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Original Article

Dysphagia and risk of aspiration pneumonia: A nonrandomized, pair-matched cohort study

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Abstract *Background/purpose:* Dysphagia was associated with increased prevalence of aspiration pneumonia (AP) in studies that were criticized for either their small sample size or lack of prospective design. Using a considerably larger nationwide, population-based database and a long-term prospective cohort design, our study aimed to explore the relationship between dysphagia and the subsequent development of AP.
Materials and methods: From 2000 to 2009, we gathered a study cohort consisting of 6979 newly diagnosed cases of dysphagia from Taiwan's National Health Insurance Research Database. For the control group, another 20,937 individuals without dysphagia were matched for age, sex, and comorbidity. The two cohorts were followed-up to observe the occurrence of AP and correlated mortality.
Results: During an average of 3.88 ± 2.73 years of follow-up, we observed 315 cases of new AP [non-dysphagia (193, 0.92%) vs. dysphagia (122, 1.75%), $p < 0.0001$], and the incidence of AP was significant in the dysphagia group. After adjusting for age, sex, and comorbidity, dysphagia-related AP [hazard ratio (HR) 2.499; 95% confidence interval (CI), 2.089–2.99; $p < 0.0001$], dysphagia related mortality [HR 3.229; 95% CI, 3.052–3.417; $p < 0.0001$], and many other systemic diseases were independently associated with a diagnosis of AP.

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Conclusion: Dysphagia was highly associated with an increased risk of AP according to data derived from a large nationwide cohort database. Nonetheless, larger prospective studies or meta-analyses are recommended to confirm our findings.

Introduction

Dysphagia is a common disorder in elderly people and is characterized by difficulty swallowing. Dysphagia occurs in approximately 3% of the general population, equally affecting both genders in the elderly population of the US.[1] Dysphagia is associated with a variety of systemic diseases, including cerebrovascular accidents and malignancies.[2] Aspiration pneumonia (AP), a catastrophic illness often presenting as acute respiratory compromise in elderly people, shares some common risk factors with dysphagia based on studies showing a high prevalence of dysphagia in patients with AP. Although taken as indicating a possible link between dysphagia and AP, these studies have been criticized for their limited sample size and lack of data from a prospective cohort.

Hypothesizing that dysphagia may contribute independently to the development of AP, we used a nationwide database to conduct a nonrandomized, pair-matched cohort study to investigate the relationship between dysphagia and subsequent development of AP, and even more importantly, mortality.

Materials and methods

The Taiwan National Health Insurance Research Database (NHIRD)

We conducted a cohort study using Taiwan's National Health Insurance Research Database (NHIRD), released by the Taiwan National Health Research Institutes. The National Health Insurance (NHI) system is a mandatory universal health insurance program that offers comprehensive medical care coverage to all residents of Taiwan. The present study was conducted using the NHIRD data set, which contains medical claim records, including coverage for outpatient and emergency department visits, hospitalization, and prescription drugs. The present study was approved by the Institutional Review Board of Taipei Veterans General Hospital (IRB-TPEVGH No.:2018-12-008BC). A cohort data set comprising 1,000,000 randomly sampled people who were alive since the year 2000 were used. This data set has been confirmed by National Health Research Institutes to be representative of the Taiwanese population.

Patient selection and definition

The study population was identified as patients who, from January 1, 2000, to December 31, 2009, had been diagnosed as having dysphagia by ICD-9-CM coding (438.82, 787.2, and 280.8) or NHI treatment coding (54032C) indicating simple swallow therapy. The date of first dysphagia diagnosis in the dataset was recorded as the index date. To avoid significant discrepancies in disease severity, the control subjects were matched with cases by age, gender, cohort entry date and Charlson Comorbidity Index (CCI), a method of classifying prognostic comorbidity in longitudinal studies that has been used in our previous work.[3] Patients with an enrolled age younger than 20 years old or with aspiration pneumonia diagnosed before January 1st, 2001 were excluded from this study. The flowchart of patient enrollment is illustrated in Fig. 1.

