as a loading dose (6-12 μg/kg/min for 10 minutes) then as a continuous infusion (0.075-0.2 μg/kg/min for 24 hours). One-way analysis of variance and the Wilcoxon test were employed.

Results: Significant improvement in several hemodynamic parameters was observed; main results are in Table 1. Levosimendan was well tolerated. At 30 days, 8 patients were event free; one patient was hospitalized; three patients received ventricular assist devices and heart transplantations; and 6 patients died.

Discussion: Our findings extend previous data on levosimendan to a population with severely compromised RV function. Augmentation in RV pressure generation indicates an increase in RV contractility rather than afterload reduction. Prospective studies with more patients are needed to support this.

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Progressive right ventricular failure is not explained by myocardial ischemia in a pig model of pulmonary embolism

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Acute pulmonary embolism (PE) is followed by high mortality when increased right ventricular (RV) afterload leads to RV dilatation and failure. Current pathophysiological concepts suggest that such RV failure is secondary to an imbalance in RV oxygen supply/demand balance, leading to progressive RV ischemia and necrosis. However, this concept has never been proven in vivo yet.

Anaesthetized farm pigs (n=18) were instrumented to measure RV peak pressure (RVpP), aortic flow (AF), RV end-diastolic segment length (RV SL) and segment-pressure loops (RV SPL), right coronary artery blood flow (RCA BF), and to withdraw RV venous blood to estimate RV oxygen consumption (RV MVO2). RVpP was increased by pulmonary artery banding (BG, n=9) that remained unchanged for 6 h. All parameters remained constant in controls (n=7). In BG at 6h, tachycardia and decreased AF demonstrated overt heart failure, while serum troponin T was increased from 0,1±0,1 (baseline) to 0,6±0,2 mg/l. RV function increased at 10min but deteriorated at 3h and 6h, as indicated by decreased RVpP, RV SPL and RV dilatation (RV SL). In contrast, RCA-BF and RV MVO2 increased throughout the protocol in BG, excluding limited oxygen supply as causative for RV failure. Histology and electron microscopy showed white cell infiltration and myocyte edema, but only single cell necrosis in BG. Pretreatment with dexamethasone (20 mg/kg, n=4) prevented white cell infiltration but did not preserve RV function.

Table 1

BG	baseline	10min	3h	6h
HR (bpm)	94±6	101±6*	113±5*,#	113±7*,#
RVpP (mmHg)	27±2	64±3*	53±1*,#	49±1*,#
AF (l/min)	6,8±0,5	5,2±0,4*	4,4±0,3*,#	4,1±0,3*,#
RV SL (mm)	14,2±0,6	15,0±0,7*	15,4±0,7*,#	15,4±0,7*,#
RV SPL (mm*mmHg)	102±18	207±49*	109±25*,#	79±19*,#
RCA BF (ml/min)	67±6	89±7*	92±6*	99±7*,#
RV MVO2 (%)	100	152±13*	216±24*,#	200±31*,#

mean±SEM, 2-way ANOVA, *:p<0,05 vs baseline, #:p<0,05 vs 10min

We conclude that progressive RV failure due to pressure load is not explained by RV ischemia, RV necrosis or inflammatory cell infiltration. We speculate that pressure and stretch-induced signal transduction cascades rather than RV ischemia mediate RV failure during PE.

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Management of heart failure and quality of care in Greater Manchester, UK in 2003

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Greater Manchester, UK has one of the highest incidences of coronary artery disease and heart failure in Europe. Within the National Health Service, both cardiologists and general medical physicians are involved in the care of such patients. In November 2003 the National Institute of Clinical Excellence (NICE), UK, published guidance for clinicians on appropriate diagnosis and management of heart failure with the aim of standardising treatment. There is, however, no documented systematic analysis of current management of in-patients with heart failure within Greater Manchester. We therefore aimed to carry out an analysis of the care offered to patients admitted with heart failure within the acute medical hospitals in this region over a period of 6 months (1st June to 30th November 2003) immediately preceding the publication of the NICE guidelines.

Methodology: all the 10 acute hospitals in Greater Manchester serving 1.5 million people were invited to participate in the study. Using the patient administration system (PAS) database, we identified all admissions with suspected acute heart failure within each hospital. The medical records of all the identified patients were then analysed to determine whether an echocardiographic confirmation of diagnosis was made and medication at discharge.

