IJC Heart & Vasculature 28 (2020) 100531

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.journals.elsevier.com/ijc-heart-and-vasculature

Cerebral microbleeds and acute myocardial infarction: Screening and disease progression

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ARTICLE INFO

Article history:
Received 25 February 2020
Received in revised form 29 April 2020
Accepted 1 May 2020

Keywords:
Cerebral microbleeds
Acute myocardial infarction
Cerebral MRI
Anticoagulant treatment
3 months

ABSTRACT

Introduction: Cerebral microbleeds (CMB) are associated with intracerebral haemorrhage. Therefore they may represent a concern if anticoagulant and/or antiplatelet therapy is needed. The aim of this study was to determine the prevalence of CMB in patients with acute myocardial infarction (AMI), and to follow their progression at 3 months under dual antiplatelet therapy (DAPT).

Methods: This prospective study included patients aged over 60 hospitalized in intensive cardiac care unit in our city for AMI. These patients underwent a first brain Magnetic resonance imaging (MRI) within 72 h of admission, that was repeated 3 months.

Results: 108 patients were included between November 2016 and December 2018. The prevalence of CMB was 21.3%, with a female predominance of 65.2% vs 32.1% (p = 0.004). Diabetes is significantly associated with the presence of CMB, 45.5% vs 21.2% (p = 0.021). Patients with at least one acute CMB had higher haemorrhagic risk as evaluated with CRUSADE score (40.5 ± 13.6 vs 31.2 ± 14.8 (p = 0.004).

Multivariate analysis showed that only female sex was associated with the presence of a CMB on the initial MRI. On repeated MRI, an increase in CMB was observed in 6% of patients.

Our results suggest that discharge treatment with anticoagulant in combination with antiplatelet therapy may be an independent predictor of early progression of CMB.

Conclusion: Our study confirms the high prevalence of CMB in patients over 60 years with AMI. The association of anticoagulant with DAPT, 3 months after stenting, may be an independent factor of CMB progression.

1. Introduction

Cerebral microbleeds (CMB) are the reflection of a chronic disorder in the small vessels of the brain.

The risk factors for CMB and coronary heart disease (particularly myocardial infarction (MI)) tend to be the same [1]. The meta-analysis by Wang et al, showed an increase in the occurrence of cerebral hemorrhagic events in patients with CMB treated with antithrombotics [2]. In a 2016 study by Wobith et al. there was a significant association between the occurrence of CMB and antiplatelet monotherapy in patients with ischemic stroke or transient ischemic attack (TIA) [3]. In coronary patients, CMB are more frequent in patients with a coronary calcium score of 100 or more [4], but no studies to our knowledge have studied the prevalence or progression of CMB under dual or triple antithrombotic therapy in patients with acute myocardial infarction (AMI).

Recently, in a study of 1447 patients with ischemic stroke or TIA anticoagulated for atrial fibrillation by vitamin K antagonist (VKA) or direct oral anticoagulant (DOA), Wilson et al. showed that CMB are an independent risk factor for symptomatic intracerebral hemorrhage (ICH) in patients treated with curative anticoagulants (HR = 3.67, IC 95% = [1.27–10.6]), particularly in the presence of at least 2 CMB [5].

In the context of shared risk factors, the impact of antiplatelet and/or anticoagulant treatments on the increased risk of intracerebral bleeding and/or on the development of CMB is a major issue.

The objectives of our study were to determine, in patients with AMI: the initial prevalence of CMB, their relationship with

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https://doi.org/10.1016/j.ijcha.2020.100531
2352-9067/

cardiovascular risk factors, and if there is a potential association between the presence of CMB and validated bleeding risk scores, including the CRUSADE score, and the BLEEDING risk described in 2016 [6]. Also, we studied their short-term progression under dual or triple antiplatelet therapy, and the factors predicting their evolution.

2. Materials and methods

2.1. Study design and inclusion criteria

Our prospective study included patients hospitalized at Dijon University Hospital for AMI between November 2016 and December 2018.

