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Doppler Ultrasound Recognition of Preclinical Changes in Arterial Wall in Diabetic Subjects: Compliance and Pulse-Wave Damping

C. S. LO, M.B., B.S., I. R. N. RELF, M.Sc., K. A. MYERS, F.R.A.C.S., AND M. L. WAHLQVIST, F.R.A.C.P.

Doppler ultrasound was used to detect early changes in arteries of the legs by two independent techniques. Pulse-wave velocity was measured to calculate arterial wall compliance and Fourier analysis was used to measure damping of the pulse-wave forms. Ten non-insulin-dependent diabetic men with no clinical evidence of peripheral arterial disease had significantly lower compliance and greater pulse-wave damping than 10 matched nondiabetic control subjects. There was a good correlation between the results for the two different techniques. DIABETES CARE 1986; 9:27–31.

Gosling[1] has shown that arterial compliance can be measured accurately using sensitive Doppler ultrasound techniques by recording the pulse-wave velocity down an arterial segment from the time difference between the start of the pulse wave at each end. Skidmore and Woodcock[2,3] have developed a mathematical technique to assess the form of the pulse wave obtained by Doppler ultrasound, using Fourier analysis to derive an index of pulse-wave damping (together with other parameters), which they consider to result from increased proximal resistance.

This article reports the results of both techniques in a group of non-insulin-dependent diabetic (NIDD) men who had no symptoms or signs of arterial disease in the lower limbs or at any other site. The aim was to determine whether Doppler studies showed greater changes in the aortoiliac and femorotibial segments in diabetic than in matched nondiabetic control subjects.

SUBJECTS AND METHODS

Subjects. Ten NIDD men treated by diet alone (mean age 61 yr, range 30–74 yr), and 10 nondiabetic men (control subjects; mean age 62 yr, range 41–78 yr) were studied. None of the subjects was hypertensive (blood pressure <150/95) and none smoked. No subject had any symptoms of peripheral arterial disease and all had apparently normal peripheral pulses. None had present or prior symptoms of coronary artery disease or cerebrovascular insufficiency. None of the diabetic subjects had clinical evidence of neuropathy, retinopathy, or nephropathy.

All patients had measurements of ankle/arm blood pressure ratio at rest and after exercise, using the Doppler stethoscope and all satisfied the criteria for a normal test, as defined by Marinelli et al.[4]

The comparison between body mass index, mean blood pressure, and biochemical measurements of carbohydrate and lipid status in the two groups are shown in Table 1.

Doppler ultrasound examination. Each subject was rested lying supine for 10 min before testing. The examination began when blood pressure was stable.

Two 4-MHz Sonicaid Doppler ultrasound probes (Sonicaid Medical Inc., Virginia) were used to calculate pulse-wave velocity. One probe was placed over the left subclavian artery in the supraclavicular fossa and the other was placed over each common femoral artery at the inguinal ligament, in turn. The two signals obtained from each of a series of 10 pulses for each test were passed through a Medishield Spectrum Analyzer (Medishield Corp. Ltd., London, U.K.) and displayed on light-sensitive paper. The pulse-wave velocity (PWV) down the aorta and iliac arterial segments was calculated from the ratio of time delay between the start of the proximal end of the distal pulse wave (T) and the measured distance between the probes (L):

$$PWV = \frac{L}{T} \text{ m, s}^{-1}$$

The arterial compliance (C), defined by Gosling[1] as the percentage lumen change caused by a 10-mm Hg pressure increment, is: $C = 66.7/(PWV)^2$.

