

## Chapter 2

# Cardiovascular Risk in Subjects with Carotid Pathologies

Fulvio Orzan, Matteo Anselmino, and Margherita Cannillo

**Abstract** Although atherosclerotic disease often becomes clinically evident only in one particular vascular distribution during a person's lifespan, it is an ubiquitous process, that can be detected in all arteries, depending on the diagnostic test adopted and the threshold chosen. Disease of the carotid arteries is frequent and the present chapter will focus on the correlation of this pathology with coronary heart disease.

**Keywords** Carotid disease • Coronary heart disease • Cardiovascular risk • Intima-media thickness • Cardiac events

Disease of the carotid arteries is frequent. Among the 5,201 subjects aged 65 years or older enrolled in the Cardiovascular Health Study, detectable carotid stenosis was present in 75% of men and 62% of women, although the prevalence of  $\geq 50\%$  stenosis was low: 7% in men and 5% in women [38].

Although atherosclerotic disease often becomes clinically evident only in one particular vascular distribution during a person's lifespan, it is an ubiquitous process, that can be detected in all arteries, depending on the diagnostic test adopted and the threshold chosen [48].

We shall review this problem focusing on the following points:

1. Carotid disease is an index of diffuse atherosclerosis, including coronary heart disease (CHD).
2. For this reason, cardiovascular risk and CHD are to be reckoned within patients with (a) symptomatic cerebrovascular disease (CVD), that is transient ischemic attack (TIA) or stroke, (b) asymptomatic CVD, (c) candidates for carotid endarterectomy.

---

F. Orzan (✉)

Division of Cardiology, Department of Internal Medicine, University of Turin,  
Corso A.M. Dogliotti, 14, 10126 Turin, Italy  
e-mail: fulvio.orzan@unito.it

3. Controversies about need for CHD testing in patients with CVD and measures to be taken in case of positive testing.
4. Role of the intima-media thickness (IMT) of the carotid artery in detecting occult coronary artery disease (CAD).

## **2.1 Carotid Disease is an Index of Diffuse Atherosclerosis, Including Coronary Heart Disease**

Disease that is manifest at one site increases the chances that it will be found at other vascular beds as well.

Pathological studies support this concept. In 200 consecutive medicolegal autopsies Mathur et al. found a significant correlation between the coronary and intracranial arterial beds. Coronary atherosclerosis appeared to develop first, about 20 years earlier than cerebral atherosclerosis [36].

Another study collected 1,042 complete sets of cerebral arteries (intracranial and extracranial), coronary arteries, and aortas from autopsied persons 10–69 years of age [51]. On a group basis there was an association between the amount of raised lesions in one artery and that in another. However, on an individual basis there was only a slight degree of association between extent of raised lesions in either aorta or coronary arteries and that in the carotid arteries and there appeared to be no correlation between either aorta or coronary arteries and the other cerebral arteries. The conclusion was that “it seems impossible to predict in individual cases the amount of atherosclerosis in the cerebral arteries from the amount of lesions in the aorta and the coronary arteries.”

Again, from 803 consecutive autopsies of neurologic patients, Gongora-Rivera et al. [21] reported a prevalence of coronary stenoses  $\geq 50\%$  in 37.5% of 341 patients with stroke. Pathologic evidence of myocardial infarction was found in 40.8%. Two-thirds of cases of myocardial infarction were clinically silent.

In a prospective series of 506 patients with extracranial CVD, coronary arteriography revealed significant CAD ( $\geq 70\%$  stenosis) in 37% of patients with clinical evidence of ischemic heart disease, compared with 16% of those without [31].

The REACH registry included 67,888 patients from North America, Latin America, Western and Eastern Europe, Middle East, Asia, Australia, and Japan. These were outpatients aged 45 or older, with established clinical CAD, CVD, or peripheral vascular disease, or with at least three atherosclerotic risk factors, defined as follows: diabetes mellitus, high blood pressure, hypercholesterolemia, current cigarette smoking, ankle-brachial index of less than 0.9, asymptomatic carotid stenosis (12,389 patients). Polyvascular disease (clinical, symptomatic disease coexistent in two or three territories) was recognized in a significant proportion, 15.9% [3].

The age of a patient under scrutiny is important, as there is a well-recognized tendency for symptomatic CVD to “lag” 10–15 years behind CAD [15, 36]. In a geriatric population one is not surprised at finding that CAD, CVD, and peripheral vascular disease are frequently coexistent [37]. However, in terms of primary

prevention, the age threshold must be kept low and the carotid artery abnormalities should be weighed together with the traditional cardiovascular risk factors (hypertension, diabetes, cholesterol, and smoking).

Subclinical atherosclerosis was examined by means of IMT and coronary calcium calcification (CAC) in more than 4,000 participants of the CARDIA and MESA studies, aged 32–50 years. The degree of both carotid IMT and CAC, was significantly higher in subjects with a high calculated lifetime cardiovascular risk, and showed a higher rate of progression [2].

