Clinical Medicine & Research
Volume 24, Number 3: 114-122
©2026 Marshfield Clinic-Sanford Health
clinmedres.org

Original Research

Timing of Post-Stroke Seizures and Functional Outcomes: Exploring Gender-Based Disparities

Erum Shariff, MD; Nehad Soltan, MD; Danah AlJaafari, MD; Abdullah Saleh AlAmri, MD; Foziah Alshamrani, MD; Mohammed AlShurem, MD; Feras Alsulaiman, MD; Majed Alabdali, MD; and Anas Salman AlDahailan, MD

Background: Post-stroke complications significantly influence functional recovery, with seizures representing a critical determinant of poor outcomes. While acute symptomatic seizures (ASS) may reflect initial injury severity, remote symptomatic seizures (RSS) potentially exacerbate neurological damage. Emerging evidence suggests gender may modulate these relationships, though comprehensive studies remain limited.

Purpose: This study aimed to: (1) evaluate the impact of seizure timing (acute vs. remote), and (2) investigate gender-specific disparities in recovery patterns.

Methods: We conducted a retrospective case-control study (2018–2021) of 232 patients (116 post-stroke seizure [PSS], 116 controls) matched by age, gender, and stroke type. Stroke severity was assessed using National Institutes of Health Stroke Scale/Score (NIHSS) Calculator, with functional outcomes measured via modified Rankin Scale (mRS) at discharge and 3 months. Statistical analyses included Fisher's exact tests for categorical variables and Mann-Whitney tests for continuous measures, with multivariable regression adjusting for confounders.

Results: PSS patients demonstrated worse functional outcomes, particularly in hemorrhagic strokes (78.3% vs. 21.7% poor outcomes, $P<0.001$) and right-sided lesions (OR 2.7, $P=0.017$). Females with RSS had markedly poorer recovery than ASS cases (OR 0.1, 95% CI 0.1–0.9, $P=0.015$), while males showed no timing-dependent differences. Vascular comorbidities (e.g., chronic kidney disease [OR 37.5], Diabetes mellitus [OR 2.3], and smoking [OR 1.4]) compounded poor outcomes.

Conclusions: RSS, especially in females, and hemorrhagic stroke are high-risk predictors of disability. Targeted seizure prophylaxis and gender-sensitive rehabilitation strategies may improve outcomes. Prospective studies should validate these associations and explore underlying mechanisms.

Keywords: Functional outcomes; Gender disparities; Post-stroke epilepsy; Seizures; Stroke

Globally, stroke ranks among the top contributors to both disability and death, creating substantial public health challenges.[1] Among its complications, post-stroke seizures (PSS) are increasingly recognized as a critical concern, particularly as advancements in acute stroke care have improved survival rates, leading to a growing population of stroke survivors.[1] Seizures complicating stroke correlate with elevated mortality, extended hospitalization durations, increased disability severity upon discharge, and consequently impacting functional outcomes and quality of life.[2]

These seizures are broadly categorized into acute symptomatic seizures (ASS), occurring within the first week of stroke, and remote symptomatic seizures (RSS), which manifest after the

Corresponding Author: Erum Shariff, MD, Department of Neurology, King Fahd Hospital of University, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia, Post Code 31952
Email: emshariff@iau.edu.sa, Tel: 966138966666 Ext 2199, Fax: 96613896670, Mobile#: +966546768278
ORCID ID: 0000-0002-2608-1107

Disclosures: The author received no financial support for the research, authorship, and/or publication of this article. The authors declare no conflicts of interest. Data will be available upon appropriate request.

Received: October 16, 2025
Revised: April 19, 2026
Accepted: August 6, 2026

doi: 10.3121/cmr.2026.2076

first week.[3] This distinction is vital, as the mechanisms and long-term consequences of ASS and RSS differ significantly. ASS are often triggered by acute metabolic stress, glutamate excitotoxicity, and cortical irritation, while RSS are associated with chronic processes such as gliosis, neurodegeneration, and persistent inflammation.[4] Current International League Against Epilepsy (ILAE) guidelines distinguish RSS (recurrence >60% at 10 years, constituting post-stroke epilepsy) from ASS (~33% recurrence rate).

This difference underscores the need for tailored management strategies based on seizure timing.[5] The incidence of PSS varies significantly, with studies reporting that 5%–20% of stroke patients develop PSS.[6,7] ASS occur in 2.2% to 33% of cases, while RSS range from 3% to 67%, reflecting variability in study definitions.[6,7] Despite this, PSS consistently show two distinct peaks: one within the first day and another between 6- and 12-months post-stroke.[6,7]

Risk factors for PSS include cortical involvement, particularly in the middle cerebral artery territory, and vascular comorbidities such as hypertension (HTN), diabetes mellitus (DM), and smoking. [8]

Diagnostic tools such as electroencephalography (EEG) and neuroimaging play a crucial role in identifying predictors of PSS, including interictal epileptiform discharges, diffuse background slowing, and large cortical infarcts.[9,10] However, their routine use in clinical practice remains underexplored. Despite the growing recognition of PSS as a significant complication, there is limited consensus on optimal management strategies, particularly regarding the timing and necessity of anti-seizure medications. While ASS may not always require long-term treatment, RSS necessitate prompt intervention to prevent recurrence and associated complications. While previous studies suggest epileptic seizures negatively impact functional, neurological, and cognitive outcomes in stroke patients, the available evidence remains inconsistent.[11] In this context, a comprehensive investigation into the clinical, electrophysiological, and radiological factors associated with PSS could offer valuable insights.

