Newly diagnosed carotid atherosclerosis in patients with coronary artery disease admitted for cardiac rehabilitation

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Background. **The association of coronary artery disease (CAD) with carotid artery disease has been well documented. However, data focusing on CAD patients participating in cardiac rehabilitation programs are lacking. We studied the prevalence of newly diagnosed carotid artery disease in CAD patients admitted for cardiac rehabilitation.**

Methods. **We performed carotid ultrasonography in 168 angiographically confirmed CAD patients admitted to two facilities. Patients with previous cerebrovascular episodes or carotid imaging were excluded.**

Results. **Out of 168 patients considered (mean age 65 ± 8 years; males 76%; chronic stable angina as the reason for cardiac rehabilitation 34%, silent ischemia 14%, and acute coronary syndrome 52%), 149 (89%) were found to have carotid atherosclerosis. Carotid atherosclerosis was present in 83, 87, 89, and 93% of patients with one-, two- and three-vessel disease and left main stem CAD respectively. Patients with severe CAD (i.e. three-vessel or left main stem) had a higher prevalence of ≥ 50% carotid stenosis as compared to patients without severe CAD (26 vs 8%, $p < 0.05$). Severe CAD had a high negative (92%) and a low positive (26%) predictive value for the presence of ≥ 50% carotid stenosis.**

Conclusions. **Silent and previously undetected carotid atherosclerosis is frequent in CAD patients admitted for cardiac rehabilitation. The absence of severe CAD reflects the absence of ≥ 50% carotid stenosis.**

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Introduction

Atherosclerosis is considered a systemic disease and a strong association between coronary and peripheral arterial lesions has been well established[1-4]. Almost 50% of patients with known coronary artery disease (CAD) have vascular disease in one or more other territories, mainly related to the carotid arteries[5,6]. Carotid atherosclerosis may also be of prognostic value in the prediction of future vascular events in patients with known CAD[7,8]. Several presentations of CAD lead to the initiation of cardiac rehabilitation programs aimed at ameliorating symptoms and implementing secondary prevention interventions. A large proportion of CAD patients is currently referred to cardiac rehabilitation facilities without a personal history or previous examination indicating the presence of concomitant carotid artery disease. To date, the correlation of CAD with silent carotid atherosclerosis has not been fully explored in this patient population.

The objectives of this study were 1) to evaluate the prevalence of newly diagnosed carotid artery disease in CAD patients admitted for cardiac rehabilitation, and 2) to compare the severity of CAD with that of concomitant carotid disease.

Methods

Subjects. We considered all consecutive patients admitted to two cardiac rehabilitation facilities in northern Italy from November 2000 through November 2002, irrespective of the clinical presentation of CAD. Patients without recent (< 6 months) angiographic confirmation of CAD were excluded. Since the aim of the present study was to assess silent and newly diagnosed carotid disease, patients known to have suffered from cerebrovascular disease or with documented carotid imaging in the past (> 1 month) were also excluded.

Assessment of coronary artery disease. Patients were classified according to the

number of diseased (≥ 50% stenosis) vessels, as documented at coronary angiography, into one of the following categories: one-vessel disease, two-vessel disease, three-vessel disease, and left main stem disease with or without other vessel disease. Three-vessel disease and left main stem disease identified severe CAD.

Assessment of carotid artery disease. Patients were studied during hospitalization by means of color Doppler ultrasonography performed using an Acuson 128 instrument (Mountain View, CA, USA) equipped with 5 and 7 MHz transducers. Ultrasonographic examinations were performed by three specially trained physicians with an intraobserver variability < 10%. Both the right and left carotid arteries were evaluated and the examined region included the common carotid artery, its bifurcation, and the accessible segment of the internal carotid artery. An intima-media thickness < 1.00 mm identified the absence of lesions, while an increased intima-media thickness identified carotid atherosclerosis. The severity of carotid atherosclerosis was evaluated by using the percentage diameter stenosis and parameters of the flow velocity pattern[9,10]. The greatest stenosis observed on the right or left side and on the common carotid artery or internal carotid artery identified the severity of carotid disease. Accordingly, all patients were classified into one of the following categories: absence of lesions; mild stenosis (< 50% diameter stenosis); moderate stenosis (50 to 69% diameter stenosis); severe stenosis (70 to 99% diameter stenosis); and occlusion (100% diameter stenosis).

