Long-Term Outcome of Acute Spinal Cord Ischemia Syndrome

Krassen Nedeltchev, MD; Thomas J. Loher, MD; Frank Stepper, MD; Marcel Arnold, MD; Gerhard Schroth, MD; Heinrich P. Mattle, MD; Matthias Sturzenegger, MD

Background and Purpose—Current knowledge of long-term outcome in patients with acute spinal cord ischemia syndrome (ASCIS) is based on few studies with small sample sizes and <2 years’ follow-up. Therefore, we analyzed clinical features and outcome of all types of ASCIS to define predictors of recovery.

Methods—From January 1990 through October 2002, 57 patients with ASCIS were admitted to our center. Follow-up data were available for 54. Neurological syndrome and initial degree of impairment were defined according to American Spinal Injury Association (ASIA)/International Medical Society of Paraplegia criteria. Functional outcome was assessed by walking ability and bladder control.

Results—Mean age was 59.4 years; 29 were women; and mean follow-up was 4.5 years. The origin was atherosclerosis in 33.3%, aortic pathology in 15.8%, degenerative spine disease in 15.8%, cardiac embolism in 3.5%, systemic hypotension in 1.8%, epidural anesthesia in 1.8%, and cryptocgenic in 28%. The initial motor deficit was severe in 30% (ASIA grades A and B), moderate in 28% (ASIA C), and mild in 42% (ASIA D). At follow-up, 41% had regained full walking ability, 30% were able to walk with aids, 20% were wheelchair bound, and 9% had died. Severe initial impairment (ASIA A and B) and female sex were independent predictors of unfavorable outcome (P=0.012 and P=0.043).

Conclusions—Considering a broad spectrum of clinical presentations and origins, the outcome in our study was more favorable than in previous studies reporting on ASCIS subgroups with more severe initial deficits. (Stroke. 2004;35:560-565.)

Key Words: anterior spinal artery syndrome ■ outcome ■ spinal cord ischemia

Acut spineal cord ischemia syndrome (ASCIS) is rare, accounting for 5% to 8% of all acute myelopathies and 1% to 2% of all vascular neurological pathologies. It usually has been associated with an unfavorable prognosis. However, current knowledge of long-term outcome is based on few studies with small sample sizes. Previous reports either included heterogeneous acute myelopathies, of which ASCIS was a subgroup, or included highly selected patients such as those with an anterior spinal artery syndrome (ASAS). Only 2 studies reported factors that could predict the potential for functional recovery.

Aiming to define predictors of functional recovery, we analyzed initial clinical presentation and long-term outcome of patients with ASCIS.

Materials and Methods

The charts of all patients who had been admitted to our institution with the final diagnosis of ASCIS between January 1990 and October 2002 were reviewed. The diagnosis was based on (1) acute neurological deficit attributable to a spinal cord lesion; (2) spinal MRI findings that were typical for an ischemic lesion and/or excluded an alternative diagnosis such as extrinsic or intrinsic cord compression; and (3) exclusion of alternative causes such as vascular malformations, myelitis, or vasculitis by means of cerebrospinal fluid (CSF) examination or vascular (ultrasound and echocardiography) and laboratory studies.

Demographic Data, Origins, and Clinical Variables

Fifty-seven patients fulfilled the inclusion criteria. We assessed the following demographic data and clinical variables: age, sex, vascular risk factors, time of symptom onset, presumed origin, neurological syndrome, neurological level, and degrees of impairment at initial presentation and follow-up.

The following vascular risk factors were assessed: hypertension, defined as systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or both; diabetes mellitus, defined as symptoms of diabetes plus random blood glucose concentration >11 mmol/L or fasting blood glucose >7 mmol/L; cigarette smoking; hypercholesterolemia, defined as total venous plasma cholesterol concentration >5 mmol/L; and positive personal and family histories of cerebrovascular events.

We considered 7 etiological groups: (1) atherosclerosis: history of or findings indicating cerebral, coronary, or peripheral artery occlusive disease or presence of >2 vascular risk factors; (2) aortic pathologies: aortic aneurysms or aortic dissections, with or without...
surgery; (3) degenerative spine disease: at the level of the cord ischemia with the potential of radiculomedullary artery compression in patients without vascular risk factors; (4) cardiac source of embolism (eg, intermittent atrial fibrillation); (5) systemic hypotension; (6) epidural anesthesia (conditions 5 and 6 were considered possible etiologies if there was a clear temporal relationship to the onset of symptoms attributable to spinal cord lesions); and (7) no detectable origin (cryptogenic).

