Multivessel versus culprit vessel percutaneous coronary intervention in ST-elevation myocardial infarction: is more worse?

Milosz Jaguszewski[1], MD; Dragana Radovanovic[2], MD; Brahmajee K. Nallamothu[3], MD; Thomas F. Lüscher[1], MD; Philip Urban[4], MD; Franz R. Eberli[5], MD; Osmund Bertel[6], MD; Giovanni B. Pedrazzini[7], MD; Stephan Windecker[8], MD; Raban Jeger[9], MD; Paul Erne[2,10]*, MD; for the AMIS Plus Investigators

1. Department of Cardiology, University Hospital Zurich, Zurich, Switzerland; 2. AMIS Plus Data Center, Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland; 3. Division of Cardiovascular Diseases, University of Michigan, Ann Arbor, MI, USA; 4. Cardiovascular Department, Hôpital de La Tour, Geneva, Switzerland; 5. Division of Cardiology, Stadtspital Triemli, Zurich, Switzerland; 6. Cardiology Centre, Klinik Im Park, Zurich, Switzerland; 7. Division of Cardiology, CardioCentro Ticino, Lugano, Switzerland; 8. Division of Cardiology, Inselspital, Bern, Switzerland; 9. Cardiology Department, University Hospital, Basel, Switzerland; 10. Division of Cardiology, Luzerner Kantonsspital, Lucerne, Switzerland

M. Jaguszewski, D. Radovanovic and B.K. Nallamothu contributed equally to this work.

KEYWORDS

- multivessel PCI
- STEMI

Abstract

Aims: We examined what type of STEMI patients are more likely to undergo multivessel PCI (MPCI) in a "real-world" setting and whether MPCI leads to worse or better outcomes compared with single-vessel PCI (SPCI) after stratifying patients by risk.

Methods and results: Among STEMI patients enrolled in the Swiss AMIS Plus registry between 2005 and 2012 (n=12,000), 4,941 were identified with multivessel disease. We then stratified patients based on MPCI use and their risk. High-risk patients were identified *a priori* as those with: 1) left main (LM) involvement (lesions, n=263); 2) out-of-hospital cardiac arrest; or 3) Killip class III/IV. Logistic regression models examined for predictors of MPCI use and the association between MPCI and in-hospital mortality. Three thousand eight hundred and thirty-three (77.6%) patients underwent SPCI and 1,108 (22.4%) underwent MPCI. Rates of MPCI were greater among high-risk patients for each of the three categories: 8.6% vs. 5.9% for out-of-hospital cardiac arrest (p<0.01); 12.3% vs. 6.2% for Killip III/IV (p<0.001); and 14.5% vs. 2.7% for LM involvement (p<0.001). Overall, in-hospital mortality after MPCI was higher when compared with SPCI (7.3% vs. 4.4%; p<0.001). However, this result was not present when patients were stratified by risk: in-hospital mortality for MPCI vs. SPCI was 2.0% vs. 2.0% (p=1.00) in low-risk patients and 22.2% vs. 21.7% (p=1.00) in high-risk patients.

Conclusions: High-risk patients are more likely to undergo MPCI. Furthermore, MPCI does not appear to be associated with higher mortality after stratifying patients based on their risk.

Corresponding author: AMIS Plus Data Center, Hirschengraben 84, CH-8001 Zurich, Switzerland.
E-mail: paul.erne@erne-net.ch

Introduction

Primary percutaneous coronary intervention (PCI) is the preferred treatment option for restoring epicardial flow and myocardial reperfusion of a culprit lesion in patients with STEMI[1]. However, the vascular process leading to myocardial infarction is frequently not limited to the culprit vessel, as multivessel disease is present in 40-65% of STEMI patients. The presence of multivessel disease is believed to worsen outcomes compared with single-vessel disease[2,3] due to dysfunction extending into the non-infarct zone, a combination of stunned and/or hibernating myocardium, and slow flow and endothelial dysfunction in non-culprit vessels[4].

Routine use of PCI in additional lesions at the time of STEMI has not been shown to be beneficial in patients with multivessel disease and, in fact, is largely felt to be harmful[5,6]. Current guidelines suggest that multivessel PCI (MPCI) at the time of STEMI is not beneficial (Class III, level of evidence C) and should be reserved for high-risk patients only[1,5,6]. A number of prospective and retrospective studies have examined this question specifically[7-13], with a recent and comprehensive meta-analysis including over 40,000 STEMI patients suggesting that MPCI should be discouraged[14]. However, this analysis combined data from studies that used mixed approaches for risk adjustment. This last point is crucial as MPCI is most likely to be done in STEMI patients who are critically ill. With no large clinical trials to guide physicians in this area, the issue remains contentious.

