Relaxin, a polypeptide hormone belonging to the insulin family, has recently attracted interest as a possible cardiovascular regulator. Though long known to prepare the birth canal for parturition, relaxin has only lately been shown to have renal and haemodynamic actions. Relaxin may also be secreted by the heart, at least when it is failing. Plasma relaxin concentrations are raised in chronic heart failure (CHF) and myocardial expression of the H1 and H2 relaxin gene is increased in proportion to the severity of CHF. Whether the heart is a source of relaxin when cardiac contractility is preserved is unknown. The lungs are commonly involved in the clearance or secretion of vasoactive peptides but their role in relaxin metabolism is unknown. The aim of this study was to measure transcardiac and transpulmonary relaxin gradients in subjects with preserved left ventricular ejection fraction. Patients undergoing coronary artery bypass grafting were studied as both pulmonary and cardiac arterial inflow and venous effluent can be readily sampled.

**METHODS**

Twenty consecutive patients were studied. Immediately before institution of cardiopulmonary bypass, blood samples were taken into chilled tubes, in rapid succession, from the aorta, coronary sinus, pulmonary artery, and pulmonary vein. A validated relaxin immunoassay was used (Immundiagnostik, Bensheim, Germany). Statistical analysis was performed using a Wilcoxon signed rank test. The study was approved by the hospital ethics committee.

**RESULTS**

Patient characteristics are shown in table 1.

There was a decrement in the concentration of relaxin between aorta and coronary sinus in 16 of the 20 subjects studied, suggesting cardiac extraction of relaxin. The mean (SD) concentration fell from 38.1 (61.3) pg/ml to 32.8 (57.8) pg/ml (p < 0.04).

No characteristic differentiated the 16 patients with cardiac extraction of relaxin from the remaining four.

There was no transpulmonary gradient in relaxin concentration. The mean (SD) concentration in the pulmonary artery was 42.0 (68.3) pg/ml v 41.8 (69.1) pg/ml in the pulmonary vein (p = NS).

**DISCUSSION**

Dschietzig and colleagues showed higher coronary sinus than left ventricular relaxin concentrations in 11 of 14 patients with severe CHF, suggesting that the failing heart may be a source of circulating relaxin. We found the opposite across the non-failing heart—that is, net extraction of relaxin. Further inspection of the data from Dschietzig and colleagues shows no transcardiac gradient in patients with moderate CHF and an aorta–coronary sinus decrement in controls, in keeping with our findings. This suggests that the contribution of the heart to circulating relaxin varies according to the presence or absence of CHF. Whether it is left ventricular systolic dysfunction, abnormal pulmonary or systemic haemodynamics, neurohumoral activation or other factors that leads to net cardiac secretion of relaxin in CHF is presently unknown.

The pattern of relaxin secretion/extraction is distinct from other hormones. A type and B type natriuretic peptide increase from aorta to coronary sinus in both the non-failing and failing heart (more notably in the latter). Adrenomedullin is also secreted by both the failing and non-failing heart. In contrast, endothelin-1 is extracted by the failing heart, whereas there seems to be either no transcardiac gradient or higher coronary sinus concentrations in non-failing hearts. There is no transcardiac gradient in plasma aldosterone concentration in the non-failing heart but an increment in coronary sinus aldosterone concentration in CHF.

Interpretation of the cardiac extraction of relaxin by the normal heart, compared to its secretion by the failing heart, is difficult. The mechanisms of relaxin clearance from the circulation are unknown. Changes in the transcardiac concentration of other peptides seem to reflect changes in receptor density/affinity—for example, decreases in endothelin concentration across the failing heart are probably caused by the increase in myocardial ET, and ET receptors. The receptors for relaxin have only recently been described and nothing is known about the effect of CHF on their expression.

The transpulmonary gradient in relaxin concentration has not been described before. Neither net extraction nor secretion occurred, which is different than for other peptides. Pulmonary extraction of A type natriuretic peptide and adrenomedullin has been described. For endothelin, some have described no transpulmonary concentration gradient, others pulmonary extraction, and others still that both secretion and extraction, which balance each other out, occurs. Relaxin also differs from other peptides in having no effect in small doses on the late gestation myometrium, suggesting a lack of a direct role in pregnancy.
pulmonary resistance arteries (whereas it is a potent
vasodilator in comparable vessels from the systemic
circulation).

In summary, in patients with coronary disease but without
CHF, there is net cardiac extraction of relaxin in contrast to
reported secretion in CHF. In patients without CHF there is no
transpulmonary gradient in relaxin.

ACKNOWLEDGEMENTS
This study was supported by the British Heart Foundation.

Authors’ affiliations
C Fisher, J J V McMurray, Department of Cardiology, Western
Infirmary, Glasgow, UK
S Al-Benna, A Kirk, Department of Cardiothoracic Surgery, Western
Infirmary
J J Morton, Neuroendocrine Laboratory, Western Infirmary

REFERENCES
1 Ivell R, Einspanier A. Relaxin peptides are new global players. Trends
Endocrinol Metab 2002;13:343.
2 Fisher C, MacLean M, Morecroft I, et al. Is the pregnancy hormone
relaxin also a vasodilator peptide secreted by the heart? Circulation
3 Dschietzig T, Richter C, Bartsch C, et al. The pregnancy hormone relaxin
4 Northridge DB, Jamieson MP, Jardine AG, et al. Pulmonary extraction
and left atrial secretion of atrial natriuretic factor during cardiopulmonary
and peripheral consumption of big endothelin and endothelin-1 in severe
heart failure: acute effects of vasodilator therapy. Circulation

IMAGES IN CARDIOLOGY

Severe pulmonary hypertension in a patient with hypertrophic cardiomyopathy: response to
alcohol septal ablation

Mild to moderate pulmonary hypertension secondary to elevation of left atrial pressure is
common in patients with hypertrophic cardiomyopathy. However, severe pulmonary
hypertension of systemic levels is unusual in these patients, especially in
the absence of severe fixed obstruction and severe mitral regurgitation.

A 74 year old woman presented with severe exertional dyspnoea. On echocardiography,
she was found to have hypertrophic obstructive cardiomyopathy with a labile left ventricular outflow
tract gradient, mild to moderate mitral regurgitation, and severe pulmonary hypertension. She underwent implantation
of a permanent pacemaker but continued to have severe symptoms. At the
time of cardiac catheterisation, there was
a labile left ventricular outflow tract gradient between 5–50 mm Hg. The
mean left atrial pressure was 20 mm Hg. The pulmonary artery pressure was 100/
35 mm Hg, at a time when the aortic
systolic pressure was 108 mm Hg (left
hand panel: LV, left ventricular pressure; Ao, aortic pressure; PA, pulmonary artery
pressure; LA, left atrial pressure).

Alcohol septal ablation was performed
without complications. Six months after
the procedure, the patient was free of
exertional symptoms. Repeat cardiac
catheterisation demonstrated resolution
of the left ventricular outflow tract
gradient and a decrease in the mean left
atrial pressure. The pulmonary artery
systolic pressure had dropped to
62 mm Hg with an aortic systolic
pressure of 160 mm Hg (right hand panel).

E S Brilakis
R A Nishimura
rnishimura@mayo.edu

Correspondence to: Professor John JV McMurray, Department of
Cardiology, Western Infirmary, Glasgow, G12 8QQ, UK;
j.mcmurray@bio.gla.ac.uk

Accepted 22 January 2003