**Scientific Letter**

The putative satiety hormone PYY is raised in cardiac cachexia associated with primary pulmonary hypertension

C W le Roux, M A Ghatel, J S R Gibbs, S R Bloom

**Methods**

Weight loss greater than 6% independently correlates with reduced survival in patients with congestive heart failure (CHF). Cardiac cachexia is a gradual and graded process, with wasting affecting muscle, bone, adipose tissue and the heart. Reduced appetite has been proposed as an important factor for weight loss caused by cardiac cachexia.

The mechanism of cardiac cachexia remains largely unclear. Gastric myoneural inhibition and gastrointestinal hypomotility with delayed gastric emptying is commonly observed, and gut hormones may also play a role, because the anorexia is often characterised by a premature feeling of fullness and loss of hunger. The gut hormone ghrelin stimulates hunger, increases food consumption, and was previously shown to be raised in patients with cardiac cachexia and CHF. Ghrelin is produced from the stomach and usually rises in anticipation of a meal and then falls after the ingestion of nutrients.

The gut hormone PYY3–36, acting as a terminator of hunger, is produced by the L cells in the distal gastrointestinal tract; it reduces appetite and 24 hour food intake by binding to the neuropeptide Y Y2 receptor in the hypothalamic arcuate nucleus.

Severe pulmonary hypertension results in a low cardiac output and neurohumoral activation. Patients frequently report loss of appetite and weight, and since it occurs in a young population they have little co-morbid disease, which itself might affect appetite. This study aimed to evaluate dynamic PYY and ghrelin responses to a standard meal in control subjects and patients with cardiac cachexia associated with pulmonary hypertension.

**Results**

There were no differences in age, sex, and BMI between control subjects and patients (table 1). PYY was 60% higher in the patients post-meal at 30 minutes (p = 0.01), 49% higher at 60 minutes (p = 0.02), and 46% higher at 90 minutes (p = 0.04) when compared with the control subjects (fig 1). There was no difference in fasting PYY concentrations (p = 0.42).

Both groups showed the expected pattern of reduction in ghrelin post-meal. The fasting ghrelin concentrations for the patients and control subjects were 704.1 (423) pmol/l and 484.6 (204) pmol/l, respectively (p = 0.13), while the 90

![Figure 1](https://www.heartjnl.com)

**Figure 1** PYY response following standard meal in cardiac cachexia associated with pulmonary hypertension and control subjects (solid circles, patients with cardiac cachexia; open circles, control subjects)

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**Table 1 Demographics of patients and control subjects**

<table>
<thead>
<tr>
<th></th>
<th>Cardiac cachexia</th>
<th>Control</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects (female)</td>
<td>6/9</td>
<td>5/9</td>
<td>0.7</td>
</tr>
<tr>
<td>Age (years)</td>
<td>38.4 (5.0)</td>
<td>29.9 (1.6)</td>
<td>0.13</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>19.8 (1.3)</td>
<td>23.6 (0.9)</td>
<td>0.052</td>
</tr>
<tr>
<td>Weight loss (kg)</td>
<td>9.0 (0.4)</td>
<td>0.2 (0.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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1. Reduced appetite has been previously shown to be raised in patients with cardiac cachexia and CHF. Ghrelin is produced from the stomach and usually rises in anticipation of a meal and then falls after the ingestion of nutrients.

2. Reduced appetite is often characterised by a premature feeling of fullness and loss of hunger. The gut hormone ghrelin stimulates hunger, increases food consumption, and was previously shown to be raised in patients with cardiac cachexia and CHF. Ghrelin is produced from the stomach and usually rises in anticipation of a meal and then falls after the ingestion of nutrients.

3. The gut hormone PYY3–36, acting as a terminator of hunger, is produced by the L cells in the distal gastrointestinal tract; it reduces appetite and 24 hour food intake by binding to the neuropeptide Y Y2 receptor in the hypothalamic arcuate nucleus.

