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Management of diabetic patients hospitalized for acute coronary syndromes: a prospective multicenter registry

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Background **Patients with diabetes mellitus and acute coronary syndrome (ACS) present an increased risk of adverse cardiovascular events. An Italian Consensus Document indicated 'three specific must' to obtain in this subgroup of patients: optimal oral antiplatelet therapy, early invasive approach and a tailored strategy of revascularization for unstable angina/non-ST-elevation-myocardial infarction (UA/NSTEMI); furthermore, glycemia at admission should be managed with dedicated protocols.**

Aim **To investigate if previous recommendations are followed, the present multicenter prospective observational registry was carried out in Lombardia during a 9-week period between March and May 2015.**

Methods and results **A total of 559 consecutive ACS patients (mean age 68.7 ± 11.3 years, 35% ≥75 years, 50% STEMI), with 'known DM' (56%) or 'hyperglycemia', this last defined as blood glucose value ≥126 mg/dl at admission, were included in the registry at 29 hospitals with an on-site 24/7 catheterization laboratory. Patients with known diabetes mellitus received clopidogrel in 51% of the cases, whereas most patients with hyperglycemia (72%) received a new P2Y12 inhibitor: according to clinical presentation in case STEMI prasugrel/ticagrelor were more prescribed than clopidogrel (70 vs. 30%, $P<0.001$); on the contrary, no significant difference was found in case of UA/NSTEMI (48 vs. 52%, $P=0.57$).**

Overall, 96% of the patients underwent coronary angiography and 85% received a myocardial revascularization (with percutaneous coronary intervention in 92% of cases) that was however performed in fewer patients with known diabetes mellitus compared with hyperglycemia (79 vs. 90%, $P=0.001$).

Among UA/NSTEMI, 85% of patients received an initial invasive approach, less than 72 h in 80% of the cases (51% <24 h); no difference was reported comparing known diabetes mellitus to hyperglycemia. Despite similar SYNTAX score, patients with known diabetes mellitus had a higher rate of Heart Team discussion (29 vs. 12%, $P=0.03$) and received a surgical revascularization in numerically more cases.

Most investigators (85%) followed a local protocol for glycemia management at admission, but insulin was used in fewer than half of the cases; diabetes consulting was performed in 25% of the patients and mainly in case of known diabetes mellitus.

Conclusion **Based on data of the present real world prospective registry, patients with ACS and known diabetes mellitus are treated with an early invasive approach in case of UA/NSTEMI and with a tailored revascularization strategy, but with clopidogrel in more cases; glycemia management is taken into account at admission.**

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Background

Patients with acute coronary syndromes (ACS) and diabetes mellitus are at increased risk of adverse cardiovascular events and mortality.[1] About one-third of ACS patients present a diagnosis of known diabetes mellitus at admission,[2] and a similar rate of undiagnosed diabetes mellitus or prediabetes has been reported.[3] These patients deserve a careful management in the acute phase of hospitalization. New oral antiplatelet agents (prasugrel and ticagrelor) result in a more intensive and consistent

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inhibition of platelet aggregation compared with clopidogrel and their use was particular efficacious in patients with ACS and diabetes mellitus.[4–6] Primary percutaneous revascularization in patients with ST-elevation myocardial infarction (STEMI) and routine invasive strategy in high-risk patients with unstable angina/non-STEMI (UA/NSTEMI) significantly reduced mortality and major cardiovascular events.[7,8] Diabetes mellitus by itself is considered as an indication to undergo coronary angiography and myocardial revascularization within 72 h in UA/NSTEMI.[8] Diabetes mellitus is usually associated with a complex coronary artery disease (CAD)[9]: despite the lack of randomized trial specifically designed to investigate percutaneous vs. surgical revascularization in ACS setting, coronary artery by pass grafting (CABG) compared with percutaneous coronary intervention (PCI) reduced repeat revascularization, myocardial infarction (MI) and mortality in diabetic patients with multivessel coronary disease.[10] An individualized strategy of revascularization within Heart Team discussion appears as mandatory in diabetic patients; in case of PCI, drug-eluting stents (DES) should be preferred over bare metal stents (BMS)[11] and in case of CABG use of arterial grafts was associated with survival improvement.[12] Furthermore, management of hyperglycemia during hospitalization is controversial, because a tight control of glycemic values did not improve clinical outcome and was associated with deleterious effects of hypoglycemia.[13]

An Italian multidisciplinary consensus document was recently published to provide practical recommendations on optimal management of patients with ACS and diabetes mellitus or hyperglycemia[14] with three specific 'must' to obtain: antiplatelet therapy optimization using the best available drug; early coronary angiography after hospitalization for patients with UA/NSTEMI followed by an individualized strategy of revascularization; and use of specific protocol for glycemia management.

