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ORIGINAL ARTICLE

The impact of a previous history of ischaemic episodes on the occurrence of left ventricular free wall rupture in the setting of myocardial infarction

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Abstract

Background: Ischaemic episodes preceding myocardial infarction (MI) are one of the defence mechanisms protecting the body from the consequences of sudden ischaemia. Left ventricular free wall rupture (LVFWR) is a rare complication of MI but leading, in a majority of patients, to sudden cardiac death.

Aim: To assess the impact of a previous history of ischaemic episodes (IEs) on the occurrence of LVFWR in patients with acute MI (AMI) managed by percutaneous coronary intervention (PCI).

Methods: The study population consisted of 270 patients who had died during hospitalisation for AMI. All the patients were managed by PCI. The study group (the LVFWR group) consisted of 49 patients who developed LVFWR during hospitalisation and the control group (the non-LVFWR group) consisted of the remaining 221 patients who had died from causes other than LVFWR. In all the patients with LVFWR the rupture was confirmed by autopsy. The data on AMI was obtained from history or medical records. The data on IEs was obtained on the basis of the symptoms that were reported by the patients in the past that directly preceded the most recent AMI or on the basis of medical records.

Results: Compared to the non-LVFWR group the LVFWR group was characterised by an older age (70.3 ± 3.4 vs. 65.2 ± 9.9 years, $p < 0.001$) and a higher percentage of females (75.0% vs. 60.2%, $p < 0.001$). The LVFWR group was also characterised by a higher percentage of IEs in the past (61.2% vs. 40.2%, $p = 0.003$), a lower percentage of patients with a history of MI (14.2% vs. 33.4%, $p = 0.004$), a higher percentage of patients with multivessel coronary artery disease (77.5% vs. 61.5%, $p = 0.03$), a longer interval from the onset of symptoms to PCI (9.0 ± 5.5 vs. 4.5 ± 3.2 h, $p < 0.001$) and a lower percentage of patients with IEs in the past but without an MI (6.1% vs. 23.9%, $p < 0.001$). Our study showed that independent risk factors for LVFWR in the setting of AMI were: older age (OR 1.1, 95% CI 1.02–1.19), male sex (OR 0.2, 95% CI 0.07–0.52) and a longer interval between the onset of symptoms and PCI (OR 1.25, 95% CI 1.07–1.47).

Conclusions: A previous history of IEs in patients without a previous history of AMI was a protective factor against the development of LVFWR in the setting of AMI.

Key words: left ventricular free wall rupture, previous history of ischaemic episodes, myocardial infarction

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INTRODUCTION

A history of ischaemic episodes (IEs) are one of the protective mechanisms currently recognised as one of the protective mechanism of the heart against the consequences of ischaemia. This is an adaptive protective mechanism in the myocardium during its ischaemia whereby brief IEs increase myocardial tolerability of subsequent, longer episodes of ischaemia, making the myocardium impervious to subsequent more extensive injury [1–3].

There has recently been a gradual increase in the number of percutaneous coronary interventions (PCI), including PCI as a management option in acute myocardial infarction (AMI). This has resulted in a considerable improvement of both in-hospital and long-term outcomes in patients with MI [4–7]. There are still, however, potentially fatal complications whose development is difficult to predict and which are difficult to manage. One such complication is left ventricular free wall rupture (LVFWR). LVFWR is a rare complication of MI which in most cases leads to sudden cardial death.

The aim of our study was to assess the impact of a previous history of IEs on the occurrence of LVFWR in patients with AMI managed by PCI.

METHODS

Over a period of 4 years a total of 4200 consecutive patients with AMI underwent PCI at the Silesian Centre for Heart Diseases. The study population consisted of 270 patients who had died during hospitalisation for AMI. All the patients were managed with PCI. Sixty-two (22.9%) of patients with LVFWR also received thrombolytic treatment prior to PCI and 72 (26.6%) patients received glycoprotein IIb/IIIa inhibitors.

The study population was divided in a group of 49 patients who had died during hospitalisation for LVFWR (the LVFWR group) and the control group of 221 patients who had died from causes other than LVFWR.

