

THE RISK OF ISCHEMIC STROKE IN PATIENTS WITH BRONCHIECTASIS

Battsetseg Turbat¹, Hsuan-Hung Lin², Wei-Sheng Chung³, Yung-Fu Chen^{1,4}

¹Department of Healthcare Administration, Central Taiwan University of Science and Technology, Taichung, Taiwan, ²Department of Management Information System, CTUST, Taichung, Taiwan, ³Department of Internal Medicine, Taichung Hospital, Ministry of Health and Welfare, Taichung, Taiwan, ⁴Department of Dental Technology and Materials Science, CTUST, Taichung, Taiwan e-mail: Jijee.promise20@gmail.com

Abstract

Background: Bronchiectasis is characterized by an irreversible dilatation of the bronchial tree caused by recurrent airway infection and inflammation. The association of atherosclerosis and inflammation is well established. However, studies on the relationship between bronchiectasis and ischemic stroke are scant. Therefore, we conducted a population-based cohort study to investigate the incidence and risk of ischemic stroke in patients with bronchiectasis.

Methods: Data of 1,295 patients newly diagnosed as bronchiectasis between 2000 and 2008 were retrieved from the Taiwan National Health Insurance Research Database. And then, a total of 6,475 controls without bronchiectasis were randomly selected from general population based on frequency-matched (1:5) age and sex. All participants were followed up to the date of occurred ischemic stroke, censoring, or the end of 2010. The patients with ischemic stroke were confirmed by computerized tomography (CT) examination. The Cox proportional hazard model was obtained to identify the risk of ischemic stroke in patients with bronchiectasis compared with those without bronchiectasis.

Results: The patients with bronchiectasis indicated a higher incidence rate of ischemic stroke (9.18 vs 4.66 per 1000 person years) than the patients without bronchiectasis, with an adjusted HR of 1.74 (95% CI= 1.28-2.35). The patients with bronchiectasis and comorbidities exhibited a 2.66-fold increased risk of ischemic stroke compared with those without either bronchiectasis or comorbidity (95% CI= 1.85-3.84). The patients with bronchiectasis exhibited a dose response risk of ischemic stroke according to the number of emergency visits and hospital admissions per year.

Conclusion: This longitudinal nationwide cohort study showed that the risk of ischemic stroke is significantly higher in patients with bronchiectasis,

especially comorbid with other diseases, than those without bronchiectasis. However, by considering the effect of comorbidity, bronchiectasis is not shown to be an

independent risk factors associated with the ischemic stroke. Furthermore, the risk of ischemic stroke showed dose response according to number of emergency visits and hospital admissions per year. Furthermore, the risk of ischemic stroke showed a dose response according to the annual number of emergency visits and hospital admissions.

Key words: bronchiectasis, ischemic stroke, comorbidity, cohort study

Introduction

Bronchiectasis is characterized by an irreversible dilatation of the bronchial tree caused by recurrent airway infection and inflammation. The diagnosis is generally confirmed by high resolution computed tomography (HRCT), which was shown to have a sensitivity as high as 97% (Goeminne et al., 2014). Chronic infection is one of the main roles in the development of bronchiectasis (Zaid et al., 2010). Respiratory symptoms, specifically those that are indicative of infection, are known to be associated with vascular events. Stroke is the rapid development of a focal neurologic deficit caused by a disruption of blood supply to the corresponding area of brain. In order to understand the association between bronchiectasis and ischemic stroke, the objective of this study was to determine the risk of ischemic stroke in patients with bronchiectasis.

Data source

Single-payer National Health Insurance (NHI) program started from March 1, 1995 in Taiwan. In 2015, more than 99.9% of Taiwan's citizens have enrolled in this program. The database has been used to study population-based public health issues, such as prevalence or incidence

of specific disease among the whole population.

Subjects

Data of patients with bronchiectasis (ICD-9-CM Code 494) confirmed by CT examination and with age ranging from 20 to 90 years old visiting healthcare centers (outpatients or inpatients) within 2000-2008 were retrieved for analysis.

