Original Article

Association of splenic contraction with stroke severity and diabetes mellitus in patients with acute ischemic stroke

Seong Ju Jeon[1#^], Yeon Kyung Woo[1#^], Seung Jae Lee[2^], Byoung-Soo Shin[3^], Hyun Goo Kang[3^]

[1]Medical School, Jeonbuk National University, Jeonju, South Korea; [2]Department of Chemistry, Institute of Molecular Biology and Genetics, Jeonbuk National University, Jeonju, South Korea; [3]Department of Neurology, Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, South Korea

Contributions: (I) Conception and design: SJ Jeon, YK Woo, HG Kang; (II) Administrative support: HG Kang, BS Shin; (III) Provision of study materials or patients: HG Kang, BS Shin; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Hyun Goo Kang, MD, PhD. Department of Neurology, Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, 20 Geonji-ro, Deokjin-gu, Jeonju-si 54907, South Korea. Email: hgkang@jbnu.ac.kr.

Background: Splenic contraction (SC) is characterized by reduced splenic volume (SV) due to the release of splenocytes into systemic circulation. This study aimed to investigate the differences between patients with acute ischemic stroke with and without SC and identify SC-associated factors.

Methods: In this retrospective study, 79 patients with acute ischemic stroke who underwent abdominal computed tomography within 5 years before and within 7 days after stroke onset were analyzed. Patients were categorized into SC (SV change ≤–5 cm^3, n=39) and non-SC (SV change >0 cm^3, n=40) groups based on changes in SV. Clinical characteristics and laboratory findings were compared between the two groups. Multivariate logistic regression analysis was performed to identify independent factors associated with SC.

Results: The SC group had significantly higher National Institutes of Health Stroke Scale (NIHSS) scores on admission compared to the non-SC group {median 7 [interquartile range (IQR) 3–12] *vs.* 5 [IQR 2–9], P=0.025}. Diabetes mellitus (DM) was less prevalent in the SC group than in the non-SC group (35.9% *vs.* 62.5%, P=0.018). Multivariate analysis revealed that higher NIHSS scores at admission were independently associated with SC [adjusted odds ratio (aOR) 1.119, 95% confidence interval (CI): 1.001–1.252, P=0.048], whereas DM was associated with a lower risk of SC (aOR 0.278, 95% CI: 0.097–0.798, P=0.017).

Conclusions: Patients with SC demonstrated significantly higher admission NIHSS scores, suggesting that SC is associated with greater neurological deficits during the acute phase of ischemic stroke. DM was associated with a lower incidence of post-stroke SC, possibly due to DM-associated pathophysiology such as blunted sympathetic response or oxidative stress-induced splenic dysfunction. These findings emphasize the potential role of the spleen in stroke pathophysiology and highlight its potential as a therapeutic target.

Keywords: Diabetes mellitus (DM); ischemic stroke; neurological deficits; spleen; splenic contraction (SC)

^ ORCID: Seong Ju Jeon, 0000-0002-1593-8224; Yeon Kyung Woo, 0009-0008-8514-5626; Seung Jae Lee, 0000-0001-9471-6808; Byoung-Soo Shin, 0000-0002-3033-0014; Hyun Goo Kang, 0000-0001-5443-3635.

Submitted Aug 08, 2025. Accepted for publication Dec 24, 2025. This article was updated on Feb 25, 2026.
The original version is available at: https://dx.doi.org/10.21037/qims-2025-1725.
doi: 10.21037/qims-2025-1725

Introduction

Stroke is the second leading cause of death and the third leading cause of death and disability combined worldwide (1). At present, the standard treatment for ischemic stroke is reperfusion therapy; however, this approach is limited owing to its narrow therapeutic time window and restricted eligibility criteria (2-5), highlighting the need for alternative management strategies (6). In this context, immunotherapy targeting neuroinflammatory responses during post-stroke damage and recovery has garnered increasing attention.

The evidence of peripheral immune system activation and neurodegeneration following stroke is well established (7-10). Lymphoid organs, including the spleen, thymus, lymph nodes, bone marrow, and gastrointestinal tract, are important contributors to these immune responses. The spleen, the largest lymphoid organ, serves as a storage site for immune cells and plays a pivotal role in the immune response to stroke. Recent insights suggest that stroke pathophysiology functions as a multi-organ network involving the brain, spleen, immune system, and circulation. Concepts such as the "cardiosplenic axis", which describe the interplay between splenic status, hemodynamics, and prognosis in heart failure, suggest that splenic volume (SV) and function are modulated by complex mechanisms. These include not only sympathetic nerve activity but also humoral modulators (such as inflammatory cytokines and hormones) and hemodynamic changes (11-14). Following stroke, these systemic interactions precipitate the release of splenocytes from the spleen into the systemic circulation and their migration to the brain, resulting in reduced SV, a phenomenon known as splenic contraction (SC) (15-23). While SC is clinically associated with post-stroke neural injury (21,22), experimental studies provide evidence for its contribution to neurodegeneration (15-17,24-27). Specifically, in rodent models, splenectomy demonstrated a protective effect against stroke compared to non-splenectomized controls (18,25,26,28), suggesting that the spleen plays a role in exacerbating neural injury.

Based on the established relationship between stroke and SC, this study aimed to investigate the differences between patients with acute ischemic stroke with and without SC by measuring changes in SV, and to identify factors associated with SC. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-2025-1725/rc).

