Immunocompromised adults hospitalized with community-acquired pneumonia in the United States: incidence, epidemiology and outcomes

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INTRODUCTION

Even though CAP is a major cause of morbidity and mortality in immunocompromised adults (ICAs), there is a significant lack literature regarding the burden of CAP in ICAs. The objectives of this study were 1) to define incidence, epidemiology, and outcomes of ICAs hospitalized with CAP in the city of Louisville, Kentucky, and 2) to estimate the burden of CAP in ICAs in the US.

METHODS

This was an ancillary study of a prospective cohort which consecutively enrolled adults hospitalized with CAP from June 1, 2014 to May 31, 2016 at any of the nine adult acute-care hospitals in Louisville, KY.

An ICA was identified using the following CDC criteria: (1) primary immunodeficiency disease; (2) advanced-stage or hematologic cancer; (3) advanced HIV infection; (4) solid organ transplantation; (5) hematopoietic stem cell transplantation; (6) receiving cancer chemotherapy; (7) receiving an immunocompromising dose of corticosteroid therapy; (8) receiving biological immune modulators; (9) receiving disease-modifying antirheumatic drugs (DMARDs). Patients with any of these criteria were considered immunocompromised.

Patient immune system function was classified into four ordinal groups: 1) normal immune system (age <65 years and no comorbidity); 2) abnormal immune system (age ≥65 years or at least one comorbidity); 3) immunocompromised (at least one criteria listed above); or 4) severely immunocompromised (more than one of the criteria listed above). Patients in groups 1 and 2 included all the non-immunocompromised adults (non-ICAs). Patients in groups 3 and 4 included all ICAs.

The annual population-based incidence of hospitalized CAP among ICAs was calculated and extrapolated to the United States. Geospatial data analysis was used to define ecological associations with poverty, race, and age. Areas of increased relative risk of hospitalization, given the underlying population density, were calculated and overlaid onto kernel density heat maps.

Mortality was evaluated up to one year after hospital discharge. Kaplan-Meier estimation was performed and mortality was compared between ICAs and non-ICAs and within the four ordinal groups of immune system function.

RESULTS

A total of 7,449 unique patients were included, with 809 (11%) ICAs identified. This corresponds to an annual hospitalized incidence of 72 ICAs per 100,000 adults living in Louisville, and an estimated 196,753 hospitalized ICAs per year in the United States. When classified according to immune system function, 6% had normal immune system, 83% had abnormal immune system, 8% were immunocompromised, and 3% were severely immunocompromised. Patient demographics and comorbidities comparing ICAs to non-ICAs are depicted in **Table 1.** The immunocompromising conditions of ICAs are depicted in **Figure 1**. The heat map of ICAs with CAP in the city of Louisville is depicted in **Figure 2A**. Heat maps depicting the density of individuals in poverty, of black or African American race, or elderly (aged ≥65) are depicted in **Figures 2B, 2C and 2D**. Time to death from hospitalization for ICAs vs non-ICAs and by patient immune function are depicted in **Figures 3A and 3B.**

Table 1. Patient demographics and medical history

	ICA 809 (11%)	non-ICA 6640 (89%)	p-value
Demographics and social history			
Age (median [IQR])	66 [57, 76]	68 [56, 80]	0.013
Sex: Male (%)	377 (46.6)	3066 (46.2)	0.848
Nursing home resident (%)	79 (9.8)	908 (13.7)	0.002
Black (%)	178 (22.0)	1297 (19.5)	0.106
Former smoker (%)	349 (43.1)	2411 (36.3)	<0.001
History of comorbid disease*			
Obesity (%)	223 (27.6)	2392 (36.0)	<0.001
Diabetes (%)	227 (28.1)	2206 (33.2)	0.004
Renal Disease (%)	218 (26.9)	1967 (29.6)	0.124
COPD (%)	361 (44.6)	3114 (46.9)	0.235
Liver disease (%)	75 (9)	460 (7)	0.018
Cerebrovascular disease (%)	75 (9.3)	880 (13.3)	0.002
Coronary artery disease (%)	195 (24.1)	2023 (30.5)	<0.001
Hypertension (%)	504 (62.3)	4649 (70.0)	<0.001
Hyperlipidemia (%)	295 (36.5)	2939 (44.3)	<0.001
Atrial fibrillation (%)	130 (16.1)	1335 (20.1)	0.007

*Comorbidities are not mutually exclusive, and a patient may have more than one comorbidity.

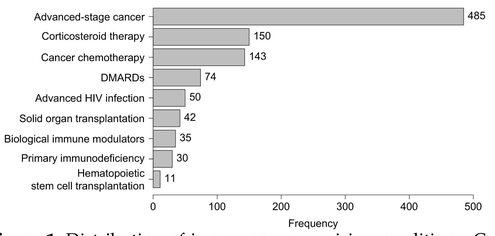

Figure 1. Distribution of immunocompromising conditions. Conditions are not mutually exclusive, and a patient may have more than one.

