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Increasing stroke severity is associated with increased risk of aspiration pneumonia: The risk is higher in medical ward compared to stroke ward

Running Title: Risk factors associated with aspiration pneumonia

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Abstract

Objective: We examined the incidence, clinical characteristics, and outcomes among ischemic stroke-related aspiration pneumonia patients in Qatar.

Methods: A prospective cohort study was analyzed retrospectively from January 2014 to April 2024. A total of 9,197 patients were included.

Results: Stroke patients who developed aspiration pneumonia tended to be older and of the male sex. Patients who developed aspiration pneumonia were also more likely to present with a higher NIHSS at admission ($p<0.001$). Patients with large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke of undetermined etiology were more likely to develop aspiration pneumonia. They also stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia (16.0 vs. 5.3 days). Patients admitted to the medicine ward had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward (aOR of 1.56, 95% confidence interval: 1.05–2.31). Patients with aspiration pneumonia had unfavorable outcome (mRS 3-6) at 90 days (74.6% vs. 30.4% for an NIHSS admission score of 5-9 and 79.6% vs. 59.5% for an NIHSS admission >10). They were also more likely to have higher mortality rates at 90 days (16.9% vs. 1.9% for an NIHSS admission score of 5-9 and 22.3% vs. 13.8% for an NIHSS admission score >10) and MACE at 1 year (23.7% vs. 3.8% for an NIHSS admission score of 5-9 and 27.5% vs. 16.2% for NIHSS >10).

Conclusion: Age, sex, admission NIHSS severity, stroke subtypes, and admission location are independent predictors of aspiration pneumonia post-stroke.

Keywords: Aspiration Pneumonia, Stroke, Dysphagia, Stroke-associated pneumonia

What is already known on this topic: Aspiration pneumonia is a common complication post-stroke that increases patient's duration of stay in hospitals and affects their prognosis post-stroke. However, there is very little data on the incidence, causes, and outcomes of aspiration pneumonia from the Middle East and North Africa (MENA) region.

What this study adds: This is the first study to specifically examine the incidence and outcomes of patients who develop aspiration pneumonia post-stroke in the MENA region. Patients with aspiration pneumonia stayed an average of 10 days longer in the hospital compared to patients without. A higher proportion of patients with aspiration pneumonia had an unfavorable outcome at 90 days. They were also more likely to have higher mortality rates at 90 days and MACE at 1 year. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward.

How this study might affect research, practice or policy: Our study demonstrates that admission location is a significant predictor of aspiration pneumonia post-stroke. Healthcare providers should be judicious of the placement of their stroke patients to reduce the incidence of aspiration pneumonia.

Introduction

Stroke is a major cause of death and disability worldwide. Early in the course of the disease, stroke patients are at risk for medical complications including dysphagia and aspiration pneumonia.[1] Dysphagia is characterized by difficulty swallowing due to weakness/reduced coordination between facial, palatal, and pharyngeal muscles (due to reduced cortical connectivity between neural regions post-stroke).[2] The incidence of dysphagia after stroke ranges from 8.1–80%,[3–7] it is frequently silent and it is highly associated with aspiration pneumonia.[8] Dysphagia causes oral or gastric contents to enter the lung, which suppresses the natural defenses of the respiratory system, increasing the risks for opportunistic infections.[9–11] Several studies have identified multiple risk factors associated with aspiration pneumonia, such as reduced level of consciousness, incorrect postures, and advanced age.[12–15]

Pneumonia is one of the leading causes of mortality for acute stroke, with a 30-day mortality rate of up to 30%.[16] Aspiration pneumonia also increases the risk of prolonged hospital stay and poor prognosis.[17] Animal and clinical studies have demonstrated that silent aspiration (micro-aspiration due to dysphagia during the night) is the primary cause of aspiration pneumonia.[18] Despite different preventative and therapeutic approaches for managing patients with aspiration pneumonia, its incidence and mortality rates remain high.[19] For example, in a case-control study comprising of 1,112,944 patients, Gupte et al[20] reported that aspiration pneumonia due to cerebrovascular disease accounted for 11.7% of deaths in the United States (62,068 deaths per year from 1999 to 2017), with increasing mortality rates since 2009. In countries such as Egypt and Brazil, the incidence of aspiration pneumonia can be as high as 44% and 76%, respectively.[19,21]

There are very few studies on the incidence, causes, and outcomes of aspiration pneumonia from the Middle East and North Africa (MENA) region.[22] This study aimed to assess the clinical characteristics and treatment outcomes among stroke-related aspiration pneumonia patients in Qatar.

Methods

Data from patients admitted with a stroke to Hamad General Hospital (HGH), Doha, Qatar from January 2014 through April 2024 were analyzed from a hospital based prospective stroke registry. HGH is a Joint Commission International (JCI) accredited 600-bed hospital, with 200 beds reserved for medical patients. It is the only tertiary care medical facility in Qatar where the stroke service is located, 95% of all strokes in Qatar requiring admission to hospital are admitted to HGH.

Ethics Considerations

The studies involving humans were approved by the Institutional Review Board of the Medical Research Centre at Hamad Medical Corporation (MRC-01-18-102). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent from the patients/participants or patients/participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Patient characteristics

Patient characteristics including age, sex, ethnicity, medical comorbidities and prior medication were collected in the Stroke Registry. National Institute of Health Stroke Scale (NIHSS) score, neuroimaging data, and post-discharge disposition were entered into the registry as well. Ischemic stroke was diagnosed according to the WHO criteria[23] and stroke subtypes were defined by the TOAST criteria.[24] The modified Rankin scale (mRS) measurements were done at discharge and at 90 days following onset of symptoms. The patients were classified as favourable (mRS ≤ 0-2) or unfavourable (mRS 3-6) outcome. We used the dichotomized mRS scale to evaluate recovery at 90 days.[25]

Diabetes was diagnosed according to the American diabetes Association (ADA) and WHO recommendation[26] and included patients with a previous diagnosis of diabetes, on medication for diabetes or an HbA1c of more than 6.5%, and the diagnosis of pre-diabetes was based on an HbA1c of 5.7-6.4% as per the 2015 ADA clinical practice recommendations. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mm Hg or a diastolic pressure ≥ 90 mm Hg, or on current treatment with antihypertensive drugs. Dyslipidemia was defined as low-density lipoprotein-cholesterol level ≥ 3.62 mmol/L, high-density lipoprotein cholesterol level ≤ 1.03 mmol/L, triglycerides ≥ 1.69 mmol/L, or current treatment with a cholesterol-lowering drug.

Data Collection

Upon identification and confirmation of diagnosis using the International Classification of Disease, 10th edition, definitions (H34.1, 163.x, 164.x, 161.x, 160.x, G45.x), patients' data were collected by trained stroke clinical nurse specialists.

Data Analysis and statistics

Descriptive results for all continuous variables were reported as mean±standard deviation (SD) for normally distributed data or median with range for data with non-normal distributions. The distribution of continuous variables was assessed before using statistical tools. Mean level comparisons between patients with aspiration pneumonia versus without aspiration pneumonia were assessed using ANOVA test and multiple comparisons were performed using Bonferroni correction. If an assumption of an ANOVA test was failed, then an alternative non-parametric Kruskal Wallis test was performed. Pearson Chi-Square test and Fisher's Exact test were performed whenever appropriate to compare the proportion of all categorical variables between the groups. Multiple logistic regression analysis was performed to assess for risk factors associated with aspiration pneumonia after selecting important and significant variables at univariate analysis. Odds ratio (OR) and the 95% confidence interval for the OR were reported. A p-value of ≤0.05 (two-tailed) was considered significant. SPSS statistical package 29.0.1.0 was used for the analysis.

Results

Patient Characteristics

A total of 9197 patients were enrolled: 380 developed aspiration pneumonia (4.1%) during hospitalization while 8817 (95.9%) of the patients did not have pneumonia. The mean age of patients was 55.3±13.4 years, with patients with aspiration pneumonia being significantly older than healthy controls (p<0.001). 80% were male, 57% had diabetes mellitus, 72% had hypertension, 46% had dyslipidemia, and 24% were active smokers. The high proportion of men is reflective of the very high male expatriate population as previously reported.[27] A summary of patients' baseline characteristics is outlined in Table 1.

Since 95.9% of our patients did not have aspiration pneumonia, we performed sub-analyses on clinical outcomes based on patients' admission NIHSS scores. Sub-analyses were performed for patients with an NIHSS of 5-9 (moderate stroke) and NIHSS >10 (severe stroke) (Table S1).

Mode of transport

Mode of transport was significantly associated with aspiration pneumonia risks ($p<0.001$). However, this was only significant for emergency medical services (EMS) versus non-medical services ($p<0.001$), with a higher proportion of patients developing aspiration pneumonia via EMS (4.5%) versus non-medical services (1.5%). Patients transported with EMS had a significantly higher NIHSS at admission (5.9±6.1 vs. 3.3±3.7, $p<0.001$). The total sample size for EMS was 6361 versus 2234 for non-medical services.

Onset Duration

Duration of stroke symptoms from the time of onset to evaluation was significantly associated with aspiration pneumonia ($p<0.001$). This was only significant for <4.5 hours vs. >24 hours ($p<0.001$) and 4.5-24 hours vs. >24 hours ($p<0.001$). A stroke onset to emergency evaluation of <4.5 hours had the highest proportion of aspiration pneumonia (5.7%) versus 4.8% for onset duration of 4.5-24 hours and 2.1% for >24 hours (Table S2).

Duration of stay in Emergency Department

Duration of stay in the ED was not significantly associated with aspiration pneumonia ($p=0.11$) (Table S2). Furthermore, when we analyzed duration of stay in the ED based on NIHSS scores (5-9 and >10), duration of stay in the ED remained non-significant ($p=0.052$ and 0.09), respectively (Table S1).

Diagnosis

Stroke diagnosis is shown in Table S2. Overall, type of stroke was significantly associated with aspiration pneumonia (p<0.001). Further analyses revealed that the risk of developing aspiration pneumonia was not significantly different between large vessel disease versus cardioembolic stroke (p=1.00), large vessel disease versus stroke of undetermined aetiology (p=1.00), cardioembolic stroke versus stroke of determined aetiology (p=0.06), cardioembolic stroke versus stroke of undetermined etiology (p=1.00), and stroke of determined aetiology versus stroke of undetermined aetiology (p=0.82).

Patients with small vessel disease had the lowest proportions of aspiration pneumonia (0.8%) compared to large vessel disease (7.4%), cardioembolic stroke (7.3%), stroke of determined etiology (4.8%), and stroke of undetermined etiology (6.8%), p<0.001 (Table 2).

Admission NIHSS Score

Admission NIHSS score was significantly associated with aspiration pneumonia (p<0.001). Fisher's exact test revealed that there was a significant association between aspiration pneumonia for patients with an NIHSS score of 0-4 (p=0.03), and NIHSS score of >10, p<0.001 (Table S3). Patients with an NIHSS > 10 had the highest proportion of aspiration pneumonia (16.5%). Moreover, patients with an NIHSS >10 and concomitant aspiration pneumonia had higher rates of mortality at 90 days (22.3%) when compared to patients with an NIHSS score of 5-9 and concomitant aspiration pneumonia (16.9%) (p<0.001) (Table S1). In patients with aspiration pneumonia, patients with an NIHSS >10 also had higher rates of major adverse cardiovascular events (MACE) at 1 year compared to patients with an NIHSS of 5-9 (27.5% vs. 23.7%, p<0.001).

Length of stay

Patients with aspiration pneumonia stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia (16.0 days vs. 5.3 days, p=0.00). When analyzed via admission NIHSS severity, patients with aspiration pneumonia stayed significantly longer in the hospital compared to those without aspiration pneumonia (17.1 days vs. 5.9 days, p<0.001 for NIHSS of 5-9, and 16.6 days vs. 9.2 days, p<0.001 for NIHSS > 10).

Admission Location

Overall, 3966 (75.1%) patients were admitted to the stroke ward and 1318 (24.9%) patients were admitted to the medical ward. A higher proportion of patients admitted to the medicine ward developed aspiration pneumonia in contrast to patients admitted to the stroke ward (5.3% vs 3.7%, p=0.01) (Table 2). 2.3% of patients with an NIHSS of 0-4 and admitted to the medicine ward developed aspiration pneumonia compared to 1.2% of patients with an NIHSS of 0-4 and admitted to the stroke ward (p=0.03) (Table S3). Similarly, 19.9% of patients with an NIHSS >10 and admitted to the stroke ward developed aspiration pneumonia compared to 9.9% of patients with an NIHSS >10 and admitted to the stroke ward (p<0.001) (Figure 1).

Modified Rankin Scale at 90 days

A higher proportion of patients with aspiration pneumonia had an unfavorable outcome (mRS 3-6) at 90 days compared to patients without aspiration pneumonia (74.6% vs. 30.4% for NIHSS of 5-9), p<0.001 (Table S1). Similar observations were seen for NIHSS > 10 (79.6% vs. 59.5%, p<0.001). Figure 2a and 2b illustrates the proportion of mRS at 90 days based on NIHSS admission scores.

Mortality at 90 days

For patients with an NIHSS score of 5-9, a higher proportion of patients with aspiration pneumonia died at 90 days (16.9%) compared to patients without aspiration pneumonia (1.9%), p<0.001. Similar observations were seen for NIHSS > 10 (22.3% vs. 13.8%, p=0.003).

Multivariate analysis for risk factors associated with aspiration pneumonia

Table 2 describes a multiple binary logistic regression model to identify significant independent factors associated with the development of aspiration pneumonia after selecting important and significant variables at bivariate analysis. Males were more likely than females to have aspiration pneumonia risks [aOR 1.56, 95% CI: 1.05–2.32, p=0.03]. Age was significantly associated with aspiration pneumonia [aOR 1.02, 95% CI: 1.01–1.03, p=0.002], with patients with aspiration pneumonia being significantly older (p<0.001). Large vessel disease was significantly associated with aspiration pneumonia [aOR 4.11, 95% CI: 2.52–6.69, p<0.001]. Similar observations were seen for cardioembolic stroke (p<0.001), stroke of determined aetiology (p<0.001), and stroke of undetermined aetiology (p<0.001), see Table 2. Patients with an NIHSS score of 5–9 and >10 also had high odds of developing aspiration pneumonia (aOR of 1.87 and 5.98, respectively). Patients admitted to the medicine ward also had 1.56 times the odds of developing aspiration pneumonia compared to the stroke ward (95% CI: 1.05–2.31, p=0.03). A forest plot of the multivariate analysis can be seen in Figure 4.

Discussion

To the best of our knowledge, this is the first study to specifically examine the incidence and outcomes of patients who develop aspiration pneumonia post-stroke in the MENA region. In our cohort, 4.1% of our patients developed aspiration pneumonia post stroke. This low number may be deceiving as the majority of patients admitted had mild symptoms [5626 (61.2%) of patients had an NIHSS of <4]. The odds of aspiration pneumonia was 1.87 in patients with

admission NIHSS of 5-9 (n=1965), increasing to 5.98 in patients with NIHSS of 10 or more (n=1606). Patients with aspiration pneumonia also stayed an average of 10 days longer in the hospital compared to patients without. A higher proportion of patients with aspiration pneumonia had an unfavorable outcome at 90 days. They were also more likely to have higher mortality rates at 90 days and MACE at 1 year. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward.

High NIHSS has also been shown to be correlated with increased rates of dysphagia and aspiration pneumonia due to stroke severity.[28] Patients with aspiration pneumonia in the Qatar dataset had comparatively higher NIHSS at presentation as compared to patients without pneumonia (14.7 v 5.1, p<0.001). Garavelli et al[29] demonstrated that an NIHSS cut-off of ≥ 10.5 was associated with higher rates of dysphagia (p=0.014) and aspiration pneumonia (p=0.006). Similarly, Jeyaseelan et al[28] demonstrated NIHSS > 9 as being moderately predictive of clinically relevant dysphagia, with dysphagia rates increasing with greater NIHSS scores (p<0.001). Okubo et al[30] also showed an NIHSS cut-off of 12 sensitive for dysphagia detection, with 14 (87.5%) of the 16 patients with dysphagia having NIHSS scores ≥ 12 and 2 (12.5%) patients having scores of 10 and 11. NIHSS >12 also has an independent association with persistent dysphagia at hospital discharge in acute ischemic stroke patients with dysphagia at stroke onset, with one of its sub-components–dysarthria–emerging as a significant independent predictor of prolonged dysphagia.[31] In our current study, the odds of developing aspiration pneumonia increased as NIHSS score increased.

Several studies have reported the adverse outcomes of aspiration pneumonia on stroke patients. In a study comprised of 610,668 stroke patients, Barlas et al[32] reported that patients with

stroke-associated pneumonia (SAP) had significantly higher odds of in-hospital mortality (OR of 2.90, 95% CI: 2.83–2.96), and longer length of stay (OR 13.11, 95% CI: 12.83–13.40). While they analyzed data from both ischemic and hemorrhagic strokes, patients with ischemic stroke were more likely to die in hospital and experience long length of stay (LOS).[32] Teh et al[33] had similar observations in his cohort of 9238 patients from the UK. SAP was found in 1083 (11.7%) patients, out of which 60.8% were aspiration pneumonia.[33] After controlling for confounders, SAP was found to be associated with increased mortality up to 1 year (inpatient, 90-day, 1 year), prolonged LOS, and poor functional outcome on discharge.[33] In our current study, patients who developed aspiration pneumonia with an admission NIHSS of 5-9 had a 16.9% mortality rate at 90 days in contrast to 1.9% for patients who did not develop aspiration pneumonia. Similarly, patients who developed aspiration pneumonia with an admission NIHSS >10 had higher mortality rates at 90 days (22.3% vs. 13.8%, p=0.003).

Dysphagia is a common feature of severe stroke and an indicator of poor prognosis. It is implicated in the development of aspiration pneumonia, and it results in longer LOS and increased mortality. In stroke patients with dysphagia, early nutritional support is vital, and the decision to initiate that depends on the outcome of the swallow study.[34] Multiple national and international guidelines recommend that people with acute stroke have their swallowing screened by a trained healthcare professional by utilizing a validated screening tool and that the patients remain nothing per oral (NPO) until a swallow screen is performed.[17] Bedside swallow screening tools include the functional bedside aspiration screen (FBAS), GLOBE-3S (the Sapienza GLObal Bedside Evaluation of Swallowing after Stroke), water swallowing test, volume-viscosity swallow test, and the Gugging swallow screen. However, despite these recommendations, in our study 34.6% of patients did not undergo swallow screen prior to PO

intake in the ED and 32.7% patient did not have SLP assessment within 24 hours of admission. Likely explanations for these findings include ED nursing inadvertently giving patients PO medications, or SLPs not being available over the weekend, hence leading to an inability to perform assessment within 24 hours of presentation.

Similar to previous reports, we observed a significantly higher risk of aspiration pneumonia in the patients admitted to the medical ward compared to the stroke ward (5.3% vs. 3.7%, p=0.01). Admission to the stroke ward, by prevention of medical complications, results in reduced length of stay, decreased incidence of complications, improved prognosis at discharge and at 90 days (higher % of mRS scores of 0-2).[35,36] Similarly, in our current study, fewer patients developed aspiration pneumonia if they were admitted to the stroke ward versus medicine ward (3.7% vs. 5.3%, p=0.01). Multivariable logistic regression identified admission location as an independent predictor of aspiration pneumonia, with patients admitted to the medicine ward having higher risks of developing aspiration pneumonia (aOR 1.56, 95% CI: 1.05–2.31). In our study population, we also observed that 19.9% patients with an NIHSS >10 and admitted to the medicine ward developed aspiration pneumonia in contrast to patients with an NIHSS > 10 and admitted to the stroke ward (9.9%; p<0.001). Thus, healthcare providers should be judicious of the placement of their stroke patients if they would like to reduce the incidence of aspiration pneumonia.

We also observed that patients with small vessel disease or subcortical stroke were less likely to develop aspiration pneumonia in contrast to patients with cardioembolic stroke, large vessel disease, stroke of undetermined etiology, and stroke of determined etiology. This is consistent with Alberts et al's study, who reported a low occurrence of aspiration in small vessel infarcts compared to those with both large- and small vessel infarcts (p=0.002).[37] Similarly,

Jitpratoom et al[38] observed that 40.7% of their patients with cardioembolic stroke developed aspiration pneumonia in contrast to 11.1% for small vessel occlusion. Multivariable logistic regression analysis revealed that type of stroke was an independent predictor of aspiration pneumonia, specifically for large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke of undetermined etiology. A potential explanation for this is that patients with small vessel disease have milder stroke symptoms and fewer neurological deficits in contrast to the other stroke subtypes,[39] therefore they might have more preserve/control of their facial, palatal, and pharyngal muscles, reducing their risks of developing dysphagia and aspiration pneumonia. However, additional studies are needed to unravel this relationship.

