

**MYOCARDIAL REVASCULARIZATION STRATEGIES IN ST ELEVATION
MYOCARDIAL INFARCTION WITHOUT URGENT REVASCULARIZATION:
INSIGHT FROM A NATIONWIDE STUDY.**

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ABSTRACT

OBJECTIVE:

To analyse the outcomes of patients presenting with ST elevation myocardial infarction (STEMI) without early (<48h) revascularization, according to percutaneous versus surgical revascularization.

PATIENTS AND METHODS:

Based on the French administrative hospital-discharge database, the study collected information for all consecutive patients seen in France, between January 1, 2010, to June 31, 2019, for a STEMI who underwent either a first percutaneous coronary intervention (PCI) or a first coronary artery bypass graft (CABG) between 48 hours to 90 days after the index hospitalization. Propensity score matching was used for the analysis of outcomes.

RESULTS:

71,365 STEMI were included in the analysis corresponding to 59,340 patients with PCI and 12,025 patients treated with CABG. In a matched analysis of 12,012 patients by arm, surgical revascularization was associated with lower rates of all cause (5.1% vs. 7.1%, HR 0.70 95%CI 0.66-0.75) and cardiovascular (2.6% vs. 3.1%, HR 0.83 95%CI 0.76-0.91) death. Rehospitalization for heart failure was less often reported after surgery (5.5% vs. 7.5%, HR 0.76 95%CI 0.71-0.81) while stroke incidence was not statistically different between the two arms (2.1% vs. 2.3%, HR 0.90 95%CI 0.80-1.00). Major bleeding was less often reported in the PCI arm (4.6% vs. 6.1% HR 1.31, 95% 1.22-1.41).

CONCLUSION:

In patients with STEMI who did not undergo urgent revascularization (i.e. within 48hours after presentation) surgical revascularization was associated with better outcomes and should be individually considered as an alternative to percutaneous coronary intervention.

Key words: STEMI, CABG, PCI

Abbreviations

ST elevation myocardial infarction (STEMI)

Percutaneous coronary intervention (PCI)

Coronary artery bypass graft (CABG)

Programme de Médicalisation des Systèmes d'Information (PMSI)

Heart failure (HF)

Standard deviation (SD)

Hazard ratios (HR)

INTRODUCTION

It is recommended to offer urgent revascularization in patients presenting with ST elevation myocardial infarction (STEMI), even in patients presenting late after symptoms onset (12 to 48 hours) (1). However, routine percutaneous coronary intervention (PCI) in an infarct related artery is not recommended after 48h (1). Therefore, revascularization strategies in patients presenting with a STEMI who did not undergo revascularization within the first 48 hours remain a challenge. PCI and coronary artery bypass graft (CABG) represent the two revascularization options that could be offered to those patients.

In non-STEMI myocardial infarction, the currently available evidence indirectly suggests that the criteria applied to patients with chronic coronary syndrome, to guide the choice of revascularization modality, should be applied to stabilized patients (2). However, no data or study are available regarding the optimal revascularization strategy in STEMI patients.

Patients who undergo CABG after myocardial infarction have higher risk of short term mortality compared to patients with elective or delayed CABG (3, 4). Deik et al revealed that CABG performed >7 days after STEMI had similar post-operative outcomes to elective CABG (5). However, the timing of surgical revascularization remains unclear after a STEMI and should be determined individually according to guidelines.

The French Programme de Médicalisation des Systèmes d'Information (PMSI), a mandatory administrative database, offers a unique opportunity to assess exhaustive and comprehensive data on all consecutive patients hospitalized in France (6, 7). Therefore, based on this large, nationwide, administrative French database, we aimed to compare the outcomes of CABG versus PCI in patient with STEMI who did not undergo revascularization within the first 48hours of hospitalization.

METHODS

Data collection

Methods have been described previously (6). All patients admitted with STEMI in France from January 2010 to June 2019 were screened using the national administrative PMSI database, through The French Data Protection Authority, covering hospital care from the entire French population, and as previously described (7,8). The study was conducted retrospectively, with no impact on patient care. Data collection and management were approved by the Commission Nationale de l'Informatique et des Libertés, which ensures that all information remains confidential and anonymous, in compliance with the Declaration of Helsinki (authorization number 1897139).

