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Impact of diabetes mellitus on pneumonia mortality in a senior population: results from the NHANES III follow-up study

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Abstract

Objective To examine whether diabetes mellitus increases the risk of pneumonia mortality among seniors in the U.S. general population. **Methods & Results** The NHANES III follow-up study data were used. After excluding individuals from other minorities, being hospitalized with pneumonia in the previous year at baseline, or death of pneumonia during the first year of follow-up, a total of 3,707 subjects aged 65 years or older (1,794 men and 1,913 women) who had no missing information on variables for the analysis were included. Approximately 16% of seniors at baseline were diabetics, which was defined as either having been diagnosed by a physician, currently taking pills/insulin lowering blood glucose, or HbA1c higher than 6.4%. During an average 11 years of follow-up, a total of 98 deaths due to pneumonia were recorded (ICD-10: J12–J18). Cox-regression models were used to estimate the risk association between pneumonia mortality and diabetes mellitus. After adjustment for the covariates at baseline, the hazard ratios of pneumonia death were 1.30 (95% CI: 0.64–2.70) for pre-diabetics and 2.28 (95% CI: 1.18–4.39) for diabetics, respectively. Among those covariates, only age (HR (95% CI); 1.16 (1.13–1.20)), gender as female (0.35 (0.22–0.61)) and physical fitness measured as having no problem walking 1^{+} mile during the previous month (0.38 (0.20–0.67)) reached statistical significance. **Conclusions** The results suggest that diabetes mellitus is a strong risk predictor of pneumonia mortality and the evaluation of physical fitness may also be useful in the risk prediction of pneumonia mortality for seniors.

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Keywords: Diabetes mellitus; Physical fitness; Senior; Pneumonia; Mortality; Follow-up

1 Introduction

Based on the 2011 National Diabetes Fact Sheet, approximately 27% of U.S. seniors (aged ≥ 65) in 2010 were diabetics; among adults with pre-diabetes, half of them were seniors.[1] Despite affecting life quality of those seniors diagnosed with diabetes mellitus,[2] diabetes mellitus in seniors is linked to higher mortality, reduced functional status, and increased risk of institutionalization and requires much more health-care resources.[3] Seniors with diabetes mellitus are at substantial risk for cardiovascular disease and its complications, but evidence suggests that diabetes mellitus may also increase the susceptibility to infectious diseases, such as pneumonia, urinary tract infections, and skin infections.[4] Pneumonia is a common and important disease in the elderly population; however, the results from previous studies in regard to the impact of diabetes mellitus on the risk of pneumonia among hospitalization patients seem to be inconsistent; some of them suggest that diabetic patients, compared to non-diabetics, are more likely to have respiratory illness, such as asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, and pneumonia;[5] they may also experience higher pneumonia-related mortality.[6] While others indicate that although patients with diabetes mellitus may have different clinical features when hospitalized with pneumonia, the pneumonia-related mortality rates, however, are similar to those without diabetes;[7] diabetes mellitus may also not be a risk for development of hospital-acquired pneumonia.[8] Although pneumonia is a frequent cause of hospitalization and death among senior adults, the examination of studies on whether diabetes in the senior population has an impact on the risk for mortality of pneumonia is scarce. Using the third National Health and Nutrition Examination Survey Mortality Follow-up Study (NHANES III follow-up Study), we explored this issue.

2 Methods

The NHANES III follow-up study was formed by linking to the death certificate data found in the National Death

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Index (NDI). The NHANES III was a stratified, multi-stage probability designed survey conducted between 1988 and 1994 involving approximately 34,000 people aged 2 months and over. The details of the survey with regards to its design and measurement procedures can be found elsewhere,[9] and the information collected during the NHANES III is considered as the baseline information. The mortality ascertainment in the NHANES III follow-up study is based upon the results from a probabilistic match between NHANES III and the NDI death certificate records to provide mortality follow-up data from the date of NHANES III survey participation (1988–1994) through December 31, 2006.[10] A total of 5,252 seniors, ages 65 years or older, were identified in the baseline of the NHANES III follow-up study. The excluding criteria considered those who were: (a) belong to "other minority"; (b) hospitalized with pneumonia during the past twelve months at baseline, and/or (c) death due to pneumonia during the first year of follow-up. The final sample size in the analysis is 3,707 (1,794 men and 1,913 women).

