Type 2 Diabetes and Pneumonia Outcomes

A population-based cohort study

JETTE B. KORNUM, MD[1]
REIMAR W. THOMSEN, MD, PHD[1]
ANDERS RIIS, MSC[1]
HANS-HENRIK LERVANG, MD, PHD[2]
HENRIK C. SCHØNHEYDER, MD, DMSC[3]
HENRIK T. SØRENSEN, MD, DMSC[1]

OBJECTIVE — We sought to examine whether type 2 diabetes increases risk of death and complications following pneumonia and to assess the prognostic value of admission hyperglycemia.

RESEARCH DESIGN AND METHODS — This was a population-based cohort study of adults with a first-time hospitalization for pneumonia between 1997 and 2004 (n = 29,900) in northern Denmark. Information on diabetes, comorbidity, laboratory findings, pulmonary complications, and bacteremia was obtained from medical databases. We used regression to compute adjusted relative risks of pulmonary complications, bacteremia, and mortality rate ratios (MRRs) within 90 days following hospitalization among patients with and without type 2 diabetes. The prognostic impact of admission hyperglycemia was studied in a subcohort (n = 13,574).

RESULTS — In total, 2,931 (9.8%) pneumonia patients had type 2 diabetes. Mortality among diabetic patients was greater than that among other patients: 19.9 vs. 15.1% after 30 days and 27.0 vs. 21.6% after 90 days, respectively, corresponding to adjusted 30- and 90-day MRRs of 1.16 (95% CI 1.07–1.27) and 1.10 (1.02–1.18). Presence of type 2 diabetes did not predict pulmonary complications or bacteremia. Adjustment for hyperglycemia attenuated the association between type 2 diabetes and mortality. High glucose level on admission was a predictor of death among patients with diabetes and more so among those without diagnosed diabetes: adjusted 30-day MRRs for glucose level ≥14 mmol/l were 1.46 (1.01–2.12) and 1.91 (1.40–2.61), respectively.

CONCLUSIONS — Type 2 diabetes and admission hyperglycemia predict increased pneumonia-related mortality.

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Mortality among adults hospitalized with community-acquired pneumonia (CAP) ranges from 6 to 14% (1). Advanced age and comorbidity are associated with increased mortality in these patients (2–4). Given the hyperglycemia, decreased immunity, impaired lung function, and chronic complications, such as renal failure, heart disease, and pulmonary microangiopathy, associated with diabetes (5), it is plausible that diabetes may predict increased severity of pneumonia. However, results of recent observational studies and a meta-analysis of pneumonia-related mortality, based on pre-1996 research, were inconsistent (6–10). The discrepancies could stem from the use of clinic-based cohorts, confounding, or incomplete follow-up. Better diagnostic surveillance of diabetic patients may result in lower-than-expected mortality from pneumonia. Most studies lack data on pneumonia severity at hospitalization in diabetic versus nondiabetic patients (6,8–10), whereas claims that diabetic pneumonia patients have an increased risk of developing bacteremia (5,11) are questionable because data on availability of blood cultures are often absent. Evidence regarding pulmonary complications in diabetic patients with pneumonia is scant (5,7), as are data on the prognostic value of acute hyperglycemia for diabetic patients with pneumonia (10).

As prevalences of diabetes (12) and pneumonia-related hospitalizations increase in the aging Western populations (4,13), accurate data are needed to understand the clinical course of and to potentially prevent pneumonia-related deaths. We examined the impact of type 2 diabetes on mortality, pulmonary complications, and bacteremia among patients hospitalized with pneumonia. We also assessed the prognostic value of acute hyperglycemia at admission.

RESEARCH DESIGN AND METHODS

Setting and study population

We conducted this population-based cohort study in the Danish counties of North Jutland and Aarhus, with a mixed rural/urban population of ~1.15 million. The cohort consisted of all adult patients with a first-time hospital discharge diagnosis of pneumonia recorded in population-based medical databases between 1 January 1997 and 31 December 2004. The Danish National Health Service provides universal tax-supported health care, including free access to primary and hospital care and reimbursement of most prescription medication costs (14). Since 1968, all Danish residents carry a unique civil registration number, encoding sex and birth date, which is used in all health databases and permits unambiguous record linkage among them.