There are several limitations with our study. Our patient sample is comprised of largely Middle Eastern ethnicity (Qatari, Arabs), South Asian and Far Eastern (Asians) (97.7% vs. 2.3% for Caucasians), therefore lacks generalizability. We also had missing data for the mRS score at 90 days for 1846 patients (out of 9197). Since Qatar's population is comprised mainly of expatriate workers, it is not possible to collect data for patients who may have moved back to their home country once their work contract ended.

Conclusion

This large study in prospectively collected patients with acute stroke identified multiple factors associated with an increased risk of aspiration pneumonia. Patients who developed aspiration pneumonia were older, presented with more severe neurological symptoms, and stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia. Patients with large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke of undetermined etiology were more likely to develop aspiration pneumonia. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in

contrast to patients admitted to the stroke ward. Our study showed that aspiration pneumonia was associated with an unfavorable prognosis (mRS 3-6) and increased mortality at 90 days in patients with moderate and severe symptoms.

Data Availability Statement

The Qatar Stroke Registry dataset will be available on reasonable request to the corresponding author.

Declaration of conflicting interests

The author(s) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Table 1. Characteristics and outcome of acute ischemic stroke patients with aspiration pneumonia

Characteristic	No Pneumonia (n=8817, 95.9%)	Aspiration Pneumonia (n= 380, 4.1%)	Total (n= 9197)	P-Value
Age	55.1±13.3	59.0±15.6	55.3±13.4	<0.001
Male Gender	7041 (79.9)	303 (79.7)	7344 (79.9)	0.95
Diabetes	5038 (57.1)	229 (60.3)	5267 (57.3)	0.22
Hypertension	6373 (72.3)	246 (64.7)	6619 (72.0)	<0.001
Dyslipidemia	4069 (46.1)	136 (35.8)	4205 (45.7)	<0.001
Prior Stroke or TIA	1156 (13.1)	63 (16.6)	1219 (13.3)	0.05
Coronary Artery Disease	1053 (11.9)	70 (18.4)	1123 (12.2)	<0.001
Atrial Fibrillation	664 (7.5)	73 (19.2)	737 (8.0)	<0.001
Active Smoking	2143 (24.3)	52 (13.7)	2195 (23.9)	<0.001
Ethnicity[a]				
Arab	2962 (33.6)	160 (42.1)	3122 (33.9)	<0.001
South Asian	4518 (51.2)	168 (44.2)	4686 (51.0)	
Far Eastern	753 (8.5)	17 (4.5)	770 (8.4)	
African	382 (4.3)	26 (6.8)	408 (4.4)	
Caucasian	202 (2.3)	9 (2.4)	211 (2.3)	
Mode of Arrival[a]				
EMS	6073 (68.9)	288 (75.8)	6361 (69.2)	<0.001
Non-Medical	2200 (25.0)	34 (8.9)	2234 (24.3)	
From Other Hospitals	372 (4.2)	15 (3.9)	387 (4.2)	
mRS prior to acute stroke[a]				
0	7595 (86.1)	282 (74.2)	7877 (85.6)	<0.001
1	132 (1.5)	9 (2.4)	141 (1.5)	
2	312 (3.5)	12 (3.2)	324 (3.5)	
3	430 (4.9)	33 (8.7)	463 (5.0)	
4	196 (2.2)	23 (6.1)	219 (2.4)	
5	151 (1.7)	21 (5.5)	172 (1.9)	
NIHSS on admission	5.1 ± 5.54	14.65 ± 8.05	5.5 ± 6.0	<0.001
Onset Duration[a]				
Less than 4.5 Hours	2822 (32.0)	169 (44.5)	2991 (32.5)	<0.001
Between 4.5 till 24 hours	2890 (32.8)	145 (38.2)	3035 (33.0)	
More than 24 hours	3105 (35.2)	66 (17.4)	3171 (34.5)	
Thrombolysis Given	962 (10.9)	73 (19.2)	1035 (11.3)	<0.001
Mechanical Thrombectomy done	350 (4.0)	43 (11.3)	393 (4.3)	<0.001
BMI on admission	28.15±43.9	27.54±5.3	28.13±43.0	0.8
RBS on admission	9.6±7.5	10.4±5.05	9.6±7.4	0.04
HbA1c	7.51±2.42	7.6±2.4	7.51±2.41	0.64
Serum Cholesterol	4.84±1.52	4.6±1.75	4.83±1.53	0.01
Serum Triglyceride	1.8±1.76	1.45±0.83	1.77±1.73	0.002
Serum HDL	1.1±3.24	1.43±6.34	1.10±3.38	0.12
Serum LDL	3.1±1.8	2.82±1.25	3.1±1.8	0.03
Systolic Blood Pressure	157.8±44.23	149.44±29.15	157.42±43.73	0.00
Diastolic Blood Pressure	91.1±22.4	86.4±19.4	90.9±22.3	0.00
Length of Stay	5.25±8.55	16.0±14.93	5.70±9.2	0.00

Disposition[a]				
Discharged Home	**5726 (64.9)**	**44 (11.6)**	**5770 (62.7)**	**<0.001**
Rehabilitation	**2079 (23.6)**	**89 (23.4)**	**2168 (23.6)**	
Long term care	**151 (1.7)**	**97 (25.5)**	**248 (2.7)**	
Transfer to other facility	**732 (8.3)**	**109 (28.7)**	**841 (9.1)**	
Died as in-patient	**129 (1.5)**	**41 (10.8)**	**170 (1.8)**	
TOAST Classification[a]				
Small Vessel Disease	**4213 (47.8)**	**36 (9.5)**	**4249 (46.2)**	**<0.001**
Large Vessel Disease	**1772 (20.1)**	**141 (37.1)**	**1913 (20.8)**	
Cardio-Embolic	**1744 (19.8)**	**137 (36.1)**	**1881 (20.5)**	
Stroke of Determined Etiology	**612 (6.9)**	**31 (8.2)**	**643 (7.0)**	
Stroke of Undetermined Etiology	**476 (5.4)**	**35 (9.2)**	**511 (5.6)**	
Swallow Screen done before oral intake	**5820 (66.0)**	**197 (51.8)**	**6017 (65.4)**	**<0.001**
Speech therapy assessment done	**6024 (68.3)**	**161 (42.4)**	**6185 (67.3)**	**<0.001**
Speech Therapy assessment duration (hours)	**31.7±309.7**	**77.9±694.32**	**32.85±325.45**	**0.07**
Antibiotics given	**626 (7.1)**	**361 (95.0)**	**987 (10.7)**	**<0.001**

Abbreviations: BMI, Body Mass Index; ED, emergency department; HDL, High density lipoprotein; ICU, intensive care unit; LDL, Low density lipoprotein; MACE, major adverse cardiac event; mRS, Modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; RBS, Random blood sugar

[a]p-value reported based on Pearson-Chi Square Test

Values are reported as mean ± standard deviation and n(%)

Table 2. Bivariate and Multivariate logistic regression analysis to identify the risk factors associated with aspiration pneumonia.

Determinants		*Bivariate logistic regression analysis*				*Multivariate logistic regression analysis*		
	No Pneumonia	**Aspiration Pneumonia**	**Standardized Beta**	**Odds ratio (95% CI)**	**p-value**	**Standardized Beta**	**Odds ratio (95% CI)**	**p-value**
Age	55.3 ± 13.4	59.0 ± 15.6	0.021	1.02 (1.01–1.03)	<.001	0.01	1.02 (1.01–1.03)	0.002
Sex								
Female	1776 (95.8)	77 (4.2)	-	1	-	-	1	-
Male	7041 (95.9)	303 (4.1)	-0.007	0.99 (0.77–1.28)	0.95	0.448	1.56 (1.05–2.32)	0.03
TOAST								
SVD	4213 (99.2)	36 (0.8)	-	1	-	-	1	-
LVD	1772 (92.6)	141 (7.4)	2.231	9.31 (6.43–13.48)	<.001	1.413	4.11 (2.52–6.69)	<.001
CE	1744 (92.7)	137 (7.3)	2.218	9.19 (6.34–13.33)	<.001	1.309	3.69 (2.23–6.12)	<.001
SDA	612 (95.2)	31 (4.8)	1.780	5.93 (3.64–9.65)	<.001	1.172	3.25 (1.75–6.03)	<.001
SUD	476 (93.2)	35 (6.8)	2.152	8.61 (5.35–13.83)	<.001	1.403	4.09 (1.98–8.46)	<.001
Mode of transport								
From Other Hospitals	372 (96.1)	15 (3.9)	-	1	-	-	1	-
EMS	6073 (95.5)	288 (4.5)	0.162	1.18 (0.69–2.00)	0.55	0.184	1.20 (0.55–2.64)	0.65
Non-Medical	2200 (98.5)	34 (1.5)	-0.959	0.38 (0.21–0.71)	0.00	0.032	1.03 (0.43–2.47)	0.94
Onset Duration								

<4.5 hours	2822 (94.3)	169 (5.7)	-	1	-	-	1	-
4.5-24 hours	3890 (96.4)	145 (3.6)	-0.177	0.84 (0.67–1.05)	<.001	0.13	1.06 (0.68–1.65)	0.79
>24 hours	3105 (97.9)	66 (2.1)	-1.036	0.36 (0.27–0.47)	<.001	0.06	1.15 (0.82–1.61)	0.43
Duration in ER								
<4 hours	809 (94.2)	50 (5.8)	-	1	-	-	1	-
4-8 hours	1711 (93.3)	122 (6.7)	0.143	1.15 (0.82–1.62)	0.41	0.34	1.41 (0.90–2.20)	0.13
>8 hours	2749 (94.8)	151 (5.2)	-0.118	0.89 (0.64–1.24)	0.48	0.21	1.24 (0.80–1.93)	0.34
NIHSS								
Mild Stroke (0-4)	5570 (99.0)	56 (1.0)	-	1	-	-	1	-
Moderate Stroke (5-14)	1906 (97.0)	59 (3.0)	1.125	3.08 (2.13–4.45)	<.001	0.62	1.87 (1.19–2.94)	0.01
Severe Stroke (>10)	1341 (83.5)	265 (16.5)	2.978	19.66 (14.64–26.38)	<.001	1.78	5.98 (3.92–9.11)	<.001
Admission Location								
Stroke Ward	3819 (96.3)	147 (3.7)	-	1	-	-	1	-
Medicine Ward	1248 (94.7)	70 (5.3)	0.377	1.46 (1.09–1.95)	0.01	0.44	1.56 (1.05–2.31)	0.03

Abbreviations: CE, cardioembolic stroke; CI, confidence interval; EMS, emergency medical services; ER, emergency room; LVD, large vessel disease; NIHSS, National Institute of Health Stroke Scale; SDA, stroke of determined etiology; SVD, small vessel disease; SUD, stroke of undetermined etiology.

Figure 1. Proportion of aspiration pneumonia between stroke ward vs. medicine ward

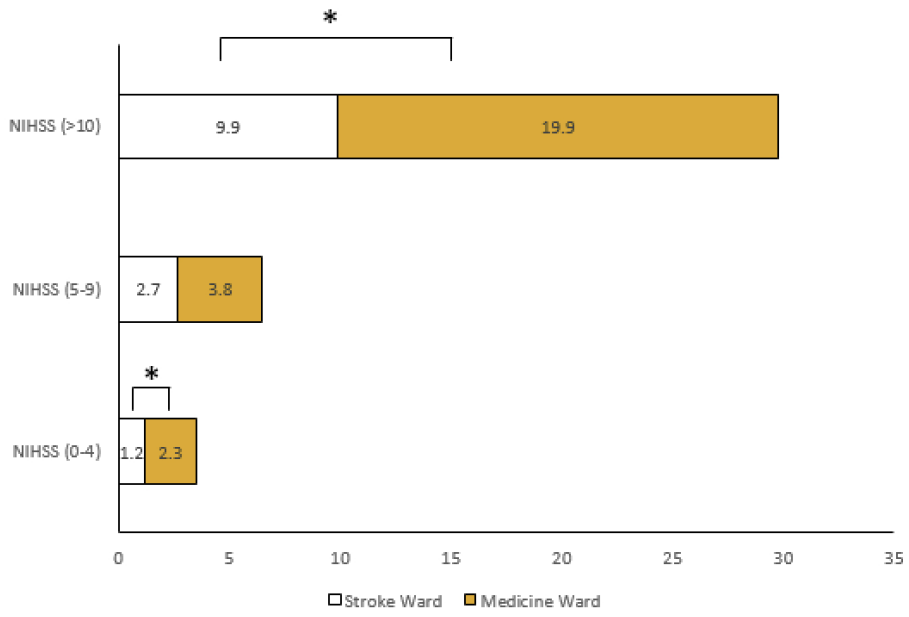
*$p \leq 0.05$

Figure 2a. Proportion of mRS at 90 days for patients with an NIHSS of 5-9

Figure 2b. Proportion of mRS at 90 days for patients with an NIHSS of >10

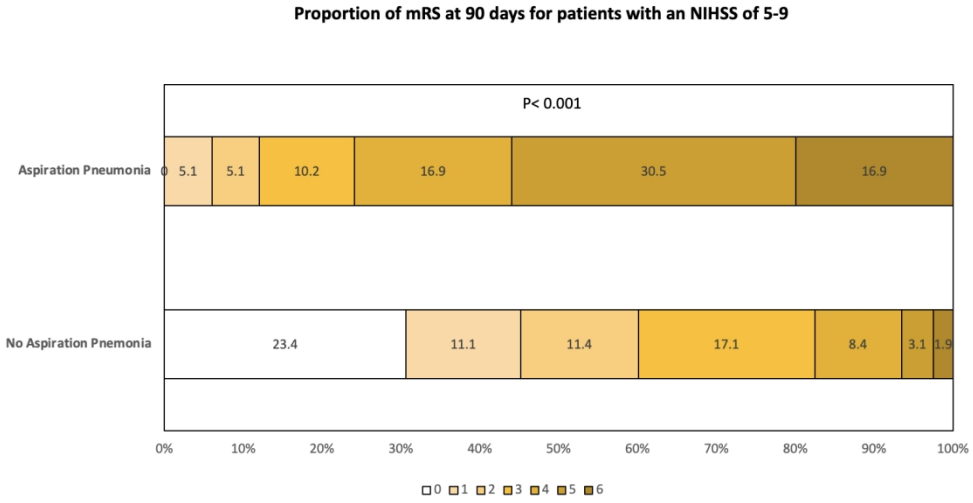
Figure 3. Forest Plot based on the results of multivariate analysis of the factors associated with aspiration pneumonia.

Abbreviations: CI, confidence interval; OR, odds ratio.



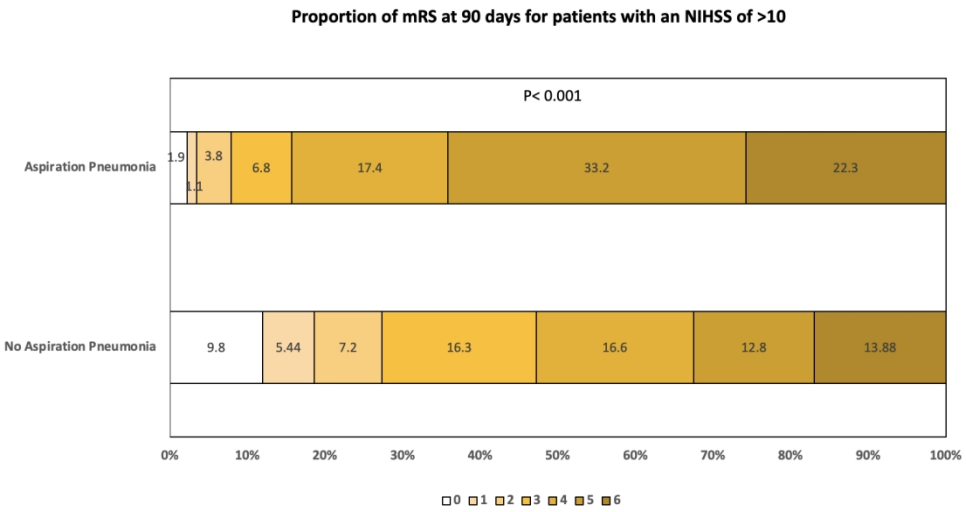
Proportion of aspiration pneumonia between stroke ward vs. medicine ward
*p≤0.05

204x136mm (144 x 144 DPI)



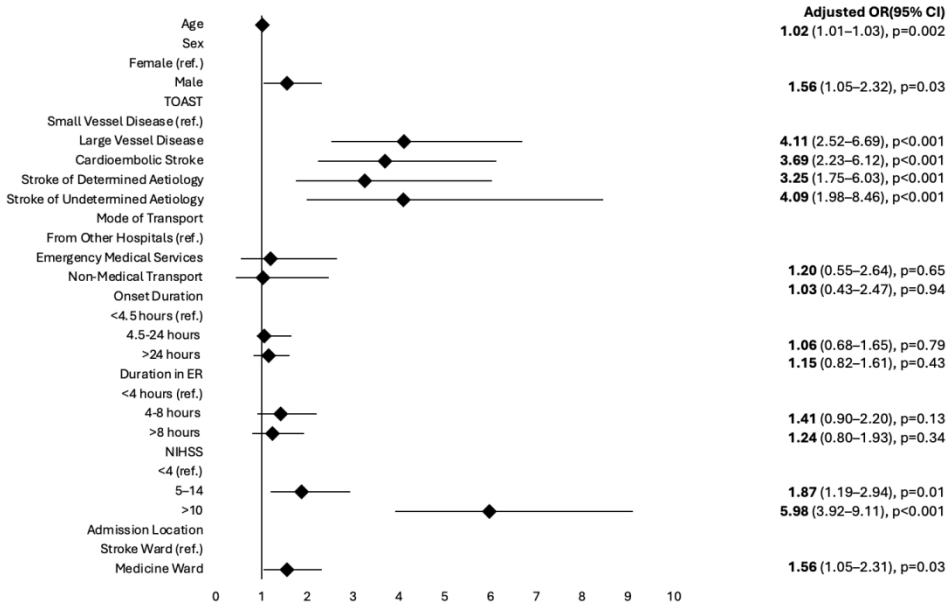
Proportion of mRS at 90 days for patients with an NIHSS of 5-9

294x156mm (144 x 144 DPI)



Proportion of mRS at 90 days for patients with an NIHSS of >10

297x156mm (144 x 144 DPI)



Forest Plot based on the results of multivariate analysis of the factors associated with aspiration pneumonia. Abbreviations: CI, confidence interval; OR, odds ratio.