Our research assessed whether seizure type (acute vs. remote) differentially impacts stroke functional outcomes and whether gender-based disparities exist, with a focus on identifying high-risk patients who may benefit from targeted interventions. By addressing gaps in current knowledge, this research seeks to improve neurological function and psychosocial well-being for stroke survivors affected by PSS.

Materials and Methods

Study Design and Setting

The present study adhered to the ethical guidelines approved by the Institutional Review Board of Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia (ID: 2023-01-477). This study included 116 patients selected from a pool of 208 patients between 2018–2021, meeting strict criteria: (1) age ≥18, (2) new-onset seizures attributed to stroke, and (3) No prior history of seizures, cerebral amyloid angiopathy, stroke mimics/conditions mimicking stroke (infection, tumor, and functional neurological disorders), and cerebral venous sinus thrombosis, or head trauma. A retrospective, control-matched design, with controls drawn from 906 patients who fulfilled same criteria except for seizure occurrence. Clinical features assessed comprised patient demographics (age and gender), the clinical progression of stroke, functional outcomes, and brain imaging findings. The study employed targeted sampling, where subjects were chosen for their specific characteristics. Seizures were defined as ASS if they occur before 7 days of the stroke, and RSS if it happens after 7 days of the stroke. Subsequently, using propensity score matching, we created comparable groups of stroke patients (with vs without seizures) in equal proportions. The parameters we included to match were: (1) age ± 10 years, (2) gender, (3) type of stroke (IS vs HS), (4) side of the lesion, (5) stroke severity, (6) stroke etiology for IS, and hemorrhage volume for HS. National Institutes of Health Stroke Scale/Score (NIHSS) was utilized to assess the stroke severity.[12] Stroke severity was reviewed during group selection but it was not possible to use it as a strict matching criterion. When an exact match was not available, the best possible match was selected based on age, sex, stroke type, and lesion side. IS were further classified by using Trial of ORG 10172 in Acute Stroke Treatment classification as; large artery atherosclerosis, Cardio-embolic, small vessel occlusion, other determined etiology, and undetermined etiology.[13] Functional outcomes were evaluated using the Modified Rankin Score (mRS) and were categorized as mild (mRS 0-1), moderate (mRS 2-3), or severe (mRS 4-5) and evaluated accordin to the mRS at discharge, and then at 3-months follow-up.

Statistical Analysis

Data were processed and analyzed with IBM SPSS Statistics software (v26.0). Categorical variables, including demographic characteristics such as gender, stroke type, vascular risk factors, and mRS outcomes, were expressed as frequencies and percentages, with between-group comparisons performed using either Pearson's χ^2 test or Fisher's exact test when expected cell frequencies fell below 5. Normally distributed continuous data (e.g., age) were summarized using means with standard deviations and compared using independent samples t-tests. For outcome analysis, we constructed adjusted binary logistic regression models to estimate the odds of poor functional outcomes associated with PSS, controlling for age, baseline NIHSS scores, infarct characteristics, and vascular comorbidities (HTN, DM, atrial fibrillation [AF]). Secondary analyses examined outcome differences based on seizure timing (acute vs remote), stratified by gender and stroke subtypes. Model assumptions were verified, including

Table 1. Comparison of baseline characteristics between cases and controls (N=232)

Characteristics	Cases (Post-stroke seizures group) n=116	Controls (Stroke only) n=116	OR with 95% CI	*P* value
Gender				
Male	66 (56.9%)	66 (56.9%)		1
Female	50 (43.1%)	50 (43.1%)		
Age (years)	61.53±15.83)	57.60±14.61	-	0.051
Stroke type				
Ischemic	92 (79.3%)	92 (79.3%)		1
Hemorrhagic	24 (20.7%)	24 (20.7%)	-	1
Stroke site				
Right	54 (46.6%)	54 (46.6%)		
Left	52 (44.8%)	52 (44.8%)		
Bilateral	10 (8.5%)	10 (8.5%)		
History of smoking	32 (27.6%)	9 (7.8%)	4.5 (2.1-10.0)	<0.001
Chronic kidney disease	33 (28.4%)	6 (5.2%)	7.3 (2.9-18.2)	<0.001
Hypertension	103 (88.8%)	72 (62.1%)	4.8 (2.4-9.6)	<0.001
Diabetes mellitus	65 (56.0%)	30 (25.9%)	3.7 (2.1-6.4)	<0.001
Dyslipidemia	69(59.5%)	79 (68.1%)	0.7 (0.4-1.2)	0.172
Ischemic heart disease	43 (37.1%)	71 (61.2%)	0.4 (0.2-0.6)	<0.001
Atrial fibrillation	23 (19.8%)	28 (24.1%)	0.8 (0.4-1.5)	0.428

assessment for multicollinearity using variance inflation factors (all visual fields < 2 indicated acceptable levels). We performed all statistical tests as two-tailed analyses, with statistical significance set at $P<0.05$. To aid clinical interpretation, effect sizes are reported alongside their 95% confidence interval (CI).

