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Association Between the Extent of Sclerotic Changes in Iliac Arteries and Long-Term Prognosis in Patients With Ischemic Heart Disease

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Abstract

Peripheral vascular disease is often complicated with ischemic heart disease and is associated with increased cardiac mortality. Latent progression of sclerotic changes in the arteries supplying the lower extremities is often present but undiagnosed. We examined the influence of sclerotic changes of the iliac arteries on the late outcome in 79 patients with ischemic heart disease. Lower abdominal aortography was performed at the time of cardiac catheterization between December 1989 and January 1991.

The degree of sclerotic change in the iliac arteries was assessed according to aortography findings such as stenosis, dilatation or bend, with higher scores representing more advanced sclerosis (aortography score). The mean aortography score of all patients was 5.8±4.6. The patients were followed up for 4.4± 1.2 years to monitor the occurrence of cardiac events (cardiac death, acute myocardial infarction, coronary bypass surgery, or coronary angioplasty for new lesion).

The cardiac event-free rate at 5 years was 76.6% in the high score group (32 patients with scores of 6 or more) and 92.9% in the low score group (47 patients with scores of 5 or less). The difference was significant ($p=0.007$) by log-rank test. The hazard rate of the aortography score for predicting risk of cardiac event was 1.11 by the Cox proportional hazards model (95% confidence intervals : 1.01–1.23, $p=0.039$). When the analysis was adjusted for coronary bypass surgery as primary therapy, the number of diseased coronary arteries, or the presence of peripheral vascular disease, similar results were obtained.

In conclusion, more severe sclerotic change in iliac arteries is associated with a higher incidence of cardiac events in patients with ischemic heart disease.

Key Words

Coronary heart disease (ischemic heart disease), Arteries (iliac), Arteriosclerosis, Follow-up studies, Prognosis (cardiac events)

INTRODUCTION

Peripheral vascular disease is usually called arteriosclerosis obliterans in Japan, and is attributable to obstructions of the arteries supplying the lower extremities. It is often complicated with ischemic heart disease[1–6]. Generalized atherosclerosis seems to be a common background of peripheral vascular

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Selected abbreviations and acronyms

CABG=coronary artery bypass graft
PVD=peripheral vascular disease
SVD=single-vessel disease

disease and ischemic heart disease. Peripheral vascular disease has been reported to increase cardiac mortality[1,3,7,8]. Symptoms of peripheral vascular disease appear when the reduction of blood flow through diseased artery becomes critical. Latent progression of sclerotic changes often occurs in the arteries supplying the lower extremities before this disease can be diagnosed. This prospective study investigated whether the prognosis of patients with ischemic heart disease is related to the extent of sclerotic changes in the iliac arteries, irrespective of whether a definite diagnosis of peripheral vascular disease had been made.

SUBJECTS AND METHODS

Patients

This study included 79 of 91 consecutive patients who underwent diagnostic cardiac catheterization for ischemic heart disease for the first time between December 1989 and January 1991 in our department. Six patients without organic coronary lesions and another six patients lost to follow-up within 6 months were excluded. Written informed consent was obtained from all patients.

Aortography score

Diagnostic cardiac catheterization included coronary angiography, and lower abdominal aortography was also performed in the anteroposterior projection.

The degree of sclerotic change was scored based on the findings of aortography. Contrasted arteries were divided into seven segments : the lower abdominal aorta, right and left common iliac arteries, right and left external iliac arteries, and right and left internal iliac arteries. Each segment was scored as follows : occlusion, 6 points; stenosis by 99–91%, 5 points; 90–76%, 4 points; 75–51%, 3 points; 50–26%, 2 points; and 25% or less, 1 point. A bend (more than 90 degrees) or dilatation (more than 1.5 times the reference diameter) was scored for an additional 1 point for each. The sum of scores from all seven segments was defined as the aortography score of the patient (**Fig. 1**). The scoring was done by two experienced cardiologists who were blinded to the clinical characteristics, including coronary angiography findings or late outcome of the patients.

The mean aortography score of all 79 patients was 5.8±4.6. Patients with an aortography score of 5 or less (n=47) and those with 6 or more (n=32) were grouped as the low score group and the high score group (**Fig. 2, Table 1**).

Coronary angiography evidence of stenosis by more than 75% was considered to be a significant coronary lesion.

