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The Impact of Malnutrition on Perioperative Ischemic Stroke in Transcatheter Aortic Valve Replacement (TAVR): A Retrospective Cohort Study of the National Inpatient Sample

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Keywords: cerebral embolic protection | ischemic stroke | malnutrition | transcatheter aortic valve replacement

ABSTRACT

Background and Aims: Ischemic stroke is a serious risk for patients undergoing transcatheter aortic valve replacement (TAVR). The relationship between malnutrition and post-TAVR ischemic stroke remains unclear. This study investigates this association using the National Inpatient Sample (NIS) data.

Methods: A retrospective observational study was conducted using NIS data from 2012 to 2021. We included patients who underwent TAVR and were diagnosed with malnutrition based on ICD-9 and ICD-10 codes. Patients under 18 years, with a history of preoperative stroke, with both ischemic and hemorrhagic strokes, or with incomplete data were excluded. Logistic regression was performed to evaluate the association between malnutrition and ischemic stroke, adjusting for potential confounders. Sensitivity analyses included stratified analysis and propensity score matching.

Results: Among 364,580 TAVR patients, 10,415 (2.86%) were diagnosed with malnutrition. Malnourished patients were older (78.04 vs. 77.40), predominantly white (85.69%), and had a higher incidence of ischemic stroke (11.47% vs. 7.25%, $p < 0.001$). After adjusting for common ischemic stroke risk factors, malnutrition was significantly associated with an increased risk of ischemic stroke (aOR: 1.51; 95% CI: 1.31–1.74). This association remained significant in the propensity-matched cohort. Subgroup analyses consistently showed associations between malnutrition and stroke risk across various demographic and clinical factors. Time trend analysis showed no significant difference in the annual incidence of perioperative ischemic stroke between malnourished patients with or without cerebral embolic protection devices ($p = 0.439$).

Abbreviations: AHRQ, agency for healthcare research and quality; AOR, adjusted odds ratio; CI, confidence interval; HCUP, healthcare cost and utilization project; ICD-10-CM, international classification of diseases, tenth revision, clinical modification; ICD-9-CM, international classification of diseases, ninth revision, clinical modification; NIS, national inpatient sample; OR, odds ratio; PSM, propensity score matching; SAVR, surgical aortic valve replacement; SMD, standard mean difference; TAVR, transcatheter aortic valve replacement.

Haowei Li and Guangzhi Cong contributed equally to this study and should be considered co-first authors.

Conclusion: Malnutrition is associated with a higher risk of ischemic stroke following TAVR, highlighting the need for targeted interventions.

1 | Introduction

Transcatheter aortic valve replacement (TAVR) has emerged as the preferred treatment modality for patients with aortic stenosis, across a spectrum of risk profiles, surpassing traditional surgical aortic valve replacement (SAVR) in efficacy and outcomes [1]. Despite technological advancements, TAVR still carries risks, including conduction block, paravalvular leak, coronary artery obstruction or myocardial infarction, local vascular complications, aortic dissection, cardiac tamponade, valve migration or detachment, acute kidney injury, and stroke.

Stroke, particularly ischemic stroke, is a severe complication following transcatheter aortic valve replacement (TAVR), with notably high rates of disability, mortality, and recurrence [2–5]. Most strokes occur within 24 h post-TAVR, with a median onset time of 6 h [6–8]. Without prompt treatment, patients may experience various complications, including sensory and motor impairments, communication difficulties, cognitive dysfunction, psychological issues, and dysfunction of other organs, imposing significant burdens on patients and their families. According to a study based on national readmission databases, the incidence of complications and hospitalized mortality significantly increases following TAVR-associated acute ischemic strokes, tripling the risk and substantially raising hospitalization costs by 32%. Additionally, there's a notable surge in the utilization of skilled nursing and intermediate care facilities by 121%, along with a 132% increase in readmission costs. Furthermore, ischemic strokes prolong hospital stays and elevate the occurrence of mechanical ventilation, gastrostomy, tracheostomy, and nonhome discharge rates [9]. Given the adverse effects and economic burden associated with ischemic strokes, identifying their risk factors is crucial for preventing ischemic strokes in TAVR patients.

The occurrence of post-TAVR ischemic stroke is closely associated not only with surgical factors but also with patient and disease-related factors [10]. A multicenter real-world study indicated that most predictive factors for stroke at 30 days and 6 months post-TAVR are patient-related, including pre-existing neurological dysfunction, diabetes, left ventricular dysfunction, and anatomical characteristics such as bicuspid valve anatomy [11]. However, given the intricate interplay between patient characteristics and surgical factors, further clinical practice and data analysis are required to explore the predictive factors for post-TAVR stroke.

Malnutrition is a common risk factor among stroke patients and is frequently observed in individuals undergoing TAVR [5, 12]. Malnourished patients undergoing TAVR exhibit significantly higher mortality rates, prolonged hospital stays, and increased incidence of acute renal injury, as well as elevated rates of pulmonary, cardiovascular, and infectious complications. Furthermore, malnutrition is associated with a greater likelihood of readmission within 30 to 90 days and incurs an average additional cost of $123,555 for inpatient care [13]. Given the predictive value of malnutrition for adverse outcomes following TAVR, we hypothesize that preoperative malnutrition may be associated with an increased risk of ischemic stroke after TAVR. However, detailed research on the relationship between malnutrition post-TAVR and ischemic stroke is currently limited. Therefore, this study aims to comprehensively analyze the detailed relationship between perioperative malnutrition in TAVR patients and the risk of ischemic stroke using data from a national inpatient sample (NIS) database.

2 | Materials and Methods

2.1 | Data

This study used the National Inpatient Sample (NIS) Healthcare Cost and Utilization Project (HCUP) database, which is funded by the Agency for Healthcare Research and Quality (AHRQ). The NIS database is an extensive compilation of data from many payers, including almost 20% of discharges from community hospitals in the United States [14]. This database, known as the largest publicly accessible all-payer inpatient database, was established as part of the Healthcare Cost and Utilization Project. The HCUP data is accessible to the public and has been stripped of any identifying information. It has been verified by AHRQ that it is not required to get Institutional Review Board permission.

2.2 | Patient Selection

We conducted a retrospective query of the database spanning from 2012 to 2021. The International Classification of Diseases Ninth Revision and Tenth Revision Clinical Modification (ICD-9-CM, ICD-10-CM) procedure codes 35.05, 35.06, 02RF3JZ, 02RF3KZ, 02RF38Z, 02RF37Z, 02RF37H, 02RF38H, 02RF3JH, 02RF3KH, and 02RF4X were used to identify TAVR admissions (Table S1). Exclusion criteria were applied as follows:

Patients aged < 18 years ($n = 91$);

Patients with preoperative stroke history (defined by ICD-9/10 codes Z86.73, I69, 438 and V12.54 in prior admissions; $n = 12{,}256$);

Patients with concurrent ischemic and hemorrhagic stroke ($n = 73$);

Patients missing critical variables (age, gender, race, ischemic stroke diagnosis codes, or malnutrition-related codes) were excluded ($n = 11{,}893$). Noncritical variables (e.g., length of stay) with missing data were retained if other essential variables were complete.

According to the Healthcare Cost and Utilization Project, malnutrition encompasses several conditions such as protein-calorie malnutrition, cachexia, nutritional neglect, weight loss due to

failure to flourish, underweight, and postsurgical nonabsorption [15]. Patients who satisfied at least one of these criteria were deemed malnourished. Corresponding ICD-9/10 codes are listed in Table S1. The malnourished group was then categorized into two subgroups depending on their use of cerebral embolic protection devices (CEP group vs. non-CEP group).

Demographic variables obtained included age, gender, race, length of stay (LOS), and hospital region distribution at admission. The primary outcomes of the study included ischemic stroke diagnosed using ICD-9 and ICD-10-CM diagnostic codes, listed in Table S1. Additionally, we identified complications before the primary analysis using ICD-9 and ICD-10-CM codes, including Peripheral Vascular Disease, Hypertension, Diabetes, Obesity, Smoking, Dyslipidemia, Coagulopathy, Endocarditis, Liver Disease, Renal Failure, Fluid And Electrolyte Disorders, Chronic Ischemic Heart Disease, Congestive Heart Failure, Obstructive Sleep Apnea, Atrial Fibrillation, and Chronic Pulmonary Disease. To ensure accuracy, two independent researchers performed data extraction and classification of ICD codes. Discrepancies (e.g., conflicting stroke subtype assignments) were resolved through arbitration by a third senior investigator.