Outcome selection and study design

The primary end point was aspiration pneumonia identified according to ICD-9-CM coding (481, 482.0, and 483.0) during hospitalization and overall mortality, defined as a death record in NHIRD from any cause. The secondary endpoints were the comorbidities percentage change, including myocardial infarction (ICD-9-CM codes 410.xx — 412.xx), congestive heart failure (ICD-9-CM code 428.x), Peripheral vascular disease & aneurysm (ICD-9-CM codes 441.xx — 444.xx), cerebrovascular disease (ICD-9-CM codes 433.xx — 437.xx), dementia, chronic obstructive pulmonary disease (COPD, ICD-9-CM codes 491.xx, 494.xx, 492.xx, and 496.xx), connective tissue disease (ICD-9-CM code 710.x), peptic ulcer disease (ICD-9-CM code 533.xx), liver disease (ICD-9-CM codes 570.x, 571.x, 573.x), diabetes with organ damage (ICD-9-CM codes 250.4x — 250.9x), hemiplegia (ICD-9-CM code 342.xx), severe chronic kidney disease (ICD-9-CM code 585), and solid tumor with or without metastasis (ICD-9-CM codes 140.xx — 239.xx). All patients were followed until they either reached the study end-point or reached the end of the study follow-up.

Statistical analysis

The Statistical Package for Social Sciences software for Windows version 17.0 (SPSS, Inc., Chicago, IL) was used in our study for data analysis. Analysis of variance was performed to determine whether there were significant differences in age, gender, medical diseases, and medication prescriptions. Cox proportional hazard regression analysis was then conducted to evaluate the impact of dysphagia on outcomes including aspiration pneumonia and total mortality after adjusting for age, gender, underling comorbidities and medications. Statistical significance was established by a two-sided P value less than 0.05.

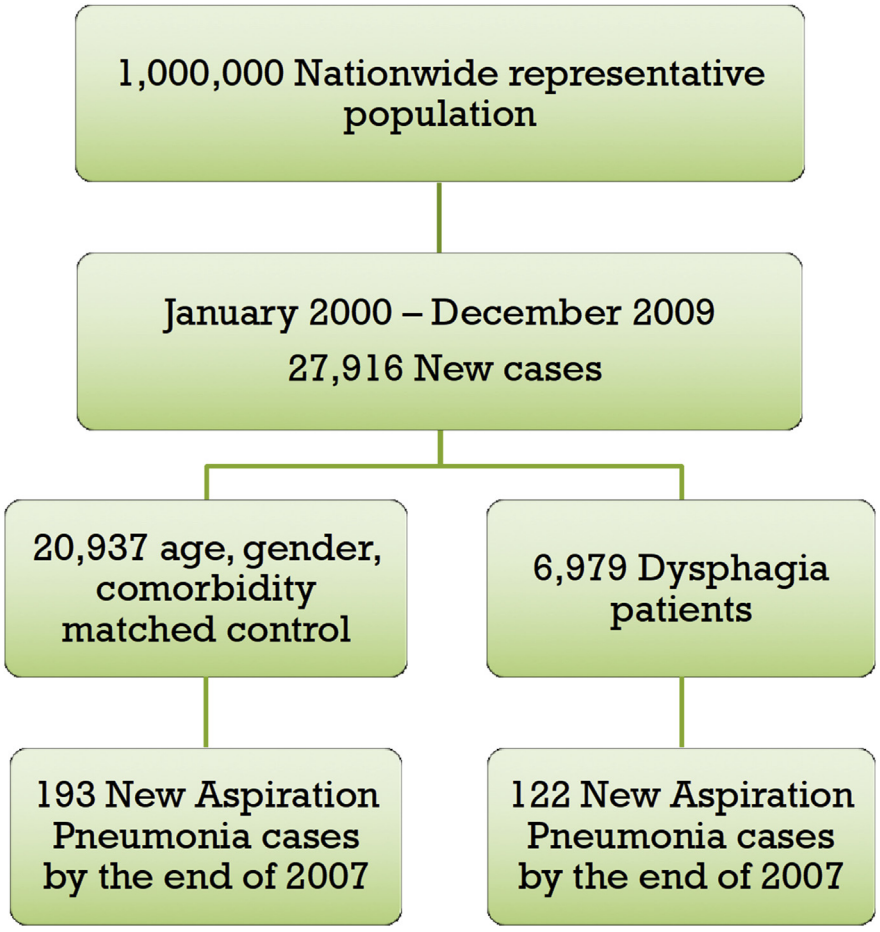

Figure 1 Flowchart illustrating the follow-up of dysphagia patients and matched controls.

Table 1 Baseline characteristics of the study population.