In conclusion, patients CAD must be evaluated within the context of diffuse, polyvascular atherosclerosis. Indeed symptomatic carotid disease or >50% obstruction of a carotid artery is now rightly considered a coronary risk equivalent by the National Cholesterol Education Program NCEP [24].

What are then the practical consequences of the association? It depends on the clinical scenario in which we encounter our CVD patient.

## **2.2 Cardiovascular Risk and CHD in Patients with Specific Conditions**

Cardiovascular risk and CHD are to be reckoned within patients with (1) asymptomatic CVD, (2) symptomatic CVD, and (3) candidates for carotid endarterectomy.

### **2.2.1 Asymptomatic CVD**

CAD is relatively rare in asymptomatic CVD: its prevalence is estimated to vary from 2 to 8% [20]. Nevertheless, when present, it importantly influences the prognosis.

In patients with asymptomatic carotid stenosis and no history of CAD, who have diabetes, or peripheral vascular disease, the risk of cardiac events is similar to that of patients with a history of CAD [9]

In the medical therapy arm of the randomized ACAS study (medical therapy vs. carotid endarterectomy for  $\geq 60\%$  asymptomatic stenosis), there was a rate of 3.8 deaths per 100 person-years, of which half were caused by myocardial infarction or other cardiac diseases [15].

### **2.2.2 Patients with TIA/Stroke**

After a stroke, short-term (<90 days) mortality due to cardiac causes ranges between 2 and 5% [1]. In the VISTA database, 161 of 864 patients (19%), experienced at least one serious cardiac adverse event (defined as a nonfatal episode of ventricular tachycardia, ventricular fibrillation, myocardial infarction, pulmonary

edema/moderate-severe cardiac failure, or cardiac death) within the 12 weeks following an ischemic stroke. At baseline, 44.7% had a diagnosis of ischemic heart disease, and 28.5% had suffered from congestive heart failure [42].

The long-term mortality from cardiac causes also is substantial, and sometimes it is even superior to that caused by recurrent stroke [1].

Already in 1982 from the Framingham study it was known that cardiovascular disease (congestive heart failure, CHD, and hypertension) was the leading cause of death for the long-term survivors of a group of 394 stroke victims (57% of whom had an atherothrombotic brain infarction) [45].

Six hundred seventy-five patients enrolled by the Oxfordshire Community Stroke Project were prospectively followed up for up to 6.5 years. After a stroke, the average annual risk of death was 9.1%, 2.3-fold the risk in people from the general population. After the first year, cardiovascular disease became the most common cause of death [10].

In the Cardiovascular Health Study, among 546 subjects with first ischemic stroke, deaths, recurrent strokes, and CHD events were identified over 3.2-year follow-up. After the first year, the stroke and CHD rates were similar (5.2 and 4.6%, respectively). Lacunar strokes had the lowest mortality (11.9%) and recurrence rates (4.3%) [26].

A meta-analysis published by Touzé et al. included 39 studies with 65,996 patients, and a mean follow-up of 3.5 years after a TIA and an ischemic stroke. The annual risk of a myocardial infarction was 2.2%, 1.1% for fatal myocardial infarction [52].

In the Nomas study 655 patients aged >40 years were followed after a stroke. Median follow-up in survivors was 4 years. There were 86 vascular deaths, including myocardial infarction ( $n=17$ ), congestive heart failure ( $n=8$ ), sudden cardiac death ( $n=15$ ), fatal strokes ( $n=39$ ), and other ( $n=7$ ). The 30-day mortality rate was 5.3%. The annual risk of myocardial infarction or vascular death among 30-day survivors was 2% [12]. The risk was strongly associated with the etiology of the stroke, being highest after an embolic type, and lowest after a lacunar type, precisely as had been found in the Cardiovascular Health Study [26].

The prevalence of cardiac disease at entry in patients who have suffered from a TIA/stroke is estimated to be 20–30% [1] but how many have no signs/symptoms of cardiac disease?

Several small studies have shown that patients with TIA and stroke have a high prevalence of asymptomatic CHD.

In a 6-month prospective study of 232 patients with cerebral ischemia, 100 (43%) had a prior history of heart disease. In 132 patients without prior heart disease, 47 (36%) were found to have cardiac disease: 6 atrial fibrillation, 31 cardiomegaly or left ventricular hypertrophy, 9 ischemic heart disease and 1 left bundle branch block [18].

After a TIA or a mild stroke, of 34 patients without clinical evidence of heart disease, 14 had abnormal cardiac scans [44].

The exercise test was positive in 26% of 140 patients with cerebral ischemia and without symptoms or electrocardiographic signs of ischemic heart disease [13].

In 33 patients with no history of CAD, 11 (33%) presented reversible ischemic defects by thallium-201 scintigraphy scan [35].

Chimowitz et al. studied 69 patients with TIA or stroke and without overt CAD with a cardiac stress test (adenosine or dipyridamole thallium myocardial perfusion imaging, exercise thallium myocardial perfusion imaging, or exercise ECG). The frequency of abnormal stress tests was 50% (15 of 30) in patients with large-artery cerebrovascular disease vs. 23% (9 of 39) in patients with other causes of brain ischemia [8].

