#### ORIGINAL RESEARCH

# Dysphagia Management and Outcomes in Elderly Stroke Patients with Malnutrition Risk: Results from Chinese Stroke Center Alliance

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**Purpose:** To investigate the effectiveness of dysphagia screening and subsequent swallowing rehabilitation in elderly stroke patients with malnutrition risk.

**Patients and Methods:** Based on the Chinese Stroke Center Alliance (CSCA) from August 1, 2015 to July 21, 2019, we compared the in-hospital adverse outcomes among stroke patients (including ischemic stroke, intracranial hemorrhage, and subarachnoid hemorrhage) over 70 years old with and without dysphagia screening. The primary outcome was in-hospital all-cause mortality. Secondary outcomes were the composite endpoint of discharge against medical advice (DAMA) or in-hospital death.

**Results:** Among 365,530 stroke patients  $\geq$  70 years old with malnutrition risk in the CSCA, documented dysphagia screening was performed for 288,764 (79.0%) participants. Of these, 41,482 (14.37%) patients had dysphagia, and 33,548 (80.87%) patients received swallowing rehabilitation. A total of 1,694 (0.46%) patients experienced in-hospital death. After adjustment for traditional risk factors, dysphagia screening was associated with a low risk of all-cause mortality in stroke patients [adjusted odds ratio (aOR): 0.75, 95% confidence interval (CI):0.65–0.87]. Compared to patients with dysphagia who did not receive swallowing rehabilitation had a reduced risk of in-hospital death (aOR:0.39, 95% CI: 0.33–0.46). Additionally, dysphagia screening had a lower risk for the composite endpoint of DAMA or in-hospital death (aOR:0.83,95% CI: 0.80–0.87), as did subsequent swallowing rehabilitation (aOR:0.43,95% CI: 0.40–0.47). Similar results were observed in the sensitivity analysis through inverse probability of treatment weighting, propensity score matching, and excluding patients without National Institutes of Health Stroke Scale scores. A similar association was observed between dysphagia management and adverse clinical outcomes in ischemic stroke and intracranial hemorrhage patients.

**Conclusion:** Dysphagia screening and swallowing rehabilitation were associated with a reduced risk of in-hospital death and composite outcome of DAMA or in-hospital death for stroke patients with malnutrition risk. Future research should concentrate on improving the quality of medical care for dysphagia management to improve patients' outcomes.

Keywords: stroke, malnutrition risk, dysphagia screening, in-hospital death, discharge against medical advice

# Introduction

China faces a great burden due to stroke. The mortality of cerebrovascular diseases in China was 149.49 per 100,000 in 2018.<sup>1</sup> Dysphagia is common among stroke survivors, affecting 27–64% of patients,<sup>2,3</sup> while affecting 25–81% of survivors 70 years

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or older.<sup>4</sup> Dysphagia can increase the risk of malnutrition, mortality, and hospitalization complications.<sup>2,3,5,6</sup> Dysphagia is a significant risk factor for malnutrition in stroke patients older than 70 years.<sup>3,6,7</sup> The nutrition screening 2002 (NRS2002) is recommended for hospital patients by the European Society of Parenteral and Enteral Nutrition (ESPEN)<sup>8</sup> and is suitable in screening malnutrition risk among Chinese geriatric inpatients older than 70 years.<sup>9</sup> According to NRS2002, stroke patients older than 70 years are defined as being at malnutrition risk.<sup>8</sup> Positive outcomes, including lower mortality, complications, and health-care costs, are common among hospitalized, older adult patients receiving enteral or oral nutrition.<sup>10–12</sup> The prevalence of malnutrition risk assessed by NRS2002 among patients with acute ischemic stroke (AIS) at admission is approximately 45%.<sup>13–15</sup> NRS2002 has a higher predictive power and can predict both short- and long-term outcomes for stroke patients.<sup>13,14</sup> Dysphagia and malnutrition influence each other and are associated with adverse outcomes (ie, pneumonia, all-cause mortality).<sup>2,4,15,16</sup> Therefore, increased attention should be paid to older adult stroke patients who are at malnutrition risk.

Multiple guidelines recommend early dysphagia screening before oral food or tablets given for stroke patients.<sup>17–20</sup> Doctors and nurses can use some screening methods to diagnose the risk of dysphagia, such as the medical history, questionnaires, and swallowing tests.<sup>4</sup> The 10 mL water swallowing test and the Gugging Swallowing Screen (GUSS) can provide information regarding dysphagia to predict poor outcomes, including pneumonia, in-hospital death, and 3-month disability.<sup>21</sup> However, a systematic review revealed that there was insufficient randomized controlled trial (RCT) data to determine whether dysphagia screening can reduce poor outcomes.<sup>22</sup>

Additionally, a meta-analysis demonstrated that swallowing therapy had no effect on case fatality but reduced the incidence of pneumonia.<sup>2</sup> However, other studies found that early dysphagia screening and intervention could reduce inhospital death or hospital-associated pneumonia.<sup>23,24</sup> Although guidelines strongly recommend dysphagia screening prior to oral food or medications, clinical evidence remains insufficient,<sup>2,22,25</sup> especially for older stroke patients who are at malnutrition risk.

Therefore, we evaluated the effectiveness of dysphagia screening and subsequent swallowing rehabilitation among older adults with stroke [including AIS, intracerebral hemorrhage (ICH), or subarachnoid hemorrhage (SAH)] based on the Chinese Stroke Center Alliance (CSCA).

