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The impact of infection on mortality in octogenarians who were admitted due to acute coronary syndrome

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ABSTRACT

Background: The prevalence of coronary artery disease is on the rise as the life expectancy of the population increases. However, treatment of acute coronary syndrome in the elderly patients has its own problems that have not been thoroughly addressed in the clinical trials. Since these patients are generally fragile and have multiple co-morbidities, the course of acute coronary syndrome can frequently be complicated. Infection, which co-exists either at the initial presentation or is acquired during the hospital stay, is a condition about which there is little published data. Therefore, in our study, we wanted to assess the impact of infection on mortality in octogenarians who have acute coronary syndrome

Methods: We retrospectively analyzed the data of 174 octogenarians who had been admitted to the coronary care unit with acute coronary syndrome. All-cause mortality was defined as the primary endpoint of the study.

Results: Overall 53 octogenarian patients (30.5%) had an infection along with acute coronary syndrome. The mean duration of follow-up was 10 months (1–25 months). Both in-hospital and long-term mortality were higher in these patients (18.9% vs 6.6%, $p = 0.01$; 52.8% vs 27.5%, $p < 0.01$; respectively). Kaplan–Meier analysis also showed lower cumulative survival. (p [log-rank] = 0.002). In multivariate Cox regression analysis; undergoing coronary angiography, infection (HR 1.96, 95% CI 1.15–3.34, $p = 0.01$), left ventricular ejection fraction and maximum C reactive protein levels were found as independent predictors of long-term survival.

Conclusion: Infection in octogenarians who were admitted due to acute coronary syndrome was frequent and increased their mortality substantially.

1. Introduction

Coronary artery disease is one of the leading causes of death worldwide (Celermajer et al., 2012 Celermajer, Chow, Marijon , Anstey, & Woo, 2012). Despite significant improvements achieved with new devices and techniques, there are still certain groups in which mortality and morbidity remain high. Today, as the life expectancy of the population increases, elderly people constitute a remarkable proportion of patients being admitted with acute coronary syndrome (ACS) (Steg et al., 2012). In this sense, octogenarians represent a specific population which has unique treatment challenges. However, the scientific data regarding these patients are scarce since they have generally been excluded from large landmark clinical trials (Bourgeois, Orenstein, Ballakur, Mandl, & Ioannidis, 2017). Moreover, it is hard to apply evidence-based guidelines since these patients have several co-morbidities that may preclude coronary angiography and subsequent revascularization (Brieger et al., 2016).

Infection is a co-morbidity that has been overlooked in octogenarians who present with ACS. Infection, by itself, creates a milieu in which septic mediators create plaque vulnerability as well as enhanced thrombogenicity all of which lead to myocardial infarction (Milbrandt et al., 2009). Also, the oxygen supply and demand mismatch that occurs during an infectious process is another mechanism of myocardial damage. When these patients are admitted to coronary care units because of myocardial infarction they are also prone to hospital-acquired infections, which further complicates their in-hospital course of care. Studies investigating the association between infection and myocardial infarction have mainly focused on the general population and reported an incidence of 3.5%–5% (Grandini & Caramelli, 2006; Piccaro de Oliveira et al., 2016). However, there is scarce data in the literature regarding the infection rate in octogenarians who are being admitted to the coronary care units with ACS. Therefore, in our study, we wanted to

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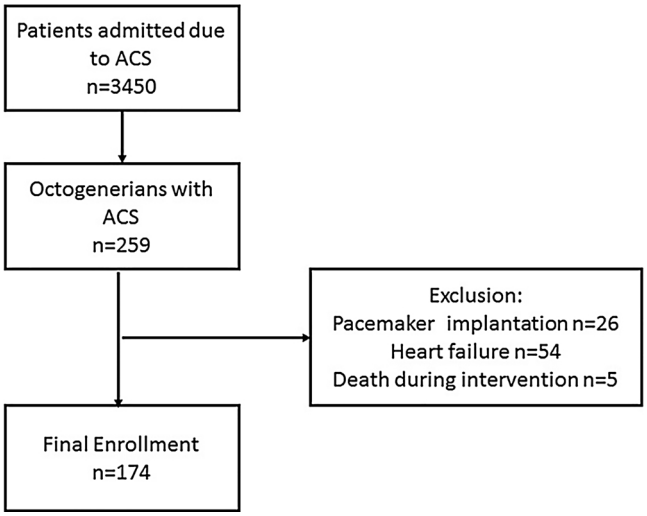

Fig. 1. Flowchart depicting patient enrollment.

assess the incidence and the impact of infections on all-cause mortality in this specific population.

