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REVIEW

Atrial Fibrillation and Acute Myocardial Infarction – an Inflammation-mediated Association

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ABSTRACT

Atrial fibrillation (AF) is an increasingly widespread healthcare problem. AF can frequently present as a complication in acute coronary syndromes (ACS), especially in ST-elevation acute myocardial infarction (AMI), in which case it is the most frequent supraventricular rhythm disturbance with an estimated incidence of 6.8–21%. The presence of AF in ACS heralds worse outcomes in comparison to subjects in sinus rhythm, and several studies have shown that in AMI patients, both new-onset and pre-existing AF are associated with a higher risk of major adverse cardiovascular and cerebrovascular events during hospitalization. The cause of new-onset AF in AMI is multifactorial. Although still incompletely understood, the mechanisms involved in the development of AF in acute myocardial ischemic events include the neurohormonal activation of the sympathetic nervous system that accompanies the AMI, ischemic involvement of the atrial myocytes, ventricular dysfunction, and atrial overload. The identification of patients at risk for AF is of great significance as it may lead to prompt therapeutic interventions and closer follow-up, thus improving prognosis and decreasing cardiovascular and cerebrovascular events. The present manuscript aims to summarize the current research findings related to new-onset AF in AMI patients, as well as the predictors and prognostic impact of this comorbid association.

Keywords: atrial fibrillation, acute myocardial infarction, risk prediction

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INTRODUCTION

Atrial fibrillation (AF) is an increasingly widespread healthcare problem, with a reported incidence of 20.9 million cases in males and 12.6 million cases in the female population worldwide.[1,2] The prevalence of this supraventricular arrhythmia is increasing with age, and it more often affects subjects with coronary artery disease, heart failure, hypertension, obesity, diabetes, or chronic renal disorders.[3–5] AF can also present as a complication in acute coronary syndromes (ACS), especially in ST-elevation myocardial infarction, in which case it is the most frequent supraventricular rhythm disturbance, with an estimated incidence of 6.8–21%.[6–9] The combination of AF and acute myocardial infarction (AMI) is of particular interest, since the development of either disorder can negatively and substantially impact the prognosis of the other. The occurrence of AF in AMI patients can lead to rapid irregular ventricular rates, thus further impairing ventricular function and coronary perfusion, with enhanced myocardial ischemia, volume overload, and elevated filling pressures.[8,9] The higher incidence of AF in AMI patients is influenced by pre-existing AF, left ventricular dysfunction, and hemodynamic disturbances with subsequent catecholamine release either as a response to low perfusion pressures, or iatrogenic due to use of ino-

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tropic or vasoactive agents. Other reported risk factors for AF include diabetes, metabolic syndrome, chronic renal failure, or extensive myocardial ischemia, which encompasses a large portion of the left ventricle as well as the atrial myocytes.[8,10,11]

The presence of AF in ACS heralds worse outcomes in comparison to subjects in sinus rhythm, since several studies have shown that both new-onset and pre-existing AF are significantly associated with the risk of major adverse cardiovascular and cerebrovascular events during hospitalization.[12,13]

In addition to the increased cardiovascular burden and impaired prognosis, the comorbid relation between AMI and AF also attracts higher healthcare costs. The estimated costs used in out-patient treatment, hospitalizations, and medical treatments for AF have been reported around 6.6 billion dollars annually, while the associated costs for a single acute coronary event have been estimated between 34,087–86,914 dollars in 2005, in the United States. The approximate costs increase by up to 40% if an ACS patient presents AF as a complication.[14–16]

The present manuscript aims to summarize the current research findings related to new-onset AF in AMI patients, as well as the predictors and prognostic impact of this comorbid association.

