New insights in management and prognosis in acute myocardial infarction

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Value of repeated measurements of NT-proBNP after acute myocardial infarction: data from the GIPS-III trial

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Abstract

Aims

N-terminal pro-brain natriuretic peptide (NT-proBNP) levels are associated with left ventricular systolic function and have important prognostic value. The optimal timing to measure NT-proBNP in relation to left ventricle ejection fraction (LVEF) and myocardial infarct size after ST-elevation myocardial infarction (STEMI) has not been well defined.

Methods and Results

The GIPS-III trial randomized STEMI patients to metformin or placebo; LVEF and infarct size were determined by cardiac magnetic resonance imaging (MRI) at 4 months. For the present analysis, 271 patients with available NT-proBNP and MRI measurements were included. NT-proBNP was measured during hospitalization at admission, 12 hours, and 24 hours after admission, and measured during follow-up visits at 2 weeks, 8 weeks and 4 months.

The median NT-proBNP levels during hospitalization increased from 80 (38-180) ng/L at admission to 965 (548-1616) ng/L at 24 hours, and declined to 174 (72-380) ng/L at 4 months. NT-proBNP levels at all time points were associated with LVEF and, except at admission, with infarct size. A higher explained variance was observed during follow-up compared to during hospitalization; for LVEF 30.0% at 8 weeks vs. 9.6% at 12 hours ($p<0.001$), and for infarct size 50.9% at 8 weeks vs. 13.0% at 12 hours ($p<0.001$). NT-proBNP levels explained more of the variability for infarct size compared to LVEF ($p=0.002$ at 8 weeks).

Conclusions

After STEMI, early NT-proBNP measurements have limited value to predict LVEF and infarct size at 4 months. However, NT-proBNP measured during follow-up are strong predictors of LVEF and even stronger predictors of myocardial infarct size.

Introduction

Patients presenting with an acute myocardial infarction are at risk of developing left ventricular (LV) dysfunction.[1,2] Left ventricular ejection fraction (LVEF) and infarct size after ST-elevation myocardial infarction (STEMI) are important predictors for morbidity and mortality.[1-5] Therefore, early identification of patients at risk of LV dysfunction is essential. A biomarker that has been well associated with LV dysfunction is N-terminal pro-brain natriuretic peptide (NT-proBNP). It is primarily produced and released in the cardiac myocytes in response to cardiac wall stretch.[6] NT-proBNP can be used for diagnostic and prognostic purposes irrespective of the LVEF.[7,8] In patients with myocardial infarction with and without heart failure NT-proBNP is commonly used as a prognostic tool.[9] The optimal timing of NT-proBNP measurements after STEMI is unknown. Therefore, we evaluated the value of NT-proBNP levels at multiple time points after STEMI in relation to LVEF and myocardial infarct size at 4 months.

Methods

Study protocol

We performed a post-hoc analyses of the GIPS-III trial.[10,11] In short, this single center study included patients without known diabetes presenting with their first myocardial infarction between January 1, 2011 and May 26, 2013. After successful primary PCI, patients were randomly assigned to metformin or placebo for 4 months. All patients received standard medication and lifestyle advises according to current guidelines.[12,13] Primary endpoint was LVEF after 4 months, determined by magnetic resonance imaging (MRI). All patients provided written informed consent. An independent committee assessed all end points, blinded to randomization and clinical results. In the GIPS-III trial, the use of metformin compared to placebo did not result in improved LVEF after 4 months.

NT-pro BNP

Laboratory measurements were performed at standardized time points. NT-proBNP was measured with a sandwich immunoassay on a Roche Modular E platform (Mannheim, Germany). NT-proBNP was measured at admission, 12 hours after PCI, 24 hours after PCI, and at the follow-up visits at 2 weeks, 8 weeks, and 4 months after discharge. When two NT-proBNP measurements were available at one time point, the levels were averaged for the current analyses. The laboratory measurement after discharge was based on the date of the follow-up visit +/- 7 days. The change of NT-proBNP levels were calculated between

admission and after 12 hours and 24 hours and between 24 hours after admission and at 2 weeks, 8 weeks and 4 months.

