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Tight systolic blood pressure control with combination therapy decreases type 2 endoleaks in patients undergoing endovascular aneurysm repair

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ABSTRACT

Background: Endovascular aneurysm repair (EVAR) has revolutionized the treatment of abdominal aortic aneurysm (AAA) disease. However, the survival advantage is lost in the long term due the occurrence of endoleaks affecting the late rupture of aneurism sac. Few data are available on the role of blood pressure control in affecting the incidence of type 2 endoleaks in patients undergoing EVAR.
Objective: Aim of this study was to evaluated whether systolic blood pressure (SBP) control to target 130 mmHg reached after preoperative cardiology consultant might decrease the incidence of type II endoleak(T2E), sac expansion and related aortic reintervention after elective endovascular aneurysm repair(EVAR).
Methods: We analyzed 386 patients undergoing EVAR between 2008 and 2016. The primary endpoints were T2E, sac expansion and related aortic re-intervention or sac shrinkage during a median follow-up of 24 months [12–48]. The secondary endpoint was every cause of vascular or cardiac morbidity and mortality.
Results: The SBP value of 130 mmHg at the time of EVAR resulted, at ROC curve analysis, the most sensitive and specific for all the analyzed endpoints (T2E, n = 74; sac expansion n = 19; re-intervention, n = 10, sac shrinkage, n = 72). The combination antihypertensive therapy showed a significant inverse relationship with T2E occurrence. The incidence of primary endpoints was significantly higher ($p < 0.001$) in patients with SBP ≥ 130 mmHg. Cardiovascular death was significantly more prevalent ($p < 0{,}001$) in patients with SBP ≥130 mmHg. These findings were confirmed at the multivariable Cox regression analysis [primary endpoint HR = 0.09(0.06–0.15), $p < 0.001$; cardiovascular death HR = 0.33(0.12–0.85), $p = 0.023$].
Conclusions: Tight SBP control at the target of 130 mmHg at the time of elective EVAR significantly decreases TE2 occurrence, need of re-intervention and cardiovascular death in a prolonged follow-up of a large sample of patients.

1. Introduction

Abdominal aorticP aneurysm (AAA) is the most common disease of aorta that particularly affects men older than 60 years [1].

Endovascular aneurysm repair (EVAR) has revolutionized the treatment of AAA disease for the lower risk of 30-day mortality and morbidity compared to open surgery (OS) [2,3,4]. However, most recent randomized trials show that the survival advantage is lost in the long term due to the late rupture of aneurism sac in patients underwent EVAR [5,6,7]. Indeed this method is burdened by complications in the follow-up related to the occurrence of endoleaks.

Endoleak is defined as continued perfusion of the aneurysm sac despite endograft placement [8]. Four types are generally considered, among which type II endoleak (T2E) occurs in 20% to 50% of patients and is caused by backflow of collateral arteries into the aneurysm sac [9,10].

Most types are favourable and resolve spontaneously after a variable period, but those with a persistent mechanism of inflow-outflow between patent branches and the sac could cause significant aneurysm sac expansion or be persistent; these cases have been reported to have a higher risk of adverse outcomes [11,12].

Although the best indicator of hemodynamic significance of a T2E is an increase in the aneurysm sac, which implies sustained systemic pressure and a higher risk of rupture, only few data are available on the role of a tight SBP control in reducing the retrograde blood flow into residual aneurysm sac.

Two studies demonstrated that systolic pressure index [13] -calculated as systolic aneurysm sac pressure divided by the systolic abdominal aortic pressure- and 2-day intensive postoperative blood pressure control [14] affect the clinical outcome of patients undergoing EVAR.

In this scenario, several recent studies suggest that the best strategy to prevent the development of T2E is a careful attention to preoperative

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strategy including optimal treatment of vascular risk factors and comorbidities [15,16].

Aim of this study was to evaluate whether preoperative BSP control, reached after preoperative cardiological assessment, might decrease T2E, sac expansion and related aortic reintervention incidence after EVAR.