Methods

Study design and participants

We conducted a retrospective study of patients admitted to Jeonbuk National University Hospital with a diagnosis of acute ischemic stroke and measured their SV during admission using abdominal computed tomography (CT). All patients were Korean and had no history of splenic disease. Between November 2020 and February 2023, we screened 1,405 patients diagnosed with ischemic stroke. We included patients who had undergone abdominal CT prior to stroke and another scan within 7 days of stroke onset. To minimize age-related changes in SV, previous CT examinations were limited to those performed within 5 years before stroke onset. Of the included patients, 89 with sufficient image quality for SV measurements were selected as the final study population. SC was defined as an SV change ≤ -5 cm^3. Accordingly, 39 patients who met this criterion were assigned to the SC group, and 40 patients with an SV change >0 cm^3 were assigned to the non-SC group. Ten patients who did not fit into either group were excluded. A flowchart showing the selection of participants for this study is presented in *Figure 1*. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Institutional Review Board of Jeonbuk National University Hospital on June 12, 2024 (CHU 2024-05-057), and the requirement for informed consent was waived because of the retrospective nature of the study. All methods were performed in accordance with relevant journal guidelines and regulations.

Definitions and classification

The following clinical data were included in the analysis: age, sex, body mass index (BMI), onset-to-CT time, hypertension status, diabetes mellitus (DM) status, dyslipidemia status, atrial fibrillation (AF) status, ischemic heart disease status, congestive heart failure status, stroke history, National Institutes of Health Stroke Scale

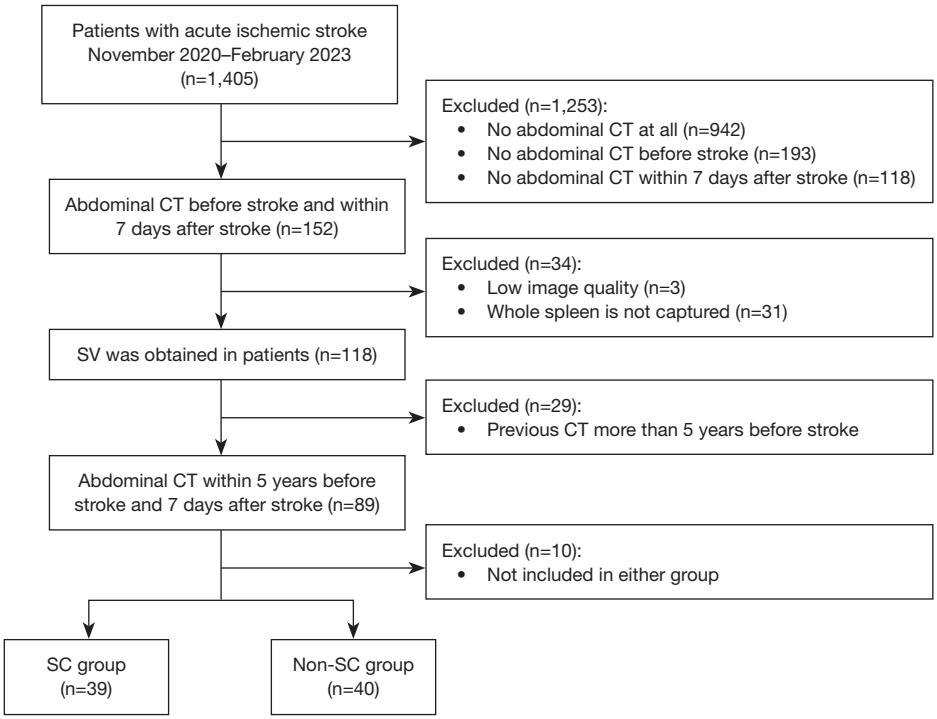

Figure 1 Flowchart showing the selection of study participants. SC group: SV change ≤–5 cm^3. Non-SC group: SV change >0 cm^3. SV change = (post-stroke SV) – (pre-stroke SV). Pre-stroke SV: SV measured before stroke. Post-stroke SV: SV measured within 7 days after stroke. CT, computed tomography; SC, splenic contraction; SV, splenic volume.

(NIHSS) scores at admission and discharge, and modified Rankin Scale (mRS) scores at 3 months after discharge. Hypertension was defined as a previous diagnosis of hypertension, persistent systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg. DM was defined as a previous diagnosis of DM, fasting blood glucose ≥126 mg/dL, or postprandial blood glucose ≥200 mg/dL within 2 h of admission. Dyslipidemia was defined as a previous diagnosis of dyslipidemia or low-density lipoprotein cholesterol ≥160 mg/dL; high-density lipoprotein cholesterol <40 mg/dL in men or <50 mg/dL in women; or triglycerides ≥175 mg/dL (29). Coronary artery disease was defined as a previous diagnosis of coronary artery disease or confirmation of angina or myocardial infarction via electrocardiography, stress myocardial perfusion imaging, exercise stress tests, echocardiography, or coronary angiography. AF was defined as a previous diagnosis of AF or confirmation of AF using electrocardiography. History of stroke was defined as a diagnosis of ischemic or hemorrhagic stroke prior to admission. Data extracted from blood tests performed after admission included total white blood cell (WBC) count, hemoglobin level, platelet count, neutrophil, lymphocyte, monocyte, eosinophil, and basophil counts (total and percentage values), D-dimer level, and hemoglobin A1c (HbA1c) level.

SV measurements

Measurements were performed using Infinitt PACS (Infinitt Healthcare Co., Seoul, South Korea). SV was directly measured and calculated from abdominal CT images. The measurements were performed by two well-trained authors (S.J.J. and Y.K.W.), with each CT measured three times, and the average value was used. In the case of discrepancies, an experienced neurologist (H.G.K.) reviewed the scans to provide a definitive interpretation. SV measurement was performed according to the method described by Prassopoulos *et al.* (30). As illustrated in *Figure 2*, the maximal width (W) was measured as the maximal diameter in the transverse section, and the maximal thickness (Th) was measured perpendicular to W, passing through the hilum. Splenic length (L) was calculated by multiplying

