Comparing patients with spinal cord infarction and cerebral infarction: clinical characteristics, and short-term outcome

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Background: To compare the clinical characteristics, and short-term outcome of spinal cord infarction and cerebral infarction.

Methods: Risk factors, concomitant diseases, neurological deficits on admission, and short-term outcome were registered among 28 patients with spinal cord infarction and 1075 patients with cerebral infarction admitted to the Department of Neurology, Haukeland University Hospital, Bergen, Norway. Multivariate analyses were performed with location of stroke (cord or brain), neurological deficits on admission, and short-term outcome (both Barthel Index [BI] 1 week after symptom onset and discharge home or to other institution) as dependent variables.

Results: Multivariate analysis showed that patients with spinal cord infarction were younger, more often female, and less afflicted by hypertension and cardiac disease than patients with cerebral infarction. Functional score (BI) was lower among patients with spinal cord infarctions 1 week after onset of symptoms ($P < 0.001$). Odds ratio for being discharged home was $5.5$ for patients with spinal cord infarction compared to cerebral infarction after adjusting for BI scored 1 week after onset ($P = 0.019$).

Conclusion: Patients with spinal cord infarction have a risk factor profile that differs significantly from that of patients with cerebral infarction, although there are some parallels to cerebral infarction caused by atherosclerosis. Patients with spinal cord infarction were more likely to be discharged home when adjusting for early functional level on multivariate analysis.

Keywords: spinal cord infarction, cerebral infarction, risk factors, short-term outcome

Spinal cord infarction is caused by acute occlusion of the blood supply to the spinal cord resulting in myelopathy with related clinical neurological deficit symptoms. Compared to cerebral infarction, spinal cord infarction is a rare condition accounting for 1% of all strokes.$^{1-3}$

Unlike cerebral infarction, little is known about the causes and risk factors associated with spinal cord infarction. Many papers have been published on anterior spinal artery syndrome in relation to aneurysm of the aorta and spinal and other surgery procedures.$^{4,6}$ However, this does not reflect the realities in neurological departments, where most of spinal cord infarctions are treated and where the most typical spinal cord infarctions are spontaneous with no preceding surgery or aortic aneurysm.$^{1,2,7}$

The aim of this study was to compare the clinical characteristics, including risk factors, concomitant diseases, and short-term outcome, of spinal cord infarction with cerebral infarction based on patients admitted to our Department of Neurology. We hypothesized that there are important similarities between patients with spinal cord infarction and patients with cerebral infarction. If so, principles of treatment of cerebral
infarction are likely to be beneficial for patients with spinal cord infarctions.

Materials and methods

Patients with spinal cord infarction
Thirty-one patients were admitted because of spinal cord stroke at the Department of Neurology, Haukeland University Hospital, Bergen, Norway, in the period 1995–2010. Three (10%) patients had spinal cord hemorrhage and 28 (90%) patients had spinal cord infarction. Only patients with spinal cord infarction were included in the subsequent analyses. The diagnosis of spinal cord infarction was based on the following criteria, which excluded other causes of myelopathy such as trauma, compression, inflammation, and infection:

1. Clinical findings: acute clinical onset of neurological spinal cord deficit symptoms developing within minutes up to a few hours with no preceding trauma or infection, in a patient with no history of systemic or neurological autoimmune condition or chronic infectious disease.
2. Magnetic resonance imaging (MRI) findings: thorough MRI investigation of the spinal cord and spinal column, including T1, T2, eco-planar, short T-inversion recovery, gadolinium contrast enhancement, and in recent years diffusion weighted imaging, showing typical well-defined spinal cord lesion corresponding to spinal cord blood vessel territory with no signs of inflammation, edema, hemorrhage and no contrast enhancement, or normal initial MRI findings. Whenever indicated, patients were followed up by one to several MRI examinations to confirm their findings. Based on level of involvement, patients were also screened with cerebral MRI and vertebro-cerebral MRI angiography.
3. Cerebro-spinal fluid (CSF) findings: a spinal lumbar puncture was performed when not contraindicated followed by CSF examination showing no pleocytosis, negative isoelectric focusing, and no neuroborreliosis tested by ELISA and Western blot.