2. Methods

We analyzed 386 consecutive patients underwent to EVAR for asymptomatic AAA larger than 5.5 cm. Three high-flow type endoleaks were recorded in this study. The high flow EL was a combination of a type Ia or Ib EL which was the inflow and a type II EL which was the outflow in 2 cases. The remaining third case was a type II EL + aorto-caval fistula which was the outflow exit of the endoleak.

In all three cases, even if a high flow EL was present, the sac reduced at the follow-up controls.

When a high-flow EL is recorded at completion angiography, these Els are monitored more closely with a follow-up every 3 months at least for the first year.

We have excluded emergency treated, inflammatory or ruptured aneurysms. All patients were treated from May 2008 to May 2016 at a single tertiary referral Hospital. All patients were treated from May 2008 and May 2016 at a single tertiary referral Hospital.

Starting from 2013 patients scheduled to EVAR have been systematically subjected to preoperative cardiologic work-up. At the moment of cardiologic consultation they already had the results of the laboratory testing including complete blood count, coagulative parameters, creatinine, two-view chest X-ray and resting electrocardiogram (ECG). They were asked to perform a home blood pressure monitoring (HMBPM) for at least 15 days before the first preoperative evaluation. Then patients received an extensive assessment of risk factors, clinical history, determination of functional capacity, physical examination, transthoracic ultrasound echocardiography and evaluation of the average systolic, diastolic BP and heart rate measurements detected at the home monitoring. In case the systolic BP is found above required target of 130 mmHg patients received a combination of at least two antihypertensive drugs until they reached a systolic pressure target. The effectiveness and tolerance of the combined treatment were evaluated after one month of combination therapy. Patients not normalized after the first drugs combination, received another titrated active principle and performed home blood pressure monitoring for two weeks more (Fig. 1).

As we needed to achieve BP control in 2–4 weeks before EVAR, we chose the combination of drugs according to the diamond-shaped strategy reported in ESC/ESH 2013 [18]. The preferred combination we have used is renin-angiotensin system (RAS) blockers along with calcium channel blockers or diuretics. In hypertensive patients with a history of myocardial infarction we have chosen beta-blockers and RAS blockers.

We considered beta-blockers whenever there was a specific indication for their use, e.g. heart failure, heart rate control, atrial fibrillation.

Each patient has continued the therapy throughout the entire period of follow-up.

The procedure was performed in a hybrid room equipped with an Artis Zee ceiling mounted angiographer (Siemens AG, Berlin, Germany). The patient was treated either under general or regional anesthesia with an intravenous total dose of 5000 IU of heparin, without withdrawal of preoperative antihypertensive treatment. Bilateral femoral cutdowns were performed routinely. All EVAR procedures were aorto-bi-iliac devices. We used different devices. Stent graft oversizing of 15–20% was routinely applied.

After obtaining approval from the institutional review board, we collected a dedicated database of patients' characteristics, SBP at the time of recovery and follow-up details. All data were analyzed retrospectively.

Outcome criteria and definitions were reported according to the Reporting standards for EVAR.

2.1. Follow-up protocol

From 2008 to 2012 all consecutive EVAR patients were scheduled for color duplex ultrasound (CDU) and plain abdominal radiography (RX) one day after the surgery. Follow-up was performed at one month and every six months. Patients were required to perform HBPM to be evaluated during every follow up visit to verify the stability of target systolic BP of 130 mmHg or less. Computed tomography angiography (CTA) was reserved for any non-diagnostic imaging at CDU. From 2012, contrast enhanced ultrasound (CEUS) was performed when (a) any endoleak was detected at CDU, (b) sac growth >5 mm within 6 months, and routinely for (c) patients with renal insufficiency (above Stage 3) or (d) iodine contrast allergy. In cases with sac shrinkage, CTA and clinical check-up was performed annually.

