Incidence, Predictors, and Outcomes of Thrombotic Events in Hospitalized Patients With Viral Pneumonia

Viral pneumonia represents a major cause of morbidity and mortality, especially among older patients.[1] Viral pneumonia may be associated with a systemic inflammatory response, which has been linked with arterial and venous thrombotic cardiovascular events.[2] During the recent COVID-19 pandemic due to the novel SARS-CoV-2 virus, anecdotal and published experience suggests high rates of thrombotic complications among hospitalized patients.[3] Due to a paucity of studies describing the incidence, predictors, and outcomes of thrombotic events among patients with viral pneumonia, the observation of thrombosis in patients with COVID-19 lacks context. Hence, we aimed to address this knowledge gap using a large nationally representative dataset.

The National Inpatient Sample (NIS) database years 2005 to 2015 was used to identify hospitalizations with primary diagnosis of viral pneumonia (influenza or noninfluenza) using International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) codes 480.x, 487.0, 487.1, 488.x1, 488.x2, 484.1, 052.1, or 055.1. Thrombotic events were defined as acute myocardial infarction (AMI), acute ischemic stroke (AIS), venous thromboembolism (VTE), or acute limb ischemia (ALI). Outcomes included in-hospital mortality, hospital costs, and length of stay (LOS) and discharge disposition (among survivors). Hospitalizations with missing data for mortality or LOS were excluded. Complex samples multivariable regression models that included patient demographics, comorbidities, and in-hospital complications (bacterial/fungal superinfection, sepsis, septic shock, acute respiratory failure, and mechanical ventilation), were used to identify factors independently associated with thrombotic events among admissions with viral pneumonia. Statistical analyses were performed using IBM SPSS Statistics, Version 20 (Armonk, New York).

The study included 455,629 hospitalizations with a primary diagnosis of viral pneumonia (83.6% with influenza pneumonia). Among these, 13,465 (3.0%) had thrombotic events (AMI 5,843 [1.3%], VTE 4,739 [1.0%], AIS 3,153 [0.7%], and ALI 217 [0.05%]). Those with thrombotic events were older, less likely to be women, and had a higher prevalence of hypertension, hyperlipidemia, diabetes mellitus, prior MI, peripheral vascular disease (PVD), and chronic kidney disease (CKD). On multivariable analysis, a number of key variables were independently associated with thrombotic complications, with mechanical ventilation posing the highest risk (OR 3.96, 95% CI 3.38 to 4.64) (Figure 1).

In-hospital mortality was significantly higher among those with versus without thrombotic events (12.8% vs 1.8%; unadjusted OR 7.90, 95% CI 6.99 to 8.93; adjusted OR 1.68, 95% CI 1.37 to 2.05; p <0.001). Compared with those who did not develop thrombotic events, those who developed thrombotic events had longer LOS (10.1 vs 4.5 days; parameter estimate 5.67, 95% CI 5.19 to 6.16; adjusted parameter estimate 2.94, 95% CI 2.56 to 3.32; p <0.001), higher total hospital costs ($30,782 vs $9,641; unadjusted parameter estimate 21,141, 95% CI 19,217 to 23,065; adjusted parameter estimate 9,322, 95% CI 7,880 to 10,764; p <0.001), and were more likely to be discharged to skilled nursing facility (41.2% vs 16.7%; unadjusted OR 3.51, 95% CI 3.22 to 3.81; adjusted OR 2.11, 95% CI 1.89 to 2.35; p <0.001).

In this nationwide observational study of >455,000 hospitalizations for viral pneumonia, we found that thrombotic events were not uncommon (~3.0%). Several baseline characteristics and comorbidities were independently associated with thrombotic events. The development of thrombotic events among these hospitalized patients was associated with increased in-hospital mortality, longer LOS, increased utilization of skilled nursing care following discharge, and higher costs. Prior studies have focused on AMI and were limited to influenza infection only.[4] The current study extends our knowledge by examining the prevalence of any thrombotic event and included any etiology of viral pneumonia. These findings are relevant to the current COVID-19 pandemic caused by SARS-CoV-2, which has been linked to an increased risk of arterial and venous thrombotic events potentially related to direct viral infection or the profound inflammatory response.[3] This analysis is limited by the observational nature of the study and potential residual confounding. The unit of analysis is the number of hospitalizations rather than individual patients, and the NIS lacks data on therapies or investigations performed as well as outcomes beyond the index