The inclusion criteria were patients over 60 years of age with AMI, with or without ST segment elevation, with elevated troponin and who received dual or triple antithrombotic therapy at discharge.

The exclusion criteria were patient refusal to participate, claustrophobia, and contraindication to brain MRI (pacemakers and defibrillators or any other equipment that could interfere with the magnetic field).

2.2. Data collection

For each patient, all cardiovascular risk factors (hypertension, diabetes, active smoking, dyslipidemia, family history of coronary disease, overweight), cardiac history and other history were collected through the *Registre des Infarctus de Côte d'Or* (RICO), a regional registry for cardiac events. For each patient in the study, an ischemic risk score (THROMBOTIC Risk Score) and two bleeding risk scores (CRUSADE, BLEEDING Risk Score) were determined [6].

2.3. Brain imaging

Each included patient received a brain MRI in the radiology department of the University Hospital of Dijon within 72 h of their admission to the cardiac intensive care unit for AMI and a second exploration at 3 months as part of their follow-up, to detect an increase in the number of CMB.

The diagnosis of CMB was generally established by the T2*-weighted gradient-echo MRI sequence, thanks to magnetic susceptibility artifacts between tissues and other structures (iron, calcium, bone, air) and artificial signal void.

In our study, a more sensitive SWI sequence, using an echo time and specific post-processing, was used. SWI sequences show a greater number of hemorrhagic lesions and smaller lesions than T2*-weighted sequences [7,8].

60% of patients underwent a MRI using 3-T MRI system (SKYRA SIEMENS), and 40% using 1.5-T MRI system(SKYRA SIEMENS). All patients had T2EG and SWI scans. The acquisition of these sequences did not require the injection of a contrast agent, thus avoiding possible allergic reactions and allowing us to include patients with kidney failure.

For The T2EG, slice thickness was 4 mm, repetition time/echo time were 887/18.9 ms and 800/19.9 ms for 1.5 T and 3 T MRI respectively.

For The SWI, slice thickness was 2.5 mm and 2 mm for 1.5 T and 3 T MRI respectively, repetition time/echo time were 47/39.3 ms and 27/20 ms for 1.5 T and 3 T MRI respectively.

CMB appeared as hyposignals (black lesions) round or ovoid, blooming effect, with diameter ranging from 2 to 10 mm and an intra-axial appearance. They were differenciated from calcifications, cavernoma and post-traumatic lesions.

Same acquisitions (T2* and SWI) were repeated for each patient included at 3 months for the second MRI. Images were analysed by experienced neuroradiologists who compared the two MRI sequences and notified the stability or the increased of the number of CMB, and revealed the new localization of CMB.

2.4. Statistical analysis

The dichotomous variables were expressed in n (%) and the continuous variables as medians (interquartile range) or means (standard deviation) according to the normality of distribution (tested by the Kolmogorov-Smirnoff test). For categorical data, a chi-square or Fischer exact test was used, while continuous data was compared with a Student's *t*-test for Gaussian variables or a Mann-Whitney test for non-Gaussian variables. Significance was set at 5%.

Multivariate logistic regression models were built to estimate the Odds Ratio (OR) of CMB presence and of CMB progression. Variables with a statistical significance threshold set at 5% in univariable analysis were included in the multivariate models.

SPSS version 12.0.1 (IBM Inc, USA) was used for all of the statistical tests. For the logistic regression analysis, levels of Nt-proBNP and CK were log transformed

3. Results

3.1. Acute phase - cerebral MRI 1

Between November 2016 and December 2018, 1692 patients were admitted to the Intensive Care Unit (ICU) at the Dijon University Hospital for AMI; 1159 were over 60 years old. Of these, 108 patients (42 female and 66 male) received a brain MRI and were included in our study. Initial brain MRI was performed within 72 h of admission (Fig. 1).

On the initial MRI, 23 patients (21.3% of the cohort), had at least one CMB (Fig. 2).

The initial MRI also showed recent ischemic stroke in 17 patients (15.7%) and ischemic stroke sequelae in 23 patients (21.3%).

Table 1 is a summary of the initial characteristics of patients with and without CMB.