	Dysphagia		P
	No (n = 20,937)	Yes (n = 6979)	
Age (y)	57.82 ± 18.7321	57.95 ± 18.7436	0.0598
Male	10,445 (49.89%)	3465 (49.65%)	0.730
Myocardial infarction	445 (2.13%)	175 (2.51%)	0.061
Congestive heart failure	923 (4.41%)	351 (5.03%)	0.031
Peripheral vascular disease & aneurysm	69 (0.33%)	25 (0.36%)	0.720
CVA: Ischemic	1202 (5.74%)	1012 (14.50%)	<0.0001
Dementia	401 (1.92%)	293 (4.20%)	<0.0001
COPD	3095 (14.78%)	1153 (16.52%)	0.001
Connective tissue disease	195 (0.93%)	50 (0.72%)	0.096
Peptic ulcer	665 (3.18%)	219 (3.14%)	0.875
Liver disease	2656 (12.69%)	560 (8.02%)	<0.0001
DM without organ damage	3531 (16.86%)	1048 (15.02%)	0.000
Hemiplegia	185 (0.88%)	277 (3.97%)	<0.0001
CKD	638 (3.05%)	182 (2.61%)	0.060
DM with organ damage	2123 (10.14%)	558 (8.00%)	<0.0001
Tumor without metastasis, leukemia, lymphoma	3429 (16.38%)	1052 (15.07%)	0.010
Metastatic solid tumor	295 (1.41%)	167 (2.39%)	<0.0001
AIDS	8 (0.04%)	4 (0.06%)	0.505
Aspiration pneumonia	193 (0.92%)	122 (1.75%)	<0.0001

Data are presented as n (%) or mean ± standard deviation. Student t test and X^2 tests were used for continuous variables and categorical variables, respectively. CVA = cerebral vascular accident; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; CKD = chronic kidney disease; AIDS = acquired immune deficiency syndrome.

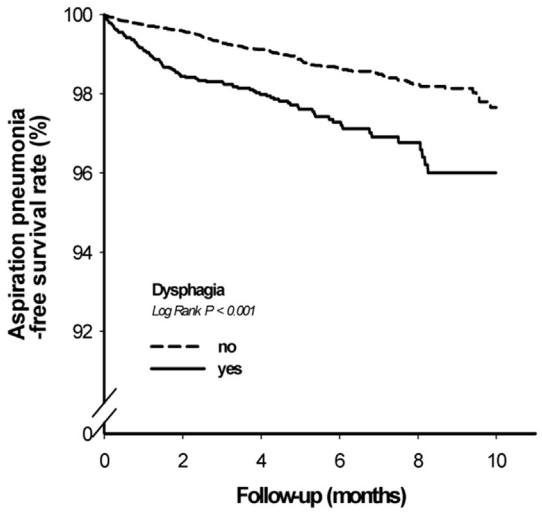

Figure 2 Kaplan-Meier estimates of aspiration pneumonia -free survival rate in patients categorized with dysphagia. The event-free survival rates were significant in the two groups ($p < 0.001$).

Results

A total of 6979 newly diagnosed dysphagia patients (mean age, 57.95 ± 18.74 years) were identified from the 1,000,000 sampled cohort database between January 2000 and December 2009. Another 20,937 patients without dysphagia (mean age, 57.82 ± 18.73 years) were matched for age, gender, and comorbidity to serve as the control group. The demographic parameters of the study participants are listed in Table 1.

During an average follow-up period of 3.88 ± 2.73 years, there was significant difference in the incidence of AP among dysphagia patients compared with that of the control group [1.75% vs. 0.92%, $p < 0.0001$]. Fig. 2 outlines the results of a Kaplan-Meier analysis and the long-rank test, showing that patients with dysphagia had significant difference in AP incidence compared to patients without dysphagia ($p < 0.001$). A comparison of patients with and without AP is shown in Table 2. Patients with AP were of similar ages, were more likely to be male and were more likely to have myocardial infarction, congestive heart failure, peripheral vascular disease and aneurysm (PAOD), ischemic cerebral vascular attack (CVA), dementia, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM) with organ damage, or metastatic solid tumor. As seen in Table 2, there was a significant difference in the incidence of mortality among AP patients compared with that of the control group [47.30% vs. 15.64%, $p < 0.0001$]. We also observed a significant difference in the incidence of mortality among dysphagia patients compared with that of the control group [23.83% vs. 13.39%]. Fig. 3 outlines the results of a Kaplan-Meier analysis and the long-rank test, showing that patients with dysphagia had a significant difference in mortality incidence compared to patients without dysphagia ($p < 0.001$).

