

Original Research Article

# Vascular Screening During Transthoracic Echocardiography: Specialty Practice-Based Prospective Monocentre Observational Study Including a Three-Year Follow-up

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Keywords

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- Real-world vascular screening
- Transthoracic echocardiography

Abstract

**Background:** Abdominal aortic aneurysm and atherosclerotic alterations of the carotid arteries are well known silent threatening conditions. Transthoracic echocardiography (TTE) is a potential tool for opportunistic screening of extra-cardiac vascular anomalies. We studied the additional diagnostic yield and therapeutic impact of vascular screening during TTE in patients referred to a practising cardiologist and therefore in a presumably high-risk patient group.

**Design, Method:** 306 patients consecutively referred to a practising cardiologist underwent vascular screening during standard TTE. Vascular recordings were made of the maximal infra-renal abdominal aorta diameter as well as the intima-media thickness (IMT) of common carotid arteries and thickness of atherosclerotic plaques in common and internal carotid arteries. After an adjusted, guideline-directed medical treatment was completed, a three-year follow-up-survey was undertaken by means of a questionnaire sent to the referring physicians.

**Results:** After exclusion of three patients for equivocal imaging, 303 patients were studied (188 males), aged  $65 \pm 15$ , of whom 89 patients (29%) were known for coronary artery disease (CAD). Abdominal aortic screening revealed 87 anomalies (28%), of which 13 were aneurysms (maximum diameter  $\geq 3$  cm) and 74 dilatations ( $\geq 2$  to  $< 3$  cm). The mean carotid IMT was  $0.8 \pm 0.2$  mm and was not significant enough to distinguish patients with CAD from the others. Carotid echo-Doppler imaging yielded significant plaques ( $\geq 1.5$  mm) in 163 patients (53%), one internal carotid occlusion and significant stenoses ( $> 50\%$ ) in 6 patients; two of these patients required short term surgery. Carotid imaging alone contributed to risk re-stratification of 47 patients (15.5%) from the low and intermediate risk groups to the high-risk group according to the basic PROCAM scoring system (PROspective Cardiovascular Munster study). Taking into account the presence of CAD and of diabetes mellitus, the initial cardiological examination shifted the number of high risk patients from 88 (29%) to 212 (69.9%).

The three-year follow-up (96% of the initial group of patients) yielded all-cause mortality of 10%, cardiovascular mortality of 6% and non-fatal cardiovascular events of 17.5%. At three years, the therapeutic impact of the cardiological key consultation was still significant for inhibitors of the renin-angiotensin system; in men, this was the case for betablockers and statins as well.

**Conclusion:** Screening of the abdominal aorta and carotid arteries during routine TTE was highly contributory to vascular diagnosis and to cardiovascular risk assessment and can be performed without additional cost or significant additional time.

## INTRODUCTION

Atherosclerosis is a major public health problem worldwide. The mortality and morbidity burden remains very high [1]. The advent of efficacious preventive measures and treatments in recent decades constitutes a real hope of reducing this burden, especially if the disease can be recognized early. Population screening programmes involve organizational and financial issues. To contribute to reducing the gap between "pure" primary prevention and "late" diagnosis of overt cardiovascular disease,

simple vascular screening tools should be utilized [2]. It therefore appears essential to benefit from all possible opportunities such as all-cause consultations by general practitioners (overall basic vascular examination for example) as well as all-cause consultations by general cardiologists. The latter group will employ specialized diagnostic tools and methods, particularly transthoracic echocardiography (TTE).

TTE is indeed a potential tool for opportunistic screening of major vascular anomalies such as abdominal aortic aneurysm [3]

and atherosclerotic alterations of the carotid arteries [4], which are well known silent threatening conditions.

## MATERIALS AND METHODS

306 patients living in a semi-rural area of Switzerland were studied on a consecutive, non-selected series basis (no other inclusion criteria applied). The fact that all patients are living in the same semi-rural area confers a quite homogeneous character to our patient group especially in terms of environmental influences. However, this is a reason not to generalize all the observations to patients living in other areas and countries. They were all referred to a practising cardiologist for a specialized evaluation including transthoracic echocardiography. The method, in particular the ultrasound modalities, were explained to the patients, and they all gave oral informed consent to their anonymised participation in the study. The history, risk factors, and medication history were obtained at the time of the cardiovascular consultation [5].

At inclusion, all patients underwent a clinical cardiovascular assessment including physical examination, resting electrocardiogram and transthoracic echocardiography. During the echocardiography, the abdominal aorta and the carotids were examined, in line with our concept of a "global approach" [6]. A PROCAM score, a numerical quantitative score based upon the main cardiovascular risk factors (age and sex, family history, smoking, lipid status, hypertension, documented atherosclerotic alterations, diabetes mellitus) [7], applied in line with the recommendations of the Swiss Society of Cardiology with its working group in lipids and atherosclerosis (SSC), was established for each patient in order to classify them in one of the three known predefined risk categories (low= <10%, intermediate= 10 to 20% and high-risk= above 20% risk of a cardiovascular event at ten years).

A three-year follow-up survey was undertaken by means of a questionnaire sent to the referring physicians (cardiovascular and all-cause mortality, non-fatal cardiovascular events, medical treatment). Where necessary, the physicians were also contacted by phone. No further study-specific contact with the patients was established for this purpose.

