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Impact of blood transfusion on in-hospital myocardial infarctions according to patterns of acute coronary syndrome: Insights from the BleeMACS registry☆

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ABSTRACT

Background: Blood transfusions (BTs) may worsen the prognosis of patients affected by acute coronary syndromes (ACS), although few data detail their impact on short-term events according to clinical presentation (ST Segment Elevation Myocardial Infarction, STEMI vs. Non-ST Segment Elevation ACS, NSTE-ACS).
Methods: Patients undergoing percutaneous coronary intervention (PCI) for ACS, with data on BTs, were selected from the BleeMACS registry. The primary end point was the incidence of myocardial infarction during hospitalization (reAMI), the secondary end-points were 30-day mortality and the combined end-point of 30-day mortality and reAMI. Sensitivity analyses were performed according to clinical presentation (STEMI vs. NSTE-ACS).
Results: Overall, 13,975 patients were included: mean age was 64.1 years, 10,651 (76.2%) were male and 7711 (55.2%) had STEMI. BTs were administered during hospitalization to 465 (3.3%) patients, who were older and presented a more relevant burden of risk factors. The primary end-point of reAMI occurred in 197 (1.4%) patients,

Abbreviations: ACS, acute coronary syndrome; BTs, blood transfusions; CV, cardiovascular; DAPT, double anti-platelet therapy; Hb, hemoglobin; NSTE-ACS, non-ST segment elevation acute coronary syndrome; NSTEMI, non-ST segment elevation myocardial infarction; OAC, oral anticoagulation; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; reAMI, recurrent acute myocardial infarction; STEMI ST, segment elevation myocardial infarction; UA, unstable angina.

☆ All the authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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of whom 102 (1.1%) with STEMI. After controlling for confounding variables, BTs independently predicted the primary end-point reAMI in patients admitted for STEMI (OR 4.059, 95% CI 2244–7.344) and not in those admitted for NSTE-ACS. Moreover, BTs independently related to 30-day mortality in STEMI and NSTE-ACS patients and to the composite of 30-day mortality and reAMI in STEMI patients.

Conclusions: In patients undergoing PCI for ACS, BTs increase the risk of reAMI only in those admitted for STEMI, and not in those with NSTE-ACS. These results may help physicians to choose appropriate BT administration according to the admission diagnosis.

1. Introduction

Anemia negatively affects the prognosis of patients hospitalized for acute coronary syndromes (ACS), increasing the mortality and incidence of adverse cardiovascular (CV) events, especially in patients with complex coronary disease [1,2]. Blood transfusions (BTs) can rapidly and effectively restore hemoglobin (Hb) and hematocrit levels, but safety and effectiveness of this practice have been increasingly doubted. Several studies reported a substantial negative effect on short and long-term outcome [3,4]. Despite these evidences, BTs are still widely administered in the ACS setting, with many challenges related to dual antiplatelet therapy [5,6,7].

Moreover, little is known about the mechanisms by which BTs could lead to adverse outcomes. Incomplete correction for confounding factors plays a significant role, as patients receiving BTs are usually more frail and present a higher comorbidity burden. A direct cause–effect relationship between BTs and CV events, however, possibly involving recurrence of acute myocardial infarction (re-AMI), has been described [8].

Furthermore, scarce data detail if different clinical presentations of ACS (ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation ACS (NSTE-ACS, which include myocardial infarction (NSTEMI) and unstable angina (UA)) may be differently affected by BTs [3]. As the pathogenesis of STEMI, as compared to NSTE-ACS, rely mainly on erythrocyte-rich red thrombus formation, it is plausible that infusion of packed red-blood cells may increase the risk of re-AMI in these patients more than in NSTE-ACS patients, even if no clinical data can corroborate this assumption [9].

We conducted the present study with the aim to investigate the occurrence of in-hospital re-AMI and the short-term mortality in patients hospitalized for ACS exposed to BTs. Moreover, our objective was also to assess if BTs may lead to different clinical outcomes in patients with STEMI as compared to those with NSTE-ACS.