Diabetes was also associated with CMB, with 45.5% of the CMB group compared to 21.2% in the no CMB group, (p = 0.021). However, no significant differences were found between the 2 groups for the other cardiovascular risk factors, including age and hypertension.

In terms of medical data (Table 2), patients with at least one CMB had a lower hemoglobin level than the no CMB group and a lower peak troponin.

No significant differences were found in terms of antiplatelet treatment (monotherapy or dual therapy), anticoagulation (DOA or VKA) before admission for AMI (Table 3). On the other hand, patients with at least one CMB on the initial MRI were more often treated with statins before admission than patients without CMB: 52.2% vs 25.9%, respectively (p = 0.016).

The CRUSADE hemorrhagic score was significantly higher in the group with CMB, 40.5 ± 13.6 vs 31.2 ± 14.8 (p = 0.004), but neither the BLEEDING Risk score (p = 0.062) nor the Syntax and Thrombotic Risk scores were significantly different in the two groups.

In multivariate analysis, only female sex was an independent factor in the presence of CMB in patients over 60 years of age hospitalized for AMI [OR (95% CI): 3.726 (1.387–10.014); p = 0.009] (Table 4).

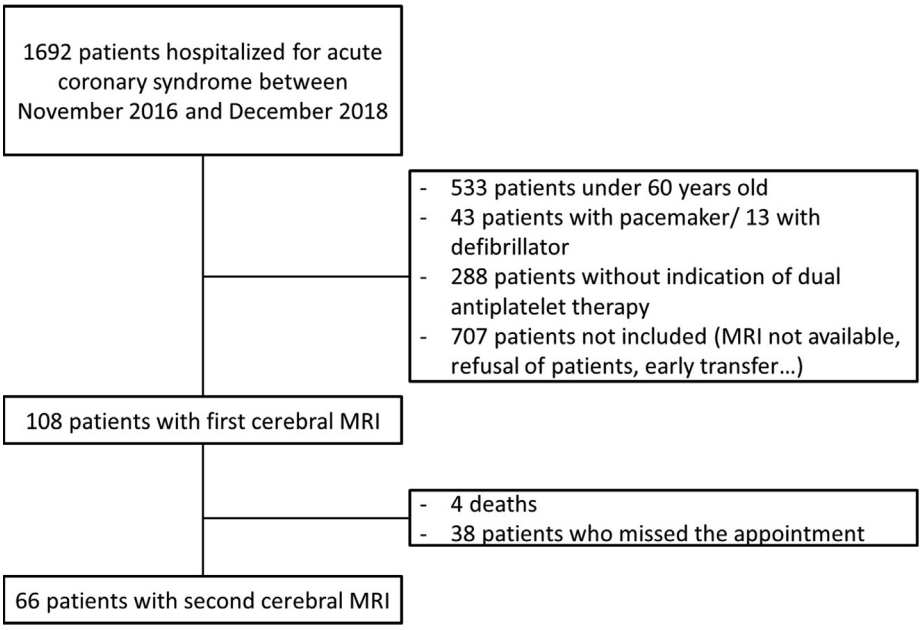

Fig 1. Population flow chart.

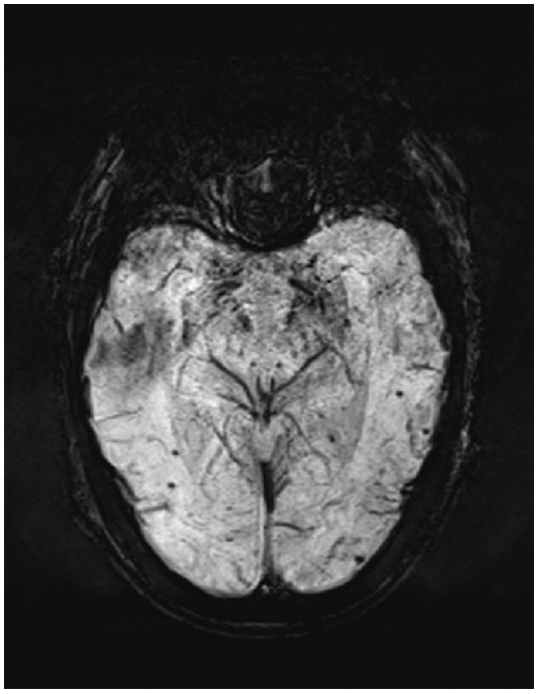

Fig. 2. Multiple lobar and deep microbleeds in a 75-year-old patient (SWI sequence - MRI 1).