In this context, we used the Swiss AMIS Plus registry to understand better what types of STEMI patients with multivessel disease are undergoing MPCI in a "real-world" setting, and then to determine whether these patients are more likely to benefit from MPCI versus single-vessel PCI (SPCI) after stratifying patients based on their risk.

Editorial, see page 895

Methods

STUDY DESIGN AND STUDY POPULATION

The AMIS (Acute Myocardial Infarction in Switzerland) Plus project founded in 1997 is an ongoing nationwide prospective registry of patients admitted with ACS to hospitals in Switzerland. Details have been previously published[15,16]. Participating centres, ranging from community institutions to large tertiary facilities, provide blinded data for each patient through standardised internet-based or paper-based questionnaires. These are checked for plausibility and consistency by the AMIS Plus Data Center in the Institute of Social and Preventive Medicine at the University of Zurich. The registry was approved by the Supra-Regional Ethics Committee for Clinical Studies, the Swiss Board for Data Security and the Cantonal Ethics Commissions. The AMIS Plus project is officially supported by the Swiss Societies of Cardiology, Internal Medicine and Intensive Care Medicine. The study design and flow of the patients are presented in **Figure 1**.

The present analysis included all patients (N=12,000) enrolled in AMIS Plus between January 2005 and June 2012, with ST-elevation myocardial infarction defined by characteristic symptoms with ECG changes and cardiac marker elevation (creatine kinase MB fraction at least twice the upper limit of normal or troponin I or T above individual hospital cut-off levels for MI). All patients were required to
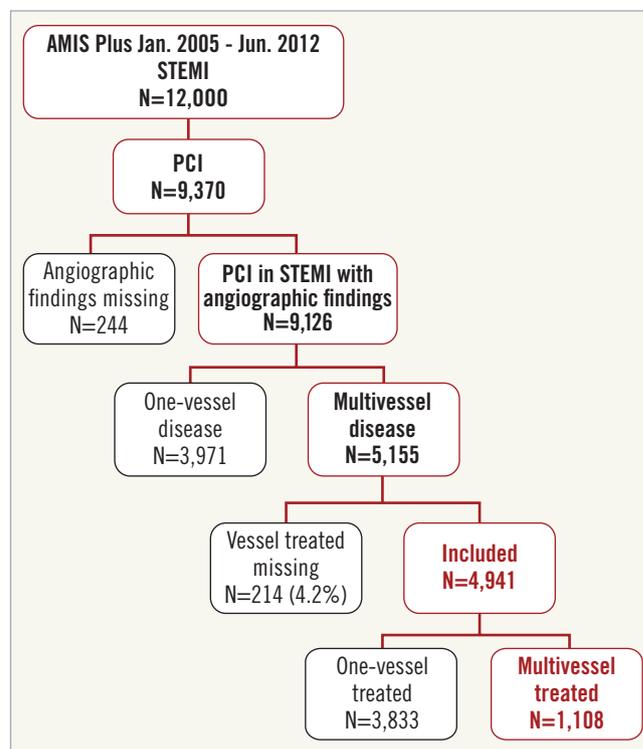

Figure 1. *Study design.*

have ST-segment elevation and/or the new development of left bundle branch block on the initial ECG at presentation. A total of 9,370 patients underwent PCI. We then further limited our study population to those patients with STEMI who also had multivessel disease (n=4,941). Three thousand eight hundred and thirty-three patients (77.6%) underwent SPCI and 1,108 (22.4%) underwent MPCI **(Figure 1)**. Multivessel disease was defined as the presence of an angiographic stenosis of ≥50% in at least two of three main coronary arteries and/or involving the LM when a surgical bypass graft was concerned.

STUDY ENDPOINTS, COVARIATE OF INTEREST AND ADDITIONAL VARIABLES

Our study endpoint of interest was in-hospital mortality. We also evaluated a secondary endpoint of in-hospital major adverse cardiac and cerebrovascular events (MACCE) that included mortality, reinfarction and cerebrovascular events. Our covariate of interest was MPCI use, which we defined as the performance of PCI in at least two or more vessels during STEMI. The MPCI population had only undergone the acute primary PCI procedure and not a staged procedure at the same hospital. Lesions that involved the left main coronary artery (LM) and that were subsequently treated were considered a separate lesion from those involving the left anterior descending and circumflex coronary arteries. The decision regarding SPCI or MPCI attempt was performed at the operating physician's discretion.

The AMIS Plus has 230 items that address medical history, comorbidities, known cardiovascular risk factors, clinical presentation, out-of-hospital management, early in-hospital management, reperfusion therapy, hospital course, diagnostic tests used or

planned, length of stay, discharge medication and discharge destination. Patients are enrolled in the registry on the basis of their final diagnosis. A number of covariates were examined in this study with regard to their association with multivessel PCI and culprit-vessel PCI only. These included: risk factors documented in the patient's medical history (dyslipidaemia, arterial hypertension and diabetes), obesity (body mass index ≥30 kg/m^2), smoking (active or not), and additional non-cardiovascular comorbidities (assessed using the Charlson index). We also included data on immediate drug treatments and discharge medication.