The LVFWR in all the patients who died from this cause during hospitalisation was confirmed by autopsy. None of the patients underwent surgery. The data on the previous history of MI was obtained from the history or medical records. The data on the previous history of IEs was obtained on the basis of the symptoms that were reported by the patients in the past that directly preceded the most recent AMI or on the basis of medical records. The duration of each IE ranged from 2 to 15 min.

Statistical analysis

The values calculated for measureable variables were expressed as arithmetic means and standard deviations. For data with normal distribution the comparative analysis was performed using the t-Student test. The distributions of the risk factors between the groups were compared using the χ^2 test. A multivariate logistic regression model was used to calculate the relationship between the set of independent variables (independent risk factors) and dependent variable (LVFWR).

RESULTS

The LVFWR occurred in 18.1% of the patients who died from AMI. The demographic data and co-morbidities in the study population are summarised in Table 1. Older age and female sex were significantly more often observed in patients with LVFWR. Table 2 summarises the results on the history of coronary artery disease (CAD), location of the MI and treatment in the study population. A previous history of IEs, no previous history of MI, multivessel CAD and a longer interval between the onset of symptoms to PCI were significantly more common in the LVFWR group. From all the obtained qualitative risk factors for LVFWR that were significantly more common in the LVFWR group, independent risk factors for LVFWR were identified using multivariate logistic regression analysis. The development of LVFWR was the dependent variable and factors that were significantly more common in the LVFWR group than in the control group. Table 3 summarises the results of the multivariate analysis.

We showed that independent risk factors for LVFWR in the setting of AMI were: older age (OR 1.1, 95% CI 1.02–1.19, p = 0.01), male sex (OR 0.2, 95% CI 0.07–0.52, p = 0.001) and a longer interval between the onset of symptoms and PCI (OR 1.25, 95% CI 1.07–1.47, p = 0.003).

A previous history of IEs in patients without a previous history of AMI was a protective factor against the development of LVFWR, which suggests that the absence of the above is an independent risk factor for LVFWR (OR 0.09, 95% CI 0.09–4.10, p = 0.01).

Table 1. Demographic data and co-morbidities

	LVFWR group (n = 49)	Non-LVFWR group (n = 221)	P
Age [years]	70.3 ± 3.2	65.2 ± 9.9	< 0.001*
Sex	37 (75%) females and 2 (25%) males	88 (60.2%) females and 133 (39.8%) males	< 0.001**
Hypertension	20 (40.8%) patients	121 (54.7%) patients	NS**
Diabetes mellitus	15 (30.6%) patients	71 (32.1%) patients	NS**

*t-Student test; **χ^2; LVFWR — left ventricular free wall rupture

Table 2. Results regarding the history of coronary artery disease and the location and treatment of acute myocardial infarction

	LVFWR group	Non-LVFWR group	P
Previous history of IEs*	30 (61.2%)	89 (40.2%)	0.003**
Previous history of MI	7 (14.2%)	74 (33.4%)	0.004**
Previous history of IEs but no previous history of MI	4 (6.1%)	53 (23.9%)	< 0.001
History of more than one MI	1 (2.0%)	19 (8.5%)	0.05
Most recent acute MI: anterior wall infraction	30 (61.2%)	129 (58,3%)	NS**
Multivessel coronary artery disease	38 (77.5%)	136 (61.5%)	0.03
Time from onset of symptoms to PCI [h]	9.0 ± 5.5	4.5 ± 3.2	< 0.001
Thrombolytic treatment	12 (24.4%)	50 (22.6%)	NS**
Glycoprotein IIb/IIIa inhibitor	10 (20.4%)	62 (28.0%)	NS**

*IEs in patients with LVFWR inclusive (with or without a history of MI); **χ^2 test; LVFWR — left ventricular free wall rupture; IEs — ischaemic episodes; MI — myocardial infarction; PCI — percutaneous coronary intervention