According to the American Diabetes Association,[11] diabetes was defined as either being diagnosed as diabetes mellitus by physicians, or currently taking prescribed medication (including insulin) for diabetes, or the baseline overnight fasting glucose > 125 mg/dL, or HbA1c > 6.4%; pre-diabetes was defined as the baseline overnight fasting glucose: > 100 mg/dL but < 126 mg/dL, or HbA1c > 5.7% but < 6.5%. The uncontrolled diabetes mellitus was defined as HbA1c > 7.5% because of the geriatric population.[12] Death due to pneumonia was defined with ICD-10 codes of J12 – J18 from the NDI records.

All analyses were conducted using survey procedures in SAS 9.3 (SAS Institute Inc., Cary, NC, USA), which take into account the weighted and clustered sampling design of NHANES. The significant level was defined at 2-tailed alpha equal or less than 0.05. Hazard ratios (HR) from partial hazard regression models were used to examine the relationship between the time for pneumonia death and diabetic status at the baseline. The following covariates at the baseline were included into the analyses, which are age, gender, ethnicity, marriage status, education, poverty income ratio, current smoking, whether walking a mile without stopping during the previous month as a proxy indicator of physical fitness, family history of diabetes, co-morbidity if reported heart attack, stroke, cancer, taking medications for hypertension or hyperlipidemia, respiratory disorder during previous year (i.e., having wheezing/whistling, asthma, or chronic bronchitis), baseline body mass index (BMI), diastolic blood pressure (DBP), and whether having an uncontrolled diabetic status.

3 Results

Approximately 26% of seniors in this study were pre-diabetics and 19% of them were diabetics. During approximately 11 years of follow-up, a total of 98 pneumonia deaths were recorded. The mortality rates of pneumonia were 16.9 per 10,000 person-years for non-diabetics, 23.1 per 10,000 person-years for pre-diabetics, and 34.1 per 10,000 person-years for diabetics, respectively. Table 1 shows the characteristics of participants at baseline. The characteristics of men are similar to women's except that they were slightly younger (72.4 *vs.* 73.8 years), more likely to be ex-smokers (57.8% *vs.* 28.7%), living with a spouse or partner (76.4% *vs.* 41.7%), and had a higher mortality rate of pneumonia (35.2 *vs.* 19.4 (per 10,000 person-years)) during the follow-up.

Table 2 shows the hazard ratios of pneumonia deaths from four models for diabetic status defined at the baseline of the study. The covariates adjusted in model one were age,

Table 1. Baseline selected characteristics of USA 3,707 elderly from the NHANES III follow-up study.

	Men	Women
	n **= 1794**	***n*** **= 1913**
Age (yrs, mean ± SE)	72.4 ± 0.2	73.8 ± 0.2
Education less than high school (%)	44.5	41.1
Non-Hispanic white (%)	89.5	89.3
Cigarette smoking (%)		
None smokers	27.6	60.8
Ex-smokers	57.8	28.7
Current smokers	14.6	10.4
Living with a spouse or a partner (%)	76.4	41.7
Poverty income ratio (mean ± SE)	3.22 ± 0.11	2.71 ± 0.10
Respiratory illness occurred during last year (%)	19.4	22.5
Diabetes (%)	20.4	17.3
Pre-diabetes (%)	26.1	25.5
Comorbidity (%)	57.1	59.9
Family history of diabetes (%)	31.3	38.0
BMI (kg/m^2, mean ± SE)	26.9 ± 0.2	26.7 ± 0.2
Systolic blood pressure (mmHg, mean ± SE)	139.8 ± 0.7	142.2 ± 0.7
Diastolic blood pressure (mmHg, mean ± SE)	75.7 ± 0.4	72.4 ± 0.4
Glycosylated hemoglobin (HbA1c (%), mean ± SE)	5.80 ± 0.04	5.83 ± 0.05
Walking 1^+ mile without stop last month (%)	44.9	36.8
Death due to pneumonia (*n*, (per 10,000 person yrs))	59 (35.2)	39 (19.4)
Follow-up time (months, mean ± SE)	120.5 ± 2.8	133.4 ± 2.4