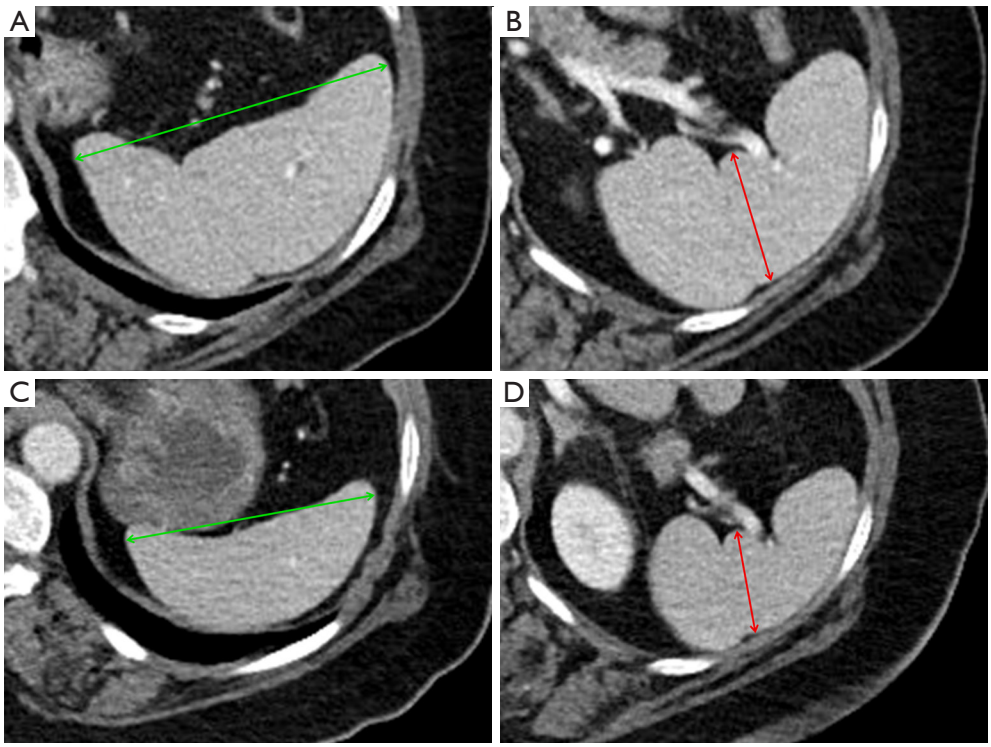

Figure 2 Measurement of SV in a representative case of a 64-year-old female patient. Abdominal CT scans were obtained 3 years prior to stroke onset (A,B) and 8 hours after stroke onset (C,D). Splenic measurements included maximal W (indicated by green arrows) in the transverse section (A,C) and maximal Th (indicated by red arrows) measured perpendicular to W in the section passing through the hilum (B,D). Pre-stroke measurements were: W =112.88 mm (A), Th =46.34 mm (B), and splenic L =120 mm, yielding a calculated SV of 394.07 cm^3. Post-stroke measurements were: W =94.66 mm (C), Th =39.23 mm (D), and L =105 mm, yielding a calculated SV of 256.15 cm^3. This represents a decrease of 137.92 cm^3 in SV following stroke, consistent with stroke-induced SC. CT, computed tomography; L, length; SC, splenic contraction; SV, splenic volume; Th, thickness; W, width.

the number of consecutive transverse CT sections by slice thickness. SV was calculated using the formula:

$$SV = 30 + 0.58(W \times L \times Th) \quad [1]$$

For each patient, the W and Th values were obtained from the same anatomical plane on the CT images when measuring the pre- and post-stroke SV.

Statistical analysis

First, patient demographics and laboratory findings were compared between the SC and non-SC groups. Pearson's Chi-squared test or Fisher's exact test was used for categorical variables, and a *t*-test was used for continuous variables. Second, multivariate analysis was performed to identify the independent factors associated with SC. To avoid variable selection caused by spurious correlations, only variables that showed a potential association (P<0.10) in univariate analysis were included as potential factors associated with SC in the multivariate logistic regression model. Statistical significance was set at P<0.05 (two-tailed). All statistical analyses were performed using SPSS 21.0 (IBM Corp., Armonk, NY, USA).

Results

In this study, we analyzed the demographic, clinical, and radiological characteristics of 79 patients with acute ischemic stroke (*Table 1*). Of these, 47 (59.5%) were male and 32 (40.5%) were female. The mean age was 75.0±10.03 years, and the mean BMI was 23.00±3.42 kg/m^2. The most common risk factor associated with stroke was hypertension, present in 59 patients (74.7%). This was followed by DM in 39 patients (49.4%) and dyslipidemia in 14 patients (17.7%).

Table 1 Clinical characteristics of the participants

Variables	Participants (n=79)
Sex (female)	32 (40.5)
Age ≥75 years	47 (59.5)
Age (years)	75.00±10.03
BMI (kg/m^2)	23.00±3.42
Hypertension	59 (74.7)
DM	39 (49.4)
Dyslipidemia	14 (17.7)
AF	21 (26.6)
Previous stroke	29 (36.7)
Ischemic heart disease	6 (7.6)
Congestive heart failure	3 (3.8)
Onset to CT time (min)	3,602.37±2,895.23
Pre-stroke SV (cm^3)	161.84±75.83
Post-stroke SV (cm^3)	163.31±84.61
SV change (cm^3)	1.47±47.72
SC group	39 (49.4)
NIHSS score at admission	6.84±4.98
NIHSS score at discharge	7.59±10.12
mRS score at 3 months	3.58±1.48
WBC (10^3/μL)	10.03±9.19
Hb (g/dL)	11.84±2.70
Platelet (10^3/μL)	244.22±100.81
Fibrinogen (mg/dL)	378.49±99.81
Neutrophil count (10^3/μL))	7.35±7.10
Lymphocyte count (10^3/μL)	1.55±0.73
Eosinophil count (10^3/μL)	0.19±0.64
Basophil count (10^3/μL)	0.05±0.07
Monocyte count (10^3/μL)	0.89±2.02
Neutrophil (%)	70.02±13.71
Lymphocyte (%)	19.48±11.11
Eosinophil (%)	2.00±4.71
Basophil (%)	0.50±0.31
Monocyte (%)	8.00±3.73
D-dimer (mg/L)	0.05±0.07
HbA1c (%)	6.51±1.44

Data are presented as number (%) or mean ± SD. SC: SV change ≤−5 cm^3. AF, atrial fibrillation; BMI, body mass index; CT, computed tomography; DM, diabetes mellitus; Hb, hemoglobin; HbA1c, hemoglobin A1c; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; SC, splenic contraction; SD, standard deviation; SV, splenic volume; WBC, white blood cell.