Results

A total of 232 participants were included in the study, with 116 in the PSS group and 116 in the stroke-only group. The baseline characteristics were comparable between the two groups in terms of gender (male: 56.9%, female: 43.1%) and stroke type (IS: 79.3%, HS: 20.7%). The mean age was slightly higher in the PSS group than in the stroke-only group (61.53±15.83 vs. 57.60±14.61; $P=0.051$). Patients with PSS exhibited significantly greater prevalence of vascular risk, including a history of smoking (27.6% vs. 7.8%; OR 4.5, 95% CI 2.1–10.0; $P<0.001$), chronic kidney disease (CKD) (28.4% vs. 5.2%; OR 7.3, 95% CI 2.9–18.2; $P<0.001$), HTN (88.8% vs. 62.1%; OR 4.8, 95% CI 2.4–9.6; $P<0.001$), and DM (56.0% vs. 25.9%; OR 3.7, 95% CI 2.1–6.4; $P<0.001$). Ischemic heart disease (IHD) was significantly lower in the PSS group (37.1% vs. 61.2%; OR 0.4, 95% CI 0.2–0.6; $P<0.001$) (Table 1). The distribution of NIHSS differed significantly between cases and controls ($P<0.001$). Mild strokes were more common in controls (48.3% vs. 4.3%), while cases had higher proportions of moderate (21.6% vs. 1.7%) and severe strokes (24.1% vs. 0%), as shown in Figure 1.

Figure 2 shows the distribution of mRS disability scores at discharge ($P<0.001$), and these findings suggest worse functional outcomes at discharge in cases compared to stroke-only controls. mRS-1 (minimal disability) was more common in controls (12.9%) than in cases (7.3%). In contrast, higher disability scores (mRS 3 and 4) were more frequent in cases (12.5% and 5.6%, respectively) compared to controls, where mRS 3 was observed in 19.4% of controls and none had mRS 4 or 5. Figure 3 compares mRS disability scores at 3 months between cases and controls and worse long-term functional outcomes were reported in cases ($P=0.015$).

Among males, the proportion of good outcomes (MRS 0–2) was relatively lower in the cases compared to controls (43.5% vs. 55.6%; OR 1.5, 95% CI 0.7–3.1; $P=0.273$), and a similar trend was observed among females (38.5% vs. 61.5%; OR 1.9, 95% CI 0.8–4.7; $P=0.171$). Patients with HS in the PSS group had significantly poorer outcomes compared to controls (poor outcomes: 78.3% vs. 21.7%; OR 11.4, 95% CI 3.0–44.0; $P<0.001$). Functional outcomes in IS patients showed no significant intergroup differences (poor outcomes: 49.6% vs. 50.4%; OR 0.9, 95% CI 0.5–1.8; $P=0.866$). Patients with right-sided strokes showed worse outcomes in the PSS group

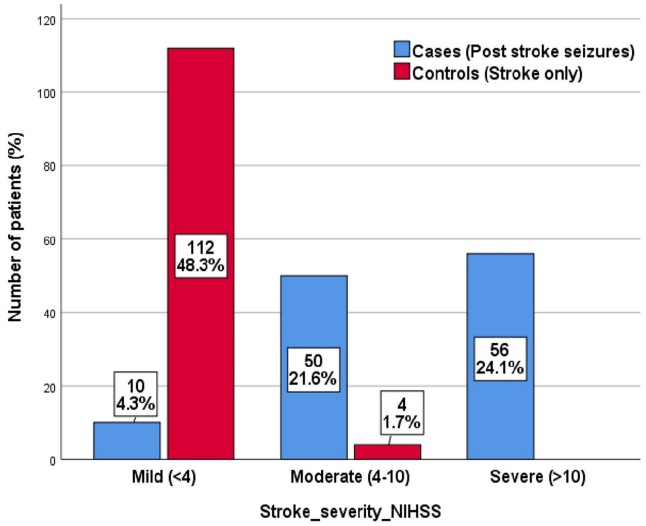

Figure 1. Distribution of Stroke Severity (NIHSS) Among Post-Stroke Seizure Cases and Stroke-Only Controls

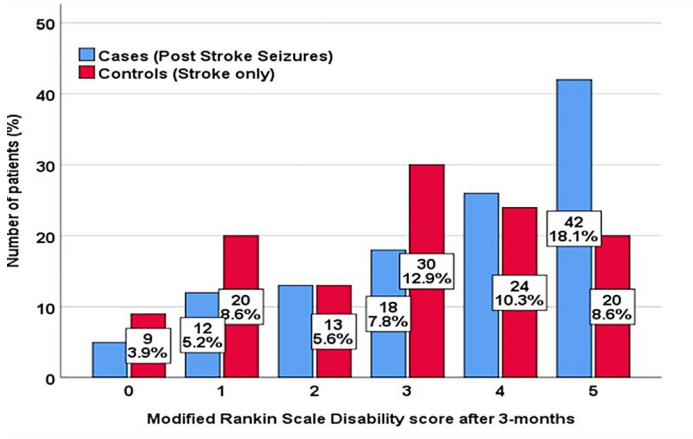

Figure 3. Distribution of Modified Rankin Scale (MRS) Disability Scores After 3 Months Among Post-Stroke Seizure Cases and Stroke-Only Controls

(poor outcomes: 58.8% vs. 41.2%; OR 2.7, 95% CI 1.2–6.0; *P*=0.017). Patients with smoking (100% vs. 0%; OR 54.8, 95% CI 2.9-104.2; *P*<0.001), DM (75.0% vs. 25.0%; OR 2.5, 95% CI 1.0–6.1; *P*=0.047), and CKD (100% vs. 0%; OR 39.0, 95% CI 2.0–747.4; *P*<0.001 in the PSS group had significantly worse outcomes than controls. HTN, AF, IHD, and dyslipidemia (DLP) did not significantly influence the functional outcomes between the two groups (Table 2).