2.3 | Data Analysis

For weighted data, categorical variables were reported as weighted percentages, and continuous variables as weighted means with corresponding confidence intervals (CIs). For unweighted and propensity score-matched data, categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD). The χ^2 test was used to compare the categorical data, while linear regression was used for the continuous variables. Malnutrition status was used to characterize the research population's baseline characteristics. Temporal trends in ischemic stroke and malnutrition incidence rates among TAVR patients were analyzed using smooth curve fitting, comparing the annual ischemic stroke incidence rates between malnourished and non-malnourished patients. Multiple regression analysis was conducted in three models. Variables were adjusted if they exhibited a significant correlation with clinical outcomes ($p < 0.1$) or if their inclusion altered the regression coefficient by ≥ 10% [16], a threshold that inherently excludes collinear variables due to their disproportionate impact on model stability (Table S2). Additionally, based on the utilization of cerebral embolic protection devices, we further examined the influence of malnutrition on perioperative ischemic stroke after TAVR. All the analyses mentioned above were conducted using weighted samples for national estimates, in conjunction with the Healthcare Cost and Utilization Project regulations for utilizing the NIS database [17].

2.4 | Sensitivity Analysis

We conducted the sensitivity analysis below to ensure the data analysis was robust: First, a stratified analysis was performed based on demographic characteristics and comorbidities to validate the stability and consistency of the primary outcomes across different subgroups. Additionally, interaction effect testing was conducted to assess the heterogeneity of outcomes across subgroups and validate the consistency of our findings. To further minimize the influence of baseline factors, we applied the propensity score matching (PSM) technique [18, 19]. Confounding variables with significant effects on the outcome were systematically identified through a combination of literature review and stepwise logistic regression analysis, ultimately resulting in a set of matching variables that included age, sex, race, and 14 comorbid conditions (Table S3). These comorbidities encompassed Peripheral Vascular Disease, Hypertension, Diabetes, Obesity, Smoking, Dyslipidemia, Coagulopathy, Renal Failure, Fluid and Electrolyte Disorders, Chronic Ischemic Heart Disease, Congestive Heart Failure, Obstructive Sleep Apnea, Atrial Fibrillation, and Chronic Pulmonary Disease. The propensity scores were matched using the 1:2 closest neighbor matching approach, with a maximum caliper width set to 0.01 times the standard deviation of the propensity scores [20]. Standardized mean differences were calculated to evaluate the balance of factors before and after the matching process, after the end of propensity score matching (PSM). An absolute value of less than 0.1 indicates effective management of confounding factors and acceptable balance [21]. The statistical analyses were performed using the R software program (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions Inc., Boston, MA). A bilateral significance level of 0.05 was used to determine whether the results were statistically significant.

3 | Results

3.1 | Patient Characteristics

Of 463,175 TAVR admissions, 364,580 met inclusion criteria (10,415 malnourished; 354,165 non-malnourished) (Figure 1). Malnourished patients were older and more often male and White. They had a significantly higher rate of non-elective admissions (40.28% vs. 15.01%, $p < 0.001$), along with increased prevalence of key comorbidities such as peripheral vascular disease, coagulopathy, renal failure, fluid and electrolyte disorders, heart failure, atrial fibrillation, and chronic pulmonary disease (Table 1).

3.2 | Temporal Trend

During the study period, the annual incidence of perioperative ischemic stroke among patients undergoing TAVR experienced a continuous decline, reaching its lowest point by 2021. Concurrently, the prevalence of malnutrition demonstrated a yearly decrease (Figure 2). However, malnourished TAVR patients showed an initial decline followed by an increase in the incidence of ischemic stroke over time, whereas non-malnourished TAVR patients demonstrated a sustained decline. Over the whole length of the study, the occurrence of ischemic stroke continually remained greater in the group of individuals who were malnourished compared to the group of individuals who were not malnourished (Figure 3).

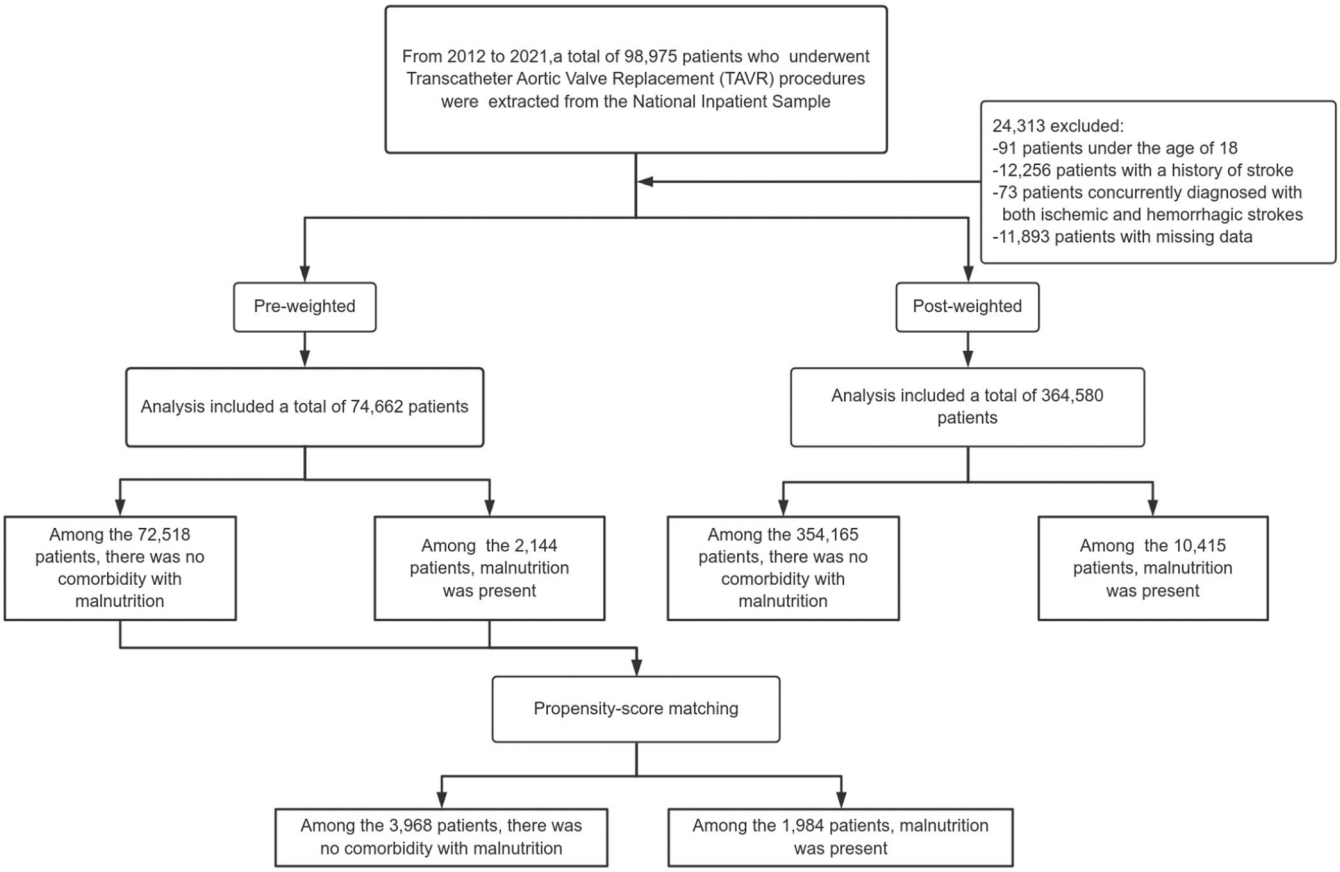


FIGURE 1 | Consort diagram for patient selection.

3.3 | Hospitalization Outcome

Malnourished patients experienced a higher incidence of perioperative ischemic stroke (11.47% vs. 7.25%; $p < 0.001$). In unadjusted analysis, malnutrition was associated with increased stroke risk (OR: 1.62; 95% CI 1.41–1.86; $p < 0.001$), and this association persisted after multivariable adjustment (adjusted OR: 1.51; 95% CI 1.31–1.74; $p < 0.001$) (Table 2, Central Illustration 1). When stratified by CEP use, malnourished patients without CEP had a significantly elevated risk (OR: 1.70; 95% CI 1.45–2.00; $p < 0.001$), whereas those with CEP showed no significant difference (OR: 1.06; 95% CI 0.45–2.52; $p = 0.892$) (Table 3). Additionally, temporal trend analysis in malnourished patients revealed no significant difference in annual ischemic stroke incidence between CEP and non-CEP users ($p = 0.439$) (Figure 4). However, subgroup analyses highlighted the context-dependent protective effects of CEP devices. Notably, the most pronounced benefits were observed in malnourished patients without specific comorbidities: CEP use was associated with substantially reduced stroke risk in those without diabetes (OR: 0.11; 95% CI: 0.01–0.78; P_interaction = 0.002), renal failure (OR: 0.23; 95% CI: 0.06–0.95; P_interaction = 0.049), or chronic pulmonary disease (OR: 0.19; 95% CI: 0.05–0.77; P_interaction = 0.004) (Table S4). These findings suggest that CEP devices may mitigate stroke risk more effectively in malnourished TAVR patients lacking complex metabolic or systemic comorbidities, potentially due to fewer competing pathophysiological pathways.