Study population

From January 1, 2010, to June 31, 2019, a total of 520,258 patients with an age of 18 years or more were hospitalized with a STEMI (ICD-10 codes: I210, I211, I212, I213) as the principal (i.e., the health problem that justified admission to hospital), the related (i.e., potential chronic disease or health state during the hospital stay), or a significantly associated (i.e., comorbidity or associated complication) diagnosis.

For the purpose of this analysis, we enrolled patients who underwent either a PCI or a CABG between 48 hours to 90 days after the index presentation for a STEMI. We did exclude all patients with revascularization during the first 48 hours of hospitalization, patients who had concomitant valvular cardiac surgery and patients with a history of previous CABG or PCI. Information regarding demographics, medical history, procedures and events during hospitalization or follow-up was collected.

Outcomes

Patients were followed until June 2019 for the occurrence of outcomes, starting from date of STEMI. Clinical outcomes for the analysis were: all-cause death, cardiovascular death, hospitalization for heart failure (HF), all-cause stroke and major bleeding. Outcomes were identified using their respective ICD-10 or procedure codes. The endpoints were evaluated with follow-up starting from date of either PCI or CABG until date of each specific outcome or date of last news in the absence of the outcome. Information on outcomes during follow-up was obtained by analyzing the PMSI codes for each patient. Mode of death (cardiovascular or non-cardiovascular) was identified based on the main diagnosis during hospitalization

resulting in death. Hospitalization was considered to be related to heart failure when heart failure was recorded as the main diagnosis. We defined major bleeding using the modified International Society on Thrombosis and Haemostasis (BARC) definitions (9). Major bleeding, based on International Society on Thrombosis and Haemostasis definition and modified to take into account the availability of information in the database, was defined as a hospitalisation with one of the three following diagnoses: haemorrhagic stroke, other critical organ or site bleeding (intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular), other bleeding with a transfusion during hospital stay, or resulting in death. Causes of death and haemoglobin result are not available to take into account not hospitalized fatal bleeding and bleeding causing a fall in haemoglobin level of 20g/l. To increase the validation of our analysis, we also evaluated incidence rates of cancer and urinary infection as negative control endpoints.

Statistical analyses

Qualitative variables are described as frequency and percentages and quantitative variable as means \pm standard deviation (SD). Comparisons were made using chi-square tests for categorical variables and the Student *t* test or non-parametric Kruskal–Wallis test, as appropriate, for continuous variables.

Owing to the non-randomized nature of the study, and considering for significant differences in baseline characteristics, propensity-score matching was used to control for potential confounders of the treatment outcome relationship. Propensity scores were calculated using logistic regression with revascularization strategy as the dependent variable. The propensity score included all variables of baseline characteristics (listed in table 1). For each patient with a PCI, a propensity score-matched patient with CABG was selected (1:1) using the one-to-one nearest neighbor method (with a caliper of 0.001 of the SD of the propensity score on the logit scale) and no replacement. Incidence rates for outcomes in each group were estimated, and cumulative incidences curves were obtained using Kaplan Meier method. A Cox regression model on all baseline parameters described in Table 1 was used to obtain adjusted hazard ratios (HR). A multivariate analysis was performed to estimate adjusted hazard ratios with their 95% confidence intervals. A *p* value $<.05$ was considered statistically significant. All analyses were performed using Enterprise Guide 7.1 (SAS Institute Inc., SAS Campus Drive, Cary, NC, USA) and STATA version 12.0 (Stata Corp, College Station, TX, USA).

RESULTS

Baseline characteristics

Between 1 January 2010 and 1 June 2019, 71,655 STEMI patients with no revascularization during the first 48 hours, and either PCI or CABG between 48 hours to 90 days were identified in the database (Figure 1). In the unmatched population of 59,340 STEMI treated with PCI and 12,025 STEMI treated with CABG, patients treated with CABG were younger, more often male and presented less often with heart failure or cardiogenic shock (Table 1). After propensity score matching, there were 12,012 patients in each group. Baseline characteristics in these populations were well matched (Table 2, supplementary Figure 1). Mean (SD) time between STEMI and PCI or CABG in the matched population was 16.7 (19.2) days (median 8, interquartile range [IQR] 4-21).