End point

LVEF and infarct size were determined by MRI 4 months after STEMI. Imaging was performed on a 3.0 Tesla MRI scanner (Achieva, Philips, The Netherlands) using a phased array cardiac receiver coil. All MRI studies were analyzed by a core MRI laboratory. Electrocardiogram-gated images were acquired during repeated breath-holds. The LV volumes were determined with cine imaging, using a segmented steady state free precession pulse sequence in multiple short axis views every 10 mm covering the entire left ventricle. On the stack of short-axis cines, the endocardial and epicardial borders were outlined in end-systolic and end-diastolic images. LV end-systolic volumes (LVESV) and LV end-diastolic volumes (LVEDV) were determined using summation of slice method multiplied by slice thickness. LVEF was calculated as 100% x (LVEDV-LVESV)/LVEDV. LV mass was determined by multiplying LV volume by the myocardial density of 1.05g/ml. Infarct size was calculated as the volume of delayed contrast-enhancement as percentage of total LV mass.

Statistical analysis

Normally distributed continuous variables are presented as means with standard deviations (SD). Skewed distributed continuous variables are presented as medians with interquartile ranges (IQR). The glomerular filtration rate was estimated using the Chronic Kidney Disease Epidemiology Collaboration equation.[14] Linear regression analysis was performed to assess the association of NT-proBNP measured at different time points on LVEF and infarct size. The levels of NT-proBNP were log transformed before linear regression analysis. The R^2 of the analysis indicate the explained variance of the outcome by NT-proBNP. The distributions of R^2 of NT-proBNP on LVEF and infarct size were compared with z-score statistics. This distribution was determined by a non-parametric bootstrapping method with 10,000 paired replicates. To adjust for potential confounders, multivariable regression analysis was performed including the residuals of established risk factors derived from the TIMI score; age, body mass index, history of diabetes, hypertension, systolic blood pressure and heart rate, anterior myocardial infarction, and time to treatment.[15] Linear regression analysis was also performed to evaluate the effect of change of NT-proBNP levels during hospitalization and follow-up on the prediction of LVEF and infarct size. Outliers of more than 4 times the standard deviation were excluded from the analyses. Models were adjusted for baseline NT-proBNP levels (i.e. admission or 24 hours after admission). Furthermore, we generated receiver operating characteristic curves to determine the area under the curve of NT-proBNP at different time points using the median LVEF and infarct size as cut-off points.
Statistical significance was defined as a two-sided p-value of less than 0.05.

Table 1 | Baseline characteristics

	Substudy n=271
General	
Age, years	57.7 ± 12
Male sex	213 (79)
Body mass index, kg/m2	26.9 ± 3
History	
Hypertension	75 (28)
Dyslipidemia	168 (62)
Current smoking	139 (51)
Blood pressure, mmHg	
Systolic	133 ± 22
Diastolic	84 ± 15
Heart rate, beats/minutes	76 ± 16
Ischemic time, minutes	155 (105-240)
Angiographic	
Infarct-related artery	
Left anterior descending	111 (41)
Circumflex	46 (17)
Right coronary artery	114 (42)
TIMI flow grade	
0 or 1	174 (64)
2 or 3	97 (36)
Multivessel disease	76 (28)
Post-procedural	
TIMI flow grade	
2	17 (6)
3	254 (94)
Myocardial blush grade	
0 or 1	24 (9)
2 or 3	245 (91)
Laboratory values	
Creatine kinase, U/L	134 (92-215)
Myocardial band of CK, U/L	17 (13-25)
Troponin, ng/L	49 (22-146)
GFR, ml/min	96 (86-103)
C-reactive protein, mg/L	1.8 (0.9-3.8)

Data are presented as mean±SD, median (IQR) or as number (%).

