Verification of the safety of early discharge (within 72 hours) in low risk patients after acute ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention. Open randomized study.

(NCT02023983)

Study protocol

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Study sponsor, principal investigator:

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Introduction:

Within past decades we can observe the clear trend towards the shortening of the hospital stay in pateints admitted with the diagnosis of myocardial infarction with ST segment elevations (STEMI).
The current Guidelines of European Society of Cardiology for the management of acute myocardial infarction with ST-segment elevation, released in 2012, state, that in the selected patients may be considered (class of recommendation IIb) early discharge (after approximately 72 hours), if adequate follow-up is arranged.
Level of evidence of cited recommendation is B, i.e. it is based on data, derived from a single randomized clinical trial or large non-randomized studies.
The overview of literature on this topic shows non-uniform mtehodology of these works and heterogenous features of studied populations (3 – 63% fulfilled criteria for early discharge!)
In the PAMI II study tle low risk was defined as following: age <70 years, left ventricule ejection fraction >45%, one- or two-vessel disease, successful percutaneous coronary intervention (PCI) and no persistent arrythmias.
In Czech Republic the issue of early discharge was investigated in PRASGUE 5 study (Jirmar et al., 2008), which after pilot phase randomized 56 low risk probands with STEMI, discharged even the next day after successful PCI. The strict inclusion criteria (fulfilled only 3% patients with acute STEMI) included age < 75 years, optimal result of primary PCI, on-vessel disease, left ventrikule ejection fraction > 40%, place of residence < 20km, exclusion criteria involved patients after Q-MI, haemodynamically or rythmically instable, with recurrent chest pain or clinical/laboratory findings requiring additional evaluation. Followed endpoints were death, reinfarction, stroke, instable angina pectoris, repeat target vessel revascularization, local groin complications requiring treatment and left ventricule ejection fraction within 30 days. This study also showed, that very early discharge in clearly defined group of patients is safe, there was just one rehospitalization due to non-cardiac cause in the group of 37 paients, discharged the next day after MI, there was no other serious event in study population.
By the verification of safety of early discharge this study wants to confirm the applicability of presented conclusions even in the regular clinical practice in our circumstances.

References:

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Design of clinical investigation

Clinical, prospective, monocentric, randomized, open study

Study objective:

The aim of the study is to prove

- that early discharge (within 72 hours) in selected group of patients with low risk of follow-up complications after myocardial infarction with elevations of ST segment, treated with primary percutaneous coronary intervention, is feasible and safe
- that early discharge is „non-inferior“ in comparison with the group of patients, discharged in a standard way accordingly with present practice and physician´s decision (usually 4th-7th day), thus it is not associated with higher incidence of complications in 30th and 90th day after myocardial infarction

Impact on other therapeutic measures:

The study hes no impact on the subsequent care, which is commonly provided to all patietnts after myocardial infarction: it does not concern the medication, control paraclinical tests and regular clinical controls, scheduled by the attending physician.

Study population:
All subjects enrolled in the study.

Study eligibility:
All inclusion and no exclusion criteria of enrolled patients mus be fulfiled.

Incluison criteria:

- Signed informed consent
- STEMI treated with successful primary PCI within 12 h of the symptom onset (TIMI flow 3 in infarct-related artery)
- Age ≥18 and ≤ 75 years
- Left ventricular ejection fraction ≥ 45%
- One- or two-vessel disease ((stenosis of major epicardial artery ≥ 70%)

- No symptoms of residual ischaemia
- Haemodynamical and rhythmical stability ((Killip class I, no arrytmia requiring treatment occurring > 2 hours after PCI)
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- 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

Exclusion kriteria:

- Symptoms of residual ischemia
- Significant comorbidities or abnormalities in paraclinical tests, requiring additional evaluation within continuing hospitalization
- Contraindication of dual antiplatelet therapy or need for anticoagulation therapy
- High risk of bleeding complications
- Participation in other clinical study

Informed consent:
All enrolled patients must give their informed consent for participation in the study.

Endpoints:

Primary endpoint:

- Composite of incidence of death, reinfarction, unstable angina pectoris, stroke, unplanned rehospitalization, repeat target vessel revascularization and stent thrombosis in 90 days after myocardial infarction

Secondary endpoint:

- Complications associated with the puncture site requiring rreatment in 30 days after myocardial infarction

Definitions:

Myocardial infarction
Criteria for the acute myocardial infarction (MI):
evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia.
Under these conditions any one of the following criteria meets the diagnosis for MI:
• Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following:

- Symptoms of ischaemia.
- New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB).
- Development of pathological Q waves in the ECG.
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- Identification of an intracoronary thrombus by angiography or autopsy.

