R
current and lengthy hospitalisation is common in
patients with heart failure and accounts for much of
the treatment cost. This has led to interventions aimed
at reducing hospitalisation, but identifying patients at risk
of hospitalisation is difficult using traditional risk factors.1
Evidence accumulates for the value of brain natriuretic
apeptide (BNP) and N-terminal brain natriuretic peptide (NT-
proBNP) in the diagnosis and management of heart failure.2
In addition, one study has compared patients with plasma
concentrations of NT-proBNP above and below a median of
825 pg/ml, observing a relative risk for hospitalisation with
heart failure of 4.7 (95% confidence interval (CI) 2.2 to 10.3;
p < 0.001).3 Patients in that study had chronic, stable heart
failure caused by coronary artery disease (CAD) and were
participating in a clinical trial. Trial exclusion criteria
included a current New York Heart Association (NYHA)
rating of IV. In the present study, we examined a UK
population cohort of incident cases of heart failure to assess
whether NT-proBNP could identify patients at risk of
subsequent hospitalisation.

METHODS
The Bromley heart failure study was designed to identify all
new cases of heart failure in Bromley, UK, through general
practitioner surveillance and daily screening of hospital
admissions.4 Heart failure was diagnosed if a patient had
symptoms (shortness of breath or fatigue) with clinical signs
of fluid retention in the presence of an underlying abnorm-
ality of cardiac structure or function.4 If doubt remained, a
positive response to treatment for heart failure confirmed the
diagnosis.

At first contact with the study cardiologist, a venous
blood sample was drawn into a glass tube containing edetic
acid and aprotonin. This was approximately 30 minutes
after arrival for 36 of 38 patients presenting in the study heart
failure clinic, within two days of admission for 46 of 72
patients hospitalised at presentation, and more than one
week after presentation for 10 patients. The blood sample
was centrifuged and the plasma stored at −80°C until
sent, while frozen, to the Hoffman-La Roche laboratory for
assay of NT-proBNP. Patients were followed up for death and
hospital admission over a median of 20 months (90% range
14–24 months). Dates and certified causes of death were
obtained from the UK National Health Service Central
Registry.

The primary outcome measure was a subsequent hospita-
lisation for worsening heart failure. The association with NT-
proBNP was evaluated using Cox’s proportional hazards
regression with patients’ follow up being censored at death.
Secondary outcomes were death before hospitalisation for
worsening heart failure, and death or subsequent hospitali-
sation for worsening heart failure.

The local research ethics committee approved this study,
and all participants gave informed consent.

RESULTS
From the 332 patients enrolled, 110 samples were available
for NT-proBNP measurement. Samples were not available
from the other patients because of early death, refusal to have
blood taken, and technical failures. Seventy one patients
were male, median age was 75 years (range 49–91 years),
CAD was the aetiology in 40 patients, 98 patients had
impaired left ventricular systolic function, and 59 patients
were NYHA rating IV at the time of first presentation. While
males (65% v 54%) were over-represented, the subsample
with NT-proBNP measurements was otherwise comparable to
the whole study cohort. Median concentration of NT-proBNP
was 637 pg/ml (90% range 110–3510 pg/ml).

Thirty patients had an unplanned admission for worsening
heart failure during follow up and 17 died before such an
admission. The results (table 1) show no evidence for an
association between NT-proBNP concentration and subse-
quent hospitalisation. By contrast, despite the small number
of deaths occurring without prior admission, there was
strong evidence of an association between higher NT-proBNP
and an increasing risk of death. The trend towards a greater
hazard of the combined outcome of hospitalisation or death
with higher NT-proBNP is because of the association with
death.

