To the Editor: The incidence of constrictive pericarditis in HIV uninfected patients with pericardial tuberculosis is very high (31.65 cases per 1000 person-years) despite modern rifampicin-based antituberculosis treatment. The cellular mediators and molecular mechanisms of post-tuberculous pericardial fibrosis are unknown. N-acetyl-serine-aspartyl-lysyl-proline (Ac-SDKP) is a ubiquitous tetrapeptide with important anti-fibrotic properties and galectin-3 is an activator of myofibroblasts, promoter of collagen and extracellular matrix deposition and is associated with organ fibrosis. Ac-SDKP, which is inactivated by ACE, exerts part of its anti-fibrotic effect by inhibiting galectin-3 (figure 1). 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 BM5 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 χ² 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 126.9–187.4)) 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 11ng/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. 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.

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.
Acknowledgements The authors are grateful to the patients who consented to be enrolled in this study, and to the physicians who contributed to the IMPI Africa Registry. Veronica Francis, Unita September and Simphiwe Nkepu are thanked for assistance with recruitment and follow-up of patients.

Mpiko Ntsekhe,1 Kerryn Matthews,1,2 Janine Wolske,1,2 Motasim Badri,1 Katalin A Wilkinson,1,2,3 Robert J Wilkinson,1,2,3,4 Edward D Sturrock,5 Bongani M Mayosi1

1The Cardiac Clinic, Department of Medicine, Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa; 2Clinical Infectious Diseases Research Initiative, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Observatory, South Africa; 3Department of Medicine, Imperial College, London, UK; 4MRC National Institute for Medical Research, London, UK; 5Division of Medical Biochemistry, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Observatory, South Africa

Correspondence to Dr Bongani M Mayosi, Department of Medicine, J Floor Old Groote Schuur Hospital, Anzio Road, Observatory, 7925, Cape Town, South Africa; bongani.mayosi@uct.ac.za

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.

Funding This work was supported by the Wellcome Trust of Great Britain (references 084323, 088316, 083226). Additional support was provided by the Medical Research Councils of the UK and South Africa and the Lily and Hausmann Research Trust.

Competing interests None.

Patient consent Obtained.

Ethics approval University of Cape Town Human Research Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

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.

REFERENCES

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

Mpho Ntsekhe, Kerryn Matthews, Janine Wolske, Motasim Badri, Katalin A Wilkinson, Robert J Wilkinson, Edward D Sturrock and Bongani M Mayosi

*Heart* published online July 26, 2012

Updated information and services can be found at: [http://heart.bmj.com/content/early/2012/07/25/heartjnl-2012-302196](http://heart.bmj.com/content/early/2012/07/25/heartjnl-2012-302196)

These include:

**References**
This article cites 5 articles, 3 of which you can access for free at: [http://heart.bmj.com/content/early/2012/07/25/heartjnl-2012-302196#BIBL](http://heart.bmj.com/content/early/2012/07/25/heartjnl-2012-302196#BIBL)

**Open Access**
This is an open-access article distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non-commercial and is otherwise in compliance with the license. See: [http://creativecommons.org/licenses/by-nc/2.0/](http://creativecommons.org/licenses/by-nc/2.0/) and [http://creativecommons.org/licenses/by-nc/2.0/legalcode](http://creativecommons.org/licenses/by-nc/2.0/legalcode).

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections

- Open access (229)

**Notes**

To request permissions go to: [http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to: [http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to: [http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)