2.2. Statistical analysis

Discrete data are expressed as frequencies, and continuous data as mean ± SD. The χ^2 test was used to compare categorical variables, and the unpaired two-tailed Student's *t*-test was used to test differences between continuous variables. In order to identify the systolic blood pressure cut-off value with the highest specificity and sensitivity for T2E, sac expansion, sac shrinkage and re-intervention ROC curve analyses were performed. Survival curves were generated with the use of the Kaplan-Meier method, and the difference between groups was assessed by log-rank test. Multivariable regression analysis to evaluate the independent contribution of demographic, clinical, procedural, and antihypertensive therapies to the endpoints was performed by the backward stepwise Cox proportional hazards model. The variables entered into the model were as follows: age, gender, BMI, SBP < 130 mmHg, hypertension, dyslipidemia, smoking habit, diabetes, chronic kidney disease, coronary artery disease, valvular heart disease, atrial fibrillation, carotid artery disease, peripheral artery disease, chronic obstructive pulmonary disease, antiplatelet/anticoagulant therapies and home blood pressure monitoring. The proportional hazard assumption was assessed and satisfied graphically by plotting log (−log) survival curves against log survival time for each predictor category and verifying whether the curves were parallel. A p-value < 0.05 was considered significant. All tests were two-sided. Analyses were performed with SPSS statistical package, Version 24 (IBM Corp., Armonk, NY, USA).

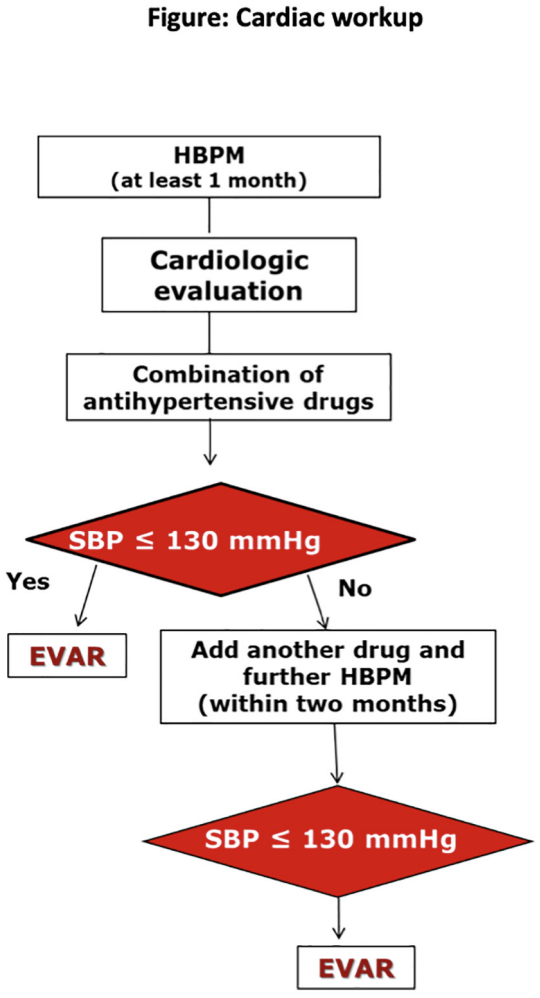

Fig. 1. Cardiac workup.

3. Results

3.1. Clinical characteristics

Between May 1, 2008 and May 1, 2016, 386 patients were recruited to undergoing EVAR. Demographic and clinical characteristics of the patients are shown in Table 1.

3.2. End-points

Primary end-points of the study were T2E, sac expansion or sac shrinkage and aneurysm-related re-intervention. Median follow-up was 24 months (interquartile range, 12–48 months). During follow-up in the study population the incidences of T2E, sac expansion and aneurysm-related re-intervention were 19.2%, 4.9% and 2.6% respectively. Sac shrinkage occurs in 18.6% of all patients.

The secondary end-point was vascular or cardiac mortality. During the follow-up, we observed 62 deaths for all-causes (16.1%), of whom 7 were aneurysm-related and 11 for cardiac-related causes.

3.3. ROC curves analyses

We performed ROC curve analyses in order to identify the SBP cut-off with the highest specificity and sensitivity for T2E, sac expansion, sac shrinkage and re-intervention. By analyzing ROC curves the cut-off was 131.5 mmHg for all outcomes. Accordingly, we divided the study population into two groups: group I patients with SBP higher than 130 mmHg at the time of EVAR and group II patients with SBP equal or lower than 130 mmHg at the time of EVAR.

