Rx	n	odds ratio	p value	95% C.I.
A + B	197	0.51	<0.01	0.33–0.79
A + B + C	558	0.58	<0.01	0.42–0.81
B	429	0.66	0.03	0.46–0.95
B + C	794	0.7	0.02	0.52–0.95
A + C	291	0.96	0.81	0.67–1.37
A	197	1.16	0.47	0.78–1.72
None	832	1.88	<0.001	1.42–2.50

Rx with A in combination with B significantly improves mortality when compared to Rx with C even after controlling for CHF. Significant differences in the prevalence of CHF in various Rx groups (53% in A and 5% in B and 11% in C) and inability to adequately control for the severity of CHF may explain the observed effect of Rx with A alone. *Conclusions: Combination Rx with A and B is preferable to Rx with C alone. It appears that mortality benefit of ACE Inhibition in patients with CAD is not limited to patients who have CHF.*

11:00

787-3 Efficacy and Safety of Early Administration of Intravenous Enalaprilat in Congestive Heart Failure Patients with Acute Pulmonary Edema

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The systemic (Swan-Ganz cathet r, brachial sphygmomanometer) and regional (2D pulsed doppler, paraaminohippurate and indocyanine green clearances) hemodynamic and blood gases effects of a single intravenous 2-h-infusion of 1 mg enalaprilat (E) were investigated within the 12 h following an acute pulmonary edema episode and compared to those of a placebo (P) in a randomized double-blind study performed in 20 CHF (III–IV NYHA) patients. The effects were investigated before and 2, 4 and 8 h after the onset of treatment infusion. At peak effect, and as compared to P, E significantly decreased pulmonary wedge pressure (−37 vs −10%, p = 0.001), diastolic and mean systemic (−21 vs −4%, p = 0.009, −18 vs −6%, p = 0.026) and pulmonary (−21 vs −8%, p = 0.040, −18 vs −9%, p = 0.046) arterial pressures, brachial and renal resistances (−44 vs −14%, p = 0.017, −22 vs −2%, p = 0.014) and significantly increased brachial and renal blood flows (+77 vs +8%, p = 0.036, +12 vs 0%, p = 0.043) arterial oxygen tension (+2 vs −8%, p = 0.041) and saturation (+1 vs −2%, p = 0.045) and finally tended to improve intra-pulmonary shunt (−18 vs −16%, p = 0.080). Simultaneously, E did not affect heart rate, cardiac output, systolic systemic and pulmonary arterial pressures, and carotid and hepato-splanchnic hemodynamics. Time courses of plasma electrolytes, creatinine and nitrogen clearances were not significantly different between E and P. We conclude that in this study early administration of intravenous enalaprilat was effective and well tolerated in CHF patients with acute pulmonary edema.

11:15

787-4 The Paradox of Low Risk Among High Risk Patients in Controlled Trials — Experience in the TRAndolapril Cardiac Evaluation Trial

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Mortality in epidemiological studies is almost always larger than in apparently similar populations selected for a clinical trial. To study this problem, patient inclusion was tracked very carefully in the Trandolapril Cardiac evaluation (TRACE) trial.

The TRACE Register includes 7001 consecutive enzyme confirmed MIs in 6676 patients screened for entry into the trial. Medical history and complications of MI were obtained for all patients. Left ventricular systolic function was determined by echocardiography in a core laboratory as wall motion index (WMI) within 6 days of the infarction. Patients with WMI ≤ 1.2 were eligible for the study (corresponding to an ejection fraction below 35%) unless an exclusion criterion was present. Patients excluded were those not tolerating or requiring an ACE inhibitor, those dying during screening phase and those unwilling/unable to participate. Survival data were available for all except 5 patients after 2–3 years.

The table shows number of MI and 1 year mortality in all patients, and patients subgroubed by left ventricular systolic function. Also shown is patients with left ventricular dysfunction subgroubed by whether they were randomised.