Patients hospitalized with pneumonia

Hospital discharge databases in Aarhus and North Jutland counties record all hospitalizations since 1977, including dates of admission and discharge, and up to 20 discharge diagnoses, coded by physicians according to the ICD-10 during the study period and ICD-8 earlier. We identified all adult (aged ≥15 years) patients with the following first-time dis-

From the [1]Department of Clinical Epidemiology, Aarhus University Hospital, Aalborg, Denmark; the [2]Department of Endocrinology, Aarhus University Hospital, Aalborg, Denmark; and the [3]Department of Clinical Microbiology, Aarhus University Hospital, Aalborg, Denmark.

Address correspondence and reprint requests to Jette B. Kornum, Department of Clinical Epidemiology, Aarhus University Hospital, Sdr. Skovvej 15, DK-9100 Aalborg, Denmark. E-mail: j.kornum@rn.dk.

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Abbreviations: ARDS, adult respiratory distress syndrome; CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

charge diagnoses: pneumonia (codes J12.x–J18.x), legionellosis (A481.x.), and ornithosis (A709.x) (4). We excluded patients who lived in the counties <1 year before the admission date (n = 1,281). Our study cohort thus comprised 29,900 patients with pneumonia, including 99 with legionellosis and 14 with ornithosis.

We were able to assess pneumonia severity among the North Jutland County patients (n = 13,574) through linkage with a laboratory database, which stores records on all specimens sent by hospitals and practitioners, including the exact time of blood sample collection. Laboratory data were unavailable for the Aarhus County subcohort. We obtained the first laboratory results available on the admission day or the following day.

Data on diabetes

Patients with diabetes were identified using combined discharge and prescription records. The prescription database tracks all filled prescriptions for the reimbursed drugs dispensed by all pharmacies in the counties (15). Diabetes was defined as present in patients with at least one prescription for insulin or an oral antidiabetes drug and/or with a discharge diagnosis of type 1 or two diabetes (ICD-8 codes 249–250 and ICD-10 codes E10–E11) predating the pneumonia admission. This definition was shown to have a predictive value of 97% (16). Cases of diabetes were classified as type 1 (those diagnosed before aged 30 years, using monotherapy with insulin, and with no history of oral antidiabetes medications) or type 2 (the remaining diabetes patients).

Data on hyperglycemia at admission

Glucose levels at admission or on the following day were available for 10,414 of 13,574 patients (77%) in the North Jutland cohort. We a priori defined glucose level categories of ≤6.10, 6.11–11.00, 11.01–13.99, and ≥14.00 mmol/l (10).

Confounding factors

We obtained data on comorbidity and other covariates from the hospital and prescription databases. From all available discharge diagnoses, except diabetes, we computed for each patient the Charlson comorbidity index score (17), defining three comorbidity levels as low (score of 0), medium (1–2), and high (≥3) (18). We also ascertained conditions not included in the Charlson index: history of alcoholism-related disorders (ICD-8 codes 291, 303, 979, 980, and 577.10; ICD-10 codes F10, K86.0, Z72.1, R78.0, T51, K29.2, G62.1, G72.1, and G31.2), history of obesity (ICD-8 code 277.99; ICD-10 codes E65.x and E66.x), use of immunosuppressants within the year before the pneumonia admission (ATC [Anatomical Therapeutic Chemical Classification System] codes L01, L04, and H02 AB), and use of systemic antibiotics within 90 days before admission (ATC code J01).

Pneumonia outcome

The main end point, defined a priori, was death from any cause within 30–90 days following the admission date. Most pneumonia-related deaths occur within 30 days of admission (19). Death within 90 days could be due to pneumonia sequelae following the initial illness (3). We ascertained mortality from the Danish Civil Registration System (20) and pulmonary complications by tracing all discharge diagnoses documented for the index hospitalization or, if a patient was discharged before day 30, until 30 days postadmission. We defined pulmonary complications as effusion (codes J90.9 and J91.9), empyema (J86.x.), lung abscess (J85.x), or adult respiratory distress syndrome (ARDS) (J80.9) (1).

