 (6.7)	7 (23.3)	0 (0.0)
Antiplatelet	8 (26.7)	6 (20.0)	13 (43.3)
Oral anticoagulant	5 (16.7)	26 (86.7)	24 (80.0)

HDL, High-density lipoprotein; *ACE*, Angiotensin-converting enzyme; *ND*, not determined.

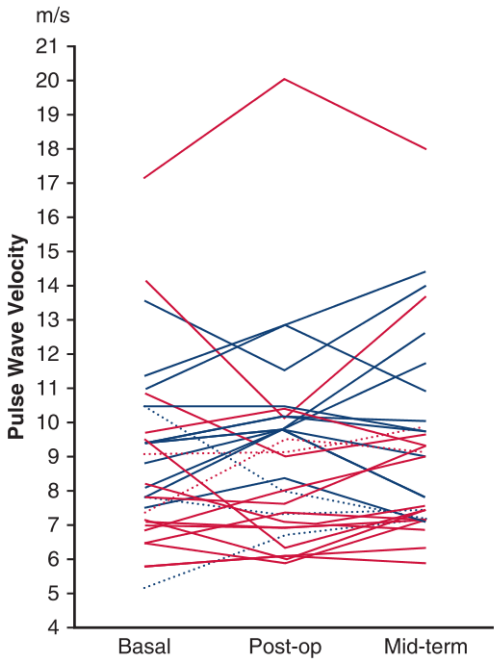

FIGURE 2. Carotid-femoral pulse wave velocity in patients with aneurysm of the ascending aorta, before surgical prosthetic replacement (basal), 5-7 days (post-op) and 18 months after surgery (mid-term). *Blue lines* refer to the patients undergoing replacement of the ascending aorta according to David, and *red lines* according to the Bentall procedure. *Dotted lines* indicate patients with Marfan syndrome.

The remarkable hemodynamic changes seen in the postop measurements are consistent with a wide literature including mathematical models and in vitro and in vivo experiments. Important areas of agreement include the increased slope of the pressure wave in the protosystolic phase, the rapid achievement of the peak of the forward wave, and the precocity of the return of the reflected waves. Using an in vitro model with fresh porcine thoracic aortas, Scharfschwerdt and colleagues[27] demonstrated an increase in the systolic peak pressure in the proximal descending aorta after prosthetic replacement of the ascending aorta. Consequently, the slope of the early systolic phase of the pressure curve (dp/dt_{max}) increased by >42% compared with the native aortic condition (from 0.45 ± 0.07 mm Hg/ms to 0.63 ± 0.08 mm Hg/ms). Similarly, Simon-Kupilik and colleagues[22] reported important hemodynamic changes in both in vitro and in vivo experiments after wrapping the ascending aorta.[22] An increase in maximum systolic pressure–time slope was shown in both a porcine in vitro model (+25%) and in vivo (+36%).

Although supported by pathophysiological considerations and by an extensive literature, interpretation of the results obtained in the postop period is hindered by the significant increase in heart rate compared with the presurgery evaluation (from 61 ± 11 bpm to 84 ± 15 bpm).

The mid-term pulse pressure waveforms recorded in this study at 16 to 20 months after surgery showed a sort of

