Galectin-3 predicts left ventricular remodelling after anterior-wall myocardial infarction treated by primary percutaneous coronary intervention

Giuseppe Di Tano,1 Giorgio Caretta,1,2 Renata De Maria,3 Marina Parolini,3 Laura Bassi,4 Sophie Testa,4 Salvatore Pirelli1

ABSTRACT

Objectives Despite modern reperfusion therapies, left ventricular remodelling (LVR) occurs frequently after an ST-elevated myocardial infarction (STEMI) and represents a strong predictor of mortality and heart failure. Galectin-3 (Gal-3), a novel biomarker involved in inflammation, tissue repair and fibrogenesis, might be a valuable predictor of LVR.

Methods We enrolled consecutively admitted patients with a first anterior STEMI and left anterior descending artery occlusion treated by primary percutaneous coronary intervention (pPCI). Galectin-3, N-terminal pro-B-type natriuretic peptide (NT-proBNP), echocardiography and cardiovascular events were evaluated 48 hours after admission, at 1 and 6 months. LVR was defined as a ≥15% increase in LV end-systolic volume.

Results We recruited 103 patients (28% women, aged 64.6±12 years, LV ejection fraction 47±11%). Median baseline Gal-3 and NT-proBNP levels were 13.2 ng/mL (10.8–17.1 ng/mL) and 2132 pg/mL (1019–4860 pg/mL) respectively. During 6 months of follow-up, 4 patients dropped out, 7 died and 26 (28.3%) of the 92 survivors developed LVR (LVR+). LVR+ patients had higher Gal-3 levels at baseline, 1 and 6 months than LVR− (<0.0001). By univariable logistic regression, age, female gender, higher baseline Gal-3 and NT-proBNP, smaller LV end-diastolic volume (LVEDV) were associated to an increased risk of LVR. By multivariable analysis, only LVEDV (OR 0.96, 95% CI 0.93 to 0.99/1 mL change) and Gal-3 levels (OR 1.22, 95% CI 1.06 to 1.42/1 ng/mL change) independently predicted LVR (C-statistics 0.84, 95% CI 0.75 to 0.93).

Conclusion Gal-3 serum levels measured during hospitalisation could be clinically useful in predicting LVR among patients admitted with anterior STEMI treated by pPCI.

INTRODUCTION

The term left ventricular (LV) remodelling (LVR) encompasses progressive changes in LV function and architecture (size, shape, structural composition), induced by deleterious adaptive mechanical and neurohormonal processes that develop after myocardial injury.1 Despite modern reperfusion therapies, LVR occurs frequently after an ST-elevated myocardial infarction (STEMI) and represents a strong predictor of mortality and heart failure (HF).2,3 Experimental and clinical studies show that LVR is a dynamic and progressive process that starts early but can last up to several months after the acute event. LVR involves infarcted and non-infarcted zones and its extent depends on infarct size, anatomic location and type and timely treatments. These changes are driven, at the histological level, by myocardial hypertrophy and apoptosis and by increased interstitial collagen deposition within scar tissue. A hallmark of LVR is the formation of fibrosis both in the early and late phases following myocardial infarction (MI).1

Galectin-3 (Gal-3) is a new biomarker that has gained interest as a marker of LVR.4–7 Gal-3 is a member of a family of proteins comprising soluble α-galactoside-binding lectins that have regulatory roles in fibrogenesis, inflammation, immunity, tissue repair and cell proliferation. Gal-3 can be measured reliably and has been shown to independently predict outcomes in patients with HF and in the general population.8 Few human studies evaluated its role on post-MI LVR.7

We aimed to assess whether Gal-3 is a useful predictor of LVR among patients with first anterior STEMI treated by primary percutaneous coronary intervention (pPCI).