In the North Jutland cohort, we identified all pneumonia patients with at least one blood culture and at least one episode of bacteremia occurring during the hospitalization for pneumonia or within 30 days following the admission date. This was done through linkage to the County Bacteremia Research Database (21), which stores prospectively collected data on all blood cultures, as well as bacteriological and clinical data on all bacteremia episodes from 1997 through 2003. We considered only the first episode of bacteremia during the hospitalization for pneumonia.

Statistical analysis

Type 2 diabetes and mortality. Follow-up extended for 90 days postadmission until death or migration, whichever came first. We constructed survival curves and computed cumulative mortality by comorbidity level. To compare mortality according to type 2 diabetes status, we used Cox's regression to estimate 30- and 90-day mortality rate ratios (MRRs) while controlling for sex, age (in categories of 15–39, 40–64, 65–79, and ≥80 years), level of comorbidity, history of alcoholism-related disorders, and preadmission use of antibiotics or immunosuppressants. Analyses were conducted with and without the obesity variable. We also adjusted for individual diseases by first computing the relative mortality rates associated with different disease categories in the Charlson index and then substituting log-transformed weights, based on these individual rates, for the Charlson index score levels in the mortality analysis. Patients with diabetes may have a higher risk of hospital-acquired pneumonia (HAP) than that for nondiabetic patients. As we were not able to clearly discriminate between CAP and HAP, we computed 30-day MRRs for type 2 diabetes separately for patients with pneumonia listed as the primary discharge diagnosis and for those with pneumonia listed as a secondary discharge diagnosis (13). To examine how much of the apparent effect of diabetes was caused by hyperglycemia, we included admission glucose level in the model for the North Jutland subcohort, both as a categorical and a continuous variable.

Type 2 diabetes, pulmonary complications, and bacteremia

We used logistic regression to estimate adjusted relative risk (RR) for pulmonary complications and bacteremia following pneumonia in patients with type 2 diabetes versus patients without diabetes.

Admission hyperglycemia and mortality

Among pneumonia patients in the North Jutland subcohort, we computed 30- and 90-day MRRs for different glucose level categories, using Cox's regression and controlling for confounders.

We analyzed data with SAS software (version 9.1.3; SAS Institute, Cary, NC). The Danish Registry Board approved the study (record no. 2006-41-6226).

RESULTS

Descriptive data

Of the 29,900 adult patients with pneumonia, 2,931 (9.8%) had type 2 diabetes. Only 92 (0.3%) patients had type 1 diabetes and were excluded. Table 1 provides descriptive data. The median age was 75 years among the diabetic patients and 73 years among the nondiabetic patients. As expected, patients with type 2 diabetes (hereafter referred to as diabetes) were more likely to have congestive heart failure, history of myocardial infarction, peripheral vascular disease, cerebrovascular disease, renal

Table 1—*Characteristics of patients hospitalized for pneumonia from 1997 to 2004 in Aarhus and North Jutland counties, Denmark*