Follow-up

The date of diagnostic cardiac catheterization was the start of observation. Survival was calculated to cardiac death, including sudden death, whereas non-cardiac death was not included. Cardiac events were counted in the remote period, when cardiac death or acute myocardial infarction occurred, or coronary bypass surgery or coronary angioplasty for a new lesion was performed. Coronary angioplasty for restenosis of a lesion was not considered a cardiac event. The patients were followed up for 4.4± 1.2 years (range : 0.4–5.7 years).

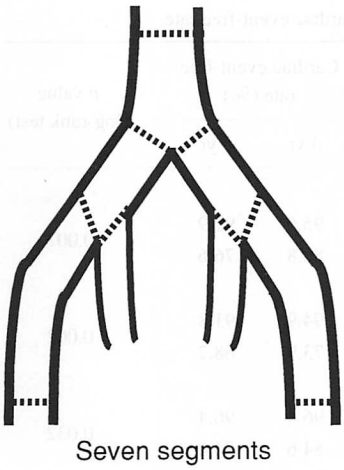
Statistical analysis

Variables are expressed as mean ± standard deviation, and the unpaired t-test was used for comparisons between pairs of groups. The χ^2 test was used to analyze categorical data. The Kaplan-Meier method was used to estimate the cardiac survival or the cardiac event-free rate, and the log-rank test was used to compare pairs of groups. The predictive power of the aortography score for cardiac events was examined by univariate analysis by the Cox proportional hazards model. A p value of less than 0.05 was considered statistically significant.

RESULTS

Baseline clinical characteristics at entry

Patients in the high score group were older than those of the low score group. The proportion of patients who underwent coronary intervention including angioplasty or bypass surgery as primary therapy at entry was not different between the two groups. Cigarette smoking was more prevalent in the high score group, although the prevalence of other risk factors were not different (**Table 1**).



Scoring in each segment

Finding		Points
Occlusion		6
Stenosis	99–91%	5
	90–76%	4
	75–51%	3
	50–26%	2
	≦25%	1
	None	0
Bend		Plus 1
Dilatation		Plus 1

Fig. 1 Scoring of the degree of sclerotic changes in lower abdominal aorta and iliac arteries

The aortogram was divided into seven segments: the lower abdominal aorta, right and left common iliac arteries, right and left external iliac arteries, and right and left internal iliac arteries. Occlusion, stenosis, bending (more than 90 degrees), and dilatation (more than 1.5 times reference diameter) in each segment were counted for scoring. The sum of the scores from seven segments was defined as the aortography score.

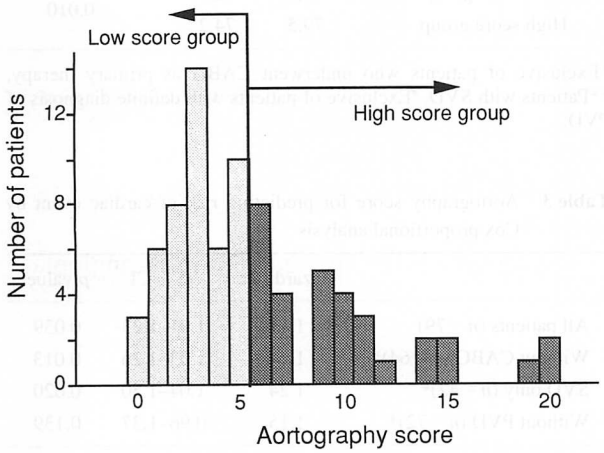


Fig. 2 Histogram of aortography score

The low score group consisted of 47 patients with aortography scores of 5 or less, and the high score group consisted of 32 patients with scores of 6 or more.

Table 1 Baseline clinical characteristics

	Low score group ($n=47$)	High score group ($n=32$)
Aortography score	≦5	≧6
(mean±SD)	(2.9±1.5)	(10.1±4.2)
Age (yr)	57.1±8.1	67.9±5.7*
Male gender	37	30
Previous MI	36	24
Coronary lesion		
Single-vessel	29	13
Multivessel	18	19
Primary coronary intervention		
Angioplasty	11	5
Bypass surgery	6	9
Risk factors		
Hypertension	22	18
Hyperlipidemia	21	12
Diabetes mellitus	8	9
Smoking	35	30#
Peripheral vascular disease	0	7*

*$p<0.01$, #$p<0.05$ vs low score group.