Table 3. Multivariate analysis results

	P	Odds ratio	95% CI lower limit	95% CI upper limit
Age [years]	0.01	1.1	1.02	1.19
Sex — males/females	0.001	0.2	0.07	0.52
Time to PCI [h]	0.003	1.25	1.07	1.47
Previous history of MI	0.84	0.89	0.27	2.86
Previous history of IEs*	0.07	2.39	0.92	6.22
Multivessel coronary artery disease	0.13	2.05	0.8	5.25
Previous history of IEs but not of MI	0.01	0.2	0.06	0.69

*IEs in patients with LVFWR inclusive (with or without a history of MI); CI — confidence interval; LVFWR — left ventricular free wall rupture; IEs — ischaemic episodes; MI — myocardial infarction; PCI — percutaneous coronary intervention

DISCUSSION

The LVFWR is always a serious complication of AMI. Despite the advent of PCI the incidence of LVFWR in AMI patients continues to be significantly high [8–11]. The LVFWR complicating AMI is nearly always fata. with most of the ruptures being discovered during postmortem. The prevalence of LVFWR is estimated at several to less than 20% of all deaths caused by AMI [8, 9, 12, 13]. A previous history of IEs in patients with AMI is associated with milder left ventricular injury [14, 15], less frequent occurrence of LVFWR in anterior wall MI [14], less frequent occurrence of heart failure and death due to AMI [16] and of ventricular fibrillation [17].

Preconditioning is a protective mechanism of the myocardium during its ischaemia that increases myocardial tolerability of subsequent episode of ischaemia. The exact pathomechanism of preconditioning is unclear, although a significant role may be played by the activation of ATP-dependent potassium channels [1, 18]. Decreased intracellular ATP levels result in the opening of potassium channels, whose activation leads to cell membrane hyperpolarisation, shortening of the action potential and reduced calcium influx into the cells. This decreases ATP consumption and reduces myocardial contractility, which spares the myocardial energy reserves.

The decreased calcium influx into the cells also results in vasodilation in the specific area of the myocardium. The effectors of preconditioning are ATP-sensitive potassium channels, closed by ATP [1, 18, 19]. Animal experimental studies have shown that the late phase of preconditioning does not exceed 70 h. However, certain clinical studies have demonstrated that the duration of the protective effect of IEs may be much longer and be maintained for up to 90 days [20]. Our study showed that patients who developed LVFWR had significantly less commonly experienced IEs than patients who died from causes other than LVFWR. This is related to the previous history of IEs, which make the myocardium "immune" to sudden ischaemia, such as the acute ischaemia caused by MI.

When we analysed a subgroup of patients with a previous history of IEs but without a previous history of IEs we found a lower rate of LVFWR. In addition, patients with LVFWR had a significantly lower rate of a previous history of MI. Several publications have also shown a higher risk of LVFWR in patients without a previous history of MI [11, 21]. It has been

hypothesised that the scar and the collateral circulation that develop during the previous MI exert protective effects against the development of LVFWR during the subsequent MI [11].

On the other hand, despite the less frequent occurrence of LVFWR in patients with a previous history of CAD our multivariate analysis showed that the previous history of MI was not an independent risk factor of LVFWR.

A study by Becker et al. [21] showed that a previous history of MI was an independent risk factor of death from causes other than LVFWR, but the participants of the study did not receive invasive treatment. In the same study, a previous history of IEs unrelated to a previous history of MI was associated with a higher incidence of LVFWR [21]. In the SHOCK registry, a history of MI was an independent factor that decreased the risk of LVFWR [11]. Also the authors of the recently published Global Registry of Acute Coronary Events (GRACE) study with a subgroup of 273 patients with LVFWR showed that a history of MI was an independent protective factor against the occurrence of LVFWR [13]. GRACE was conducted in patients with ST-elevation MI (STEMI), non-STEMI and unstable angina. In addition, in the GRACE registry, STEMI was an independent risk factor of LVFWR [13]. It should also be noted that the populations assessed for the impact of a previous history of MI on the development of LVFWR differed between each other in terms of the clinical course and treatment [11, 13, 21].