Characteristics	Patients with type 2 diabetes	Patients without diabetes
n	2,931	26,877
Age (years)		
15–39	30 (1)	2,170 (8)
40–64	610 (21)	6,349 (24)
65–79	1,342 (46)	10,165 (38)
≥80	949 (32)	8,193 (30)
Sex		
Women	1,300 (44)	12,693 (47)
Men	1,631 (56)	14,184 (53)
Comorbidity		
Congestive heart failure	662 (23)	2,571 (10)
Peripheral vascular disease	394 (13)	1,855 (7)
Former myocardial infarction	481 (16)	2,373 (9)
Chronic pulmonary disease	639 (22)	5,209 (19)
Cerebrovascular disease	655 (22)	3,586 (13)
Hemiplegia	13 (0)	135 (1)
Dementia	95 (3)	521 (2)
Connective tissue disease	172 (6)	1,237 (5)
Moderate/severe renal disease	168 (6)	762 (3)
Any type of malignancy	467 (16)	4,294 (16)
Any liver disease	91 (3)	409 (2)
AIDS	0 (0)	23 (0)
Alcoholism-related disorders	184 (6)	1,257 (5)
Obesity	347 (12)	473 (2)
Comorbidity index*		
Low (0)	809 (28)	11,588 (43)
Medium (1–2)	1,349 (46)	10,866 (40)
High (≥3)	773 (26)	4,423 (16)
Immunosuppressive drugs	513 (18)	5,011 (19)
Systemic antibiotic therapy before admission	1,157 (39)	10,417 (39)
Pneumonia as primary discharge diagnosis	1,744 (60)	17,261 (64)
Pneumonia as secondary discharge diagnosis	1,187 (40)	9,616 (36)
Duration of hospital stay	7 (4–13)	7 (3–12)
Laboratory findings (n = 13,574)†	1,415	12,159
Arterial pH (ref. 7.35–7.42)	7.42 (7.37–7.46)	7.43 (7.38–7.47)
PaO_2 (ref. 10.0–14.5) (kPa)	8.1 (6.8–9.7)	8.2 (6.9–9.7)
Hematocri (female ref. 0.35–0.46, male ref. 0.40–0.50)	0.38 (0.34–0.42)	0.38 (0.34–0.42)
Hemoglobin (female ref. 7.4–9.6, male ref. 8.4–10.8) (mmol/l)	7.9 (7.1–8.8)	8.1 (7.2–8.8)
Urea nitrogen (ref. 3.0–7.5) (mmol/l)	9.2 (6.1–16.3)	6.9 (4.8–10.8)
Creatinine (female ref. 55–115, male ref. 60–125) (μmol/l)	106 (82–146)	92 (74–120)
Sodium (ref. 136–147) (mmol/l)	137 (134–140)	138 (134–140)
Leukocyte count (ref. 4.0–11.0) (10^9/l)	12.7 (9.5–17.2)	12.1 (8.9–16.2)
C-reactive protein (ref. <10) (mg/l)	85 (32–176)	88 (34–181)
Glucose (ref. 3.1–7.8) (mmol/l)	9.3 (6.6–13.6)	6.0 (5.2–7.2)

Data are n (%) or median (interquartile range). *Level of Charlson index score (see text). †Laboratory findings on the date of admission (or the day after, if unavailable) in patients hospitalized with pneumonia in North Jutland County. Results available for >90% of patients, except for arterial pH, PaO_2, hematocrit, and urea nitrogen (available for 40–52% of patients) and glucose (available for 90% of diabetic and 71% of other patients).

disease, and obesity (which was likely underreported).

The median duration of hospital stay was 7 days and did not differ by diabetes status. In the North Jutland subcohort, patients with diabetes had higher median levels of urea nitrogen, creatinine, and glucose but nearly the same levels of C-reactive protein, leukocyte counts, and PaO_2 at admission, compared with the nondiabetic patients.

Type 2 diabetes and mortality

Mortality among diabetic patients was 19.9 vs. 15.1% among other patients after 30 days (mortality difference 4.8% [95% CI 3.3–6.3]) and 27.0 vs. 21.6% after 90 days (5.3% [3.7–7.0]). Patients with diabetes had higher cumulative mortality, independent of comorbidity (Fig. 1). Adjusted 30- and 90-day MRRs for diabetic pneumonia patients were 1.16 (95% CI 1.07–1.27) and 1.10 (1.02–1.18), compared with nondiabetic pneumonia patients (Table 2). Further adjustment for obesity yielded virtually identical 30- and 90-day MRRs (1.18 [95% CI 1.08–1.29]