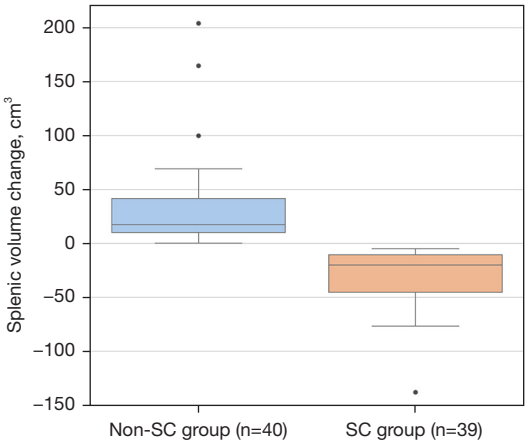

Figure 3 Box-and-whisker plot of SV change by group. The plot compares the distribution of SV change values between the non-SC group (n=40; SV change >0 cm^3) and the SC group (n=39; SV change ≤−5 cm^3). The horizontal line within each box indicates the median, the box represents the IQR, and the whiskers extend to 1.5 times the IQR. Outliers are indicated by black dots. IQR, interquartile range; SC, splenic contraction; SV, splenic volume.

Other notable risk factors included AF in 21 patients (26.6%), history of stroke in 29 patients (36.7%), ischemic heart disease in six patients (7.6%), and congestive heart failure in three patients (3.8%). Stroke severity evaluated using the NIHSS score at admission was 6 [interquartile range (IQR) 3–10], the NIHSS score at discharge was 4 (IQR 2–10), and the mRS score at 3 months post-discharge was 3 (IQR 3–4). In addition, the average time from stroke onset to CT imaging was 3,602.37±2,895.23 min. Radiological analysis of the CT findings revealed that the mean SV prior to stroke was 161.84±75.83 cm^3, and the mean post-stroke SV was 163.31±84.61 cm^3. The average change in SV before and after stroke was 1.47±47.72 cm^3.

The 79 patients were divided into the SC group (SV change ≤−5 cm^3) and non-SC group (SV change >0 cm^3) based on their SV change; a box-and-whisker plot visualizing the distribution of SV change values for these two groups is presented in *Figure 3*. The clinical and demographic characteristics of these groups were then compared (*Table 2*). The SC group showed a significantly higher proportion of female patients than the non-SC group (53.8% *vs.* 27.5%, P=0.017). In addition, the NIHSS score at admission was significantly higher in the SC group (median 7, IQR 3–12) than in the non-SC group (median 5, IQR 2–9, P=0.025). Conversely, the prevalence of DM was significantly lower in the SC group than in the non-SC

Table 2 Comparison of the clinical characteristics in patients with or without SC

Variables	SC (n=39)	Non-SC (n=40)	P value
Demographic and clinical factors			
Sex (female)	21 (53.8)	11 (27.5)	0.017
Age (years)	75.28±11.54	74.73±8.44	0.808
BMI (kg/m^2)	22.70±3.79	23.29±3.04	0.453
NIHSS score at admission	8.10±5.38	5.60±4.28	0.025
NIHSS score at discharge	7.51±7.77	7.68±12.08	0.944
mRS score at 3 months	3.59±1.53	3.56±1.46	0.939
Stroke risk factors			
Hypertension	30 (76.9)	29 (72.5)	0.651
DM	14 (35.9)	25 (62.5)	0.018
AF	15 (38.5)	6 (15.0)	0.018
Dyslipidemia	7 (17.9)	7 (17.5)	0.958
Previous stroke	17 (43.6)	12 (30.0)	0.210
Ischemic heart disease	3 (7.7)	3 (7.7)	1.000
Congestive heart failure	1 (2.6)	2 (5.1)	1.000
Laboratory findings			
WBC (10^3/μL)	9.21±3.71	10.83±12.41	0.437
Hb (g/dL)	11.65±2.94	12.02±2.46	0.541
Platelet (10^3/μL)	245.23±84.47	243.23±115.63	0.930
HbA1c (%)	6.03±0.94	6.96±1.68	0.005
Fibrinogen (mg/dL)	372.84±98.02	384.31±102.67	0.627
Neutrophil count (10^3/μL)	6.89±3.73	7.81±9.32	0.565
Lymphocyte count (10^3/μL)	1.53±0.67	1.57±0.79	0.793
Eosinophil count (10^3/μL)	0.09±0.09	0.28±0.89	0.181
Basophil count (10^3/μL)	0.04±0.02	0.06±0.10	0.187
Monocyte count (10^3/μL)	0.67±0.32	1.10±2.82	0.345
Neutrophil (%)	70.93±13.67	69.14±13.86	0.567
Lymphocyte (%)	19.50±11.29	19.46±11.07	0.988
Eosinophil (%)	1.26±1.52	2.72±6.40	0.193
Basophil (%)	0.46±0.27	0.55±0.35	0.754
Monocyte (%)	7.86±3.33	8.13±4.11	0.793
D-dimer (mg/L)	3.61±4.43	2.55±3.78	0.254

Data are presented as number (%) or mean ± SD. SC: splenic volume change ≤–5 cm^3. AF, atrial fibrillation; BMI, body mass index; DM, diabetes mellitus; Hb, hemoglobin; HbA1c, hemoglobin A1c; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; SC, splenic contraction; SD, standard deviation; WBC, white blood cell.

