CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES IN VASCULAR SURGERY
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MARRIOTT RIVE GAUCHE & CONFERENCE CENTER
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Does TEVAR affect the heart?

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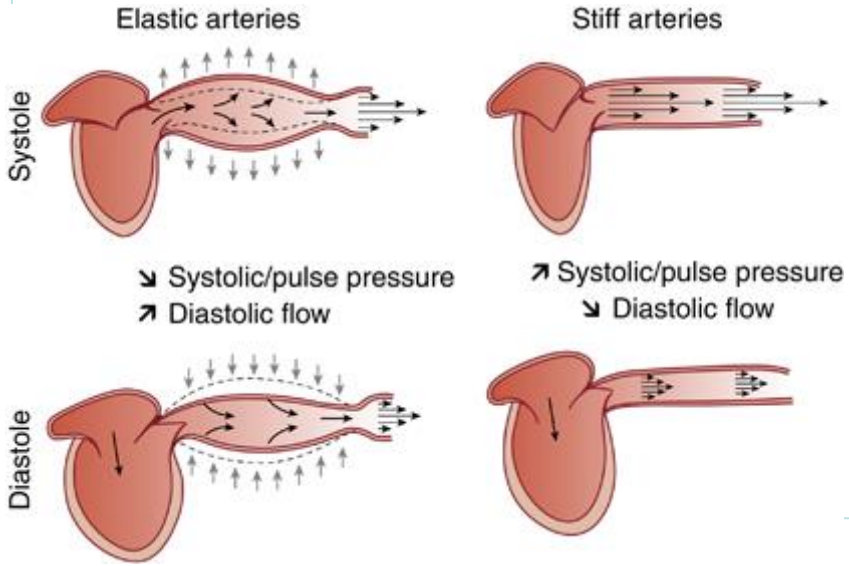
NO DISCLOSURES RELATED TO THE TOPIC

Arterial Stiffness and cardiac outcomes

- Arterial stiffness has been correlated with long-term cardiovascular outcomes independent of traditional cardiovascular risk factors (e.g. hypertension, diabetes, obesity, dyslipidemia, smoking)

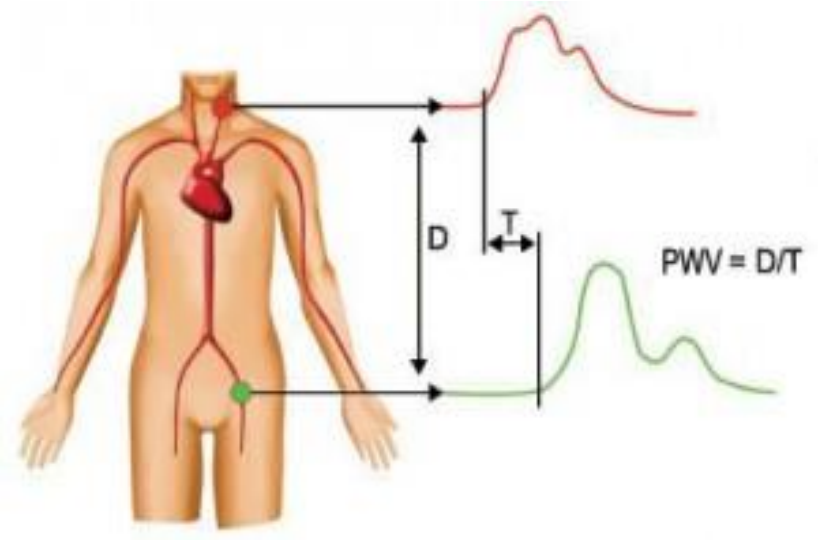


- Arterial stiffening results in increased pulse pressure, left ventricular hypertrophy, subendocardial ischemia, endothelial dysfunction and cardiac fibrosis

Liao J et al Curr Ather Reports 2014

Pulse wave velocity (PWV) and cardiac outcomes

- **Pulse wave velocity (PWV)**: the gold standard method of arterial stiffness measurement and a strong independent predictor of cardiovascular morbidity and mortality.

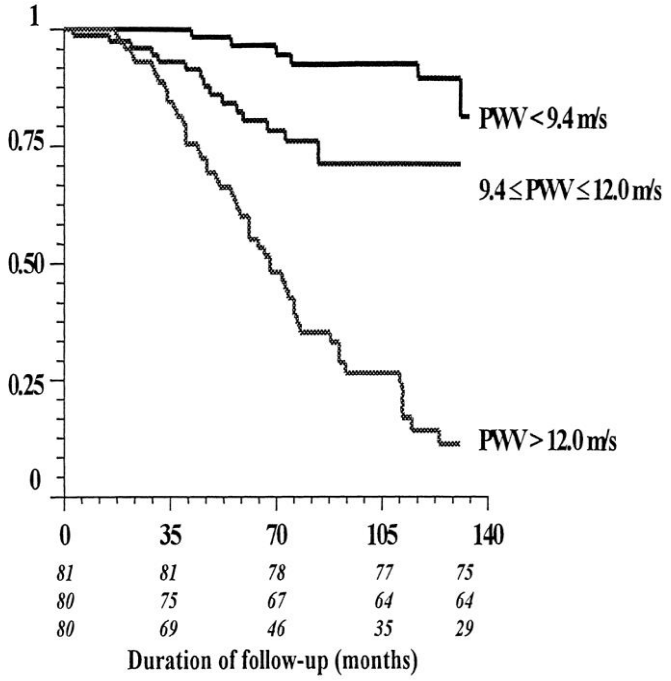


- Therapeutic modalities reducing PWV are associated with less cardiovascular events rate and improved prognosis

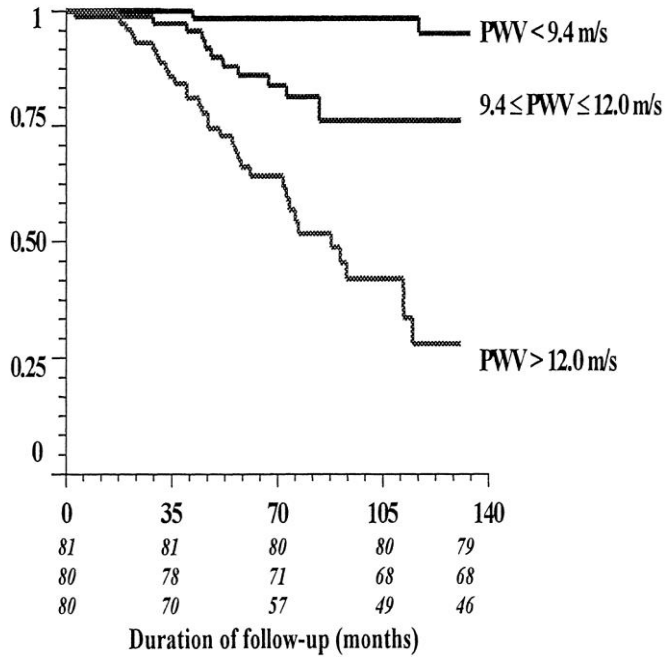
Cavalcante JL et al JACC 2011; Ben-Shlomo Y et al JACC 2013

