Concomitant Peripheral Vascular and Coronary Artery Disease: A New Dimension for the Global Endovascular Specialist?

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Summary

Background: Early and accurate diagnosis of peripheral atherosclerosis is of paramount importance for global management of patients with known coronary artery disease (CAD).

Hypothesis: We sought to evaluate retrospectively the prevalence and clinical relevance of significant abdominal vessel stenosis or aneurysm (AVA) in patients undergoing coronary angiography.

Methods: Medical records of consecutive patients who underwent coronary angiography at two public institutions over a 12-month period were evaluated. Angiographic results of patients who underwent diagnostic abdominal aorta angiography, based on clinical criteria, to evaluate abdominal vessels at the same time as coronary angiography were analyzed.

Results: During the study period, AVA was reported in 180 (35.7%) of 504 consecutive patients (335 men, mean age 68 ± 13.8 years): renal artery stenosis was found in 13.1% of cases (66 patients), aortoiliac artery disease in 13.7% (69 patients), and aortic aneurysmal disease in 8.9% (45 patients). Logistic regression analyses revealed ≥ 3 -vessel CAD (odds ratio [OR] 9.917, $p = 0.002$), age > 65 years (OR 3.817, $p = 0.036$), ≥ 3 risk factors (OR 2.8, $p = 0.048$) as independent predictors of AVA.

Conclusion: Multiple vascular atherosclerotic distributions are frequent in elderly patients who have multivessel CAD and

a high-risk profile, suggesting the usefulness of a more global and comprehensive cardiovascular approach.

Key words: coronary disease, catheterization, angiography, peripheral vascular disease

Introduction

An early and accurate diagnosis of peripheral atherosclerosis (renal, abdominal, and aortoiliac localizations) is of paramount importance for global management and prognosis because of its major additional mortality impact in patients with known coronary artery disease (CAD),^{1,2} especially those who are candidates for coronary or cardiac revascularization.^{3,4} We sought to evaluate retrospectively the prevalence and clinical relevance of significant renal and/or aortoiliac artery stenosis or aneurysm (AVA) in patients undergoing coronary angiography who were at risk of peripheral atherosclerosis but in whom the presence of AVA was suspected but unconfirmed at the time of examination.

Materials and Methods

Medical records of consecutive patients who underwent coronary angiography at two 700-bedded public institutions over a 12-month period were reviewed. On the basis of clear clinical and angiographic criteria (Table I), patients also underwent diagnostic abdominal aorta angiography to evaluate renal, abdominal, and iliac vessels and the results were analyzed. Written informed consent was obtained from all patients. Pretreatment with 0.45% saline at a rate of 1 ml/kg/h for 12 h was administered to all patients. Repeated serum creatinine was obtained during hospital admission and every 2 weeks thereafter until return to baseline values in patients exhibiting procedure-related kidney dysfunction (increase in serum creatinine of ≥ 0.5 mg/dl). In the peripheral angio-

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TABLE I Abdominal aorta angiography enrollment criteria

Severe hypertension (systolic blood pressure ≥ 180 or diastolic ≥ 110 mmHg regardless of drug therapy)
Unexplained renal dysfunction (Cockcroft-Gault creatinine clearance < 50 ml/min without clearly established causes)
Abnormal abdominal pulsation or murmur
Absent or reduced femoral pulses

graphic protocol, a pigtail catheter was positioned at the level of the L1 vertebral body in the anterior-posterior to depict the abdominal aorta slightly above the renal arteries to the origin of femoral arteries using a powered injection of ≥ 30 ml of Iopromide (Ultravist 370, Schering, Milan, Italy). Alternatively, a Judkins right coronary catheter was used for selective renal artery angiography in the 20–25° left or right oblique projections using 4–8 ml. Digital subtractive technique was used preferentially. Moderate to severe vascular arterial stenosis ($> 50\%$ stenosis), vessel occlusion, and aneurysmal vessels were noted as significant angiographic findings. Contrast-induced nephropathy was defined as a rise in serum creatinine of $\geq 25\%$ from baseline.

Statistical Analysis

Data are expressed as mean $\pm$ standard deviation (SD) and as percentages. Univariate and multivariate logistic regression analyses were used to determine independent predictors of extra-cardiac atherosclerotic involvement. A significant level

was defined as $p < 0.05$. All analyses were performed using the Statistical Package for Social Sciences 10.0 (SPSS Inc., Chicago, Ill., USA).