A Cox proportional hazard regression model was used to determine the factors independently associated with the development of AP and consequent mortality. After adjusting for age, gender, and the above comorbidity, congestive heart failure, PAOD, connectice tissue disease,

Table 2 Baseline characteristics of the study population.

	Aspiration pneumonia		P
	No (n = 27,601)	Yes (n = 315)	
Age (y)	57.8 ± 18.7291	57.95 ± 18.7436	<0.0001
Male	13,723 (49.72%)	187 (59.37%)	0.001
Myocardial infarction	600 (2.17%)	20 (6.35%)	<0.0001
Congestive heart failure	1247 (4.52%)	27 (8.57%)	0.001
Peripheral vascular disease & aneurysm	89 (0.32%)	5 (1.59%)	0.000
CVA: Ischemic	2150 (7.79%)	64 (20.32%)	<0.0001
Dementia	675 (2.45%)	19 (6.03%)	<0.0001
COPD	4142 (15.01%)	106 (33.65%)	<0.0001
Connective tissue disease	241 (0.87%)	4 (1.27%)	0.453
Peptic ulcer	876 (3.17%)	8 (2.54%)	0.523
Liver disease	3172 (11.49%)	44 (13.97%)	0.171
DM without organ damage	4503 (16.31%)	76 (24.13%)	0.000
Hemiplegia	448 (1.62%)	14 (4.44%)	<0.0001
CKD	803 (2.91%)	17 (5.40%)	0.009
DM with organ damage	2633 (9.54%)	48 (15.24%)	0.001
Tumor without metastasis, leukemia, lymphoma	4422 (16.02%)	59 (18.73%)	0.193
Metastatic solid tumor	450 (1.63%)	12 (3.81%)	0.003
AIDS	12 (0.04%)	0 (0.00%)	0.003
Dysphagia	6857 (24.84%)	122 (38.753%)	<0.0001
Mortality	4317 (15.64%)	149 (47.30%)	<0.0001

Data are presented as n (%) or mean ± standard deviation. Student t test and X^2 tests were used for continuous variables and categorical variables, respectively. CVA = cerebral vascular accident; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; CKD = chronic kidney disease; AIDS = acquired immune deficiency syndrome.

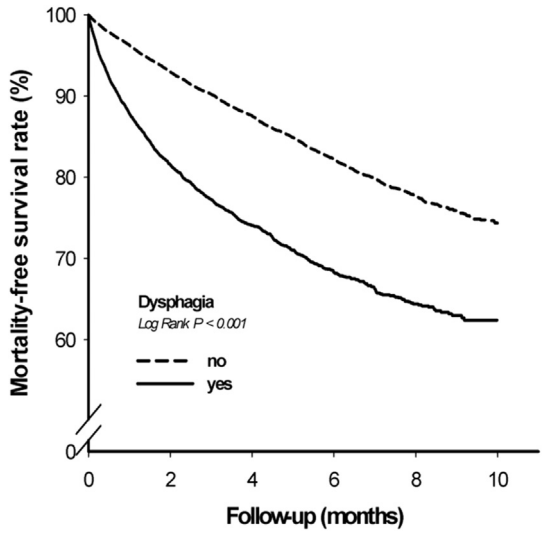

Figure 3 Kaplan-Meier estimates of survival free mortality events in patients categorized with dysphagia. The event-free survival rates were significant in the two groups ($p < 0.001$).

peptic ulcer, hemiplegia, and metastatic solid tumor were independently associated with the development of AP after dysphagia happened. And only hemiplegia was independently associated with the development of mortality after dysphagia occurred (Figs. 4 and 5).

Discussion

Using a large nationwide database, we found that dysphagia was associated with future risk of AP. In the Taiwanese general population, the incidence of aspiration pneumonia was 1.13% (non-dysphagia: 0.92%, dysphagia: 1.75%). This incidence is lower than the 3% seen for the United States population. The reason could be the high prevalence of nasogastric intubation and feeding gastrostomy rates in Taiwan.[4] Furthermore, our study that confirmed male gender, myocardial infarction, congestive heart failure, peripheral vascular disease and aneurysm, ischemic CVA, dementia, COPD, DM with or without organ damage, hemiplegia, CKD, metastatic solid tumor, and AIDS were independent predictors for AP events, consistent with the results of previous studies.[5–9] All these systemic diseases will induce varying degrees of disability. Subsequent muscle