Aim of the present registry was to assess whether these recommendations about antiplatelet therapy, timing and strategies of revascularization and glycemic control were followed during hospitalization of patients with ACS and diabetes mellitus.

Methods

This present registry was a multicenter, observational, prospective data collection carried out in Lombardia (Italy) during a 9-week period and included consecutive ACS patients hospitalized in the Cardiology Division or Coronary Care Unit with known diabetes mellitus or hyperglycemia at admission. The registry was led 9 months after the publication of the Italian consensus document; in the meantime, the content was illustrated in a series of national and local scientific meetings.

Study population

Eligible patients were identified for inclusion after they received a diagnosis of ACS (STEMI or UA/NSTEMI) with a concomitant known diabetes mellitus or hyperglycemia at admission. Diagnosis of known diabetes mellitus was based on previous history referred by the patient or on use of at least one oral antidiabetic drug or insulin; hyperglycemia was defined as first blood glucose value $\geq$126 mg/dl at admission.[15] STEMI was defined as typical symptoms lasting at least 20 min and persistent ST-elevation at least 1 mm (not known to be preexisting or resulting from a coexisting disorder) in at least two contiguous leads and or new or presumed-new left bundle-branch block and planned primary PCI (defined as PCI within the first 24 h after symptom onset). NSTEMI was defined as new onset/worsening of angina pain (or equivalent) and elevated cardiac biomarkers of necrosis (troponin I or T upper limit of normal at study site) and/or electrocardiographic changes (ST-depression, transient ST-elevation and T-wave inversion).

Study protocol, informed consent and case report form were approved by the local ethical committee of all participating hospitals and the written informed consent was required before any study procedure.

Data collection and management

At hospital admission, the following data were collected: demographic characteristics, cardiovascular risk factors, previous cardiac events or procedures, use of medications, values of hemoglobin, creatinine, estimated glomerular filtration rate, troponin and blood glucose.

The main focuses of the registry were on antiplatelet therapy, timing and strategies of revascularization (for patients with UA/NSTEMI) and glycemia management.

Investigators had to report the type and timing of P2Y12 inhibitors loading dose related to time of angiography and the antithrombotic therapy administered during myocardial revascularization; at discharge, the choice and duration of dual antiplatelet therapy (DAPT) were required.

Time to angiography for UA/NSTEMI patients was reported as less than 2 h, less than 24 h, less than 72 h or more than 72 h after hospital admittance. Individual risk assessment was estimated using the Global Registry of Acute Coronary Events (GRACE) score[16] and bleeding risk with the Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines score.[17]

Extent and complexity of baseline CAD were quantified using the SYNTAX score[18] and risk related to CABG with the EuroSCORE.[19] If the choice between PCI and CABG was performed after a Heart Team discussion, it had to be specified, and details about the quality of revascularization itself were collected.

Each center had to report if a specific local protocol for hyperglycemia management was followed, particularly with use or not of insulin (iv or sc) and if a diabetic consultation was required during hospitalization.

In-hospital outcome was collected as all cause-death and safety as major bleeding according to Thrombolysis in Myocardial Infarction (TIMI) classification.[20]

A prespecified analysis comparing patients with known diabetes mellitus vs. hyperglycemia was performed.

The registry received the endorsement of the Italian Society of Interventional Cardiology (SICI-GISE). The study was sponsored by SICI-GISE receiving an unrestricted grant from Daiiky Sankio Co. (Tokyo, Japan) and Eli Lilly (Indianapolis, Indiana, USA): the sponsors had no role in study design, data collection, data monitoring, analysis, interpretation or in drafting and editing the present article.

Statistical analysis

Categorical variables are presented as number and percentages and compared by the chi-squared test or Fischer exact test, where indicated. Continuous variables are presented as mean and SD and compared by analysis of variance. A P value less than 0.05 was considered statistically significant. Analyses were performed with IBM SPSS Statistics for Windows, version 21, Armonk, NY: IBM Corp.