3.4 | Sensitivity Analysis

Stratified analyses based on demographic characteristics and comorbidities showed that the effect of malnutrition on the incidence of ischemic stroke during perioperative TAVR was consistent across subgroups stratified by age (< 70 and ≥ 70), gender, diabetes, smoking, dyslipidemia, coagulopathy, and congestive heart failure (Table 4). However, further analysis highlighted significant heterogeneity in the magnitude of malnutrition's effects, which were influenced by gender and comorbid conditions. Notably, female patients exhibited a substantially elevated risk of ischemic stroke compared to males (OR: 2.03, 95% CI: 1.69–2.44 vs. OR: 1.29, 95% CI: 1.05–1.58; P_interaction = 0.001), suggesting potential sex-specific vulnerabilities linked to hormonal or metabolic disparities. Additionally, malnutrition synergized with coagulopathy to amplify stroke risk (OR: 2.60, 95% CI: 2.06–3.27; P_interaction < 0.001), highlighting hemostatic dysregulation as a critical pathway in mediating this association. While initial unadjusted interaction tests suggested a higher stroke risk in malnourished patients without dyslipidemia, this finding was contrary to prior study [22]. However, multivariable adjustment revealed alignment with established evidence, confirming that comorbid dyslipidemia significantly heightened stroke risk (adjusted OR: 3.17, 95% CI: 2.39–4.20; P_interaction < 0.001, Table S5). Collectively, these findings underscore the importance of integrating gender, coagulation status, and dyslipidemia into preoperative risk stratification to optimize stroke prevention strategies in malnourished TAVR patients.

TABLE 1 | Baseline characteristics before and after propensity score matching.[a–d]

	Before PSM			After PSM			
	Non-malnutrition	Malnutrition	*p* value	Non-malnutrition	Malnutrition	SMD	*p* value
N	354,165	10,415		3968	1984		
Age	77.40 (77.18, 77.62)	78.04 (77.00, 79.09)	0.200	76.46 ± 10.36	78.65 ± 10.94	0.21 (0.15, 0.26)	< 0.001***
Female	43.38 (42.84, 43.93)	46.71 (43.92, 49.52)	0.022*	1755 (44.23%)	951 (47.93%)	0.07 (0.02, 0.13)	0.007**
Race			0.037*			0.03 (−0.03, 0.08)	0.654
White	87.89 (87.37, 88.40)	85.69 (82.89, 88.11)		3379 (85.16%)	1676 (84.48%)		
Black	3.87 (3.59, 4.18)	5.38 (4.25, 6.78)		206 (5.19%)	114 (5.75%)		
Other	8.23 (7.73, 8.77)	8.93 (7.19, 11.04)		383 (9.65%)	194 (9.78%)		
Selective admission	84.99 (84.05, 85.87)	59.72 (57.22, 62.18)	< 0.001***	3247 (81.83%)	1176 (59.27%)	0.51 (0.46, 0.57)	< 0.001***
Hospital distribution			0.596			0.16 (0.11, 0.21)	< 0.001***
New England	11.08 (7.05, 17.00)	12.87 (4.67, 30.79)		246 (6.20%)	123 (6.20%)		
Middle Atlantic	16.91 (15.41, 18.52)	18.39 (15.00, 22.34)		724 (18.25%)	408 (20.56%)		
East North Central	15.55 (14.13, 17.09)	15.89 (12.90, 19.42)		660 (16.63%)	337 (16.99%)		
West North Central	7.28 (6.47, 8.18)	8.40 (6.50, 10.80)		299 (7.54%)	178 (8.97%)		
South Atlantic	19.75 (18.24, 21.34)	15.22 (12.54, 18.34)		858 (21.62%)	330 (16.63%)		
East South Central	5.96 (5.23, 6.79)	4.56 (3.46, 5.98)		232 (5.85%)	95 (4.79%)		
West South Central	8.10 (7.27, 9.01)	10.23 (7.99, 13.00)		342 (8.62%)	212 (10.69%)		
Mountain	5.21 (4.63, 5.86)	4.94 (3.67, 6.63)		226 (5.70%)	103 (5.19%)		
Pacific	10.16 (9.16, 11.25)	9.51 (7.52, 11.94)		381 (9.60%)	198 (9.98%)		
Peripheral vascular disease	21.65 (21.10, 22.22)	25.88 (21.91, 30.28)	0.028*	993 (25.03%)	552 (27.82%)	0.06 (0.01, 0.12)	0.020*
Hypertension	86.06 (85.20, 86.88)	79.16 (76.56, 81.55)	< 0.001***	3214 (81.00%)	1565 (78.88%)	0.05 (−0.00, 0.11)	0.053
Diabetes	36.44 (35.26, 37.63)	27.08 (25.07, 29.18)	< 0.001***	1458 (36.74%)	530 (26.71%)	0.22 (0.16, 0.27)	< 0.001***
Obesity	22.35 (21.56, 23.16)	7.44 (6.04, 9.14)	< 0.001***	924 (23.29%)	164 (8.27%)	0.42 (0.37, 0.48)	< 0.001***
Smoking	39.29 (38.63, 39.96)	34.52 (29.42, 40.00)	0.080*	1657 (41.76%)	734 (37.00%)	0.10 (0.04, 0.15)	< 0.001***
Dyslipidemia	73.30 (72.65, 73.95)	55.88 (47.62, 63.83)	< 0.001***	2588 (65.22%)	1189 (59.93%)	0.11 (0.06, 0.16)	< 0.001***
Coagulopathy	13.52 (12.81, 14.28)	24.82 (22.60, 27.18)	< 0.001***	910 (22.93%)	481 (24.24%)	0.03 (−0.02, 0.08)	0.260
Endocarditis	0.52 (0.45, 0.60)	3.22 (2.38, 4.34)	< 0.001***	23 (0.58%)	67 (3.38%)	0.20 (0.15, 0.26)	< 0.001***
Liver disease	3.59 (3.30, 3.92)	5.33 (4.20, 6.74)	0.003**	176 (4.44%)	115 (5.80%)	0.06 (0.01, 0.12)	0.022*
Renal failure	30.63 (29.99, 31.28)	41.91 (37.83, 46.11)	< 0.001***	1450 (36.54%)	794 (40.02%)	0.07 (0.02, 0.13)	0.009**
Fluid and electrolyte disorders	15.18 (14.47, 15.91)	36.29 (34.00, 38.66)	< 0.001***	1166 (29.39%)	717 (36.14%)	0.14 (0.09, 0.20)	< 0.001***

(Continues)

TABLE 1 | (Continued)

	Before PSM			After PSM			
	Non-malnutrition	Malnutrition	*p* value	Non-malnutrition	Malnutrition	SMD	*p* value
Chronic ischemic heart disease	67.11 (66.38, 67.84)	65.53 (60.42, 70.31)	0.525	2516 (63.41%)	1348 (67.94%)	0.10 (0.04, 0.15)	< 0.001***
Congestive heart failure	68.83 (67.59, 70.04)	78.59 (75.95, 81.01)	< 0.001***	2681 (67.57%)	1579 (79.59%)	0.28 (0.22, 0.33)	< 0.001***
Obstructive sleep apnea	14.67 (14.27, 15.08)	6.82 (5.48, 8.46)	< 0.001***	745 (18.78%)	140 (7.06%)	0.35 (0.30, 0.41)	< 0.001***
Atrial fibrillation	37.47 (37.03, 37.91)	51.08 (43.87, 58.25)	< 0.001***	1711 (43.12%)	932 (46.98%)	0.08 (0.02, 0.13)	0.005**
Chronic pulmonary disease	26.39 (25.72, 27.06)	33.22 (31.26, 35.24)	< 0.001***	1323 (33.34%)	671 (33.82%)	0.01 (−0.04, 0.06)	0.712

Abbreviations: CI, confidence interval; PSM, propensity score matching; SD, standard deviation; SMD, standardized mean difference.

[a]Before propensity score matching: For continuous variables: survey-weighted mean (95% CI), *p* value was by survey-weighted linear regression. For categorical variables: survey-weighted percentage (95% CI), *p* value was by survey-weighted χ^2 test.

[b]Aftre propensity score matching: Values are presented as mean ± SD or *n* (%). Standardized mean differences (SMD) were calculated as the difference in means or proportions divided by the pooled standard deviation; SMD < 0.1 indicates acceptable balance.

[c]Statistical significance markers: $^*p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

[d]Subgroup definitions: "Other" race: Nonwhite/nonblack; "Selective Admission": Elective admission (planned, nonurgent) vs. nonselective admission (emergency/urgent).

