


Spontaneous spinal cord infarction in Austria: a two-center comparative study

Slaven Pikija, Alexander B. Kunz, Raffaele Nardone, Christian Enzinger, Johannes A.R. Pfaff, Eugen Trinkla, Thomas Seifert-Held* and Johann Sellner* 

Abstract

Background: Spinal cord infarction (SCI) is a neurological emergency associated with high rates of persistent neurological deficits. Knowledge about this rare but potentially treatable condition needs to be expanded.

Objective: To describe the characteristics of spontaneous SCI in a large retrospective series of patients treated at two tertiary care centers in Austria.

Methods: We performed a descriptive and comparative analysis of spontaneous SCI treated at the University Hospitals of Salzburg and Graz between the years 2000 and 2020. The analysis included pre- and in-hospital procedures, clinical presentation, etiology, diagnostic certainty, reperfusion therapy, and functional outcome at discharge.

Results: We identified 88 cases, 61% were ascertained in the second half of the study period. The median age was 65.5 years [interquartile range (IQR) = 56–74], 51.1% were women. Anterior spinal artery infarction was the predominant syndrome (82.9%). Demographics, vascular comorbidities, and clinical presentation did not differ between the centers. The most frequent etiology and level of diagnostic certainty were distinct, with atherosclerosis (50%) and definite SCI (42%), and unknown (52.5%) and probable SCI (60%) as front runners in Salzburg and Graz, respectively. Patients arrived after a median of 258.5 min (IQR = 110–528) at the emergency room. The first magnetic resonance imaging (MRI) of the spinal cord was performed after a median of 148 min (IQR = 90–312) from admission and was diagnostic for SCI in 45%. Two patients received intravenous thrombolysis (2.2%). The outcome was poor in 37/77 (48%).

Conclusion: Demographics, clinical syndromes, and quality benchmarks for spontaneous SCI were consistent at two Austrian tertiary care centers. Our findings provide the foundation for establishing standards for pre- and in-hospital care to improve outcomes.

Keywords: ischemic myelopathy, outcome, paraplegia, spinal cord infarction, stroke

Received: 11 November 2021; revised manuscript accepted: 7 January 2022.

Introduction

Spinal cord infarction (SCI) is among the infrequent causes of acute non-traumatic myelopathies and ischemic stroke.¹ The rarity can be explained, on one hand, by the high level of collaterals maintaining the vascular supply of the spinal cord.² On the other hand, spinal arteries are less susceptible to atheroma formation than their cerebral counterparts. Still, atherosclerosis is among the most frequent causes of spontaneous SCI.³ The spectrum of conditions leading to spontaneous SCI is broad; among the more frequent reasons are aortic

disease, systemic hypoperfusion, cardiogenic embolism, vertebral artery dissection, and pathologies of the spine.⁴ Spontaneous SCI needs to be distinguished from periprocedural SCI. Complications of aortic surgery, spinal decompression, and epidural steroid injection are among the more frequent causes of the latter.⁵

Abrupt onset of back and limb pain, which is usually located at the dermatomal level of the affected spinal cord, followed by the development of neurological symptoms, is the characteristic clinical

Ther Adv Neurol Disord

2022, Vol. 15: 1–14

DOI: 10.1177/
17562864211076321

© The Author(s), 2022.
Article reuse guidelines:
sagepub.com/journals-
permissions

Correspondence to:

Johann Sellner
Department of Neurology,
Landeskrankenhaus
Mistelbach-Gänserndorf,
Lichtensteinst. 67, 2130
Mistelbach, Austria.

Department of Neurology,
Christian Doppler Medical
Center, Paracelsus
Medical University,
Salzburg, Austria.

Department of Neurology,
Klinikum rechts der Isar,
Technische Universität
München, München,
Germany.

johann.sellner@mistelbach.lknoe.at

Slaven Pikija
Department of Neurology,
Christian Doppler Medical
Center, Paracelsus
Medical University,
Salzburg, Austria.

Alexander B. Kunz
Department of Neurology,
Christian Doppler Medical
Center, Paracelsus
Medical University,
Salzburg, Austria.

Karl Landsteiner Institute
for Neurorehabilitation
and Space Neurology,
Salzburg, Austria

Raffaele Nardone
Karl Landsteiner Institute
for Neurorehabilitation
and Space Neurology,
Salzburg, Austria

Department of Neurology,
Hospital of Merano
(SABES-ASDAA), Merano,
Italy; Spinal Cord Injury
and Tissue Regeneration
Center, Salzburg, Austria

Christian Enzinger
Department of Neurology,
Medical University of Graz,
Graz, Austria

Division of Neuroradiology,
Vascular and
Interventional Radiology,
Department of Radiology,
Medical University of Graz,
Graz, Austria

Johannes A.R. Pfaff
University Institute for
Neuroradiology, Christian
Doppler Medical Center,
Paracelsus Medical
University, Salzburg,
Austria

Eugen Trinka

Department of Neurology,
Christian Doppler Medical
Center, Paracelsus
Medical University,
Salzburg, Austria

Karl Landsteiner Institute
for Neurorehabilitation
and Space Neurology,
Salzburg, Austria

Neuroscience Institute,
Christian Doppler Medical
Center and Center for
Cognitive Neuroscience,
Paracelsus Medical
University, Salzburg,
Austria

Thomas Seifert-Held

Department of Neurology,
Medical University of Graz,
Graz, Austria

*Thomas Seifert-Held
and Johann Sellner
contributed equally.

manifestation of SCI.^{3,6,7} The neurologic presentation of SCI depends on the affected level of the spinal cord and vascular territory involved. The symptoms peak within the first 12h in four out of five patients.⁷ Transient ischemic attack (TIA) with rapid onset of severe myelopathic deficits followed by prompt resolution precedes spontaneous SCI in just 3% of the cases.⁸ Anterior spinal artery (ASA) syndrome is the most common clinical presentation characterized by pronounced motor and sensory deficits that develop abruptly or over a few to several hours. If the cervical cord is affected, all four limbs are involved, which may also be accompanied by respiratory compromise. The disability caused by spinal stroke is frequently severe and permanently disabling, with about half of the patients requiring gait aid.⁷ Significantly, the outcome is determined by the initial severity of neurological defects.⁶ Prognosis may be improved by treatment strategies translated from a cerebral stroke. This concept includes strategies directed at reperfusion, and however, the translation of stroke unit standards. Yet, the efforts are hampered by delayed hospital presentation and awareness of a potentially treatable condition.³ In addition, standardized and rapid exclusion of differentials is challenging. SCI is, therefore, a frequently under- and misdiagnosed condition. Thus, the introduction of diagnostic criteria for spontaneous SCI proposed by Zalewski in 2019 was well-received.⁷ Yet, inception studies in independent cohorts are lacking. Moreover, prior studies of SCI were monocentric and mainly incorporated small patient numbers, and a subsequent reporting bias is likely. Furthermore, only a few larger studies focused exclusively on spontaneous SCI and there is heterogeneity for the classification of the individual etiology of the condition.^{9–11}

This study aimed to analyze pre- and in-hospital procedures, clinical presentation, etiology, diagnostic certainty, reperfusion therapy, and functional outcome at the discharge of spontaneous SCI in two tertiary care centers in Austria.