Coronary artery stenosis was observed by computed tomography in 25.4% of stroke patients without previous clinical evidence of CHD [49].

The Stroke Council and the Council on Clinical Cardiology of the American Heart Association/American Stroke Association estimate that 20–40% of stroke patients may have abnormal test for silent cardiac ischemia [1].

In conclusion, patients with CVD, both asymptomatic, and after a TIA/stroke have an increased risk of myocardial infarction and cardiac death.

Patients with an ischemic stroke (except possibly those with a lacunar stroke) and those with a 50% carotid artery obstruction must be considered to have a coronary risk equivalent [7].

Patients who have suffered from a large-vessel atherosclerotic stroke should be considered for cardiac screening [1].

### 2.2.3 *Candidates for Carotid Endarterectomy*

Of 335 consecutive patients who underwent carotid endarterectomy between 1969 and 1973 at the Cleveland Clinic, fatal myocardial infarction accounted for 60% of early deaths within 30 days of operation and occurred in 1.8% of the entire series. Among the patients who survived operation, the 5-year mortality rate was 27%, and the 11-year mortality rate was 48%. Myocardial infarction caused 37% of the deaths that occurred within 5 years after operation and 38% of the deaths that have occurred within 11 years. Improvement in actuarial survival ( $p < 0.05$ ) and reduction in the late mortality rate ( $p < 0.01$ ) were statistically significant for the subset of patients with suspected CAD who had aortocoronary bypass graft procedures [30].

At the Mayo Clinic 177 patients who underwent carotid endarterectomy were stratified as to the presence ( $n = 64$ ) or absence ( $n = 93$ ) of overt CAD or prior myocardial revascularization ( $n = 20$ ) at the time of endarterectomy. 8-year relative survival was 89% in those without and 75% in those with overt CAD. The cumulative incidence of a cardiac event at 8 years after carotid endarterectomy was greater in those with overt CAD than in those without (61 vs. 25%,  $p < 0.0001$ ). In multivariate analysis, untreated CAD and diabetes were the only independent predictors of subsequent cardiac events [43].

In the NASCET study, 2,985 patients were randomized either to carotid endarterectomy or to medical therapy. In the first month after surgery the rate of cardiovascular complications was 8.1 vs. 1.2% in those allocated to medical treatment. Only a history of myocardial infarction or angina and a history of hypertension were statistically significant risk factors for medical complications [41].

The Swedish vascular registry reported a substantial reduction in long-term survival for 631 asymptomatic patients who underwent carotid endarterectomy. Among the predictors of decreased longevity were diabetes, cardiac disease, and previous vascular surgery. Patients with a cardiovascular event after carotid endarterectomy demonstrated a statistically significant decreased 5-year survival (2.2% among those alive vs. 11.4% among those dead;  $p < 0.001$ ) [29].

Given this background, at the Cleveland Clinic coronary arteriography before carotid endarterectomy has been the policy since 1978. In a prospective series of 506 patients (32–94 years old, mean 65) with extracranial CVD and previous neurologic symptoms ( $N=288$ ) or asymptomatic carotid bruits ( $N=218$ ), CAD ( $\geq 70\%$  stenosis) was documented in 37% of patients with clinical evidence of ischemic heart disease, compared with 16% of those without. Severe inoperable coronary disease was especially common (14%) among diabetics [31].

Among the 1,662 patients of the ACAS study (carotid endarterectomy for asymptomatic carotid artery stenosis), 8.4% had a positive history for CAD, defined by the presence of angina, myocardial infarction, previous CABG, or an abnormal electrocardiogram [15].

These observations are confirmed by the aforementioned NASCET study, in which the risk of combined outcome of severe myocardial infarction and cardiac death was evaluated according to the baseline history of ischemic heart disease (angina, myocardial infarction) and of risk factors (age  $\geq 75$  years, history of diabetes, history of hypertension, smoking in past year, left ventricular hypertrophy on ECG, myocardial infarction on ECG, or creatinine  $> 115 \mu\text{mol/L}$ ). With history of ischemic heart disease at entry (1,124 patients), the 5-year risk of combined outcome of severe myocardial infarction and cardiac death was 16.5%. Without history at entry (1,691 patients), risk was 6.7%. The 5-year risk of severe myocardial infarction or cardiac death increased to 33.9% for patients with  $\geq 4$  risk factors (age  $\geq 75$  years, history of diabetes, history of hypertension, smoking in past year, left ventricular hypertrophy on ECG, myocardial infarction on ECG, or creatinine  $> 115 \mu\text{mol/L}$ ) plus a history of ischemic heart disease and to 23.5% for those without history of ischemic heart disease [17].

In addition, patients with EF of 35% or less are at increased risk for perioperative cardiac complications and reduced overall survival following carotid surgery [27].