High-risk patients were identified *a priori* as those with: 1) LM involvement that required treatment with PCI; 2) out-of-hospital cardiac arrest; or 3) Killip class III/IV. We selected these specific categories since they represent clinical scenarios under which patients with STEMI are at high risk for in-hospital mortality and additional revascularisation is believed to be worthwhile.

STATISTICAL ANALYSIS

The results are presented as percentages for categorical variables and analysed using the non-parametric Pearson χ^2 test or Fisher's exact test as appropriate. Continuous normally distributed variables are expressed as means±1 standard deviation (SD) and compared using the Student's unpaired t-test. Continuous non-normally distributed variables are expressed as median and interquartile ranges and analysed using the Mann-Whitney U test. All statistical tests were two-tailed and a p-value <0.05 was considered statistically significant.

A multivariate logistic regression model was examined to determine predictors of MPCI use and included the following variables: age, gender, LM involvement, Killip class >2, Charlson comorbidities weighted index ≥2 and out-of-hospital cardiac arrest.

Moreover, we assessed the association between MPCI and in-hospital mortality. To determine in-hospital mortality predictors, a multivariate logistic regression model included the following variables: age, gender, vessel treated, LM involvement, Killip class >2, Charlson comorbidities weighted index ≥2 and out-of-hospital cardiac arrest. We did this in the entire cohort and after stratifying patients based on risk. Adjusted odds ratios in all models are reported from the multivariate models. IBM SPSS software version 19 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

Results

STUDY POPULATION AND MPCI PREDICTORS

Out of 12,000 patients admitted with a diagnosis of STEMI between 2005 and 2012, we identified 4,941 patients (41.2%) with multivessel disease who underwent PCI. Three thousand eight hundred and thirty-three patients (77.6%) underwent SPCI and 1,108 (22.4%) underwent MPCI **(Figure 1)**. Baseline characteristics stratified by MPCI use are presented in **Table 1**. In general, rates of MPCI were greater among sicker patients. High-risk patients, identified by the three characteristics, all had higher rates of MPCI use after age and gender adjustment: 8.6% vs. 5.9% for out-of-hospital cardiac arrest (OR 1.49, 95% CI: 1.16-1.92, p=0.002); 12.3% vs. 6.2% for Killip III/IV (OR 2.14, 95% CI: 1.71-2.68, p<0.001); and 14.5% vs. 2.7%

for LM involvement (OR 6.27, 95% CI: 4.84-8.12, p<0.001). In addition, drugs, i.e., glycoprotein IIb/IIIa inhibitors, beta-blockers and ACE inhibitors/AT antagonists, were used less frequently in patients treated with MPCI (33.2% vs. 39.4%, OR 0.75, 95% CI: 0.65-0.87, p<0.001; 59.3% vs. 62.8%, OR 0.85, 95% CI: 0.74-0.98, p=0.034; 50.0% vs. 61.8%, OR 0.61, 95% CI: 0.54-0.70, p<0.001, respectively). After accounting for additional risk factors, the presence of LM (OR 5.87, 95% CI: 4.53-7.63, p<0.001) and a Killip class III/IV (OR 1.79, 95% CI: 1.39-2.32, p<0.001) were the only factors independently predictive of MPCI use during STEMI **(Table 2)**.

IN-HOSPITAL OUTCOMES AND PREDICTORS OF MORTALITY

Overall, in-hospital mortality after MPCI was higher when compared with SPCI (7.3% vs. 4.4%, OR 1.80, 95% CI: 1.37-2.38; p<0.001) as well as MACCE (8.6% vs. 5.8%, OR 1.59, 95% CI: 1.24-2.05, p<0.001, **Table 3**). Age (per additional year), Charlson weighted index ≥2, out-of-hospital cardiac arrest and Killip III/IV were identified as predictors of in-hospital mortality (OR 1.06, 95% CI: 1.04-1.07, p<0.001; OR 1.83, 95% CI: 1.32-2.54, p<0.001; OR 4.62, 95% CI: 3.18-6.72, p<0.001; OR 12.2, 95% CI: 8.81-16.8, p<0.001, respectively, **Table 4**) but not MPCI use (OR 1.22, 95% CI: 0.86-1.71, p=0.26). Differences in in-hospital mortality were completely eliminated when patients were stratified by risk: in-hospital mortality for MPCI vs. SPCI was 2.0% vs. 2.0% (p=1.00) in low-risk patients and 22.2% vs. 21.7% (p=0.93) in high-risk patients **(Figure 2** and **Table 5)**.