An 8-MHz Vasculab Blood Velocimeter Doppler ultrasound probe (Medsonics, Kendall Hospital Corp., California) was used to record pulse waves over each common femoral artery at the inguinal ligament, and over each posterior tibial artery

TABLE 1
Comparison of means (±SE) for various characteristics of control and NIDD men

Subject	N	BMI*	Mean BP†	Fasting blood sugar (mmol/L)	GTT area‡	GHb (g/100 g)	Total cholesterol (mmol/L)	High-density lipoprotein cholesterol (mmol/L)	Triglyceride (mmol/L)
NIDD	10	27 ± 2	98 ± 3	10.7 ± 1.2	16.1 ± 1.5	7.8 ± 0.8	5.5 ± 0.2	0.96 ± 0.07	2.4 ± 0.4
Control	10	27 ± 2	98 ± 3	5.2 ± 0.2	6.9 ± 0.5	6.0 ± 0.4	6.1 ± 0.4	1.37 ± 0.18	2.0 ± 0.3
Significance (P)		NS	NS	<0.01	<0.001	<0.05	NS	<0.05	NS

* BMI, body mass index, wt (kg)/ht² (m²).
† Mean BP, systolic blood pressure + (2 × diastolic blood pressure)/3.
‡ GTT area, area under 2-h glucose tolerance curve (mmol·L⁻¹·h).

at the ankle. These Doppler recordings were analyzed by the Medishield Doppler Spectrascan Mark II (Medishield Corp. Ltd., London, U.K.) for Fourier analysis. The spectrum of blood velocity signals for each pulse was displayed on an oscilloscope and recorded on paper and audio tape. The best fit for maximum frequencies through each pulse was then extracted from the tape by a maximum-frequency follower. This signal was then analyzed by a Data General Nova II computer (Data General Corp., Massachusetts) to give a discrete Fourier transform equation, F(S), which can be solved by using an inverse Laplace transformation

$$F(S) = \frac{1}{(S^2 + 2\,\delta\omega_o + \omega_o^2)\,(S + \gamma)}$$

where δ is an independent variable termed the damping factor, which has been shown to measure proximal arterial resistance[2,3] (ω_o is related to arterial wall compliance and γ is related to distal resistance). Changes in these parameters will be reported in subsequent articles.

The mean of 10 recordings was analyzed for each site. The reproducibility of the measurements for the individual limbs was assessed on separate occasions. The mean coefficient of variation was 6.6% (range 1.7–10.2%) for measurements of compliance and 6.8% (range 3.2–10.0%) for proximal resistance at the common femoral artery. A comparison of the findings for the right and the left legs was also made; the mean coefficient of variation between the legs was 8.4% for compliance, 16.6% for proximal resistance at the common femoral artery, and 13.0% for proximal resistance at the posterior tibial artery.

Statistical comparison of the groups was made on the basis of Student's *t*-test and the relationships were examined by linear regression analysis.

RESULTS

Mean compliance was significantly lower in the NIDD (0.49 ± 0.18) than in the control group (1.02 ± 0.23) (Figure 1). The mean proximal resistance was significantly higher in the NIDD (0.44 ± 0.14) than in the control group (0.29 ± 0.05) at the common femoral artery level and the proximal resistance was significantly higher in the NIDD (0.54 ± 0.13) than in the control group (0.35 ± 0.13) at the posterior tibial artery level (Figure 2). There was a significant correlation between compliance and proximal resistance at the common femoral artery level (r = 0.68) (Figure 3) and between proximal resistance at the common femoral artery level and proximal resistance at the posterior tibial level (r = 0.56) (Figure 4).

