Trends in the incidence of the free wall cardiac rupture in acute myocardial infarction. Observational study: experience of a single center

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Abstract

Purpose: Free wall cardiac rupture (CR) is one of the most common cause of in-hospital death in acute myocardial infarction (AMI). The early diagnosis of CR and selection of the patients predisposed to CR become an important clinical tool. Aim: assessing the occurrence of CR in patients with AMI, to determine the factors which could help to identify the patients threatened with CR.

Material and methods: 2320 consecutive patients with AMI. CR was proved by autopsy or by echocardiography performed during cardio-pulmonary resuscitation (CPR).

Results: In-hospital mortality was 11% (254 patients). 50 patients (2%) died from CR. CR was the cause of 20% of total in-hospital death. Patients with CR were older than survivors (72 vs 60 years, $p<0.0001$). Women prevailed in CR group: (62% in CR group vs 27% in the survivors, $p<0.01$). 29% of patients were treated with thrombolytics (Th+). Out of 58 patients from Th (+) group who died, 17 (29.3%) died because of CR. CR occurred in 33 (16.8%) patients out of 196 died in Th (-) group. In the logistic regression analysis only age and sex remained as predictors of CR. 16 patients died from CR during first 24 h from admission (ECR). In 34 patients CR occurred >24 h (LCR). In ECR group were no prevalence of women, while in LCR women constituted 68%. In ECR group all but one patient had no previous history of MI ($p=0.06$). Frequency of thrombolythic therapy was equal.

Conclusions: Advanced age patients, particularly women with first AMI are at risk of CR. Decision of thrombolytic treatment in this group of patients must be very cautious.

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Introduction

Free wall cardiac rupture (CR) became a second most important cause of death in acute myocardial infarction (AMI). Almost inevitably CR leads to death and is considered to be a hopeless situation. Some data suggest, that CR occurs more often than it is clinically diagnosed and in case of subacute CR conservative or surgical treatment could be lifesaving [1,2]. On the other hand different kind of reperfusion therapy (trombolysis or primary PCI) seems to influence the occurrence of CR [3-5]. Therfore the early diagnosis of CR and selection of the patients predisposed to CR become an important clinical tool.

The aim of the study was to assess the trends of occurrence and frequency of CR in patients suffering from AMI admitted to our department and to determine the demographic and clinical factors which could help to identify the patients especially threated with CR.

Material and methods

2320 consecutive patients with AMI admitted to Cardiological Department of Wrocław County Hospital from 1985 to 2001 were retrospectively analysed.

Diagnosis of AMI was established according to the "old" WHO definition: retrosternal pain not responding to sublingual nitrates, ST elevation in at least 2 ECG leads and/or CPK elevation (>2 x normal level).

In respect of AMI localisation, we divided patients into 3 groups: group 1 – anterior Q wave AMI, group 2 – inferior Q wave AMI, group 3 – patients with isolated lateral MI, MI of uncertain localisation, non-Q AMI.

Until 1987 AMI treatment consisted of administration of unfractionated Heparin and intravenous Nitroglycerin. Since

Table 1. **Baseline characteristics of study population by sex**

	All (%) n=2320	Women (%) n=672	Men (%) n=1648	P value
Age	60.9±12	66.0±11	58.6±12	<0.001
AMI localisation				
anterior	910 (*39.2*)	269 (*40.0*)	641 (*38.9*)	
inferior	1083 (*46.7*)	293(*43.6*)	790 (*48.0*)	NS
other	325 (*14.0*)	110 (*16.4*)	215 (*13.1*)	
Thrombolysis	661 (*28.5*)	186 (*27.7*)	475 (*28.9*)	NS
Total mortality	254 (*11.0*)	111 (*16.5*)	143 (*8.7*)	<0.001
CR	50 (*2.2*)	31 (*4.6*)	19 (*1.2*)	<0.00001
OD	204 (*8.8*)	80 (*11.9*)	124 (*7.5*)	<0.001

