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Observational Study

Prognostic impact of body mass index on in-hospital bleeding complications after ST-segment elevation myocardial infarction

Delphine Ingremeau, Sylvain Grall, Florine Valliet, Laurent Desprets, Fabrice Prunier, Alain Furber, Loïc Bière

ORCID number: Delphine Ingremeau (0000-0001-7321-3873); Sylvain Grall (0000-0002-4251-3643); Florine Valliet (0000-0003-2170-1749); Laurent Desprets (0000-0001-9412-9179); Fabrice Prunier (0000-0002-6637-1141); Alain Furber (0000-0002-5918-0419); Loïc Bière (0000-0002-9321-3739).

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Delphine Ingremeau, Sylvain Grall, Fabrice Prunier, Alain Furber, Loïc Bière, Department of Cardiology, Angers University Hospital, Angers 49933, France

Sylvain Grall, Fabrice Prunier, Alain Furber, Loïc Bière, UMR CNRS 6015 - INSERM U1083, Institut MitoVasc, University of Angers, Angers 49100, France

Florine Valliet, Department of Cardiology, Saumur Hospital, Saumur 49403, France

Laurent Desprets, Department of Cardiology, Cholet Hospital, Cholet 49300, France

Corresponding author: Loïc Bière, MD, PhD, Assistant Professor, Associate Professor, Doctor, Senior Scientist, Department of Cardiology, Angers University Hospital, Institut MitoVasc, 3 rue Roger Amsler, Angers 49933, France. lobiere@chu-angers.fr

Abstract

BACKGROUND

ST-elevation myocardial infarction (STEMI) remains a major cause of mortality despite early revascularization and optimal medical therapy. Tailoring individual management by considering patients' specificities may help in improving post-STEMI survival.

AIM

To evaluate whether in-hospital bleeding complications may be involved in post STEMI prognosis among overweight patients.

METHODS

We prospectively included 2070 patients with a STEMI between January 2005 and December 2012 in the French observational cohort, "Registre d'Infarctus Maine-Anjou". Bleeding Academic Research Consortium (BARC) in-hospital bleeding complications were recorded.

RESULTS

Of 705 patients (35.3%) were presented as being of normal weight, defined as a body mass index (BMI) < 25 kg/m², 877 (43.9%) had a BMI between 25 and 30 kg/m² and 416 (20.8%) had a BMI ≥ 30 kg/m². One-year cardiovascular mortality was lower for BMI ≥ 25 kg/m² (5.3% and 7.1%) patients than for normal weight patients (10.8%) ($P = 0.001$). We found an interaction between the effect of BARC 3 on mortality and BMI groups. While a BARC 3 was related to a higher 1-year mortality in general (HR: 2.58, 95%CI: 1.44-4.64, $P \leq 0.001$), prognosis was even worse in normal weight patients (HR: 2.97, 95%CI: 1.61-5.5, $P < 0.001$) than for patients with a BMI ≥ 25 kg/m² (HR: 1.94, 95%CI: 1.02-3.69, $P = 0.041$).

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CONCLUSION

Normal weight patients presented higher rates of in-hospital bleeding complications and lower survival after a STEMI. Excess mortality might be due to greater vulnerability to bleeding amongst normal weight patients.

Key words: Myocardial infarction; Body mass index; Bleeding complications; Obesity paradox

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Core tip: There was an obesity paradox, with body mass index (BMI) ≥ 25 kg/m² ST-elevation myocardial infarction patients presenting better survival. Normal weight patients presented more in-hospital bleeding than others. In-hospital bleeding was related to 1-year cardiovascular mortality. Presenting a normal BMI increased the effect of bleeding on mortality.

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INTRODUCTION

The prevalence of overweight people in France [Body Mass Index (BMI) between 25 and 30 kg/m²] in 2012 was 32% and obesity rates (BMI greater than 30 kg/m²) were at 15% according to the “National Epidemiological Study on excess weight and obesity” (*ObÉpi*)^[1]. In the United States of America, the obesity rate more than doubled from 15% in 1980 to 34% in 2006^[2]. It is an independent risk factor for cardiovascular (CV) disease, conducive to the occurrence of ST-segment elevation myocardial infarction (STEMI)^[3].

Yet, increasingly, studies also suggest that obesity might also have a protective role in some chronic diseases once they are established, including coronary artery disease. Recent studies have demonstrated an “obesity paradox” after percutaneous coronary intervention, whereby overweight and obese patients seem to have better outcomes than normal weight individuals^[4]. There are multiple explanations. Obese patients may be more likely to receive full-dose guideline-based medical therapy during hospital admission and at discharge^[4]. They present greater coronary diameters^[5]. Thin patients may present higher rates of comorbidities such as cancer^[6], but also a higher rate of bleeding^[7].