METHODS

GALAMI was a prospective, observational, single-centre study that included 103 consecutive patients admitted for acute anterior STEMI and treated by pPCI. Inclusion criteria were as follows: age ≥18 years, ischaemic symptoms since <12 hours, eligible for pPCI, ECG with ST-segment elevation ≥2 mm in ≥2 adjacent anterior precordial/peripheral leads (V3–4, V6+DI, aVL) or new left bundle branch block or new significant Q wave in ≥2 adjacent anterior precordial/peripheral derivations, left anterior descending artery or left main as infarct-related artery. Exclusion criteria were previous STEMI/non-STEMI, pre-existing LV dysfunction (LV ejection fraction (LVEF) <50%), mineralocorticoid receptor antagonists (MRAs), severe renal dysfunction (plasma creatinine level >220 μmol/L and/or creatinine clearance <30 mL/min), severe liver disease (Child-Pugh Class 3), cancer, life expectancy <6 months, cardiac arrest lasting >10 min, inability or unwillingness to comply with the treatment or follow-up visits. Written informed consent was obtained from the patient or a member of the family or the person of confidence, if the patient was unable to provide informed consent.
The study protocol complied with the Declaration of Helsinki and was approved by the local ethics committee (protocol number 8686/13).

At baseline, blood was sampled for routine biochemistry and cardiac troponin I (cTnI), Gal-3 and N-terminal pro-B-type natriuretic peptide (NT-proBNP) assays. Two-dimensional echocardiography was performed 36–48 hours after pPCI. Follow-up after STEMI included a clinical visit and blood sampling for Gal-3 and NT-proBNP measurements at 1 and 6 months, when a two-dimensional echocardiogram was again obtained.

Gal-3 levels were measured with the VIDAS automated enzyme-linked fluorescent assay (ELFA) (bioMérieux, France). Blood was collected into chilled tubes containing potassium EDTA (1 mg/mL blood) and aprotinin (50 KIU/mL blood) and centrifuged within 1 hour at 2000 g for 15 min at ambient temperature. Plasma was extracted and stored at −70°C until batched blinded analysis after trial completion. Each aliquot was subjected to two freeze-thaw cycles. The coefficient of variation for the assay was <10% and the limit of detection was 2.2 ng/mL. NT-proBNP was measured on serum samples with the quantitative VIDAS ELFA (bioMérieux, France). Physicians who performed biomarker assays were unaware of clinical information and echocardiographic results.

Echocardiography was performed with patients lying in left lateral decubitus with a digital ultrasonic device system (Vivid 7, GE Vingmed Ultrasound, Horten, Norway). Grey scale 4-chamber, 2-chamber and long-axis apical views and parasternal short-axis views of LV at either basal or apical level were obtained at a high frame rate (60–80 frames/s) using second harmonic (1.7/3.4 MHz) imaging. LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) were measured according to Simpson’s biplane method and LVEF was calculated as [(LVEDV − LVESV)/LVEDV]. Physicians who performed echocardiographic assessments were unaware of biomarkers results. Inter-observer and intra-observer variabilities for LV volume measurement in our laboratory were as follows: LVEDV 8% and LVESV 10% for inter-observer variability, LVEDV 5% and LVESV 6% for intra-observer variability. LV was defined as an increase of ≥15% from baseline in LVESV at 6-month echocardiography. We also performed a sensitivity analysis using a more stringent criterion for LV (LVESV increase ≥20%).

Statistical analysis

Based on previous studies, we hypothesised that 30% of patients with anterior STEMI would develop LVH: a sample of 100 patients had to be recruited to obtain a power of 90% and a two-tailed α of 0.05.

Discrete variables are presented as count and frequency (%). Continuous variables are shown as mean±SD or median and IQR when they had a skewed distribution. Continuous variables were compared using either the t-test or the Mann-Whitney U test and categorical variables were compared by the χ² test or Fisher’s exact test, depending on whether the data followed a normal distribution. A generalised linear mixed model with Bonferroni correction was used to test changes with time by presence of LVH in chamber size and function and the biomarkers Gal-3 and NT-proBNP levels after logarithmic transformation of the latter skewed variables. Correlations between logGal-3 and logNT-proBNP were tested by Pearson’s coefficient.

