Body Temperature – A Marker of Infarct Size in the Era of Early Reperfusion

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Fever after acute myocardial infarction (AMI) is a common finding [1]. Body temperature may rise on average by more than 1°C as early as 4–8 h after onset of infarction and usually resolves by the 4th–5th day [2]. Sixty-six years ago, Master et al. [3] stated that fever was one of the cardinal signs of coronary thrombosis and a reliable guide to the severity of infarction. Fever may impair cardiovascular function by increasing myocardial oxygen requirements, possibly predisposing to extension of the infarct and arrhythmias [4]. Elevation of body temperature may also aggravate thrombosis and necrosis during AMI and worsen the ‘no-reflow phenomenon’ [5]. Several studies performed over 2 decades ago showed that early treatment with \( \beta \)-adrenoceptor blockade in AMI lowered body temperature, presumably limiting infarct size [6–8].

The underlying mechanism of fever in AMI remains unclear. Some have reported that the severity of fever reflects the mass of infarcted myocardium and correlates with the levels of cardiac enzymes associated with necrosis [6, 8–10]. Others have found no correlation between the magnitude of fever and infarct size, and have attributed fever to a nonspecific inflammatory response, as reflected by increased levels of acute phase reactants [11].

The frequency and severity of fever after ST elevation AMI and its significance remain unknown. Thrombolytic

Key Words
Myocardial infarction · Fever · Body temperature · Inflammation · Infarct size

Abstract
We measured body temperature in 40 consecutive patients treated for a first ST elevation acute myocardial infarction (AMI) with primary percutaneous coronary interventions. Left ventricular function was assessed by echocardiography, and blood samples were drawn for highly sensitive C-reactive protein (hs-CRP), white blood cell (WBC) count, fibrinogen, creatine kinase (CK), and cardiac troponin I levels (cTnI). The median (25th, 75th quartiles) peak 24-hour temperature was 37.4°C (36.9°C, 37.6°C). Variables significantly associated with peak 24-hour temperature were CK (\( p = 0.01, r = 0.42 \)), wall motion index (\( p = 0.01, r = 0.41 \)), hs-CRP (\( p = 0.01, r = 0.41 \)), and cTnI (\( p = 0.03, r = 0.35 \)). There was no significant correlation between peak 24-hour temperature and WBC count (\( p = 0.39, r = 0.14 \)) and fibrinogen (\( p = 0.12, r = 0.21 \)). Thus, peak 24-hour body temperature after ST elevation AMI probably reflects infarct size rather than a nonspecific inflammatory response.
agents like streptokinase may also induce a fever given their immunologic properties. Therefore, the aims of our study were to define the range of body temperatures in patients with ST elevation AMI treated with primary percutaneous coronary interventions (PCI), and to correlate peak body temperature 24 h after admission to infarct size (assessed by echo and biomarkers) and inflammatory indices.

Methods

We prospectively followed 40 consecutive patients with a first ST elevation AMI treated with primary PCI within 6 h of symptom onset. Exclusion criteria included age <18 years, previous AMI, treatment with fibrinolytic agents, known or suspected bacterial or viral infection within the week prior to admission or during hospitalization, positive blood or urine cultures, infiltrates on chest X-ray, chronic inflammatory conditions, early pericarditis, and the use of antipyretic drugs or antibiotics. Written informed consent was obtained from all patients before enrollment.

All patients were evaluated for baseline demographic and clinical characteristics, treatment modalities before and during the hospital course, and electrocardiographic parameters, including the location and the sum of ST elevation.