Table 3 Multivariate analysis of factors associated with SC

Variables	Univariate analysis		Multivariate analysis	
	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Female	3.076 (1.205–7.851)	0.019	1.556 (0.530–4.567)	0.421
NIHSS score at admission	1.114 (1.011–1.226)	0.029	1.119 (1.001–1.252)	0.048
DM	0.336 (0.135–0.839)	0.020	0.278 (0.097–0.798)	0.017
AF	3.542 (1.201–10.443)	0.022	2.502 (0.722–8.671)	0.148

SC: splenic volume change ≤–5 cm^3. AF, atrial fibrillation; CI, confidence interval; DM, diabetes mellitus; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SC, splenic contraction.

group (35.9% *vs.* 62.5%, P=0.018). The prevalence of AF was significantly higher in the SC group (38.5% *vs.* 15.0%, P=0.018). Regarding laboratory findings, HbA1c levels were significantly lower in the SC group than in the non-SC group (6.03±0.94 *vs.* 6.96±1.68, P=0.005).

Univariate and multivariate logistic regression analyses were performed to evaluate factors associated with SC (*Table 3*). In univariate analysis, female sex, NIHSS scores, DM, and AF were significantly associated with the occurrence of SC. However, in multivariate analysis, only the NIHSS score [adjusted odds ratio (aOR) 1.119, 95% confidence interval (CI): 1.001–1.252, P=0.048] and DM (aOR 0.278, 95% CI: 0.097–0.798, P=0.017) were identified as independent factors that significantly affected the occurrence of SC.

Discussion

Recent studies on the relationship between stroke and the immune system have made significant progress (7-10). However, our understanding of the mechanisms underlying this interaction is limited, highlighting the need for further studies. We selected the spleen, which is the largest lymphoid organ, as the research target to investigate the association between ischemic stroke and the immune system. The spleen allows for the quantitative evaluation of the immune response using SC. Furthermore, the impairment or removal of splenic function is associated with a relatively acceptable risk, as splenectomy has been widely performed in patients with hematological diseases and trauma (31). The well-established risks associated with splenectomy support the rationale for considering the spleen as a potential therapeutic target.

Previous animal studies have demonstrated the effects of the removal of splenic function through splenectomy on stroke. The groups that underwent splenectomy prior to ischemic stroke induction had smaller infarction volume (18,25,28), less immune cell infiltration such as microglia, macrophages, and neutrophils in brain parenchyma (18,28), lower IFNγ levels in brain parenchyma (18,25,26), and milder neurological deficits (26) compared with groups that did not undergo splenectomy. In contrast, adoptive splenocyte transfer after splenectomy eliminated the protective effects of splenectomy (26). These results suggest that the spleen plays a significant role in post-stroke immune responses, emphasizing the need for a further exploration of the relationship between the spleen and stroke.

In this study, we categorized patients with acute ischemic stroke into two groups based on the occurrence of SC and analyzed their characteristics. SC after stroke has been observed not only in animal studies (15-18) but also in clinical studies (19-23); it is caused by sympathetic nerve signaling and the release of splenocytes (27). Given these observations, several studies have investigated the effects of SC on stroke. In the present study, the NIHSS score at admission was significantly higher in the SC group than in the non-SC group. This finding is consistent with that of previous experimental studies (15-18,24-28), suggesting that SC contributes to brain damage caused by post-stroke immune responses. In a clinical study by Vahidy *et al.* (21), patients in the SC group presented with higher initial and mean serial NIHSS scores compared with those in the non-SC group. Nous *et al.* (22) reported that the SC group had higher NIHSS scores than the control group at admission and on the third day of hospitalization. Our study is concordant with these results, as the SC group showed greater neurological deficits at the time of admission (the acute phase). However, there was no significant difference in the NIHSS scores at discharge between the two groups. This pattern—where SC correlated with stroke severity

at admission but not at discharge—suggests that SC's contribution to neurological deficit may be largely confined to the acute phase. The correlation with initial severity likely reflects how sympathetic activation and subsequent splenocyte release drive immediate neuroinflammation and brain damage. Over time, however, other factors may become more influential in determining outcomes, including acute treatments such as tissue plasminogen activator, post-admission complications such as infections, or varying lengths of hospitalization. In addition, it is important to consider the potential role of the immune system not only in brain injury but also in the repair processes following stroke. Furthermore, our study showed that the mRS scores at 3 months were unrelated to post-stroke SC. These findings raise questions about whether SC affects long-term stroke severity and prognosis beyond the acute stage. Alternatively, the absence of significant correlations at later time points may represent a false negative due to our limited sample size. A larger, prospective study would be necessary to establish whether a long-term association also exists.

Moreover, there were no significant differences in the WBC and differential counts between the SC and non-SC groups. A previous clinical study showed that SC was associated with an increase in the total WBC count (19), whereas another study did not find a statistical relationship between the two (20). In addition, other clinical studies have reported an association between SC and lymphocytes, with some showing increased levels (20,23) and others showing decreased levels (22). Similarly, neutrophils have been observed to increase (19) or decrease (20,23) relative to SC. Thus, the results of WBC and differential counts in existing clinical studies, including ours, are inconsistent, which may be due to the different time points of WBC measurements. In animal experiments that clearly demonstrated the release of immune cells following SC, evaluations were performed using cell counts (17,18,24,26,28), proinflammatory cytokine/chemokine levels (15,18,24-26), and gene expression (15,16) in the spleen or brain parenchyma, which may be more sensitive and accurate indicators than blood cell counts. Similarly, in a clinical study by Vahidy *et al.* (21), blood pro-inflammatory cytokine levels, measured as indicators of the immune response, were significantly higher in the SC group than in the control group.

