Efficacy of invasive treatment and the occurrence of cardiac rupture in acute ST-elevation myocardial infarction

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Abstract

Background: Cardiac rupture is a rare but potentially lethal complication of acute myocardial infarction with ST-elevation (STEMI). Primary percutaneous coronary intervention (pPCI) is a preferable treatment method of acute STEMI. Reperfusion at vascular and myocardial levels may be the key parameters determining probability of cardiac rupture.

Aim: To analyse the relationship between reperfusion parameters and cardiac rupture occurrence in a group of patients with STEMI treated with pPCI.

Methods: Twenty three patients with cardiac rupture were selected out of 2800 patients with acute STEMI hospitalised and treated with pPCI from 2000 to 2007. Free wall or interventricular septum rupture was diagnosed on echocardiography or autopsy. The control group consisted of 255 patients with STEMI and pPCI treatment, but without cardiac rupture. The TIMI flow score was used to assess blood flow in an infarct-related artery (IRA). Myocardial perfusion was evaluated with the use of the myocardial blush grade (MBG) score.

Results: Female gender accounted for 47.8% of patients with cardiac rupture. Mean age was 72.9 ± 4.8 years for women and 64.3 ± 11.5 years for men. In 12 (52%) patients anterior descending artery was the IRA. Before the pPCI, the average blood flow in IRA was significantly lower in patients with subsequent cardiac rupture (0.41 ± 0.59) than in the reference group (0.81 ± 1.15; p < 0.05), and remained lower after pPCI (1.96 ± 0.93 in comparison to 2.93 ± 0.36; p < 0.05). Adequate blood flow (TIMI 3) was achieved only in 30.4% (7) of patients with cardiac rupture and in 95.3% (243) of the control group (p < 0.05). Myocardial tissue perfusion, assessed by MBG, was also lower (0.76 ± 1 vs 1.92 ± 1.13; p < 0.05). In-hospital mortality in patients with cardiac rupture reached 56.5% (13 subjects) compared to 3 (1.2%) patients in the reference group (p < 0.05). Multivariable analysis confirmed independent effects of lower TIMI and MBG after PCI as well as female gender on the occurrence of cardiac rupture.

Conclusions: Poorer blood flow in IRA and worse tissue microvascular perfusion after pPCI are important risk factors of cardiac rupture occurrence in patients with STEMI.

Key words: myocardial infarction, primary percutaneous coronary intervention, cardiosurgical treatment, myocardial blush grade, TIMI flow grade

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INTRODUCTION

Cardiac rupture (CR) in the acute phase of ST-elevation myocardial infarction (STEMI) occurs rarely, but it represents the second (after cardiogenic shock) most frequent cause of death in patients with MI [1]. Despite the progress in the diagnosis and therapy of the STEMI patients, the proportion of rupture-related deaths is as high as 2% [2]. The majority of ruptures involve left ventricular (LV) free wall (free wall rupture, FWR) [3, 4]. Less than a half of FWR cases occur within 24 h from infarct onset [2], before the significant inflow of neutrophils into the infarcted area. It means that also non-inflammatory factors play a role in the development of this complication. These include degradation of connective tissue intercellular matrix and cardiomyocyte apoptosis [5, 6]. The increased rate of early rupture related to fibrinolytic treatment drew attention to the potential role of blood extravasation and haemostasis disturbances within the peri-infarct zone, between the necrotic and the healthy myocardium [7]. The abrupt increase of blood pressure caused by Valsalva manoeuvre or physical exercise can act as a trigger [8–10].

Primary percutaneous coronary intervention (pPCI) is the method of choice in the treatment of STEMI patients, aiming at flow restoration in the infarct-related artery (IRA) and adequate tissue perfusion [11]. Reperfusion achieved by pPCI reduces the risk of FWR in comparison with thrombolysis [12–15]. Taking into account the pathophysiology of the acute phase of infarction, it seems that the key parameter that can potentially affect the rate of CR is the effectiveness of reperfusion at the level of the IRA as well as at the myocardial level. The success of reperfusion in patients receiving invasive treatment can be assessed by TIMI flow grade, which estimates blood flow in the epicardial vessels. However, the complete reflow (TIMI 3) does not necessarily mean good myocardial perfusion in the infarcted area [16]. This can be assessed by the myocardial blush grade (MBG) that describes myocardial reperfusion based on the extent of myocardial contrast dynamics during coronary angiography [17].

