Risk for prolonged hospitalization and mortality in aged community acquired pneumonia patients: a retrospective study in Japan

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(Received 25 May, 2020; Accepted 29 May, 2020; Published online 31 July, 2020)

The present study aimed to reveal; i) risk for prolonged hospitalization and mortality in aged community acquired pneumonia patients, and ii) whether swallowing ability was related to rehospitalization. The present retrospective study included 92 patients older than 75 years hospitalized with community acquired pneumonia in Takagi Hospital between April 2017 and March 2018. The patients were classified into 3 groups; discharged within 17 days (group I): hospitalized more than 18 days (group II): died during the hospitalization (group III). Swallowing ability was evaluated if available. Univariate analysis indicated males and body mass index (BMI) in group I (n = 24) were higher than group II (n = 46). Group III (n = 22) had low serum albumin, low BMI, and severe disease progression compared with group I. Multivariate analysis demonstrated that group II BMI was lower than group I [odds ratio (OR) = 1.18, p = 0.042]. Group III had lower serum albumin level compared with group I (OR = 81.01, p = 0.025). Diabetes mellitus (p = 0.009), but not swallowing disability, was risk for readmission. Malnutrition represented by low albumin enhanced mortality rate in the pneumonia patients, and low BMI and diabetes mellitus might increase the pneumonia risk.

Key Words: serum albumin, body mass index, CURB-65, comorbidity, swallowing ability

rommunity and hospital acquired pneumonia is still one of - the major lethal causes in Japan, especially in aged generations,⁽¹⁻⁷⁾ whereas several preventive medical practices including vaccination for pneumonia have been performed.(8-10) In aged populations, majority of community acquired pneumonia might be caused by aspiration and/or dysphagia, which might lead to a high recurrence rate and poor prognosis of the disease.^(2-4,6,11,12) In a real world clinical situation, definition and diagnosis of aspiration pneumonia and/or community acquired pneumonia have not been well-established and therapeutic approaches might be the almost same between aspiration and non-aspiration pneumonia.^(3,6,12) Whereas several studies suggested the several risks for community acquired pneumonia including aspiration pneumonia, the reports which demonstrated the risk factors for prolonged hospitalization and patients' prognosis of the disease were limited in Japan.^(4,6,13,14)

The present retrospective chart review in the Japan single institute in aimed to reveal risk factors for prolonged stay and mortality is newly hospitalized community acquired pneumonia patients more than 75 years old in order to take steps for medical care for aged pneumonia patients. In addition, the present study examined if swallowing ability was related to the repeated hospitalization of the pneumonia patients.

Methods

In the present retrospective study, 92 patients older than 75 years who hospitalized with community acquired pneumonia in department of respiratory of Kouhou-kai Takagi Hospital between April 2017 and March 2018 were examined. Patients of hospital acquired pneumonia were not included. The patients were classified into 3 groups according to their clinical courses; the patients who discharged within 17 days from the admission (group I): the patients who hospitalized more than 18 days (group II): the patients who died during the hospital stay (group III). The factors collected from the medical records were as follows; age, gender, body mass index, serum albumin, pneumonia severity, general condition, comorbidities, and repeated hospitalization within one year. CURB-65 (score 1 or 0; confusion, blood urea nitrogen >19 mg/dl, respiratory rate ≥ 30 breaths/min, low blood pressure, age ≥ 65 years) was used as index for pneumonia severity at admission.⁽⁷⁾ The general condition of the patients was evaluated by Eastern Cooperative Oncology Group Performance Status at admission as follows; status 0: fully active, able to carry on all predisease performance without restriction, status 1: restricted in physically strenuous activity but ambulatory and able to carry out work of a light sedentary nature like light house work and office work, status 2: ambulatory and capable of all self-care but unable to carry out any work activities up and about more than 50% of waking hours, status 3: capable of only limited self-care confined to bed or chair more than 50% of waking hours, status 4: completely disabled and not able to carry on any self-care totally confined to bed and/or chair.⁽¹⁵⁾ In addition, the swallowing ability was evaluated, if available, with the informed consent. The speech therapist tested the swallowing ability with a repetitive saliva swallowing test, a modified water swallow test, and a food test as previous demonstrated.⁽¹⁶⁾ The patients were categorized into grade 1 to 10 with comprehensive judgement as indicated in Table 1. Grades 1 to 3 cannot eat by mouth; grades 4 to 6 relate to varying degrees of oral feeding with non-oral supplementation (nasogastric or gastrostomy tube feeding or parenteral nutrition); grades 7 to 9 relate to varying degrees of oral feeding without non-oral supplementation; grade 10 is normal. All procedures