Table 2. Hazard ratios of death from pneumonia for diabetes diagnosed at baseline.

	HR	95% CI	*P*-value for trends
Model 1			
Non-diabetes	1.00		0.01
Pre-diabetes	1.30	0.63–2.68	
Diabetes	2.41	1.28–4.51	
Model 2			
Non-diabetes	1.00		< 0.02
Pre-diabetes	1.30	0.64–2.62	
Diabetes	2.29	1.20–4.37	
Model 3			
Non-diabetes	1.00		< 0.02
Pre-diabetes	1.28	0.63–2.61	
Diabetes	2.21	1.19–4.12	
Model 4			< 0.03
Non-diabetes	1.00		
Pre-diabetes	1.31	0.63–2.69	
Diabetes	2.57	1.23–5.35	

Model 1: adjusted for age, sex, ethnicity, education, and family diabetes history; Model 2: further adjusted for current smoking status and whether walking a mile without stop; Model 3: further adjusted for body mass index and diastolic blood pressure; Model 4: further adjusted for whether having comorbidity (heart attack, stroke, cancer, hypertension and/or dyslipidemia), whether having respiratory disorder during last 12 months and whether diabetes being controlled at baseline.

gender, ethnicity, education, and family history of diabetes; compared to seniors without diabetes at the baseline, the HR of pneumonia deaths were 1.30 (95% CI: 0.63–2.68) for those with pre-diabetes and 2.41 (95% CI: 1.28–4.51) for those with diabetes, respectively (*P*-value for trends was 0.01). When further adjusted for other potential confounding variables (models two–four), the risk association between diabetic status at baseline and pneumonia deaths during the follow-up did not change.

Among those covariates, only age, gender and physical fitness reached statistically significance (Figure 1). Every one year increase in age was associated with 16% increased risk of pneumonia death (95% CI: 1.13–1.20); the HRs of pneumonia death was 0.35 (95% CI: 0.22–0.61) for women in comparison to men and 0.38 (95% CI: 0.20–0.67) for those who had no problem walking 1^{+} mile during the previous month at baseline in comparison to those who experienced difficulty.

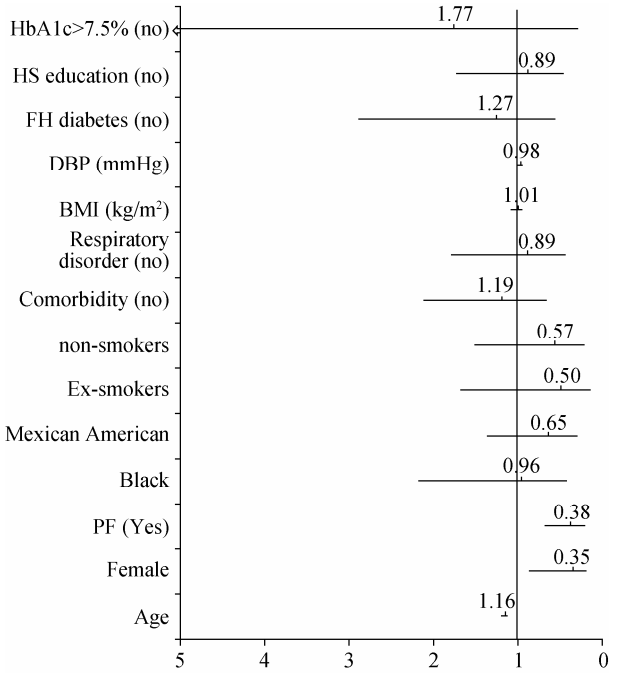

Figure 1. Hazard ratios of pneumonia death. BMI: body mass index; DBP: diastolic blood pressure; FH: family history; HS: high school; PF: physical fitness.