ETIOLOGY AND CONSEQUENCES OF AF IN AMI

The cause for new-onset AF in AMI subjects is multifactorial, various factors as well as a genetic dimension being reported. AF leads to the deterioration of coronary perfusion and ischemia, with a negative impact on patient outcomes. Although still incompletely understood, the mechanisms involved in the development of AF in acute myocardial ischemic events include the neurohormonal activation of the sympathetic nervous system that accompanies the AMI, ischemic involvement of the atrial myocytes, ventricular dysfunction, and atrial overload.[17,18] In general, AF is triggered by focal automaticity and electrical re-entry in the area surrounding the pulmonary veins. Several factors have been reported to be associated with AF in AMI patients, such as hypertension, metabolic disorders, structural or valvular heart disease. The arrhythmia itself leads to a structural remodeling of the atria with subsequent fibrosis, adipose infiltration, inflammatory infiltrates, which will ultimately lead to the so-called "electrical remodeling" that is optimal for developing reentrant circuits within the atrial wall and perpetuation of the arrhytmia.[19–21] The various physiopathological mechanisms in AF initiation and persistence include stretch-induced myocardial fibrosis, which may be caused by left ventricular overload, and dysfunction secondary to acute infarctions. In acute coronary events, AF can also result from a decreased contractility of the atrial myocardium, caused by involvement of the atrial branch of the coronary artery, by fatty infiltration or inflammation, or by calcium imbalance.[22–25]

ATRIAL ISCHEMIA

The ischemia of atrial myocytes as a trigger for new-onset AF has been suggested by a study that had experimentally induced atrial branch occlusions on animal models, leading to prolonged atrial conduction, increased electrical heterogeneity, and higher rates of induced atrial fibrillation episodes. These episodes had an increased likelihood to persist, compared to controls or to animals with left anterior descendant occlusions.[26] A study on 149 patients with ACS, out of which 4.9% had developed AF during hospitalization, showed that although there were no differences regarding the cardiovascular risk profile and associated disease, patients with atrial branch atherosclerosis or ischemic involvement of the atrial vasculature were more expected to present supraventricular arrhythmia.[27] These studies suggest that the arrhythmia is triggered by the compromised atrial coronary vasculature rather than neurohormonal activation.

ATRIAL STRETCH AND NEUROHORMONAL ACTIVATION

Increased stretch of the atrial wall is caused by various disorders that lead to increased volume overload either directly, as in atrioventricular valve regurgitation, or secondary to left ventricular increased pressures, in congestive heart failure, acute heart failure caused my myocardial ischemia, aortic valve disease, or structural cardiac diseases. The increased left ventricular pressure is transmitted to the left atrium, leading to neurohormonal activation, which has been implicated in fibrosis formation and cardiac remodeling via the renin-angiotensin-aldosterone pathways. In addition, the increased left ventricular wall stress leads to overstimulation of the same neurohormonal system, consequent heart failure and atrial remodeling, both structurally and electrically.[28–30] The acute myocardial ischemia, as well as the mitral regurgitation due to papillary ischemia, enhance the atrial overload and trigger AF with rapid ventricular response, which will, in turn, worsen the already altered coronary perfusion, decrease the cardiac output secondary to the loss of atrial contraction, and also impair the diastolic and

systolic function of the left ventricle. The decreased cardiac output will further stimulate the sympathetic nervous system, with secondary adrenergic stimulation that leads to the creation of a vicious circle, with higher ventricular overload, more enhanced atrial stretch, and even more increased neurohormonal activation, ultimately leading to extension of the infarction and worse outcomes.[31–34]

INFLAMMATORY RESPONSE AS A TRIGGER FOR AF IN THE POST-INFARCTION PERIOD

Several studies have linked an increased inflammatory response with the development and persistence of AF.[35–38] The independent association between AF and the serum level of C-reactive protein (CRP), which is illustrative for an acute-phase inflammatory response, increases the likelihood of AMI patients to develop the supraventricular arrhytmia.[39,40]