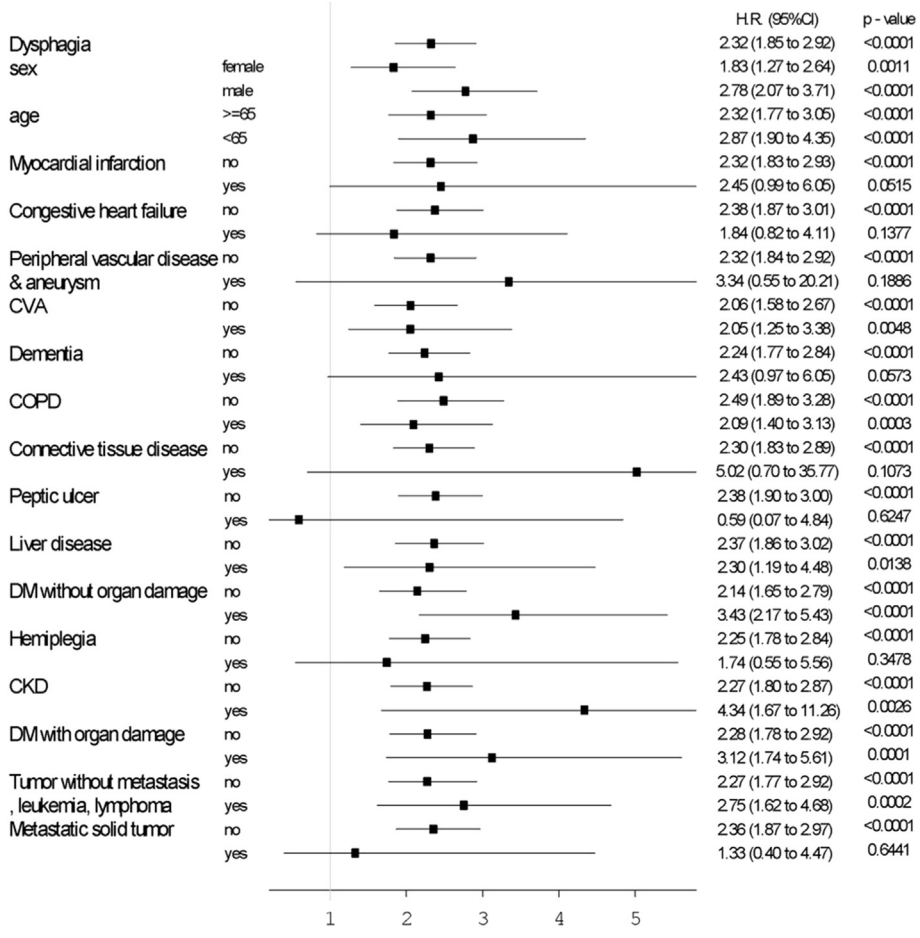

Figure 4 Hazard ratios, with 95% confidence intervals, for aspiration pneumonia events, according to prespecified dysphagia subgroups. CVA = cerebral vascular accident; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; CKD = chronic kidney disease.