2. Methods

2.1. Study population

The present study is a sub-analysis of the BleeMACS project, a voluntary contemporary quality improvement international registry, which enrolled 15,401 consecutive unselected patients undergoing percutaneous coronary intervention (PCI) for ACS and who survived the in-hospital phase. Full study protocol has been already published [10], and more detailed data can be found in the BleeMACS webpage (http://bleemacs.wix.com/registry) and in clinicaltrials.gov (Identifier: NCT02466854). Briefly, recruitment was conducted between 2003 and 2014 in 15 centers from ten countries from North America (Canada), South America (Brazil), Europe (Germany, Poland, Netherlands, Spain, Italy, Greece), and Asia (China and Japan). Baseline clinical characteristics and in-hospital procedures and events were recorded for all patients. A one-year follow-up after the discharge from index hospitalization was conducted and data about vital status, bleeding complications, CV events and other adverse events were collected from hospital records, by telephonic contact with patients or their relatives or their primary care physician if deemed necessary.

For the purpose of this analysis, for which approval of the scientific committee of the BleeMACS initiative was obtained, all patients with available information pertaining treatment with BTs (patients treated with BTs vs. not treated with BTs) during index hospitalization were included. Informed consent was obtained from each patient. The study was conducted in accordance with the Declaration of Helsinki and was approved by local institutional review boards.

2.2. Study end-point

The primary end-point of the study was the incidence of in-hospital reAMI. Secondary end-points were 30-day mortality and the combined end-point of in-hospital reAMI and 30-day mortality. Sensitivity analyses were performed according to the clinical presentation of ACS (STEMI vs. NSTE-ACS).

2.3. Data definition

In-hospital re-AMI was defined as the occurrence of any new MI during index hospitalization after PCI, intended both as peri-procedural MI (type 4a MI) and as a new spontaneous MI occurred during index hospitalization [11]. Thirty-day mortality was inferred from the original registry based on time-to-death. History of bleeding included prior bleeding and in-hospital bleeding. Prior bleeding included any episode of serious bleeding previous to the qualifying ACS hospitalization, and was defined as intracranial bleeding or any other bleeding leading to hospitalization and/or red blood transfusion. In-hospital bleeding was defined as any TIMI (Thrombolysis In Myocardial Infarction) major or minor bleeding, or any GUSTO (Streptokinase and t-PA for Occluded Coronary Arteries) severe or moderate bleeding, or any BARC (Bleeding Academic Research Consortium) type 3 bleeding [12,13,14]. Vascular disease was defined as prior stroke/transient ischemic attack or peripheral arterial disease (PAD). Malignancy was defined as any active cancer or any non-active cancer diagnosed during the last 5 years.

2.4. Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), categorical variables were expressed as number and percentages (%). Correlations between parameters and study groups were tested in cross tabulation tables by means of Pearson Chi Square test or Fisher exact test for categorical variables and by One-Way Analysis of Variance (ANOVA) for continuous variables.

Logistic regression analysis was performed to test the predictive ability of parameters relating to study end-points. A different model was run for each end-point stratified by clinical presentation of ACS (i.e. STEMI vs. NSTE-ACS) including main variables significantly relating to those same end-points at univariate analysis [15]. Calibration and accuracy of each model were tested by Hosmer–Lemenshow test and by ROC curves analysis. A two-sided <0.05 p-value was considered as statistically significant; all analysis were performed with SPSS 21.0 (IBM Corporation, Armonk, NY, USA).

3. Results

3.1. Baseline features

After excluding 1426 patients due to the absence of data pertaining in-hospital treatment with BTs, 13,975 patients were included in the present analysis, of whom 10,651 (76.2%) were males, with a mean age of 64.1 ± 12.7 years. BTs during index hospitalization were administered to 465 (3.3%) patients.

As shown in Table 1, patients treated with BTs were older, more frequently of female sex and were characterized by a higher burden of CV risk factors and comorbidities. Dyslipidemia was more frequent in patients not treated with BTs.

At admission, a diagnosis of STEMI was adjudicated in 294 (63.2%) patients treated with BTs as compared to 7417 (54.9%) in those not treated with BTs ($p < 0.001$), while NSTE-ACS were more frequent among patients not treated with BTs (6093, 45.1% vs. 171, 36.8%, $p < 0.001$). The difference was mainly driven by the different rate of UA (6.7% vs. 14.1%, $p < 0.001$), while rate of NSTEMI was similar between the two groups. Patients treated with BTs (Table 2) showed a significantly higher prevalence of multivessel disease, were more likely to receive femoral access and to undergo PCI without stent implantation and presented a lower rate of complete revascularization. These same

Table 1
Baseline characteristics of study population.