# **Materials and Methods**

### Study Design

The study was based on the data derived from the CSCA and enrolled 1,006,798 patients with acute stroke/ transient ischemic attacks (TIA) from August 1, 2015, to July 21, 2019.<sup>26,27</sup> The CSCA program was designed to develop stroke centers and treat patients in a manner consistent with accepted national guidelines. Patients aged  $\geq 18$  years and within 7 days of symptom onset were enrolled in the program. The CSCA was approved by the ethics committee of Beijing Tiantan Hospital (KY 2018–061-02). The study protocol conforms to the ethical guidelines of the Declaration of Helsinki. The data were collected and managed via a web-based tool. Participating hospitals in the CSCA collected data without the individual information and exemption from their Institutional Review Board.<sup>26</sup>

# Study Population

NRS2002 involves three factors: age, disease severity, and nutritional impairment. The NRS2002 score of participants with stroke and age  $\geq$  70 were assessed for 2 and 1, respectively. Patients with a score of NRS2002  $\geq$  3 were at malnutrition risk. The present study included stroke patients  $\geq$  70 years old from the CSCA who were at risk of malnutrition based on the NRS2002.<sup>8</sup> Patients were excluded if they met the following criterion: diagnosed with TIA and unspecified stroke, stroke patients aged  $\leq$  70 years, patients who died within 72 hours, admission department was intensive care unit (ICU) or neurological intensive care unit (NICU), and missing data for dysphagia screening or mortality. Finally, a total of 365,530 stroke patients under malnutrition risk were included for analyses (Figure 1).

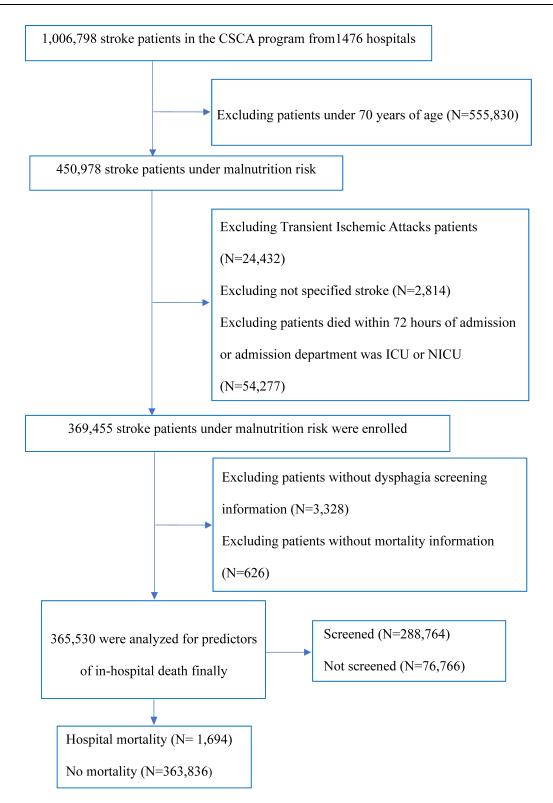


Figure I Flow chart of patient selection.

Abbreviations: CSCA, Chinese Stroke Center Alliance; ICU, intensive care unit; NICU, neurological intensive care unit.

### Variables and Outcomes

Data were collected via the web-based patient data collection and management tool (Medicine Innovation Research Center, Beijing, China). Data were collected for patient demographics, insurance status, medical history, National Institutes of Health Stroke Scale (NIHSS) score on admission, and the hospital characteristics (geographic region, hospital grade). The body mass index (BMI) was calculated as weight [kg] divided by height squared [m<sup>2</sup>]. Dysphagia screening was defined as the patient's swallowing function as assessed by medical care personnel before any oral intake during hospitalization. The dysphagia screen, Eating Assessment Tool-10, Clinical Swallowing Function Assessment Form, and so on.<sup>17–20</sup> Swallowing rehabilitation was provided by a professional physiatrician for swallowing function according to the condition of the patients. The manner of swallowing rehabilitation included acupuncture treatment, medication, neuromuscular electrical stimulation, pharyngeal electrical stimulation, transcranial direct current stimulation, etc.<sup>26,27</sup>

The primary outcome was in-hospital all-cause mortality. Secondary outcomes were the composite outcomes including death and discharge against medical advice (DAMA), and hospital-associated pneumonia. DAMA was defined as a patient leaving the hospital against the advice of their care provider. Hospital-associated pneumonia was diagnosed by the clinician through clinical symptoms, physical examination, and radiological or etiological evidence.<sup>26,27</sup>

### Statistical Analysis

Continuous variables were described as mean  $\pm$  standard deviation or median and interquartile range (*IQR*). Categorical variables were presented as absolute numbers with percentages. We compared the differences in the baseline characteristics between patients with and without dysphagia screening using the standardized difference. An absolute standardized difference (ASD) of >10% indicated significant differences in the variable between the two groups.<sup>28</sup>

Multivariable logistic regression models were performed to determine the risk of dysphagia screening or swallowing rehabilitation for poor outcomes among stroke patients as odds ratios (*OR*) and 95% confidence intervals (*CI*). The age,; sex; initial NIHSS score; BMI; medical history, including stroke, hypertension, diabetes mellitus, coronary heart disease/ myocardial infarction, dementia, heart failure, and atrial fibrillation; current smoking; alcoholism; medication history; and the hospital characteristics (geographic region, hospital grade) were adjusted in the multivariable models.