Patients with ischemic stroke (ICD-9-CM Code 433-435) diagnosed before the index date were excluded.

Statistical analysis

SPSS 22.0 software (IBM.SPSS) was adopted for all statistical analyses⁸ such as Chi-square test, Cox proportional hazard regression and Kaplan-Meier analysis. We evaluated the overall, age-specific, and comorbidity-specific incidence of ischemic stroke in both bronchiectasis and non-bronchiectasis.

Results

The patients with bronchiectasis exhibited a higher incidence rate of ischemic stroke (9.18 vs 4.66 per 1000 person years) than those without bronchiectasis with a crude HR of 1.93 (95%

CI 1.43-2.61) and an adjusted HR of 1.74 (95% CI=1.28-2.35) after controlling for age, sex and comorbidities. The incidence rate of ischemic stroke increased with age and the male exhibited a higher incident rate in both cohorts. The risk of ischemic stroke of the bronchiectasis patients was significantly higher than non-bronchiectasis cohort in both male (Crude HR=1.98, 95% CI=1.32-2.97) and female (Crude HR=1.89, 95% CI=1.21-2.96). After adjusting for covariates, the risk of ischemic stroke was the higher in the patients aged 50- 65 years (Adjust HR=4.79, 95% CI=1.88-12.17) and over 65 years (Adjust HR=11.76, 95% CI=4.76-29.07) compared to the younger age group (<50 years old).

The bronchiectasis patients with comorbidities presented a higher incidence rate of ischemic stroke (12.43 vs 7.29 per 1000PY) than the non-bronchiectasis cohort with comorbidities (Crude HR=1.66, 95% CI=1.21-2.28). The patients with any types of comorbidities exhibited a 2.66-fold (95% CI=1.85-3.84) increased risk of ischemic stroke compared with those without comorbidity.

Table 1-Cox proportional hazard regression analysis for the risk of bronchiectasis-associated ischemic stroke with joint effect of individual comorbidity

Bronchiectasis	Comorbidity [‡]	Patient (N)	Ischemic Stroke (n)	Adjusted HR [†] (95% CI)	
Bronchiectasis	Hypertension				
No	No	4076	63		1(Reference)
No	Yes	2399	100	1.98	(1.43, 2.74)***
Yes	No	819	18	1.58	(0.94, 2.67)
Yes	Yes	476	40	4.46 (2.97	, 6.68)***
Bronchiectasis	Diabetes				
No	No	5457	107		1(Reference)
No	Yes	1018	56	2.36	(1.70, 3.26)***
Yes	No	1087	38	1.98	(1.37, 2.87)***
Yes	Yes	208	20	4.70 (2.91	, 7.58)***
Bronchiectasis	Hyperlipi- demia				
No	No	5489	132		1(Reference)
No	Yes	986	31	1.23	(0.83, 1.82)
Yes	No	1124	46	1.91	(1.37, 2.67)***
Yes	Yes	171	12	2.96 (1.64	, 5.36)***
Bronchiectasis	CAD				
No	No	5626	120		1(Reference)
No	Yes	849	43	1.71	(1.20, 2.43)*
Yes	No	1078	38	1.86	(1.29, 2.68)***
Yes	Yes	217	20	3.60 (2.24	, 5.80)***
Bronchiectasis	CHF				
No	No	6294	152		1(Reference)
No	Yes	181	11	1.73	(0.93, 3.20)
Yes	No	1192	49	1.91	(1.38, 2.64)***
Yes	Yes	103	9	3.30 (1.69	, 6.52)***
Bronchiectasis	COPD				
No	No	5922	136		1(Reference)
No	Yes	553	27	1.38	(0.91, 2.10)
Yes	No	663	24	1.88 (1.22	, 2.91)***
Yes	Yes	632	34	2.25 (1.54	, 3.28)***
Bronchiectasis	AF				
No	No	6402	158		1(Reference)
No	Yes	73	5	1.96	(0.80, 4.79)
Yes	No	1270	52	1.86	(1.37, 2.55)***
Yes	Yes	25	6	7.45 (3.28	, 16.88)***