Myocardial ischemia has been linked to increased inflammatory response.[41–46] Acute myocardial ischemia leads to an intense inflammatory response which is of utmost importance for the process of cardiac repair. The exacerbation of this normal repair mechanism can lead to further promotion of myocardial damage and left ventricular remodeling, with subsequent development of heart failure following MI.[47–49] C-reactive protein as a marker for sustained inflammation following an acute MI can be induced by myocardial ischemia and existing unstable coronary plaques and has been established as a novel predictor for cardiovascular disease, as well as a predictor for adverse outcomes in MI.[50–53] Other inflammatory biomarkers that present elevated serum levels following an AMI include tumor necrosis factor alpha, interleukin-6, or macrophage migration inhibitory factor, which have also been linked to mortality rates and adverse events following an acute coronary syndrome.[54–56]

Inflammation has also been incriminated in the development and persistence of AF.[57,58] The first observation that led to the hypothesis that inflammation may have a role in the genesis of the supraventricular arrhythmia was its higher incidence in patients with clinical conditions that are associated with enhanced inflammatory response, such as pericarditis and myocarditis, or cardiac surgery.[59] The contribution of the inflammatory process in AF has been proved by histological studies on atrial biopsies in patients with lone atrial fibrillation in which several inflammatory infiltrates were observed.[60]

Several studies have shown the connection between increased levels of pro-inflammatory biomarkers and AF; however, there are still uncertainties whether the arrhythmia is caused by inflammation, or that the inflammation is a consequence of the arrhythmia. A study that included 5,806 subjects from the Cardiovascular Risk Study, with a mean follow-up period of 6.9 ± 1.6 years, showed that CRP was significantly associated with AF (fourth quartile – mean CRP levels <3.41 mg/L vs. first quartile – mean CRP levels <0.97 mg/L, adjusted HR 1.31, 95% CI 1.08 to 1.58, p = 0.005), and also, elevated CRP levels predicted the risk for future arrhythmia development (adjusted hazard ratio for 1-SD increase 1.24, 95% CI 1.11 to 1.40, p <0.001).[61] Chung *et al.* have shown that higher levels of CRP were present in patients with permanent AF compared to paroxysmal AF, which could indicate that inflammation is related to the burden of AF.[62] Alternatively, a study on 52 subjects with persistent AF (over 3 months) who underwent electrical conversion, showed that those with recurrence at 1 month presented significantly higher baseline high-sensitivity CRP (hs-CRP) levels compared to those who remained in sinus rhythm (0.5 ± 0.18 mg/dL vs. 0.29 ± 0.13 mg/dL, respectively, p <0.001). Also, there was a significant decrease in hs-CRP levels after sinus rhythm restoration (0.29 ± 0.13 mg/dL before vs. 0.10 ± 0.06 mg/dL after, p <0.001), whereas patients with recurrence presented similar levels (0.05 ± 1.8 mg/dL before vs. 0.56 ± 0.24 mg/dL after, p = 0.42).[63]

In a study that analyzed 971 patients with significant coronary artery disease, several inflammatory cytokines, such as interleukin-6, as well as an increased left atrial diameter have been shown to correlate with the genesis and duration of AF.[64] Elevated levels of TNF-alpha, interleukin-8, interleukin-10, and monocyte chemoattractant protein-1 (MCP-1) were found in a higher number of patients with persistent AF compared to paroxysmal AF and arrhythmic patients compared to sinus-rhythm controls.[65–67]

The enhanced inflammatory response expressed either locally or at a systemic level,[68] seems to be also one of the factors intertwined in the thrombogenic milieu present in the atria of AF subjects, alongside endothelial dysfunction and platelet activation.[35,59] A study has shown that increased serum interleukin-6 was an independent predictor for stroke and death in a follow-up period of 6 years,[69] while another research has linked high CRP values with the incidence of spontaneous echo contrast in the left atrial cavity and appendage.[70]

This bidirectional relationship, inflammation – arrhythmia – inflammation, in the sense that AF is triggered but also generates an inflammatory response, could be one of the explanations of the "AF begets AF" concept. Fast irregular atrial depolarizations lead to atrial fibrosis