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Table 1. Grading the oral feeding and swallowing ability

Grade 1: Nothing by mouth (no adaptation to swallowing training)

Grade 2: Nothing by mouth (adaptation only to fundamental swallowing training)

Grade 3: Nothing by mouth (possible of swallow training with food in appropriate situation)

Grade 4: Minimal food attempts for pleasure (need non-oral supplementation)

Grade 5: Oral diet to certain extent in one or two meal with non-oral supplementation

Grade 6: Oral diet to certain extent in every meal with non-oral supplementation

Grade 7: Dysphagia diet in every meal

Grade 8: Total oral diet without food which is difficult to swallow

Grade 9: Total oral diet with no restriction, but requiring watching

Grade 10: Normal swallowing ability

 Table 2. Characteristics of patients of subdivided administrated pneumonia patients with their clinical courses

		Group I	Group II	p value	Group III	<i>p</i> value
Number of patients		24	46		22	
Age (mean \pm SD, year)		$\textbf{84.3} \pm \textbf{5.0}$	$\textbf{85.2} \pm \textbf{5.2}$	0.529	$\textbf{85.4} \pm \textbf{6.7}$	0.540
Gender, males/females		17/7	21/25	0.045*	13/9	0.403
BMI (kg/m²)		$\textbf{22.5} \pm \textbf{4.8}$	$\textbf{19.4} \pm \textbf{3.5}$	0.004*	$\textbf{18.2} \pm \textbf{4.6}$	0.004*
Serum albumin (mg/dl)		$\textbf{3.4} \pm \textbf{0.36}$	$\textbf{3.2}\pm\textbf{0.41}$	0.080	$\textbf{2.6} \pm \textbf{0.56}$	<.0001*
CURB-65	1	17 (70.8%)	23 (50.0%)	0.138	4 (18.2%)	0.001*
	2	7 (29.2%)	18 (39.1%)		9 (40.9%)	
	3	0 (0.0%)	2 (4.4%)		6 (27.3%)	
	4	0 (0.0%)	3 (6.5%)		3 (13.6%)	
ECOG PS	0	8 (33.3%)	9 (19.6%)	0.404	3 (13.6%)	0.057
	1	10 (41.7%)	17 (37.0%)		5 (22.7%)	
	2	3 (12.5%)	8 (17.4%)		4 (18.2%)	
	3	3 (12.5%)	7 (15.2%)		5 (22.7%)	
	4	0 (0.0%)	5 (10.9%)		5 (22.7%)	
Comorbidity						
Congestive heart failure		1 (4.1%)	2 (4.3%)	NA	1 (4.5%)	NA
Chronic kidney disease		0 (0.0%)	1 (2.2%)	NA	0 (0.0%)	NA
Cerebrovascular disease		5 (20.8%)	14 (30.4%)	0.391	5 (22.7%)	0.876
Neuromuscular disease		0 (0.0%)	6 (13.0%)	0.088	2 (9.1%)	NA
Chronic pulmonary disease		14 (53.8%)	18 (39.1%)	0.126	10 (45.5%)	0.382
Psychosis		0 (0.0%)	3 (6.5%)	NA	1 (4.5%)	NA
Dementia		1 (4.1%)	5 (10.9%)	NA	3 (13.6%)	NA
Diabetes mellitus		5 (20.8%)	7 (15.2%)	0.554	3 (13.6%)	0.520
Collagen disease		0 (0.0%)	3 (6.5%)	NA	0 (0.0%)	NA
Swallowing ability (n)		8.5 ± 0.7 (2)	6.9 ± 1.9 (14)	0.268	6.1 ± 1.9 (8)	0.130
Readmission		8 (33.3%)	20 (43.5%)	0.411		

*Statistical significance. Group I: patients who discharged within 17 days from the admission. Group II: patients who hospitalized more than 18 days. Group III: patients who died during the hospital stay. CURB-65, confusion; blood urea nitrogen >19 mg/dl, respiratory rate \geq 30 breaths/min, low blood pressure, age \geq 65. CURB-65 was evaluated in 3 groups, 1/2/3 + 4. ECOG PS, Eastern Cooperative Oncology Group performance status. PS was evaluated in 4 groups, 0/1/2/3 + 4. BMI, body mass index; NA, not available.

performed in the present study were approved by the Kouhou-kai Takagi Hospital Ethics Committee.