4 Discussion

Although inconsistent results were found from the previous studies among hospitalized-patients in regard to the impact of diabetic status on the risk of pneumonia death,[5–8,13,14] the results from this prospective cohort study indicated that diabetic status is a strong risk factor for pneumonia mortality among seniors in the general population. This risk association between diabetic status at baseline and pneumonia death during the follow-up is independent from many known risk factors for pneumonia, such as age, male gender, ethnicity, cigarette smoking, co-morbidity, and other respiratory illness.[15,16]

Similar to the results of the study conducted among hospitalized-patients, this study confirmed that age and male gender are important risk predictors of pneumonia mortality.[16] However, certain risk factors, such as ethnicity, cigarette smoking, co-morbidity, other respiratory illness and/or uncontrolled diabetic status at baseline, seemed to have no impact on the risk prediction of pneumonia mortality as observed in hospitalized-patients. This might be due to the fact that the subjects in this study were from the general population; while the subjects from the previous studies were mainly from the hospitalized patients.

In addition, some other risk factors related to all-cause mortality, such as BMI,[17,18] blood pressure,[19] and educa-

tion,[20] were not associated with pneumonia mortality in this study. Interestingly, however, physical fitness measured as a person who can walk a mile or more without stopping during the previous month is a strong predictive indicator for pneumonia death among this senior population; our results suggest that those who could walk a mile or more without stopping during the previous month at the baseline were 62% less likely to die of pneumonia in comparison to those who could not. The impact of physical fitness on the risk of pneumonia mortality appears never to have been examined before. This may be because those hospital orientated studies were most likely derived from the hospital-registration database, which usually did not have physical fitness information. The results from studies conducted among subjects from the general population suggest that cardiorespiratory fitness (e.g., measured with treadmill) is strongly and negatively associated with the risk of all-cause mortality.[21] Although no information on treadmill measured physical fitness is in this study, however, a simple question whether the senior can walk 1^{+} mile without stopping during the previous month was asked. It seems that this question is a useful tool to probe the physical fitness status of seniors and shows a stronger predictor of pneumonia mortality among seniors.

Based on our knowledge, this is the first report of the impact of diabetes on pneumonia mortality among seniors in the general population. There are several strengths of this study. They are: (1) the NHANES III follow-up study is a well-designed population-based study with rigorously standardized medical and laboratory examinations; (2) the exclusion of those who have been hospitalized with pneumonia during the previous year at baseline, or pneumonia death occurring during the first year of follow-up made the conclusion stronger, which could reduce a potential bias when including those subjects into the study; and (3) a number of well-known risk factors have been included into the analysis. Yet, no information on those newly developed diabetics during the follow-up can be a limitation, because it may affect the observed risk association. However, it is doubtful that the direction of the risk association between diabetic status and pneumonia mortality will be changed, since seniors who were in the pre-diabetic group also have an elevated risk for pneumonia mortality, though it did not reach statistical significance.

In conclusion, diabetes mellitus is a strong risk predictor of pneumonia death among seniors in the general population. Physical fitness in the elderly may also be a valuable predictor for the risk predication of pneumonia mortality. Indeed, further study is urgently needed to confirm their roles on the pneumonia related outcomes in the senior population.

References

1 Prevention., C.f.D.C.a., National Diabetes Fact Sheet: National Estimates and General Information on Diabetes and Prediabetes in the United States. , C.f.D.C.a.P. US Department of Health and Human Services, Ed.; 2011: Atlanta, GA, USA.