• Cardiac death with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes or new LBBB,but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.
• Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values (>5 x 99th percentile URL) in patients with normal

baseline values (≤99th percentile URL) or a rise of cTn values >20% if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischaemia or (ii) new ischaemic ECG changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.
• Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischaemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.
• Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (>10 x 99th percentile URL) in patients with normal baseline cTn values (≤99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Criteria for prior myocardial infarction
Any one of the following criteria meets the diagnosis for prior MI:
• Pathological Q waves with or without symptoms in the absence of non-ischaemic causes.
• Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischaemic cause.
• Pathological findings of a prior MI.

ST-segment elevation – ECG characteristics
New ST elevation at the J point in two contiguous leads with the cut-points: ≥0.1 mV in all leads other than leads V2–V3 where the following cut points apply:≥0.2 mV in men ≥40 years;≥0.25 mV in men <40 years, or ≥0.15 mV in women.

Percutaneous coronary intervention
Refers to all interventional cardiology methods for treatment coronary artery disease

Unstable angina
is considered to be present in patients with ischemic symptoms suggestive of an ACS and no elevation in troponin, with or without ECG changes indicative of ischemia (eg, ST segment depression or transient elevation or new T wave inversion).

Stroke

Presence of focal neurological deficit, occuring due to brain vessel lesion, persisting > 24 hours or lasting < 24 hours, if the pharmacological or non-pharmacological treatment was applied

Target vessel revascularization

Any repeat percutaneous intervention or surgical bypass of any segment of target vessel

Stent thrombosis:

Definite

The presence of an angiographic confirmation of stent thrombosis (the presence of a thrombus that originates in the stent or in the segment 5 mm proximal or distal to the stent) is associated with the presence of at least one of the following criteria within a 48-hour window: acute onset of ischaemic symptoms at rest, new ischaemic electrocardiographic changes that suggest acute ischaemia or typical rise and fall in cardiac biomarkers; or in the presence of a pathological confirmation of stent thrombosis (evidence of recent thrombus within the stent determined at autopsy or via examination of tissue retrieved following thrombectomy). The incidental angiographic documentation of stent occlusion in the absence of clinical signs or symptoms is not considered a confirmed stent thrombosis (silent occlusion).

Probable

Probable stent thrombosis is defined as the presence of any unexplained death within the first 30 days after stent implantation, or in the presence of any MI related to documented acute ischaemia in the territory of the implanted stent without angiographic confirmation of stent thrombosis and in the absence of any other obvious cause, irrespective of the time after the index procedure.

Possible

Possible stent thrombosis is defined as any unexplained death from 30 days after intracoronary stenting until the end of follow-up.

TIMI (Thrombolysis In Myocardial Infarction) classification:

developed by TIMI study group to semiquantitatively assess coronary artery perfusion beyond point of occlusion on coronary angiography.

TIMI 3 – complete perfusion: normal flow with complete filling of the distal territory

