

Single-vessel versus multivessel PCI in patients with acute coronary syndrome and multivessel coronary artery disease

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Summary

Aims: Optimal management of patients with acute coronary syndromes (ACS) presenting with multivessel coronary artery disease (CAD) is controversial. We compared the outcome of three different treatment strategies: single-vessel (SV) PCI of the infarct-related artery only, multivessel PCI during the index procedure (MV_{index}) and staged multivessel PCI (MV_{staged}).

Methods and results: Between July 2007 and December 2008, 387 patients presented with ACS and multivessel CAD. In-hospital mortality was 2.4% for SV PCI, 1.9% for MV_{index} PCI and 0.8% for MV_{staged} PCI ($p = 0.566$). The in-hospital rate of myocardial infarction, acute stent thrombosis, cerebrovascular accident and unplanned revascularisation did not differ. MV_{index} PCI was associated with a higher rate of inguinal haematoma (0.5%, 9.4%, and 2.4% for SV PCI, MV_{index} PCI and MV_{staged} PCI respectively, $p = 0.001$). After 1 year death had occurred in 4.6% with SV PCI, in 4.0% with MV_{index} PCI and in 4.9% of the patients with MV_{staged} PCI ($p = 0.966$). Rates for major cardiovascular events including death, myocardial infarction, cerebrovascular accident and unplanned revascularisation were 13.1%, 12.1% and 13.4%, for SV PCI, MV_{index} PCI and MV_{staged} PCI respectively ($p = 0.981$).

Conclusion: Multivessel coronary artery PCI performed during the index procedure on presentation of the ACS was associated with a higher rate of inguinal haematoma. Long-term outcome of the three treatment strategies did not differ. Revascularisation of the infarct-related artery only might provide equal benefit to multivessel revascularisation, but needs to be determined prospectively in a larger patient population.

Key words: *treatment strategy; acute coronary syndrome; multivessel disease; staged revascularisation; percutaneous coronary intervention*

Introduction

Patients with acute coronary syndrome (ACS) frequently present with angiographically-documented multivessel disease at the time of acute percutaneous coronary intervention (PCI). This has been associated with increased morbidity and mortality [1–3]. Current guidelines from the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) recommend PCI of the infarct-related artery (IRA) in patients who are haemodynamically stable. Multivessel revascularisation is encouraged in patients presenting in cardiogenic shock, especially if the stenotic vessel serves a large area of myocardium [4,5].

For several years past, progress in instrumental technology, stent design (in particular the introduction of drug-eluting stents) and the development of potent antiplatelet drugs has made an aggressive approach with multivessel revascularisation in ACS patients feasible and hence more attractive. Many interventionalists perform PCI of all angiographically relevant lesions either simultaneously at the time of the initial PCI or in a staged procedure. It is conceivable that the former approach, alleviating all areas of ischaemia, may be associated with a reduced incidence of adverse events at follow-up and thus also be more cost-effective [6]. On the other hand, early simultaneous multivessel PCI may result in an increased periprocedural risk due to a larger quantity of contrast dye, longer procedural time, ischaemia in non-infarcted myocardial regions and a higher risk of stent thrombosis [7]. In addition, treatment of clinically silent lesions is very possible. Unfortunately, data supporting either of these strategies are relatively sparse.

Funding / potential competing interests:

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Thus, optimal management of multivessel coronary artery disease in the context of an ACS treated by PCI remains uncertain. It was therefore the aim of this study to compare short- and long-term outcomes of single-vessel PCI, multivessel PCI during the index procedure, and staged multivessel revascularisation (either during the index hospitalisation or a second hospitalisation) in patients with ACS and multivessel coronary artery disease.

Patients and methods

Patient population

The University Hospital Zurich, where this retrospective single-centre study was performed, is a tertiary referral clinic treating some 500 patients with ACS (i.e. unstable angina pectoris, non-ST elevation myocardial infarction [NSTEMI] and ST elevation myocardial infarction [STEMI]) per year. Between July 2007 and December 2008, 727 ACS patients were treated by primary PCI. Only patients with multivessel coronary artery disease (CAD) were eligible for this study. Multivessel CAD was defined as >50% diameter stenosis of at least two main coronary arteries (i.e. left anterior descending artery, left circumflex artery and right coronary artery) or their major branches [8–10]. The only exclusion criterion was presentation in cardiogenic shock at admission (Killip class IV). Treatment of multiple lesions in one major vessel during primary PCI was not an exclusion criterion. For analysis, patients were divided into three groups as follows: (1) single-vessel PCI (SV PCI), (2) multivessel PCI during the index procedure (MV_{index} PCI), and (3) staged multivessel PCI (MV_{staged} PCI). Due to the retrospective character of this study there were no predefined criteria for treatment selection. The study was approved by the local ethics committee and a waiver of consent was granted.