278x189mm (144 x 144 DPI)

Table S1. Characteristics and outcome of acute ischemic stroke patients with aspiration pneumonia based on their NIHSS admission

Characteristic or Investigation	No Pneumonia (n=8817, 95.9%)	Aspiration Pneumonia (n= 380, 4.1%)	Total (n= 9197)	P-Value
NIHSS Severity				
Mild Stroke (NIHSS 0-4)	5570 (63.2)	56 (14.7)	5626 (61.2)	<0.001
Moderate Stroke (NIHSS 5-9)	1906 (21.6)	59 (15.5)	1965(21.4)	
Severe Stroke (NIHSS 10 or more)	1341 (15.2)	265 (69.7)	1606 (17.5)	
NIHSS (5-9)				
90-Days Mortality	36 (1.9)	10 (16.9)	46 (2.3)	<0.001
MACE at 1 year	72 (3.8)	14 (23.7)	86 (4.4)	<0.001
Admission Location				
Stroke Ward	1281 (67.2)	35 (59.3)	1316 (67.0)	
Medicine Ward	250 (13.1)	10 (16.9)	45 (13.2)	0.31
Duration of ED Stay Category[a]				
<4 hours	249 (13.1)	2 (3.4)	251 (12.8)	
4-8 hours	555 (29.1)	23 (39.0)	578 (29.4)	
>8 hours	750 (39.3)	26 (44.1)	776 (39.5)	0.052
Length of Stay	5.89±10.0	17.1±19.4	6.23±10.5	<0.001
Prognosis – At Discharge				
Good (mRS 0–2)	814 (42.7)	4 (6.8)	818 (41.6)	<0.001
Poor (mRS 3-6)	1092 (57.3)	55 (93.2)	1147 (58.4)	
Prognosis – At 90 Days				
Good (mRS 0–2)	876 (46.0)	6 (10.2)	882 (44.9)	<0.001
Poor (mRS 3-6)	580 (30.4)	44 (74.6)	624 (31.8)	
Mortality at Discharge	9 (0.5)	7 (11.9)	16 (0.8)	<0.001
90 Days Mortality	36 (1.9)	10 (16.9)	46 (2.3)	<0.001
mRS at 90 Days[a]				
0	446 (23.4)	0 (0)	446 (22.7)	
1	212 (11.1)	3 (5.1)	215 (10.4)	
2	218 (11.4)	3 (5.1)	221 (11.2)	
3	325 (17.1)	6 (10.2)	331 (16.8)	<0.001
4	160 (8.4)	10 (16.9)	170 (8.7)	
5	59 (3.1)	18 (30.5)	77 (3.9)	
6	36 (1.9)	10 (16.9)	46 (2.3)	
NIHSS (>10)				
90-Days Mortality	185 (13.8)	59 (22.3)	244 (15.2)	0.003
MACE at 1 year	217 (16.2)	73 (27.5)	290 (18.1)	<0.001
Admission Location				
Stroke Ward	834 (62.2)	92 (34.7)	926 (57.7)	
Medicine Ward	166 (12.4)	40 (15.1)	206 (12.8)	<0.001
Duration of ED Stay Category[a]				
<4 hours	288 (21.5)	41 (15.5)	329 (20.5)	
4-8 hours	446 (33.3)	87 (32.8)	533 (33.2)	0.09
>8 hours	470 (35.0)	103 (38.9)	573 (35.7)	
Length of Stay	9.2±9.8	16.6±14.6	10.4±11.2	<0.001
Prognosis – At Discharge				
Good (mRS 0–2)	247 (18.4)	5 (1.9)	252 (15.7)	<0.001
Poor (mRS 3-6)	1094 (81.6)	260 (98.1)	1354 (84.3)	

Prognosis – At 90 Days				
Good (mRS 0–2)	301 (22.4)	18 (6.8)	319 (19.9)	<0.001
Poor (mRS 3-6)	798 (59.5)	211 (79.6)	1009 (62.8)	
Mortality at Discharge	105 (7.8)	30 (11.3)	135 (8.4)	0.07
90 Days Mortality	185 (13.8)	59 (22.3)	244 (15.2)	<0.001
mRS at 90 Days[a]				
0	132 (9.8)	5 (1.9)	137 (8.5)	<0.001
1	72 (5.4)	3 (1.1)	75 (4.7)	
2	97 (7.2)	10 (3.8)	107 (6.7)	
3	219 (16.3)	18 (6.8)	237 (14.8)	
4	223 (16.6)	46 (17.4)	269 (16.7)	
5	171 (12.8)	88 (33.2)	259 (16.1)	
6	185 (13.8)	59 (22.3)	244 (15.2)	

Abbreviations: ED, emergency department; NIHSS, National Institute of Heath Stroke Scale; MACE, major adverse cardiovascular event; mRS, modified Rankin Scale

	Overall	No Pneumonia	Aspiration Pneumonia	Overall Significance	SVD vs. LVD[1]	SVD vs. CE[1]	SVD vs. SDA[1]	SVD vs. SUD[1]	LVD vs. CE[1]	LVD vs. SDA[1]	LVD vs. SUD[1]	CE vs. SDA[1]	CE vs. SUD[1]	SDA vs. SUD[1]
TOAST				<.001	<.001	<.001	<.001	<.001	1.00	0.25	1.00	0.06	1.00	0.82
Small vessel disease	4249 (46.2)	4213 (99.2)	36 (0.8)	–	–	–	–	–	–		–	–	–	–
Large vessel disease	1913 (20.8)	1772 (92.6)	141 (7.4)	–	–	–	–	–	–		–	–	–	–
Cardioembolic	1881 (20.5)	1744 (92.7)	137 (7.3)	–	–	–	–	–	–		–	–	–	–
Determined etiology	643 (7.0)	612 (95.2)	31 (4.8)	–	–	–	–	–	–		–	–	–	–
Undetermined etiology	511 (5.6)	476 (93.2)	35 (6.8)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**EMS vs. NM[1]**	**EMS vs. OH[1]**	**NM vs. OH[1]**							
Mode of transport				<.001	<.001	1.00	0.07							
EMS	6361 (69.2)	6073 (95.5)	288 (4.5)	–	–	–	–	–	–		–	–	–	–
Non-Medical	2234 (24.3)	2200 (98.5)	34 (1.5)	–	–	–	–	–	–		–	–	–	–
From Other Hospitals	387 (4.2)	372 (96.1)	15 (3.9)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**<4.5 hours vs. 4.5-24 hours[1]**	**<4.5 hours vs. >24 hours[1]**	**4.5-24 hours vs. >24 hours[1]**							
Onset Duration				<.001	0.26	<.001	<.001							
<4.5 hours	2991 (32.5)	2822 (94.3)	169 (5.7)	–	–	–	–	–	–		–	–	–	–
4.5-24 hours	3035 (33.0)	2890 (95.2)	145 (4.8)	–	–	–	–	–	–		–	–	–	–
>24 hours	3171 (34.5)	3105 (97.9)	66 (2.1)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**<4 hours**	**<4 hours vs. >8**	**4-8 hours**							

					vs. 4-8 hours[1]	hours [1]	vs. >8 hours[1]							
Duration in ER				0.11	1.00	1.00	0.11							
<4 hours	859 (15.4)	809 (94.2)	50 (5.8)	–	–	–	–	–	–	–	–	–	–	
4-8 hours	1833 (32.8)	1711 (93.3)	122 (6.7)	–	–	–	–	–	–	–	–	–	–	
>8 hours	2900 (51.9)	2749 (94.8)	151 (5.2)	–	–	–	–	–	–	–	–	–	–	
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**0-4 vs. 5-14[1]**	**0-4 vs. >15[1]**	**5-14 vs. >15[1]**							
NIHSS				<.001	<.001	<.001	<.001							
Mild Stroke (0-4)	5626 (61.2)	5570 (99.0)	56 (1.0)	–	–	–	–	–	–	–	–	–	–	
Moderate Stroke (5-9)	1965 (21.4)	1906 (97.0)	59 (3.0)	–	–	–	–	–	–	–	–	–	–	
Severe Stroke (>10)	1606 (17.5)	1341 (83.5)	265 (16.5)	–	–	–	–	–	–	–	–	–	–	

Table S2. Clinical characteristics among patients with aspiration pneumonia versus those without aspiration pneumonia

[1] Bonferroni corrections have been applied to the p-values reported

Abbreviations: CE, cardioembolic; EMS, emergency medical service; LVD, large vessel disease; NM, non-medical; OH, other hospitals; SDA, stroke of determined etiology; SUD, stroke of undetermined etiology; SVD, small vessel disease.

NIHSS	No Pneumonia	Aspiration Pneumonia	Stroke Ward vs. Medicine Ward
Mild Stroke (0-4)			
Admission Location			
Stroke Ward	1704 (98.8)	20 (1.2)	0.03*
Medicine Ward	832 (97.7)	20 (2.3)	
Moderate Stoke (5-9)			
Admission Location			
Stroke Ward	1281 (97.3)	35 (2.7)	0.31
Medicine Ward	250 (96.2)	10 (3.8)	
Severe Stroke (>10)			
Admission Location			
Stroke Ward	834 (90.1)	92 (9.9)	<.001*
Medicine Ward	166 (80.1)	40 (19.9)	

Abbreviations: NIHSS, National Institute of Health Stroke Scale.
*p≤0.05

Table S3. Comparison of NIHSS score and admission location among patients with aspiration pneumonia versus those without aspiration pneumonia using Fisher's Exact Test

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Increasing stroke severity is associated with increased risk of aspiration pneumonia: The risk is higher in medical ward compared to stroke ward

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Increasing stroke severity is associated with increased risk of aspiration pneumonia: The risk is higher in medical ward compared to stroke ward

Running Title: Risk factors associated with aspiration pneumonia

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Abstract

Objective: Aspiration pneumonia is a common complication post-stroke that increases patient's duration of stay in hospital, mortality, and morbidity. We examined the incidence, clinical characteristics, and outcomes among ischemic stroke-related aspiration pneumonia patients in Qatar.

Methods: A retrospective cohort study was analyzed from January 2014 to April 2024. A total of 9,197 patients were included.

Results: Stroke patients who developed aspiration pneumonia tended to be older and of the male sex. Patients who developed aspiration pneumonia were also more likely to present with a higher NIHSS at admission ($p<0.001$). Patients with large vessel disease, cardioembolic stroke, stroke

of determined etiology and stroke of undetermined etiology were more likely to develop aspiration pneumonia. They also stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia (16.0 vs. 5.3 days). Patients admitted to the medicine ward had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward (aOR of 1.56, 95% CI: 1.05–2.31). Patients with aspiration pneumonia had unfavorable outcome (mRS 3-6) at 90 days (74.6% vs. 30.4% for an NIHSS admission score of 5-9 and 79.6% vs. 59.5% for an NIHSS admission >10). They were also more likely to have higher mortality rates at 90 days (16.9% vs. 1.9% for an NIHSS admission score of 5-9 and 22.3% vs. 13.8% for an NIHSS admission score >10) and major adverse cardiovascular event at 1 year (23.7% vs. 3.8% for an NIHSS admission score of 5-9 and 27.5% vs. 16.2% for NIHSS >10).

Conclusion: Age, sex, admission NIHSS severity, stroke subtypes, and admission location are independent predictors of aspiration pneumonia post-stroke.

Keywords: Aspiration Pneumonia, Stroke, Dysphagia, Stroke-associated pneumonia

Strengths and limitations of this study:

1) This is the first study to specifically examine the incidence and outcomes of patients who develop aspiration pneumonia post-stroke in the Middle East and North Africa (MENA) region.
2) This study is based on a large stroke registry with 9197 acute ischemic stroke patients enrolled over a 10-year period.
3) This is the first study in the MENA region to demonstrate that patients with aspiration pneumonia stayed an average of 10 days longer in the hospital compared to patients without. A higher proportion of patients with aspiration pneumonia had an unfavorable

outcome at 90 days. They were also more likely to have higher mortality rates at 90 days and MACE at 1 year. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward.

4) Our patient sample is comprised of largely Middle Eastern ethnicity, South Asian and Far Eastern, therefore lacks generalizability.

Introduction

Stroke is a major cause of death and disability worldwide. Early in the course of the disease, stroke patients are at risk for medical complications including dysphagia and aspiration pneumonia.[1] Dysphagia is characterized by difficulty swallowing due to weakness/reduced coordination between facial, palatal, and pharyngeal muscles (due to reduced cortical connectivity between neural regions post-stroke).[2] The incidence of dysphagia after stroke ranges from 8.1–80%,[3–7] it is frequently silent and it is highly associated with aspiration pneumonia.[8] Dysphagia causes oral or gastric contents to enter the lung, which suppresses the natural defenses of the respiratory system, increasing the risks for opportunistic infections.[9–11] Several studies

have identified multiple risk factors associated with aspiration pneumonia, such as reduced level of consciousness, incorrect postures, and advanced age.[12–15]

Pneumonia is one of the leading causes of mortality for acute stroke, with a 30-day mortality rate of up to 30%.[16] Aspiration pneumonia also increases the risk of prolonged hospital stay and poor prognosis.[17] Animal and clinical studies have demonstrated that silent aspiration (micro-aspiration due to dysphagia during the night) is the primary cause of aspiration pneumonia.[18] Despite different preventative and therapeutic approaches for managing patients with aspiration pneumonia, its incidence and mortality rates remain high.[19] For example, in a case-control study comprising of 1,112,944 patients, Gupte et al[20] reported that aspiration pneumonia due to cerebrovascular disease accounted for 11.7% of deaths in the United States (62,068 deaths per year from 1999 to 2017), with increasing mortality rates since 2009. In countries such as Egypt and Brazil, the incidence of aspiration pneumonia can be as high as 44% and 76%, respectively.[19,21]

There are very few studies on the incidence, causes, and outcomes of aspiration pneumonia from the Middle East and North Africa (MENA) region.[22] This study aimed to assess the clinical characteristics and treatment outcomes among stroke-related aspiration pneumonia patients in Qatar.

Methods

Data from patients admitted with a stroke to Hamad General Hospital (HGH), Doha, Qatar from January 2014 through April 2024 were analyzed from a hospital based prospective stroke registry. HGH is a Joint Commission International (JCI) accredited 600-bed hospital, with 200 beds reserved for medical patients. It is the only tertiary care medical facility in Qatar where the stroke service is located, 95% of all strokes in Qatar requiring admission to hospital are admitted

to HGH. The program provides 24-hour thrombolysis and thrombectomy services for acute stroke management. Patients are evaluated by the stroke team in the emergency department (ED), and urgent decisions about treatment are made. Hyperacute stroke patients are admitted to a dedicated 12-bed stroke unit or Medical ICU as necessary. Non-urgent stroke patients are admitted under the medical team, with neurology consultation in the ED. HGH has the required laboratory, neuroradiological, and neurosurgical infrastructure to manage stroke patients effectively. The stroke team is readily available to make immediate treatment decisions for acute stroke cases.

Patient characteristics

Patient characteristics including age, sex, ethnicity, medical comorbidities and prior medication were collected in the HGH Stroke Registry. National Institute of Health Stroke Scale (NIHSS) score, neuroimaging data, and post-discharge disposition were entered into the registry as well. Ischemic stroke was diagnosed according to the WHO criteria[23] and stroke subtypes were defined by the TOAST criteria.[24] The modified Rankin scale (mRS) measurements were done at discharge and at 90 days following onset of symptoms. The patients were classified as favourable (mRS ≤ 0-2) or unfavourable (mRS 3-6) outcome. We used the dichotomized mRS scale to evaluate recovery at 90 days.[25]

Diabetes was diagnosed according to the American diabetes Association (ADA) and WHO recommendation[26] and included patients with a previous diagnosis of diabetes, on medication for diabetes or an HbA1c of more than 6.5%, and the diagnosis of pre-diabetes was based on an HbA1c of 5.7-6.4% as per the 2015 ADA clinical practice recommendations. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mm Hg or a diastolic pressure ≥ 90 mm Hg, or on current treatment with antihypertensive drugs. Dyslipidemia was defined as

low-density lipoprotein-cholesterol level ≥ 3.62 mmol/L, high-density lipoprotein cholesterol level ≤ 1.03 mmol/L, triglycerides ≥ 1.69 mmol/L, or current treatment with a cholesterol-lowering drug.

Data Collection and inclusion/exclusion criteria

Upon identification and confirmation of diagnosis using the International Classification of Disease, 10th edition, definitions (H34.1, 163.x, 164.x, 161.x, 160.x, G45.x), patients' data were collected by trained stroke clinical nurse specialists. For our study, we only included patients diagnosed with acute ischemic stroke and excluded patients diagnosed with intracerebral hemorrhage, transient ischemic attacks, stroke mimics, and cerebral venous thrombosis. As for the diagnosis of post-stroke aspiration pneumonia, clinical diagnosis was made via assessing symptoms like fever, cough, dyspnea, and purulent sputum. Radiological imagings (CT and chest X-rays) were also performed to identify lung consolidation or infiltrates indicative of pneumonia. Microbiological testing including sputum culture, blood cultures, and bronchoalveolar lavage were also performed.

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Data Analysis and statistics

Descriptive results for all continuous variables were reported as mean±standard deviation (SD) for normally distributed data or median with range for data with non-normal distributions. The distribution of continuous variables was assessed before using statistical tools. Mean level comparisons between patients with aspiration pneumonia versus without aspiration pneumonia were assessed using ANOVA test and multiple comparisons were performed using Bonferroni

correction. If an assumption of an ANOVA test was failed, then an alternative non-parametric Kruskal Wallis test was performed. Pearson Chi-Square test and Fisher's Exact test were performed whenever appropriate to compare the proportion of all categorical variables between the groups. Multiple logistic regression analysis was performed to assess for risk factors associated with aspiration pneumonia after selecting important and significant variables at univariate analysis. Odds ratio (OR) and the 95% confidence interval for the OR were reported. A p-value of ≤0.05 (two-tailed) was considered significant. SPSS statistical package 29.0.1.0 was used for the analysis.

Results

Patient Characteristics

A total of 9197 patients were enrolled: 380 developed aspiration pneumonia (4.1%) during hospitalization while 8817 (95.9%) of the patients did not have pneumonia. The mean age of patients was 55.3±13.4 years, with patients with aspiration pneumonia being significantly older than healthy controls (p<0.001). 80% were male, 57% had diabetes mellitus, 72% had hypertension, 46% had dyslipidemia, and 24% were active smokers. The high proportion of men is reflective of the very high male expatriate population as previously reported.[27] A summary of patients' baseline characteristics is outlined in Table 1.

Since 95.9% of our patients did not have aspiration pneumonia, we performed sub-analyses on clinical outcomes based on patients' admission NIHSS scores. Sub-analyses were performed for patients with an NIHSS of 5-9 (moderate stroke) and NIHSS >10 (severe stroke) (Table 2).

Mode of transport

Mode of transport was significantly associated with aspiration pneumonia risks ($p<0.001$). However, this was only significant for emergency medical services (EMS) versus non-medical services ($p<0.001$), with a higher proportion of patients developing aspiration pneumonia via EMS (4.5%) versus non-medical services (1.5%). Patients transported with EMS had a significantly higher NIHSS at admission (5.9±6.1 vs. 3.3±3.7, $p<0.001$). The total sample size for EMS was 6361 versus 2234 for non-medical services.

Onset Duration

Duration of stroke symptoms from the time of onset to evaluation was significantly associated with aspiration pneumonia ($p<0.001$). This was only significant for <4.5 hours vs. >24 hours ($p<0.001$) and 4.5-24 hours vs. >24 hours ($p<0.001$). A stroke onset to emergency evaluation of <4.5 hours had the highest proportion of aspiration pneumonia (5.7%) versus 4.8% for onset duration of 4.5-24 hours and 2.1% for >24 hours (Table S1).

Duration of stay in Emergency Department

Duration of stay in the ED was not significantly associated with aspiration pneumonia ($p=0.11$) (Table S1). Furthermore, when we analyzed duration of stay in the ED based on NIHSS scores (5-9 and >10), duration of stay in the ED remained non-significant ($p=0.052$ and 0.09), respectively (Table 2).

Stroke Diagnosis

Stroke diagnosis is shown in Table S1. Overall, type of stroke was significantly associated with aspiration pneumonia ($p<0.001$). Further analyses revealed that the risk of developing aspiration pneumonia was not significantly different between large vessel disease versus cardioembolic stroke ($p=1.00$), large vessel disease versus stroke of undetermined aetiology ($p=1.00$), cardioembolic stroke versus stroke of determined aetiology ($p=0.06$),

cardioembolic stroke versus stroke of undetermined etiology (p=1.00), and stroke of determined aetiology versus stroke of undetermined aetiology (p=0.82).

Patients with small vessel disease had the lowest proportions of aspiration pneumonia (0.8%) compared to large vessel disease (7.4%), cardioembolic stroke (7.3%), stroke of determined etiology (4.8%), and stroke of undetermined etiology (6.8%), p<0.001 (Table 3).

Admission NIHSS Score

Admission NIHSS score was significantly associated with aspiration pneumonia (p<0.001). Fisher's exact test revealed that there was a significant association between aspiration pneumonia for patients with an NIHSS score of 0-4 (p=0.03), and NIHSS score of >10, p<0.001 (Table S2). Patients with an NIHSS > 10 had the highest proportion of aspiration pneumonia (16.5%). Moreover, patients with an NIHSS >10 and concomitant aspiration pneumonia had higher rates of mortality at 90 days (22.3%) when compared to patients with an NIHSS score of 5-9 and concomitant aspiration pneumonia (16.9%) (p<0.001) (Table 2). In patients with aspiration pneumonia, patients with an NIHSS >10 also had higher rates of major adverse cardiovascular events (MACE) at 1 year compared to patients with an NIHSS of 5-9 (27.5% vs. 23.7%, p<0.001).

Length of stay

Patients with aspiration pneumonia stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia (16.0 days vs. 5.3 days, p=0.00). When analyzed via admission NIHSS severity, patients with aspiration pneumonia stayed significantly longer in the hospital compared to those without aspiration pneumonia (17.1 days vs. 5.9 days, p<0.001 for NIHSS of 5-9, and 16.6 days vs. 9.2 days, p<0.001 for NIHSS > 10).

Admission Location

Overall, 3966 (75.1%) patients were admitted to the stroke ward and 1318 (24.9%) patients were admitted to the medical ward. A higher proportion of patients admitted to the medicine ward developed aspiration pneumonia in contrast to patients admitted to the stroke ward (5.3% vs 3.7%, p=0.01) (Table 3). 2.3% of patients with an NIHSS of 0-4 and admitted to the medicine ward developed aspiration pneumonia compared to 1.2% of patients with an NIHSS of 0-4 and admitted to the stroke ward (p=0.03) (Table S2). Similarly, 19.9% of patients with an NIHSS >10 and admitted to the stroke ward developed aspiration pneumonia compared to 9.9% of patients with an NIHSS >10 and admitted to the stroke ward (p<0.001) (Figure 1).

