Safety of early discharge in low risk patients after acute ST-segment elevation myocardial infarction, treated with primary percutaneous coronary intervention. Open label, randomized trial

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Background. The length of hospital stay in patients with acute myocardial infarction and ST-segment elevation (STEMI) has been shortened in recent years with corresponding savings in costs, but there is limited available data on its implementation in clinical practice. The aim of this trial was to determine whether early discharge in selected patients after STEMI is feasible and safe.

Methods. 151 patients with STEMI successfully treated with primary percutaneous coronary intervention (PCI) who fulfilled the inclusion criteria of low risk were randomly assigned to two groups on a 1:1 ratio: early (within 48-72 h of admission) and standard (after 72 h) discharge. The primary end point was the composite of death, myocardial infarction (MI), unstable angina, stroke, unplanned rehospitalization, repeated target vessel revascularization and stent thrombosis at 90 days after discharge. The study is registered with ClinicalTrials.gov (identifier NCT02023983).

Results. The primary end point occurred in 5 patients in the early group and 6 in the standard group (6.6% vs. 8.0%, $P=0.765$). There were no significant differences in the incidence of individual components of the primary end point at 90 days. The length of hospital stay was significantly shorter in the intervention group (60.8 ± 8.5 vs. 92.1 ± 12.1 h, $P<0.0001$).

Conclusion. This study confirms that early discharge within 48-72 h in selected low risk patients after STEMI treated with successful primary PCI is feasible and safe, with outcomes comparable to the later discharge. This strategy applies to more than a quarter of all STEMI patients.

Key words: ST elevation myocardial infarction, percutaneous coronary intervention, patient discharge, feasibility, safety

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INTRODUCTION

There is now a substantially reduced length of hospital stay in patients with a diagnosis of myocardial infarction and ST-segment elevation¹. Significant reduction in health cost associated with this strategy has been consistently found²⁻⁴.

At the time when this study was designed, the Guidelines of the European Society of Cardiology (ESC) recommended that early discharge (after around 72 h) after myocardial infarction (MI) with ST-segment elevation, could be considered in selected patients (class of recommendation IIb, level of evidence B), if adequate follow-up was arranged⁵. However, there is limited available data on its implementation in clinical practice.

The aim of this trial was to determine whether early discharge (within 48-72 h) in patients with low risk of complications after STEMI, treated with successful primary PCI, is feasible and safe, and that early discharge is equal to patients discharged, according to current local practice and the physician's decision (usually 3rd-5th

day). A third aim was to observe whether or not this approach is associated with higher incidence of complications in the following 90 days after myocardial infarction.

MATERIALS AND METHODS

This was a prospective, open-label, randomized, single centre study enrolling low risk patients with STEMI, successfully treated with primary PCI. The study was carried out in agreement with the Declaration of Helsinki and registered with ClinicalTrials.gov (identifier NCT02023983). The approval of the local Ethics committee of the Municipal Hospital Ostrava was gained prior to the start of recruitment. All individual participants included in the trial signed an informed consent at the study outset.

Calculated sample size for non-inferiority margin 10% was 126 subjects per group.

Inclusion criteria, definition of low risk and thus eligibility for enrollment in the study, are listed in Table 1. The trial scheme is shown in Fig. 1.

Fig. 1. Study scheme.

The participants were randomly (simple envelope method) assigned to two groups in a 1:1 ratio. Patients with complications or serious comorbidities, requiring additional evaluation within extended primary hospitalization at the discretion of treating physician, were excluded.

The primary end point was the composite of death, MI, unstable angina, stroke, unplanned rehospitalization, repeated target vessel revascularization and stent thrombosis within 90-days of follow-up.

The participants were admitted to the coronary care unit and then discharged from this unit or stepdown intermediate unit. No patient was transported back to the referring hospital. Echocardiography was used for evaluation of left ventricular function. Clinical check-up of patients randomized to the intervention group was performed at an outpatient visit no later than 4 days after discharge. The following 30-day and 90-day check-ups were done at the clinic or by telephone.