Aortic Stiffness

OVERALL SURVIVAL



CARDIOVASCULAR SURVIVAL



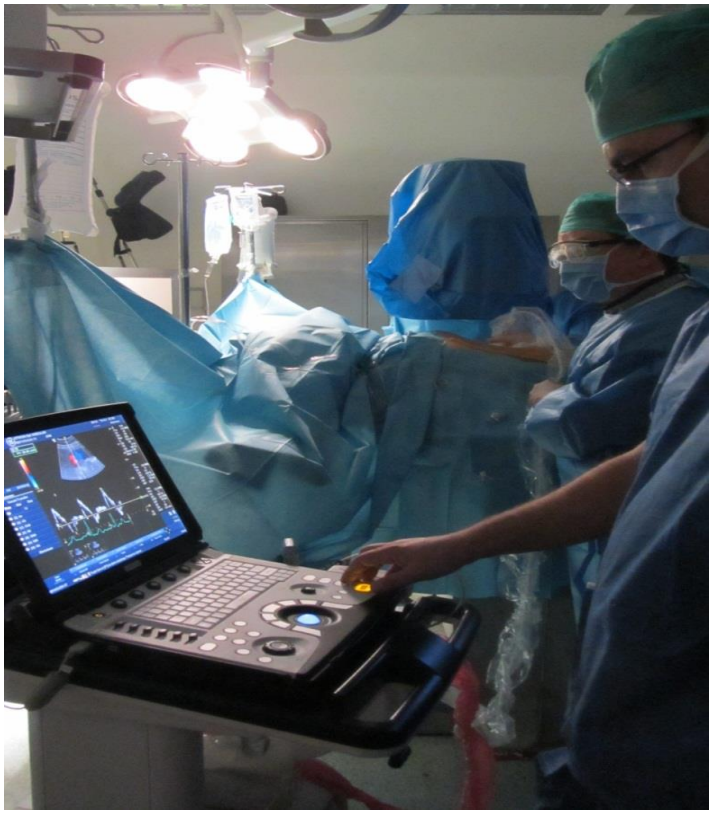
Probabilities of overall survival (A) and event-free survival (cardiovascular mortality, B) in study population according to level of PWV divided into tertiles.

American Heart Association

Blacher J. et al Circulation. 1999;99:2434-2439

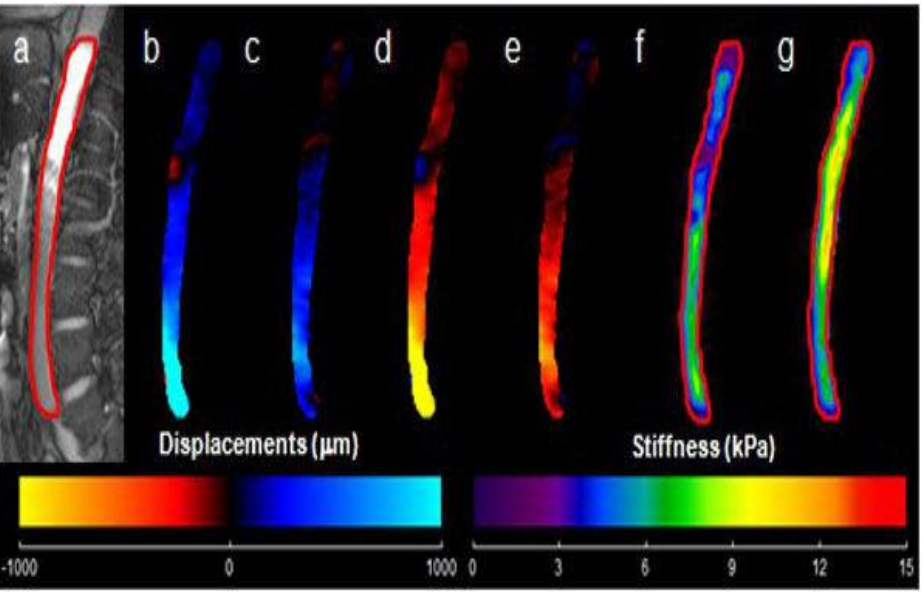
Changes in arterial stiffness in patients undergoing EVAR and TEVAR

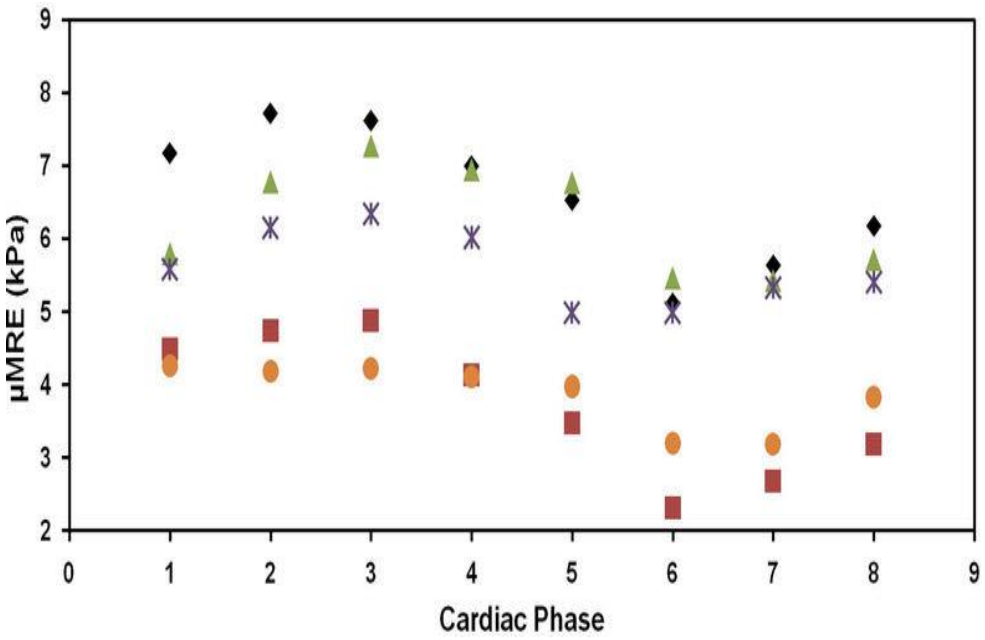
Computational Fluid Dynamics
Ongoing Trial



