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Review article

Patients with atrial fibrillation and coronary artery disease – Double trouble

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ABSTRACT

Coronary artery disease (CAD) is the most common cardiovascular disease while atrial fibrillation (AF) is the most common cardiac arrhythmia. Both diseases share associated risk factors – hypertension, diabetes mellitus, sleep apnea, obesity and smoking. Moreover, inflammation plays a causative role in both diseases. The prevalence of CAD in patients with AF is from 17% to 46.5% while the prevalence of AF among patients with CAD is low and it is estimated from 0.2% to 5%. AF is a well-established factor of poor short- and long-term prognosis in patients with acute myocardial infarction (AMI) and is associated with a marked increase in overall mortality.

The arrhythmia is common after cardiac surgeries and occurs in about 20 to 40% of patients after coronary artery bypass graft (CABG) surgery. It is predicted that between 5 and 15% of AF patients will require stenting at some point in their lives and will receive triple therapy with aspirin, clopidogrel or ticagrelor and oral anticoagulation (OAC). This requires careful consideration of antithrombotic therapy, balancing bleeding risk, stroke risk, and in-stent thrombosis with subsequent acute coronary syndromes. Co-prescription of OAC with antiplatelet therapy, in particular triple therapy, increases the absolute risk of major bleeding. In addition, major bleeding is associated with an up to 5-fold increased risk of death following an acute coronary syndrome. Coexistence of AF and CAD worsens the prognosis even in carefully treated patients.

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1. Introduction

Coronary artery disease (CAD) is the most common cardiovascular disease [1], while atrial fibrillation (AF) is the most common cardiac arrhythmia [2]. The prevalence of angina in population-based studies increases with age, from 5 to 7% in women aged 45–64 years to 10–12% in women aged 65–84 and from 4 to 7% in men

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aged 45–64 years to 12–14% in men aged 65–84 [3]. In 2013 CAD was the most common cause of death globally, resulting in 8.14 million deaths (16.8%) up from 5.74 million deaths (12%) in 1990 [4].

Atrial fibrillation occurs in 2% of the general population and increases with age from 0.14% in those younger than 50 years old, 4% in patients between 60 and 70 years old, to 14% in population over 80 years old [2]. Both diseases share associated risk factors–hypertension, diabetes mellitus, sleep apnea, obesity and smoking. Moreover, inflammation plays a causative role in both diseases [5–7].

The prevalence of CAD in patients with AF ranges from 17% to 46.5% [8–12]. In the ROCKET-AF (Rivaroxaban Once daily oral direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in atrial fibrillation) [13] and RELY (Randomized Evaluation of Long-term anticoagulant therapY with dabigatran etexilate) [14] large randomized trials CAD was present in ~ 17% of the AF patients. Van Gelder et al. who investigated only patients with permanent AF, detected an incidence of CAD of 18% [15]. Kralev et al. in the study of AF patients undergoing coronary angiography showed that stable CAD was diagnosed in 13% of AF patients and in 21% of the patients with CAD percutaneous coronary intervention (PCI) or CABG were performed [16]. The prevalence of permanent type of AF was similar in both groups – with and without CAD (30% vs 27%, respectively) [16]. On the other hand, Lip et al. described an incidence of CAD up to 46% of the patients [10]. On the other hand, the prevalence of AF among patients with CAD is low and it is estimated from 0.2% to 5% [17–20].

1.1. Atrial fibrillation and myocardial infarction as co-occurring events

Acute myocardial infarction (AMI) is an established risk factor for an AF episode with AF occurring in 6% to 21% of patients with AMI [21]. One out of ten subjects who present with MI have a documented history of AF [22]. Moreover, one out of four subjects without prior AF will develop AF at or after MI [22]. The case control study of 2460 patients with AMI showed that coronary disease affecting the atrial branches is a predictor for the development of AF early after MI, independent of age, gender, left ventricular ejection fraction, left atrial size, time to reperfusion or TIMI flow after coronary intervention [22].