Materials and methods

Study design and patient selection

We performed a retrospective study of patients admitted to the Departments of Neurology at Christian Doppler University Hospital and the Medical University of Graz. Both are tertiary care centers in Western and Southern Austria,

respectively. The study period included the years between 2000 and 2020, and searches within the institutional electronic patient record databases aimed to identify cases of spontaneous SCI. The search terms were SCI, spinal cord stroke, anterior spinal artery, posterior spinal artery, ischemic, and vascular myelopathy. We subsequently reviewed the data of all patients to verify the diagnosis. The ethics committee of Bundesland Salzburg evaluated and approved the study (415-EP/73/750-2017). Written informed consent was not required according to national regulations for the analysis of retrospective anonymized data.

Diagnostic criteria

We used the diagnostic criteria for spontaneous SCI proposed by Zalewski *et al.*⁷ These included ‘definite’ (1, 2A, 2B, 2C, 4), ‘probable’ (1, 2A, 2B, 3, 4), and ‘possible’ SCI (1, 4). The criteria are as follows:

1. Acute non-traumatic myelopathy with onset to the nadir of severe motor or sensory deficits within 12h;
2. MRI:
 - (a) No spinal cord compression;
 - (b) Supportive intramedullary T2-hyperintense spinal cord lesion;
 - (c) Specific (1 of): DWI/ADC restriction, vertebral body infarction, arterial dissection/occlusion adjacent to the lesion;
3. Cerebrospinal fluid (CSF): non-inflammatory (normal cell count, IgG Index within limits, no oligoclonal bands);
4. Exclusion of alternative diagnoses.

Spinal cord TIA was defined as acute myelopathy that lasted less than 24h in patients who made a full recovery. Paraplegia was classified as no movement of the lower extremities, and quadriplegia as no movement in all extremities.

Diagnostic workup: laboratory and CSF examination

A comprehensive diagnostic workup was undertaken at both centers. Brain and spinal cord magnetic resonance imaging (MRI) were mandatory investigations to ascertain the causal condition and exclude differentials. The examinations commonly included cervical CT or MR angiography, sonography of the carotid and vertebral arteries, thoracoabdominal CT or MR angiography, digital subtraction

angiography, spinal tap, and transthoracic/esophageal cardiac echocardiography. Metabolic, infectious, and autoimmune conditions were evaluated when deemed relevant. The investigations included serum levels of vitamin B12, copper, zinc, serology for syphilis, *Borrelia*, varicella-zoster virus, human immunodeficiency virus, human T-lymphotropic virus 1, antinuclear antibody, antibodies to extractable nuclear antigens, anti-cyclic citrullinated peptide, and antineutrophil and cytoplasmic antibodies. The vascular profile was evaluated by the study of coagulation parameters and antiphospholipid antibodies. Further serological exams included aquaporin-4/IgG and paraneoplastic antibodies. Some patients had electromyography/nerve conduction studies.

CSF evaluations included white blood cell count, red blood cell count, protein, glucose, and cytology. Further examinations, when deemed relevant, were testing for IgG index, oligoclonal bands, Gram stain, and bacterial culture, as well as appropriate examination to exclude neurological manifestations of syphilis and borreliosis, cryptococcal antigen, and angiotensin-converting enzyme. Further optional examinations were PCR for a varicella-zoster virus, Epstein–Barr virus, cytomegalovirus, enterovirus, and mycobacterium tuberculosis.

Clinical evaluation

The medical records were reviewed for age, sex, and time from onset to hospital admission. Further parameters of interest included motor deficits, presence of acute pain at neck, shoulder, scapula, chest, abdomen, and back; sensory level (the most caudal segment of the spinal cord with normal bilateral sensory functions); joint position sense and vibration tests; urine or stool retention; and acute respiratory failure requiring mechanical ventilator support.

Vascular risk factors

Vascular risk factors included hypertension defined as systolic blood pressure >140mmHg, diastolic blood pressure >90mmHg, or current use of anti-hypertensive medication; diabetes mellitus: symptoms of diabetes plus fasting blood glucose >126mg/dl and postprandial blood glucose >200mg/dl or current use of antidiabetic agents; hyperlipidemia: cholesterol >200mg/dl, triglyceride >150mg/dl, or use of lipid-lowering drugs; atrial fibrillation.

Previous stroke or TIA (clinical history and chart records); myocardial infarction (clinical history, chart records, and ECG); heart diseases (congestive heart failure, arrhythmia, and valvular heart disease); and cigarette smoking.

Assessment of etiology

The etiology adapted from the classification by Nedeltchev *et al.*:¹²

1. High risk of atherosclerosis: history or objective examinations indicating previous stroke or TIA, myocardial infarction, or multiple vascular risk factors;
2. Aortic disease: aortic aneurysm, dissection, or atheroma, with or without surgery;
3. Cardiac embolism;
4. Adjacent spinal disease/degenerative disease: coincident with spinal cord ischemia, which might be caused by spinal artery compromise in patients without multiple vascular risk factors;
5. Systemic hypotension;
6. Iatrogenic;
7. Unknown cause.

The category ‘undetermined’ was used if an examination was missed to classify for points 1–7.

MRI

The minimum requirements for spinal cord MRI were sagittal T1-weighted fast spin-echo sequences, sagittal T2-weighted images, and axial T2-weighted images at the lesion level. All images were re-examined. The spinal columns were evaluated for vertebral body infarction. The diagnosis of longitudinally extensive lesions required the presence of T2-hyperintensities expanding over three or more vertebral segments.

Definition of clinical syndromes

We distinguished anterior spinal artery (ASA), posterior spinal artery (PSA), and transverse SCI. Further options for ASA infarctions included anterior unilateral, anterior bilateral, and central cord involvement.