Patients in group I were significantly older than patients in group II, whereas the other clinical characteristics did not significant differ between group I and group II (Supplementary Table 1).

Patients of group I (SBP > 130 mmHg) had significantly higher incidence of the primary end-points (T2E, sac expansion or sac shrinkage and aneurysm-related re-intervention) than patients of group II (SBP ≤ 130 mmHg). Cardiac mortality was more prevalent in group I than in group II (Table 1).

As shown in Table 2, group I patients were less frequently treated with ACE-inhibitors, calcium antagonists, mineralcorticoid receptor antagonists and diuretics than patients of group II.

Most of the patients in the group I (SBP > 130 mmHg) were treated with one (42.3%) or two (35.9%) antihypertensive drugs, and only 5.1% of patients was treated with three or more active principles.

In group II (SBP ≤ 130 mmHg), only 10% was treated with monotherapy, 44.8% was treated with two antihypertensive drugs and 35.8% with three or more active principles.

A single pill with fixed combination of antihypertensive drugs was administered in 73 (18.9%) patients: 23.1% in group II and 2.6% in group I ($p < 0.001$).

Any outcome was affected by the type of stentgraft implanted as reported in Supplementary Table 2.

In order to identify the predictors of primary and secondary outcomes we performed univariate and multivariate Cox regression analysis. The results are shown in Table 3. At the univariate analysis SBP ≤ 130 mmHg and the home blood press monitoring were independent predictors of a reduced incidence of T2E; at the multivariate analysis, adjusted for confounding variables, only the SBP ≤ 130 mmHg remained a significant protective factor for T2E [0.05 (0.03–0.10) 95% CI, $p < 0.001$]. As for what concerns the other end-points, the Cox regression analyses, after adjustment for confounders, demonstrated that SBP ≤ 130 mmHg was a significant and independent predictive factor for the occurrence of sac expansion, sac shrinkage and re-intervention [HR = 0.08 (0.03–0.29) 95%CI, $p < 0.001$; HR = 2.40 (1.01–6.19), $p = 0.045$; HR = 0.08 (0.01–0.38) 95%CI, $p < 0.008$ respectively]. As shown in Table 3 SBP ≤ 130 mmHg significantly reduced the risk of cardiovascular mortality and this association was maintained also after adjustment for several confounders [HR = 0.19 (0.03–0.99) 95%CI, $p = 0.042$). We did not perform the Cox regression analysis for aneurysm-related deaths, because of the low number of cases.

Table 1
Primary and secondary end-points according to SBP (> or ≤130 mmHg).

	Group I (PA > 130 mmHg) (n = 78)	Group II (PA ≤ 130 mmHg) (n = 308)	p value
Type 2 Endoleak, n (%)	**61 (78.2)**	**13 (4.2)**	**<0.001**
Sac expansion, n (%)	**11 (14.1)**	**8 (2.6)**	**<0.001**
Sac shrinkage, n (%)	**5 (6.4)**	**68 (22.1)**	**0.001**
Re-intervention, n (%)	**8 (10.3)**	**1 (0.3)**	**<0.001**
Ruptured aneurysm, n (%)	3 (3.8)	4 (1.3)	0.150
Cardiac mortality, n (%)	**6 (7.7)**	**5 (1.6)**	**0.011**

In bold the results with a statistical significance.

4. Discussion

This study shows that a tight blood pressure control with combination antihypertensive therapy, started at the time of preoperative cardiologic evaluation, is associated with a significant reduction in the incidence of T2E, sac expansion and related aortic re-intervention during a median follow-up of 24 months after EVAR. These findings have never been reported in literature and in our opinion this strategy should be considered in all EVAR patients.

The value of 130 mmHg of systolic pressure at the time of surgery has been identified as the threshold with the best sensitivity and specificity for the primary endpoints. Noteworthy, our results identified the same cut-off reported by the 2017 ACC/AHA guidelines on the diagnosis of hypertension which recommend treatment target of <130/80 mmHg for patients on stage 1 of hypertension with known cardiovascular disease or 10-year atherosclerotic event risk of 10% or higher [17], as our patients undergoing EVAR.