Among PSS patients, 57 had ASS, and 59 had RSS. Outcomes among males were similar between acute and remote PSS groups (poor outcomes: 43.5% vs. 56.5%; OR 0.9, 95% CI 0.3–2.7; *P*=0.909). However, females with RSS had significantly poorer outcomes compared to ASS (poor outcomes: 52.5% vs. 47.5%; OR 0.1, 95% CI 0.1–0.9; *P*=0.015). Outcomes for IS showed a higher proportion of poor outcomes in the RSS group (60.3% vs. 39.7%; OR 0.5, 95% CI 0.2–1.2; *P*=0.114); whereas, HS outcomes were similar between the groups (poor outcomes: 66.7%; OR 1.0, 95% CI 0.1–7.1; *P*=1). CKD and AF were associated with worse outcomes in RSS compared to ASS, although these differences were not statistically significant (*P*=0.084, *P*=0.076 respectively) (Table 3).

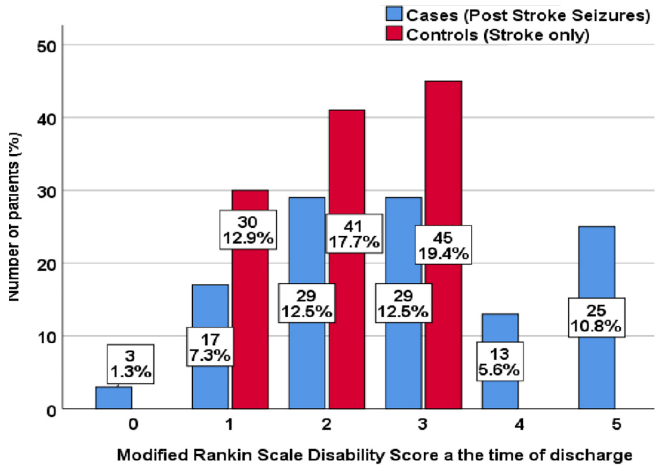

Figure 2. Distribution of Modified Rankin Scale (MRS) Disability Scores at Discharge Among Post-Stroke Seizure Cases and Stroke-Only Controls

Discussion

Stroke represents the predominant cause of acquired epilepsy in older adults,[15] with seizures occurring in both acute (ASS) and chronic (RSS) post-stroke phases, each carrying distinct pathophysiological mechanisms and clinical implications. These seizures eventually significantly compromise neurological recovery and functional outcomes, creating an escalating public health challenge as global aging populations produce more stroke survivors. The anticipated growth of PSS underscores the urgent need to delineate differential risk factors, recurrence patterns, and long-term outcomes between ASS and RSS, particularly given their varying impacts on rehabilitation potential and quality of life. Such investigations are crucial for developing targeted prevention strategies and optimizing post-stroke management in an increasingly vulnerable demographic. Our case-control study reveals gender-specific vulnerabilities in PSS, with females experiencing significantly worse functional outcomes following RSS compared to other groups.

Table 2. Comparison mRS based outcomes among study groups after 3 months

		Groups			
Characteristics	**mRS**	**Cases (n=116)**	**Controls (n=116)**	**OR with 95% CI**	***P* value**
Gender					
Male	Good	20 (43.5%)	26 (55.6%)	Ref.	0.273
	Poor	46 (53.5%)	40 (46.5%)	1.5 (0.7-3.1)	
Female	Good	10 (38.5%)	16 (61.5%)	Ref.	0.171
	Poor	40 (54.1%)	34 (45.9%)	1.9 (0.8-4.7)	
Age (years)	Good	57.13±14.92	54.00±13.02	-	0.090
	Poor	63.07±15.94	59.65±15.15	-	0.095
Stroke type					
Ischemic	Good	24 (51.1%)	23 (48.9%)	Ref.	0.866
	Poor	68 (49.6%)	69 (50.4%)	0.9 (0.5-1.8)	
Hemorrhagic	Good	6 (24.0%)	19 (76.0%)	Ref.	<0.001
	Poor	18 (78.3%)	5 (21.7%)	11.4 (3.0-44.0)	
Site of stroke					
Right	Good	14 (35.0%)	26 (65.0%)	Ref.	0.017
	Poor	40 (58.8%)	28 (41.2%)	2.7 (1.2-6.0)	
Left	Good	16 (53.3%)	14 (46.7%)	Ref.	0.665
	Poor	36 (48.6%)	38 (51.4%)	0.8 (0.4-1.9)	
Bilateral	Good	-	2 (100%)	-	0.136
	Poor	10 (55.6%)	8 (44.4%)	-	
Smoking	Good	8 (47.1%)	9 (52.9%)	Ref.	<0.001
	Poor	24 (100%)	-	54.8 (2.9-104.2)	
Chronic kidney disease	Good	8 (57.1%)	6 (42.9%)	Ref.	<0.001
	Poor	25 (100%)	-	39.0 (2.0-747.4)	
Diabetes mellitus	Good	17 (54.8%)	14 (45.2%)	Ref.	0.047
	Poor	48 (75.0%)	16 (25.0%)	2.5 (1.0-6.1)	
Hypertension	Good	28 (54.9%)	23 (45.1%)	Ref.	0.495
	Poor	75 (60.5%)	49 (39.5%)	1.3 (0.7-2.4)	
Dyslipidemia	Good	18 (39.1%)	28 (60.9%)	Ref.	0.220
	Poor	51 (50.0%)	51 (50.0%)	1.6 (0.8-3.2)	
Ischemic heart disease	Good	9 (27.3%)	24 (72.7%)	Ref.	0.142
	Poor	34 (42.0%)	47 (58.0%)	1.9 (0.8-4.7)	
Atrial fibrillation	Good	6 (46.2%)	7 (53.8%)	Ref.	0.929
	Poor	17 (44.7%)	21 (55.3%)	0.9 (0.3-3.3)	