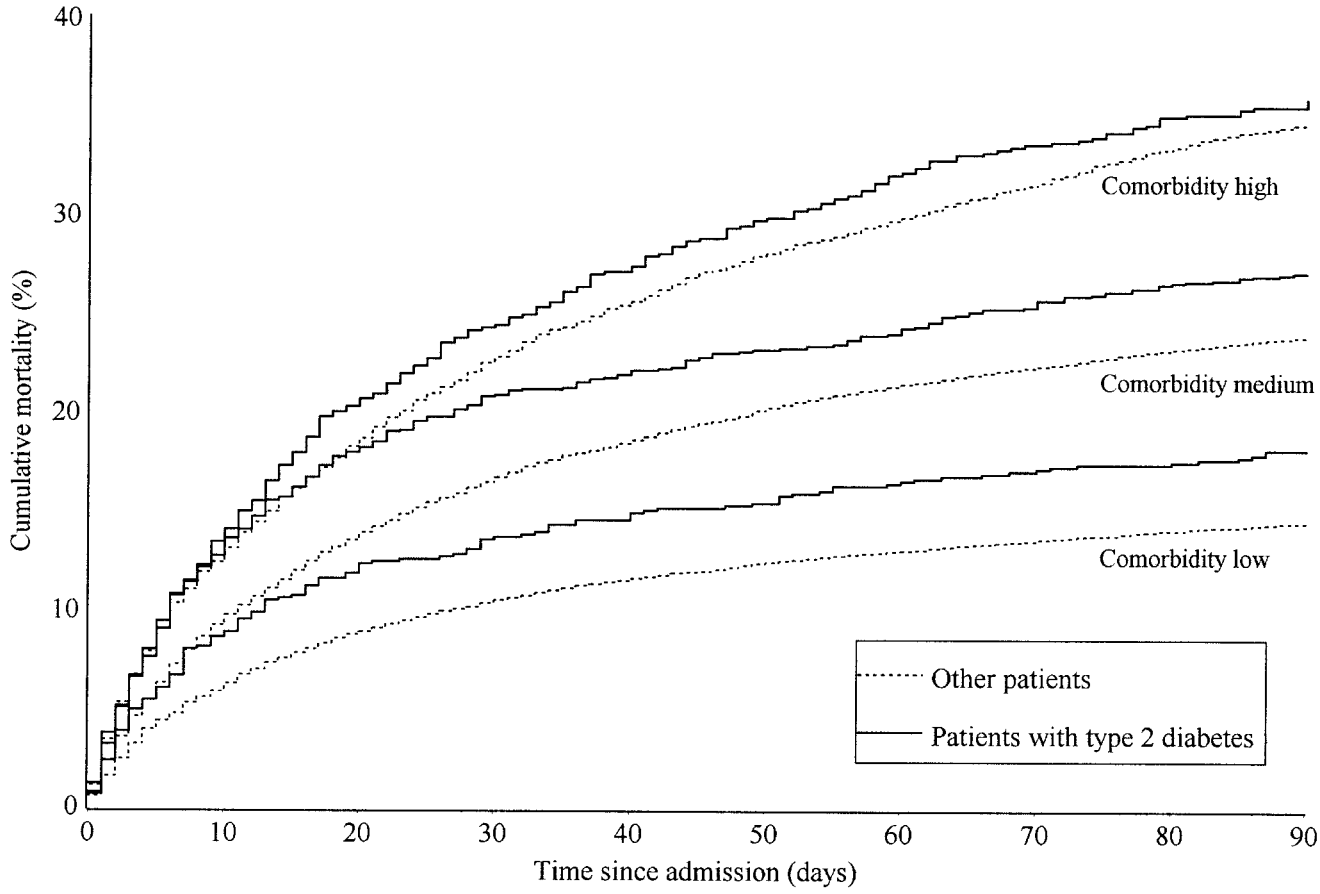

Figure 1—*Mortality curves for patients with type 2 diabetes compared with other patients hospitalized with pneumonia, according to level of Charlson index score.*

and 1.12 [1.04–1.20]), as did adjustment for individual disease categories in lieu of Charlson index score levels (1.17 and 1.11, respectively).

Patients with type 2 diabetes were slightly more likely than other pneumonia patients to have pneumonia listed as a nonprimary discharge diagnosis (40.5 vs. 35.8%). The adjusted 30-day MRR was 1.18 (95% CI 1.05–1.34) for diabetic patients with pneumonia listed as a secondary discharge diagnosis and 1.13 (1.00–1.27) for those with pneumonia listed as the primary discharge diagnosis.

