Methods and Results: In six patients (mean age 59±7 years) with sever LV dysfunction the NES delivery system (Optimizer) was implanted. Three patients had ischemic cardiomyopathy (CM), and 3 with dilated CM. Mean left ventricular ejection fraction and QRS duration were 17±4 % and 116±16 ms, respectively. The NES was delivered using two bipolar electrodes placed at the right ventricular septum. Holter recording were performed 2, 3, 4, 5 and 6 weeks on a daily basis post implant.Mean heart rate (HR), QTc, number of premature ventricular tachycardia (PVC), non-sustained ventricular tachycardia episodes (NSVT), and sustained monomorphic ventricular tachycardia episodes (MSVT) were analyzed from 24-hour Holter. Changes in electrocardiographic parametes and arrhythmias were compared prior (group a), during (group b) and after (group c) NES delivery:

	Group a	Group b	Group c
HR	83±14	77±17*	80±16
QTc	403±15	393±17*+	405±16
PVCs	1007±2868	170±421*+	760±1088
NSVT	12±26	3±3*+	10±4
MSVT	5±4	0	5±3

* p<0.0001 comparison with group a; + p<0.0001 comparison with group c

Conclusion: Non-excitatory signal delivery seems to have an antiarrhythmic effect in patients with severe LV dysfunction by slowing the HR and suppressing ventricular arrhythmias.

1037-154 Significance of Atrial Fibrillation in Patients With Acute Myocardial Infarction and Symptomatic or Asymptomatic Left Ventricular Dysfunction: Data From the OPTIMAAL Study

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Background; Atrial fibrillation (AF) is associated with the presence of chemic heart disease and/or congestive heart failure (HF). The prognostic importance of AF after myocardial infarction (MI) is unclear.

Methods; The OPTIMAAL Study randomised patients with clinical evidence of HF during the acute phase of a MI, patients with a new anterior Q wave MI, or patients with a re-infarction in the presence of a previous anterior Q wave MI to treatment with losartan or captopril in addition to standard treatment.

Results; 5477 patients, 71 % males, 67.4 ± 9.9 years were included. In 626 patients AF was present at baseline while 273 developed AF.

	Total population	No AF at base	AF at base	No AF during study	AF during study
Number of patients	5477	4851	626	4578	273
Age	67.4 ± 9.9	66.7 ± 9.8	73.1 ± 8.6 p< 0.001	66.4 ± 9.8	70.5 ± 8.7 p< 0.001
Signs of HF at base, %	68	67	82	66	74

Patients with AF at randomisation had a Hazard Ratio (HR) for death of 2.1 (p < 0.001) and stroke of 2.1 (p < 0.001) respectively, compared to patients without AF. Development of AF at any time (pre-randomisation or during the trial) was associated with a HR of 2.6 (p< 0.001) for death and 2.5 (p<0.001) for stroke.

Conclusion; In patients with acute MI and LV-dysfunction with or without HF those who had AF or developed AF, were older and HF was more prevalent. Both the presence of AF at baseline and the development of AF during the study are associated with an adverse prognosis after acute MI.

1037-155 Ventricular Arrhythmias in Decompensated Heart Failure: Role of Endothelin

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INTRODUCTION: Patients with congestive heart failure (CHF) have a high incidence of ventricular arrhythmias and sudden arrhythmic death. Endothelin-1 (ET-1), a potent vasoconstrictor, is elevated in patients with CHF and has been implicated as an important mediator of increased cardiac filling pressures, pulmonary hypertension, and the progression of circulatory failure. Animal studies suggest that ET-1 may be proarrhythmic (Cardiovasc Res 2001;49:272-280), but whether ET-1 contributes to arrhythmias in human CHF is not known.

METHODS: We studied 83 patients admitted to the hospital for treatment of decompensated CHF. Neurohormonal and cytokine activation was assessed by measuring plasma renin activity, aldosterone, norepinephrine, ET-1, tumor necrosis factor-alpha, and interleukin-6 levels. Ventricular arrhythmic events were assessed by 24-hour Holter monitoring.

RESULTS: A moderate, but highly significant, positive relation was found between plasma ET-1 levels and the average hourly total premature ventricular beats (r = 0.33, p = 0.003), the frequency of ventricular pairs (r = 0.39, p = 0.0003), and the frequency of ventricular tachycardia episodes (r = 0.35, p = 0.001).

To exclude possible effects of clinical variables, drug effects, neurohormones, and cytokines on the relation between ET-1 and ventricular ectopic activity, multiple linear regression analyses were performed using measures of ventricular ectopy as dependent variables. In a multivariate regression analysis, the positive relationship between plasma ET-1 level and the average hourly total premature ventricular beats (p = 0.008), the frequency of ventricular pairs (p = 0.007), and ventricular tachycardia episodes (p = 0.009) remained significant and independent. No associations between other neurohormones or cytokines and ventricular arrhythmic events were found.