Clinical outcomes

Mean (SD) follow-up was 2.6 (2.7) years, (median 1.8, IQR 0.1-4.6). In the whole population, all-cause death was recorded in 11,477 patients and cardiovascular death was recorded in 5142 patients. Predictors of all-cause death are reported in table 3 and predictors of all-cause death are in table 4. Treatment with CABG (vs. PCI) was independently associated with a lower risk of all-cause death (HR 0.73, 95% CI 0.69-0.78) and of cardiovascular death (HR 0.88, 95% CI 0.82-0.96).

In the matched population, all-cause death was recorded in 2202 (7.1%) patients who underwent PCI versus 1596 (5.1%) who underwent CABG (HR 0.70, 95% CI 0.66-0.75; Table 5 and Figure 2). The incidence of cardiovascular death was also lower in the CABG group (2.6% versus 3.1%; HR 0.83, 95% CI 0.76–0.91; Table 5 and Figure 2).

Incidences of rehospitalization for worsening heart failure was reported lower after CABG (1569 patients, 5.5%) versus PCI (2026 patients, 7.5%) (HR 0.76, 95% CI 0.71-0.81; Table 5 and Figure 3) while all-cause stroke were not statistically different between the two groups (2.1% versus 2.3%; (HR 0.89, 95% CI 0.80-1.00; Table 3 and Figure 3).

Major bleeding was reported in 1309 (4.6%) patients in the PCI arm versus 1658 (6.1%) patients in the CABG arm (HR 1.31, 95% 1.22-1.41; Table 3, Figure 4).

DISCUSSION

Our nationwide analysis showed that:

- In real life setting, 13% of patients admitted with STEMI in France between 2010 to 2019 underwent either PCI or CABG outside the criteria of urgent myocardial revascularization (<48h)
- In patients with STEMI who did not undergo a PCI within the first 48 hours, surgical revascularization was associated with better long-term outcomes

Patients with STEMI should be revascularized as soon as possible within a 48 hours window from symptoms onset. Indeed, timing of intervention is crucial in STEMI, where myocardial salvage in the infarct related artery territory is usually possible within 48hours. However, it is not uncommon that patients do present very late and urgent revascularization could not be achieved in this time frame. In our national database around 13% of STEMI did undergo either PCI or CABG between 48hours to 90 days following admission.

Outcomes following CABG in STEMI patients are controversial. A recent analysis comparing outcomes of CABG in STEMI and non-STEMI treated within the first 48hours of hospitalization showed twice higher in hospital mortality after CABG for STEMI with similar long-term outcomes (10). Another study showed improved long-term survival after CABG in STEMI versus non-STEMI when performed during the first 48 hours (11).

A large US nationwide analysis confirmed that observed mortality rates after CABG during the index hospitalization of a STEMI patient appeared low (12), while another recent US dataset showed poorer outcomes for STEMI treated with CABG during the first 24 hours after admission (13). Pooled together those data suggest that CABG might be safely performed in selected STEMI patients in a timely fashion, which should be individually evaluated in Heart Team.

When compared to PCI, a large monocentric registry (14) compared outcomes of PCI vs CABG in STEMI and showed that despite higher risk and unfavourable in-hospital course, long-term outcomes of patients treated with early CABG were similar to patients treated with PCI. Our data are in favour of lower rates of cardiovascular death and rehospitalisation for heart failure in patients with STEMI treated with CABG between 48hours to 90 days when compared to PCI. Major bleeding appear to be higher after CABG during the whole follow

up. While short-term bleeding are related to the surgery, this difference in bleeding tends to become less significant over time.

In this nationwide study, timing of intervention demonstrates that when the 48 hours windows is outdated, revascularization, even percutaneous, is usually performed after few days (mean delay of 10 days for PCI). In addition to surgery timing (13), several other factors emerged in the literature as predictors for adverse outcomes in STEMI patients undergoing CABG such as age, female gender, preoperative cardiogenic shock or heart failure, CABG after failed PCI or fibrinolysis, and the degree of preoperative myocardial injury as quantified by cardiac troponin (10-14). In our cohort, we observed that in France patients who underwent CABG between 48 hours to 90 days were sicker than those who had PCI. Even if slightly younger, frailty index was higher in CABG patients, while heart failure and cardiogenic shock at presentation more frequently observed.

We assume that improved technology and equipment, in combination with optimized medical treatment prior to the procedure, contributed to the improved outcomes in the patients who underwent CABG. In addition, improvement in medical infrastructure and treatment of short-term post-CABG complications also contributed to improved long-term outcomes.

