B-type natriuretic peptide for predicting morbidity and mortality after non-cardiac surgery

B-type natriuretic peptide (BNP) is a polypeptide released by cardiomyocytes in the left ventricle in response to excessive stretching; it is an indicator of systolic dysfunction. BNP binds to and activates atrial natriuretic factor receptors. This reduces systemic vascular resistance and promotes natriuresis, which promotes an increase in cardiac output as a result of reduced afterload and more favourable positioning on the Frank–Starling curve. BNP has been used as a biomarker of disease severity in heart failure for some time and is established as a predictor of disease progression and mortality. More recently it has been suggested as a predictor of perioperative morbidity and mortality.

The value of B-type natriuretic peptide

BNP, measured by immunoassay, is a relatively cheap and easy blood test to perform. Initial investigations of this biomarker demonstrated that patients suffering with postoperative acute coronary syndromes had statistically significant elevations in BNP preoperatively (Gibson et al, 2007). This has since been shown to be an independent predictor of cardiac morbidity in a variety of patient groups undergoing major surgery. More recently preoperative BNP levels have been shown to predict long-term survival in a single centre after major non-cardiac surgery (Payne et al, 2011). This association holds true for vascular and non-vascular patients alike as well as those without a diagnosis of ischaemic heart disease.

Meta-analysis was performed by Karthikeyan et al (2009) on nine studies including more than 3000 patients who had preoperative BNP measurements. All the studies reported a statistically significant association between elevated BNP levels and cardiac complications perioperatively. Meta-analysis demonstrated an odds ratio of 19.3 (95% confidence interval (CI) =8.5–43.7) for cardiac death or non-fatal myocardial infarction. The authors concluded that preoperative BNP is a powerful independent predictor of cardiac complications in the first 30 days after surgery.

Ryding et al (2009) carried out a meta-analysis of a larger group of studies (15 papers) with similar findings. The authors found increased risk of immediate cardiac complications (odds ratio = 19.77; 95% CI = 13.18–29.65; $P<0.0001$), 30-day all-cause mortality (odds ratio = 9.28; 95% CI = 3.51–24.56; $P<0.0001$), cardiac death (odds ratio = 23.88; 95% CI = 9.43–60.43; $P<0.00001$) and long-term all-cause mortality (odds ratio = 4.77; 95% CI = 2.99–7.46; $P<0.00001$).

Problems with the use of B-type natriuretic peptide

Assay of BNP for prediction of perioperative morbidity and mortality is still in its infancy. Evidence for its use in this setting comes from single centre cohort studies and their meta-analysis. No large multicentre randomized controlled trials have been performed, nor has sub-group analysis been done. There is little standardization of outcome measures from study to study.

Difficulties in interpretation also arise because of the suggested 'normal' values and those that should be used as an indicator of increased risk. Normal values are greater in women than in men and tend to increase with age. At the age of 50 years, men may have a range from 4–40 pg/ml whereas women would show 8–80 pg/ml. This increases to 9–86 pg/ml in men and 16–155 pg/ml in women at the age of 80 years. Each of the investigations of BNP use different cut-off values for elevated concentration and therefore increased risk.

Payne et al (2011) performed receiver operating characteristics analysis to try and remove this problem. They suggested a BNP concentration of 87.5 pg/ml giving a combined sensitivity (65.7%) and specificity (78.6%) for predicting long-term mortality. In 345 patients undergoing major surgery mean survival was 732 days in those with BNP >87.5 pg/ml compared to 1285 days in those with lower concentrations preoperatively. This is in the expected range of a healthy 60-year-old woman.

There is no consensus on how clinicians should respond to increased concentrations of BNP. It is not yet clear whether this indicates a modifiable risk or how it should be set in the context of other disease.

Discussion

It is highly desirable to have a single cheap, rapid, easy to perform, objective test that demonstrates good correlation with surgical outcome. BNP shows some promise and can be used in conjunction with other risk stratification tools to improve their accuracy (Biccard and Rodseth, 2011). It appears to have predictive value in a variety of surgical patients undergoing major surgery. Further work is required to establish cut-off values and confirm the predictive value in patient sub-groups. It may be some time before consensus is reached on how the clinician should respond to evidence of increased risk demonstrated by elevated BNP concentrations. BJHM

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