The aim of the study was to assess the correlation of selected parameters of pPCI success and CR occurrence in invasively treated patients with STEMI.

METHODS

The records of 2800 STEMI patients hospitalised in our department between 2000 and 2007 were analysed. The final analysis included 23 cases of FWR or inter-ventricular septum rupture diagnosed based on autopsy protocols or in-hospital records. The control group consisted of 255 randomly selected STEMI patients treated with pPCI between 2002–2005, in whom CR did not occur.

In coronary angiography, the IRA was determined and the significance of lesions in the remaining vessels was evaluated. The flow in the IRA was assessed prior to and after pPCI according to the TIMI flow grade (0–3) and myocardial perfusion was assessed with MBG (0–3) [16, 17].

Statistical analysis

Results are presented as mean ± SD or numbers and percentages. Differences between analysed parameters were analysed using Student t-test, chi-square test and multi-variable regression analysis test where appropriate. The STATISTICA 9 statistical package was used and a p value < 0.05 was considered statistically significant.

RESULTS

Clinical characteristics are presented in Table 1. Nearly a half of the CR patients were female, whereas women represented as little as 1/4 of the control group. Patients with CR were significantly older than their counterparts without CR. The difference was related mainly to the more advanced age of women in the CR group (Table 1).

In subjects with CR, left anterior descending coronary artery (LAD) was the IRA in 52.2% of cases. In the control group, however, LAD was the IRA significantly less frequently (35.3%) (Table 2). Localisation of infarct was related to the frequency of LAD occlusion. The majority of infarcts occurred in the anterior wall (47.8%; n = 11) or in the inferior wall (30.4%; n = 7). In 60.9% of patients rupture occurred in the free wall and 39.1% — in the inter-ventricular septum.

The TIMI score assessed prior to pPCI and after intervention was significantly lower in the CR patients than in controls (Table 2). The mean MBG value in CR patients was also lower in the CR group (Table 2).

<table>
<thead>
<tr>
<th>Table 1. Characteristics of the study group</th>
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<td><strong>Patients with cardiac rupture (n = 23)</strong></td>
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<td>Female gender</td>
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<td>Mean age [years]:</td>
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<tr>
<td>Females</td>
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<tr>
<td>Males</td>
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<tr>
<td>All</td>
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<tr>
<td>Ejection fraction (ECHO) [%]</td>
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Beside the mean values of these parameters, the groups were also different in terms of the maximum values achieved in both scoring systems. In patients with CR, normal flow (TIMI 3) was achieved in only 30.4% of patients, while in the control group this proportion was 95.3% (p < 0.001) (Fig. 1). Adequate myocardial perfusion (MBG 2–3) in the area supplied by the IRA, was also seen less frequently in patients in whom CR later occurred (21.7% vs 65.1%, respectively; p < 0.05) (Fig. 2). Moreover, a trend towards a more pronounced myocardial perfusion defects in patients in whom IRA patency was restored was noted in this group. For example, there were 3 patients, in whom despite achieving TIMI 3 flow myocardial perfusion was not restored (TIMI 3; MBG 0).

Multivariable logistic analysis revealed a significant and independent effects of impaired myocardial perfusion after PCI (MBG) (p = 0.005; Wald statistics 7.89), lower epicardial flow (TIMI) (p = 0.0004; Wald statistics 12.6) and female sex (p = 0.004; Wald statistics 8.2) on occurrence of CR.

The mortality rate in the CR group was high and amounted to 56.5% (13 patients). The size of the group was not sufficient to achieve statistical significance in terms of survival assessment, but the lower effectiveness of myocardial reperfusion in patients who died of CR, can be appreciated (Table 2).