In parallel, the unfavourable impact on the prognosis of bleeding complications after STEMI was recently highlighted in various studies. A meta-analysis based on 133597 patients presenting an acute coronary syndrome pointed to major bleeding as a strong predictor of in-hospital or 30-d death and acute myocardial infarction^[8]. Evaluating the relationship between bleeding events and BMI could explain the obesity paradox^[7]. The objective of this study is to evaluate the impact of BMI on the occurrence of bleeding complications and its further relationship with prognosis after a STEMI.

MATERIALS AND METHODS

Study population

We studied 2070 patients consecutively from the “Registre d’Infarctus Maine-Anjou” (RIMA) survey^[9]. We prospectively included all patients presenting with a STEMI in a Western region of France, in which the only available 24 h-7 d coronary angiography service was in Angers University Hospital. Patients were recruited between January 2005 and December 2012. Comparisons were carried out between 3 groups: Normal weight (BMI < 25 kg/m²) ($n = 705$, 35.3%), overweight (25 kg/m² \leq BMI < 30 kg/m²) ($n = 877$, 43.9%), and obese (BMI ≥ 30 kg/m²) ($n = 416$, 20.8%) (Figure 1).

Patients with missing weight or height data ($n = 28$), or a BMI < 18.5 kg/m² ($n = 44$)

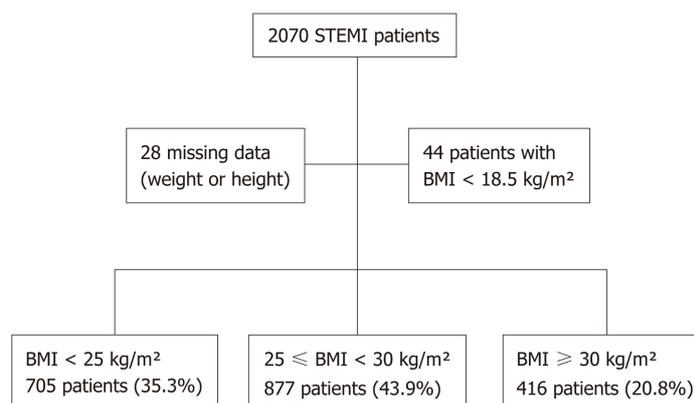


Figure 1 Flow chart. BMI: Body mass index; STEMI: ST elevation myocardial infarction.

were not considered for analysis. This study was carried out in accordance with the Declaration of Helsinki and the protocol was approved by the ethics committee of Angers University Hospital.

Study definitions

STEMI was defined as the presence of symptoms attributed to myocardial ischemia for at least 30 min accompanied with ST-segment elevation of ≥ 1 mm in at least two contiguous limb leads or ≥ 2 mm in precordial leads, or new or undetermined left bundle-branch block, as well as elevation of cardiac biomarkers^[10].

In-hospital bleeding complications were defined according to the Bleeding Academic Research Consortium (BARC)^[11] bleeding classification. The BARC classification identified STEMI patients at risk of 1-year mortality^[12]. We considered type 3 and 5 for analysis: BARC 3a was defined as haemorrhage (haematoma ≥ 4 cm at the site of vascular puncture, or gastrointestinal blood loss, or retroperitoneal bleeding verified by either ultrasound or computed tomography imaging, or intracranial bleeding^[10]) plus haemoglobin drop equal to between 3 g/dL and < 5 g/dL or any transfusion with bleeding; BARC 3b was defined as haemorrhage plus haemoglobin drop ≥ 5 g/dL, cardiac tamponade, haemorrhage requiring surgical intervention for control (excluding dental/nasal/skin/haemorrhoids) or haemorrhage requiring intravenous vasoactive agents; BARC 3c was defined as intracranial haemorrhage; BARC 5 bleeding was defined as fatal haemorrhage^[12].

Data collection

Data on demographics (age, sex, BMI), CV risk factors (smoker, diabetes history, hypertension, dyslipidaemia, family history of premature coronary vascular disease^[13], obstructive sleep apnoea), medical history (prior MI, stroke, peripheral vascular disease, renal failure, cancer) and admission characteristics (systolic blood pressure) were prospectively recorded for each patient at admission. The CRUSADE^[14] and HEMORR2HAGES^[15] bleeding risk scores were calculated based on the patient's initial characteristics.

