Comparative Analysis of Pre-existing Comorbidities, Symptomology, and Clinical Course of Young and Older Stroke Patients: A Retrospective Study from Aseer Region

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Abstract:

Background**:** Although advanced age is a well-known non-modifiable risk factor for stroke, the prevalence of stroke has been increasing in younger adults. However, only a few studies have instigated the differences in comorbidities and symptom presentation between young and older stroke patients. Therefore, the primary objective of this retrospective study is to systematically compare pre-existing comorbidities, symptoms, and clinical outcomes of young (<45 years) and older (≥ 45 years) hospitalized stroke patients.
Methods**:** This single-centered study utilized data from Aseer Central Hospital (Abha City, Kingdom of Saudi Arabia) from inception to 2019 to avoid potential confounding effects of the COVID-19 pandemic. Multivariable analysis was performed to detect differences in symptomology and clinical course of young versus older stroke patients.
Results**:** Young patients were significantly more likely to present with elevated HbA1c [OR=1.927 (95%CI 1.195-3.107); p=0.007] and visual symptoms [OR=16.429 (95%CI 3.92-68.865); p<0.0001] than older patients. However, younger patients were less likely to have pre-existing hypertension [OR=0.0472 (95%CI 0.006-0.342); p=0.003] and T2DM [OR=0.080 (95%CI 0.016-0.392); p=0.002] or present with arm weakness [OR=0.197 (95%CI 0.046-0.844); p=0.028], and slurred speech [OR=0.159 (95%CI 0.035-0.731); p=0.018] than older patients.
Conclusion**:** Pre-existing comorbidities and stroke symptoms vary considerably between young and older patients.

Keywords: Stroke; Young; Comorbidities; Symptomology; Aseer.

Introduction

Stroke is the third-leading cause of global deaths and disability (1). The global prevalence of stroke was estimated at 101 million people in 2019, with over 12 million incident cases each year. Among the modifiable risk factors of incident stroke, hypertension, type 2 diabetes mellitus (T2DM), and dyslipidemia are prominent and correlate well with the presence of atherosclerosis (2-4) Age is a crucial non-modifiable risk factor for incident stroke (5). Although stroke is traditionally associated with advanced age, a growing number of stroke cases is being reported in young and middle-aged adults. In 2019, about one-fourth of the patients with stroke globally were under the age of 50. Furthermore, females had a slightly higher prevalence than men (56% vs. 44%)(1). Stroke risk factors, etiologies, and prognosis can also vary substantially by region and country (6-8).

Stroke is increasingly recognized as a "soaring epidemic" in the Kingdom of Saudi Arabia (KSA) (9, 10). Although stroke incidence is substantially

lower in the KSA than in other high-income countries such as the United States (114.9 versus 138.95 cases per 100,000 people), the disease burden measured in disability-adjusted life years (DALY; 1168.7 versus 1166.6 DALYs per 100,000 people) is comparable between the two countries (11). Patients with first-time stroke in KSA also tend to be younger (mean age=63 years) than in the United States (mean age=69 years)12 despite the differences in population aging; the median age of the KSA population is 30.8 years versus 38.5 years in the United States (12). Importantly, modeling studies show that the incidence of first-time stroke is expected to grow by 57-67% over ten years in KSA and pose a severe burden to the healthcare system (13). The currently available workforce for stroke care in the KSA, including stroke neurologists, interventional neuroradiologists, and occupational therapists, is inadequate to deal with the increasing burden of stroke (14).

Other studies from KSA report important age-related differences in cerebrovascular risk profiles between juvenile and young-to-middle-aged adults(15), comprehensive stroke knowledge between patients aged <45 years and ≥45 years (16), functional outcomes post-stroke among patients aged <65 years and ≥65 years(17), and mortality risks among patients aged <60 and ≥65 years(18) . Also, earlier studies indicate that stroke risk profiles and etiologies vary considerably from one region to another within KSA (15). Therefore, caution should be exercised when generalizing data and findings from one population to another, and a comprehensive understanding of the regional epidemiology and distinctive characteristics of stroke is essential for developing effective prevention and treatment strategies(5).

