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Norepinephrine Level as a Predictor of Mortality After First Myocardial Infarction*

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*The objective of this study was to determine whether the magnitude of adrenergic activation, as measured by plasma norepinephrine concentration (PNE) in the acute phase of myocardial infarction, may be useful as an independent predictor of long-term morbidity and mortality following acute myocardial infarction (AMI). Plasma norepinephrine was obtained within 3 days of admission to the cardiac intensive care unit in 146 randomly selected patients presenting with their first AMI. We analysed the relationship between the initial PNE and the clinical outcomes of death, reinfarction, and congestive heart failure during the subsequent 18 months. Patients with initial PNE over 565 pg/ml ($n = 54$) were found to have a significantly higher likelihood of cardiac death within the following 18 months ($RR = 4.22$; $p = 0.04$), as compared with patients with a lower PNE ($n = 98$). Even adjustment for variables significant on the univariate level, the difference in mortality remained significant ($RR = 4.67$; $p = 0.03$). No correlation was found between PNE and subsequent incidence of reinfarction and congestive heart failure in these patients ($RR = 0.087$; $p = 0.80$ and $RR = 1.00$; $p = 0.09$, respectively). Our observations support the hypothesis that PNE obtained early in the course of myocardial infarction can be a useful independent prognostic tool for post-AMI mortality. **J Clin Basic Cardiol 2005; 8: 55–8.***

Key words: myocardial infarction, norepinephrine, cardiac death

The activation of the sympathetic nervous system early in the course of an acute myocardial infarction (AMI) manifested by increased concentrations of norepinephrine in the blood and urine has been of interest to investigators for almost three decades. Increased levels of plasma norepinephrine (PNE) have been associated with a number of adverse clinical events after myocardial infarction, including congestive heart failure, cardiogenic shock [1–3], ventricular arrhythmias [1, 2, 4, 5], and death [1, 4, 6, 7]. McAlpine et al. observed that in addition to plasma catecholamine elevation, renin and angiotensin II were elevated up to ten days after an AMI in patients with heart failure and ventricular tachycardia [1]. Elevation of these neurohormones was associated with death during hospitalisation due to pump failure and arrhythmias. Increase in PNE has also been correlated with higher levels of myocardial enzyme release [1, 6, 8], which signify the extent of myocardial damage.

These observations have given support for the use of beta-adrenergic blocking agents for the treatment of AMI. Since norepinephrine appears to be related to a number of adverse events occurring in the acute phase of myocardial infarction, it is possible that its concentration obtained during hospitalisation could provide an important predictor of long-term survival after an AMI. In order to examine the predictive potential of norepinephrine, plasma concentrations of norepinephrine were measured in patients within the first 72 hours of their first AMI. Patients were subsequently followed for occurrence of death, congestive heart failure (CHF) and reinfarction for 18 months after their initial hospitalisation.

Methods

Patients were enrolled consecutively into the study during a three-year period between 1991 and 1993. Study subjects were part of a larger study of 511 patients admitted to the Coronary Intensive Care Unit with their first AMI, based upon established electrocardiographic and enzymatic criteria

(see below). From the total population of patients with their first AMI (Q-wave and non-Q-wave), 146 were randomly selected to have a blood sample drawn for plasma norepinephrine. The samples were taken within the first three days of admission, at an average time from admission of 2 days. Those patients with previous history of myocardial infarction or an ECG-evidence of remote infarction, patients with valvular heart disease, hypertrophic obstructive cardiomyopathy, congenital heart disease, and previous documented heart failure were excluded. Informed consent was obtained in all patients prior to enrollment in the study.

All patients in the study underwent complete history and physical examination by a senior staff cardiologist, including a history of risk factors of coronary artery disease, family history of hypertension, hypercholesterolaemia, diabetes mellitus, cigarette smoking, and drug abuse. At the time of admission, an electrocardiogram and serial cardiac enzymes were obtained.