Discussion

Our analysis has several key findings. First, we identified that patients more likely to undergo MPCI are sicker in general and at high risk. Second, MPCI is associated with higher rates of in-hospital mortality and MACCE, but these differences are largely negated after stratifying patients based on risk. The latter finding indicates that MPCI in non-critically ill STEMI patients does not negatively influence in-hospital outcome.

Patients with STEMI and multivessel disease are likely to have a substantial increase in cardiovascular morbidity and mortality due to several factors – and not just the performance of MPCI [2-4]. First of all, STEMI patients with multivessel disease are likely to have more extensive coronary disease and lower LV ejection fraction compared to those with single-vessel disease [17]. It has also been hypothesised that acute myocardial infarction slows flow globally throughout the coronary vessels, due to increased systemic inflammatory response and vasospasm, which may exacerbate outcomes [18-20].

There is a large body of literature investigating whether PCI procedures should be extended during the course of STEMI in patients with multivessel disease or whether it should be confined to culprit vessel [5,6,14]. Existing data are somewhat conflicting and controversial [14]. Several studies suggested that MPCI during the course of STEMI is associated with increased mortality, MACE and stent thrombosis [11,13,21-24]. On the contrary, Qarawani et al and Politi et al supported MPCI in the acute phase of STEMI as a feasible and safe attempt resulting in an improved acute clinical course after MPCI and a lower MACE rate at long-term follow-up [8,25]. Another

Table 1. Baseline characteristics of the STEMI patients according to vessel treatment (n/N [%]).

		Single-vessel PCI	Multivessel PCI	*p*-value	OR adjusted for age and gender (95% CI)
Number of patients		3,833	1,108		
Sex, male (%)		2,911/3,833 (77.3)	221/1,108 (79.2)	0.19	
Age in years, mean (SD)		64.8 (12.0)	64.0 (12.1)	0.080	
Delay hr:min	Median	3:00	3:07	0.21	
	(IQR)	1:41, 6:40	1:45, 6:40		
Resuscitation prior to admission		225/3,833 (5.9)	95/1,108 (8.6)	0.002	1.49 (1.16-1.92)
CPR (%)		155/3,817 (4.1)	64/1,108 (5.8)	0.020	1.44 (1.06-1.94)
cardioversion/defibrillation (%)		200/3,817 (5.2)	79/1,108 (7.1)	0.018	1.37 (1.05-1.80)
Symptoms at admission	pain (%)	3,437/3,719 (92.4)	984/1,069 (92.0)	0.70	0.94 (0.73-1.22)
	dyspnoea (%)	885/3,312 (26.7)	324/961 (33.7)	<0.001	1.41 (1.21-1.64)
Vital signs at admission, mean (SD)	systolic blood pressure (mmHg)	133 (29)	133 (29)	0.75	
	diastolic (mmHg)	79 (18)	80 (24)	0.23	
	heart rate (beats/min)	77 (19)	80 (19)	<0.001	
Killip class III/IV		238/3,811 (6.2)	135/1,100 (12.3)	<0.001	2.14 (1.71-2.68)
Risk factors	Family history (%)	1,125/3,251 (34.6)	351/920 (38.2)	0.051	1.15 (0.99-1.34)
	Smoking (%)	1,479/3,478 (42.5)	418/964 (43.4)	0.66	0.96 (0.82-1.12)
	Dyslipidaemia (%)	1,819/3,356 (54.2)	503/953 (52.8)	0.44	0.94 (0.82-1.09)
	Hypertension (%)	2,182/3,593 (60.7)	600/1,024 (58.6)	0.22	0.95 (0.82-1.10)
	Diabetes (%)	670/3,659 (18.3)	208/1,033 (20.1)	0.19	1.15 (0.99-1.37)
	Obesity (BMI >30) (%)	670/3,306 (20.3)	182/917 (19.8)	0.82	0.96 (0.80-1.16)
Coronary artery disease (%)		1,178/3,791 (31.1)	306/1,087 (28.2)	0.067	0.88 (0.75-1.02)
Charlson score ≥2 (%)[§]		631/3,833 (16.5)	195/1,108 (17.6)	0.39	1.12 (0.94-1.35)
Two vessels treated		--	939 (84.7)		
Three vessels treated		--	161 (14.5)		
Four vessels treated		--	8 (0.7)		
LM (%)		102/3,833 (2.7)	161/1,108 (14.5)	<0.001	6.27 (4.84-8.12)

Data are shown for single-vessel PCI versus multivessel PCI. BMI: body mass index; CPR: cardiopulmonary resuscitation; IQR: interquartile range; LM: left main; PCI: percutaneous coronary intervention. [§]The Charlson comorbidity index gives an estimate of survival based on the following variables: cerebrovascular disease, chronic pulmonary disease, congestive heart failure, connective tissue disease, dementia, hemiplegia, leukaemia, malignant lymphoma, myocardial infarction, peripheral vascular disease, ulcer disease, diabetes mellitus, liver disease, renal disease, malignant solid tumour, and acquired immune deficiency syndrome status

Table 2. Predictors for use of multivessel PCI.