Outcome

The outcome was based on ambulation at discharge and dichotomized as good (able to walk

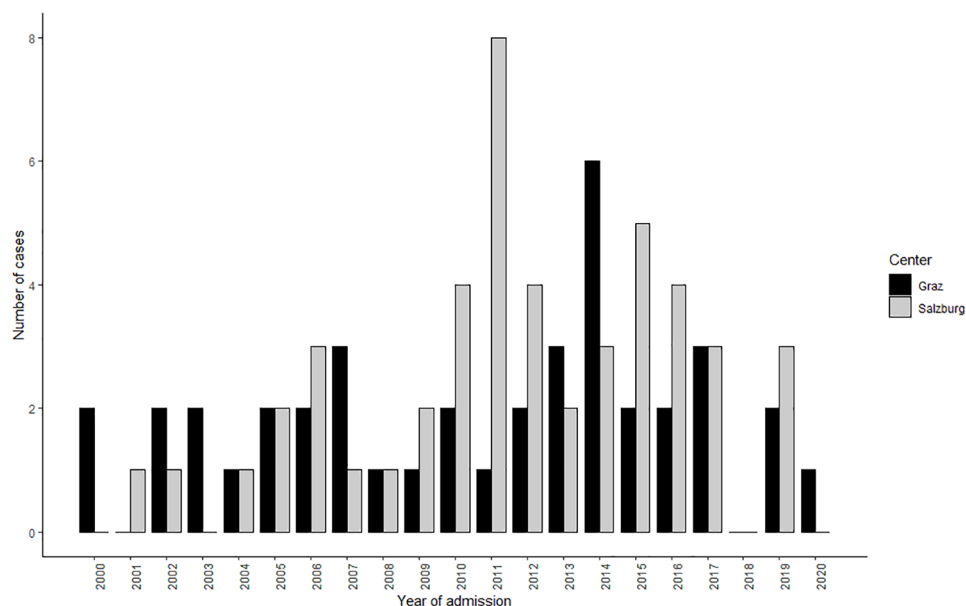


Figure 1. Number of cases with spontaneous SCI per year (2000–2020) treated at two Austrian tertiary centers: Salzburg ($N=48$) and Graz ($N=40$).

independently or with one aid) and poor (death, unable to walk, or able to walk with two aids).

Statistical analysis

We used the χ^2 test, with Yate's correction or Fisher's exact test, to compare qualitative variables and the non-parametric Kruskal–Wallis test to compare quantitative variables. Values of p less than 0.05 were considered statistically significant. The analysis was performed using STATA SE 13.0 for Windows (StataCorp LP, TX, USA).

Results

Patient demographics and hospital transfer

We identified a total of 96 patients. Excluded were four patients with spinal TIA and four in whom the time from symptom onset to imaging of the spine was more than 10 days (4.2% each).

In the study cohort of 88 patients, 48 (54%) patients were from the center in Salzburg. Thirty-nine patients from the Salzburg cohort were reported in a previous study. In addition, a subset of patients with PSA infarctions from Graz was summarized in a short communication.^{3,13}

The median age was 65.5 years [interquartile range (IQR) = 56–74], and 45 (51%) were women. There were no differences in demographics (age, gender) between Salzburg and Graz. The time trends for case identification revealed that 39% of cases were ascertained in the first and 61% in the second half of the study period (Figure 1). The annual patient numbers peaked in 2011 ($n=8$) in Salzburg and 2014 ($n=6$) in Graz. The exact time from symptom onset to hospital admission was available in 36 patients (40%). The median time (IQR) was 258 min (110–528) and did not differ between the centers.

Vascular risk factors

One or more vascular risk factors were present in 79 patients (82%). Most frequent were hypertension (69%), hyperlipidemia (33%), and diabetes mellitus (25%). There were no differences regarding the frequencies of these comorbidities between the two centers. However, a higher prior stroke and TIA rate were recorded in Salzburg (19% versus 2%). Further comparative details are shown in Table 1.

Etiology of SCI

There were eight different etiologies present in the Salzburg cases, whereas only four were in the

Table 1. Demographics, presumed etiology, and comorbidities of spontaneous spinal cord infarction..

	Entire cohort (N=88)	Salzburg (N=48)	Graz (N=40)	p-value
Age ^a , years (IQR)	65.5 (56.3–74.2)	67.9 (58.7–75.0)	62.0 (49.8–74.0)	0.200
Female gender (%)	45 (51.1)	17 (42.5)	26 (54.2)	0.293
Etiology (%)				< 0.001
Atherosclerosis	40 (45.5)	24 (50.0)	16 (40.0)	
Aortic pathology	5 (5.7)	4 (8.3)	1 (2.5)	
Degenerative spinal disease	5 (5.7)	5 (10.4)	0 (0.0)	
Cardiac embolism	3 (3.4)	3 (6.2)	0 (0.0)	
Iatrogenic	3 (3.4)	3 (6.2)	0 (0.0)	
Hypotension	2 (2.3)	2 (4.2)	0 (0.0)	
Vasculitis	1 (1.1)	0 (0.0)	1 (2.5)	
Dissection of the vertebral artery	1 (1.1)	1 (2.1)	0 (0.0)	
Various causes	1 (1.1)	0 (0.0)	1 (2.5)	
Unknown	27 (30.7)	6 (12.5)	21 (52.5)	
Vascular comorbidity (%)				
Hypertension	52 (59.1)	28 (58.3)	24 (60.0)	1.000
Diabetes	22 (25.0)	12 (25.0)	10 (25.0)	1.000
Angina pectoris/peripheral arterial occlusive disease	17 (19.3)	8 (16.7)	9 (22.5)	0.591
Hyperlipidemia	29 (33.0)	12 (25.0)	17 (42.5)	0.111
Medical history (%)				
Prior TIA/stroke	10 (11.4)	9 (18.8)	1 (2.5)	0.019
History of neoplasia	10 (11.4)	8 (16.7)	2 (5.0)	0.104
Number of vascular comorbidities				0.840
0	17 (19.3)	10 (20.8)	7 (17.5)	
1	28 (31.8)	15 (31.2)	13 (32.5)	
2	23 (26.1)	12 (25.0)	11 (27.5)	
3	16 (18.2)	9 (18.8)	7 (17.5)	
4	3 (3.4)	1 (2.1)	2 (5.0)	
5	1 (1.1)	1 (2.1)	0 (0.0)	
Time from symptom onset to hospital admission (min) ^b	258.5 (109.5–527.5)	225.0 (96.0–486.0)	315.0 (110.0–510.0)	0.657

IQR, interquartile range; TIA, transient ischemic attack.

^aMedian.^bDetails are missing in 52 patients (59%), which included 29 (60%) in Salzburg and 23 (57%) in Graz.

cohort from Graz. Although cases of aortic pathology, degenerative spine disease, hypotension, and iatrogenic made up a substantial proportion in the cohort from Salzburg (29%), this either was either rare (total 2% for aortic pathology) or absent (degenerative, cardiac, iatrogenic) in Graz. Atherosclerosis was the most common etiology in Salzburg (50%), whereas most frequently, the cause remained unknown in Graz (52.5%). The group of patients with unknown etiology was on average 8 years younger (median = 57 years, IQR = 45–69, $p=0.003$) when compared to the group with atherosclerotic pathogenesis (median = 69 years, IQR = 61–76) and other etiologies (median = 64 years, IQR = 53–75). Moreover, the rate of women was higher in the group with unknown etiology (67% versus 51% in the entire cohort, $p=0.115$).