The clinical features of ASCIS were classified according to the International Standards for Neurological and Functional Classification of Spinal Cord Injury proposed by the American Spinal Injury Association (ASIA) and the International Medical Society of Paraplegia (IMSOP). The following clinical syndromes were distinguished: ASAS, posterior spinal artery syndrome (PSAS), Brown-Séquard syndrome (BSS), and complete spinal cord transection (CSCT). Neurological level was defined by the most caudal segment of the spinal cord with normal sensory and motor function on both sides. We divided the patients into 3 groups according to neurological level: cervical, thoracic, and lumbosacral. The initial degree of impairment was measured by the ASIA impairment scale (ASIA grades A, B, C, and D). In addition, we assessed the initial motor score, ie, the sum of the graded strength of the key muscles on a 6-point scale (0=full paralysis, 5=normal active movement). Finally, we evaluated the functional independence measure (FIM) in the acute phase.

MR Imaging
All patients underwent at least 1 spinal cord MRI on a 1.5-T MR system (Siemens). In the sagittal plane, T1-weighted fast spin-echo sequences with and without DTPA gadolinium and T2-weighted sequences were performed. T2-weighted sequences were also performed in the axial plane. In addition, 5 patients underwent an echo-planar diffusion-weighted MRI.

Laboratory Findings
We performed serum analyses, including routine laboratory tests and anti-nuclear and anti-cardiolipin antibodies. The following serologies were routinely performed: syphilis, Lyme borreliosis, HIV, cytomegalovirus, herpes simplex virus, varicella-zoster virus, enterovirus, Coxsackievirus A and B, adenovirus, and Epstein-Barr virus. A CSF analysis was done in all patients and included cell count, protein level, and electrophoresis. Serological tests of the CSF were performed when results were positive in the serum or when CSF cell count was increased.

Outcome Parameters
After obtaining approval from the local ethics committee to conduct the study, we sent a letter to all patients in which we described the aim of the study and the analyses we intended to perform with their personal data. Patients were asked to give their informed consent, and after obtaining it, we sent a form addressing questions on current mobility and bladder control. Finally, a structured telephone interview was performed to control the accuracy of the previous data. Outcome data could not be obtained from 3 patients because they had moved.

Clinical improvement was recognized if patients who had been completely dependent in the acute phase were able to walk with or without aids at follow-up or if patients who had been “modified dependent” in the acute phase reached full walking ability at follow-up.

Clinical outcome was assessed by 2 major aspects of functional recovery: mobility and bladder control. In terms of mobility, 3 outcome categories were considered: full walking ability, walking with aids, and wheelchair bound. For bladder control, patients were divided into 3 groups: normal, intermittently incontinent, or performing a self-catheterization or having a permanent catheter.

Statistical Analysis
Demographic data and time intervals are given as means and SD. The motor and FIM scores are given as medians. The Kruskal-Wallis test was used to compare differences between subpopulations for nominal variables. Ordinal data were analyzed by use of Spearman’s rho rank correlation. Values of P<0.05 were considered statistically significant. Logistic regression analysis including the variables that showed significant differences on univariate comparison was performed. To identify variables that might indicate a poor functional outcome, mobility at follow-up was dichotomized into wheelchair users and those able to walk.

Results
Demographic data, vascular risk factors, and origins of the initial sample of 57 patients are given in Table 1. The study population consisted of 28 men and 29 women. Their mean±SD age was 59.4±17 years (range, 16 to 92 years). Thirty-eight patients (67%) had at least 1 vascular risk factor; 18 patients (32%) had ≥2 vascular risk factors.

The most prevalent origin was atherosclerosis (33.3%), followed by aortic pathologies with or without surgery (15.8%) and degenerative spine disease (15.8%). Cardiac embolism, systemic hypotension, and epidural anesthesia were rare causes of spinal cord ischemia. In 17 patients (28%), the cause remained unclear.

The initial motor deficit was severe in 30% (ASIA grades A and B), moderate in 28% (ASIA C), and mild in 42% (ASIA D) (Table 2). The neurological syndrome was ASAS in 67%, BSS in 18%, CSCT in 12%, and PSAS in 3%. Of the 38 patients with ASAS, 10 (26%) had a severe (ASIA grade B), 14 (37%) had a moderate (ASIA grade C), and 14 (37%) had a mild motor deficit (ASIA grade D). PSAS was always associated with a mild motor deficit. BSS caused either a moderate (20%) or only a mild (80%) motor deficit. CSCT was always associated with a loss of motor and sensory functions below the neurological level (ASIA grade A).

The neurological level was cervical in 21%, thoracic in 39%, and lumbosacral in 40%. There was no association between the neurological level and the long-term outcome.
between neurological level and severity of neurological impairment (Table 2).