Recent research on the cardiosplenic axis highlights how hemodynamic disturbances can influence SV. In our study, AF was significantly more prevalent in the SC group (38.5% *vs.* 15.0%). Although AF did not remain significant in multivariate analysis, its high prevalence in the SC group aligns with the concept of the "cardiosplenic axis", where hemodynamic disturbances and congestion are known to influence SV (11-14). This suggests that AF may serve as a marker of shared pathophysiological mechanisms—such as heightened sympathetic activity, systemic inflammation, and hemodynamic instability—rather than acting as a sole independent driver of SC (32,33).

DM is associated with a high prevalence and recurrence of stroke, poor outcomes, and a high risk of death (34-37). We found that patients with DM had a lower incidence of SC than those without DM. The absence of SC may reduce immune response-related damage during stroke, which contradicts previous findings regarding the negative effect of DM on stroke. The reason for this apparent protective effect of DM against SC is likely multifactorial. First, post-stroke SC is primarily driven by sympathetic nerve signaling (27). It is well-established that patients with long-standing DM are at high risk for developing diabetic autonomic neuropathy, which can lead to a significant impairment in autonomic nervous system control (38-41). This reduced sympathetic drive may inhibit the spleen's ability to contract and mobilize immune cells (27,42-44) in response to the acute stress of an ischemic stroke. Second, the chronic state of DM facilitates the production of reactive oxygen species (ROS), leading to systemic oxidative stress (45). This oxidative stress can directly damage the immune system, including the splenic tissue, and impair its function (46-48).

This cumulative damage to the splenic parenchyma and microvasculature may reduce its contractile capacity, which is consistent with splenic atrophy previously observed in chronic diseases (46,48,49). However, past research on post-stroke SC has not found an association with DM (21,23). A distinguishing feature of our study was the measurement of baseline SV before stroke onset, allowing for direct comparison with post-stroke SV in the same patients. This methodology contrasts with previous studies that assessed SV after stroke and compared it with that in healthy volunteers (19,21,23). With these prior approaches, it is possible that splenic atrophy had occurred before stroke onset in patients with DM due to persistent oxidative stress (46,48,49). In such cases, patients without SC may have been misclassified as having SC, resulting in an insignificant relationship between DM and SC.

This study not only showed that SC can affect stroke severity but also demonstrated that patients with DM have a lower tendency to develop SC, which may result in a partially protective effect against stroke injury. This

relationship between DM and SC is noteworthy in the context of post-stroke therapeutic interventions. Several studies have proposed therapeutic strategies targeting the spleen, such as low-dose splenic irradiation (50), sympathetic nerve inhibitors (27,42), and stem cell administration (51). Our study suggests that DM may alter the efficacy of such interventions, making it a potentially critical factor in determining the optimal treatment strategy for individual patients.

This study had some limitations. First, the study participants were restricted to patients who underwent abdominal CT at a single institution, which may not be representative of the broader population of patients with stroke. Patients who underwent abdominal CT may have had specific clinical indications such as abdominal symptoms, suspected complications, or particular risk factors that prompted imaging, whereas patients without these features would not have been included. These underlying conditions or clinical characteristics could be associated with both SC and stroke severity, potentially introducing selection bias. However, considering that none of the patients were confirmed to have known splenic disease, the impact was considered limited. In addition, because this study was conducted retrospectively, it was not feasible to control all potential confounding variables that may have affected SC and stroke severity. For instance, the study did not differentiate between various ischemic stroke subtypes such as large artery atherosclerotic, cardioembolic, or lacunar strokes, which might have confounded the findings. Autonomic and immune responses may differ substantially depending on stroke subtype, as the underlying pathophysiological mechanisms, infarct locations, and tissue injury patterns vary. Future studies should investigate whether the relationship between SC and stroke severity differs across these subtypes, as this could provide insights into the mechanisms linking sympathetic activation, splenic immune response, and neurological outcomes. Furthermore, although this study analyzed the mRS scores 3 months after discharge for stroke prognosis, long-term follow-up data beyond that time point were not obtained. Moreover, the finding regarding the inverse association between DM and SC is based on a limited cohort size of 79 patients, meaning this relationship should be considered exploratory, requiring further investigation in significantly larger, prospective multicenter studies. Therefore, a prospective cohort study with a larger sample size is required to address these limitations. Lastly, we evaluated splenic function by measuring SC using CT images; however, a more accurate evaluation of splenic function could be achieved using methods such as scintigraphy with ^{99m}Tc-labelled, heat-altered erythrocytes (52).

Conclusions

We investigated the relationship between SC and acute ischemic stroke as well as the factors associated with SC. The SC group had significantly higher NIHSS scores at admission than the non-SC group, suggesting that SC contributes to the severity of neurological deficits in the acute phase of stroke. The presence of DM was associated with a lower incidence of post-stroke SC. This effect may be attributed to DM-associated pathophysiology, such as impaired autonomic reactivity, blunting the sympathetic stress response, or chronic oxidative stress-induced splenic dysfunction. In particular, the relationship between DM and SC warrants further investigation, as it may affect the efficacy of potential spleen-targeted therapies in patients with stroke and comorbid DM.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-2025-1725/rc

Data Sharing Statement: Available at https://qims.amegroups.com/article/view/10.21037/qims-2025-1725/dss

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-2025-1725/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Institutional Review Board of Jeonbuk National

University Hospital on June 12, 2024 (CHU 2024-05-057), and the requirement for informed consent was waived because of the retrospective nature of the study.