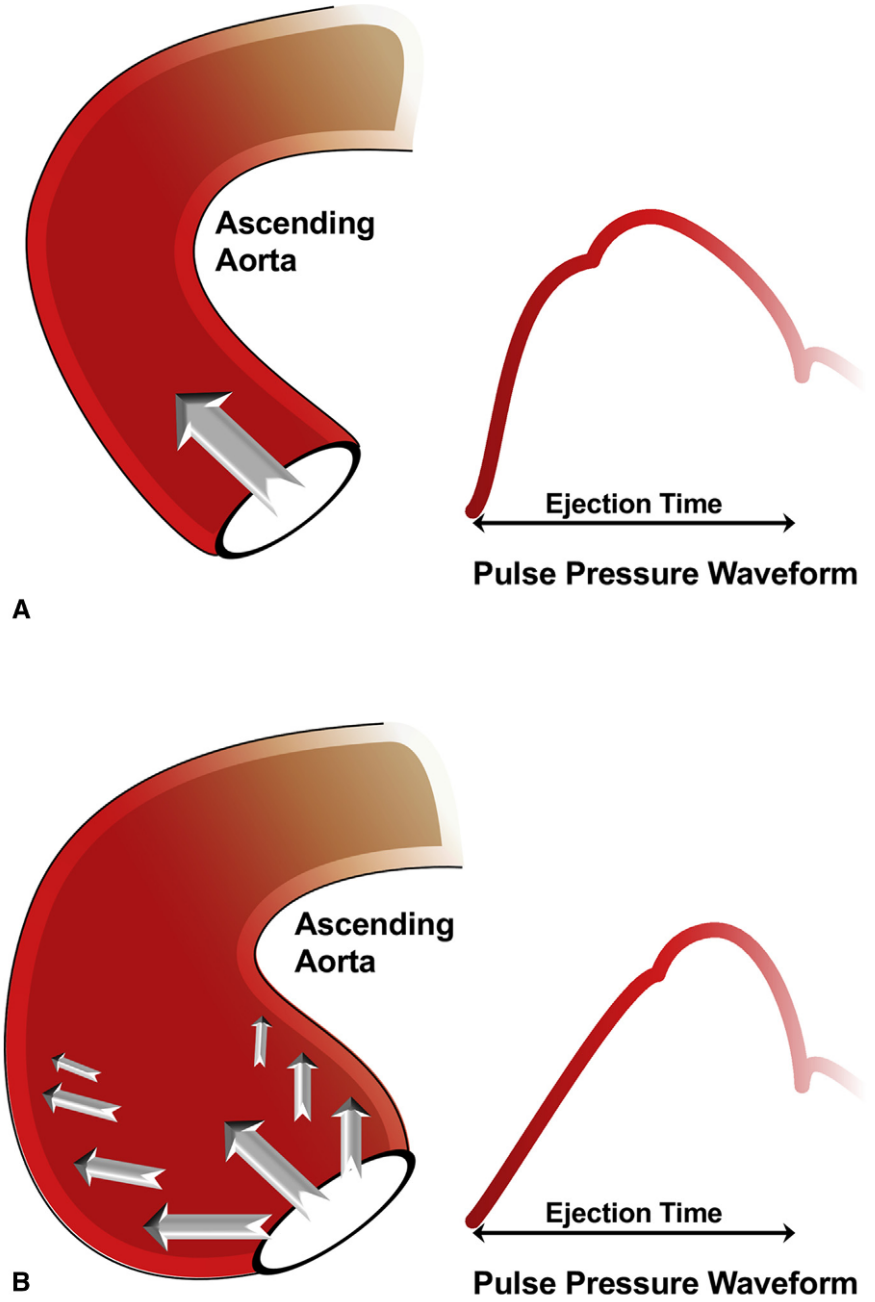

FIGURE 3. Mechanism underlying the pulsus tardus in the presence of an aneurysm of the ascending aorta. A, Normal morphology of the arterial pressure curve. B, The aneurysmal dilatation of the aortic root and ascending thoracic aorta significantly increases the surface against which the cardiac output is addressed. The pressure in the ascending aorta is damped and reaches the maximum pressure peak more slowly.

"normalization" of the pressure waveform, with values of the early systolic pulse pressure slope becoming comparable to those of the control group.

The main limitation of this study is the heterogeneity of the recruited patients by disease (Marfan syndrome, bicuspid aortic valve, other diseases), type of surgery (David or Bentall procedure), associated valve disease, and medical treatment. This inhomogeneity does not allow us to distinguish different hemodynamic behaviors in different pathologies or in different types of surgery from a statistical standpoint.

CONCLUSIONS

In our cohort, no worsening of the viscoelastic properties of the total aorta was observed after insertion of a rigid prosthesis in the ascending aorta (Video 1). Thus, this study does not support the assumption that substituting the viscoelastic ascending aorta with a rigid prosthesis can cause serious

VIDEO 1. Prosthetic replacement of the ascending thoracic aorta causes significant pulse waveform changes in the postop measurements but does not cause any worsening of aortic distensibility downstream. Video available at: https://www.jtcvs.org/article/S0022-5223(20)31250-2/fulltext.

hemodynamic alterations downstream. The ascending thoracic aortic aneurysm is associated with a pulsus tardus; however, this characteristic is already lost in the mid-term after surgery, with the restoration of morphology found in subjects with regular aortic arteries. In other words, the pressure curves recorded in the medium term after surgery are comparable to those of the subjects of the control group for both PWV and morphology.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: aortic distensibility, arterial stiffness, ascending aortic aneurysm, pulse wave velocity, thoracic aortic surgery, vascular prosthesis