To control for the influence of confounding variables, the Propensity Score Matching (PSM) method was used to equalize the baseline covariates [23]. Following a 1:2 propensity score matching procedure, a total of 1984 malnourished patients were matched with 3968 non-malnourished patients. The SMDs of most covariates were markedly reduced after matching, as shown in Table S3, indicating successful adjustment of confounding factors. In the group of patients matched based on propensity score, the occurrence of ischemic stroke during the perioperative phase after TAVR was greater in malnourished individuals compared to those who were not malnourished (9.68% vs. 7.79%; $p = 0.013$) (Table 2). In multivariate regression analysis after PSM, malnourished patients still had a higher risk of perioperative ischemic stroke during TAVR compared to non-malnourished patients (OR: 1.26; 95% CI: 1.04–1.51; $p = 0.016$) (Central Illustration).

4 | Discussion

We performed a retrospective study using the National Inpatient Sample database from 2012 to 2021. Our analysis revealed several noteworthy findings: (1) Between 2012 and 2021, 2.86% of patients undergoing transcatheter aortic valve replacement (TAVR) and included in the National Inpatient Sample were identified as malnourished. (2) Malnourished patients have a greater likelihood of experiencing perioperative ischemic stroke compared to patients who are not malnourished. (3) Throughout the study period, the occurrence of perioperative ischemic stroke in TAVR patients decreased each year. However, malnourished patients consistently had a higher incidence of ischemic stroke compared to non-malnourished patients. (4) There was no significant difference in the trend of perioperative ischemic stroke incidence between malnourished TAVR patients who used cerebral embolic protection (CEP) and those who did not use CEP.

Preoperative malnutrition is widely acknowledged to be closely associated with unfavorable postoperative outcomes. A study investigating preoperative serum albumin levels in patients undergoing transcatheter aortic valve replacement (TAVR) demonstrated a significant correlation between hypoalbuminemia and increased all-cause mortality rates at both 30 days and 1 year postoperatively [24]. Furthermore, a systematic review and meta-analysis involving 10 studies and 5936 subjects revealed a higher all-cause mortality rate among malnourished patients undergoing TAVR compared to non-malnourished patients [25]. Additionally, an analysis of the 2011–2016 National Readmissions Database identified an independent association between malnutrition and elevated mortality risks, neurological complications, readmissions, and increased resource utilization among recipients of TAVR [13]. Notably, this analysis did not specifically examine the independent relationship between preoperative malnutrition in TAVR patients and perioperative stroke, particularly ischemic stroke. Given that ischemic strokes are predominant in post-TAVR cases [26], our study provides compelling evidence on the association between preoperative malnutrition and ischemic stroke after TAVR, utilizing recent data that reflects current clinical practices and technological advancements.

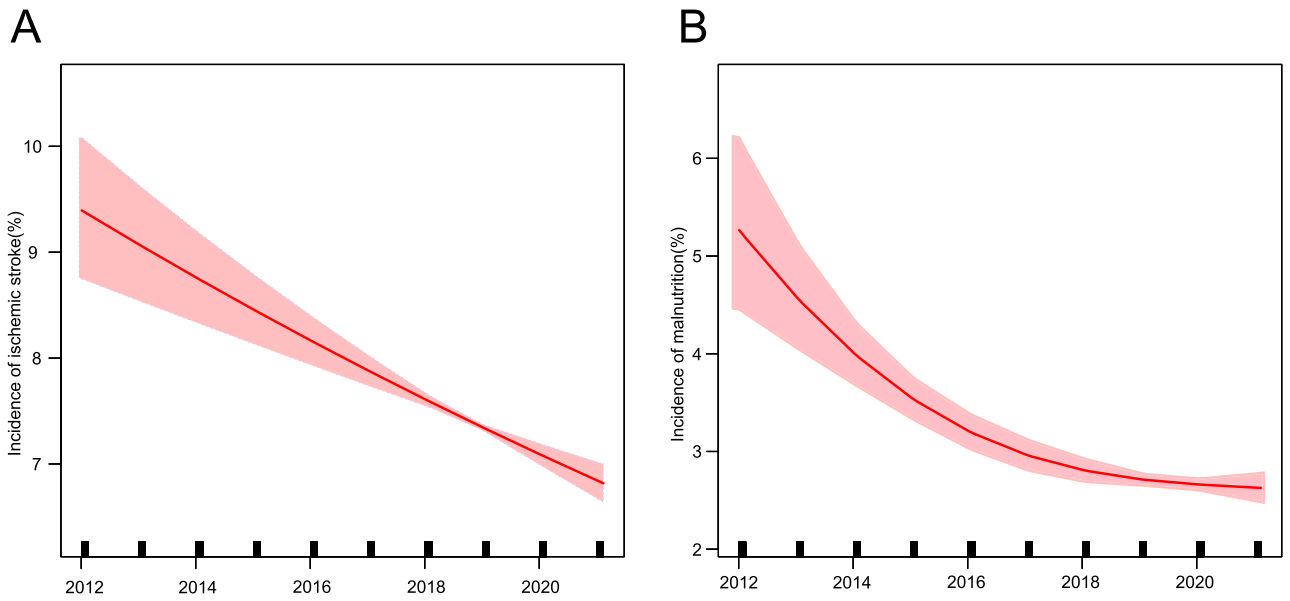


FIGURE 2 | Time trends in the incidence of ischemic stroke and malnutrition in TAVR patients from 2012 to 2021. (A) The trend of ischemic stroke occurrence in patients with TAVR. (B) The trend of malnutrition occurrence in patients with TAVR. TAVR = Transcatheter Aortic Valve Replacement.

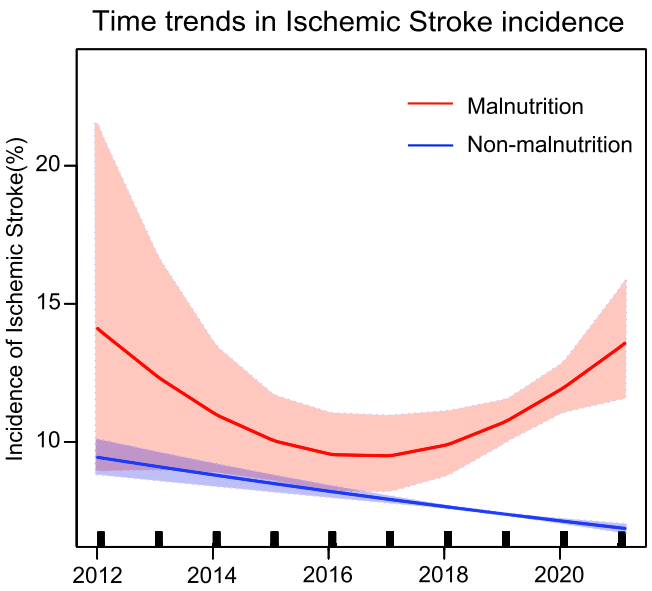


FIGURE 3 | Time trend of 10-year incidence of ischemic stroke.

Several mechanisms might explain the relationship between malnutrition and perioperative ischemic stroke in TAVR patients. Firstly, malnutrition alters blood composition by increasing red cell mass and impairing platelet function, which elevates blood viscosity and thrombosis risk [27]. Vitamin K deficiency further disrupts hemostasis by impairing γ-carboxylation of both procoagulant factors (II, VII, IX, X) and anticoagulant proteins (C, S), creating a thrombogenic imbalance [28, 29]. The resultant imbalance between procoagulant and anticoagulant pathways not only elevates bleeding risk but also paradoxically promotes thrombosis due to impaired regulation of thrombin generation [30]. Our finding of a higher prevalence of coagulopathy in malnourished patients (OR: 2.60; $p < 0.001$) underscores the critical role of nutritional status in maintaining hemostatic equilibrium. Secondly, malnutrition induces a pro-inflammatory state—elevated IL-6, TNF-α, and CRP [31] —that impairs endothelial function by reducing nitric oxide bioavailability, increasing oxidative stress, and vascular permeability [32], and accelerates atherosclerosis via macrophage activation and foam cell formation [33]. Our findings of higher peripheral vascular disease (25.88% vs. 21.65%) and chronic pulmonary disease (33.22% vs. 26.39%) rates in malnourished patients align with this pathway, as both conditions are driven by systemic inflammation and endothelial dysfunction. Inflammation-driven endothelial dysfunction, combined with deficiencies in vascular-protective nutrients (e.g., vitamin D, B12, folate), likely accelerates vascular stiffening and plaque instability, further elevating stroke risk [34], which is consistent with previous findings on the prognostic value of immunonutritional status in cardiovascular disease [35]. Thirdly, malnutrition disrupts metabolic homeostasis, causing electrolyte imbalances (e.g., hypokalemia) and renal dysfunction. Hypokalemia increases arrhythmia susceptibility [36], which may explain the higher incidence of atrial fibrillation (51.08% vs. 37.47%) and heart failure (78.59% vs. 68.83%) in malnourished patients [37, 38]. Such arrhythmias and hemodynamic instability directly predispose to cerebral hypoperfusion and embolic event [39]. Fourthly, we observed significant heterogeneity across patient subgroups (Table 4). Female patients faced nearly double the risk of males, potentially driven by postmenopausal estrogen decline, which exacerbates metabolic inflexibility and inflammation [40], or sociocultural factors influencing nutritional access and dietary patterns. Despite higher absolute risk in the elderly (≥ 70 years: OR = 1.63 vs. < 70 years: OR = 1.59), the lack of significant interaction (P_interaction = 0.908) underscores that malnutrition elevates stroke risk universally across age groups, advocating for routine nutritional screening in all TAVR candidates. Emerging evidence implicates gut dysbiosis in malnutrition-related stroke risk. Reduced fiber intake lowers short-chain fatty acid (SCFA) production (e.g., butyrate), exacerbating systemic inflammation, while elevated trimethylamine N-oxide (TMAO) promotes