	Overall n = 13,975	Patients treated with blood transfusions n = 465	Patients not treated with blood transfusions n = 13,510	p value
Age	64.1 ± 12.6	71.7 ± 11.7	63.8 ± 12.6	<0.001
Female sex	3324 (23.8)	236 (50.8)	3088 (22.9)	<0.001
Hypertension	8195 (58.6)	310 (66.7)	7885 (58.4)	<0.001
Diabetes mellitus	3327 (23.8)	168 (36.1)	3159 (23.4)	<0.001
Dyslipidemia	7243 (51.8)	173 (37.2)	7070 (52.3)	<0.001
Peripheral arterial disease	859 (6.1)	63 (13.5)	796 (5.9)	<0.001
Prior MI	1719 (12.3)	76 (16.3)	1643 (12.2)	0.007
Prior PCI	1818 (13.0)	56 (12.0)	1762 (13.0)	0.529
Prior CABG	495 (3.5)	33 (7.1)	462 (3.4)	<0.001
Stroke/transient ischemic attack	801 (5.7)	44 (9.5)	757 (5.6)	<0.001
Chronic heart failure	439 (3.6)	33 (10.1)	406 (3.4)	<0.001
STEMI	7711 (55.2)	294 (63.2)	7417 (54.9)	<0.001
NSTE-ACS	6264 (44.8)	171 (36.8)	6093 (45.1)	<0.001
LVEF	53.3 ± 11.5	48.5 ± 13.8	53.5 ± 11.3	<0.001
Chronic kidney disease	185 (3.0)	29 (22.3)	156 (2.6)	<0.001
Creatinine (mg/dl)	0.96 ± 0.49	1.33 ± 0.99	0.94 ± 0.46	<0.001
Hb admission	14 ± 1.8	11.9 ± 2.3	14.1 ± 1.7	<0.001
Hb discharge	13 ± 2.5	10.2 ± 1.7	13.1 ± 2.5	<0.001
Peptic ulcus	167 (4.8)	6 (5.5)	161 (4.8)	0.760
Malignancy	879 (6.3)	63 (13.5)	816 (6.0)	<0.001
History of bleeding	759 (5.5)	42 (9.2)	717 (5.3)	<0.001
Aspirin	13,790 (98.7)	444 (95.5)	13,346 (98.8)	<0.01
Clopidogrel	12,048 (86.2)	412 (88.6)	11,636 (86.1)	0.128
Ticagrelor	600 (4.3)	2 (0.4)	598 (4.4)	<0.001
Prasugrel	665 (4.8)	2 (0.4)	663 (4.9)	<0.001
Oral anti-coagulation	727 (5.2)	61 (13.1)	666 (4.9)	<0.001
Beta-blockers	11,232 (80.4)	333 (72.1)	10,899 (81.1)	<0.001
ACE-inhibitors or ARB	10,521 (75.3)	311 (67.3)	10,210 (75.9)	<0.001
Statins	12,981 (92.9)	375 (80.6)	12,606 (93.3)	<0.001

ARB, angiotensin-receptor blockers; CABG, coronary artery by-pass graft; Hb, hemoglobin LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

patterns were encountered also when stratifying patients by clinical presentation (STEMI and NSTE-ACS, Table 3).

Patients treated with BTs were also more likely to be undertreated from a medical therapy standpoint (Table 1): 401 (86.2%) patients received double anti-platelet therapy (DAPT) as compared to 12,761 (94.5%) in those not treated with BTs ($p < 0.001$).

3.2. Study end-points

During hospitalization, 197 (1.4%) patients experienced the primary end-point of in-hospital reAMI. Patients treated with BT reported a significantly higher incidence of the primary end-point (25, 5.4% vs. 440, 1.3%, Fig. 1). At univariate analysis, moreover, PAD, PCI without stent, multivessel disease, OAC prescription, Killip class ≥2 at admission and in-hospital heart failure or bleeding were more frequent among patients with in-hospital reAMI, while complete revascularization, dyslipidemia and femoral access were less frequent.

Out of 7710 STEMI patients, 99 (1.3%) experienced the primary end-point of in-hospital reAMI, as compared to 98 (1.5%) with NSTE-ACS. BTs related to in-hospital reAMI only in patients presenting with STEMI and not in those presenting with NSTE-ACS: among patients with STEMI, 21 (7.1%) patients treated with BTs experienced in-hospital reAMI as compared to 78 (1.1%, $p < 0.001$) not treated with BTs, while among NSTE-ACS patients these same figures were respectively 4 (2.3%) and 94 (1.5%, p 0.408, see Fig. 1). Univariate predictors of in-hospital reAMI for each clinical presentation of ACS are shown in Tables 4 and 5.