mRS, modified Rankin Scale; OR, odds ratio; CI, confidence interval
mRS Good: 0-2; Bad:4-6

Our study found a trend toward older age in PSS patients (*P*=0.051), aligning with most literature linking advanced age to PSS risk.[16] However, this association remains controversial, as some studies report no age relationship[17,18] or even inverse associations.[18,19] These discrepancies may reflect differences in study populations (e.g., stroke subtypes) or PSS classification methods, underscoring the need for standardized age-stratified analyses in future research. We did not document differences in PSS based on gender. Notably, demographic factors like age and gender show inconsistent associations with PSS across studies, suggesting vascular pathophysiology rather than baseline characteristics drives seizure susceptibility. These findings highlight three critical research priorities: (1) mechanistic studies to separate acute compensatory (e.g., perfusion-preserving) versus chronic detrimental (e.g., microvascular injury) effects of vascular risks on epileptogenesis; (2) time-stratified analyses of blood pressure's dual-phase impact; and (3) prospective trials

Table 3. Comparison mRS based Outcomes with respect to Early versus Late Post-Stroke Seizures after 3 months

Characteristics		MRS	Post-stroke seizures			
			Early (n=57)	Late (n=59)	OR with 95% CI	*P* value
Gender	Male	Good	9 (45.0%)	11 (55.0%)	Ref.	0.909
		Poor	20 (43.5%)	26 (56.5%)	0.9 (0.3-2.7)	
	Female	Good	9 (90.0%)	1 (10.0%)	Ref.	**0.015**
		Poor	19 (47.5%)	21 (52.5%)	0.1 (0.1-0.9)	
Age (years)		Good	57.12±15.80	55.50±9.91	-	0.508
Poor		62.84±15.93	63.38±15.99	-	0.856	
Stroke type	Ischemic	Good	14 (58.3%)	10 (41.7%)	Ref.	0.114
		Poor	27 (39.7%)	41 (60.3%)	0.5 (0.2-1.2)	
	Hemorrhagic	Good	4 (66.7%)	2 (33.3%)	Ref.	1‡
		Poor	12 (66.7%)	6 (33.3%)	1 (0.1-7.1)	
Site of stroke	Right	Good	8 (57.1%)	6 (42.9%)	Ref.	0.434
		Poor	18 (45.0%)	22 (55.0%)	0.6 (0.2-1.8)	
	Left	Good	10 (62.5%)	6 (37.5%)	Ref.	0.229
		Poor	16 (34.8%)	20 (65.2%)	0.5 (0.1-1.6)	
	Bilateral	Good	-	-	-	-
		Poor	5 (50.0%)	5 (50.0%)	-	
Smoking		Good	4 (50.0%)	4 (50.0%)	Ref.	0.533‡
		Poor	9 (37.5%)	15 (62.5%)	0.6 (0.1-3.0)	
Chronic kidney disease		Good	6 (75.0%)	2 (25.0%)	Ref.	0.084‡
		Poor	10 (40.0%)	15 (60.0%)	0.2 (0.1-1.3)	
Diabetes mellitus		Good	10 (58.8%)	7 (41.2%)	Ref.	0.285
		Poor	21 (43.8%)	27 (56.2%)	0.5 (0.2-1.4)	
Hypertension		Good	17 (60.7%)	11 (39.3%)	Ref.	0.205
		Poor	35 (46.7%)	40 (53.3%)	0.6 (0.2-1.4)	
Dyslipidemia		Good	9 (50.0%)	9 (50.0%)	Ref.	0.344
		Poor	19 (37.3%)	32 (62.7%)	0.6 (0.2-1.8)	
Ischemic heart disease		Good	4 (44.4%)	5 (55.6%)	Ref.	0.889‡
		Poor	16 (47.1%)	18 (52.9%)	1.1 (0.3-4.5)	
Atrial fibrillation		Good	5 (83.3%)	1 (16.7%)	Ref.	0.076‡
		Poor	7 (41.2%)	10 (58.8%)	0.1 (0.1-1.5)	

mRS, modified Rankin Scale; OR, odds ratio; CI, confidence interval
Odds ratio compares the odds of early versus late seizures in the poor outcome group relative to the good outcome group within each subgroup. Good outcome served as the reference category.
Percentages are calculated row-wise, using the total number of patients within each subgroup and mRS category as the denominator.
‡Fisher's exact test used because of small cell counts. For other categorical comparisons, chi-square test was used. Continuous variables were compared using independent-samples t-test.

validating statins' potential antiepileptogenic effects through lipid-mediated and pleiotropic pathways.