Certainty according to diagnostic criteria

Applying the Zalewski *et al.*⁷ criteria, 32 (36%) were classified as definite, 35 (40%) probable, and 21 (24%) possible SCI. The diagnosis of definite SCI was more frequent in the Salzburg cohort than in Graz [20 (42%) versus 12 (30%)]. However, the cases classified as possible SCI were lower in Salzburg than in Graz [11 (23%) versus 24 (60%), $p<0.001$].

Clinical presentation and syndromes

Motor dysfunction was the most consistently found neurological impairment and present in 76 (86%). The pain was reported from 65% and localized adjacent to the level of the spinal cord lesion in 54 (61%). Sensory disturbances (paresthesia or dysesthesia) were noted by 60% of the patients. A stratification of clinical symptoms at presentation and etiology is shown in Table 2.

The predominant syndrome was bilateral ASA infarction (73%). The less frequent manifestations are illustrated in Table 3.

CSF and evoked potentials

A total of 64 patients (72%) underwent CSF examination. A pleocytosis was found in 4 patients (4%) and elevated CSF protein in 39/47 (83%). There was no case with the presence of CSF-specific oligoclonal bands. Evoked potentials were done in 31 (36%) of patients; the rates did not differ among the centers ($p=0.07$).

Neuroimaging

The details of in-hospital triage were reconstructed in 56 patients. The median time from admission to spinal cord MRI was 148 min (IQR = 90–312) and did not differ between the centers. Time to first MRI in the period from 2016–2020 (median = 127 min, IQR = 60–234) shortened by almost half an hour compared to the first 15 years of study (median = 155 min, IQR = 104–350).

Regardless of positivity on T2 or DWI sequences (radiological reports missing in 12% of patients), the first MRI was diagnostic for SCI in 40 (45%). An unremarkable neuroimaging result was reported in 29 (33%), whereas the remaining cases were rated as unspecific. A second MRI was performed in 70 patients (80%). At this examination, lesions (T2 or DWI) were defined as SCI in 42 (60%). The second MRI was specific for SCI in 19 (70%) patients with initially normal or unspecific MRI. In nine patients (13%), the second MRI did not show a spinal cord lesion. The median time from admission to the second MRI was 3 days (IQR = 2–5), $N=41/88$ (46%).

DWI was part of the first MRI exam of the spinal cord in 43 cases (49%). DWI positivity was present in 13 (30%). In the second MRI exam, DWI was used in 19 patients with a previously normal examination. In this group, 15/19 patients (78%) had newly appearing DWI lesions (i.e. DWI conversion). DWI positivity (first and second MRI combined) was more frequent in younger patients ($p=0.033$). The median age of patients with DWI positivity was 61 (IQR = 52–69) and 68 (59–75) without changes. Also, the chance of detecting a DWI lesion was higher in the isolated cervical spine (9/27, 33%) and combined thoracolumbar involvement (8/27, 30%) than in other localizations. There was a trend for a higher chance of DWI positivity later in the period, that is, after the year 2015; however, this observation was not statistically significant ($p=0.089$).

Spinal angiography was performed in 17 (19%) of patients. There was a non-significant difference between the centers for this exam (27% in Salzburg and 10% in Graz, $p=0.058$). One patient had a vertebral body infarction at the level of the sixth thoracic vertebra, which corresponded to the spinal infarction level.

Table 2. Spontaneous spinal cord infarction: clinical presentation and outcome with stratification according to etiology..

	Total N=88	Atherosclerosis, N = 40	Unknown, N = 27	Aortic pathology, N = 5	Degenerative spine disease, N = 5	Cardiac embolism, N = 3	Systemic hypotension, N = 2	Isatrogenic, N = 3	Undetermined, N = 1	Vasculitis, N = 1	Vertebral artery dissection, N = 1	p-value
Demographics												
Age ^a , years (IQR)	65.5 (56.3–74.2)	69.2 (61.0–76.0)	57.0 (45.5–69.0)	74.9 (51.6–75.3)	61.8 (58.2–64.0)	70.4 (70.2–77.2)	84.0 (83.2–84.7)	45.0 (33.0–58.7)	45	63	60	
Female gender	44 (51.1)	19 (47.5)	18 (66.7)	2 (40.0)	2 (40.0)	2 (66.7)	1 (50.0)	1 (33.3)	–	–	–	
Clinical presentation												
Motor dysfunction	76 (86.4)	34 (85.0)	25 (92.6)	4 (80.0)	4 (80.0)	2 (66.7)	1 (50.0)	3 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	0.524
Pain	57 (64.8)	29 (72.5)	20 (74.1)	1 (20.0)	5 (100.0)	–	–	–	1 (100.0)	1 (100.0)	–	< 0.001
Sensory dysfunction ^b	52 (59.8)	22 (55.0)	20 (74.1)	2 (50.0)	4 (80.0)	1 (33.3)	2 (100.0)	–	1 (100.0)	–	–	0.073
Autonomic dysfunction	47 (53.4)	18 (45.0)	20 (74.1)	3 (60.0)	1 (20.0)	2 (66.7)	–	1 (33.3)	1 (100.0)	1 (100.0)	–	0.057
Outcome on discharge ^c												
Good	40 (45.5)	18 (45.0)	13 (48.1)	1 (20.0)	3 (60.0)	–	–	2 (66.7)	1 (100.0)	1 (100.0)	1 (100.0)	0.052
Poor	37 (42.0)	17 (42.5)	14 (51.9)	2 (40.0)	1 (20.0)	1 (33.3)	1 (50.0)	1 (33.3)	–	–	–	
Unknown	11 (12.5)	5 (12.5)	–	2 (40.0)	1 (20.0)	2 (66.7)	1 (50.0)	–	–	–	–	
Mobility on discharge												
Able to walk with help	14 (15.9)	4 (10.0)	6 (22.2)	–	–	–	–	2 (66.7)	1 (100.0)	1 (100.0)	–	
Wheelchair	32 (36.4)	15 (37.5)	9 (33.3)	3 (60.0)	2 (40.0)	1 (33.3)	1 (50.0)	1 (33.3)	–	–	–	
Bedridden	11 (11.4)	5 (12.5)	5 (18.5)	–	1 (20.0)	–	–	–	–	–	–	
Self-ambulatory	18 (20.5)	9 (22.5)	7 (25.9)	–	1 (20.0)	–	–	–	–	–	1 (100.0)	
Unknown	13 (14.8)	7 (17.5)	–	2 (40.0)	1 (20.0)	2 (66.7)	1 (50.0)	–	–	–	–	
Additional outcome												
Autonomic failure	43 (52.4)	18 (46.2)	18 (78.3)	2 (50.0)	–	1 (33.3)	1 (50.0)	1 (33.3)	1 (100.0)	–	1 (100.0)	0.011
Therapy at discharge												
Antiplatelet versus other	71 (80.7)	33 (82.5)	23 (85.2)	4 (80.0)	4 (80.0)	1 (33.3)	2 (100.0)	2 (66.7)	0 (0.0)	1 (100.0)	1 (100.0)	0.307
IQR, interquartile range. Data are shown as n (%).												
^a Median.												
^b Sensory dysfunction: paresthesia or hypesthesia.												
^c Good was defined as able to walk independently or with one aid, and poor as death, unable to walk or able to walk with two aids.												