We collected data concerning acute stage management, including thrombolytic use, time from symptom onset to first medical contact or to admission in the coronary angiography room, coronary angiogram findings [infarct location, vessel disease, puncture access, duration of the procedure and final thrombolysis in myocardial infarction (TIMI) flow], and the medical therapy given before and in the first 24 h after the first medical contact (antiplatelet therapy, antithrombotic therapy). Anticoagulants and their doses were mandated by a single protocol (see supplementary file). During the hospital stay, an echocardiography was obtained for the evaluation of left ventricular ejection fraction (LVEF) by the biplane Simpson method. Blood samples were collected to measure serum haemoglobin at admission and during hospitalisation to determine the haemoglobin drop, haematocrit and creatine phosphokinase peak. In-hospital complications were examined by two physicians and included death, bleeding event, transfusion, necrosis recurrence, heart failure and stroke. The 1-year follow-up for survival was available for all patients who were initially included.

Statistical analysis

Patient characteristics, in-hospital and 1-year events were compared relating to the BMI group. Continuous variables are expressed as the median (interquartile range).

Continuous variables were analysed using the Mann-Whitney *U*-test for 2-group comparisons and the Kruskal-Wallis test for 3-group comparisons. Qualitative variables were expressed as frequencies and percentages. The Pearson χ^2 test or Fisher's exact test were used to carry out comparisons between qualitative variables and in-hospital event rates.

Binomial logistic regression was carried out to determine correlates of in-hospital BARC 3 or 5 bleeding. The variables entered into the model were gender, age, history of hypertension, BMI, smoking, renal failure, puncture access, duration of the procedure, number of diseased vessel(s), final TIMI flow, creatine phosphokinase peak, LVEF and pre-use of antivitamin K. Interactions between BMI and procedure duration and puncture access were evaluated.

Univariate Cox analysis was made to identify predictors of 1-year CV mortality. Overweight and obese patients were grouped for analysis, and variables demonstrating a $P < 0.05$ were included in an exploratory Cox proportional hazards model to assess 1-year CV mortality. Interactions between the effect of BMI groups and independent variables on mortality (BARC 3, in-hospital heart failure, history of cancer, stroke) were calculated and included in the multivariate model when significant. $P < 0.05$ was considered significant. Statistical tests were performed using SPSS software (Version 17; SPSS, Inc., Illinois, United States).

RESULTS

Baseline characteristics and initial management

Obese patients were younger than overweight and normal weight patients [respectively 61 (51, 74) years old *vs* 64 (53, 76) and 67 (53, 79)]. They presented more CV risk factors such as hypertension, diabetes, dyslipidaemia and obstructive sleep apnoea. The main characteristics are summarised in [Table 1](#). There was no difference in medical history and infarct characteristics among the three groups. There was less use of femoral access for obese patients (51.5%) than for the other groups (60.1% and 59.5%) ($P = 0.021$).

In-hospital events and bleeding

Among the population, 150 patients (7.5%) presented a BARC 3 or 5 bleeding event. These patients were older (70.2 ± 13.9 *vs* 64.1 ± 14.73 , $P < 0.001$) and the use of femoral access was higher (71.5% *vs* 56.6%, $P = 0.001$). Normal weight patients had higher rates of BARC 3 and 5 bleeding than overweight and obese patients (9.5% *vs* 6.2% and 6.2%, $P = 0.031$) ([Table 2](#)). Independent variables associated with in-hospital BARC 3 or 5 bleeding were duration of the procedure, puncture access and LVEF ([Table 3](#)). The other in-hospital outcomes were not different among the three groups.

Cardiovascular mortality

One-year CV mortality was significantly lower for BMI ≥ 25 kg/m² (5.3% and 7.1%) patients than for normal weight patients (10.8%) with $P = 0.001$ ([Table 2](#)). Independent variables associated with 1-year CV mortality were age, prior myocardial infarction, prior stroke, cancer, creatine phosphokinase peak, in-hospital heart failure and BARC 3 bleeding ([Table 4](#)). BMI was not an independent variable in this multivariate analysis although there was an interaction between BARC 3 and BMI (HR: 2.58, 95% CI: 1.44-4.64, $P = 0.001$), demonstrating BARC 3 bleeding to have a stronger clinical impact among normal weight patients (HR: 2.97, 95% CI: 1.61-5.5, $P < 0.001$) than for BMI ≥ 25 kg/m² patients (HR: 1.94, 95% CI: 1.02-3.69, $P = 0.041$) ([Figure 2](#)).

DISCUSSION

The 1-year cardio-vascular mortality of patients with BMI ≥ 25 kg/m² in the RIMA cohort was lower than for normal weight patients, yet BMI was not an independent predictor for mortality, while an in-hospital bleeding event was. We found a BMI ≥ 25 kg/m² to be related to the bleeding event have less of an effect on prognosis.

Population characteristics

The 416 patients in our study with BMI ≥ 30 kg/m² were younger, predominantly male and their prevalence of diabetes, hypertension and dyslipidaemia was higher. These are typical characteristics as identified in populations with acute coronary syndrome^[16], including STEMI^[17]. Nevertheless, there was no difference in regard of infarct location, reperfusion success, and LVEF.