Multi vessel disease is a frequent finding in STEMI patients (15). In chronic coronary syndrome or stabilized non-STEMI with multivessel disease, CABG has shown to be an efficient revascularization strategy with better long-term outcomes, mostly regarding the rate of re intervention, when compared to PCI (16). Moreover, complete revascularization after STEMI is associated with better prognosis (17) and more often achieved with CABG. Following the COMPLETE study results, a multivessel percutaneous revascularization in STEMI appeared to be preferred to medical therapy for non-culprit coronary lesions (17). Indeed, complete revascularization was associated with lower risk of myocardial infarction and ischemia driven revascularization. Therefore, the optimal management of STEMI who have not been revascularized in emergency poses a challenge to the cardiologist. On one arm, PCI represents a less invasive approach to allow semi-urgent revascularization in those patients. On the other arm, CABG may achieve more complete revascularization and may be associated with improved long-term outcomes. However, no direct comparison of PCI versus CABG in this setting is existing so far.

Limitations

We recognize several limitations to our analysis. A main limitation is inherent to the retrospective, observational nature of the study and its potential biases. Specifically, the study was based on administrative data, with limitations inherent to such methodology (6 – 8). The PMSI database makes use of diagnoses coded using ICD-10; such diagnoses are the physician's responsibility and were not comprehensively checked, leading to a potential information bias. Nevertheless, the large scale of the database and the regular audit of coded diagnoses (linked with reimbursement) are expected to mitigate possible bias and errors. The large population of patients admitted for STEMI is likely to represent a heterogeneous group of patients, each with various kinds of illnesses and severities, which may have affected prognosis. Moreover, relevant clinical or procedural information, as well as the usage of pharmacotherapies were not evaluated. Furthermore, the complete evaluation of the clinical circumstances (such as failed PCI or salvage CABG) that may have influenced treatment decisions on CABG was not available. However, the time frame (48 hours after hospital admission) should reduce this bias.

Analyses were restricted to the variables coded in the database, excluding precise results of coronary angiograms, biological parameters, echocardiographic measurements or use of medications. Comparisons between groups might not be fully appropriate, as the presence of other missing confounding factors cannot be ruled out. Coronary anatomy and SYNTAX score, which are pivotal element in the decision between PCI and CABG in stable and stabilized non-STEMI patients, were not available for this analysis. Despite having no access to a precise evaluation of left ventricular ejection fraction, we do report heart failure and cardiogenic shock at baseline. Moreover, CABG details (off pump versus on pump, arterial versus venous graft, complete revascularization) were not available for this analysis.

Conclusions

In patients with STEMI who did not undergo urgent revascularization (i.e. within 48hours after presentation) surgical revascularisation was associated with better outcomes and should be considered as an alternative to percutaneous coronary intervention after individualized Heart Team evaluation.

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Table 1. Characteristics of patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