TABLE 2 | Multivariable regression equations for ischemic stroke and overall stroke before and after propensity score matching.[a–d]

Exposure	Before PS matching				After PS matching	
	N	Non-adjusted	Adjust I	Adjust II	*N*	Non-adjusted
Ischemic Stroke						
Non-malnutrition	25,677 (7.25%)	1	1	1	309 (7.79%)	1
Malnutrition	1195 (11.47%)	1.62 (1.41, 1.86) < 0.001***	1.55 (1.35, 1.78) < 0.001***	1.51 (1.31, 1.74) < 0.001***	192 (9.68%)	1.26 (1.04, 1.51) 0.016*
Overall Stroke						
Non-malnutrition	25,819 (7.29%)	1	1	1	313 (7.89%)	1
Malnutrition	1205 (11.57%)	1.62 (1.42, 1.86) < 0.001***	1.55 (1.35, 1.78) < 0.001***	1.51 (1.31, 1.73) < 0.001***	194 (9.78%)	1.25 (1.04, 1.51) 0.016*

Abbreviations: CI, confidence interval; OR, odds ratio; PSM, propensity score matching.

[a]Y: Ischemic Stroke; Overall Stroke. X: Malnutrition. Outcome Definitions: Overall Stroke: All stroke types (ischemic, hemorrhagic, and unspecified).

[b]Odds ratios (OR) and 95% confidence intervals (CI) from logistic regression models. Non-adjusted models include only malnutrition status. Adjust I models additionally adjust for age (continuous, years), sex (reference = male), race (reference = White), admission type (reference = elective), and hospital region.(reference = New England). Adjust II models further adjust for comorbidities selected by literature review and stepwise logistic regression (variables with $p < 0.1$ in univariate analysis or altering the malnutrition coefficient by ≥ 10%): peripheral vascular disease, hypertension, diabetes, obesity, smoking, dyslipidemia, coagulopathy, renal failure, fluid and electrolyte disorders, chronic ischemic heart disease, congestive heart failure, obstructive sleep apnea, atrial fibrillation, and chronic pulmonary disease.

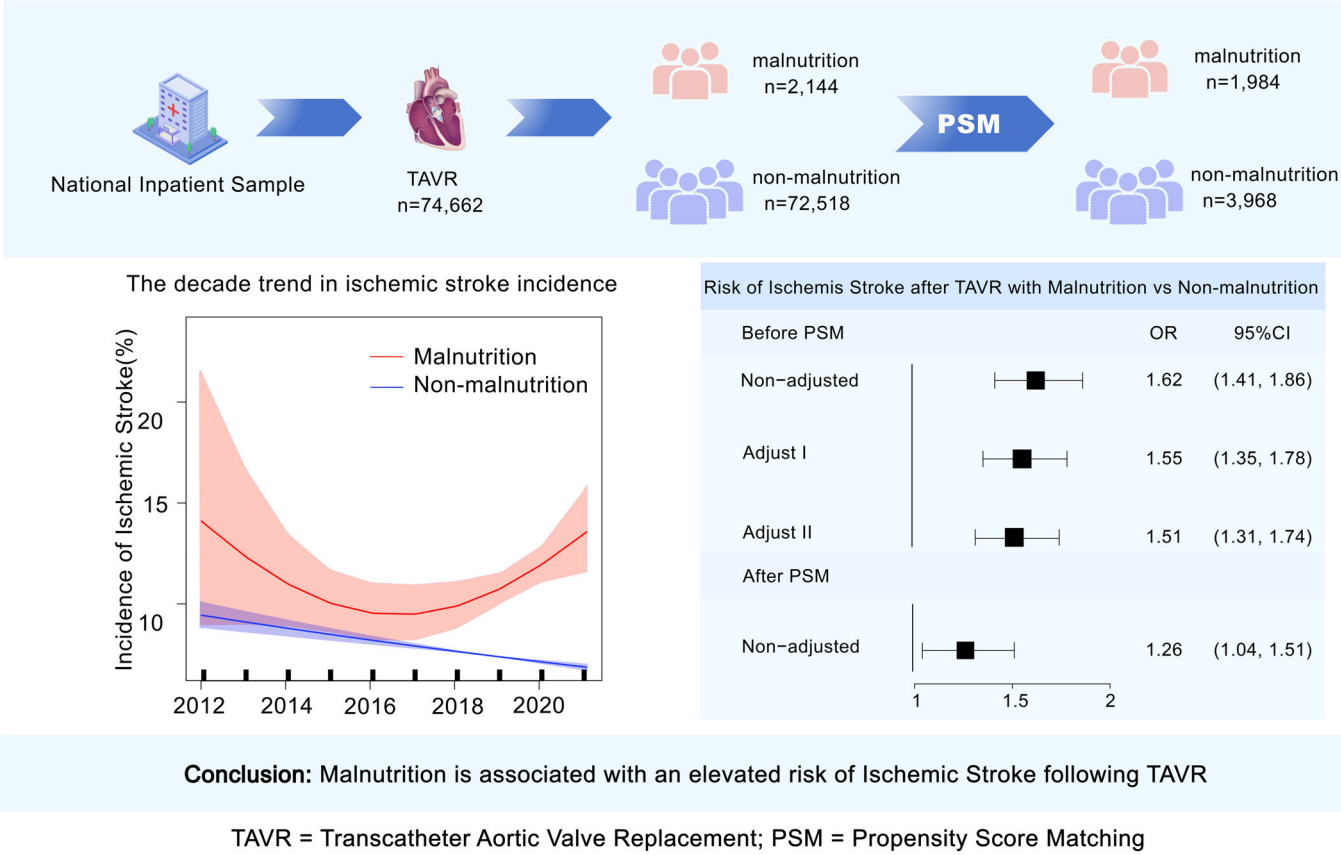
[c]Propensity scores were estimated via logistic regression on the above covariates; 1:2 nearest-neighbor matching without replacement, caliper = 0.01 SD. Balance was assessed by standardized mean differences (|SMD| < 0.1 indicating acceptable balance).

[d]Statistical significance markers: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

atherosclerosis [41]. Although our study did not assess gut microbiota or metabolites, this pathway provides a novel direction for future research linking nutrition, microbial ecology, and cerebrovascular health. Finally, malnutrition compromises immunity, increasing infection risk—a known driver of thromboembolism via inflammation-induced hypercoagulability [42]. This pathway may further explain the elevated stroke risk in malnourished patients, particularly those with chronic comorbidities. While our analysis adjusted for multiple clinical confounders, residual bias from unmeasured variables (e.g., dietary patterns, substance use, or socioeconomic status) may persist. For example, malnourished patients with limited access to nutrient-rich diets or preventive care may simultaneously experience compounded vascular risks [43]. Previous studies have reported symptomatic new-onset stroke rates of 2%–5% after TAVR. In contrast, our ICD-based analysis identified a higher overall incidence of 7.41%, likely reflecting broader capture of mild or asymptomatic events in administrative data and improved detection over time through advances in neuroimaging and heightened clinical awareness. Despite this elevated baseline, we observed a steady annual decline in stroke rates, which corresponds to ongoing refinements in TAVR device design, growing operator expertise, and enhanced perioperative management. Concurrently, the proportion of malnourished patients decreased, suggesting that preoperative nutritional screening and multidisciplinary care pathways may already have an impact.

When stratified by nutritional status, however, divergent patterns became evident. Non-malnourished patients experienced a continuous decrease in stroke incidence throughout the study period, whereas malnourished patients experienced an initial reduction followed by a gradual increase. At every time point, the malnourished cohort had a higher incidence than their non-malnourished counterparts. These persistent disparities suggest that malnutrition may attenuate the benefits of evolving TAVR practice and underscore the continued importance of nutritional status in perioperative ischemic stroke risk. Therefore, our findings highlight the urgent need for targeted nutritional interventions, such as preoperative supplementation and postoperative dietitian-led protocols, to improve outcomes in this vulnerable population.

