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

Kamil Novobilsky, Roman Stipal, Petr Cerny, Ivo Horak, Vladimir Kaucak, Jan Mrozek, Jan Vaclavik, Radim Kryza

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

INTRODUCTION

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

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 arranged. 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.
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 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
Screened patients with STEMI (n = 578)

- Excluded (n = 427):
  - Multiple reasons (n = 161)
  - Haemodynamical instability and/or LV EF < 45% (n = 96)
  - CPR and intubation before admission (n = 23)
  - Comorbidities (n = 36)
  - Acute or subacute stent thrombosis (n = 3)
  - Age (n = 26)
  - Arrhythmias (n = 4)
  - Non-compliance (n = 16)
  - Contrast-induced nephropathy (n = 2)
  - Staged procedure within index hospitalization (n = 14)
  - Multi-vessel disease (n = 12)
  - Declined consent (n = 3)
  - Anticoagulation (n = 6)
  - Other (n = 25)

Randomized patients (n = 151)

- Early discharge (n = 76)
- Standard discharge (n = 75)

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
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 occurrence. 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, 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.

<table>
<thead>
<tr>
<th>Event</th>
<th>Early discharge</th>
<th>Standard discharge</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite endpoint</td>
<td>5</td>
<td>6</td>
<td>0.765</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
<td>2</td>
<td>0.620</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Unplanned rehospitalization</td>
<td>5</td>
<td>6</td>
<td>0.765</td>
</tr>
<tr>
<td>Repeated target vessel revasculariza</td>
<td>1</td>
<td>3</td>
<td>0.367</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>0</td>
<td>2</td>
<td>0.245</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

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.

Acknowledgement: The authors kindly thank Mgr. Jana Zapletalová, Dr., Department of Medical Biophysics, Faculty of Medicine and Dentistry, Palacky University Olomouc, for her help with statistical analysis. Author contributions: KN: conception, study design, literature search, execution, data collection, data analysis and data interpretation of the data, manuscript writing; RS: execution and interpretation of the data; PC, IH, VK, JM: conception; JV: conception, data interpretation, manuscript writing; RK: conception. Conflict of interest statement: The authors state that there are no conflicts of interest regarding the publication of this article.
REFERENCES