3.2. Evolution at 3 months - cerebral MRI 2

In total, 66 patients underwent the second MRI 3 months after they were admitted to the hospital for AMI. Four patients died before the second scheduled MRI appointment.

The 3-month MRI indicated that the CMB had progressed in 4 patients (6%) with: the appearance of a lobar CMB in one patient taking aspirin and ticagrelor; the expansion of 2 CMB in a patient taking aspirin and VKA (2 CMB, one lobar and one deep, detected on the initial MRI); the appearance of a lobar CMB in a patient prescribed aspirin, clopidogrel and VKA at discharge and the appearance of a deep CMB in another patient on aspirin, clopidogrel and DOA.

We compared patients with a disease progression on cerebral MRI at 3 months to those with stable results. Patients with an increase in the number of CMB tended to be older than those with stable results (85 ± 5 vs 75 ± 8 years, p = 0.016).

In multivariate analysis, only discharge treatment with DOA or VKA was an independent predictive factor for the progression of CMB at 3 months: OR (95% CI): 13.882 (1.111–173.511); p = 0.041] (Table 5).

4. Discussion

Our study found that CMB were common in patients over 60 years of age (21.3%). The female sex was the only independent predictor of CMB in this selected population. Patients with CMB had a higher risk of bleeding than patients without CMB according to the CRUSADE score.

According to the follow-up (3 months after stenting), new CMB were found in 6% of patients who underwent a second MRI. VKA or DOA treatment at discharge may be an independent predictor of early progression of CMB 3 months after AMI but without intracerebral hemorrhage.

4.1. Prevalence of initial CMBs and their association with cardiovascular risk factors

This prevalence is in line with studies conducted on the general population, in particular the Rotterdam study where a systematic screening of 3979 controls (average age 60 years) found that 15.3% had at least one CMB [8]. In our study, only patients over 60 years of age were included, but a relationship between age and CMB has been clearly established; for instance, in 2010 Poels et al. reported an incidence of 11.5% in individuals between 50 and 59 years of age, 16.8% at between 60 and 69 years, 28.9% at between 70 and 79 years and 35.7% after 80 years [8]. Diabetes was significantly associated with CMB on the initial MRI. This result is in agreement with the meta-analysis of Cordonnier et al. whose included 9073 participants from 54 studies [7].

Table 1
Comparison of cardiovascular risk factors and cardiovascular history between patients without CMB and patients with CMB or patients with ≥ 2 CMB.