Risk factors [8,9]: Resting blood pressure was measured according to the ESC recommendations by means of a standard sphygmomanometer. The results were rounded to the nearest 5 mmHg. Subjects were considered hypertensive based on a history of hypertension, use of antihypertensive medication and current blood pressure of >140/90 mmHg.

Patients were considered diabetic based on documented diabetes, current use of antidiabetic drugs, available blood-glucose and HbA1c values. For dyslipidaemia, available results of recent blood sampling were collected. Patients were considered dyslipidaemic in case of a current specific treatment and according to the above-mentioned criteria. To respect the completely non-invasive character of the study, no blood samples were taken at the cardiovascular evaluation.

Abdominal aorta assessment included longitudinal and cross-

sectional ultrasound imaging of the infra-renal abdominal aorta and its bifurcation, with the patient placed in a semi-left lateral position [3]. Images were acquired using a conventional (cardiac) 2.25 MHz probe of a commercially available echocardiograph ("Vivid 7 dimension", GE medical Systems, Horton, Norway). The maximum diameter of the infra-renal abdominal aorta was noted for each patient as the largest diameter measured on either longitudinal or transverse images. The range of normal abdominal aortic dimensions is 1.4 to <2 cm [10]; dilatation and aneurysm are defined as dimensions of  $\geq 2$  cm to <3cm and  $\geq 3$  cm, respectively. All imaging and measurements were done by a single operator. For practical reasons, an analysis of the ilio-femoral axis was not performed.

For the carotid assessment [11], both sides were visualized following a standardized protocol that includes the common carotid artery, the carotid bifurcation and the proximal extracranial portion of the internal and external carotid artery. A conventional 10 MHz probe of the same echocardiograph was used. To measure IMT, the image was focused on the posterior (far) wall of the common carotid artery, approximately 10 mm proximal to the bifurcation, and gain settings were used to optimize image quality. Mean IMT was obtained semi-automatically by the means of a dedicated commercially available software built into the Vivid 7-dimension device used (Vivid 7 BT08 IMT). IMT was recorded for each patient as mean left common carotid and mean right common carotid thickness and their average. Carotid plaque was defined as a focal structure encroaching into the arterial lumen with a thickness of  $\geq 1.5$  mm. Carotid stenosis was defined as loss of more than 50% of carotid lumen. The yield in terms of risk stratification of the described global approach by vascular screening during TTE was evaluated. The sole exclusion criterion was inconclusive imaging results.

For the definitive allocation to the PROCAM risk categories [12], the following observations induced a change in PROCAM risk categories (low to high and intermediate to high): newly diagnosed diabetes, newly diagnosed coronary artery disease (CAD) and the existence of a carotid plaque.

### Follow-up

After the prescription of adjusted guideline-directed medical treatment, a three-year follow-up survey was undertaken by means of a questionnaire sent to the referring physicians. The impact of the changes on allocation to the risk categories was evaluated after a mean follow-up of 39 months, particularly in terms of cardiovascular events and treatment changes.

### Statistical analysis

Patient characteristics were summarized using means and standard deviations (SD) for continuous variables and frequencies and percentage for categorical variables. P-values for differences across groups were estimated using  $X^2$  or Fisher's exact test or simple logistic regression in case of binary variables and multinomial logistic regression in case of categorical variables. We used Student's t-test or linear regression to estimate differences in the case of continuous variables. The association

between age and aortic diameter was visualized in a scatterplot and estimated using the Pearson correlation. Differences between medical treatment as baseline and at three-year follow-up across subgroups were assessed using McNemar's  $X^2$  test for paired nominal data. All hypotheses were two sided and  $p < 0.05$  was deemed statistically significant. The analyses were performed using the statistical package Stata (version 14.1).

## RESULTS

### General results

After exclusion of three patients for inconclusive imaging results, 303 patients were analysed. Table 1 shows their baseline characteristics. The mean age of the patients was  $65 \pm 15$  years (ranging from 17 to 88 years). A large number of them (48%) were referred for echocardiographic evaluation of left ventricular function. Other referral reasons include follow-up of valvular disease (26%), heart murmurs (7.5%), cerebrovascular events (2.6%), heart failure (1.6%) and other indications (15.8%). Roughly a quarter of this population was previously known to the cardiologist.

Men had 20% more risk factors than women. The difference was striking for smoking (47.3% versus 29.6%;  $p = 0.0022$ ) and for dyslipidaemia (47.1% versus 28.6%;  $p = 0.0016$ ). Hypertension was slightly though statistically non-significantly more prevalent in women (49.1% versus 43.6%;  $p = 0.35$ ), while there was no significant difference for diabetes (13.9% in men and 12.5% in women;  $p = 0.73$ ). 58% of women and 38% of men presented no or only one risk factor. Men presented four or five risk factors more often than women (11.7% vs. 7.8%). Body mass index (BMI) was similar in both sex groups (26 in women and 26.8 kg/m<sup>2</sup> in men;  $p = 0.19$ ).

### Vascular screening

**Abdominal aorta screening:** Mean abdominal aortic diameter was  $1.9 \pm 0.6$  cm (Figure 1). We observed a positive although weak correlation between age and aortic dimensions (Pearson correlation = 0.33).