Baseline characteristics of three groups' patients were compared using Chi-squared or Fisher's exact test for categorical variables. For multivariate analysis, we applied the multivariable logistic regression model with explanatory variables which has the significance levels (univariate p < 0.15 on statistical tests). The odds ratios (OR) and 95% confidence interval (CI) were shown in tables. JMP Pro 14 was used for all analyses. Statistical significance was defined as p < 0.05.

Results

All the 92 pneumonia patients were divided into group I, group

II and group III. Table 2 indicated the baseline characteristics of the patients; i) discharged within 17 days (group I, n = 24), ii) the patients who hospitalized more than 18 days (group II, n = 46) and, iii) the patients who died during the hospital stay (group III, n = 22). Group I vs group II and group I vs group III were compared using univariate analysis regarding age, gender, body mass index (BMI), serum albumin, pneumonia severity with CURB-65, performance status with ECOG PS, comorbidity (congestive heart failure, chronic kidney disease, cerebrovascular disease, neuromuscular disease, chronic pulmonary disease, psychosis, dementia, diabetes mellitus, and collagen disease), and functional level of swallowing ability. Comparing group I with group II, gender of males and BMI were higher in group I, and other factors including pneumonia severity at admission,

performance status at admission, comorbidities and the swallowing ability did not affect the length of the hospitality stay of the pneumonia patients. Readmission rate was not different between groups I and II. Regarding group III who died during the hospital stay, the serum albumin level and BMI were lower and disease progression of pneumonia was more severe compared with group I. Other factors including performance status, comorbidities and swallowing ability were not different between the two groups.

A multivariate analysis was performed regarding group I and group II or group I and group III to reveal risk for hospitalization and life prognosis (Table 3). The variable factors with p<0.15 and more than 5 were selected. Group II patients had lower BMI compared with group I patients (OR = 1.18, 95% CI: 1.01–1.39, p = 0.042). Group III patients had lower serum albumin level compared with group I patients (OR = 81.01, 95% CI: 1.76–3,728.54, p = 0.025).

The characteristics of readmitted patients caused by repeated pneumonia and no-readmitted patients who evaluated functional level of swallowing were indicated in Table 4. There was no significant difference between readmitted patients and noreadmitted patients regarding age, gender, and nutrition status, severity of pneumonia, PS, and swallowing ability. Regarding comorbidity, there was more diabetes patients in readmitted patients compared with no-readmitted patients.

Table 3. Multivariate analysis compared group I with group II or group III

	OR (95% CI)	<i>p</i> value
Group I vs Group II		
Gender (males)	2.76 (0.76–9.96)	0.122
BMI	1.18 (1.01–1.39)	0.042*
Serum albumin	2.53 (0.44–14.53)	0.299
CURB-65	0.40 (0.12–1.40)	0.153
Chronic pulmonary disease	2.46 (0.72–8.45)	0.152
Group I vs Group III		
BMI	1.39 (0.81–2.39)	0.228
Serum albumin	81.0 (1.76–3,728.54)	0.025*
CURB-65	0.03 (0.001–1.39)	0.073

Analyzed factors: p values less than 0.15 in univariate analysis and having more than 5 data in each group. *Statistical significance. Group I: patients who discharged within 17 days from the admission. Group II: patients who hospitalized more than 18 days. Group III: patients who died during the hospital stay. OR, odds ratio; CI, confidence interval; BMI, body mass index; CURB-65, confusion; blood urea nitrogen >19 mg/dl, respiratory rate ≥30 breaths/min, low blood pressure, age ≥65.

 Table 4. Clinical background of patients evaluated the swallowing ability were compared between the discharged patients without readmission caused by repeated pneumonia