Group	CMB (−) N = 85	CMB (+) N = 23	p	CMB ≥ 2 N = 9	P
Age (Median)	76.6 (69–84)	79.3 (73–84)	0.169	79 (72–89)	0.258
Female, n (%)	27 (32.1)	15 (65.2)	0.004	6 (66.7)	0.062
HBP, n (%)	63 (74.1)	19 (82.6)	0.398	9 (1 0 0)	0.110
Smoking, n (%)			0.815		0.885
Never smoker	45 (52.9)	10 (43.5)		4 (44.4)	
Previous smoker	32 (37.7)	11 (47.8)		4 (44.4)	
Active	8 (9.4)	2 (8.7)		1 (11.1)	
Coronary family history, n (%)	19 (23.2)	3 (13.6)	0.255	0 (0)	0.196
Diabetes, n (%)	18 (21.2)	10 (45.5)	0.021	5 (55.6)	0.037
Hypercholesterolemia, n (%)	41 (48.2)	14 (63.6)	0.198	7 (77.8)	0.159
BMI (kg/m2)	27 ± 4	28 ± 5	0.230	30 ± 7	0.214
History of MI, n (%)	12 (14.5)	3 (13)	0.584	0 (0)	0.599
Stroke / TIA, n (%)	10 (11.8)	3 (13.0)	1	1 (11.1)	1
PAD, n (%)	2 (2.4)	2 (8.7)	0.20	1 (11.1)	0.263
AAA, n (%)	2 (2.4)	0 (0)	1	0 (0)	1
AS, n (%)	2 (2.4)	0 (0)	1	0 (0)	1
Chronic kidney disease, n (%)	4 (4.9)	3 (13)	0.176	1 (11.1)	0.402
COPD, n (%)	5 (5.9)	0 (0)	0.582	0 (0)	1
Alzheimer's, n (%)	2 (2.4)	0 (0)	1	0 (0)	1
History of Angioplasty, n (%)	14 (16.7)	1 (4.3)	0.183	1 (11.1)	1
History of CABG, n (%)	2 (2.4)	2 (8.7)	0.198	1 (11.1)	0.263
History of AF, n (%)	7 (8.2)	3 (13)	0.36	3 (33.3)	0.068
ST-segment elevation, n (%)	44 (53)	8 (36.4)	0.165	3 (33.3)	0.311
LVEF (%)	55 (45–60)	45 (40–60)	0.276	60 (48–70)	0.217

AAA = Abdominal aortic aneurysm; AF = Atrial fibrillation; AN = Aortic stenosis; BMI = Body Mass Index; CABG = Coronary artery bypass graft; CMB = cerebral microbleeds; COPD = Chronic obstructive pulmonary disease; HBP = Hypertension; LVEF = Left ventricular ejection fraction; MI = Myocardial infarction; PAD = Peripheral arterial disease; TIA = Transient ischemic attack.

Table 2
Comparison of biological data in the population without CMB and patients with CMB or patients with ≥ 2 CMB.

Criteria	CMB (−) N = 85	CMB (+) N = 23	p	CMB ≥ 2 N = 9	p
Hemoglobin g/100 mL	14.1 (12.4–15.1)	13.3 (11.0–13.9)	0.012	12.2 (9.9–13.9)	0.014
HbA1c %	5.9 (5.6–6.5)	6.3 (5.7–6.8)	0.171	6.1 (5.9–7.0)	0.177
Total cholesterol (g/l)	2.16 (1.68–2.48)	1.96 (1.64–2.34)	0.379	1.78 (1.17–2.26)	0.097
LDL (g/l)	1.25 (0.96–1.58)	1.19 (0.81–1.56)	0.603	0.99 (0.53–1.43)	0.150
HDL (g/l)	0.56 (0.43–0.71)	0.45 (0.37–0.63)	0.060	0.44 (0.41–0.53)	0.086
Triglycerides (g/l)	1.07 (0.78–1.50)	1.41 (0.97–2.34)	0.051	1.25 (0.83–3.39)	0.272
Troponin I (ng/ml)	26.70 (3.35–65.00)	6.60 (0.35–20.00)	0.009	6.60 (1.83–15.00)	0.083
CK peak, UI/L	860 (234–1360)	295 (122–506)	0.013	338 (105–465)	0.031
eCCr (ml/min)	71.4 ± 30.0	60.5 ± 28.3	0.122	63.4 ± 30.0	0.449
NT-proBNP (pg/ml)	499 (150–2332)	2537 (1448–4916)	0.001	1867 (1010–2728)	0.076
CRP ≥ 3 mg/l	52 (61.2)	17 (73.9)	0.259	7 (77.8)	0.476
TSH	1.47 (0.90–2.39)	1.30 (0.88–3.02)	0.981	1.13 (0.60–3.03)	0.556
Homocysteine	13 (11–16)	16 (11–21)	0.133	19 (9–35)	0.100

CK=: Creatinin Kinase; CMB = cerebral microbleeds; CRP = C-reactive protein; eCCr = estimated creatinine clearance rate; HbA1c = glycosylated hemoglobin; HDL-C = high-density lipoprotein; LDL-C = low-density lipoprotein; Nt pro BNP =: N-Terminal Pro-Brain Natriuretic Peptide; TSH = thyroid stimulating hormone.