Our cohort revealed a significantly higher prevalence of vascular risk factors in PSS, including smoking, CKD, HTN, and DM (all $P<0.001$) while some studies report lower HTN in ASS,[19] others identify smoking as a key predictor.[14] Paradoxically, IHD was less prevalent in PSS patients ($P<0.001$), aligning with studies reporting no IHD-PSS association.[16,19] These findings highlight the selective vascular risk profile associated with PSS, though literature remains inconsistent. HTN demonstrates particularly complex, phase-

dependent associations with PSS. Our data and multiple studies[21,22] support HTN as a risk factor for PSS, potentially through chronic cerebrovascular remodeling. Conversely, acute HTN may transiently reduce ASS risk by maintaining cerebral perfusion in ischemic penumbra,[20] though this putative protective effect must be balanced against risks of hemorrhagic transformation.[23] Although HTN and DLP contribute to PSS pathogenesis,[22] cholesterol's specific mechanistic role requires clarification. Emerging evidence of statins' protective effects[24] suggests lipid metabolism may modulate epileptogenesis, particularly in high-DLP populations.[25] This warrants targeted studies examining: (1) cholesterol-mediated blood-brain barrier disruption, (2) neuroinflammatory pathways, and (3) statins' pleiotropic antiepileptic properties. Although AF is a recognized risk factor for cardioembolic stroke and cortical injury, both linked to PSS,[26] our study, consistent with prior reports,[27] found no independent association between AF and PSS. This discrepancy may stem from confounding variables such as infarct location, stroke severity, or the protective effects of antithrombotic therapy, which could modulate the apparent association between AF and seizure risk. Alternatively, the systemic effects of AF, including cerebral hypoperfusion and microemboli, might contribute differently to epileptogenesis compared to localized cortical injury. Further studies incorporating advanced neuroimaging, detailed infarct characterization, and anticoagulation data are needed to clarify whether AF's role in PSS is mediated by indirect mechanisms rather than direct causation.

The distribution of stroke severity differed significantly between cases and controls (P<0.001), with more severity related to PSS. This is in line with the literature that higher NIHSS in severe strokes linked to more PSS.[17,19] While a case control study revealed NIHSS was not different with and without PSS,[18] their analysis revealed a trend toward greater stroke severity in PSS patients compared to controls (P=0.21), though this difference did not achieve statistical significance.

Patients with PSS had significantly higher mRS scores at discharge and 3-month follow-up compared to stroke-only (P<0.001), indicating worse functional outcomes, a finding consistent with prior studies.[17] While the association between PSS and poorer recovery is well-documented, the underlying mechanisms remain debated. Some evidence suggests the timing of PSS may influence outcomes, with RSS linked to worse functional recovery than ASS.[14] Our case-control study reveals significant gender disparities in PSS outcomes: (1) females with RSS showed relatively worse functional recovery than males (38.5% vs 61.5% good outcomes); (2) we notably identify a novel gender-timing interaction as females with RSS fared worst, a finding unexplained by prior studies,[28] despite known female disadvantages in stroke recovery.[29] Potential mechanisms include hormonal influences (estrogen withdrawal lowering seizure thresholds[30] or rehabilitation disparities. These results advocate gender-specific monitoring, particularly aggressive seizure prophylaxis and early rehabilitation for females developing RSS. Prospective studies should validate these associations and explore biological (e.g., hormonal status) and care-related mediators through advanced imaging/biomarkers.

Our study revealed striking differences in how PSS impact functional outcomes based on stroke type and seizure timing. Patients with HS and PSS suffered dramatically worse outcomes (P<0.001), suggesting seizures may exacerbate the already compromised neural environment in HS through mechanisms like increased metabolic demand in perihematomal regions or seizure-induced blood-brain barrier disruption. Conversely, IS outcomes showed more nuanced associations with RSS correlating with poorer recovery, while ASS and RSS demonstrated no significant difference in HS patients. These findings partially align with Misra et al.'s[12] observations of seizure-associated poor outcomes in both stroke types, though we identified important temporal distinctions they did not report. The divergent patterns may reflect fundamental pathophysiological differences: in IS, RSS could indicate maladaptive plasticity in chronically hypoperfused tissue; whereas in HS, ASS may trigger cascades of secondary injury through inflammatory mediators like IL-1β and matrix metalloproteinases. Clinically, these results argue for particularly vigilant seizure monitoring in HS patients and suggest the therapeutic window for neuroprotection may differ between stroke types, potentially requiring earlier intervention in HS and more sustained prophylaxis in IS. Future research should employ advanced imaging biomarkers to track how seizures interact with stroke evolution in these distinct contexts.