		Readmission	No-readmission	<i>p</i> value
Number of patients		7	9	
Age (mean \pm SD, year)		$\textbf{84.9} \pm \textbf{4.9}$	$\textbf{85.6} \pm \textbf{5.7}$	0.799
Gender, males/females		6/1	4/5	0.091
BMI (kg/m²)		$\textbf{21.4} \pm \textbf{3.2}$	$\textbf{18.9} \pm \textbf{3.2}$	0.151
Serum albumin (mg/dl)		$\textbf{3.2}\pm\textbf{0.4}$	$\textbf{2.9} \pm \textbf{0.5}$	0.161
CURB-65	1	4 (57.1%)	2 (22.2%)	0.152
	2	3 (42.9%)	6 (66.7%)	
	3	0 (0.0%)	0 (0.0%)	
	4	0 (0.0%)	1 (11.1%)	
ECOG PS	0	1 (14.3%)	1 (11.1%)	0.484
	1	2 (28.6%)	4 (44.4%)	
	2	1 (14.3%)	3 (33.3%)	
	3	3 (42.9%)	1 (11.1%)	
	4	0 (0.0%)	0 (0.0%)	
Length of hospital stay (days)		$\textbf{38.7} \pm \textbf{21.4}$	63.6 ± 56.4	0.290
Comorbidity				
Congestive heart failure		0 (0.0%)	0 (0.0%)	NA
Chronic kidney disease		1 (14.3%)	0 (0.0%)	NA
Cerebrovascular disease		2 (28.6%)	3 (33.3%)	0.839
Neuromuscular disease		1 (14.3%)	2 (22.2%)	0.687
Chronic pulmonary disease		1 (14.3%)	2 (22.2%)	0.687
Psychosis		0 (0.0%)	0 (0.0%)	NA
Dementia		2 (28.6%)	2 (22.2%)	0.771
Diabetes mellitus		4 (57.1%)	0 (0.0%)	0.009*
Collagen disease		1 (14.3%)	1 (11.1%)	1.000
Swallowing ability		7.3 ± 1.7	$\textbf{7.0} \pm \textbf{2.0}$	0.767

*Statistical significance. BMI, body mass index; CURB-65, confusion; blood urea nitrogen >19 mg/dl, respiratory rate \geq 30 breaths/min, low blood pressure, age \geq 65. CURB-65 was evaluated in 3 groups, 1/2/3 + 4. ECOG PS, Eastern Cooperative Oncology Group performance status. PS was evaluated in 4 groups, 0/1/2/3 + 4. NA, not available.

Discussion

The present retrospective chart review evaluated by multivariate analysis indicated; i) the risk factor for the prolonged hospitalization in the aged community acquired pneumonia patients more than 75 years old was low BMI, and ii) the risk factor for mortality in the pneumonia patients was low serum albumin. In addition, univariate analysis for the pneumonia patients revealed that the gender of females was the risk for prolonged hospitalization and that pneumonia severity and low BMI were the risks for mortality. The risk for repeated hospitalization with pneumonia was the patients of diabetes mellitus, and the swallowing ability was not directly related to the repeated hospitalization.

The low serum albumin level and severity of pneumonia on the admission were the risk factors for mortality in the aged community acquired pneumonia patients in the present study. The low serum albumin level, an indicator of malnutrition,⁽¹⁷⁾ was applicable for evaluation of the disease prognosis including the patients with severe sepsis and percutaneous endoscopic gastrostomy.⁽¹⁸⁻²⁰⁾ Several reports showed that serum albumin levels were associated with mortality and/or prognosis of the pneumonia,^(4,21,22) which was consistent with the result of the present study. Several indicators including procalcitonin,⁽²³⁻²⁵⁾ which was not evaluated in the present study, might be applicable for evaluation for prognosis of the pneumonia.

Low BMI on admission, a kind of an indicator for malnutrition, was a risk factor for the prolonged hospitalization in the aged pneumonia with multivariate analysis and was related to the mortality with univariate analysis. The result emphasized the nutrition status was an important factor for disease prognosis of aged hospitalized patients with community acquired pneumonia. Evaluation of the nutrition status with BMI was essential in prognosis of other pulmonary disease patients including the chronic obstructive pulmonary disease and the nosocomial infection.⁽²⁶⁻²⁹⁾

The present study suggested that the gender of females might be risk for the prolonged hospitalization. The reason why the hospitalization stay tended to be long in the aged females pneumonia patients was not clear,⁽³⁰⁾ as the number of the patients

