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Predictors of adverse events among patients undergoing primary percutaneous coronary intervention: insights from a pooled analysis of the COMFORTABLE AMI and EXAMINATION trials

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KEYWORDS

- drug-eluting stent
- percutaneous coronary intervention
- primary angioplasty
- ST-segment elevation myocardial infarction

Abstract

Aims: The aim of this study was to identify predictors of adverse events among patients with ST-elevation myocardial infarction (STEMI) undergoing contemporary primary percutaneous coronary intervention (PCI).

Methods and results: Individual data of 2,655 patients from two primary PCI trials (EXAMINATION, N=1,504; COMFORTABLE AMI, N=1,161) with identical endpoint definitions and event adjudication were pooled. Predictors of all-cause death or any reinfarction and definite stent thrombosis (ST) and target lesion revascularisation (TLR) outcomes at one year were identified by multivariable Cox regression analysis. Killip class III or IV was the strongest predictor of all-cause death or any reinfarction (OR 5.11, 95% CI: 2.48-10.52), definite ST (OR 7.74, 95% CI: 2.87-20.93), and TLR (OR 2.88, 95% CI: 1.17-7.06). Impaired left ventricular ejection fraction (OR 4.77, 95% CI: 2.10-10.82), final TIMI flow 0-2 (OR 1.93, 95% CI: 1.05-3.54), arterial hypertension (OR 1.69, 95% CI: 1.11-2.59), age (OR 1.68, 95% CI: 1.41-2.01), and peak CK (OR 1.25, 95% CI: 1.02-1.54) were independent predictors of all-cause death or any reinfarction. Allocation to treatment with DES was an independent predictor of a lower risk of definite ST (OR 0.35, 95% CI: 0.16-0.74) and any TLR (OR 0.34, 95% CI: 0.21-0.54).

Conclusions: Killip class remains the strongest predictor of all-cause death or any reinfarction among STEMI patients undergoing primary PCI. DES use independently predicts a lower risk of TLR and definite ST compared with BMS. The COMFORTABLE AMI trial is registered at: http://www.clinicaltrials.gov/ct2/show/NCT00962416. The EXAMINATION trial is registered at: http://www.clinicaltrials.gov/ct2/show/NCT00828087

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Introduction

Mortality after acute ST-segment elevation myocardial infarction (STEMI) has considerably declined during the last two decades owing to improved access to and the widespread use of reperfusion therapy[1]. Primary percutaneous coronary intervention (PCI) has emerged as the reperfusion therapy of choice due to its lower risk of reinfarction and haemorrhagic stroke and improved vessel patency, translating into lower mortality as compared to fibrinolysis[2]. However, cardiac mortality is still observed in up to 4% of patients undergoing primary PCI at one-year follow-up[3,4]. Moreover, STEMI patients undergoing primary PCI remain at risk for reinfarction, stent thrombosis and repeat revascularisation, underlining the need to identify predictors of adverse clinical outcomes in this high-risk population.

The impact of clinical characteristics on prognosis among STEMI patients has been investigated in numerous studies during the fibrinolysis era, which consistently identified Killip class, age, heart rate, and anterior MI as independent predictors of mortality[5,6]. More recently, impaired left ventricular ejection fraction (LVEF) and angiographic variables – such as multivessel disease and small vessel diameter – have been reported to predict mortality among STEMI patients undergoing primary PCI[7,8]. However, these findings were based on studies without systematic use of P2Y12 receptor inhibitors, thrombus aspiration and stent implantation, which have significantly improved clinical outcomes[9-13,14]. In addition, the results of two large-scale randomised clinical trials have recently suggested that the use of new-generation drug-eluting stents (DES) among STEMI patients undergoing primary PCI is associated with a lower risk of repeat revascularisation, reinfarction and stent thrombosis (ST) compared with bare metal stents through to one year[15,16]. The purpose of the present study was therefore to identify predictors of all-cause death or any reinfarction and definite ST, target lesion revascularisation (TLR) among patients with STEMI undergoing primary PCI in a pooled analysis of two contemporary primary PCI trials (EXAMINATION and COMFORTABLE AMI)[15,16].