Statistical analysis

All patients completed the 90-day follow-up and were included in the analysis. Statistical data were processed using SPSS Statistics software package, version 22 (IBM Corporation, Armonk, NY, USA). Fischer's exact test was used for comparison of qualitative variables. For comparison of quantitative variables we applied the Mann-Whitney U test or Student's t-test (age). The normality of the data was assessed with the Shapiro-Wilk test. $P < 0.05$ were considered statistically significant.

RESULTS

578 consecutive patients with a diagnosis of STEMI, treated with successful primary PCI, were admitted to our hospital within the period October 15, 2013 and November 23, 2016. 151 (26.1%) fulfilled the inclusion

Table 1. Inclusion criteria.

- STEMI treated with successful primary PCI within 12 h of the symptom onset (TIMI flow 3 in infarct-related artery)
- Age ≤ 75 years
- Left ventricular ejection fraction $\geq 45\%$
- Single- or two-vessel disease
- No symptoms of residual ischaemia
- Haemodynamical and rhythmical stability (Killip class I, no arrhythmia requiring treatment occurring > 2 h after PCI)
- Absence of comorbidities, requiring continuation of hospitalization
- Absence of contraindication for dual antiplatelet treatment or need for anticoagulation
- Supposed cooperation, adherence to medical measures and social background

TIMI – thrombolysis in myocardial infarction

criteria, were recruited for study and randomized to two groups in a 1:1 ratio. 18% were females. The patients flow is described in Fig. 2, where the reasons for exclusion are likewise listed. The interim results of this study have been published⁶.

The baseline characteristics of the groups, the procedural data and left ventricular ejection fraction are shown in Table 2, with the exception of body-mass index, the cohorts were similar. The most frequent risk factors were smoking, dyslipidemia and hypertension.

Inferior localization of MI clearly dominated (62.3%), the distribution of infarct related arteries between groups was slightly different ($P=0.049$). The radial approach as well as the use of drug eluting stents were preferred. Aspiration thrombectomy was used in less than half of the cases, glycoprotein IIb/IIIa inhibitors were administered as bailout therapy only (14.5% vs. 16%) – no significant differences between groups. Before PCI, about half of infarct related arteries were occluded (TIMI 0 flow), on the contrary more than a quarter of patients (28.9% vs. 26.7%) showed normal (TIMI 3) flow – with no significant difference between groups. Mean left ventricular ejection fraction was practically normal and there were no differences between groups. The length of stay was significantly ($P < 0.0001$) shorter in the intervention group (Table 3, Fig. 3).

With regard to the medication at discharge, all patients took dual antiplatelet therapy (aspirin and P2Y₁₂ inhibitors) and a statin. There were no differences between groups in terms of β -blockers or renin-angiotensin-aldosterone system inhibitors (angiotensin-converting enzyme inhibitor or angiotensin II receptor blockers) administration (88.2% vs. 85.3%, $P=0.639$ and 98.7% vs. 97.3%, $P=0.620$, respectively).

The primary end point at 3 months occurred in 5 patients in the intervention group and 6 patients in the standard group (6.6% vs. 8%, $P=0.765$). There were no

Fig. 2. Patient flow.

Fig. 3. Distribution of length of stay in compared groups.

significant differences in the incidence of individual components of the primary endpoint. No patient died and no stroke occurred within the 90-day follow-up (Table 4).

2 stent thromboses were registered in the group with standard discharge (19th and 88th day, the first of them 12 days after patient cessation of P2Y₁₂ inhibitor). No adverse event occurred between early discharge and the first clinical check-up in the outpatient clinic 2–4 days after discharge. 1 symptomatic (prolonged mild wrist pain) radial artery occlusion was detected in the group with early discharge. No other complications associated with the puncture site requiring treatment occurred.

DISCUSSION

This study shows that early discharge in selected patients with STEMI treated with primary PCI is possible and safe and is not associated with higher risk of complications in the following 90 days compared to deferred discharge.

Primary percutaneous coronary intervention is currently the most effective method of reperfusion in patients presenting with acute STEMI (ref.⁷). As a logical consequence of advances in therapy and hospital care, including early rehabilitation and mobilization, the length of hospital stay in STEMI patients has been significantly

Table 2. Baseline clinical characteristics of the analyzed cohorts. Procedural data of PCI and left ventricular ejection fraction.