**DISCUSSION**

Cardiac rupture in the course of MI is not a frequent phenomenon, but unfortunately it results in patient’s death in the majority of cases. Thus, the identification of patients who may be predisposed to this complication is important. This would allow for immediate implementation of close monitoring and adequate surgical or medical treatment. The identification of

<table>
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<th>Table 2. Angiographic parameters</th>
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<tr>
<td><strong>Survivors with CR</strong></td>
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<td>(n = 10)</td>
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<tr>
<td>IRA:</td>
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<tr>
<td>LAD</td>
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<td>Cx</td>
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<td>RCA</td>
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<td>Other</td>
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<td>Prior to pPCI</td>
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<td>After pPCI</td>
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<td>MBG</td>
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CR — cardiac rupture; HR — heart rupture; IRA — infarct related artery; LAD — left anterior descending; Cx — left circumflex; RCA — right coronary artery; Other — marginal branch, diagonal branch; pPCI — primary percutaneous coronary intervention; MBG — myocardial blush grade

Figure 1. TIMI score after angioplasty in patients with CR and in the control group (p < 0.05; χ² test); TIMI — blood flow in the infarct-related artery

Figure 2. Myocardial blush grade (MBG) after angioplasty in patients with CR and in the control group (p < 0.05; χ² test)
The sequence of events leading to the rupture in the infarcted area begins immediately after flow cessation in the coronary artery. The extent of the rupture depends on connective tissue structural injury [5], the number of apoptotic cardiomyocytes [6] and also on the high LV pressure values [8]. In autopsy studies it was demonstrated that patients who died of FWR had higher amounts of subepicardial fat [21]. This phenomenon is particularly pronounced in elderly patients and it promotes local expression of proinflammatory factors [21]. Also other factors contribute to the increased susceptibility of the elderly to cardiac rupture. Young et al. [22] in an experimental study observed that in the population of older, (12-month old) mice, increased density of macrophages and neutrophils and increased expression of proinflammatory cytokines were observed. Moreover, in the elderly mice, intra-ventricular systolic and diastolic pressures were higher and the MMP-9 activity increased [22]. On the other hand, the incidence of CR in mice with MI and MMP-2 deletion or pharmacological inhibition was significantly lower than in mice without such MMP-2 modification [23–25].

In our work, as well as in the previously published studies [26], there was a trend towards a more frequent CR occurrence in the elderly patients, particularly women over 70. Additionally, single-vessel disease and the lack of history of angina are probably related to the absence of collaterals capable of at least minimal blood supply to the infarcted region [26, 27]. Our results demonstrate the importance of the assessment of the patency of IRA and myocardial perfusion analysis in the infarcted area after pPCI. In the previously published studies referring to the relationship between therapy and CR occurrence, the parameter used for evaluation of the therapy effectiveness was only vessel patency [28–30]. Also, the type of therapy (thrombolysis vs pPCI) and time from symptom onset to reperfusion were analysed. A positive correlation between the incidence of myocardial rupture and parameters of coronary flow impairment was noted [30]. However, despite achieving full patency of the IRA, myocardial perfusion is not always equally restored in the infarcted area. Hence, the assessment of IRA patency is not sufficient to fully evaluate the success of pPCI, and complete assessment should include MBG scoring, which reflects the real myocardial reperfusion status [19].

It should be underlined that multivariable analysis demonstrated independent value of the assessment of pPCI success at the epicardial (TIMI) and microvascular (MBG) levels. Similar to previously published studies, it also confirmed that female gender plays a role [26, 27], but contrary to these studies, it did not confirm the independent effects of age as a risk factor. Most probably this is due to the fact that in our population, as in other similar studies [31, 32], women were older and the treatment effectiveness was also somewhat lower in the elderly (age correlation with MBG r = –0.16 and with TIMI r = –0.17). Thus, the age did not contribute significantly to the multivariable model. However, other mechanisms of the effects of ageing on the pathomechanism of CR in thrombolysed [26, 27] and interventional treated patients can not be excluded.

**Limitations of the study**

The limitations of our study result from the fact that it presents single centre data. Also, the number of the studied cases is limited, and the analysis was carried out retrospectively. However, we describe a relatively small population of patients in whom CR occurred despite interventional treatment. Low incidence of CR in our population was related to the fact that medical records did not allow for clinical status assessment immediately before the rupture and the cause of death determination in all patients. Not all the deceased patients had an autopsy performed. In the literature, electromechanical dissociation was automatically treated as the symptom of cardiac rupture [1]. However, in our study, only the confirmed cases of CR were analysed. Before 2002, complete data concerning the number of hospitalised patients with MI was not available. Hence, it was impossible to find out whether the treatment with PCI had an impact on the reduction of CR.