After controlling for confounding factors in a logistic regression model including age, treatment with BTs, creatinine value at admission, complete revascularization and PCI without stent implantation, BTs independently related to in-hospital reAMI in patients presenting with STEMI (OR 4.06, 95% CI 2.27–7.27, Fig. 2). On the contrary, BTs did not relate to recurrent myocardial infarction in patients with NSTE-ACS at multivariate analysis (OR 1.31, 95% CI 0.45–3.8, Fig. 3).

Concerning the secondary end-point of 30 day-mortality, 100 patients (0.7%) died after 30 days from the index event, of whom 68 (0.9%) with STEMI, 33 (0.5%) with NSTE-ACS. Patients treated with BTs reported a higher incidence of 30-day mortality (Fig. 1; Supplementary Tables 1 and 2 show univariate parameters associated with this end-point). After controlling for confounding factors at logistic regression, BTs independently related to this end-point in both patients with STEMI (OR 3.70, 95% CI 1.98–6.92) and with NSTE-ACS (OR 3.99, 95% CI 1.51–10.53) (Supplementary Figs. 1 and 2).

Table 2
Procedural characteristics of patients undergoing PCI.

	Overall n = 13,975	Patients treated with blood transfusions n = 465	Patients not treated with blood transfusions n = 13,510	p value
Multivessel disease	4565 (47.6)	220 (56.8)	4345 (47.2)	<0.001
Femoral access	6864 (54.7)	308 (75.7)	6556 (54.0)	<0.001
DES	4929 (35.3)	150 (32.3)	4779 (35.4)	0.167
PCI without stent	542 (3.9)	50 (10.8)	492 (3.6)	<0.001
Thrombolysis	202 (1.4)	3 (0.6)	199 (1.5)	0.141
Complete revascularization	6306 (60.5)	187 (45.7)	6119 (61.1)	<0.001

DES, drug-eluting stent; PCI, percutaneous coronary intervention.

Table 3
Baseline features of patients presenting with ST-segment elevation myocardial infarction and with non ST-segment elevation acute coronary syndromes, stratified according to the treatment with blood transfusions.

	STEMI			NSTE-ACS		
	Patients treated with blood transfusions	Patients not treated with blood transfusions	p value	Patients treated with blood transfusions	Patients not treated with blood transfusions	p
	n = 294	n = 7417		n = 171	n = 6093	
Age	70.7 ± 12.1	62.3 ± 12.9	<0.001	73.5 ± 10.6	65.6 ± 12.1	<0.001
Female sex	161 (54.8)	1652 (22.3)	<0.001	75 (43.9)	1436 (23.6)	<0.001
Hypertension	163 (55.4)	3776 (50.9)	0.127	147 (86.0)	4109 (67.4)	<0.001
Diabetes mellitus	80 (27.2)	1438 (19.4)	0.001	88 (51.5)	1721 (28.2)	<0.001
Dyslipidemia	84 (28.6)	3433 (46.3)	<0.001	89 (52.0)	3637 (59.7)	0.045
Peripheral arterial disease	31 (10.5)	359 (4.8)	<0.001	32 (18.7)	437 (7.2)	<0.001
Prior MI	32 (10.9)	583 (7.9)	0.061	44 (25.7)	1060 (17.4)	0.005
Prior PCI	25 (8.5)	652 (8.8)	0.864	31 (18.1)	1110 (18.2)	0.976
Prior CABG	9 (3.1)	110 (1.5)	0.031	24 (14.0)	352 (5.8)	<0.001
Stroke/transient ischemic attack	21 (7.1)	397 (5.4)	0.184	23 (13.5)	360 (5.9)	<0.001
Chronic heart failure	9 (5.8)	162 (2.8)	0.029	24 (14.0)	244 (4.0)	<0.001
LVEF	45 ± 13.1	51.2 ± 11.2	<0.001	51.8 ± 13.6	55.8 ± 11.1	<0.001
Chronic kidney disease	9 (14.1)	59 (2.3)	<0.001	20 (30.3)	97 (2.9)	<0.001
Creatinine (mg/dl)	1.17 ± 0.76	0.92 ± 0.39	<0.001	1.61 ± 1.24	0.97 ± 0.53	<0.001
Hb admission	12.4 ± 2.3	14.2 ± 1.7	<0.001	11.1 ± 2.1	14.0 ± 1.7	<0.001
Hb discharge	10.2 ± 1.7	13.2 ± 2.7	<0.001	10.2 ± 1.6	13.0 ± 2.3	<0.001
Peptic ulcus	3 (5.9)	71 (5.2)	0.840	3 (5.1)	89 (4.5)	0.839
Malignancy	37 (12.6)	412 (5.6)	<0.001	26 (15.2)	404 (6.6)	<0.001
History of bleeding	24 (8.4)	331 (4.5)	0.002	18 (10.5)	386 (6.3)	0.028
Multivessel disease	131 (50.8)	2373 (43.7)	0.026	89 (69.0)	1972 (52.2)	<0.001
Femoral access	225 (83.0)	4083 (60.3)	<0.001	83 (61.0)	2473 (46.2)	0.001
DES	71 (24.1)	2171 (29.3)	0.058	79 (46.2)	2608 (42.8)	0.376
PCI without stent	36 (12.2)	357 (4.8)	<0.001	14 (8.2)	135 (2.2)	<0.001
Thrombolysis	3 (1.0)	195 (2.6)	0.087	0 (0.0)	4 (0.1)	0.738
Complete revascularization	127 (48.8)	3551 (61.3)	<0.001	60 (40.3)	2568 (60.9)	<0.001