Urbini et al. [53] stratified 172 patients with symptomatic carotid stenosis 70–99% into four groups: (1) no coronary symptoms, no ischemia; (2) coronary ischemia (by exercise ECG and/or Thallium scanning) without symptoms; (3) unable to exercise; (4) cardiac ischemic symptoms. Kaplan–Meier estimated curves of survival free from fatal and nonfatal coronary events were 97, 51, 49, and 59%, respectively. The rate of events was higher for patients with cardiac ischemia, whether with or without symptoms ( $p < 0.001$ , group 1 vs. groups 2 and 3;  $p < 0.01$ , group 1 vs. group 4).

In an effort to identify patients at risk, Ombrellaro et al. tested 174 carotid endarterectomy patients with preoperative dipyridamole myocardial scintigraphy. Preoperative histories of myocardial infarction and chest pain were significant independent predictors of adverse cardiac outcomes ( $p < 0.05$ ) while scintigraphy was not [40].

Landesberg et al. [32] reported an observational study of 255 carotid endarterectomy candidates who underwent Thallium scanning. Those with moderate to severe reversible defects or with multiple reversible defects were referred for coronary arteriography and subsequent coronary revascularization. Patients who underwent coronary revascularization had a survival rate similar to that of patients with a normal or mildly abnormal thallium scan. Their survival was better than that of patients with a significantly abnormal scan, who did not receive a coronary revascularization. It is noteworthy, however, that 47% of the entire group had a history of ischemic heart disease.

### 2.3 Controversies About Need for CHD Testing in Patients with CVD and Measures to Be Taken in Case of Positive Testing

A general start of how to deal with cardiovascular risk in candidates for carotid endarterectomy is to follow the ACC/AHA 2007 guidelines on perioperative cardiac evaluation and care for noncardiac surgery, in which carotid endarterectomy is classified as bearing an intermediate cardiac risk (1–5%) [16]. In the guidelines cardiovascular risk evaluation is based on the Revised Cardiac Index [33] and six steps are suggested:

1. *Emergency surgery?*  $\Rightarrow$  Vital signs, ECG, Blood chemistry  $\Rightarrow$  *Proceed to surgery.*
2. Nonemergent surgery  $\Rightarrow$  *Active cardiac conditions present?* (listed below)  $\Rightarrow$  *Cardiac evaluation* is recommended:
  - (a) Unstable angina (CCS class III/IV stable, if sedentary)
  - (b) Decompensated heart failure (NYHA functional class IV; worsening or new-onset heart failure)
  - (c) Significant arrhythmias
    - High-grade atrioventricular block
    - Mobitz II atrioventricular block
    - Third-degree atrioventricular heart block
    - Symptomatic ventricular arrhythmias
    - Supraventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (HR greater than 100 bpm at rest)
    - Symptomatic bradycardia
    - Newly recognized ventricular tachycardia
  - (d) Severe valvular disease
    - Severe aortic stenosis
    - Symptomatic mitral stenosis
3. Nonemergent surgery, no active cardiac conditions present, *Low risk surgery?*  $\Rightarrow$  *Proceed to surgery.*
4. Intermediate risk surgery? (carotid endarterectomy)  $\Rightarrow$  *Functional capacity* (4 METS, “climbing 1 flight of stairs”).

### 5. Low functional capacity? Assess clinical risk factors:

- (a) Ischemic heart disease, defined as: class I/II angina, previous MI, positive cardiac ischemia test, ECG with abnormal Q waves
- (b) History of previous congestive heart failure, presence of peripheral edema, bilateral rales, S3, or X-ray with pulmonary vascular redistribution
- (c) Preoperative insulin treatment for diabetes mellitus
- (d) Preoperative creatinine greater than 2 mg/dL

No clinical risk factors  $\Rightarrow$  *Proceed to surgery.*

Risk Factor(s) present: consider testing *if it will change management.*

To summarize:

1. In a nonemergent condition a minimum work-up should include: History, Physical Examination, ECG, Blood and urinalysis.
2. An active cardiac condition calls for cardiac consultation.
3. In the absence of active cardiac conditions, an assessment of functional capacity is recommended.
4. The presence of risk factors does not necessarily call for cardiac testing; this is “considered” only if the result will change management.
5. History taking is instrumental (active cardiac conditions, clinical risk factors).

Unfortunately point 3 is ambiguous: functional capacity is either assessed rather imprecisely on clinical grounds (much as the NYHA classification), or it requires cardiac testing. This leads to the ambiguity of point 4: testing should change management only if we have reasonable evidence that action taken following the result of the test will prevent adverse events (myocardial infarction, serious arrhythmias, acute heart failure) or death. Searching for CAD in individuals with CVD is relevant if the prevalence of CAD in a population is high and if there is a demonstrated benefit in treating such patients [5, 52]. Such crucial information is at the moment lacking or conflicting, and the reader is referred to the exchange by Gregoratos and Brett for an exhaustive review of these points [23].

Although addressed at vascular surgery, not specifically at carotid artery disease, Kertai has produced a thorough review about whether and how to screen such patients, and how best to treat them [28].

Finally an attempt is also made at defining the “high-risk cardiac patient” in relation to carotid endarterectomy. In the SAPPHERE study it has been defined as “Clinically significant cardiac disease: congestive heart failure, abnormal stress test, or need for open-heart surgery” [57].