The first symptom was sensory in 36 patients (63%), motor in 20 patients (35%), and autonomic in 1 patient (2%). Initial symptoms were sudden and severe spinal (back) pain in 34 patients (60%), loss of bladder control in 33 (58%), and loss of bowel control in 21 (37%). The mean interval from symptom onset to symptom maximum was 7.8 ± 23 hours (median, 1 hour).

Spinal MRI performed within 21 days of symptom onset (median, 1 day) showed signal changes of the cord compatible with ischemia in 45%.

Outcome was assessed at a mean of 4.5 ± 4 years. During this period, 25 patients (46%) experienced clinical improvement (Table 3). Clinical improvement was less frequent in ASIA grade A (14%) than in ASIA grades B (50%), C (40%), and D (59%).

At follow-up, 41% of the patients had regained full walking ability, 30% were able to walk with aids, and 20% were wheelchair bound. The best clinical outcome was found in patients with ASIA grade D: 68% were able to walk without aids, 23% walked with aids, and only 4.5% used wheelchairs. ASIA grade A patients had the worst clinical outcome with regard to walking ability: 2 of 7 were able to

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### TABLE 2. Clinical Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ASIA Impairment Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial degree of impairment, n (%)</td>
<td>A (7) B (10) C (16) D (24) Total (57)</td>
</tr>
<tr>
<td>Neurological syndrome, n (%)</td>
<td></td>
</tr>
<tr>
<td>ASAS</td>
<td>0 (100) 10 (87.5) 14 (87.5) 14 (58.3) 38 (67)</td>
</tr>
<tr>
<td>PSAS</td>
<td>0 (0) 0 (0) 0 (2) 8 (3.3) 2 (3)</td>
</tr>
<tr>
<td>BSS</td>
<td>0 (0) 0 (2.1.5) 2 (12.5) 8 (33.3) 10 (18)</td>
</tr>
<tr>
<td>CSCT</td>
<td>7 (100) 0 (0) 0 (0) 0 (0) 7 (12)</td>
</tr>
<tr>
<td>Neurological level, n (%)</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>1 (14) 3 (30) 2 (12) 6 (25) 12 (21)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>4 (57) 2 (20) 7 (44) 9 (37.5) 22 (39)</td>
</tr>
<tr>
<td>Lumbosacral</td>
<td>2 (29) 5 (50) 7 (44) 9 (37.5) 23 (40)</td>
</tr>
<tr>
<td>First symptom, n (%)</td>
<td></td>
</tr>
<tr>
<td>Motor</td>
<td>1 (14) 2 (20) 9 (56) 8 (33.3) 20 (35)</td>
</tr>
<tr>
<td>Sensory</td>
<td>5 (71) 8 (80) 7 (44) 16 (66.6) 36 (63)</td>
</tr>
<tr>
<td>Autonomic</td>
<td>1 (14) ... ... ... 1 (2)</td>
</tr>
<tr>
<td>Mean (SD) time to maximum, h</td>
<td>1.4 (0.6) 4.2 (8) 13 (39) 7.8 (18) 7.8 (23)</td>
</tr>
<tr>
<td>Initial motor score (median)</td>
<td>50 62 74 89 75</td>
</tr>
<tr>
<td>Initial FIM (median)</td>
<td>70 70 76 99 77</td>
</tr>
</tbody>
</table>

---

### TABLE 3. Clinical Improvement and Functional Outcome at Follow-Up

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ASIA Impairment Scale*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) follow-up, y</td>
<td>A (n=7) B (n=10) C (n=15) D (n=22) Total (n=54)†</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>1 (14) ... 3 (20) 2 (9) 5 (9)</td>
</tr>
<tr>
<td>Clinical improvement, n (%)</td>
<td>1 (14) 5 (50) 6 (40) 13 (59) 25 (46)</td>
</tr>
<tr>
<td>Walking ability</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>... 3 (30) 4 (27) 15 (68) 22 (41)</td>
</tr>
<tr>
<td>Walk with aids</td>
<td>2 (29) 6 (60) 3 (20) 5 (23) 16 (30)</td>
</tr>
<tr>
<td>Use wheelchair users</td>
<td>4 (57) 1 (10) 5 (33) 1 (4.5) 11 (20)</td>
</tr>
<tr>
<td>Bladder control</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1 (14) 3 (30) 4 (27) 14 (64) 22 (41)</td>
</tr>
<tr>
<td>Intermittently incontinent</td>
<td>... 2 (20) 2 (13) 6 (27) 10 (19)</td>
</tr>
<tr>
<td>Catheterization</td>
<td>5 (71) 5 (50) 6 (40) 1 (5) 17 (31)</td>
</tr>
</tbody>
</table>

*Allocation to the corresponding grade of the ASIA impairment scale represents initial severity of the spinal cord injury.