Statistical analysis. The χ^2 test was used to detect statistically significant relationships between categorical variables. The Yate's correction or Fisher's exact test were used where appropriate. A two-tailed p value < 0.05 was considered statistically significant. The sensitivity, specificity, and predictive values of severe CAD for the presence of moderate-severe carotid stenosis were calculated. The SPSS package (SPSS Inc., Chicago, IL, USA) was used to perform statistical analysis.

Results

Baseline evaluation. Of 241 patients considered for enrolment, 73 (30%) were excluded because they had no recent coronary angiography (n = 15, 6%) and because of a previous history of cerebrovascular disease (n = 23, 10%), and documentation of carotid imaging in the past (n = 35, 14%). The characteristics of the 168 eligible patients, with regard to the reason for cardiac rehabilitation, are shown in table I. Seventy-seven per cent of patients started cardiac rehabilitation after coronary artery bypass graft (CABG) surgery, and a preoperative carotid screening was documented in 99 (77%) of them.

Table I. Clinical characteristics of the study population.

Age (years)	65 ± 8 (47-84)
Sex (M/F)	127/41
Smoking status	
Active smokers	53 (31%)
Ex-smokers	21 (12%)
Hypercholesterolemia	101 (60%)
Hypertension	107 (63%)
Diabetes mellitus	50 (30%)
Family history of vascular events	88 (53%)
Ejection fraction < 50%	43 (26%)
Clinical presentation of CAD	
Silent ischemia	23 (14%)
Chronic stable angina	58 (34%)
ACS	87 (52%)
Coronary revascularization*	154 (92%)
CABG	129 (77%)
PTCA	25 (15%)
Duration of the rehabilitation program (days)	18 ± 9

ACS = acute coronary syndrome (i.e. unstable angina and myocardial infarction); CABG = coronary artery bypass graft; CAD = coronary artery disease; PTCA = percutaneous transluminal coronary angioplasty with or without stenting. * as a result of the clinical presentation of CAD.

Globally, 149 patients out of 168 (89%) had carotid atherosclerosis, with severe stenosis in 11 cases (7%). No carotid occlusion was documented. Females had a significantly higher prevalence of diabetes than males (46 vs 24%, p < 0.05) and more carotid lesions (100 vs 85%, p < 0.05). The prevalence of carotid lesions did not significantly vary between patients with and without impaired ejection fraction (88 vs 90%, p = NS) (Table II). All severe carotid stenoses were found in CABG patients. Of these, 5 out of 11 (45%) were identified at preoperative carotid screening and were treated by concomitant carotid endarterectomy during CABG. Globally, the prevalence of severe carotid stenosis in patients without a preoperative carotid screening was 20% (6 out of 30 patients). With regard to the location of the most severe carotid stenosis, the bulb was the most common site (71 cases, 48%), followed by the internal carotid artery (n = 60, 40%) and the common carotid artery (n = 18, 12%).

The distribution of the entire study population according to the severity of CAD and carotid atherosclerosis is listed in table III. Carotid atherosclerosis was present in 83, 87, 89 and 93% of patients with one-, two-, three-vessel disease and left main stem disease respectively. Patients with severe CAD had a higher prevalence of moderate-to-severe carotid stenosis (i.e. ≥ 50% stenosis) than patients without severe CAD (26 vs 8%, p < 0.05). In the entire study population, the documentation of severe CAD had a high sensitivity (89%), a low specificity (33%), a low positive (26%), and a high negative (92%) predictive value for the presence of moderate-to-severe carotid stenosis.

Table II. Prevalence and severity of carotid atherosclerosis in coronary artery disease patients.