Definitions and endpoints

To group the coronary artery diseases into single-vessel and multivessel coronary diseases we used the definition of the coronary-artery-tree-segments based on the classification proposed by the American Heart Association and modified for the ARTS I and II trials [11, 12]. By this approach the three epicardial coronary arteries with their branches are divided into 16 segments.

Clinical and procedural data of our patients were collected from hospital records. Patients were also followed up in the out-hospital clinic or by phone interviews.

Adverse cardiovascular events included death, myocardial infarction, acute stent thrombosis, stroke, unplanned PCI or coronary artery bypass grafting and major bleeding. Major bleeding was defined as (a) inguinal haematoma ≥ 5 cm or requiring intervention,

(b) retroperitoneal bleeding and (c) other bleeding such as intracranial or intraocular haemorrhage; any gastrointestinal haemorrhage; urogenital haemorrhage; a need for transfusion of packed red blood cells; a decrease in haemoglobin ≥ 4 g/dL; any other major bleeding. Additionally, peak creatinine was analysed as an in-hospital outcome parameter.

Endpoints at follow-up were death, myocardial infarction, stroke and the need for any unplanned revascularisation (i.e. target vessel revascularisation, target lesion revascularisation and coronary artery bypass grafting). We also analysed a combined endpoint including all the above events [13]. One year follow-up was available in 340 (88%) of the patients.

Statistical analysis

Statistical analysis was performed using SPSS 15 (SPSS Inc., Chicago, USA). If not otherwise indicated, data are presented as mean \pm the standard deviation for continuous variables and as number and frequencies for categorical variables. Continuous variables were compared using student's t-test and categorical variables using the chi-square test and Fisher's exact test. Kaplan-Meier estimates were used to calculate 1-year outcome. They were compared using the log rank test. A cox regression analysis was performed to compare single-vessel and multivessel treatment. For all tests a two-sided $p < 0.05$ was considered statistically significant.

Results

Patients and procedures

Between July 2007 and January 2009, 727 patients presenting with ACS were treated at our clinic, of whom 409 (56%) presented with multivessel coronary disease. After exclusion of patients in cardiogenic shock at admission, a total of 387 patients were analysed. Of these, 209 patients were treated by SV PCI, 53 by MV_{index} PCI and the remaining 129 by MV_{staged} PCI. Forty-three (81%) of the patients undergoing MV_{index} PCI were considered completely revascularised. Staged revascularisation was carried out during the same hospitalisation in 20 (16%) of the patients. In the remaining patients elective revascularisation was performed during a second hospitalisation 1–12 weeks (median 4 weeks) after the index event.

Baseline characteristics of the three treatment groups are shown in table 1. Age, sex and prevalence of cardiovascular risk factors did not differ between the two groups. Patients with SV PCI presented more often with a history of prior PCI (19%, 9% and 7% for patients with SV PCI, MV_{index} PCI and MV_{staged} PCI respectively, $p = 0.006$).

Procedural characteristics are presented in table 2. Patients with MV_{index} revascularisation presented significantly more often with NSTEMI and unstable AP,

Table 1

Baseline characteristics.

| Variable | Single-vessel PCI (n = 209) | Multivessel PCI index procedure (n = 53) | Multivessel PCI staged (n = 125) | p value |
|-----------------------|-----------------------------|--|----------------------------------|---------|
| Age (years) | 66 ± 12 | 64 ± 11 | 64 ± 12 | 0.476 |
| Male sex | 158 (76%) | 38 (72%) | 125 (82%) | 0.208 |
| Hypertension | 119 (58%) | 35 (67%) | 75 (62%) | 0.456 |
| Diabetes | 46 (22%) | 8 (15%) | 22 (18%) | 0.418 |
| Hypercholesterolaemia | 91 (44%) | 24 (46%) | 46 (38%) | 0.421 |
| Current smoker | 82 (40%) | 27 (52%) | 42 (34%) | 0.222 |
| Family history of CAD | 57 (28%) | 12 (23%) | 37 (30%) | 0.614 |
| PVD | 16 (8%) | 6 (11%) | 7 (6%) | 0.412 |
| Prior MI | 45 (22%) | 7 (13%) | 15 (12%) | 0.062 |
| Prior CABG | 19 (9%) | 3 (6%) | 5 (4%) | 0.200 |
| Prior PCI | 40 (19%) | 5 (9%) | 9 (7%) | 0.006 |
| Prior CVA | 4 (2%) | 0 (0%) | 1 (1%) | 0.457 |
| Creatinine (µmol/L) | 95 ± 50 | 88 ± 22 | 90 ± 47 | 0.543 |

CAD: coronary artery disease; PVD: peripheral vascular disease; MI: myocardial infarction; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention; CVA: cerebrovascular accident.