Modified Rankin Scale at 90 days

A higher proportion of patients with aspiration pneumonia had an unfavorable outcome (mRS 3-6) at 90 days compared to patients without aspiration pneumonia (74.6% vs. 30.4% for NIHSS of 5-9), p<0.001 (Table 2). Similar observations were seen for NIHSS > 10 (79.6% vs. 59.5%, p<0.001). Figure 2 and 3 illustrates the proportion of mRS at 90 days based on NIHSS admission scores.

Mortality at 90 days

For patients with an NIHSS score of 5-9, a higher proportion of patients with aspiration pneumonia died at 90 days (16.9%) compared to patients without aspiration pneumonia (1.9%), p<0.001. Similar observations were seen for NIHSS > 10 (22.3% vs. 13.8%, p=0.003).

Multivariate analysis for risk factors associated with aspiration pneumonia

Table 3 describes a multiple binary logistic regression model to identify significant independent factors associated with the development of aspiration pneumonia after selecting important and significant variables at bivariate analysis. Males were more likely than females to have aspiration pneumonia risks [aOR 1.56, 95% CI: 1.05–2.32, p=0.03]. Age was significantly

associated with aspiration pneumonia [aOR 1.02, 95% CI: 1.01–1.03, p=0.002], with patients with aspiration pneumonia being significantly older (p<0.001). Large vessel disease was significantly associated with aspiration pneumonia [aOR 4.11, 95% CI: 2.52–6.69, p<0.001]. Similar observations were seen for cardioembolic stroke (p<0.001), stroke of determined aetiology (p<0.001), and stroke of undetermined aetiology (p<0.001), see Table 3. Patients with an NIHSS score of 5–9 and >10 also had high odds of developing aspiration pneumonia (aOR of 1.87 and 5.98, respectively). Patients admitted to the medicine ward also had 1.56 times the odds of developing aspiration pneumonia compared to the stroke ward (95% CI: 1.05–2.31, p=0.03). A forest plot of the multivariate analysis can be seen in Figure 4.

Discussion

To the best of our knowledge, this is the first study to specifically examine the incidence and outcomes of patients who develop aspiration pneumonia post-stroke in the MENA region. In our cohort, 4.1% of our patients developed aspiration pneumonia post stroke. This low number may be deceiving as the majority of patients admitted had mild symptoms [5626 (61.2%) of patients had an NIHSS of <4]. The odds of aspiration pneumonia was 1.87 in patients with admission NIHSS of 5-9 (n=1965), increasing to 5.98 in patients with NIHSS of 10 or more (n=1606). Patients with aspiration pneumonia also stayed an average of 10 days longer in the hospital compared to patients without. A higher proportion of patients with aspiration pneumonia had an unfavorable outcome at 90 days. They were also more likely to have higher mortality rates at 90 days and MACE at 1 year. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward.

High NIHSS has also been shown to be correlated with increased rates of dysphagia and aspiration pneumonia due to stroke severity.[28] Patients with aspiration pneumonia in the Qatar dataset had comparatively higher NIHSS at presentation as compared to patients without pneumonia (14.7 v 5.1, p<0.001). Garavelli et al[29] demonstrated that an NIHSS cut-off of ≥ 10.5 was associated with higher rates of dysphagia (p=0.014) and aspiration pneumonia (p=0.006). Similarly, Jeyaseelan et al[28] demonstrated NIHSS > 9 as being moderately predictive of clinically relevant dysphagia, with dysphagia rates increasing with greater NIHSS scores (p<0.001). Okubo et al[30] also showed an NIHSS cut-off of 12 sensitive for dysphagia detection, with 14 (87.5%) of the 16 patients with dysphagia having NIHSS scores ≥ 12 and 2 (12.5%) patients having scores of 10 and 11. NIHSS >12 also has an independent association with persistent dysphagia at hospital discharge in acute ischemic stroke patients with dysphagia at stroke onset, with one of its sub-components–dysarthria–emerging as a significant independent predictor of prolonged dysphagia.[31] In our current study, the odds of developing aspiration pneumonia increased as NIHSS score increased.

Several studies have reported the adverse outcomes of aspiration pneumonia on stroke patients. In a study comprised of 610,668 stroke patients, Barlas et al[32] reported that patients with stroke-associated pneumonia (SAP) had significantly higher odds of in-hospital mortality (OR of 2.90, 95% CI: 2.83–2.96), and longer length of stay (OR 13.11, 95% CI: 12.83–13.40). While they analyzed data from both ischemic and hemorrhagic strokes, patients with ischemic stroke were more likely to die in hospital and experience long length of stay (LOS).[32] Teh et al[33] had similar observations in his cohort of 9238 patients from the UK. SAP was found in 1083 (11.7%) patients, out of which 60.8% were aspiration pneumonia.[33] After controlling for confounders, SAP was found to be associated with increased mortality up to 1 year (inpatient, 90-day, 1 year),

prolonged LOS, and poor functional outcome on discharge.[33] In our current study, patients who developed aspiration pneumonia with an admission NIHSS of 5-9 had a 16.9% mortality rate at 90 days in contrast to 1.9% for patients who did not develop aspiration pneumonia. Similarly, patients who developed aspiration pneumonia with an admission NIHSS >10 had higher mortality rates at 90 days (22.3% vs. 13.8%, p=0.003).

Dysphagia is a common feature of severe stroke and an indicator of poor prognosis. It is implicated in the development of aspiration pneumonia, and it results in longer LOS and increased mortality. In stroke patients with dysphagia, early nutritional support is vital, and the decision to initiate that depends on the outcome of the swallow study.[34] Multiple national and international guidelines recommend that people with acute stroke have their swallowing screened by a trained healthcare professional by utilizing a validated screening tool and that the patients remain nothing per oral (NPO) until a swallow screen is performed.[17] Bedside swallow screening tools include the functional bedside aspiration screen (FBAS), GLOBE-3S (the Sapienza GLObal Bedside Evaluation of Swallowing after Stroke), water swallowing test, volume-viscosity swallow test, and the Gugging swallow screen. However, despite these recommendations, in our study 34.6% of patients did not undergo swallow screen prior to PO intake in the ED and 32.7% patient did not have SLP assessment within 24 hours of admission. Likely explanations for these findings include ED nursing inadvertently giving patients PO medications, or SLPs not being available over the weekend, hence leading to an inability to perform assessment within 24 hours of presentation.

Similar to previous reports, we observed a significantly higher risk of aspiration pneumonia in the patients admitted to the medical ward compared to the stroke ward (5.3% vs. 3.7%, p=0.01). Admission to the stroke ward, by prevention of medical complications, results in

reduced length of stay, decreased incidence of complications, improved prognosis at discharge and at 90 days (higher % of mRS scores of 0-2).[35,36] Similarly, in our current study, fewer patients developed aspiration pneumonia if they were admitted to the stroke ward versus medicine ward (3.7% vs. 5.3%, p=0.01). Multivariable logistic regression identified admission location as an independent predictor of aspiration pneumonia, with patients admitted to the medicine ward having higher risks of developing aspiration pneumonia (aOR 1.56, 95% CI: 1.05–2.31). In our study population, we also observed that 19.9% patients with an NIHSS >10 and admitted to the medicine ward developed aspiration pneumonia in contrast to patients with an NIHSS > 10 and admitted to the stroke ward (9.9%; p<0.001). Thus, healthcare providers should be judicious of the placement of their stroke patients if they would like to reduce the incidence of aspiration pneumonia.

We also observed that patients with small vessel disease or subcortical stroke were less likely to develop aspiration pneumonia in contrast to patients with cardioembolic stroke, large vessel disease, stroke of undetermined etiology, and stroke of determined etiology. This is consistent with Alberts et al's study, who reported a low occurrence of aspiration in small vessel infarcts compared to those with both large- and small vessel infarcts (p=0.002).[37] Similarly, Jitpratoom et al[38] observed that 40.7% of their patients with cardioembolic stroke developed aspiration pneumonia in contrast to 11.1% for small vessel occlusion. Multivariable logistic regression analysis revealed that type of stroke was an independent predictor of aspiration pneumonia, specifically for large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke of undetermined etiology. A potential explanation for this is that patients with small vessel disease have milder stroke symptoms and fewer neurological deficits in contrast to the other stroke subtypes,[39] therefore they might have more preserve/control of their

facial, palatal, and pharyngal muscles, reducing their risks of developing dysphagia and aspiration pneumonia. However, additional studies are needed to unravel this relationship.

There are several limitations with our study. Our patient sample is comprised of largely Middle Eastern ethnicity (Qatari, Arabs), South Asian and Far Eastern (Asians) (97.7% vs. 2.3% for Caucasians), therefore lacks generalizability. We also had missing data for the mRS score at 90 days for 1846 patients (out of 9197). Since Qatar's population is comprised mainly of expatriate workers, it is not possible to collect data for patients who may have moved back to their home country once their work contract ended.

Conclusion

This large study in prospectively collected patients with acute stroke identified multiple factors associated with an increased risk of aspiration pneumonia. Patients who developed aspiration pneumonia were older, presented with more severe neurological symptoms, and stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia. Patients with large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke of undetermined etiology were more likely to develop aspiration pneumonia. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward. Our study showed that aspiration pneumonia was associated with an unfavorable prognosis (mRS 3-6) and increased mortality at 90 days in patients with moderate and severe symptoms.

Data Availability Statement

The Qatar Stroke Registry dataset will be available on reasonable request to the corresponding author.

Ethics Statement

The studies involving humans were approved by the Institutional Review Board of the Medical Research Centre at Hamad Medical Corporation (MRC-01-18-102). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent from the patients/participants or patients/participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Declaration of conflicting interests

The author(s) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors Contribution

KHT: Writing—original draft, Formal analysis.

NA: Formal analysis, Methodology, Supervision, Reviewing draft.

AA: Writing, Reviewing draft

SJ: Data curation and Validation.

RU: Data curation and Validation.

DM: Data curation and Validation.

BB: Data curation, Methodology.

AS: Conceptualization, reviewing, editing & guarantor.

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Table 1. Characteristics and outcome of acute ischemic stroke patients with aspiration pneumonia

Characteristic	No Pneumonia (n=8817, 95.9%)	Aspiration Pneumonia (n= 380, 4.1%)	Total (n= 9197)	P-Value
Age	55.1±13.3	59.0±15.6	55.3±13.4	<0.001
Male Gender	7041 (79.9)	303 (79.7)	7344 (79.9)	0.95
Diabetes	5038 (57.1)	229 (60.3)	5267 (57.3)	0.22
Hypertension	6373 (72.3)	246 (64.7)	6619 (72.0)	<0.001
Dyslipidemia	4069 (46.1)	136 (35.8)	4205 (45.7)	<0.001
Prior Stroke or TIA	1156 (13.1)	63 (16.6)	1219 (13.3)	0.05
Coronary Artery Disease	1053 (11.9)	70 (18.4)	1123 (12.2)	<0.001
Atrial Fibrillation	664 (7.5)	73 (19.2)	737 (8.0)	<0.001
Active Smoking	2143 (24.3)	52 (13.7)	2195 (23.9)	<0.001
Ethnicity[a]				
Arab	2962 (33.6)	160 (42.1)	3122 (33.9)	<0.001
South Asian	4518 (51.2)	168 (44.2)	4686 (51.0)	
Far Eastern	753 (8.5)	17 (4.5)	770 (8.4)	
African	382 (4.3)	26 (6.8)	408 (4.4)	
Caucasian	202 (2.3)	9 (2.4)	211 (2.3)	
Mode of Arrival[a]				
EMS	6073 (68.9)	288 (75.8)	6361 (69.2)	<0.001
Non-Medical	2200 (25.0)	34 (8.9)	2234 (24.3)	
From Other Hospitals	372 (4.2)	15 (3.9)	387 (4.2)	
mRS prior to acute stroke[a]				
0	7595 (86.1)	282 (74.2)	7877 (85.6)	<0.001
1	132 (1.5)	9 (2.4)	141 (1.5)	
2	312 (3.5)	12 (3.2)	324 (3.5)	
3	430 (4.9)	33 (8.7)	463 (5.0)	
4	196 (2.2)	23 (6.1)	219 (2.4)	
5	151 (1.7)	21 (5.5)	172 (1.9)	
NIHSS on admission	5.1 ± 5.54	14.65 ± 8.05	5.5 ± 6.0	<0.001
Onset Duration[a]				
Less than 4.5 Hours	2822 (32.0)	169 (44.5)	2991 (32.5)	<0.001
Between 4.5 till 24 hours	2890 (32.8)	145 (38.2)	3035 (33.0)	
More than 24 hours	3105 (35.2)	66 (17.4)	3171 (34.5)	
Thrombolysis Given	962 (10.9)	73 (19.2)	1035 (11.3)	<0.001
Mechanical Thrombectomy done	350 (4.0)	43 (11.3)	393 (4.3)	<0.001
BMI on admission	28.15±43.9	27.54±5.3	28.13±43.0	0.8
RBS on admission	9.6±7.5	10.4±5.05	9.6±7.4	0.04
HbA1c	7.51±2.42	7.6±2.4	7.51±2.41	0.64
Serum Cholesterol	4.84±1.52	4.6±1.75	4.83±1.53	0.01
Serum Triglyceride	1.8±1.76	1.45±0.83	1.77±1.73	0.002
Serum HDL	1.1±3.24	1.43±6.34	1.10±3.38	0.12
Serum LDL	3.1±1.8	2.82±1.25	3.1±1.8	0.03
Systolic Blood Pressure	157.8±44.23	149.44±29.15	157.42±43.73	0.00
Diastolic Blood Pressure	91.1±22.4	86.4±19.4	90.9±22.3	0.00
Length of Stay	5.25±8.55	16.0±14.93	5.70±9.2	0.00

Disposition[a]				
Discharged Home	**5726 (64.9)**	**44 (11.6)**	**5770 (62.7)**	**<0.001**
Rehabilitation	**2079 (23.6)**	**89 (23.4)**	**2168 (23.6)**	
Long term care	**151 (1.7)**	**97 (25.5)**	**248 (2.7)**	
Transfer to other facility	**732 (8.3)**	**109 (28.7)**	**841 (9.1)**	
Died as in-patient	**129 (1.5)**	**41 (10.8)**	**170 (1.8)**	
TOAST Classification[a]				
Small Vessel Disease	**4213 (47.8)**	**36 (9.5)**	**4249 (46.2)**	**<0.001**
Large Vessel Disease	**1772 (20.1)**	**141 (37.1)**	**1913 (20.8)**	
Cardio-Embolic	**1744 (19.8)**	**137 (36.1)**	**1881 (20.5)**	
Stroke of Determined Etiology	**612 (6.9)**	**31 (8.2)**	**643 (7.0)**	
Stroke of Undetermined Etiology	**476 (5.4)**	**35 (9.2)**	**511 (5.6)**	
Swallow Screen done before oral intake	**5820 (66.0)**	**197 (51.8)**	**6017 (65.4)**	**<0.001**
Speech therapy assessment done	**6024 (68.3)**	**161 (42.4)**	**6185 (67.3)**	**<0.001**
Speech Therapy assessment duration (hours)	**31.7±309.7**	**77.9±694.32**	**32.85±325.45**	**0.07**
Antibiotics given	**626 (7.1)**	**361 (95.0)**	**987 (10.7)**	**<0.001**

Abbreviations: BMI, Body Mass Index; ED, emergency department; HDL, High density lipoprotein; ICU, intensive care unit; LDL, Low density lipoprotein; MACE, major adverse cardiac event; mRS, Modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; RBS, Random blood sugar

[a]p-value reported based on Pearson-Chi Square Test

Values are reported as mean ± standard deviation and n(%)

Table 2. Characteristics and outcome of acute ischemic stroke patients with aspiration pneumonia based on their NIHSS admission

Characteristic or Investigation	No Pneumonia (n=8817, 95.9%)	Aspiration Pneumonia (n= 380, 4.1%)	Total (n= 9197)	P-Value
NIHSS Severity				
Mild Stroke (NIHSS 0-4)	5570 (63.2)	56 (14.7)	5626 (61.2)	<0.001
Moderate Stroke (NIHSS 5-9)	1906 (21.6)	59 (15.5)	1965(21.4)	
Severe Stroke (NIHSS 10 or more)	1341 (15.2)	265 (69.7)	1606 (17.5)	
NIHSS (5-9)				
90-Days Mortality	36 (1.9)	10 (16.9)	46 (2.3)	<0.001
MACE at 1 year	72 (3.8)	14 (23.7)	86 (4.4)	<0.001
Admission Location				
Stroke Ward	1281 (67.2)	35 (59.3)	1316 (67.0)	
Medicine Ward	250 (13.1)	10 (16.9)	45 (13.2)	0.31
Duration of ED Stay Category[a]				
<4 hours	249 (13.1)	2 (3.4)	251 (12.8)	
4-8 hours	555 (29.1)	23 (39.0)	578 (29.4)	
>8 hours	750 (39.3)	26 (44.1)	776 (39.5)	0.052
Length of Stay	5.89±10.0	17.1±19.4	6.23±10.5	<0.001
Prognosis – At Discharge				
Good (mRS 0–2)	814 (42.7)	4 (6.8)	818 (41.6)	<0.001
Poor (mRS 3-6)	1092 (57.3)	55 (93.2)	1147 (58.4)	
Prognosis – At 90 Days				
Good (mRS 0–2)	876 (46.0)	6 (10.2)	882 (44.9)	<0.001
Poor (mRS 3-6)	580 (30.4)	44 (74.6)	624 (31.8)	
Mortality at Discharge	9 (0.5)	7 (11.9)	16 (0.8)	<0.001
90 Days Mortality	36 (1.9)	10 (16.9)	46 (2.3)	<0.001
mRS at 90 Days[a]				
0	446 (23.4)	0 (0)	446 (22.7)	
1	212 (11.1)	3 (5.1)	215 (10.4)	
2	218 (11.4)	3 (5.1)	221 (11.2)	
3	325 (17.1)	6 (10.2)	331 (16.8)	<0.001
4	160 (8.4)	10 (16.9)	170 (8.7)	
5	59 (3.1)	18 (30.5)	77 (3.9)	
6	36 (1.9)	10 (16.9)	46 (2.3)	
NIHSS (>10)				
90-Days Mortality	185 (13.8)	59 (22.3)	244 (15.2)	0.003
MACE at 1 year	217 (16.2)	73 (27.5)	290 (18.1)	<0.001
Admission Location				
Stroke Ward	834 (62.2)	92 (34.7)	926 (57.7)	
Medicine Ward	166 (12.4)	40 (15.1)	206 (12.8)	<0.001
Duration of ED Stay Category[a]				
<4 hours	288 (21.5)	41 (15.5)	329 (20.5)	
4-8 hours	446 (33.3)	87 (32.8)	533 (33.2)	0.09
>8 hours	470 (35.0)	103 (38.9)	573 (35.7)	
Length of Stay	9.2±9.8	16.6±14.6	10.4±11.2	<0.001
Prognosis – At Discharge				
Good (mRS 0–2)	247 (18.4)	5 (1.9)	252 (15.7)	<0.001
Poor (mRS 3-6)	1094 (81.6)	260 (98.1)	1354 (84.3)	

Prognosis – At 90 Days				
Good (mRS 0–2)	**301 (22.4)**	**18 (6.8)**	**319 (19.9)**	**<0.001**
Poor (mRS 3-6)	**798 (59.5)**	**211 (79.6)**	**1009 (62.8)**	
Mortality at Discharge	**105 (7.8)**	**30 (11.3)**	**135 (8.4)**	**0.07**
90 Days Mortality	**185 (13.8)**	**59 (22.3)**	**244 (15.2)**	**<0.001**
mRS at 90 Days[a]				
0	**132 (9.8)**	**5 (1.9)**	**137 (8.5)**	**<0.001**
1	**72 (5.4)**	**3 (1.1)**	**75 (4.7)**	
2	**97 (7.2)**	**10 (3.8)**	**107 (6.7)**	
3	**219 (16.3)**	**18 (6.8)**	**237 (14.8)**	
4	**223 (16.6)**	**46 (17.4)**	**269 (16.7)**	
5	**171 (12.8)**	**88 (33.2)**	**259 (16.1)**	
6	**185 (13.8)**	**59 (22.3)**	**244 (15.2)**	

Abbreviations: ED, emergency department; NIHSS, National Institute of Heath Stroke Scale; MACE, major adverse cardiovascular event; mRS, modified Rankin Scale.

Table 3. Bivariate and Multivariate logistic regression analysis to identify the risk factors associated with aspiration pneumonia.