Methods

PATIENT POPULATION

Individual patient data from COMFORTABLE AMI and EXAMINATION were pooled for the purpose of the present study. The details and primary results of the COMFORTABLE AMI and EXAMINATION trials have been described previously[15,16]. In summary, 1,161 STEMI patients undergoing primary PCI at 11 sites in Europe and Israel between September 2009 and January 2011 were randomly assigned to treatment with biolimus-eluting stents with biodegradable polymer coating (BioMatrix™; Biosensors Europe SA, Morges, Switzerland), or bare metal stents (Gazelle™; Biosensors Europe SA) in the COMFORTABLE AMI trial. In the EXAMINATION trial, 1,504 STEMI patients undergoing primary PCI at 12 sites in Europe between December 2008 and May 2010 were randomly assigned to treatment with everolimus-eluting stents with durable polymer coating (XIENCE V; Abbott Vascular, Santa Clara, CA, USA), or bare metal stents (MULTI-LINK VISION™; Abbott Vascular). Overall, 10 out of 2,665 patients withdrew consent after randomisation (six patients in EXAMINATION and four patients in COMFORTABLE AMI). For the purpose of this analysis, 2,655 patients allocated to new-generation DES (N=1,326) or bare metal stents (N=1,329) were pooled. A summary of the principal trial characteristics is reported in **Table 1**.

ENDPOINT DEFINITIONS AND EVENT ADJUDICATION

The same clinical endpoint definitions were used in COMFORTABLE AMI and EXAMINATION[15,16]. All-cause mortality included cardiac death, vascular death, and non-cardiovascular death. All deaths were considered cardiac unless an unequivocal non-cardiac cause could be established. Reinfarction was defined according to the WHO extended historical definition[17]. Target lesion revascularisation (TLR) was defined as any repeat revascularisation due to a stenosis within the index stent or within a 5 mm border proximal and distal to the index stent. Stent thrombosis (ST) was defined according to the Academic Research Consortium criteria[18]. In both the COMFORTABLE AMI

Table 1. Summary of included trials.

Study	No. of patients	Stent type	Primary endpoint	Inclusion criteria	Exclusion criteria	Baseline characteristics								
						Mean age, years (SD)	Male,%	Diabetes,%	LVEF, mean	Hyperlipidaemia, %	Hypertension, %	Smoking, %	Family history, %	Clinical follow-up
COMFORTABLE AMI	1,161	BES vs. BMS	Composite of cardiac death, target vessel MI, clinically indicated TLR at 1 year	Primary PCI within 24 hours, evidence of ischaemia	Age <18, intolerance to medication, use of vitamin K agents secondary to ST, mechanical complications, planned surgery within 6 months	60.6 (11.7)	79.3	15.0	49.5	56.4	47.0	49.5	32.1	1 year
EXAMINATION	1,504	EES vs. BMS	Composite of death, any MI, TVR at 1 year	Primary PCI within 48 hours, evidence of ischaemia	Age <18, intolerance to medication, use of vitamin K agents secondary to ST	61.2 (12.5)	83.0	17.2	51.1	43.7	48.4	72.2	16.8	1 year

BES: biolimus-eluting stent; BMS: bare metal stent; EES: everolimus-eluting stent; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention; SD: standard deviation; ST: stent thrombosis; TLR: target lesion revascularisation; TVR: target vessel revascularisation

and EXAMINATION trials, adverse events were independently adjudicated by a clinical events committee, chaired by the same investigator (PV), unaware of treatment allocation. The pre-specified primary endpoint of the present analysis was the composite of all-cause death and any reinfarction. Secondary endpoints were definite ST and target lesion revascularisation. Angiograms were centrally assessed by the independent core laboratory at Bern University Hospital, Bern, Switzerland, and Cardialysis, Rotterdam, The Netherlands by personnel blinded to stent type and outcome. Killip class I includes patients without clinical signs of heart failure. Killip class II includes patients with rales or crackles of <50% in both lung fields as well as the presence of an audible S3 heart sound, and elevated jugular venous pressure. Killip class III includes patients with rales or crackles of >50% in both lung fields as well as the presence of an audible S3 heart sound, and elevated jugular venous pressure. Killip class IV includes patients in cardiogenic shock or hypotension, and evidence of peripheral vasoconstriction.