Results: eight of the 10 acute hospitals in Greater Manchester opted to participate in the study. 699 admissions with suspected heart failure in the 8 hospitals during the study period were identified. Twenty five patients were excluded (insufficient data), resulting in a final study sample of 674 patients. Overall, 72% (483 patients) of the study population had an echocardiographic examination for confirmation of diagnosis but this varied between hospitals (range 57-83%). Speciality wise, 82% of patients under cardiology had an echocardiogram, compared with 67% under care of general medicine. Of the 483 patients with echocardiographic assessment, 73% (352 patients) were confirmed to have LV systolic dysfunction with 86% of these discharged on diuretics, 76% on an ACEI or AIIRA, 32% on a beta-blocker, 31% on spironolactone, and 12% on digoxin (but 52% of those in AF).

Conclusions: the management and quality of care of heart failure within Greater Manchester in 2003 differed considerably between hospitals, with low rates of initiation of some therapies. It is plausible that some of these therapies may have been initiated after discharge. In view of the recommendations of the now published NICE guidelines on heart failure we plan another review of the service in 3 years.

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Eplerenone benefit in patients with elevated baseline heart rate in the EPHESUS trial

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EPHESUS demonstrated that patients with AMI complicated by heart failure (HF) and LVSD experienced significant reductions in all-cause mortality (ACM), cardiovascular mortality/CV hospitalization (CVM/H), CVM, and sudden cardiac death (SCD) with eplerenone (EPL) added to standard therapy. Because elevated heart rate (HR) increases risk in post-AMI patients with HF, the analysis of EPHESUS explores the impact of EPL on outcomes according to baseline HR.

Patients with post-AMI HF and LVSD (EF ≤40%) on standard therapies

were randomized 3-14 days after the index AMI to EPL (25 mg titrated to 50 mg QD; n=3319) or placebo (PBO; n=3313). Patients were followed for up to 2.5 years (mean=16 months). End point analyses were performed with a Cox proportional hazards regression model with treatment group as the only factor, stratified by geographic region. Treatment-by-HR ($\leq$90/>90 bpm) factor interaction was based on the Wald's test of the interaction term in the Cox model.

The rate of all-cause mortality in PBO-treated patients was 25.2% in those with baseline HR >90 bpm and 15.9% with baseline HR $\leq$90 bpm. Reductions in risk with EPL relative to PBO according to baseline HR are in Figure. Although most of the treatment-by-factor interaction P-values were not significant, the reduction in risk for SCD in patients with HR >90 bpm was greater compared to patients with HR <90 bpm (treatment-by-factor interaction P-value=0.04).
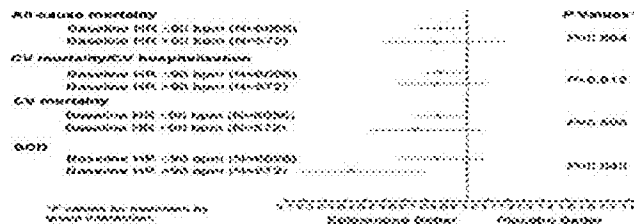

Figure 1. Relative Risk of End points by Baseline HR.

At an average of 16 months of follow-up, EPL treatment demonstrated a consistent effect on the risk of ACM, CVM/H, and CVM in EPHESUS patients with baseline HR $\leq$90 and >90 bpm. While EPL treatment reduced the risk of SCD in patients with HR $\leq$90 and >90 bpm, patients with a baseline HR >90 bpm may derive a larger treatment effect for this end point.

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The impact of statin therapy on the efficacy of eplerenone

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In EPHESUS, treatment with eplerenone (EPL) significantly reduced mortality and morbidity in patients with acute myocardial infarction (AMI) and LVSD with signs of heart failure (HF) when used with standard therapies. Because post-AMI HF patients often receive statin therapy, this retrospective analysis evaluated the treatment effect of EPL used concurrently with standard HF treatment in EPHESUS patients w/ and w/out concomitant statin therapy.

Patients w/ post-AMI HF and LVEF </= 40% on standard therapy were randomized 3-14 days after index AMI to EPL (25 mg titrated to 50 mg QD; N=3319) or placebo (PBO; N=3313) and followed for up to 2.5 years. The comparative analyses of treatment effects in patients who received statins from baseline (from index AMI up to 14 days post-AMI) and those who did not were performed using a Cox proportional hazards regression analysis stratified by the geographical region. Treatment-by-statin interaction was tested using Cox model.