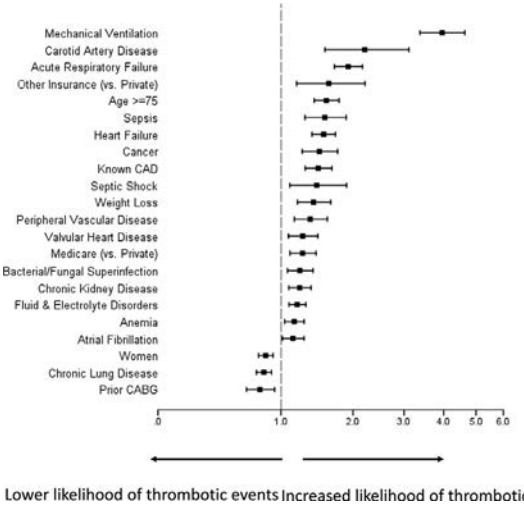

Figure 1. Forest plot for factors independently associated with thrombotic events on multivariable regression analysis. CABG = coronary artery bypass surgery; CAD = coronary artery disease.

hospitalization. Despite these limitations, our study provides important insights into the incidence, risk factors, and outcomes of thrombotic events in hospitalized patients with viral pneumonia and may serve as a comparator once similar data emerge for SARS-CoV-2 pneumonia.

Disclosures

The authors have no conflicts of interest to disclose.

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Transcatheter Aortic Valve Implantation Outcomes in Chronic Kidney Disease Versus End-Stage Kidney Disease

Patients with end stage kidney disease on dialysis (ESKD-D) have a high risk of developing aortic stenosis (AS). The dystrophic calcification of the aortic annulus and leaflets occurs with worsening renal function, leading to an onset 10 to 20 years earlier than the general population, as well as faster progression.[1] Similarly, patients with less advanced chronic kidney disease (CKD) have been associated with increased postoperative mortality after cardiac procedures.[2] There is little data to answer the question of whether TAVI is safe in dialysis patients as they were excluded from the large trials and small trials offered mixed results.[3] The aim of our study was to evaluate the impact of different stages of CKD on outcomes after TAVI.

We performed a retrospective cohort study using the National Readmissions Database (NRD), released by the Agency for Healthcare Research and Quality. The study population included patients with severe AS and CKD (IIIa, IIIb, IVa, and IVb) or ESKD-D who underwent TAVI between January 2012 and December 2017. We excluded patients with CKD stages I-II as they are considered clinically normal from a nephrology point of view and therefore may be underreported. We used ICD-9 and ICD-10 codes to identify eligible patients operated before and after October 2015, respectively.

We assessed the in-hospital outcomes including in-hospital mortality, stroke, permanent pacemaker implantation, blood transfusion, acute myocardial infarction (AMI), sepsis, length of hospital stay, and discharge with disability. "Discharge with disability" was defined as any disposition category not reported as routine discharge (including transfer to other care facilities, home health care, and discharge against medical advice). To assess 30-day readmission rates, we excluded patients who died during the index admission and patients who were discharged in December of each year to allow for at least 30 days of follow-up.

Our study included 42,147 CKD patients who underwent TAVI, including 36,070 patients who had CKD stage III, IV, or V not requiring dialysis, and 6,077 patients who had ESKD-D. The median age was 83 years in patients with CKD versus 75 years in patients with ESKD-D ($p < 0.001$). CKD patients were more likely to have congestive heart failure, atrial fibrillation, peripheral vascular disease, obesity, history of alcohol and drug abuse, but less likely to have coronary atherosclerosis, hypertension, diabetes mellitus, dyslipidemia, coagulopathy, smoking, and anemia (Table 1).

The median length of stay following TAVI was 6 days in patients with ESKD-D compared to 4 days in CKD patients not requiring dialysis ($p < 0.001$). In-hospital mortality was higher in ESKD-D group compared to the CKD not requiring dialysis group (5.2% vs 3%, $p < 0.001$). Further, patients with ESKD-D were more likely to develop in-hospital AMI (6% vs 3.7%, $p < 0.001$), in-hospital sepsis (5% vs 1.7%, $p < 0.001$), require blood transfusion (21.6% vs 14.2%, $p < 0.001$), and need permanent pacemaker implantation (12.3% vs 11.2%, $p < 0.001$) following TAVI. The rates of in-hospital stroke and discharge with disability did not differ between both groups. Patients with ESKD-D were more likely to be readmitted within 30 days following discharge (25.5% vs 17.3%, $p < 0.001$) (Table 1).

The present study shows that ESKD-D patients who underwent TAVI were associated with a higher risk of in-hospital mortality, AMI, blood transfusion, sepsis, and 30-day readmission, as well as longer length of hospital stay, compared with CKD patients not requiring dialysis. However, the risk of in-hospital stroke and discharge with disability were similar between the two groups. These results are concordant with former studies in the literature.[4,5] Despite the limitations of NRD data (including possible ICD-10 code misclassification, lack of data on procedural characteristics, and short follow-up), our results indicate that being on dialysis increases the risk of worse outcomes after TAVI. Future studies are encouraged to develop optimal risk stratification and outcome improvement strategies for patients undergoing TAVI with different CKD stages.