Laboratory investigation
All patients with spinal cord infarction underwent thorough routine serological and blood sample laboratory investigation on admission to our department, including hematologic parameters, hormones, blood coagulation parameters, liver, and renal function tests, electrolytes, glucose, albumin, cholesterol, inflammatory, and infection parameters. ECG was obtained in all patients. All patients had spinal cord MRI examination as described above. Patients had thoraco-abdominal CT scan or ultrasound examination of the aorta. Twenty-two patients underwent spinal lumbar puncture with CSF examination as described previously. None of these patients had elevated CSF leukocyte cell counts and none had oligoclonal bands in isoelectric focusing of the serum and CSF. None of the patients tested positive for neuroborreliosis in serum or CSF laboratory tests. Virological investigation of the CSF was not indicated in these patients since all had normal CSF cell counts.

CSF investigation was not carried out in seven patients: two patients woke up after surgery with typical clinical and MRI findings, and spinal lumbar puncture was contraindicated due to post-surgery low molecular heparin treatment. Three patients with typical clinical findings improved rapidly after ictus and a CSF investigation was therefore not indicated (one with a typical spinal cord MRI lesion and two with normal MRI findings). Two other patients had a rupturing aorta aneurysm where immediate surgery was needed and the cause of their spinal cord infarction was indisputable, hence there was no indication for CSF investigation.

Clinical evaluation
Patients underwent thorough medical history and risk factor investigation. Clinical neurological examination was done on a daily basis. Complete medical records were available for all patients. Blood pressure, temperature, ECG, and blood tests were obtained on admission. Patients were evaluated using National Institute of Health Stroke Scale (NIHSS) on admission, and Barthel Index (BI) and modified Rankin Scale score (mRS) 7 days after symptom onset.

Patients with cerebral infarction
In total, 1075 patients with acute cerebral infarction admitted to the Stroke Unit, Department of Neurology, Haukeland University Hospital between February 2006 and September 2009 were prospectively registered in a database (The Bergen Stroke Registry). Cerebral infarction was defined in accordance with the Baltimore-Washington Cooperative Young Stroke Study Criteria comprising neurological deficits lasting more than 24 hours because of ischemic lesions or transient ischemic attacks where CT or MRI showed infarctions related to the clinical findings.

Stroke severity on admission was assessed by the NIHSS score. ECG, blood pressure, body temperature, and blood sample including hematology, C-reactive protein (CRP), cholesterol, and electrolytes were obtained on admission.
Isolated acute ischemic lesions on CT or MRI were defined as lacunar infarctions (LI) if <1.5 cm and located subcortical or in the brainstem. All other acute ischemic lesions were defined as non-lacunar infarction. Non-lacunar infarction comprised subcortical and brainstem infarction $\geq 1.5$ cm, cortical infarction, mixed cortical and subcortical infarction, and cerebellar infarction.

Concomitant diseases and risk factors for patients with spinal cord infarction or cerebral infarction

Risk factors including hypertension, smoking, diabetes mellitus, myocardial infarction, angina pectoris, peripheral artery disease, and atrial fibrillation were registered on admittance. Hypertension was defined as prior use of antihypertensive medication. Current smoking was defined as smoking at least one cigarette per day. Diabetes mellitus was considered present if the patient was on glucose-lowering diet or medication. Angina pectoris, myocardial infarction, and peripheral artery disease were considered present if diagnosed by a physician any time before stroke onset. Atrial fibrillation required ECG confirmation any time prior to stroke onset. A history of prior cerebral infarction was registered.

Statistical analyses

Binominal test, Fisher’s exact test, Mann–Whitney test, and Student’s t-test were used when appropriate. Multiple logistic regression analyses and multiple linear regression analyses were performed to identify variables associated with stroke location (cerebrum or cord), neurological score on admission, and short-term outcome as detailed in the results. Age, NIHSS score, BI, mRS, glucose, and systolic blood pressure were treated as continuous variables whereas the other variables were dichotomized in the multivariate analyses. Variables of presumed biological importance were used as independent variables in the multivariate analyses. $P$ values $\leq 0.05$ were considered statistically significant.