STATISTICAL METHODS

For the purpose of the present study, patient-level data from the EXAMINATION and COMFORTABLE AMI trials were pooled and analysed. Continuous variables are expressed as means±standard deviation and compared by means of ANOVA. Categorical data are expressed as frequencies and percentages and are compared using the χ^2 and Fisher's exact tests. Mixed effects logistic regressions with random effect of the study (EXAMINATION or COMFORTABLE AMI) were used for the analyses of all-cause death or any reinfarction, TLR or definite ST. Odds ratios (OR) with 95% confidence intervals (95% CI) are reported. Univariable and multivariable mixed effects logistic regressions tested the association of single and multiple risk factors, respectively, with outcomes of interest (all-cause death or any reinfarction, TLR and definite ST). Multivariable risk factors with a p-value below 0.05 were retained for each minimal model, with OR (95% CI) reported. Estimates for the multivariable and minimal models are after multiple imputation of missing data per study using chained equations. For illustrative purposes, a classification and regression tree (CART) for time-to-death or reinfarction was constructed from the minimal model (with splits set at p-value <0.05, with each group after the split including a minimum of 10 patients and/or 10 events) using non-missing data only. All p-values shown are from two-sided tests, and the level of statistical significance was set at 0.05. Analyses were performed using Stata 12 (StataCorp, College Station, TX, USA).

Results

One-year follow-up was available in 2,617 of 2,655 patients (98.6%). At one year, the composite of all-cause death and any reinfarction occurred in 144 patients (5.4%), definite ST in 35 patients (1.3%), and TLR in 96 patients (3.6%).

PREDICTORS OF ALL-CAUSE DEATH AND ANY REINFARCTION

Baseline clinical, angiographic, and procedural characteristics according to the occurrence of all-cause death or any reinfarction at one year are summarised in **Table 2**. Patients who experienced all-cause death or any reinfarction after primary PCI were older, more likely to be female, and more frequently had increased heart rate, hypertension, non-smoking habits, diabetes mellitus, impaired left ventricular ejection fraction, previous MI, Killip class III or IV, longer stent length, final TIMI flow 0-2, and higher CK peak value. Independent predictors of all-cause death or any reinfarction after multivariable analysis are shown in **Figure 1** and comprise in decreasing order: Killip class III or IV (OR 5.11, 95% CI: 2.48-10.52), left ventricular ejection fraction <0.30 (OR 4.77, 95% CI: 2.10-10.82), final TIMI flow 0-2 (OR 1.93, 95% CI: 1.05-3.54), hypertension (OR 1.69, 95% CI: 1.11-2.59), age (OR 1.68, 95% CI: 1.41-2.01), and CK peak (OR 1.25, 95% CI: 1.02-1.54).

Table 2. Baseline characteristics of patients with and without all-cause death or any reinfarction at one year.