Cardiovascular magnetic resonance elastography

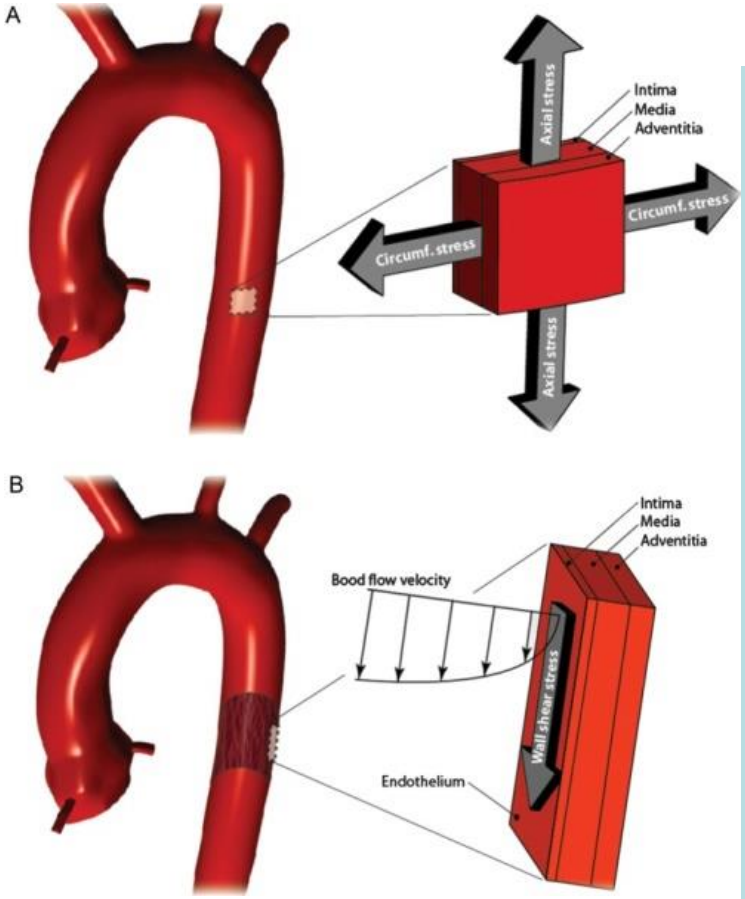
Magnetic resonance elastography (MRE) is a phase-contrast magnetic resonance imaging technique that measures tissue stiffness non-invasively.





Khan S. et.al NMR in Biomedicine. 2017

Arterial stiffness in patients with abdominal (AAA) or thoracic aortic aneurysms (TAA)



- Men with AAA presented with significantly elevated PWV levels compared to age-matched controls
- Mean blood pressure, AAA diameter and age: independent determinants of PWV in AAA
- TAA is associated with increased augmentation index

Shingu Y, et al Ann Thorac Surg 2009;
Kadoglou NPE, Liapis C et al J Endovasc Surg 2012

Arterial stiffness, circulating vascular calcification inhibitors and inflammatory mediators in pts with AAA

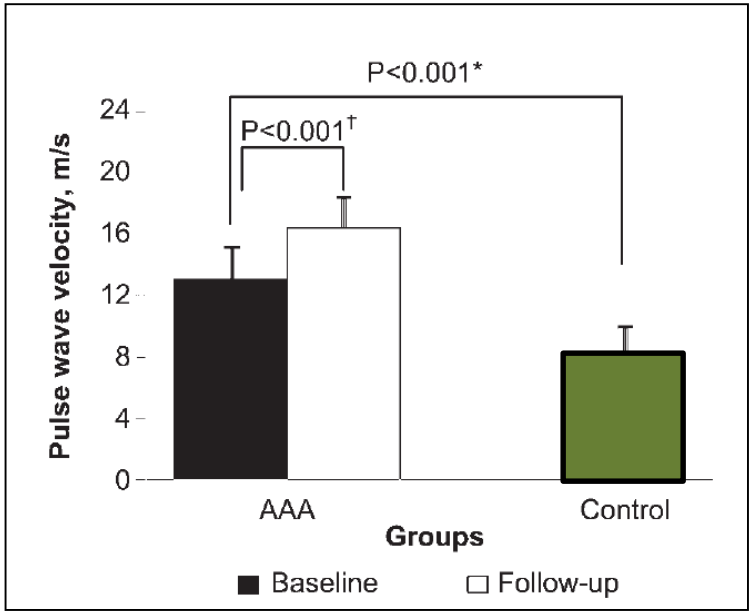
	AAA group (N = 108)	CO group (N = 42)	p
hsCRP (mg/L)	5.90 ± 2.05	2.96 ± 1.02	<0.001
WBC (cells/μL)	9870 ± 2231	8850 ± 2001	0.039
TC (mg/dl)	218 ± 31	184 ± 48	0.118
HDL (mg/dl)	42 ± 11	45 ± 13	0.501
LDL (mg/dl)	137 ± 19	113 ± 22	0.098
TG	148 ± 56	130 ± 39	0.319
PWV (m/s)	12.99 ± 3.75	10.03 ± 1.57	<0.001
Osteoprotegerin (pmol/L)	16.11 ± 3.01	12.13 ± 1.98	<0.001
Osteopontin (ng/ml)	54.4 ± 16.05	42.33 ± 13.72	0.047
IL-6 (pg/ml)	5.51 ± 2.42	4.22 ± 1.63	0.038

	B	p
MBP	0.501	<0.001
OPG	0.405	0.022
OPN	0.204	0.272
IL-6	0.251	0.189
AAA diameter	0.348	0.006

- **PWV and hsCRP, WBC, IL-6, Osteoprotegerin were significantly upregulated in pts with AAA.**
- **Independent association of PWV with mean blood pressure, OPG and AAA diameter**

Kadoglou NP, Liapis CD et al. Arterial stiffness and novel biomarkers in patients with abdominal aortic aneurysms. Regul Pept. 2012

Changes in arterial stiffness in patients undergoing AAA repair



Stent-graft implantation (n=48) was associated with significant increase in PWV 6 months following EVAR

Open surgical repair (n=39) of AAA induced modest increase of PWV and decreased by 8,5% the Augmentation index

- **Kadoglou NP, Moulakakis KG, Liapis CD.** Changes in aortic pulse wave velocity of patients undergoing endovascular repair of abdominal aortic aneurysms. J Endovasc Ther. 2012
- **Lantelme P et al** J Hypertens 2009

EVAR and cardiovascular Outcome

- **A non-significant tendency toward cardiovascular deaths was apparent in the EVAR trial in the endovascular group during the 24-month interval.**

- **Cardiovascular mortality was primarily due to the poor general health status of those patients or the required secondary interventions.**

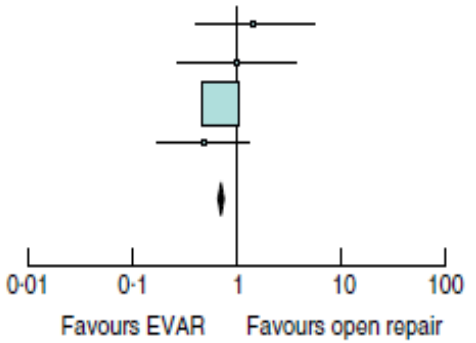
- **A harmful effect of even slight alterations in aortic stiffness induced by endografts should be considered.**

1. Brown LC, et al. EVAR trial participants. Incidence of cardiovascular events and death after open or endovascular repair of abdominal aortic aneurysm in the randomized EVAR trial 1. Br J Surg. 2011
2. Brown LC, et al. EVAR trial participants. Does EVAR alter the rate of cardiovascular events in patients with AAA considered unfit for open repair? Results from the randomized EVAR trial 2. Eur J Vasc Endovasc Surg. 2010