Table 2

Procedural characteristics of the primary intervention.

| Variable | Single-vessel PCI (n = 209) | Multivessel PCI index procedure (n = 53) | Multivessel PCI staged (n = 125) | p value |
|-------------------------------|-----------------------------|--|----------------------------------|---------|
| Type of ACS | | | | |
| STEMI | 125 (60%) | 18 (34%) | 75 (60%) | 0.002 |
| NSTEMI | 63 (30%) | 26 (49%) | 43 (34%) | 0.034 |
| Unstable AP | 21 (10%) | 9 (17%) | 7 (6%) | 0.058 |
| Three vessel disease | 83 (40%) | 22 (42%) | 48 (38%) | 0.925 |
| Left main stenosis ≥50% | 13 (6%) | 10 (19%) | 5 (4%) | 0.002 |
| CTO of LAD | 19 (9%) | 6 (11%) | 13 (10%) | 0.857 |
| CTO of CX | 12 (6%) | 2 (4%) | 5 (4%) | 0.712 |
| CTO of RCA | 31 (15%) | 5 (9%) | 8 (6%) | 0.056 |
| Ejection fraction (%) | 52 ± 14 | 53 ± 12 | 53 ± 9 | 0.822 |
| Systolic BP (mm Hg) | 126 ± 25 | 124 ± 24 | 123 ± 24 | 0.658 |
| Diastolic BP (mm Hg) | 69 ± 13 | 70 ± 12 | 70 ± 13 | 0.884 |
| Medication before angiography | | | | |
| Aspirin | 209 (100%) | 53 (100%) | 125 (100%) | N/A |
| Clopidogrel | 106 (51%) | 27 (51%) | 77 (62%) | 0.135 |
| Heparin | 143 (68%) | 34 (64%) | 86 (69%) | 0.813 |
| Low molecular weight heparin | 47 (23%) | 11 (21%) | 29 (23%) | 0.938 |
| Medication for PCI | | | | |
| Heparin | 94 (45%) | 29 (55%) | 57 (46%) | 0.433 |
| Heparin and GpIIb/IIIa | 79 (38%) | 16 (30%) | 45 (36%) | 0.588 |
| Bivalirudin | 35 (17%) | 8 (15%) | 23 (18%) | 0.853 |
| Number of stents | 1.69 ± 1.43 | 2.10 ± 0.77 | 1.47 ± 0.63 | 0.005 |
| DES use | 134 (64%) | 38 (72%) | 76 (61%) | 0.282 |
| Total stent length (mm) | 32 ± 18 | 44 ± 20 | 30 ± 14 | <0.001 |
| IABP use | 18 (9%) | 11 (21%) | 10 (8%) | 0.021 |

ACS: acute coronary syndrome; STEMI: ST segment elevation myocardial infarction; NSTEMI: non-ST segment elevation myocardial infarction; AP: angina pectoris; CTO: chronic total occlusion; LAD: left anterior descending; CX: circumflex; RCA: right coronary artery; BP: blood pressure; DES: drug eluting stent; IABP: intra-aortic balloon pump.

and less often with STEMI. However, an IABP was inserted more frequently in patients with MV_{index} PCI. As expected, a larger number of stents were also used in such patients and total stent length was more than in SV PCI and MV_{staged} PCI patients. Antithrombotic medication before angiography and for PCI did not differ between the treatment groups.