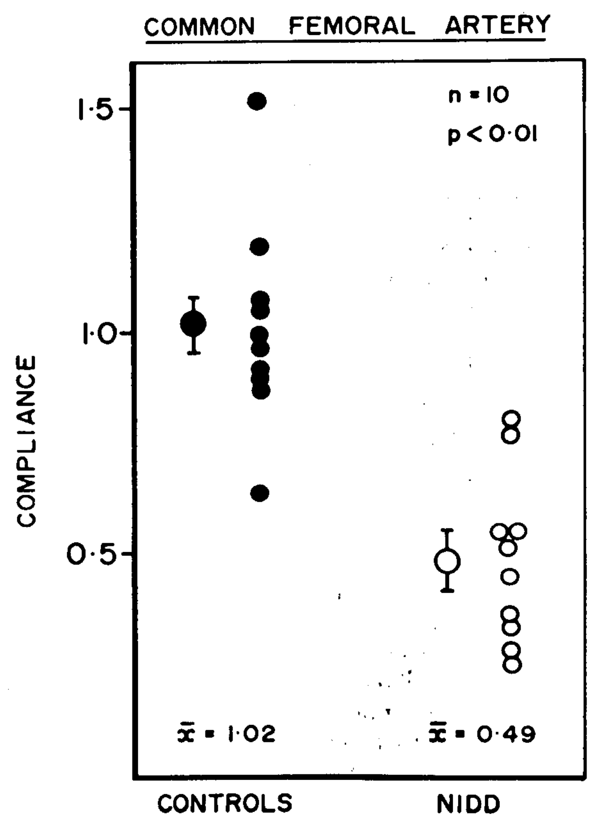

FIG. 1. Arterial wall compliance at level of common femoral artery in control and NIDD subjects.