AF is a well-established marker of poor short- and long-term prognosis in patients with AMI [24–28] and is associated with a large increase in overall mortality [23]. Patients presenting with AMI and a history of AF have increased mortality rate compared with patients without AF [23]. Population-based data indicate that, one half of first-ever documented AF cases after AMI are developed in the first month post-AMI onset [29]. The risk imparted by AF varies according to its timing, with a 2-fold increase in the risk of death for AF occurring 30 days after the incident of AMI compared with patients without AF [23,27,28,30–32]. Pilgrim et al. showed that among patients with CAD undergoing revascularization with drug-eluting stent, AF confers an increased risk of ischaemic stroke and intracranial bleeding [33]. In large, community-wide study involving more than 6000 patients with AMI it was observed that new-onset AF is a common and lethal complication of AMI [34]. AF was associated with a higher risk for in-hospital death and readmission within 30 days [34]. Furthermore, there was a greater-than 2-fold higher risk for acute stroke and death during hospitalization in patients admitted with an AMI and AF [34]. These results are consistent with those of the Global Registry of Acute Coronary Events (GRACE) study where it was observed that patients with new-onset AF had a 3-fold increased risk of death during hospitalization for an acute coronary syndrome (ACS) compared with those who did not develop AF [35]. Patients with new-onset AF after AMI were almost twice more likely to have a hospital course complicated by heart failure and more than 3 times more likely to develop cardiogenic shock [34]. In a single-center data-base of 2980 consecutive patients presenting with AMI, comparing the outcomes between particular AF types, only the permanent AF and new-onset AF groups had significantly higher short- and long-term mortality than patients without AF [36,37]. Furthermore, patients with known paroxysmal AF had the lowest observed 30-day mortality (7.3%) among the subgroups, similar to that of patients without AF (5.2%). The 10-year mortality rate was high and did not differ significantly among AF subgroups [37].

Conversely, sporadic cases of thromboembolic AMI also have been reported in patients with AF [38–44]. AF is associated with systemic signs of inflammation that could promote a prothrombotic state and eventually AMI [45]. Systemic inflammation may depend on AF per se or on the concomitant presence of the classic atherosclerotic risk factors, which are typically associated with AF [46]. In addition to atherosclerosis, AMI may occur in AF by other mechanisms. For example, episodes of AF with high ventricular rates may yield type 2 MI, which is characterized by an imbalance between demand and blood supply, and is usually associated with non-ST elevation MI [47]. In the large randomized trial ROCKET-AF myocardial infarction occurred in 101 patients in the rivaroxaban group and in 126 patients in the warfarin group (0.9% and 1.1% per year, respectively) [13]. The RE-LY trial reported a lower number of myocardial infarction: 0.53% per year with warfarin and 0.72% per year with dabigatran 110 mg bid and 0.74% per year with dabigatran 150 mg bid [14].

1.2. Atrial fibrillation after coronary artery bypass surgery

The arrhythmia is common after cardiac surgeries and occurs in about 20 to 40% of patients after coronary artery bypass graft (CABG) surgery [48,49]. Post-operative AF usually occurs 2–4 days after the procedure. Generally, it is well tolerated, but it can be life-threatening, especially in the elderly and patients with left ventricular dysfunction [50]. It is also associated with an increased risk of thromboembolic events, stroke and lengthened hospital stay [48,51–53]. Aranki et al. in his study showed that the mean length of hospitalization after surgery was 15.3 +/– 28.6 days for patients with AF compared with 9.3 +/– 19.6 days for patients without AF [48]. Several studies reported association with increasing age and the risk of AF after CABG [48,49,52].

1.3. Angiographic findings among patients with AF

AF patients may present with chest pain, which can be accompanied by transient ischemic-type ST-segment changes with marginally elevated cardiac markers, thus mimicking symptoms of CAD [54]. The rapid ventricular rate is often seen in patients with AF, and ST depression occurring at these rates has been attributed to subendocardial myocardial ischemia. In the study of Tsigkas et al. ST depression was seen in 38% of the patients with rapid AF and half of them had CAD at angiography [55]. Only 4% of the patients without ST depression during rapid AF had positive noninvasive tests for myocardial ischemia and CAD at angiography [56,57].

Nevertheless ST segment depression can often occur during rapid rates, even without CAD, and is not specific for ischemia particularly if the depression is <2 mm [56,58]. Another study showed troponin release in 15% of AF patients with symptoms of myocardial ischemia, usually in the absence of CAD at angiography [59]. In a retrospectively collected database of patients presenting for selective coronary angiography, the presence or history of AF was a factor associated with non-significant coronary disease [60]. In conclusion, the presence of AF alone, without other risk factors