Results

During the study period, angiographically significant AVA was observed in 180 of 504 (35.7%) patients (335 men, mean age 68 ± 13.8 years) undergoing concomitant abdominal aorta angiography (Table II): renal artery stenosis was found in 13.1% (66 patients), aortoiliac artery disease in 13.7% (69 patients), and aortic aneurysmal disease in 8.9% (45 patients), including patients with combined renal artery and aortic stenosis, renal artery stenosis and abdominal aneurysm, and iliac stenosis/occlusion and thoracoabdominal aneurysmal disease (Table III). Significant AVA was associated with CAD in 98.8% (Table IV). Complications of combined coronary and subclavian or abdominal vessel angiography included six cases of contrast-induced nephropathy (1.2%); no patient required renal replacement therapy. The additional contrast volume used for abdominal aorta and/or renal angiography was 38 ± 15 ml, while the additional fluoroscopy time was 5.0 ± 1.1 min. Among candidates for coronary surgery (89/180, 49.4%), abdominal angiography was useful in determining the need for prior percutaneous peripheral interventions in 48

TABLE II Demographic and clinical data

Male/female	335/169
Risk factors, no. (%)	
Hypertension	382 (75.8)
Hypercholesterolemia	386 (76.6)
Diabetes	129 (25.7)
Smoking	301 (59.7)
No. of risk factors/patient	1.9 ± 1.2
Indications for coronary angiography, no. (%)	
AMI	126 (25.1)
Non-ST-elevation ACS	117 (23.2)
Silent ischemia	103 (20.4)
Heart valve disease	158 (31.3)
Criteria for abdominal aortography, no. of patients	
Abdominal pulsation or murmur	69
Absent or reduced femoral pulses and history of claudication not previously investigated	152
Severe hypertension ^a	246
Unexplained renal dysfunction ^b	37

^a Systolic > 180 mmHg and/or diastolic > 110 mmHg despite compliance to full medical treatment.

^b When all other forms of nonvascular etiologies have been excluded. Abbreviations: ACS = acute coronary syndrome, AMI = acute myocardial infarction.

TABLE III Angiographic findings

	No. of patients (%)
Renal stenosis	(11.5)
Monolateral	38
Bilateral	20
Aortoiliac occlusive disease	(12.5)
Aortic stenosis	4
Monolateral common iliac artery stenosis	35
Bilateral common iliac artery stenosis	11
Common iliac artery occlusion	13
Abdominal aortic-iliac aneurysmal disease	(7.7)
Iliac aneurysm	10
Infrarenal abdominal aortic aneurysm	21
Thoraco-abdominal aneurysm	8
Renal and aortic stenosis	4 (0.8)
Abdominal aortic aneurysm and renal stenosis	4 (0.8)
Iliac artery stenosis and thoraco-abdominal aortic aneurysm	2 (0.4)

TABLE IV Relationship between AVA and CAD

	No CAD	CAD 1-vessel	CAD 2-vessel	CAD > 3-vessel
No. of patients (%)	49 (9.6)	90 (17.9)	136 (27.1)	229 (45.4)
% Significant findings (patient/total no.)	5 (2/49)	10.8 (10/90)	30.8 (42/136)	50.7 (116/229)

Abbreviations: AVA = abdominal vessel aneurysm, CAD = coronary artery disease.

patients, concomitant or staged vascular surgery in 41 patients, and unsuitability for any postcardiac surgery aortic balloon pumping in 14 patients. Globally, on the basis of standard clinical indications, endovascular treatment was necessary in 40% (72 patients) and surgical vascular repair in 22.2% (40 patients) of cases. The remaining patients were managed medically for peripheral vascular disease and are currently being followed up. Multivariate logistic regression analyses revealed $\geq$ triple-vessel CAD (odds ratio [OR] 9.917, 95% confidence interval [CI] 2.2–43.8; $p = 0.002$), age > 65 years (OR 3.817, 95% CI 2.2–6.5.8; $p = 0.036$), $\geq$ three risk factors (OR 2.8, CI 95% 0.63–9.1; $p = 0.048$) as independent predictors of AVA (Table V).

Discussion

Although no definite evidence of the clinical benefit of combined coronary and peripheral angiography can be drawn from this registry, data reported in this retrospective study suggest that the association of AVA with CAD is high and clinically relevant when evaluated by angiography. Some differences exist in the current literature regarding the prevalence of the association of CAD with different sites of atherosclerotic involvement. Renal artery stenosis (RAS) is a relatively uncommon but potential cause of renal failure as well as a cause of refractory hypertension and recurrent pulmonary edema. It is independently associated with mortality in patients undergoing coronary artery angiography, and its severity has an in-

cremental effect on survival prognosis. Four-year unadjusted survival for patients with RAS is 65% compared with 86% for patients undergoing catheterization without significant RAS. Factors associated with decreased 4-year survival included advanced age, increased serum creatinine, the presence of RAS, peripheral vascular disease, congestive heart failure, diabetes, hypertension, and reduced ejection fraction.⁵ Progression of even mild stenosis is reported in a large number of patients.⁶ Moreover, RAS has been reported to have a high prevalence in patients with CAD.^{7, 8} It is not surprising that many authors have advocated the usefulness of renal angiography screening in patients undergoing coronary angiography, especially those with unexplained renal insufficiency, uncontrolled or severe hypertension, and previous vascular surgery or a clinical history of cerebral ischemic attack and hypertensive pulmonary edema (Table VI). A recent report⁹ has demonstrated that severe RAS may be present in 7% of patients with severe atherosclerosis, 3% of patients with renal dysfunction, 9% with hypertension, 22% with acute pulmonary edema and hypertension, and 39% with proteinuria.