Cardiac survival

Six patients suffered cardiac death, including four patients who died of apparent cardiac causes and another two with sudden death. Four patients were in the high score group and two in the low score group, although the difference in survival between the two groups was not significant (**Fig. 3**).

Cardiac event-free rate

Cardiac events occurred in 11 patients, including cardiac death in 6, non-fatal acute myocardial infarction in 1, coronary bypass surgery in 1, and coronary angioplasty for a new lesion in 3. The incidence of cardiac events in the high score group was higher than in the low score group, and the difference in the cardiac event-free rate between the two groups was significant ($p=0.007$; **Fig. 4**, **Table 2**).

When patients who underwent coronary bypass surgery as primary therapy were excluded, the analysis also showed a significant difference in the cardiac event-free rate between the two groups ($p=0.002$; **Table 2**). When only patients with single-vessel coronary disease were included in the analysis, the cardiac event-free rate was also lower in the high score group than in the low score group ($p=0.032$; **Table 2**). If the seven patients with a definite diagnosis of peripheral vascular disease were excluded from the high score group, the difference in the cardiac event-free rate between the two groups was the same ($p=0.010$; **Table 2**).

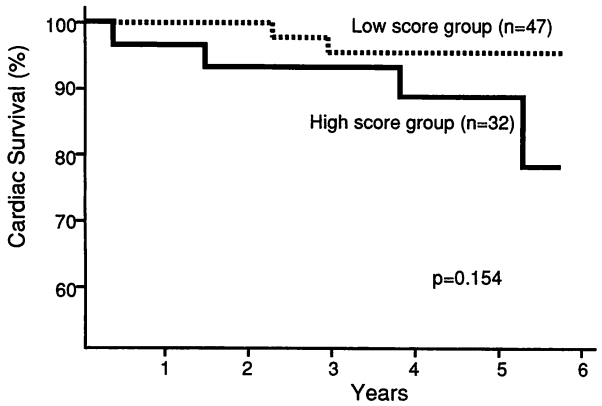


Fig. 3 Cardiac survival of each group by Kaplan-Meier analysis
Five-year survival rate was 95.6% in the low score group and 89.2% in the high score group.

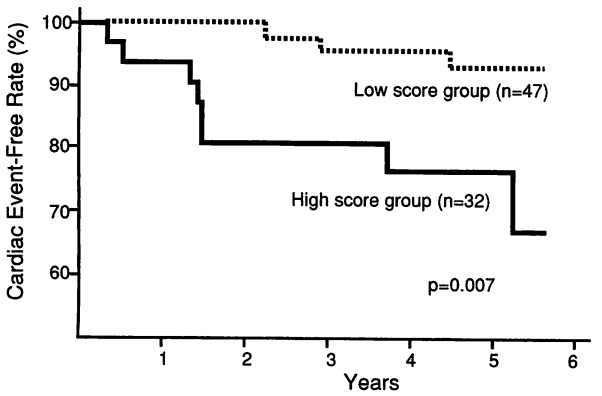


Fig. 4 Cardiac event-free rate of each group by Kaplan-Meier analysis
The difference was significant by log-rank test.

Table 2 Cardiac event-free rate

	Cardiac event-free rate (%)		*p* value (log-rank test)
	3 yr	5 yr	
All patients ($n=79$)			
Low score group	95.6	92.9	0.007
High score group	80.8	76.6	
Without CABG ($n=64$)*			
Low score group	94.9	91.8	0.002
High score group	73.9	68.2	
SVD only ($n=42$)**			
Low score group	96.4	96.4	0.032
High score group	84.6	74.0	
Without PVD ($n=72$)#			
Low score group	95.6	92.9	0.010
High score group	79.5	74.2	

*Exclusive of patients who underwent CABG as primary therapy, **Patients with SVD, #Exclusive of patients with definite diagnosis of PVD.

Table 3 Aortography score for predicting risk of cardiac event by Cox proportional analysis

	Hazard rate	95% CI	*p* value
All patients ($n=79$)	1.11	1.01–1.23	0.039
Without CABG ($n=64$)*	1.14	1.03–1.26	0.013
SVD only ($n=42$)*	1.24	1.04–1.50	0.020
Without PVD ($n=72$)*	1.15	0.96–1.37	0.139

*See footnote in Table 2.
CI=confidence intervals.

