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Short communication

Serum free light chains in patients with ST elevation myocardial infarction (STEMI): A possible correlation with left ventricle dysfunction

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ABSTRACT

Background: Light chains are proteins produced by plasma cells, also called light chains kappa and lambda, are tied together with other proteins (heavy chains) to form the intact immunoglobulins or antibodies. Recent studies have shown a possible role of combined free light chains (cFLC) as an inflammatory marker in patients with chronic heart failure (HF). HF is a significant contributor to overall mortality in the community, but often patients with chronic HF also have chronic renal failure, which could alter the concentration of cFLC.
Methods: We evaluated the FLC in patients with STEMI ($n = 113$), who were treated with primary angioplasty in the Cardiology Department of the University Hospital "Tor Vergata". For each patient during hospitalization we have determined blood concentration of cFLC, in addition to routine blood tests and we also performed an echocardiogram to evaluate cardiac function.
Results: We performed cFLC serum concentration in 113 patients with STEMI and observed that the cFLC concentration correlates with Left Ventricle Ejection Fraction (LVEF). We identified that the majority of patients (97%) who had one of the two positive light chains also had a reduced systolic function (LVEF <50%).
Conclusions: For the first time in this paper we highlight the increase of serum free light chains concentrations in acute ischemic heart failure in patients with STEMI and without kidney failure.
The cFLC could be proposed as a new biomarker for left ventricle dysfunction, further studies are required to confirm these results.

1. Introduction

Until recently, limited information was available on polyclonal combined free light chains (cFLC, summation of FLC κ and λ) elevations, when there is no obvious predominance of either chain. Recent studies have shown a possible role of cFLC as an inflammatory marker in patients with chronic heart failure (HF). Many studies describe that inflammation is an important factor in cardiovascular diseases and can led to the evaluation of HF also as an inflammatory disease [1]. HF is a significant contributor to overall mortality in the community, and high levels of cFLC were associated with increased mortality in the general population [2]. The potential causes of inflammation in patients with HF are numerous, including the activation of innate immune responses following tissue injury [3], neuro-hormonal activation, oxidative stress, as well as translocation of bacteria or their products from the gut due to intestinal edema.

However, patients with chronic heart failure often have comorbidities that could increase the concentration of cFLC, such as chronic renal failure. Thus the role of cFLC in patients with heart failure is still poorly understood.

The aim of our study is to evaluate the concentration of cFLC in patients with ST elevation myocardial infarction (STEMI), and consequent acute ischemic cardiac dysfunction, to verify if cFLC can be considered a new biomarker for cardiac dysfunction in patients with normal kidney markers. The patients were treated with primary angioplasty in the Cardiology Department of the University Hospital "Tor Vergata", Rome.

2. Methods

We evaluated the FLC in patients with STEMI ($n = 113$), who were treated with primary angioplasty in the Cardiology Department of the University Hospital "Tor Vergata". Inclusion criteria: patient with STEMI in the absence of previous cardiovascular diseases. Exclusion criteria: chronic heart failure, diabetes, haematological diseases, kidney failure. For each patient during hospitalization we have determined blood concentration of cFLC, in addition to routine blood tests and we also performed an echocardiogram to evaluate cardiac function. Left ventricular ejection fraction (LVEF) was measured by 2-dimensional echocardiography. Analysis was performed offline, using the biplane method of discs (modified Simpson's rule) by a single operator blinded to patient information.

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Reduced systolic function was defined as LVEF <50%. Whole blood was drawn from venipuncture into serum and plasma vacutainers. Samples were processed immediately by centrifugation at 3000g for 15 min and serum and plasma fractions were aliquoted for storage at −80 °C until assay. The blood samples were taken immediately before the echocardiogram. The FLCs measurement was performed using N Latex FLC kit based on a mixture of monoclonal antibodies for use on the BN ProSpec® System analyzer (Siemens Healthcare Diagnostics GmbH, Marburg, Germany). Positive concentrations of FLCs were defined as >22,4 mg/L and >27,0 mg/L for k FLC and λ FLC respectively [4]. Data were analyzed for statistical analysis using Student's *t* -test for normally distributed data or the Mann-Whitney *U* test for non-normally distributed data. Data are reported as significant where p was <0.05. Normal data are presented as mean ± standard deviation, non-normal data are shown as median + interquartile range.

The study was approved by the local Ethics Committee and has been carried out in accordance with the Declaration of Helsinki. All patients signed an informed consent.

3. Results

We performed FLC serum concentration in 113 patients with STEMI and we observed that the FLC concentration correlates with LVEF. We identified that the majority of patients (97%) who had one of the two positive light chains also had a reduced systolic function (LVEF <50%).

Only 2 patients out of 61 are positive for one of the light free chains and have a normal systolic function (3%) (Fig. 1).