Body temperature was measured rectally every 8 h using a standard clinical mercury thermometer for up to 48 h after admission. Blood samples were drawn for creatine kinase (CK) levels at admission and every 8 h thereafter for the first 48 h. The maximum CK activity was defined as the highest value obtained from the cumulative enzyme release curve. Blood samples for highly sensitive C-reactive protein (hs-CRP), white blood cell (WBC) count, fibrinogen, and cardiac troponin I levels (cTnI) were drawn after 24 h. hs-CRP was assayed using the Roche/Integra 800 Analyzer by a particle-enhanced immunoturbidimetric method, using latex particles coated with monoclonal anti-CRP antibodies. The day-to-day variation (expressed as CV%) was 3.5% at 0.43 mg/dl, 2.9% at 2.0 mg/dl and 1.7% at 5.0 mg/dl. Troponin I analysis was performed using the DPC Immulite turbo kit. Based on the 98th percentile, the recommended cutoff value was 1.0 ng/ml. The within-run precision at this level was 3.3%. The detection limit was 0.5 ng/ml, with a within-run precision of 8.8%. The day-to-day variation (expressed as CV%) was 13.7% at 0.7 ng/ml and 6.2% at 12.5 ng/ml.

In all patients, left ventricular (LV) function was assessed by two-dimensional echocardiography. Wall motion index was calculated based on a 16-segment model with segments graded as being normokinetic, hypokinetic, akinetic, or dyskinetic and respectively scored on a scale ranging from 1 to 4 [12]. The total wall motion score was divided by 16 to derive the wall motion index.

The location (anterior, inferior, lateral, or other) of AMI was defined from the electrocardiographic tracings, and the magnitude of the ST segment deviation calculated.

Statistical Analysis

Statistical analyses were done using the SPSS statistical software version 11. Continuous variables are expressed as mean ± standard deviation. Differences between continuous variables were assessed using Students’ t test. Categories were compared by using the χ² test. Significance was set at p < 0.05. Bivariate correlations were assessed by using the bivariate correlation test. To evaluate the independent relation between body temperature and LV systolic function, confounders associated with temperature and systolic function were evaluated in a multivariable logistic regression. Receiver operating curves (ROC) were constructed to compare the best predictor of systolic function.

Results

Our cohort included 40 patients (table 1). All but 3 patients presented with Killip class I; 1 patient (2.5%) presented with cardiogenic shock, and 2 (5%) presented with Killip class II. Forty-two percent of the patients had anterior wall involvement. The mean ST-segment elevation was 10.0 mm, and the mean ST-segment depression was 3.7 mm. All patients had successful PCI, defined as residual diameter stenosis of the culprit artery <20% and TIMI 3 flow.

<table>
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<tr>
<th>Table 1. Patient characteristics, results of coronary angiography and treatment</th>
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<td><strong>Patient characteristics</strong></td>
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<td><strong>Results of coronary angiography</strong></td>
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The median (25th, 75th quartiles) peak temperature was 37.4°C (36.9°C, 37.6°C), with a range of 36.1–39.1°C. The mean temperature of patient with anterior wall AMI was 37.5°C, with a mean of 37.2°C for the other patients.

The median wall motion index was 1.56 (1.23, 1.88), and 35, 25, and 40% of the patients had good, mildly impaired, and moderately to severely impaired LV function, respectively.

The median hs-CRP level, WBC count, fibrinogen, peak CK and cTnI levels were 3.24 mg/dl, 12,160 × 10^3/µl, 360 mg/dl, 1978.5 U/l, and 100 ng/ml, respectively.

Variables significantly associated with peak 24-hour temperature were peak CK (p = 0.01, r = 0.42) (fig. 1a), wall motion index (p = 0.01, r = 0.41) (fig. 1b), hs-CRP (p = 0.01, r = 0.41) (fig. 1c), and cTnI (p = 0.03, r = 0.35) (fig. 1d). There was no significant correlation between peak 24-hour temperature and WBC count (p = 0.39, r = 0.14) (fig. 2a), fibrinogen levels (p = 0.12, r = 0.21) (fig. 2b), and the sum of ST elevation (p = 0.24, r = 0.18) (fig. 2c).

Using ROC analysis, peak CK level was the best predictor of wall motion index. Using multivariate analysis, peak hs-CRP levels, but not peak 24-hour body temperature, were independently associated with regional wall motion index.

**Discussion**

**Main Findings**

Now, In the era of early reperfusion with primary PCI for ST elevation AMI, we found that peak 24-hour body temperature was 37.4°C in 50% of patients. Moreover, peak body temperature correlated with markers of infarct size, but not with nonspecific inflammatory indices.