2 Speight J, Sinclair AJ, Browne JL, *et al*. Assessing the impact of diabetes on the quality of life of older adults living in a care home: validation of the ADDQoL Senior. *Diabet Med* 2012; 30: 74–80.

3 Brown AF, Mangione CM, Saliba D, *et al*. Guidelines for improving the care of the older person with diabetes mellitus. *J Am Geriatr Soc* 2003; 51(5 Suppl Guidelines): S265–S280.

4 Benfield T, Jensen JS, Nordestgaard BG. Influence of diabetes and hyperglycaemia on infectious disease hospitalisation and outcome. *Diabetologia* 2007; 50: 549–554.

5 Ehrlich SF, Quesenberry CP Jr, Van Den Eeden SK, *et al*. Patients diagnosed with diabetes are at increased risk for asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, and pneumonia but not lung cancer. *Diabetes Care* 2010; 33: 55–60.

6 Kornum JB, Thomsen RW, Riis A, *et al*. Diabetes, glycemic control, and risk of hospitalization with pneumonia: a population-based case-control study. *Diabetes Care* 2008; 31: 1541–1545.

7 Di Yacovo S, Garcia-Vidal C, Viasus D, *et al*. Clinical features, etiology, and outcomes of community-acquired pneumonia in patients with diabetes mellitus. *Medicine* (*Baltimore*) 2013; 92: 42–50.

8 Yende S, van der Poll T, Lee M, *et al*., The influence of pre-existing diabetes mellitus on the host immune response and outcome of pneumonia: analysis of two multicentre cohort studies. *Thorax* 2010; 65: 870–877.

9 CDC, NHANES III. National Center for Health Statistics. http://www.cdc.gov/nchs/nhanes/nh3data.htm. Accessed on March 9, 2013.

10 CDC, NHANES III Linked Mortality File. National Center for Health Statistics. http://www.cdc.gov/nchs/data_access/data_linkage/mortality/nhanes3_linkage.htm. Accessed on March 9, 2013.

11 Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010; S62–S69.

12 Sue Kirkman M, Briscoe VJ, Clark N, *et al*. Diabetes in older adults: a consensus report. *J Am Geriatr Soc* 2012; 60: 2342–2356.

13 Kornum JB, Thomsen RW, Riis A, *et al*. Type 2 diabetes and pneumonia outcomes: a population-based cohort study. *Diabetes Care* 2007; 30: 2251–2257.

14 Valdez R, Narayan KM, Geiss LS, *et al*. Impact of diabetes mellitus on mortality associated with pneumonia and influenza among non-Hispanic black and white US adults. *Am J Public Health* 1999; 89: 1715–1721.

15 Welte T. Risk factors and severity scores in hospitalized pa-

tients with community-acquired pneumonia: prediction of severity and mortality. *Eur J Clin Microbiol Infect Dis* 2011; 31: 33–47.

16 Welte T. Risk factors and severity scores in hospitalized patients with community-acquired pneumonia: prediction of severity and mortality. *Eur J Clin Microbiol Infect Dis* 2012; 31: 33–47.

17 Veronese N, De Rui M, Toffanello ED, *et al*. Body mass index as a predictor of all-cause mortality in nursing home residents during a 5-year follow-up. *J Am Med Dir Assoc* 2013; 14: 53–57.

18 Flegal KM, Kit BK, Orpana H, *et al*. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA* 2012; 309: 71–82.

19 Vamos EP, Harris M, Millett C, *et al*. Association of systolic and diastolic blood pressure and all cause mortality in people with newly diagnosed type 2 diabetes: retrospective cohort study. *BMJ* 2012; 345: e5567.

20 Zajacova A, Hummer RA. Gender differences in education effects on all-cause mortality for white and black adults in the United States. *Soc Sci Med* 2009; 69: 529–537.

21 Lee DC, Sui X, Ortega FB, *et al*. Comparisons of leisure-time physical activity and cardiorespiratory fitness as predictors of all-cause mortality in men and women. *Br J Sports Med* 2011; 45: 504–510.