**CONCLUSIONS**

The majority of patients with CR had reduced blood flow in IRA prior to pPCI. Reduced blood flow in the IRA, and, particularly, impaired myocardial perfusion at the microvascular level after the intervention represent significant risk factors for CR in patients with STEMI treated with pPCI.

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**Conflict of interest:** none declared
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Pęknięcie serca u pacjentów z zawałem serca z uniesieniem odcinka ST. Wpływ skuteczności leczenia inwazyjnego

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Streszczenie

Wstęp: Pęknięcie serca jest rzadkim powiklaniem zawału serca z uniesieniem odcinka ST (STEMI), jednak stanowi jedną z głównych przyczyn śmiertelności wewnątrzszpitalnej. Dzięki rozpowszechnieniu pierwotnej przezskórnej interwencji wieńcowej (pPCI) jako metody z wyboru w leczeniu ostrej fazy zawału, częstość pęknięć serca zmaleła. Brakuje jednak dokładnych opracowań czynników ryzyka wystąpienia pęknięcia serca w populacji chorych leczonych interwencyjnie. Wydaje się, że kluczowym parametrem mogącego wpływać na częstość występowania tego powikłania jest skuteczność reperfuzji zarówno na poziomie naczynia odpowiedzialnego za zawał, jak i mikrokrążenia.

Cel: Celem pracy była ocena relacji między wybranymi parametrami skuteczności przezskórnej angioplastyki wieńcowej a wystąpieniem pęknięcia serca u pacjentów ze STEMI leczonych interwencyjnie.


Wyniki: Wśród pacjentów z pęknięciem serca 47,8% populacji stanowiły kobiety. Średni wiek w tej grupie wynosił 72,9 ± 4,8 roku wśród kobiet i 64,3 ± 11,5 roku wśród mężczyzn. W koronarografii wykazano, że w 12 (52%) przypadkach naczyniem odpowiedzialnym za zawał była gałąź przednia zstępująca lewej tętnicy wieńcowej. Średni przepływ w tętnicy wieńcowej przed zabiegiem był istotnie statystycznie niższy w populacji chorych z pęknięciem (odpowiednio 0,41 ± 0,59 w porównaniu z grupą referencyjną 0,81 ± 1,15; $p < 0,05$). Po wykonaniu pPCI przepływ był nadal istotnie niższy w grupie badanej (odpowiednio 1,96 ± 0,93 v. 2,93 ± 0,36; $p < 0,05$). Pełen przepływ w naczyniu odpowiedzialnym za zawał (TIMI 3) osiągnięto jedynie u 30,4% (7) osób z grupy z pęknięciem i u 95,3% (243) z grupy odniesienia (p < 0,05). Perfuzja mięśnia zaopatrywanego przez tętnicę odpowiedzialną za zawał oceniana w skali MBG była również istotnie statystycznie niższa u osób, u których doszło później do pęknięcia miokardium (odpowiednio 0,76 ± 1 v. 1,92 ± 1,13; $p < 0,05$). Śmiertelność wewnątrzszpitalna w przypadku zawału powikłanego pęknięciem wynosiła w populacji leczonej pPCI 56,5% (13 osób), natomiast w grupie referencyjnej zmarł jedynie 3 osoby (1,2%; $p < 0,05$). Analiza wieloczynnikowa wykazała, że niezależnymi czynnikami wpływającymi na wystąpienie pęknięcia serca są: gorszy przepływ TIMI w naczyniu, słabsza perfuzja tkankowa MBG po interwencji wieńcowej i płeć żeńska.

Wnioski: Zajęcie gałęzi przedniej zstępującej, niepełny przepływ w naczyniu odpowiedzialnym za zawał i upośledzenie mikrokrążenia po interwencji wieńcowej są istotnymi angiograficznymi czynnikami ryzyka wystąpienia pęknięcia mięśnia sercowego u chorych ze STEMI leczonych pierwotną interwencją wieńcową.

Słowa kluczowe: pęknięcie serca, zawał serca, przezskórna interwencja wieńcowa, MBC, TIMI

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