Patients not on statin therapy appeared to have increased risk for end points compared with those on statins; the rate of all-cause mortality in PBO-treated patients was 19.5% and not on statins and 13.6% in those on statin therapy. Risk reductions with EPL relative to PBO for patients w/ and w/out concomitant statin therapy were similar (P >/=0.12) for

each endpoint (Figure 1). There was no evidence of toxicity related to the coadministration of EPL and statins, and the incidence of adverse events with EPL was similar to PBO.
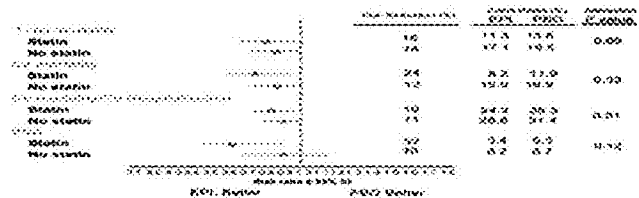

Figure 1. Relative Risk of Endpoints in EPHESUS by Baseline Statin Treatment.

EPL treatment provided mortality and morbidity benefits in post-AMI HF patients w/ and w/out concomitant statin therapy, with greater benefits in those receiving concomitant statin therapy. For each end point, event rates were lower with EPL than PBO, independent of statin treatment.

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Clinical parameters on admission: can they predict in-hospital heart failure after acute coronary syndromes?

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Introduction: heart failure (HF) is a frequent complication of acute coronary syndromes (ACS) and is associated with poor prognosis. Our goal was to find clinical parameters on admission that could predict HF, thereby helping select the most suitable management strategy.

Methods: we studied 1045 patients (61.4±12.5 years-old, 71.7% males) consecutively admitted in our cardiology department with ACS. Clinical and laboratory parameters were obtained during the first 48 hours. The outcome was development of clinical signs of HF during hospitalisation.

Results: cardiovascular risk factors were found in a significant proportion of our sample (hypertension in 55.9%, diabetes mellitus in 29.1%, current or previous smoking in 50%, dyslipidaemia in 62.2%, body mass index > 30 Kg/m^2 in 20%). Forty-three percent of the patients had ACS with ST segment elevation (STEMI) and 40% had left ventricular systolic dysfunction (LVSD). Multivessel and/or left main coronary artery disease were found in 52.3%. Revascularisation was performed in 60.7%. Heart failure occurred in 15.9%. Variables associated with development of HF in univariate analysis were: male sex (OR 0.446, 95%CI 0.317-0.629), age (OR 1.061, 95%CI 1.045-1.068), smoking (OR 0.463, 95%CI 0.328-0.655), hypertension (OR 1.528, 95%CI 1.083-2.157), diabetes (OR 2.639, 95%CI 1.878-3.709), dyslipidaemia (OR 0.531, 95%CI 0.380-0.742), LVSD (OR 8.042, 95%CI 5.378-12.025), STEMI (OR 2.130, 95%CI 1.519-2.987), revascularisation (OR 0.513, 95%CI 0.358-0.736), serum creatinine (OR 1.173, 95%CI 1.044-1.318), hematocrit (OR 0.9, 95%CI 0.871-0.929), glycaemia (OR 1.07, 95%CI 1.05-1.091) and troponin I (OR 1.004, 95%CI 1.002-1.006). Multivariate analysis, using a stepwise binary logistic regression method, revealed that the only ones with independent predictive value were: age (OR 1.056, 95%CI 1.036-1.076), LVSD (OR 6.381, 95%CI 4.009-10.156), STEMI (OR 1.628, 95%CI 1.056-2.510), hematocrit (OR 0.916, 95%CI 0.882-0.952) and glycaemia (OR 1.064, 95%CI 1.039-1.090, for each 10 mg/dl increment). Using the predicted probabilities of this model we constructed a ROC curve. Its AUC was 0.85 (p<0.001 vs ND). Using the best cut-off of predicted probabilities this model showed a sensitivity of 88.3%, specificity of 64.5%, positive predictive value of 33% and negative predictive value of 96.7%.

Conclusion: in-hospital post-ACS heart failure might be predicted on admission using common practice clinical and laboratory data.