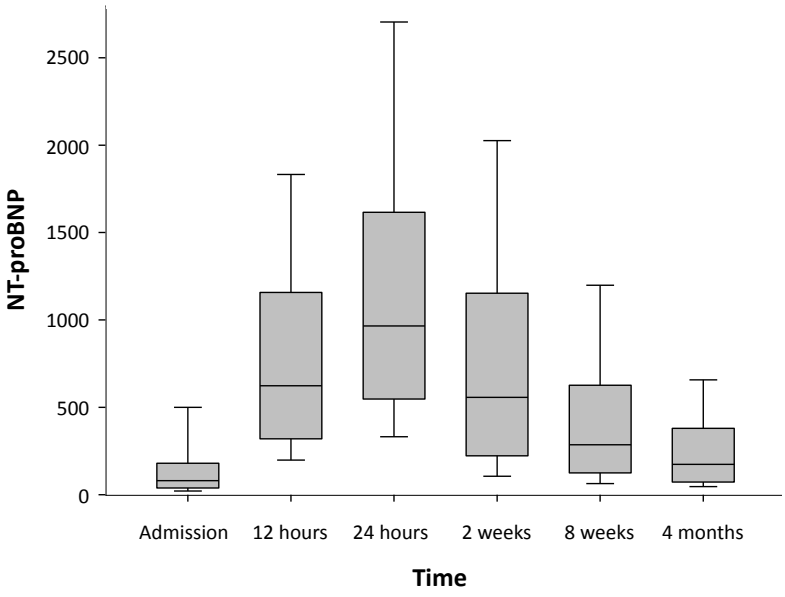
PCI: Percutaneous Coronary Intervention, TIMI: Thrombolysis In Myocardial Infarction, GFR: Glomerular Filtration Rate.

Statistical analysis was performed using SPSS software version 22.0 (Chicago, USA) and R version 3.0.

Results

Baseline characteristics are presented in Table 1. The median (IQR) time points of the NT-proBNP measurements were; a) admission: -0.5 hours (-0.7- -0.37) before PCI b) 12 hours: 11.7 (11.3-12.2), c) 24 hours: 23.6 (23.0-24.0). The NT-proBNP measurements after discharge were; d) at 2 weeks: 2.8 (2.4-3.3), e) at 8 weeks: 8.0 (7.3-8.3), and f) at 4 months: 4.1 (4.0-4.2). The highest median level of NT-proBNP was measured at 24 hours after admission (Figure 1). The distribution of the NT-proBNP levels were alike across the randomization treatment of the GIPS III trial.