The screening yielded 74 abdominal aortic dilations (24%, mean age  $72 \pm 8$  y, 59 males) and 13 abdominal aortic aneurysms (4.3%, mean age  $75.8 \pm 5.5$  y; 12 males). 77% of the aneurysm patients and 35% of the patients with aortic dilation had overt CAD. 46% of the aneurysm patients were smokers, 61% had hypertension, 30% were known for diabetes and 84% had dyslipidaemia. There is a significant difference for IMT between normal and dilated/aneurysmal aorta variants ( $0.7 \pm 0.2$  versus  $0.8 \pm 0.2$ ,  $p = 0.0007$ ), but no significant difference for carotid plaques (5 out of the 6-significant carotid stenoses were discovered in patients with normal abdominal aorta dimensions).

**Carotid screening, plaque and IMT:** 53% of the studied population showed significant carotid plaques; their mean age was 13 years higher than the general mean age. Carotid examination revealed significant plaques in 61% of men and 43% of women. BMI was equivalent in patients with and without plaques.

Plaques were present in 53% of male smokers and 34% of female smokers, in 55% of men and 63% women with hypertension, in 62% of men and 48% of women with dyslipidaemia, and in 16% of male and 18% of female diabetics. There were 55% more risk factors in the group of patients with significant carotid plaques than in patients without plaques.

Among patients with carotid plaques, we found six severe stenoses. They were on average 12 years older than the patients without plaques, were mostly non-diabetic men (83%) and only one had an aortic anomaly (dilatation). Four of them (66%) were known for coronary disease. Mean aortic dimension was lower in this group ( $1.7 \pm 0.3$  versus  $1.9 \pm 0.6$  in the non-stenosis group). The mean IMT was  $0.8 \pm 0.2$  in men and  $0.7 \pm 0.2$  in women. Regarding the initial numerical PROCAM risk group assessment,

**Table 1:** General characteristics.

Characteristic	Overall (n=303)	Women (n=115)	Men (n=188)	p-value
Age (years)	65.0±15.0	63.5±16.3	66.0±14.1	0.174
BMI (kg/m <sup>2</sup> )	26.5±4.6	26.0±5.5	26.8±3.9	0.191
Systolic pressure (mmHg)	142.3±16.5	143.5±18.8	141.5±14.9	0.311
Diastolic pressure (mmHg)	86.3±7.7	86.3±8.5	86.2±7.3	0.930
LVEF	59.3±12.3	62.8±10.5	57.1±12.8	0.000
Cardiovascular risk factors	1.7±1.3	1.5±1.3	1.9±1.3	0.004
Diabetes	40 (13.4)	14 (12.5)	26 (13.9)	0.73
Dyslipidaemia	120 (40.1)	32 (28.6)	88 (47.1)	0.002
Hypertension	138 (45.7)	56 (49.1)	82 (43.6)	0.352
Family history	65 (21.7)	14 (12.5)	51 (27.3)	0.003
Active or former smoker	123 (40.6)	34 (29.6)	89 (47.3)	0.002
<i>Abdominal aorta</i>				
Diameter	1.9±0.6	1.7±0.4	2.0±0.7	<0.0001
Classification of the aortic diameter				<0.0001
Normal (<2 cm)	211 (70.8)	98 (86.0)	113 (61.4)	
Dilatation (≥2 to <3 cm)	74 (24.8)	15 (13.2)	59 (32.1)	
Abdominal aorta aneurysm (≥3 cm)	13 (4.4)	1 (0.9)	12 (6.5)	
<i>Carotid arteries</i>				
Intima-media thickness	0.8±0.2	0.7±0.2	0.8±0.2	0.123
Plaque	163 (53.8)	49 (42.6)	114 (60.6)	0.002
Plaque thickness	2.7±0.8	2.4±0.7	2.8±0.8	0.004
Significant stenosis	6 (2.0)	1 (0.9)	5 (2.7)	0.414
<i>Coronary arteries</i>				<0.0001
Known coronary artery disease	47 (15.5)	18 (15.7)	29 (15.4)	
No coronary artery disease	89 (29.4)	15 (13.0)	74 (39.4)	
Unknown	167 (55.1)	82 (71.3)	85 (45.2)	

Displayed numbers are n (%) or mean (SD); BMI=Body Mass Index; LVEF=Left Ventricular Ejection Fraction; SD=Standard Deviation. P-values for differences across gender are estimated using  $X^2$  or Fisher's exact test in case of binary variables, multinomial logistic regression in case of categorical variables, and Student's t-test in case of continuous variables.

56% of the non-plaque population and 41% of the plaque group had previously been placed in the low risk category including four of the six patients presenting significant carotid stenoses.

There was a tendency to association with diffuse arterial wall disease: the prevalence of CAD was 10 times higher in the group with significant plaques than in the patients without plaques. All the aortic aneurysms were found in patients with significant carotid plaques. Aortic dilatation was twice as frequent in patients with plaques, and the mean aortic diameter was 15% higher in patients with plaques.

**The coronary artery disease population:** 89 patients (29% of the total population studied) were known for CAD. Their mean age was 70±10 years (versus 64±15 years for non-CAD-patients). Their mean aortic diameter was 2.1±0.9 cm. 13 patients (11.8%) had an aortic aneurysm (and 30.6% had aortic dilatation), 91%

had significant carotid plaques.