In line with this need, a growing number of stroke-related studies from KSA are reporting the data at a regional level, especially from more populated provinces such as Riyadh, Makkah, Jizan, and the Eastern province(9). Recently, several studies have investigated stroke incidence and risk factors in the Aseer region in the southwest part of KSA (4, 19-21). For instance, Alhazzani et al. (19) showed stroke incidence of 8.41 and 32.66 cases per 100,000 in the <40 and 40-44 age groups which progressively increased to 851.81 cases per 100,000 in the 70+ age group. Overall, the incidence of stroke in the Aseer region of Saudi Arabia is 57.64 per 100,000 person 19, higher than in other regions, such as Medina (13.89 per 100,000 persons) (22). In another study, Alhazzani et al. (4) showed that T2DM, hypertension, obesity, and dyslipidemia were associated with a significantly elevated risk of incident stroke in hospitalized first-time stroke patients in 2016 from the Aseer region compared to age- and gender-matched non-stroke hospitalized patients.

Although the age-specific incidence rate of stroke in the Aseer region is well reported, age-specific comorbidities and symptom presentation, if any, have not been reported. Therefore, the primary objective of this retrospective study is to systematically compare pre-existing morbidities, symptoms, and clinical outcomes of young (<45 years) and older (≥ 45 years) hospitalized stroke patients within the Aseer region. By doing so, the study aims to fill a crucial gap in the current research on stroke in this locale, ultimately providing invaluable insights that can shape and improve local healthcare policies and the allocation of medical resources. In addition to its local implications, the data and findings gleaned from this analysis are expected to contribute to the broader, global discourse on stroke, aiding in understanding how the disease uniquely affects different age groups across diverse regions and contexts.

Methods

This study utilized data from the Neurology department of Aseer Central Hospital in Abha City. 2019 was used as the cutoff point for data collection to avoid potential confounding effects of the COVID-19 pandemic.

The initial dataset included files of 173 stroke patients. To maintain the robustness and integrity of our research, we executed a meticulous data cleaning process, aiming to address any inconsistencies or errors that might have arisen from data entry mistakes or missing values, and 21 patient files were excluded in this process. The final dataset for analysis comprised data from 152 patients: 36 young and 116 middle-aged or older patients. We defined "young" patients as those under the age of 45. This categorization resonates with the prevailing view in the literature that individuals under 45 years of age are typically classified as young stroke patients(23, 24).

Descriptive statistics comprised patient demographics, the prevalence of pre-existing comorbidities, stroke characteristics, stroke-specific clinical symptoms at presentation, non-specific clinical parameters such as complete blood count and metabolic panel, blood pressure, and body temperature, and admission characteristics, which we tabulate as frequency (percentage), median (interquartile range), or mean ± standard deviation. The differences in the descriptive statistics between young and older stroke patients were assessed for statistical significance using the Chi-Square or Exact Test.

In addition, beta coefficients, odds ratio (OR), and 95% confidence intervals (CI) were calculated during multivariable analysis to detect the likelihood of occurrence of pre-existing morbidities and symptoms of young stroke patients at the time of hospitalization, which were the primary outcomes of interest of this study. In the multivariable analysis, the study considered several factors, including Sex, Body Mass Index (BMI), Elevated HbA1c, LDL, Total Cholesterol, HDL, Hypertension, T2DM, Smoking, Myocardial Infarction, ICU Admission, First Event, Visual Symptoms, Arm Weakness, Leg Weakness, and Slurred Speech.

Statistical significance was determined based on p-values, with a value less than 0.05 considered statistically significant. All statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) Software (Version 25, SPSS, Inc, Chicago, IL, USA).

Results

Population Characteristics

Patient demographics, prevalence of pre-existing comorbidities, and stroke characteristics are presented in Table 1. The average age for young patients was 33 years, with a standard deviation of 9. Conversely, the average age for older patients was 71 years, with a standard deviation of 12. There was a significantly higher proportion of females in the younger cohort (20/36; 55.6%), while the older cohort had a higher proportion of males (78/116; 67.8%). In terms of pre-existing comorbidities, the younger cohort was more likely to be on hormone therapy (11.1% vs. 1.7%, p=0.028). In comparison, the older population has a higher prevalence of hypertension (11.1% vs. 63.8%, p=0.001) and T2DM (11.1% vs. 63.8%, p<0.0001). Over half of the strokes occurred in the evening (55.6% vs. 51.7%, p=0.047), with ischemic stroke as the most prevalent type (100% vs. 96.6%, p=0.57) in both patient groups. However, a significantly greater proportion of patients in the younger group experienced a single event (83.3% vs. 60.3%, p=0.011) and exhibited large artery atherosclerosis (16.7% vs. 5.2%, p=0.036).