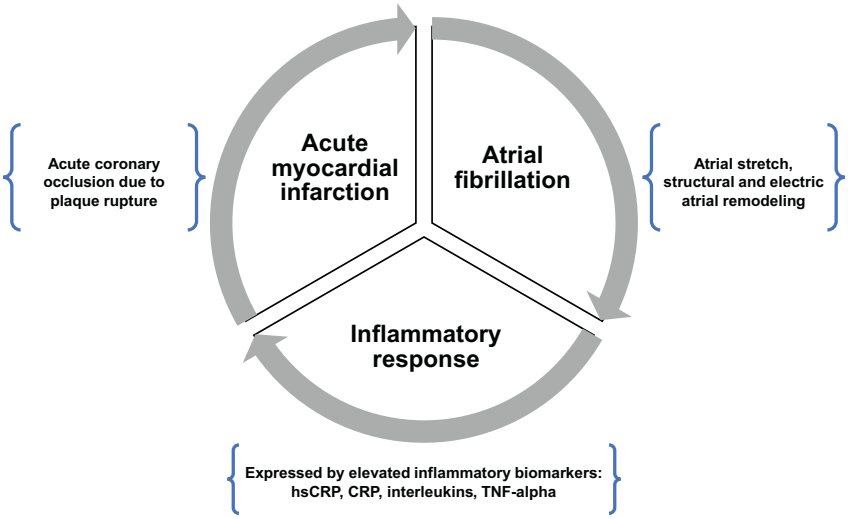

FIGURE 1. Inflammatory response in acute myocardial infarction triggers onset and persistence of atrial fibrillation, which will further enhance inflammation with subsequent atrial structural and electrical remodeling

and necrosis of myocardial fibers, which in turn generates a low inflammatory response with further structural and electrical atrial remodeling, a cycle that illustrates the impact of both inflammation and remodeling in the initiation, persistence, recurrence, and burden of AF.

The inflammatory response secondary to an AMI is not limited to the infarcted myocardium, but it is also present in the remote non-infarcted areas, which can explain how pro-inflammatory cytokine release can indorse AF in these patients (Figure 1). A study published in 2007, which included 1,209 patients admitted for AMI, showed that patients who had developed new-onset AF presented a positive and significant association with hs-CRP measured at 12 and 24 hours from onset of symptoms, respectively (p for trend <0.001).[71] This was one of the first studies to demonstrate the impact of enhanced inflammatory response in the development of AF in the early post-infarction period. Another study conducted on 409 consecutive AMI patients showed similar results, that hs-CRP levels were significantly higher in patients with early AF (within 24 h from onset of the acute coronary event) compared to patients in sinus rhythm (14.5 mg/L vs. 6.5 mg/L, p = 0.01), and that there was a progressive increase in early-onset AF with increasing tertiles of hs-CRP (3.6% in the first tertile, 8.9% in the second, and 14.1% in the third tertile, respectively, p = 0.02). However, their results were only applicable for patients without left atrial dilation, showing that hs-CRP levels as biomarkers for enhanced inflammatory response in the post-infarction period could contribute to the process of left atrial remodeling and dilation.[72] A meta-analysis published in 2015, which included 6 studies and 4,153 AMI patients (363 with and 3,790 without new-onset AF), aimed to evaluate the role of CRP levels in the occurrence of AF in AMI. Their results showed that elevated CRP levels are associated with a higher risk of new-onset AF, but that CRP was not independently linked to the development of the arrhythmia, other potential risk factors including age, gender, time to revascularization, or infarct location.[73]