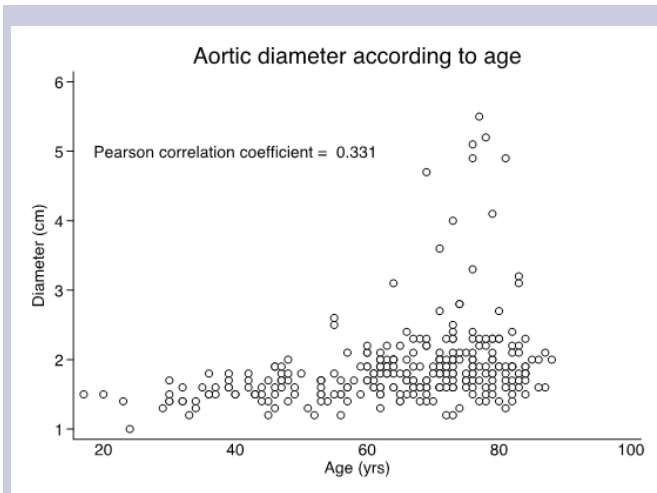
**PROCAM risk groups:** There was no significant sex difference for the initial numerical PROCAM score adapted for Switzerland. The risk level increased with age. 47% of the population studied were considered at low risk before reclassification. Among the men, 45% were considered at low risk, 25% at medium risk and 30% at high risk. Among the women, 52% were considered at low risk, 21% at medium risk and 27% at high risk.

All patients in the "low" and "intermediate" risk groups with newly defined coronary disease and/or diabetes were shifted to the "high" risk group. Patients with newly diagnosed carotid plaques as a proof of atherosclerosis at the time of the initial cardiological examination were also shifted to the high-risk category (Table 2 and Table 3).

**Table 2:** Patients' characteristics after re-classification.

Characteristic	Low risk unchanged (N=71)	Intermediate risk unchanged (N=20)	High risk unchanged (N=88)	Low to high risk (N=73)	Intermediate to high risk (N=51)	p-value
Women	38 (53.5)	10 (50.0)	31 (35.2)	22 (30.1)	14 (27.5)	0.0113
Age (years)	49.9±17.4	61.0±13.2	70.5±9.5	69.4±11.2	72.0±8.6	<0.0001
BMI (kg/m <sup>2</sup> )	25.7±4.7	24.8±6.4	27.2±4.0	26.5±4.2	27.1±5.0	0.1055
Systolic pressure (mmHg)	134.9±14.0	136.0±19.4	145.2±17.6	144.2±13.0	147.2±17.4	<0.0001
Diastolic pressure (mmHg)	85.0±7.1	85.2±9.7	86.5±7.4	86.6±6.6	87.5±9.7	0.4513
LVEF	63.5±11.2	60.8±14.5	57.7±12.8	57.5±11.6	58.1±11.7	0.0149
Cardiovascular risk factors	0.8±0.9	1.2±1.1	2.1±1.3	1.9±1.3	2.2±1.2	<0.0001
Diabetes	0 (0.0)	0 (0.0)	11 (12.6)	18 (24.7)	11 (22.0)	0.1211
Dyslipidaemia	10 (14.5)	3 (15.0)	41 (47.1)	39 (53.4)	27 (54.0)	<0.0001
Hypertension	18 (25.7)	3 (15.0)	52 (59.1)	38 (52.1)	27 (52.9)	<0.0001
Family history	10 (14.5)	4 (20.0)	21 (24.1)	12 (16.4)	18 (36.0)	0.0555
Active or former smoker	13 (18.3)	10 (50.0)	50 (56.8)	26 (35.6)	24 (47.1)	<0.0001
<i>Abdominal aorta</i>						
Diameter	1.6±0.2	1.8±0.4	1.9±0.4	2.0±0.6	2.2±1.0	<0.0001
Classification of the aortic diameter						0.0001
Normal (<2 cm)	64 (90.1)	13 (65.0)	59 (70.2)	45 (61.6)	30 (60.0)	
Dilatation (≥2 to <3 cm)	7 (9.9)	7 (35.0)	23 (27.4)	24 (32.9)	13 (26.0)	
Abdominal aorta aneurysm (≥3 cm)	0 (0.0)	0 (0.0)	2 (2.4)	4 (5.5)	7 (14.0)	
<i>Carotid arteries</i>						
Intima-media thickness	0.6±0.2	0.7±0.1	0.8±0.2	0.8±0.2	0.8±0.2	<0.0001
Plaque	0 (0.0)	1 (5.0)	51 (58.0)	66 (90.4)	45 (88.2)	<0.0001
Plaque thickness	Not enough observations	Not enough observations	2.9±1.0	2.6±0.8	2.7±0.6	0.2855
Significant stenosis	0 (0.0)	0 (0.0)	2 (2.3)	4 (5.5)	0 (0.0)	0.2839
<i>Coronary arteries</i>						0.000
Known coronary artery disease	13 (18.3)	5 (25.0)	11 (12.5)	11 (15.1)	7 (13.7)	
No coronary artery disease	1 (1.4)	1 (5.0)	27 (30.7)	32 (43.8)	28 (54.9)	
Unknown	57 (80.3)	14 (70.0)	50 (56.8)	30 (41.1)	16 (31.4)	

Displayed numbers are n (%) or mean (SD); BMI=Body Mass Index; LVEF=Left Ventricular Ejection Fraction; SD=Standard Deviation. P-values for differences across groups are estimated using simple or multinomial logistic regression in case of binary and categorical variables, and linear regression in case of continuous variables.