Short-term vs. long-term MI following EVAR and Open AAA Repair

Reference	Event rate: EVAR	Event rate: Open repair	Weight (%)	Odds ratio
a Myocardial infarction				
ACE[33]	6 of 150	4 of 149	0·3	1·51 (0·42, 5·47)
DREAM[35]	5 of 173	5 of 178	0·3	1·03 (0·29, 3·62)
Medicare[9]	1598 of 22 830	2146 of 22 830	99·0	0·73 (0·68, 0·78)
OVER[38]	6 of 444	12 of 437	0·5	0·49 (0·18, 1·30)
Total	1615 of 23 597	2167 of 23 594	100·0	0·73 (0·68, 0·78)

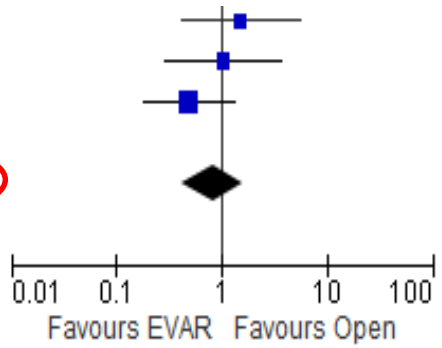
Heterogeneity: $\tau^2 = 0{\cdot}00$; $\chi^2 = 2{\cdot}18$, 3 d.f., $P = 0{\cdot}54$; $I^2 = 0\%$
Test for overall effect: $Z = 9{\cdot}33$, $P < 0{\cdot}001$



b

ACE	6	150	4	149	27.0%	1.51 [0.42, 5.47]
DREAM	5	173	5	178	28.2%	1.03 [0.29, 3.62]
OVER	6	444	12	437	44.8%	0.49 [0.18, 1.30]
Total (95% CI)		**767**		**764**	**100.0%**	**0.82 [0.41, 1.61]**
Total events	17		21			

Heterogeneity: Tau² = 0.01; Chi² = 2.07, df = 2 (P = 0.35); I² = 4%
Test for overall effect: Z = 0.59 (P = 0.56)



Stather et.al *British Journal of Surgery 2013;* 100: 863–872

Cardiac effect of endovascular repair

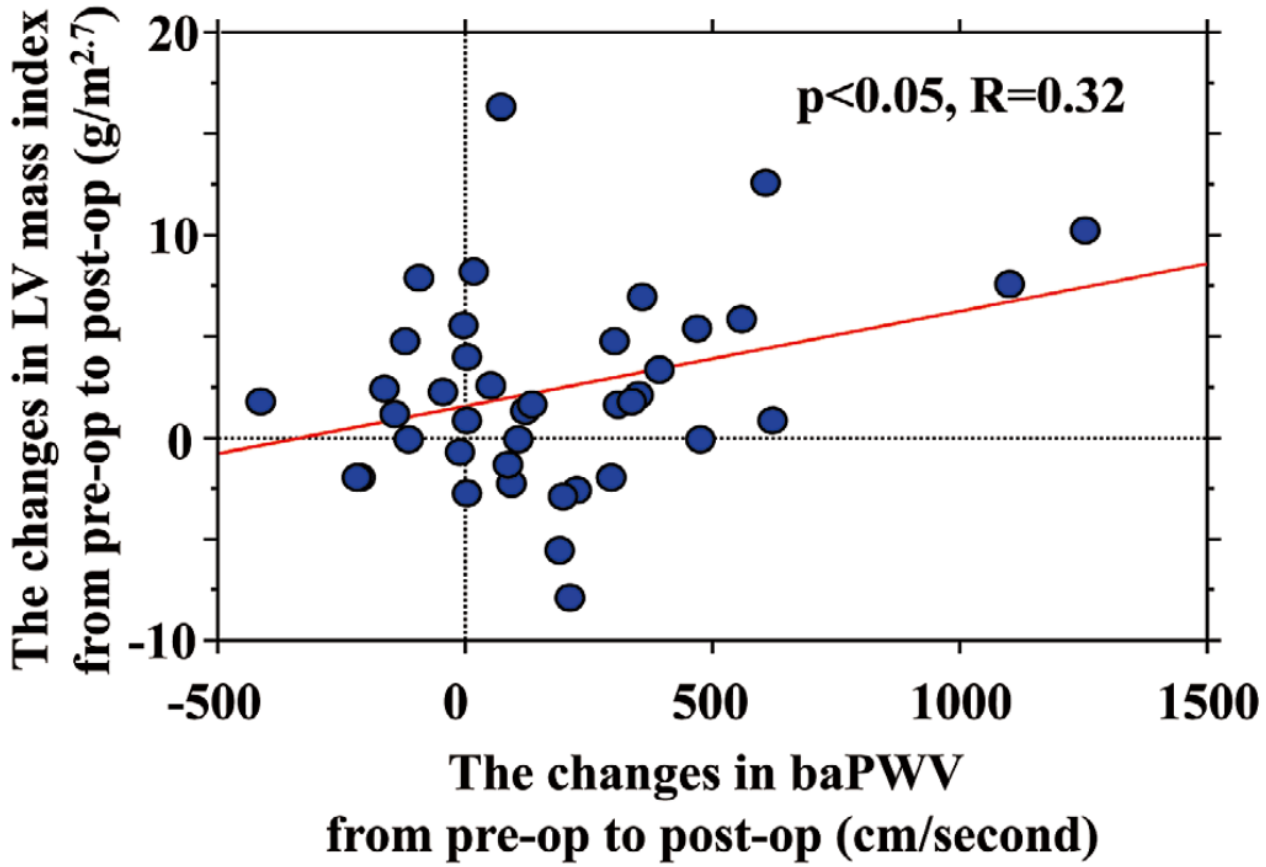
Table 2. Baseline (Pre-Op) Characteristics of Patients and 7-Day (Post-Op) Outcomes After Endovascular Aortic Repair

Characteristic	Pre-op (n=40)	Post-op (n=40)	P value
Systolic blood pressure (mmHg)	131±15	128±15	0.075
Diastolic blood pressure (mmHg)	76±8	72±9	<0.05
Heart rate (beats/min)	65±10	69±12	<0.05
baPWV (cm/s)	1,914±389	2,096±459	<0.05
Inferior vena cava dimension (mm)	12±3	12±3	0.574
LV volume index at end-diastole (ml/m$^{2.7}$)	28.3±4.9	29.1±4.0	0.096
Left atrial volume index (ml/m$^{2.7}$)	13.7±4.4	15.4±4.6	<0.05
LVEF (%)	68±5	67±4	0.127
IVST at end-diastole (mm)	9.0±2.3	9.1±2.3	0.623
LV PWT at end-diastole (mm)	8.7±1.1	8.9±0.9	0.118
LV PWT at end-systole (mm)	15.0±2.0	15.1±2.1	0.749
DWS	0.41±0.09	0.40±0.09	0.429
LV mass index (g/m$^{2.7}$)	42±10	45±11	<0.05
Relative wall thickness	0.35±0.05	0.35±0.04	0.663
E/A ratio	7.8±1.3	0.78±0.20	0.427
Deceleration time of E wave (ms)	244±37	243±39	0.886
E' (cm/s)	7.8±1.3	7.8±1.5	0.773
E/E' ratio	8.2±1.8	8.4±1.5	0.385

Values are expressed as the mean±SD.
A, peak velocity of transmitral flow velocity curve at atrial contraction; baPWV, brachial-ankle pulse wave velocity; DWS, diastolic wall strain; E, peak early diastolic flow velocity of transmitral flow velocity curve; E', peak early diastolic velocity of the tissue Doppler imaging of the mitral annulus movement at septal position; EF, ejection fraction; IVST, interventricular septal thickness; LV, left ventricular; PWT, posterior wall thickness.