In the North Jutland cohort, the prognostic impact of type 2 diabetes was slightly lower than that in the overall cohort, and the association between diabetes and mortality vanished after adjustment for confounding (30-day MRR 0.98 [95% CI 0.86–1.11]); 90-day MRR 0.97 [0.87–1.09]). Among the subset of patients with bacteremic pneumonia, mortality from diabetes was slightly lower, with MRR 0.86 (95% CI 0.54–1.38) and 0.92 (0.62–1.36), respectively. After the categorical variable for the glucose level at admission was added to the regression model, the adjusted 30- and 90-day MRRs for patients with diabetes markedly decreased, respectively, from 0.98 and 0.97 to 0.82 (0.71–0.95) and 0.89 (0.79–1.00). Using glucose level as a continuous variable yielded similar estimates (data not shown).

Type 2 diabetes, pulmonary complications, and bacteremia

The cumulative incidence of recorded pulmonary complications was 2% among patients with or without diabetes. Except for ARDS, pneumonia patients with dia-

Table 2—*Crude and adjusted mortality within 30 and 90 days among patients hospitalized for pneumonia*

Prognostic factor	*n*	Deaths	Mortality (%)	Crude MRR (95% CI)	Adjusted MRR (95% CI)*	*P*
30 day						
No diabetes	26,877	4,048	15.1	1.0 (ref.)	1.0 (ref.)	
Type 2 diabetes	2,931	582	19.9	1.36 (1.25–1.48)	1.16 (1.07–1.27)	<0.01
90 day						
No diabetes	26,877	5,818	21.6	1.0 (ref.)	1.0 (ref.)	
Type 2 diabetes	2,931	791	27.0	1.30 (1.21–1.40)	1.10 (1.02–1.18)	0.02

Data are *n* unless otherwise indicated. *Adjusted for sex, age group, level of comorbidity, alcoholism-related conditions, and use of antibiotics and immunosuppressive drugs before admission.

Table 3—*Crude and adjusted mortality within 30 days among pneumonia patients with available glucose values on admission*

30-day glucose level (mmol/l)	*n*	Deaths	Mortality (%)	Crude MRR (95% CI)	Adjusted MRR (95% CI)*	*P*
All patients	10,414					
≤6.1	5,129	727	14.2	1.0 (ref.)	1.0 (ref.)	
6.11–11.0	4,446	903	20.3	1.49 (1.36–1.65)	1.37 (1.25–1.51)	<0.01
11.01–13.99	383	86	22.5	1.68 (1.35–2.10)	1.49 (1.19–1.86)	<0.01
≥14	456	107	23.5	1.79 (1.46–2.20)	1.71 (1.40–2.10)	<0.01
Patients with type 2 diabetes	1,307					
≤6.1	279	52	18.6	1.0 (ref.)	1.0 (ref.)	
6.11–11.0	545	95	17.4	0.93 (0.66–1.30)	0.96 (0.69–1.35)	0.82
11.01–13.99	188	40	21.3	1.18 (0.78–1.78)	1.24 (0.82–1.88)	0.31
≥14	295	65	22.0	1.24 (0.86–1.78)	1.46 (1.01–2.12)	0.04
Other patients	9,107					
≤6.1	4,850	675	13.9	1.0 (ref.)	1.0 (ref.)	
6.11–11.0	3,901	808	20.7	1.56 (1.41–1.73)	1.43 (1.29–1.59)	<0.01
11.01–13.99	195	46	23.6	1.81 (1.34–2.44)	1.65 (1.23–2.23)	<0.01
≥14	161	42	26.1	2.07 (1.51–2.82)	1.91 (1.40–2.61)	<0.01

Data are *n* unless otherwise indicated. *Adjusted for sex, age group, level of comorbidity, alcoholism-related conditions, and use of antibiotics and immunosuppressive drugs before admission.

betes had pulmonary complication rates similar to those among other pneumonia patients. The overall adjusted RR for pulmonary complications was 1.02 (95% CI 0.75–1.40). The adjusted RR for ARDS among patients with diabetes was 4.86 (1.17–20.22). Overall, 60.2% of patients with diabetes and 59.7% of other pneumonia patients had at least one blood culture. *Streptococcus pneumoniae* was the pathogen in 51.1% of all bacteremia episodes. Among pneumonia patients with blood cultures available, the adjusted RR for bacteremia in diabetic versus nondiabetic patients was 1.02 (0.78–1.33). Patients with diabetes had a risk similar to that of their nondiabetic counterparts for pneumococcal bacteremia (adjusted RR 1.17 [95% CI 0.84–1.62]), a greater risk of bacteremia due to gram-positive pathogens other than *S. pneumoniae* (1.69 [1.02–2.80]), and a lower risk for gram-negative bacteremia (0.72 [0.42–1.23]).