Determinants		*Bivariate logistic regression analysis*				*Multivariate logistic regression analysis*		
	No Pneumonia	**Aspiration Pneumonia**	**Standardized Beta**	**Odds ratio (95% CI)**	**p-value**	**Standardized Beta**	**Odds ratio (95% CI)**	**p-value**
Age	55.3 ± 13.4	59.0 ± 15.6	0.021	1.02 (1.01–1.03)	<.001	0.01	1.02 (1.01–1.03)	0.002
Sex								
Female	1776 (95.8)	77 (4.2)	-	1	-		1	-
Male	7041 (95.9)	303 (4.1)	-0.007	0.99 (0.77–1.28)	0.95	0.446	1.56 (1.05–2.32)	0.03
TOAST								
SVD	4213 (99.2)	36 (0.8)	-	1	-		1	-
LVD	1772 (92.6)	141 (7.4)	2.231	9.31 (6.43–13.48)	<.001	1.43	4.11 (2.52–6.69)	<.001
CE	1744 (92.7)	137 (7.3)	2.218	9.19 (6.34–13.33)	<.001	1.396	3.69 (2.23–6.12)	<.001
SDA	612 (95.2)	31 (4.8)	1.780	5.93 (3.64–9.65)	<.001	1.179	3.25 (1.75–6.03)	<.001
SUD	476 (93.2)	35 (6.8)	2.152	8.61 (5.35–13.83)	<.001	1.428	4.09 (1.98–8.46)	<.001
Mode of transport								
From Other Hospitals	372 (96.1)	15 (3.9)	-	1	-		1	-
EMS	6073 (95.5)	288 (4.5)	0.162	1.18 (0.69–2.00)	0.55	0.184	1.20 (0.55–2.64)	0.65
Non-Medical	2200 (98.5)	34 (1.5)	-0.959	0.38 (0.21–0.71)	0.00	0.032	1.03 (0.43–2.47)	0.94
Onset Duration								

<4.5 hours	2822 (94.3)	169 (5.7)	-	1	-		1	-
4.5-24 hours	3890 (96.4)	145 (3.6)	-0.177	0.84 (0.67–1.05)	<.001	0.116	1.06 (0.68–1.65)	0.79
>24 hours	3105 (97.9)	66 (2.1)	-1.036	0.36 (0.27–0.47)	<.001	0.061	1.15 (0.82–1.61)	0.43
Duration in ER								
<4 hours	809 (94.2)	50 (5.8)	-	1	-		1	-
4-8 hours	1711 (93.3)	122 (6.7)	0.143	1.15 (0.82–1.62)	0.41	0.311	1.41 (0.90–2.20)	0.13
>8 hours	2749 (94.8)	151 (5.2)	-0.118	0.89 (0.64–1.24)	0.48	0.211	1.24 (0.80–1.93)	0.34
NIHSS								
Mild Stroke (0-4)	5570 (99.0)	56 (1.0)	-	1	-		1	-
Moderate Stroke (5-14)	1906 (97.0)	59 (3.0)	1.125	3.08 (2.13–4.45)	<.001	0.625	1.87 (1.19–2.94)	0.01
Severe Stroke (>10)	1341 (83.5)	265 (16.5)	2.978	19.66 (14.64–26.38)	<.001	1.788	5.98 (3.92–9.11)	<.001
Admission Location								
Stroke Ward	3819 (96.3)	147 (3.7)	-	1	-		1	-
Medicine Ward	1248 (94.7)	70 (5.3)	0.377	1.46 (1.09–1.95)	0.01	0.422	1.56 (1.05–2.31)	0.03

Abbreviations: CE, cardioembolic stroke; CI, confidence interval; EMS, emergency medical services; ER, emergency room; LVD, large vessel disease; NIHSS, National Institute of Health Stroke Scale; SDA, stroke of determined etiology; SVD, small vessel disease; SUD, stroke of undetermined etiology.

Figure 1. Proportion of aspiration pneumonia between stroke ward vs. medicine ward

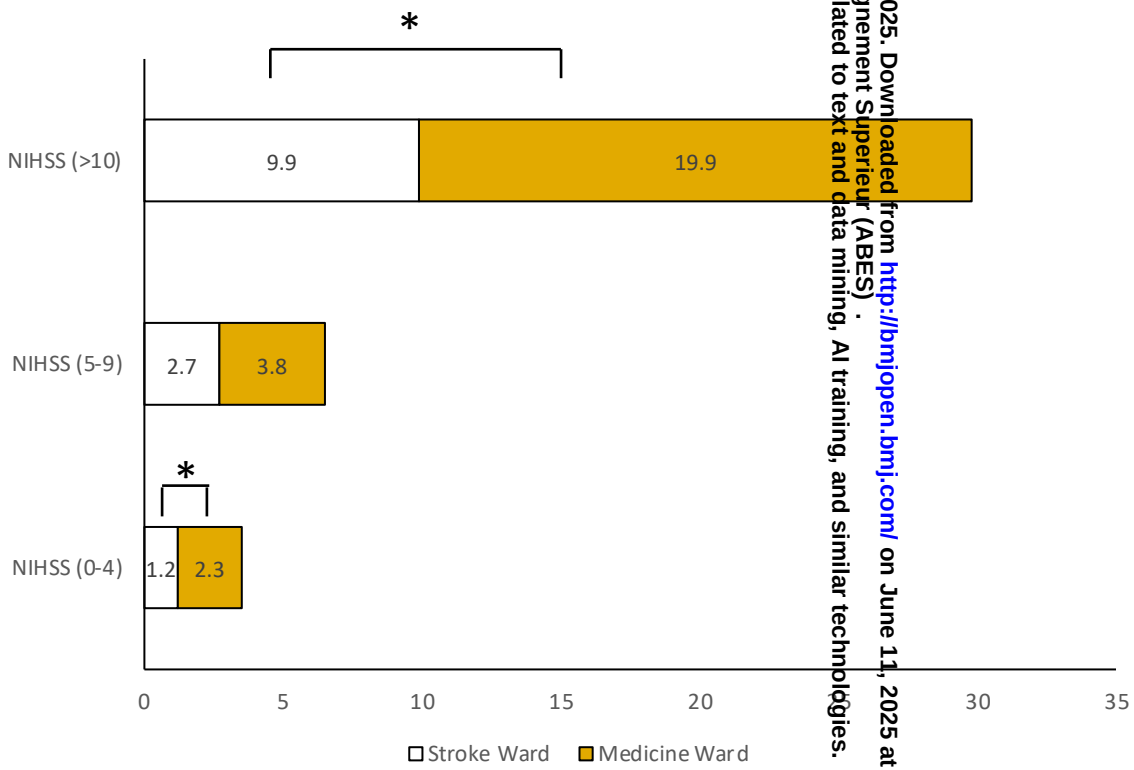
*p $\leq$ 0.05

Figure 2. Proportion of mRS at 90 days for patients with an NIHSS of 5-9

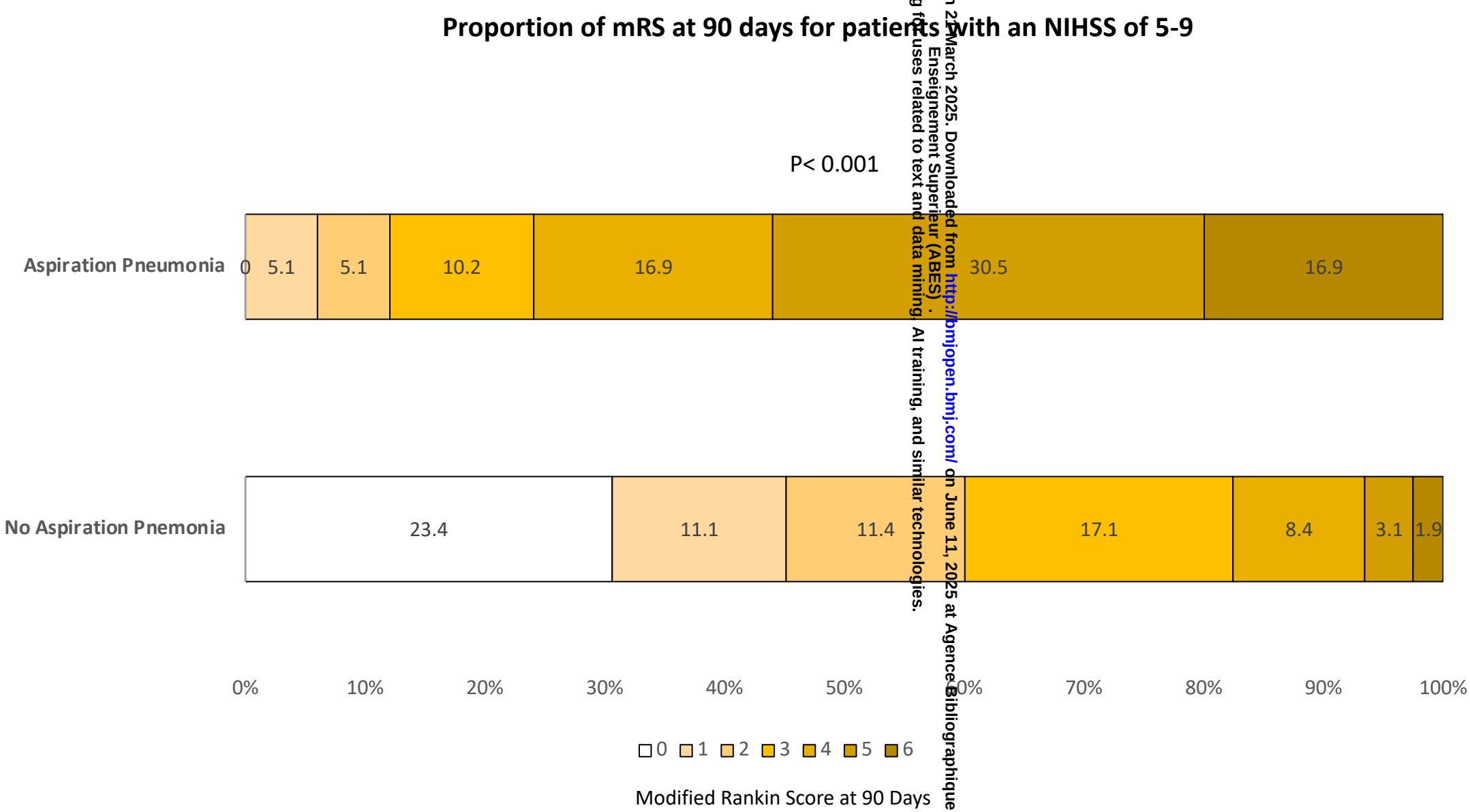
Figure 3. Proportion of mRS at 90 days for patients with an NIHSS of >10

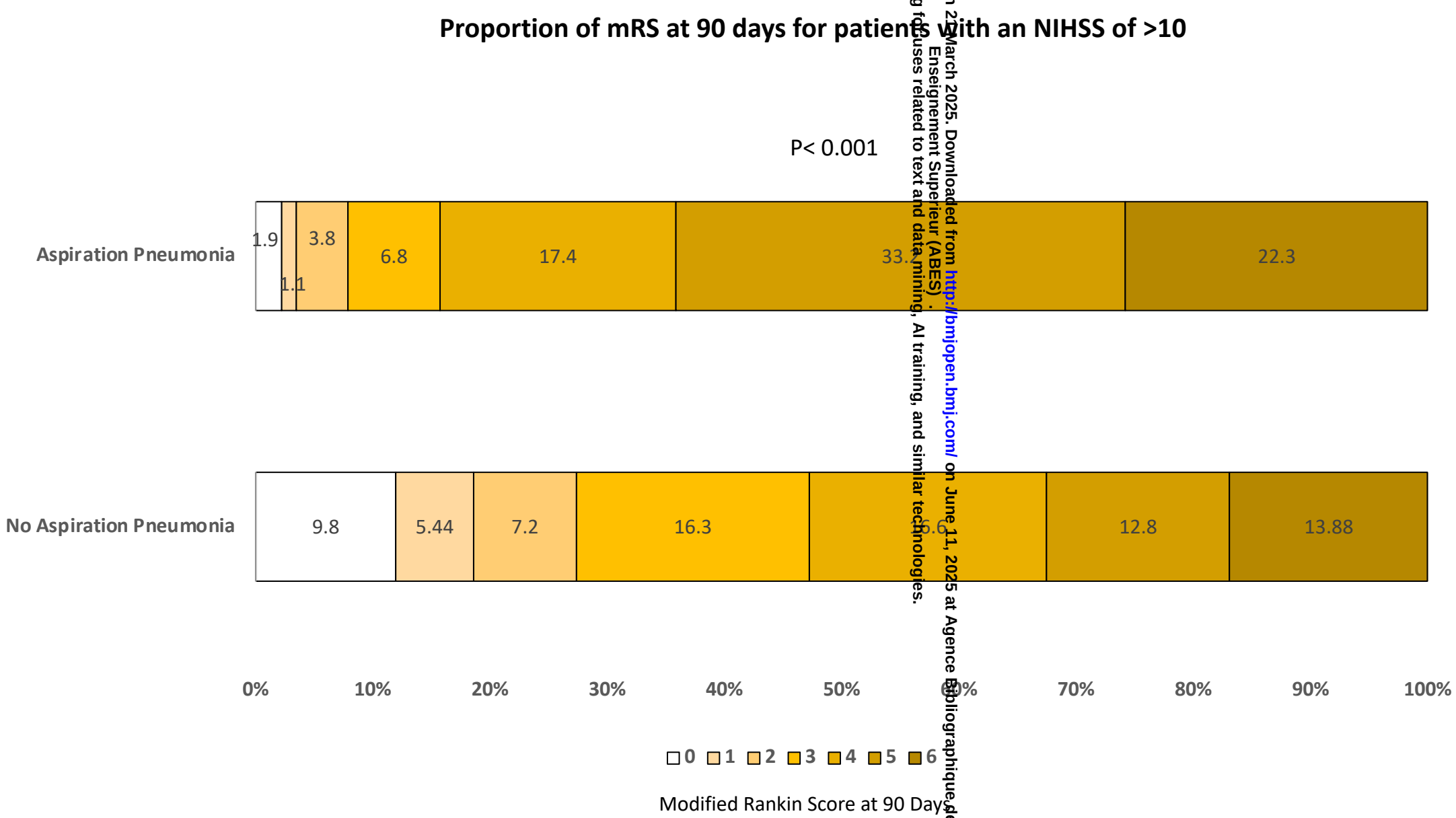
Figure 4. Forest Plot based on the results of multivariate analysis of the factors associated with aspiration pneumonia.

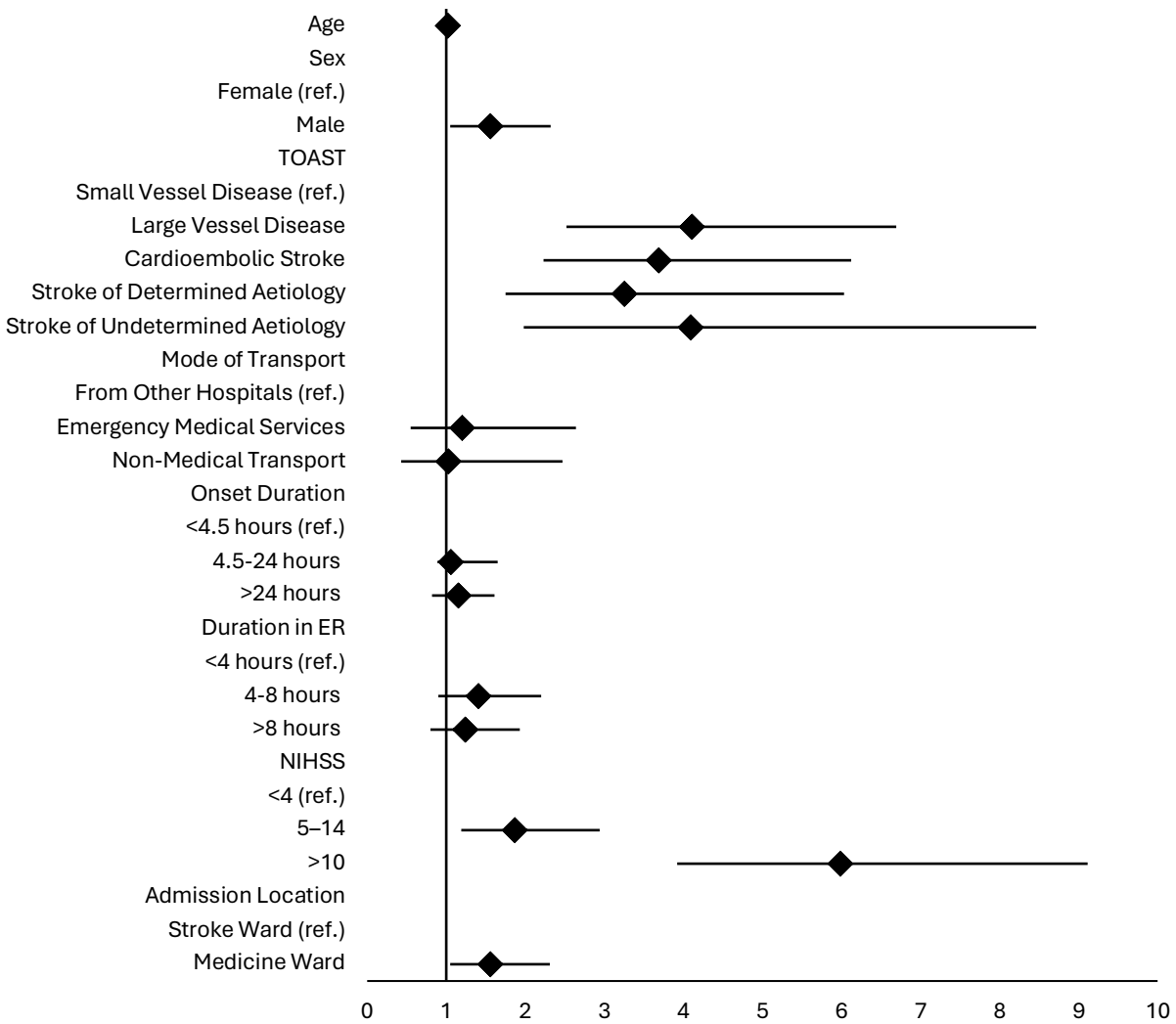
Abbreviations: CI, confidence interval; OR, odds ratio.



Proportion of aspiration pneumonia between stroke ward vs. medicine ward
*p≤0.05







Adjusted OR(95% CI)

1.02 (1.01–1.03), p=0.002

1.56 (1.05–2.32), p=0.03

4.1 (2.52–6.69), p<0.001

3.7 (2.23–6.12), p<0.001

3.2 (1.75–6.03), p<0.001

4.09 (1.98–8.46), p<0.001

1.20 (0.55–2.64), p=0.65

1.03 (0.43–2.47), p=0.94

1.06 (0.68–1.65), p=0.79

1.15 (0.82–1.61), p=0.43

1.41 (0.90–2.20), p=0.13

1.24 (0.80–1.93), p=0.34

1.87 (1.19–2.94), p=0.01

5.98 (3.92–9.11), p<0.001

1.56 (1.05–2.31), p=0.03

	Overall	No Pneumonia	Aspiration Pneumonia	Overall Significance	SVD vs. LVD[1]	SVD vs. CE[1]	SVD vs. SDA[1]	SVD vs. SUD[1]	LVD vs. CE[1]	LVD vs. SDA[1]	LVD vs. SUD[1]	CE vs. SDA[1]	CE vs. SUD[1]	SDA vs. SUD[1]
TOAST				<.001	<.001	<.001	<.001	<.001	1.00	0.25	1.00	0.06	1.00	0.82
Small vessel disease	4249 (46.2)	4213 (99.2)	36 (0.8)	–	–	–	–	–	–		–	–	–	–
Large vessel disease	1913 (20.8)	1772 (92.6)	141 (7.4)	–	–	–	–	–	–		–	–	–	–
Cardioembolic	1881 (20.5)	1744 (92.7)	137 (7.3)	–	–	–	–	–	–		–	–	–	–
Determined etiology	643 (7.0)	612 (95.2)	31 (4.8)	–	–	–	–	–	–		–	–	–	–
Undetermined etiology	511 (5.6)	476 (93.2)	35 (6.8)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**EMS vs. NM[1]**	**EMS vs. OH[1]**	**NM vs. OH[1]**							
Mode of transport				<.001	<.001	1.00	0.07							
EMS	6361 (69.2)	6073 (95.5)	288 (4.5)	–	–	–	–	–	–		–	–	–	–
Non-Medical	2234 (24.3)	2200 (98.5)	34 (1.5)	–	–	–	–	–	–		–	–	–	–
From Other Hospitals	387 (4.2)	372 (96.1)	15 (3.9)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**<4.5 hours vs. 4.5-24 hours[1]**	**<4.5 hours vs. >24 hours[1]**	**4.5-24 hours vs. >24 hours[1]**							
Onset Duration				<.001	0.26	<.001	<.001							
<4.5 hours	2991 (32.5)	2822 (94.3)	169 (5.7)	–	–	–	–	–	–		–	–	–	–
4.5-24 hours	3035 (33.0)	2890 (95.2)	145 (4.8)	–	–	–	–	–	–		–	–	–	–
>24 hours	3171 (34.5)	3105 (97.9)	66 (2.1)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**<4 hours**	**<4 hours vs. >8**	**4-8 hours**							

					vs. 4-8 hours[1]	hours [1]	vs. >8 hours[1]							
Duration in ED				0.11	1.00	1.00	0.11							
<4 hours	859 (15.4)	809 (94.2)	50 (5.8)	–	–	–	–	–	–	–	–	–	–	
4-8 hours	1833 (32.8)	1711 (93.3)	122 (6.7)	–	–	–	–	–	–	–	–	–	–	
>8 hours	2900 (51.9)	2749 (94.8)	151 (5.2)	–	–	–	–	–	–	–	–	–	–	
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**0-4 vs. 5-14[1]**	**0-4 vs. >15[1]**	**5-14 vs. >15[1]**							
NIHSS				<.001	<.001	<.001	<.001							
Mild Stroke (0-4)	5626 (61.2)	5570 (99.0)	56 (1.0)	–	–	–	–	–	–	–	–	–	–	
Moderate Stroke (5-9)	1965 (21.4)	1906 (97.0)	59 (3.0)	–	–	–	–	–	–	–	–	–	–	
Severe Stroke (>10)	1606 (17.5)	1341 (83.5)	265 (16.5)	–	–	–	–	–	–	–	–	–	–	

Table S1. Clinical characteristics among patients with aspiration pneumonia versus those without aspiration pneumonia

[1] Bonferroni corrections have been applied to the p-values reported

Abbreviations: CE, cardioembolic; EMS, emergency medical service; LVD, large vessel disease; NM, non-medical; OH, other hospitals; SDA, stroke of determined etiology; SUD, stroke of undetermined etiology; SVD, small vessel disease.