	OR	95% CI	*p*
Left main	5.87	4.53-7.63	<0.001
Female gender	0.90	0.76-1.08	0.25
Age (per additional year)	0.99	0.98-1.00	0.041
Charlson weighted index ≥2	1.07	0.89-1.29	0.48
Resuscitation prior to admission	1.10	0.83-1.46	0.51
Killip class >2	1.79	1.39-2.32	<0.001

study revealed incomplete revascularisation as a strong and independent risk factor of death and MACE in patients with STEMI[26]. The HELP-AMI multicentre, randomised trial found one-time full revascularisation to be a safe procedure[7]. Investigators concluded, however, that the staged approach to MPCI during the acute phase of MI avoids treating non-relevant lesions unneccesarily[7]. Also, no economic advantages of one-time MPCI were documented[7].

All the studies on MPCI versus SPCI in patients with STEMI and multivessel disease (MVD) were performed on a small population[8,25,26].

Table 3. Complications and in-hospital outcome according to vessel treatment.

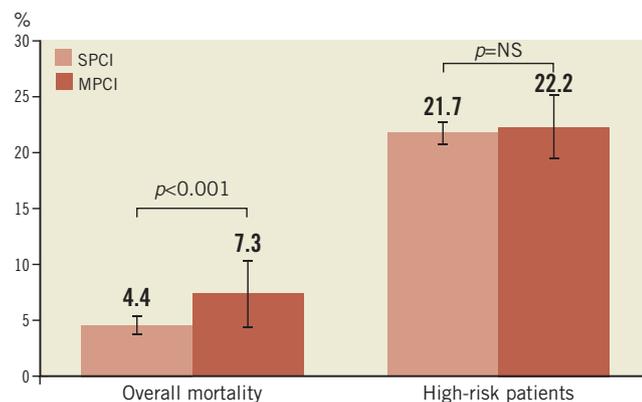|	Single-vessel PCI	Multivessel PCI	*p*-value	OR adjusted for age and gender (95% CI)
Number of patients	**3,833**	**1,108**		
Reinfarction (%)	42/3,821 (1.1)	9/1,106 (0.8)	0.50	0.75 (0.37-1.55)
Cerebrovascular event (%)	31/3,821 (0.8)	10/1,106 (0.9)	0.71	1.13 (0.55-2.31)
Mortality (%)	168/3,833 (4.4)	81/1,108 (7.3)	<0.001	1.80 (1.37-2.38)
MACCE (%)	220/3,821 (5.8)	95/1,107 (8.6)	0.001	1.59 (1.24-2.05)

MACCE: major adverse cardiac and cerebrovascular events

Table 4. Predictors for in-hospital mortality.

	OR	95% CI	p
Multivessel treatment	1.22	0.86-1.71	0.26
Left main	1.64	0.99-2.70	0.056
Female gender	0.90	0.64-1.27	0.56
Age (per additional year)	1.06	1.04-1.07	<0.001
Charlson weighted index =>2	1.83	1.32-2.54	<0.001
Resuscitation prior to admission	4.62	3.18-6.72	<0.001
Killip class >2	12.2	8.81-16.8	<0.001

In a meta-analysis of patients with STEMI and MVD, a strategy of staged complete revascularisation appeared to be the best choice in patients with STEMI[4,14]. In another recently published meta-analysis, one-time MPCI was not beneficial for patients with STEMI, although it did not worsen the mortality rate[27].

The rate of MPCI among STEMI patients has reportedly ranged between 0% and 38%[10]. Full revascularisation, including non-culprit vessels, has been suggested to be most relevant for high-risk patients with cardiogenic shock leading to reduced ischaemia and improved survival[28,29]. Indeed, currently published guidelines recommend MPCI only in unstable STEMI patients[1,5,6]. In non-shock STEMI patients, the use of PCI should be focused on the infarct-related or culprit vessel only. However, these recommendations remain based on observational studies where there has been a mixed application of risk-adjustment methods.

