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Original Article

Arterial vascular properties in individuals with spina bifida

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Study design: Observational cross-sectional study.
Objective: To assess the vascular characteristics of the arterial circulation in individuals with spina bifida (SB) in comparison with individuals with spinal cord injury (SCI) and able-bodied controls (C).
Setting: University Medical Centre, Nijmegen, The Netherlands.
Methods: Six spina bifida (SB), 15 spinal cord injury (SCI) and 10 C were included. Red blood cell velocities and arterial diameter of the common carotid artery and common femoral artery were measured using echo-Doppler ultrasound in a supine position. A venous blood sample was withdrawn for determination of blood viscosity.
Results: In the common carotid artery, blood flow and wall shear stress were not different between the three groups. The diameter was smaller in SB compared with SCI and C. In the common femoral artery, blood flow was smaller in SB than in SCI and C. Wall shear stress was significantly higher in SB and SCI compared with C. High wall shear stress may lead to endothelial dysfunction and related cardiovascular disease.
Conclusion: Deteriorating vascular properties are present in SB as well as in spinal-cord-injured individuals in comparison with C. These properties tend to be more pronounced in SB than in SCI.
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Keywords: spinal cord injury; wall shear stress; congenital; inactivity; endothelium; circulation

Introduction

It is well known that a spinal cord injury (SCI) leads to paralysis and concomitant muscle atrophy and consequently, blood flow below the lesion level will decrease. This may result in an 'atrophied' vascular bed supplying the muscles in the legs. Previous studies[1,2] observed a decreased blood flow in the femoral artery of spinal-cord-injured compared with able-bodied individuals.

This change in blood flow was mainly because of a decrease in diameter. Wall shear stress represents the frictional force exerted by the circulating blood on the intimal surface of arteries and is known to be a key factor in endothelial function.[3,4] A recent study showed higher levels of wall shear stress in the SCI population compared with able-bodied controls (C) in the common femoral artery.[5]

In spina bifida (SB), the neural tube has not completely closed, early in gestation. This results in paralysis, loss of sensation and loss of autonomic control below the affected level. We hypothesise that leg-vascular properties are more severely affected in SB individuals who are paralysed from birth compared to SCI individuals who have normal development of their muscles and vascular system before the injury. Although it is known that individuals with SB, like those with SCI, are prone to secondary complications because of a poor circulation, for example, decubitus and poor wound healing,[6–8] vascular properties in individuals with SB have never been studied.

The purpose of this study was therefore to examine the vascular characteristics, such as diameter, blood flow and wall shear stress, of the arterial circulation in individuals with SB. Vascular characteristics of the common carotid artery and common femoral artery in individuals with SB will be compared with individuals with SCI and C.

Methods

Subjects

A total of 31 individuals volunteered to participate in this study: six individuals with SB, 15 individuals with

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SCI of traumatic origin at thoracic level and 10 C. Neurological examinations of the motor and sensor neurological system revealed completeness and level of the lesion. In the SB group, one subject had a cervical lesion, one a thoracic lesion and four had a lesion at lumbo-sacral level. One SB and all but two SCI subjects had a complete motor and sensory lesion (ASIA A).[9] One SB and one SCI subject had a complete motor lesion, but were sensory incomplete (ASIA B). The other SB and SCI subjects had an incomplete sensor and motor lesion, although the motor activity was not functional (ASIA C). Group characteristics, including time since injury and physical activity, are summarised in Table 1.

All subjects completed a local medical health questionnaire to assure that the participants did not meet the exclusion criteria. Five SB and three SCI subjects used chronic medication. The study was approved by the Faculty Ethics Committee and all subjects signed an informed consent before starting the tests.

Protocol
All subjects refrained from caffeine, nicotine and alcohol for at least 12 h before starting the test. A venous blood sample was obtained from all subjects for determination of blood viscosity. The tests were performed in one experimental room in which the temperature was maintained in a range between 22 and 24°C, and were started between 11.00 am and 14.00 pm. After completing the medical health questionnaire, the subjects were positioned on a bed in supine position for the measurements.

After a 15-min supine rest period, red blood cell velocity of the left common carotid artery was measured for 2 min, followed by measurement of the diameter of this artery. This was followed by measurement of both entities of the left common femoral artery.