Hyperglycemia at admission and mortality

Ninety percent of diabetic and 71% of nondiabetic patients in the North Jutland subcohort had blood glucose values measured at admission or on the following day. Among patients without diabetes, the 30-day mortality increased from 13.9% at glucose values ≤6 mmol/l to 26.1% at glucose values ≥14 mmol/l (Table 3). Hyperglycemia was also associated with increased mortality in patients with diabetes, but the association was restricted to those with admission glucose values of >11 mmol/l. In the adjusted analyses, a high glucose level at admission remained a strong predictor of death among patients with diabetes but more so among those without diagnosed diabetes: adjusted 30-day MRRs for glucose levels ≥14 mmol/l were 1.46 (95% CI 1.01–2.12) and 1.91 (1.40–2.61), respectively. When we included admission glucose values as a continuous variable, each 1-mmol/l increase augmented the mortality rate among all patients by 3.3% after 30 days and by 2.1% after 90 days. For the diabetic patients, the respective increases were 3.2 and 1.8% and for other patients were 4.1 and 3.0%. However, the linear model did not fit the data well, with both very low and high glucose levels associated with increased mortality.

CONCLUSIONS — In this population-based cohort study, type 2 diabetes was a clear marker of increased mortality from pneumonia, although this was largely explained by differences in patient age and comorbidity. The relative mortality increase conferred by type 2 diabetes appeared to be the highest in the early phase of infection but persisted for at least 90 days. Type 2 diabetes did not predict pulmonary complications or bacteremia. Admission glucose levels of >11 mmol/l in type 2 diabetic patients and of >6 mmol/l in other patients predicted increased mortality.

In a Canadian study of 2,471 patients with CAP, including 401 patients with diabetes, McAlister et al. (10) found that a diabetes history did not predict in-hospital mortality. They did find hyperglycemia on admission to be associated with a poor prognosis for both diabetic and nondiabetic patients with CAP, which corroborates our findings. Based on 623,718 U.S. patients aged >65 years and hospitalized for CAP, Kaplan et al. (9) reported no association between in-hospital mortality and diabetes: adjusted RR 0.96 (95% CI 0.93–0.99). The patients with diabetes were identified from hospital records, thus excluding diabetic patients who were never hospitalized. The 1996 meta-analysis of CAP prognosis by Fine et al. (8) put a relative mortality at 1.3 (1.1–1.5) for diabetic compared with nondiabetic patients. The results of this analysis, which did not adjust for confounding, are similar to those of the crude 30-day MRR in our study. A recent Spanish study of 660 patients with CAP found that diabetes was associated with markedly increased 30-day mortality (adjusted RR 2.14 [95% CI 1.09–4.19]) (7). However, this study relied on a selected cohort of diabetic patients hospitalized at a university hospital, who were likely to have greater disease severity compared with patients in our population-based cohort.

Our study's strengths include its large size, population-based design, adjustment for important confounders, complete follow-up for mortality, and detailed information on blood chemistry and bacteremia in one of the study regions. Use of routinely recorded health care data, collected independently of the study hypothesis, reduced the risk of information bias.

One of the most important limitations is the possibility of surveillance bias, as

physicians could be more likely to hospitalize diabetic patients with infection. Such bias, inevitable in observational studies on this topic, would cause underestimation of the diabetes-related mortality. However, comparable preadmission use of antibiotics, similar levels of inflammatory parameters, and similar proportions of patients with at least one blood culture among diabetic and nondiabetic patients all speak against a severe bias.

The validity of our estimates depends on the accuracy of pneumonia and diabetes records. Despite inevitable coding errors, the estimated predictive value of a discharge diagnosis of pneumonia in Denmark is 90% (4). Some type 2 diabetic patients could be missed if they had not been hospitalized or treated with antidiabetes drugs, causing mortality underestimation. However, if patients identified with type 2 diabetes had greater-than-average disease severity, mortality would be overestimated. Still, it has been shown that 89% of known diabetes patients in Denmark could be identified by combining discharge diagnoses records with prescription data (22).