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NIHSS	No Pneumonia	Aspiration Pneumonia	Stroke Ward vs. Medicine Ward
Mild Stroke (0-4)			
Admission Location			
Stroke Ward	1704 (98.8)	20 (1.2)	0.03*
Medicine Ward	832 (97.7)	20 (2.3)	
Moderate Stoke (5-9)			
Admission Location			
Stroke Ward	1281 (97.3)	35 (2.7)	0.31
Medicine Ward	250 (96.2)	10 (3.8)	
Severe Stroke (>10)			
Admission Location			
Stroke Ward	834 (90.1)	92 (9.9)	<.001*
Medicine Ward	166 (80.1)	40 (19.9)	

Abbreviations: NIHSS, National Institute of Health Stroke Scale.
*p≤0.05

Table S2. Comparison of NIHSS score and admission location among patients with aspiration pneumonia versus those without aspiration pneumonia using Fisher's Exact Test

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Impact of Stroke Severity on Aspiration Pneumonia Risks in the Medical Ward versus the Stroke Unit: A 10-Year Retrospective Cohort Study

Running Title: Risk factors associated with aspiration pneumonia

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Abstract

Objective: Aspiration pneumonia is a common complication post-stroke that increases patient's duration of stay in hospital, mortality, and morbidity. We examined the incidence, clinical characteristics, and outcomes among ischemic stroke-related aspiration pneumonia patients in Qatar.

Settings and participants: The Qatar Stroke database was reviewed for acute ischemic stroke patients admitted to Hamad General Hospital, a tertiary care medical facility, between January 2014 to April 2024.

Outcomes: Patients were prospectively assessed for mortality at 90 days, modified Rankin Score at 90 days, and length of stay. Several clinical characteristics were also compared between acute ischemic stroke patients who developed aspiration pneumonia versus those without.

Results: Stroke patients who developed aspiration pneumonia tended to be older and of the male sex. Patients who developed aspiration pneumonia were also more likely to present with a higher NIHSS at admission ($p<0.001$). Patients with large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke of undetermined etiology were more likely to develop aspiration pneumonia. They also stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia (16.0 vs. 5.3 days). Patients admitted to the medicine ward had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward (aOR of 1.56, 95% CI: 1.05–2.31). Patients with aspiration pneumonia had unfavorable outcome (mRS 3-6) at 90 days (74.6% vs. 30.4% for an NIHSS admission score of 5-9 and 79.6% vs. 59.5% for an NIHSS admission >10). They were also more likely to have higher mortality rates at 90 days (16.9% vs. 1.9% for an NIHSS admission score of 5-9 and 22.3% vs. 13.8% for an NIHSS admission score >10) and major adverse cardiovascular event at

1 year (23.7% vs. 3.8% for an NIHSS admission score of 5-9 and 27.5% vs. 16.2% for NIHSS >10).

Conclusion: Age, sex, admission NIHSS severity, stroke subtypes, and admission location are independent predictors of aspiration pneumonia post-stroke.

Keywords: Aspiration Pneumonia, Stroke, Dysphagia, Stroke-associated pneumonia

Strengths and limitations of this study:

1) This study is based on a large stroke registry with 9197 acute ischemic stroke patients enrolled over a 10-year period.
2) Our patient sample is comprised of largely Middle Eastern ethnicity, South Asian and Far Eastern, therefore lacks generalizability.

Introduction

Stroke is a major cause of death and disability worldwide. Early in the course of the disease, stroke patients are at risk for medical complications including dysphagia and aspiration pneumonia.[1] Dysphagia is characterized by difficulty swallowing due to weakness/reduced coordination between facial, palatal, and pharyngeal muscles (due to reduced cortical connectivity between neural regions post-stroke).[2] The incidence of dysphagia after stroke ranges from 8.1–80%,[3–7] it is frequently silent and it is highly associated with aspiration pneumonia.[8] Dysphagia causes oral or gastric contents to enter the lung, which suppresses the natural defenses of the respiratory system, increasing the risks for opportunistic infections.[9–11] Several studies have identified multiple risk factors associated with aspiration pneumonia, such as reduced level of consciousness, incorrect postures, and advanced age.[12–15]

Pneumonia is one of the leading causes of mortality for acute stroke, with a 30-day mortality rate of up to 30%.[16] Aspiration pneumonia also increases the risk of prolonged hospital stay and poor prognosis.[17] Animal and clinical studies have demonstrated that silent aspiration (micro-aspiration due to dysphagia during the night) is the primary cause of aspiration pneumonia.[18] Despite different preventative and therapeutic approaches for managing patients with aspiration pneumonia, its incidence and mortality rates remain high.[19] For example, in a case-control study comprising of 1,112,944 patients, Gupte et al[20] reported that aspiration pneumonia due to cerebrovascular disease accounted for 11.7% of deaths in the United States (62,068 deaths per year from 1999 to 2017), with increasing mortality rates since 2009. In countries such as Egypt and Brazil, the incidence of aspiration pneumonia can be as high as 44% and 76%, respectively.[19,21]

There are very few studies on the incidence, causes, and outcomes of aspiration pneumonia from the Middle East and North Africa (MENA) region.[22] This study aimed to assess the clinical characteristics and treatment outcomes among stroke-related aspiration pneumonia patients in Qatar.

Methods

Data from patients admitted with a stroke to Hamad General Hospital (HGH), Doha, Qatar from January 2014 through April 2024 were analyzed from a hospital based prospective stroke registry. HGH is a Joint Commission International (JCI) accredited 600-bed hospital, with 200 beds reserved for medical patients. It is the only tertiary care medical facility in Qatar where the stroke service is located, 95% of all strokes in Qatar requiring admission to hospital are admitted to HGH. The program provides 24-hour thrombolysis and thrombectomy services for acute stroke management. Patients are evaluated by the stroke team in the emergency department (ED), and urgent decisions about treatment are made. Hyperacute stroke patients are admitted to a dedicated 12-bed stroke unit or Medical ICU as necessary. Non-urgent stroke patients are admitted under the medical team, with neurology consultation in the ED. HGH has the required laboratory, neuroradiological, and neurosurgical infrastructure to manage stroke patients effectively. The stroke team is readily available to make immediate treatment decisions for acute stroke cases.

Study Variables

The primary outcome variables were duration of stay in the emergency department, length of stay, modified Rankin Score at 90 days, and mortality at 90 days.

The independent variables were age, sex, development of post-stroke pneumonia, and admission location (stroke ward versus medical ward).

Patient characteristics

Patient characteristics including age, sex, ethnicity, medical comorbidities and prior medication were collected in the HGH Stroke Registry. National Institute of Health Stroke Scale (NIHSS) score, neuroimaging data, and post-discharge disposition were entered into the registry as well. Ischemic stroke was diagnosed according to the WHO criteria[23] and stroke subtypes were defined by the TOAST criteria.[24] The modified Rankin scale (mRS) measurements were done at discharge and at 90 days following onset of symptoms. The patients were classified as favourable (mRS ≤ 0-2) or unfavourable (mRS 3-6) outcome. We used the dichotomized mRS scale to evaluate recovery at 90 days.[25] NIHSS score was developed by the National Institutes of Health and is widely referenced in clinical settings for stroke assessment. The tool is highly regarded for its reliability and ability to track neurological changes over time.[26] The Modified Rankin Scale (mRS) is a widely used tool to assess the degree of disability or dependence in individuals who have suffered a stroke or other neurological events. It measures the functional outcome of a patient after a neurological injury, such as a stroke, and evaluates the level of independence in daily activities.[27]

Diabetes was diagnosed according to the American diabetes Association (ADA) and WHO recommendation[28] and included patients with a previous diagnosis of diabetes, on medication for diabetes or an HbA1c of more than 6.5%, and the diagnosis of pre-diabetes was based on an HbA1c of 5.7-6.4% as per the 2015 ADA clinical practice recommendations. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mm Hg or a diastolic pressure ≥ 90 mm Hg, or on current treatment with antihypertensive drugs. Dyslipidemia was defined as low-density lipoprotein-cholesterol level ≥ 3.62 mmol/L, high-density lipoprotein cholesterol

level ≤ 1.03 mmol/L, triglycerides ≥ 1.69 mmol/L, or current treatment with a cholesterol-lowering drug.

Data Collection and inclusion/exclusion criteria

Upon identification and confirmation of diagnosis using the International Classification of Disease, 10th edition, definitions (H34.1, 163.x, 164.x, 161.x, 160.x, G45.x), patients' data were collected by trained stroke clinical nurse specialists. For our study, we only included patients diagnosed with acute ischemic stroke and excluded patients diagnosed with intracerebral hemorrhage, transient ischemic attacks, stroke mimics, and cerebral venous thrombosis. Clinical diagnosis (via assessing symptoms like fever, cough, dyspnea, and purulent sputum) and/or radiological imaging (CT and chest X-rays to identify lung consolidation or infiltrates indicative of pneumonia) were used to confirm the diagnosis of post-stroke aspiration pneumonia. Microbiological testing including sputum culture, blood cultures, and bronchoalveolar lavage were also performed when clinical or imaging diagnoses were inconclusive. The methods used are consistent with current guidelines.[29,30]

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Data Quality Control

Data quality control in the HGH Stroke Registry was ensured through several key practices. Stroke coordinators received training on data collection and International Classification of Diseases (ICD)-10 coding, and standardized procedures are followed to maintain consistency. Diagnoses were confirmed using ICD-10 codes, and registry entries are cross-checked with patient records to ensure accuracy. Automated tools flag errors, and manual

reviews ensure corrections are made when necessary. Routine audits and continuous monitoring of data help identify and correct errors, maintaining the integrity of the registry. These measures help ensure high-quality, reliable data for stroke care analysis and improvement.

Data Analysis and statistics

Descriptive results for all continuous variables were reported as mean±standard deviation (SD) for normally distributed data or median with range for data with non-normal distributions. The distribution of continuous variables was assessed before using statistical tools. Mean level comparisons between patients with aspiration pneumonia versus without aspiration pneumonia were assessed using ANOVA test and multiple comparisons were performed using Bonferroni correction. If an assumption of an ANOVA test was failed, then an alternative non-parametric Kruskal Wallis test was performed. Pearson Chi-Square test and Fisher's Exact test were performed whenever appropriate to compare the proportion of all categorical variables between the groups. Multiple logistic regression analysis was performed to assess for risk factors associated with aspiration pneumonia after selecting important and significant variables at univariate analysis. Odds ratio (OR) and the 95% confidence interval for the OR were reported. A p-value of ≤0.05 (two-tailed) was considered significant. SPSS statistical package 29.0.1.0 was used for the analysis.

Results

Patient Characteristics

A total of 9197 patients were enrolled: 380 developed aspiration pneumonia (4.1%) during hospitalization while 8817 (95.9%) of the patients did not have pneumonia. The mean age of patients was 55.3±13.4 years, with patients with aspiration pneumonia being significantly older than healthy controls (p<0.001). 80% were male, 57% had diabetes mellitus, 72% had

hypertension, 46% had dyslipidemia, and 24% were active smokers. The high proportion of men is reflective of the very high male expatriate population as previously reported.[31] A summary of patients' baseline characteristics is outlined in Table 1.

Since 95.9% of our patients did not have aspiration pneumonia, we performed sub-analyses on clinical outcomes based on patients' admission NIHSS scores. Sub-analyses were performed for patients with an NIHSS of 5-9 (moderate stroke) and NIHSS >10 (severe stroke) (Table 2).

Mode of transport

Mode of transport was significantly associated with aspiration pneumonia risks ($p<0.001$). However, this was only significant for emergency medical services (EMS) versus non-medical services ($p<0.001$), with a higher proportion of patients developing aspiration pneumonia via EMS (4.5%) versus non-medical services (1.5%). Patients transported with EMS had a significantly higher NIHSS at admission (5.9±6.1 vs. 3.3±3.7, $p<0.001$). The total sample size for EMS was 6361 versus 2234 for non-medical services.

Onset Duration

Duration of stroke symptoms from the time of onset to evaluation was significantly associated with aspiration pneumonia ($p<0.001$). This was only significant for <4.5 hours vs. >24 hours ($p<0.001$) and 4.5-24 hours vs. >24 hours ($p<0.001$). A stroke onset to emergency evaluation of <4.5 hours had the highest proportion of aspiration pneumonia (5.7%) versus 4.8% for onset duration of 4.5-24 hours and 2.1% for >24 hours (Table S1).

Duration of stay in Emergency Department

Duration of stay in the ED was not significantly associated with aspiration pneumonia ($p=0.11$) (Table S1). Furthermore, when we analyzed duration of stay in the ED based on NIHSS

scores (5-9 and >10), duration of stay in the ED remained non-significant (p=0.052 and 0.09), respectively (Table 2).

Stroke Diagnosis

Stroke diagnosis is shown in Table S1. Overall, type of stroke was significantly associated with aspiration pneumonia (p<0.001). Further analyses revealed that the risk of developing aspiration pneumonia was not significantly different between large vessel disease versus cardioembolic stroke (p=1.00), large vessel disease versus stroke of undetermined aetiology (p=1.00), cardioembolic stroke versus stroke of determined aetiology (p=0.06), cardioembolic stroke versus stroke of undetermined etiology (p=1.00), and stroke of determined aetiology versus stroke of undetermined aetiology (p=0.82).

Patients with small vessel disease had the lowest proportions of aspiration pneumonia (0.8%) compared to large vessel disease (7.4%), cardioembolic stroke (7.3%), stroke of determined etiology (4.8%), and stroke of undetermined etiology (6.8%), p<0.001 (Table 3).

Admission NIHSS Score

Admission NIHSS score was significantly associated with aspiration pneumonia (p<0.001). Fisher's exact test revealed that there was a significant association between aspiration pneumonia for patients with an NIHSS score of 0-4 (p=0.03), and NIHSS score of >10, p<0.001 (Table S2). Patients with an NIHSS > 10 had the highest proportion of aspiration pneumonia (16.5%). Moreover, patients with an NIHSS >10 and concomitant aspiration pneumonia had higher rates of mortality at 90 days (22.3%) when compared to patients with an NIHSS score of 5-9 and concomitant aspiration pneumonia (16.9%) (p<0.001) (Table 2). In patients with aspiration pneumonia, patients with an NIHSS >10 also had higher rates of major adverse

cardiovascular events (MACE) at 1 year compared to patients with an NIHSS of 5-9 (27.5% vs. 23.7%, p<0.001).

Length of stay

Patients with aspiration pneumonia stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia (16.0 days vs. 5.3 days, p=0.00). When analyzed via admission NIHSS severity, patients with aspiration pneumonia stayed significantly longer in the hospital compared to those without aspiration pneumonia (17.1 days vs. 5.9 days, p<0.001 for NIHSS of 5-9, and 16.6 days vs. 9.2 days, p<0.001 for NIHSS > 10).

Admission Location

Overall, 3966 (75.1%) patients were admitted to the stroke ward and 1318 (24.9%) patients were admitted to the medical ward. A higher proportion of patients admitted to the medicine ward developed aspiration pneumonia in contrast to patients admitted to the stroke ward (5.3% vs 3.7%, p=0.01) (Table 3). 2.3% of patients with an NIHSS of 0-4 and admitted to the medicine ward developed aspiration pneumonia compared to 1.2% of patients with an NIHSS of 0-4 and admitted to the stroke ward (p=0.03) (Table S2). Similarly, 19.9% of patients with an NIHSS >10 and admitted to the stroke ward developed aspiration pneumonia compared to 9.9% of patients with an NIHSS >10 and admitted to the stroke ward (p<0.001) (Figure 1).

Modified Rankin Scale at 90 days

A higher proportion of patients with aspiration pneumonia had an unfavorable outcome (mRS 3-6) at 90 days compared to patients without aspiration pneumonia (74.6% vs. 30.4% for NIHSS of 5-9), p<0.001 (Table 2). Similar observations were seen for NIHSS > 10 (79.6% vs. 59.5%, p<0.001). Figure 2 and 3 illustrates the proportion of mRS at 90 days based on NIHSS admission scores.

Mortality at 90 days

For patients with an NIHSS score of 5-9, a higher proportion of patients with aspiration pneumonia died at 90 days (16.9%) compared to patients without aspiration pneumonia (1.9%), p<0.001. Similar observations were seen for NIHSS > 10 (22.3% vs. 13.8%, p=0.003).

Multivariate analysis for risk factors associated with aspiration pneumonia

Table 3 describes a multiple binary logistic regression model to identify significant independent factors associated with the development of aspiration pneumonia after selecting important and significant variables at bivariate analysis. Males were more likely than females to have aspiration pneumonia risks [aOR 1.56, 95% CI: 1.05–2.32, p=0.03]. Age was significantly associated with aspiration pneumonia [aOR 1.02, 95% CI: 1.01–1.03, p=0.002], with patients with aspiration pneumonia being significantly older (p<0.001). Large vessel disease was significantly associated with aspiration pneumonia [aOR 4.11, 95% CI: 2.52–6.69, p<0.001]. Similar observations were seen for cardioembolic stroke (p<0.001), stroke of determined aetiology (p<0.001), and stroke of undetermined aetiology (p<0.001), see Table 3. Patients with an NIHSS score of 5–9 and >10 also had high odds of developing aspiration pneumonia (aOR of 1.87 and 5.98, respectively). Patients admitted to the medicine ward also had 1.56 times the odds of developing aspiration pneumonia compared to the stroke ward (95% CI: 1.05–2.31, p=0.03). A forest plot of the multivariate analysis can be seen in Figure 4.

Discussion

To the best of our knowledge, this is the first study to specifically examine the incidence and outcomes of patients who develop aspiration pneumonia post-stroke in the MENA region. In our cohort, 4.1% of our patients developed aspiration pneumonia post stroke. This low number may be deceiving as the majority of patients admitted had mild symptoms [5626 (61.2%) of

patients had an NIHSS of <4]. The odds of aspiration pneumonia was 1.87 in patients with admission NIHSS of 5-9 (n=1965), increasing to 5.98 in patients with NIHSS of 10 or more (n=1606). Patients with aspiration pneumonia also stayed an average of 10 days longer in the hospital compared to patients without. A higher proportion of patients with aspiration pneumonia had an unfavorable outcome at 90 days. They were also more likely to have higher mortality rates at 90 days and MACE at 1 year. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward.