Table 1 Baseline clinical characteristics according to body mass index

	Total n = 1998	BMI < 25 kg/m ² n = 705	25 ≤ BMI < 30 kg/m ² n = 877	BMI ≥ 30 kg/m ² n = 416	P value
Cardiovascular risk factors					
Age (yr)	64 (53-77)	67 (53-79) ^{ae}	64 (53-76) ^{ac}	61 (51-74) ^{ce}	< 0.001
Male	1485 (74.3)	493 (69.6) ^a	693 (79.0) ^{ac}	302 (72.6) ^c	< 0.001
Hypertension	986 (49.3)	308 (43.6) ^e	422 (48.2) ^c	257 (61.9) ^{ce}	< 0.001
Diabetes mellitus	492 (24.6)	134 (19.1) ^{ae}	211 (24.3) ^{ac}	147 (35.6) ^{ce}	< 0.001
Dyslipidaemia	1001 (50.1)	323 (45.8) ^{ae}	442 (50.8) ^{ac}	236 (57.0) ^{ce}	0.001
Smoker	708 (35.4)	261 (37) ^{ae}	299 (34.2) ^a	148 (35.8) ^e	0.006
Family history of coronary artery disease	442 (22.1)	134 (19.1) ^{ae}	210 (24.4) ^a	98 (24.0) ^e	0.032
Prior myocardial infarction	171 (8.6)	53 (7.5)	83 (9.5)	35 (8.5)	0.36
Obstructive sleep apnoea	22 (1.1)	0 (0.0) ^{ae}	10 (1.5) ^{ac}	12 (3.7) ^{ce}	< 0.001
History					
Stroke	86 (4.3)	34 (4.8)	37 (4.2)	15 (3.6)	0.4
Renal failure	59 (3.0)	21 (3.0)	29 (3.3)	9 (2.2)	0.52
Cancer	158 (7.9)	61 (8.7)	71 (8.1)	27 (6.5)	0.41
Clinical presentation					
Systolic blood pressure (mmHg)	139 (120-159)	135 (116-155) ^{ae}	140 (120-160) ^{ac}	141 (127-162) ^{ce}	< 0.001
HEMORR2HAGES score	1 (0-2)	1 (0-2)	1 (0-2)	1 (0-2)	0.09
CRUSADE score	24 (14-37)	29 (18-42) ^{ae}	21 (12-33) ^{ac}	18 (9-33) ^{ce}	< 0.001
Infarct characteristics					
Time from symptoms to first medical contact (h)	2.25 (1-5.5)	2.3 (1.2-5.7)	2 (1-4) ^c	2 (1-6) ^c	0.024
Time from symptoms to admission (h)	3 (1.9-6.5)	3.1 (2-6.3)	2 (1-6) ^c	3 (2-7) ^c	0.025
Anterior infarction	820 (41)	294 (41.6)	362 (41.3)	166 (40.2)	0.57
Multivessel disease	1003 (53)	356 (53.2)	433 (52.5)	217 (54.5)	0.75
Femoral access	1017 (57.5)	365 (59.5) ^e	463 (58.7) ^c	191 (51.5) ^{ce}	0.021
Duration of the angioplasty procedure (min)	39 (22-60)	40 (22-59)	38 (22-60)	40 (21-60)	0.8
Fibrinolysis	307 (15.4)	100 (14.1)	153 (17.4)	55 (13.3)	0.06
Final TIMI 3 flow	1508 (92.8)	527 (92.5)	670 (93.3)	314 (92.4)	0.7
LVEF (%)	50 (40-55)	47 (36-58)	49 (38-59)	48 (38-59)	0.09
Creatine phosphokinase peak (UI/L)	1404 (606-2675)	1374 (520-2565) ^e	1367 (626-2711)	1526 (728-2683) ^e	0.048
Prior medication					
Antivitamin K	62 (3.1)	21 (3)	29 (3.3)	12 (2.9)	0.91
In-hospital medication					
Aspirin	1964 (98.3)	696 (98.9)	863 (98.6)	408 (98.8)	0.95
Clopidogrel	1777 (88.9)	627 (89.1)	786 (89.9)	367 (88.9)	0.74
Prasugrel	223 (11.2)	75 (11.5)	95 (11.4)	53 (13.6)	0.48
Antivitamin K	35 (1.8)	13 (1.9)	12 (1.4)	10 (2.4)	0.4
LMWH	1481 (74.1)	511 (72.7)	671 (76.7)	302 (73.3)	0.06
UFH	454 (22.7)	166 (23.6)	180 (20.6)	108 (26.2)	0.06
LMWH + UFH	198 (9.9)	71 (10.1)	78 (8.9)	49 (11.9)	0.25
Bivalirudin (since 2010, for information)	136	55	55	26	0.41

Data given as number (%) or median (interquartile range).