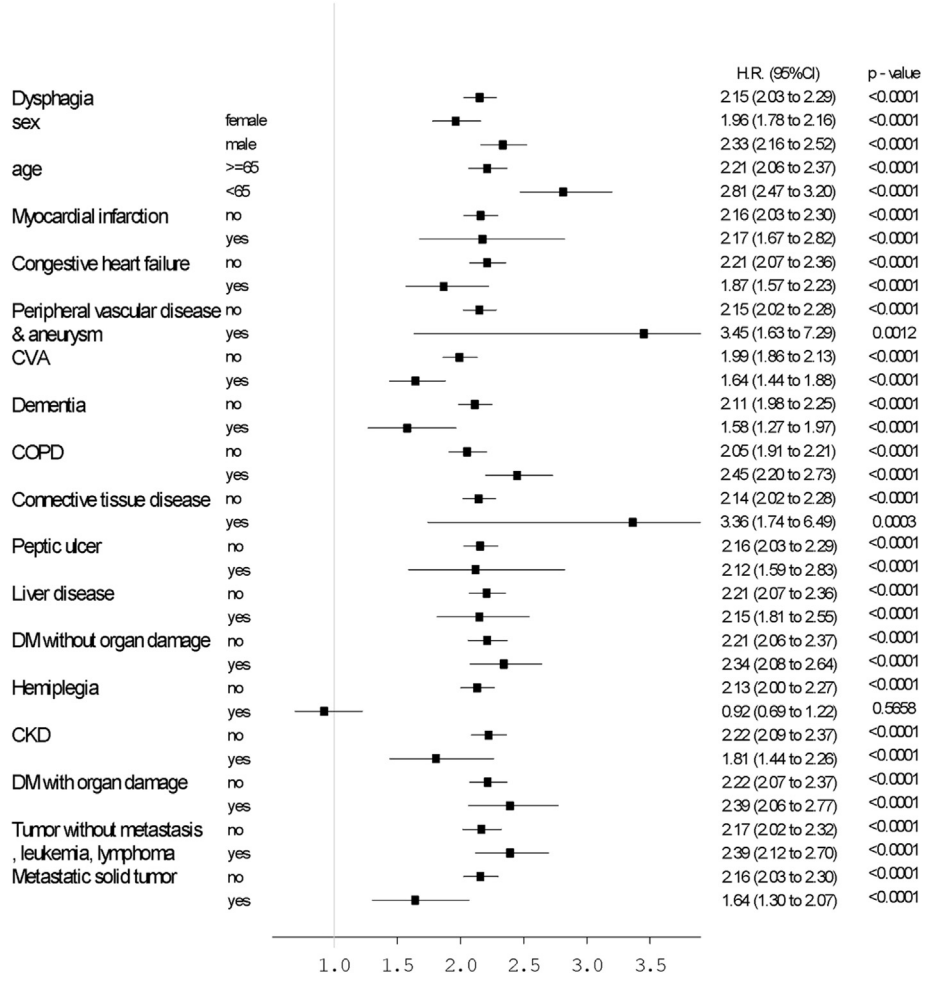

Figure 5 Hazard ratios, with 95% confidence intervals, for mortality events, according to prespecified dysphagia subgroups. CVA = cerebral vascular accident; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; CKD = chronic kidney disease.

weakness and sarcopenia happen thereafter. Muscle weakness and sarcopenia are now known to contribute to oropharyngeal dysphagia (OD).[10] Maeda et al. found that low muscle mass induced aspiration pneumonia and even mortality after 90 days of AP diagnosis.[8] In particular, the risk of AP associated with poor nutrition, and the mortality from aspiration pneumonia can be improved after adequate nutritional support.[11] These studies provide important insights into the current awareness of dysphagia, associated factors, and nutritional strategies.

An association between dysphagia and AP has been reported in clinical observations. Poor swallowing function is known to be related to aging, head and neck irradiation, myopathies, stroke, and neuromuscular disease.[5,6,12–14] Dysphagia is a major healthcare problem, as it increases the risk of malnutrition, dehydration, aspiration pneumonia, and death.[11] Our findings correlate with the results of previous studies.[10]

Using a nationwide cohort study, our study confirmed that male gender, myocardial infarction, congestive heart failure, PAOD, ischemic CVA, dementia, COPD, DM with organ damage, or metastatic solid tumor were important risk factors for developing AP, as previously reported.[9,15–17]

The main strength of our study was use of a nationwide population-based database that can be used to trace nearly all cases of dysphagia and AP in Taiwan over the study period, as all ENT doctors and chest specialists' practices are covered in our insurance system. Additionally, the large sample size and cohort study design with controls afforded considerable statistical power for detecting real differences between the two cohorts, including subtle ones.

There were some limitations of this study worth noting. Importantly, diagnoses of dysphagia and AP that rely on administrative claims data registered by physicians or hospitals may be less accurate than diagnoses made according to standardized criteria. However, AP is always a serious condition in elderly people and is usually diagnosed at a hospital with imaging and blood studies. Therefore, these diagnoses should be correct. In addition, because AP was identified through ICD codes in an insurance claims database, it is possible that the incidence of AP may have been underestimated. However, the incidence of AP found in our study was consistent with that of previously reported

cases, suggesting that our identification of AP was reliable. Additionally, some personal information was not available in the administrative data used, including bed-ridden status, swallowing efficiency, and chewing capacity.

In conclusion, using a large nationwide database, we showed that dysphagia was associated with a great risk of aspiration pneumonia. Furthermore, our study confirmed that male gender, myocardial infarction, congestive heart failure, PAOD, ischemic CVA, dementia, COPD, DM with organ damage, and metastatic solid tumor were independent predictors for AP, consistent with the results of previous studies. Larger prospective studies or meta-analyses are recommended to confirm our findings.

Declarations of interest

The authors have no conflicts of interest to declare.

Acknowledgments

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