	PCI	CABG	p value	Standardized difference, CABG vs PCI (%)	Total
	(n=59,340)	(n=12,025)			(n=71,365)
Age, years	68.5±13.7	66.2±10.8	<.001	-18.2	68.1±13.3
Sex (male)	41292 (69.6)	9678 (80.5)	<.001	25.4	50970 (71.4)
Charlson comorbidity index	3.9±2.9	4.2±2.9	<.001	9.7	3.9±2.9
Frailty index	5.3±3.1	5.6±2.8	<.001	12.0	5.3±3.1
Obesity	9469 (16.0)	2296 (19.1)	<.001	8.3	11765 (16.5)
Dyslipidemia	19486 (32.8)	4986 (41.5)	<.001	17.9	24472 (34.3)
Diabetes mellitus	15023 (25.3)	3775 (31.4)	<.001	13.5	18798 (26.3)
Hypertension	32121 (54.1)	6965 (57.9)	<.001	7.6	39086 (54.8)
Smoker	12737 (21.5)	2815 (23.4)	<.001	4.7	15552 (21.8)
Alcohol related diagnoses	2957 (5.0)	664 (5.5)	.01	2.4	3621 (5.1)
Illicit drug use	274 (0.5)	48 (0.4)	.35	-1.0	322 (0.5)
Dilated cardiomyopathy	2679 (4.5)	648 (5.4)	<.001	4.0	3327 (4.7)
Heart failure with congestion	3752 (6.3)	710 (5.9)	.08	-1.7	4462 (6.3)
Aortic stenosis	1737 (2.9)	390 (3.2)	.06	1.8	2127 (3.0)
Aortic regurgitation	1063 (1.8)	262 (2.2)	.01	2.8	1325 (1.9)
Mitral regurgitation	3437 (5.8)	979 (8.1)	<.001	9.2	4416 (6.2)
Tricuspid regurgitation	268 (0.5)	75 (0.6)	.01	2.4	343 (0.5)
Ischemic stroke	1805 (3.0)	330 (2.7)	.08	-1.8	2135 (3.0)
Atrial fibrillation	9023 (15.2)	2081 (17.3)	<.001	5.7	11104 (15.6)
Previous pacemaker or ICD	1193 (2.0)	142 (1.2)	<.001	-6.6	1335 (1.9)
Vascular disease	5598 (9.4)	1324 (11.0)	<.001	5.2	6922 (9.7)
Abnormal renal function	3185 (5.4)	551 (4.6)	<.001	-3.6	3736 (5.2)
Liver disease	1635 (2.8)	391 (3.3)	.01	2.9	2026 (2.8)
Lung disease	6924 (11.7)	1338 (11.1)	.09	-1.7	8262 (11.6)
COPD	4172 (7.0)	804 (6.7)	.18	-1.4	4976 (7.0)
Sleep apnea syndrome	2390 (4.0)	525 (4.4)	.09	1.7	2915 (4.1)
Anaemia	5386 (9.1)	1314 (10.9)	<.001	6.2	6700 (9.4)
Previous cancer	5966 (10.1)	855 (7.1)	<.001	-10.5	6821 (9.6)
Thyroid diseases	3222 (5.4)	486 (4.0)	<.001	-6.5	3708 (5.2)
Cognitive impairment	2284 (3.8)	212 (1.8)	<.001	-12.7	2496 (3.5)
Depression	3639 (6.1)	589 (4.9)	<.001	-5.4	4228 (5.9)
Poor nutrition	2455 (4.1)	322 (2.7)	<.001	-8.1	2777 (3.9)
Anterior MI	25306 (42.6)	4664 (38.8)	<.001	-7.9	29970 (42.0)
Inferior MI	18797 (31.7)	3478 (28.9)	<.001	-6.0	22275 (31.2)
MI with other location	15237 (25.7)	3883 (32.3)	<.001	14.6	19120 (26.8)
HF at the acute phase	16367 (27.6)	4196 (34.9)	<.001	15.8	20563 (28.8)
Pulm. edema / shock at the acute phase	2851 (4.8)	850 (7.1)	<.001	9.6	3701 (5.2)
Time between STEMI and PCI/CABG (days)	10.4±15.0	17.0±17.9	<.001	40.1	11.5±15.7
Death during follow-up	9881 (16.7)	1596 (13.3)	<.001	-	11477 (16.1)
Cardiovascular death	4326 (7.3)	816 (6.8)	.05	-	5142 (7.2)

Values are mean ± standard deviation, or n (%).

AF = atrial fibrillation; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ICD, implantable cardiac defibrillator; STEMI = ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation.

Table 2. Characteristics of matched patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