^aP < 0.05 to compare body mass index (BMI) < 25 kg/m² with BMI between 25 kg/m² and 30 kg/m²;

^cP < 0.05 to compare BMI between 25 kg/m² and 30 kg/m² with BMI ≥ 30 kg/m²;

^eP < 0.05 to compare BMI < 25 kg/m² with BMI ≥ 30 kg/m². BMI: Body mass index; LVEF: Left ventricular ejection fraction; LMWH: Low molecular weight heparin; TIMI: Thrombolysis in Myocardial Infarction; UFH: Unfractionated heparin.

The obesity paradox

Bucholz *et al*^[18] studied 2334 patients with an infarction in the PREMIER registry. The 4-year mortality was 24.1% for normal weight patients, 17.2% for overweight patients and 12.4% for obese patients. The increase of 1 BMI point in the RICO cohort led to a reduction of 5% in the risk of death after one-year [OR: 0.95, (0.93-0.98), P < 0.001]^[19]. Despite a higher coronary risk, in-hospital and one-year mortality was lower for

Table 2 In-hospital and one-year events

	Total	BMI < 25 kg/m ²	25 ≤ BMI < 30 kg/m ²	BMI ≥ 30 kg/m ²	P value
	n = 1998	n = 705	n = 877	n = 416	
In-hospital events					
Duration of hospitalisation in intensive care (d)	5 (3-7)	5 (4-7)	5 (3-7)	5 (3-6)	0.21
Heart failure	417 (20.9)	153 (21.7)	176 (20.1)	89 (21.5)	0.56
Stent thrombosis	38 (1.9)	19 (2.5)	11 (1.3)	8 (1.9)	0.16
Atrial fibrillation	196 (9.8)	75 (10.6)	92 (10.5)	29 (7.0)	0.06
Stroke	39 (2.0)	14 (2)	19 (2.2)	6 (1.4)	0.65
Tamponade	22 (1.1)	10 (1.4)	7 (0.8)	5 (1.2)	0.56
Mortality	115 (5.8)	54 (7.6) ^{ac}	43 (4.9) ^a	18 (4.3) ^e	0.018
Cardiovascular mortality	112 (5.6)	54 (7.6) ^{ac}	40 (4.6) ^a	18 (4.3) ^e	0.013
In-hospital bleeding events					
Input Haemoglobin (g/dL)	14.4 (13.3-15.5)	14.1 (13-15.3) ^{ac}	14.6 (13.5-15.6) ^a	14.7 (13.5-15.7) ^e	< 0.001
Haemoglobin drop (g/dL)	1.9 (0.9-2.9)	2 (1-3.2) ^{ac}	1.7 (0.8-2.9) ^a	1.8 (0.9-2.7) ^e	0.016
Input haematocrit (%)	42.6 (39.6-45.5)	42 (38.9-44.9) ^{ac}	42.8 (40-45.8) ^a	43.3 (40.2-45.6) ^e	< 0.001
Haematocrit drop (%)	5.3 (2.8-8.4)	6.1 (3.1-9.3) ^{ac}	5 (2.6-8.1) ^a	4.9 (2.8-7.8) ^e	< 0.001
Haemorrhagic stroke	9 (0.5)	6 (0.8)	3 (0.3)	0 (0.0)	0.07
Gastrointestinal bleeding	25 (1.3)	12 (1.7)	8 (0.9)	5 (1.2)	0.45
Haematoma at the puncture site	138 (6.9)	56 (7.9)	58 (6.6)	24 (5.8)	0.22
Surgical repair of the haematoma	9 (0.5)	3 (0.4)	4 (0.5)	2 (0.5)	0.98
Use of amines in bleeding	33 (1.7)	18 (2.5)	10 (1.1)	6 (1.4)	0.13
Transfusion	82 (4.1)	42 (5.9) ^a	25 (2.9) ^a	15 (3.6)	0.011
Fatal bleeding (BARC 5)	9 (0.5)	6 (0.8)	2 (0.2)	1 (0.2)	0.17
BARC 3 or 5	146 (7.3)	67 (9.5) ^{ac}	54 (6.2) ^a	26 (6.2) ^e	0.031
One-year events					
Mortality	198 (9.9)	93 (13.1) ^{ac}	82 (9.4) ^{ac}	23 (5.5) ^{ce}	< 0.001
CV mortality	160 (8.0)	76 (10.8) ^{ac}	62 (7.1) ^a	22 (5.3) ^e	0.001

^aP < 0.05 to compare body mass index (BMI) < 25 kg/m² with BMI between 25 kg/m² and 30 kg/m²;

^cP < 0.05 to compare BMI between 25 kg/m² and 30 kg/m² with BMI ≥ 30 kg/m²;

^eP < 0.05 to compare BMI < 25 kg/m² with BMI ≥ 30 kg/m². BARC: Bleeding Academic Research Consortium; BMI: Body mass index; CV: Cardiovascular.

patients with BMI ≥ 25 kg/m².