Figure 1 | NT-proBNP levels at different time points

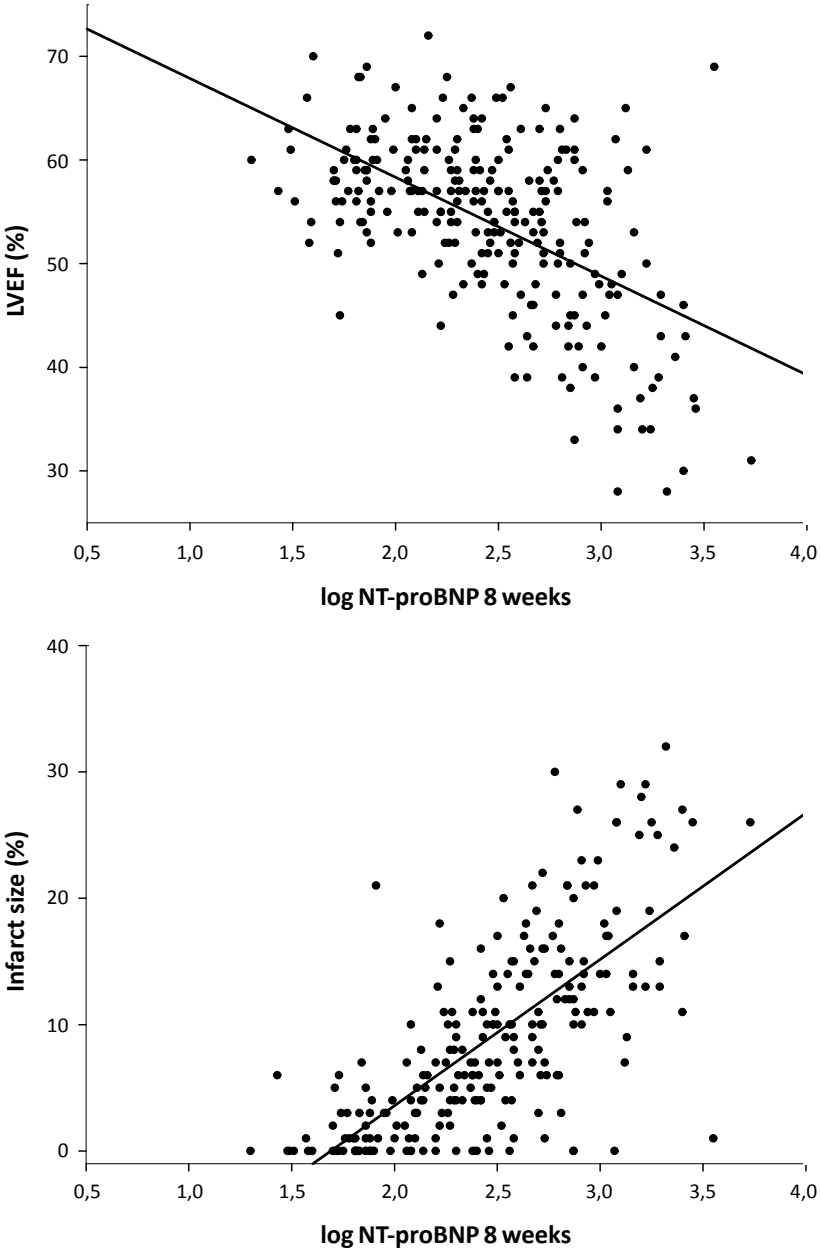


NT-proBNP levels (ng/L) are presented as median (IQR); At admission 80 ng/L (38-180) n=267, 12 hours after PCI 623 ng/L (320-1157) n=258, 24 hours after PCI 965 ng/L (548-1616) n=192, 2 weeks after discharge 557 ng/L (222-1153) n=250, 8 weeks after discharge 286 ng/L (125-627) n=246, and 4 months after discharge 174 ng/L (72-380) n=244.

The LVEF and infarct size determined by MRI were available in 271 and 257 patients, respectively. At 4 months, the mean LVEF was 53.9% [95% CI, 52.9%-55.0%] and median

infarct size was 7.0% (IQR, 2.1%-13.7%). Other parameters of LV systolic function determined by MRI were; LVEDV 194.6 ± 46 ml, LVESV 91.7 ± 36 ml, cardiac output 6.0 ± 1.4 L/min, and LV mass 101.9 ± 24 grams.

Figure 2 | Predictive value of log NT-proBNP levels at 8 weeks on left ventricular ejection fraction and infarct size



Left ventricular ejection fraction

The association of log-transformed NT-proBNP levels at different time points on LVEF at 4 months is shown in Figure 2. In univariable linear regression, NT-proBNP at all time points, peak and area under the curve during hospitalization were associated with LVEF (Table 2a).

Table 2a | Predictive value of log NT-proBNP on left ventricular ejection fraction

Log NT-proBNP	β	SE (β)	p-value	Rsquare
At admission	-2.57	0.95	0.007	0.027
12 hours	-6.50	1.25	<0.001	0.096
24 hours	-7.03	1.63	<0.001	0.089
2 weeks	-8.89	0.95	<0.001	0.260
8 weeks	-9.53	0.93	<0.001	0.300
4 months	-8.72	0.95	<0.001	0.257
Peak during hospitalization	-4.51	1.12	<0.001	0.057
Peak of all time points	-7.60	1.18	<0.001	0.135
AUC during hospitalization	-6.71	1.62	<0.001	0.085

NT-proBNP: N-Terminal pro-Brain Natriuretic Peptide, AUC: Area Under the Curve.