In addition, Sharma et al. [9] showed on 1760 patients with stable coronary artery disease or peripheral vascular disease who had a brain MRI that 29.3% of the population have at least one CMB.

Our study shows that female sex is an independent factor for the existence of at least one CMB, which is at odds with current literature. Nevertheless, cerebral amyloid angiopathy, which is most often responsible for lobar CMB, is more common in women than in men.

In the two groups of our cohort, no significant differences in lipid profile were found. A 2017 study published by Mitaki et al. [10] which included 4024 controls aged 62 years on average with no neurological history, found that patients with deep CMB had significantly lower total cholesterol and High density Lipoprotein (HDL-Cs) levels than patients without CMB, even after adjustment for other risk factors. It should also be noted, however, that many of our patients were treated with statins before they were hospitalized for AMI: 52.2% of CMB patients and 25.9% of no-CMB patients.

4.2. Evolution of CMB after 3 months of dual or triple antithrombotic therapy

The originality of our work was the second cerebral MRI 3 months after AMI, making it possible to judge the progression of the individual cerebral lesions. We found that the brain lesions were stable in the majority of patients, but 6% of the population experienced a progression. Our study suggests that discharge treatment with VKA or DOA in combination with antiplatelet therapy may be an independent predictor of early progression of CMB, but these data certainly need to be validated by larger series. Also, longer-term follow-up of 1 year at least will be necessary to validate these results.

Data in the literature regarding the progression of CMB in patients receiving antithrombotic therapy are inconsistent and, more importantly, are derived from data in the post-stroke or post-TIA setting.

Table 3
Associations between cerebral microbleeds and bleeding risk scores, AMI treatment or previous treatments in patients without CMB, with CMB and with ≥ 2 CMB.

	CMB (−) N = 85	CMB (+) N = 23	P	CMB ≥ 2 N = 9	P
PREVIOUS TREATMENT					
Antiplatelets*, n(%)			0.330		0.214
None	60 (70.6)	13 (56.5)		4 (44.4)	
Monotherapy	23 (27.1)	9 (39.1)		5 (55.6)	
Dual therapy	2 (2.4)	1 (4.4)		0 (0)	
VKA, n (%)	5 (5.9)	2 (8.7)	0.462	1 (11.1)	0.463
DOA, n (%)	3 (3.5)	1 (4.4)	0.622	0 (0)	1
DOA or VKA, n (%)	8 (9.4)	3 (13)	0.428	1 (11.1)	1
Antiplatelet* or DOA or VKA, n(%)	31 (36.5)	13 (56.5)	0.098	6 (66.7)	0.148
Statins, n (%)	22 (25.9)	12 (52.2)	0.016	5 (55.6)	0.114
CORONARY ANGIOGRAPHY					
Multivessel disease	46/85 (54.1)	15 (65.2)	0.479	6 (66.7)	0.727
Thrombolysis	1 (1.2)	0 (0.0)	1	0 (0.0)	1
PCI	75/85 (88.2)	16 (69.6)	0.019	5 (55.6)	0.015
CABG	2 (2.5)	2 (9.1)	0.199	2 (22.2)	0.048
RISK SCORES					
Crusade	31.2 ± 14.8	40.5 ± 13.6	0.004	42 ± 12	0.038
Bleeding risk	5.3 ± 2.4	6.1 ± 1.7	0.062	6 (4–7)	0.360
Thrombotic risk	3.5 ± 1.6	4.1 ± 1.6	0.05	4 (3–6)	0.124
Syntax	13 ± 8	17 ± 13	0.182	17 ± 14	0.184
GRACE	158 ± 27	160 ± 36	0.785	157 ± 30	0.822

CABG: Coronary artery by-pass graft; CMB = cerebral microbleeds; DOA: Direct oral anticoagulant; PCI: Percutaneous coronary intervention; VKA: Vitamin K antagonist.
*Acetylsalicylic acid +/− clopidogrel or prasugrel or ticagrelor.