In the sensitivity analysis, the associations were further assessed using the inverse probability of treatment weighting and greedy, nearest-neighbor propensity score matching (PSM). Inverse probability of treatment weighting estimation was then defined as the inverse of the estimated propensity score for patients with dysphagia screening and the inverse of one minus the estimated propensity score for those without dysphagia screening.<sup>29</sup> Propensity scores were calculated for each patient based on a multivariable logistic regression model. This model included demographic variables (age, sex); inpatients' medical insurance; stroke severity (NIHSS score) at admission; history of stroke, hypertension, diabetes mellitus, dyslipidemia, coronary heart disease/ myocardial infarction, dementia, heart failure, atrial fibrillation, carotid stenosis; current smoking, alcoholism; medication history of antiplatelet drugs, anticoagulant drugs, antihypertensive drugs, lipid-lowering drugs; and the hospital characteristics (geographic region, hospital grade). We also matched patients without and with dysphagia screening in a 1:4 ratio using the greedy, nearest-neighbor method without replacement, with a caliper of 0.01 of the propensity score.<sup>30</sup> Given that there were more missing values in the NIHSS score, we excluded patients without the NIHSS scores in a sensitivity analysis. Additionally, we evaluated the balance of covariates between groups in the matched samples and determined the risk of dysphagia screening or swallowing rehabilitation for the poor outcomes in patients with different types of stroke.

All tests were two-tailed with P-values <0.05 considered as statistically significant. All statistical analyses were performed using SAS version 9.4 statistical software (SAS Institute Inc., Cary, North Carolina, USA).

# Results

### **Baseline Characteristics**

According to the NSR2002 criterion, 450,978 (44.79%) stroke patients were  $\geq$  70 years old. A total of 365,530 patients were ultimately included in the study and 288,764 (79.0%) received dysphagia screening before oral food or tablets given

were provided. Before PSM, patients who received dysphagia screening had a higher likelihood of mild to moderate stroke severity and a lower proportion of middle geographic region. There were no significant differences between the two groups in the demographic characteristics or medical history according to ASD. According to the inverse probability of treatment weighting, patients with and without dysphagia screening were similar with respect to age, sex, NIHSS score at admission, previous medical history, medication history, and hospital characteristics. After the greedy, nearest-neighbor PSM, baseline characteristics between 177,433 patients with dysphagia screening and 45,302 patients without dysphagia screening were well balanced (Table 1).

# Primary Outcome: In-hospital Death

A total of 1694 (0.46%) stroke patients died during hospitalization. Patients who died during hospitalization were significantly older and had higher NIHSS scores, and had a higher likelihood of previous medical history and dysphagia, whereas a lower proportion of dysphagia screening and swallowing rehabilitation than survivors (<u>Table S1</u>). After adjusting for age, sex, NIHSS score at admission, BMI, the medical history of stroke/TIA, hypertension, etc. medication history, and the hospital characteristics (grade and region), dysphagia screening was associated with a reduced risk of inhospital death [adjusted OR (aOR): 0.75, 95% CI:0.65–0.87]. After adjusting for the same confounders, dysphagia was significantly associated with the occurrence of in-hospital death (aOR: 6.13, 95% CI: 5.18–7.27). Older age, severity of stroke (NIHSS score at admission), the medical history of stroke or TIA, diabetes mellitus, coronary heart disease/ previous myocardial infarction, atrial fibrillation, heart failure, dementia and tertiary grade hospital were risk factors for all-cause mortality in stroke patients. Meanwhile, the associations were consistent after PSM and inverse probability of treatment weighting estimation (Table 2).

Among the 288,764 stroke patients with documented dysphagia screening, 41,482 (14.37%) patients had dysphagia, and 33,548 (80.87%) patients received swallowing rehabilitation (<u>Table S2</u>). Compared to patients with dysphagia but who did not receive swallowing rehabilitation, swallowing rehabilitation significantly reduced the risk of death (aOR: 0.39, 95% CI: 0.33–0.46) (Table 3).

### Secondary Outcomes: Composite Outcomes and In-hospital Pneumonia

A total of 19,909 (5.45%) deaths and DAMA occurred; the proportion of DAMA patients was 4.98% (18,215), and 51,649 (14.13%) patients were diagnosed with in-hospital pneumonia. After adjusting for the confounders, dysphagia screening prior to oral intake reduced the risk of the composite outcome, including DAMA and death (aOR: 0.83, 95*CI*: 0.80–0.87). However, dysphagia screening was associated with an increased risk for hospital-associated pneumonia (aOR: 1.54, 95CI: 1.49–1.59). Swallowing rehabilitation also reduced the risk of DAMA and death (aOR: 0.43, 95*CI*: 0.40–0.47) among stroke patients with dysphagia. Similar results were observed using propensity score approaches with inverse probability of treatment weighting and PSM (Table 3).

# Sensitivity Analysis and Subgroup Analysis for the Association Between Dysphagia Management and Clinical Outcomes

We performed a sensitivity analysis for dysphagia management and clinical outcomes among stroke patients after excluding patients who lacked NIHSS scores. Dysphagia management including dysphagia screening and swallowing rehabilitation was also associated with a lower risk of in-hospital death and the composite outcome (Table 4).

In the subgroup analysis, dysphagia screening (aOR: 0.74, 95% CI: 0.63–0.87) and swallowing rehabilitation (aOR: 0.40, 95% CI: 0.33–0.48) were also associated with a reduced risk of all-cause mortality among ischemic stroke patients. We also observed that dysphagia screening (aOR: 0.87, 95% CI: 0.83–0.91) and swallowing rehabilitation (aOR: 0.42, 95% CI: 0.39–0.45) reduced the risk of the composite outcome including DAMA and death for ischemic stroke patients (Table 5). A similar relationship was observed for intracranial hemorrhage but not subarachnoid hemorrhage stroke patients (Tables S3 and S4).