4. Severe pulmonary hypertension results in a low cardiac output and neurohumoral activation. Patients frequently report loss of appetite and weight, and since it occurs in a young population they have little co-morbid disease, which itself might affect appetite. This study aimed to evaluate dynamic PYY and ghrelin responses to a standard meal in control subjects and patients with cardiac cachexia associated with pulmonary hypertension.

5. Parametric statistical analysis was done using SigmaStat v2.0 (SPSS Science, Chicago, Illinois, USA). The PYY, ghrelin, and body mass index (BMI) data were normally distributed and statistical comparisons were made using an unpaired t test. Linear regression was used to evaluate the correlation between BMI, fasting ghrelin, and peak PYY. A probability level of p < 0.05 (5%) was considered significant.
minute post-meal values were 470.9 (231) pmol/l and 325.4 (154) pmol/l (p = 0.08).
There was no correlation between BMI and peak PYY response in either the control subjects (p = 0.19) or the cardiac cachexia patients (p = 0.53), and no correlation between BMI and fasting ghrelin for either the control subjects (p = 0.28) or the cardiac cachexia patients (p = 0.53).

**DISCUSSION**

Patients with cardiac cachexia caused by severe pulmonary hypertension have an exaggerated and early PYY response to a 720 kcal meal when compared to control subjects, while ghrelin showed the same post-meal pattern in both groups. The pattern of PYY is consistent with previous studies and clinical observations which reported that patients with cardiac cachexia experience a change in appetite, possibly reaching satiety earlier and consequently consuming less food per day. A reduction in food intake of as little of 100 kcal per day, if sustained, could lead to weight loss similar to that observed in patients with cardiac cachexia associated with pulmonary hypertension.

Previous studies demonstrated fasting concentrations of ghrelin 61% higher in 28 patients with CHF and cardiac cachexia compared to 46 patients with CHF without cachexia. We observed fasting ghrelin concentrations 45% higher in the patients with pulmonary hypertension than control subjects (p = 0.13). This is the first study to describe the dynamic pattern of ghrelin following standard meals in these patients, showing similar decreases in ghrelin to control subjects. Raised fasting ghrelin concentrations in cardiac cachexia may reflect weight loss and the negative energy balance. It is unlikely that PYY and ghrelin are the only factors governing appetite. The mechanism for the elevation of PYY in patients with pulmonary hypertension is not known. It may form part of a metabolic syndrome related to low cardiac output and/or congestion of the gastrointestinal system which leads to the release of these hormones.

In conclusion, the PYY response of patients with cardiac cachexia associated with primary pulmonary hypertension is premature and exaggerated and may play a role in the aetiology of premature hunger termination and reduced daily calorie intake in patients with cardiac cachexia.

**ACKNOWLEDGEMENTS**

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**References**


**Images in Cardiology**

Severe tricuspid regurgitation following a stab to the heart

A 28 year old man sustained an isolated stab injury to the left third intercostal space in the moclavicular line. The weapon was reported to be a kitchen knife 12 cm in length. A transthoracic echocardiogram revealed a pericardial effusion. He was transferred to our department and was taken to theatre for emergency surgery. A median sternotomy was performed. An entry wound was found over the anterior aspect of the right ventricular outflow tract, and an exit wound on the inferior surface of the right ventricle near the atrioventricular groove (panel A). Cardiopulmonary bypass was instituted because of haemodynamic instability. Both ventricular tears were repaired with interrupted 5'0 polypropylene sutures. An intraoperative transoesophageal echocardiogram was performed following weaning from bypass to assess intracardiac structures. This revealed severe regurgitation through the anterior leaflet of the tricuspid valve (panels B and C).

Bypass was re-instituted with bicaval cannulation. The right atrium was opened directly on beating heart and a defect confirmed in the tricuspid leaflet. This was repaired with interrupted 5’0 polypropylene sutures. The patient made an uneventful recovery and was discharged home.

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