The recent Controversies in Carotid Artery Revascularization have proposed the following definition: congestive heart failure (NYHA class III–IV); unstable angina (CCS class III/IV); myocardial infarction in the last 30 days; severe CAD (left main,  $\geq 2$  vessel disease); left ventricular ejection fraction  $\leq 30\%$ ; heart surgery planned in the next 30 days [55].

The merit of different clinical indices of cardiac risk, and their weaknesses are well explained and discussed by Devereaux et al. [11].



The optimal management of an asymptomatic CVD patient whose cardiac testing turns positive is controversial. In fact, revascularization is not recommended in asymptomatic patients by the guidelines [16].

In patients with stable CAD, prophylactic coronary revascularization before high-risk noncardiac surgery does not confer any beneficial effects, when compared with optimized medical management, in terms of perioperative mortality, myocardial infarction, long-term mortality, or adverse cardiac events [56].

Even in high-risk patients undergoing major vascular surgery preoperative coronary revascularization was not associated with improved postoperative or long-term outcome compared with the best medical treatment [47].

## **2.4 Intima-media Thickness of the Carotid Artery and Cardiac Risk**

### ***2.4.1 Correlation with Coronary Angiography***

In 1994 Geroulakos et al. examined with high-resolution B-mode ultrasound 75 patients who underwent coronary angiography for assessment of chest pain and 40 normal controls matched for age and sex. The IMT of the common carotid artery for the controls was  $0.71 \pm 0.16$  mm and for the patients  $0.91 \pm 0.18$  mm ( $p < 0.005$ ). In patients with normal coronary angiogram the IMT was  $0.73 \pm 0.1$  mm. In the group with one-vessel disease it increased to  $0.91 \pm 0.17$  mm ( $p < 0.05$ ), in the group with two-vessel disease it was  $0.96 \pm 0.17$  mm ( $p < 0.01$ ), and in the group with three-vessel disease it was  $0.99 \pm 0.21$  mm ( $p < 0.01$ ). There was a significant linear trend between IMT and the number of involved vessels ( $p < 0.0001$ ,  $r = 0.44$ ) [19].

Kafetzakis et al. reported in their study of 184 patients submitted to coronary angiography and to duplex ultrasonography of the carotid, femoral, and popliteal arteries. IMT of the carotid and femoral arteries were independent predictive factors of obstructive CAD [25].

### ***2.4.2 Correlation with Cardiac Events***

The association of preexisting CHD, CVD, and peripheral vascular disease with carotid and popliteal IMT (measured by B-mode ultrasound) was assessed in 13,870 subjects enrolled in the Atherosclerosis Risk in Communities (ARIC) Study. A substantially greater arterial wall thickness was observed in middle-aged adults with prevalent cardiovascular disease. Both carotid and popliteal arterial IMT were related to clinically manifest cardiovascular disease affecting distant vascular beds, such as the cerebral, peripheral, and coronary artery vascular beds [6].

In the Rotterdam study, the risk of myocardial infarction increased 43% per standard deviation increase (0.163 mm) in common carotid IMT. The risk was particularly increased in subjects with an IMT in the upper quintile of the distribution (0.908 mm) relative to the reference category (0.75 mm), but the association between IMT and risk of myocardial infarction did not show a clearly linear pattern. Those who developed myocardial infarction had at baseline a higher prevalence of hypercholesterolemia and diabetes, and had more frequently suffered already from a heart attack, so that adjustment for cardiovascular risk factors attenuated the magnitude of the associations and their statistical significance [4].

The combined measure of IMT was significantly associated with the risk of myocardial infarction in 5,858 participants to the Cardiovascular Health Study, whose carotid arteries were evaluated with high-resolution B-mode ultrasonography [39].

A meta-analysis in 2007 confirmed that carotid IMT is a strong predictor of future vascular events, both stroke and myocardial infarction [34].

However, after reviewing 18 studies, Wald and Beswick [54] concluded that neither carotid plaque nor IMT is sufficiently discriminatory between affected and unaffected individuals to be a worthwhile screening test for CHD. While it is true that the relative risk is higher for those with a very high IMT compared with a very low IMT, this only confirms that an association is present. Because the groups being compared are mutually exclusive, and most people in the middle of the distribution are not considered in the analysis, the value of the ultrasound exam as a screening test is low, in the range of that of serum cholesterol or diastolic blood pressure.

Needless to say, the quality of the ultrasound study must be kept high [14] in case of therapeutic decisions. For IMT measurement, it should meet the criteria meticulously described by the American Society of Echocardiography, which has produced a specific protocol [50] (Table 2.1).