MI	n	1 year mortality
All	7001	23 ± 1%
WMI not available	475	50 ± 4%
WMI > 1.2	3920	12 ± 1%
WMI ≤ 1.2	2606	34 ± 2%
WMI ≤ 1.2 Randomised	1747	24 ± 1%
WMI ≤ 1.2 Excluded	859	54 ± 3%

Conclusion: Even though the target population of high risk patients with reduced left ventricular function was successfully identified, the final study population had a 1 year mortality similar to unselected patients. This was caused by exclusion of patients at extreme risk.

11:30

787-5 Systemic Effect of Ramipril on Endothelin, but not on Eicosanoid Levels in Patients with Coronary Artery Disease

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Study aim: Neurohumoral effects of ramipril (R) alone or in combination with isosorbide dinitrate (ISDN) compared to ISDN or placebo.

Study design: Placebo-controlled double-blind parallel group trial.

Methods: 32 patients with coronary artery disease (CAD) received placebo, R 5 mg, ISDN 20 mg slow release b.i.d. or R + ISDN for one week. A 24 hour kinetic profile of ramipril and its metabolite, of ace activity (ACE-A) and of related hormones (renin and aldosterone), of endothelin and of prostaglandins (PG), thromboxane B2 (TXB2), PGF2a, 6-keto PGF1a, the stable metabolite of prostacyclin (PGI2-M) was studied after the first dose. Measurements were repeated after 8 days of treatment before and 3 hours after the morning dose.

Results: Hormone measurements are presented as means of percent difference of patients treated with R (n = 16) vs. those without ace-inhibitor (n = 16).

Time (hrs)	0	1	2	3	4	6	8	24	0–8	3–8
Ramipril(mg/l)	0	*8*	*5*	*4*	*3*	*2*	*1*	*0.4*	*1*	*7*
Ramiprilat(mg/l)	0	*6*	*11*	*10*	*8*	*7*	*5*	*1*	*2*	*14*
ACE-A (%)	−6	*−78*	*−95*	*−98*	*−98*	*−97*	*−96*	*−80*	*−82*	*−98*
Aldosteron (%)	9	−5	−31	−34	−21	−27	−23	−34	–	–
Renin (%)	−9	−7	7	19	13	17	53	32	–	–
Endothelin (%)	−17	−13	*−25*	−19	−16	−15	−4	0	–	–
TXB2 (%)	4	10	4	5	–	5	–	0	12	−3
PGF2a (%)	10	17	0	0	–	8	–	2	2	−9
PGI2-M (%)	7	0	−3	8	–	−5	9	−1	−7	13

– = not done; significant differences are printed in *italics* (two-tailed t-test)

A single oral dose of 5 mg R reduced ACE activity ($p < 0.001$), decreased aldosterone and increased renin ($p < 0.1$). R did not influence plasma levels of the vasoconstricting (TXB2, PGF2a) or vasodilating (PGI2-M) eicosanoid mediators, but decreased endothelin ($p < 0.1$).

Conclusion: R, in a dose that results in significant systemic inhibition of the renin angiotensin aldosteron system, does not induce measurable changes of circulating eicosanoid concentrations, but seems to diminish systemic release of endothelin.

11:45

787-6 Hypotension Induced by Captopril in Patients with Primary Autonomic Failure Occurs Independently of Plasma Renin Levels and Sympathetic Nervous Activity

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We have investigated the haemodynamic and hormonal responses to angiotensin converting enzyme inhibition in 12 patients with primary autonomic failure (AF, 5 pure autonomic failure, 7 multiple system atrophy) and 7 normal subjects. Measurements of blood pressure (BP), heart rate (HR), stroke distance (SD) and cardiac index (CI, continuous wave Doppler, forearm blood flow (FBF, strain gauge plethysmography) and digital skin blood flow (DSBF, laser Doppler flowmetry) were made non-invasively. Plasma renin activity (PRA) and noradrenaline (NORAD) were measured before and at 30 min intervals after captopril (50 mg, oral).

Basal supine BP was higher in AF compared to normals ($p < 0.05$). After captopril, mean BP fell in AF (117 ± 6 to 103 ± 5 mmHg, $p < 0.05$), but not in normals (99 ± 4 to 97 ± 5 mmHg, ns). HR was unchanged after captopril in both groups. The depressor response in AF was accompanied by a fall in SD