Building on the findings above, our CEP-stratified analysis demonstrated that malnutrition significantly increased the risk of perioperative ischemic stroke in patients without CEP devices, whereas no significant effect was observed in those receiving CEP. Among malnourished patients, temporal trends in stroke incidence from 2017 to 2021 did not differ significantly between CEP and non-CEP groups, a finding that is consistent with previous randomized controlled trials involving 3000 subjects [44]. Interestingly, our stratified analysis revealed that for malnourished TAVR patients, cerebral embolic protection devices may confer protective benefit in subgroups without comorbid diabetes, renal failure, or chronic pulmonary diseases. The nonsignificant overall trend (Figure 4) contrasts with marked CEP benefits in comorbidity-free subgroups (Table S4). This discrepancy suggests that complex comorbidities (e.g., diabetes-related endothelial damage) may attenuate CEP efficacy, whereas simpler pathophysiology allows embolus interception. Such heterogeneity underscores the need for



CENTRAL ILLUSTRATION 1 | The Impact of Malnutrition on perioperative Ischemic Stroke in TAVR: A National Inpatient Sample Analysis.

TABLE 3 | Multifactorial analysis shows the impact of malnutrition on ischemic stroke after using or not using cerebral protection devices (with reference to individuals with normal nutrition).[a–c]

Exposure	*N*	Adjusted odds ratio [95% CI]	*p* Value
Malnutrition			
Non-CEP group	20,697/282,360 7.33%	1.70 (1.45, 2.00)	< 0.001***
CEP group	1196/23,080 5.18%	1.06 (0.45, 2.52)	0.892

Abbreviations: OR, Odds ratio; CI, Confidence interval; CEP, Cerebral embolic protection; TAVR, Transcatheter aortic valve replacement.
[a]Statistical Analysis: Adjusted odds ratios (OR) and 95% confidence intervals (CI) from multivariable logistic regression. Adjusted covariates: Age, sex, race, admission type, hospital region, and comorbidities (peripheral vascular disease, hypertension, diabetes, obesity, smoking, dyslipidemia, coagulopathy, renal failure, fluid/electrolyte disorders, chronic ischemic heart disease, congestive heart failure, obstructive sleep apnea, atrial fibrillation, chronic pulmonary disease).
[b]Key Definitions: Non-CEP group: Patients without cerebral embolic protection devices during TAVR. CEP group: Patients with cerebral embolic protection devices during TAVR.
[c]Statistical significance markers: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

personalized device selection. However, these findings did not account for other potential influencing factors in patients, such as the degree of vascular calcification, valve type, and surgical approach. Future studies should further explore the impact of these factors on the effectiveness of cerebral protection devices to offer more comprehensive guidance for clinical practice.

In summary, our findings highlight the marked effect of malnutrition on perioperative ischemic stroke risk in TAVR patients and underscore the need for comprehensive nutritional strategies. To translate these findings into practice, we propose a three-phase clinical pathway: First, preoperative assessment should integrate a rapid screening tool (e.g., Mini Nutritional Assessment–Short Form or CONUT score) with key laboratory markers (serum albumin and lymphocyte count) to stratify nutritional risk; patients with moderate to severe malnutrition should receive individualized optimization—from oral or enteral supplementation to brief procedural delay for parenteral nutrition. Second, intraoperative management should focus on maintaining hemodynamic and metabolic stability—avoiding prolonged hypotension or hypothermia—to minimize catabolic stress. Third, postoperative care should follow dietitian-led protocols with defined caloric (25–30 kcal/kg/day) and protein (1.2–1.5 g/kg/day) targets, adding immunonutrition for patients

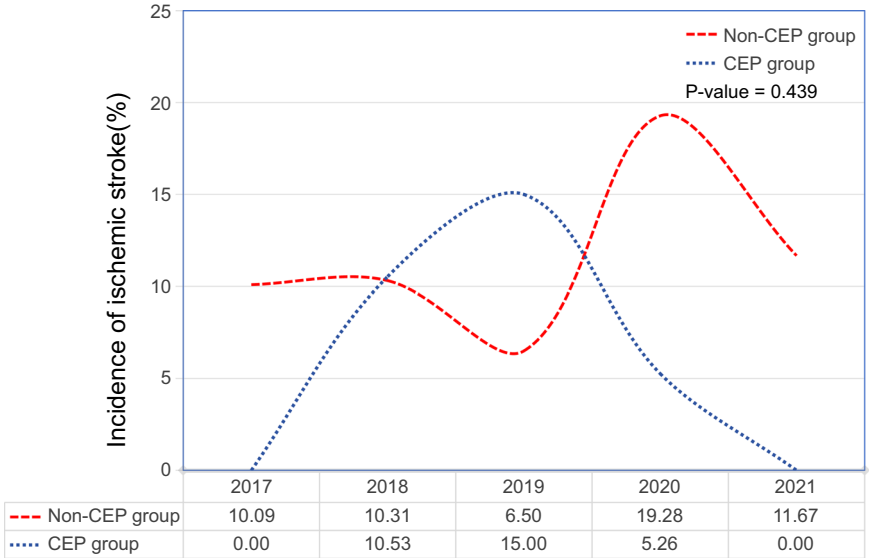


FIGURE 4 | Time trends of ischemic stroke occurrence in malnourished populations (CEP group vs. Non-CEP group).

with marked inflammatory responses. A core multidisciplinary team—including cardiologists, dietitians, and rehabilitation specialists—should oversee individualized plans and ensure seamless transition to outpatient follow-up.

Future research should prioritize validating nutritional interventions through randomized controlled trials to assess the efficacy of preoperative strategies such as protein supplementation and micronutrient repletion in reducing stroke risk. Mechanistic studies integrating biomarkers (e.g., homocysteine for folate deficiency, inflammatory cytokines) are essential to elucidate the pathways linking malnutrition to cerebrovascular injury. Furthermore, incorporating socioeconomic indices (e.g., income, education) and granular lifestyle data—such as dietary patterns, physical activity, and substance use—could disentangle the complex interplay between malnutrition, healthcare disparities, and vascular risk. Finally, prospective cohorts with extended follow-up are needed to evaluate the long-term impact of malnutrition on post-TAVR recovery, cardiovascular outcomes, and healthcare utilization. Refining these approaches aims to enhance surgical outcomes and improve long-term cardiovascular health for TAVR patients.

4.1 | Strengths

Our study offers several strengths in investigating the relationship between malnutrition and perioperative ischemic stroke in TAVR patients. To our knowledge, this is the first study to examine in detail the relationship between malnutrition and perioperative ischemic stroke in TAVR patients. Additionally, based on this foundational analysis, we further elucidated the impact of Cerebral Embolic Protection devices on the incidence of ischemic stroke in this specific malnourished patient population. Our study employed a comprehensive diagnostic definition of malnutrition [15], which accelerates the research process, minimizes subjective biases, and facilitates effective preoperative risk stratification for identifying high-risk patients, potentially reducing postoperative risks [13]. Furthermore, we accurately reflect current clinical practices by utilizing a larger sample size and contemporary data from a national inpatient database. This enables us to provide comprehensive regional and national assessments of patient outcomes and healthcare utilization, offering valuable insights for improving patient care on a broader scale.

4.2 | Limitations

However, our study has several limitations. First, as a retrospective observational study using administrative claims data, it is subject to inherent selection biases. Specifically, the exclusion of patients with missing critical variables ($n = 11{,}893$) may have systematically underrepresented populations with fragmented healthcare access (e.g., marginalized or socioeconomically disadvantaged groups), potentially skewing the cohort toward individuals with more complete medical records. Second, the diagnosis of malnutrition relied solely on ICD codes, which lack clinical granularity (e.g., serum albumin levels or body composition metrics). This may lead to misclassification bias, as mild or subclinical malnutrition cases could be overlooked, while severe cases might be overrepresented. Third, the NIS database captures only hospitalized patients in the United States, limiting generalizability to outpatient or international TAVR populations. Fourth, despite adjusting for common risk factors via propensity score matching, the data set does not capture detailed lifestyle factors (e.g., alcohol consumption, dietary habits, physical activity), overall physical status, or preoperative nutritional interventions—variables that might independently influence both malnutrition and stroke risk [45, 46]. Fifth, the absence of long-term follow-up data restricts our analysis of perioperative outcomes, leaving the sustained impact of malnutrition on post-TAVR recovery unexplored. Despite these limitations, our use of propensity score matching and sensitivity analyses aimed to mitigate measurable biases. The large sample size and standardized data collection across US

TABLE 4 | Stratified analysis and interaction tests of malnutrition on ischemic stroke risk in patients undergoing TAVR.[a–c]