The NT-proBNP levels during follow-up explained more of the variance of LVEF (30.0% at 8 weeks) compared to the NT-proBNP levels during hospitalization (9.6% at 12 hours, p<0.001), the peak levels during hospitalization (5.7%, p<0.001), the peak levels of all time points (13.5%, p<0.001) or the area under the curve during hospitalization (8.5%, p<0.001). In the multivariable regression analysis, NT-proBNP levels at all time points remained an independent predictor of LVEF at 4 months after adjustment for residuals of established risk factors, except for NT-proBNP at admission (Table 3a).

Table 3a | Predictive value of log NT-proBNP on left ventricular ejection fraction adjusted for established risk factors

Log NT-proBNP	β	SE (β)	p-value	Rsquare
At admission	-1.78	0.94	0.057	0.014
12 hours	-4.74	1.25	<0.001	0.053
24 hours	-5.09	1.62	0.002	0.049
2 weeks	-7.88	0.96	<0.001	0.215
8 weeks	-8.60	0.94	<0.001	0.255
4 months	-7.86	0.95	<0.001	0.220

* adjusted for age, body mass index, history of diabetes, hypertension, systolic blood pressure and heart rate, anterior myocardial infarction, and time to treatment (symptom onset to first intervention).

The explained variance of NT-proBNP levels were highest during follow-up; 21.5-25.5% versus 1.4-5.3% during hospitalization.

The change between NT-proBNP levels at admission and after 12 hours and 24 hours was associated with LVEF at 4 months (Table 4a). Also the change between NT-proBNP levels 24 hours after admission and NT-proBNP levels at 2 weeks, and 8 weeks was associated with LVEF. However, the explained variance of the change in NT-proBNP levels was between 2.2-6.9%.

Table 4a | Predictive value of the change of NT-proBNP levels on left ventricular ejection fraction adjusted for baseline log NT-proBNP

Change of NT-proBNP	β	SE (β)	p-value	Rsquare
Admission – 12 hours	-0.003	0.001	<0.001	0.051
Admission – 24 hours	-0.002	0.001	<0.001	0.069
24 hours – 2 weeks	-0.002	0.001	0.001	0.061
24 hours – 8 weeks	-0.002	0.001	0.015	0.034
24 hours – 4 months	-0.002	0.001	0.050	0.022

The receiver operating characteristic curves showed higher areas under the curves of NT-proBNP levels during follow-up (0.720-0.756) compared to those obtained during hospitalization (0.571-0.660) for predicting an LVEF of 55% or more. Using different cutoff values for LVEF, this trend of higher area under the curves during follow-up remained.

Infarct size

NT-proBNP at all time points, except at admission, peak and area under the curve during hospitalization were associated with infarct size (Table 2b).

Table 2b | Predictive value of log NT-proBNP on infarct size

Log NT-proBNP	β	SE (β)	p-value	Rsquare
At admission	1.29	0.89	0.148	0.008
12 hours	6.76	1.12	<0.001	0.130
24 hours	8.59	1.43	<0.001	0.166
2 weeks	10.34	0.77	<0.001	0.434
8 weeks	11.53	0.74	<0.001	0.509
4 months	9.97	0.87	<0.001	0.363
Peak during hospitalization	6.00	1.03	<0.001	0.119
Peak of all time points	8.93	1.03	<0.001	0.227
AUC during hospitalization	7.17	1.47	<0.001	0.119

NT-proBNP: N-Terminal pro-Brain Natriuretic Peptide, AUC: Area Under the Curve.

The variability of infarct size explained by NT-proBNP levels is highest during follow-up (50.9% at 8 weeks) compared to NT-proBNP levels during hospitalization (13.0% at 12 hours, p<0.001), the peak levels during hospitalization (11.9%, p<0.001), the peak levels of all time points (22.7%, p<0.001) or the area under the curve during hospitalization (11.9%, p<0.001). Furthermore a higher explained variance by NT-proBNP levels at 8 weeks was observed for infarct size compared to LVEF (p=0.002).