References

- Okazaki T, Ebihara S, Mori T, Izumi S, Ebihara T. Association between sarcopenia and pneumonia in older people. *Geriatr Gerontol* 2020; 20: 7–13.
- 2 Manabe T, Fujikura Y, Mizukami K, Akatsu H, Kudo K. Pneumoniaassociated death in patients with dementia: a systematic review and metaanalysis. *PLoS One* 2019; 14: e0213825.
- 3 Miyashita N, Yamauchi Y. Bacterial pneumonia in elderly Japanese populations. Jpn Clin Med 2018; 9: 1179670717751433.
- 4 Nonaka S, Fujii S, Hara M, et al. Incidence of aspiration pneumonia during hospitalization in Japanese hospitalized cases did not increase whereas concern factors were exacerbated in a time-dependent manner: analysis of diagnosis procedure combination (DPC) data. J Clin Biochem Nutr 2018; 63: 66–69.
- 5 Momosaki R. Rehabilitative management for aspiration pneumonia in elderly patients. J Gen Fam Med 2017; 18: 12–15.
- 6 Komiya K, Rubin BK, Kadota JI, et al. Prognostic implications of aspiration pneumonia in patients with community acquired pneumonia: a systematic review with meta-analysis. Sci Rep 2016; 6: 38097.
- 7 Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003; 58: 377–382.
- 8 Ihara H, Kikuchi K, Taniguchi H, et al. 23-valent pneumococcal polysaccharide vaccine improves survival in dialysis patients by preventing cardiac events. *Vaccine* 2019; 37: 6447–6453.
- 9 Noguchi S, Yatera K, Akata K, et al. Distribution and annual changes in the proportion of *Streptococcus pneumoniae* serotypes in Japanese adults with pneumococcal pneumonia from 2011 to 2017. J Infect Chemother 2019; 25: 925–929.
- 10 Sando E, Suzuki M, Furumoto A, et al. Impact of the pediatric 13-valent

with good performance status (0 + 1) was not different between males (14 cases) and females (13 cases) and there was no significance difference between the genders regarding the other factors evaluated in the present study.

The complication of diabetes mellitus for the community acquired pneumonia was a risk factor for the repeated hospitalization with the pneumonia in the present study, although decrease in the swallowing ability did not enhance the repeated hospitalization. Repeated hospitalization with diabetes mellitus was compatible with several previous reports which demonstrated that pneumonia-related hospitalization was closely associated with diabetes mellitus,^(31–34) and that increase in HbA1c exacerbated the risk of the community acquired pneumonia.⁽³⁵⁾ The reasons for no relationship between the swallowing disability and repeated hospitalization were partly due to specialized diet for protection of dysphagia during hospitalization and the small number of the tested patients, which warrant further exploration.

There are several limitations in the present study; i) a retrospective study in a single institute with a relatively small sample size, ii) observation period for repeated hospitalization was one year, and iii) limited number of patients for evaluation of the swallowing ability.

In conclusion, the present retrospective chart review indicated risk of the poor prognosis of the mortality rate and the prolonged hospitalization in the aged community acquired pneumonia patients was due to malnutrition represented by the low serum albumin and the low BMI in addition to disease severity of the pneumonia.

Acknowledgments

The authors would gratefully acknowledge the speech therapists for the examination of swallowing ability.

Conflict of Interest

No potential conflicts of interest were disclosed.

pneumococcal conjugate vaccine on serotype distribution and clinical characteristics of pneumococcal pneumonia in adults: the Japan Pneumococcal Vaccine Effectiveness Study (J-PAVE). *Vaccine* 2019; **37**: 2687–2693.

- 11 Lanspa MJ, Jones BE, Brown SM, Dean NC. Mortality, morbidity, and disease severity of patients with aspiration pneumonia. *J Hosp Med* 2013; 8: 83–90.
- 12 Hayashi M, Iwasaki T, Yamazaki Y, et al. Clinical features and outcomes of aspiration pneumonia compared with non-aspiration pneumonia: a retrospective cohort study. J Infect Chemother 2014; 20: 436–442.
- 13 Kose E, Hirai T, Seki T. Assessment of aspiration pneumonia using the Anticholinergic Risk Scale. *Geriatr Gerontol Int* 2018; 18: 1230–1235.
- 14 Tamayose M, Fujita J, Parrott G, et al. Correlations between extent of X-ray infiltration and levels of serum C-reactive protein in adult non-severe community-acquired pneumonia. J Infect Chemother 2015; 21: 456–463.
- 15 Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982; 5: 649–655.
- 16 Teramoto S, Matsuse T, Fukuchi Y, Ouchi Y. Simple two-step swallowing provocation test for elderly patients with aspiration pneumonia. *Lancet* 1999; 353: 1243.
- 17 Wan GY, Zheng LY, Li HQ, Yuan H, Xue H, Zhang XY. Effects of enteral nutritional rich in n-3 polyunsaturated fatty acids on the nutritional status of gastrointestinal cancer patients: a systematic review and meta-analysis. *Eur J Clin Nutr* 2020; 74: 220–230.
- 18 Yin M, Si L, Qin W, et al. Predictive value of serum albumin level for the prognosis of severe sepsis without exogenous human albumin administration: a prospective cohort study. J Intensive Care Med 2018; 33: 687–694.
- 19 Tominaga N, Shimoda R, Iwakiri R, et al. Low serum albumin level is risk factor for patients with percutaneous endoscopic gastrostomy. Internal Med