Results

A total of 559 consecutive ACS patients were included in the study at 29 hospitals between 2 March and 8 May 2015. Half of the cases had a diagnosis of UA/NSTEMI. All participating centers had an on-site 24/7 catheterization laboratory (Cath Lab).

Baseline clinical characteristics are summarized in Table 1. Patients with known diabetes mellitus compared with hyperglycemia were significantly older, with a higher rate of previous MI, previous coronary revascularization, history of peripheral artery disease, worse renal function, higher levels of baseline glucose and were hospitalized for UA/NSTEMI in more cases.

The rate of known diabetes mellitus compared with hyperglycemia was significantly higher in patients with age at least 75 (62 vs. 38%, $P < 0.001$) but not in those less than 75 (52 vs. 48%, $P = 0.57$).

Antithrombotic therapy

At hospitalization about 52% of patients were already on treatment with aspirin and 6% on DAPT. Pretreatment with an oral P2Y12 inhibitor loading dose was reported in 55% of the cases and more frequently performed in UA/NSTEMI patients compared with STEMI (63 vs. 45%, $P = 0.004$). We found no difference between diabetes mellitus vs. hyperglycemia related to P2Y12 pretreatment (57 vs. 50%, $P = 0.09$), with a wider use of clopidogrel rather than of prasugrel/ticagrelor (57 vs. 43%, $P = 0.015$) in diabetic patients.

Table 2 summarizes antithrombotic therapy at discharge: aspirin and P2Y12 inhibitors were prescribed respectively to 95 and 88% of the whole population, but more patients with hyperglycemia compared with diabetes mellitus received the second drug (92 vs. 85%, $P = 0.02$). Figure 1 summarizes oral P2Y12 inhibitors prescription at discharge according to clinical presentation and diabetic status: patients with known diabetes mellitus received clopidogrel in 51% of the cases and a new inhibitor (32% ticagrelor, 17% prasugrel) in 49%, whereas almost three-quarters of patients with hyperglycemia were treated with new P2Y12 inhibitors (46% ticagrelor, 27% prasugrel) ($P < 0.05$). Patients with STEMI were more treated with new drugs than with clopidogrel, even if statistical significance was obtained only for patients with hyperglycemia ($P < 0.05$). On the contrary, patients with UA/NSTEMI were more frequently treated with clopidogrel (Fig. 1).

Table 1 Baseline characteristics of the study population and comparison between patients with known diabetes mellitus and hyperglycemia

	Overall, $N = 559$	DM, $N = 310$	HG, $N = 249$	P value
Age, years	68.7 ± 11.3	70.4 ± 10.1	66.6 ± 12.3	0.0001
Age ≥75 years (%)	195 (35)	120 (39)	75 (30)	0.03
BMI (k/m^2)	27.3 ± 4.6	27.8 ± 4.6	26.8 ± 4.6	0.007
Female, *n* (%)	163 (29.2)	85 (27.4)	78 (31.3)	0.313
Smoking, *n* (%)	155 (27.7)	66 (21.3)	89 (35.7)	<0.001
Arterial hypertension, *n* (%)	427 (76)	260 (84)	167 (33)	<0.001
Dyslipidemia, *n* (%)	215 (38.7)	101 (33)	114 (46)	0.002
Previous MI, *n* (%)	160 (28.6)	117 (37.7)	43 (17.3)	<0.001
Previous revascularization, *n* (%)	172 (30.8)	131 (42.3)	41 (16.5)	<0.001
PAD, *n* (%)	136 (24.3)	105 (33.9)	31 (12.4)	<0.001
Previous TIA/stroke, *n* (%)	62 (11.1)	39 (12.6)	23 (9.2)	0.211
Glycemia at admission (mg/dl)	189.9 ± 76	207 ± 89.4	167.6 ± 46.3	<0.001
Creatinine clearance (ml/min)	76.3 ± 35.3	71.2 ± 34.2	82.7 ± 35.7	<0.001
STEMI at admission, *n* (%)	275 (50)	107 (35.5)	168 (67.4)	<0.001
UA/NSTEMI at admission, *n* (%)	275 (50)	194 (64.4)	81 (32.5)	<0.001

DM, known diabetes; HG, hyperglycemia (blood glucose ≥126 mg/dl at admission); MI, myocardial infarction; PAD, peripheral arterial disease; Revascularization (PCI or CABG); STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack; UA/NSTEMI, unstable angina/non-ST-elevation-myocardial infarction.

