

CHANGE IN THE LOWER LIMB DEEP VENOUS FLOW IN PERIPHERAL ATHEROSCLEROTIC ARTERIAL DISEASE

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Abstract

Aim. This prospective study was undertaken to determine how peripheral atherosclerotic disease influences the flow in the deep veins of the leg.

Material and method. Thirty one subjects with peripheral atherosclerotic disease and 23 age matched control subjects were studied. The popliteal vein flow velocity was measured at rest and during reactive hyperemia by means of color duplex ultrasound scanning. Patient age, ankle-brachial index (ABI) and the presence of risk factors for venous thrombosis were also recorded.

Results. There was a negative correlation between the ankle-brachial index and venous flow velocity among subjects with peripheral arterial disease ($p=0.001$). There was a negative correlation between dyslipidemia and resting venous flow velocity ($p=0.049$). During reactive hyperemia, venous flow velocity increased less in subjects with peripheral arterial disease than it did in control subjects ($p=0.007$). The subjects with dyslipidemia showed no changes in venous flow velocity in reactive hyperemia measurements ($p=0.908$).

Conclusion. Increasing the venous flow velocity in peripheral arterial disease, may confer some protection against the deep venous thrombosis.

Keywords: peripheral arterial disease, popliteal venous flow, venous thrombosis, risk factors.

Introduction

Peripheral arterial disease and venous disease often coexist and they have common risk factors [1,2].

If Virchow's triad is accepted as a basis for the development of venous thrombosis [3], peripheral vascular disease has a number of characteristics which are likely to promote venous thrombosis.

First, compared to normal subjects, blood flow increased to a lesser extent in patients with peripheral arterial disease during exercise and reactive hyperemia [4].

Second, there is an increased concentration of metabolites such as complement C3 and C5, free oxygen radicals and lipid peroxides produced in relation to distal tissue ischaemia which, at least in vitro, upregulate the procoagulant properties of the vascular endothelium [5,6].

With the use of color duplex ultrasound scanning, veins may be identified and their dimensions may be measured. By analyzing the spectrum of the doppler signal, the velocity can be estimated [7].

To find out how peripheral arterial disease influences deep venous flow in the lower limbs, we undertook a prospective controlled study examining velocity flow in the popliteal vein with color duplex ultrasound scanning.

Methods

Thirty-one subjects who had chronic peripheral arterial disease (24 men and 7 women), were recruited for the study: 19 complained of claudication alone, 18 suffered from rest pain and 21 had gangrene. Four patients had thigh amputation. Twenty-three control subjects (16 men and 7 women) without peripheral arterial disease of similar age who were awaiting general surgical procedures were also invited to take part in the study. The presence or absence of peripheral arterial disease was confirmed by the history of the disease and measurement of the ankle-brachial index (ABI). Patients with deep venous thrombosis, chronic venous insufficiency as well as incompressibility of the leg arteries detected while measuring the ABI were excluded. Control subjects with an ABI of 0.8 or less were excluded from the study.

All subjects underwent B mode ultrasonography of a popliteal vein. Ultrasound scanning took place in the labora-

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Table 1. Demographic and clinical characteristics of the study populations and drugs used (all values are means \pm standard deviation for continuous variables and the number for categorical variables)

Characteristic	Patients (n=31)	Controls (n=23)
Age (in years)	66.58 \pm 11.051	54.09 \pm 8.954
Gender (M vs F)	24 vs 7	16 vs 7
Arterial hypertension (n, %)	33 (74.2%)	9 (39.1%)
Blood glucose levels (mg/dl)	117.87 \pm 49.432	124.52 \pm 37.768
Cholesterol levels (mg/dl)	214.61 \pm 59.710	201.22 \pm 48.67
Smoking (n,%)	23 (74.19%)	9 (39.13%)
Statins (n, %)	13 (42.93%)	9 (39.13%)
Antihypertensive drugs (n, %)	14 (45.26%)	7 (30.43%)
Antidiabetic drugs (n, %)	9 (29.3%)	3 (13.04)
Insulin (n, %)	5 (16.13)	3 (13.04)

tory, were the ambient temperature was 25°C. The equipment used was a Diasonics Ultrasound, coupled with 4MHz transmitted frequency for doppler measurements. Venous blood flow velocity was estimated by the ultrasound scanner as time averaged peak velocity. The popliteal vein was chosen as the target for the ultrasound measurements because the anatomical position makes it an easy target for ultrasound examination. In all patients and control subjects a mean of three measurements of the venous flow velocity was recorded, and the average was calculated, at rest. Then, a 20 cm wide femoral blood pressure cuff was placed around the thigh and inflated 50 mmHg above the systolic blood pressure for 5 minutes. After the cuff was released, the maximum venous flow velocity were recorded during 60 seconds. This test is flow mediated dilatation or reactive hyperemia.