References

1. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, et al. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. Circulation 2023;147:e93-e621.
2. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2019;50:e344-418.
3. Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention: a systematic review. JAMA 2015;313:1451-62.
4. Cohen DL, Kearney R, Griffiths M, Nadesalingam V, Bathula R. Around 9% of patients with ischaemic stroke are suitable for thrombectomy. BMJ 2015;351:h4607.
5. Tawil SE, Cheripelli B, Huang X, Moreton F, Kalladka D, MacDougal NJ, McVerry F, Muir KW. How many stroke patients might be eligible for mechanical thrombectomy? Eur Stroke J 2016;1:264-71.
6. Marko M, Posekany A, Szabo S, Scharer S, Kiechl S, Knoflach M, Serles W, Ferrari J, Lang W, Sommer P, Greisenegger S; Austrian Stroke Unit Registry Collaborators. Trends of r-tPA (Recombinant Tissue-Type Plasminogen Activator) Treatment and Treatment-Influencing Factors in Acute Ischemic Stroke. Stroke 2020;51:1240-7.
7. Amantea D, Nappi G, Bernardi G, Bagetta G, Corasaniti MT. Post-ischemic brain damage: pathophysiology and role of inflammatory mediators. FEBS J 2009;276:13-26.
8. Anthony S, Cabantan D, Monsour M, Borlongan CV. Neuroinflammation, Stem Cells, and Stroke. Stroke 2022;53:1460-72.
9. Monsour M, Borlongan CV. The central role of peripheral inflammation in ischemic stroke. J Cereb Blood Flow Metab 2023;43:622-41.
10. Stephens R, Grainger JR, Smith CJ, Allan SM. Systemic innate myeloid responses to acute ischaemic and haemorrhagic stroke. Semin Immunopathol 2023;45:281-94.
11. Hiraiwa H, Okumura T, Sawamura A, Kondo T, Kazama S, Kimura Y, Shibata N, Arao Y, Oishi H, Kato H, Kuwayama T, Yamaguchi S, Furusawa K, Morimoto R, Murohara T. Spleen size improvement in advanced heart failure patients using a left ventricular assist device. Artif Organs 2020;44:700-8.
12. Hiraiwa H, Okumura T, Sawamura A, Araki T, Mizutani T, Kazama S, Kimura Y, Shibata N, Oishi H, Kuwayama T, Kondo T, Furusawa K, Morimoto R, Murohara T. Splenic size as an indicator of hemodynamics and prognosis in patients with heart failure. Heart Vessels 2022;37:1344-55.
13. Hiraiwa H, Okumura T, Murohara T. The cardiosplenic axis: the prognostic role of the spleen in heart failure. Heart Fail Rev 2022;27:2005-15.
14. Hiraiwa H, Yura Y, Okumura T, Murohara T. Interplay of the heart, spleen, and bone marrow in heart failure: the role of splenic extramedullary hematopoiesis. Heart Fail Rev 2024;29:1049-63.
15. Offner H, Subramanian S, Parker SM, Afentoulis ME, Vandenbark AA, Hurn PD. Experimental stroke induces massive, rapid activation of the peripheral immune system. J Cereb Blood Flow Metab 2006;26:654-65.
16. Bao Y, Kim E, Bhosle S, Mehta H, Cho S. A role for spleen monocytes in post-ischemic brain inflammation and injury. J Neuroinflammation 2010;7:92.
17. Offner H, Subramanian S, Parker SM, Wang C, Afentoulis ME, Lewis A, Vandenbark AA, Hurn PD. Splenic atrophy in experimental stroke is accompanied by increased regulatory T cells and circulating macrophages. J Immunol 2006;176:6523-31.
18. Seifert HA, Leonardo CC, Hall AA, Rowe DD, Collier LA, Benkovic SA, Willing AE, Pennypacker KR. The spleen contributes to stroke induced neurodegeneration through interferon gamma signaling. Metab Brain Dis 2012;27:131-41.
19. Sahota P, Vahidy F, Nguyen C, Bui TT, Yang B, Parsha K, Garrett J, Bambhroliya A, Barreto A, Grotta JC,

