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Detection of influenza myocarditis using national healthcare safety network surveillance definitions accounting for fever in older adults

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To the Editor—Cardiovascular complications following influenza infection are often severe.^{1,2} National Healthcare Safety Network (NHSN) surveillance definitions monitor cardiovascular complications such as myocarditis. However, NHSN surveillance definitions for myocarditis do not account for immunosenescence in older adults. Specifically, older adults frequently have lower baseline temperatures and blunted febrile responses.³ Accordingly, Infectious Diseases Society of America (IDSA) guidelines for older adults define fever as (1) a single oral temperature >100° F; (2) repeated oral temperatures >99°F; or (3) an increased temperature >2°F above baseline.⁴ This is important because older adults incur high risks of influenza-associated complications,⁵ and 2017 NHSN criteria define fever exclusively as temperature >100.4°F.

We compared the detection of myocarditis following influenza infection using the 2017 NHSN definition and a proposed modified definition that accounts for fever in older adults. We performed a cohort study of all inpatients ≥18 years of age with influenza A or influenza B between November 1, 2014, and April

30, 2015, and November 1, 2015, and April 30, 2016, at Yale New Haven Hospital, a 1,541-bed tertiary-care medical center in New Haven, Connecticut. Influenza was detected using real-time Taqman polymerase chain reaction according to the protocol developed by the Yale New Haven Hospital Clinical Virology Laboratory. The Yale Human Investigation Committee approved this study.

We identified all patients developing myocarditis within 30 days following influenza detection using the 2017 NHSN definition and proposed modified definition. The 2017 NHSN definition considered myocarditis as meeting 1 of the following criteria: (1) influenza identified from myocardial tissue or (2) ≥2 clinical features including fever (>100.4°F), chest pain, paradoxical pulse, or increased heart size with no other recognized cause plus ≥1 additional parameter including an EKG consistent with myocarditis, histological evidence of myocarditis, 4-fold rise in paired sera from IgG antibody titer, or pericardial effusion. Our proposed modified definition had criteria identical to those of the 2017 NHSN definition except for fever, which was defined according to the IDSA guidelines for older adults ≥65 years of age.⁴

For all patients, we recorded demographics, comorbidities, antiviral therapy, receipt of seasonal influenza vaccine, hospital characteristics, all-cause mortality, and whether NHSN criteria were present. Influenza infection was categorized as community-acquired versus hospital-acquired based on detection within 48 hours of admission. We compared differences in the proportions of myocarditis detected with the 2017 NHSN definition versus the proposed modified definition using the McNemar test.

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PREVIOUS PRESENTATION: This work was presented in part at IDWeek 2017 (Abstract no. 64324) in San Diego, California, in the Adult Viral Infection Session (Poster no. 1042) on October 6, 2017.

Cite this article: Datta R, et al. (2018). Detection of influenza myocarditis using national healthcare safety network surveillance definitions accounting for fever in older adults. *Infection Control & Hospital Epidemiology* 2018, 39, 1145–1147. doi: 10.1017/ice.2018.147

Table 1. Descriptive Characteristics of Adult Patients With Influenza

Characteristic	2014–15 Season (N = 454), No. (%)	2015–16 Season (N = 304), No. (%)
Female gender	257 (57)	162 (53)
White race	313 (69)	171 (56)
Acquisition type		
Community-acquired	415 (91)	275 (90)
Hospital-acquired	39 (9)	29 (10)
Influenza type		
A	380 (84)	251 (83)
B	74 (16)	53 (17)
Comorbidities		
Chronic obstructive pulmonary disease	163 (36)	110 (36)
Solid organ tumor	96 (21)	46 (15)
Diabetes mellitus	113 (25)	68 (22)
End-stage renal disease	21 (5)	9 (3)
Pregnancy	6 (1)	5 (2)
Cerebrovascular disease	171 (38)	83 (27)
Immunocompromised	50 (11)	38 (13)
Body mass index > 40	46 (10)	38 (13)
Admission location		
Home	373 (82)	259 (85)
Skilled nursing facility	63 (14)	30 (10)
Transfer	8 (2)	7 (2)
Other	10 (2)	8 (3)
Discharge disposition		
Home	282 (62)	218 (72)
Skilled nursing facility	132 (29)	63 (21)
Death	23 (5)	15 (5)

Overall, we identified 758 influenza-positive patients. Median age was 66 years (range, 18–97 years). Table 1 provides patient characteristics. Among all patients, 181 patients (23.9%) received the seasonal influenza vaccine, and 534 patients (70.4%) received antiviral therapy. The median length of stay was 4 days (interquartile range, 2–9 days).

There was no difference in detection of influenza-associated myocarditis using the proposed modified (N = 6, 0.8%) versus the 2017 NHSN (N = 5, 0.7%) definition ($P = .32$). Among the 6 myocarditis cases, 4 patients were ≥ 65 years of age. The additional case was detected using the proposed modified definition; this patient had fever (defined by a single temperature $> 100^\circ\text{F}$) and repeated temperatures $> 99^\circ\text{F}$. Overall, 5 cases met both definitions. The most common criteria included EKG findings (N = 6), fever (N = 5), and chest pain (N = 4). Furthermore, 3 case patients

required intensive care, 2 patients required intubation and inotropic support, and 1 patient died.

Although not statistically significant, our results suggest that the 2017 NHSN definition may underestimate the frequency of myocarditis when compared to a proposed modified definition that accounts for fever in older adults per IDSA guidelines. Despite an absolute difference of 1 case, the differential detection of myocarditis may be more pronounced across larger populations with predominantly older adults, such as that cared for by the Veterans Health Administration. Moreover, these data contribute to the limited body of evidence evaluating myocarditis surveillance definitions. Collectively, our findings underscore the need for increased recognition for cardiovascular complications following influenza infection in older adults.

The variable presentation of myocarditis from asymptomatic infection to cardiogenic shock has implications for surveillance.^{4,6,7} Without myocardial biopsy, which is often reserved for fulminant cases, we show that NHSN criteria may selectively detect nonsevere cases. Additionally, EKG changes in myocarditis are variable, which may impact sensitivity and specificity of surveillance definitions.⁸ Revised NHSN criteria accounting for immunosenescence in older adults may broaden recognition of influenza-associated myocarditis and promote early supportive care.

This work has several limitations. First, our analysis is limited by the small number of cases consistent with the rarity of myocarditis. Second, referenced IDSA guidelines were established for long-term care facilities.⁴ However, the frequency of admissions from long-term care facilities and prevalence of multiple comorbidities and functional disabilities among inpatients suggest that these guidelines may be generalizable. Finally, data collection was subject to observation bias.

In summary, $\sim 1\%$ of adult inpatients with laboratory-proven influenza meet criteria for myocarditis within 30 days of influenza detection. When applying a proposed modified definition of myocarditis that accounts for fever in older adults, only 1 additional case was detected compared to the 2017 NHSN definition. Larger studies are needed to compare differences in myocarditis detection using surveillance definitions that account for immunosenescence in older adults.

Acknowledgments. We thank the Yale New Haven Hospital Department of Infection Prevention for their support of this work.

Financial support. This work was supported by the Section of Infectious Diseases at Yale School of Medicine (grant no. 2T32AI007517-16).

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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