Preexisting atrial fibrillation and myocardial infarction: only 10% of infarcts directly linked to atrial fibrillation

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The aim of the study was to evaluate the incidence and prognosis of type 1 myocardial infarction (T1MI) and type 2 MI (T2MI) in patients with acute MI and known atrial fibrillation (AF) to identify MI directly linked to AF. Among the 669 patients, four patients with hyperthyroidism were excluded, and among the remaining 665 patients, about two-thirds were diagnosed with T1MI, and the remaining third were diagnosed with T2MI. AF was the direct cause of MI in 9.8% of our overall population [1.8% of T1MI type C (coronary embolism), 4.9% of T2MI type A and 3.1% of T2MI type B]. Among patients with T2MI, 30-day mortality was lower when the trigger was AF than for the other triggers, for both type 2A (6% vs. 11%) and type 2B (0% vs. 13%). Most cases of AF-related MI are, thus, T2MI, for which therapeutic guidelines are lacking. Given the diverse triggers in T2MI, a specific approach using etiological patterns is needed to properly determine the optimal therapeutic. ***Cardiovasc Endocrinol Metab*** **11: 1–4**

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Acute myocardial infarction (MI) and atrial fibrillation (AF) are common conditions with mutual interplay. Patients with AF often suffer from acute MI, and there is an increased risk of AF in patients with acute MI. However, so far no study has evaluated the extent to which AF is directly responsible for MI or is an associated condition.

The Fourth Universal Definition of MI proposes a classification for the subgroups of MI [1]. The first, type 1 MI (T1MI), is caused by an acute atherothrombotic event that is usually precipitated by atherosclerotic plaque disruption (rupture or erosion). In contrast, type 2 MI (T2MI) designates the pathophysiological mechanism leading to ischemic myocardial injury in the context of an imbalance between oxygen supply and demand, in the absence of an atherothrombotic event [1,2]. T2MI is thought to have multiple causes [3]. It was recently suggested that T2MI be further classified into subgroups of patients with or without coronary artery disease (CAD) and that T1MI be classified according to the cause of the acute coronary obstruction [4].

This new subclassification of MI makes it possible to identify MI directly linked to AF. Among MI patients with previous AF, two types of relationship may exist: (a) AF is an underestimated cause of coronary artery embolism (CE) (type 1A), or (b) AF leads to T2MI through either increased oxygen demand due to tachyarrhythmia, or a reduced supply via brady-arrhythmia related or not to drugs with bradycardic effects, or anemia related to anticoagulants (type 2A and type 2B) [5].

In contrast to T1MI, the diagnostic criteria for T2MI are not firmly validated because they are reflected through heterogeneous triggers. However, identifying the type of MI is a key requirement for optimizing management. In addition, the combination of anticoagulant and antiplatelet agents has not proven efficient in T2MI, which is characterized by a high risk of bleeding.

We currently have only a limited understanding of the occurrence and outcomes associated with acute MI subtypes, even though these data are important for estimating individual prognosis. In view of the lack of data on this subject, we aimed to evaluate the incidence and prognosis of T1MI and T2MI in patients with acute MI and known AF by enrolling consecutive patients from a large cohort of acute MI patients.