Table 2 Antithrombotic therapy at discharge in patients with known diabetes mellitus and hyperglycemia

	Overall, $N=537$	DM, $N=292$	HG, $N=245$	P value
ASA, *n* (%)	512 (95.3)	274 (93.8)	238 (97.1)	0.07
P2Y12 inhibitor, *n* (%)	475 (88)	249 (85)	226 (92)	0.02
Clopidogrel, *n* (%)	189 (39)	126 (50.6)	63 (27.9)	<0.001
Ticagrelor, *n* (%)	184 (38)	81 (32.5)	103 (45.6)	<0.001
Prasugrel, *n* (%)	102 (23)	42 (16.9)	60 (26.5)	0.003
VKA, *n* (%)	41 (8)	31 (10.6)	10 (4.1)	0.005
NOAC, *n* (%)	11 (2)	7 (2.4)	4 (1.6)	0.54

ASA, aspirin; DM, known diabetes mellitus; HG, hyperglycemia (blood glucose ≥126 mg/dl); NOAC, nonvitamin K oral anticoagulant; VKA, vitamin K antagonist oral anticoagulant.

In patients aged less than 75, more patients were treated with prasugrel/ticagrelor compared with clopidogrel, both in case of know diabetes mellitus (58 vs. 42%, $P=0.023$) and of hyperglycemia (84 vs. 16%, $P<0.001$); in patients aged at least 75, clopidogrel was more prescribed than prasugrel or ticagrelor: the difference was significant among known diabetes mellitus (64 vs. 36%, $P<0.001$), but not in the case of hyperglycemia (58 vs. 42%, $P=0.08$).

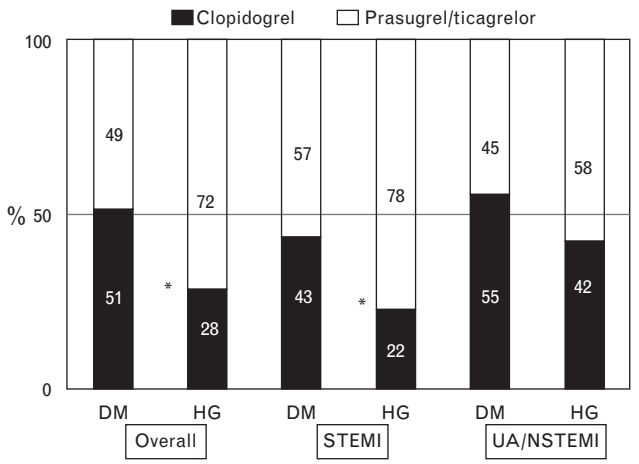
At discharge, DAPT was prescribed for 12 months in 76% of patients; fewer than 1% of investigators considered a therapy over 1 year.

Glycoprotein IIb/IIIa receptor inhibitors were used with upstream strategy in only 2% of the cases and downstream in 18%, with tirofiban choice in about two-thirds of them.

At admission more than half of patients were treated with unfractioned heparin (UHF), one-third with enoxaparin and 9% with fondaparinux. In Cath Lab, UHF was used in 94% of PCI and bivalirudin in the remaining 6%.

Long-term oral anticoagulant therapy (OAC) was prescribed to 10% of the patients, in more cases of known diabetes mellitus compared with hyperglycemia (Table 2).

Fig. 1



MI, myocardial infarction; DM, known diabetes; HG, hypergycaemia (blood gluxose ≥ 126 mg/dl at admission); UA/NSTEMI, unstable angina/non-ST-elevation MI; STEMI, ST-elevation MI; *P<0.05 DM vs HG

P2Y12 inhibitors at discharge according to diabetic status and clinical presentation.

Timing of angiography and strategies of revascularization

Table 2 summarizes type, strategies and quality of revascularization of the whole ACS population. 529 patients (96%) underwent coronary angiography and overall 85% of patients received a myocardial revascularization that was nevertheless significantly less performed in patients with known diabetes mellitus compared with hyperglycemia (79 vs. 90%, $P=0.001$). PCI was the most used strategy of revascularization, and CABG was performed in 8% of the cases. A complete revascularization was obtained in 61% of the treated patients, but it was less common in diabetes mellitus vs. hyperglycemia (56 vs. 66%, $P=0.017$). For patients treated with PCI, at least one DES was used in 82% of the patients with no difference between diabetes mellitus and hyperglycemia, but BMS use was not negligible and surprisingly in more patients with known diabetes mellitus.