Predictive accuracy of Gal-3 levels was assessed by the C-statistics. Sensitivity, specificity, negative and positive predictive values of cut-off derived from the receiver operating characteristic (ROC) curve were calculated.

Univariable and multivariable logistic regression analyses were performed to evaluate the relation between LVH at 6-month follow-up and the following baseline variables: age, sex, multivessel disease, history of hypertension, diabetes, serum creatinine levels, Killip class (I vs > I) peak cTnI levels, LVEDV, LVEF, NT-proBNP levels and Gal-3 levels. Variables with a probability value <0.20 by univariable analysis were entered as covariates in the multivariable model. Model calibration was assessed by Hosmer-Lemeshow goodness-of-fit test and predictive accuracy by the C-statistics. Time-to-first event Kaplan-Meier event-free survival curves for the combined end point of death or HF admission at 6 months by Gal-3 cut-off were compared by the log rank test.

A p value <0.05 was considered statistically significant. Statistical analysis was performed with the SPSS software package (SPSS (V.20.0), International Business Machines Armonk, New York, USA).

RESULTS

From March 2013 to October 2014, 205 patients with STEMI were consecutively admitted to the coronary care unit of the ASST Hospital of Cremona and were treated with pPCI. Among them, 103 patients had anterior STEMI and were included in the study. Four patients withdrew consent during follow-up. Thus, data of 99 patients were analysed. Mean age was 64.6 years and 71.8% were men. Baseline post-PCI LVEF was 46.3%.

Median baseline Gal-3 and NT-proBNP levels were 13.2 ng/mL (10.8–17.1 ng/mL) and 2132 pg/mL (1019–4860 pg/mL), respectively. During 6-month follow-up, seven patients died and six were readmitted for HF; respectively. Overall, 12 patients met the combined end point of death or HF admission. Six-month event-free survival rates according to baseline Gal-3 level above or below the manufacturer-provided normal cut-off (>17.7 ng/mL) were 65% versus 92% (p<0.001, figure 1).

Figure 1 Kaplan-Meier curves showing event-free survival from hospitalisation for heart failure (HF) according to baseline galectin-3 (Gal-3) levels below or above the normal cut-off (>17.7 ng/mL).
Table 1  Baseline characteristics of all patients and stratified by presence of LVR at 6 months