Figure 2. *In-hospital mortality according to high risk in STEMI patients who underwent single or multivessel PCI.*

Why would MPCI be potentially harmful in STEMI patients? PCI in acute coronary syndromes could cause coronary microembolisation due to the erosion or rupture of a vulnerable atherosclerotic plaque occurring spontaneously[30]. This leads to periprocedural MIs, contractile dysfunction and reduced coronary reserve[30]. These potential complications in a non-culprit artery may be poorly tolerated due to simultaneous impairment of the infarct-related and non-related areas[22]. Second, in the acute phase of STEMI, the significance of the lesion of the non-culprit vessel could be overestimated due to vasoconstriction and endothelial dysfunction[31], leading to overtreatment of vessels where the benefit is unlikely to be substantial. In this setting, an initial conservative strategy is likely to be more effective[32]. Additional reasons for culprit-vessel PCI only include its lower contrast use, which could reduce the risk of acute kidney injury – a powerful predictor of outcomes in STEMI patients. The advantage for staged PCI is that non-culprit lesions can be discussed within a Heart Team to determine the best individual management strategy[5,6].

PCI for non-culprit vessels in the acute course of STEMI, excluding the cardiogenic shock setting, is discouraged in recently published ESC guidelines and has been labelled as "inappropriate" in a recent report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force[33,34]. The accurate treatment strategy in case of STEMI and MVD is still not well established by RCTs[33].

In our observational experience, after stratifying patients based on risk, MPCI does not appear to be associated with higher mortality, supporting its potential use for selected patients during the course of STEMI. MPCI may be considered by physicians in terms of convenience for the patients and potential cost reduction compared to post-STEMI staged PCI of non-culprit vessels[35].

Study limitations

Our study should be assessed in the context of its limitations, many of which are inherent to registry studies. First, there is the potential for residual confounding factors due to a lack of data on relevant clinical features that could have impacted both on the choice to use MPCI as well as on outcomes. Therefore, to identify the high-risk setting we selected the clinical and angiographic variables, since we were not able to provide more accurate risk stratification based on the GRACE or TIMI score. Second, although the AMIS Plus registry provides data on the number of vessels treated with PCI, the precise anatomical distribution of the lesions and technical features

Table 5. In-hospital mortality according to high risk in STEMI patients who underwent single or multivessel PCI.

Mortality	Single-vessel PCI (n=3,833)	Multivessel PCI (n=1,108)	p-value	OR adjusted for age and gender (95% CI)
All study patients	168/3,833 (4.4)	81/1,108 (7.3)	<0.001	1.80 (1.37-2.38)
No high risks	66/3,359 (2.0)	16/807 (2.0)	1.00	1.13 (0.64-1.97)
One or more high risks	98/452 (21.7)	65/293 (22.2)	0.93	1.01 (0.70-1.45)
One high risk	53/346 (15.3)	28/207 (13.5)	0.62	0.86 (0.52-1.42)
Two high risks	43/102 (42.2)	32/75 (42.7)	1.00	0.96 (0.52-1.79)
Three high risks (all)	2/4 (50.0)	5/11 (45.5)	1.00	Small number of pts.

of the procedure itself are unknown. Third, we have no information regarding subsequent treatment of non-culprit vessels (CABG, staged in-hospital revascularisations, and conservative treatment) or follow-up data on the patients following discharge.

Conclusions

STEMI patients with multivessel disease who have undergone MPCI are sicker than those who underwent culprit-vessel PCI only. Furthermore, MPCI does not appear to be associated with higher mortality after stratifying patients based on their risk. Therefore, although MPCI in STEMI patients should continue to be reserved for high-risk groups, physicians should not be reluctant to use this approach when their clinical judgement suggests potential benefit. Large-scale prospective trials should be organised to guide the appropriateness of MPCI during the course of STEMI. The current observation reflects a "real-world" practice which encourages us to perform a randomised clinical trial of MPCI in STEMI in the near future.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN, Lange RA, Mauri L, Mehran R, Moussa ID, Mukherjee D, Nallamothu BK, Ting HH. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation.* 2011;124:e574-651.

2. Sorajja P, Gersh BJ, Cox DA, McLaughlin MG, Zimetbaum P, Costantini C, Stuckey T, Tcheng JE, Mehran R, Lansky AJ, Grines CL, Stone GW. Impact of multivessel disease on reperfusion success and clinical outcomes in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. *Eur Heart J.* 2007;28:1709-16.

3. Goldstein JA, Demetriou D, Grines CL, Pica M, Shoukfeh M, O'Neill WW. Multiple complex coronary plaques in patients with acute myocardial infarction. *N Engl J Med.* 2000;343:915-22.

4. Bangalore S, Kumar S, Poddar KL, Ramasamy S, Rha SW, Faxon DP. Meta-analysis of multivessel coronary artery revascularization versus culprit-only revascularization in patients with ST-segment elevation myocardial infarction and multivessel disease. *Am J Cardiol.* 2011;107:1300-10.

5. Kushner FG, Hand M, Smith SC Jr, King SB 3rd, Anderson JL, Antman EM, Bailey SR, Bates ER, Blankenship JC, Casey DE Jr, Green LA, Hochman JS, Jacobs AK, Krumholz HM, Morrison DA, Ornato JP, Pearle DL, Peterson ED, Sloan MA, Whitlow PL, Williams DO. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005

guideline and 2007 focused update) a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2009;54:2205-41.

6. Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS); European Association for Percutaneous Cardiovascular Interventions (EAPCI), Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, Garg S, Huber K, James S, Knuuti J, Lopez-Sendon J, Marco J, Menicanti L, Ostojic M, Piepoli MF, Pirlet C, Pomar JL, Reifart N, Ribichini FL, Schalij MJ, Sergeant P, Serruys PW, Silber S, Sousa Uva M, Taggart D. Guidelines on myocardial revascularization. *Eur Heart J.* 2010;31:2501-55.

7. Di Mario C, Mara S, Flavio A, Imad S, Antonio M, Anna P, Emanuela P, Stefano DS, Angelo R, Stefania C, Anna F, Carmelo C, Antonio C, Monzini N, Bonardi MA. Single vs multivessel treatment during primary angioplasty: results of the multicentre randomised HEpacoat for cuLPrit or multivessel stenting for Acute Myocardial Infarction (HELP AMI) Study. *Int J Cardiovasc Intervent.* 2004;6:128-33.

8. Politi L, Sgura F, Rossi R, Monopoli D, Guerri E, Leuzzi C, Bursi F, Sangiorgi GM, Modena MG. A randomised trial of target-vessel versus multi-vessel revascularisation in ST-elevation myocardial infarction: major adverse cardiac events during long-term follow-up. *Heart.* 2010;96:662-7.

9. Khattab AA, Abdel-Wahab M, Rother C, Liska B, Toelg R, Kassner G, Geist V, Richardt G. Multi-vessel stenting during primary percutaneous coronary intervention for acute myocardial infarction. A single-center experience. *Clin Res Cardiol.* 2008;97:32-8.

10. Cavender MA, Milford-Beland S, Roe MT, Peterson ED, Weintraub WS, Rao SV. Prevalence, predictors, and in-hospital outcomes of non-infarct artery intervention during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction (from the National Cardiovascular Data Registry). *Am J Cardiol.* 2009;104:507-13.

11. Corpus RA, House JA, Marso SP, Grantham JA, Huber KC Jr, Laster SB, Johnson WL, Daniels WC, Barth CW, Giorgi LV, Rutherford BD. Multivessel percutaneous coronary intervention in patients with multivessel disease and acute myocardial infarction. *Am Heart J.* 2004;148:493-500.

12. Hannan EL, Samadashvili Z, Walford G, Holmes DR Jr, Jacobs AK, Stamato NJ, Venditti FJ, Sharma S, King SB 3rd. Culprit vessel percutaneous coronary intervention versus multivessel and staged percutaneous coronary intervention for ST-segment elevation myocardial infarction patients with multivessel disease. *JACC Cardiovasc Interv.* 2010;3:22-31.

13. Toma M, Buller CE, Westerhout CM, Fu Y, O'Neill WW, Holmes DR Jr, Hamm CW, Granger CB, Armstrong PW. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. *Eur Heart J.* 2010;31:1701-7.

14. Vlaar PJ, Mahmoud KD, Holmes DR Jr, van Valkenhoef G, Hillege HL, van der Horst IC, Zijlstra F, de Smet BJ. Culprit

vessel only versus multivessel and staged percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction: a pairwise and network meta-analysis. *J Am Coll Cardiol.* 2011;58:692-703.

15. Radovanovic D, Erne P. AMIS Plus: Swiss registry of acute coronary syndrome. *Heart.* 2010;96:917-21.

16. Radovanovic D, Urban P, Simon R, Schmidli M, Maggiorini M, Rickli H, Stauffer JC, Seifert B, Gutzwiller F, Erne P. Outcome of patients with acute coronary syndrome in hospitals of different sizes. A report from the AMIS Plus Registry. *Swiss Med Wkly.* 2010;140:314-22.

17. Muller DW, Topol EJ, Ellis SG, Sigmon KN, Lee K, Califf RM. Multivessel coronary artery disease: a key predictor of short-term prognosis after reperfusion therapy for acute myocardial infarction. Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) Study Group. *Am Heart J.* 1991;121:1042-9.

18. Gibson CM, Ryan KA, Murphy SA, Mesley R, Marble SJ, Giugliano RP, Cannon CP, Antman EM, Braunwald E. Impaired coronary blood flow in nonculprit arteries in the setting of acute myocardial infarction. The TIMI Study Group. Thrombolysis in myocardial infarction. *J Am Coll Cardiol.* 1999;34:974-82.