Among UA/NSTEMI, 232 (85%) patients underwent coronary angiography that was performed less than 72 h in 80% of the cases (51% <24 h): lower risk (57%), comorbidities (37%) and patient refusal (6%) were reported by investigators as the main causes of a conservative strategy. A similar rate of patients with known diabetes mellitus compared with hyperglycemia were treated with an invasive approach (83 vs. 87%, $P=0.33$) and in fewer cases less than 72 h (77 vs. 87%, $P=0.07$). SYNTAX score was not different between patients with diabetes mellitus vs. hyperglycemia (18.2 ± 11.5 vs. 17.6 ± 12.5, $P=0.71$), but the first group had a higher rate of Heart Team discussion (29 vs. 12%, $P=0.03$) and received a surgical revascularization in numerically more cases (16 vs. 10%, $P=0.21$) (Table 3).

Hyperglycemia management

More than 85% of investigators claimed to follow an antidiabetic protocol in the setting of ACS: in more than half of the cases insulin was not used, but if chosen the subcutaneous administration was preferred. Diabetes consulting was performed in one-quarter of patients (known diabetes mellitus 33% vs. hyperglycemia 14%, $P<0.001$). A total of 84% UA/NSTEMI patients with diabetes mellitus interrupted metformin before angiography and 66% with chronic kidney disease received contrast-induce nephropathy prophylaxis. A total of 16 patients with hyperglycemia at admission had a diagnosis of established diabetes mellitus at discharge and received a long-term hypoglycemic treatment (Table 4).

Table 3 Strategies of revascularization in patients with known diabetes mellitus and hyperglycemia

	Overall, $N=545$	DM, $N=297$	HG, $N=248$	P value
Revascularization, *n* (%)	460 (85)	236 (79)	224 (90)	0.001
PCI, *n* (%)	402 (87)	196 (83)	206 (92)	0.004
CABG, *n* (%)	38 (8.3)	31 (13)	7 (3)	<0.001
Hybrid, *n* (%)	5 (1.1)	1 (0.4)	4 (2)	0.16
Multistage, *n* (%)	15 (3)	8 (3)	7 (3)	0.87
Percutaneous revascularization				
BMS, *n* (%)	61 (15)	22 (11)	39 (19)	0.025
DES, *n* (%)	330 (82)	163 (83)	167 (81)	0.60
BVS, *n* (%)	14 (4)	7 (4)	7 (4)	0.99
DEB, *n* (%)	18 (5)	12 (6)	6 (3)	0.14
Surgical revascularization				
Arterial graft per patient (mean ± SD)	1.18 ± 0.7	1.15 ± 0.36	1.2 ± 0.46	0.72
SYNTAX score	18.2 ± 13	18.4 ± 14.6	17 ± 11	0.59
EuroSCORE	10.3 ± 13.1	12.1 ± 14.2	8.2 ± 11.4	0.001
Heart Team discussion, *n* (%)	96 (20)	67 (23)	29 (12)	0.001
Complete revascularization, *n* (%)	313 (68)	154 (56)	159 (66)	0.01

BMS, bare metal stent; BVS, bioresorbable vascular scaffold; DEB, drug-eluting balloon; DES, drug-eluting stent; DM, known diabetes mellitus; HG, hyperglycemia (blood glucose ≥126 mg/dl at admission).

In-hospital clinical outcome

Median hospital stay was 8 (6–13) days. Total mortality was 1.6% (diabetes mellitus 2.3% vs. hyperglycemia 0.8%, $P=0.170$) and a major bleeding, using TIMI criteria, was reported in 2% of the cases (diabetes mellitus 3% vs. hyperglycemia 1.6%, $P=0.304$). Incidence of stroke/transient ischemic attack was extremely low (0.9%) and so was hemorrhagic bleeding (0.4%).

Discussion

The principal findings of the present registry are: in patients hospitalized for ACS the presence of diabetes does not influence the use of ticagrelor or prasugrel compared with clopidogrel; most patients with UA/NSTEMI are treated with an early invasive approach and with a tailored strategy of revascularization regardless of diabetic status; and glycemia management is taken into account at time of hospitalization.