AF AS A PROGNOSTIC FACTOR IN AMI

AF occurring as a complication of acute myocardial ischemic events has been shown to negatively impact patient outcome and mortality rates, both during hospitalization and during the long-term follow-up. Despite its negative impact on outcomes, AF is not perceived by clinicians as a critical complication in the acute post-infarction period, in contrast to ventricular arrhythmias, acute heart failure, cardiogenic shock, or mechanical complications. However, AF is associated with a more than 40% increase in mortality compared to AMI subjects in sinus rhythm, as shown by a meta-analysis published by Jabre *et al.* (2011), on 43 studies including 278,854 patients.[13] The study also showed that negative outcomes are persistently independent of the arrhythmia onset, while new-onset AF is significantly associated with higher death rates even after adjustments for age, diabetes, increased blood pressure, chronic congestive heart failure, previous myocardial infarction, or coronary revascularization, which have all been associated with increased mortality both in patients with AMI and chronic AF.[13] New-onset AF in the context of acute myocardial isch-

emia can lead to impaired patient outcomes due to its effect on the already unstable hemodynamic status via loss of atrial contraction and atrioventricular synchrony, and irregular rapid ventricular response with subsequent decrease in cardiac output.[74] The irregular rapid ventricular response caused by AF may also trigger severe ventricular tachyarrhythmias due to irregular R-R intervals, ischemia, or overactivation of the sympathetic nervous system.[75,76] A prospective study on 600 patients in sinus rhythm on admission, with ST-elevation and non-ST elevation AMI (Vukmirovic *et al.*, 2017), aimed to evaluate the prognostic role of new-onset AF, both during hospitalization as well as during a follow-up period of 84 months after discharge. Their results showed that the strongest predictors for new-onset AF included older age, increased left atrial diameter, moderate to severe mitral regurgitation, increased serum levels of brain-natriuretic peptide (BNP), and obesity. Also, the study revealed that subjects who had developed AF during hospital admission presented significantly higher mortality rates, both during hospital stay, as well as on the long term, compared to patients in sinus rhythm.[77] Another meta-analysis published in 2012 (Angeli *et al.*), on 24 clinical studies that evaluated the prognostic role of AF in the early post-infarction period on all-cause mortality during hospitalization, revealed that AF occurring during AMI, irrespective of its onset, was significantly associated with all-cause death rates (OR 2.00, 95% CI 1.93 to 2.08, p <0.0001), and that not only new-onset (OR 3.38, 95% CI 2.98 to 3.83, p <0.0001), but also uncertain onset (OR 1.90, 95% CI 1.83 to 1.98, p <0.0001) and permanent AF (OR 2.01, 95% CI 1.70 to 2.38, p <0.0001) were linked to higher death rates.[12] The Cooperative Cardiovascular Project (CCP), which included 106,780 elderly subjects aged over 65 years with AMI and AF of various onset types, showed that subjects with supraventricular arrhythmia had significantly worse outcomes compared to those in sinus rhythm, including during hospitalization (25.3% vs. 16.0%, p = 0.001, OR 1.77, 95% CI 1.71 to 1.84), at 30 days (29.3% vs. 19.1%, p = 0.001, OR 1.76, 95% CI 1.71 to 1.82), and during the 1-year follow-up (48.3% vs. 32.7%, p = 0.001, OR 1.92, 95% CI 1.87 to 1.98), even after adjustment for demographical, clinical, and therapeutic parameters. The same study revealed that AF was more frequently associated with reinfarction, cerebrovascular accidents, congestive heart failure, and admissions in the Intensive Care Unit (ICU), while the overall hospitalization period was significantly longer in arrhythmic subjects compared to sinus rhythm controls (9.6 days vs. 7.6 days, p <0.0001).[9]

PREDICTORS FOR AF IN AMI

Given the associated risk of AF in AMI and its prognostic value in patients with ACS, it would be useful to identify patients at risk for the new onset of this supraventricular arrhythmia.

