CORRESPONDENCE

Comparison between cardiac troponin T and creatinine kinase MB mass in the diagnosis of myocardial infarction

To the Editor: Recently, Paul Collinson and colleagues¹ reported some results and perspectives about the diagnosis of myocardial infarction (MI). Here, we want to show some results in a public hospital of the State of Rio Grande do Sul, Brazil.

Cardiac troponin T (cTnT) is considered the 'gold standard' in the diagnosis of MI since 2000, because of its high specificity for the heart muscle;² however, due to high complexity and high cost of all services in Nether, the diagnosis for MI is done according to the symptomatology.²⁻³ Creatinine kinase MB (CK-MB) mass is a biomarker with a little less specificity, nevertheless with low cost and more accessibility, useful in places with less technology.⁴

Information about the diagnosis of MI in public services in Brazil has so far not been published. Our aim is to present some data in a public hospital and establish a comparison between cTnT and CK-MB mass, evaluating the correlation and analysing the benefits for a public service.

During the period of 1 year (October 2010 until September 2011) we analysed 148 patients of both genders. It was found that there is a significant correlation between the biomarkers. The correlation between cTnT and CK-MB mass was stronger in women. Strong correlation ($p < 0.005$) was also demonstrated in patients in the age group of 60–69 years and 80–89 years. So, both biomarkers were effective for the diagnosis of MI. It is important to note that the time of MI was not analysed.

In conclusion, when in the scarcity of cTnT, the use of CK-MB is acceptable. We agree with Paul Collinson and colleagues¹ that the additional measurement of myoglobin and CK-MB does not provide further information in the diagnosis but we propose the use of CK-MB in centres that do not have cTnI or cTnT.

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Contributors The relevance of this correspondence is based on scarcity of information about the diagnosis of MI in public services in Brazil. Our aim was to present some data in a public hospital and establish a comparison between cTnT and CK-MB mass, evaluating the correlation and analysing the benefits for a public service.

Competing interests None.

Ethics approval Ethics approval was provided by Comitê de Ética em Pesquisa - Unicruz.

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Comparison between cTnT and CK-MB mass in the diagnosis of myocardial infarction: the response

The Authors' reply In our recent study, we found the measurement of the MB isoenzyme of creatine kinase by a mass measurement (CK-MB mass) to be significantly inferior to the measurement of cardiac troponin.¹ Currently, the universal definition of myocardial infarction recommends the measurement of cardiac troponin either as cardiac troponin T (cTnT) or cardiac troponin I (cTnI).² CK-MB is accepted as an alternative although acknowledged as being both less sensitive and less specific. This is in broad agreement with the findings of the authors although they do not state the diagnostic criteria they used.

Logistical reasons, or financial arguments, are advanced as explanations for the failure to measure cardiac troponin in routine clinical practice. Neither category truly stands up to scrutiny. The logistical explanation is a lack of appropriate technology for measurement. Currently available commercial laboratory immunoassay systems support troponin measurement as part of an extensive menu of tests, and cover a range of laboratory workloads. When there is a very small throughput of tests, such as in an emergency care laboratory or a satellite laboratory, robust point-of-care testing (POCT) systems are available. POCT troponin measurement, although of lower diagnostic sensitivity (for the most part), is superior to CK-MB mass measurement if a conventional laboratory-based troponin assay is unavailable.

The financial argument is based on the relative cost of the assays. The price of cardiac troponin assays has now significantly fallen, and is comparable with measurement of CK-MB mass measurement, regardless

of whether or not a laboratory or POCT-measurement is used. With an appropriately designed investigation strategy, it is preferable to perform a correctly timed troponin measurement rather than multiple measurements of CK-MB mass. This can be achieved at a lower cost. Finally, the major cost in healthcare that remains is the patient episode cost rather than the investigation cost. An appropriate decision-making pathway incorporating even a slightly higher laboratory cost can be translated into a significant patient episode cost saving, especially if coronary intervention is involved.

For these reasons, I cannot agree that CK-MB measurement is an acceptable substitute. The challenge is to provide a service. This requires clinician/laboratory cooperation and communication. Lack of clinician/laboratory interaction and dialogue were highlighted as a significant deficiency in a recent survey of laboratory practice,³ although it is the first of the 10 commandments of troponin.⁴

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Scientific letter: Ac-SDKP (N-acetylseryl-aspartyl-lysyl-proline) and Galectin-3 levels in tuberculous pericardial effusion: implications for pathogenesis and prevention of pericardial constriction

To the Editor: The incidence of constrictive pericarditis in HIV uninfected patients with pericardial tuberculosis is very high (31.65

Figure 1 Hypothesised mechanism by which the tetrapeptide N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) inhibits fibrosis. Ac-SDKP is generated from the G-actin binding peptide, thymosin β 4, by prolyl oligopeptidase (POP) through one-step enzymatic cleavage. ACE hydrolyses Ac-SDKP into inactive dipeptides. ACE inhibitors (ACEi) increase the concentration of Ac-SDKP whereas POP inhibitors (POPi) decrease Ac-SDKP production. Ac-SDKP prevents the galectin-3 induced effect on fibrosis by inhibiting the transforming growth factor beta (TGF- β)/Smad2 signalling pathway. Ac-SDKP may also inhibit fibrosis directly by blocking collagen synthesis.