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=92)</th>
<th>LVR– (n=66)</th>
<th>LVR+ (n=26)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>64 (56–75)</td>
<td>63 (56–71)</td>
<td>74 (60–79)</td>
<td>0.009</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>22 (23.9)</td>
<td>10 (15.2)</td>
<td>12 (54.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>53 (57.3)</td>
<td>36 (54.2)</td>
<td>17 (66.7)</td>
<td>0.483</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>11 (11.9)</td>
<td>8 (12.1)</td>
<td>3 (11.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>EDV, mL</td>
<td>109 (89–120)</td>
<td>117 (97–133)</td>
<td>91 (74–109)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESV, mL</td>
<td>54 (41–77)</td>
<td>57 (46–81)</td>
<td>43 (34–58)</td>
<td>0.01</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>48 (40–55)</td>
<td>48 (40–55)</td>
<td>50 (42–57)</td>
<td>0.32</td>
</tr>
<tr>
<td>Symptoms-to-balloon hours</td>
<td>3 (2–4)</td>
<td>3 (2–5)</td>
<td>2 (2–3.25)</td>
<td>0.88</td>
</tr>
<tr>
<td>Killip class on admission n (%)</td>
<td>86 (93)</td>
<td>62 (94)</td>
<td>24 (92)</td>
<td>1.00</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.90 (0.80–1.14)</td>
<td>0.90 (0.79–1.15)</td>
<td>0.90 (0.79–1.06)</td>
<td>0.76</td>
</tr>
<tr>
<td>cTnI (peak), ng/mL</td>
<td>27 (10–98)</td>
<td>21 (9–134)</td>
<td>46 (26–86)</td>
<td>0.81</td>
</tr>
<tr>
<td>Gal-3 (baseline), ng/mL</td>
<td>13.2 (10.8–17.1)</td>
<td>12.3 (10.5–15.0)</td>
<td>15.3 (13.1–22.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>NT-proBNP (baseline), pg/mL</td>
<td>2132 (1019–4860)</td>
<td>1374 (835–3726)</td>
<td>3219 (1149–8334)</td>
<td>0.018</td>
</tr>
<tr>
<td>Killip class on admission n (%)</td>
<td>66 (71.7)</td>
<td>48 (72.7)</td>
<td>18 (69.2)</td>
<td>0.679</td>
</tr>
<tr>
<td>I</td>
<td>19 (20.7)</td>
<td>12 (18.2)</td>
<td>7 (26.6)</td>
<td></td>
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<tr>
<td>II</td>
<td>1 (1.1)</td>
<td>1 (1.5)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>6 (6.5)</td>
<td>5 (7.6)</td>
<td>1 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Multi-vessel disease—n (%)</td>
<td>35 (38.0)</td>
<td>25 (37.8)</td>
<td>10 (38.4)</td>
<td>0.57</td>
</tr>
<tr>
<td>Any stent—n (%)</td>
<td>87 (94.5)</td>
<td>61 (92.4)</td>
<td>26 (100)</td>
<td>0.071</td>
</tr>
<tr>
<td>Bare metal stent</td>
<td>41 (44.5)</td>
<td>25 (37.9)</td>
<td>16 (61.5)</td>
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<tr>
<td>Drug eluting stent</td>
<td>46 (50.0)</td>
<td>36 (54.5)</td>
<td>10 (38.5)</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors—n (%)</td>
<td>79 (85.8)</td>
<td>56 (84.8)</td>
<td>23 (88.5)</td>
<td>0.75</td>
</tr>
<tr>
<td>β-blocker—n (%)</td>
<td>84 (91.3)</td>
<td>59 (89.4)</td>
<td>25 (91.6)</td>
<td>0.433</td>
</tr>
</tbody>
</table>

Mid-term LVR
Among the 92 survivors at 6 months, 26 patients (28.2%) showed LVR (LVR+). The baseline characteristics of the population are summarised in table 1. LVR+ patients were older, more likely to be women and had higher serum levels of Gal-3 and NT-proBNP. At baseline, LVR+ patients had smaller LVVs than LVR−, although LVEF did not differ between groups. At 6-month echocardiography, as compared with baseline, LVR+ patients showed increased LVEDV and decreased LVEF. Conversely, in LVR− patients, LVEDV decreased, while LVEF increased (p for time-group interaction = 0.001 for LVEF and = 0.003 for LVEDV by multivariable analysis).

Temporal trends for Gal-3 and NT-proBNP
Log-Gal-3 and logNT-proBNP were correlated at baseline (R=0.409, p<0.001), at 1 month (R=0.514, p<0.001) and 6 months (R=0.457, p<0.001).
However, the two biomarkers showed different trends, as shown in figure 3. Gal-3 concentrations were significantly increased throughout follow-up in LVR+ than in LVR− (generalised linear mixed model of log-Gal; time p=0.466, group p<0.001 and time-group interaction p=0.801). NT-proBNP concentrations were also significantly higher in LVR+ than in LVR− and similarly decreased over time in the two groups (generalised linear mixed model of log-NT-proBNP; time p<0.001, group p=0.009 and time-group interaction, p=0.661).