Measurements
Peak (V_{peak}), mean (V_{mean}) and minimal (V_{min}) red blood cell velocity, and longitudinal systolic and diastolic vessel diameter were measured with a pulsed colour-coded Doppler device (ATL 5000 HDI. Bothell, USA). A 7 MHz broadband linear array transducer with a range of 4–7 MHz (L7–4) was used. The sample volume was placed in the centre of each vessel, 2 cm before bifurcation of the left common femoral artery into the deep and superficial femoral artery, and 1.5 cm before the bifurcation of the left common carotid artery into the external and internal carotid artery. All measurements were performed by the same experienced examiner. In the common carotid artery and common femoral artery, red blood cell velocity was measured beat to beat for 2 min and stored once every 10 s. An average of 12 values (2 min) was used to calculate V_{peak} and V_{mean} of common carotid artery, and V_{peak} and V_{min} of common femoral artery. V_{mean} in the common femoral artery was calculated off-line using the equation $(\frac{1}{2}(\frac{1}{4}V_{peak} + \frac{1}{6}V_{min}))$ (60 heart rate^{-1}).[10] Systolic (the largest) and diastolic (the smallest) vessel diameters of the common carotid artery and common femoral artery were measured three times off-line and averaged values were calculated.

Blood viscosity was measured with a rotational viscometer ($50\,s^{-1}$) (Emilia Rheometer, Reciprotor, Denmark). Calibration was performed with a physiologic solution (0.9% NaCl) before every measurement. All measurements were performed in duplicate by the same analyst and the two values were averaged.

Data analysis
Mean diameter (D_m) (cm) was calculated as ($\frac{1}{3}$ systolic diameter $+\frac{2}{3}$ diastolic diameter). Blood flow (1/min) was calculated as $V_{mean}\pi(\frac{1}{2}D_m)^2$. Peak wall shear stress (PWSS) in pascals was calculated as the V_{peak} (m/s) multiplied by four times blood viscosity (Pa s) and divided by the systolic diameter (m). Mean wall shear stress (MWSS) in pascals was obtained from the V_{mean} (m/s) multiplied by four times blood viscosity and divided by the D_m (m).

Statistical analysis
Differences in mean arterial diameter, blood flow and wall shear stress (PWSS and MWSS) in the common carotid artery and common femoral artery and in blood viscosity were assessed between the C and SB groups, and between the SCI and SB groups, using Student's *t*-tests for independent groups or Mann–Whitney test, depending on the presence of a normal distribution, which was verified by calculating skewness. All variables, except for blood flow and MWSR in common carotid artery and PWSS in common femoral artery, were normally distributed. *P*-values smaller than 0.05

Table 1 Subject characteristics

Group	*N*	*BM (kg)*	*Height (m)*	*BMI (kg/m^2)*	*Age (years)*	*TL (years)*
SB	6	78.8 (15)	1.56 (0.5)*	32.2 (5.6)*	40.2 (8.2)	40.2 (8.2)
SCI	14	71.5 (14)	1.82 (0.1)	21.6 (2.9)	36.3 (8.5)	10.0 (6.3)
C	10	70.8 (7.6)	1.78 (0.1)	22.6 (2.4)	34.0 (12)	—

Body mass (BM), body mass index (BMI) and time since lesion (TL) of the group with spina bifida (SB), the group with spinal cord injury (SCI) and control group (C) expressed as mean (SD). *$P<0.05$ from SCI and C.

were considered to indicate statistical significance. Results are expressed as mean ± SD.

Results

Height and body mass index were significantly different in SB compared with C and SCI. No significant differences were found in any of the other subject characteristics between the three groups (Table 1). Red blood cell velocity and diameter of the common carotid artery of one SB subject could not be measured. Therefore, the group characteristics of the common carotid artery were calculated for five instead of six SB subjects. Two subjects of the SCI group did not have a three-phasic spectrum in the common femoral artery. As a result, the used formula for off-line calculation was not applicable, and therefore V_{mean} of the common femoral artery could not be calculated for these two subjects.

Blood flow

Mean diameters of the common carotid artery and common femoral artery are smaller in SB than in C and SCI (Table 2, Figures 1a, 2a). No differences in blood flow in the common carotid artery were observed between any of the groups (Table 2, Figure 1a). In the common femoral artery, blood flow in SB was significantly lower compared with C and SCI (Table 2, Figure 2a).

V_{peak} in the common carotid artery was significantly higher in C (103.3 ± 23.5 cm/s) than in SB (73.9 ± 10.9 cm/s) and SCI (97.6 ± 15.4 cm/s). No significant differences were observed in V_{peak} in common femoral artery between SB (101.8 ± 26.0 cm/s), and C (86.6 ± 17.2 cm/s) and SCI (98.9 ± 28.0 cm/s). No differences were observed in V_{mean} in the common carotid artery or in the common femoral artery between SB (common carotid artery: 40.7 ± 8.8 cm/s; common femoral artery: 8.7 ± 3.4 cm/s), and C (common carotid artery: 40.0 ± 6.6 cm/s; common femoral artery: 7.2 ± 2.0 cm/s) and SCI (common carotid artery: 42.6 ± 8.7 cm/s; common femoral artery: 8.8 ± 3.6 cm/s).