ECG and Enzymatic Criteria for AMI

The diagnosis of a Q-wave AMI was based on the presence of typical symptoms, in association with a new Q-wave in at least two consecutive ECG leads. The anatomical location of the myocardial infarction was established using criteria described by Chou [9]. A non-Q-wave AMI was diagnosed in the presence of typical symptoms associated with concurrent changes in the ST and T waves without development of Q-waves. Enzymatic criteria for both Q-wave and non-Q-wave AMI included total peak serum creatine phosphokinase (CPK) > 400 IU/l and serum MB isoenzyme (CKMB) > 3 % total CPK. Enzyme evaluations were initiated upon admission and repeated 3 times, 8 hours apart.

Follow-Up

Patients had a two-dimensional transthoracic echocardiogram performed within 36 hours from admission and at discharge. During each follow-up visit, complete interval cardiac history, physical examination, and 2D-echo were performed.

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Echocardiographic Evaluation

Two-dimensional echocardiograms were used to quantify left ventricular (LV) mass, cavity volume, and regional wall motion in accordance with the recommendations of the American Society of Echocardiographers [10]. All echocardiographic studies were performed by an experienced sonographer and reviewed for quality by one of the investigators. End-systolic and end-diastolic cavity volumes were computed from the dimensions and area measures obtained from paired apical views. Left ventricular volumes were calculated using the disc summation method (modified Stimson rule) [11]. Left ventricular mass was determined by the method of Helak and Reichel [12].

Norepinephrine concentration was analysed in a pre-determined dichotomous fashion by separating patients above and below 565 pg/ml. The concentration of 565 pg/ml is the upper limit of normal norepinephrine levels used by the Henry Ford Hospital Biochemical Laboratory. This upper limit of normal equals the mean plus two standard deviations obtained by prior analysis of catecholamine levels in a group of 56 healthy volunteers.

Statistical Methods

Association of plasma norepinephrine levels with baseline factors was analysed using either the χ -squared test (for categorical variables) or Student's *t*-test (for continuous variables), where appropriate. The three types of adverse cardiac events followed were cardiac death, reinfarction, and congestive heart failure. On a multivariate level, the association of plasma norepinephrine levels with adverse cardiac events as defined above was analysed using a Cox proportional hazards model (Proc. Phreg. in SAS). The outcome in all models was time to event. Time started three days after the date of AMI, the approximate date when PNE levels were drawn. Therefore, individuals who had heart failure or reinfarction within three days of their AMI were excluded from the models that used heart failure or reinfarction as the outcome event. This excluded 41 patients from the heart failure models and 2 individuals from the reinfarction models. Individuals who did not experience an event were censored at their last day of follow-up or 18 months, whichever came first. Initial model fitting included only high PNE as an explanatory variable to obtain a crude risk ratio for survival. Additional model fitting included variables that were significant at the univariate level to obtain an adjusted risk estimate for high PNE. Time from study enrollment to each event was also analysed with Kaplan-Meier survival curves and log rank χ -square tests.

Results

Of the 146 patients enrolled in the study, 53 (36.3 %) had PNE-levels greater than 565 pg/ml. Table 1 compares the baseline characteristics between high-PNE and low-PNE groups. With the exception of mean age, history of hypocholesterolaemia, history of former smoking, and use of angiotensin converting enzyme (ACE) inhibitors, the patients in both groups were quite similar.

Table 2 shows differences in catecholamine levels and echocardiographic characteristics between the two groups. Only the LV score index was significantly greater in the high-PNE group. During the 18-months follow-up period the study group experienced 10 cardiac-related deaths, 19 episodes of CHF, and 15 reinfarctions. 84.2 % (16/19) of the CHF events occurred during the initial hospitalisation following PNE testing, whereas 80 % (12/15) of reinfarctions and all of the 10 cardiac-related deaths occurred after discharge.

Table 1. Comparison of baseline characteristics between low and high PNE groups (n = 146)