Stratification variable	Subgroup	*N*	Ischemic stroke (OR, 95% CI)	*p* value	P interaction
Age	< 70	13,615	1.59 (1.12, 2.27)	< 0.010**	0.908
	≧ 70	61,047	1.63 (1.40, 1.89)	< 0.001***	
Gender	Male	42,099	1.29 (1.05, 1.58)	0.015*	0.001***
	Female	32,563	2.03 (1.69, 2.44)	< 0.001***	
Race	White	65,624	1.64 (1.42, 1.90)	< 0.001***	0.708
	Black	2928	1.89 (1.02, 3.50)	0.044*	
	Other	6110	1.37 (0.82, 2.27)	0.226	
Selective admission	No	11,826	1.19 (0.94, 1.51)	0.154	0.002**
	Yes	62,836	1.87 (1.58, 2.21)	< 0.001***	
Hospital distribution	New England	8294	4.09 (3.04, 5.49)	< 0.001***	< 0.001***
	Middle Atlantic	12,929	1.24 (0.87, 1.77)	0.239	
	East North Central	11,785	1.23 (0.85, 1.78)	0.281	
	West North Central	5464	1.52 (0.95, 2.42)	0.079	
	South Atlantic	14,735	1.62 (1.15, 2.27)	0.006**	
	East South Central	4319	1.67 (0.86, 3.25)	0.132	
	West South Central	5949	1.01 (0.64, 1.58)	0.978	
	Mountain	3794	1.18 (0.51, 2.72)	0.700	
	Pacific	7393	1.34 (0.80, 2.26)	0.266	
Peripheral vascular disease	No	58,334	1.81 (1.53, 2.13)	< 0.001***	0.006**
	Yes	16,328	1.20 (0.94, 1.53)	0.143	
Hypertension	No	11,155	1.27 (0.90, 1.79)	0.167	0.096
	Yes	63,507	1.73 (1.49, 2.01)	< 0.001***	
Diabetes	No	47,658	1.70 (1.45, 1.99)	< 0.001***	0.209
	Yes	27,004	1.39 (1.05, 1.83)	0.020*	
Obesity	No	58,386	1.58 (1.37, 1.82)	< 0.001***	0.982
	Yes	16,276	1.57 (0.93, 2.64)	0.089	
Smoking	No	45,490	1.78 (1.51, 2.10)	< 0.001***	0.063
	Yes	29,172	1.35 (1.05, 1.72)	0.017*	
Dyslipidemia	No	20,360	2.77 (2.27, 3.39)	< 0.001***	< 0.001***
	Yes	54,302	1.27 (1.05, 1.54)	0.014*	
Coagulopathy	No	64,232	1.28 (1.08, 1.52)	0.005**	< 0.001***
	Yes	10,430	2.60 (2.06, 3.27)	< 0.001***	
Endocarditis	No	74,227	1.61 (1.40, 1.85)	< 0.001***	0.720
	Yes	435	1.40 (0.66, 2.95)	0.378	
Liver disease	No	71,941	1.66 (1.44, 1.90)	< 0.001***	0.202
	Yes	2721	1.02 (0.47, 2.22)	0.965	
Renal failure	No	51,449	2.05 (1.73, 2.42)	< 0.001***	< 0.001***
	Yes	23,213	1.07 (0.85, 1.36)	0.570	
Fluid and electrolyte disorders	No	62,802	1.84 (1.56, 2.17)	< 0.001***	< 0.001***
	Yes	11,860	1.12 (0.87, 1.44)	0.366	

(Continues)

TABLE 4 | (Continued)

Stratification variable	Subgroup	*N*	Ischemic stroke (OR, 95% CI)	*p* value	P interaction
Chronic ischemic heart disease	No	24,503	3.38 (2.73, 4.19)	< 0.001***	< 0.001***
	Yes	50,159	1.15 (0.96, 1.38)	0.126	
Congestive heart failure	No	22,982	1.47 (1.08, 2.00)	0.015*	0.493
	Yes	51,680	1.65 (1.42, 1.92)	< 0.001***	
Obstructive sleep apnea	No	63,951	1.63 (1.42, 1.88)	< 0.001***	0.506
	Yes	10,711	1.34 (0.75, 2.38)	0.319	
Atrial fibrillation	No	46,277	1.14 (0.92, 1.42)	0.240	< 0.001***
	Yes	28,385	2.20 (1.84, 2.63)	< 0.001***	
Chronic pulmonary disease	No	54,496	1.87 (1.59, 2.20)	< 0.001***	0.002**
	Yes	20,166	1.16 (0.89, 1.50)	0.270	

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Statistical Analysis: Odds ratios (OR) and 95% confidence intervals (CI) from logistic regression models. Interaction tests (P interaction < 0.05 indicates significant heterogeneity) were performed via likelihood ratio tests comparing models with and without interaction terms.
[b]Statistical significance markers: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
[c]Subgroup definitions: "Other" race: Nonwhite/nonblack; "Selective Admission": Elective admission (planned, nonurgent) vs. nonselective admission (emergency/urgent).

hospitals strengthen the validity of the observed association. Future prospective studies should incorporate objective nutritional assessments (e.g., Mini Nutritional Assessment) and long-term follow-up to validate these findings and explore causal mechanisms.

5 | Conclusion

Our research thoroughly investigates the influence of malnutrition on perioperative ischemic stroke in individuals who are receiving TAVR. The results emphasize that malnutrition is common among patients undergoing transcatheter aortic valve replacement (TAVR) and greatly increases the likelihood of perioperative ischemic stroke. Importantly, this heightened risk is present independent of cerebral protective devices, indicating that patients' nutritional condition plays a crucial role in their outcomes, which cannot be fully improved by procedural advancements alone. Further research is warranted to explore targeted nutritional interventions that may help reduce the incidence of ischemic stroke in this high-risk population.

Author Contributions

Haowei Li: data curation, methodology, writing – original draft. **Guangzhi Cong:** resources, writing – review and editing. **Xueping Ma:** project administration, supervision. **Bo Shi:** data curation, visualization. **Congyan Ye:** data curation, validation. **Rui Yan:** formal analysis, investigation. **Shizhe Fu:** data curation, software. **Kairu Wang:** conceptualization, formal analysis. **Shaobin Jia:** funding acquisition, project administration. **Jingjing Wang:** funding acquisition, project administration, writing – review and editing.

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Disclosure

All authors have read and approved the final version of the manuscript. Jingjing Wang and Haowei Li had full access to all of the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Ethics Statement

This study utilized data from the National Inpatient Sample (NIS), a publicly available, deidentified database. As the data used are fully anonymized and in compliance with the Health Insurance Portability and Accountability Act (HIPAA), this study did not require institutional review board (IRB) approval or patient consent.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study. The data that support the findings of this study are openly available in The National (Nationwide) Inpatient Sample (NIS) at https://hcup-us.ahrq.gov/nisoverview.jsp.

Transparency Statement

The lead author Jingjing Wang affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

References

1. P. M. Ndunda, M. R. Vindhyal, T. M. Muutu, and Z. Fanari, "Clinical Outcomes of Sentinel Cerebral Protection System Use During Transcatheter Aortic Valve Replacement: A Systematic Review and Meta-Analysis," *Cardiovascular Revascularization Medicine* 21, no. 6 (2020): 717–722.

2. R. Burgos, I. Bretón, E. Cereda, et al., "ESPEN Guideline Clinical Nutrition in Neurology," *Clinical Nutrition* 37, no. 1 (2018): 354–396.

3. Y. Chen, X. Yang, Y. Zhu, X. Zhang, J. Ni, and Y. Li, "Malnutrition Defined by Geriatric Nutritional Risk Index Predicts Outcomes in Severe Stroke Patients: A Propensity Score-Matched Analysis," *Nutrients* 14, no. 22 (2022): 4786.

4. V. Huppertz, S. Guida, A. Holdoway, et al., "Impaired Nutritional Condition After Stroke From the Hyperacute to the Chronic Phase: A Systematic Review and Meta-Analysis," *Frontiers in Neurology* 12 (2022): 20.

5. T. Sabbouh and M. T. Torbey, "Malnutrition in Stroke Patients: Risk Factors, Assessment, and Management," *Neurocritical Care* 29, no. 3 (2018): 374–384.

6. S. Khera, A. N. Koshy, G. H. L. Tang, et al., "Prevention and Management of Stroke After Transcatheter Aortic Valve Replacement: The Mount Sinai Stroke Initiative," *Journal of the American Heart Association* 12, no. 4 (2023): e028182.

7. D. C. Miller, E. H. Blackstone, M. J. Mack, et al., "Transcatheter (TAVR) Versus Surgical (AVR) Aortic Valve Replacement: Occurrence, Hazard, Risk Factors, and Consequences of Neurologic Events in the PARTNER Trial," *Journal of Thoracic and Cardiovascular Surgery* 143, no. 4 (2012): 832–843.e13.

8. E. L. W. Tay, R. Gurvitch, N. Wijesinghe, et al., "A High-Risk Period for Cerebrovascular Events Exists After Transcatheter Aortic Valve Implantation," *JACC: Cardiovascular Interventions* 4, no. 12 (2011): 1290–1297.

9. K. S. Eduardo, P. S. Rodrigo, P. T. Ana, et al., "Routine Use of Cerebral Protection Devices During Transcatheter Aortic Valve Implantation: What Does the Evidence Say?," *Vessel Plus* 4 (2020): 41.

10. S. Stortecky and S. Windecker, "Stroke: An Infrequent but Devastating Complication in Cardiovascular Interventions," *Circulation* 126, no. 25 (2012): 2921–2924.