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Variables		Unadjusted		IPTW	Propensity Score Matching				
	DS N=288764 (79.0%)	Without DS N=76766 (21.0%)	ASD (%)	DS N=285209	Without DS N=285266	ASD (%)	DS N=177433	Without DS N=45302	ASD (%
Age, (year)	76.66±7.22	76.31±7.37	4.80	76(72,81)	76(72,81)	0.07	76.50(7.13)	76.49(7.07)	0.14
Gender, Male	160,898(55.72)	42,602(55.50)	0.45	158,738(55.66)	158,689(55.63)	0.06	98,582(55.56)	25,201(55.63)	0.14
Race, Han	280,532(97.15)	74,204(96.66)	2.83	277,451(97.28)	276,076(96.78)	2.95	172,715(97.34)	43,856(96.81)	3.15
Insurance Status									
NRCMS	120013(41.56)	32,788(42.71)	2.33	117,265(42.12)	117,786(41.29)	1.68	74,639(42.07)	18,764(41.42)	1.32
Other	11,490(3.98)	3862(5.03)	5.06	10,836(3.80)	10,764(3.77)	0.16	6904(3.89)	1819(4.02)	0.67
Self	14,058(4.87)	3349(4.36)	2.43	12,880(4.52)	12,735(4.46)	0.29	6833(3.85)	1765(3.90)	0.26
UEBMI	84845(29.38)	23,103(30.10)	1.58	85,890(30.11)	85,860(30.10)	0.02	54,635(30.79)	14,185(31.31)	1.12
URBMI	58358(20.21)	13,664(17.80)	6.15	58,338(20.45)	58,122(20.37)	0.20	34,422(19.40)	8769(19.36)	0.10
Admission NIHSS score	4(2,7)	4(2,8)	11.62	4(2,7)	4(2,8)	2.20	4(2,7)	4(2,8)	7.72
0–3	142,174(59.29)	26,316(58.08)	2.46	168,476(59.07)	168,450(59.05)	0.04	104,585(58.94)	26,315(58.09)	1.72
4–14	79,163(33.00)	14,021(30.94)	4.42	93,180(32.67)	93,104(32.64)	0.06	55,507(31.28)	14,021(30.95)	0.71
≥15	18,568(7.74)	4976(10.98)	11.14	23,553(8.26)	23,713(8.31)	0.18	17,341 (9.77)	4966(10.96)	3.90
BMI, kg/m <sup>2</sup>	23.14±4.10	23.40±5.25	5.52	23.14±4.37	23.31±10.99	2.03	23.12±4.04	23.30±4.53	4.19
Medical history									
Stroke/TIA	100601(34.84)	28,541(37.18)	4.88	98,755(34.63)	99,158(34.76)	0.27	62,923(35.46)	16,494(36.41)	1.98
Hypertension	192,764(66.75)	48,616(63.33)	7.19	189,815(66.55)	190,144(66.65)	0.21	114,584(64.58)	29,084(64.20)	0.79
Diabetes Mellitus	57,501(19.91)	13,804(17.98)	4.93	56,824(19.92)	56,858(19.93)	0.03	32,754(18.46)	8331(18.39)	0.18
Dyslipidemia	19,320(6.69)	5552(7.23)	2.12	19,356(6.79)	19,408(6.80)	0.04	12,004(6.77)	3189(7.04)	1.06
CHD/Previous MI	32898(11.39)	8036(10.47)	2.95	30,183(10.58)	30,369(10.65)	0.23	15,893(8.96)	4079(9.00)	0.14
Atrial Fibrillation	23,845(8.26)	5332(6.95)	4.95	24,030(8.43)	24,144(8.46)	0.11	13,327(7.51)	3477(7.68)	0.64
Carotid Stenosis	4141(1.43)	969(1.26)	1.49	4047(1.43)	4100(1.44)	0.08	2167(1.22)	569(1.26)	0.36
Heart Failure	4854(1.68)	1168(1.52)	1.27	5026(1.76)	5081(1.78)	0.15	2801(1.58)	744(1.64)	0.48
Dementia	2602(0.90)	520(0.68)	3.48	2462(0.86)	2537(0.89)	0.32	1155(0.65)	309(0.68)	0.37
Current smoking	43,954(15.22)	10,371(13.51)	4.88	43,942(15.41)	44,106(15.46)	0.14	25,844(14.57)	6545(14.49)	0.23
Alcoholism	48,902(16.94)	12,132(19.88)	7.59	48,563(17.03)	48,486(17.00)	0.08	28,998(16.34)	7470(16.49)	0.40
Medication at admission									
Antiplatelet	61,656(21.35)	17,433(22.71)	3.28	62,314(21.85)	62,245(21.82)	0.07	39,866(22.47)	10,535(23.26)	1.88
Anticoagulant	11,795(4.08)	4007(5.22)	5.42	11,175(3.92)	11,101(3.89)	0.15	7653(4.31)	2117(4.67)	1.74
Antihypertensive	143,784(49.79)	34,879(45.44)	8.72	142,164(49.85)	142,484(49.95)	0.20	84,469(47.61)	21,332(47.09)	1.04
Lipid-lowering	43,792(15.17)	12,422(16.18)	2.78	44,107(15.46)	43,991(15.42)	0.11	28,424(16.02)	7594(16.76)	1.99

#### Table I Baseline Characteristics Before and After Inverse Probability of Treatment Weighted in Stroke Patient (with DS and Without DS)