CABG, coronary artery by-pass graft; Hb, hemoglobin LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; DES, drug-eluting stent; PCI, percutaneous coronary intervention.

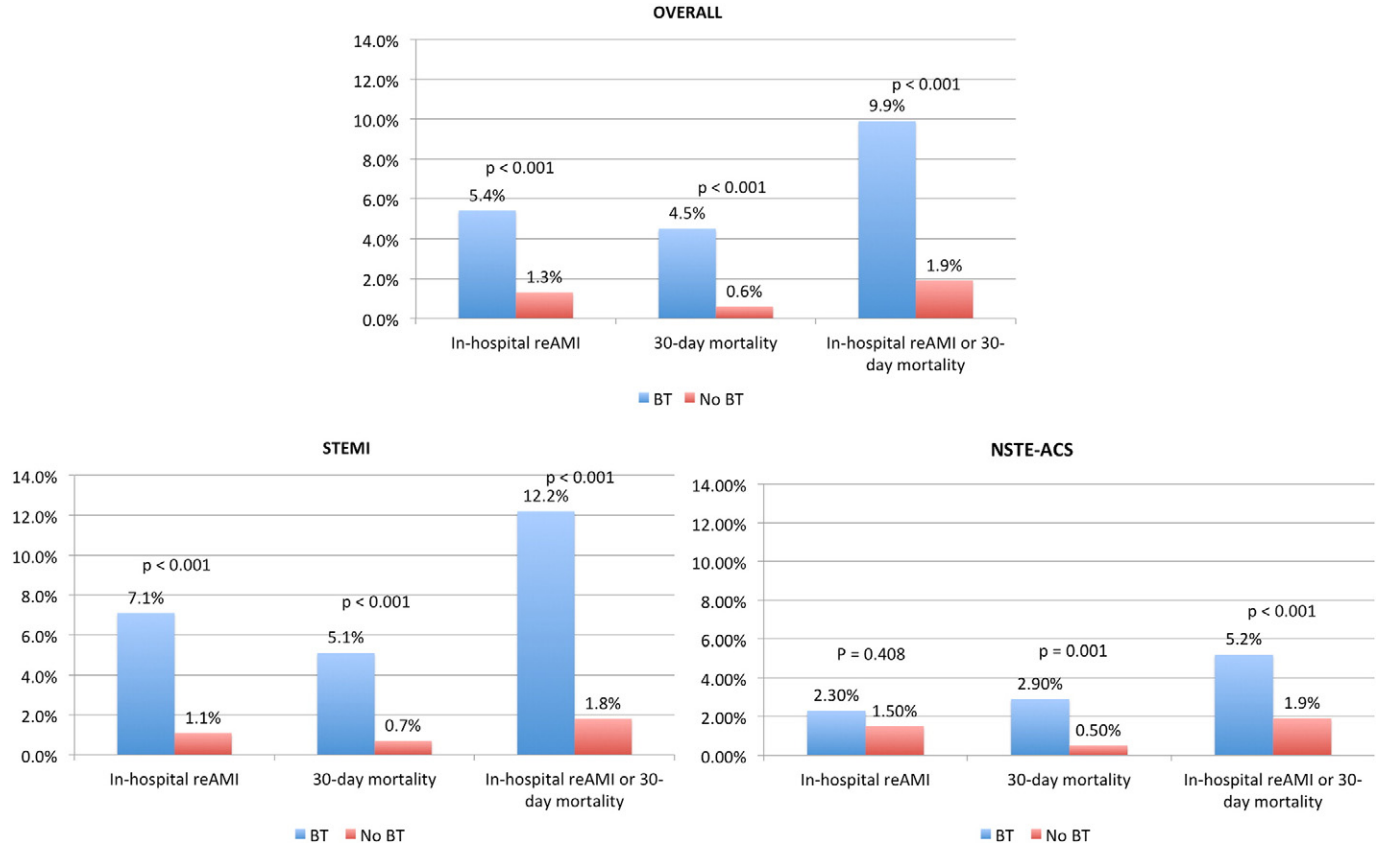

Fig. 1. Incidence of study end-points in the overall population and stratified according to the clinical presentation of acute coronary syndrome (BT, blood transfusion; reAMI, recurrent acute myocardial infarction; NSTE-ACS, non-ST-segment elevation acute coronary syndromes; STEMI, ST-segment elevation myocardial infarction).

Table 4
Parameters significantly associated to in-hospital reAMI at univariate analysis in patients presenting with STEMI.

	In-hospital recurrent myocardial infarction n = 99	No in-hospital recurrent myocardial infarction n = 7611	p value
Age	66.4 ± 12.6	62.6 ± 12.9	0.003
LVEF	48.4 ± 13.0	51.1 ± 11.2	0.046
Creatinine at admission	1.02 ± 0.68	0.93 ± 0.41	0.034
Killip class ≥2	21 (22.1)	865 (14.2)	0.029
Multivessel disease	49 (54.4)	2455 (43.9)	0.045
PCI without stent	13 (13.1)	380 (5.0)	<0.001
Complete revascularization	36 (39.6)	3641 (61.0)	<0.001
In-hospital bleeding	29 (29.3)	541 (7.1)	<0.001
Blood transfusion	21 (21.2)	273 (3.6)	<0.001
In-hospital heart failure	17 (23.0)	405 (6.9)	<0.001
Aspirin	94 (94.9)	7495 (98.5)	0.005
Oral anti-coagulation	13 (13.1)	407 (5.3)	0.001
Statins	88 (88.9)	7134 (93.7)	0.049

LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Regarding the composite secondary end-point of in-hospital reAMI and 30-day mortality (Fig. 1; Supplementary Tables 3 and 4), an independent association between BTs and this end-point was encountered only for STEMI patients (OR 4.68, 95% CI 3.04–7.20), while only a trend towards significance was defined for NSTE-ACS patients (OR 1.98, 95% CI 0.98–3.98; Supplementary Figs. 3 and 4).

4. Discussion

The main findings of our study are:

1) BTs are associated with a higher risk of in hospital reAMI in patients presenting with ACS
2) BTs relate to an increased risk of reAMI only in patients presenting with STEMI and not in those presenting with NSTE-ACS. This finding highlights a potential peculiar mechanism of harm in these patients.
3) BTs increase 30-day mortality in both STEMI and NSTE-ACS patients.

BTs are a known factor associated with unfavorable prognosis in patients presenting with ACS. A restrictive approach towards the administration of BTs in the ACS setting is to date recommended as it has been demonstrated to be at least non-inferior to a more liberal approach [4,16,17,18]. BTs have been identified as independent predictors of a worsened short and long-term outcome, with higher mortality rates and incidence of CV events [5,19,20]. In conditions of severe anemia, however, an inversion of the risk/benefit ratio has been observed: BTs are recommended when Hb levels fall below <7 g/dl according to European Society of Cardiology or <8 g/dl according to American Heart Association/American College of Cardiology [21,22,23].