†Follow-up data were available for 54 patients because 1 patient with ASIA grade C and 2 patients with ASIA grade D had moved without providing a new address.

‡Mortality was taken into account when percentages were calculated.
walk with aids, and 4 of 7 were wheelchair-bound. In a univariate model, walking ability at follow-up was associated with ASIA grade (P<0.001), initial motor score (P<0.001), neurological syndrome (P=0.003), and initial FIM score (P=0.006).

Outcome walking ability was not influenced by age, vascular risk factors, and time from symptom onset to symptom maximum.

Regarding bladder control, 41% had normal sphincter functions, 19% were intermittently incontinent, and 31% performed a self-catheterization or had a permanent indwelling catheter. We observed an association between bladder control and neurological syndrome, the sphincter function being more frequently altered in patients with ASAS and CSCT than in those with PSAS and BSS (P=0.023). Bladder control at follow-up correlated also with ASIA grade (P<0.001), initial motor score (P=0.002), and initial FIM score (P<0.001). Age, sex, vascular risk factors, neurological syndrome, and time from symptom onset to symptom maximum had no influence on bladder control at follow-up.

Logistic regression analyses showed that ASIA grades A and B (P=0.012) and female sex (P=0.043) were independent predictors of poor functional outcome.

**Discussion**

ASCIS is a rare syndrome. The frequency of ASCIS was 1.2% of all admissions for stroke to a community hospital during a 52-month period. In a rehabilitation center for spinal cord injuries, infarctions constituted 4.2% of all admissions. Because of the low incidence, knowledge of long-term outcome is based on few studies with small sample sizes and heterogeneous inclusion criteria.

Methodological differences make the comparison of previous studies difficult. In some series, ASCIS has been added to acute myelopathies of other origins. Other studies included only patients with ASAS or those who had spinal cord signal changes on MRI. The presumed origins varied considerably and in general reflected the referral patterns of the particular centers. Clinical approaches differed even within a study. MRI was routinely performed only in studies from the last decade. Follow-up time varied from 6 months to <2 years on average (Table 4). The definitions of improvement and outcome, even though always encompassing motor function, walking ability, and sphincter control, were also heterogeneous.

Regarding origin, atherosclerosis was presumed in 33.3% of our series. Atherosclerotic changes in the arteries supplying the spinal cord are rarely diagnosed because spinal angiography is not a routine diagnostic examination. Therefore, we considered an atherosclerotic origin if cerebral, coronary, or peripheral arteries were affected or if there were multiple vascular risk factors. Such an approach is reasonable given the systemic character of atherosclerosis. Aortic pathology was the second most prevalent cause in our series. It was the leading cause in several previous studies (Table 4).

Because of a 3% to 5% risk of cord ischemia in aortic dissection and a 1% to 10% risk in aortic surgery, large vascular surgery centers see a certain number of patients with this complication. The origin “degenerative spine disease” is certainly disputable. The idea is that spondylotic vertebral spurs may compress spinal arteries (the Figure).

Whether this explanation alone is sufficient, given the extensive perimedullary collateral network, is difficult to prove in the individual case. There is a long list of rare causes associated with ASCIS, including cardiac embolism, decompression sickness, coagulopathy, spinal arteriovenous malformations, systemic hypotension, epidural anesthesia, radiation-induced vasculopathy, vasculitis, sympathetomy, gastrectomies, esophagectomy, and others. In 7% to 36.1%, the cause remains undefined. This number certainly depends on the type of diagnostic workup used. In our series, despite extensive workup, the cryptogenic group still made up 28%. Previous studies observed a more favorable outcome in