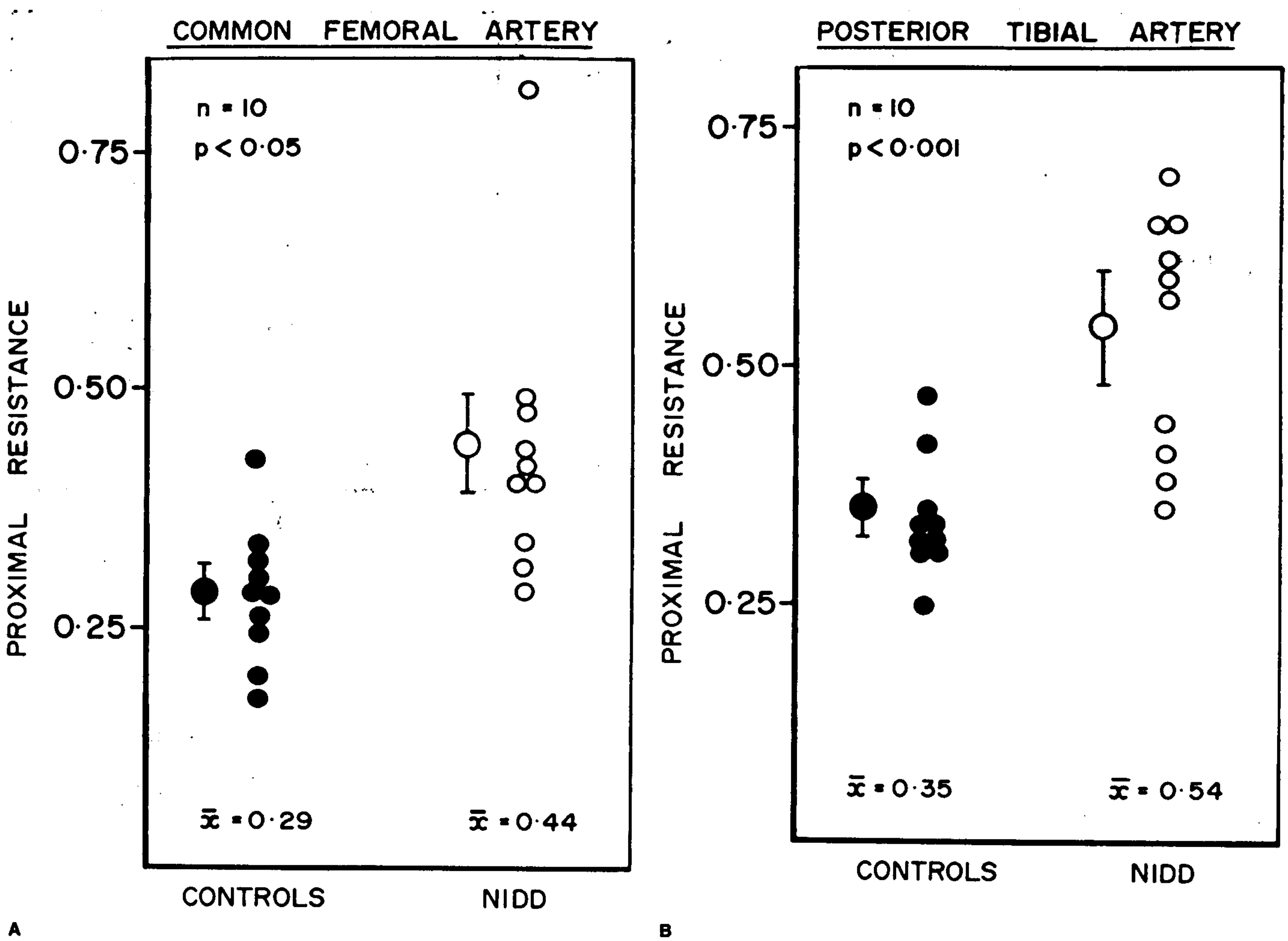

FIG. 2. Proximal resistance at level of common femoral artery (A) *and posterior tibial artery* (B) *in control and NIDD subjects.*

DISCUSSION

The present study showed a significant decrease in compliance and increase in pulse-wave damping in the NIDD group compared with control subjects. There was a good correlation between the two techniques used to assess changes in the proximal arteries. The results indicate that changes are present in both the aortoiliac and femorotibial segments in the diabetic group to a greater degree than in control subjects.

The changes were apparent in diabetic subjects who otherwise had no apparent clinical abnormality relating to the vascular system. The only defined differences between NIDD and control men that might have led to these arterial changes were in carbohydrate status or related variables. There were no differences in body mass index, blood pressure, or lipids; all subjects were nonsmokers; and the two groups were age matched. The significant differences between the two groups indicate that changes in the arterial wall may be recognized by noninvasive measurements even in individuals with mild diabetes and that these differences can be attributed to abnormalities in carbohydrate status rather than other conventional risk factors. However, it is not possible to state with certainty that these changes are due to arterial disease and, if so, whether they result from atherosclerosis, medial sclerosis, or other disorders such as glycosylation of proteins in the arterial wall.[5] If they do reflect early disease, then this would have considerable significance, for accelerated atherosclerosis in coronary and cerebral arteries is responsible for three-quarters of all deaths in diabetic individuals,[6] while diabetes also predisposes to macrovascular disease in arteries to the lower limbs.[7] Peripheral arterial disease predicts an increased risk of future myocardial infarction and stroke.[8] If arterial disease could be detected early, then good diabetes control and other risk factor intervention might delay disease progression.

A technique for measuring compliance similar to that used in this study showed reduced compliance in the femoral to tibial artery segment in asymptomatic diabetic men,[9] although another study found changes only in diabetic patients with foot ulcers.[10] Skidmore et al.[11] used the technique of Fourier analysis of the pulse wave to measure the damping factor to distinguish patients with normal, mildly diseased, and severely diseased iliac arteries. Baird et al.[12] used the technique