High NIHSS has also been shown to be correlated with increased rates of dysphagia and aspiration pneumonia due to stroke severity.[32] Patients with aspiration pneumonia in the Qatar dataset had comparatively higher NIHSS at presentation as compared to patients without pneumonia (14.7 v 5.1, p<0.001). Garavelli et al[33] demonstrated that an NIHSS cut-off of ≥ 10.5 was associated with higher rates of dysphagia (p=0.014) and aspiration pneumonia (p=0.006). Similarly, Jeyaseelan et al[32] demonstrated NIHSS > 9 as being moderately predictive of clinically relevant dysphagia, with dysphagia rates increasing with greater NIHSS scores (p<0.001). Okubo et al[34] also showed an NIHSS cut-off of 12 sensitive for dysphagia detection, with 14 (87.5%) of the 16 patients with dysphagia having NIHSS scores ≥ 12 and 2 (12.5%) patients having scores of 10 and 11. NIHSS >12 also has an independent association with persistent dysphagia at hospital discharge in acute ischemic stroke patients with dysphagia at stroke onset, with one of its sub-components–dysarthria–emerging as a significant independent predictor of prolonged dysphagia.[35] In our current study, the odds of developing aspiration pneumonia increased as NIHSS score increased.

Several studies have reported the adverse outcomes of aspiration pneumonia on stroke patients. In a study comprised of 610,668 stroke patients, Barlas et al[36] reported that patients with stroke-associated pneumonia (SAP) had significantly higher odds of in-hospital mortality (OR of 2.90, 95% CI: 2.83–2.96), and longer length of stay (OR 13.11, 95% CI: 12.83–13.40). While they analyzed data from both ischemic and hemorrhagic strokes, patients with ischemic stroke were more likely to die in hospital and experience long length of stay (LOS).[36] Teh et al[37] had similar observations in his cohort of 9238 patients from the UK. SAP was found in 1083 (11.7%) patients, out of which 60.8% were aspiration pneumonia.[37] After controlling for confounders, SAP was found to be associated with increased mortality up to 1 year (inpatient, 90-day, 1 year), prolonged LOS, and poor functional outcome on discharge.[37] In our current study, patients who developed aspiration pneumonia with an admission NIHSS of 5-9 had a 16.9% mortality rate at 90 days in contrast to 1.9% for patients who did not develop aspiration pneumonia. Similarly, patients who developed aspiration pneumonia with an admission NIHSS >10 had higher mortality rates at 90 days (22.3% vs. 13.8%, p=0.003).

Dysphagia is a common feature of severe stroke and an indicator of poor prognosis. It is implicated in the development of aspiration pneumonia, and it results in longer LOS and increased mortality. In stroke patients with dysphagia, early nutritional support is vital, and the decision to initiate that depends on the outcome of the swallow study.[38] Multiple national and international guidelines recommend that people with acute stroke have their swallowing screened by a trained healthcare professional by utilizing a validated screening tool and that the patients remain nothing per oral (NPO) until a swallow screen is performed.[17] Bedside swallow screening tools include the functional bedside aspiration screen (FBAS), GLOBE-3S (the Sapienza GLObal Bedside Evaluation of Swallowing after Stroke), water swallowing test, volume-

viscosity swallow test, and the Gugging swallow screen. However, despite these recommendations, in our study 34.6% of patients did not undergo swallow screen prior to PO intake in the ED and 32.7% patient did not have SLP assessment within 24 hours of admission. Likely explanations for these findings include ED nursing inadvertently giving patients PO medications, or SLPs not being available over the weekend, hence leading to an inability to perform assessment within 24 hours of presentation.

Similar to previous reports, we observed a significantly higher risk of aspiration pneumonia in the patients admitted to the medical ward compared to the stroke ward (5.3% vs. 3.7%, p=0.01). Admission to the stroke ward, by prevention of medical complications, results in reduced length of stay, decreased incidence of complications, improved prognosis at discharge and at 90 days (higher % of mRS scores of 0-2).[39,40] Similarly, in our current study, fewer patients developed aspiration pneumonia if they were admitted to the stroke ward versus medicine ward (3.7% vs. 5.3%, p=0.01). Multivariable logistic regression identified admission location as an independent predictor of aspiration pneumonia, with patients admitted to the medicine ward having higher risks of developing aspiration pneumonia (aOR 1.56, 95% CI: 1.05–2.31). In our study population, we also observed that 19.9% patients with an NIHSS >10 and admitted to the medicine ward developed aspiration pneumonia in contrast to patients with an NIHSS > 10 and admitted to the stroke ward (9.9%; p<0.001). Thus, healthcare providers should be judicious of the placement of their stroke patients if they would like to reduce the incidence of aspiration pneumonia.

We also observed that patients with small vessel disease or subcortical stroke were less likely to develop aspiration pneumonia in contrast to patients with cardioembolic stroke, large vessel disease, stroke of undetermined etiology, and stroke of determined etiology. This is

consistent with Alberts et al's study, who reported a low occurrence of aspiration in small vessel infarcts compared to those with both large- and small vessel infarcts (p=0.002).[41] Similarly, Jitpratoom et al[42] observed that 40.7% of their patients with cardioembolic stroke developed aspiration pneumonia in contrast to 11.1% for small vessel occlusion. Multivariable logistic regression analysis revealed that type of stroke was an independent predictor of aspiration pneumonia, specifically for large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke of undetermined etiology. A potential explanation for this is that patients with small vessel disease have milder stroke symptoms and fewer neurological deficits in contrast to the other stroke subtypes,[43] therefore they might have more preserve/control of their facial, palatal, and pharyngal muscles, reducing their risks of developing dysphagia and aspiration pneumonia. However, additional studies are needed to unravel this relationship.

There are several limitations with our study. Our patient sample is comprised of largely Middle Eastern ethnicity (Qatari, Arabs), South Asian and Far Eastern (Asians) (97.7% vs. 2.3% for Caucasians), therefore lacks generalizability. We also had missing data for the mRS score at 90 days for 1846 patients (out of 9197). Since Qatar's population is comprised mainly of expatriate workers, it is not possible to collect data for patients who may have moved back to their home country once their work contract ended.

Conclusion

This large study in prospectively collected patients with acute stroke identified multiple factors associated with an increased risk of aspiration pneumonia. Patients who developed aspiration pneumonia were older, presented with more severe neurological symptoms, and stayed an average of 10 days longer in the hospital compared to patients without aspiration pneumonia. Patients with large vessel disease, cardioembolic stroke, stroke of determined etiology and stroke

of undetermined etiology were more likely to develop aspiration pneumonia. Patients who were admitted to the medicine ward also had higher odds of developing aspiration pneumonia in contrast to patients admitted to the stroke ward. Our study showed that aspiration pneumonia was associated with an unfavorable prognosis (mRS 3-6) and increased mortality at 90 days in patients with moderate and severe symptoms.

Data Availability Statement

The Qatar Stroke Registry dataset will be available on reasonable request to the corresponding author.

Ethics Statement

The studies involving humans were approved by the Institutional Review Board of the Medical Research Centre at Hamad Medical Corporation (MRC-01-20-1135). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent from the patients/participants or patients/participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Declaration of conflicting interests

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Authors contribution:

KHT: Writing—original draft, Formal analysis.

NA: Formal analysis, Methodology, Supervision, Reviewing draft.

AA: Writing, Reviewing draft

SJ: Data curation and Validation.

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Table 1. Characteristics and outcome of acute ischemic stroke patients with aspiration pneumonia

Characteristic	No Pneumonia (n=8817, 95.9%)	Aspiration Pneumonia (n= 380, 4.1%)	Total (n= 9197)	P-Value
Age	55.1±13.3	59.0±15.6	55.3±13.4	<0.001
Male Gender	7041 (79.9)	303 (79.7)	7344 (79.9)	0.95
Diabetes	5038 (57.1)	229 (60.3)	5267 (57.3)	0.22
Hypertension	6373 (72.3)	246 (64.7)	6619 (72.0)	<0.001
Dyslipidemia	4069 (46.1)	136 (35.8)	4205 (45.7)	<0.001
Prior Stroke or TIA	1156 (13.1)	63 (16.6)	1219 (13.3)	0.05
Coronary Artery Disease	1053 (11.9)	70 (18.4)	1123 (12.2)	<0.001
Atrial Fibrillation	664 (7.5)	73 (19.2)	737 (8.0)	<0.001
Active Smoking	2143 (24.3)	52 (13.7)	2195 (23.9)	<0.001
Ethnicity[a]				
Arab	2962 (33.6)	160 (42.1)	3122 (33.9)	<0.001
South Asian	4518 (51.2)	168 (44.2)	4686 (51.0)	
Far Eastern	753 (8.5)	17 (4.5)	770 (8.4)	
African	382 (4.3)	26 (6.8)	408 (4.4)	
Caucasian	202 (2.3)	9 (2.4)	211 (2.3)	
Mode of Arrival[a]				
EMS	6073 (68.9)	288 (75.8)	6361 (69.2)	<0.001
Non-Medical	2200 (25.0)	34 (8.9)	2234 (24.3)	
From Other Hospitals	372 (4.2)	15 (3.9)	387 (4.2)	
mRS prior to acute stroke[a]				
0	7595 (86.1)	282 (74.2)	7877 (85.6)	<0.001
1	132 (1.5)	9 (2.4)	141 (1.5)	
2	312 (3.5)	12 (3.2)	324 (3.5)	
3	430 (4.9)	33 (8.7)	463 (5.0)	
4	196 (2.2)	23 (6.1)	219 (2.4)	
5	151 (1.7)	21 (5.5)	172 (1.9)	
NIHSS on admission	5.1 ± 5.54	14.65 ± 8.05	5.5 ± 6.0	<0.001
Onset Duration[a]				
Less than 4.5 Hours	2822 (32.0)	169 (44.5)	2991 (32.5)	<0.001
Between 4.5 till 24 hours	2890 (32.8)	145 (38.2)	3035 (33.0)	
More than 24 hours	3105 (35.2)	66 (17.4)	3171 (34.5)	
Thrombolysis Given	962 (10.9)	73 (19.2)	1035 (11.3)	<0.001
Mechanical Thrombectomy done	350 (4.0)	43 (11.3)	393 (4.3)	<0.001
BMI on admission	28.15±43.9	27.54±5.3	28.13±43.0	0.8
RBS on admission	9.6±7.5	10.4±5.05	9.6±7.4	0.04
HbA1c	7.51±2.42	7.6±2.4	7.51±2.41	0.64
Serum Cholesterol	4.84±1.52	4.6±1.75	4.83±1.53	0.01
Serum Triglyceride	1.8±1.76	1.45±0.83	1.77±1.73	0.002
Serum HDL	1.1±3.24	1.43±6.34	1.10±3.38	0.12
Serum LDL	3.1±1.8	2.82±1.25	3.1±1.8	0.03
Systolic Blood Pressure	157.8±44.23	149.44±29.15	157.42±43.73	0.00
Diastolic Blood Pressure	91.1±22.4	86.4±19.4	90.9±22.3	0.00
Length of Stay	5.25±8.55	16.0±14.93	5.70±9.2	0.00

Disposition[a]				
Discharged Home	**5726 (64.9)**	**44 (11.6)**	**5770 (62.7)**	**<0.001**
Rehabilitation	**2079 (23.6)**	**89 (23.4)**	**2168 (23.6)**	
Long term care	**151 (1.7)**	**97 (25.5)**	**248 (2.7)**	
Transfer to other facility	**732 (8.3)**	**109 (28.7)**	**841 (9.1)**	
Died as in-patient	**129 (1.5)**	**41 (10.8)**	**170 (1.8)**	
TOAST Classification[a]				
Small Vessel Disease	**4213 (47.8)**	**36 (9.5)**	**4249 (46.2)**	**<0.001**
Large Vessel Disease	**1772 (20.1)**	**141 (37.1)**	**1913 (20.8)**	
Cardio-Embolic	**1744 (19.8)**	**137 (36.1)**	**1881 (20.5)**	
Stroke of Determined Etiology	**612 (6.9)**	**31 (8.2)**	**643 (7.0)**	
Stroke of Undetermined Etiology	**476 (5.4)**	**35 (9.2)**	**511 (5.6)**	
Swallow Screen done before oral intake	**5820 (66.0)**	**197 (51.8)**	**6017 (65.4)**	**<0.001**
Speech therapy assessment done	**6024 (68.3)**	**161 (42.4)**	**6185 (67.3)**	**<0.001**
Speech Therapy assessment duration (hours)	**31.7±309.7**	**77.9±694.32**	**32.85±325.45**	**0.07**
Antibiotics given	**626 (7.1)**	**361 (95.0)**	**987 (10.7)**	**<0.001**

Abbreviations: BMI, Body Mass Index; ED, emergency department; HDL, High density lipoprotein; ICU, intensive care unit; LDL, Low density lipoprotein; MACE, major adverse cardiac event; mRS, Modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; RBS, Random blood sugar

[a]p-value reported based on Pearson-Chi Square Test

Values are reported as mean ± standard deviation and n(%)

Table 2. Characteristics and outcome of acute ischemic stroke patients with aspiration pneumonia based on their NIHSS admission

Characteristic or Investigation	No Pneumonia (n=8817, 95.9%)	Aspiration Pneumonia (n= 380, 4.1%)	Total (n= 9197)	P-Value
NIHSS Severity				
Mild Stroke (NIHSS 0-4)	5570 (63.2)	56 (14.7)	5626 (61.2)	<0.001
Moderate Stroke (NIHSS 5-9)	1906 (21.6)	59 (15.5)	1965(21.4)	
Severe Stroke (NIHSS 10 or more)	1341 (15.2)	265 (69.7)	1606 (17.5)	
NIHSS (5-9)				
90-Days Mortality	36 (1.9)	10 (16.9)	46 (2.3)	<0.001
MACE at 1 year	72 (3.8)	14 (23.7)	86 (4.4)	<0.001
Admission Location				
Stroke Ward	1281 (67.2)	35 (59.3)	1316 (67.0)	
Medicine Ward	250 (13.1)	10 (16.9)	45 (13.2)	0.31
Duration of ED Stay Category[a]				
<4 hours	249 (13.1)	2 (3.4)	251 (12.8)	
4-8 hours	555 (29.1)	23 (39.0)	578 (29.4)	
>8 hours	750 (39.3)	26 (44.1)	776 (39.5)	0.052
Length of Stay	5.89±10.0	17.1±19.4	6.23±10.5	<0.001
Prognosis – At Discharge				
Good (mRS 0–2)	814 (42.7)	4 (6.8)	818 (41.6)	<0.001
Poor (mRS 3-6)	1092 (57.3)	55 (93.2)	1147 (58.4)	
Prognosis – At 90 Days				
Good (mRS 0–2)	876 (46.0)	6 (10.2)	882 (44.9)	<0.001
Poor (mRS 3-6)	580 (30.4)	44 (74.6)	624 (31.8)	
Mortality at Discharge	9 (0.5)	7 (11.9)	16 (0.8)	<0.001
90 Days Mortality	36 (1.9)	10 (16.9)	46 (2.3)	<0.001
mRS at 90 Days[a]				
0	446 (23.4)	0 (0)	446 (22.7)	
1	212 (11.1)	3 (5.1)	215 (10.4)	
2	218 (11.4)	3 (5.1)	221 (11.2)	
3	325 (17.1)	6 (10.2)	331 (16.8)	<0.001
4	160 (8.4)	10 (16.9)	170 (8.7)	
5	59 (3.1)	18 (30.5)	77 (3.9)	
6	36 (1.9)	10 (16.9)	46 (2.3)	
NIHSS (>10)				
90-Days Mortality	185 (13.8)	59 (22.3)	244 (15.2)	0.003
MACE at 1 year	217 (16.2)	73 (27.5)	290 (18.1)	<0.001
Admission Location				
Stroke Ward	834 (62.2)	92 (34.7)	926 (57.7)	
Medicine Ward	166 (12.4)	40 (15.1)	206 (12.8)	<0.001
Duration of ED Stay Category[a]				
<4 hours	288 (21.5)	41 (15.5)	329 (20.5)	
4-8 hours	446 (33.3)	87 (32.8)	533 (33.2)	0.09
>8 hours	470 (35.0)	103 (38.9)	573 (35.7)	
Length of Stay	9.2±9.8	16.6±14.6	10.4±11.2	<0.001
Prognosis – At Discharge				
Good (mRS 0–2)	247 (18.4)	5 (1.9)	252 (15.7)	<0.001
Poor (mRS 3-6)	1094 (81.6)	260 (98.1)	1354 (84.3)	

Prognosis – At 90 Days				
Good (mRS 0–2)	**301 (22.4)**	**18 (6.8)**	**319 (19.9)**	**<0.001**
Poor (mRS 3-6)	**798 (59.5)**	**211 (79.6)**	**1009 (62.8)**	
Mortality at Discharge	**105 (7.8)**	**30 (11.3)**	**135 (8.4)**	**0.07**
90 Days Mortality	**185 (13.8)**	**59 (22.3)**	**244 (15.2)**	**<0.001**
mRS at 90 Days[a]				
0	**132 (9.8)**	**5 (1.9)**	**137 (8.5)**	**<0.001**
1	**72 (5.4)**	**3 (1.1)**	**75 (4.7)**	
2	**97 (7.2)**	**10 (3.8)**	**107 (6.7)**	
3	**219 (16.3)**	**18 (6.8)**	**237 (14.8)**	
4	**223 (16.6)**	**46 (17.4)**	**269 (16.7)**	
5	**171 (12.8)**	**88 (33.2)**	**259 (16.1)**	
6	**185 (13.8)**	**59 (22.3)**	**244 (15.2)**	

Abbreviations: ED, emergency department; NIHSS, National Institute of Heath Stroke Scale; MACE, major adverse cardiovascular event; mRS, modified Rankin Scale.

Table 3. Bivariate and Multivariate logistic regression analysis to identify the risk factors associated with aspiration pneumonia.

Determinants			*Bivariate logistic regression analysis*			*Multivariate logistic regression analysis*		
	No Pneumonia	**Aspiration Pneumonia**	**Standardized Beta**	**Odds ratio (95% CI)**	**p-value**	**Standardized Beta**	**Odds ratio (95% CI)**	**p-value**
Age	55.3 ± 13.4	59.0 ± 15.6	0.021	1.02 (1.01–1.03)	<.001	0.01	1.02 (1.01–1.03)	0.002
Sex								
Female	1776 (95.8)	77 (4.2)	-	1	-		1	-
Male	7041 (95.9)	303 (4.1)	-0.007	0.99 (0.77–1.28)	0.95	0.446	1.56 (1.05–2.32)	0.03
TOAST								
SVD	4213 (99.2)	36 (0.8)	-	1	-		1	-
LVD	1772 (92.6)	141 (7.4)	2.231	9.31 (6.43–13.48)	<.001	1.43	4.11 (2.52–6.69)	<.001
CE	1744 (92.7)	137 (7.3)	2.218	9.19 (6.34–13.33)	<.001	1.396	3.69 (2.23–6.12)	<.001
SDA	612 (95.2)	31 (4.8)	1.780	5.93 (3.64–9.65)	<.001	1.179	3.25 (1.75–6.03)	<.001
SUD	476 (93.2)	35 (6.8)	2.152	8.61 (5.35–13.83)	<.001	1.428	4.09 (1.98–8.46)	<.001
Mode of transport								
From Other Hospitals	372 (96.1)	15 (3.9)	-	1	-		1	-
EMS	6073 (95.5)	288 (4.5)	0.162	1.18 (0.69–2.00)	0.55	0.184	1.20 (0.55–2.64)	0.65
Non-Medical	2200 (98.5)	34 (1.5)	-0.959	0.38 (0.21–0.71)	0.00	0.032	1.03 (0.43–2.47)	0.94
Onset Duration								

<4.5 hours	2822 (94.3)	169 (5.7)	-	1	-		1	-
4.5-24 hours	3890 (96.4)	145 (3.6)	-0.177	0.84 (0.67–1.05)	<.001	0.116	1.06 (0.68–1.65)	0.79
>24 hours	3105 (97.9)	66 (2.1)	-1.036	0.36 (0.27–0.47)	<.001	0.061	1.15 (0.82–1.61)	0.43
Duration in ER								
<4 hours	809 (94.2)	50 (5.8)	-	1	-		1	-
4-8 hours	1711 (93.3)	122 (6.7)	0.143	1.15 (0.82–1.62)	0.41	0.311	1.41 (0.90–2.20)	0.13
>8 hours	2749 (94.8)	151 (5.2)	-0.118	0.89 (0.64–1.24)	0.48	0.211	1.24 (0.80–1.93)	0.34
NIHSS								
Mild Stroke (0-4)	5570 (99.0)	56 (1.0)	-	1	-		1	-
Moderate Stroke (5-14)	1906 (97.0)	59 (3.0)	1.125	3.08 (2.13–4.45)	<.001	0.625	1.87 (1.19–2.94)	0.01
Severe Stroke (>10)	1341 (83.5)	265 (16.5)	2.978	19.66 (14.64–26.38)	<.001	1.788	5.98 (3.92–9.11)	<.001
Admission Location								
Stroke Ward	3819 (96.3)	147 (3.7)	-	1	-		1	-
Medicine Ward	1248 (94.7)	70 (5.3)	0.377	1.46 (1.09–1.95)	0.01	0.412	1.56 (1.05–2.31)	0.03

Abbreviations: CE, cardioembolic stroke; CI, confidence interval; EMS, emergency medical services; ER, emergency room; LVD, large vessel disease; NIHSS, National Institute of Health Stroke Scale; SDA, stroke of determined etiology; SVD, small vessel disease; SUD, stroke of undetermined etiology.