Written informed consent was obtained from all participants.

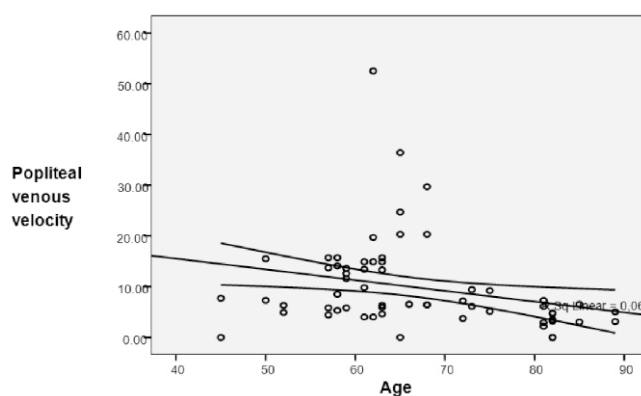
Statistical analysis. Measured values were expressed as median. Measurements from the patient and control groups were compared with the Mann-Whitney test. Linear correlation analysis was used, and the result was expressed as Pearson's correlation coefficient to determine the relationship between paired variables. A p value less than 0.05 was considered statistically significant.

Results

The demographic and clinical data in the study population are shown in Table 1. Resting popliteal venous flow velocity did not show a significant difference between subjects with peripheral arterial disease 9.501 \pm 5.616 cm/sec (3.1-21.6 95%CI 7.833-11.169) and controls 9.270 \pm 7.858 cm/sec (1.8-45.7 95%CI 7.307-11.233); p=0.621, but in limbs with an ABI less than 0.9 venous flow velocity was significantly higher 16.557 \pm 19.656 (2.9-52.5 95%CI 1.622-34.736) than in limbs with an ABI of 0.9 or more 12.673 \pm 5.792 (3.1-24.7 95%CI 9.46-15.81); p=0.001.

Venous flow velocity appeared to be greater among younger subjects, and decreased in elderly subjects (p=0.042) (Figure 1)

Interestingly, resting venous flow velocity appeared to be greater among subjects without dyslipidemia

**Figure 1.** Correlation analysis between age and flow venous velocity in the popliteal vein at rest among subjects with peripheral arterial disease

10.042 \pm 8.26 cm/sec versus 9.635 \pm 10.177 in those with dyslipidemia, although this difference did not quite reach statistical significance (p=0.057). Furthermore, among patients with peripheral arterial disease there was a negative correlation between dyslipidemia and resting popliteal vein flow velocity (p=0.049).

During reactive hyperemia venous flow velocity increased in all subjects, but to a significantly lesser extent in subjects with peripheral arterial disease: 9.532 \pm 5.665 (7.071-9.643 95%CI 2.3-21.1) versus controls 10.559 \pm 4.696 (2.7-11.953 95%CI 10.559-18.1) p=0.007. The degree of this velocity showed significant positive correlation with ankle-brachial index (p=0.001). Venous flow in reactive hyperemia conditions was not statistically influenced in diabetic subjects and in those with dyslipidemia (p=0.251 versus p=0.908).