Several theories have been developed to explain this phenomenon. One hypothesis is that thin patients are older and have more comorbidities than overweight patients, notably in term of higher prevalence of cancer. This hypothesis was developed by Witassek *et al*^[20] in the Swiss AMIS Plus registry. The prevalence of history of cancer among the three groups in the RIMA appeared to be similar, despite the fact that normal weight patients were older. Other explanations have been put forward, such as obtaining targeted and adapted therapeutic doses in overweight and obese patients, which was not the case for thin patients^[4,9], particularly regarding anticoagulants^[16].

In our study, factors conducive to 1-year cardio-vascular mortality were age, history of infarction or stroke; history of cancer, creatine phosphokinase peak, in-hospital heart failure, and a BARC 3 in-hospital haemorrhagic event. While BMI did not appear to be an independent factor for mortality *per se*, BMI was an effect modifier of the impact of haemorrhagic complications. Of note, bleeding events were more frequent among BMI < 25 kg/m² patients compared to others (Table 2).

Haemorrhagic complications

The prevalence for bleeding events varies in the literature from 3.9% in a GRACE-derived report^[21] to 22% in a STEMI cohort^[22]. In our study, we defined bleeding events by the BARC scoring system, which is robust and takes into account quantitative parameters such as a haemoglobin drop. Consequently, we reported a bleeding prevalence of 7.3% in the RIMA cohort; and we showed this prevalence to be higher among normal weight patients than among the other groups. Das *et al*^[17] found the same relationship in 49329 patients with STEMI, as already reported by other sources^[4,6,19,23-26]. The main location of bleeding events was at the puncture site.

Table 3 Predictor of Bleeding Academic Research Consortium 3 and 5 bleeding by univariate and multivariate analysis

	Univariate analysis	Multivariate analysis	Odds ratio (95%CI)
	P value	P value	
Male	0.001	0.19	
Age (per decade)	< 0.001	0.08	
Hypertension	0.001	0.18	
BMI < 25 kg/m ²	0.006	0.75	
Smoker	0.005	0.31	
Renal failure	0.032	0.77	
Radial puncture access	0.001	0.036	0.54 (0.3-0.96)
Duration of the procedure	< 0.001	0.004	1 (1-1.01)
Multivessel disease	0.003	0.76	
Final TIMI flow	0.005	0.46	
Creatine phosphokinase peak (per 500 UI/L)	< 0.001	0.15	
Left ventricular ejection fraction	< 0.001	0.017	0.97 (0.94-0.99)
Antivitamin K use before	0.016	0.48	

BMI: Body mass index; TIMI: Thrombolysis in myocardial infarction.

According to Hamon *et al*^[8], predictive factors for haemorrhagic complications are being female, low weight (BMI < 19 kg/m²), aged 75 or more, severe renal failure, history of stroke and uncontrolled arterial hypertension. Indeed, pharmacokinetics of anticoagulants may be driven by body composition, as patients with a lower ratio of lean body mass are exposed to supra-therapeutic dose of anticoagulants. Moreover, the management of antiplatelet therapy being mostly unadjusted to body weight, normal weight patients may receive relatively greater doses. In the present study, independent correlates to bleeding events were longer procedure duration, lower LVEF and a femoral puncture site. Of note, a femoral puncture site was responsible for higher rates of bleeding events BARC 3 or 5 (Figure 2). It should be noted that a femoral puncture site was responsible for higher rates of BARC 3 or 5 bleeding events (Table 3)^[27].

These bleeding complications are also associated with a more severe prognosis in normal weight patients than for other patients (Figure 2). The originality of this report was the evidence of lower prevalence and a poorer prognostic impact of bleeding complications in normal weight patients (Figure 3). Special concerns should be given to the management of antithrombotic therapies, including following drug requirements, stopping anticoagulants early after effective angioplasty^[28], avoiding changing anticoagulants several times^[29], and encouraging low-risk strategies when invasive management is uncertain^[30]. Even though the benefits of newer antiplatelet therapy is unquestionable in terms of prevention of stent thrombosis, a switch to clopidogrel – as soon as one month after angioplasty - may lower bleeding events^[31].