In general, patients with CKD, smoking, and DM in the PSS group exhibited significantly worse functional outcomes compared to controls (P<0.001, P<0.001, and P=0.047, respectively). In contrast, HTN, AF, IHD, and DLP did not demonstrate a statistically significant impact on outcomes between the two groups. Regarding seizure timing, CKD and AF were associated with poorer outcomes in RSS compared to ASS, though these differences did not reach statistical significance (P=0.084, P=0.076 respectively). Higher prevalence of vascular risk factors in PSS being one of the contributors to unfavorable functional outcomes already established.[31]

Our study identified significantly worse functional outcomes in patients with right-sided strokes who developed PSS (P=0.017), while left-sided and bilateral strokes showed no PSS-related outcome differences. This lateralized effect contrasts with the findings of Agarwal et al[19] in which no association between stroke laterality and outcomes, potentially reflecting differences in study populations or outcome measures was found. The right hemisphere's dominance for attention and spatial processing may render it particularly vulnerable to seizure-induced network disruptions,

compounding existing deficits in activities of daily living. Alternatively, the apparent laterality effect could stem from under-recognition of left hemisphere seizure symptoms (e.g., aphasic seizures being misclassified as stroke progression) or variations in rehabilitation access for right hemisphere deficits. These discrepancies highlight the need for future studies to incorporate standardized seizure monitoring (including continuous EEG for non-motor seizures) and lesion-mapping approaches to clarify whether right hemisphere strokes truly confer higher PSS-related disability risks or if this represents an epiphenomenon of assessment biases. Regardless, clinicians should be particularly vigilant for seizures in right hemisphere stroke patients and consider prompt neurorehabilitation referrals when PSS occurs.

This study has several notable strengths. As a single-center investigation, it employed standardized diagnostic as well as inclusion/exclusion criteria, with all participants undergoing consistent 3-month follow-ups. This approach minimized inter-center variability, strengthening internal validity. Consecutive enrollment of both ischemic and hemorrhagic stroke patients improved the generalizability of results, while the 1:1 case-control design facilitated rigorous comparative analyses. Clinically, the use of mRS assessments at discharge and 3 months provided practical insights into long-term functional recovery, a metric aligned with real-world rehabilitation benchmarks.

Limitations include; the study's retrospective design introduces potential documentation bias, particularly for non-convulsive seizures, which may have been underreported in medical records. Functional outcomes were measured only with the mRS, which is practical but less detailed than repeated NIHSS assessments. Unaccounted confounders, such as rehabilitation adherence, socioeconomic factors, and infarct volume precision, could further influence interpretations. Smaller subgroups (e.g., hemorrhagic stroke [HS; n=24] and chronic kidney disease [n=33]) risk overestimating effect sizes due to limited statistical power. Future prospective studies should integrate standardized seizure monitoring and multidimensional functional assessments to address these gaps.

Conclusion

Our study reveals clinically meaningful differences in outcomes between stroke patients with and without PSS. The PSS group demonstrated greater initial stroke severity and significantly poorer functional recovery. These findings persisted after adjusting for confounding factors, suggesting PSS may independently worsen recovery trajectories through multiple pathways: (1) direct seizure-related neuronal injury exacerbating initial stroke damage, (2) disruption of neurorehabilitation due to ictal events, and (3) potential interactions between antiseizure medications and neuroplasticity. Notably, we observed temporal and gender-specific patterns, RSS was particularly detrimental for females and IS patients, possibly reflecting hormonal influences on epileptogenesis or gender differences in care access. The elevated prevalence of vascular risk factors in PSS patients suggests shared pathophysiology between cerebrovascular disease and post-stroke epileptogenesis.

Acknowledgements

This study made use of the computational resources and technical services of the Scientific & High-Performance Computing Center at Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. The authors would like to acknowledge the assistance of Mr. Muhammad Amir Latif (RESnTEC, Institute of Research, Bahawalpur, Pakistan) for his assistance with the statistical analysis presented in this paper.

References

1. Katan M, Luft A. Global Burden of Stroke. Semin Neurol. 2018;38(2):208-211 doi:10.1055/s-0038-1649503. Published online May 23, 2018.
2. Tanaka T, Ihara M. Post-stroke epilepsy. Neurochem Int. 2017;107:219-228. doi:10.1016/j.neuint.2017.02.002.
3. Wang JZ, Vyas MV, Saposnik G, Burneo JG. Incidence and management of seizures after ischemic stroke: Systematic review and meta-analysis. Neurology. 2017;89(12):1220-1228. doi:10.1212/WNL.0000000000004407
4. Chen J, Ye H, Zhang J, Li A, Ni Y. Pathogenesis of seizures and epilepsy after stroke. Acta Epileptologica. 2022;4(1):2. doi:10.1186/s42494-021-00068-8.
5. Fisher RS, Cross JH, D'Souza C, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia. 2017;58(4):531-542. doi:10.1111/epi.13671
6. Stefanidou M, Das RR, Beiser AS, et al. Incidence of seizures following initial ischemic stroke in a community-based cohort: The Framingham Heart Study. Seizure. 2017;47:105-110. doi:10.1016/j.seizure.2017.03.009.
7. Arboix A, Comes E, García-Eroles L, Massons JB, Oliveres M, Balcells M. Prognostic value of very early seizures for in-hospital mortality in atherothrombotic infarction. Eur Neurol. 2003;50(2):78-84. doi:10.1159/000072503.
8. Zhang C, Wang X, Wang Y, et al. Risk factors for post-stroke seizures: A systematic review and meta-analysis. Epilepsy Res. 2014;108(10):1806-1816. doi:10.1016/j.eplepsyres.2014.09.030.
9. Bentes C, Martins H, Peralta AR, et al. Early EEG predicts poststroke epilepsy. Epilepsia Open. 2018;3(2):203-212. doi:10.1002/epi4.12103.
10. De Reuck J, Goethals M, Claeys I, Van Maele G, De Clerck M. EEG findings after a cerebral territorial infarct in patients who develop early- and late-onset seizures. Eur Neurol. 2006;55(4):209-213. doi:10.1159/000093871.