Results

Table 1 shows characteristics of patients with spinal cord infarction and patients with cerebral infarction. Patients with spinal cord infarctions were younger (61.8 versus 70.6 years, $P = 0.002$). Patients with cerebral infarction had cardiac diseases more often (myocardial infarction, $P = 0.04$, and atrial fibrillation, $P = 0.06$). Hypertension ($P < 0.001$) and high systolic blood pressure on admission ($P < 0.001$) were more common among patients with cerebral infarction. There were no differences for diabetes mellitus, peripheral artery disease, prior cerebral infarction, and smoking. There was no difference in NIHSS score on admission between patients with spinal cord infarction and patients with cerebral infarction. Patients with spinal cord infarction scored significantly worse than patients with cerebral infarction on mRS score and BI 7 days after symptom onset. Median hospital stay before discharge home or to other institution was 9 days for patients with spinal cord infarction and 7 days for patients with cerebral infarction ($P = 0.05$).

Multiple logistic regression with spinal cord infarction versus cerebral infarction as dependent variable showed that spinal cord infarction was associated with females, young age, no hypertension, no atrial fibrillation, and high mRS score 7 days after symptom onset (Table 2).

### Table 1 Characteristics of patients with spinal cord infarction and patients with cerebral infarction

|                        | Spinal cord infarction | Cerebral infarction | $P$  |
|------------------------|------------------------|---------------------|------|
| N (%)                  |                        |                     |      |
| Females                | 16 (57.1)              | 462 (43.0)          | 0.18 |
| Prior cerebral infarction | 1 (3.6)              | 164 (15.3)          | 0.11 |
| Prior TIA              | 3 (10.7)               | 101 (9.4)           | 0.74 |
| Myocardial infarction  | 0 (0)                  | 135 (12.6)          | 0.04 |
| Angina pectoris        | 1 (3.6)                | 147 (13.7)          | 0.16 |
| Peripheral atherosclerosis | 2 (7.1)              | 82 (7.7)            | 1.00 |
| Hypertension           | 4 (14.3)               | 547 (51.1)          | <0.001 |
| Diabetes mellitus      | 4 (14.8)               | 150 (14.1)          | 0.76 |
| Atrial fibrillation    | 1 (3.6)                | 185 (17.3)          | 0.06 |
| Smoking                | 5 (17.9)               | 256 (23.8)          | 0.46 |
| Married                | 14 (51.9)              | 618 (58.8)          | 0.55 |
| Employed              | 12 (42.9)              | 282 (27.5)          | 0.09 |
| Discharged home        | 13 (46.4)              | 633 (58.9)          | 0.19 |

| Mean (SD)              | Mean (SD)              |                     |      |
| Age (years)            | 61.8 (20)              | 70.6 (14)           | 0.002 |
| Systolic blood pressure| 145 (26)               | 167 (32)            | <0.001 |
| Body temperature       | 36.9 (0.6)             | 36.5 (0.8)          | 0.02 |
| Serum glucose (mmol/L) | 6.7 (2.0)              | 6.8 (2.5)           | 0.80 |
| Hemoglobin (g/dL)      | 14.0 (1.1)             | 14.1 (1.6)          | 0.65 |
| Leucocytes (10$^9$/L)  | 8.2 (2.8)              | 8.7 (4.4)           | 0.56 |
| Creatinine (umol/L)    | 71 (16)                | 85 (31)             | 0.02 |
| Urate (umol/L)         | 268 (90)               | 347 (100)           | 0.01 |
| CRP (mg/L)             | 23 (55)                | 12 (29)             | 0.03 |
| Cholesterol (mmol/L)   | 5.9 (1.0)              | 5.4 (1.3)           | 0.18 |
| CK (U/L)               | 275 (500)              | 155 (297)           | 0.08 |
| NIHSS                  | 7.4 (3.7)              | 6.3 (7.0)           | 0.41 |
| mRS (day 7)            | 3.5 (1.5)              | 2.3 (1.6)           | <0.001 |
| Barthel Index (day 7)  | 44 (34)                | 79 (33)             | <0.001 |