Methods

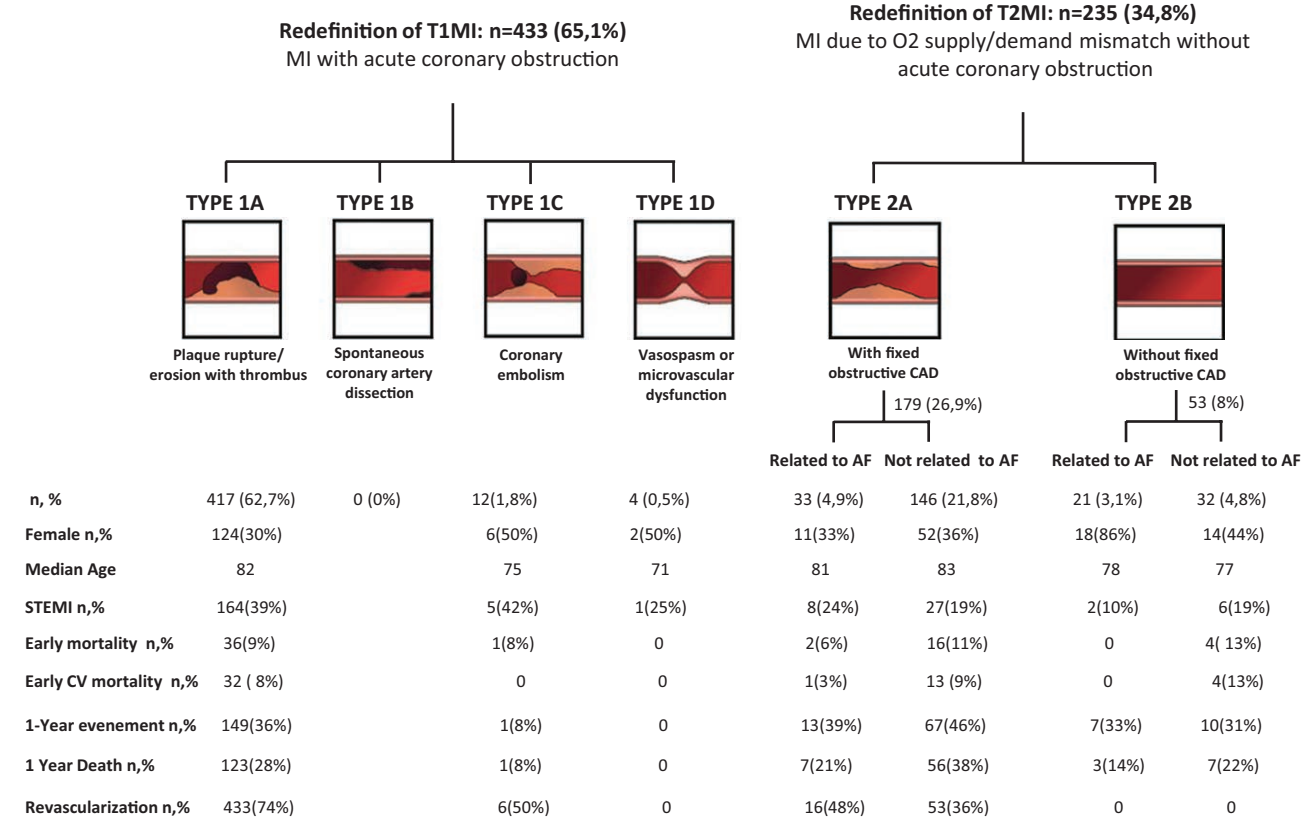
From the Registre des Infarctus de la Côte d'Or (RICO) survey, all consecutive patients with preexisting AF admitted to the coronary care unit of Dijon University Hospital for an acute MI from October 2012 to February 2020 and who underwent coronary angiography were prospectively included [6]. Patients less than 18 years or time delay from symptom onset to admission of more than 12H were excluded from the study. All of the participants

Table 1 **Baseline characteristics of patients with acute coronary syndrome with preexisting atrial fibrillation [*n* (%), or median (IQR)]**

				Type 2A *n* = 179		Type 2B *n* = 53	
Baseline characteristics	Type 1 A *n* = 417	Type 1C *n* = 12	Type 1D *n* = 4	Related to AF *n* = 33	Not related to AF *n* = 146	Related to AF *n* = 21	Not related to AF *n* = 32
Age, years, mean (min–max)	81 (73–86)	75 (71–85)	71 (62–80)	81 (72–86)	83	78 (67–82)	77 (68–84)
Sex (female), *n* (%)	124 (30)	5 (42)	2 (50)	11 (33)	53 (36)	18 (86)	14 (44)
Diabetes, *n* (%)	135 (32)	3 (25)	0 (0)	17 (52)	60 (41)	6 (28)	8 (25)
Hypertension, *n* (%)	330 (79)	9 (75)	3 (75)	27 (82)	127 (87)	20 (95)	27 (84)
BMI, mean (min–max)	26 (24–29)	28 (24–30)	28 (23–31)	27 (25–31)	25 (23–30)	27 (25–32)	28 (24–32)
Dyslipidemia, *n* (%)	222 (53)	7 (58)	3 (75)	23 (70)	89 (61)	11 (52)	18 (56)
Current smoker, *n* (%)	39 (9)	1 (8)	0 (0)	5 (15)	13 (9)	3 (14)	3 (9)
Family history, *n* (%)	94 (23)	1 (8)	0 (0)	7 (21)	19 (13)	4 (19)	8 (25)
Chronic renal failure, *n* (%)	34 (8)	1 (8)	0 (0)	3 (9)	12 (8)	1 (5)	2 (6)

Chronic renal failure (glomerular filtration rate < 60 ml/min/1.73 m^2).
AF, atrial fibrillation; IQR, interquartile range.

Fig. 1



n, %	417 (62,7%)	0 (0%)	12(1,8%)	4 (0,5%)	33 (4,9%)	146 (21,8%)	21 (3,1%)	32 (4,8%)
Female n,%	124(30%)		6(50%)	2(50%)	11(33%)	52(36%)	18(86%)	14(44%)
Median Age	82		75	71	81	83	78	77
STEMI n,%	164(39%)		5(42%)	1(25%)	8(24%)	27(19%)	2(10%)	6(19%)
Early mortality n,%	36(9%)		1(8%)	0	2(6%)	16(11%)	0	4(13%)
Early CV mortality n,%	32 (8%)		0	0	1(3%)	13 (9%)	0	4(13%)
1-Year evenement n,%	149(36%)		1(8%)	0	13(39%)	67(46%)	7(33%)	10(31%)
1 Year Death n,%	123(28%)		1(8%)	0	7(21%)	56(38%)	3(14%)	7(22%)
Revascularization n,%	433(74%)		6(50%)	0	16(48%)	53(36%)	0	0