Recent European Guidelines and position paper documents highlight the clinical relevance of a careful management of diabetic patients hospitalized for ACS[8]; particularly, a document promoted by Italian Scientific Societies (Associazione Nazionale Medici Cardiologi Ospedalieri ANMCO, Società Italiana di Cardiologia Interventistica GISE, Associazione Medici Diabetologi AMD, Società Italiana di Diabetologia SID) recommends three specific 'must' to optimize the treatment of these high-risk patients: optimal antiplatelet therapy, early invasive approach and individualized revascularization strategy and careful glycemia management.[14] Therefore, after a series of national and local meetings focusing on sharing with the community of cardiologists the advice contained in the document, the present registry was performed to investigate if these recommendations were adopted during hospitalization of patients with ACS and known diabetes mellitus. Based on these results, only two of the three targets had been obtained.

Due to higher baseline platelet reactivity of diabetic patients, a more intensive oral antiplatelet therapy should be selected in diabetic patients.[4] However, according to our data, patients with known diabetes mellitus were less treated with DAPT; despite recommendations their higher baseline risk profile did not influence the choice of the oral antiplatelet agent: at discharge prasugrel or ticagrelor were more prescribed than clopidogrel considering the whole population without a difference between patients with or without known diabetes mellitus. In particular, diabetic patients with UA/NSTEMI were more frequently treated with clopidogrel than with newer oral antiplatelet agents. Actually, in our population, patients aged less than 75 were more frequently treated with prasugrel/ticagrelor irrespective of diabetes status, and those aged at least 75 received clopidogrel in more cases. This paradox, underlying a separation between guidelines recommendations and daily clinical practice, has already been shown in larger registries, in which patients treated with prasugrel/ticagrelor compared with clopidogrel were younger, with significantly less previous MI, previous myocardial revascularization and prior stroke.[21,22] Clinical scenario at presentation, with more patients hospitalized for UA/NSTEMI in the known diabetes mellitus group, had probably an influence on initial approach, on strategy of revascularization and consequently on choice of the antiplatelet therapy: it is known that patients with UA/NSTEMI (due to higher comorbidities), compared with STEMI, receive clopidogrel in more cases and are treated with coronary angiography and PCI in fewer cases, but more with CABG.[23] More patients with known diabetes mellitus of our registry had an indication for long-term treatment with OAC; this is not surprisingly because it is known that incidence of atrial fibrillation is higher in diabetic patients,[24] and diabetes mellitus by itself is one of the conditions included in the CHA2DS2-VASC.[25] Because of prasugrel/ticagrelor contraindication, patients receiving OAC were treated with clopidogrel: however, their exclusion

Table 4 Strategies of revascularization patients hospitalized for unstable angina/non-ST-elevation-myocardial infarction

UA/NSTEMI, $N=275$	DM, $N=194$	HG, $N=81$	P value
Coronaroangiography, *n* (%)	161 (83)	71 (87)	0.33
Early <72 h angiography, *n* (%)	124 (77)	62 (87)	0.07
GRACE score	148 ± 33.5	147.8 ± 32.4	0.945
SYNTAX score	18.2 ± 11.53	17.5 ± 12.53	0.678
Heart Team discussion, *n* (%)	53 (29)	10 (12.5)	0.003
Myocardial revascularization, *n* (%)	140 (87)	65 (91)	0.31
PCI, *n* (%)	118 (84)	59 (90)	0.21
CABG, *n* (%)	22 (16)	6 (10)	0.21

CABG, coronary artery bypass grafting; DM, known diabetes mellitus; GRACE, Global Registry of Acute Coronary Events; HG, hyperglycemia (blood glucose ≥126 mg/dl at admission); PCI, percutaneous coronary intervention; UA/NSTEMI, unstable angina/non-ST-elevation myocardial infarction.

did not influence the results, because patients with known diabetes mellitus compared with hyperglycemia still received clopidogrel in more cases (42 vs. 23%, $P < 0.001$).

At least 25% of patients admitted for ACS have a prevalence of prediabetes or undiagnosed diabetes mellitus[3]; there is no consensus about the cutoff to define acute hyperglycemia in this clinical setting, and a direct relation between glycemic values and adverse outcome has been reported.[26,27] However, for diabetologists involved in our consensus document a value at least 126 mg/dl was sufficient to define hyperglycemia.[14] After enrollment, the choice of antithrombotic therapy was left to investigator discretion, so an influence of this parameter on P2Y12 inhibitors use cannot be extrapolated; furthermore in our registry we do not have a control group with normal glycemic values at admission to use as a comparator. At univariate analysis diabetes mellitus was a predictor of clopidogrel use at discharge, but not at multivariate; no significance was found for hyperglycemia (data not shown).