Discussion

This study documents the change in venous flow in peripheral arterial disease. There are conflicting reports regarding the relationship between deep venous disease and peripheral arterial disease in the lower limbs [8]. We chose the popliteal vein as a representative area for both anatomic

and technical reasons. Our observations indicate that the deep veins of the lower limb constrict in response to ischemia and the deep venous flow increased. The degree of this constriction is related to the severity of the peripheral arterial disease. During reactive hyperemia, when the hypoxia was augmented by the preceding arterial occlusion, the venous flow increased. The endothelium has been recognized as the key regulator of vascular homeostasis. Healthy endothelium produces a wide range of factors that regulate vascular tone, adhesion of circulating blood cells to the vessel wall, thrombus formation, smooth muscle cell proliferation, and vessel wall inflammation, which is the key mechanism of the thrombosis process [9,10]. One of the most important functions of the endothelium is its effect on the vascular tone. Consequently, some humoral factor related to tissue ischemia must be involved in producing this venoconstriction. Perhaps there are change in the endothelial production of nitric oxide or endothelins, which may be responsible for the contraction of the vascular smooth muscle [11]. Venous flow velocity decreases with age, which may be attributable in part to decreased nitric oxide release and to diminished smooth muscle cell responsiveness in older subjects [12]. We also observed an increase in resting venous flow velocity among subjects with peripheral vascular disease that was dependent on the severity of the disease. This change in velocity is the result of the constriction of the veins. The correlation between ankle-brachial index and venous flow velocity was significant in subjects with peripheral arterial disease. During reactive hyperemia venous flow velocity increases to a lesser extent in subjects with peripheral arterial disease as compared to subjects. Reduced venous flow has long been considered to be an important factor in the development of venous thrombosis [13,14].

Conclusion

It is likely that increased venous flow velocity, resulting from venoconstriction, has an important protective role for the development of deep venous thrombosis. As the activity of the coagulation system is also increased, it is surprising that deep vein thrombosis does not have a higher incidence. Future studies as well as investigation of blood

coagulation are necessary to show the link between peripheral arterial disease and the venous disorder.

Reference

1. Braekkan S, Hald E, Mathiesen B, et al. Competing risk of atherosclerotic risk factors for arterial and venous thrombosis in a general population: the Tromso Study. *Arterioscler Thromb Vasc Biol*, 2012; 32:487-491.
2. Franchini M, Mannucci P. Association between venous and arterial thrombosis: Clinical implications. *Eur J Intern Med*, 2012; 23:333-337.
3. Bergandal A, Bremme K, Hedenmalm K. Risk factors for venous thromboembolism in pre and post menopausal women. *Thromb Res*, 2012; 130(4):596-601.
4. Vardi M, Nini A. Near-infrared spectroscopy for evaluation of peripheral vascular disease. A systematic review of literature. *Eur J Vasc Endovasc Surg*, 2008; 35(1):68-74.
5. Brueggemann A, Noltze A, Lange T, Kaun M. Significant C3a increase in free flaps after prolonged ischemia. *J Surg Res*, 2008; 150(1):125-130.
6. Rosario R, Nuzzi A, Origliani G. Prognostic role of flow mediated dilation and cardiac risk factors in postmenopausal women. *J Am Coll Cardiol*, 2008; 51(10):997-1002.
7. Osada T, Radegran G. Alterations in the blood velocity profile influence the blood flow response during muscle contractions and relaxations. *J Physiol Sci*, 2006; 56(3):195-203.
8. Willem M, Lijfering MD, Flinterman MS, et al. Relationship between venous and arterial thrombosis: a review of the literature from a causal perspective. *Semin Thromb Hemost*, 2011; 37:885-896.
9. Namrataa C. Endothelial dysfunction – a predictor of atherosclerosis. *Int J Med*, 2009; 4(1):33-41.
10. Hirase T, Node K. Endothelial dysfunction as a cellular mechanism for vascular failure. *Am J Physiol Heart Circ Physiol*, 2012; 302(3):H499-505.
11. Poredos P, Jezovnik M. Testing endothelial function and its clinical relevance. *J Atheroscler Thromb*, 2013; 20:1-8.
12. Parker BA, Ridout SJ, Proctor DN. Age and flow mediated dilation: a comparison of dilatory responsiveness in brachial and popliteal arteries. *Am J Physiol Heart Circ Physiol*, 2006; 291:3043-3049.
13. Turpie A, Chin B. Venous thromboembolism: pathophysiology, clinical features and prevention. *BMJ*, 2002; 325:887-890.
14. Poredos P, Jezovnik M. The role of inflammation in venous thromboembolism and the link between arterial and venous thrombosis. *Int Angiol*, 2007; 26(4):306-311.