	All-cause death or any reinfarction		
	Yes (N=144)	No (N=2,511)	*p*-value
Age (yrs)	69.6±13.0	60.43±11.88	<0.001
Male gender	96 (66.7%)	2,066 (82.3%)	<0.001
Body mass index (kg/m^2)	26.9±4.6	27.3±4.0	0.22
Heart rate on admission	80.4±18.1	76.3±16.6	0.004
Blood pressure - systolic (mmHg)	126.4±28.1	127.7±23.1	0.54
Hypertension	97 (67.4%)	1,172 (46.7%)	<0.001
Family history of CAD	28 (20.9%)	597 (25.0%)	0.35
Smoking at baseline	50 (35.2%)	1,281 (51.3%)	<0.001
Dyslipidaemia	70 (49.0%)	1,237 (49.4%)	0.93
Diabetes mellitus	41 (28.5%)	391 (15.6%)	<0.001
Left ventricular ejection fraction <30%	14 (13.0%)	27 (1.3%)	<0.001
Previous MI	15 (10.4%)	128 (5.1%)	0.012
Previous PCI	8 (5.6%)	99 (3.9%)	0.38
Killip class III or IV	23 (16.1%)	37 (1.5%)	<0.001
Primary PCI (<12 hrs)	121 (84.0%)	2,198 (87.6%)	0.20
Multivessel treatment	8 (5.6%)	103 (4.1%)	0.39
Number of lesions treated per patient	1.2±0.5	1.2±0.4	0.50
Treatment of LAD	64 (44.4%)	1,049 (41.8%)	0.54
Total stent length per patient (mm)	30.7±16.6	27.7±14.6	0.019
Maximal stent diameter (mm)	3.2±0.4	3.2±0.4	0.97
TIMI flow 0-2 before PCI	119 (83.8%)	2,069 (82.8%)	0.82
Final TIMI flow 0-2	29 (20.4%)	128 (5.1%)	<0.001
Thrombus aspiration	96 (66.7%)	1,604 (63.9%)	0.53
Drug-eluting stent allocation	65 (45.1%)	1,261 (50.2%)	0.27
Any dual antiplatelet therapy	136 (94.4%)	2,363 (94.1%)	1.00
CK peak value	2,935.3±2,867.7	2,123.3±1,993.1	<0.001

Values are n (%) or mean±SD. CAD: coronary artery disease; CK: creatine kinase; LAD: left anterior descending artery; MI: myocardial infarction; PCI: percutaneous coronary intervention; TIMI: Thrombolysis In Myocardial Infarction

CART ANALYSIS

Figure 2 shows the results of a CART analysis, depicting the most important variables which influenced the likelihood of all-cause death or any reinfarction in a hierarchical order through to one

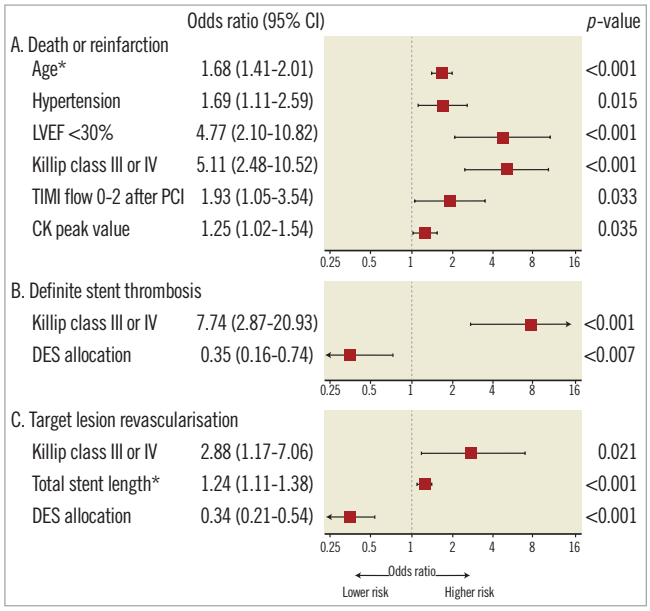

Figure 1. *Independent predictors of adverse events. Multivariate analysis of predictors of (A) all-cause death or any reinfarction, (B) definite stent thrombosis, and (C) target lesion revascularisation. CK: creatine kinase; DES: drug-eluting stent; LVEF: left ventricular ejection fraction; OR: odds ratio; TIMI: Thrombolysis In Myocardial Infarction. *OR per 10 units increase for age (year) and total stent length (mm). **OR per log-transformed CK peak value.*

year. Killip class was the strongest predictor followed by age, left ventricular ejection fraction, and final TIMI flow 0-2. A patient with Killip class I or II, age ≤80, left ventricular ejection fraction ≥30%, and final TIMI 3 flow has a one-year mortality as low as 2.6%. Conversely, a patient with Killip class III or IV, age >80, left ventricular ejection fraction <30%, and final TIMI 0-2 flow has a considerably increased risk of all-cause death or any reinfarction ranging from 6.5% to 36.5% at one year.