11. R. Gorla, L. Tua, P. D'Errigo, et al., "Incidence and Predictors of 30-day and 6-month Stroke After TAVR: Insights From the Multicenter OBSERVANT II Study," *Catheterization and Cardiovascular Interventions* 102, no. 6 (2023): 1122–1131.

12. D. van Erck, M. Tieland, N. W. Adriaens, et al., "GLIM-Based Malnutrition, Protein Intake and Diet Quality in Preprocedural Transcatheter Aortic Valve Implantation (TAVI) Patients," *Clinical Nutrition ESPEN* 51 (2022): 481–485.

13. S. Emami, S. Rudasill, N. Bellamkonda, et al., "Impact of Malnutrition on Outcomes Following Transcatheter Aortic Valve Implantation (From a National Cohort)," *American Journal of Cardiology* 125, no. 7 (2020): 1096–1101.

14. "NIS Database Documentation," accessed April 25, 2024, https://hcup-us.ahrq.gov/db/nation/nis/nisdbdocumentation.jsp.

15. K. R. Fingar, A. J. Weiss, M. L. Barrett, et al., "All-Cause Readmissions Following Hospital Stays for Patients With Malnutrition, 2013: Statistical Brief #218," *Healthcare Cost and Utilization Project (HCUP), December 2016, Agency for Healthcare Research and Quality, Rockville, MD*, accessed June 18, 2019, https://www.hcup-us.ahrq.gov/reports/statbriefs/sb218-Malnutrition-Readmissions-2013.jsp.

16. W. N. Kernan, C. M. Viscoli, L. M. Brass, et al., "Phenylpropanolamine and the Risk of Hemorrhagic Stroke," *New England Journal of Medicine* 343, no. 25 (2000): 1826–1832.

17. R. L. Houchens, A. Elixhauser, "Using the HCUP Nationwide Inpatient Sample to Estimate Trends," *HCUP Methods Series Report #2006-05. August 18, 2006, Agency for Healthcare Research and Quality, Rockville, MD*, accessed August 1, 2024, https://www.hcup-us.ahrq.gov/reports/2006_05_NISTrendsReport_1988-2004.pdf.

18. S. Deb, P. C. Austin, J. V. Tu, et al., "A Review of Propensity-Score Methods and Their Use in Cardiovascular Research," *Canadian Journal of Cardiology* 32, no. 2 (2016): 259–265.

19. P. C. Austin, "An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies," *Multivariate Behavioral Research* 46, no. 3 (2011): 399–424.

20. J. A. Rassen, A. A. Shelat, J. Myers, R. J. Glynn, K. J. Rothman, and S. Schneeweiss, "One-To-Many Propensity Score Matching in Cohort Studies," *Pharmacoepidemiology and Drug Safety* 21 (2012): 69–80.

21. J. E. Pustejovsky and M. A. Rodgers, "Testing for Funnel Plot Asymmetry of Standardized Mean Differences," *Research Synthesis Methods* 10, no. 1 (2019): 57–71.

22. E. Aradine, Y. Hou, C. A. Cronin, and S. Chaturvedi, "Current Status of Dyslipidemia Treatment for Stroke Prevention," *Current Neurology and Neuroscience Reports* 20, no. 8 (2020): 31.

23. E. Baumfeld Andre, R. Reynolds, P. Caubel, L. Azoulay, and N. A. Dreyer, "Trial Designs Using Real-World Data: The Changing Landscape of the Regulatory Approval Process," *Pharmacoepidemiology and Drug Safety* 29, no. 10 (2020): 1201–1212.

24. G. Liu, X. Hu, M. Long, Z. M. Du, Y. Li, and C. H. Hu, "Meta-Analysis of the Impact of Pre-Procedural Serum Albumin on Mortality in Patients Undergoing Transcatheter Aortic Valve Replacement," *International Heart Journal* 61, no. 1 (2020): 67–76.

25. M. Dong, "Malnutrition Predicts Adverse Outcomes After Transcatheter Aortic Valve Replacement: A Systematic Review and Meta-Analysis," *Anatolian Journal of Cardiology* 27, no. 5 (2023): 240–248.

26. M. Megaly, P. Sorajja, J. Cavalcante, et al., "TCT CONNECT-6 Ischemic Stroke With Cerebral Protection System During Transcatheter Aortic Valve Replacement," *Journal of the American College of Cardiology* 76, no. 17 (2020): B3–B4.

27. M. Leary and L. Caplan, "Cardioembolic Stroke: An Update on Etiology, Diagnosis and Management," *Annals of Indian Academy of Neurology* 11 (2008): 52.

28. S. Perrone, S. Raso, and M. Napolitano, "Clinical, Laboratory, and Molecular Characteristics of Inherited Vitamin K-Dependent Coagulation Factors Deficiency," *Seminars in Thrombosis and Hemostasis* 51, no. 2 (2025): 170–179.

29. O. Benzakour, "Vitamin K-Dependent Proteins: Functions in Blood Coagulation and Beyond," *Thrombosis and Haemostasis* 100, no. 4 (2008): 527–529.

30. S. Bassam, S. Mansour, and R. Ajrouche, et al., "Drug-Related Problems and Factors Involved in the Imbalance of Oral Anticoagulants in Lebanese Patients: A Cross Sectional Study," *Dr. Sulaiman Al Habib Medical Journal* 4, no. 2 (2022): 77–85.

31. P. C. Calder, "Nutrition and Immunity: Lessons for COVID-19," *European Journal of Clinical Nutrition* 75, no. 9 (2021): 1309–1318.

32. P. M. Ridker, "From C-Reactive Protein to Interleukin-6 to Interleukin-1: Moving Upstream To Identify Novel Targets for Atheroprotection," *Circulation Research* 118, no. 1 (2016): 145–156.

33. P. Libby, "Inflammation in Atherosclerosis," *Arteriosclerosis, Thrombosis, and Vascular Biology* 32, no. 9 (2012): 2045–2051.

34. D. Mozaffarian, E. J. Benjamin, A. S. Go, et al., "Heart Disease and Stroke Statistics—2015 Update," *Circulation* 131, no. 4 (2015): e29–e322.

35. L. Peng, J. Tang, N. Zhang, Z. Zhang, D. Wang, and Y. He, "Association Between Controlling Nutritional Status Score and the Prognosis of Patients With Acute Myocardial Infarction: A Systematic Review and Meta-Analysis," *Frontiers in Nutrition* 11 (2025): 15.

36. O. E. Osadchii, B. H. Bentzen, and S. P. Olesen, "Chamber-Specific Effects of Hypokalaemia on Ventricular Arrhythmogenicity in Isolated, Perfused Guinea-Pig Heart," *Experimental Physiology* 94, no. 4 (2009): 434–446.

37. G. M. Reaven, "The Metabolic Syndrome: Time to Get Off the Merry-Go-Round?," *Journal of Internal Medicine* 269, no. 2 (2011): 127–136.

38. B. F. Palmer and D. J. Clegg, "Physiology and Pathophysiology of Potassium Homeostasis," *Advances in Physiology Education* 40, no. 4 (2016): 480–490.

39. S. Yusuf, S. Hawken, and S. Ounpuu, "Effect of Potentially Modifiable Risk Factors Associated With Myocardial Infarction in 52 Countries (The INTERHEART Study): Case-Control Study," *Lancet* 364, no. 9450 (2004): 2020.

40. K. M. Rexrode, T. E. Madsen, A. Y. X. Yu, C. Carcel, J. H. Lichtman, and E. C. Miller, "The Impact of Sex and Gender on Stroke," *Circulation Research* 130, no. 4 (2022): 512–528.

41. K. E. Bach Knudsen, H. N. Lærke, M. S. Hedemann, et al., "Impact of Diet-Modulated Butyrate Production on Intestinal Barrier Function and Inflammation," *Nutrients* 10, no. 10 (2018): 1499.

42. P. C. Calder, "Nutrition and Immunity: Lessons for COVID-19," *Nutrition & Diabetes* 11, no. 1 (2021): 19.

43. E. Gakidou, A. Afshin, A. A. Abajobir, et al., "Global, Regional, and National Comparative Risk Assessment of 84 Behavioural, Environmental and Occupational, and Metabolic Risks or Clusters of Risks, 1990-2016: A Systematic Analysis for the Global Burden of Disease Study 2016," *Lancet* 390, no. 10100 (2017): 1345–1422.

44. S. R. Kapadia, R. Makkar, M. Leon, et al., "Cerebral Embolic Protection During Transcatheter Aortic-Valve Replacement," *New England Journal of Medicine* 387, no. 14 (2022): 1253–1263.

45. G. A. Roth, G. A. Mensah, C. O. Johnson, et al., "Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019," *Journal of the American College of Cardiology* 76, no. 25 (2020): 2982–3021.

46. P. Braveman and L. Gottlieb, "The Social Determinants of Health: It's Time to Consider the Causes of the Causes," supplement, *Public Health Reports®* 129, no. S2 (2014): 19–31.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.