Because admission diagnoses were unavailable in our database, we could not discriminate between CAP and HAP. The crude mortality rates from HAP range from 30 to as high as 70% (23). A recent Danish study showed that only 13% of pneumonia episodes in the hospital discharge database from North Jutland County were hospital acquired (4). If patients with diabetes were relatively more susceptible to HAP due to more frequent hospitalizations, failure to discriminate between CAP and HAP could partly explain the greater diabetes-related mortality found in our study compared with that in the study by Kaplan et al. (9). However, similarly increased mortality associated with type 2 diabetes was observed regardless of pneumonia being listed as the primary discharge diagnosis. Lack of data precluded adjustment for pneumococcal and influenza vaccinations, which have been associated with reduced mortality among patients hospitalized with pneumonia (24,25). Even if patients with type 2 diabetes were vaccinated at higher rates than others, this would lead to underestimation of the relative mortality associated with diabetes and therefore would not alter our conclusions.

Biological mechanisms underlying increased mortality among diabetic patients hospitalized for pneumonia may include decreased leukocyte function and harmful effects of hyperglycemia (5,10,26). In fact, after controlling for admission glucose level in the subset of patients with available glucose measurements, type 2 diabetes no longer predicted increased mortality following pneumonia and even tended to be associated with improved prognosis. However, the estimates from the regression model are difficult to interpret for several reasons. First, it is conceptually difficult to separate blood glucose levels from diabetes, since hyperglycemia is included in the definition of diabetes. Second, MRR estimates associated with diabetes were lower in the North Jutland subcohort than in the total cohort. This may be due to chance, increased surveillance of diabetic patients in this region, or demographic differences (e.g., pneumonia patients in this region were older and had more comorbidities and thus were more likely to die regardless of diabetes status).

Still, our analysis suggests that much of the increased mortality associated with type 2 diabetes is mediated through the glucose level. The impact of hyperglycemia on mortality was lower among patients with type 2 diabetes than that among other patients. In nondiabetic patients, hyperglycemia could signal physiological stress and thus greater pneumonia severity (27). Furthermore, some nondiabetic patients with hyperglycemia could have been undiagnosed and therefore untreated diabetic patients (27), experiencing a poor outcome following pneumonia. By contrast, in diabetic patients, hyperglycemia could be due to poorly controlled diabetes, stress, or both, since we did not know their baseline concentration of glucose (28). In addition, patients with type 2 diabetes might be more likely to receive insulin for hyperglycemia (28) during pneumonia-related hospitalization, thus improving outcome among critically ill patients (29). Hyperglycemia can cause intracellular and extracellular dehydration, electrolyte abnormalities, and depressed immunity (27). Furthermore, impaired lung function and pulmonary microangiopathy have been observed among diabetic patients (5). The elevated mortality that we observed in diabetic patients did not appear to be mediated through more pulmonary complications. Rather, patients with diabetes had more underlying renal disease and considerably higher levels of urea nitrogen and creatinine at the time of admission. Urea nitrogen level on admission predicts CAP outcome and is included in prognosis prediction rules such as the Pneumonia Severity Index score (26).

We did not observe an elevated risk of bacteremia in diabetic pneumonia patients. In the subgroup of bacteremic pneumonia patients, mortality ratio estimates for those with diabetes indicated protective effect, confirming previous findings for diabetic patients with pneumococcal bacteremia (30). It has been suggested that diabetic patients with sepsis may be protected from severe complications, such as ARDS, via a less active inflammatory cascade (30,31). However, we observed, though based on little data, that diabetic pneumonia patients were more likely to have a record of ARDS.

In conclusion, patients with type 2 diabetes have an increased risk of death associated with pneumonia hospitalization. Risk of hyperglycemia at admission was increased among the diabetic patients, while high glucose levels were associated with increased mortality in all patients. Our results showed that glucose on admission is a very important clinical indicator among patients with pneumonia. Our results also suggest that current hospitalization routines and surveillance during and after pneumonia-related hospitalization of patients with type 2 diabetes could be improved.

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