PREDICTORS OF STENT THROMBOSIS

Baseline clinical, angiographic, and procedural characteristics according to the occurrence of definite ST at one year are summarised in **Table 3**. Patients suffering definite ST more frequently presented with Killip class III or IV and were less frequently treated with DES. All definite ST events among patients with Killip class III or IV occurred within six days. After multivariable analysis, Killip class III or IV (OR 7.74, 95% CI: 2.87-20.93) and use of DES (OR 0.35, 95% CI: 0.16-0.74) emerged as independent predictors of definite ST **(Figure 1)**.

PREDICTORS OF TARGET LESION REVASCULARISATION

Baseline clinical, angiographic, and procedural characteristics according to the occurrence of TLR at one year are summarised in **Table 4**. Patients undergoing TLR more frequently had previous PCI and Killip class III or IV, had a higher number of lesions to be treated resulting in longer total stent length, and had less frequently

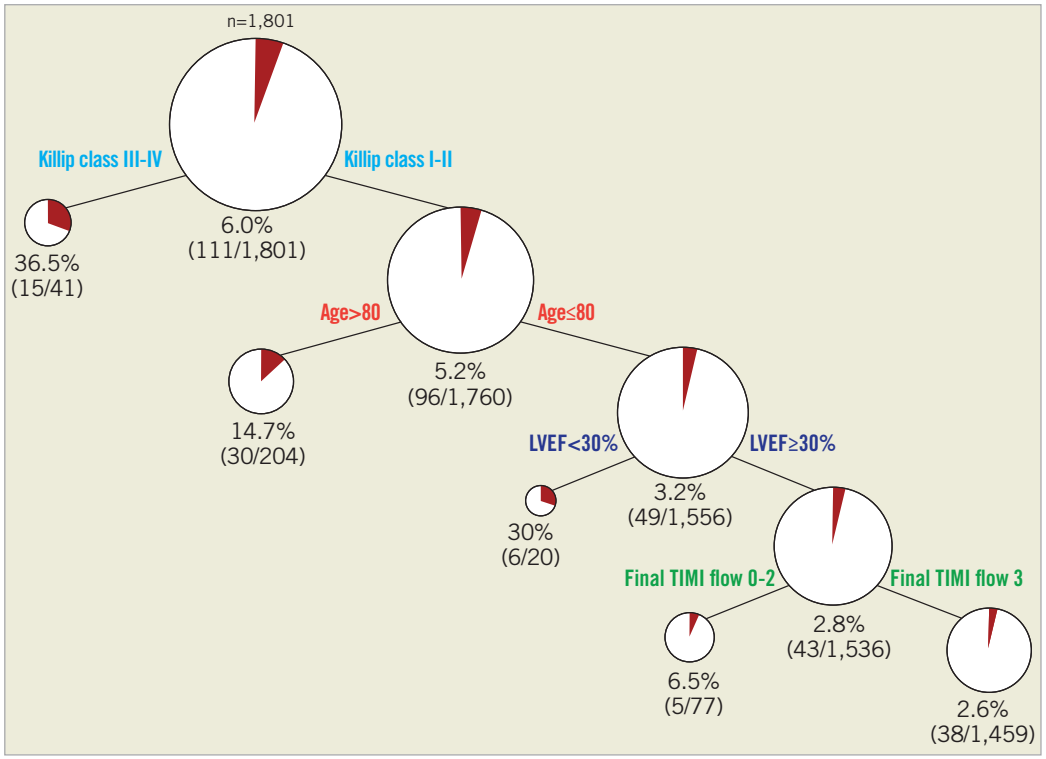

Figure 2. *CART model of predictors of all-cause death or reinfarction. CART analysis showing in a hierarchical order the most important variables influencing the likelihood of all-cause death or reinfarction at one year. LVEF: left ventricular ejection fraction; TIMI: Thrombolysis In Myocardial Infarction*

Table 3. Baseline characteristics of patients with and without definite stent thrombosis at one year.