	PCI (n=12,012)	CABG (n=12,012)	p value	Standardized difference, CABG vs PCI (%)	Total (n=24,024)
Age, years	66.1±13.7	66.2±10.8	.25	1.5	66.2±12.3
Sex (male)	9721 (80.9)	9665 (80.5)	.36	-1.1	19386 (80.7)
Charlson comorbidity index	4.3±3.0	4.2±2.9	.6	-2.4	4.2±3.0
Frailty index	5.7±3.0	5.6±2.8	.23	-1.5	5.6±2.9
Obesity	2296 (19.1)	2291 (19.1)	.93	-0.1	4587 (19.1)
Dyslipidemia	5015 (41.7)	4973 (41.4)	.58	-0.7	9988 (41.6)
Diabetes mellitus	3773 (31.4)	3768 (31.4)	.94	-0.1	7541 (31.4)
Hypertension	6920 (57.6)	6953 (57.9)	.67	0.6	13873 (57.8)
Smoker	2821 (23.5)	2810 (23.4)	.87	-0.2	5631 (23.4)
Alcohol related diagnoses	686 (5.7)	662 (5.5)	.5	-0.9	1348 (5.6)
Illicit drug use	44 (0.4)	48 (0.4)	.68	0.5	92 (0.4)
Dilated cardiomyopathy	681 (5.7)	647 (5.4)	.34	-1.3	1328 (5.5)
Heart failure with congestion	719 (6.0)	710 (5.9)	.81	-0.3	1429 (5.9)
Aortic stenosis	404 (3.4)	390 (3.2)	.61	-0.7	794 (3.3)
Aortic regurgitation	276 (2.3)	261 (2.2)	.51	-0.9	537 (2.2)
Mitral regurgitation	960 (8.0)	974 (8.1)	.74	0.5	1934 (8.1)
Tricuspid regurgitation	80 (0.7)	75 (0.6)	.69	-0.6	155 (0.6)
Ischemic stroke	359 (3.0)	330 (2.7)	.26	-1.4	689 (2.9)
Atrial fibrillation	2078 (17.3)	2076 (17.3)	.97	0.0	4154 (17.3)
Previous pacemaker or ICD	128 (1.1)	142 (1.2)	.39	0.9	270 (1.1)
Vascular disease	1337 (11.1)	1320 (11.0)	.73	-0.5	2657 (11.1)
Abnormal renal function	545 (4.5)	551 (4.6)	.85	0.2	1096 (4.6)
Liver disease	386 (3.2)	390 (3.2)	.88	0.2	776 (3.2)
Lung disease	1367 (11.4)	1337 (11.1)	.54	-0.8	2704 (11.3)
COPD	836 (7.0)	803 (6.7)	.4	-1.1	1639 (6.8)
Sleep apnea syndrome	512 (4.3)	524 (4.4)	.7	0.5	1036 (4.3)
Anaemia	1328 (11.1)	1310 (10.9)	.71	-0.5	2638 (11.0)
Previous cancer	838 (7.0)	855 (7.1)	.67	0.5	1693 (7.0)
Thyroid diseases	468 (3.9)	486 (4.0)	.55	0.7	954 (4.0)
Cognitive impairment	212 (1.8)	212 (1.8)	.99	0.0	424 (1.8)
Depression	594 (4.9)	589 (4.9)	.88	-0.2	1183 (4.9)
Poor nutrition	340 (2.8)	322 (2.7)	.48	-0.8	662 (2.8)
Anterior MI	4740 (39.5)	4658 (38.8)	.28	-1.4	9398 (39.1)
Inferior MI	3402 (28.3)	3478 (29.0)	.28	1.4	6880 (28.6)
MI with other location	3870 (32.2)	3876 (32.3)	.93	0.1	7746 (32.2)
HF at the acute phase	4231 (35.2)	4185 (34.8)	.53	-0.8	8416 (35.0)
Pulm. edema / shock at the acute phase	859 (7.2)	849 (7.1)	.80	-0.4	1708 (7.1)
Time between STEMI and PCI/CABG (days)	16.5±20.6	17.0±17.8	.05	3.0	16.7±19.2
Death during follow-up	2202 (18.3)	1596 (13.3)	<.001	-	3798 (15.8)
Cardiovascular death	951 (7.9)	816 (6.8)	0.01	-	1767 (7.4)

Values are mean ± standard deviation, or n (%).

AF = atrial fibrillation; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ICD, implantable cardiac defibrillator; STEMI = ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation.

Table 3. Predictors of all-cause death during the whole follow-up in unmatched patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