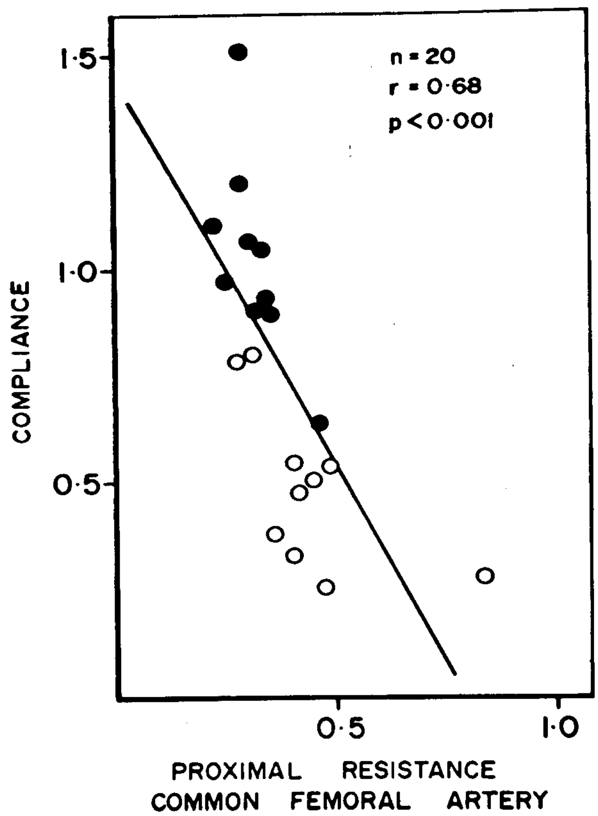

FIG. 3. Correlation between compliance and proximal resistance at the common femoral artery level in all subjects: ●, *control;* ○, *NIDD.*

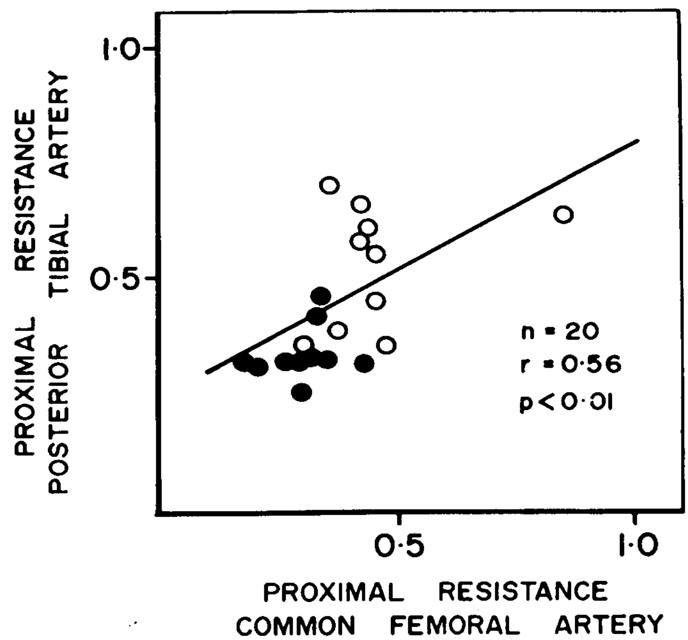

FIG. 4. Correlation between proximal resistance at the common femoral artery level and at the posterior tibial artery level in all subjects: ●, *control;* ○, *NIDD.*

to detect hemodynamically significant iliac lesions in patients with femoral artery disease. Both studies demonstrated that the damping coefficient measured proximal resistance and was essentially independent of changes in peripheral resistance.

These previous studies consistently demonstrated decreased damping factor measurements at the common femoral artery level in patients long before there was apparent change in common femoral pulses, either at rest or after exercise, but at a stage where there was early arteriographic evidence of stenosis.[13] Before the present study, however, changes in the damping factor suggesting increased proximal resistance have not been demonstrated in apparently normal subjects who might have preclinical disease. Thus, any implications that these changes necessarily imply accelerated arterial disease must be proffered with caution, pending further experimental validation of the technique.

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From the Department of Vascular Surgery, Prince Henry's Hospital, Melbourne; the Department of Surgery, Monash University, Melbourne (I.R.N.R. and K.A.M.); and the Department of Human Nutrition, Deakin University, Geelong, Australia (C.S.L. and M.L.W.).

Address reprint requests to K. A. Myers, Department of Vascular Surgery, Prince Henry's Hospital, St. Kilda Road, Melbourne 3004, Australia.

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