CR – cardiac rupture; OD – other death

Figure 1. **Bar graphs demonstrating percentage men/women over analysed period**

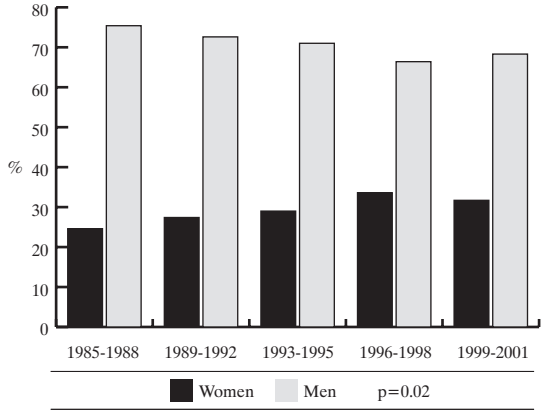
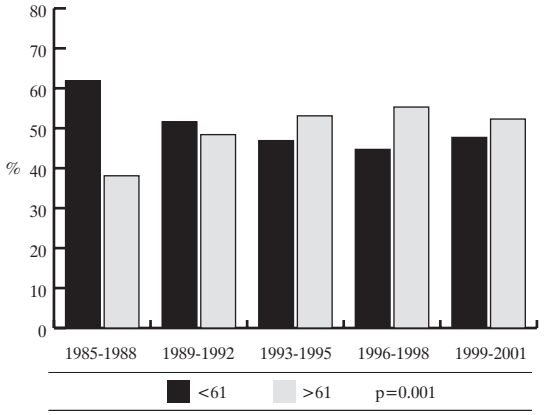


Figure 2. **Bar graphs demonstrating aging of study population (median = 61 years)**



1987 fibrinolytic treatment with streptokinase was introduced, since 1990 – new generations of thrombolytics (t-PA, rt-PA, TNK-tPA) were applied as well as a routine administration of aspirin. Up to 2001 primary percutaeous interventions (PCI) were not performed.

CR was diagnosed in 50 patients. In 39 of them on autopsy. The other 11 patients were included in the CR group on the basis of the signs of electromechanical dissociation (EMD) during cardiopulmonary resuscitation, with CR confirmed by echocardiography. Echocardiographic diagnose of CR was made when liquid layer (more than 1 cm) was present in the pericardial sac, distributed regularly around the heart. Sometimes hyperechogenic structures (clots) were visible.

CR population was divided into 2 subgroups: early CR (ECR) subgroup consisted of 16 patients who died within 24 hours after hospital admission. The remaining 34 patients were included to the late CR (LCR) subgroup.

We analysed demographic and clinical data, localisation of the AMI as well as influence of fibrinolytic treatment. In the CR group we assessed also the anamnestic data like previous myocardial infarction, preceding angina and hypertension, thrombolytic treatment.

Statistical analysis

Results are presented as a mean ± standard deviation (SD) for continuous and normally distributed variables, as median and as percentage for categorical data. Analysis of normality was performed with Kolmogorov-Smirnov test. For continuous variables comparisons between two groups were performed with unpaired two-tailed t-test. Categorical data and proportion were analysed using Chi-square test. Stepwise logistic regression model was developed to analyse the effect of baseline characteristics for the prediction of CR. A p value < 0.05 was considered statistically significant.

Results

Characteristic of the study group is shown in *Tab. 1*.

There were 29% women in study population. Women were significantly older than men. During observation time, the percentage of women with AMI was growing up significantly, AMI population was growing old (*Fig. 1*,*2*).

254 patients (11%) died. During study period hospital mortality ranged from 15.9% to 5.7% and significantly decreased (p=0.01). CR constituted 19.7% of whole deaths. The frequency of CR fluctuated, but increased (*Fig. 3*). CR as a cause of death was noted significantly more often in women than in men. The mean age of AMI survivors (S) was nearly 7 years lower, than those who died, and more than 11 years lower than those who died of CR (*Tab. 2*).

In whole AMI group, inferior wall MI occurred slightly more often, in CR group anterior wall MI was in prevalence.

Cardiac rupture and thrombolysis

661 patients (28.5%) received thrombolytic treatment. Frequency of thrombolytic therapy rose rapidly, with maximum in 1999, when 53% of patients received this kind of treatment. There was difference in mortality between groups in favour of those who received thrombolytic treatment Th (+): (8.8% vs 11.8% respectively, p=0.033).