Aortography score and cardiac events

The Cox proportional hazards model showed the aortography score can be used as a predictor for the risk of cardiac events, and the hazard rate was 1.11 per point of the score (95% confidence intervals: 1.01–1.23, $p=0.039$; **Table 3**).

The aortography score of 11 patients with cardiac events was significantly higher than that of the cardiac event-free patients (8.6 ± 6.2 vs 5.4 ± 4.1, $p=0.033$; **Fig. 5**).

DISCUSSION

Peripheral vascular disease often coexists with ischemic heart disease. The prevalence of intermittent claudication is higher in patients with than in those without ischemic heart disease[1], and the prevalence of ischemic heart disease is higher in patients with intermittent claudication[2,3]. Coronary artery obstructions are frequently documented by coronary angiography performed before peripheral vascular surgery[4,5]. In the Framingham study, the incidence of intermittent claudication was greater in a cohort consisting of patients with than in those without coronary heart disease, and the incidence of coronary heart disease was greater in a cohort with intermittent claudication[6]. Generalized atherosclerosis seems to be a common underlying background shared by peripheral vascular disease and ischemic heart disease. Risk factors of arterial sclerosis influence both diseases[3], although the significance of each risk factor is somewhat different between the diseases[1,2].

These diseases are also associated in their prognoses. Among patients with intermittent claudication, the death rate was higher in a subgroup with evidence of ischemic heart disease[9]. After an operation for peripheral revascularization, the incidence of cardiac events is higher in patients with than in

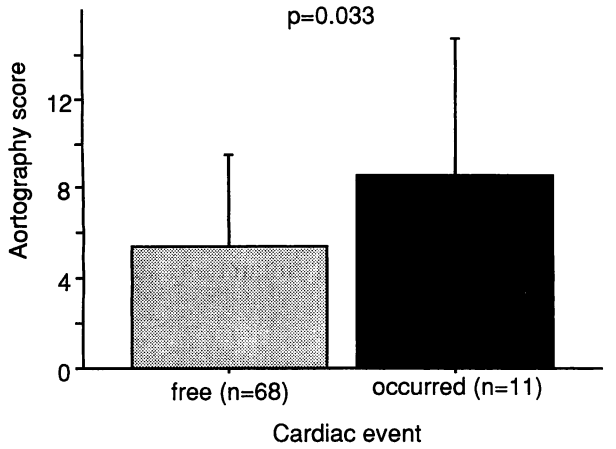


Fig. 5 Comparison of aortography score between patients who encountered cardiac events and cardiac event-free patients

those without ischemic heart disease[10].

On the other hand, the presence of peripheral vascular disease leads to a less favorable prognosis. In the general population, overall mortality and cardiac mortality are higher in those who have intermittent claudication[1-3,6] or noninvasively diagnosed peripheral vascular disease[7,8] than in those who do not. In patients with ischemic heart disease after coronary bypass surgery, late mortality and the cardiac event rate are higher in the subgroup with peripheral vascular disease[11,12].

Thus, peripheral vascular disease could be one of the predictors of late outcome in patients with ischemic heart disease. However, symptoms of peripheral vascular disease begin relatively late in life, and sclerotic changes in the iliac arteries or lower peripheral arteries may exist latently before symptoms or detectable impairment of flow appear, especially in patients with other arterial sclerotic disorders such as ischemic heart disease. In the present study, we examined the influence of the degree of sclerotic changes derived from findings of lower abdominal aortography on the late outcome in patients with ischemic heart disease, irrespective of whether or not a definite diagnosis of peripheral vascular disease has been made. The degree of sclerosis was expressed by the aortography score, and the cardiac event rate was significantly higher in the high score group than in the low score group. The proportional hazards model showed the aortography score could be a predictor of cardiac events. More severe sclerotic changes in the lower abdominal aorta and iliac arteries were associated with a higher cardiac event rate in patients with ischemic heart disease.

The cardiac events included in this study were cardiac death, acute myocardial infarction, coronary bypass surgery, and coronary angioplasty for a new lesion. Their occurrence might be related to the progression of coronary arterial sclerosis. Coronary angioplasty for restenosis of an old lesion was not considered to be a cardiac event to avoid bias attributable to the original angioplasty, because it does not reflect the natural course of coronary arterial sclerosis.