Adjusted HR[†]: Adjusted for age and sex; Comorbidity[‡]: Only one of the following comorbidities was considered: hypertension, diabetes, hyperlipidemia, CAD, CHF, COPD, and AF; Statistical analysis with * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$

Table 2- Cox proportional hazard regression analysis for the risk of bronchiectasis-associated ischemic stroke with joint effect of comorbidity

Bronchiectasis	Comorbidity [‡]	Patient (N)	Ischemic Stroke (n)	Adjusted HR [†] (95% CI)
No	No	3159	34	1(Reference)
No	Yes	3316	129	2.17 (1.47, 3.20)***
Yes	No	377	4	1.24 (0.44, 3.48)
Yes	Yes	918	54	4.03 (2.61, 6.22)***

Adjusted HR[†]: Adjusted for age and sex with

* $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$; Comorbidity[‡]: Only to have one of the comorbidities: hypertension, diabetes, hyperlipidemia, CAD, CHF, COPD, and AF

Conclusion

This is the first Asian nationwide based study to examine the associations between bronchiectasis and ischemic stroke. Our analysis exhibited the risk of ischemic stroke is significantly higher in patients with bronchiectasis, especially co-morbid with other diseases, than those without bronchiectasis. However, by considering the effect of comorbidity, bronchiectasis is not shown to be an independent risk factor associated with the ischemic stroke. Furthermore, the risk of ischemic stroke showed dose response according to numbers of emergency visits and hospital admissions per year.

References

1. Altin, R., Savranlar, A., Kart, L., Mahmutyazicioglu, K., Ozdemir, H., Akdag, B., & Gundogdu, S. (2004). Presence and HRCT quantification of bronchiectasis in coal workers. *Eur J Radiol*, 52(2), 157-163. doi: 10.1016/j.ejrad.2004.03.017
2. Chang, A. B., & Bilton, D. (2008). Exacerbations in cystic fibrosis: 4-- Non-cystic fibrosis bronchiectasis. *Thorax*, 63(3), 269-276. doi: 10.1136/thx.2006.060913
3. Goeminne, P. C., Nawrot, T. S., Rutters, D., Seys, S., & Dupont, L. J. (2014). Mortality in non-cystic fibrosis bronchiectasis: a prospective cohort analysis. *Respir Med*, 108(2), 287-296. doi: 10.1016/j.rmed.2013.12.015
4. Gursel, G. (2006). Does coexistence with bronchiectasis influence intensive care unit outcome in patients with chronic obstructive pulmonary disease? *Heart & Lung: The Journal of Acute and Critical Care*, 35(1), 58-65.
5. Johansen, H. L., Wielgosz, A. T., Nguyen, K., & Fry, R. N. (2006). Incidence, comorbidity, case fatality and readmission of hospitalized stroke patients in Canada.

Canadian Journal of Cardiology, 22(1), 65-71.

6. Millett, E., Hurst, J., Thomas, S., Smeeth, L., Hubbard, R., Brown, J., & Navaratnam, V. (2014). The association between bronchiectasis and cardiovascular disease: a population based study. *Am J Respir Crit Care Med*, 189, A3618.

7. Neves, P. C., Guerra, M., Ponce, P., Miranda, J., & Vouga, L. (2011). Non-cystic fibrosis bronchiectasis. *Interact Cardiovasc Thorac Surg*, 13(6), 619-625. doi: 10.1510/icvts.2011.284208

8. Pasteur, M. C., Helliwell, S. M., Houghton, S. J., Webb, S. C., Foweraker, J. E., Coulden, R. A., & Keogan, M. T. (2000). An investigation into causative factors in patients with bronchiectasis. *Am J Respir Crit Care Med*, 162(4), 1277-1284.

9. Wannamethee, S. G., Shaper, A. G., & Ebrahim, S. (1995). Respiratory function and risk of stroke. *Stroke*, 26(11), 2004-2010.

10. Zaid, A. A., Elnazir, B., & Greally, P. (2010). A decade of non-cystic fibrosis bronchiectasis 1996-2006. *Irish medical j*