The Cooperative Cardiovascular Project was one of the largest patient cohorts (106,780 included subjects) that evaluated the clinical characteristics of patients with new-onset AF in the context of acute coronary events. Their results revealed that compared to patients in sinus rhythm, those in AF were significantly older (mean age 79.2 years vs. 76.8 years, p <0.0001), presented significantly higher heart rate on admission (95.8 bpm vs. 86.8 bpm, p <0.0001), more advanced heart failure (Killip class IV: 4% vs. 2%, p = 0.001), and higher frequency of previous MI (34.2% vs. 32.3%, p = 0.001) and revascularization. At the same time, multivariate analysis in this study showed that advanced acute heart failure with Killip class IV was the most important predictor of AF development (OR 1.58, 95% CI 1.45 to 1.73).[9] Another study conducted in 2017 showed that by logistic regression analysis, the most powerful predictors of AF during hospitalization for AMI were age over 70 years (OR 2.37, 95% CI 1.23 to 4.58, p = 0.010), obesity defined as a body mass index over 25 kg/m^2 (OR 1.17, 95% CI 1.04 to 1.33, p = 0.012), significant mitral insufficiency (OR 3.56, 95% CI 1.25 to 10.32, p = 0.018), and elevated levels of BNP (OR 2.12, 95% CI 1.24 to 3.33, p = 0.048). Also, patients with new-onset AF presented significantly lower left ventricular ejection fraction (41.7 ± 4.6% vs. 43.9 ± 4.9%, p = 0.003), larger left atrium diameter (43.6 ± 3.9 mm vs. 40.4 ± 3.6 mm, p <0.001), higher frequency of moderate to severe mitral regurgitation (25% vs. 7.3%, p <0.001), higher heart rate upon admission (85.5 bpm vs. 77 bpm, p <0.001), and also a higher incidence of ventricular tachycardia during hospital stay (18.8% vs. 7.6%, p = 0.014).[77] Vukmirovic *et al.* also analyzed levels of cardiac biomarkers in association with the risk of developing AF and showed that while hemoglobin levels and anemic patients were not significantly different between AF and non-AF patients, there was a significantly higher number of AF cases that developed contrast-induced nephropathy (37.5% vs. 15.0% p <0.001). AF patients also presented significantly higher levels of BNP as an illustrator of neurohormonal activation (272 vs. 64.5, p <0.001), and higher levels of hs-CRP (83.5 vs. 24.5, p <0.001).[77]

Obesity was shown to be associated with increased risk of AF, due to its association with a chronic pro-inflammatory status and increased oxidative stress, both leading to onset and persistence of the supraventricular arrhyth-

mia.[78] Furthermore, an increased body mass index has also been linked to an increased volume of the left atrium that triggers the remodeling and inflammatory process, ultimately causing AF.[79]

Laboratory markers evaluated on presentation for AMI and their role in the development of new-onset AF were also analyzed by the TRIUMPH cohort, which found that both hs-CRP and BNP levels were correlated with the risk of arrhythmia. Surprisingly, troponin was not related to this risk. The study revealed that two times higher levels of NT pro-BNP associated an 18% increase in the rate of AF (OR 1.17, 95% CI 1.02 to 1.34; p <0.02) and a 2-fold increase in hs-CRP levels led to a 15% higher frequency of the arrhythmia (OR 1.15, 95% CI 1.02 to 1.30; p = 0.02), while no association was reported in relation to the increase of troponin (OR 0.94, 95% CI 0.84 to 1.06, p = 0.3).[80] Other observations of the same study were that patients with AF were, as expected, older (mean age 64.6 ± 13.2 years vs. 57.5 ± 11.9 years, p <0.001), Caucasian (77.2% vs. 67.9%, p = 0.021), more likely to present diabetes (42.1% vs. 30.5%), chronic renal failure (11.4% vs. 6.1%, p = 0.024), chronic pulmonary disorders (14% vs. 6.4%, p = 0.002), or hypertension (74.6% vs. 64.8%, p = 0.033). Surprisingly, patients with AF were less likely to smoke compared to those in sinus rhythm (24.8% vs. 43.6%, p <0.001).[80]