cases per 1000 person-years) despite modern rifampicin-based antituberculosis treatment.¹ The cellular mediators and molecular mechanisms of post-tuberculous pericardial fibrosis are unknown. N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) is a ubiquitous tetrapeptide with important antifibrotic properties and galectin-3 is an activator of myofibroblasts, promoter of collagen and extracellular matrix deposition and is associated with organ fibrosis.^{2–5} Ac-SDKP, which is inactivated by ACE, exerts part of its antifibrotic effect by inhibiting galectin-3 (figure 1).⁴ Currently, it is not known whether endogenous Ac-SDKP and galectin-3 are present in normal pericardial effusion, and whether there are any changes in the context of pericarditis.

METHODS

We conducted a pilot study of adults (≥ 18 years) with a normal pericardium and cases with tuberculous pericarditis to define the levels of endogenous Ac-SDKP and galectin-3 in normal pericardial fluid, and to assess the effect of pericardial infection with

tuberculosis on levels of these factors. All participants gave written informed consent and the study was approved by the University of Cape Town Human Research Ethics Committee (HREC REF: 402/2008). Eligible participants had echocardiographic evidence of a moderate or large effusion. The pericardial fluid was considered tuberculous if it was an inflammatory exudate with one of the following criteria: *Mycobacterium tuberculosis* was identified by microscopy, culture or by PCR; levels of interferon- γ were >50 pg/ml or adenosine deaminase >40 IU/l.

Patients undergoing elective coronary bypass surgery were used as normal controls. Participants with either a history of pericardial disease or evidence of prior myocardial infarction (by history or ECG) were excluded. The SPIBIO-A05881 was used to measure Ac-SDKP while the BenderMed BMS 279/2CE ELISA kit was used for measurement of galectin-3.

The Shapiro-Wilk test was used to test if the measured levels were normally distributed. Differences between the two groups (cases with tuberculosis and controls without pericardial disease) were tested using the Student t test, or Mann-Whitney test, where appropriate for continuous variables, and the χ^2 test for categorical variables. All tests were two-sided and a p value <0.05 was considered significant.

RESULTS

Ac-SDKP and galectin-3 levels were assayed in 49 and 52 patients with tuberculous pericarditis, respectively. The levels were compared with those of 20 control participants with no pericardial disease. The median level of Ac-SDKP in the participants with tuberculous pericarditis (156 pg/ml (IQR 126.8–187.4)) was significantly lower than normal controls (412 pg/ml (IQR 146.7–717.9)), $p=0.029$ (figure 2A). The median level of galectin-3 measured in the cell free pericardial fluid of patients with tuberculous pericarditis was 11 ng/ml (IQR 7.55–15.6). This was similar to the 12 ng/ml (IQR 7.49–19.62) found in the pericardial fluid of normal controls ($p=0.191$) (figure 2B).

DISCUSSION

In this pilot study we have shown, for the first time, that Ac-SDKP and galectin-3 are

detectable in normal pericardial fluid, and that tuberculous pericarditis is associated with low levels of pericardial Ac-SDKP and normal galectin-3 levels. These observations pertaining to the levels of Ac-SDKP and galectin-3 in normal pericardial fluid and tuberculous pericardial effusion are important for a number of reasons. The findings suggest that Ac-SDKP and galectin-3 play a housekeeping function within the normal pericardium similar to that in ventricles and kidneys.⁵ Furthermore, our results raise the possibility that both molecules play an important role maintaining the health of the pericardium during times of physiological or pathological stress. The depressed levels of Ac-SDKP in conjunction with normal or low levels of galectin-3 within the pericardium may provide a novel explanation for the high incidence of constrictive pericarditis associated with tuberculous pericarditis.¹

Thus, further elucidation of the physiological and pathological role of Ac-SDKP and galectin-3 could enhance the limited understanding of the constitution and function of normal pericardial fluid, the pathogenesis of pericardial inflammation and fibrosis, and provide important information on the prospect of using these molecules as novel pharmacological targets for the prevention of constriction.

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Figure 2 Scatter plots of pericardial Ac-SDKP levels in pg/ml (A) and pericardial galectin-3 levels in ng/ml (B) grouped by cases with tuberculous pericarditis (1) and controls undergoing cardiac surgery without pericarditis (0).

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Contributors The idea of the study was conceived by BMM and EDS. BMM, EDS, MN, KAW and RJW were involved in the design of the experiment. The experimental work was carried out by MN, KM and JW. MB conducted the statistical analysis of the data. MN wrote the first draft of the manuscript, and all authors participated in the finalisation of the manuscript.

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Competing interests None.

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Ethics approval University of Cape Town Human Research Ethics Committee.

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Data sharing statement Normal pericardial fluid and pericardial fluid infected with *Mycobacterium tuberculosis* is available for the participants in this study. These biological materials are owned by the IMPI Registry Investigators. Investigators may propose sub-studies based on the biological material to the IMPI Registry Steering Committee.

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