Prediction of LVR
By univariable logistic regression (table 2) age, male gender, baseline Gal-3 and NT-proBNP and LVEDV were associated with LVR. Figure 4 (left) represents the unadjusted ROC curve and C-statistics for LVR at 6 months of baseline Gal-3 levels (C-statistics 0.72, 95% confidence interval (CI) 0.60 to 0.84).
In the multivariable model, only LVEDV (OR 0.96, 95% CI 0.93 to 0.99/1 mL increase) and Gal-3 levels (OR 1.14, 95% CI 1.02 to 1.25/1 ng/mL increase) were independent predictors of LVR. The C-statistics of the model predicted probability was 0.84 (95% CI 0.75 to 0.93) (figure 4, right); the Hosmer-Lemeshow index was 0.871, indicating good model fit.
Gal-3 measured at 1 month preserved its predictive role by multivariable analysis (OR 1.14 95% CI 1.02 to 1.25/1 ng/mL increase) but did not provide incremental predictive value over baseline levels (C-statistics 0.81, 95% CI 0.71 to 0.91). Gal-3 levels at 6 months were not associated to LVR.

Sensitivity, specificity, negative and positive predictive values of the Gal-3 cut-off value derived from the ROC curve (≥ 13.5 ng/ml) were 76.9%, 65.2%, 87.8% and 46.5%, respectively. Conversely, when the upper limit of normal cut-off value for Gal-3 indicated by the manufacturer (>17.7 ng/mL) was used, sensitivity, specificity, negative and positive predictive values were 30.8%, 90.9%, 76.9% and 57.1%, respectively.

A sensitivity analysis using a more stringent cut-off for LVR (LVEV increase ≥20%, n=23, 25%) confirmed baseline Gal-3, adjusted by age, gender and LVEDV as independent predictor of LVR (OR 1.22, 95% CI 1.04 to 1.42, p=0.013) (C-statistics 0.84, 95% CI 0.74 to 0.93).

DISCUSSION
This study demonstrates that Gal-3 plasma levels measured during the acute post-MI phase after pPCI might be clinically useful in predicting the development of LVR among patients admitted with a reperfused anterior STEMI.
Post-MI LVR is a key precursor of the development of overt HF and an important predictor of mortality. LVR is reported to occur frequently after anterior STEMI, despite achievement of early flow in the infarct-related artery. Early identification of patients at risk may have important implications for post-discharge therapy and follow-up.

Over one-fourth (28.3%) of our successfully reperfused patients developed LVR after 6 months, a rate consistent with previous reports among similar populations. Furthermore, LVR+ patients had a fivefold higher rate of HF hospitalisation during follow-up than LVR−. In our cohort, Gal-3 was an accurate predictor of mid-term LVR (C-statistics value adjusted by age, gender and LVEDV 0.84).

Gal-3, a β-galactoside-binding lectin secreted by activated macrophages, has recently been proposed as a marker (and possibly a key mediator) of inflammation and fibrosis, central to the processes pathophysiological of LVR. Experimental evidences suggest that Gal-3 is involved in fibrotic process following MI. Only few studies, based on subgroup analyses from randomised controlled trials, described Gal-3 levels in patients with acute MI. These studies were limited to the assessment of Gal-3 relationship with scar extension or LV function. Among 100 patients with reduced LVEF after acute MI, Weir et al found an inverse correlation between baseline Gal-3 and LVEF after 6 months. However, they found no relationships between Gal-3 and LV parameters at baseline or any changes over time in any parameter. van der Velde et al recently reported similar findings among 247 post-MI patients. Patients with elevated Gal-3 levels at the time of acute MI had lower LVEF by cardiac MRI (CMR) after 4 months and baseline Gal-3 levels were independent predictors of lower LVEF and bigger infarct-related scars at 4 months; however, no baseline measures of LVEF or LV volumes were available. Since LVR implies a change over time in LV geometry, whether Gal-3 was a marker of the extension of the acute injury or a predictor of eventual LVR remained unclear from these reports.

Of note, we elected to focus our study on patients with anterior STEMI, who are at higher risk of developing LVR. In our cohort, baseline Gal-3 predicted an increase of at least 15% of LVEF after 6 months, which is a validated definition of LVR and a strong predictor of outcome after MI, irrespective of LVEF or LVEDV.