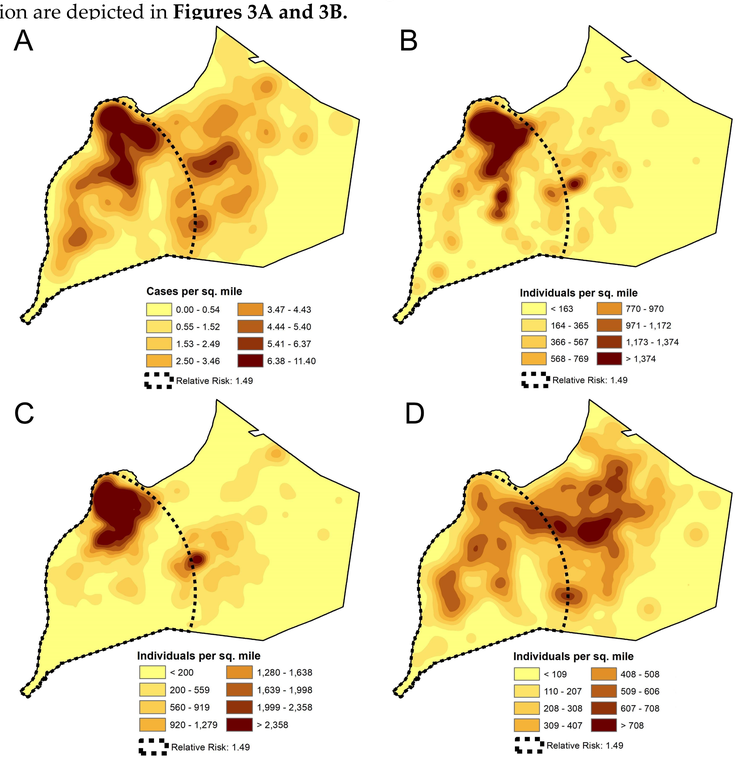

Figure 2. Kernel density heat maps of Louisville, KY, with areas of risk overlaid. **A)** Kernel density heat map of ICAs. **B)** Kernel density heat map of persons in poverty. **C)** Kernel density heat map of black or African American persons. **D)** Kernel density heat map of elderly persons.

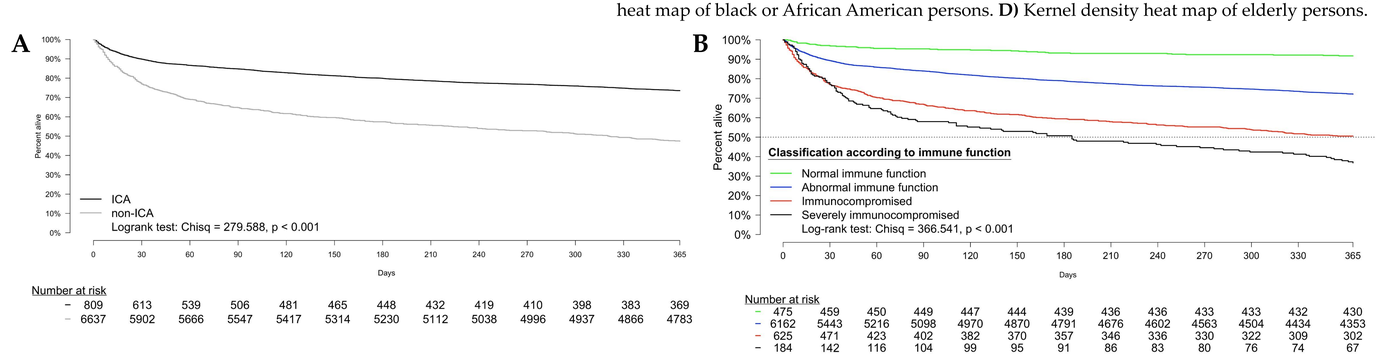

Figure 3. (left) Time to death from hospitalization, comparing ICAs to non-ICAs. (right) Time to death from hospitalization, comparing the four groups based on immune system function.

DISCUSSION

Approximately 11% of hospitalized patients with CAP are immunocompromised, with a total of nearly 200,000 hospitalizations of ICAs with CAP each year in the US.

The most common immunocompromising condition of ICAs was cancer, followed by corticosteroid therapy. ICAs were more likely to be former smokers, with lung cancer being the most frequent cancer diagnosis. Non-ICAs had higher rates of other comorbidities such as obesity, diabetes, and coronary artery disease.

Geospatial epidemiology indicates that areas in the city of Louisville with a high incidence of ICAs hospitalized with CAP overlap with areas with a high proportion of impoverished residents and black or African American residents. The increased risk for hospitalization due to CAP among the most socially disadvantaged immunocompromised population argues for pneumonia prevention strategies prioritizing these groups. The majority of ICAs and non-ICAs hospitalized due to CAP were older than 65 years of age. However, we did not find an ecological association of older adult patients in Louisville and ICAs hospitalized with CAP, likely due to the fact that older adults in Louisville are less clustered than poverty and race. Our data suggest that the risk for hospitalization due to CAP in ICAs is associated with both socioeconomic and/or racial groups. Further studies evaluating the epidemiology of ICAs hospitalized with CAP should examine these disparity patterns.

Mortality for ICAs was almost doubled when compared to mortality in non-ICAs during hospitalization, at 30 days, at 6 months and 1 year after diagnosis of CAP. Nearly one out of two ICAs died within one year after a hospitalization due to CAP. Evaluating mortality based on the four ordinal groups of immune system function showed that mortality increased as immune function decreased. Further studies are needed to evaluate the role CAP plays in the high mortality of these patients.

CONCLUSIONS

In conclusion, this study demonstrates a significant burden of immunocompromised adults hospitalized with CAP in the United States. Our data suggest that socioeconomic disparities may contribute to hospitalization of ICAs due to CAP. Further studies examining drivers for mortality and prevention measures in these high-risk patients are necessary.

FUNDING AND CONFLICTS OF INTEREST

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