Coronary angiography was performed in 85% of the UA/NSTEMI population, and less than 72 h after admission in 80% of the cases, with no influence of diabetic status on this strategy. Based on data of previous Italian registries, in 2001 less than one-third of patients with NSTEMI underwent coronary angiography: this rate increased to almost 70% in 2010 up to 83% in 2015, with a concomitant significant reduction of the time from hospital admission to angiography.[28] No specific data investigating the role of diabetes mellitus as a determinant of invasive strategy are available; diabetic status is not included in the GRACE score, but it is considered as a criterion for an invasive approach less than 72 h, even with a score less than 140: in our population, mean GRACE score value of more than 140 both in patients with known diabetes mellitus and hyperglycemia may have influenced the choice of the early invasive approach.[8] Furthermore, in our registry, all participating hospitals had an on-site Cath Lab and in a previous survey this last was the strongest predictor of early coronary angiography[29]: this logistic aspect was likely the main determinant of strategy selection and of short time to angiography. The high rate of coronary angiography was followed by a high rate of myocardial revascularization, obtained in 85% of the patients of the whole population.

Type of ACS at presentation influenced the choice of revascularization, because half of the included patients were admitted for STEMI with planned PCI: they received a percutaneous revascularization in more than 90% of the cases; in UA/NSTEMI patients, a surgical revascularization was performed in 13% of the patients, twice compared with FAST-MI data.[23] In these patients, known diabetes mellitus was likely considered by investigators as a key feature for revascularization strategy decision; despite similar anatomical coronary complexity (SYNTAX score did not differ between groups), Heart Team discussion was significantly higher in diabetic patients compared with hyperglycemia, leading to a numerical higher rate of CABG in the first case. Our SYNTAX score values are lower compared with previous studies involving diabetic patients with mutlivessel-CAD and comparing surgical vs. percutaneous revascularization,[10] but not so different by the ones reported for example in the GEPRESS study.[30] However, an underestimation of the score value (directly reported by the investigator and not analyzed by an independent Core-Lab) cannot be excluded. Patients with known diabetes mellitus received a lower rate of complete revascularization: this result could be expected, because a large randomized trial reported that diabetes was significantly associated with incomplete revascularization related to a greater burden of anatomical coronary complexity.[31] Use of arterial graft was high and comparable with previous registries.[29]

Most centers followed a specific protocol for glycemia management in the acute phase; however, insulin was used in half of the cases with a preference for sc administration; only 7% of patients with known diabetes mellitus (with a mean glycemic value of 200 mg/dl) received an iv infusion: in this group, furthermore undergoing less myocardial revascularization, a higher rate of infusive insulin could be expected. Metformin was stopped in almost all patients with UA/NSTEMI (most treated with an early invasive approach) suggesting a careful prophylaxis of contrast-induced renal failure in this high-risk population. Diabetic consulting during hospitalization was low but comparable with previous reported data.[32]

Limitations

The small number of patients included and the short period of enrollment are the first and major limitations of the present work, but very few data on diabetic patients in the real world have been reported. Second, some factors that could have an influence on clopidogrel choice might be not taken into account (e.g. recent bleedings).

All enrolling hospitals had an on-site 24/7 Cath Lab leading to the very high rate of the early invasive approach and making our conclusions not representative of different areas. Data about clinical indication to OAC at discharge were not collected; despite possibly being important, it was not for the purpose of the present analysis: in all cases, clopidogrel is the drug of choice, and an influence on in-hospital bleeding is unlikely. In addition, first value of blood glucose was not collected necessarily fasting, with a possible overestimation of patients with hyperglycemia, but only 16 patients (6%) of this group received a diagnosis of established diabetes mellitus. No data about obtained optimal glycemic control during hospital phase and at discharge have been collected. Finally, no conclusion about clinical outcome can be performed because of the small sample size and without an independent event committee adjudicating the events.

Conclusion

In the present registry aimed to measure the quality of medical care administered to patients with ACS and known diabetes mellitus, we showed that these patients were treated with an early invasive approach in case of UA/NSTEMI and with a tailored revascularization strategy, but with use of clopidogrel in more cases. As some categories of high-risk ACS patients such as elderly and diabetics are usually underrepresented in randomized clinical trials generating guidelines recommendations, specific indications for their treatment should be obtained by consensus documents, and their applications should be verified in periodic surveys or real world registries.

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