Abbreviations: CK, creatine kinase; CRP, C-reactive protein; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; SD, standard deviation; TIA, transient ischemic attack.
Table 2 Logistic regression with spinal cord infarction versus cerebral infarction as dependent variable

|          | OR   | P     |
|----------|------|-------|
| Female   | 2.2  | 0.055 |
| Age      | 0.97 | 0.012 |
| Hypertension | 0.24 | 0.013 |
| Atrial fibrillation | 0.1  | 0.036 |
| Rankin score | 1.7  | <0.001 |

Abbreviation: OR, odds ratio in favor of spinal cord infarction.

Table 3 Linear regression with NIHSS score on admission as dependent variable

|          | Partial correlation | P     |
|----------|---------------------|-------|
| Sex      | −0.05               | 0.089 |
| Age      | 0.16                | <0.001|
| Systolic blood pressure | −0.19 | <0.001 |
| Glucose  | 0.12                | <0.001|
| Spinal cord infarction | 0.02 | 0.47   |

Note: *Versus cerebral infarction.
Abbreviation: NIHSS, National Institute of Health Stroke Scale.

Table 4 Linear regression with Barthel score after a week as dependent variable

|          | Partial correlation | P     |
|----------|---------------------|-------|
| Sex      | −0.003              | 0.91  |
| Age      | −0.23               | <0.001|
| NIHSS score on admittance | −0.66 | <0.001 |
| Spinal cord infarction | 0.22  | <0.001 |

Note: *Versus cerebral infarction.
Abbreviation: NIHSS, National Institute of Health Stroke Scale.

Table 5 Logistic regression with discharge home versus other institution as dependent variable

|          | Odds ratio | P     |
|----------|------------|-------|
| Age      | 0.99       | 0.15  |
| Sex      | 0.8        | 0.43  |
| Spinal cord infarction | 5.5      | 0.019 |
| Barthel Index | 1.1     | <0.001 |

Note: *Versus cerebral infarction.

Discussion

Our results suggest that there are important differences in risk factor profiles between patients with spinal cord infarction and patients with cerebral infarction. Patients with spinal cord infarctions were younger than patients with cerebral infarction and the frequency of females was higher among patients with spinal cord infarctions.1,2 Hypertension, an important risk factor for cerebral infarction,10 seems to be less important for patients with spinal cord infarctions. Univariate analyses comparing patients with spinal cord infarction and patients with lacunar stroke showed that patients with spinal cord infarctions were younger (61.8 versus 68.1 years, P = 0.037), had significantly less frequent hypertension (P < 0.001), and had lower blood pressure on admission (P < 0.001). There were no significant differences for diabetes mellitus, cardiac diseases, prior cerebral infarctions, peripheral artery disease, and smoking. Univariate analyses comparing patients with spinal cord infarction and patients with non-lacunar stroke showed that patients with spinal cord infarctions were younger (61.8 versus 68.5 years, P = 0.018), had significantly less hypertension (P < 0.001), had lower blood pressure on admission (P < 0.001), and had less frequent cardiac disease (myocardial infarction, P = 0.063, and atrial fibrillation, P = 0.006). There were no significant differences for diabetes mellitus, prior cerebral infarctions, peripheral artery disease, and smoking.

On univariate analyses, patients with spinal cord infarction had significantly lower creatinine and urate whereas CRP and creatinine kinase were significantly higher than in patients with cerebral infarction (Table 1). On logistic regression (with spinal cord infarction versus cerebral infarction as dependent variable) including sex and age these differences were no longer significant.

Linear regression with NIHSS score on admission as dependent variable showed that high NIHSS score (severe neurological deficits) was associated with high age, low systolic blood pressure, and high glucose on admission, but not with location of infarction (cord or brain) (Table 3).

Linear regression with BI 7 days after stroke onset as dependent variable showed that poor function (low BI) was significantly associated with high age, high NIHSS score on admission, and spinal cord infarction (Table 4).