Table 1.

Comparison of stroke characteristics and outcomes between young and older patients

	Variables	Patients <45	Patients ≥ 45	
		Mean ± SD	***Mean ± SD***	
	Age in years	33±*9*	71±*12*	-
		n (%)	***n (%)***	***p***
Patient Demographics	Total	36 (23.7%)	116 (76.3%)	
	Gender			
	Female	20 (55.6%)	38 (32.8%)	0.014*
	Male	16 (44.4%)	78 (67.2%)	
	Area of residence			
	Low altitude	2 (5.6%)	18 (15.5%)	0.16
	High altitude	34 (94.4%)	98 (84.5%)	
	Body mass index			
	Underweight	0 (0.0%)	2 (1.7%)	
	Normal Weight	8 (22.2%)	26 (22.4%)	0.82
	Overweight	12 (33.3%)	46 (39.7%)	
	Obesity	16 (44.4%)	42 (36.2%)	
Comorbidities	Hypertension	4 (11.1%)	74 (63.8%)	0.001*
	Myocardial infarction	2 (5.6%)	18 (15.5%)	0.12
	Type 2 Diabetes Miletus	4 (11.1%)	74 (63.8%)	<0.0001*
	Dyslipidemia	2 (5.6%)	16 (13.8%)	0.24
	Carotid artery stenosis	2 (5.6%)	8 (6.9%)	1
	Smoking	2 (5.6%)	6 (5.2%)	1
	Hormone therapy	4 (11.1%)	2 (1.7%)	0.028#
	Time of stroke			
	Morning	6 (16.7%)	40 (34.5%)	
	Evening	20 (55.6%)	60 (51.7%)	0.047*
	Midnight	10 (27.8%)	16 (13.8%)	
	Type of stroke			
	Ischemic	36 (100.0%)	112 (96.6%)	0.57
	Hemorrhagic	0 (0.0%)	4 (3.4%)	
Stroke Characteristics	Stroke history			
	First	30 (83.3%)	70 (60.3%)	0.011*
	Multiple	6 (16.7%)	46 (39.7%)	
	Thrombus/embolism	2 (5.6%)	14 (12.1%)	0.26
	Extracranial vessel involvement	2 (5.6%)	12 (10.3%)	0.52
	Large artery atherosclerosis	6 (16.7%)	6 (5.2%)	0.036#
	Small artery occlusion	0 (0.0%)	6 (5.2%)	0.33

*p < 0.05, statistical significance using the Chi-Square Test. #p < 0.05, statistical significance using the Exact Test.

Symptom presentation and admission characteristics

The symptoms varied considerably between the two groups (Table 2). While visual symptoms (38.9% vs. 5.2%; p=<0.0001) were more prevalent in the younger cohort, a more significant proportion of older patients exhibited arm (16.7% vs. 77.6%; p<0.0001) and leg (22.2% vs. 74.1%; p=0.0001) weakness, language im-pairment (0% vs. 19%; p=0.005), and slurred speech (16.7% vs. 37.9%; p=0.018). The occurrence of sensory symptoms was comparable between the two groups (6.9% vs 5.6%, p=0.777). Nonetheless, only a small proportion of patients in both cohorts required ICU admission (16.7% vs 15.5%) or had complications during admission (11.1% vs. 15.5%) with no between-group differences (Table 2).

Table 2: Comparison of clinical symptoms and admission characteristics between young and older stroke patients

Clinical symptoms	**Patients <45** *n (%)*	**Patients ≥ 45** *n (%)*	***P***
Impaired level of consciousness	4 (11.1%)	26 (22.4%)	0.13
Visual symptoms	14 (38.9%)	6 (5.2%)	<0.0001#
Facial asymmetry	2 (5.6%)	14 (12.1%)	0.26
Arm weakness	6 (16.7%)	90 (77.6%)	<0.0001*
Leg weakness	8 (22.2%)	86 (74.1%)	<0.0001*
Sensory symptoms	2 (5.6%)	8 (6.9%)	0.777
Language impaired	0 (0.0%)	22 (19.0%)	0.005*
Slurred speech	6 (16.7%)	44 (37.9%)	0.018*
ICU admission	6 (16.7%)	24 (20.7%)	0.60
Complications during admission	4 (11.1%)	18 (15.5%)	0.51

*p < 0.05, statistical significance using the Chi-Square Test. #p < 0.05, statistical significance using the Exact Test.