19. Chan MY, Andreotti F, Becker RC. Hypercoagulable states in cardiovascular disease. *Circulation*. 2008;118:2286-97.

20. Kereiakes DJ, Gurbel PA. Peri-procedural platelet function and platelet inhibition in percutaneous coronary intervention. *JACC Cardiovasc Interv.* 2008;1:111-21.

21. Roe MT, Cura FA, Joski PS, Garcia E, Guetta V, Kereiakes DJ, Zijlstra F, Brodie BR, Grines CL, Ellis SG. Initial experience with multivessel percutaneous coronary intervention during mechanical reperfusion for acute myocardial infarction. *Am J Cardiol.* 2001;88:170-3, A6.

22. Kornowski R, Mehran R, Dangas G, Nikolsky E, Assali A, Claessen BE, Gersh BJ, Wong SC, Witzenbichler B, Guagliumi G, Dudek D, Fahy M, Lansky AJ, Stone GW; HORIZONS-AMI Trial Investigators. Prognostic impact of staged versus "one-time" multivessel percutaneous intervention in acute myocardial infarction: analysis from the HORIZONS-AMI (harmonizing outcomes with revascularization and stents in acute myocardial infarction) trial. *J Am Coll Cardiol.* 2011;58:704-11.

23. Dziewierz A, Siudak Z, Rakowski T, Zasada W, Dubiel JS, Dudek D. Impact of multivessel coronary artery disease and noninfarct-related artery revascularization on outcome of patients with ST-elevation myocardial infarction transferred for primary percutaneous coronary intervention (from the EUROTRANSFER Registry). *Am J Cardiol.* 2010;106:342-7.

24. Pedrazzini GB, Radovanovic D, Vassalli G, Surder D, Moccetti T, Eberli F, Urban P, Windecker S, Rickli H, Erne P. Primary percutaneous coronary intervention for unprotected left main disease in patients with acute ST-segment elevation myocardial infarction the AMIS (Acute Myocardial Infarction in Switzerland) plus registry experience. *JACC Cardiovasc Interv.* 2011;4:627-33.

25. Qarawani D, Nahir M, Abboud M, Hazanov Y, Hasin Y. Culprit only versus complete coronary revascularization during primary PCI. *Int J Cardiol.* 2008;123:288-92.

26. Kalarus Z, Lenarczyk R, Kowalczyk J, Kowalski O, Gasior M, Was T, Zebik T, Krupa H, Chodór P, Poloński L, Zembala M. Importance of complete revascularization in patients with acute myocardial infarction treated with percutaneous coronary intervention. *Am Heart J.* 2007;153:304-12.

27. Sethi A, Bahekar A, Bhuriya R, Singh S, Ahmed A, Khosla S. Complete versus culprit only revascularization in acute ST elevation myocardial infarction: a meta-analysis. *Catheter Cardiovasc Interv.* 2011;77:163-70.

28. Thiele H, Allam B, Chatellier G, Schuler G, Lafont A. Shock in acute myocardial infarction: the Cape Horn for trials? *Eur Heart J.* 2010;31:1828-35.

29. Hochman JS, Sleeper LA, Webb JG, Dzavik V, Buller CE, Aylward P, Col J, White HD. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. *JAMA.* 2006;295:2511-5.

30. Heusch G, Kleinbongard P, Bose D, Levkau B, Haude M, Schulz R, Erbel R. Coronary microembolization: from bedside to bench and back to bedside. *Circulation*. 2009;120:1822-36.

31. Hanratty CG, Koyama Y, Rasmussen HH, Nelson GI, Hansen PS, Ward MR. Exaggeration of nonculprit stenosis severity during acute myocardial infarction: implications for immediate multivessel revascularization. *J Am Coll Cardiol.* 2002;40:911-6.

32. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL, Chaitman BR, Shaw L, Gosselin G, Nawaz S, Title LM, Gau G, Blaustein AS, Booth DC, Bates ER, Spertus JA, Berman DS, Mancini GB, Weintraub WS; COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med.* 2007;356:1503-16.

33. Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Giannuzzi P, Halvorsen S, Huber K, Juni P, Kastrati A, Knuuti J, Lenzen MJ, Mahaffey KW, Valgimigli M, van 't Hof A, Widimsky P, Zahger D. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J.* 2012;33:2569-619.

34. Patel MR, Dehmer GJ, Hirshfeld JW, Smith PK, Spertus JA. ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 Appropriate use criteria for coronary revascularization focused update: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol.* 2012;59:857-81.

35. Ochala A, Smolka GA, Wojakowski W, Dudek D, Dziewierz A, Krolikowski Z, Gasior Z, Tendera M. The function of the left ventricle after complete multivessel one-stage percutaneous coronary intervention in patients with acute myocardial infarction. *J Invasive Cardiol.* 2004;16:699-702.