2010; 49: 2283-2288.

- 20 Ayman AR, Khouny T, Cohen J, et al. PEG insertion in patients with dementia does not improve nutritional status and has worse outcomes as compared with PEG insertion for other indications. J Clin Gastroenterol 2017; 51: 417–420.
- 21 Lee JH, Kim J, Kim K, et al. Albumin and C-reactive protein have prognostic significance in patients with community-acquired pneumonia. J Crit Care 2011; 26: 287–294.
- 22 Yamagata A, Ito A, Nakanishi Y, Ishida T. Prognostic factors in nursing and healthcare-associated pneumonia. J Infect Chemother 2020; 26: 563–569.
- 23 Ito A, Ito I, Inoue D, et al. The utility of serial procalcitonin measurements in addition to pneumonia severity scores in hospitalised community-acquired pneumonia: a multicentre, prospective study. Int J Infect Dis 2020; 92: 228– 233.
- 24 Akagi T, Nagata N, Miyazaki H, *et al.* Procalcitonin is not an independent predictor of 30-day mortality, albeit predicts pneumonia severity in patients with pneumonia acquired outside the hospital. *BMC Geriatr* 2019; **19**: 3.
- 25 Haga T, Ito K, Sakashita K, Iguchi M, Ono M, Tatsumi K. Risk factors for death from psychiatric hospital-acquired pneumonia. *Intern Med* 2018; 57: 2473–2478.
- 26 Landbo C, Prescott E, Lange P, Vestbo J, Almdal TP. Prognostic value of nutritional status in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999; 160: 1856–1861.
- 27 Suzuki Y, Yoshimura K, Enomoto Y, et al. Distinct profile and prognostic impact of body composition changes in idiopathic pulmonary fibrosis and idiopathic pleuroparenchymal fibroelastosis. Sci Rep 2018; 8: 14074.
- 28 Ishii M, Yamaguchi Y, Hamaya H, Ogawa S, Imura M, Akishita M. Characteristics of factors for decreased lung function in elderly patients with type 2 diabetes. *Sci Rep* 2019; 9: 20206.
- 29 Cosquéric G, Sebag A, Ducolombier C, Thomas C, Piette F, Weill-Engerer

S. Sarcopenia is predictive of nosocomial infection in care of the elderly. *Br J Nutr* 2006; **96**: 895–901.

- 30 Nishizawa T, Sakitani K, Suzuki H, et al. Adverse events associated with bidirectional endoscopy with midazolam and pethidine. J Clin Biochem Nutr 2020; 66: 78–81.
- 31 Ehrlich SF, Quesenberry CP Jr, Van Den Eeden SK, Shan J, Ferrara A. 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.
- 32 Konomura K, Nagai H, Akazawa M. Economic burden of communityacquired pneumonia among elderly patients: a Japanese perspective. *Pneumonia* (*Nathan*) 2017; 9: 19.
- 33 Harada S, Aoki K, Yamamoto S, *et al.* Clinical and molecular characteristics of *Klebsiella pneumoniae* isolates causing bloodstream infections in Japan: occurrence of hypervirulent infections in health care. *J Clin Microbiol* 2019; 57: e01206–e01219.
- 34 Fujii S, Hara M, Nonaka S, *et al.* Infectious disease during hospitalization is the major causative factor for prolonged hospitalization: multivariate analysis of diagnosis procedure combination (DPC) data of 20,876 cases in Japan. J *Clin Biochem Nutr* 2016; **59**: 49–52.
- 35 Kornum JB, Thomsen RW, Riis A, Lervang HH, Schønheyder HC, Sørensen HT. Diabetes, glycemic control, and risk of hospitalization with pneumonia: a population-based case-control study. *Diabetes Care* 2008; **31**: 1541–1545.