Table 3. Spontaneous spinal cord infarction: clinical syndromes and MRI findings stratified for etiology.

Clinical syndrome	Total N = 88	Atherosclerosis, N = 40	Unknown, N = 27	Aortic pathology, N = 5	Degenerative spine disease, N = 5	Cardiac embolism, N = 3	Systemic hypotension, N = 2	Isatrogenic, N = 3	Undetermined, N = 1	Vasculitis, N = 1	Vertebral artery dissection, N = 1
Bilateral anterior SA	64 (72.7)	26 (65.0)	23 (85.2)	3 (60.0)	3 (60.0)	3 (100.0)	2 (100.0)	3 (100.0)	1 (-)	-	-
Unilateral anterior SA	9 (10.2)	7 (17.5)	-	-	1 (20.0)	-	-	-	-	-	1 (-)
Bilateral PA	2 (2.3)	1 (2.5)	-	1 (20.0)	-	-	-	-	-	-	-
Unilateral PA	1 (1.1)	-	1 (3.7)	-	-	-	-	-	-	-	-
Central	6 (6.8)	4 (10.0)	-	-	1 (20.0)	-	-	-	-	1 (-)	-
Complete	6 (6.8)	2 (5.0)	3 (11.1)	1 (20.0)	-	-	-	-	-	-	-
MRI detection of lesion ^a											
Positive DWI, overall	27 (36.0)	11 (33.3)	7 (31.8)	3 (75.0)	1 (20.0)	1 (33.3)	-	2 (66.7)	1 (-)	-	1 (-)
Positive T2, overall	66 (76.7)	27 (71.1)	25 (92.6)	4 (80.0)	3 (60.0)	1 (33.3)	-	3 (100.0)	1 (-)	1 (-)	1 (-)
First MRI											
Specific	40 (45.5)	16 (40.0)	14 (51.9)	3 (60.0)	3 (60.0)	-	-	1 (33.3)	1 (-)	1 (-)	1 (-)
Non-specific	8 (9.1)	2 (5.0)	4 (14.8)	-	-	1 (33.3)	1 (50.0)	-	-	-	-
Normal	29 (33.0)	17 (42.5)	8 (29.6)	2 (40.0)	-	-	-	2 (66.7)	-	-	-
Unknown	11 (12.5)	5 (12.5)	1 (3.7)	-	2 (40.0)	2 (66.7)	1 (50.0)	-	-	-	-
Second MRI											
Specific	42 (60.0)	17 (53.1)	17 (85.0)	1 (25.0)	2 (50.0)	1 (33.3)	-	3 (100.0)	-	1 (-)	-
Non-specific	3 (4.3)	2 (6.2)	-	-	1 (25.0)	-	-	-	-	-	-
Normal	9 (12.9)	6 (18.8)	2 (10.0)	-	-	-	-	-	1 (-)	-	-
Unknown	16 (22.9)	7 (21.9)	1 (5.0)	3 (75.0)	1 (25.0)	2 (66.7)	2 (100.0)	-	-	-	-
Lesion distribution on MRI											
Cervical	16 (18.2)	7 (17.5)	6 (22.2)	1 (20.0)	1 (20.0)	-	-	-	-	-	1 (-)
Cervico-thoracal	5 (5.7)	1 (2.5)	3 (11.1)	-	1 (20.0)	-	-	-	-	-	-
Thoracal	14 (15.9)	9 (22.5)	2 (7.4)	1 (20.0)	-	-	-	2 (66.7)	-	-	-
Thoraco-lumbar	29 (33.0)	11 (27.5)	11 (40.7)	2 (40.0)	-	1 (33.3)	1 (50.0)	1 (33.3)	1 (-)	1 (-)	-
Lumbar	5 (5.7)	1 (2.5)	3 (11.1)	-	1 (20.0)	-	-	-	-	-	-
None	19 (21.6)	11 (27.5)	2 (7.4)	1 (20.0)	2 (40.0)	2 (66.7)	1 (50.0)	-	-	-	-

DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; PA, posterior spinal artery; SA, spinal artery.

^aDWI was not done in 45 (51%) first MRIs and in 53 (74%) second MRIs (16 patients without second MRI). First MRI data missing for T2 in 11 (12%) and for second MRI in 34 (39%).

First MRI: a combined analysis of T2 and DWI

The presence of SCI-specific findings in the first MRI (including those with DWI positivity) in the cohort of 77 patients was significantly associated with motor symptoms compared to patients with unspecific or normal MRI findings ($p=0.004$). The most common spinal MRI localization with SCI-specific findings on the first MRI was the combined thoracolumbar region (40%). In addition, the most common presentation of motor deficits in patients with SCI-specific MRI findings was monoparesis (42%), whereas the least common was paraparesis (5%).

Time to hospital presentation and the location of the spinal cord lesion

The analysis of pre-hospital transfer times revealed that 17/36 (47.2%) presented at the ER within the potential time window for intravenous (IV) thrombolysis (< 4.5 h). The mean times did not differ between the centers (47% in Salzburg and 58% in Graz, $p=0.73$). DWI was positive in three patients (19%), arriving within 4.5 h, whereas SCI-specific findings employing positivity in either DWI or T2 were present in 6/17 (37%) patients.

IV thrombolysis

Two patients (2.2% of the entire cohort and 6% of patients with available time from symptom onset to arrival) received systemic IV thrombolysis. The cases were admitted within the 4.5 h time window, one each in Graz (initially assumed to be middle cerebral artery stroke syndrome) and Salzburg (initially processed as SCI). Patient #1 was a 57-year-old woman, she presented with an ASA syndrome and had a corresponding MRI lesion at the cervical level. The etiology was classified as unknown, and her outcome was poor (mRS = 5). Patient #2 was a 57-year-old man who had a clinical syndrome involving the anterior and posterior segment of the spinal cord, and repeat MRI did not show a lesion. The etiology was classified as atherosclerosis, and the outcome was good (mRS = 3).