Variable	PNE > 565 (n = 53)	PNE ≤ 565 (n = 93)	p-value
Age	61.7 ± 14.5	56.5 ± 13.0	0.026
Male sex	29 (54.7)	64 (68.8)	0.088
Black race	19 (35.9)	30 (32.3)	0.659
Diabetes	9 (17.0)	18 (19.4)	0.722
Hypertension	28 (52.8)	42 (45.2)	0.372
Hypercholesterolaemia	18 (34.0)	17 (18.3)	0.033
Current smoker	25 (47.1)	46 (49.5)	0.790
Former smoker	14 (26.4)	12 (12.9)	0.040
Ever smoker	39 (73.4)	58 (62.4)	0.167
History of PTCA	19 (35.9)	37 (39.8)	0.638
History of CABG	2 (3.8)	7 (7.5)	0.488
LVH at baseline	20 (38.5)	36 (40.0)	0.857
Q-wave MI	41 (77.4)	73 (78.5)	0.873
Thrombolytic use	30 (56.6)	57 (61.3)	0.579
Anterior MI	19 (35.9)	26 (28.0)	0.321
Rx with β -blockers	39 (86.7)	94 (93.1)	0.210
Rx with ACEI	33 (73.3)	47 (46.5)	0.003
Rx with Ca ²⁺ blockers	3 (6.7)	6 (5.9)	1.000
Rx with Digitalis	8 (17.8)	15 (14.9)	0.654

PNE: plasma norepinephrine; MI: myocardial infarction; Rx: treatment; ACEI: angiotensin converting enzyme inhibitors. Numbers in parentheses are percentages

Table 2. Comparison of catecholamine levels, echocardiographic characteristics and peak CPK concentrations between low and high PNE groups (n = 146)

Variable	PNE > 565 (n = 53)	PNE ≤ 565 (n = 93)	p-value
PNE	840 ± 363	346 ± 108	N/A
Plasma Epinephrine	49.4 ± 33.6	48.2 ± 52.4	0.868
Plasma Dopamine	50.3 ± 61.4	45.8 ± 131.9	0.783
Ejection fraction	50.0 ± 10.7	50.1 ± 10.2	0.518
ESVI	26.9 ± 11.0	27.9 ± 8.4	0.561
LV score index	1.79 ± 0.47	1.59 ± 0.39	0.005
Peak CPK level	2192 ± 1724	2059 ± 1510	0.628

PNE: plasma norepinephrine; LV: left ventricle; ESVI: end-systolic volume index; CPK: creatine phosphokinase

Table 3 shows the univariate relationships between the various clinical variables and adverse cardiac outcomes. Besides the high PNE, the peak CPK, and thrombolytic use were also significantly associated with cardiac death during the follow-up period. The summary of adverse events in the high and low PNE group is seen in Table 4. By multivariate analysis for each adverse outcome at the end of follow-up (18 months), there was no statistical difference in the occurrence of reinfarction or heart failure between the two groups. However, the occurrence of cardiac death was significantly greater in the high PNE group. After adjustments were made for those variables significant on the univariate level, differences were still statistically significant (RR = 4.67; p = 0.03).

The Kaplan-Meier crude survival curve for cardiac death is shown in Figure 1. A clear separation between the groups was observed (χ -square 2.75; p = 0.097).

Discussion

The results of our study show that there is a significant correlation between the PNE measured within 72 hours of admission of AMI patients and their survival to 18 months. Although this study failed to prove a similar correlation with other clinical outcomes, it appears that PNE may be a useful biomarker for long-term survival in patients presenting with

Table 3. Relationship between study risk factors and adverse cardiac outcomes

Variable	Cardiac-Related Death			Congestive Heart Failure			YES (n = 15)
	YES (n = 10)	NO (n = 136)	p-value	YES (n = 19)	NO (n = 89)	p-value	
PNE	647 ± 246	516 ± 338	0.230	445 ± 247	518 ± 366	0.413	526 ± 274
PNE > 565 (%)	70.0	35.3	0.029	31.6	32.6	0.934	33.3
Age	64.3 ± 18.8	57.9 ± 13.3	0.158	60.5 ± 12.2	56.2 ± 13.4	0.206	61.1 ± 20.0
Male sex (%)	80.0	62.5	0.328	47.4	72.1	0.037	46.7
Black race (%)	30.0	33.8	0.805	21.1	33.7	0.282	33.3
Diabetes (%)	0	20.0	0.209	31.6	15.1	0.092	20.0
HTN (%)	60.0	47.1	0.521	79.0	37.2	0.001	73.3
Peak CPK	3262 ± 2217	2022 ± 1507	0.017	3023 ± 2043	1786 ± 1309	0.020	2806 ± 1837
Ant MI (%)	50.0	29.4	0.285	36.8	23.3	0.251	40.0
EF (%)	50.3 ± 7.8	50.8 ± 10.6	0.895	49.2 ± 11.1	52.4 ± 1.4	0.230	44.5 ± 10.3
ESVI	27.4 ± 10.3	27.5 ± 9.4	0.952	27.3 ± 7.8	27.2 ± 9.4	0.952	31.5 ± 10.4
Thrombolytics (%)	100.0	56.6	0.006	52.6	61.6	0.469	73.3