There were seven patients with a definite diagnosis of peripheral vascular disease, all of whom belonged to the high score group. It is unlikely that the inclusion of these seven patients per se was responsible for the statistical difference in prognosis between the two groups, because the cardiac event-free rate was still lower in the high score group when these seven patients were excluded from the analysis.

Coronary bypass surgery is generally accepted to improve the prognosis of ischemic heart disease regardless of the presence or absence of peripheral vascular disease[5,11,13,14], whereas the influence of percutaneous transluminal coronary angioplasty on the late outcome of ischemic heart disease is both limited and controversial[15]. To determine the effect of bypass surgery, we analyzed the subgroup excluding those who underwent coronary bypass operation, and similar results with better statistical values were obtained.

Patients with less severe coronary lesions are expected to have a better prognosis than those with more severe lesions. So, analysis limited to patients with single-vessel coronary disease is also of interest. The association between sclerotic changes of the iliac arteries and the cardiac event rate was also shown to be significant.

On cardiac mortality, however, the influence of the degree of sclerosis in the iliac arteries did not reach statistical significance. This suggests that the subclinical extension of arterial sclerosis has less power to predict cardiac mortality than the presence of a definite diagnosis of peripheral vascular disease. The small number of patients studied may also contribute to the lack of significance, which is a limitation of the present study.

Another limitation is the distinct difference in age between the two groups in this study. Although age itself was not predictive of cardiac event rate by

univariate analysis (hazard rate : 1.05, $p=0.219$), the extent of sclerosis in the lower abdominal aorta and iliac arteries, which is represented by the aortography score, is not independent of age or risk factors, and would reflect generalized arterial sclerosis.

Our results suggest that the progression of coronary lesions might be faster in patients with already advanced systemic arterial sclerosis. Although lower abdominal aortography itself is an invasive examination, it is very easy to include this procedure at the time of routine cardiac catheterization study. Information about iliac arteries has implications for predicting the late outcome of patients with ischemic heart disease.

CONCLUSIONS

In patients with ischemic heart disease, the extent of sclerotic changes in the iliac arteries and lower abdominal aorta has a predictive value for the incidence of cardiac events including coronary angioplasty for a new lesion, coronary bypass surgery, acute myocardial infarction, and cardiac death.

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要　約

虚血性心疾患患者における腸骨動脈硬化程度と長期予後の関連

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虚血性心疾患では閉塞性動脈硬化症をしばしば合併し，合併患者では心臓死の頻度が高くなる．また，下肢を灌流する動脈の硬化は，閉塞性動脈硬化症の確定診断に至らない段階で潜在しうる．今回，虚血性心疾患患者において，下位腹部大動脈から腸骨動脈にかけての硬化の程度と長期予後とがいかに関連するかを検討した．

対象は1989年12月から約1年間に，虚血性心疾患の精査目的で当科で心臓カテーテル検査を行った連続91例のうち，冠動脈に器質病変を有し，かつ追跡可能であった79例である．

心臓カテーテル検査時に下位腹部大動脈造影を行い，その所見に基づいて動脈硬化の程度をスコア化した．すなわち，下位腹部大動脈，左右の総腸骨動脈，左右の外腸骨動脈，左右の内腸骨動脈の計7部位のそれぞれにおいて，閉塞，狭窄，蛇行，拡張の有無で加点し(硬化の強いほど高得点)，全7部位の総計をその患者の「大動脈造影スコア」とした(全例で5.8±4.6点)．6点以上を高スコア群(32例)，5点以下を低スコア群(47例)とし，心事故(心臓死，急性心筋梗塞発症，冠動脈バイパス術施行，新病変に対する経皮的冠動脈形成術施行)の発生について観察(4.4±1.2年)した．

心事故回避率は，5年で低スコア群92.9%，高スコア群76.6%で，log-rank testにて有意差を認めた($p=0.007$)．比例ハザードモデルによるこのスコアの心事故発生に関するハザード比は1.11(95%信頼区間：1.01–1.23，$p=0.039$)であった．また，冠動脈バイパス術を初期治療とした患者を除いた64例での検討，冠動脈一枝病変患者のみ(42例)での検討，閉塞性動脈硬化症合併者を除いた72例での検討でも，それぞれ心事故発生に関して全患者の場合と同様の結果が得られた．

以上より，下位腹部大動脈から腸骨動脈にかけての潜在的な硬化の程度は虚血性心疾患患者の予後の推定に有用で，硬化が強ければ心事故発生率は高い．

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