**Figure 1:** Abdominal aortic dimension related to age. Plotted is the abdominal aortic dimension (in cm) against age (in years). The association between the two variables is estimated with the Pearson correlation.

Overall (Figure 2), 124 patients were shifted to the high-risk group (73 from the low risk and 51 from the intermediate-risk group). 88 out of these 124 patients were men. On the sole basis of discovery of carotid plaques, 47 patients were shifted to the high-risk category (15.5%; 18 men and 12 women from low to high risk and 9 men and 8 women from intermediate to high risk). Amongst these 124 patients, 37 were known for abdominal aortic dilatation. All the aortic aneurysm patients were ultimately placed in the high-risk group (only two initially considered at high risk). Considering the presence of overt CAD and of diabetes mellitus, the initial cardiological examination raised the number of high risk patients from 88 (29%) to 212 (69.9%).

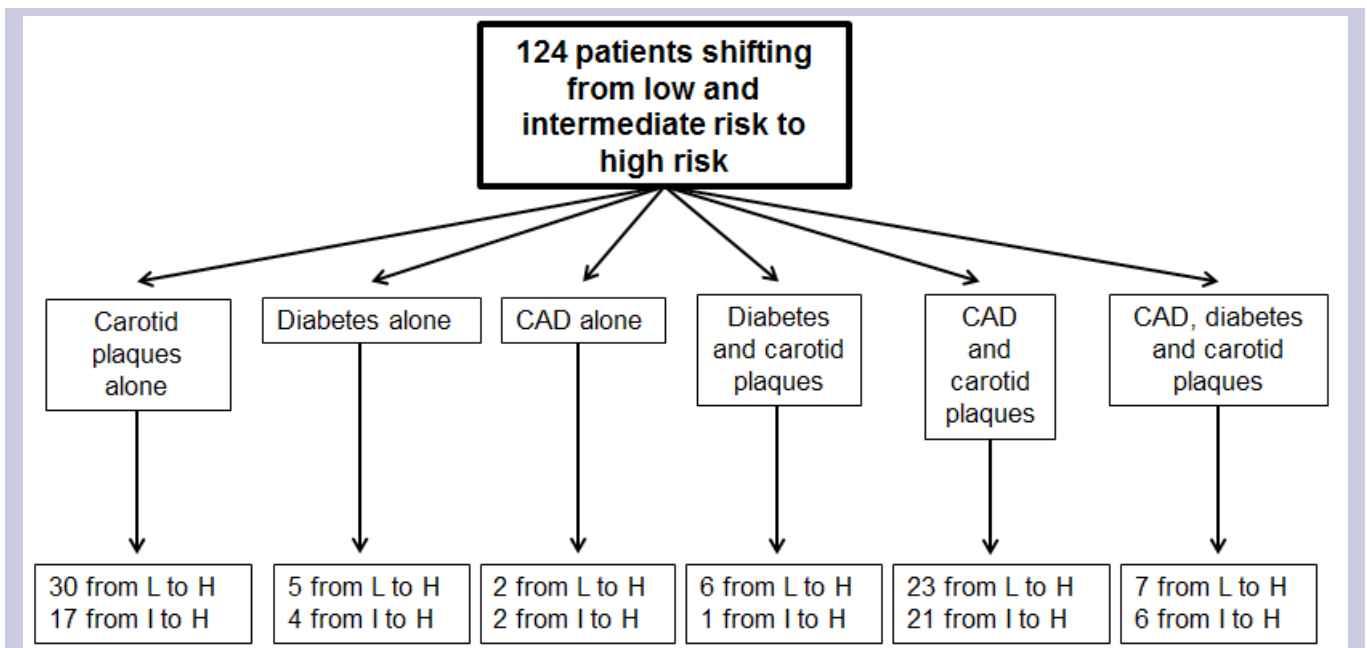
**Follow-up results**

**Mortality, morbidity:** Follow-up was obtained at an average of 39.5±5.9 months. By that time, 31 patients (10.2%) had passed away, 20 from cardiovascular causes (6.6%, mean age 72 years, 90% men; LVEF was lower than in the group of living patients: 39±17% versus 60±11%) and 11 from non-cardiac causes. 15 patients (4.9%) were lost to follow-up. We found a statistically significant association between death and four baseline characteristics (data not shown): age (p=0.015), aortic diameter (p=0.002), carotid stenosis (p=0.0001) and coronary disease (p=0.006.)

Among the deceased patients, 40% were initially at high risk while 50% had been reclassified to the high-risk group at the time of the initial cardiological examination (six from the low risk group and four from the intermediate-risk group). 60% were known for CAD, 50% for smoking, 47% for hypertension, 10% for diabetes and 50% for dyslipidaemia. 75% of them had carotid plaques (versus 51% for the living patients and 72% for the non-cardiovascular deaths). One deceased patient had been classified in the low risk group and another in the intermediate-risk group. There was no aortic aneurysm in this group; 36.8% presented aortic dilatation (versus 24.3% in the living patients).