Upon admission, the older patient group had significantly higher serum hemoglobin (12.83±2.15 vs. 13.79±2.32 g/dL; p=0.029), serum LDL (99.5±24.1 vs. 101.1±34 mg/dL; p<0.0001), and systolic blood pressure (127.72±20.42 vs. 155.22±30.14 mmHg; p<0.0001) albeit with lower serum total cholesterol (166±25 vs. 161±46 mg/dL; p=0.0001), serum HDL (44.2±14.8 vs. 36.3±10.7 mg/dL; p=0.001), HbA1c (8.28±1.42 vs. 7.71±1.37 %; p=0.017), international normalized ratio (1.89±0.81 vs. 1.21±0.31; p<0.0001), BMI (29.09±6.12 vs. 28.59±5.02 kg/m²); p<0.0001), and heart rate (89.39±17.14 vs. 82.53±18.19 bpm; p<0.0001) (Table 3).

Table 3: Comparison of clinical parameters during admission between young and older stroke patients

Variables	**Patients <45**		**Patients ≥ 45**		**P**
	Mean ±SD	**Median**	**Mean ±SD**	**Median**	
Hemoglobin, g/dL	12.83±2.15	13.15	13.79±2.32	14.05	0.029*
Red blood cell count, M/µL	5±1	5	5±1	5	0.986
Cholesterol, mg/dL	166±25	160	161±46	158	<0.0001*
HDL, mg/dL	44.2±14.8	38.8	36.3±10.7	35.8	0.001*
LDL, mg/dL	99.5±24.1	91.0	101.1±34.0	97.5	0.000*
HbA1c, %	8.28±1.42	8.27	7.71±1.37	7.55	0.017*

Erythrocyte sedimentation rate, mm/hr	27.78±14.11	31.75	35.22±18.03	32.50	0.079
International normalized ratio	1.89±0.81	2.11	1.21±0.31	1.10	<0.0001#
Ferritin, ng/mL	16.27±3.70	15.89	15.79±0.75	15.89	0.10
Body mass index, kg/m²	29.09±6.12	28.98	28.59±5.02	28.20	<0.0001*
Systolic blood pressure, mmHg	127.72±20.42	128.00	155.22±30.14	155.00	<0.0001*
Diastolic blood pressure, mmHg	79.00±12.58	79.50	80.78±14.60	80.50	0.54
Heart rate, beats per min	89.39±17.14	86.00	82.53±18.19	82.50	<0.0001*
Respiratory rate, breaths per min	20.17±1.08	20.00	19.79±2.96	20.00	0.28
Temperature, °C	36.96±0.17	37.00	36.84±0.33	36.95	0.032#

*Significant t-test; #Significant Mann-Whitney test

Clinical Outcomes

In terms of clinical outcomes, younger patients had a significantly longer median length of hospitalization (8 vs. 5 days; p=0.042), although the median length of ICU stay (3 vs. 4 days; p=0.83), the proportion of pa-tients requiring referral to rehabilitation unit (22.2% vs. 32.8%, p=0.22), or mortality rate (0% vs. 3.4%, p=0.57) did not differ significantly between the two groups (Table 4).

Table 4: Comparison of clinical outcomes between young and older stroke patient

Parameter	Patients <45	Patients ≥ 45	*P*
Median ICU stay duration, days	5	3	0.83
Median Hospital stays, days	8	5	0.042#
Discharge, n (%)	34 (94.4%)	112 (96.6%)	0.62
Rehabilitation unit referral, n (%)	8 (22.2%)	38 (32.8%)	0.22
Died, n (%)	0 (0.0%)	4 (3.4%)	0.57