Figure 3. **Free wall cardiac rupture ploted against thrombolytic treatment**

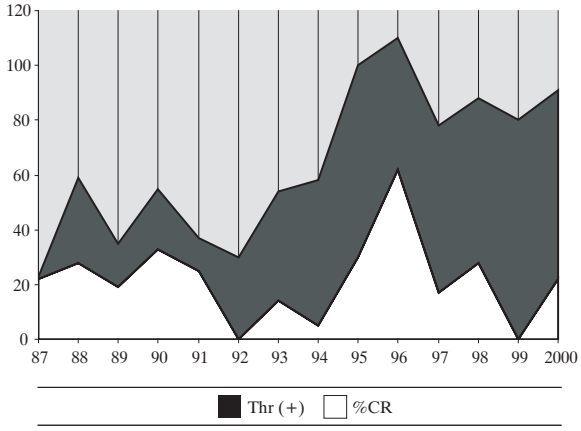


Table 2. **Subgroup analysis: hospital outcomes**

	S (%) n=2066	CR (%) n=50	OD (%) n=204	P value
Age	60.0±12	71.7±9	68.1±12	<0.001
Sex				
women	561 (*27.2*)	31 (*62*)	80 (*39.2*)	<0.01
men	1505 (*72.8*)	19 (*38*)	124 (*60.8*)	
AMI localisation				
anterior	805 (*39.0*)	25 (*50.0*)	80 (*39.2*)	
inferior	991 (*48.0*)	20 (*40.0*)	72 (*35.3*)	NS
other	268 (*13.0*)	5 (*10.0*)	52 (*25.5*)	
Thrombolysis	603 (*29*)	17 (*34.0*)	41 (*20.1*)	p=0.034
Time to death (day) Median		4.1±3.6 4	5.6±10 2	NS

CR – cardiac rupture; OD – other death; S – survivors

Table 3. **Demographic and clinical data in patients with (CR) divided into early and late rupture (ECR and LCR)**

	CR (%) n=50	ECR (%) n=16	LCR (%) n=34
Age	71.7±9	69±9	73±8
sex			
women	31 (*62*)	8 (*50*)	23 (*68*)
men	19 (*38*)	8 (*50*)	11 (*32*)
Previous MI	11 (*24*)	1 (*7*)	10 (*32*)
Previous angina	14 (*32*)	3 (*23*)	11 (*36*)
Hypertension	23 (*46*)	6 (*38*)	17 (*50*)
AMI localisation			
anterior	25 (*50*)	9 (*56*)	16 (*47*)
inferior	22 (*44*)	6 (*38*)	16 (*47*)
other	3 (*6*)	1 (*6*)	2 (*6*)
Thrombolysis	17 (*34*)	6 (*38*)	11 (*32*)

CR – cardiac rupture; ECR – early cardiac rupture; LCR – late cardiac rupture

Out of 58 patients from Th (+) group who died, 17 (29.3%) died because of CR. Out of 196 patients who died and did not received thrombolytic treatment (Th (-) group) frequency of CR was lower: 33 patients (16.8%) p=0.036. Only 2 patients (12%) who died from CR received thrombolytic treatment later than 6 h from the onset of chest pain. In first case time interval was 7 h, in second one 12 h after beginning of chest pain.

32% of CR occurred during first 24 hours after admission (ECR group). The differences between ECR and LCR groups were not signifficant. However, in ECR group were no prevalence of women, while in LCR women constituted 68% (*Tab. 3*). In ECR group only one patient had previous history of MI while in LCR 11 (p=0.06). Frequency of thrombolythic therapy was equal in both groups.

All investigated variables were included in a logistic regression analysis for the prediction of CR. In the forward stepwise procedure the variables that remained as predictors of CR were age (OR 1.072 CI 1.042 – 1.103) and sex (OR 0.349 CI 0.187 – 0.652) both for p<0.001.

Discussion

Our study had an observational character and consisted of unselected consecutive patients with AMI treated in one cardiac centre during consecutive 17 years. Thrombolysis was the only one reperfusion therapy administered.

We noticed significant improvement of survival in patients with AMI during analysed period in spite of growing old population and increasing percentage of women resulted in well known fact of greater mortality in this subgroups of patients [6-10].