	Definite stent thrombosis		
	Yes (N=35)	No (N=2,620)	*p*-value
Age (yrs)**	61.3±10.5	60.9±12.2	0.85
Male gender	31 (88.6%)	2,131 (81.3%)	0.38
Body mass index (kg/m^2)**	28.2±4.2	27.3±4.0	0.20
Heart rate on admission**	75.7±17.1	76.5±16.7	0.78
Blood pressure - systolic (mmHg)**	122.3±25.7	127.7±23.4	0.19
Hypertension	19 (54.3%)	1,250 (47.7%)	0.50
Family history of CAD	11 (34.4%)	614 (24.6%)	0.22
Smoking at baseline	16 (45.7%)	1,315 (50.5%)	0.61
Dyslipidaemia	16 (45.7%)	1,291 (49.4%)	0.76
Diabetes mellitus	7 (20.0%)	425 (16.2%)	0.49
Left ventricular ejection fraction <30%	1 (3.2%)	40 (1.9%)	0.46
Previous MI	4 (11.4%)	139 (5.3%)	0.12
Previous PCI	2 (5.7%)	105 (4.0%)	0.65
Killip class III or IV	5 (14.3%)	55 (2.1%)	0.001
Primary PCI (<12 hrs)	32 (91.4%)	2,287 (87.4%)	0.61
Multivessel treatment	0 (0.0%)	111 (4.2%)	0.40
Number of lesions treated per patient	1.1±0.4	1.2±0.4	0.64
Treatment of LAD	12 (34.3%)	1,101 (42.0%)	0.39
Total stent length per patient (mm)**	29.6±10.8	27.8±14.8	0.49
Maximal stent diameter (mm)	3.3±0.5	3.2±0.4	0.26
TIMI flow 0-2 before PCI	30 (85.7%)	2,158 (82.8%)	0.82
Final TIMI flow 0-2	2 (5.7%)	155 (5.9%)	1.00
Thrombus aspiration	26 (74.3%)	1,674 (63.9%)	0.22
Drug-eluting stent allocation	9 (25.7%)	1,317 (50.3%)	0.006
Any dual antiplatelet therapy	34 (97.1%)	2,465 (94.1%)	0.72
CK peak value***	2,672.0±2,329.6	2,161.5±2,055.0	0.17

Values are n (%) or mean±SD. CAD: coronary artery disease; CK: creatine kinase; LAD: left anterior descending artery; MI: myocardial infarction; PCI: percutaneous coronary intervention; TIMI: Thrombolysis In Myocardial Infarction

Table 4. Baseline characteristics of patients with and without target lesion revascularisation at one year.

	TLR		
	Yes (N=96)	No (N=2,559)	*p*-value
Age (yrs)**	62.9±10.7	60.9±12.2	0.11
Male gender	83 (86.5%)	2,079 (81.2%)	0.23
Body mass index (kg/m^2)**	27.9±3.9	27.3±4.0	0.15
Heart rate on admission**	76.0±14.8	76.5±16.7	0.73
Blood pressure - systolic (mmHg)**	127.3±5.6	127.6±23.3	0.90
Hypertension	52 (54.2%)	1,217 (47.6%)	0.21
Family history of CAD	30 (32.3%)	595 (24.5%)	0.09
Smoking at baseline	44 (45.8%)	1,287 (50.6%)	0.41
Dyslipidaemia	46 (47.9%)	1,261 (49.4%)	0.84
Diabetes mellitus	21 (21.9%)	411 (16.1%)	0.16
Left ventricular ejection fraction <30%	2 (2.4%)	39 (1.9%)	0.67
Previous MI	7 (7.3%)	136 (5.3%)	0.36
Previous PCI	9 (9.4%)	98 (3.8%)	0.014
Killip class III or IV	6 (6.3%)	54 (2.1%)	0.020
Primary PCI (<12 hrs)	88 (91.7%)	2,231 (87.3%)	0.27
Multivessel treatment	8 (8.3%)	103 (4.0%)	0.06
Number of lesions treated per patient	1.3±0.6	1.2±0.4	0.002
Treatment of LAD	42 (43.8%)	1,071 (41.9%)	0.75
Total stent length per patient (mm)**	33.6±17.2	27.7±14.6	<0.001
Maximal stent diameter (mm)	3.2±0.5	3.2±0.4	0.12
TIMI flow 0-2 before PCI	72 (75.8%)	2,116 (83.1%)	0.07
Final TIMI flow 0-2	5 (5.2%)	152 (6.0%)	1.00
Thrombus aspiration	58 (60.4%)	1,642 (64.2%)	0.45
Drug-eluting stent allocation	25 (26.0%)	1,301 (50.8%)	<0.001
Any dual antiplatelet therapy	94 (97.9%)	2,405 (94.0%)	0.12
CK peak value***	2,275.1±2,441.2	2,164.7±2,044.0	0.64