Variable	Carotid atherosclerosis	Carotid stenosis		
		< 50%	50-70%	> 70%
Males (n=127)	108 (85%)	87 (81%)	14 (13%)	7 (6%)
Females (n=41)	41 (100%)	27 (66%)	10 (24%)	4 (10%)
Silent ischemia (n=36)	36 (100%)	26 (72%)	6 (17%)	4 (11%)
Chronic stable angina (n=27)	27 (100%)	22 (81%)	4 (15%)	1 (4%)
ACS (n=105)	86 (82%)	66 (77%)	14 (16%)	6 (7%)
Absence of coronary revascularization (n=14)	11 (79%)	8 (73%)	3 (27%)	0
CABG (n=129)	120 (93%)	90 (75%)	19 (16%)	11 (9%)
PTCA (n=25)	18 (72%)	16 (89%)	2 (11%)	0
Ejection fraction ≥ 50% (n=125)	112 (90%)	85 (76%)	20 (18%)	7 (6%)
Ejection fraction < 50% (n=43)	37 (86%)	29 (78%)	4 (11%)	4 (11%)

ACS = acute coronary syndrome; CABG = coronary artery bypass graft; PTCA = percutaneous transluminal coronary angioplasty.

Table III. Distribution of patients according to the severity of coronary artery disease and carotid artery disease.

	Absence of carotid lesions	Carotid stenosis			
		Any	< 50%	50-70%	> 70%
One-vessel disease (n=24, 14%)	4 (17%)	20 (83%)	17 (71%)	2 (8%)	1 (4%)
Two-vessel disease (n=24, 14%)	3 (12%)	21 (87%)	20 (83%)	1 (4%)	0
Three-vessel disease (n=79, 47%)	9 (11%)	70 (89%)	53 (67%)	11 (14%)	6 (8%)
Left main stem disease (n=41, 25%)	3 (7%)	38 (93%)	24 (59%)	10 (24%)	4 (10%)
Total (n=168, 100%)	19 (12%)	149 (88%)	114 (68%)	24 (14%)	11 (6%)

Discussion

Our findings showed a high prevalence of previously undetected carotid atherosclerosis in patients who start cardiac rehabilitation after a clinical manifestation of CAD, with a significant correlation between severe CAD and moderate-to-severe carotid disease.

Autopsy studies[11] and large observational studies have demonstrated a close correlation between CAD and carotid artery disease. The prevalence and severity of carotid atherosclerosis has been related to the prevalence of symptomatic CAD[1,12-14] and to the risk of development of CAD in normal subjects[2,15]. Focusing on the cardiac rehabilitation setting, we restricted the analysis to patients without previously diagnosed carotid disease and found that angiographic confirmation of CAD *per se* reflected the presence of silent carotid atherosclerosis in up to 90% of cases. Most of these had mild carotid atherosclerosis; however moderate-to-severe carotid stenosis was present in up to one fifth of patients. The documentation of severe carotid stenosis during cardiac rehabilitation could be of great importance for the planning of appropriate carotid revascularization and in order to adapt stress tests and physical training. Whether all or only selected CAD patients should be screened for carotid disease during cardiac rehabilitation still needs to be addressed. The severity of CAD could be useful to guide selective screening of patients, but several limits have to be considered. Unfortunately, in our patient population, analysis of the predictive values revealed that the presence of severe CAD did not reflect the presence of moderate-to-severe carotid disease. On the other hand, the absence of severe CAD reflected the absence of moderate-to-severe carotid disease.

The percentage of patients with severe carotid stenosis who underwent CABG without preoperative carotid screening (55%) was surprisingly high. Our CABG patients were discharged by a large network of 24 surgery units, thus minimizing the risk of inclusion bias. These findings provided supportive evidence for extensive carotid screening before CABG.

Although there is increasing evidence regarding the prognostic importance of carotid assessment in patients with CAD[8], data confirming the predictive value of carotid atherosclerosis for future vascular events after cardiac rehabilitation are not available at the moment.

In conclusion, these data suggest that the presence of silent carotid atherosclerosis should always be considered in CAD patients admitted for cardiac rehabilitation. Further studies are required in order to identify the determinants of carotid disease which provide the best prognostic value in this patient population.

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