The reasons explaining the unfavorable outcome following BTs are not fully elucidated. Part of this association has to be ascribed to the inability of statistical analysis to fully account for confounding factors and to the "confounding by indication" bias [24], that is, the bias occurring "when studying the effect of a treatment, while the indication for the treatment causes the outcome" and by which "patients with the indication are more likely both to receive the treatment and to experience the outcome, even if the treatment is not actually causing the outcome" [25]. Patients receiving BTs are indeed more frail and burdened by a heavier load of comorbidities [26]: in our study, out of the 13,975 undergoing PCI for ACS in the Bleemacs registry, the 465 (3.3%) treated with BTs were older, had higher CV profile risk, a lower LVEF and a higher prevalence of renal impairment, PAD, history of bleedings, prior MI and revascularization (both surgical and percutaneous), and presented more often with STEMI and signs of heart failure (Killip class ≥ II). Patients receiving BTs presented a more complex coronary artery profile, as multivessel disease was more common and complete revascularization less frequent. The higher frailty and profile risk of these patients was also reflected by the under-treatment observed pertaining medical therapy (lower rates of prescription of DAPT, Aspirin, Prasugrel, Ticagrelor, ACE-inhibitors or Angiotensin receptor blockers, statins).

Table 5
Parameters significantly associated to in-hospital reAMI at univariate analysis in patients presenting with NSTE-ACS.

	In-hospital recurrent myocardial infarction n = 98	No in-hospital recurrent myocardial infarction n = 6297	p value
Peripheral arterial disease	17 (17.3)	463 (7.4)	<0.001
Dyslipidemia	43 (43.9)	3761 (59.7)	0.002
Femoral access	28 (30.4)	2601 (47.0)	0.002
DES	59 (60.2)	2668 (42.4)	<0.001
Complete revascularization	42 (44.2)	2713 (61.6)	<0.001
In-hospital heart failure	7 (7.1)	148 (2.4)	0.002
Proton pump inhibitors	42 (44.2)	2340 (67.1)	0.001

DES, drug-eluting stent.

A direct detrimental effect of BTs, however, should be accounted for [8]. Despite the differences between the two study groups, which could apparently suffice to account for the different outcome of these patients, our analysis suggests that the increased rate of in-hospital re-AMI determined by BTs bears the potential to directly, negatively affect prognosis. A significantly increased rate of re-AMI following BTs and relating to unfavorable outcomes has been reported for patients in multiple analyses [4,8,19,27], both in PCI and non-PCI settings [28,29]. Reasons explaining the increased incidence of re-AMI following BTs are however not completely understood, with many mechanisms called in to cause. Increased platelet activation in vitro after BTs has been reported [30], along with damages in function and morphology of stored red cells, with nitric oxide and 2,3-diphosphoglicerate depletion possibly increasing oxidative stress, and shape changes from discoid to spherical [31]. All these factors, moreover, combine with the proinflammatory and hyperviscosity state encountered during the course of ACS [20].

Primary objective of our study was to assess if the clinical presentation of ACS (STEMI vs. NSTE-ACS) may affect the outcome of subjects undergoing PCI and receiving BTs. Based on our results, BTs bear an increased risk of in hospital re-AMI in patients presenting with STEMI, but not in those presenting with NSTE-ACS. A really scarce amount of data is available in literature pertaining this topic; to the best of our knowledge, this is the first experience reporting similar results. We can hypothesize that, as the peculiar substrate of STEMI is the erythrocyte-rich red thrombus, the abrupt infusion of a conspicuous amount of erythrocytes could lead to hyper-viscosity and increased platelet shear-stress, affecting this pattern of ACS to a different extent as compared to NSTE-ACS, which are mainly characterized by the presence of white, fibrin-rich, thrombi [9]. No previous studies addressed directly if different clinical presentations of ACS are differently affected by BTs: Chatterjee and colleagues found in their meta-analysis a possible limited harm of BTs in patients with STEMI as compared to NSTEMI and UA, but value of these results are limited as they are not patient-level and neither validated by meta-regression analysis [3]. Other studies found an increased risk of reAMI in patients treated with BTs and presenting with MI, STEMI or ACS, but direct comparisons are, to the best of our knowledge, lacking [5,8,19].

