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EDITORIAL

Influenza Vaccine: Routine Secondary Prevention for Patients With Cardiovascular Disease?

The association between influenza and cardiovascular disease was first recognized with the observation that all-cause mortality increases with influenza epidemics, and evidence of more specific associations with myocardial infarction, stroke, and other cardiovascular outcomes has accrued since then (1). In their article, Chow and colleagues (2) confirm that cardiovascular events are an important contributor to the morbidity and mortality associated with influenza. They studied 80 261 adults with confirmed influenza and determined that almost 12% had an acute cardiovascular event, most commonly acute heart failure (6.2%) or acute ischemic heart disease (5.7%). This study also showed that patients with the combination of influenza and acute cardiovascular events have high care needs: Median length of stay was 5 days, 31.2% of patients required intensive care, and 7.3% died in the hospital. Of fatal cases, 1 in 4 had an associated acute cardiovascular event, reflecting potentially preventable influenza-related cardiovascular mortality.

The respiratory morbidity and mortality of influenza are well recognized; however, the cardiovascular burden is also substantial but often unrecognized. In 1 study, the rate of influenza infection in persons admitted to the hospital with acute myocardial infarction was almost 8% (3). Another study found that 12.4% of patients admitted with acute myocardial infarction had unrecognized and undiagnosed influenza (4).

Most studies to date have looked at the prevalence of influenza in patients with acute cardiovascular events. Chow and colleagues (2) add to this body of evidence by showing that among all diagnosed influenza admissions, acute cardiovascular disease is common. Yet, influenza may be substantially underdiagnosed. In the United States, influenza-related hospitalizations were estimated to be underdetected by a factor of 3.2 for adults aged 18 to 65 years and by more than 5 times in adults older than 65 years (5). Therefore, the true rate of simultaneous influenza and acute cardiovascular disease may be even greater than suggested by this research.

Because of the clear relationship between influenza and acute cardiovascular events, all patients with influenza should be assessed for cardiovascular health and vaccination status. Conversely, clinicians should consider influenza in patients presenting with acute cardiovascular events during the influenza season. There is an argument for testing patients with acute cardiovascular events at any time of the year, given that influenza can occur outside the typical season. The clinical recognition of influenza in patients presenting with other clinical syndromes, such as cardiovascular disease, is challenging. Unlike children, in whom fever is common with influenza, only 30% of adults with influenza have fever (6). Thus, influenza may go undiagnosed unless tested for regardless of fever. Diagnosis allows early commencement of antiviral therapy, which may mitigate potential complications. In 1 study, oseltamivir reduced the rate of cardiovascular events from more than 20% to 8.5% (7).

Influenza may unmask undiagnosed cardiovascular disease and may exacerbate known disease. It may trigger acute cardiovascular events (such as stroke or myocardial infarction), acting through direct viral effects on the myocardium, vasculature, and receptors and through indirect effects, including cytokine production, plaque disruption, acute thrombosis, vasoconstriction, tachycardia, and hypoxia (8). Persons with some degree of preexisting atherosclerotic disease, even subclinical disease, are susceptible to influenza-related acute cardiovascular disease. Influenza may precipitate acute thrombosis of a subcritical stenosis of a coronary artery or acute heart failure in the setting of previously stable left ventricular dysfunction. Thus, influenza vaccination can be considered important as secondary prevention for acute cardiovascular events. A meta-analysis estimated that vaccination reduces the risk for serious cardiovascular events by 36% (9). Yet, as pointed out by Chow and colleagues (2), rates of influenza vaccination in adults who have or are at risk for cardiovascular disease are suboptimal.

If vaccination prevents infection altogether, the triggering effects of influenza can be avoided. However, in older adults (who are at higher risk for cardiovascular disease), age-related immunosenescence makes vaccines less immunogenic. The development of high-dose and adjuvanted influenza vaccines that are more immunogenic in older adults may help. However, Chow and colleagues (2) showed that vaccination was beneficial even when it did not prevent influenza. Among study patients hospitalized with influenza, those who were vaccinated were significantly less likely to develop acute heart failure and acute ischemic heart disease than those who were unvaccinated. This finding shows that the benefit of influenza vaccination extends beyond simply preventing infection—influenza vaccination prevents severe complications of infection when infection occurs despite vaccination. Cardiovascular disease is the leading cause of morbidity and mortality globally, so by preventing a proportion of acute cardiovascular events, influenza vaccination will have a substantial public health benefit (8) and will likely be cost-beneficial (10).

The estimated efficacy of influenza vaccines for secondary prevention of cardiovascular events is 15% to 45%, similar to that of statins, antihypertensive agents, and smoking cessation (8). We accept the important role of the latter interventions in secondary prevention of cardiovascular disease, but influenza vaccination continues to be overlooked. It is time to recognize the significant and preventable cardiovascular morbidity

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and mortality associated with influenza and to view influenza vaccination as a routine secondary preventive measure for cardiovascular events.

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