The study population had an overall very high cardiovascular risk: in particular, hypertension prevalence was 87%. After the preoperative cardiological assessment and the subsequent cardiac follow-up, nearly 69% of patients achieved a blood pressure target of <130 mmHg before EVAR.

As recommended by European hypertension guidelines, HBPM has been used as an educational tool in hypertensive patients for improving the understanding and accountability about their disease and follow-up, allowed the detection of white-coat and masked hypertension and had the additional advantages, such as wide availability and a very low cost [18,19]. In our study HBPM was the strategy adopted to achieved the pressure target, thus, in a real-world scenario, we demonstrate that it is an appropriate method for the long-term follow-up of treated hypertension.

Our approach, based on a prevention strategy, consisting in preoperative haemodynamic stabilization, has dropped the rate of re-interventions after EVAR from 10.3% to 0.3% in patient with a systolic pressure target of <130 mmHg [20]. Literature has showed so far that re-interventions are more frequent after EVAR than open abdominal aortic repair and one of the most frequent cause is endoleak presence. There are different types of endoleaks. The high flow types I and III endoleaks affect short and long-term outcome and the trend is to repair immediately with definitive secondary intervention; on the contrary, there are many controversies and limited consensus on the need for treatment of the low-flow T2E. Some authors manage T2E conservatively by a 'wait-and-watch' strategy to detect aneurysm sac enlargement, and risk of rupture [7,21–28]. In fact, T2E have a mostly benign prognosis, if there is no sac expansion of the AAA but their natural history is still not completely understood. Any kind of endoleak, if pressurize the sac and make it growth, can lead to a continuous sac expansion until rupture.

Therefore, the prevention of T2E might be very appealing than the treatment even if it is feasible. Some Authors have assessed models to predict high risk for T2E at the time of initial procedure using anatomic features, number and size of patent feeding arteries, and other factors. These groups have then looked at pre-emptive coil embolization to prevent T2E [27,29–34], but a strong and definitive benefit failed has to be proved.

In the last decades a careful and rigorous postoperative lifelong follow-up with computed tomography and color Duplex Ultrasound to detect aneurysmal sac growth and related risk of rupture is performed in most centres. If the sac is stable or decreasing in size, the risk is likely to be less and about half of them undergo spontaneous shrinkage [35].

However, despite an imaging follow-up continue to be essential for all patients after EVAR, several reports showed that >90% of EVAR patients do not benefit from surveillance, since imaging alone may lead to unnecessary interventions in 1.4–9% patients [36–38].

Several recent studies have attempted to assess preoperative risk factors for the development of T2E. A number of demographic factors,

Table 2
Antihypertensive treatment strategy according to SBP (> or ≤130 mmHg).

	Group I (PA > 130 mmHg) (n = 78)	Group II (PA ≤ 130 mmHg) (n = 308)	p value
ACE inhibitor, n (%)	**30 (38.5)**	**180 (58.4)**	**0.002**
Angiotensin receptor blockers, n (%)	12 (15.4)	73 (23.7)	0.127
Diidrophyridine calcium antagonist, n (%)	**19 (24.4)**	**139 (45.1)**	**0.001**
Beta-blockers, n (%)	25 (32.1)	107 (34.7)	0.691
Diuretics, n (%)	**7 (9.0)**	**118 (38.3)**	< **0.001**
Mineralcorticoid receptor antagonist, n (%)	**2 (2.6)**	**0 (0.0)**	**0.040**
Alfa blockers, n (%)	7 (9.0)	40 (13.0)	0.439
Nitrates, n (%)	1 (1.3)	12 (3.9)	0.480
Single pill with fixed combination, n (%)	**2 (2.6)**	**71 (23.1)**	<**0.001**
Anti-platelet/anti-coagulant therapies, n (%)	68 (87.2)	265 (86.0)	0.068

In bold the results with a statistical significance.

comorbidities, anatomic details of the aneurysm, and intraoperative factors have been actively investigated.