In total, 13 (46.4%) patients with spinal cord infarction versus 633 (58.9%) with cerebral infarction were discharged home (P = 0.19). Table 5 shows logistic regression analysis with discharged home or not as dependent variable. Discharged home was associated with spinal cord infarction (odds ratio = 5.5; P = 0.019) when adjusting for BI 1 week after symptom onset.

Based on diffusion weighted MR imaging, 215 (27.4%) patients with cerebral infarction had lacunar stroke whereas 570 (72.6%) had non-lacunar stroke. Univariate analyses comparing patients with spinal cord infarction and patients with lacunar stroke showed that patients with spinal cord infarctions were younger (61.8 versus 68.1 years, P = 0.037), had significantly less frequent hypertension (P < 0.001), and had lower blood pressure on admission (P < 0.001). There were no significant differences for diabetes mellitus, cardiac diseases, prior cerebral infarctions, peripheral artery disease, and smoking. Univariate analyses comparing patients with spinal cord infarction and patients with non-lacunar stroke showed that patients with spinal cord infarctions were younger (61.8 versus 68.5 years, P = 0.018), had significantly less hypertension (P < 0.001), had lower blood pressure on admission (P < 0.001), and had less frequent cardiac disease (myocardial infarction, P = 0.063, and atrial fibrillation, P = 0.006). There were no significant differences for diabetes mellitus, prior cerebral infarctions, peripheral artery disease, and smoking.
less frequent among patients with spinal cord infarctions. However, there were no differences for diabetes mellitus, peripheral artery disease, smoking, and cholesterol. These are risk factors especially associated with atherosclerosis. Thus, a cautious interpretation of our findings is that spinal cord infarction is associated with atherosclerosis, but not with cardiac disease.

In addition to cardiac disease and atherosclerosis small vessel disease causing lacunar stroke is a frequent cause of cerebral infarction. One might hypothesize that small vessel disease is an important cause of spinal cord infarctions. However, except for low frequency of cardiac disease among patients with lacunar stroke, the characteristics of patients with lacunar strokes were more similar to those of patients with non-lacunar strokes than to those of patients with spinal cord infarctions. Thus, our data do not support that small vessel disease is an important cause of spinal cord infarction.

Multivariate analyses showed that severe neurological deficits on admission were associated with high age, low systolic blood pressure on admission, and high glucose, but not location of infarction (cord or brain). Studies including patients with cerebral infarction only, have shown that poor prognosis is associated with low blood pressure and high glucose on admission. Our data suggest that patients with spinal cord infarction should be treated in the same way as patients with cerebral infarction for blood pressure and glucose. Current guidelines recommend that cautious treatment should be considered if blood pressure is >220/120 mmHg and glucose >8.0 mmol/L in the acute phase of cerebral infarction.

One week after onset of symptoms, function was significantly worse among patients with spinal cord infarction. This was confirmed on multivariate analysis adjusting for neurological score on admission. A possible interpretation is that 1 week improvement is slower among patients with spinal cord infarction than in patients with cerebral infarction. However, on discharge there was no significant difference in the percentage going home. Others have found similar outcome after spinal cord infarction. Multivariate analysis showed that the odds ratio for going home was significantly higher among patients with spinal cord infarction than among patients with cerebral infarction when adjusting for early functional level (BI 1 week after symptom start). A possible explanation is that many patients with cerebral infarction have cognitive dysfunction, making discharge to home more difficult even though functional level as assessed by BI may be comparable. Another possibility is that patients with spinal cord infarction have better functional progress after the first week in hospital. These possibilities need to be addressed in future studies.

One of the limitations of the present study is that spinal cord infarction was registered retrospectively. Another limitation is the low number of patients with spinal cord infarction. However, spinal cord infarction is rare and all published series have included similar numbers or less. One of the strengths of the present study is that all patients were admitted to the same neurological department and thus underwent similar investigations and treatment.

In conclusion, patients with spinal cord infarction have a risk factor profile that differs significantly from that of patients with cerebral infarction, although there are some parallels to cerebral infarction caused by atherosclerosis. Even though functional level early in the disease course was low among many patients with spinal cord infarction, more of these patients were discharged home than were patients with cerebral infarction with comparable function.

Disclosure
The authors declare no conflicts of interest.

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