The occurrence of CR was consistent with previously published papers [11,12]. Probably the percentage could be greater, if as in most studies, all patients died with signs of EMD were qualified as CR. Some authors consider appearance of EMD as diagnostic for CR [13,14]. In our study we considered only incontestable cases of CR confirmed on autopsy and/or by echocardiography.

In our material, as in previous studies CR occurred in significantly older patients, with prevalence of women [15-17]. The prevalence of CR in women population is not obvious. Significantly higher mean age of women is of great importance. The different course of CAD in women plays also an important role. The differences concern anatomical properties of coronary circulation and atherosclerotic plaque [19,20].

Cardiac rupture in respect of thrombolysis

There are three mechanisms possibly responsible for an increased occurrence of CR in patients received thrombolysis: 1) hemorrhage to the ischemic zone resulting loose of strength of muscular tissue [20,21]; 2) thrombolytic agents increase degradation of collagen and restrain its synthesis [22]; 3) lymphocyte migration to the infarct zone initiate absorbtion of collagen and proteolysis [21].

The results of GISSI-1 trial and Honan investigation showed, that percentage of CR positively correlates with the delay of thrombolytic treatment [23,24]. LATE trial did not confirm this results, suggesting that the late thrombolysis (>12

hours), did not increase the risk of CR, but accelerated occurrence of CR as compared to placebo group [13]. Other authors suggest, that thrombolysis decrease the rate of CR and the lack of reperfusion of the culprit vessel is responsible for increased risk of CR [25]. In fundamental anlysis concerning CR based on U.S. registry of 35000 patients with AMI, Becker found, that in the thrombolytic era, percentage of CR as a cause of death increased. Moreover, thrombolysis accelerates occurrance of CR as compared to patients who did not received thrombolysis [12].

We found higher percentage of CR in patients treated with thrombolytics but in logistic regression analysis this difference did not reach statistical significance perhaps because of small sample size. We cannot confirm an observation concerning acceleration of CR by late administration of thrombolytics as well as an observation concerning shorter time interval from the onset of chest pain to CR in patients treated with thrombolythics.

There are no clear classification of CR. Generally 2 classification are proposed: acute CR (death within 30 min) and subacute CR (30% of cases) or early CR (up to 72 h) and late CR [1,2,26]. We were searching for the predisposing factors for CR during first 24 hours hospitalisation when the choice of reperfusion therapy takes place. We can not explain why the significant prevalence of women in CR group did not concern the ECR subgroup, where the proportion between men and women were equal. Some authors had similar observation [1,2]. In contrary to ECR group, in LCR group 50% of patients suffered from hypertension which is regarded by some authors as a factor increasing the risk of CR [11]. All but one patient from the ECR group had previously MI, only a few had history of angina. More severe course of MI and greater tendency to CR was described in patients suffered from the first MI with no preinfarction angina [27]. This observation may be explained by lack of the effect of ischemic preconditioning. According to some authors CR occurres frequently in patient with one vessel disease, when the collateral circulation is not developed. Mentioned above differences between the ECR and LCR group suggest not homogenous mechanisms leading to CR. Cardiomyocyte apoptosis, neutrophylic infiltration and the importance of defective metalloproteinases (MMPs) activation during LV remodeling after AMI could lead to CR [5,28]. On a mouse model of AMI it has been demonstrated that MMPs inhibition may prevent CR [29]. Genetic susceptibility for CR (i.e. polymorphism in MPPs promoters) is also taken into consideration [5].

Some investigators call in question the advantage of thrombolytic therapy in patients >75 years, because of high risk of such treatment [30]. The optimal reperfusion therapy in this group of patients is now widely discussed. Primary PCI reduces the risk of CR, although its influence on frequency of CR occurrence in AMI is now the matter of investigation [31,32].

Conclusions

Selection of patients with AMI particulary threaten with CR may be possible. This are the patients older than 70 years with first AMI, particulary women. In this group of patients, thrombolytic therapy if given should be followed by careful (probably echocardiographic) observation.

Limitations: The material presented was analysed in most cases retrospectively, so it was impossible to focus on same important problems like eventual analysis of subacute CR. The obduction was not performed in all patients died because of AMI, even in patients died within signs of EMD, which with no doubt influenced on lowering the percentage of CR in our material.

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