Mean IMT was similar in cardiovascular deaths, non-cardiovascular deaths and patients alive (0.8±0.2). However, there was a significant association between experiencing a cardiovascular event and having an IMT higher or lower than 0.8 (p=0.014) (Figure 3). The probability of having a cardiovascular event was 1.94 times higher (p=0.015) for patients having an IMT above 0.8 than for those with an IMT equal or lower than 0.8.

**Non-fatal cardiovascular events (Figure 4):** During the follow-up, we observed 60 non-fatal cardiovascular events in



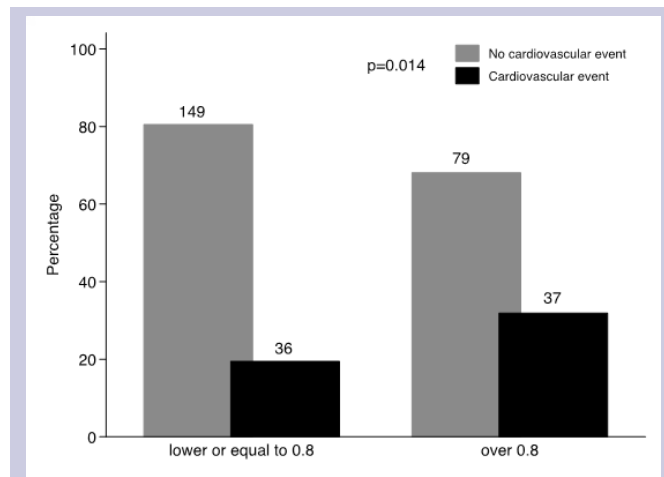
**Figure 2:** Patients changing risk groups depending upon newly diagnosed CAD, diabetes and carotid plaques. L stands for low-risk group, I for intermediate-risk group and H for high-risk group. CAD for coronary artery disease.

**Table 3:** Discovered aortic aneurysms and carotid pathologies by systematic screening during TTE.

	Aortic aneurysms	Aortic dilatations	Carotid stenosis	Significant Carotid plaques	Mean IMT	Total anomalies
Initial low-risk	4 (2.8)	31 (21.5)	4 (2.8)	66 (45.8)	0.7±0.2	105
Initial intermediate-risk	7 (10)	20 (28.6)	0	46 (64.8)	0.8±0.2	73
Initial high-risk	2 (2.4)	23 (27.4)	2 (2.3)	51 (58)	0.8±0.2	78
Low-risk reclassified	0	7 (9.9)	0	0	0.6±0.2	7
Intermediate-risk reclassified	0	7 (35)	0	0	0.7±0.1	7
High-risk reclassified	13 (6.3)	60 (29)	6 (2.8)	163 (76.4)	0.8±0.2	242

Displayed numbers are n (%) or mean (SD).

53 patients (17.5 %); 66% were men, and their mean age was 68±11 years: 18 coronary complications (34%), 14 arrhythmic events (26.4%), ten cardiovascular surgical interventions (18.8%, aortic, valvular, carotid interventions), five acute cardiac decompensations (9.5%), five cerebral ischaemic events (9.5%) and eight others (5.7%).



**Figure 3:** Relationship between IMT (upper normal limit of 0.8) and presence of cardiovascular event at follow-up.

The depicted numbers in the plot represent the absolute frequencies, while the bars represent the relative frequencies of presence and absence of cardiovascular events according to risk group. The p-value for the association between IMT and presence of cardiovascular event at follow-up was estimated using the  $\chi^2$  test.

LVEF was lower than in the living patients without cardiovascular events (56±13% versus 60±11%). Of those patients, 41% were known for coronary disease, 47% for smoking, 55% for hypertension, 17% for diabetes and 47% for dyslipidaemia. Four abdominal aortic aneurysms were present in this group and 15% presented aortic dilatation (versus 28% in the living group of patients). Mean aortic diameter was higher than in patients with cardiovascular death (1.96±0.8 versus 1.84±0.3).

40% of these patients were considered at high risk initially, 26% had been upgraded from low to high, 24% from intermediate to the high-risk group. Three patients from the unchanged intermediate-risk and two from the unchanged low risk groups presented cardiovascular events.

**Therapeutic impact:** The impact of optimal, guideline-directed medical treatment at mid-term of a unique cardiological consultation including TTE, abdominal aortic imaging and echo-Doppler examination of the extracranial carotid arteries was analysed based on the follow-up questionnaire.

