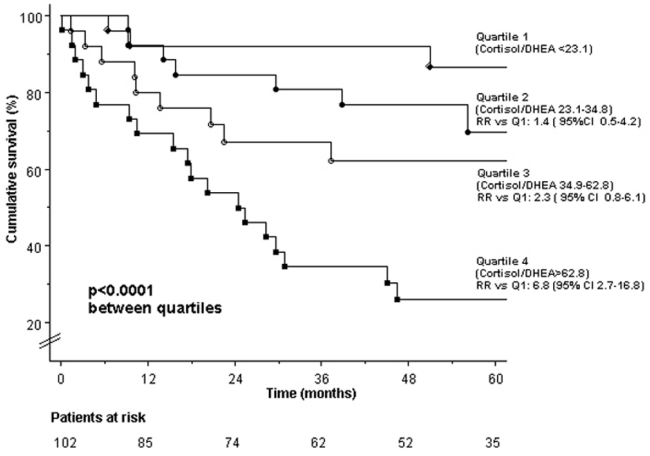
P1140 Prognostic significance of an altered steroid profile in patients with chronic heart failure

D.O. Okonko[1], M. Crosato[1], P. Kalra[1], M. Cicoira[1], S. Von Haehling[1], G. Diller[1], P.A. Poole-Wilson[1], S.D. Anker[2]. [1]*National Heart Lung Institute, Cardiology, London, United Kingdom;* [2]*Charité campus, Virchow-Klinikum, Applied Cachexia Research, Berlin, Germany*

Background: Chronic heart failure (CHF)is characterised by a shift of adrenocortical biosynthesis from Dehydroepiandrosterone (DHEA; anabolic) to cortisol (catabolic) production. Therefore, the cortisol/DHEA ratio (CDR) is a marker of catabolic/anabolic steroid imbalance. Its prognostic utility in CHF is unknown.
Method & Results: Survival and CDR were analysed in 102 stable, male CHF patients (age 62±11y, NYHA class 2.6±0.7, CDR 50±5, urate 468±136 μmol/L, creatinine 124±43 μmol/L, BMI 26.1±4.4 kg/m^2, LVEF 26±11%, peak VO2 18.1±5.8 mL/kg/min, VE/VCO2-slope 38±13. During follow-up (55±40 months, all survivors: >16 months), 48 patients died (12-month mortality 15%, at 36 months: 38%). In univariant Cox analysis only CDR, urate, creatinine, NYHA, VE/VCO2, peak VO2, age (all $p<0.01$) and BMI ($p=0.03$) predicted survival. In bivariant models CDR was predictive of survival, independently of all other parameters. Urate, NYHA, VE/VCO2 and peak VO2 predicted survival, independently of CDR. In multivariant analysis, CDR ($p<0.0001$), urate ($p=0.008$), NYHA class ($p=0.002$), VE/VCO2 ($p=0.04$) but not peak VO2 ($p>0.2$) were independent prognosticators. We subdivided patients by CDR quartiles (Q, see Figure 1). Survival at 36 months for patients in Q1, Q2, Q3 and Q4 was 92, 81, 67 and 35%, respectively.



Conclusion: An altered steroid profile with an increase in catabolic/anabolic steroid imbalance(quantified by the cortisol/DHEA ratio) independently predicts impaired survival in CHF. Therapeutic strategies blunting catabolism and/or augmenting anabolism may confer prognostic benefits in CHF.

P1141 Effects of combined administration of vitamin E and atorvastatin on endothelial function and inflammatory process, in patients with ischaemic heart failure

D. Tousoulis[1], C.A. Antoniades[2], C. Tentolouris[1], K. Marinou[1], C. Tsioufis[1], S. Brilli[1], C. Pitsavos[1], C. Stefanadis[1]. [1]*Athens University, Cardiology Dept. Hippokration Hospital, Athens, Greece;* [2]*Hippokration Hospital, Cardiology Unit, Athens, Greece*

Previous studies have shown that ischemic heart failure is associated with endothelial dysfunction and increased levels of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-a) and soluble form of vascular cell adhesion molecule (sVCAM-1). Statins as well as antioxidant vitamins, improve endothelial function in patients with coronary atherosclerosis, while their role in heart failure is unknown.
Aim: We assessed the effect of atorvastatin alone or in combined with vitamin E on endothelial function and inflammatory process in patients with ischemic heart failure.
Methods: Thirty-eight (38) patients with ischemic heart failure (NYHA II-IV) were enrolled. Seventeen (17) patients received atorvastatin 10mg/day (ATR), 7 patients received atorvastatin 10 mg/day plus vitamin E 400IU/day (ATR+E) and 14 received no treatment for 4 weeks (Controls). Forearm blood flow was measured using venous occlusion strain-gauge plethysmography. Endothelium dependent dilation (EDD) and endothelium independent dilation (EID) were expressed as the % change of flow from baseline to the maximum flow during reactive hyperemia or after sublingual nitroglycerin administration respectively.
Results: EDD was significantly improved in ATR group (from 40±5 to 88±13%, $p<0.01$) but not in ATR+E (from 45±6 to 65±15%, p=ns) or control group (from 50±5 to 46±6%, p=ns). Levels of IL-6, sVCAM-1 and TNF-a were decreased only in ATR group (from 7.9±0.8, 665±69 and 3.7±0.49 to 5.8±0.8 pg/ml $p<0.05$, 473±53 ng/ml $p<0.01$ and 2.62±0.17 pg/ml $p<0.05$, respectively) while remained unaffected in ATR+E (from 5.4±1.5, 868±91 and 3.99 ±0.80 to 3.2±0.8 pg/ml, 749±63 ng/ml and 3.01 ±0.77 pg/ml respectively, p=ns for all) and in controls (from 7.4±0.8, 610±65 and 4.54±0.91 to 6.2±0.9 pg/ml, 594±70 ng/ml and 4.32±0.58 pg/ml respectively, p=ns for all). EID remained unchanged in all groups (from 64±8, 66±12 and 71±6 to 66±9%, 72±13% and 68±9% respectively, p=ns for all)
Conclusions: Atorvastatin improves endothelial function and reduces inflammatory process in patients with heart failure while co-administration of vitamin E and atorvastatin may reduce these beneficial effects of atorvastatin.