Region									
East	13,714(47.50)	33,754(43.97)	7.09	137,900(48.35)	138,165(48.43)	0.16	82,243(46.35)	20,566(45.40)	1.91
Middle	83,383(28.88)	26,962(35.12)	13.41	82,138(28.80)	81,968(28.74)	0.13	56,959(32.10)	14,905(32.90)	1.71
West	68,207(23.62)	16,050(20.91)	6.51	65,172(22.85)	65,134(22.83)	0.05	38,231(21.55)	9831(21.70)	0.36
Hospital grade									
Secondary	113,565(39.33)	31,166(40.60)	2.59	112,284(39.37)	112,480(39.42)	0.10	71,264(40.16)	18,185(40.14)	0.04
Tertiary	175,199(60.67)	45,600(59.40)	2.59	172,925(60.63)	172,787(60.53)	0.10	106,169(59.84)	27,117(59.86)	0.04

Notes: Continuous variables are expressed as mean ± SD or as median (interquartile range, IQR). Categorical variables are expressed as frequency (%).

Abbreviations: ASD, absolute standardized difference; BMI, body mass index; CHD, coronary heart disease; DS, dysphagia screening; IPTW, inverse probability of treatment weighted; MI, myocardial infarction; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attacks; NRCMS, new rural cooperative medical scheme; UEBMI, urban employees' basic medical insurance; URBMI, urban residents' basic medical insurance.

Variable	OR (95% CI, P-value)							
	Unadjusted	IPTW	Propensity Score Matching					
DS done prior to oral intake <sup>a</sup>	0.75(0.65–0.87, <0.001)	0.79(0.73–0.86, <0.001)	0.74(0.64–0.86, <0.001)					
Swallowing function, Normal (Reference)								
Dysphagia <sup>a</sup>	6.13(5.18–7.27, <0.001)	6.11(5.23–7.12, <0.001)	6.04 (4.95–7.37, <0.001)					
Age (per I years)	1.07(1.06–1.08, <0.001)	1.07(1.07–1.08, <0.001)	1.07(1.06–1.08, <0.001)					
Male (vs Female)	1.33(1.16–1.52, <0.001)	1.52(1.38–1.66, <0.001)	1.35(1.16–1.57, 0.001)					
Admission NIHSS score (vs 0–3)								
4–14	3.77(3.14-4.62, <0.001)	3.62(3.20-4.09, <0.001)	3.74 (3.02–4.63, <0.001)					
≥15	18.18(15.21–21.74, <0.001)	18.74(16.61–21.14, <0.001)	18.76(15.32–22.97, <0.001)					
Medical history								
Stroke/TIA	1.26(1.10–1.43, <0.001)	1.36(1.24–1.48, <0.001)	1.26(1.09–1.46, 0.002)					
Hypertension	0.98(0.82-1.17, 0.80)	1.01(0.89–1.14, 0.91)	0.93(0.77-1.13, 0.48)					
Dyslipidemia	1.08(0.87-1.34,0.48)	1.07(0.92-1.24,0.38)	1.08(0.85-1.37,0.55)					
Diabetes mellitus	1.62(1.41–1.86, <0.001)	1.63(1.49–1.80, <0.001)	1.63(1.40–1.91, <0.001)					
CHD/previous MI	1.81(1.56–2.09, <0.001)	1.67(1.51–1.85, <0.001)	1.63(1.37–1.94, <0.001)					
Atrial fibrillation	1.56(1.35–1.81, <0.001)	1.51(1.37–1.68, <0.001)	1.44(1.21–1.70, <0.001)					
Heart failure	2.16(1.73-2.69, <0.001)	2.16(1.85–2.52, <0.001)	2.38(1.85-3.05, <0.001)					
Dementia	1.96(1.40–2.75, <0.001)	2.24(1.80-2.79, <0.001)	1.79(1.17–2.73, 0.007)					
Antiplatelet drugs	0.93(0.78-1.11, 0.44)	0.95(0.84–1.07, 0.39)	0.89(0.72-1.08, 0.23)					
Anticoagulant drugs	0.90(0.73-1.09, 0.40)	0.84(0.69-1.01, 0.06)	0.94(0.71-1.23, 0.63)					
Antihypertensive drugs	1.28(1.08-1.51, 0.004)	1.21(1.08–1.35, <0.001)	1.23(1.02–1.48, 0.03)					
Lipid-lowering drugs	0.89(0.73-1.09,0.26)	0.84(0.73–0.96,0.01)	0.92(0.73-1.15,0.44)					
Hospital grade (Tertiary vs Secondary)	1.49(1.30–1.70, <0.001)	1.68(1.53–1.84, <0.001)	1.61(1.39–1.87, <0.001)					
Region, East (Reference)								
Middle	1.12(0.96-1.30, 0.15)	1.25(1.13–1.38, <0.001)	1.06(0.90-1.25, 0.48)					
West	1.57(1.37–1.81, <0.001)	1.41(1.28–1.55, <0.001)	1.42(1.21–1.21, <0.001)					

Table 2 Multivariable Analysis of Risk Factors Associated with Hos	pital Mortality in Stroke Patients
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Notes: <sup>a</sup>Model adjusted for age, sex, initial NIHSS score, body mass index, history of stroke, hypertension, diabetes mellitus, dyslipidemia, coronary heart disease/ myocardial infarction, dementia, heart failure, atrial fibrillation, carotid stenosis, current smoking, alcoholism, antiplatelet drugs, anticoagulant drugs, antihypertensive drugs, lipid-lowering drugs, the hospital characteristics (geographic region, hospital grade).

Abbreviations: ASD, absolute standardized difference; CHD, coronary heart disease; CI, confidence interval; DS, dysphagia screening; IPTW, inverse probability of treatment weighting; MI, myocardial infarction; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; TIA, transient ischemic attacks.