Takeda Y. et al Circ J 2014;78:322-328

Cardiac effect of endovascular repair



Positive correlation between PWV and LV mass

Takeda Y. et al Circ J 2014;78:322-328

EVAR alters cardiac structure and function

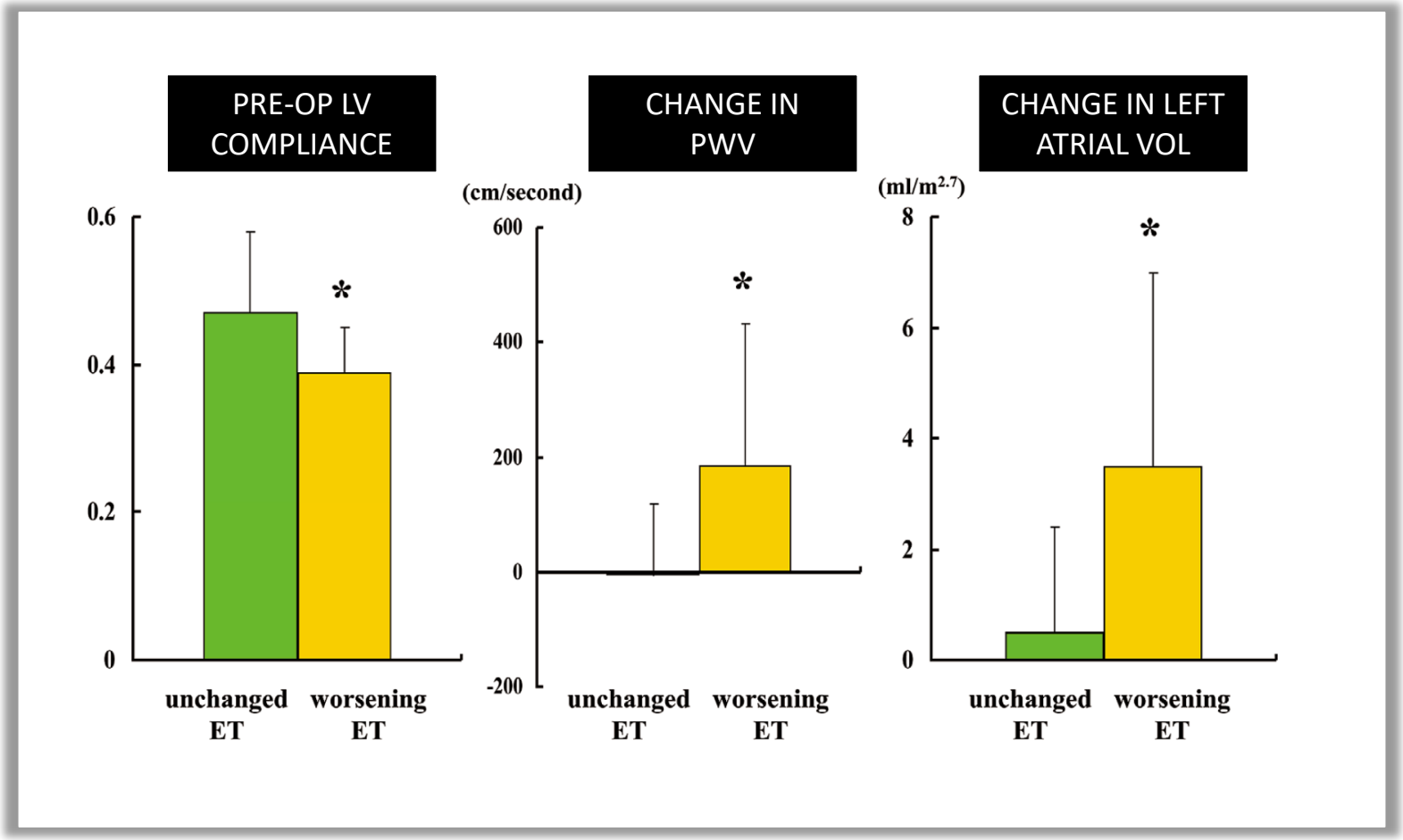
Table 3. Baseline (Pre-Op) Characteristics of Patients and 1-Year (Follow-up) Outcomes After Endovascular Aortic Repair

Characteristic	Pre-op (n=22)	Follow-up (n=22)	P value
Specific activity scale score	6.0±1.6	5.3±1.9	<0.05
Systolic blood pressure (mmHg)	131±15	131±16	0.953
Diastolic blood pressure (mmHg)	75±8	74±10	0.476
Heart rate (beats/min)	64±9	62±10	0.283
baPWV (cm/s)	1,834±329	1,942±387	<0.05
Inferior vena cava dimension (mm)	12±3	12±2	0.606
LV volume index at end-diastole (ml/m$^{2.7}$)	29.2±4.8	27.2±4.4	<0.05
Left atrial volume index (ml/m$^{2.7}$)	14.0±5.3	16.2±4.7	<0.05
LVEF (%)	68±5	68±5	0.866
IVST at end-diastole (mm)	9.5±2.6	9.8±2.8	0.088
LV PWT at end-diastole (mm)	8.6±1.0	9.0±1.0	0.201
LV PWT at end-systole (mm)	15.0±1.7	14.8±2.4	0.646
DWS	0.42±0.09	0.38±0.10	0.066
LV mass index (g/m$^{2.7}$)	43±11	45±11	<0.05
Relative wall thickness	0.35±0.05	0.37±0.04	<0.05
E/A ratio	0.82±0.21	0.75±0.19	<0.05
Deceleration time of E wave (ms)	249±32	246±47	0.733
E' (cm/s)	7.8±1.5	7.3±1.8	0.060
E/E' ratio	8.5±1.7	8.6±2.1	0.052

increased baPWV and induced **left ventricular hypertrophy, left atrium enlargement and impaired diastolic function**

Takeda Y et al Circ J 2014

Exercise tolerance



Takeda Y. et al Circ J 2014;78:322-328

Changes in Arterial Stiffness and N-terminal pro-brain natriuretic peptide Levels after Endovascular Repair of Descending Thoracic Aorta

Twenty-seven patients with TAA underwent elective TEVAR. Blood samples were obtained preoperatively, 24 hr, 48 hr, and 6 months postoperatively.

Serum levels of NT-proBNP were measured. PWV was determined before and 6 months after TEVAR.