**Table 4. Clinical Characteristics and Outcome: A Comparison With Previous Studies**

<table>
<thead>
<tr>
<th>Source</th>
<th>Patients</th>
<th>Mean Follow-up</th>
<th>Most Frequent Origin, %</th>
<th>Neurological Syndrome, %</th>
<th>Severity of Initial Motor Deficit</th>
<th>Clinical Improvement, %</th>
<th>Outcome, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheshire et al</td>
<td>44</td>
<td>1.2 ± 2 y</td>
<td>Aortic pathology, 43</td>
<td>ASAS, 100</td>
<td>Unimproved, 24</td>
<td>Full walking ability, 11</td>
<td>Full, 22</td>
</tr>
<tr>
<td>Iseli et al</td>
<td>28</td>
<td>6 mo</td>
<td>Aortic pathology, 43</td>
<td>ASAS, 100</td>
<td>Significant ASIA motor score improvement</td>
<td>Full walking ability or ability to walk with aids, 25</td>
<td>Full, 25</td>
</tr>
<tr>
<td>de Seze et al</td>
<td>11</td>
<td>1 y</td>
<td>No data</td>
<td>ATM, 63</td>
<td>Severe, 100%</td>
<td>Able to walk with aids or wheelchair bound, 93</td>
<td>Able, 93</td>
</tr>
<tr>
<td>Salvador de la Barrera et al</td>
<td>36</td>
<td>19.9 ± 30 mo</td>
<td>Aortic pathology, 33.3</td>
<td>ASAS, 100</td>
<td>Unimproved, 52.8</td>
<td>Full walking ability, 18</td>
<td>Full, 18</td>
</tr>
<tr>
<td>Present study</td>
<td>57</td>
<td>4.5 ± 4 y</td>
<td>Atherosclerosis, 33.3</td>
<td>ASAS, 67</td>
<td>Unimproved, 45</td>
<td>Full walking ability, 41</td>
<td>Full, 41</td>
</tr>
</tbody>
</table>

ATM indicates acute transverse myelopathy; APTM, acute partial transverse myelopathy.
ischemic myelopathy of cryptogenic origin. However, the origin had no predictive value in our series.

The presenting clinical syndrome in this series was ASAS in 67%, BSS in 18%, CSCT in 12%, and PSAS in 3%. In a univariate model, the neurological syndrome was associated with clinical outcome, with ASAS and CSCT having worse prognoses. However, logistic regression analysis failed to confirm this result because of the interactions between the neurological syndrome and the degree of the initial impairment, with ASAS, for example, comprehensively having more severe neurological deficits than BSS. The considerably poorer prognosis of ASCIS in the study reported by Salvador de la Barrera et al., in which 57% were wheelchair bound after a mean follow-up of 20 months compared with 20% in our series after 4.5 years, is explained partly by patient selection. All patients in that study had ASAS.

An important step toward methodological standardization was the implementation of the ASIA/IMSOP criteria. With these criteria, the initial degree of impairment was severe in 30% (ASIA grades A and B), moderate in 28% (ASIA grade C), and mild in 42% of the patients (ASIA grade D). At follow-up, 41% had regained full walking ability, 30% were able to walk with aids, 20% were wheelchair bound, and 9% had died. Independent predictors of poor outcome were severe initial impairment (ASIA grade A and B) and female sex.

Four studies with sample sizes >10 patients have assessed the outcome of patients with ASCIS (Table 4). Two used the ASIA/IMSOP criteria. Clinical improvement and outcome were defined in a similar manner, assessing motor functions, walking ability, and sphincter control. MRI examinations were carried out in a considerable proportion of the patients.

Compared with the other 4 studies, the overall outcome in our series was clearly better. One explanation is the greater proportion of patients with a mild degree of initial deficits (ASIA grade D) in our series (42% compared with 19% in the study of Salvador de la Barrera et al.). This assumption is also in agreement with the lower mortality rate observed in our study (9% versus 22%).

As found by Iseli et al. and Salvador de la Barrera et al., initial severity of the impairment was the best predictor of functional recovery. Waters et al. observed a poor clinical outcome in patients with complete motor deficit persisting for >1 month, and Little et al. stated that the lack of an M-response from muscles, with motor neurons originating in cord segments caudal to the spinal cord injury upper level, predicts an unfavorable outcome.

In accordance with these observations, only 1 of the 7 patients (14%) with complete spinal cord transection (ie, ASIA grade A) showed improvement during follow-up. On the contrary, if sensory and/or motor functions were preserved in the sacral segments (ASIA grades B, C and D), clinical improvement was much more frequent (50%, 40%, and 59%, respectively). It seems that preservation of spinal cord functions below the neurological level, at least to some extent, is essential for the recovery process.

Female sex was another independent predictor of poor functional outcome in our series. The worse prognosis as a result of being female is surprising in view of experimental studies done over the past decade that show a lesser vulnerability of young adult female animals to cerebral ischemia. This has been shown to be due to the neuroprotective effects of estrogen and to some extent progesterone. It might be that after menopause the drop in neuroprotective female hormones results in a greater vulnerability than if the women never had estrogen and progesterone on which to rely.

Advanced age, which has been reported to correlate with poor outcome, did not have a prognostic value in our series.

In summary, the functional long-term outcome of ASCIS depends on the degree of the initial neurological deficits, especially motor deficits. Given the variety of presenting clinical syndromes and origins, the outcome of ASCIS in our study was better than previously reported.
Acknowledgments
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References
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