Also in the multivariable regression analysis, NT-proBNP levels at all time points, except at admission, remained an independent predictor of LVEF at 4 months after adjustment for residuals of established risk factors (Table 3b).

Table 3b | Predictive value of log NT-proBNP on infarct size adjusted for established risk factors

Log NT-proBNP	β	SE (β)	p-value	Rsquare
At admission	0.56	0.87	0.517	0.002
12 hours	4.95	1.13	<0.001	0.073
24 hours	6.42	1.46	<0.001	0.096
2 weeks	9.08	0.79	<0.001	0.359
8 weeks	10.27	0.78	<0.001	0.427
4 months	8.72	0.89	<0.001	0.292

* adjusted for age, body mass index, history of diabetes, hypertension, systolic blood pressure and heart rate, anterior myocardial infarction, and time to treatment (symptom onset to first intervention).

NT-proBNP levels explained more of the variability during follow-up (29.2-42.7%) compared to during hospitalization (0.2-9.6%).

Similar to the association with LVEF, the change between NT-proBNP levels at admission and after 12 hours and 24 hours was also associated with infarct size at 4 months (Table 4b). Also, the changes between NT-proBNP levels 24 hours after admission and NT-proBNP levels at 2 weeks, and 8 weeks were all associated with infarct size. The highest explained variance was 13.6%.

Table 4b | Predictive value of the change of NT-proBNP levels on infarct size adjusted for baseline log NT-proBNP

Change of NT-proBNP	β	SE (β)	p-value	Rsquare
Admission – 12 hours	0.004	0.001	<0.001	0.089
Admission – 24 hours	0.003	0.001	<0.001	0.136
24 hours – 2 weeks	0.003	0.001	<0.001	0.090
24 hours – 8 weeks	0.002	0.001	0.009	0.041
24 hours – 4 months	<0.001	0.001	0.627	0.001

The receiver operating characteristic curve analyses to predict an infarct size of at least 7.0% by NT-proBNP levels showed higher areas under the curves during follow-up (0.807-0.882) compared to during hospitalization (0.520-0.681).

Additional determinants of LV systolic function

Additional MRI parameters of LV systolic function showed similar results (Table 5, supplement). The NT-proBNP levels during follow-up were significantly associated with LVEDV (R^2= 5.5-7.9%), but levels during hospitalization were not. For LVESV, NT-proBNP levels were all associated, but a higher explained variance (17.3-21.8%) was seen for levels during follow-up compared to the explained variance (1.8-7.2%) for levels during hospitalization. Cardiac output was associated with NT-proBNP levels at admission (R^2= 1.5%) and during follow-up (R^2= 1.9-2.1%). The same was true for LV mass, with an explained variance of 1.6% for NT-proBNP levels at admission and an explained variance between 2.2-3.8% for levels during follow-up.

Table 5 | Predictive value of log NT-proBNP on other determinants of left ventricular systolic function

		LVEDV (ml)		
Log NT-proBNP	**β**	**SE (β)**	**p-value**	**Rsquare**
At admission	5.32	5.23	0.309	0.004
12 hours	17.77	7.10	0.013	0.024
24 hours	17.48	9.34	0.063	0.018
2 weeks	22.20	5.87	<0.001	0.055
8 weeks	26.49	5.81	<0.001	0.079
4 months	23.34	5.89	<0.001	0.061
		LVESV (ml)		
Log NT-proBNP	**β**	**SE (β)**	**p-value**	**Rsquare**
At admission	8.95	4.05	0.028	0.018
12 hours	24.24	5.42	<0.001	0.072
24 hours	26.61	7.17	<0.001	0.068
2 weeks	31.01	4.31	<0.001	0.173
8 weeks	34.17	4.15	<0.001	0.218
4 months	30.97	4.07	<0.001	0.193
		Stroke volume (ml)		
Log NT-proBNP	**β**	**SE (β)**	**p-value**	**Rsquare**
At admission	-3.55	2.41	0.141	0.008
12 hours	-6.47	3.27	0.048	0.015
24 hours	-9.17	4.25	0.032	0.024
2 weeks	-8.87	2.70	0.001	0.042
8 weeks	-7.77	2.75	0.005	0.032