In-hospital outcome

In-hospital outcome is shown in table 3. In-hospital mortality was 2.4 % for patients with SV PCI, 1.9% for patients with MV_{index} PCI and 0.8% for patients with MV_{staged} PCI ($p = 0.566$). Thus, in-hospital mortality for multivessel revascularisation (MV_{index} and MV_{staged} PCI) was 1.1% ($p = 0.351$ compared to single-vessel revascularisation). Myocardial infarction occurred in 1.4%, 0% and 1.6% for SV PCI, MV_{index} PCI and MV_{staged} PCI respectively, $p = 1.000$. Acute stent thrombosis occurred in two patients with SV PCI, two with MV_{staged} PCI and none with MV_{index} PCI respectively, $p = 0.798$. While no cerebrovascular accidents occurred in the patients with SV PCI or MV_{index} PCI, cerebrovascular accidents occurred in 2 patients with MV_{staged} PCI. The

rate for unplanned PCI and need for coronary artery bypass grafting did not differ. Peak creatinine was not higher in patients undergoing MV_{index} PCI. In the subgroup of patients presenting with STEMI, in-hospital mortality was 3/125 (2.4%), 1/18 (5.6%) and 0/75 (0%) for patients treated by SV PCI, MV_{index} PCI and MV_{staged} PCI respectively, $p = 0.222$. Significantly more patients presented with an inguinal haematoma after undergoing MV_{index} PCI (0.5%, 9.4% and 2.4% for SV PCI, MV_{index} PCI and MV_{staged} PCI respectively, $p = 0.001$). Possible causes of inguinal haematoma in MV_{index} PCI patients included need for an intra-aortic balloon pump (IABP) in 2 patients, use of a Gp2b3a inhibitor for 12 h after PCI in 1 patient. One patient already presented with inguinal haematoma after diagnostic catheterisation in the referring hospital. In one patient no specific reason for inguinal haematoma could be found.

None of the patients in the MV_{staged} PCI group had an adverse cardiovascular event within 30 days of staged revascularisation.

As shown in table 2, a total of 28 patients presented with left main stenosis $\geq 50\%$. These patients were more often treated with MV_{index} PCI. In-hospital

Table 3

In-hospital outcome.

| Variable | Single-vessel PCI (n = 209) | Multivessel PCI index procedure (n = 53) | Multivessel PCI staged (n = 129) | p value |
|---------------------------------------|-----------------------------|--|----------------------------------|---------|
| Death | 5 (2.4%) | 1 (1.9%) | 1 (0.8%) | 0.566 |
| Myocardial infarction | 3 (1.4%) | 0 (0%) | 2 (1.6%) | 1.000 |
| Acute stent thrombosis | 2 (1.0%) | 0 (0%) | 2 (1.6%) | 0.798 |
| CVA | 0 (0%) | 0 (0%) | 2 (1.6%) | 0.211 |
| Unplanned PCI | 1 (0.5%) | 1 (1.9%) | 2 (1.6%) | 0.457 |
| CABG | 3 (1.4%) | 0 (0%) | 0 (0%) | 0.548 |
| Major bleeding | 8 (3.8%) | 6 (11.3%) | 5 (4.0%) | 0.068 |
| Inguinal haematoma | 1 (0.5%) | 5 (9.4%) | 3 (2.4%) | 0.001 |
| Retroperitoneal bleeding | 3 (1.4%) | 0 (0%) | 0 (0%) | 0.276 |
| Other bleeding | 4 (1.9%) | 1 (1.9%) | 2 (1.6%) | 0.978 |
| Peak creatinine ($\mu\text{mol/L}$) | 111 \pm 78 | 97 \pm 35 | 101 \pm 74 | 0.403 |

CVA: cerebrovascular accident; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting.

Table 4

Kaplan Meier estimates of 1-year outcome.

| Variable | Single-vessel PCI | Multivessel PCI index procedure | Multivessel PCI staged | p value |
|-----------------------------|-------------------|---------------------------------|------------------------|---------|
| Death | 8 (4.6%) | 2 (4.0%) | 4 (4.9%) | 0.966 |
| Myocardial infarction | 4 (2.5%) | 1 (3.4%) | 2 (1.6%) | 0.924 |
| CVA | 0 (0%) | 0 (0%) | 1 (1.2%) | 0.126 |
| Unplanned revascularisation | 21 (13.2%) | 3 (8.1%) | 8 (9.4%) | 0.525 |
| Combined endpoint | 21 (13.1%) | 5 (12.1%) | 12 (13.4%) | 0.981 |

CVA: cerebrovascular accident. Data in parentheses represent Kaplan-Meier estimates for 1-year event rate. P values indicate overall comparison using the log-rank test.

mortality (7.1% vs. 1.4%, $p = 0.028$), the rates of unplanned CABG (7.1% vs. 0.3%, $p = 0.014$) and of major bleeding (14.3% vs. 4.2%, $p = 0.040$) were higher in these patients. Rates of CVI, MI and unplanned PCI did not differ.