# Discussion

In the present study, we investigated the association between dysphagia management and poor clinical outcomes among stroke patients at malnutrition risk based on the CSCA. For the 365,530 stroke patients enrolled in our study, documented dysphagia screening was performed for 288,764 (79.0%) patients; 41,482 (14.37%) patients had dysphagia, and 33,548 (80.87%) patients received swallowing rehabilitation. We found that the dysphagia status after dysphagia screening was an independent risk factor for in-hospital death. Dysphagia screening performed prior to oral intake and subsequent swallowing rehabilitation could reduce the risk of in-hospital death; and composite poor outcomes, including DAMA and death. Unexpectedly, we found that dysphagia screening and swallowing rehabilitation were associated with a higher likelihood of developing hospital-related pneumonia.

A total of 288,764 (79.0%) patients underwent dysphagia screening in our study, which is similar to that of approximately 80% reported in previous studies.<sup>5,31,32</sup> However, the performance of dysphagia screening was higher than that of 69.2% in the HeadPoST program conducted in China from March 2015 to November 2016.<sup>31</sup> The GWTG–Stroke program from 2003–2009 reported 68.9% of patients were documented to have been provided dysphagia screening.<sup>33</sup> The higher rate of dysphagia

Adverse Outcomes	N (%)	Dysphagia Screening		N (%)	Swallowing Rehabilitation	
		OR (95% CI)	P value		OR (95% CI)	P value
Mortality <sup>a</sup>						
Unadjusted	1233(0.43)	0.75(0.65,0.87)	<0.001	540(1.56)	0.39(0.33,0.46)	<0.001
After IPTW PSM	1121(0.39)	0.79(0.73,0.86)	<0.001	502(1.44)	0.39(0.34,0.46)	<0.001
After nearest-neighbor PSM	703(0.40)	0.74(0.64,0.86)	<0.001	326(1.48)	0.43(0.36,0.52)	<0.001
Mortality + DAMA <sup>a</sup>						
Unadjusted	15,049(5.21)	0.83(0.80,0.87)	<0.001	3676(10.63)	0.43(0.40,0.47)	<0.001
After IPTW PSM	14829(5.20)	0.83(0.81,0.85)	<0.001	3715(10.75)	0.44(0.41,0.47)	<0.001
After nearest-neighbor PSM	9368(5.28)	0.83(0.79,0.87)	<0.001	2473(11.24)	0.45(0.42,0.49)	<0.001
Pneumonia <sup>a</sup>						
Unadjusted	43,027(14.90)	1.54(1.49,1.59)	<0.001	15,197(43.93)	0.99(0.93,1.05)	0.61
After IPTW PSM	41667(14.61)	1.54(1.51,1.56)	<0.001	15,265(43.67)	0.98(0.93,1.03)	0.43
After nearest-neighbor PSM	25909(14.60)	1.54(1.48,1.59)	<0.001	9683(44.00)	0.96(0.89,1.02)	0.19

#### Table 3 The Hospital Poor Outcomes in Stroke Patients with and without DS and Swallowing Rehabilitation

**Notes**: <sup>a</sup>Model adjusted for age, sex, initial NIHSS score, body mass index, history of stroke, hypertension, diabetes mellitus, dyslipidemia, coronary heart disease/ myocardial infarction, dementia, heart failure, atrial fibrillation, carotid stenosis, current smoking, alcoholism, antiplatelet drugs, anticoagulant drugs, antihypertensive drug, lipid-lowering drugs, the hospital characteristics (geographic region, hospital grade).

Abbreviations: Cl, confidence interval; OR, odds ratio; DAMA, discharge against medical advice; PSM, propensity Score Matching; IPTW, inverse probability of treatment weighted.

Adverse Outcomes	N (%)	N (%) Dysphagia Screening OR (95% CI) P value		N (%)	Swallowing Rehabilitation	
					OR (95% CI)	P value
Mortality <sup>a</sup>						
Unadjusted	633(0.38)	0.75(0.62,0.91)	0.004	310(1.48)	0.44(0.35,0.55)	<0.001
After IPTW PSM	702(0.37)	0.78(0.70,0.86)	<0.001	344(1.44)	0.44(0.36,0.54)	<0.001
After nearest-neighbor PSM	386(0.40)	0.75(0.61,0.92)	0.006	199(1.58)	0.44(0.33,0.57)	<0.001
Mortality + DAMA <sup>a</sup>						
Unadjusted	8460(5.01)	0.81 (0.76,0.86)	<0.001	2202(10.51)	0.44(0.40,0.49)	<0.001
After IPTW PSM	9586(5.03)	0.82(0.80,0.85)	<0.001	2524(10.55)	0.44(0.41,0.48)	<0.001
After nearest-neighbor PSM	4967(5.16)	0.79(0.75,0.84)	<0.001	1417(11.24)	0.43(0.38,0.48)	<0.001
Pneumoniaª						
Unadjusted	24,007(14.23)	1.50(1.43,1.57)	<0.001	9100(43.44)	1.08(1.00,1.17)	0.042
After IPTW PSM	27243(14.30)	1.52(1.48,1.55)	<0.001	10,429(43.57)	1.08(1.00,1.15)	0.045
After nearest-neighbor PSM	14187(14.74)	1.50(1.43,1.58)	<0.001	5639(44.74)	1.04(0.95,1.15)	0.41

Table 4 Hospital Poor Outcomes in Stroke Patients Excluded Missing of NIHSS Score with and without DS and SwallowingRehabilitation

Notes: <sup>a</sup>Model adjusted for age, sex, initial NIHSS score, body mass index, history of stroke, hypertension, diabetes mellitus, dyslipidemia, coronary heart disease/ myocardial infarction, dementia, heart failure, atrial fibrillation, carotid stenosis, current smoking, alcoholism, antiplatelet drugs, anticoagulant drugs, antihypertensive drugs, lipid-lowering drugs, the hospital characteristics (geographic region, hospital grade).