DISCUSSION: The results of the present study suggest that increased ET-1 concentrations may be involved in promoting the occurrence of ventricular arrhythmic events in CHF patients. Proarrhythmic effects may account, in part, for the poor outcome associated with increased ET-1 levels in patients with left ventricular dysfunction.

1037-156 Benefit of Slowing the Ventricular Rate for Left Ventricular Systolic Performance During Atrial Fibrillation in Subjects With Myocardial Infarction

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Background: Slowing ventricular rate during atrial fibrillation (AF) by post-ganglionic vagal nerve stimulation (PGVS) is expected to improve left ventricular (LV) systolic performance in coronary artery disease. We reported that LV systolic parameters during AF correlated well with the ratio of preceding and pre-preceding RR intervals (RR_1/RR_2), and the value at $RR_1/RR_2 = 1$ in the linear regression line could estimate LV systolic function in lone AF.

Purpose: We evaluated the effect of ventricular rate slowing by PGVS on LV systolic function in a canine myocardial infarction (MI) and AF model using this index.

Methods: Data were obtained in 8 healthy mongrel dogs at baseline sinus rhythm (N-SR). MI was created by ligating left anterior descending coronary artery (MI-SR). AF was triggered (MI-AF) and PGVS was subsequently applied (MI-PGVS). LV systolic function was estimated by max dP/dt and aortic peak flow rate (AoF) during AF using $RR_1/RR_2 = 1$ index.

Results: 1) LV systolic function during sinus rhythm deteriorated after coronary ligation and further worsened by AF. 2) RR interval was significantly shortened by AF (530 to 404 msec) and prolonged by PGVS (547 msec). 3) Max dP/dt and AoF significantly decreased by AF and increased by PGVS.

Conclusion: 1) Slowing ventricular rate by PGVS during AF improved LV systolic performance in the subjects with coronary artery disease. 2) The systolic parameters at $RR_1/RR_2 = 1$ accurately evaluated LV systolic function during AF even in impaired ventricles.

	N-SR	MI-SR	MI-AF	MI-PGVS
Max dP/dt (mm Hg)	3429 ± 213	2409 ± 812	1979 ± 747	2389 ± 661
AoF (L/min)	11.6 ± 1.7	8.6 ± 2.1	5.5 ± 1.5	7.5 ± 2.4

1037-157 Effects of Sauna Therapy on Cardiac Arrhythmia in Patients With Chronic Heart Failure

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Background: We have previously reported that repeated 60 degree C dry sauna bathing, a thermal therapy, improves hemodynamics and clinical symptoms in patients with chronic heart failure (CHF). Since cardiac arrhythmia is an important target in the treatment of CHF, we investigated the effects of thermal therapy on cardiac arrhythmia. Patients and Methods: Twenty six patients with CHF (59±18 years) with NYHA functional class II or III and at least 200 premature ventricular contractions (PVCs) / 24hrs were studied. Their medication had not been changed for at least 2 weeks before and during the study. They had 60 degree C far infrared-ray dry sauna for 15 min and were kept at bed rest with blankets for 30 min once a day. Before and at the day after 2-week sauna therapy, the effect of the sauna was evaluated with 24-hour Holter recordings for arrhythmia and heart rate variability (HRV), chest X-ray and measurement of plasma brain natriuretic peptide (BNP) concentration. Results: All patients enrolled in the study completed it. No patient experienced dyspnea, angina pectoris, or palpitations during sauna bathing. Body weight and hematocrit did not change after 2-week sauna treatment (53±12 to 53±12 kg, 38±5 to 37±5 %, respectively). After 2-week sauna therapy, 1) PVCs / 24hrs decreased significantly compared with baseline value (2993±905 to 1476±592 /24hrs, P<0.01), 2) HRV significantly increased compared with baseline value (9.2±1.4 to 11.8±2.4, P<0.05) in 15 patients without atrial fibrillation (Af), however mean heart rate did not change, 3) in two of 11 patients with Af sustained for at least 4 days, Af was converted to sinus rhythm. Plasma BNP concentrations and cardio-thoracic ratios significantly decreased in comparison with baseline value (514±141 to 204±92 pg/ml, P<0.01, 60±2 to 57±%, P<0.01, respectively). Conclusion: Sauna therapy decreases cardiac arrhythmia in patients with chronic heart failure, probably due to improvement of cardiac function and autonomic nerve function.

1037-158 Polygenic Risk Assessment Improves Usefulness of Genotyping in Heart Failure Populations: Additive Effects of ACE and eNOS Polymorphisms

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Background: Genetic risk assessment that combines data on multiple genes may be a more powerful prognostic tool than single gene strategies. The angiotensin converting enzyme deletion polymorphism (ACE D) and the endothelial nitric oxide synthase Asp298 variant (eNOS T) both adversely influence heart failure survival. We evaluated the prognostic value of an analysis which combined eNOS and ACE genotype data in a study of heart failure patients.

Method:463 patients (mean age 55.8 ± 12, 49% ischemic, 71% male) referred to the Cardiomyopathy Clinic at the University of Pittsburgh with an LVEF≤ 0.45 were enrolled,