Having considered the studies published so far, we analysed an additional subgroup of patients with a previous history of IEs but without a previous history of MI and found that this was an independent risk factor of LVFWR. We concluded that a previous history of IEs without a previous history of MI is a better protection against LVFWR during AMI than a previous history of both IEs and MI. In the era of invasive treatment our data allow us to confirm the fact that myocardial preconditioning through repeated episodes of ischaemia is an important mechanism that provides protection against LVFWR in patients with AMI.

We also found that the presence of a post-MI scar weakens the beneficial effect of a previous history of IE preceding AMI.

It has been hypothesised that the differences in stresses between the scar and the myocardium not affected by necrosis and the related abnormalities of contractility may impair the function of ATP-dependent potassium channels.

CONCLUSIONS

A previous history of IEs and a previous history of MI are significantly less common in patients with LVFWR in the setting of AMI managed with PCI.

No previous history of IEs in patients without a history of MI, older age, female sex and a longer interval from the onset of symptoms to PCI are independent risk factors of LVFWR as a serious complication of MI.

Conflict of interest: *none declared*

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Wpływ przebytych epizodów niedokrwiennych na pęknięcie wolnej ściany lewej komory w przebiegu zawału serca

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Streszczenie

Wstęp: Epizody niedokrwienne poprzedzające zawał serca (MI) stanowią jeden z mechanizmów obronnych przed skutkami nagłego niedokrwienia. Pęknięcie wolnej ściany lewej komory (CR) jest rzadkim powikłaniem MI, prowadzącym w większości przypadków do nagłego zgonu sercowego.

Cel: Celem pracy była ocena wpływu przebytych epizodów niedokrwiennych (IE) na wystąpienie CR u chorych z ostrym MI (AMI) leczonych metodą przezskórnej interwencji wieńcowej (PCI).

Metody: Badaniem objęto populację 270 pacjentów, u których w okresie wewnątrzszpitalnym wystąpił zgon w przebiegu AMI; wszyscy chorzy byli poddani PCI. Grupa badana (grupa CR) składała się z 49 osób, u których w okresie wewnątrzszpitalnym wystąpiło CR, a grupę kontrolną (grupa non-CR) stanowiło 221 chorych, u których zgon wystąpił z innego powodu niż CR. U wszystkich pacjentów CR potwierdzono sekcyjnie. Dane dotyczące przebytego MI uzyskano z wywiadu bądź na podstawie dokumentacji medycznej, a informacje na temat IE na podstawie obecności dolegliwości zgłaszanych przez chorego w przeszłości lub poprzedzających bezpośrednio wystąpienie obecnego AMI lub na podstawie dokumentacji medycznej.

Wyniki: Chorzy, u których doszło do CR, byli starsi (70,3 ± 3,2 v. 65,2 ± 9,9 roku; $p < 0,001$), częściej CR dotyczyło kobiet (w grupie CR kobiety stanowiły 75%, a w grupie non-CR 60,2%; $p < 0,001$). W grupie chorych z CR częściej obserwowano przebyte IE (61,2% *v.* 40,2%; $p = 0,003$), rzadziej przebyty MI (14,2% *v.* 33,4%; $p = 0,004$), częściej wielonaczyniową chorobę wieńcową (77,5% *v.* 61,5%; $p = 0,03$), dłuższy czas od początku objawów do PCI (9,0 ± 5,5 v. 4,5 ± 3,2 h; $p < 0,001$) oraz rzadziej przebyte IE bez przebytego MI (6,1% *v.* 23,9%; $p < 0,001$). Niezależnymi czynnikami ryzyka wystąpienia CR w przebiegu AMI był starszy wiek (OR 1,1; 95% Cl 1,02–1,19), płeć żeńska (OR 0,2 dla płci męskiej; 95% Cl 0,07–0,52) i dłuższy czas od wystąpienia objawów do PCI (OR 1,25; 95% Cl 1,07–1,47).

Wnioski: Obecność uprzednich IE u chorych bez przebytego MI stanowiła czynnik ochronny przed wystąpieniem CR w przebiegu AMI.

Słowa kluczowe: pęknięcie lewej komory, przebyte niedokrwienie, zawał serca

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