DISCUSSION
Our results suggest that the previous study may have
overestimated the relation between NT-proBNP and the
subsequent risk of hospitalisation for worsening heart fail-
ure.1 This discrepancy may have arisen because our study is of
a population based cohort of acutely ill patients with heart
failure arising from a number of different aetiologies and a
wide range of disease severity. Perhaps there is a stronger
association in patients with specific aetiologies, such as CAD.1
Alternatively, the timing of NT-proBNP measurement may be
an important factor in maximising its predictive value for
subsequent hospitalisation. While in our study NT-proBNP
was measured shortly after first diagnosis, in the study by
Richards and colleagues, patients were enrolled, and their
NT-proBNP measured when they were in a stable state.1 A
recent study has addressed this issue directly, comparing
measurements of NT-proBNP made on arrival at, and on
discharge from, a coronary care unit.1 Both measurements
were available for 34 patients, who subsequently experienced
19 events (death, hospital admissions for heart failure, or
worsening heart failure without hospitalisation). With both
measurements included in the same regression analysis, only
the pre-discharge concentration of NT-proBNP was indepen-
dently associated with the composite outcome.1 This limited
evidence suggests that if the objective is to identify patients at

Abbreviations: BNP, brain natriuretic peptide; CAD, coronary artery
disease; NYHA, New York Heart Association; NT-proBNP, N-terminal
brain natriuretic peptide
In our study we have found a strong association between NT-proBNP measured at diagnosis and subsequent survival. We suggest that the most likely reason for our failure to find a similar association with hospitalisation for worsening heart failure is the limited potential for any single patient characteristic to predict that outcome, as such admission arises through interplay of medical, social, and health service factors. We have previously found only age to be independently predictive of admission in patients with heart failure. This association is conceivably because of age acting as a marker for several factors simultaneously, such as the resilience of the patient to heart failure, and the availability of social support.

While the increasing clinical use of NT-proBNP and BNP is supported by strong associations with diagnosis and mortality, our study suggests that their value for identifying patients at risk of future hospitalisation is not yet established.

ACKNOWLEDGEMENTS
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REFERENCES

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Conflicts of interest: MRC advises several companies that manufacture assays for natriuretic peptides. MRC was the clinical adviser for the NICE guideline on the diagnosis and management of chronic heart failure, but the views expressed here are his own and should not be taken to necessarily reflect those published in the guideline.

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Table 1 Event rates for patients with NT-proBNP above and below the median value

<table>
<thead>
<tr>
<th>Event point</th>
<th>Event rate for patients with NT-proBNP</th>
<th>Hazard ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admission†</td>
<td>16/55 14/55</td>
<td>1.03 (0.79 to 1.35)</td>
<td>0.83</td>
</tr>
<tr>
<td>All cause mortality without prior hospital admission†</td>
<td>3/55 14/55</td>
<td>1.54 (1.08 to 2.19)</td>
<td>0.016</td>
</tr>
<tr>
<td>Hospital admission or all cause mortality†</td>
<td>19/55 28/55</td>
<td>1.19 (0.96 to 1.48)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* Calculated using Cox’s proportional hazards regression.
† Unplanned hospital admission for worsening heart failure only.

Hazard ratios indicate the increased hazard of an event with a doubling of plasma NT-proBNP concentration at time of first presentation.

Images in Cardiology

Left subclavian artery stenosis with subclavian–subclavian bypass

An arch aortography demonstrates an occluded brachiocephalic trunk and subclavian–subclavian bypass graft (SSBG) in a 56 year old woman with left main and triple coronary artery disease requiring coronary artery bypass graft (CABG) surgery. A selective left subclavian arteriography revealed a moderate stenosis with a 40 mm Hg gradient proximal to the origin of the left vertebral artery and left internal mammary artery (LIMA). Stenting of the left subclavian stenosis was performed to improve distal flow and the utilisation of LIMA during CABG. To minimise cerebral embolisation of atherosclerotic material into the left vertebral artery and right carotid through the SSBG, left subclavian stenting was performed using induced hyperaemia of the left upper extremity and temporary manual compression of the SSBG. The procedure was uneventful and the patient was doing well one month later.

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