Limitations

However, there are limits to this real-life cohort study. It only included hospitalised patients, leading to a bias in the recruitment of survivors. The BMI is not the best criterion for evaluating abdominal obesity, our study did not include a measurement of the waist size and the waist-to-hip ratio, and did not take into account for confounders like chronic inflammatory disease or coagulation disorder in the database.

In conclusion, in the present study, we show in-hospital bleeding to be more prevalent amongst normal weight patients (BMI < 25 kg/m²) with greater impact on prognosis. Normal weight did not impact on one-year CV mortality *per se*, but increased the effect of bleeding on mortality. Here, we raise one explanatory hypothesis of the obesity paradox, with in-hospital bleeding in BMI ≥ 25 kg/m² patients related to lower impact on one-year mortality after STEMI.

Table 4 Predictor of one-year cardiovascular mortality by univariate and multivariate analysis

	Univariate analysis	Multivariate analysis	Hazard ratio (95%CI)
	P value	P value	
Male	< 0.001	0.5	
Age (per decade)	< 0.001	< 0.001	1.56 (1.31-1.87)
Hypertension	< 0.001	0.28	
BMI < 25 kg/m ²	< 0.001	0.5	
Smoker	< 0.001	0.62	
Diabetes mellitus	0.042	0.71	
Prior myocardial infarction	0.011	0.015	1.91 (1.13-3.22)
Stroke history	< 0.001	0.011	2.07 (1.17-3.64)
Renal failure	< 0.001	0.43	
Cancer	0.002	0.02	1.83 (1.09-3.06)
Radial puncture access	< 0.001	0.06	
Creatine phosphokinase peak (per 500 UI/L)	0.003	< 0.001	1.05 (1.03-1.07)
In-hospital heart failure	< 0.001	< 0.001	5.29 (3.44-8.13)
BARC 3 among BMI < 25 kg/m ²	< 0.001	< 0.001	2.97 (1.61-5.5)
BARC 3 among BMI ≥ 25 kg/m ²	< 0.001	0.041	1.94 (1.02-3.69)

BARC: Bleeding Academic Research Consortium; BMI: Body mass index; TIMI: Thrombolysis in myocardial infarction.

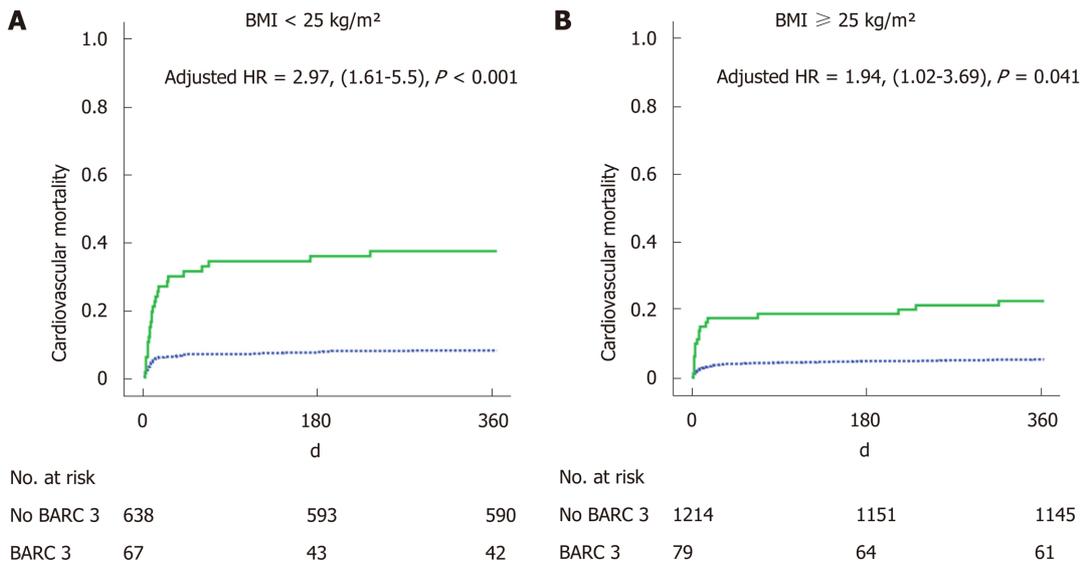


Figure 2 Time-to-event curves for the primary end-point. A: Occurrence of 1-year cardiovascular mortality according to Bleeding Academic Research Consortium (BARC) 3 in body mass index (BMI) < 25 kg/m² patients; B: Occurrence of 1-year cardiovascular mortality according to BARC 3 in BMI ≥ 25 kg/m² patients. BARC: Bleeding Academic Research Consortium; BMI: Body mass index; HR: Hazard ratio.