One-way analysis of variance by ranks was used to test the alterations in PWV (from baseline to 6 months) and NT-proBNP (along the 4 phases of evaluation). Post hoc analyses were appropriately performed.

Moulakakis K., Liapis CD et.al. Ann Vasc Surg 2017

Arterial stiffness and thoracic endografts

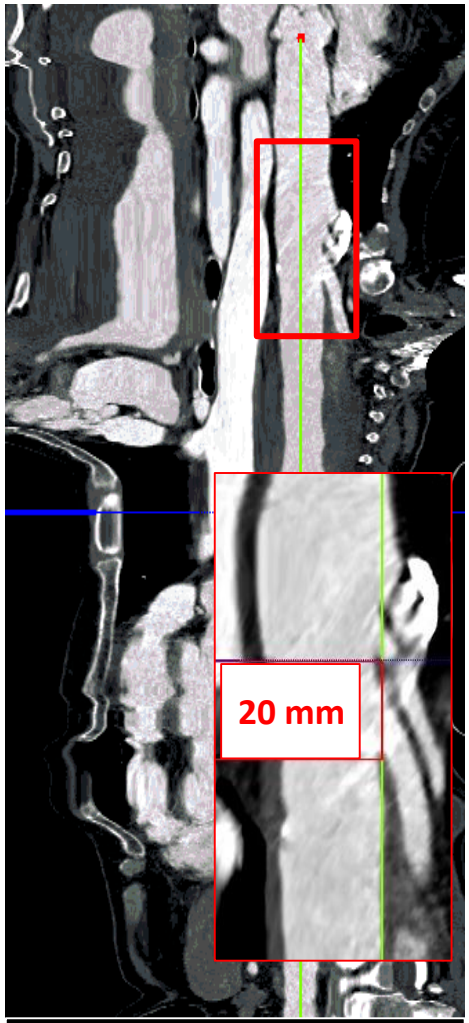
M, 79y,
Symptomatic
8cm TAA
Medtronic
VALIANT
Thoracic
40X40, 46X46