P1142 Pravastatin reduces the inflammatory response to cardiopulmonary bypass after coronary revascularization

G. Teixeira Filho, R.A.K. Kalil, P.R. Prates, J.R.M. Sant'Anna, L.C. Pellanda, A. Homsi-Neto, I.A. Nesralla. *Instituto de Cardiologia do RS/FUC, Cirugia, Porto Alegre, Brazil*

Background: The effects of pravastatin have been documented in reducing LDL levels. In constrast, the effect of pravastatin in inflammatory function has not yet been demonstrated. This study was designed to evaluate action of pravastatin on inflammatory reaction after extracorporeal circulation.
Methods: In a prospective, randomized study, 20 patients undergoing eletive coronary artery bypass grafting were investigated. Ten patients received 80mg p.o. of pravastatin 36 and 12h before surgery, and a control group of 10 did not. Plasma levels of C-reactive protein, tumor necrosis factor-alfa, interleukin-6, interleukin-8 and postoperative blood loss were analysed before and after cardiopulmonary bypass.
Results: Interleukin-6 in both groups significantly increased after Cardiopulmonary bypass (CPB) when comparing to the measures pre bypass and there was no significant diferences between the two groups. Interleukin-8 increased ($p=0.017$) in group control at 6h after CPB compared with group P. C-reative protein was increased ($p=0.015$) in group pravastatin before CPB compared with control. Median levels are 9.9 (7.0-15.6) and 5.0 (5.0-9.3) mg/dL. Despite this previous elevation, at 24h after CPB group P showed significantly lower levels than group control ($p=0.004$). Median levels are 62 (38.7-73.6) and 109.0 (104.0-112.0) mg/dL in groups P and C, respectively. Postoperative blood loss was significantly lower in group pravastatin than in group control ($p=0.019$).
Conclusions: Our data suggest that pravastatin pre-treatment preceding CPB reduced systemic inflammatory response. The effects of administration are immediate and antinflammatory action is not mediated by lipid lowering. Pravastatin also reduced mediastinal postoperative bleeding.

P1143 The Relationship of High Sensitivity C Reactive Peptide (hsCRP) measurements to known prognostic indicators in patients assessed for heart failure in an outpatient setting

J.D. Windram, P.H. Loh, C. Constantin, D.H. Reddy, K. Lalukota, A.L. Clark, J.G.F. Cleland. *Hull Royal Infirmary, Academic Cardiology, Hull, United Kingdom*

Background: A raised high sensitivity CRP (hsCRP) has been shown in several recent epidemiological trials to be an independent risk factor in the development of congestive heart failure. HsCRP levels have also been noted to correlate with the severity of heart failure, as well as readmission rate to hospital.
Methods: We analysed 1091 patients who attended our outpatient clinic for assessment of symptoms suggesting a possible diagnosis of heart failure. All patients had a standard clinical history and medications recorded. All patients had a hsCRP measurement taken together with a full biochemical and haematological profile. They also completed a 6 min walk test, quality of life questionnaire and underwent echocardiographic assessment of left ventricular (LV) function at their clinic visit. Heart failure was diagnosed according to ESC criteria.
Results: 622 (57%) were men, the mean age of the population was 71±10 yrs. The median and inter-quartile range of hsCRP in those diagnosed with heart failure (n=577) was 4.1 (range 2.4 to 9), which was not significantly different from patients without heart failure (n=514); 4 (range 2.2 to 6.8). Amongst patients with heart failure, hsCRP was significantly higher in patients with more severe symptoms, and shorter corridor walk distance but was poorly related to LVEF. Median (IQR) hsCRP in patients with NYHA class I (n=104) was 3.4 (range 1.6-5.1) but 6.5 (range 4.2 to 11) in NYHA class IV (n=13) In patients with a 6min walk test distance >500m (n=17), hsCRP was 2.8 (range 1.0 to 5), and in those with distance <250m (n=184), 5.6 (range 3.3 to 12). However, comparing patients with mild (LVEF 40-49%) to patients with severe LV systolic dysfunction (LVEF <30%), hsCRP was similar 4 (range 2.5 to 8.6), n=83, versus 4.1 (range 1.8 to 11),n= 97, respectively.
Conclusion: High sensitivity CRP does not appear to be a useful diagnostic tool in patients with suspected heart failure. It is increased in patients with more severe symptoms and greater functional limitation but is poorly related to the underlying severity of LV systolic dysfunction.

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