Figure 1. Proportion of aspiration pneumonia between stroke ward vs. medicine ward

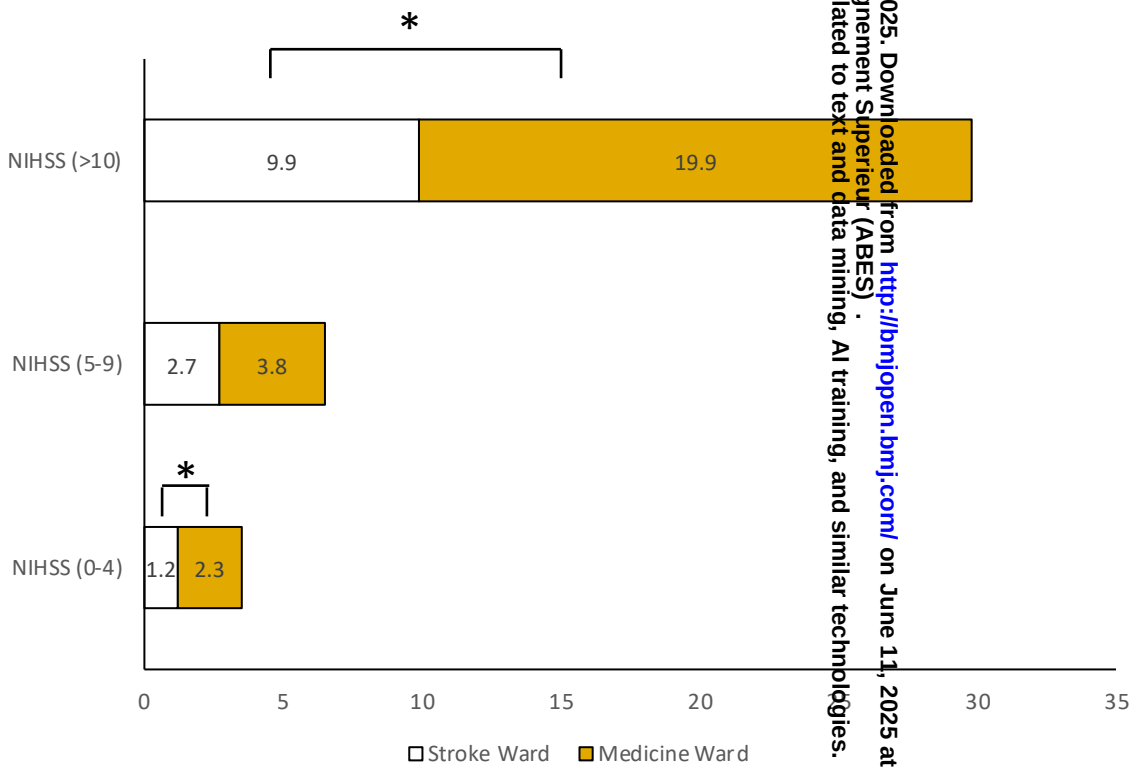
*$p \leq 0.05$

Figure 2. Proportion of mRS at 90 days for patients with an NIHSS of 5-9

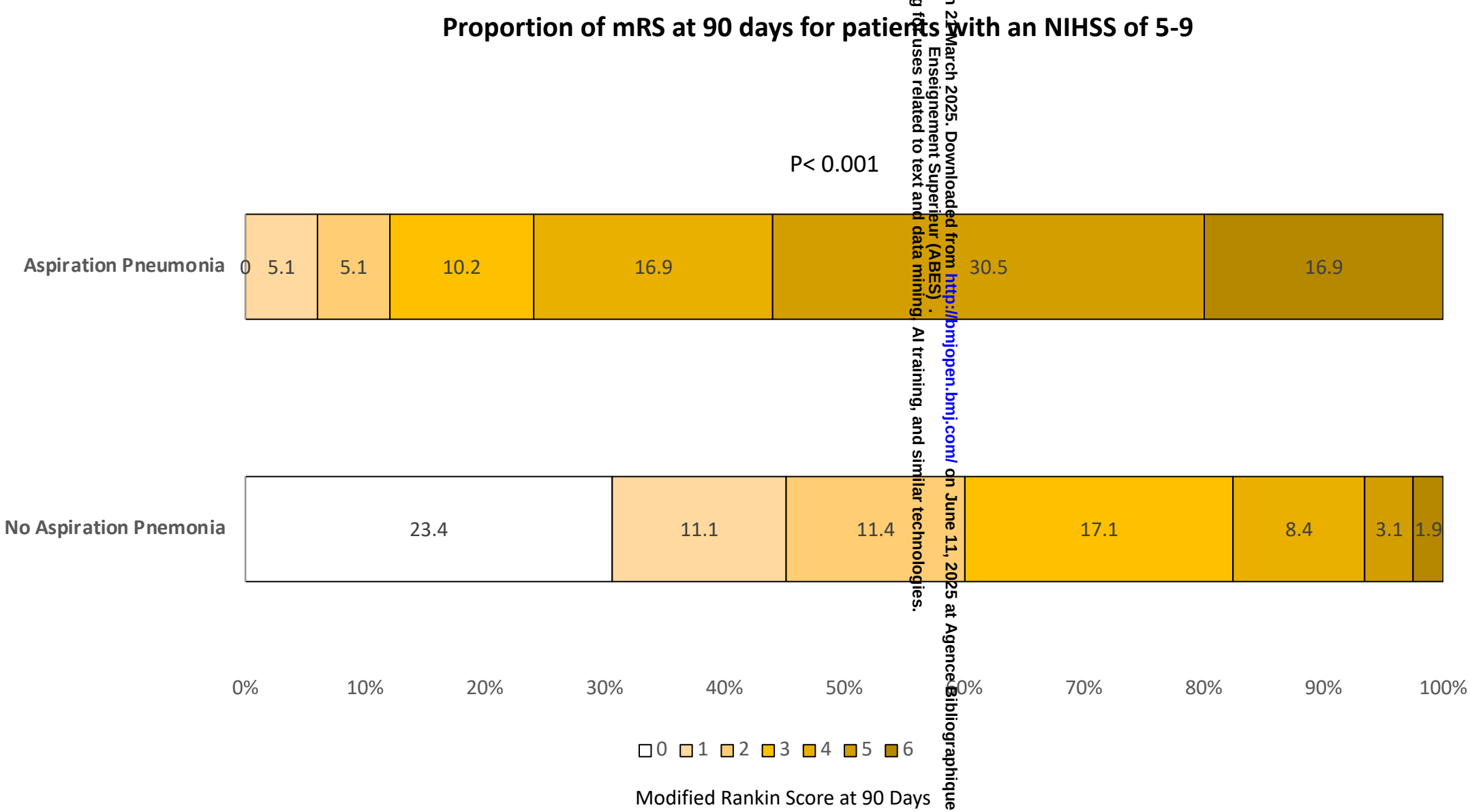
Figure 3. Proportion of mRS at 90 days for patients with an NIHSS of >10

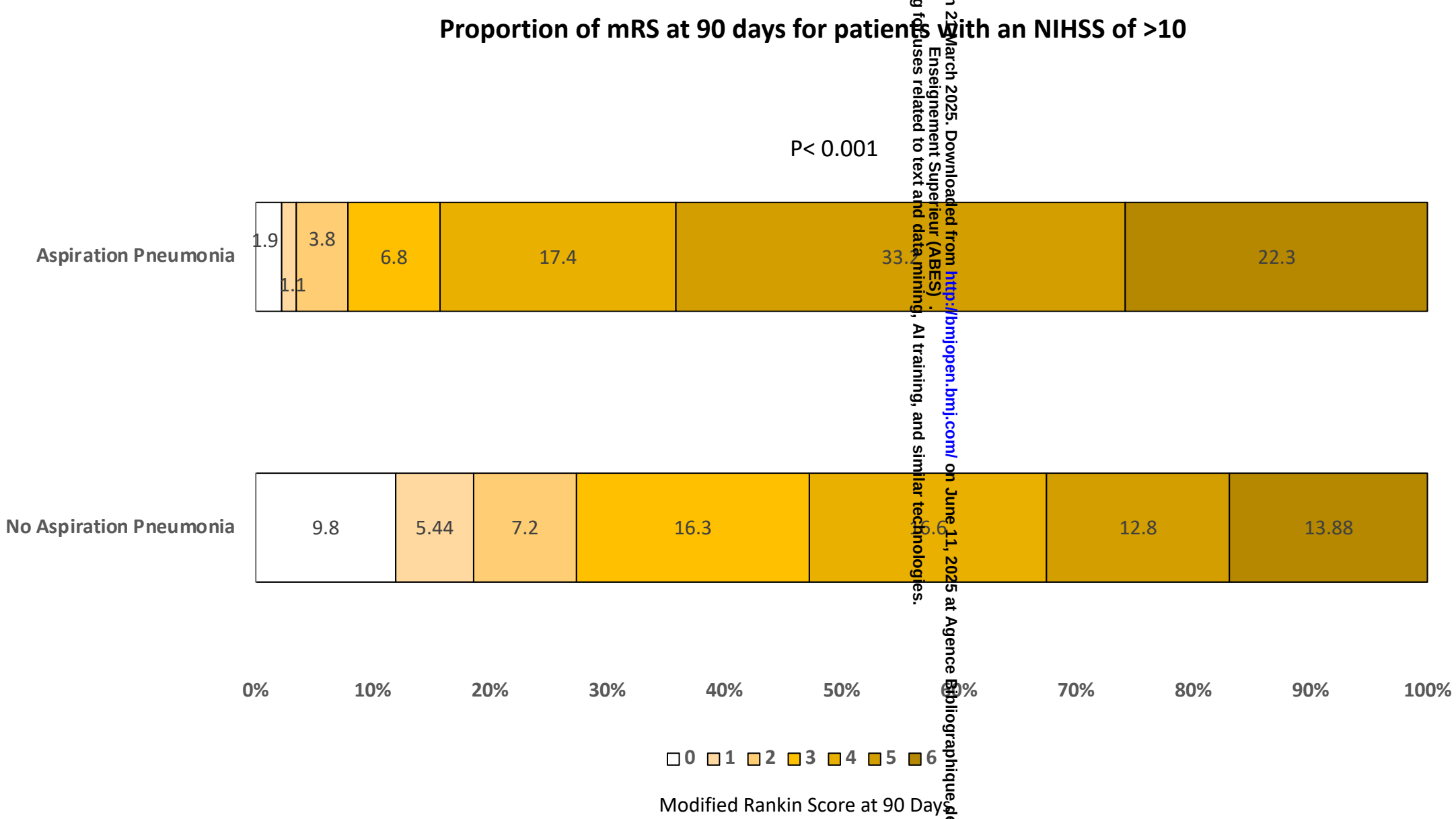
Figure 4. Forest Plot based on the results of multivariate analysis of the factors associated with aspiration pneumonia.

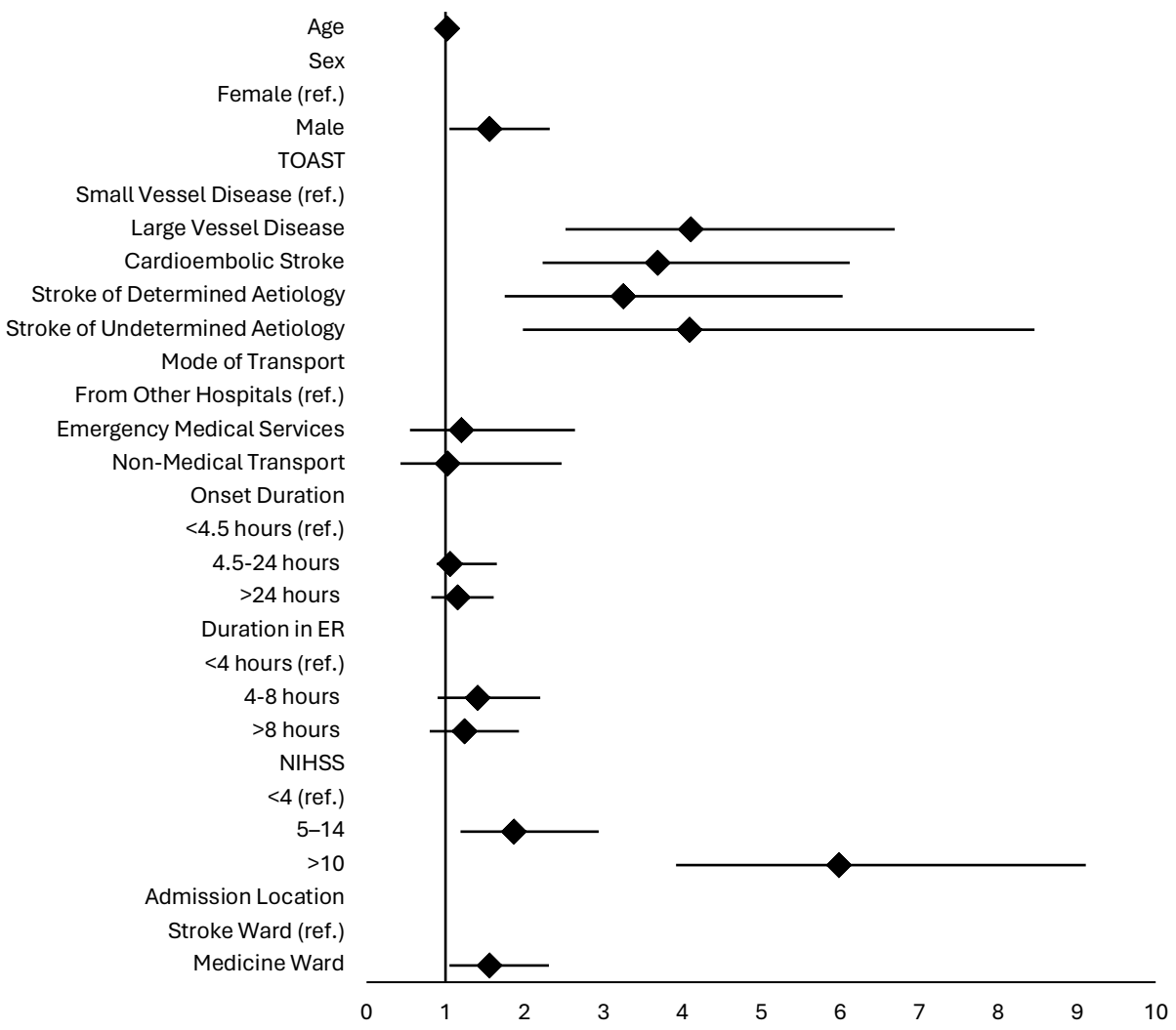
Abbreviations: CI, confidence interval; OR, odds ratio.



Proportion of aspiration pneumonia between stroke ward vs. medicine ward
*p≤0.05







Adjusted OR(95% CI)

1.02 (1.01–1.03), p=0.002

1.56 (1.05–2.32), p=0.03

4.1 (2.52–6.69), p<0.001

3.7 (2.23–6.12), p<0.001

3.2 (1.75–6.03), p<0.001

4.09 (1.98–8.46), p<0.001

1.20 (0.55–2.64), p=0.65

1.03 (0.43–2.47), p=0.94

1.06 (0.68–1.65), p=0.79

1.15 (0.82–1.61), p=0.43

1.41 (0.90–2.20), p=0.13

1.24 (0.80–1.93), p=0.34

1.87 (1.19–2.94), p=0.01

5.98 (3.92–9.11), p<0.001

1.56 (1.05–2.31), p=0.03

	Overall	No Pneumonia	Aspiration Pneumonia	Overall Significance	SVD vs. LVD[1]	SVD vs. CE[1]	SVD vs. SDA[1]	SVD vs. SUD[1]	LVD vs. CE[1]	LVD vs. SDA[1]	LVD vs. SUD[1]	CE vs. SDA[1]	CE vs. SUD[1]	SDA vs. SUD[1]
TOAST				<.001	<.001	<.001	<.001	<.001	1.00	0.25	1.00	0.06	1.00	0.82
Small vessel disease	4249 (46.2)	4213 (99.2)	36 (0.8)	–	–	–	–	–	–		–	–	–	–
Large vessel disease	1913 (20.8)	1772 (92.6)	141 (7.4)	–	–	–	–	–	–		–	–	–	–
Cardioembolic	1881 (20.5)	1744 (92.7)	137 (7.3)	–	–	–	–	–	–		–	–	–	–
Determined etiology	643 (7.0)	612 (95.2)	31 (4.8)	–	–	–	–	–	–		–	–	–	–
Undetermined etiology	511 (5.6)	476 (93.2)	35 (6.8)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**EMS vs. NM[1]**	**EMS vs. OH[1]**	**NM vs. OH[1]**							
Mode of transport				<.001	<.001	1.00	0.07							
EMS	6361 (69.2)	6073 (95.5)	288 (4.5)	–	–	–	–	–	–		–	–	–	–
Non-Medical	2234 (24.3)	2200 (98.5)	34 (1.5)	–	–	–	–	–	–		–	–	–	–
From Other Hospitals	387 (4.2)	372 (96.1)	15 (3.9)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**<4.5 hours vs. 4.5-24 hours[1]**	**<4.5 hours vs. >24 hours[1]**	**4.5-24 hours vs. >24 hours[1]**							
Onset Duration				<.001	0.26	<.001	<.001							
<4.5 hours	2991 (32.5)	2822 (94.3)	169 (5.7)	–	–	–	–	–	–		–	–	–	–
4.5-24 hours	3035 (33.0)	2890 (95.2)	145 (4.8)	–	–	–	–	–	–		–	–	–	–
>24 hours	3171 (34.5)	3105 (97.9)	66 (2.1)	–	–	–	–	–	–		–	–	–	–
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**<4 hours**	**<4 hours vs. >8**	**4-8 hours**							

					vs. 4-8 hours[1]	hours [1]	vs. >8 hours[1]							
Duration in ED				0.11	1.00	1.00	0.11							
<4 hours	859 (15.4)	809 (94.2)	50 (5.8)	–	–	–	–	–	–	–	–	–	–	
4-8 hours	1833 (32.8)	1711 (93.3)	122 (6.7)	–	–	–	–	–	–	–	–	–	–	
>8 hours	2900 (51.9)	2749 (94.8)	151 (5.2)	–	–	–	–	–	–	–	–	–	–	
	Overall	**No Pneumonia**	**Aspiration Pneumonia**	**Overall Significance**	**0-4 vs. 5-14[1]**	**0-4 vs. >15[1]**	**5-14 vs. >15[1]**							
NIHSS				<.001	<.001	<.001	<.001							
Mild Stroke (0-4)	5626 (61.2)	5570 (99.0)	56 (1.0)	–	–	–	–	–	–	–	–	–	–	
Moderate Stroke (5-9)	1965 (21.4)	1906 (97.0)	59 (3.0)	–	–	–	–	–	–	–	–	–	–	
Severe Stroke (>10)	1606 (17.5)	1341 (83.5)	265 (16.5)	–	–	–	–	–	–	–	–	–	–	

Table S1. Clinical characteristics among patients with aspiration pneumonia versus those without aspiration pneumonia

[1] Bonferroni corrections have been applied to the p-values reported

Abbreviations: CE, cardioembolic; EMS, emergency medical service; LVD, large vessel disease; NM, non-medical; OH, other hospitals; SDA, stroke of determined etiology; SUD, stroke of undetermined etiology; SVD, small vessel disease.

NIHSS	No Pneumonia	Aspiration Pneumonia	Stroke Ward vs. Medicine Ward
Mild Stroke (0-4)			
Admission Location			
Stroke Ward	1704 (98.8)	20 (1.2)	0.03*
Medicine Ward	832 (97.7)	20 (2.3)	
Moderate Stoke (5-9)			
Admission Location			
Stroke Ward	1281 (97.3)	35 (2.7)	0.31
Medicine Ward	250 (96.2)	10 (3.8)	
Severe Stroke (>10)			
Admission Location			
Stroke Ward	834 (90.1)	92 (9.9)	<.001*
Medicine Ward	166 (80.1)	40 (19.9)	

Abbreviations: NIHSS, National Institute of Health Stroke Scale.
*p≤0.05

Table S2. Comparison of NIHSS score and admission location among patients with aspiration pneumonia versus those without aspiration pneumonia using Fisher's Exact Test