Endovascular repair

Centre Hospitalier Régional Universitaire de Lille

Access

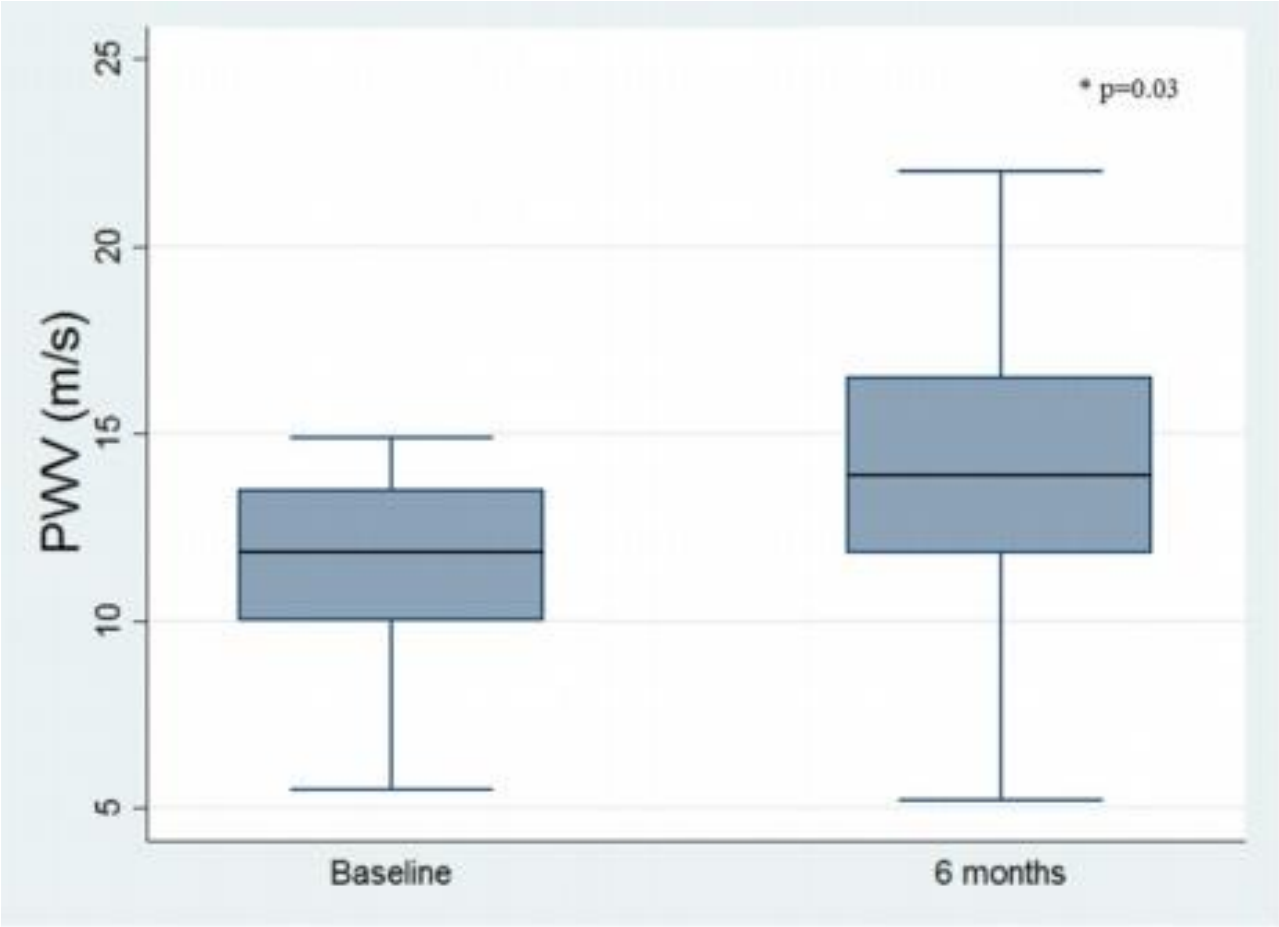
Narrow true lumen



Proximal landing zone

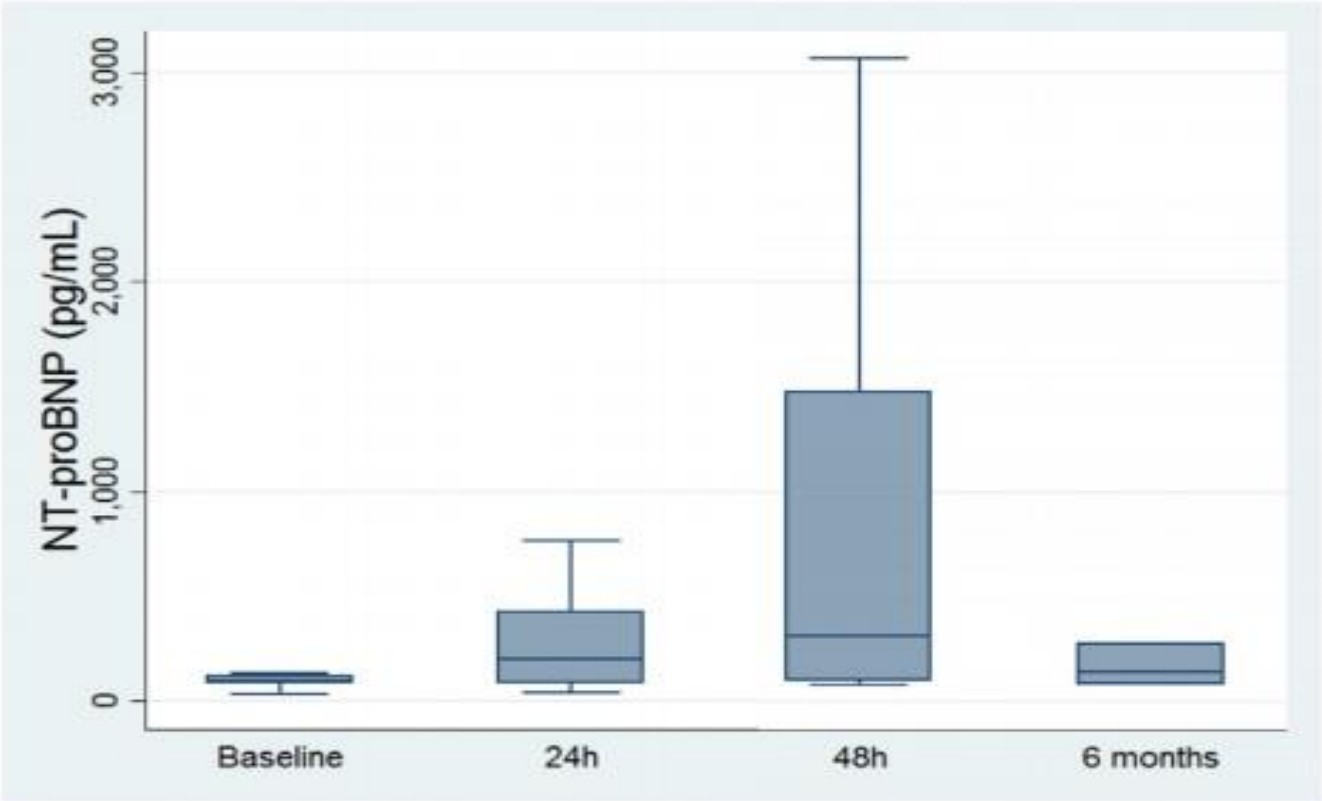
Courtesy of Rachel Clough

PWV (m/sec) in baseline and 6 monts after TEVAR



Moulakakis K., Liapis CD et.al. Ann Vasc Surg 2017

NT-proBNP (pg/mL) among the different time points of evaluation after TEVAR



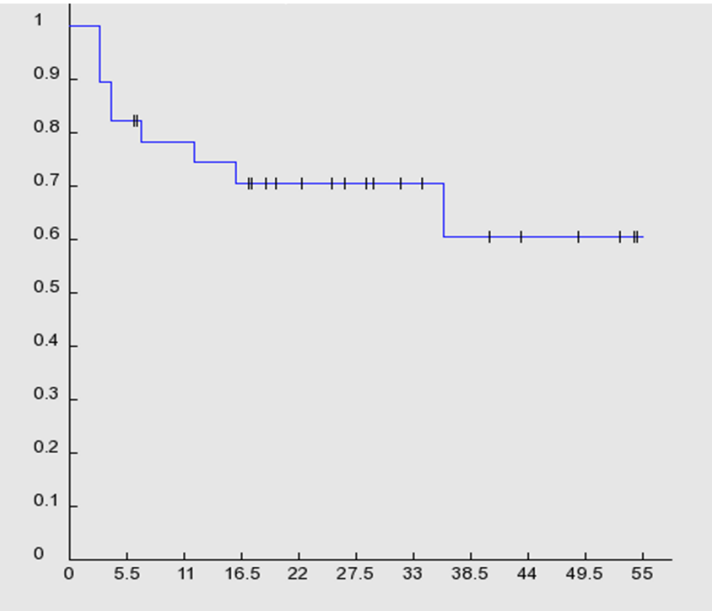
	Baseline	24h	48h
Baseline			
24h	**12.9 (0.02)**		
48h	**20.5 (<0.001)**	**7.5 (0.13)**	
6 months	**12.7 (0.03)**	**0.3 (0.49)**	**7.7 (0.15)**

Moulakakis K., Liapis CD et.al. Ann Vasc Surg 2017

Arterial stiffness and NT-proBNP changes following TEVAR

Kaplan – Meier survival curve estimate in follow up

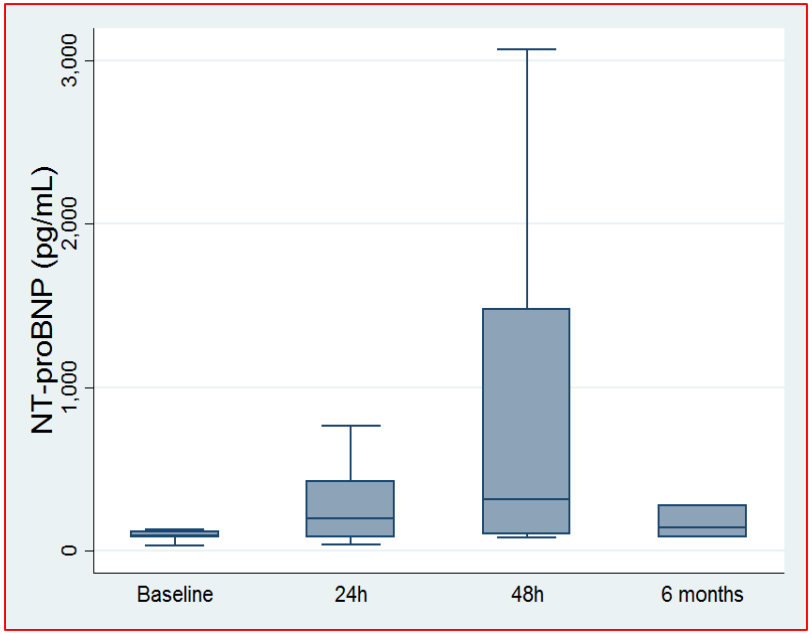
TEVAR Group, N=27, Baseline Characteristics	
Variable	**Mean ± SD or n (%)**
Age (years)	68.8 ± 11.3
Male Gender	24 (88.8)
BMI (kg/m^2)	27.25 ± 4.6
Indication for TEVAR	
▪ Atherosclerotic Aneurysm	23 (85.2)
▪ Dissecting Aneurysm	2 (7.4)
▪ Pseudoaneurysm	1 (3.7)
▪ Intramural Hematoma	1 (3.7)
TAA Diameter (N=26) (cm)	6.19 ± 1.3
Chronic Obstructive Pulmonary Disease	7 (25.9)
Dyslipidemia	11 (40.7)
CAD	9 (33.3)
Diabetes Mellitus	6 (22.2)
Smoking	15 (55.5)
Hypertension	19 (70.3)
History of Ascending Aorta Reconstruction	1 (3.7)
History of AAA Reconstruction	10 (37)
Operative Characteristics	
▪ Aortic Pathology Length (cm)	14.91±8.67
▪ Subclavian Artery Coverage	6 (22.2)
▪ Carotid - Subclavian Bypass	2 (7.4)
▪ Celiac artery Coverage	6 (22.2)
▪ Number of endografts placed: 1/2/3	13/11/3
▪ Duration of surgery (min)	121.7± 47.8
▪ Blood loss (mL)	164.7 ± 99.3
Follow-up	23.4 ± 16.4
30-day Mortality	0
Mortality in Follow-up	9 (33.3)