	Univariate analysis		Multivariable analysis	
	HR, 95%CI	p	HR, 95%CI	p
Age, years	1.053 (1.052-1.055)	<.001	1.042 (1.039-1.044)	<.001
Sex (male)	0.774 (0.744-0.804)	<.001	1.070 (1.026-1.116)	.01
Charlson comorbidity index	1.195 (1.189-1.200)	<.001	1.082 (1.073-1.090)	<.001
Frailty index	1.050 (1.049-1.052)	<.001	1.012 (1.010-1.014)	<.001
Obesity	0.989 (0.941-1.040)	.67	0.914 (0.866-0.964)	.01
Dyslipidemia	0.974 (0.938-1.012)	.18	0.858 (0.823-0.894)	<.001
Diabetes mellitus	1.601 (1.541-1.663)	<.001	1.090 (1.044-1.140)	<.001
Hypertension	1.717 (1.651-1.786)	<.001	0.962 (0.920-1.005)	.08
Smoker	0.683 (0.649-0.718)	<.001	0.979 (0.925-1.036)	.47
Alcohol related diagnoses	1.482 (1.377-1.594)	<.001	1.352 (1.246-1.468)	<.001
Illicit drug use	0.809 (0.565-1.158)	.25	1.218 (0.849-1.746)	.29
Dilated cardiomyopathy	1.872 (1.747-2.005)	<.001	1.037 (0.965-1.113)	.32
Heart failure with congestion	3.293 (3.130-3.465)	<.001	1.713 (1.608-1.825)	<.001
Ischemic stroke	2.007 (1.844-2.185)	<.001	1.101 (1.009-1.200)	.03
Atrial fibrillation	2.273 (2.182-2.368)	<.001	1.176 (1.126-1.229)	<.001
Previous pacemaker or ICD	2.233 (2.027-2.460)	<.001	1.002 (0.907-1.108)	.96
Vascular disease	2.356 (2.248-2.470)	<.001	1.233 (1.170-1.300)	<.001
Abnormal renal function	2.731 (2.577-2.895)	<.001	1.187 (1.114-1.265)	<.001
Liver disease	2.651 (2.450-2.869)	<.001	1.360 (1.248-1.483)	<.001
Lung disease	2.128 (2.033-2.226)	<.001	1.209 (1.125-1.299)	<.001
COPD	2.161 (2.047-2.281)	<.001	1.085 (0.996-1.181)	.06
Sleep apnea syndrome	1.202 (1.102-1.311)	<.001	0.874 (0.798-0.957)	0.003
Anaemia	2.584 (2.464-2.710)	<.001	1.221 (1.159-1.287)	<.001
Previous cancer	2.496 (2.379-2.617)	<.001	1.396 (1.325-1.470)	<.001
Thyroid diseases	1.457 (1.356-1.566)	<.001	0.944 (0.876-1.017)	.13
Cognitive impairment	2.250 (2.088-2.425)	<.001	1.091 (1.008-1.181)	.03
Depression	1.472 (1.376-1.576)	<.001	0.967 (0.899-1.039)	.36
Poor nutrition	2.945 (2.747-3.157)	<.001	1.226 (1.139-1.319)	<.001
Anterior MI	1.104 (1.064-1.145)	<.001	0.944 (0.904-0.985)	0.01
Inferior MI	0.705 (0.676-0.735)	<.001	0.868 (0.826-0.912)	<.001
HF at the acute phase	1.821 (1.754-1.890)	<.001	1.402 (1.341-1.465)	<.001
Pulm. edema / shock at the acute phase	4.434 (4.212-4.668)	<.001	2.946 (2.784-3.118)	<.001
CABG (vs PCI)	0.727 (0.690-0.767)	<.001	0.734 (0.695-0.775)	<.001

AF = atrial fibrillation; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ICD, implantable cardiac defibrillator; STEMI = ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention.

Table 4. Predictors of cardiovascular death during the whole follow-up in unmatched patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