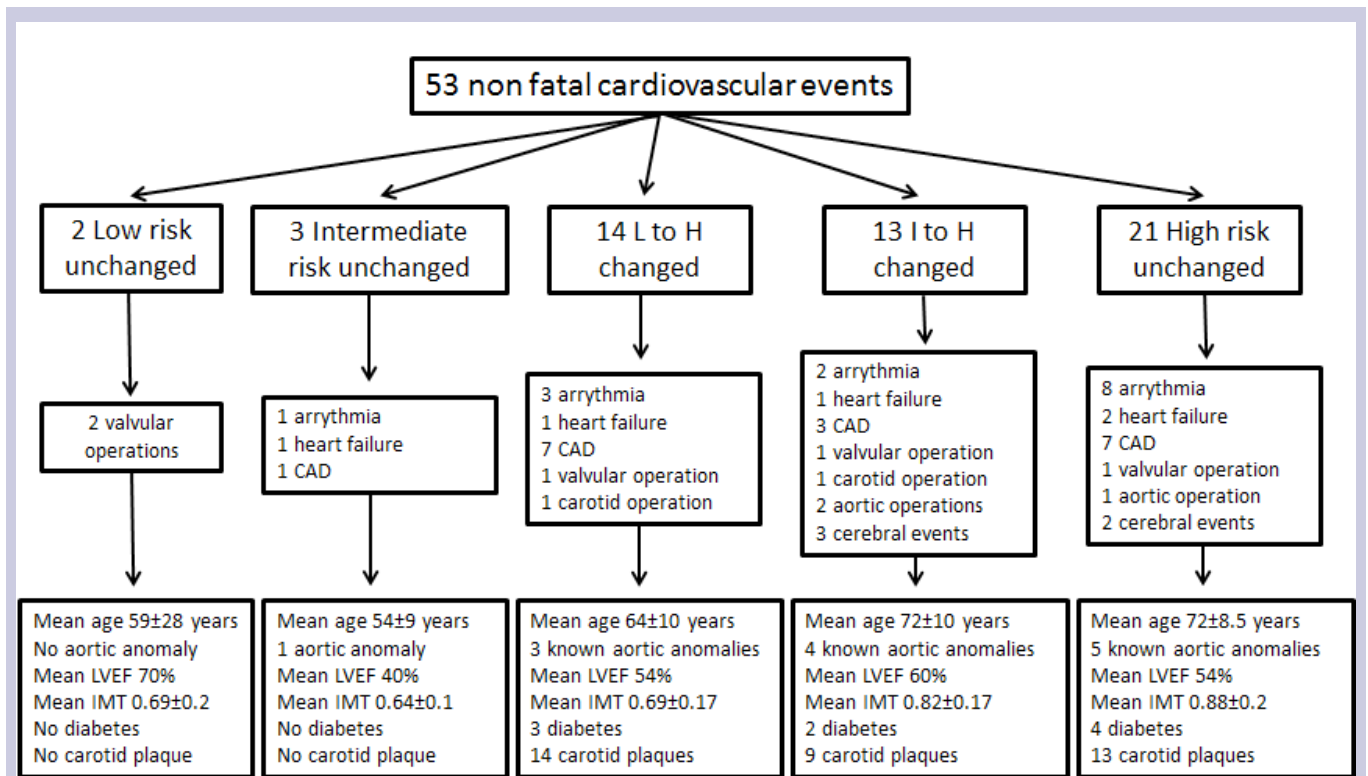
Referring physicians and patients followed the specialized counselling to some extent. In patients reclassified to the high-risk category, it was observed that an intensification of preventive drug therapy persisted at three years. Regardless of gender, the difference was significant only for Ace-I/ARBs (p=0.001). In terms of gender, men presented a significant difference not only for Ace-I/ARBs but also for beta-blockers and statins (Figure 5).

## DISCUSSION

Early diagnosis of subclinical atherosclerotic alterations, risk stratification and its prevention are challenges in daily practice [13;14]. Our prospective monocentre observational study aimed to discover the advantage of opportunistic detection and specialized counselling of patients at risk during a cardiological examination including the impact of carotid and aortic screening [15], looking for silent threatening conditions and markers of subclinical atherosclerosis [16].

The risk stratification we obtained based on a unique non-invasive cardiological work-up confirmed our hypothesis that outpatients referred to a cardiologist are a high-risk population. Indeed, 70% of the patients were classified in the PROCAM high risk category (>20% risk of experiencing a cardiovascular event within 10 years). This high risk is reflected in a quite high mortality of 10% within three years with a 6.6% mortality of cardiovascular origin. Of the 20 patients who died from cardiovascular events, ten (50%) had been shifted from the low and intermediate-risk to the high-risk group and all presented significant carotid plaques.

Carotid imaging revealed six significant stenoses, and two patients benefited from surgery. Four of these patients with significant stenoses presented an initially low numerical risk score. This carotid anomaly is a statistically significant variable regarding short term death (p=0.0001). Interestingly, diabetes was not statistically significant regarding the presence of atherosclerosis in this location.

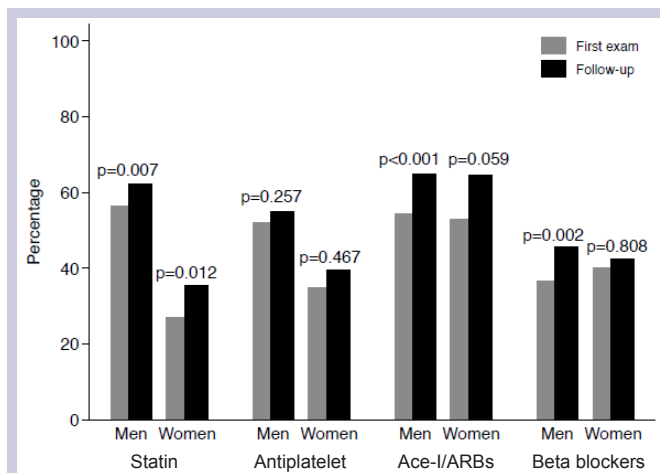


**Figure 4:** Non-fatal cardiovascular events during 39 months' follow-up. L stands for low-risk group, I for intermediate-risk group and H for high-risk group, CAD for coronary artery disease.

