Influence of atrial fibrillation on acute myocardial infarction

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ABSTRACT

Atrial fibrillation is an increasingly common significant arrhythmia with potentially serious outcomes. Myocardial infarction is a common consequence of atherosclerosis and coronary artery disease. When the two conditions occur together, the consequences can be compounded. This article briefly reviews some of the potentials for the relationship.

KEYWORDS

Atrial Fibrillation; Myocardial Infarction; Acute Myocardial Infarction; Cardiovascular Risks

1. INTRODUCTION

A relationship between atrial fibrillation (AF) and acute myocardial infarction (AMI) has been established for sometime, with an earlier attempt at characterization in the 1970s by M. Klass and L. J. Haywood; they reviewed data from 31 patients with myocardial infarction and AF with an incidence of 7.5% and associated mortality of 42%. Since that time multiple studies have shown varying incidences ranging from 7% to 21% [1], documenting that AF is commonly associated with AMI.

Whereas there is consensus on the association of AF with AMI, the question of its prognostic significance is an area of debate. Multiple studies have reported an adverse impact on mortality [2-8] while others have failed to find this association [9-13]. Studies reporting an adverse impact of AF on mortality have been limited by the need to control for potential confounders in the AMI setting (e.g. age, left ventricular systolic and diastolic dysfunction, functional mitral regurgitation), raising the question of whether AF independently predicts mortality or simply denotes a sicker underlying substrate.

The mechanisms responsible for the onset of AF in the setting of AMI appear complex, and the understanding incomplete. Animal studies reveal that AF is inducible when intra-atrial pressure is raised acutely by passive stretch of the left atrium [14]. This mechanism may be particularly pertinent in the setting of AMI, where an acute elevation of left atrial pressure is frequently observed [15,16]. Others have hypothesized that excessive neurohormonal activation, inflammation, and/or left ventricular dysfunction which is commonly present in the peri-infarct period provide a substrate for arrhythmia [15-17].

We will focus on the current data with regards to the incidence and timing of AF in the setting of AMI, as well as attempt to assess whether AF may independently impact mortality. With regards to the timing, we have chosen to separate the occurrence of AF into three main categories: preexisting, new-onset AF occurring within 30 days of infarction, and new-onset AF occurring beyond 30 days. Although arbitrary, these categories are in line with most current reported data when defining the incidence of short versus long-term AF in the setting of AMI. We will bring attention to the debate surrounding this topic and invite the reader to review the topic based on the available data.

Preexisting AF in the Setting of AMI

Reported incidences of preexisting AF in the setting of AMI range from 1% - 13% [18]. When attempting to chart this temporal relationship, confounding factors can result in incorrect categorization. Some studies have failed to document the presence of preexisting AF in the setting of AMI, simply designating patients as being with or without AF at the time of presentation. Many patients with asymptomatic or paroxysmal AF may remain undiagnosed until hospitalization for AMI, resulting in an erroneous categorization as new-onset AF. In addition,

the timing of AF in relation to the AMI may be misclassified secondary to delays in seeking medical attention after symptom onset. Conversely, the apparent increased occurrence of AF in the immediate post-MI period could partially reflect previously undetected AF that manifests during hospitalization. Lastly, when attempting to follow these patients long-term, detection of AF is reliant mainly on ECG and/or physical exam at the time of follow-up, and those with asymptomatic or paroxysmal arrhythmias can be missed, leading to delayed or even failed detection of AF.

This being said, many of the more well-controlled studies have found an association between pre-existing AF and mortality. One prospective multicenter registry with one year outcome data on 3393 patients with ACS reported that 387 patients (11.4%) had preexisting AF. This study concluded that new-onset AF was associated with worse short-term outcomes, but only preexisting AF was associated with greater mortality at 12 months (hazard ratio 1.42, p < 0.05) [19]. Similarly, in the TRAndolapril Cardiac Evaluation (TRACE) study which included 6676 patients with AMI, 5 year mortality was increased (RR 1.3) and was similar for patients with new-onset and preexisting AF [5]. In both studies, patients with AF were significantly older and had a greater cardiovascular disease burden as well as cardiovascular risk factor profiles. In a post hoc analysis of the OPTIMAAL trial (The Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan), which included 5477 patients with AMI who developed clinical signs of heart failure or evidence of left ventricular dysfunction within 10 days of hospitalization, 12% of patients were found to have AF at baseline [20]. In this study, patients with preexisting AF had significantly higher total mortality, cardiovascular death, stroke, and all-cause mortality when adjusted for multiple major baseline characteristics as well as for the severity of heart failure at randomization. The impact on mortality was found both during hospitalization as well as at long-term follow-up for three years. Conversely, a retrospective analysis of the GRACE trial (Global Registry of Acute Coronary Events) which included 21,785 patients, found that both preexisting and new-onset AFs were associated with clinical characteristics known to be related to poorer outcomes in patients with AMI (e.g. advanced age, diabetes, prior congestive heart failure), and the presence of AF conveyed a worse in-hospital prognosis. Yet, the independent impact of previous AF on in-hospital mortality was lost on multivariate regression analysis [21]. A recent very comprehensive meta-analysis involving 43 studies and over 278,000 patients (4) found a significant and similar association between AF and mortality between new-onset AF (OR 1.37) and prior AF (OR 1.28) in the setting of AMI. This effect appeared to be attenuated very little by the temporal rela-

tionship of AF to the myocardial infarct [18].