	Univariate analysis		Multivariable analysis	
	HR, 95%CI	p	HR, 95%CI	p
Age, years	1.057 (1.054-1.060)	<.001	1.050 (1.046-1.053)	<.001
Sex (male)	0.665 (0.628-0.704)	<.001	0.959 (0.901-1.020)	.18
Charlson comorbidity index	1.127 (1.119-1.136)	<.001	0.984 (0.971-0.997)	.02
Frailty index	1.035 (1.032-1.038)	<.001	0.996 (0.992-1.000)	.03
Obesity	1.019 (0.947-1.096)	.62	0.944 (0.872-1.022)	.15
Dyslipidemia	1.019 (0.963-1.079)	.52	0.875 (0.822-0.930)	<.001
Diabetes mellitus	1.715 (1.621-1.814)	<.001	1.408 (1.319-1.503)	<.001
Hypertension	1.794 (1.691-1.904)	<.001	0.996 (0.932-1.064)	.90
Smoker	0.606 (0.560-0.655)	<.001	0.942 (0.863-1.028)	0.18
Alcohol related diagnoses	1.233 (1.097-1.385)	<.001	1.330 (1.170-1.512)	<.001
Illicit drug use	0.603 (0.334-1.090)	.09	1.169 (0.644-2.119)	.61
Dilated cardiomyopathy	1.988 (1.802-2.194)	<.001	1.049 (0.948-1.162)	.35
Heart failure with congestion	3.529 (3.282-3.793)	<.001	2.304 (2.098-2.530)	<.001
Ischemic stroke	2.148 (1.907-2.420)	<.001	1.377 (1.218-1.557)	<.001
Atrial fibrillation	2.487 (2.343-2.639)	<.001	1.220 (1.145-1.301)	<.001
Previous pacemaker or ICD	2.415 (2.107-2.766)	<.001	1.068 (0.928-1.230)	.36
Vascular disease	2.525 (2.359-2.703)	<.001	1.545 (1.431-1.668)	<.001
Abnormal renal function	2.745 (2.524-2.986)	<.001	1.352 (1.232-1.483)	<.001
Liver disease	2.513 (2.237-2.823)	<.001	1.625 (1.433-1.842)	<.001
Lung disease	1.908 (1.781-2.045)	<.001	1.289 (1.161-1.432)	<.001
COPD	1.803 (1.655-1.963)	<.001	0.997 (0.877-1.134)	.97
Sleep apnea syndrome	1.094 (0.957-1.250)	.19	0.834 (0.725-0.958)	.01
Anaemia	2.264 (2.106-2.433)	<.001	1.117 (1.032-1.209)	.01
Previous cancer	1.552 (1.430-1.684)	<.001	1.098 (1.005-1.199)	.04
Thyroid diseases	1.535 (1.383-1.703)	<.001	0.970 (0.871-1.080)	.58
Cognitive impairment	2.102 (1.881-2.349)	<.001	1.176 (1.045-1.324)	.01
Depression	1.411 (1.274-1.562)	<.001	1.007 (0.904-1.122)	.89
Poor nutrition	2.381 (2.140-2.649)	<.001	1.092 (0.977-1.221)	.12
Anterior MI	1.176 (1.113-1.242)	<.001	0.978 (0.917-1.043)	.49
Inferior MI	0.668 (0.626-0.712)	<.001	0.860 (0.797-0.927)	<.001
HF at the acute phase	2.147 (2.032-2.268)	<.001	1.767 (1.652-1.891)	<.001
Pulm. edema / shock at the acute phase	5.881 (5.492-6.297)	<.001	3.824 (3.544-4.127)	<.001
CABG (vs PCI)	0.856 (0.794-0.922)	<.001	0.884 (0.818-0.956)	.01

AF = atrial fibrillation; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ICD, implantable cardiac defibrillator; STEMI = ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention.

Table 5. Clinical outcomes during the whole follow-up (mean [SD] 2.6 [2.7], median [IQR] 1.8 [0.1-4.6] years) in matched patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

	PCI (n=12012)	CABG (n=12012)	HR (95% CI) for CABG vs PCI	p (uncorrected)
All-cause death	2202 (7.1)	1596 (5.1)	0.70 (0.66-0.75)	<.001
Cardiovascular death	951 (3.1)	816 (2.6)	0.83 (0.76-0.91)	<.001
Non-cardiovascular death	1251 (4.1)	780 (2.5)	0.61 (0.56-0.66)	<.001
Worsening heart failure	2026 (7.5)	1569 (5.5)	0.76 (0.71-0.81)	<.001
All-cause stroke	699 (2.3)	638 (2.1)	0.89 (0.80-1.00)	0.04
Major bleeding	1309 (4.6)	1658 (6.1)	1.31 (1.22-1.41)	<.001
Negative control analysis:				
Cancer	1187 (4.1)	1120 (3.8)	0.92 (0.85-1.00)	0.04
Urinary infection	808 (2.7)	841 (2.8)	1.04 (0.94-1.14)	0.46

Values are n (incidence rate, %/year). CI=confidence interval; HF=heart failure; HR=hazard ratio; STEMI = ST-segment elevation myocardial infarction.

Figures legends

Figure 1: Flow chart of the study

Figure 2: Cumulative incidence of all-cause death (top panel) and of cardiovascular death (lower panel) in matched patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

Figure 3: Cumulative incidence of rehospitalization for heart failure (top panel) and of ischemic stroke (lower panel) in matched patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

Figure 4: Cumulative incidence of major bleeding in matched patients with STEMI treated with PCI or CABG in day 3-90 after STEMI.

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