Abbreviations: Cl, confidence interval; OR, odds ratio; DAMA, discharge against medical advice; PSM, propensity score matching; IPTW, inverse probability of treatment weighted.

screening in our study relative to previous studies could be due to several reasons. The stroke patients enrolled in our study were  $\geq$  70 years old. Patients who received documented dysphagia screening tended to be older.<sup>5,31,34</sup> The older age was significantly associated with dysphagia screening ( $\geq$  80 versus < 60 years, adjusted OR, 1.44; 95% CI: 1.18–1.75).<sup>5</sup> Moreover, with multiple national and international guidelines recommending dysphagia screening and management for stroke patients,<sup>17–20</sup> clinicians and nurses may pay increased attention to dysphagia screening, especially for older adults or patients at malnutrition risk.<sup>4,6</sup> Further, the quality of stroke care in China has improved in overall adherence to guideline-recommended performance measures,

Adverse Outcomes	N (%)	Dysphagia Screening		N (%)	Swallowing Rehabilitation	
		OR (95% CI)	P value		OR (95% CI)	P value
Mortality <sup>a</sup>						
Unadjusted	956(0.35)	0.74(0.63,0.87)	<0.001	435(1.40)	0.40(0.33,0.48)	<0.001
After IPTW PSM	935(0.35)	0.79(0.72,0.86)	<0.001	427(1.33)	0.40(0.34,0.47)	<0.001
After nearest-neighbor PSM	569(0.34)	0.73(0.62,0.87)	<0.001	271(1.37)	0.43(0.35,0.53)	<0.001
Mortality + DAMA <sup>a</sup>						
Unadjusted	13,054(4.84)	0.87(0.83,0.91)	<0.001	3113(9.98)	0.42(0.39,0.45)	<0.001
After IPTW PSM	13327(4.93)	0.86(0.84,0.89)	<0.001	3271(10.15)	0.42(0.39,0.45)	<0.001
After nearest-neighbor PSM	8296(5.00)	0.87(0.83,0.91)	<0.001	2094(10.55)	0.43(0.40,0.48)	<0.001
Pneumonia <sup>a</sup>						
Unadjusted	37,589(13.94)	1.60(1.55,1.66)	<0.001	13,279(42.59)	0.98(0.92,1.04)	0.55
After IPTW PSM	37663(13.94)	1.60(1.58,1.63)	<0.001	13,790(42.80)	0.98(0.92,1.03)	0.38
After nearest-neighbor PSM	22876(13.79)	1.60(1.54,1.66)	<0.001	8536(43.00)	0.99(0.93,1.07)	0.85

Table 5 The Hospital Poor Outcomes in Ischemic Stroke Patients with and without DS and Swallowing Rehabilitation

Notes: <sup>a</sup>Model adjusted for age, sex; initial NIHSS score, body mass index, history of stroke, hypertension, diabetes mellitus, dyslipidemia, coronary heart disease/ myocardial infarction, dementia, heart failure, atrial fibrillation, carotid stenosis, current smoking, alcoholism, antiplatelet drugs, anticoagulant drugs, antihypertensive drugs, lipid-lowering drugs; the hospital characteristics (geographic region, hospital grade); We matched patients in a 1:4 ratio using the greedy, nearest-neighbor PSM without replacement.

Abbreviations: CI, confidence interval; OR, odds ratio; DAMA, discharge against medical advice; PSM, propensity score matching; IPTW, inverse probability of treatment weighted.

including dysphagia screening.<sup>32</sup> The patients in our study were from the CSCA program, which was designed to improve stroke care quality and outcomes. The CSCA have been implemented to promote the progress of stroke center construction and the standard of clinical practice in China.<sup>26</sup> Therefore, the performance of dysphagia screening in our study may have improved significantly in recent years.<sup>27</sup>

We observed that dysphagia screening could reduce the risk of adverse in-hospital outcomes. Similar to our results, a cluster RCT revealed that stroke care pathways consisting of dysphagia screening could reduce the risk of all-cause mortality at 90-days (adjusted OR: 0.33; 95% *CI*: 0.12–0.90).<sup>35</sup> Early dysphagia screening and intervention could reduce hospital-associated death or pneumonia in some studies.<sup>23,24</sup> Additionally, in the Quality in Acute Stroke Care (QASC) study, patients who received intervention for acute stroke (ie, fever, sugar, and swallowing management) were significantly less likely to be dependent or die (mRS  $\geq$ 2) at 90 days than patients in the control group [236 (42%) vs 259 (58%), P=0.002], but this was not the case for all-cause mortality [21 (3.7%) vs 24 (5.3%), *P*=0.36].<sup>36</sup> Unexpectedly, we observed that dysphagia screening was associated with an increased risk of pneumonia. The GWTG–Stroke program also reported that dysphagia screening was associated with a higher OR for pneumonia.<sup>33</sup> However, we suggest that the causal relationships may be reversed. Firstly, stroke patients at higher risk of pneumonia may be more likely to receive dysphagia screening in clinical practice. Furthermore, patients with documented dysphagia screening were more likely to have a medical history (ie, atrial fibrillation, current smoking) that could increase the risk of pneumonia.<sup>37</sup> Meanwhile, our results demonstrate that the dysphagia status as a result of the dysphagia screening was also associated with a higher risk of in-hospital death (adjusted OR: 6.13, 95% CI: 5.18–7.27), which is consistent with other studies.<sup>5,23,31</sup>