**Body Temperature and Infarct Size**

Previous studies from the late 1980s have by and large correlated body temperature after AMI with infarct size, as estimated by CK levels. In the era prior to reperfusion therapy, Gibson et al. [13] found that 65.3% of the patients with AMI had fever (>38°C), which was more common in transmural (77.2%) than nontransmural (50.7%) AMI. Fever was most common on day 2 of AMI and rarely exceeded 39.5°C. No significant correlation could be found between temperature severity, degree of enzyme

![Fig. 1. Correlation between peak 24-hour body temperature and peak CK levels (a), wall motion index (b), hs-CRP levels (c), and cTnI levels (d).](image-url)
elevation, and leukocyte count. Others [9] reported that the severity of fever (a measurement which takes into account the time-course as well as the magnitude of the fever) was related to serum enzyme change in AMI. In the era of thrombolytic therapy, Fernandes et al. [14] showed that body temperature was higher in patients not receiving thrombolytic therapy, as compared to those receiving thrombolytic therapy. In the non-thrombolytic group, there was a positive relation between peak body temperature and peak CK levels.

In our study, performed in patients after primary PCI, rather than fibrinolysis, we assessed infarct size by biomarker levels and echocardiography. We found a statistically significant, correlation between peak 24-hour body temperature and CK levels, cTnI levels, and wall motion index, indicating that fever after ST elevation AMI correlates with the extent of myocardial necrosis. Although body temperature was correlated with wall motion index, using ROC analysis, peak CK level was the best predictor of wall motion index.

**Body Temperature and Inflammatory Response**

Fever in the setting of AMI may reflect a nonspecific inflammatory response, unrelated to the mass of damaged myocardium. In our study, we found a significant correlation between body temperature and hs-CRP levels, but not with WBC count or fibrinogen levels.

The association between acute coronary syndrome and elevated serum concentration of acute phase reactants, such as CRP [15–17] serum amyloid A [16, 17], and interleukin-6 [18], suggests that chronic inflammation of the coronary arterial wall may play an important role in the pathogenesis of acute coronary syndrome. Increased serum CRP concentrations at admission are markers for a worse short- and long-term prognosis in patients with a non-ST elevation acute coronary syndrome [16, 19–24]. Elevated levels of CRP may also predict the risk for recurrent in-hospital cardiac events after AMI [25].

The correlation between CRP levels and infarct size remains controversial. De Beer et al. [26] and Yano et al. [27] reported a correlation between CRP and infarct size. De Sutter et al. [28] and Hori et al. [29] found no correlation between CRP and infarct size. Verstraete et al. [30] reported a correlation between CRP and infarct size only with an occluded infarct-related coronary artery after thrombolytic therapy, but not if the artery was patent. Umemura et al. [31] found that elevated CRP levels immediately after onset of AMI were associated with less myocardial damage and better LV function in reperfused anterior AMI.

CRP levels may thus reflect myocardial processes, not only atherosclerotic processes. Moreover, CRP itself may mediate some of these myocardial effects [32, 33]. We therefore postulate that body temperature reflects myocardial processes that are also reflected by hs-CRP, and hence the correlation between the two. It seems that although body temperature and hs-CRP levels may be elevated in the presence of a generalized inflammatory response, body temperature does not reflect a generalized, nonspecific inflammatory response, given the lack of association between body temperature and WBC count and fibrinogen levels on the one hand and the correlation between body temperature and infarct size on the other hand.
Conclusions

Body temperature is frequently elevated after successful reperfusion for ST segment elevation AMI. Peak 24-hour body temperature after ST elevation AMI in the era of early reperfusion with primary PCI may be a simple marker of myocardial damage. It is related to infarct size, but not to a nonspecific inflammatory response.

Acknowledgment

This study was funded in part by an unrestricted grant from Dyn Diagnostics, Israel.

References


Fever and Infarct Size

Cardiology 2005;103:169–173 173