As recently reported, CAD was associated with aortoiliac lesions in 40.5% of patients undergoing coronary angiography and in a significant proportion of patients with aortic aneurysmal disease.²⁰ The extent of CAD was directly related to the frequency and extent of the aortoiliac lesions. Frequencies of aortoiliac lesions were strongly related to a history of smoking and intermittent claudication and directly related to the extent of CAD. The prevalence of aortic aneurysmal disease associated with CAD has been reported to range from 4.4 to 7%.^{21, 22} However, the real incidence of aortic aneurysmal disease was underestimated in our patients because of the well-known limitations of angiography in detecting aortic aneurysms. Our data correlated well with the literature on the issue. A knowledge of aortic involvement in such atherosclerotic phenomena may influence the operative strategy in patients undergoing urgent coronary angiography resulting in complete revascularization, thus reducing the risk of cardiac events in patients undergoing thoracic aortic surgery; or, in the case of severe thoraco-abdominal aneurysm, by referring the patient for combined surgical management, which has low mortality and good event-free survival rates.^{23–28} Abdominal aortography should be considered not only for assessing the renal artery but also for evaluating aortoiliac occlusive diseases.^{29, 30} Differences in entry criteria, imaging techniques and protocols, and lesion severity evaluation methods may contribute to this variety of results. Our study, although limited by its retrospective nature and the limited resolution of invasive angiography for the aortic aneurysmal disease, showed that a simple low-volume con-

TABLE V Results of univariate and multivariate logistic regression analyses

Variable	OR (95% CI)	p Value
1-Vessel CAD	2.00 (0.34–11.6)	0.44
2-Vessel CAD	3.76 (0.82–17.2)	0.87
≥ 3 -Vessel CAD	9.91 (2.24–43.8)	0.002
2 Risk factors	1.90 (0.71–7.2)	0.067
≥ 3 Risk factors	3.80 (0.63–9.1)	0.010
Hypertension	1.851 (1.03–7.9)	0.054
Age > 65 years	3.817 (2.2–6.5)	0.036
Diabetes	1.91 (0.9–5.4)	0.058
Smoking	1.98 (0.86–5.3)	0.062
Hypercholesterolemia	1.84 (0.96–5.9)	0.053

Abbreviations: CAD = coronary artery disease, OR = odds ratio, CI = confidence interval.

TABLE VI Review of the current literature

Abdominal aorta angiography				
Author (Ref. No.), year	No. of patients	Study type	RAS (%)	Selection criteria
Harding <i>et al.</i> (7) 1992	1,302	Prospective	15	Female gender, age, HP, congestive heart failure, elevated serum creatinine, PVD
Valentine <i>et al.</i> (9) 1993	346	Retrospective	28	Uncontrolled HP, mild renal insufficiency, CAD, PVD
Conlon <i>et al.</i> (5) 1998	14,152	Retrospective	6.3	Elevated serum creatinine, CAD, PVD, HP, cerebrovascular disease, age, female gender, and family history of CAD
Gross <i>et al.</i> (8) 2000	609	Retrospective	25	Triple-vessel CAD
Song <i>et al.</i> (10) 2000	427	Retrospective	5.6	Age, HP, PVD
Conlon <i>et al.</i> (11) 2001	3,987	Retrospective	4.8	Female gender, age, HP, congestive heart failure, elevated serum creatinine
Shen <i>et al.</i> (12) 2001	280	Prospective	15.3	CAD, elevated serum creatinine, HP
Rihal <i>et al.</i> (13) 2002	297	Prospective	19.2	HP, carotid artery disease, CAD
Yamashita <i>et al.</i> (14) 2002	289	Retrospective	7	HP, multivessel CAD
Rath <i>et al.</i> (15) 2002	1,000	Prospective	2.5	Multiple risk factors, CAD
Khosla <i>et al.</i> (16) 2003	2,439	Retrospective	19	Refractory HP
Buller <i>et al.</i> (17) 2004	837	Prospective	14.3	Female gender, age, HP, elevated serum creatinine, PVD, carotid artery disease
Leandri <i>et al.</i> (18) 2004	467	Retrospective	9	Double- or triple-vessel CAD, age, creatinine clearance 30–60 ml/min
Rigatelli <i>et al.</i> (19) 2004	112	Retrospective	6	Age, HP, $\geq$ double-vessel CAD, ≥ 3 risk factors

Abbreviations: BP = blood pressure, CAD = coronary artery disease, PVD = peripheral vascular disease, DM = diabetes mellitus, HP = hypertension, RAS = renin-angiotensin system.

trast medium injection through a standard diagnostic catheter may contribute to a prompt diagnosis of abdominal vessel atherosclerosis in patients undergoing coronary angiography. More important, the analysis of the angiographic data suggests that this strategy is more efficient in patients aged > 60 years with multivessel CAD and multiple risk factors. Finally, our data confirm that angiographically significant AVA associated with CAD is quite frequent and clinically relevant: aged patients with multivessel CAD have a high-risk profile and multiple vascular atherosclerotic distributions, suggesting the usefulness of a more global and comprehensive cardiovascular approach. The clinical effectiveness of this strategy based on coronary angiography and, when indicated, concomitant abdominal aortography needs to be tested in terms of cost saving and thus expediting endovascular or surgical management.

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