Outcome

The outcome was studied at hospital discharge, and the exact clinical condition was available to 77 patients (88%). There were 40 cases (46%) with good outcomes and no differences between

the two centers. The rate of patients with unknown outcome was ten folds higher in Salzburg (21% *versus* 2%, $p=0.013$). Four patients died in hospital in the Salzburg cohort, contrasting one in Graz. Almost half of the patients had vegetative disturbances at discharge 39 (48%), most frequently with overlapping localization 19 (39%) and anterior artery syndrome 38 (78%). Eighteen patients (20%) were able to walk home at discharge, 14 (16%) needed help to ambulate, 32 (36%) were mobile with a wheelchair, and 11 (13%) were bedridden. The bedridden patients were significantly younger than other functional outcomes (age 57 years, IQR = 53–61 years *versus* 63, 55–73; $p=0.037$). Patients with cervical localization of the SCI had a good outcome, with seven patients (39%) fully ambulatory at discharge. Further details of the outcome concerning different etiologies are shown in Table 2.

One patient in the Graz cohort had recurrent SCI. He presented initially with paraparesis; DWI positivity was located at the ASA territory and spanned from the Th10 to the L1 levels. The etiology was classified as unknown, presumably coagulopathy. At the end of his first hospitalization, he could walk with help and be discharged with anticoagulation therapy. The second event occurred five months later and involved the same spinal cord region.

Clinical outcome at discharge in relationship with localization and SCI syndrome

The combined analysis of MRI localization (eight categories) and SCI syndrome (seven categories) yielded 56 entities distributed over three outcome categories. Patients with cervical localization and anterior spinal cord syndrome ($n=12$, 14%) had the best prognosis, with 8/40 (20%) falling into the category of a good outcome. The worst outcome was observed with overlapping affection of the spinal cord (i.e. two or more segments in MRI) and ASA syndrome. In this subgroup, 15/37 (41%) had a poor outcome. Most of our patients were discharged with antiplatelet therapy, as shown in Table 2.

Discussion

This retrospective study of 88 patients with spontaneous SCI treated at two tertiary care centers in Austria over 20 years corroborates the current

understanding and extends the knowledge of this rare condition. In this cohort, 32 cases were classified as definite (36%), 35 as probable (40%), and 21 as possible spontaneous SCI (24%). The clinical presentation varies, and the classical apoplectic onset, presence of pain, and motor impairment may be missing in a subgroup of patients. While SCI is framed as a diagnosis of exclusion in the acute setting to be considered after eliminating alternative etiologies such as spinal cord compression, we found delays in hospital admission and workup. Furthermore, almost half of the patients had a poor outcome. In addition, we identified four cases of spinal cord TIA (4.2% of the entire cohort), which is in line with the 3% reported in the only comprehensive study on this topic so far.⁸

Most importantly, there were no site-related differences concerning age and gender. Our study confirms that spontaneous SCI, despite a significant heterogeneity in the etiology, is a disease at the transition from the end of middle to advanced age. The median age was 65.5 years, 51.5% of the patients were women. Our findings are mainly comparable to the prospective multi-center study in France study with 28 patients and a median age of 62 years (29% women), and the US American retrospective study with 102 patients and a median age of 60 years (53% women).^{6,7} The study period for the French study was January 2001 to January 2004 and for the monocentric US American series 1997 to 2017. A study from Taiwan reported that patients with dissection as the cause of SCI are younger than with other etiologies (39.8 versus 59.8 years).⁹ Of note, a series of 75 cases of procedural SCI reported a median age of 68 years.⁵ Our study summarizes patients diagnosed with spontaneous SCI between 2000 and 2020 and disclosed an increasing number of case identification after 2015. The reason for this observation remains speculative but may be related to a combination of increased awareness, consideration of SCI in elderly patients, and increasing availability of MRI. Transverse myelitis has been a significant differential of SCI, and misdiagnosis may have occurred less frequently.^{14,15} We need to acknowledge the change from 1.5 to 3 Tesla scanners throughout the study. Differences in the sensitivity of field strength to identify lesions related to SCI have not been studied so far but the analysis of lesions related to multiple sclerosis at 1.5 and 3 T did not reveal discrepancies.¹⁶ While we found an equal

distribution across gender, several recent series also confirmed a male predominance for spontaneous SCI. There might be a sample bias for these studies; the rate of women in a Spanish series of 41 patients, an Indian series of 17 patients, and a Korean series of 14 patients were 41.5%, 35.3%, and 42.9%, respectively.^{11,17,18}

In our series, patients without vascular comorbidities were in the minority (18%). The front runners among vascular risk factors were hypertension and hyperlipidemia. In the US American series, the rate of patients lacking vascular risk factors was even higher (24%).⁷ There were no differences between the sites for vascular comorbidities but a higher rate of prior stroke and a history of neoplasia in the Salzburg cohort. The finding of a distinct distribution of suspected etiologies at the two sites is interesting. This may be related to differences in the classification of the causative condition, as Graz had a predominance of cases with unknown etiology and the rate of patients with possible SCI was higher. The findings from Graz are in line with a recent study of 41 cases of spontaneous SCI, which classified the etiology as undetermined (29%), despite the presence of vascular comorbidities in 9/12 patients (75%).¹¹ This calls for the necessity to refine the etiological classification and subsequent inception studies. We also evidenced changes for the etiological classification in the scientific literature over time. In a Swiss study of 27 patients (study period between 1990 and 2003) and a Taiwanese study of 22 patients (1993–2007), the causative condition was not identifiable in 74% and 60%, respectively.^{19,20} These observations contrast our study, where we defined a cause in two-thirds of the cases. Fibrocartilaginous embolism (FCE) was the proposed etiology in a subgroup of patients in case series from the United States (5.5% and 14%, respectively).^{7,21} We did not classify FCE as the cause of SCI in our cohort, mostly due to the high rate of vascular comorbidities and prior cerebrovascular events. It needs to be acknowledged that the diagnostic criteria for FCE are inconsistent, and have not been evaluated in inception studies.^{21,22}

It is also likely that the rate of unclear etiologies further diminishes over time as rarer and less considered causes are considered in clinical practice. For instance, there is emerging evidence that degenerative cervical spondylosis is frequently overseen as a cause of SCI. Some authors assume

that dynamic cord compression may cause vascular redistribution phenomenon, leading to spinal cord ischemia.²³ The pathophysiology may be shared in part with surfer's myelopathy, a condition that develops in the aftermath of abrupt hyperextension.²⁴ Intersegmental artery dissection proximal to the artery of Adamkiewicz was reported recently as a cause of spontaneous SCI.²⁵ The diagnosis required catheter angiography, a procedure that was performed in less than one-fifth of our cohort.