Figure 2 Time course of echocardiographic parameters for left ventricular ejection fraction (LVEF) (above) and left ventricular end-diastolic volume (LVEDV) (below) is shown.

Figure 3 Time course of galectin-3 levels (above) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) (below) among patients with left ventricular remodelling (LVR) (LVR +) and without LVR (LVR −) is shown.
infarct size. Moreover, the predictive value of Gal-3 was confirmed using a higher, more stringent cut-off, for LVESV increase.

Gal-3 has previously been associated with levels of matrix metalloproteinase-3 and monocyte chemoattractant protein-1, which are involved in LVR. Gal-3 remained high in our LVR+ patients 1 month after MI, when it maintained its independent predictive value, but after 6 months no relationship with LVR was observed. These data suggest that Gal-3 acts its pathophysiologises role in pro-remodelling pathways early post-MI, when high levels may reflect greater macrophage activation, extracellular matrix turnover and fibrosis and ensuing LVR.

NT-proBNP was elevated early after MI in the present study, although it decreased significantly over time. NT-proBNP is elevated in symptomatic and asymptomatic LV systolic dysfunction and predicts mortality among patients with chronic HF and major adverse cardiac events after MI. Gal-3 correlated with NT-proBNP at all time points, as previously reported after acute coronary syndromes and in patients with HF. However, patterns and time trends during follow-up differed markedly between these two biomarkers (figure 3) and presumably reflect the difference between the pro-fibrotic effects of Gal-3 and the load-dependent nature of natriuretic peptide release. NT-proBNP tends to fall with reduction in myocardial stretch and unloading therapies, such as ACE inhibitors and diuretics. Gal-3 levels express the process of inflammation and fibrogenesis aimed at myocardial repair after acute injury.

Reports on the prognostic role of Gal-3 measured in the acute post-MI phase are scanty and limited to the short term. High levels of Gal-3 have shown prognostic value in HF and have been suggested to represent integrated predictors for long-term incident HF even in the general population. In our cohort, patients with abnormal Gal-3 levels had lower event-free survival rates at 6 months.

Biomarker-targeted treatment is a very attractive therapeutic strategy. However, to date there are no convincing clinical data to suggest a specific treatment driven by elevated Gal-3 levels. Weir et al reported no significant treatment effect of eplerenone on serum Gal-3 levels over the 24-week study period, while the post-hoc analysis by van der Velde et al suggested that MRAs might be used to lower Gal-3 levels and, indirectly, reduce the

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**Table 2** Predictors of LVR: univariable and multivariable logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable OR (95% CI)</th>
<th>Univariable p value</th>
<th>Multivariable OR (95% CI)</th>
<th>Multivariable p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>1.06 (1.01 to 1.11)</td>
<td>0.007</td>
<td>1.01 (0.96 to 1.06)</td>
<td>n.s</td>
</tr>
<tr>
<td>Male</td>
<td>0.21 (0.07 to 0.58)</td>
<td>0.003</td>
<td>0.92 (0.27 to 4.23)</td>
<td>n.s</td>
</tr>
<tr>
<td>Multi-vessel disease</td>
<td>1.02 (0.40 to 2.60)</td>
<td>0.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.95 (0.23 to 3.9)</td>
<td>0.94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (baseline), %</td>
<td>1.02 (0.98 to 1.07)</td>
<td>0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDV (baseline)/1 mL change</td>
<td>0.96 (0.93 to 0.98)</td>
<td>&lt;0.0001</td>
<td>0.95 (0.92 to 0.98)</td>
<td>0.004</td>
</tr>
<tr>
<td>LVESV (baseline)/1 mL change</td>
<td>0.96 (0.93 to 0.98)</td>
<td>0.02</td>
<td></td>
<td>n.s</td>
</tr>
<tr>
<td>NT-proBNP (baseline)/1000 ng/mL change</td>
<td>1.15 (1.04 to 1.27)</td>
<td>0.007</td>
<td></td>
<td>n.s</td>
</tr>
<tr>
<td>GAL-3 (baseline)/1 ng/mL change</td>
<td>1.22 (1.09 to 1.38)</td>
<td>0.0001</td>
<td>1.22 (1.06 to 1.39)</td>
<td>0.005</td>
</tr>
<tr>
<td>Troponin I (peak) ng/mL</td>
<td>1.00 (0.99 to 1.04)</td>
<td>0.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Killip class &gt;1</td>
<td>1.18 (0.44 to 3.20)</td>
<td>0.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIMI flow 3 vs &lt;3</td>
<td>0.78 (0.13 to 4.51)</td>
<td>0.78</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GAL-3, galectin-3; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVR, left ventricular remodelling; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