**Table 2.1** Highlights

Coronary artery disease must be evaluated within the context of diffuse, polyvascular atherosclerosis
Patients with cerebrovascular disease, both asymptomatic, and after a TIA/stroke present an increased risk of myocardial infarction and cardiac death
Symptomatic carotid disease or >50% obstruction of a carotid artery is a coronary risk equivalent
Patients who have suffered from a large-vessel atherosclerotic stroke should be considered for cardiac screening
Carotid endarterectomy is an intermediate cardiac risk surgery:
1. In a nonemergent condition a minimum work-up should include: History, Physical Examination, ECG, Blood, and urinalysis
2. An active cardiac condition calls for cardiac consultation
3. In the absence of active cardiac conditions, an assessment of functional capacity is recommended
4. The presence of risk factors does not necessarily call for cardiac testing, that should be considered only if the result will change management
5. History taking is instrumental (active cardiac conditions, clinical risk factors)

## 2.5 Conclusions

In summary, the increased attention to cardiac (coronary) conditions in patients with carotid disease is wholly justified both for subjects with asymptomatic disease, patients after a TIA or stroke, and patients before a planned carotid endarterectomy (and afterwards).

This increased awareness should translate in more stringent primary and secondary prevention of the atherosclerotic disease [22, 24, 46].

Whether one should screen for CAD the patient with carotid disease who has no cardiac symptoms, but significant risk factors, the test to be adopted, and which therapy should be subsequently implemented are issues that await the results of controlled clinical trials.

## References

1. Adams RJ, Chimowitz MI, Alpert JS, Awad IA, Cerqueria MD, Fayad P, Taubert KA. Coronary risk evaluation in patients with transient ischemic attack and ischemic stroke. A scientific statement for healthcare professionals from the Stroke Council and the Council on Clinical Cardiology of the American Heart Association/American Stroke Association. *Circulation* 2003;108:1278–1290
2. Berry JD, Liu K, Folsom AR, Lewis CE, Carr JJ, Polak JF, Shea S, Sidney S, O’Leary DH, Chan C, Lloyd-Jones DM. Prevalence and progression of subclinical atherosclerosis in younger adults with low short-term but high lifetime estimated risk for cardiovascular disease: the Coronary Artery Risk Development in Young Adults Study and Multi-Ethnic Study of Atherosclerosis. *Circulation* 2009;119:382–389
3. Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas J-L, Goto S, Liao C-S, Richard AJ, Roether J, Wilson PWF. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA* 2006;295:180–189
4. Bots ML, Hoes AW, Koudstaal PJ, et al. Common carotid intima-media thickness and risk of stroke and myocardial infarction (The Rotterdam Study). *Circulation* 1997;96:1432–1437
5. Brett AS. Coronary assessment before noncardiac surgery. Current strategies are flawed. *Circulation* 2008;117:3145–3151
6. Burke GL, Evans GW, Riley WA, Sharrett AR, Howard G, Barnes RW, Rosamond W, Crow RS, Rautaharju PM, Heiss G. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study Stroke. 1995 Mar;26(3):386–91
7. Chaturvedi S. Should stroke be considered both a brain attack and a heart attack? *Stroke* 2007;38:1713–1714
8. Chimowitz MI, Poole RM, Starling MR, Schwaiger M, Gross MD. Frequency and severity of asymptomatic coronary disease in patients with different causes of stroke. *Stroke* 1997;28:941–945
9. Chimowitz MI, Weiss DG, Cohen SL, et al. Cardiac prognosis of patients with carotid stenosis and no history of coronary artery disease: Veterans Affairs Cooperative Study Group 167. *Stroke* 1994;25:759–765
10. Dennis MS, Burn JP, Sandercock PA, Bamford JM, Wade DT, Warlow CP. Long-term survival after first-ever stroke: the Oxfordshire Community Stroke Project. *Stroke* 1993;24:796–800
11. Devereaux PJ, Goldman L, Yusuf S, Gilbert K, Leslie K, Guyatt GH. Surveillance and prevention of major perioperative ischemic cardiac events in patients undergoing noncardiac surgery: a review. *CMAJ* 2005;173:779–788