4 months	-7.76	2.93	0.009	0.028
		Cardiac output (L/min)		
Log NT-proBNP	**β**	**SE (β)**	**p-value**	**Rsquare**
At admission	-0.32	0.16	0.043	0.015
12 hours	-0.40	0.22	0.068	0.013
24 hours	-0.35	0.31	0.254	0.007
2 weeks	-0.40	0.18	0.027	0.020
8 weeks	-0.40	0.19	0.030	0.019
4 months	-0.43	0.19	0.023	0.021
		left ventricular mass (grams)		
Log NT-proBNP	**β**	**SE (β)**	**p-value**	**Rsquare**
At admission	5.16	2.69	0.038	0.016
12 hours	6.67	3.70	0.073	0.013
24 hours	6.25	5.06	0.218	0.008
2 weeks	7.14	3.09	0.019	0.022
8 weeks	9.33	3.02	0.002	0.038
4 months	9.625	3.21	0.003	0.036
		Infarct size (grams)		
Log NT-proBNP	**β**	**SE (β)**	**p-value**	**Rsquare**
At admission	2.44	1.10	0.027	0.019
12 hours	8.85	1.40	<0.001	0.142
24 hours	11.17	1.85	<0.001	0.169
2 weeks	12.34	1.00	<0.001	0.393
8 weeks	12.83	0.93	<0.001	0.449
4 months	11.43	1.05	<0.001	0.341

LVESV: Left ventricular end-systolic volumes: LVEDV: Left ventricular end-diastolic volumes (LVEDV).

Discussion

In patients presenting with first acute myocardial infarction treated according to current guidelines, early measurements of NT-proBNP have limited value in predicting LVEF or infarct size at 4 months. However, NT-proBNP measured during follow-up can predict up to 30% and 51% of the variability of LVEF and infarct size, respectively. Furthermore, NT-proBNP levels during follow-up are stronger predictors for infarct size compared to LVEF.

The reason of using data of the GIPS III trial was that the patients were included after their first myocardial infarction, assuming normal LVEF prior to inclusion. NT-proBNP was

measured on standardized time points and patients were treated following the current guidelines with primary PCI, standard medication and received advices for improving lifestyle.[10-13] The primary endpoint of this study was LVEF determined by MRI and assessed by a core lab blinded to other patient characteristics.

Left ventricular dysfunction

Myocardial infarction is one of the most common causes of LV dysfunction.[16] Early and successful revascularization of the infarct-related artery is the most important treatment in preserving LV function. Myocardial dysfunction occurs (sub)acutely when myocardial loss is not prevented by revascularization. The initiated temporary neurohormonal cascade attempts to compensate for the declined contractile myocardial function to maintain sufficient cardiac output.[17] In the following months, myocardial remodeling occurs including infarct expansion, myocardial hypertrophy, and fibrosis resulting in reduced LVEF and LV dilatation.[17] The clinical syndrome of heart failure often ensues from LV dysfunction; mortality is much higher in patients who develop heart failure after myocardial infarction.[1,18] MRI is the most accurate available noninvasive imaging technique for determination of LV function.[19] Infarct size measured by MRI is highly reproducible[20] and associated with cardiovascular mortality and morbidity.[5]

Predictive value of NT-proBNP

Clearly, sophisticated imaging of LV function is more laborious and more costly to perform than assessing a biomarker. For that reason, a single level of a biomarker measured during follow-up, with a strong association with LV function determined by MRI, would be a useful tool in routine clinical practice.