As corroborated in our study, back or neck pain often adjacent to the level of the infarction accompanies spontaneous SCI. Two-thirds of the patients presented with bilateral ASA syndrome, mostly related to infarction in the thoracolumbar area. However, 14% of our patients did not have any motor dysfunction. Clinical presentations with isolated sensory disturbance and autonomic symptoms were noted in almost one-third of our patients. Thus, increased awareness for the clinical heterogeneity and the stuttering course of SCI in some patients might be required to assure rapid recognition of the potentially treatable condition and initiation of appropriate diagnostic measures. In this regard, almost every second initial MRI revealed SCI-specific findings. The remainder, however, had a normal spinal cord exam or unspecific findings, primarily due to susceptibility artifacts. The second MRI revealed SCI-specific findings in half of initially negative MRIs in our cohort. Physicians, therefore, need to be aware of this time gap where normal imaging findings can be expected in a substantial proportion. While a CT scan in acute cerebral stroke is used to rule out brain hemorrhage and other differentials but is insensitive for detecting early brain infarction, the translation to SCI might not be obvious. DWI was positive in only 30% of cases, and DWI conversion on the second MRI was observed in only 23% of initially DWI-negative patients. T2 positivity on the second scan occurred in substantially more cases (77%), supporting the use of this sequence as a primary imaging modality. In turn, further studies are required to assess whether the time-consuming DWI is obsolete in SCI. Younger age, cervical localization, and ASA syndrome was significantly associated with diagnostic MRI findings (including DWI positivity). Contrast-enhanced MRI is sometimes ordered in an acute setting and could obscure the diagnosis and hinder approaches toward reperfusion therapy when positive. Indeed, contrast-enhancing lesions are

relatively common in SCI (up to 39%). The enhancement pattern is rather typical, that is, a linear craniocaudal strip of enhancement.⁷ Furthermore, the median time from admission to MRI of the spine was 176 min needs to be emphasized. SCI is a neurological emergency and needs to be prioritized for rapid workup as this has been implemented for cerebral stroke.²⁶

If the brain stroke therapeutic paradigm can be translated to spontaneous SCI, most patients arrived at the ER beyond the theoretical therapeutic opportunity of 4.5 h for recanalization therapy. In contrast, 17 patients arrived within this potential therapeutic window. Two patients received IV thrombolysis in an off-label setting. Currently, there are just anecdotal reports on the use of alteplase in spontaneous SCI.²⁷⁻²⁹ Given the characteristic stuttering nature of clinical progress, one can conceive more penumbra to be salvaged when timely intervention ensues. With recent extensions of the thrombolytic therapeutic window for acute ischemic stroke for up to 9 h, based on advanced imaging, there is a chance that future studies could translate this paradigm to the treatment of SCI.²⁶ Certainly, aortic dissection, which accounted for SCI in 14% of the Chinese study patients and 6% in our cohort, is a clear contraindication for thrombolysis.²⁰ Whether IV thrombolysis is contraindicated with aortic aneurysm or intimal aortic wall bleeding as a potential cause of SCI is unclear. At the upper cervical level, vertebral dissection could cause SCI, as seen in one of our cases. This pathology is not a contraindication for IV thrombolysis in case of cerebral stroke. Of note, there is an ongoing clinical trial examining the safety and efficacy of IV thrombolysis in patients with ASA infarcts who present within 6 h from symptom onset (NCT02232084). There is also recent evidence for the feasibility of direct intra-arterial thrombolysis using selective angiography.³⁰ What are the practical considerations for possible thrombolytic administration in the setting of SCI? When the lesion is high (i.e. cervical) and there is no clinical evidence for aortic pathologies, such as pulse divergence and sharp interscapular pain, one could proceed with IV thrombolysis following exclusion of major differentials on spinal cord MRI. Whether tissue can be saved by reperfusion therapy in the presence of a T2 lesion in the spinal cord remains to be determined, and a T2/DWI mismatch concept may not be feasible in this setting. Furthermore, in case DWI and T2

are both negative, does this preclude the usage of recanalization therapies?

However, when the lesion is mid-thoracic, as in 44% in our cohort, there could be some chance of aortic pathology, and acute CT angiography should be ordered. Both CTA and MR angiography have a near 100% sensitivity and specificity for detecting major aortic pathologies such as aneurysm or dissection. However, MRA is better at imaging the aortic vessel wall that could benefit in evaluating a possible cause of SCI.³¹ From our experience, aortic pathology in the form of aortic vessel wall bleeding can be seen as a potential cause of SCI.

Hemodynamic augmentation would make sense but has not been investigated for spontaneous SCI in clinical trials.⁴ Studies with continuous intra-arterial blood pressure monitoring and sequential spinal cord MRI would be of value to understand the impact of the autonomic nervous system on the evolution of reversible tissue damage. Thus, the current management approach relies on risk factor modification, tailored secondary prevention, and symptomatic treatment.^{10,32} Admission to the intensive care unit (ICU) may be required in case of respiratory compromise, complications, and intensified pain treatment.³³ Given that most SCI is due to atherosclerotic pathology, secondary prevention for recurrent cerebrovascular events will be in line with brain stroke guidelines. Most of our patients received antiplatelet therapy.

Conclusion

Spontaneous SCI is a rare but often devastating disorder caused by a wide array of pathologic states. Our study disclosed the need for a harmonization of diagnostic procedures and inception studies for the classification of the cause. Moreover, concepts for therapeutic measures are eagerly awaited.

Acknowledgements

The authors thank all patients for participating in the study, and all the members of Neuroimmune Team in the Department of Neurology for various supports.

Author contributions

Slaven Pikija: Conceptualization; Data curation; Formal analysis; Investigation; Methodology;

Project administration; Visualization; Writing – original draft; Writing – review & editing.

Alexander Baden, Kunz: Formal analysis; Methodology; Writing – review & editing.

Raffaele Nardone: Formal analysis; Validation; Writing – review & editing.

Christian Enzinger: Formal analysis; Project administration; Writing – review & editing.

Johannes Pfaff: Formal analysis; Writing – review & editing.

Eugen Trink, MD, MSc: Formal analysis; Project administration; Writing – review & editing.

Thomas Seifert-Held: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Writing – original draft; Writing – review & editing.

Johann Sellner: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Writing – original draft; Writing – review & editing.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethics statement

The Local Ethics Committee evaluated and approved the study (415-EP/73/750-2017).

ORCID iD

Johann Sellner  <https://orcid.org/0000-0001-8749-5533>

Data sharing statement

Anonymized individual participant data collected for this study will be made available on reasonable request.

References

1. Heldner MR, Arnold M, Nedeltchev K, *et al.* Vascular diseases of the spinal cord: a review. *Curr Treat Options Neurol* 2012; 14: 509–520.