PNE: plasma norepinephrine; HTN: hypertension; Ant MI: anterior myocardial infarction; EF: ejection fraction; ESVI: end-systolic volume index

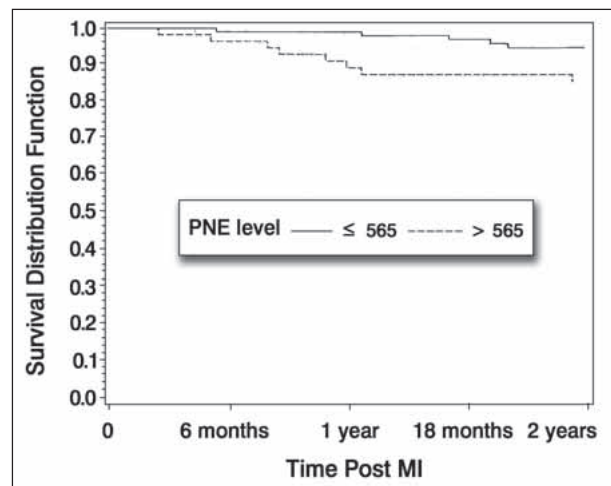
Table 4. Crude and adjusted risk estimates for high norepinephrine levels (PNE > 565 pg/ml) for different event outcomes at 18 months

Event	Risk Estimate	95 % CI	p-value
Death: (n = 146)			
Crude	4.22	1.09–16.33	0.04
Adjusted*	4.67	1.20–18.63	0.03
CHF: (n = 105)#			
Crude	1.00	0.38–2.62	0.99
Adjusted	0.86	0.33–2.30	0.77
Reinfarction: (n = 144)**			
Crude	0.87	0.30–2.55	0.80
Adjusted	0.76	0.26–2.24	0.62

*Adjusted for variables significant for each outcome by univariate analysis at $p < 0.10$ level; #41 individuals omitted from the analysis who had CHF before entry into study; **2 individuals omitted from the analysis who had reinfarcted before entry into study

their first AMI and may be used as a convenient adjunct to other well established tests, such as two-dimensional echocardiogram or maximum serum CPK levels.

AMI is associated with the activation of the sympathetic nervous system and the renin-angiotensin system. This neurohumoral activation is expressed by the marked increase of plasma catecholamines, renin, vasopressin, brain (BNP), and atrial natriuretic peptide protein (ANP), prolactin, adrenocorticotrophic hormone (ACTH), and glucagon [13, 14]. Elevated plasma levels of these markers are detected within minutes to hours after the ischaemic event and are not altered by early reperfusion [15]. Neurohumoral activation manifested by the marked elevation of catecholamine levels is also observed in patients with LV dysfunction without acute myocardial ischaemia [16]. Results of several studies suggest that elevations of ANP and PNE especially are prognostic markers in patients with AMI and/or LV dysfunction, and predict long-term clinical outcome [6, 7, 16–18]. In a subanalysis of 534 patients from the SAVE study, neurohormone levels, including PNE, were measured a mean of 12 days after an AMI. Higher PNE levels were independently related to later cardiovascular events by univariate analysis [18]. However, this relation was much weaker after adjusting for other known mortality correlates in the multivariate analysis [18]. Other studies have also shown that, after correction for clinical CHF or degree of LV dysfunction in these patients, increased PNE did not reach statistical significance as an inde-

**Figure 1.** Kaplan Meier crude survival curve for cardiac death based on baseline norepinephrine above and below the upper limit of laboratory normal showing ($p = 0.097$)

pendent outcome predictor [7]. In some studies, elevated PNE was related to the extent of myocardial damage reflected by peak CPK and development of clinical heart failure and cardiogenic shock [1, 2, 4, 6, 13, 16, 19, 20]. Therefore, it is still uncertain, whether acute elevation of norepinephrine after AMI is an independent prognostic marker after correction for the above covariates. We observed significantly better LV function as measured by baseline LV score index in the high PNE group compared with the low PNE group. We did not see any significant difference in peak CPK levels between the two groups.