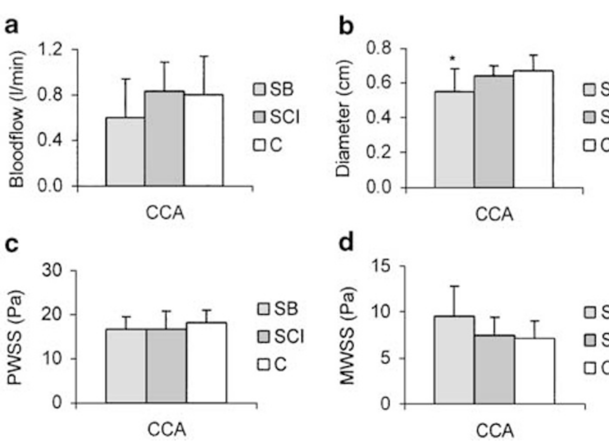

Figure 1 Blood flow (**a**), diameter (**b**), peak (**c**) and mean wall shear stress (**d**) in the common carotid artery (CCA) in spina bifida (SB), the group with spinal cord injury (SCI) and the control group (C). The error bars represent the standard deviation. $*P<0.05$ from SCI and C

Wall shear stress

Blood viscosity was not significantly different between SB (3.10 ± 0.49 Pa s) and C (2.96 ± 0.48 Pa s) or SCI (2.83 ± 0.56 Pa s). Duplo measurements of blood viscosity showed a relative error of 2%.

No differences were observed in PWSS and MWSS in the common carotid artery between SB (PWSS: 16.7 ± 2.9 Pa; MWSS: 9.56 ± 3.25 Pa), and C (PWSS: 18.2 ± 6.7 Pa; MWSS: 7.14 ± 1.89 Pa) and SCI (PWSS: 16.7 ± 4.22 Pa; MWSS: 7.5 ± 2.0 Pa) (Figure 1c, d). In the common femoral artery, PWSS and MWSS were higher in SB (PWSS: 20.8 ± 7.1 Pa; MWSS: 2.0 ± 0.7 Pa) and SCI (PWSS: 14.2 ± 3.9 Pa ($P>0.05$); MWSS: 1.4 ± 0.6 Pa ($P>0.05$)) than in the C group (PWSS: 10.2 ± 2.9 Pa ($P=0.002$); MWSS: 0.90 ± 0.3 Pa ($P=0.001$)) (Figure 2c, d). Shear stress values tended to be higher in SB compared with SCI.

Discussion

This is the first study to examine the vascular properties in the lower extremities of individuals with SB. We compared a group with SB with SCI by trauma and C. The main finding of this study is that deteriorating vascular properties (small diameter, low flow, high shear stress) are more pronounced in SB than in SCI and differ

Table 2 Blood flow and diameter

	Blood flow (l/min)		*Diameter (cm)*	
Group	*CCA*	*CFA*	*CCA*	*CFA*
SB	0.60 (0.34)	0.13 (0.05)*	0.55 (0.05)*	0.56 (0.09)*
SCI	0.83 (0.26)	0.20 (0.10)	0.64 (0.06)	0.71 (0.12)
C	0.88 (0.34)	0.31 (0.09)	0.67 (0.09)	0.96 (0.08)

Blood flow and mean diameter in the common carotid artery (CCA) and the common femoral artery (CFA) in the group with spina bifida (SB), the group with spinal cord injury (SCI) and the control group (C). Values are expressed as mean (SD). $*P<0.05$ from SCI and C.

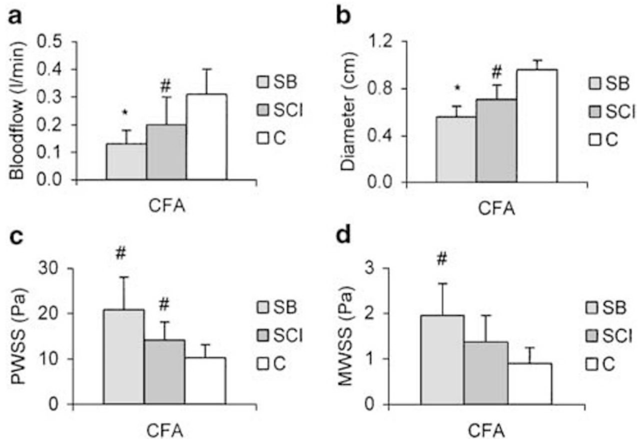

Figure 2 Blood flow (**a**), diameter (**b**), peak (**c**) and mean wall shear stress (**d**) in the common femoral artery (CFA) in spina bifida (SB), the group with spinal cord injury (SCI) and the control group (C). The error bars represent the standard deviation. $^{\#}P<0.05$ from C, $^{*}P<0.05$ from SCI and C

significantly from control values in able-bodied individuals.