12. Dhamoon M, Tai W, Boden-Albala B, Runek T, Paik MC, Sacco RL, Elkind MSV. Risk of myocardial infarction or vascular death after first ischemic stroke: the Northern Manhattan study. *Stroke* 2007;38:1752–1758
13. Di Pasquale G, Pinelli G, Grazi P, et al. Incidence of silent myocardial ischaemia in patients with cerebral ischaemia. *Eur Heart J* 1988;9(suppl N):104–107
14. Elgersma OE, van Leeuwen MS, Meijer R, Eikelboom BC, van der Graaf Y. Lumen reduction measurements of the internal carotid artery before and after Levovist enhancement: reproducibility and agreement with angiography. *J Ultrasound Med* 1999;18:191–201
15. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA* 1995;273:1421–1428
16. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikoff E, Fleischmann KE, Freeman WK, Froelich JB, Kasper EK, Kersten JR, Riegel B, Robb JF. ACC/AHA 2007 guidelines on perioperative cardiac evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2007;116:1971–1996
17. Gates PC, Eliasziw M, Algra A, Barnett HJ, Gunton RW; North American Symptomatic Carotid Endarterectomy Trial Group. Identifying patients with symptomatic carotid artery disease at high and low risk of severe myocardial infarction and cardiac death. *Stroke* 2002;33:2413–2416
18. Gates P, Peppard R, Kempster P, Harris A, Pierce M. Clinically unsuspected cardiac disease in patients with cerebral ischaemia. *Clin Exp Neurol* 1987;23:75–80
19. Geroulakos G, O’Gorman DJ, Kalodiki E, et al. The carotid intima-media thickness as a marker of the presence of severe symptomatic coronary artery disease. *Eur Heart J* 1994;15:781–785
20. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, DeGraba TJ, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JV, Sacco RL. Primary prevention of ischemic stroke. A guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: The American Academy of Neurology affirms the value of this guideline. *Stroke* 2006;37:1583
21. Gongora-Rivera F, Labreuche J, Jaramillo A, Steg PG, Hauw JJ, Amarencu P. Autopsy prevalence of coronary atherosclerosis in patients with fatal stroke. *Stroke* 2007;38:1203–1210
22. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, DeGraba TJ, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JV, Sacco RL. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2006;113:e873–e923
23. Gregoratos G. Current guideline-based preoperative evaluation provides the best management of patients undergoing noncardiac surgery. *Circulation* 2008;117:3134–3144
24. Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, Pasternak RC, Smith SC Jr, Stone NJ; National Heart, Lung, and Blood Institute, American College of Cardiology Foundation, American Heart Association. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. *Circulation* 2004;110:227–239
25. Kafetzakis A, Kochiadakis G, Laliotis A, Peteinarakis I, Touloupakis E, Igoumenidis N, Katsamouris A. Association of subclinical wall changes of carotid, femoral, and popliteal arteries with obstructive coronary artery disease in patients undergoing coronary angiography. *Chest* 2005;128:2538–2543
26. Kaplan RC, Tirschwell DL, Longstreth WT Jr, Manolio TA, Heckbert SR, Lefkowitz D, El-Saed A, Psaty BM. Vascular events, mortality, and preventive therapy following ischemic stroke in the elderly. *Neurology* 2005;65:835–842

27. Kazmers A, Cerqueira MD, Zierler RE. The role of preoperative radionuclide left ventricular ejection fraction for risk assessment in carotid surgery. *Arch Surg* 1988;123:416–419
28. Kertai MD. Preoperative coronary revascularization in high-risk patients undergoing vascular surgery: a core review. *Anesth Analg* 2008;106:751–758
29. Kragstern B, Bjorck M, Lindback J, Bergqvist D, Parsson H. Long-term survival after carotid endarterectomy for asymptomatic stenosis. *Stroke* 2006;37:2886–2891
30. Hertzner NR, Lees CD. Fatal myocardial infarction following carotid endarterectomy: three hundred thirty-five patients followed 6–11 years after operation. *Ann Surg* 1981;194:212–218
31. Hertzner R, Young JR, Beven EG, Graor RA, O'Hara PJ, Ruschhaupt WF, deWolfe VG, Maljovec LC. Coronary angiography in 506 patients with extracranial cerebrovascular disease. *Arch Intern Med* 1985;145:849–852
32. Landesberg G, Wolf Y, Schechter D, Mosseri M, Weissman C, Anner H, Chisin R, Luria MH, Kovalski N, Bocher M, Erel J, Berlitzky Y. Preoperative thallium scanning, selective coronary revascularization, and long-term survival after carotid endarterectomy. *Stroke* 1998;29:2541–2548
33. Lee TH, Marcantonio ER, Mangione CM, Thomas Eric J, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KKL, Ludwig LE, Pedan A, Goldman L. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999;100:1043–1049
34. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness. *Circulation* 2007;115:459–467
35. Love BB, Grover-McKay M, Biller J, et al. Coronary artery disease and cardiac events with asymptomatic and symptomatic cerebrovascular disease. *Stroke* 1992;23:939–945
36. Mathur KS, Kashyap SK, Kumar V. Correlation of the extent and severity of atherosclerosis in the coronary and cerebral arteries. *Circulation* 1963;27:929–934
37. Ness J, Aronow WS. Prevalence of coexistence of coronary artery disease, ischemic stroke, and peripheral arterial disease in older persons, mean age 80 years, in an academic hospital-based geriatrics practice. *J Am Geriatr Soc* 1999;47:1255–1256
38. O'Leary DH, Polak JF, Kronmal RA, Kittner SJ, Bond MG, Wolfson SK, Bommer W, Price TR, Gardin JM, Savage PJ. Distribution and correlates of sonographically detected carotid artery disease in the cardiovascular health study. The CHS Collaborative Research Group. *Stroke* 1992;23:1752–1760
39. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *N Engl J Med* 1999;340:14–22
40. Ombrellaro MP, Dieter RA III, Freeman M, Stevens SL, Goldman MH. Role of dipyridamole myocardial scintigraphy in carotid artery surgery. *J Am Coll Surg* 1995;181(5):451–458
41. Paciaroni M, Eliasziw ML, Kappelle, LJ, et al. Medical complications associated with carotid endarterectomy. *Stroke* 1999;30:1759–1763
42. Prosser J, MacGregor L, Lees KR, Diener H-C, Hacke W, Davis S; VISTA Investigators. Predictors of early cardiac morbidity and mortality after ischemic stroke. *Stroke* 2007;38:2295–2302
43. Rihal CS, Gersh BJ, Whisnant JP, Rooke TW, Sundt TM Jr, O'Fallon WM, Ballard DJ. Influence of coronary heart disease on morbidity and mortality after carotid endarterectomy: a population-based study in Olmsted County, Minnesota (1970–1988). *J Am Coll Cardiol* 1992;19:1254–1260
44. Rokey R, Rolak LA, Harati Y, Kutka N, Verani MS. Coronary artery disease in patients with cerebrovascular disease: a prospective study. *Ann Neurol* 1984;16:50–53
45. Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke: the Framingham Study. *Stroke* 1982;13:290–295
46. Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American

- Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke* 2006;37:577–617
47. Schouten O, van Kuijk JP, Flu WJ, Winkel TA, Welten GM, Boersma E, Verhagen HJ, Bax JJ, Poldermans D; DECREASE Study Group. Long-term outcome of prophylactic coronary revascularization in cardiac high-risk patients undergoing major vascular surgery (from the randomized DECREASE-V Pilot Study). *Am J Cardiol* 2009;103:897–901
  48. Shah AM, Banerjee T, Mukherjee D. Coronary, peripheral and cerebrovascular disease: a complex relationship. *Herz* 2008;33:475–480
  49. Seo WK, Yong HS, Koh SB, Suh SI, Kim JH, Yu SW, Lee JY. Correlation of coronary artery atherosclerosis with atherosclerosis of the intracranial cerebral artery and the extracranial carotid artery. *Eur Neurol* 2008;59(6):292–298
  50. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, Najjar SS, Rembold CM, Post WS; American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr* 2008;21:93–111
  51. Solberg LA, McGarry PA, Moossy J, Strong JP, Tejada C, Löken AC. Severity of atherosclerosis in cerebral arteries, coronary arteries, and aortas. *Ann N Y Acad Sci* 1968;149:956–973
  52. Touzé E, Varenne O, Chatellier G, Peyrard S, Rothwell PM, Mas JL. Risk of myocardial infarction and vascular death after transient ischemic attack and ischemic stroke: a systematic review and meta-analysis. *Stroke* 2005 36:2748–2755
  53. Urbinati S, Di Pasquale G, Andreoli A, Lusa AM, Carini G, Grazi P, Labanti G, Passarelli P, Corbelli C, Pinelli G. Preoperative noninvasive coronary risk stratification in candidates for carotid endarterectomy. *Stroke* 1994;25:2022–2027
  54. Wald DS, Beswick JP. Carotid ultrasound screening for coronary heart disease: results based on a meta-analysis of 18 studies and 44861 subjects. *J Med Screen* 2009;16:147–154
  55. White CJ, Beckman JA, Cambria RP, Comerota AJ, Gray WA, Hobson RW II, Iyer SS; Writing Group 5. Atherosclerotic Peripheral Vascular Disease Symposium II: controversies in carotid artery revascularization. *Circulation* 2008;118:2852–2859
  56. Wong EY, Lawrence HP, Wong DT. The effects of prophylactic coronary revascularization or medical management on patient outcomes after noncardiac surgery – a meta-analysis. *Can J Anaesth* 2007;54:705–717
  57. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Whitlow P, Strickman NE, Jaff MR, Popma JJ, Snead DB, Cutlip DE, Firth BG, Ouriel K; Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493–1501

## Biographies

*Fulvio Orzan*, MD, PhD, is currently Assistant Professor on faculty of the Department of Internal Medicine and Cardiology of the University of Torino (Torino, Italy). He is also on faculty of the Cardiology Unit of the S. Giovanni Battista “Molinette” Hospital of Torino. His research interests are related to the investigation and treatment of cardiac and cardiovascular pathologies.



*Matteo Anselmino* (12-03-1978). During his PhD at Karolinska Institutet, Stockholm, Sweden he worked on the “Euro Heart Survey on Diabetes and the Heart” focusing on treatment patterns in patients with coronary artery disease with and without abnormal glucose regulation. To date he is Assistant Professor at the Cardiology Division of the Internal Medicine Department of the University of Turin, Italy committed to clinical and research experience at the Cardiac Pacing and Electrophysiology Unit.

*Margherita Cannillo*, MD, PhD, obtained the Italian Laurea in Medicine and Surgery from the University of Torino (Torino, Italy) in 2008. She is now specializing at the Cardiology School of the University of Torino. Her principal research interests are related to the morpho-functional assessment of the right ventricle in subjects with septal defects.

<http://www.springer.com/978-1-4419-7221-7>

Atherosclerosis Disease Management

Suri, J.; Kathuria, C.; Molinari, F. (Eds.)

2011, XIV, 946 p. 282 illus., 182 illus. in color.,

Hardcover

ISBN: 978-1-4419-7221-7