#Significant Mann-Whitney test

In multivariate analysis, young patients were significantly more likely to present with elevated HbA1c [OR=1.927 (95%CI 1.195-3.107); p=0.007] and visual symptoms [OR=16.429 (95%CI 3.92-68.865); p<0.0001] than older patients. However, younger patients were less likely to have pre-existing hypertension [OR=0.0472 (95%CI 0.006-0.342); p=0.003] and T2DM [OR=0.080 (95%CI 0.016-0.392); p=0.002] or present with arm weakness [OR=0.197 (95%CI 0.046-0.844); p=0.028], and slurred speech [OR=0.159 (95%CI 0.035-0.731); p=0.018] than older patients (Table 5). Other variables, such as gender, BMI, LDL, total cholesterol, myocardial infarction, smoking status, ICU admission, and leg weakness, were not associated with a significant change **Table 5: Multivariable analysis of factors associated with young stroke patients.**

Variables	Coefficient (B)	Odds Ratio (OR)	95% CI for OR	*P*
Sex (Female)	-.579	0.561	0.126 to 2.492	0.447
Body mass index	.119	1.126	0.978 to 1.297	0.099

Elevated HbA1c	.656	1.927	1.195 to 3.107	0.007*
LDL	.004	1.004	0.977 to 1.031	0.794
Total cholesterol	-.004	0.996	0.978 to 1.014	0.635
HDL	.056	1.058	0.993 to 1.127	0.080
Hypertension	-3.066	0.047	0.006 to 0.342	0.003*
Type 2 Diabetes Miletus	-2.524	0.080	0.016 to 0.392	0.002*
Smoking	2.305	10.026	0.804 to 125.061	0.073
Myocardial infarction	.564	1.758	0.213 to 14.494	0.600
ICU admission	.578	1.782	0.242 to 13.129	0.571
First event	.532	1.702	0.383 to 7.567	0.485
Visual symptoms	2.799	16.429	3.92 to 68.865	<0.0001
Arm weakness	-1.625	0.197	0.046 to 0.844	0.028*
Leg weakness	-1.434	0.238	0.055 to 1.025	0.054
Slurred speech	-1.837	0.159	0.035 to 0.731	0.018*

*Significant p-value at 0.05 level

Discussion

The population characteristics observed in this study are consistent with the population characteristics of stroke patients reported by previous studies from the Aseer region, providing validity for our dataset. For instance, Alhazzani et al (19). reported that while overall stroke incidence was higher among males (65.52 vs. 48.14 per 100,000 persons), the data was influenced by strongly disproportionate incidence among men in the ≥ 65 years age group. In the 45-49 age group, females had a higher incidence (42.14 vs. 80.18 per 100,000), while the incidence was comparable between males and females in the other age groups. It is noteworthy that the incidence reported by Alhazzani et al (19). only included first-stroke patients admitted to all hospitals in the Aseer region in 2016, while we report a slightly higher proportion of females in the younger cohort (55.6%) and a higher proportion of males (67.8%) in the older cohort since inception to 2019 but from just one hospital in the Aseer region. Furthermore, another study by the same research group showed that the overall case fatality rate did not differ significantly by gender or age group among in-hospital first-time stroke patients. The presence of hypertension, current smoking status, and drowsy, unconscious, or immobile at admission were predictors of in-hospital mortality risk(25).

In terms of the primary study outcomes, younger stroke patients were less likely to present with arm weakness or slurred speech but were more likely to present with visual symptoms compared to older patients. Only a few studies have previously investigated the differences in stroke symptoms at presentation between young and older patients. In the sifap1 study, arm/paresis (57.7%) and speech symptoms (55.4%) were the most common presenting symptoms in young stroke patients aged 18–55 years than facial (38.5%) or visual (Hemianopia: 14.4%; Diplopia:10.3%; Amaurosis fugax: 2.3%) symptoms although 55.6% patients presented with somatosensory deficits(26). However, Eddelien et al.(27) reported lower odds of presenting with sensory symptoms with each year increment in age but no changes in odds of other symptoms. In contrast, an analysis of the National Acute Stroke ISraeli registry showed a significantly lower prevalence of speech (34.5% vs. 45.5%) but a higher prevalence of sensory (47% vs. 27%) symptoms in patients ≤50 years than those aged >50 years with comparable proportion of patients presenting with motor weakness (68.8% vs. 71.1%) or visual symptoms (14% vs. 11.7%) in the two groups (28).