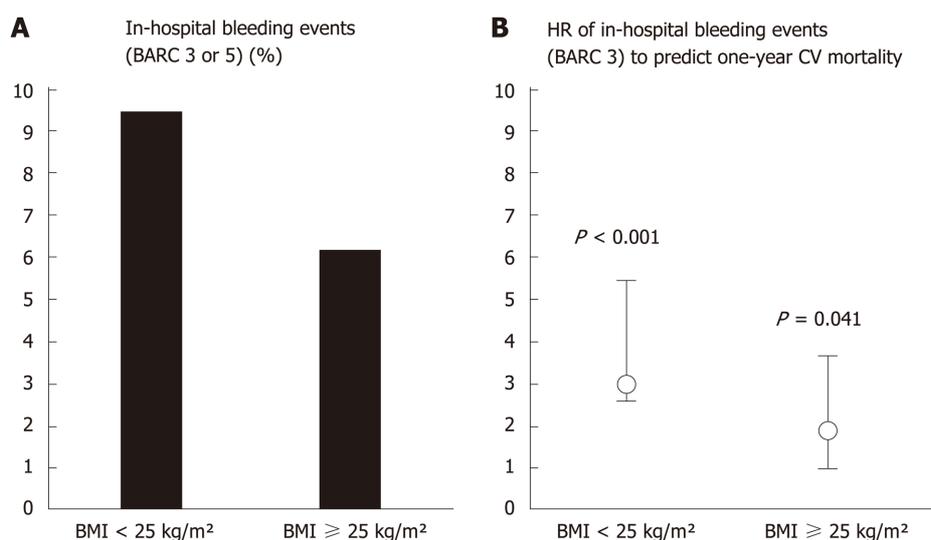


Figure 3 Bleeding events and prognosis. A: In-hospital bleeding events [Bleeding Academic Research Consortium (BARC) 3 or 5] prevalence; B: Hazard ratios (HR) of in-hospital bleeding event (BARC 3) to predict one-year cardiovascular mortality. *P* values for HR in each body mass index subgroup. BARC: Bleeding Academic Research Consortium; BMI: Body mass index; CV: Cardiovascular; HR: Hazard ratio.

ARTICLE HIGHLIGHTS

Research background

ST-segment elevation myocardial infarction (STEMI) remains a major cause of mortality despite early revascularization and optimal medical therapy. Tailoring individual management by considering patients' specificities may help in improving post-STEMI survival.

Research motivation

While overweight and obesity are correlated with common cardiovascular (CV) risk factors and outcomes, overweight and obese patients present better survival after suffering from myocardial infarction. This obesity paradox is not elucidated.

Research objectives

To assess whether the obesity paradox might be explained by bleeding events after a first STEMI.

Research methods

We studied 2070 patients consecutively from the "Registre d'Infarctus Maine-Anjou" survey, that prospectively included all patients presenting with a STEMI in a Western region of France, in which the only available 24 h-7 d coronary angiography service was in Angers University Hospital. Median age was 64 (interquartile range 53-77) years, 74.3% were male, 41% presented with anterior infarction and 81% underwent primary percutaneous coronary intervention. Outcomes were gathered during the year following MI. Bleeding Academic Research Consortium (BARC) 3 and 5 bleeding events were used to assess in-hospital bleeding complications. Cox regression analyses were performed to assess correlates for 1-year mortality.

Research results

One-year CV mortality was significantly lower for body mass index (BMI) ≥ 25 kg/m² (5.3% and 7.1%) patients than for normal weight patients (10.8%) with *P* = 0.001. Independent variables associated with 1-year CV mortality were age, prior myocardial infarction, prior stroke, cancer, creatine phosphokinase peak, in-hospital heart failure and BARC 3 bleeding. BMI was not an independent variable in this multivariate analysis although there was an interaction between BARC 3 and BMI (HR: 2.58, 95%CI: 1.44-4.64, *P* = 0.001), demonstrating BARC 3 bleeding to have a stronger clinical impact among normal weight patients (HR: 2.97, 95%CI: 1.61-5.5, *P* < 0.001) than for BMI ≥ 25 kg/m² patients (HR: 1.94, 95%CI: 1.02-3.69, *P* = 0.041).

Research conclusions

We show in the present study the role that in-hospital bleeding may play in the obesity paradox. Indeed, not only in-hospital bleeding events were lower among overweight patients, but also presented a weaker impact on 1-year CV mortality. The results of this study first suggest a need to adjust antithrombotic therapies in normal weight patients. Lowering doses to lower bleeding events must be balanced with anti-ischemic efficacy. Second, the reasons why intra-hospital bleeding presents a lower impact on overweight patients raise question and need further investigation.

Research perspectives

Randomized control trials are needed to better monitor anti-thrombotic therapies in STEMI patients. Beside age, gender and clinical presentation, BMI might be a valuable feature to assess.

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