	Early discharge	Standard discharge	<i>P</i>
n	76	75	
Female	15 (19.7%)	12 (16%)	0.672
Age – mean	56.7 ± 9.2	58.0 ± 8.7	
- median	56.5	58.0	0.345
- minimum	36.0	35.0	
- maximum	75.0	75.0	
Hypertension	41 (53.9%)	41 (54.7%)	1
Diabetes	7 (9.2%)	7 (9.3%)	0.655
IGT	8 (10.5%)	12 (16%)	
Hyperliproteinemia	54 (71.1%)	58 (77.3%)	0.458
Previous MI	3 (3.9%)	6 (8.0%)	0.327
Previous PCI	2 (2.6%)	6 (8.0%)	0.167
Previous stroke / TIA	2 (2.6%)	2 (2.7%)	1
Peripheral arterial disease	2 (2.6%)	1 (1.3%)	1
Smoking	56 (73.7%)	45 (60.0%)	0.180
Ex-smoking	8 (10.5%)	10 (13.3%)	
Body-mass index	29.9	27.3	0.002
Vessel – LAD	19 (25.0%)	27 (36.0%)	
- C + M	18 (23.7%)	9 (12.0%)	0.049
- RCA	30 (39.5%)	36 (48.0%)	
- other	9 (11.8%)	3 (4.0%)	
1-vessel disease	48 (63.2%)	39 (52.0%)	0.189
2-vessel disease	28 (36.8%)	36 (48.0%)	
Radial approach	75 (98.7%)	75 (100%)	1
Drug eluting stent	64 (84.2%)	70 (93.3%)	0.121
Initial TIMI flow 0	41 (53.9%)	37 (49.3%)	
1	6 (7.9%)	8 (10.7%)	0.788
2	7 (9.2%)	10 (13.3%)	
3	22 (28.9%)	20 (26.7%)	
GP IIb/IIIa inhibitors	11 (14.5%)	12 (16.0%)	0.824
Aspiration thrombectomy	35 (46.1%)	35 (46.7%)	1
Left ventricular EF (%)	55.8 ± 5.1	54.6 ± 5.8	0.225

IGT – impaired glucose tolerance, TIA – transient ischemic attack,

LAD – left anterior descending artery, C – circumflex branch, M – marginal branch, RCA – right coronary artery, GP IIb/IIIa inhibitors – glycoprotein IIb/IIIa inhibitors, EF – ejection fraction

shortened within the past 50 years. An overview of the relevant literature showed wide methodological variation in given publications with e.g. 3–63% of probands fulfilling the criteria for early discharge! The current guidelines proceed from limited data derived from randomized trials.

At present, the low risk STEMI population requiring shorter in-hospital observation is well defined⁸⁻¹². Grines et al. in the PAMI II study, defined low risk as: age < 70 years, left ventricular ejection fraction > 45%, single- or two-vessel disease, successful percutaneous coronary intervention and no persistent arrhythmias. STEMI patients were randomized to accelerated care (4.2 ± 2.3 days) and traditional care (7.1 ± 4.7 days) and at 6 months there were no significant differences in mortality, unstable ischaemia, reinfarction, stroke, heart failure or their combined occurrence⁴. Substantial cost reduction was demonstrated as well. De Luca et al.¹¹ created a practical score (Zwolle Risk Score for STEMI) for risk stratification of patients with STEMI, treated with primary PCI. They identified age, anterior infarction, Killip class, ischemic time,

Table 3. Length of hospital stay.

	Early discharge	Standard discharge	<i>P</i>
Average (h)	60.8 ± 8.5	92.1 ± 12.1	
Median (h)	61.0	91.0	< 0.0001
Minimal (h)	43.0	74.0	
Maximal (h)	72.0	132.0	

postprocedural TIMI flow in infarct related artery and multi-vessel disease as independent predictors of 30-day mortality. Score ≤ 3 designates low-risk patients.