Flow chart of patients with myocardial infraction and preexisting atrial fibrillation, according to the proposed redefinition of the Fourth Universal Definition of Myocardial infarction (according to De Lemos *et al.* [4]). CV, cardiovascular; T1MI, type 1 myocardial infarction; T2MI, type 2 myocardial infarction.

provided consent prior to inclusion, and the Ethics Committee of the University Hospital of Dijon approved the protocol (BIOCARDIS-2016–9205AAO034S02117). Patients with hyperthyroidism were excluded; MI types were systematically adjudicated by two blinded investigators according to the recent modification proposal by De Lemos *et al.* [4].

Results

Among 665 patients with MI and previous AF, about two-thirds (433; 65.1%) were diagnosed with T1MI, and the remaining third (232; 34.8%) were diagnosed with T2MI. All of these patients were included in the RICO cohort, whose characteristics have been described elsewhere (Table 1) [7]. Thus, 16 patients (12 with CE and four

with coronary spasm) were classified as type 1 (Fig. 1) [4,8].

Our population had a percentage of T1MI linked to AF-related coronary embolism (i.e. type 1C) (1.8%) that was similar to the report by Shibata *et al.* [9]. Among the patients with AF in their study (158 patients), the percentage of type 1C was 25%, but only 39% of patients with CE were treated with vitamin-K antagonists, and the median international normalized ratio was 1.42 (range, 0.95–1.80) [9].

Among patients with T2MI in our study, 179 presented fixed CAD (type 2A) and 53 had no fixed CAD (type 2B). Triggering factors were classified into 'AF-related' (rapid AF or bradycardia AF) and 'non-AF-related' (bleeding, infection, ventricular tachycardia and respiratory failure). Only few T2MI [54 (23.2%)] were related to AF, including 33 patients with type 2A and 21 patients with type 2B. Among the cohort, four patients had hyperthyroidism, and hyperthyroidism was the trigger for type 2 infarction in three patients. The other triggers of type 2A and 2B infarct were: infection (33.7% vs. 22.2%, respectively), heart failure or shock (22.1% vs. 24.1%), bleeding (7.2% vs. 1.9%), respiratory failure (3.9% vs. 0%) and hypertensive crisis (2.2% vs. 1.9%). Overall, in patients with known AF, the percentage of T2MI A and T2MI B directly related to AF appeared to be low, suggesting that rhythm management was good.

Among patients with T2MI, 30-day mortality was lower when the trigger was AF than for the other triggers, for both type 2A (6% vs. 11%) and type 2B (0% vs. 13%). One-year mortality was also lower in T2MI related to AF in both the type 2A (20% vs. 38%) and type 2B groups (14% vs. 22%).

Discussion

Our prognostic data can be compared to the study by Schoepfer *et al.* [8], which included patients in the emergency department with symptoms suggestive of MI, and with 30-day all-cause mortality of 3.6% for T1MI type 1A and 2.9% for T2MI type 2A. These major differences in short- and medium-term mortality confirm the need for a specific cohort study. In addition, the prognostic significance of underlying CAD during the management of T2MI (type 2A vs. type 2B) is a key issue. Chapman *et al.* [10] demonstrated that CAD is an independent predictor of major adverse cardiovascular events at 5 years in patients who presented with T2MI [hazard ratio, 1.71 (1.31–2.24); $P < 0.001$].

We recognize that the present study has some limitations. First, the study was conducted in the ICU of a single hospital. In addition, AF patients with severe hemorrhage are usually not hospitalized in the coronary care unit but in other units such as gastroenterology or surgery. The percentage of patients with T2MI is, therefore, underestimated, which is why these patients were classified separately. Second, the classification of T2MI remains difficult even for experienced cardiologists. Third, the patients with known AF tend to be elderly with a complex cardiovascular history, which explains the high percentage of T2MI. Moreover, it is often difficult to differentiate between T2MI and myocardial injury, which we excluded.

In conclusion, AF was the direct cause of MI in 10.3% of our overall population (1.8% of T1MI type C, 5.2% of T2MI type A and 3.3% of T2MI type B). Most cases of AF-related MI are, thus, T2MI, for which therapeutic guidelines are lacking. Given the diverse triggers in T2MI, a specific approach using etiological patterns is needed to properly determine the optimal therapeutic response. This is particularly true among AF patients, for whom reduction/slowing down strategies are available.

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Ethics approval and consent to participate: informed consent was obtained for each patient prior to inclusion in the study. The study protocol was authorized by the Ethics Committee of the Dijon University Hospital.

Conflicts of interest

Y.C. reports having received grants, consulting fees, honoraria and/or delivering lectures for Servier, Novartis, Boehringer, Pfizer, MSD, and Bayer. M.Z. received research grants from Amarin Corp. For the remaining authors, there are no conflicts of interest.

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