B-type natriuretic peptide (BNP) is synthesized and released by the myocardium, especially the ventricular tissue, in response to cardiac stretch and overload, in parallel to the severity of the trigger.[21] During an acute myocardial infarction, the synthesis and release is also stimulated by ischemia and up regulated due to local stretch mechanisms in the area surrounding the jeopardized myocardium. Upon cardiac injury, the natriuretic peptides have protective effects on circulatory homeostasis through multiple actions. BNP lowers blood pressure by its vasodilatory actions and effects on sodium handling, but also has several direct effects on the heart, such as anti-fibrotic and anti-apoptotic effects.[6] The natriuretic peptides are considered the physiological counter players of the renin angiotensin system (RAS) – in healthy individuals, the RAS and the natriuretic peptide system is in tight equilibrium. Since BNP has a short half-life, with associated considerable fluctuations within individuals and between individuals[6], often the biologically inactive but more stable cleavage product NT-proBNP is measured, as we did in this study.

In our study we found a stronger association of NT-proBNP levels with LVEF and

infarct size during follow-up compared to the levels measured during hospitalization. The stronger association during follow-up may, be explained by that NT-proBNP levels are upregulated after clinical stabilization mainly due to stretched LV wall caused by infarct scar in comparison to upregulation due to the acute ischemia.[6,22] Also progressive LV remodeling and the longer half-life of NT-proBNP may influence the magnitude of these differential associations. A similar association of NT-proBNP levels with LVEF and infarct size during follow-up compared to early measurements is also shown in other studies.[23-27]

We also found that NT-proBNP is a better predictor of infarct size than of LVEF. This is in line with other previous studies.[23,24] Possibly infarct size is a better determinant of the myocardial damage in patients after their first acute myocardial infarction than LVEF. Infarct size determined by MRI, only includes irreversible injured myocardium due to unsuccessful (microvascular) reperfusion.[28] This contributes to the LVEF measured after myocardial infarction; however the LVEF may be, unlike infarct size, influenced by multiple factors already present before the myocardial infarction.

Opportunities of risk assessment

Risk assessment gives the opportunity to initiate early treatment that reduces progression to symptomatic heart failure and the associated morbidity and mortality. Improved and routine use of invasive strategies and multiple pharmacotherapies have improved myocardial salvage after myocardial infarction, therefore lowering the risk of LV dysfunction and developing heart failure[1] Examples of treatment strategies that improve outcome in high risk patients for LV dysfunction after myocardial infarction are; prevention of reinfarction by early revascularization of significant coronary artery disease and antithrombotic medication and/or attenuation of the remodeling process by angiotensin-converting enzyme-inhibitors, angiotensin-receptor blockers or mineralocorticoid receptor antagonists.[12,13,19] More aggressive and early treatment in patients with high risk for LV dysfunction may improve outcome for this patient group. Noteworthy, the prescription and adherence of pharmacotherapy is often suboptimal in patients with LV dysfunction.[3,4,29,30]

Multiple risk models are known to predict the outcome after myocardial infarction; baseline characteristics that have been associated with outcome most of the time are: age, heart rate, systolic blood pressure, prior heart failure, diabetes, left bundle-branch block, anterior myocardial infarction.[3,4,15] After adjustments for these established risk factors, NT-proBNP at all time points remained independent predictor of LVEF and infarct size at 4 months, with the strongest association for NT-proBNP measured during follow-up.

Potential implications

As our study implicates that the association of NT-proBNP during hospitalization and LVEF is modest, costs can be reduced by omitting NT-proBNP measurements during hospitalization

in routine clinical practice. Moreover, measuring NT-proBNP during follow-up could be used as a surrogate endpoint for LV function in smaller studies including patients with myocardial infarction.

Limitations

In the context of the study design, we included patients after their first myocardial infarction without known diabetes mellitus. This resulted in a low percentage of patients with significant LV dysfunction. Therefore, our findings can only be interpreted in patients with relatively preserved LV function. The same is true for the relative small infarct sizes. However, despite this, a strong association could be found. Furthermore, we could not relate NT-proBNP to hard endpoints, as there were hardly any major adverse events during this study.

Conclusion

After STEMI, NT-proBNP levels measured during hospitalization are of limited value in predicting LVEF and infarct size. However, NT-proBNP measured during follow-up are strong predictors of LVEF and even stronger predictors of myocardial infarct size.

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