2. NEW ONSET

2.1. Short Term AF in the Setting of AMI

In The Global Use of Strategies To Open occluded coronary arteries (GUSTO-III) study, 13,858 patients were followed at 30 days and 1 year postinfarction (of which 906 developed AF during hospitalization) to evaluate whether new-onset AF independently influenced mortality [8]. At 30 days, the mortality rate was higher in the AF group (15%) relative to the no-AF group (6%, P < 0.001). The median time to death was 5.7 (2.2 to 9.4) days in the AF group versus 1.2 (0.2 to 4.9) days in the no-AF group. The rate of early death (within the first 2 days) was 3% in both groups. In the unadjusted 30-day death model, the OR for death among AF patients was 2.74. After adjusting for significant differences in baseline predictors (age, systolic blood pressure, weight, Killip class, heart rate, infarct location, hypertension, diabetes mellitus, prior angioplasty, cerebrovascular disease, and prior bypass surgery), the OR decreased to 1.63 (95% CI, 1.31-2.02). Jabre *et al.* [22] reviewed a community-based cohort of 3220 patients hospitalized for AMI and found that 729 patients developed AF subsequent to the acute event. When considering death within 30 days after MI, similar associations were seen for prior and early AF (new-onset AF within 2 days of AMI) as were observed for all deaths. However, the association between intermediate AF (3 to 30 days post-MI) and 30-day mortality was much stronger; patients with intermediate AF had a 5-fold increased risk of death within 30 days after adjustment for baseline characteristics (HR 5.86). When adjusted for heart failure in addition to other baseline characteristics, the association remained (HR 4.99). Also, over the follow-up period, 1638 deaths occurred, 314 of these within the first month after MI, equating to a 30-day case fatality rate of 10% (95% CI 9% - 11%).

2.2. Long Term AF in the Setting of AMI

In the Global Use of Strategies To Open occluded coronary arteries (GUSTO-III) study [8], at 1 year postinfarction, the unadjusted 1-year death model, the OR for AF patients was 2.93 (95% CI, 2.48 - 3.46). After adjusting for the significant baseline predictors (age, systolic blood pressure, weight, Killip class, heart rate, infarct location, diabetes mellitus, hypercholesterolemia, prior MI, angina, heart failure, cerebrovascular disease, prior angioplasty, and prior bypass surgery), the OR decreased to 1.82 (95% CI, 1.51 - 2.20). The in-hospital, pre-AF complications that were predictors of 1-year death were identical to those predictive of 30-day death. When they were added to the model (by using the same base-

line adjustment), the adjusted OR of 1-year death for patients with delayed onset AF was 1.64 (95% CI, 1.35 - 2.01). The important findings were that patients who had AF during hospitalization had more in-hospital complications even before the onset of AF, and AF predicted worse 30-day and 1-year mortality rates independent of both baseline characteristics and pre-AF complications. (The community-based cohort study by Jabre *et al.* [22] reviewed at 5 years, mortality was 34% (95% CI 32% - 36%) within the entire MI incidence cohort. Most deaths were from cardiovascular causes [n = 933 (57%)], while 218 deaths (13%) were attributed to cancer, and 428 (26%) to other causes.)

2.3. Conclusions/Summary

Since the early attempt to quantify the effect of AF on patients with AMI was published in the 1970's, [23] many other studies have extended these observations by establishing AF as an independent predictor of early and long-term mortality after AMI.

The studies clearly demonstrate that AF in MI patients is associated with an increased risk of death even after adjustment for relevant confounders. Two important findings deserve emphasis. First, patients presenting with acute MI and a history of AF have increased mortality compared with patients without AF. Second, the occurrence of AF at any time after MI is associated with a large increase in overall mortality; moreover, AF developing more than 30 days post-MI is associated with the highest mortality risk compared to patients without AF and possibly related to the extent of left atrial enlargement and left ventricular remodeling.

AF in the setting of AMI portends a worse prognosis and arguably can be used as a marker of higher risk individuals. However, it is currently unclear how this information can be used to adjust treatment plans, and represents an opportunity for future research.

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