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**Figure 4** Unadjusted receiver operating characteristic (ROC) curve and C-statistics for left ventricular remodelling (LVR+) of galectin-3 (Gal-3) (left) are shown. ROC curve and C-statistics for LVR+ of Gal-3 adjusted by age, sex, Killip class and left ventricular end-diastolic volume (right) are shown.
risk of developing LV dysfunction. Recently, among patients with chronic HF and elevated Gal-3 concentrations, no specific benefit from addition or intensification of MRA therapy was found.\(^{23}\) In our study, MRA treatment was an exclusion criterion. Our data suggest that patients at risk of LVR with elevated Gal-3 levels might benefit from early therapy with MRA after MI beyond current guideline recommendations\(^{24}\) to reduce the risk of LVR and possibly adverse outcomes related to LV dysfunction. Further studies with Gal-3-modifying therapies are warranted.

**Study limitations**

Our study has certain limitations that should be considered. First, only patients with anterior STEMI were included; thus, the results cannot be extrapolated to patients with other STEMI locations or non-STEMI. Second, our study population was relatively small and was limited to patients with a first MI treated with pPCI in a single centre, with few complications. Therefore, selection bias and low statistical power should be taken into account when interpreting our findings.

Third, we evaluated our patients with two-dimensional echocardiography, a widely available, low-cost imaging method, to reflect real-life practice. Although CMR is more accurate and also allows reliable estimation of the infarct size and the extension of fibrosis, its costs and restricted availability make echocardiography still the most common non-invasive tool used to quantify LV volumes and function, especially during the acute phase after MI or for serial evaluations.\(^{25}\) Echocardiography has been demonstrated to correlate well with CMR when quantifying LV volumes\(^{26}\) and it has been widely used in landmark studies assessing the prognostic role of LVR in post-MI patients\(^{12,14,25}\) or the predictive value of serum biomarkers.\(^{27}\)

Finally, we did not obtain the overall enzymatic curve but used a single-point (peak) troponin value to estimate infarct size. However, peak troponin correlated with baseline ventricular function consistently with previous studies that cumulatively indicated single time points for troponin measurements to be as accurate as the area under the enzymatic curve.\(^{28}\)

**Conclusion**

In our population, Gal-3 serum levels measured within 48 hours after pPCI were independently associated with LVR in patients with anterior STEMI. To our knowledge, this is the first study to document a role of Gal-3 in predicting post-infarction LVR. Gal-3 measured during hospitalisation could be clinically useful in identifying patients at high risk of development of LV remodelling after acute MI.

**Acknowledgements**

bioMérieux provided the reagents for Gal-3 determinations.

**Contributors**

GDT, GC and SP designed of the study, submitted the study protocol to the ethics committee and collected the data. LB and ST performed laboratory tests. RDM, GC and MP performed data analysis and interpretation. GDT, GC, RDM and SP drafted the article and performed a critical revision. All authors contributed to the final approval of the version to be published.

**Competing interests**

None declared.

**Ethics approval**

Ethics Committee of ASST Cremona Hospital.

**Provenance and peer review**

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