11. Brondani R, de Almeida AG, Cherubini PA, et al. Risk factors for epilepsy after thrombolysis for ischemic stroke: a cohort study. Front Neurol. 2020;10:1256. doi:10.3389/fneur.2019.01256.
12. Kwah LK, Diong J. National Institutes of Health Stroke Scale (NIHSS). J Physiother. 2014;60(1):61. doi:10.1016/j.jphys.2013.12.012.
13. Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24(1):35-41. doi:10.1161/01.str.24.1.35
14. Misra S, Kasner SE, Dawson J, et al. Outcomes in Patients With Poststroke Seizures: A Systematic Review and Meta-Analysis. JAMA Neurol. 2023;80(11):1155-1165. doi:10.1001/jamaneurol.2023.3240
15. Sen A, Jette N, Husain M, Sander JW. Epilepsy in older people. Lancet. 2020;395(10225):735-748. doi:10.1016/S0140-6736(19)33064-8.
16. Samake B, Houot M, Zavanone C, et al. Late but not early seizures impact negatively early post stroke recovery: A case-control study. Eur Stroke J. 2023;8(3):784-791. doi:10.1177/23969873231182493.
17. Ferreira-Atuesta C, Döhler N, Erdélyi-Canavese B, et al. Seizures after ischemic stroke: a matched multicenter study. Ann Neurol. 2021;90(5):808-820. doi:10.1002/ana.26212.
18. Castro-Apolo R, Huang JF, Vinan-Vega M, Tatum WO. Outcome and predictive factors in post-stroke seizures: A retrospective case-control study. Seizure. 2018;62:11-16. doi:10.1016/j.seizure.2018.09.007.
19. Agarwal A, Sharma J, Padma Srivastava MV, et al. Early Post-Stroke Seizures in Acute Ischemic Stroke: A Prospective Cohort Study. Ann Indian Acad Neurol. 2021;24(4):580-585. doi:10.4103/aian.AIAN_1283_20
20. Hundozi Z, Shala A, Boshnjaku D, et al. Hypertension on admission is associated with a lower risk of early seizures after stroke. Seizure. 2016;36:40-43. doi:10.1016/j.seizure.2016.01.016.
21. Ma S, Fan X, Zhao X, Wang K, Wang H, Yang Y. Risk factors for early-onset seizures after stroke: A systematic review and meta-analysis of 18 observational studies. Brain Behav. 2021;11(6):e02142. doi:10.1002/brb3.2142
22. Pitkänen A, Roivainen R, Lukasiuk K. Development of epilepsy after ischaemic stroke. Lancet Neurol. 2016;15(2):185-197. doi:10.1016/S1474-4422(15)00248-3.
23. Hong JM, Kim DS, Kim M. Hemorrhagic transformation after ischemic stroke: mechanisms and management. Front Neurol. 2021;12:703258. doi:10.3389/fneur.2021.703258.
24. Li Y, Zhang B, Zhang L, Xie D, Li Y. Efficacy of Statin therapy in post-stroke seizure prophylaxis: Clues from an observational study of routine secondary prevention treatment. Seizure. 2019;71:185-189. doi:10.1016/j.seizure.2019.07.010.
25. AlMuhaidib S, AlBuhairan F, Tamimi W, et al. Prevalence and factors associated with dyslipidemia among adolescents in Saudi Arabia. Sci Rep. 2022;12(1):16888. doi:10.1038/s41598-022-21262-9.
26. Dziadkowiak E, Guziński M, Chojdak-Łukasiewicz J, Wieczorek M, Paradowski B. Predictive factors in post-stroke epilepsy: Retrospective analysis. Adv Clin Exp Med. 2021;30(1):29-34. doi:10.17219/acem/128745.
27. Do PT, Chen LY, Chan L, Hu CJ, Chien LN. Risk factors for postischemic stroke epilepsy in young adults: a nationwide population-based study in Taiwan. Front Neurol. 2022;13:880661. doi:10.3389/fneur.2022.880661.
28. Hung KH, Lai JCY, Hsu KN, et al. Gender gap and risk factors for poor stroke outcomes: a single hospital-based prospective cohort study. J Stroke Cerebrovasc Dis. 2018;27(8):2250-2258. doi:10.1016/j.jstrokecerebrovasdis.2018.04.014.
29. Zhou Y, Gisinger T, Lindner SD, et al. Sex, gender, and stroke recovery: Functional limitations and inpatient care needs in Canadian and European survivors. Int J Stroke. 2025;20(2):215-225. doi:10.1177/17474930241288033.
30. Røste LS, Taubøll E, Svalheim S, Gjerstad L. Does menopause affect the epilepsy? Seizure. 2008;17(2):172-175. doi:10.1016/j.seizure.2007.11.019. Published online December 27, 2007.
31. Li X, Breteler MMB, de Bruyne MC, Meinardi H, Hauser WA, Hofman A. Vascular determinants of epilepsy: the Rotterdam Study. Epilepsia. 1997;38(11):1216-1220. doi:10.1111/j.1528-1157.1997.tb01219.x.

Author Affiliations

Erum Shariff, MD; Nehad Soltan, MD*; Danah AlJaafari, MD*; Abdullah Saleh AlAmri, MD*; Foziah Alshamrani, MD*; Mohammed AlShurem, MD*; Feras Alsulaiman, MD*; Majed Alabdali, MD*; and Anas Salman AlDahailan, MD**

**Department of Neurology, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia*