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Impact of diabetes on epicardial reperfusion and mortality in a contemporary STEMI population undergoing mechanical reperfusion: Insights from the ISACS STEMI COVID 19 registry

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ABSTRACT

Background and aim: Diabetes has been shown in last decades to be associated with a significantly higher mortality among patients with ST-segment elevation myocardial infarction (STEMI) treated with primary PCI (PPCI). Therefore, the aim of current study was to evaluate the impact of diabetes on times delays, reperfusion and mortality in a contemporary STEMI population undergoing PPCI, including treatment during the COVID pandemic.

Methods and results: The ISACS-STEMI COVID-19 is a large-scale retrospective multicenter registry involving PPCI centers from Europe, Latin America, South-East Asia and North-Africa, including patients treated from 1st of March until June 30, 2019 and 2020. Primary study endpoint of this analysis was in-hospital mortality. Secondary endpoints were postprocedural TIMI 0–2 flow and 30-day mortality. Our population is represented by 16083 STEMI patients. A total of 3812 (23,7 %) patients suffered from diabetes. They were older, more often males as compared to non-diabetes. Diabetic patients were less often active smokers and had less often a positive family history of CAD, but they were more often affected by hypertension and hypercholesterolemia, with higher prevalence of previous STEMI and previous CABG. Diabetic patients had longer ischemia time, had more often anterior MI, cardiogenic shock, rescue PCI and multivessel disease. They had less often out-of-hospital cardiac arrest and in-stent thrombosis, received more often a mechanical support, received less often a coronary stent and DES. Diabetes was associated with a significantly impaired postprocedural TIMI flow (TIMI 0–2: 9.8 % vs 7.2 %, adjusted OR [95 % CI] = 1.17 [1.02–1.38], p = 0.024) and higher mortality (in-hospital: 9.1 % vs 4.8 %, Adjusted OR [95 % CI] = 1.70 [1.43–2.02], p < 0.001; 30-day mortality: 10.8 % vs 6 %, Adjusted HR [95 % CI] = 1.46 [1.26–1.68], p < 0.001) as compared to non-diabetes, particularly during the pandemic.

Conclusions: Our study showed that in a contemporary STEMI population undergoing PPCI, diabetes is significantly associated with impaired epicardial reperfusion that translates into higher in-hospital and 30-day mortality, particularly during the pandemic.

1. Introduction

Diabetes Mellitus is one of the major cardiovascular (CV) risk factors [1]. Its worldwide prevalence continues to increase, rising to 10 % of the population in countries such as China and India, which are now embracing western lifestyles; in 2017 about 60 million adult Europeans were thought to have T2DM (half undiagnosed). Patients with type 2 DM are likely to have multiple ASCVD risk factors (including dyslipidaemia and hypertension), each of which mediates an increased risk of both ASCVD and non-ASCVD. Large efforts have been done to investigate new factors and mechanisms associated to the observed increased risk [2–6].

Several previous reports have shown that diabetes is associated with longer ischemia time, impaired reperfusion, distal embolization and worse outcome at short and long-term follow-up [7–9].

However, most of the available data are quite outdated, whereas in the last decade better organized regional networks, allowing a timely reperfusion, and improvements in arterial access [10], stent technology [11,12], thrombus management [13] and adjunctive antithrombotic therapies [14–20], have contributed to improve clinical outcome.

Furthermore, during this pandemic period, most of the resources have comprehensibly been focused on the treatment of COVID19 patients, thereby reducing the access to the health care services for people affected by chronic disease, like Diabetes Mellitus (DM) [21,22]. In fact, it has been shown that it has significant impacted delays in hospital presentation, due to the fear of contagion, and mortality [23,24]. No data has so far investigated the prognostic impact of diabetes in a contemporary population, including those patients treated during the pandemic, that is therefore the aim of the present study.

2. Methods

The International Study on Acute Coronary Syndromes – ST Elevation Myocardial Infarction (ISACS-STEMI) COVID-19 was established in response to the emerging outbreak of COVID-19 to provide a European snapshot and aimed to estimate the true impact of the COVID- 19 pandemic on the treatment and outcome of STEMI patients treated by primary angioplasty [24,25], promoted by the Eastern Piedmont University, Novara, Italy. The inclusion period was from 1st of March until June 30, 2019 and 2020. Detailed data have previously been reported [24,25].

2.1. Inclusion criteria

STEMI treated by primary angioplasty (including mechanical reperfusion for failed thrombolysis).

2.2. Data collection

Anonymized data were collected through a dedicated CRF. Each center identified a local Principal Investigator. We collected demographic, clinical, procedural data including total ischemia time, door-to-balloon time (DTB), referral to primary PCI facility, COVID positivity, PCI procedural data, in-hospital and 30-day mortality. Diabetes was defined as known history of diabetes at admission, treated with or without medical therapy. After collection, each participating center submitted the CRF to the coordinating unit (Eastern Piedmont University), in charge of reporting all data into the central electronic database. Data were finally checked for missing or contradictory entries.

2.3. Study outcomes

Primary study outcomes: 1) In-hospital death. Secondary study outcomes: 1) 30-day mortality; 2) Postprocedural TIMI 0–2 flow.

2.4. Statistics

Data analysis was performed using SPSS Statistics Software 23.0 (IBM SPSS Inc., Chicago, Illinois). Quantitative variables were described using median and interquartile range. Absolute frequencies and percentages were used for qualitative variables. ANOVA or Mann-Whitney and chi-square test were used for continuous and categorical variables, respectively. Normal distribution of continuous variables was tested by the Kolmogorov-Smirnov test).

Multivariable Cox and logistic regression analyses were performed to

identify the impact of diabetes on primary and secondary study endpoints after adjustment for baseline confounding factors between the two groups (entered in block; p value entry <0.05; p value removal >0.1).

We additionally used the propensity score technique to further account for potential confounding between groups using logistic regression analysis, as previously described [26]. For each patient, a propensity score indicating the likelihood of being diabetic. was calculated through logistic regression analysis that identified variables independently associated with diabetes. We included significant baseline clinical variables associated with diabetes at univariable analysis (entered in block; p value entry <0.05; p value removal >0.1). The following variables were entered into the model: age, gender, smoking, hypertension, hypercholesterolemia, Family History of CAD, Previous STEMI, Previous PCI, Previous CABG, Type of referral, ischemia time, door-to-balloon time, Anterior STEMI, Out-of-hospital cardiac arrest, Cardiogenic shock, Rescue PCI for failed thrombolysis, In-Hospital RASI therapy, COVID Positivity, year of revascularization (2019 vs 2020), radial aceess, In-stent thrombosis, multivessels disease, preprocedural TIMI 0–2 flow, postprocedural TIMI 3 flow, stenting, DES, mechanical support, DAPT, additional PCI. The discriminatory performance of the propensity score was assessed by the receiver operating characteristic curve method, which indicated a good accuracy of the propensity score model (area under the curve = 0.76).

The consistency of the main results for the primary outcome of the study was investigated according to propensity score values (quartiles), as much as in major subgroups according to age, gender, hypertension, smoking, hypercholesterolemia, year of treatment, continent and propensity score. A $p < 0.05$ was considered statistically significant.

Finally, a multiple logistic regression analysis was performed to identify independent predictors of in-hospital mortality among diabetic patients, with a forward stepwise selection (p value entry <0.05 and p value removal >0.1). The stepwise selection of variables and estimation of significant probabilities were computed by means of maximal likelihood ratio test. The χ^2 value was calculated from the log of the ratio of maximal partial likelihood functions. The additional value of each category of variables added sequentially was evaluated on the basis of the increases in the overall likelihood statistic ratio.

The data coordinating center was established at the University of Messina, Messina, Italy.

3. Results

Our population is represented by a total of 16083 STEMI patients, including 3812 (23.7 %) patients suffering from diabetes. A total of 8698 patients were treated in 2019, including 2030 patients with diabetes (23.3 %), whereas 7385 patients were treated in 2020, including 1774 with diabetes (24 %).

3.1. Baseline demographic and clinical characteristics

Table 1 shows baseline characteristics of the 2 groups of patients according to the year, with several statistically significant differences. Patients with diabetes were older, with larger prevalence of hypertension, hypercholesterolemia, female gender, previous STEMI, previous PCI and previous CABG, whereas had less often family history of CAD and were less often smokers.

We observed a significant difference in referral to primary PCI facility, with a larger number of patients reaching the primary PCI center by ambulance with direct transfer from community. Despite a greater proportion of patients presenting by the most efficient route, patients with diabetes had a significantly longer total ischemia and door-to-

Table 1
Baseline demographic and clinical characteristics according to diabetes.

	OVERALL POPULATION (N = 16083)			YEAR 2019 (N = 8698)			YEAR 2020 (N = 7385)		
	Diabetes (n = 3812)	Non Diabetes (n = 12271)	P value	Diabetes (n = 2038)	Non diabetes (n = 6660)	P value	Diabetes (n = 1774)	Non DIabetes (n = 5611)	P value
Age (median, IQR)	65 [56–73]	62 [53–71]	<0.001	65 [57–74]	62 [54–71]	<0.001	65 [56–73]	62 [53–71]	<0.001
Age >75 year – n. (%)	888 (23.1)	2167 (17.7)	<0.001	490 (24)	1192 (17.9)	<0.001	390 (22)	975 (17.4)	<0.001
Male gender – n. (%)	2686 (70.5)	9478 (77.2)	<0.001	1458 (71.5)	5113 (76.8)	<0.001	1228 (69.2)	4365 (77.8)	<0.001
Hypertension- n (%)	2777 (72.8)	6036 (49.2)	<0.001	1475 (72.4)	3270 (49.1)	<0.001	1302 (73.4)	2766 (49.3)	<0.001
Hypercholesterolemia - n (%)	1978 (51.9)	4375 (35.7)	<0.001	1036 (50.8)	2409 (36.2)	<0.001	942 (53.1)	1966 (35)	<0.001
Smokers – n (%)	1794 (47.1)	6992 (57)	<0.001	692 (34)	3080 (46.2)	<0.001	632 (35.6)	2415 (43)	<0.001
Family History of CAD - n (%)	664 (17.4)	2634 (21.5)	<0.001	367 (18)	1468 (22)	<0.001	297 (16.7)	1166 (20.8)	<0.001
Previous STEMI- n (%)	496 (13)	1047 (8.5)	<0.001	253 (12.4)	579 (8.7)	<0.001	243 (13.7)	468 (8.3)	<0.001
Previous PCI – n (%)	705 (18.5)	1288 (10.5)	<0.001	355 (17.4)	683 (10.3)	<0.001	350 (19.7)	605 (10.8)	<0.001
Previous CABG - n (%)	119 (3.1)	153 (1.2)	<0.001	64 (3.1)	80 (1.2)	<0.001	55 (3.1)	73 (1.3)	<0.001
Referral to Primary PCI Hospital									
Ambulance (from community) – n (%)	1670 (43.8)	6068 (49.4)	<0.001	887 (43.5)	3275 (49.2)	<0.001	783 (44.1)	2793 (49.8)	<0.001
Time delays									
Ischemia time, median [25 - 75th]	240 [135–450]	200 [120–360]	<0.001	225 [130–420]	186 [120–330]	<0.001	252 [140–480]	210 [127–384]	<0.001
Total Ischemia time >12 h – n (%)	515 (13.5)	1147 (9.3)	<0.001	246 (12.1)	546 (8.2)	<0.001	269 (15.2)	601 (10.7)	<0.001
Door-to-balloon time, median [25 - 75th]	40 [26–74]	40 [25–65]	<0.001	40 [25–72]	38 [24–61]	<0.001	40 [27–74]	40 [25–65]	<0.001
Door-to-balloon time >30 min (%)– n (%)	2394 (62.8)	7256 (59.1)	<0.001	1275 (62.6)	3844 (57.7)	<0.001	1119 (63.1)	3412 (60.8)	0.087
Clinical Presentation									
Anterior STEMI – n (%)	1832 (48.1)	5614 (45.8)	0.013	978 (48)	3008 (45.2)	0.025	854 (48.1)	2606 (46.4)	0.212
Out-of-hospital cardiac arrest – n (%)	169 (4.4)	787 (6.4)	<0.001	90 (4.4)	425 (6.4)	0.001	79 (4.5)	362 (6.5)	0.002
Cardiogenic shock– n (%)	349 (9.2)	819 (6.7)	<0.001	179 (8.8)	446 (6.7)	0.001	170 (9.6)	374 (6.7)	<0.001
Rescue PCI for failed thrombolysis – n (%)	304 (8)	795 (6.5)	0.001	163 (8)	442 (6.6)	0.035	141 (7.9)	353 (6.3)	0.015

*Mann-Whitney test.
CAD = Coronary Artery Disease; STEMI = ST-segment Elevation Myocardial Infarction; PCI = Percutaneous Coronary Intervention; CABG 0 Coronary Artery Bypass Graft.

balloon time.

As shown in Table 2, patients with diabetes presented more often with anterior infarct location, cardiogenic shock, failed thrombolysis treated by rescue PCI, but had less often out-of- hospital cardiac arrest.

These differences were almost similarly observed in both patients treated in 2019 and 2020.

3.2. Procedural characteristics

Table 2 shows procedural characteristics. Patients with diabetes had less often radial approach, in-stent thrombosis, use of thrombectomy, intravenous antiplatelet therapies, and DES, but a higher prevalence of multivessel disease, preprocedural recanalization, implantation of mechanical support devices.

Diabetes was associated with impaired postprocedural TIMI flow (TIMI 0–2: 9.8 % vs 7.2 %, OR [95 % CI] = 1.4 [1.23–1.59], p value < 0.001), similarly observed in 2019 and 2020 (Fig. 1 and Fig. 1S; p interaction 0.18). The results were confirmed in major high-risk subgroups (Fig. 1S), the continent, and after adjustment for all baseline confounding factors (age, gender, smoking, hypertension, hypercholesterolemia, Family History of CAD, Previous STEMI, Previous PCI, Previous CABG, Type of referral, ischemia time, door-to-balloon time, Anterior STEMI, Out-of-hospital cardiac arrest, Cardiogenic shock, Rescue PCI for failed thrombolysis, In-Hospital RASI therapy, COVID Positivity, year of revascularization (2019 vs 2020), radial access, In-stent thrombosis, multivessel disease, preprocedural TIMI 0–2 flow, stenting, DES, mechanical support, DAPT, additional PCI) (Adjusted OR [95 % CI] = 1.17 [1.02–1.38], p = 0.024).

A total of 938 patients died during hospitalization. Diabetes was associated with a significantly higher mortality (9.1 % vs 4.8 %, OR [95 % CI] = 1.97 [1.72–2.26], p < 0.001) similarly observed in 2019 and 2020 (Fig. 2 and Fig. 2S; p interaction 0.54). The results were confirmed in major high-risk subgroups (Fig. 2S), the continent and after adjustment for all confounders (age, gender, smoking, hypertension, hypercholesterolemia, Family History of CAD, Previous STEMI, Previous PCI, Previous CABG, Type of referral, ischemia time, door-to-balloon time, Anterior STEMI, Out-of-hospital cardiac arrest, Cardiogenic shock, Rescue PCI for failed thrombolysis, In-Hospital RASI therapy, COVID Positivity, year of revascularization (2019 vs 2020), radial access, In-stent thrombosis, multivessel disease, preprocedural TIMI 0–2 flow, postprocedural TIMI flow, stenting, DES, mechanical support, DAPT, additional PCI) (Adjusted OR [95 % CI] = 1.70 [1.43–2.02], p < 0.001).

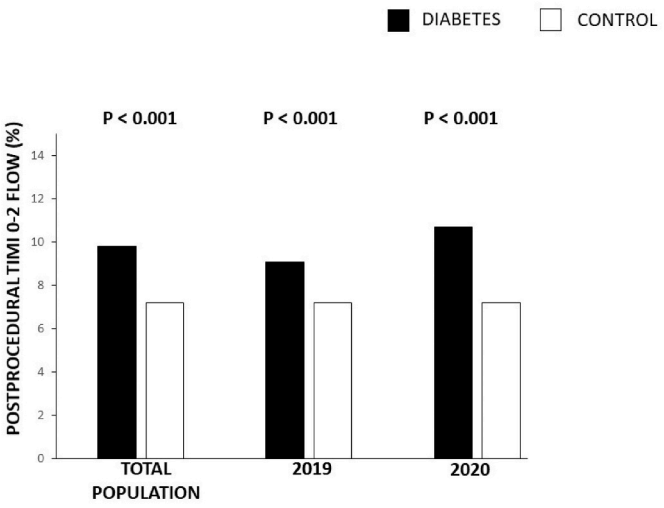

Fig. 1. Bar graphs show the impact of diabetes on postprocedural TIMI 0–2 flow in overall population, in 2019 and 2020.

Table 2
Angiographic and procedural characteristics according to diabetes.

	OVERALL POPULATION (N = 16083)			YEAR 2019 (N = 8698)			YEAR 2020 (N = 7385)		
	Diabetes (n = 3812)	Non Diabetes (n = 12271)	P value	Diabetes (n = 2038)	Non diabetes (n = 6660)	P value	Diabetes (n = 3812)	Non Diabetes (n = 12271)	P value
Radial Access (%)	2740 (71.9)	9528 (77.6)	<0.001	1461 (71.7)	5062 (76)	<0.001	1279 (72.1)	4466 (79.6)	<0.001
Culpirt vessel			<0.001			0.010			0.033
Left main – n (%)	71 (1.9)	181 (1.5)		37 (1.8)	104 (1.6)		34 (1.9)	77 (1.4)	
LAD– n (%)	1780 (46.7)	5578 (45.5)		957 (47)	3030 (45.5)		823 (46.6)	2548 (45.4)	
Circumflex – n (%)	503 (13.2)	1847 (15.1)		261 (12.8)	985 (14.8)		242 (13.6)	862 (15.4)	
RCA – n (%)	1415 (37.1)	4586 (37.4)		760 (37.3)	2500 (37.5)		655 (36.9)	2086 (37.2)	
Anterolateral Branch – n (%)	9 (0.2)	32 (0.3)		6 (0.3)	19 (0.3)		3 (0.2)	13 (0.2)	
SVG – n (%)	34 (0.9)	45 (0.4)		17 (0.8)	20 (0.3)		17 (1)	25 (0.4)	
In-stent Thrombosis – n (%)	445 (3.6)	187 (4.9)	<0.001	99 (4.9)	240 (3.6)	0.010	88 (5)	205 (3.7)	0.014
Multivessel disease – n (%)	2195 (57.6 %)	5691 (46.45 %)	<0.001	1154 (56.6)	3082 (46.3)	<0.001	1041 (58.7)	2609 (46.5)	<0.001
Preprocedural TIMI 0 flow – n (%)	2468 (64.7)	8263 (67.3)	0.003	1316 (64.6)	4450 (66.8)	0.061	1152 (64.9)	3813 (68)	0.018
Thrombectomy– n (%)	560 (14.7)	2003 (16.3)	0.016	299 (14.7)	1103 (16.6)	0.042	261 (14.7)	900 (16)	0.181
Stenting– n (%)	3446 (90.4)	11320 (92.3)	0.001	1849 (90.7)	6149 (92.3)	0.004	1597 (90)	5172 (92.2)	0.020
Drug-eluting stent– n (%)	3321 (87.1)	10933 (89.1)	0.001	1760 (86.4)	5896 (88.5)	0.008	1561 (88)	5037 (89.8)	0.035
Mechanical support – n (%)	167 (4.4)	330 (2.7)	<0.001	78 (3.8)	168 (2.5)	0.002	89 (5)	162 (2.9)	<0.001
Postprocedural TIMI 3 Flow – n (%) –	3437 (90.2)	11384 (92.8)	<0.001	1852 (90.9)	6178 (92.8)	<0.001	1585 (89.3)	5206 (92.8)	0.005
Gp IIb-IIIa inhibitors/ Cangrelor – n (%)	712 (18.7)	2555 (20.8)	0.004	373 (18.3)	1380 (20.7)	0.017	339 (19.1)	1175 (20.9)	0.096
Bivalirudin– n (%)	11 (0.3 %)	41 (0.3 %)	0.66	9 (0.4)	25 (0.4)	0.675	2 (0.1)	16 (0.3)	0.199
Additional PCI			0.092			0.715			0.066
During the index procedure – n (%)	392 (10.3)	1184 (9.6)		191 (9.4)	596 (8.9)		201 (11.3)	588 (10.5)	
Staged– n (%)	367 (9.6)	1319 (10.7)		200 (9.8)	686 (10.3)		167 (9.4)	633 (11.3)	
DAPT therapy – n (%)	3768 (98.8)	12137 (98.9)	0.748	2017 (99)	6576 (98.7)	0.404	1751 (98.7)	5561 (99.1)	0.132
In Hospital Death	346 (9.1)	592 (4.8)	<0.001	163 (8)	294 (4.4)	<0.001	183 (10.3)	298 (5.3)	<0.001
Death- n (%)	375 (10.8)	652 (6.0)	<0.001	175 (9.4)	329 (5.6)	<0.001	200 (12.3)	323 (6.5)	<0.001

TIMI = Thrombolysis in Myocardial Infarction; DAPT = Dual Antiplatelet Therapy.

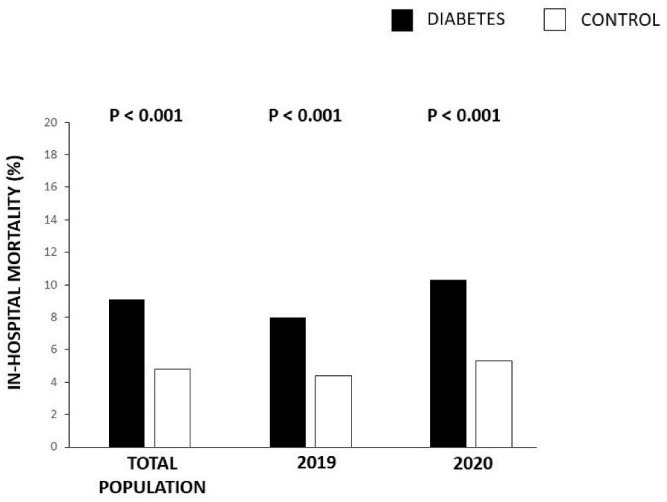

Fig. 2. Bar graphs show the impact of diabetes on in-hospital mortality in overall population, in 2019 and 2020.

Table 3
Independent predictors of in-hospital mortality among diabetic patients.

Variable	Adjusted Odds Ratio	95 % CI	P value
Age >75	2.88	2.16–3.83	<0.001
Hypertension	1.61	1.14–2.26	0.007
Hypercholesterolemia	0.48	0.36–0.65	<0.001
Ischemia time >12 h	2.34	1.67–3.29	<0.001
OHCA	3.07	1.95–4.84	<0.001
Cardiogenic shock	10.1	7.13–14.37	<0.001
Radial Access	0.57	0.44–0.76	<0.001
TIMI 0 pre	1.46	1.07–1.99	0.016
TIMI 0–2 Post	3.83	2.75–5.33	<0.001
DES	0.69	0.49–0.98	0.039
Mechanical Support	2.3	1.48–3.58	<0.001
DAPT	0.32	0.13–0.81	0.016
MVD	1.59	1.17–2.15	0.003
Additional PCI	0.61	0.46–0.8	<0.001

Table 3 reports independent predictors of in-hospital mortality in diabetic patients.

A total of 1027 patients died within 30 days. Diabetes was associated with a significantly higher mortality (10.8 % vs 6 %, HR [95 % CI] = 1.82 [1.6–2.06.], p < 0.001) similarly observed in 2019 and 2020 (Fig. 3 and Fig. 3S; p interaction 0.31). The results were confirmed in major high-risk subgroups (Fig. 3S), the continent and after adjustment for all confounders (age, gender, smoking, hypertension, hypercholesterolemia, Family History of CAD, Previous STEMI, Previous PCI, Previous CABG, Type of referral, ischemia time, door-to-balloon time, Anterior STEMI, Out-of-hospital cardiac arrest, Cardiogenic shock, Rescue PCI for failed thrombolysis, In-Hospital RASI therapy, COVID Positivity, year of revascularization (2019 vs 2020), radial access, In-stent thrombosis, multivessel disease, preprocedural TIMI 0–2 flow, postprocedural TIMI flow, stenting, DES, mechanical support, DAPT, additional PCI) (Adjusted HR [95 % CI] = 1.46 [1.26–1.68], p < 0.001) (Fig. 4).

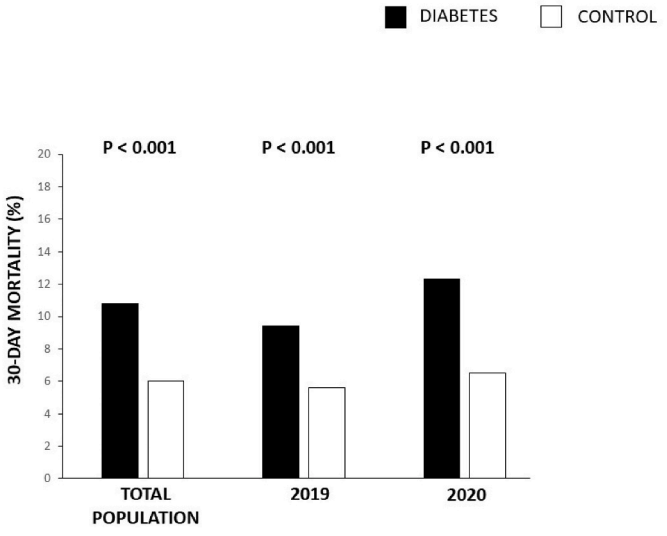

Fig. 3. Bar graphs show the impact of diabetes on 30-day mortality in overall population, in 2019 and 2020.

4. Discussion

The ISACS-STEMI COVID-19 registry represents the largest study of patients with STEMI undergoing mechanical reperfusion during the COVID pandemic, to date. The main finding of the current study was that diabetes was independently associated with a significantly worse coronary reperfusion and higher mortality.

Coronary artery disease is a major cause of mortality in western countries. The organization of well-run networks has greatly contributed to the improvement in the management of ST-segment elevation acute myocardial infarction by a fast diagnosis and treatment with subsequently shorter ischemia time [27–29] and improved survival. However, the outcome is still unsatisfactory in some high-risk subsets of patients [30–32], including those with diabetes [7–9], that currently represents a

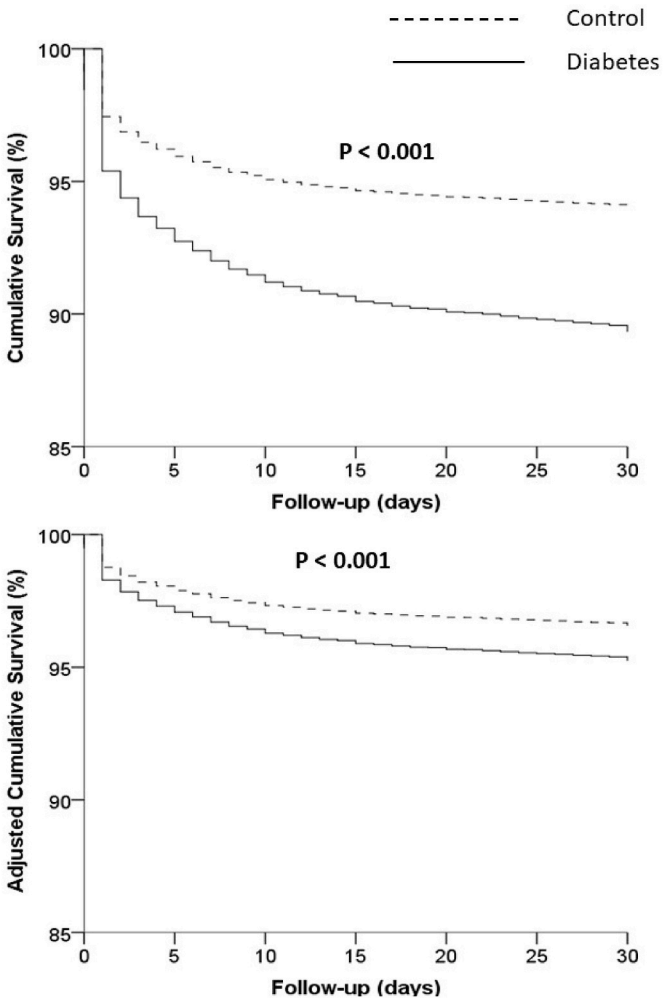

Fig. 4. Unadjusted and adjusted survival curves according to diabetes.

major risk factor and prognostic determinant in patients suffering from STEMI. Large attention has been paid to mechanicistic insights to explain the negative prognostic impact of diabetes on cardiovascular outcomes [33–42].

Hyperglycemia at admission, even in the absence of diabetes (stress hyperglycemia), is associated with larger infarct size and worse survival in STEMI patients [43–47]. In fact, several in vitro and in vivo experiments demonstrated the involvment of hyperglycemia in the reperfusion injury [48–53]. Acute hyperglycemia increases intercellular adhesion molecule-1 levels [48], which could, in turn, increase plugging of leukocytes in the capillaries [49].

Furthermore, hyperglycemia induce alterations in some signaling pathways [50,51], such as reperfusion injury signaling kinase (RISK) pathway including PI3K/Akt signaling cascade, and survivor activating factor enhancement (SAFE) pathway including JAK2/STAT3 signaling cascade, that represent a key elements for myocardial protection.

Chronic hyperglycemia can also disrupt mitochondria by increasing dynamin-related protein 1 (DRP1) expression [52], blocking the mitochondrial K_{ATP} channel [53] and inactivating hypoxia-inducible factor-1 (HIF-1α) [54], reducing the efficacy of potential therapeutic interventions against ischemia-reperfusion injury. In particular, all the above mentioned alterded pathways may clearly contribute to the impaired mechanisms of preconditioning observed in the presence of diabetes [55].

Furthermore, elevated glycaemia may additionally favour thrombus formation. It has been shown that blood glucose is independently associated with platelet-dependent thrombosis, even in the normal range [56] that may impair myocardial reperfusion. In fact, it has been shown that microthrombus in the capillaries play a crucial role in the no-reflow phenomenon after STEMI [57]. In a previous report, De Luca et al. [58] found that among patients treated with glycoprotein IIb-IIIa inhibitors, diabetes was associated with higher occurrences of distal embolization and impaired myocardial reperfusion and higher mortality. So far, after initial enthusiasm and despite the strong rationale, the routine use of thrombectomy has not proven significant beneficial effects in terms of mortality. However, neither randomized studies nor prespecified subanalyses have been strictly conducted on thrombectomy in diabetic patients with STEMI.

Several studies have shown the significant negative impact on survival of diabetes in STEMI. An analysis from the TASTE registry-based study [59], including 7224 STEMI patients, showed no difference in the thrombus grade ($p = 0.909$) and the location of the culprit coronary lesion between patients with or without DM. Patients with diabetes had higher mortality (9 % vs 4.9 %), whereas no significant difference was observed in terms of recurrent MI (4.0 % vs. 2.5 %) or stent thrombosis (1.0 % vs. 0.8 %). Within the DM group, the insulin-treated patients displayed significantly higher 1-year mortality (12.6 % vs. 6.6 %) when compared with DM patients without insulin treatment. After adjustments for all confounders, diabetes was independently associated with mortality at 1 year. The negative impact of diabetes on mortality has been confirmed at log-term follow-up.

In a previous large study, including 6298 patients, De Luca G et al. [8] showed that, despoite no difference in postprocedural TIMI flow, diabetes was independently associated with higher mortality (19.1 % vs. 7.4 %), reinfarction (10.4 % vs. 7.5 %), stent thrombosis (7.6 % vs. 4.8 %) and target vessel revascularization (18.6 % vs. 15.1 %) up to 4-year follow-up. Brugaletta et al. [7], in a smaller study including a population of 1498 STEMI patients undergoing primary PCI with a follow-up extended up to 10 years, confirmed the negative impact of diabetes on repeated revascularization, without a significant difference in mortality (29 % vs 19.56 %) presumably due to the limited statistical power.

This is one of the largest and most recent study so far conducted to evaluate the prgnostic impact of diabetes, including more than 16000 STEMI patients treated by PPCI, mostly with DES and radial approach. Furthermore, we included patients treated in both precovid and covid-19 pandemic. In fact, the pandemic has been shown to increase delays to reperfusion and therefore can negatively impact in a larger quote of MACEs rate, especially in diabetic patients. As expected, diabetic patients showed a worse clinical profile, and were associated with impaired epicardial perfusion, confirmed after adjustment for all baseline and procedural confounders. The negative impact on reperfusion clearly translated into higher in-hospital and 30-day mortality, that was confirmed even after adjustment for all confounders. The results were similarly observed in both prepandemic and pandemic period.

Future large randomized trials should be certainly dedicated to this high-risk subgroup of patients, focusing on pharmacological therapies to minimize reperfusion injury and reduce the occurrence of microvascular obstruction.

5. Limitations

This study which assessed data from 109 high-volume PPCI centers, mainly European, is limited by its retrospective, non-randomized design. As may be expected, patients with diabetes had a significantly worse cardiovascular risk profile and differed from the control population in several procedural characteristics. However, our results were confirmed after adjustment for all baseline and procedural confounders. Furthermore, our research was conducted during a pandemic emergency, which was a challenge and expected to encounter some missing data. Unfortunately, data on the type of chronic treatment at admission (insulin vs oral vs no medical treatment), new diagnosed diabetes and glycosylated haemoglobin were not routinely collected and therefore not available for this analysis.

Finally, we included only patients undergoing PPCI, excluding those who died before hospital admission or prior to angiography, and STEMI patients managed conservatively. Therefore, caution should be exercised in the interpretation of our results.

6. Conclusions

Our study showed that in a contemporary STEMI population undergoing primary angioplasty, diabetes is significantly associated with impaired epicardial reperfusion that translates into higher in-hospital and 30-day mortality, particularly during the pandemic.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2024.09.031.

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