Starting from the assumption that the hemodynamic significance of T2E is an increase in the aneurysm sac, which implies sustained systemic pressure and a higher risk of rupture, some Authors have emphasized the importance of measuring aneurysm sac pressure to confirm whether EVAR is complete, and to evaluate the early outcomes of EVAR [39–41,14]. The concept of preventing T2E at the time of procedure with tight blood pressure control was applied for the first time by Miura and colleagues [14]. They performed elective EVAR under general anesthesia and then administered intravenous antihypertensive medication (nicardipine) in all patients placed in the intensive care unit (ICU). They found decreased incidence of T2E and enhanced sac shrinkage at 1 year. But this type of perioperative care is not standard and it is very expensive as patients undergoing EVAR are not placed in ICU unless they develop complications.

Mostly the advantages of the endovascular approach has been toward less invasive, shorter hospital stays, since patients are discharged on the second day, with studies looking at same-day discharge.

The biggest advantage of our method of decreasing T2E has been to obtain a tight BP control in less expensive settings and by less invasive methods.

All patients included in our study are at high cardiovascular risk, most of all, have a very poor control of blood pressure at the preoperative cardiological visit. We found that the only statistically significant risk factor for development of T2E was SBP >130 mmHg.

It is unquestionable that in these patients, controlling blood pressure can reduce the risk of cardiovascular disease [42].

Despite this, recent observations show that in the proportion of treated hypertensive patients only 30–40% are controlled to the recommended target [43–44].

There is strong evidence that in high-risk people blood pressure control is more difficult and requires more frequently the combination of more than two agents to control BP within goal [43–45].

Starting treatment with a combination may allow to achieve BP targets earlier than with monotherapy and it is potentially beneficial in high-risk with higher BP values or whose blood pressures are more above their optimal target.

Failure to achieve control with a two drugs combination at full dosage may require switching to another two drugs combination, or adding a third drug [18,46].

Evidence suggests that this approach will improve the speed, efficiency, and consistency of initial BP lowering and BP control, and is well tolerated by patients [47,48].

Accordingly, renin-angiotensin system blockers can be combined with either thiazide diuretics or calcium channel blockers [49,50].

Another combination to be prioritized consists of a calcium channel blocker with a thiazide diuretic used either as initial randomized treatment[52] or as combination during follow-up[53–56].

Patients with asymptomatic aortic aneurysm need to be operated within one to two months of cardiologic counselling. Thanks to the combination therapy, in particular to single pill fixed (SPF) dose we managed them to reach target ≤130 mmHg within one-two months.

Our finding confirm the results of previous studies, showing that patients receiving SPF combinations have superior compliance compared with those taking the individual components.

In our series no patient with a SPF developed endoleak.

Limitations of our study are the limited sample size and period of follow-up as well as the low frequencies of some variables included as end-points which can cause a statistical type II error.

Table 3
Univariate Cox regression analysis for T2E, sac expansion, sac shrinkage, re-intervention, and cardiovascular mortality.