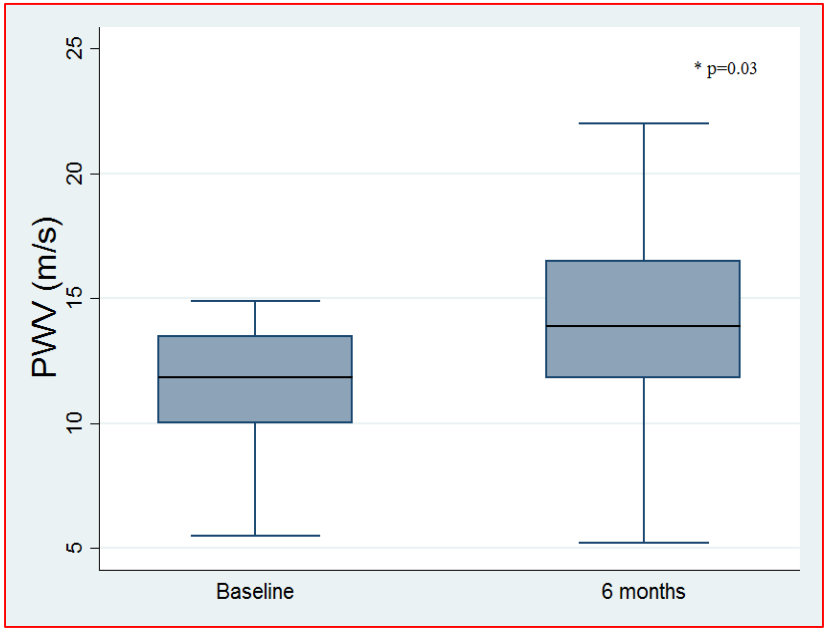


Follow-up: 23.4 ± 16.4 months (range 3-54 months).
Overall Mortality : 33.3%

Moulakakis K., Liapis CD et.al. Ann Vasc Surg 2017

PWV and NT-proBNP changes in pts following TEVAR





Endovascular treatment of descending thoracic aortic aneurysms is associated with **significantly increased NT-proBNP levels and arterial stiffness**.

An increased cardiac risk for patients with already impaired cardiac compensatory mechanism ?

Moulakakis K., Liapis CD et.al. Ann Vasc Surg 2017

Differential effects of stent-graft fabrics on arterial stiffness in patients undergoing EVAR

Structural Characteristics of the Stent-Grafts Used in the Study

Stent-Graft	Device Structure	Fabric and Skeleton	Fixation
Anaconda	Modular	Polyester and nitinol	Friction and hooks
Excluder	Modular	ePTFE and nitinol	Anchors
Talent	Modular	Polyester and nitinol	Suprarenal stent
Endurant	Modular	Polyester and nitinol	Suprarenal stent with anchor pins on the proximal end
Zenith FB	Modular	Polyester and stainless steel and nitinol	Suprarenal bare stent with anchoring barbs

Demographic and Clinical Characteristics of 118 Male Patients Undergoing Endovascular Aneurysm Repair According to the Type of Endograft

	PTFE (n=46)	Polyester (n=72)	p
Age, y	70±9	71±7	0.568
CAD	14 (30.4%)	29 (40.3%)	0.382
Diabetes	8 (17.4%)	15 (20.8%)	0.793
History of carotid surgery	3 (6.5%)	5 (6.9%)	0.482
Smokers			
Baseline	21 (45.6%)	24 (33.3%)	0.195
End	5 (10.9%)	6 (8.2%)	0.312
Statins			
Baseline	24 (52.2%)	44 (61.1%)	0.582
End	38 (82.6%)	66 (91.7%)	0.656
Antihypertensive medications			
Baseline	39 (84.8%)	56 (77.8%)	0.711
End	42 (91.3%)	68 (94.4%)	0.819
AAA diameter, cm	6.02±0.78	5.62±0.68	0.456
Aortoiliac length, cm	14.9±1.7	15.1±1.9	0.812
Endograft proximal diameter, cm	2.65±0.24	2.69±0.33	0.944
Endograft length, cm	13.75±1.63	13.67±1.75	0.912
Type of endograft	Excluder	Anaconda (38) Zenith (28) Endurant (5) Talent (1)	

Prospective study

N=118 pts

Kadoglou NP, Moulakakis KG, Liapis CD. Differential effects of stent-graft fabrics on arterial stiffness in patients undergoing endovascular aneurysm repair. J Endovasc Ther. 2014

Differential effects of stent-graft fabrics on arterial stiffness in patients undergoing EVAR

N=118 pts

Values of PWV and novel biomarkers at **baseline** and **after 12 months**

Pulse Wave Velocity and Novel Biomarkers in Patients Undergoing Endovascular Aneurysm Repair According to the Type of Endograft

	PTFE (n=46)		Polyester (n=72)			
	Baseline	End	Baseline	End	p1†	p2†
PWV, m/s	12.05±2.55	14.87±2.43*	12.63±2.75	16.75±2.88*	0.685	0.033
OPG, pmol/L	15.18±3.78	10.51±4.46*	15.72±5.02	12.45±4.94*	0.803	0.048
IL-8, pg/mL	11.27±5.09	17.97±8.1*	10.27±5.02	25.68±11.11*	0.681	<0.001
IL-6, pg/mL	3.81±1.51	3.69±1.37	3.89±4.56	3.58±1.50	0.944	0.883
IL-10, pg/mL	5.35±1.57	8.39±2.22*	4.36±2.08	7.64±1.52	0.271	0.518

PWV, OPG and IL-8 increase was more pronounced in Polyester Woven group compared to PTFE group (p=0.033, p=0.048, p<0.001 respectively)

Kadoglou NP, Moulakakis KG, Liapis CD. Differential effects of stent-graft fabrics on arterial stiffness in patients undergoing endovascular aneurysm repair. J Endovasc Ther. 2014

Conclusions (I)

- **TEVAR and EVAR are associated with lower perioperative mortality and morbidity rates compared to open surgical repair BUT this advantage is blunted at long term, mainly due to an increase in cardiovascular complications.**

- **Arterial stiffening together with adverse cardiac function after stent graft implantation may explain this change in the long-term outcome**

Conclusions (II)

- **There is evidence of increased arterial stiffness after EVAR related to graft type (polyester more than PTFE). The effect of endograft type in the thoracic aorta is under investigation.**

- **Arterial stiffness should be taken into consideration by the industry when designing new endografts**


Thank you for your attention