Table 4
Multivariate analyses for predicting the presence of microbleeds.

	Multivariate Model 1		Multivariate Model 2		Multivariate Model 3	
	OR (CI)	p	OR (CI)	p	OR (CI)	p
Female gender	3.493 (1.263–9.656)	0.016	2.658 (0.839–8.425)	0.097	3.726 (1.387–10.014)	0.009
Diabetes	2.236 (0.764–6.541)	0.142	2.380 (0.850–6.668)	0.099	2.526 (0.914–6.984)	0.074
SYNTAX score	1.035 (0.984–1.089)	0.186	X		X	
CRUSADE	X		1.022 (0.983–1.062)	0.274	X	
Quality indexes	−2LL = 95.847; pHL = 0.298; %class = 80.2		−2LL = 99.164; pHL = 0.323; %class = 76.9		−2LL = 100.381; pHL = 0.560; %class = 76.9	

In 2011, Ge et al. retrospective work on 300 patients with ischemic cerebrovascular disease assessed the impact of aspirin taken for more than one year before the episode [11]. This study found a higher frequency of CMB and ICH in long-term aspirin patients, with 40% versus 12% ($p < 0.001$) and 28% versus 1% ($p < 0.0001$), respectively. Also, patients taking aspirin for more than 5 years had a higher risk of CMB than those treated for <5 years. In our series, 28% of patients were taking aspirin before admission, but the duration of treatment was unknown.

In 2015, the CHANCE study randomly assigned two treatments (1/ clopidogrel 75 mg/d + aspirin 75 mg/d for 21 days and clopidogrel alone for up to 90 days, or 2/ aspirin alone at a dose of 75 mg/d for 90 days) to 129 patients after a high-risk TIA or a mild ischemic stroke [12]. On the 3-month MRI, the percentage of patients with CMB was similar in the 2 groups (52.7%). While dual therapy did not increase the number of CMB, the appearance of new CMB was proportional to the number of pre-existing CMB, especially if the number was greater than 3, and to the location of CMB in the cortical/subcortical region. The analysis of patients with CMB on initial MRI and dual therapy is important because it reflects cardiological practices. The CMB progression rate was 50% in the CHANCE study compared with only 6% in our study despite a longer duration of dual therapy. Though our work was done in the context of AMI, it underlines the importance of monitoring high-risk populations.

The potential associations between anticoagulants and CMB have also been the object of scrutiny. In a series of 204 patients, Orken et al. studied the impact of warfarin therapy on the development of new CMB after ischemic stroke [13]. After two years of treatment, the authors found a progression rate of 14% on the second MRI; the difference was more pronounced if CMB were identified on the initial MRI (26% versus 12%).

In 2015, Saito et al. assessed the effect of DOA on CMB [14]. The study included 69 patients with atrial fibrillation who received two cerebral MRI scans one year apart. The analysis of 3 groups (DOA, Warfarin and Warfarin + aspirin) found no new CMB under DOA, but an increase of 23.8% under warfarin and 33.3% under warfarin + aspirin.

Our work has also shown that CMB progress more in older patients, which is consistent with the literature. Wobith and al. reported that the 6-month progression rate was significantly influenced by age (70 years and older) in patients with ischemic stroke or transient ischemic attack and treated with antiplatelet monotherapy [3].

Certainly, our study did not provide solid proof of the incrimination of anticoagulant treatment in the progression of microbleeds, but it is important to note that this result is in harmony with what has been found in other recent studies dealing with this subject. A recent meta-analysis, including forty-seven studies (25 245 participants), published in 2019, by Cheng Y. revealed that anticoagulant use is associated with higher prevalence and incidence of CMB; also, this association appears to be more related to lobar CMB, and to the type of anticoagulant (warfarin) [15].

4.3. CMB and bleeding risk scores

Our study found that the patients in the CMB group had the highest CRUSADE scores, underlining the interest of this score for

Table 5
Univariate and multivariate analyses for predicting an increase in the number of microbleeds.