Aronowski J, Rahbar MH, Savitz S. Changes in spleen size in patients with acute ischemic stroke: a pilot observational study. Int J Stroke 2013;8:60-7.
20. Chiu NL, Kaiser B, Nguyen YV, Welbourne S, Lall C, Cramer SC. The Volume of the Spleen and Its Correlates after Acute Stroke. J Stroke Cerebrovasc Dis 2016;25:2958-61.
21. Vahidy FS, Parsha KN, Rahbar MH, Lee M, Bui TT, Nguyen C, Barreto AD, Bambhroliya AB, Sahota P, Yang B, Aronowski J, Savitz SI. Acute splenic responses in patients with ischemic stroke and intracerebral hemorrhage. J Cereb Blood Flow Metab 2016;36:1012-21.
22. Nous A, Peeters I, Nieboer K, Vanbinst AM, De Keyser J, De Raedt S. Post-stroke infections associated with spleen volume reduction: A pilot study. PLoS One 2020;15:e0232497.
23. Zha A, Vahidy F, Randhawa J, Parsha K, Bui T, Aronowski J, Savitz SI. Association Between Splenic Contraction and the Systemic Inflammatory Response After Acute Ischemic Stroke Varies with Age and Race. Transl Stroke Res 2018;9:484-92.
24. Seifert HA, Hall AA, Chapman CB, Collier LA, Willing AE, Pennypacker KR. A transient decrease in spleen size following stroke corresponds to splenocyte release into systemic circulation. J Neuroimmune Pharmacol 2012;7:1017-24.
25. Seifert HA, Collier LA, Chapman CB, Benkovic SA, Willing AE, Pennypacker KR. Pro-inflammatory interferon gamma signaling is directly associated with stroke induced neurodegeneration. J Neuroimmune Pharmacol 2014;9:679-89.
26. Jin R, Zhu X, Liu L, Nanda A, Granger DN, Li G. Simvastatin attenuates stroke-induced splenic atrophy and lung susceptibility to spontaneous bacterial infection in mice. Stroke 2013;44:1135-43.
27. Ajmo CT Jr, Collier LA, Leonardo CC, Hall AA, Green SM, Womble TA, Cuevas J, Willing AE, Pennypacker KR. Blockade of adrenoreceptors inhibits the splenic response to stroke. Exp Neurol 2009;218:47-55.
28. Ajmo CT Jr, Vernon DO, Collier L, Hall AA, Garbuzova-Davis S, Willing A, Pennypacker KR. The spleen contributes to stroke-induced neurodegeneration. J Neurosci Res 2008;86:2227-34.
29. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019;140:e563-95.
30. Prassopoulos P, Daskalogiannaki M, Raissaki M, Hatjidakis A, Gourtsoyiannis N. Determination of normal splenic volume on computed tomography in relation to age, gender and body habitus. Eur Radiol 1997;7:246-8.
31. Weledji EP. Benefits and risks of splenectomy. Int J Surg 2014;12:113-9.
32. Chen PS, Chen LS, Fishbein MC, Lin SF, Nattel S. Role of the autonomic nervous system in atrial fibrillation: pathophysiology and therapy. Circ Res 2014;114:1500-15.
33. Hu YF, Chen YJ, Lin YJ, Chen SA. Inflammation and the pathogenesis of atrial fibrillation. Nat Rev Cardiol 2015;12:230-43.
34. Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, Ingelsson E, Lawlor DA, Selvin E, Stampfer M, Stehouwer CD, Lewington S, Pennells L, Thompson A, Sattar N, White IR, Ray KK, Danesh J. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet 2010;375:2215-22.
35. Zhang L, Li X, Wolfe CDA, O'Connell MDL, Wang Y. Diabetes As an Independent Risk Factor for Stroke Recurrence in Ischemic Stroke Patients: An Updated Meta-Analysis. Neuroepidemiology 2021;55:427-35.
36. Zhu S, McClure LA, Lau H, Romero JR, White CL, Babikian V, Nguyen T, Benavente OR, Kase CS, Pikula A. Recurrent vascular events in lacunar stroke patients with metabolic syndrome and/or diabetes. Neurology 2015;85:935-41.
37. Echouffo-Tcheugui JB, Xu H, Matsouaka RA, Xian Y, Schwamm LH, Smith EE, Bhatt DL, Hernandez AF, Heidenreich PA, Fonarow GC. Diabetes and long-term outcomes of ischaemic stroke: findings from Get With The Guidelines-Stroke. Eur Heart J 2018;39:2376-86.
38. Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. Diabetes Care 2003;26:1553-79.
39. Balcıoğlu AS, Müderrisoğlu H. Diabetes and cardiac autonomic neuropathy: Clinical manifestations, cardiovascular consequences, diagnosis and treatment. World J Diabetes 2015;6:80-91.
40. Agashe S, Petak S. Cardiac Autonomic Neuropathy in Diabetes Mellitus. Methodist Debakey Cardiovasc J 2018;14:251-6.
41. Schmidt RE. Neuropathology and pathogenesis of diabetic autonomic neuropathy. Int Rev Neurobiol 2002;50:257-92.

42. Yan FL, Zhang JH. Role of the sympathetic nervous system and spleen in experimental stroke-induced immunodepression. Med Sci Monit 2014;20:2489-96.
43. Atef Y, Ito T, Masuda A, Kato Y, Nishimura A, Kanda Y, Kunisawa J, Kusakabe T, Nishida M. Diabetic Mice Spleen Vulnerability Contributes to Decreased Persistence of Antibody Production after SARS-CoV-2 Vaccine. Int J Mol Sci 2024;25:10379.
44. Vinik AI, Erbas T, Casellini CM. Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. J Diabetes Investig 2013;4:4-18.
45. Baynes JW. Role of oxidative stress in development of complications in diabetes. Diabetes 1991;40:405-12.
46. Konrad P, Forsgren A, Husberg BS, Nilsson L. The immunosuppressive effect of streptozotocin-induced diabetes in rats. Res Exp Med (Berl) 1986;186:455-62.
47. Manna P, Ghosh J, Das J, Sil PC. Streptozotocin induced activation of oxidative stress responsive splenic cell signaling pathways: protective role of arjunolic acid. Toxicol Appl Pharmacol 2010;244:114-29.
48. Sutradhar S, Deb A, Singh SS. Melatonin attenuates diabetes-induced oxidative stress in spleen and suppression of splenocyte proliferation in laboratory mice. Arch Physiol Biochem 2022;128:1401-12.
49. Orzechowski A, Ostaszewski P, Wilczak J, Jank M, Bałasińska B, Wareski P, Fuller J Jr. Rats with a glucocorticoid-induced catabolic state show symptoms of oxidative stress and spleen atrophy: the effects of age and recovery. J Vet Med A Physiol Pathol Clin Med 2002;49:256-63.
50. Ostrowski RP, Schulte RW, Nie Y, Ling T, Lee T, Manaenko A, Gridley DS, Zhang JH. Acute splenic irradiation reduces brain injury in the rat focal ischemic stroke model. Transl Stroke Res 2012;3:473-81.
51. Acosta SA, Tajiri N, Hoover J, Kaneko Y, Borlongan CV. Intravenous Bone Marrow Stem Cell Grafts Preferentially Migrate to Spleen and Abrogate Chronic Inflammation in Stroke. Stroke 2015;46:2616-27.
52. de Porto AP, Lammers AJ, Bennink RJ, ten Berge IJ, Speelman P, Hoekstra JB. Assessment of splenic function. Eur J Clin Microbiol Infect Dis 2010;29:1465-73.

Cite this article as: Jeon SJ, Woo YK, Lee SJ, Shin BS, Kang HG. Association of splenic contraction with stroke severity and diabetes mellitus in patients with acute ischemic stroke. Quant Imaging Med Surg 2026;16(2):117. doi: 10.21037/qims-2025-1725