In addition, we noted that younger patients were less likely to have pre-existing hypertension or T2DM but had a higher likelihood of presenting with elevated HbA1c. Earlier studies indicate that while T2DM is a significant risk factor for incident stroke(29), HbA1c levels are not associated with cerebrovascular lesions in ischemic stroke patients after adjustment for age and hypertension (30, 31). It is noteworthy that HbA1c levels typically increase with age in non-diabetic individuals but decrease in diabetic patients(31-33). In our cohort, younger patients had higher median HbA1c levels (8.27% vs. 7.55%) but a disproportionately low prevalence of T2DM (11.1% vs. 63.8%) than older patients. Therefore, the patient's age and diabetic status must be concurrently assessed if the HbA1c level is to be used as a prognostic indicator(32).

Moreover, Al-Saleem et al (34) showed suboptimal hypertension-related training of doctors and nurses, the proportion of patients with controlled blood pressure, and patient compliance in the Aseer region. Low medication adherence has also been reported in a nationally representative sample of post-stroke patients from KSA (35). Hence, future healthcare policies and patient care guidelines must incorporate training healthcare professionals and educating stroke patients to manage stroke-related risk factors.

Our findings also underscore the need to improve the availability and access to occupational therapists in KSA, given that an outsize proportion of stroke patients were older with a vastly greater prevalence of motor and speech-related symptoms at presentation than younger patients. Yet, the referral rate to the rehabilitation unit was not statistically significant between the two groups. Several authors have identified the lack of training programs for stroke rehabilitation professionals on par with international standards or to cope with the current and projected local demand for stroke rehabilitation (14, 36). In addition to the need to increase the number of stroke neurologists and interventional neuroradiologists(14), researchers have called for the introduction of post-professional programs monitored by the Saudi Commission for Health Specialties (36) with the inclusion of stroke rehabilitation programs in the national clinical guideline (37). Such efforts are likely to have a significant positive impact on the burden of stroke care. In a cost-effectiveness study, Al-Senani et al (38) showed that a more comprehensive stroke care development program may produce better health outcomes regarding quality-adjusted life-years and estimated savings of $602 million in healthcare expenditure over 15 years.

Another key issue in Saudi Arabia is the lack of comprehensive stroke awareness. In a recent study in which three-fourths of the participants were under 40 years old, only 2.2% of the participants recognized all fourteen risk factors of stroke (39). The most recognized risk factors were hypertension (81.7%), history of stroke (74.1%), dyslipidemia (57.2%), smoking (55.1%), and sedentary lifestyle (50.8%)[39]. A recent survey of diabetic patients from the Aseer region showed that a higher proportion of participants (69.1%) had good knowledge of stroke, defined as a knowledge item score of ≥60%, albeit with better score among participants aged 50-65 years (74.4%) than those aged 25-34 (65.6%) and 35-49 (68.18%) years(40).

However, the study has certain limitations, including its retrospective design, which may have introduced selection bias. The single-center setting also poses a potential limitation, restricting the generalizability of the findings to other regions or countries. For future research, it would be beneficial to conduct prospective studies with a larger sample size and multiple centers. This approach would allow for a more in-depth investigation into the differences in stroke symptoms and comorbidities between young and older patients.

Furthermore, future studies could concentrate on developing targeted prevention and treatment strategies for stroke in young and middle-aged adults. Additionally, there is a need to allocate medical resources effectively to address the

escalating burden of stroke in the region. Investigating the etiology of stroke in young and middle-aged adults could provide valuable insights, aiding in the development of targeted prevention and treatment strategies.

Conclusions

We conclude that young stroke patients were less likely to present with arm weakness, slurred speech, pre-existing hypertension, and T2DM but were more likely to present with visual symptoms and elevated HbA1c than older patients.

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Institutional Review Board Statement: Ethical approval was secured from the Ethics Committee of Aseer Central Hospital. All procedures and methodologies employed were in strict accordance with the institution-al ethical standards, the 1964 Helsinki Declaration, and its later amendments. Any personal identifiers were removed or altered to ensure the confidentiality and anonymity of the patient data.

Informed Consent Statement: The requirement for securing informed consent was waived due to the study's retrospective nature.

Data Availability Statement: Due to privacy and ethical constraints, the raw patient data cannot be publicly disclosed. Interested researchers may request access to de-identified and aggregated data through a formal application process, contingent upon approval by the institutional review board and compliance with data protection regulations. For inquiries regarding data availability and access procedures, please contact the corresponding author.

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