In recent years, several randomized trials have shown the possibility of length of stay shorter than 72 h. Kotowycz et al.¹³, Azzalini et al.¹⁴ and Jirmář et al.¹⁵ provide evidence of the feasibility of early discharge in their small studies (with 54-100 probands).

Noman et al. carried out a retrospective analysis of 2448 STEMI patients treated with primary PCI and surviving to hospital discharge¹⁶. Patients with TIMI 3 flow

Table 4. Results.

	Early discharge		Standard discharge		<i>P</i>
	n	%	n	%	
Primary composite endpoint	5	6.6	6	8.0	0.765
Death	0	0	0	0	-
Myocardial infarction	1	1.3	2	2.7	0.620
Unstable angina	1	1.3	1	1.3	1
Unplanned rehospitalization	5	6.6	6	8.0	0.765
Repeated target vessel revascularization	1	1.3	3	4.0	0.367
Stent thrombosis	0	0	2	2.7	0.245
Stroke	0	0	0	0	-

in infarct related artery and without haemodynamic or arrhythmic complications were considered for early discharge at the discretion of the attending physician: a total of 1542 patients (63%) were discharged within 2 days of admission (early discharge group) and the remaining 37% after 2 days (late discharge). The 30-day post-discharge mortality rate was 0.71% in the early group and 1.66% in the late group. During a mean follow-up of 584 days, mortality was 4.3% vs. 12.3% ($P<0.0001$). To the best of our knowledge only two larger randomized studies have been published on this issue: Melberg et al.¹⁷ randomized 215 patients to either early discharge (≤ 3 days) or usual routine discharge. During follow-up there were no deaths, and similar readmission rate (3.7% vs. 2.8%, $P=0.69$) in the early vs. usual discharge group respectively. No differences in the 30 days health status measurements were registered. In a recent large trial, Satilmisoglu et al.¹⁸ randomly assigned 769 probands with STEMI to early (within 48 to 56 h of uneventful course) or standard discharge group. The inclusion criteria were as follows: acute STEMI, a successful primary PCI procedure, an uneventful 24-hour follow-up period, single epicardial artery to be treated. Primary outcomes were all-cause mortality and readmission at 30 days. There were no significant differences in mortality or readmissions between groups ($P=0.684$ and $P=0.061$, respectively) and the patients reported similar health status at 30 days.

In contrast to Melberg and Satilmisoglu's studies we extended the follow-up to 90 days and our study confirmed the intermediate-term safety of the early discharge of selected low-risk patients with STEMI within 48-72 h after admission. Our results further support the recently released new version of ESC guidelines for STEMI (ref.¹⁹) in terms of the level of evidence for the strategy with the shorter recommended length of hospital stay (48-72 h).

However, we agree with Azzalini et al. that even earlier discharge within 48 h is unreasonable¹⁴. It should be stressed that the shorter uneventful hospital stay provides only limited time for proper patient rehabilitation, education and titration of medication. It is therefore advisable to carry out early clinical post-discharge check-up and arrange subsequent regular care, as we did in our study.

The limitation of this trial is the single centre character and limited patient sample. Because of various reasons calculated sample size was not reached, so the statistical power could be questioned.

Further trials are needed to evaluate whether less strict criteria (multivessel disease, more depressed left ventricle function, older population) could be applied for selection of patients in this setting.

CONCLUSION

This prospective, open-label, randomized study showed that early discharge (within 48 – 72 h) in selected low risk patients after STEMI treated with successful primary PCI is feasible and safe. This strategy applies to more than a quarter of all STEMI patients and may be adopted in everyday clinical practice, provided the appropriate follow-up management is arranged to ensure adequate secondary prevention measures.

ABBREVIATIONS

STEMI, myocardial infarction and ST-segment elevation; PCI, percutaneous coronary intervention; MI, myocardial infarction; ESC, European Society of Cardiology; TIMI, thrombolysis in myocardial infarction; IGT, impaired glucose tolerance; TIA, transient ischemic attack; LAD, left anterior descending artery; C, circumflex branch; M, marginal branch; RCA, right coronary artery; GP IIb/IIIa inhibitors, glycoprotein IIb/IIIa inhibitors; EF, ejection fraction.

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