SUPPLEMENTARY METHODS

Haemodynamic measurements

All patients had Swan-Ganz catheters inserted before surgery that provided measures of pulmonary artery and pulmonary capillary wedge pressures and cardiac output that were recorded immediately after induction of anaesthesia.

Biochemistry

All blood samples were collected from the radial artery cannula of fasted patients before anaesthesia and plasma stored at -80°C. Estimated glomerular filtration rate was calculated from the Modification of Diet in Renal Disease formula.[1] ß-cell function (HOMA2-%B), insulin sensitivity (HOMA2-%S), and insulin resistance (HOMA2-IR) were calculated using the HOMA calculator version 2.2.[2] Amino-terminal-pro-B-type natriuretic peptide was measured by electrochemiluminescence immunoassay using an Elecsys instrument (Roche Diagnostics, Basel, Switzerland). Carboxy-terminal propeptide of procollagen type I was measured by ELISA (Takara Bio Inc. Otsu, Shiga, Japan) and intact amino-terminal propeptides of procollagens type 1 and III were measured by radioimmunoassay (Orion Diagnostica, Espoo, Finland).

Advanced glycation end products (AGEs) N^{ε}-(carboxymethyl)lysine (CML) and low molecular weight fluorophores (LMWF) were measured by ELISA (Microcoat, Penzberg, Germany) and by fluorescence spectroscopy,[3] respectively. Soluble receptor for AGEs (sRAGE), vascular endothelial growth factor (VEGF)-A, soluble VEGF receptor (sVEGFR)-1, sVEGFR-2, angiopoietin-1, angiopoietin-2, Tie-1, Tie-2, fibroblast growth factor basic, endostatin, placental growth factor, and hepatocyte growth factor were measured by ELISA (R&D Systems Inc., Minneapolis, MN). The LMWF assay had intra- and inter-assay coefficients of variation (CV) of 4.7% and 6.4%,[3] whereas the ELISAs had intra- and inter-assay CVs of <10% and <12%, respectively.

Histological analysis

Details of tissue collection and histological analysis have been previously described.[4-6] All histological analyses were performed blind to patient identity and clinical, haemodynamic, and echocardiography results. Picrosirius red-stained 4 μm paraffin sections were analyzed for fibrosis by quantitative morphometry of digitized images of the whole myocardial section (Aperio Technologies, Inc., CA). Myocardial total fibrosis was calculated using the positive pixel count algorithm as the area of collagen staining expressed as a percentage of the total myocardial tissue area, after excluding the pericardium, whereas interstitial fibrosis was calculated as described for total fibrosis, with exclusion of perivascular fibrosis. The same individual performed all measurements of total and interstitial fibrosis with CV for duplicate sections from the same patient of 11% and 12%, respectively.

Perivascular fibrosis, cardiomyocyte width and capillary length density were measured, and immunohistochemistry for collagens I and III, CML and RAGE was performed and quantified as previously described.[4-6]

References

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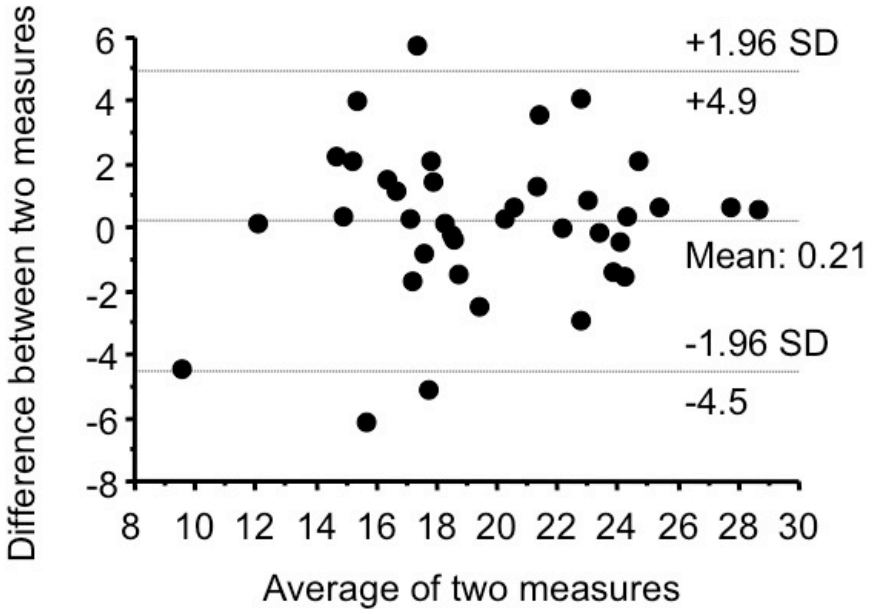
SUPPLEMENTARY FIGURE



Bland-Altman plot for the two measures of calibrated integrated backscatter.