In the present study, we observed that subsequent swallowing rehabilitation had beneficial effects on all-cause mortality for patients with stroke (adjusted OR: 0.39, 95% CI: 0.33–0.46), AIS (adjusted OR: 0.40, 95% CI: 0.33–0.48) and intracranial hemorrhage (adjusted OR: 0.28, 95% CI: 0.20–0.39). Compared with conventional discharge, DAMA was likely to increase the risk of hospital readmission, and mortality.<sup>38,39</sup> Swallowing rehabilitation also significantly decreased the risk of composite outcomes, including in-hospital death and DAMA in our study. Some meta-analyses showed that acupuncture may have beneficial effects on swallowing function and dependency, but no data were reported for mortality.<sup>40,41</sup> However, another meta-analysis revealed that swallowing therapy did not affect case fatality (OR: 1.00, 95% CI: 0.66–1.52), but could reduce the incidence of pneumonia (OR: 0.36, 95% CI: 0.16–0.78).<sup>2</sup>

Swallowing rehabilitation may decrease the risk of adverse outcomes, but the association was significant, such that we consider it may be overstating the effect. Firstly, the socioeconomic status and compliance of patients in undertaking swallowing rehabilitation may have been superior and, hence, improved treatment outcomes.<sup>42</sup> Further, the hospitals that provided swallowing rehabilitation may have adhered to evidence-based performance measures and improved multi-faceted intervention quality, including intravenous recombinant tissue plasminogen activator (rt-PA), deep venous thrombosis prophylaxis, evidence-based medications after admission, and dysphagia management that prevented and reduced in-hospital and long-term mortality.<sup>43</sup>

Dysphagia interventions involve behavioral therapy and rehabilitative methods, and behavioral approaches include modification of fluid and food consistencies.<sup>4</sup> Some high-quality RCTs report that dietary adjustments or nutritional support could reduce the risk of death. The FOOD trials showed that a supplemented diet reduced the absolute risk of death in stroke patients with dysphagia [7%, 95% CI: -1.4-2.7; P= 0.5)].<sup>44</sup> The Effect of early nutritional support on Frailty, Functional Outcomes, and Recovery of malnourished medical inpatients Trial revealed that assessing patients by NRS2002 could decrease the risk of a composite adverse clinical outcome defined as all-cause mortality, admission to intensive care, non-elective hospital readmission, major complications, and decline in functional status at 30 days (HR: 0.81, 95% CI: 0.68–0.97) and all-cause mortality (HR: 0.65, 95% CI: 0.48–0.88) within 30 days.<sup>45</sup> The abovementioned findings indicate the importance of performing dysphagia screening and management to reduce the risk of adverse outcomes, especially for stroke patients who are older or at malnutrition risk.

We acknowledge several limitations in our study. Firstly, there may have been heterogeneity in the type of dysphagia screening or swallowing rehabilitation among the multicenter hospitals. The detailed information was not collected on the heterogeneity for further analysis. Secondly, there may have been selection bias, as our study patients with stroke at malnutrition risk were screened based on age ( $\geq 70$  years old), which meets two items of malnutrition risk defined by NRS-2002. Therefore, some patients who were < 70 years old but might be screened as at malnutrition risk according to other items in the NRS-2002 were not included in our study. However, several previous studies reported that the average age of stroke patients at malnutrition risk was  $\geq$  70 years.<sup>13,46</sup> Positive outcomes were more likely among older patients  $\geq$  70 years old who received nutritional support.<sup>10-12</sup> Therefore, we focused on this segment of patients at malnutrition risk in our study. Hence, caution should be taken when generalizing the findings to other populations at malnutrition risk. A major strength of our study is the large sample size of stroke patients at malnutrition risk from multicenter, and the main purpose was to provide evidence for reducing poor outcomes through dysphagia management among specific patients, specifically, older adults. In addition, the primary endpoint included in-hospital death and complication but not outcomes after discharge. Finally, some other potential confounding factors (ie, modified Rankin score at admission, activities of daily living) may have influenced the results. However, the quality of these related variables was not sufficient for inclusion in the analysis in our study. Further studies are needed to validate that dysphagia screening may reduce the risk of short- and long-term adverse outcomes and investigate its effect in a larger scope of populations at malnutrition risk.

### Conclusion

Dysphagia screening and swallowing rehabilitation were associated with reducing the risk of death and the composite outcome of DAMA and in-hospital death among stroke patients. Future research should concentrate on improving the quality of medical care for dysphagia management to improve patients' outcomes.

# Abbreviations

AIS, acute ischemic stroke; ASD, absolute standardized difference; CI, confidence interval; CSCA, Chinese Stroke Center Alliance; DAMA, discharge against medical advice; IPTW, inverse probability of treatment weight; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; NRS 2002, nutrition screening 2002; PSM, propensity score matching; TIA, transient ischemic attacks.

# **Data Sharing Statement**

The data are available to researchers on reasonable request for purpose of reproducing the results or replicating the procedure from the corresponding author.

# **Ethics Approval and Consent to Participate**

The CSCA was approved by the ethics committee of Beijing Tiantan Hospital (KY 2018-061-02). The study protocol conforms to the ethical guidelines of the Declaration of Helsinki. The data was collected and managed via the web-based tool. Participating hospitals in CSCA collected data without the individual information and exemption from their Institutional Review Board.

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# Disclosure

The authors report no conflicts of interest in this work.

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