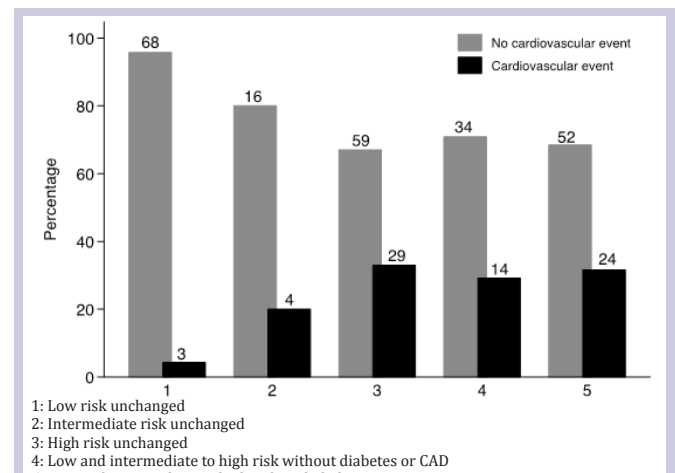
Abdominal aortic imaging was feasible in all but three patients. 29% of them showed abnormal diameters and a statistically significant link with advancing age, male sex, IMT, presence of carotid plaque and CAD. The presence of an abnormal abdominal aortic diameter is statistically significant for cardiovascular death (and non-cardiovascular death). All patients with aneurysms were in the PROCAM corrected high risk group.

Vascular screening and therefore the refinement of risk estimation and therapeutic counselling were feasible in nearly all patients (equivocal images in less than 1% - three patients - led

to exclusion from the study). Vascular screening yielded many abdominal aortic alterations (74), especially 13 aneurysms, a well-known threatening silent condition. Similarly striking were the observations at the carotid level. 163 patients (53%) had significant plaques justifying their inclusion in or transfer to the high-risk category. In 47 patients (15.5%) carotid imaging alone motivated this shift. Furthermore, two patients underwent surgical thromboendarterectomy shortly thereafter. Statistical regression analysis showed that the probability of experiencing a cardiovascular event is 1.94 times higher ( $p=0.015$ ) for patients having an IMT above 0.8 than for those with an IMT equal or



**Figure 5:** Medical treatment at baseline and at three-year follow-up for the group of patients shifted to the high-risk category according to gender. The p-value for the difference between medical treatment as baseline and at three-year follow-up across gender was estimated using McNemar's  $\chi^2$  test.



**Figure 6:** Mortality and morbidity as a function of risk groups. The depicted numbers in the plot represent the absolute frequencies, while the bars represent the relative frequencies of presence and absence of cardiovascular events according to risk group.

lower than 0.8 [17]. Figure 6 highlights the impact of carotid atherosclerosis discovery and the need for short term preventive measures. Consequently, guideline-directed treatment changes can be firmly recommended.

The therapeutic impact of counselling resulting from a unique cardiological examination, including TTE and opportunistic vascular screening, was modest when the current treatment was considered three years later; still, there was a significant improvement in patient adherence regarding statins and beta-blockers in men as well as Ace-I/ARBs in the whole population. However, considering the patients' (and the physicians') well-known suboptimal adherence with treatment over time [18], it can be speculated that the impact may have been more significant initially.

Our study has several limitations. First, for country-specific reasons, at the time of the first observations we employed a less widely used risk scoring system, the PROCAM score adjusted to Switzerland, instead of the ESC or Framingham scoring systems. The main advantage of this system is its goal of considering mortality as well as morbidity. Yet, like the other scores, it does not include many factors considered by physicians in their daily work such as physical activity, psychological stress and social deprivation. Furthermore, the follow-up observations were collected solely based on a questionnaire sent to the referring physicians, so that slight variations in communication quality were unavoidable in this setting. It is inherent to this method that we lack dynamic information during the three years of follow-up.

## CONCLUSION

Vascular screening during TTE is feasible and does not involve additional costs or significant additional examination time, at least in our country-specific administrative and political reimbursement system. It yields a fairly large number of vascular alterations, necessitating treatment adjustments in the high-risk population referred to a cardiologist by the managing physicians. These additional observations and adjustments must be adequately explained to the patients and their physicians to clarify the individual situation and to avoid unduly induced anxiety.

Our observations underscore the need for a truly global approach to the patients [19], especially by opportunistic screening during TTE [3], that can reduce the gap between pure primary prevention by population-based information and a delayed diagnosis of an overt symptomatic atherosclerotic disease.

The total three-year mortality of 10% (with cardiovascular mortality of 6.6%), confirms that patients referred to a cardiologist are indeed at high risk and therefore need optimal individual preventive treatment according to the guidelines. Patient and physician adherence is still far from optimal, and greater attention should be paid to continuing education [20]. We therefore recommend opportunistic vascular screening during TTE in cardiology patients [21].

## DISCLOSURE

The authors declare no conflicts of interest.

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