The GUSTO 1 trial, which included 40,000 patients with AMI in the thrombolytic era, also found that the most important predictors for the development of AF are acute ventricular dysfunction at presentation (Killip I vs. Killip IV class: OR 3.28, 95% CI 2.28 to 4.71) and older age (OR 3.2, 95% CI 2.99 to 3.43).[81] Data from the Osaka Acute Coronary Insufficiency trial revealed, once again, that patients with a higher risk of presenting AF presented more advanced Killip class IV (OR 2.06, 95% CI 1.07 to 3.94), male gender (OR 1.89, 95% CI 1.23 to 2.90), older age (OR 1.06, 95% CI 1.04 to 1.07), and heart rate over 100 bpm during admission (OR 3.0, 95% CI 1.94 to 4.64).[82] Other studies found that females were more prone to develop arrhythmia, and other baseline characteristics that were commonly found in patients with AF and AMI were diabetes, hypertension, increased left atrial diameter, lower left ventricular ejection fraction, and impaired renal function.[83–87]

The type of reperfusion treatment applied for the AMI (thrombolysis or percutaneous revascularization) was not shown to significantly impact the risk of AF.[88] Furthermore, as shown by the RICO study on a cohort of 1,701 patients, there were no differences in the rate of new-onset AF in patients with ST-elevation and non-ST elevation AMI (7.6% vs. 7.7% respectively, p = 0.334).[89] Another study showed no significant difference in the rate of AF in patients receiving fibrinolytic treatment (sinus rhythm – 5.8% vs. AF – 5.3%, p = 0.318), but patients presenting this arrhythmia were more likely to benefit from in-hospital percutaneous revascularization (sinus rhythm – 29.7% vs. AF – 46.5%, p <0.001), to have beta-blocker treatment upon hospital arrival (sinus rhythm – 13.1% vs. AF – 21.9%, p = 0.007), as well as calcium channel blocker (sinus rhythm – 41.1% vs. AF – 50.9%, p = 0.039) compared to subjects in sinus rhythm, an observation which could indicate the pre-existing cardiac disorders.[80] Kosmidou *et al*. (2018) performed a study on 1,812 patients with left main coronary atherosclerosis in sinus rhythm, out of which 162 (8.9%) had developed AF after a mean period of 2.7 ± 2.5 days of hospitalization. The arrhythmia was present in a significantly higher number of subjects that underwent coronary artery by-pass grafting (CABG) compared to those who benefited from percutaneous coronary revascularization of the left main (18% vs. 0.1%, p <0.0001).[90] Furthermore, the occurrence of AF in CABG patients was associated with subsequent death (11.4% vs. 4.3%, adjusted HR 3.02, 95% CI 1.60 to 5.70, p = 0.0006), stroke (6.6% vs. 2.4%, adjusted HR 4.19, 95% CI 1.74 to 10.11, p = 0.001), and with the composite end-point of death, myocardial infarction, and stroke (22.6% vs. 12.8%, adjusted HR 2.13, 95% CI 1.39 to 3.25, p = 0.0004) at the three-year follow-up.90 Other studies reported post-CABG AF frequency of 11–40% of patients.[91–94] CABG is associated with an increased inflammatory response, which could explain the higher rate of arrhythmias compared to the minimally invasive percutaneous coronary revascularization.

CONCLUSIONS

AF developing in the context of an AMI can negatively and substantially impact patient outcomes during hospitalization as well as on the long term. Identification of patients at risk is of great significance, as it may lead to prompt therapeutic interventions and closer follow-up, thus improving prognosis and decreasing cardiovascular and cerebrovascular events that are linked to this comorbid association. Predictors for AF in AMI patients include advanced acute heart failures, higher Killip class on admission, increased admission heart rate, older age, female gender, previous cardiovascular disease, impaired renal function, diabetes, or low left ventricular ejection fraction. Laboratory parameters associated with an increased risk for AF include elevated levels of BNP and NT-proBNP, as well as hs-CRP, which are illustrative for the enhanced neurohormonal activation and the inflammatory response in the post-infarction period.

CONFLICT OF INTEREST

Nothing to declare.

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