	Univariate		Multivariate Model 1		Multivariate Model 2	
	OR (IC)	p	OR (IC)	p	OR (IC)	p
Female gender		0.442	X		X	
Age	1.183 (1.003–1.396)	0.046	1.175 (0.952–1.450)	0.133	1.189 (0.988–1.430)	0.067
BMI		0.459	X		X	
HBP	NA		X		X	
Diabetes		0.911	X		X	
Dyslipidemia		0.894	X		X	
Coronary heredity	NA		X		X	
Tobacco use	NA		X		X	
Previous ODA		0.101	X		X	
Previous ODA or VKA	40.500 (3.390–483.918)	0.003	29.902 (2.086–428.617)	0.012	X	
DOA at discharge		0.357	X		X	
DOA or VKA at discharge	15.600 (1.470–165.582)	0.023	X		13.882 (1.111–173.511)	0.041
Chronic antiplatelet*	NA		X		X	
Antiplatelet* at discharged	NA		X		X	
Chronic antiplatelet* or DOA or VKA		0.170	X		X	
Antiplatelet* or DOA or VKA at discharged	NA		X		X	
PCI		0.525	X		X	
CABG		0.098	X		X	
Multivessel disease		0.298	X		X	
CK peak (log)		0.220	X		X	
Troponin I peak		0.249	X		X	
Nt-ProBNP (log)		0.364	X		X	
Hemoglobin		0.210	X		X	
GRACE		0.154	X		X	
SYNTAX		0.722	X		X	
CRUSADE		0.090	X		X	
Bleeding risk		0.202	X		X	
Thrombotic risk		0.613	X		X	
Quality indexes			−2LL = 16,468; pHL = 0.980 ; % class = 93.5		−2LL = 19.281 ; pHL = 0.995 ; % class = 92.4	

BMI = Body Mass Index; CABG = Coronary artery bypass graft; CK = Creatinin Kinase; HBP = Hypertension; DOA = Direct oral anticoagulant; Nt pro BNP = N-Terminal Pro-Brain Natriuretic Peptide PCI = Percutaneous coronary intervention; VKA = Vitamin K agonist.
* Acetylsalicylic acid or prasugrel or clopidogrel or ticagrelor.

the quantification of bleeding risk. Taha et al.'s meta-analysis, which included 9 studies and 13,759 patients, showed that only the CRUSADE score was valid for ST elevation myocardial infarction (STEMI) and Non ST segment elevation myocardial infarction (NSTEMI) AMI patients. In a similar context, registry data show that severe bleeding occured in 2.6% of patients still in hospital and in the same proportion of patients in the post-AMI year [16]. While there is no specific score for post-AMI stroke risk, registry data indicate that strokes occur in 1.4% of patients who are still in hospital recovering from AMI, among which 11.4% are hemorrhagic strokes [17]. In addition, in the year after AMI, 0.6% of patients presented with a stroke, 4.4% of which were hemorrhagic.

There are common elements in the "Crusade score" and the "Bleeding Risk Score" as renal function and hemoglobin. However Crusade score includes diabetes and female gender which can't be found in the bleeding risk score: Diabetes is more associated with CMB+ patients; Also, in our study, female gender was an independent risk factor for CMB. These elements can explain the higher crusade score in CMB+ Patients.

4.4. Limitations of the study

Our study is monocentric, and has included only a limited number of patients to date. The second MRI in the 3rd month may be too soon after the coronary event, though this is usual practice in post-stroke registries.

5. Conclusion

Our study confirms that CMB are common in patients over 60 years of age with AMI and 6% of patients had an increased number of CMB after 3 months of treatment.

Further work is needed to assess the impact of physiological anomalies and the potential adverse effects of treatment. The presence of CMB could also be used as a parameter when evaluating bleeding risk in an effort to optimize individual management in the medium and long term.

Funding

This work was supported by the University Hospital of Dijon, the Association de Cardiologie de Bourgogne, and by grants from the Agence Régionale de Santé (ARS) de Bourgogne Franche-Comté, Institut National de la Santé et de la Recherche Médicale (INSERM) and from the Regional Council of Bourgogne Franche-Comté.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100531.

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