Values are n (%) or mean±SD. CAD: coronary artery disease; CK: creatine kinase; LAD: left anterior descending artery; MI: myocardial infarction; PCI: percutaneous coronary intervention; TIMI: Thrombolysis In Myocardial Infarction; TLR: target lesion revascularisation

received DES. Independent predictors of TLR after multivariable analysis are shown in **Figure 1**, and include Killip class III or IV (OR 2.88, 95% CI: 1.17-7.06), stent length (OR 1.24, 95% CI: 1.11-1.38), and DES allocation (OR 0.34, 95% CI: 0.21-0.54).

Discussion

The findings of this analysis reporting predictors of adverse events among STEMI patients undergoing contemporary primary PCI in two large-scale randomised trials can be summarised as follows:

– One-year rates of all-cause death and any reinfarction are relatively low in the contemporary primary PCI era.

– Killip class III or IV remains the strongest predictor of all-cause death or any reinfarction, definite ST, and TLR.

– The use of DES independently predicts a lower risk of TLR and definite ST as compared with BMS.

The introduction of reperfusion strategies with the use of fibrinolytic agents as well as aspirin have significantly reduced mortality in STEMI patients[19,20]. More recently, mechanical reperfusion by means of primary PCI with stenting, in conjunction with potent platelet inhibitors, has further reduced in-hospital mortality to as low as 3%. It is worth noting that the decline in early mortality was consistently observed in nationwide surveys in the United States and Europe[21,22]. However, there is a paucity of information on predictors of all-cause death and reinfarction among patients with STEMI undergoing contemporary reperfusion with primary PCI.

PREDICTORS OF ALL-CAUSE DEATH AND ANY REINFARCTION

The present analysis shows that independent predictors of all-cause death and any reinfarction have not changed significantly despite changes in reperfusion and adjunctive therapy. Killip class at presentation was identified as a predictor of mortality in the fibrinolysis era, as reported in the GUSTO-I and TIMI trials[5,23]. Similar findings have been observed in the BMS era (CADILLAC), and more recently in the HORIZONS-AMI trial comparing early-generation

paclitaxel-eluting stents and BMS[7,24,25]. The fact that Killip class remains the strongest predictor of all-cause death and any reinfarction, irrespective of left ventricular function and extent of coronary artery disease at baseline, reflects the degree of haemodynamic compromise in these patients which can be recognised easily on clinical grounds.

In addition to Killip class, other predictors of death and reinfarction identified in our analysis included age, hypertension, left ventricular ejection fraction, final TIMI flow and CK peak value, which have traditionally been considered major risk factors of ischaemic adverse events after STEMI and have been consistently identified in previous reports as predictors of death and reinfarction among STEMI patients treated with fibrinolysis as well as primary PCI[5,7,23,26].

PREDICTORS OF STENT THROMBOSIS AND TARGET LESION REVASCULARISATION

Beyond Killip class, other independent predictors of definite ST and TLR are all device-related. Given the fact that all definite ST among patients with Killip class III or IV occurred within six days of PCI, it appears important to ensure optimal procedural results avoiding residual dissections, inadequate stent expansions, and to install adequate antithrombotic treatment during and after the procedure.