Long-term outcome

Kaplan-Meier estimates of event rate at one-year follow-up are reported in table 4. Mortality and adverse event rates did not differ between treatment strategies. Mortality was 4.6%, 4.0% and 4.9% for patients with SV, MV_{index} and MV_{staged} PCI respectively, $p = 0.966$. Cumulative event rate including death and major cardiovascular events was 13.1%, 12.1% and 13.4% for patients with SV, MV_{index} and MV_{staged} PCI respectively, $p = 0.981$. Cumulative event rate is also shown in figure 1.

Table 5

Cox-regression analysis of multivessel PCI (during the index procedure or staged) compared to single-vessel PCI.

| Endpoint | Hazard ratio | 95% CI | p value |
|-----------------------------|--------------|-------------|---------|
| Death | 0.90 | 0.31–2.59 | 0.841 |
| Myocardial infarction | 0.752 | 0.179–3.155 | 0.697 |
| Unplanned revascularisation | 0.675 | 0.34–1.34 | 0.260 |
| Combined endpoint | 1.059 | 0.571–1.965 | 0.855 |

CI: confidence interval

Figure 1

Kaplan-Meier estimates of survival free from major cardiovascular events in patients with multivessel coronary artery disease according to treatment strategy.

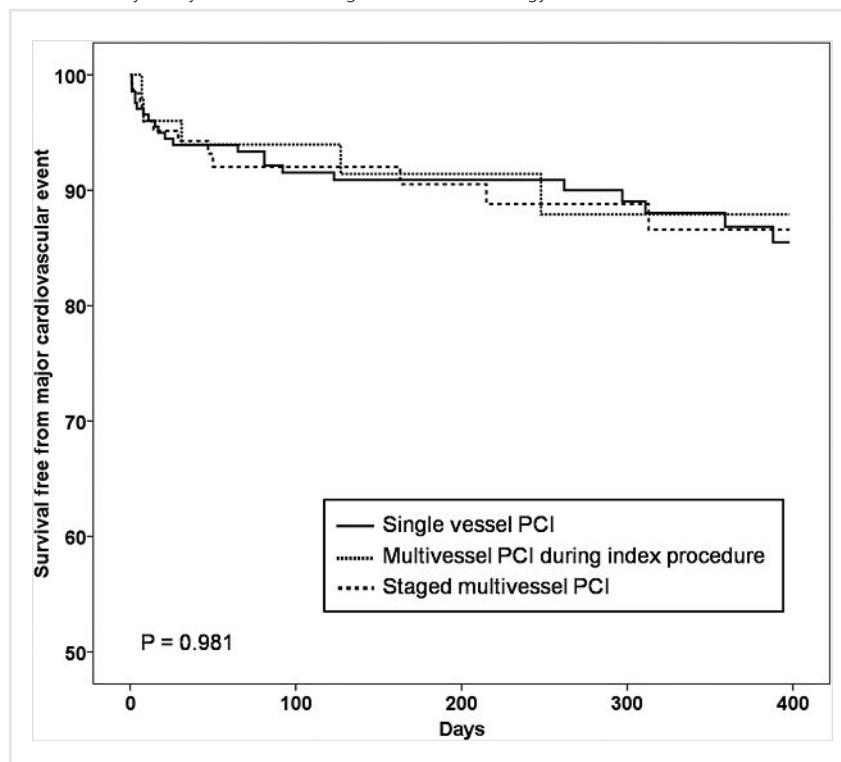


Table 5 compares long-term outcome between single-vessel revascularisation and multivessel revascularisation (MV, including MV_{index} and MV_{staged} PCI). Mortality was the same in SV and MV PCI (HR 0.90, 95% CI 0.31–2.59). Cumulative event rate did not differ (HR 1.06, 95% CI = 0.57 – 1.97).

Discussion

In the present study we compared three different treatment strategies: (1) single-vessel treatment of the IRA only, (2) multivessel revascularisation during the index procedure and (3) staged multivessel revascularisation. Inguinal haematoma was significantly more frequent in patients undergoing MV_{index} PCI. However, in two of these patients inguinal haematoma was associated with use of an IABP, and an IABP was significantly more often inserted in patients undergoing MV_{index} PCI. Otherwise, short- and long-term mortality and the rate of major adverse cardiovascular events were similar in all three treatment groups. In-hospital mortality in patients treated with multivessel PCI was indeed as low as 1.1% and compared well with the 2.4% rate in patients treated by single-vessel revascularisation. The low in-hospital mortality of all treatment groups may be explained at least in part by the exclusion of patients presenting in cardiogenic shock. This may have limited the power of this study to detect differences between groups. On the other hand, the combined event rate during the first year was relatively high, probably due to the presence of multivessel disease and hence selection of a patient population at high risk of future adverse cardiovascular events. Peak creatinine was not higher in patients undergoing MV revascularisation during the index procedure.