Several investigators reported an association between the level of norepinephrine in patients with myocardial infarction and development of ventricular arrhythmias [1–5]. Hayashi et al. found a temporal relation of catecholamine elevations to the onset of arrhythmias by serial urine sampling [21]. This correlation could not be confirmed by a later study by Videbaek et al. [22]. Pathophysiologic mechanisms investigated in animal models proposed a relationship between elevated catecholamines and increased mortality. Catecholamines were shown to be involved in coronary thrombosis [23] and cardiotoxicity [24]. While epinephrine seemed to be thrombogenic in a canine model, norepinephrine had the opposite effect [23]. Infusion of exogenous norepinephrine

caused multifocal microscopic myocardial necrosis in rabbits [25] and significantly increased the infarct area in isolated rabbit hearts, with or without β -blockers [24]. Treatment with metoprolol prevented norepinephrine-induced myocardial damage in isolated rat hearts [26]. It has been proposed that catecholamines are cardiotoxic by their autooxidation and release of oxygen free radicals [24]. Overall, the possibility of catecholamines having any direct effect upon the infarct size, subsequent left ventricular dysfunction or arrhythmias deserves further investigation.

For the purpose of the dichotomous analysis, we chose a PNE level cut-off of 565 pg/ml, i.e. the upper limit of normal range in our laboratory. Norepinephrine levels are typically elevated in the acute phase of myocardial infarction and this somewhat arbitrary level provided a very practical cut-off point for the dichotomous statistical analysis.

Although the study excluded patients with overt heart failure, a known predictor of norepinephrine elevation, it is possible that even subclinical heart failure was present and provided a sufficient stimulus for catecholamine release. It has been documented in prior studies that elevated catecholamines tend to persist in subjects developing CHF after a myocardial infarction, whereas they decrease in those without clinical signs of heart failure [1, 6, 20, 27, 28]. However, the incidence of CHF in the post-MI period did not correlate with the initial PNE.

Our observations support the hypothesis that an increase in PNE early after myocardial infarction may provide, together with other established criteria such as assessment of LV function and volumes, peak CPK, and clinical CHF/shock, a useful prognostic tool for long-term clinical outcome. More research is still needed to explain the role of early catecholamine release in the pathophysiology of post-AMI morbidity and mortality.

References:

- McAlpine HM, Morton JJ, Leckie B, Rumley A, Gillen G, Dargie HJ. Neuroendocrine activation after acute myocardial infarction. *Br Heart J* 1988; 60: 117-24.
- Januszewicz W, Sznajderman M, Wocial B, Preibisz J. Urinary excretion of free norepinephrine and free epinephrine in patients with acute myocardial infarction in relation to its clinical course. *Am Heart J* 1968; 76: 345-52.
- Siggers DC, Salter C, Fluck DC. Serial plasma adrenaline and noradrenaline levels in myocardial infarction using a new double isotope technique. *Br Heart J* 1971; 33: 878-83.
- Jewitt DE, Reid D, Thomas M, Mercer CJ, Valori E, Shillingford JP. Free noradrenaline and adrenaline excretion in relation to the development of cardiac arrhythmias and heart failure in patients with acute myocardial infarction. *Lancet* 1969; 1: 635-41.
- McDonald L, Baker C, Bray C, McDonald A, Restieaux N. Plasma catecholamines after cardiac infarction. *Lancet* 1969; 2: 1021-4.
- Karlsberg RP, Cryer PE, Roberts R. Serial plasma catecholamines response early in the course of clinical acute myocardial infarction. Relationship to infarct extent and mortality. *Am Heart J* 1981; 102: 24-9.
- Omland T, Aarland T, Aakvaag A, Lie RT, Dickstein K. Prognostic value of plasma atrial natriuretic factor, norepinephrine and epinephrine on acute myocardial infarction. *Am J Card* 1993; 72: 255-259.
- Gazes PC, Richardson JA, Woods EF. Plasma catecholamine concentrations in myocardial infarction and angina pectoris. *Circulation* 1959; 19: 657-61.
- Chou TC. *Electrophysiology in clinical practice*. Grune and Stratton, 1979; 146-215.
- Schiller NB. Two-dimensional echocardiographic evaluation of the left ventricular volume, systolic function and mass. Summary and discussion of the 1089 recommendations of the American Society of Echocardiography. *Circulation* 1991; 84: 1-280.
- Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, Gutgesell H, Reichek N, Sahn D, Schnittger I, Silverman NH, Tajik AJ. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards Subcommittee. *J Am Soc Echocardiogr* 1989; 2: 358.
- Helak JW, Reichek N. Quantitation of human left ventricle mass and volume by two-dimensional echocardiography: in vitro anatomic validation. *Circulation* 1981; 63: 1398-407.
- Ferrari R, Ceconi C, Rodella A, Harris P, Visioli O. Hormonal response in untreated myocardial infarction. *Cardioscience* 1990; 1: 55-60.
- Foy SG, Crozier IG, Richards AM, Nicholls MG, Turner SG, Frampton CM, Ikram H. Neurohumoral changes after acute myocardial infarction. Relationships with hemodynamic indices and effects of ACE inhibition. *Eur Heart J* 1995; 16: 770-8.
- Ray SG, Morton JJ, Dargie HJ. Neuroendocrine activation and markers of early reperfusion in the acute phase of myocardial infarction. *Eur Heart J* 1993; 14: 1615-21.
- Benedict CR, Shelton B, Johnstone DE, Francis G, Greenberg B, Konstam M, Probstfield JL, Yusuf S. Prognostic significance of plasma norepinephrine in patients with asymptomatic left ventricular dysfunction. SOLVD investigators. *Circulation* 1996; 94: 690-7.
- Huttel S, Nussberger J, Lehmann K, Hasford J, Brunner HR, Delius W. Beneficial clinical effect of very early enalapril treatment in patients with acute left ventricular failure complicating myocardial infarction. *Clin Cardiol* 1995; 18: 317-23.
- Rouleau JL and other SAVE Investigators. Prognostic value of neurohumoral activation in patients with an acute myocardial infarction: effect of captopril. *J Am Coll Cardiol* 1994; 24: 583-91.
- Sigurðsson A. Neurohumoral activation in patients with acute myocardial infarction or chronic congestive heart failure. With special reference to treatment with angiotensin converting enzyme inhibitors. *Blood Press* 1995; Suppl 1: 1-45.
- Valori C, Thomas M, Shillingford J. Free noradrenaline and adrenaline excretion in relation to clinical syndromes following myocardial infarction. *Am J Cardiol* 1967; 20: 605-10.
- Hayashi KG, Moss AJ, Yun PN. Urinary catecholamine excretion in myocardial infarction. *Circulation* 1969; 40: 473-81.
- Videbaek J, Christensen NJ, Sterndorff B. Serial determination of plasma catecholamines in myocardial infarction. *Circulation* 1972; 46: 846-55.
- Lin H, Young DB. Opposing effects of plasma epinephrine and norepinephrine on coronary thrombosis in vivo. *Circulation* 1995; 91: 1135-42.
- Rump AF, Klaus W. Evidence for norepinephrine cardiotoxicity mediated by superoxide anion radicals in isolated rabbit hearts. *Naunyn Schmiedeberg Arch Pharmacol* 1994; 349: 295-300.
- Gavras H, Kremer D, Brown JJ, Gray B, Lever AF, MacAdam RF, Medina A, Morton JJ, Robertson JI. Angiotensin- and norepinephrine-induced myocardial lesions: experimental and clinical studies in rabbits and man. *Am Heart J* 1975; 89: 321-32.
- Waldenstrom AP, Hjalmarson AC, Thornell L. A possible role of noradrenaline in the development of acute myocardial infarction: and experimental study in the isolated rat heart. *Am Heart J* 1978; 95: 43-51.
- Sigurðsson A, Held P, Swedberg K. Short- and long-term neurohumoral activation following acute myocardial infarction. *Am Heart J* 1993; 126: 1068-76.
- Benedict CR, Grahame-Smith DG. Plasma adrenaline and noradrenaline concentrations and dopamine-beta-hydroxylase activity in myocardial infarction with and without cardiogenic shock. *Br Heart J* 1979; 42: 214-20.

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