	T2E		Sac expansion		Sac shrinkage		Re-intervention		Cardiovascular mortality	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Male sex	1.84 (0.80–4.26)	0.154	1.61 (0.27–9.76)	0.606	1.06 (0.45–2.52)	0.897	0.98 (0.83–1.17)	0.835	0.90 (0.07–5.39)	0.719
Age, years	0.99 (0.95–1.02)	0.304	0.97 (0.90–1.03)	0.266	1.04 (0.99–1.08)	0.051	1.69 (0.09–10.45)	0.488	1.07 (0.97–1.18)	0.115
BMI (kg/m^2)	0.99 (0.94–1.04)	0.577	0.93 (0.81–1.07)	0.317	1.00 (0.93–1.09)	0.910	1.22 (0.97–1.52)	0.084	0.88 (0.74–1.03)	0.105
BMI > 25 kg/m^2	1.02 (0.67–2.08)	0.943	1.02 (0.29–3.01)	0.672	0.92 (0.66–1.55)	0.355	3.05 (0.89–48.5)	0.171	0.63 (0.56–2.50)	0.389
SBP < 130 mmHg	0.05 (0.03–0.10)	<0.001	0.08 (0.03–0.29)	<0.001	2.40 (1.01–6.19)	0.045	0.08 (0.01–0.38)	0.008	0.19 (0.03–0.99)	0.042
Home BP monitoring	0.79 (0.17–0.99)	0.049	0.38 (0.05–1.34)	0.087	1.34 (0.77–2.32)	0.296	1.14 (0.70–25.9)	0.100	1.65 (0.04–3.08)	0.323
Smoking habit	0.79 (0.36–1.74)	0.563	0.98 (0.65–1.43)	0.526	1.20 (0.49–2.94)	0.696	0.99 (0.10–5.46)	0.353	0.36 (0.08–1.62)	0.184
Diabetes	1.63 (0.87–3.05)	0.127	2.20 (0.45–10.8)	0.332	0.95 (0.41–2.18)	0.910	0.67 (0.04–18.5)	0.815	3.90 (0.90–16.9)	0.070
Dyslipidemia	0.90 (0.54–1.51)	0.700	0.42 (0.13–1.41)	0.160	1.98 (1.12–3.30)	0.019	0.28 (0.05–3.28)	0.248	0.51 (0.13–2.03)	0.336
Coronary artery disease	1.04 (0.62–1.76)	0.884	0.29 (0.09–0.94)	0.042	0.91 (0.51–1.61)	0.778	0.32 (0.11–1.24)	0.093	0.89 (0.21–3.82)	0.870
Valvular heart disease	1.31 (0.63–2.73)	0.466	4.11 (1.07–15.8)	0.039	1.56 (0.41–2.86)	0.571	0.38 (0.10–13.7)	0.596	0.26 (0.03–2.65)	0.253
Atrial fibrillation	0.77 (0.31–1.67)	0.502	0.48 (0.06–3.71)	0.482	1.09 (0.49–2.88)	0.777	3.65 (0.76–12.7)	0.1350	1.17 (0.22–7.15)	0.687
Carotid artery disease	0.88 (0.50–1.52)	0.636	0.95 (0.29–3.10)	0.931	0.74 (0.43–1.28)	0.278	2.64 (0.56–25.7)	0.190	0.81 (0.18–3.53)	0.253
Peripheral artery disease	0.96 (0.58–1.53)	0.602	0.54 (0.11–2.54)	0.436	1.50 (0.82–2.76)	0.189	0.28 (0.03–4.33)	0.365	2.16 (0.55–8.56)	0.273
Chronic obstructive polmonary disease	1.34 (0.83–2.18)	0.234	1.10 (0.39–3.09)	0.856	0.64 (038–1.07)	0.087	1.99 (0.23–17.1)	0.533	0.91 (0.24–3.44)	0.889
Renal chronic failure	0.94 (0.46–1.91)	0.953	2.37 (0.69–9.41)	0.133	0.66 (0.34–1.29)	0.361	2.53 (0.20–10.4)	0.528	1.21 (0.48–5.41)	0.705
Antiplatelet/anti-coagulant therapies	0.73 (0.37–1.45)	0.334	0.41 (0.10–1.71)	0.219	0.45 (0.24–0.99)	0.045	10.8 (0.15–79.8)	0.577	2.48 (0.01–23.9)	0.278

Furthermore, the change of follow-up method could condition the results of the study. However, computed tomography angiography (CTA) was reserved for any non-diagnostic imaging at CDU before 2012. From 2012, contrast enhanced ultrasound (CEUS) was performed and it was demonstrated that a CEUS based protocol for EVAR follow up is safe and effective and it is similar to a CTA based follow up protocol with regard to identification of endoleaks in a mid-term period [38].

5. Conclusion

Type II endoleak following EVAR and its related reinterventions can be reduced adopting a non-interventional approach by using a combination antihypertensive therapy on a home blood pressure monitoring pre-operative protocol. This approach which has become our standard of care is safe and cost-effective and we suggest to be undertaken it in all EVAR patients. The cardiac work-up in patients undergoing EVAR is worthwhile either to control risk factors or to prevent some complications related to EVARP.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.02.066.

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