Importantly, DES allocation predicted a reduced risk of both ST and TLR. The higher effectiveness of DES compared with BMS, leading to a reduced risk of restenosis and repeat revascularisation procedures, has been evidenced since the introduction of DES in clinical practice among patients with stable angina as well as STEMI[13]. However, safety concerns were raised with respect to the use of early-generation sirolimus-eluting and paclitaxel-eluting stents in the setting of STEMI[27]. Two recent network meta-analyses have reported a lower risk of ST with new-generation DES compared with BMS[28,29]. Similar results were observed in the EXAMINATION trial[30]. These findings can be explained at least in part by a lower thrombogenicity observed *in vitro* with new-generation DES compared with BMS[31]. In line with these recent reports, the present large-scale patient-level analysis shows that DES allocation reduced the risk of definite ST by 70% in patients with STEMI at one year. Of note, BioMatrix and Gazelle have identical stent platforms, and the same applies to XIENCE V and MULTI-LINK VISION. Therefore, the differences between the DES used and their BMS comparators were limited to polymer coatings and antiproliferative agent release. Whether this benefit persists beyond the first year after PCI will need to be confirmed by longer-term follow-up of available trials as well as by future studies powered for safety endpoints.

As it relates to device effectiveness, stent length independently predicted TLR in our analysis. Several reports have associated stent length with an increased risk of repeat revascularisation after PCI in patients with stable angina and STEMI[32,33]. This may be related to the higher degree of vascular injury after implantation of longer and/or overlapping metallic stents[34].

Study limitations

Some limitations of the present analysis deserve discussion. First, time from symptom onset to reperfusion was not available. However, both the COMFORTABLE AMI and EXAMINATION trials were conducted in European countries with developed STEMI networks. Therefore, one can assume a low degree of variability in time-to-reperfusion across the centres involved in the two trials. Second, baseline characteristics captured in the COMFORTABLE AMI and EXAMINATION trials were not identical. Therefore, we cannot exclude that unmeasured variables, such as renal failure and anaemia, might have emerged as independent predictors of adverse events if available for analysis. Third, high-volume European tertiary centres recruited patients in the COMFORTABLE AMI and EXAMINATION trials. For this reason, our findings may not be generalisable to different healthcare settings. Fourth, the currently available universal definition of MI was not applied in this study which would probably have resulted in somewhat higher event rates, particularly during the follow-up phase. However, one of the strengths of this pooled analysis is the uniform definition as well as the adjudication of the endpoint MI in both studies. Fifth, the aim of this analysis was to identify baseline predictors of adverse events. Evaluating the impact of any changes in adherence to medications over time was beyond the scope of this analysis. Finally, clinical follow-up was limited to one year. It cannot be excluded that predictors of longer-term outcomes might differ from the ones identified in this analysis. Nevertheless, it is notable that over 60% of adverse events in patients with STEMI occur during the first year of follow-up[35]. Therefore, predictors of one-year outcomes remain of importance to identify high-risk subsets among patients with STEMI undergoing percutaneous reperfusion in the contemporary era of primary PCI.

Conclusions

Killip class remains the strongest predictor of all-cause death or reinfarction among STEMI patients undergoing primary PCI. DES use independently predicts a lower risk of TLR and definite ST compared with BMS.

Impact on daily practice

Patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) remain at high risk of adverse events, including death, reinfarction, stent thrombosis and repeat revascularisation. This underlines the need to identify predictors of impaired clinical outcomes in order to recognise higher-risk patients in contemporary practice of primary PCI. According to our findings, Killip class remains the strongest predictor of death or reinfarction in STEMI patients undergoing primary PCI, which highlights that a simple clinical assessment remains of key importance in this setting. In addition, the use of DES independently predicts a lower risk of definite stent thrombosis and target lesion revascularisation compared with bare metal stents, suggesting that DES should be considered the standard of care in STEMI patients undergoing primary PCI.

Conflict of interest statement

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