Serious adverse event

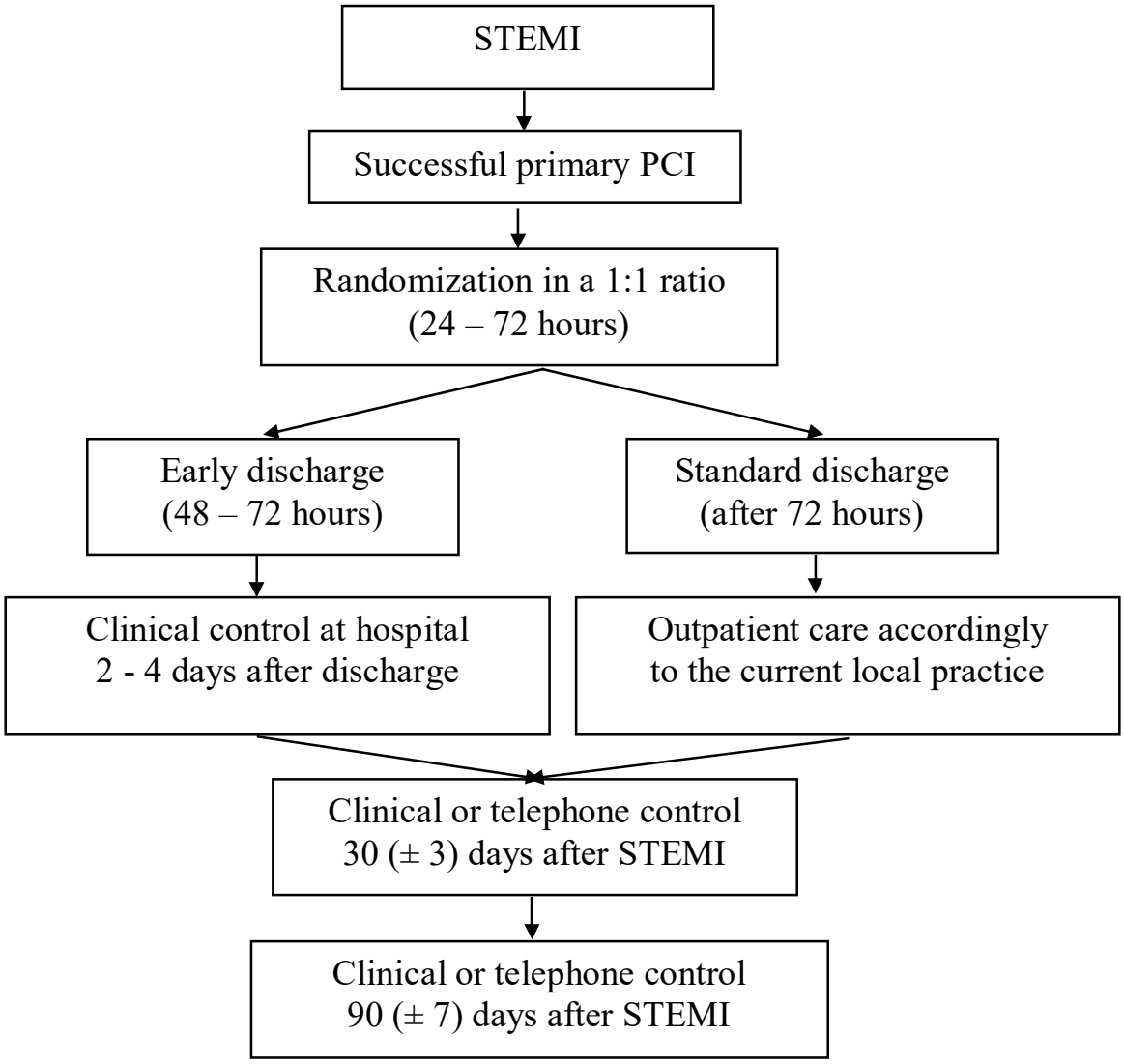
Any adverse drug experience occurring at any dose that results in any of the following outcomes:

- Life-threatening
- Death
- Hospitalization/prolongation of hospitalization
- Congenital anomaly
- Persistent or significant disability/incapacity
- Required intervention to prevent permanent impairment/damage

Other adverse events

Adverse events that are not Serious adverse events

Plan of study:



Number of probands:
Enrollment of about 150-200 patients is planned

Expected total duration of clinical investigation:
3 years

Randomization:
Patients will be assigned into the study groups by the method of simple randomization in ratio 1:1.

The ending or interruption of study:
Whenever in the course of study the patient can end his participation in study on basis of his decision. He will inform promptly his physician about this decisoin.
The recruitment of the subjects will be interrupted, when the preliminary analysis in the course ot the trial shows significant difference in the incidence of endpoints between the study groups.

Statistic:
All subjects, participating in the study and completing the follow-up, will be involved into the statistical analysis. Considered rate of probands lost within follow-up is 2%.
The adequate methods of statistical evaluation of the study results will be used. Baseline demographic, clinical, angiographic, periprocedural data and results will be summarized using descriptive summary statistics.
Fischer´s exact test will be used for comparison of qualitative variables between two groups. For comparison of quantitative variables Mann-Whitney U test, respectively Student´s t-test will be used. Normality of data will be assessed with Shapiro-Wilk test. The value $p < 0.05$ will be considered as statistically significant.

Open access to source data / documents:

The investigator in case of need and submission of written request gives access to source data/documents for the purposes of clinical investigation monitoring to ethics commitees or controlling authorities inspection.

Data manipulation and retaining of records:
All information concerning the studied subjects will be kept in confidence to the extent, appropriate laws and directions. Medical records and information, obtained within clinical investigation, can be studied by doctors or medical staff practicing the study, local healthcare authorities, auditors, ethics comitees. No personal data of subjects participating in study will be published. Patients will sign the informed consent with collection, transmission, processing and archiving of personal data, including state of health in the connection with conducted study.

Declaration of Helsinki, Ethics comitee:
Trial will be performed in agreement with Declaration of Helsinki. The approval of local Ethics committee will be gained prior to the start of patients recruitment.

Financing:
Clinical investigation does not require special financial support.

Study registration:
Study will be registered in the international register of clinical trials www.clinicaltrials.gov.

Publication activities:
The rseults of study will be published in reviewed medical journal and presented on professional medical congresses.