Our results have a potential relevant impact on clinical practice: incidence of in-hospital reAMI increased only in STEMI patients, highlighting a potential peculiar mechanism of harm of BTs in these patients. It is plausible that STEMI patients resent more significantly of the direct detrimental effect of BTs and that a more restrictive approach to BTs should be reserved to this subset of patients. BTs, not surprisingly, increased short-term mortality in both STEMI and NSTE-ACS patients, as prognostic implications of BTs range far more widely than from reAMI. However, we believe that our finding of a differential effect of BTs on the outcome of different presentations of ACS is noteworthy

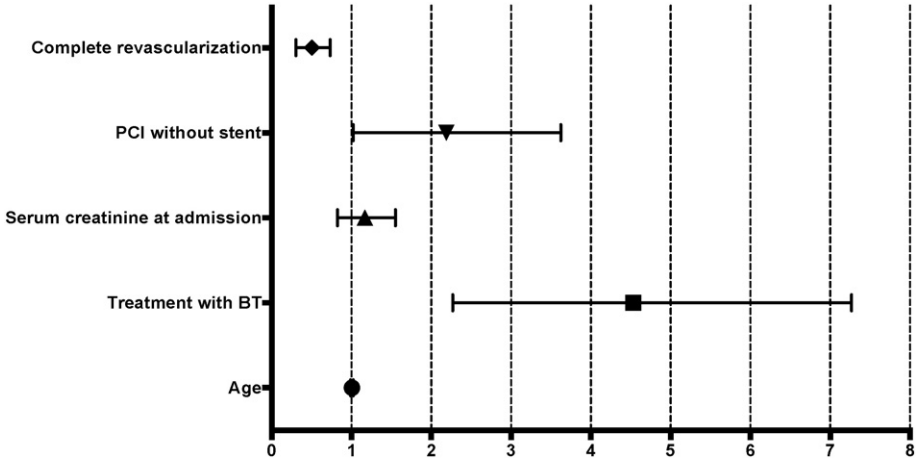

Fig. 2. Independent predictors of in-hospital recurrent acute myocardial infarction in patients presenting with ST-segment elevation myocardial infarction at logistic regression analysis (BT, blood transfusion; PCI, percutaneous coronary intervention).

and should deserve further evaluation in future studies aiming to assess if a differential approach to STEMI as compared to NSTE-ACS patients may determine also a different outcome.

5. Limitations

This is a retrospective, registry-based study, whose findings should warrant confirmation in a prospective setting. The main limitation of the present analysis is the lack of the Hb value at which BTs were performed. However, the main objective of the analysis was to compare the outcome of different presentations of ACS: considering that the main guidelines provided by the scientific societies do not differentiate cut-offs for BTs based on clinical presentation of ACS and that STEMI and NSTE-ACS patients were treated in the same centers, we can suppose a similar approach to BTs in these different clinical presentations.

6. Conclusions

BTs may increase the risk of in hospital reAMI in patients presenting with STEMI and not in those presenting with NSTE-ACSA. Thirty-day mortality is increased by BTs in both patients with diagnosis of STEMI and NSTE-ACS. Our results suggest that a more restrictive approach to BTs could be more beneficial to STEMI patients as compared to NSTE-ACS patients.

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Conflicts of interest/financial disclosures

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2016.07.075.

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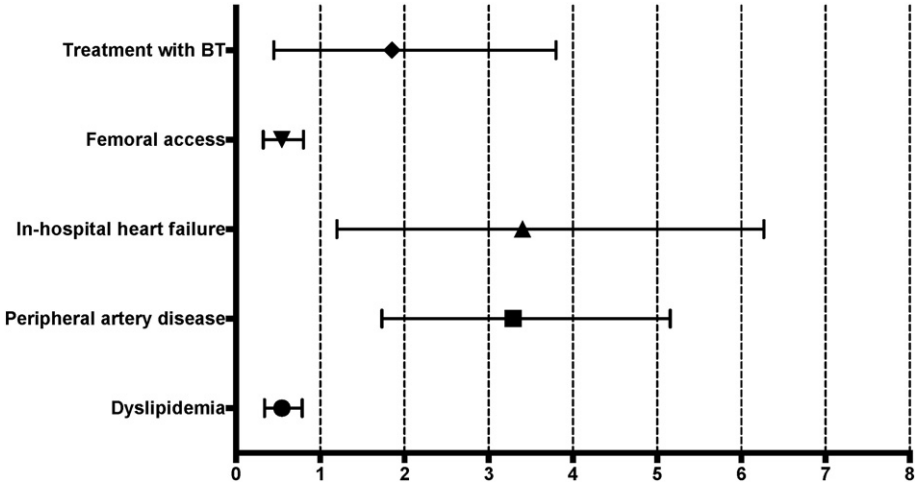

Fig. 3. Independent predictors of in-hospital recurrent acute myocardial infarction in patients presenting with non-ST-segment elevation acute coronary syndromes at logistic regression analysis (BT, blood transfusion).

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