2. Kramer CL. Vascular disorders of the spinal cord. *Continuum* 2018; 24: 407–426.
3. Pikija S, Mutzenbach JS, Kunz AB, *et al.* Delayed hospital presentation and neuroimaging in non-surgical spinal cord infarction. *Front Neurol* 2017; 8: 143.
4. Nardone R, Pikija S, Mutzenbach JS, *et al.* Current and emerging treatment options for spinal cord ischemia. *Drug Discov Today* 2016; 21: 1632–1641.
5. Zalewski NL, Rabinstein AA, Krecke KN, *et al.* Spinal cord infarction: clinical and imaging insights from the periprocedural setting. *J Neurol Sci* 2018; 388: 162–167.
6. Masson C, Pruvo JP, Meder JF, *et al.* Spinal cord infarction: clinical and magnetic resonance imaging findings and short term outcome. *J Neurol Neurosurg Psychiatry* 2004; 75: 1431–1435.
7. Zalewski NL, Rabinstein AA, Krecke KN, *et al.* Characteristics of spontaneous spinal cord infarction and proposed diagnostic criteria. *JAMA Neurol* 2019; 76: 56–63.
8. English SW, Rabinstein AA, Flanagan EP, *et al.* Spinal cord transient ischemic attack: insights from a series of spontaneous spinal cord infarction. *Neurol Clin Pract* 2020; 10: 480–483.
9. Hsu JL, Cheng MY, Liao MF, *et al.* The etiologies and prognosis associated with spinal cord infarction. *Ann Clin Transl Neurol* 2019; 6: 1456–1464.
10. Nasr DM and Rabinstein A. Spinal cord infarcts: risk factors, management, and prognosis. *Curr Treat Options Neurol* 2017; 19: 28.
11. Ros Castillo V, Sanchez Sanchez A, Natera Villalba E, *et al.* Spinal cord infarction: aetiology, imaging findings, and prognostic factors in a series of 41 patients. *Neurologia*. Epub ahead of print 12 June 2021. DOI: 10.1016/j.nrleng.2020.11.004.
12. Nedeltchev K, Loher TJ, Stepper F, *et al.* Long-term outcome of acute spinal cord ischemia syndrome. *Stroke* 2004; 35: 560–565.
13. Struhal W, Seifert-Held T, Lahrmann H, *et al.* Clinical core symptoms of posterior spinal artery ischemia. *Eur Neurol* 2011; 65: 183–186.
14. Sellner J, Luthi N, Schupbach WM, *et al.* Diagnostic workup of patients with acute transverse myelitis: spectrum of clinical presentation, neuroimaging and laboratory findings. *Spinal Cord* 2009; 47: 312–317.
15. Zalewski NL, Flanagan EP and Keegan BM. Evaluation of idiopathic transverse myelitis revealing specific myelopathy diagnoses. *Neurology* 2018; 90: e96–e102.
16. Hagens MHJ, Burggraaff J, Kilsdonk ID, *et al.* Three-Tesla MRI does not improve the diagnosis of multiple sclerosis: a multicenter study. *Neurology* 2018; 91: e249–e257.
17. Park D, Kim BH, Lee SE, *et al.* Spinal cord infarction: a single center experience and the usefulness of evoked potential as an early diagnostic tool. *Front Neurol* 2020; 11: 563553.
18. Yadav N, Pendharkar H and Kulkarni GB. Spinal cord infarction: clinical and radiological features. *J Stroke Cerebrovasc Dis* 2018; 27: 2810–2821.
19. Novy J, Carruzzo A, Maeder P, *et al.* Spinal cord ischemia: clinical and imaging patterns, pathogenesis, and outcomes in 27 patients. *Arch Neurol* 2006; 63: 1113–1120.
20. Cheng MY, Lyu RK, Chang YJ, *et al.* Spinal cord infarction in Chinese patients. Clinical features, risk factors, imaging and prognosis. *Cerebrovasc Dis* 2008; 26: 502–508.
21. Mateen FJ, Monrad PA, Leep Hunderfund AN, *et al.* Clinically suspected fibrocartilaginous embolism: clinical characteristics, treatments, and outcomes. *Eur J Neurol* 2011; 18: 218–225.
22. AbdelRazek MA, Mowla A, Farooq S, *et al.* Fibrocartilaginous embolism: a comprehensive review of an under-studied cause of spinal cord infarction and proposed diagnostic criteria. *J Spinal Cord Med* 2016; 39: 146–154.
23. Stember DM, Hanson RM and Staudinger R. Spinal cord infarction in degenerative cervical spondylosis: an underdiagnosed phenomenon. *Neurol Clin Pract* 2020; 10: e33–e34.
24. Alva-Diaz C, Rodriguez-Lopez E, Lopez-Saavedra A, *et al.* Is Surfer's myelopathy an acute hyperextension-induced myelopathy? A systematic synthesis of case studies and proposed diagnostic criteria. *J Neurol*. Epub ahead of print 3 September 2021. DOI: 10.1007/s00415-021-10775-4.
25. Gailloud P, Deib G, Pearl MS, *et al.* Intersegmental artery dissection resulting in spinal infarction. *Neurol Clin Pract* 2020; 10: 535–537.
26. Berge E, Whiteley W, Audebert H, *et al.* European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *Eur Stroke J* 2021; 6: I–LXII.
27. Focke JK and Seitz R. Reversal of acute spinal cord ischemia by intravenous thrombolysis. *Neurol Clin Pract* 2021; 11: e975–e976.

28. Koch M, Sepp D, Prothmann S, *et al.* Systemic thrombolysis in anterior spinal artery syndrome: what has to be considered? *J Thromb Thrombolysis* 2016; 41: 511–513.
29. Etgen T and Hocherl C. Repeated early thrombolysis in cervical spinal cord ischemia. *J Thromb Thrombolysis* 2016; 42: 142–145.
30. Haynes J, Shapiro M, Raz E, *et al.* Intra-arterial thrombolytic therapy for acute anterior spinal artery stroke. *J Clin Neurosci* 2021; 84: 102–105.
31. Bhave NM, Nienaber CA, Clough RE, *et al.* Multimodality imaging of thoracic aortic diseases in adults. *JACC Cardiovasc Imaging* 2018; 11: 902–919.
32. Kleindorfer DO, Towfighi A, Chaturvedi S, *et al.* 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke* 2021; 52: e364–e467.
33. Grassner L, Marschallinger J, Dunser MW, *et al.* Nontraumatic spinal cord injury at the neurological intensive care unit: spectrum, causes of admission and predictors of mortality. *Ther Adv Neurol Disord* 2016; 9: 85–94.

Visit SAGE journals online
[journals.sagepub.com/
home/tan](https://journals.sagepub.com/home/tan)

 SAGE journals