On the contrary, 55 patients who were not positive for free light chains, only one resulted in a reduced systolic function (2%). Data are shown in Fig. 1. cFLC serum concentration of patients with left ventricular ejection fraction (LVEF) >50 (36.25 ± 6.22 mg/L, $n = 54$) and <50 (81.59 ± 51.6, $N = 59$) shows a significative difference (Independent *t*-Test; $p < 0.001$; Fig. 2). Both the k and λ FLC correlate significantly with the systolic function; with the increase in the concentration of the FLCs correspond low values of LVEF (Pearson correlation $r = 0.56$, $p < 0.01$ for k FLC; $r = 0.51$, p < 0.01 for λ FLC). All patients had normal serum kidney markers.

4. Discussion

Elevated polyclonal serum FLC levels have been associated with increased mortality and disease activity in many conditions [5]. Jackson et al. showed that free light chains may be a prognostic marker in patients with chronic HF [6]. However, patients with chronic HF often also have chronic kidney failure. Several studies have shown an increase in FLC in patients with chronic renal failure [7]. Therefore it was necessary to clarify whether to increase cFLC was cardiac pathology or kidney failure. We evaluated cFLC in patients with STEMI who showed normal kidney markers and we demonstrated that cFLC concentration correlated with left ventricular dysfunction. Recent study provides the analysis of cFLC in patients with STEMI and showed a relatively small but significant increase of cFLC levels during the follow up period with peak concentrations determined on day 7 and were still increased on day 30 [8].

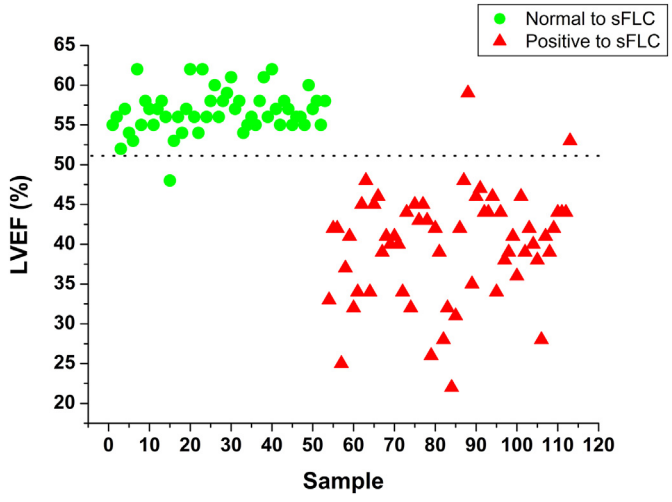

Fig. 1. Left ventricular ejection fraction (LVEF) respect to cFLC serum concentration (samples $N = 113$).

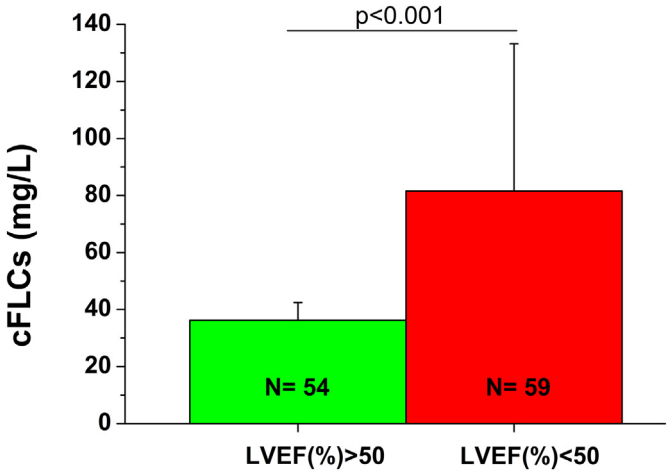

Fig. 2. cFLC serum patients concentration with left ventricular ejection fraction (LVEF) > 50 ($n = 54$) and < 50 ($N = 59$). The two groups show a significative difference (Independent *t*-Test; $p < 0.001$).

In this study, in fact, a positive linear relationship was found between LVEF and both FLC-κ and FLC-λ levels.

It can be hypothesized that a reduction of left ventricle function and of ejection fraction increases the systemic inflammation and activates the neurohormonal system, such as to increase the cFLC. Depending on the ejection fraction greater or <50%, we have observed in almost all cases a correlation with the concentration of cFLC. Our data confirm the hypothesis that an increase in the level of FLC in patients with HF is thought to be influenced by mediators of mast cell origin, which play an important role in activation of inflammation and neuroendocrine response [6].

We have shown for the first time that cFLC correlates with left ventricle dysfunction in patients with STEMI. The cFLC could be proposed as a new biomarker for left ventricle dysfunction, further studies are required to confirm these results.

Aim of the study

The aim of the study is to evaluate, for the first time, the concentration of cFLC in patients with ST elevation myocardial infarction (STEMI), and consequent acute ischemic cardiac dysfunction, to verify if cFLC can be considered a new biomarker of left ventricle dysfunction in patients with normal kidney markers. The patients were treated with primary angioplasty in the Cardiology Department of the University Hospital "Tor Vergata", Rome. No similar study, to our knowledge, has ever been published.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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