Blood flow

The diameter of the common femoral artery was significantly lower in the SB group compared with the SCI and C groups. No other studies have examined arterial diameter in SB. Studies on SCI groups reported diameters of the common femoral artery between 5 and 7 mm in SCI,[1,11,12] and Sandgren *et al*[13] reported values between 8 and 10 mm for healthy human controls. Values found in the present study in SCI and C are in line with those studies. A previous study showed that the diameter of the common femoral artery was not significantly different between individuals with SCI with spastic or flaccid paralysis, which was again confirmed in the present study (SCI spastic, 0.66 ($n=9$) versus SCI flaccid, 0.63 ($n=5$)).[5] The smaller diameter in SB may be explained by the high level of muscle atrophy as well as the lack of proper development of the legs in SB, since the lesion existed from prebirth. The smaller height of the SB individuals may be an indication of this lack of development.

Blood flow of the common femoral artery in SB is significantly smaller than in SCI and C. Earlier studies reported lower blood flow in SCI than in C, which is confirmed in the present study ($P=0.004$).[1] It may be expected that the effects of paralysis and concomitant chronic inactivity, as well as the lack of development of the muscular and vascular system below the lesion level, are more pronounced in the SB group than in the SCI group, which may explain the even lower blood flow in SB. Low blood flow has been associated with poor wound healing and high incidence of pressure sores in SCI,[8,14] and may partly explain the high incidence of pressure sores (26%) in SB.[15] The diameter of the common carotid artery was significantly smaller in SB than in SCI and C. The diameter values of the common carotid artery in SCI and C are in agreement with previously reported results.[12,16–19] The smaller diameter in SB is not easy to explain, especially since this vessel represents the area above the lesion level and therefore we assumed that this vessel would not be affected. However, a study of Polak *et al*[20] showed a positive correlation between height and diameter of the common carotid artery, indicating that larger individuals have larger arterial lumen. Another possible explanation is the inactive lifestyle from birth on in SB and the retarded development of parts of the body may lead to overall adaptations in the circulation, reflected here in the common carotid artery.

Blood flow in the common carotid artery did not show significant differences between groups although a trend towards a lower flow in SB can be observed. This may be explained in analogy to the smaller diameter of common carotid artery in SB.

Wall shear stress

Blood viscosity showed no differences between the three groups. No earlier studies have measured blood viscosity in SB and SCI individuals. Owing to the different methods of measurement of blood viscosity, comparison of absolute values between studies is not always valid. Previous studies[21,22] reported blood viscosity values of 3.6 and 3.8 Pa s, whereas in the present study, with good relative errors of 2%, values between 2.5 and 4.3 Pa s were found.

PWSS and MWSS levels in common carotid artery did not show any difference between groups and are in agreement with earlier findings in a healthy population,[16,17,23] but in contrast, that is, markedly lower, with values of wall shear rate in the common carotid artery of healthy humans reported in another study.[18] This may be explained by the differences in methods to calculate red blood cell velocity using echo-Doppler. The inclusion of a double reference group (C and SCI), measured with the same technique and by the same examiner as in the present study, is therefore of great importance. In addition, the coefficient of variance for the measurement set up in this study, assessed in six subjects who were all measured twice within 2 weeks, was 6% (diameter) and 14% (shear stress) in the femoral artery and 6% (diameter) and 10% (shear stress) in the carotid artery, which includes physiological as well as physical variation. This reproducibility data are in line with values found by Demolis *et al*,[24] who reported a variation coefficient of 4–5% for the diameter and 10–12% for red blood cell velocity in the femoral and carotid arteries.

The higher wall shear stress levels in the femoral artery of SB compared with SCI and C may again be explained by the deteriorating circulatory adaptations to the lack of development because of the congenital spine defect and concomitant paralysis. The shear stress levels in SCI in the present study are higher than in C, which is in accordance with previously reported results.[11,25] The high shear stress levels in both SCI and SB may lead to endothelial cell damage and consequently to an early onset of endothelial dysfunction. Endothelial cell damage or dysfunction is widely regarded as a critical initiating factor in the development of atherosclerosis and many other vascular diseases.[26] Additional research is needed to assess the consequences of high shear stress levels on endothelial function and clinical outcome.

Conclusion

The present study demonstrates that deteriorating vascular properties (small diameter, low flow, high shear stress) are present in individuals with SB as well as in those with a SCI in comparison with the C group. These deteriorating properties tend to be more pronounced in SB than in SCI.

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