2. Methods

2.1. Patients

We retrospectively analyzed the hospital records of patients who had been admitted to the coronary care unit due to acute coronary syndrome between April 2015 and May 2017. Our institution is a tertiary care center and approximately 3000 coronary angiograms are performed each year. In total, 3450 patients with acute coronary syndrome were identified, and among those, 174 octogenarians with ACS were found eligible and enrolled in our study (Fig. 1).

The diagnosis of acute coronary syndrome was based on the presence of at least two of the following: typical chest pain, dynamic ECG changes and elevated troponin levels consistent with acute coronary syndrome. Octogenarians who had been admitted for other reasons and those who presented with cardiogenic shock and died during the intervention were excluded. SYNTAX scores were calculated in a blinded fashion by two interventional cardiologists via the following website: http://www.syntaxscore.com. To calculate baseline SYNTAX score, the pre-PCI angiograms were assessed and scored. To calculate residual SYNTAX score, the final post-PCI angiogram was scored to assess untreated disease. Ethical board approval was provided by the local ethics committee.

2.2. Infection

Development of infection within the first 72 h of admission was considered a community-acquired infection whereas development of infection after this time period was considered a hospital-acquired infection, which is in accordance with the criteria established by the Centers for Disease Control and Prevention (Anonymous, 2015). The diagnosis was first established by the attending physician if any signs and symptoms of infection were detected. Later, the presence of infection was validated by the consultant infectious disease specialist and appropriate antibiotics were administered. During the course of the hospital stay, any change in antibiotic regimens was tailored according to the infectious disease specialist

2.3. Clinical outcome

All-cause mortality was the primary endpoint of our study. In-hospital mortality was evaluated through review of hospital records. 30-day and long-term mortality were identified according to the national death notification system.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 20 software (SPSS Inc., Chicago, Illinois). Distribution of data was assessed using the Kolmogorov-Smirnov test. The data for continuous variables were reported as means ± standard deviation if normally distributed, median and interquartile ranges were reported if the data were not normally distributed. Categorical variables were reported as numbers and percentages. Continuous variables were compared between groups using independent sample *T*-test or Mann-Whitney as appropriate. Categorical data were compared using the chi-square or Fisher Exact test. Event-free survival curves were generated using the Kaplan–Meier method. Differences in survival curves among the groups were assessed using the log-rank test. A 2-tailed p-value < 0.05 was considered statistically significant. To assess the impact of infection on mortality we developed a model using Cox regression analysis where we included ACS type, undergoing coronary angiography, infection, diabetes mellitus, acute renal failure, left ventricular ejection fraction, admission, glucose maximum, troponin, hemoglobin and C reactive protein as covariates (by “forward method” method). When building the model, covariates that are found to be significant in univariate analysis ($P < 0.1$) or have clinical significance were entered into the model. In order to identify multicollinearity, either Pearson correlation analysis for continues variables or chi-square test for dichotomous variables were used.

3. Results

In our study, 53(30.5%) patients had an infection. Of these, 73% (n = 38) of the infections occurred in the first 72 h after admission. The most common site of infection was pulmonary (47.2%) followed by urinary tract infections (15.1%). Only 3.5% of patients had primary bacteremia and the remaining patients had either other loci or unidentified primary infection site (34.2%). The main pathogens identified on positive cultures and considered to be responsible for the infections were: Streptococcus species, *Staphylococcus aureus, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. Octogenarians with infection had more acute renal failure, need for inotropic support and higher mortality (Table 1).

The clinical and demographic characteristics of the study population are presented in Table 1. There were no differences between the two groups in terms age and other comorbid conditions. The majority of the patients were admitted as Non-ST elevation myocardial infarction (NSTEMI) (n = 118, 67.8%). In total, 109(62.6%) patients underwent coronary angiography and 82(47.1%) had a PCI procedure. Among those who did not undergo coronary angiography (n = 65), 27 (41.5%) of them did not give consent and the rest had severe comorbid conditions that precluded the procedure. Laboratory results are presented in Table 2. Patients with infection had higher admission glucose, WBC, CRP, and troponin I levels. They also reached higher maximum WBC counts and CRP and troponin I levels during the hospital stay.

Coronary angiographic and procedural details are given in Table 3. There was no difference between the two groups in terms of coronary angiography or PCI results. In addition there was also no statistical difference in baseline and residual SYNTAX scores as well as the type and length of stents implanted.

3.1. Clinical outcomes

Patients with infection had higher in-hospital, 30-day and long-term mortality (18.9% vs 6.6% p = .01; 30.2% vs 14.9% p = .01; 52.8% vs 27.5% p < .01 respectively). The mean duration of follow-up was 10 months (1–25 months). The results of the Cox regression analysis of