Comparison to previous studies

Current guidelines recommend single vessel PCI of the IRA only in haemodynamically stable patients [4, 5]. There is ongoing debate as to whether or not complete revascularisation may improve prognosis in patients presenting with an

acute coronary syndrome, since by this approach all areas of potential ischaemia are effectively treated. A recent metaanalysis has suggested that elective revascularisation may improve outcome in patients with recent myocardial infarction, but not in patients without such an event [14]. Furthermore, use of drug eluting stents has led to lower rates of revascularisation and mortality in patients with acute myocardial infarction [15–17].

A number of retrospective studies comparing single-vessel and multivessel treatment of patients with myocardial infarction have been published. Most of the studies have compared outcome of SV and MV_{index} PCI [18–22] only. A few studies have included patients treated by MV_{staged} PCI [23–26]. Altogether, the conclusions of these studies were inhomogeneous: indeed, in Corpus et al. [23], reporting on patients with prior myocardial infarction treated in early 2000, multivessel PCI was associated with higher rates of reinfarction, revascularisation and major adverse cardiac events at 1-year follow-up. They concluded that in patients with multivessel disease PCI should be restricted to the infarct-related artery. However, the majority of these patients were treated with bare metal stents. Rigattieri et al. [24] reported in 2008 that multivessel, staged PCI was associated with a lower incidence of adverse events at follow-up (9.3% vs 23.9%, $P = 0.037$), but this strategy was associated with a higher incidence of in-hospital major adverse cardiac events. In contrast, evaluation of the combined endpoint at one year did not show any difference between multivessel, staged PCI and single-vessel PCI, which is in line with our results. Han et al. [25] used drug-eluting stents in more than 90% of their patients and found no difference in major adverse cardiovascular events or mortality during a 12-month follow-up. However, the rate of recurrent angina and depressed left ventricular ejection fraction was lower in patients undergoing multivessel revascularisation with the second intervention performed 7–15 days after the index procedure. Finally, Hannan et al. [26] recently reported increased in-hospital mortality in patients undergoing multivessel revascularisation during the index procedure but lower 12-month mortality in patients with MV_{staged} PCI performed within 60 days of the index procedure, including during the index admission.

Overall, 218 patients in this study presented with ST elevation myocardial infarction. Only 18 (8%) were treated by multivessel PCI. This is in line with a recent state-of-the-art paper suggesting that default strategy in patients with ST elevation myocardial infarction and multivessel disease should be single vessel PCI [27].

Clinical relevance

Clinical practice and several studies have highlighted the fact that multivessel disease is frequently present in patients presenting with ACS. In previously published series of patients with acute myocardial infarction, multivessel CAD was found in about 40–50% of the cases [28, 29]. In our study the rates of multivessel disease tended to be even higher and were 52%, 63% and 58% for patients with STEMI, NSTEMI and unstable angina pectoris respectively. It is therefore important to define an optimal treatment strategy in such patients. The results of the present study suggest that multivessel PCI in patients presenting with ACS is safe but does not outperform single-vessel revascularisation during a 1-year follow-up. However, as no additional hospitalisation is required, multivessel PCI during the index procedure may be cost-effective compared to staged multivessel PCI.

Limitations

This is a retrospective non-randomised single-centre study without predefined criteria for treatment selection. Moreover, coronary lesions were classified on the basis of the respective operator's visual estimation, which involves uncertainty. Tests for the detection of ischaemia such as pressure wires or scintigraphy were not routinely used. Also, the number of patients included in this study was small and confidence intervals were relatively wide. Finally, the follow-up time of one year was relatively short and may lead to underestimation of the benefits of multivessel revascularisation [19]. Indeed, one year of follow-up may not be long enough to show differences in outcome of a disease that may take decades to develop its complications [30], particularly in patients receiving optimal medical care.

Conclusion

We conclude, with respect to the limitations of this study, that multivessel PCI in patients with ACS did not outperform single-vessel revascularisation during a 1-year follow-up. Multivessel PCI during the index procedure was associated with a higher rate of inguinal haematoma. Prospective, randomised trials including a larger patient population and long-term follow-up are needed to determine the optimal treatment strategy in patients with ACS and multivessel disease.

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