BNP and NT-proBNP in heart failure
Hogenhuis, Jochem

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2006

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Summary
Summary

The diagnostic and prognostic properties of B-type Natriuretic Peptide (BNP) and N-terminal proBNP (NT-proBNP) in patients with heart failure have been well established during the past years. Today, measurement of natriuretic peptides is frequently used in clinical practice. However, although very promising, there are several factors that might limit the diagnostic and prognostic use of these peptides. This thesis provided a critical appraisal on the benefits and limitations of the use of natriuretic peptides in heart failure patients.

The primary aims of this thesis were:
1. To assess the influence of age, renal dysfunction, anaemia, functional capacity and quality of life on levels of BNP and/or NT-proBNP.
2. To identify the independent predictors of the discharge diagnosis heart failure, and to develop an easy applicable scoring rule using these independent predictors and BNP and/or NT-proBNP levels.
3. To investigate the value of the currently available cut-off value of BNP levels for exclusion of heart failure in a setting of discharge from the hospital after admission for heart failure.

Since most studies on BNP and NT-proBNP have been performed in emergency department settings and because only little evidence is available on their usefulness in a setting of discharge after admission for heart failure, we studied BNP and NT-proBNP levels in a population of patients that were about to be discharged after admission for suspected heart failure. We described the criteria of this population, which was included in the COACH study, in chapter 2.

In healthy subjects, natriuretic peptide levels are higher with increasing age, but it remained unknown whether the same is true for patients with heart failure. In chapter 3 we described that all studied natriuretic peptides were significantly related to age (p<0.05) on multivariate regression analysis, with partial correlation coefficients of 0.18, 0.29, 0.28 and 0.25 for ANP, NT-ANP, BNP and NT-proBNP respectively. The relative increase of both BNP and NT-proBNP with age were more pronounced than the relative increase of ANP and NT-ANP with age (p<0.01). Furthermore, the relative increase of BNP with age was markedly larger than of NT-proBNP (p<0.01). Levels of all natriuretic peptides were also significantly related to cardiothoracic ratio, renal function and left ventricular ejection fraction.

Other phenomena that may possibly influence BNP and NT-proBNP levels are anaemia (by increasing plasma volume) and renal dysfunction (by decreasing clearance), although this was not been well described in heart failure patients. We therefore aimed to study the influence of anaemia and renal dysfunction on BNP and NT-proBNP levels in heart failure patients. In chapter 4 we showed that in a heart failure population of 541 patients, 30% (n=159) was anaemic (Hb<7.5 mmol/L for women and Hb<8.1 mmol/L for men). Of the 159 anaemic patients, 73% had renal dysfunction (estimated GFR <60 ml/min/1.73m²) and of the non-anaemic patients, 57% had renal dysfunction. Multivariable analysis demonstrated that both plasma haemoglobin and estimated GFR were independently related to the level of both BNP and NT-proBNP (standardized beta’s of -0.20, -0.13 [BNP] and -0.26, -0.28 [NT-proBNP] respectively, P-values <0.01).
Both BNP and the 6-minute walk test are related to severity and prognosis of heart failure. However, in chapter 5 we did not find a correlation between BNP and the 6-minute walk test, indicating that BNP and the 6-minute walk test represented different aspects of the clinical syndrome of heart failure ($r=0.01$, $P=0.87$). Further results of our study suggested that BNP plasma levels were more related to cardiac function, while the 6-minute walk test reflected functional capacity and physical dimensions of quality of life.

Early validation studies showed that 18% - 33% of patients admitted for suspected heart failure received a false-positive discharge diagnosis of heart failure. We aimed to identify the most important independent predictors of a (false) heart failure discharge diagnosis and to construct a score to improve the discharge diagnosis of heart failure (chapter 6). The outcome panel that we put together, identified 6% of our research population that was admitted for suspected heart failure ($n=540$) with a discharge diagnosis other than heart failure. Univariable predictors of the discharge diagnosis heart failure were dyspnoea at rest, absence of COPD/ asthma, absence of anaemia, renal dysfunction, BNP > 100 pg/ml and NT-proBNP > 300 pg/ml. In multivariable logistic analyses, all of these, except BNP > 100 pg/ml, remained independent predictors of a heart failure discharge diagnosis. The ROC area of a model combining these predictors was 0.78. These independent predictors were combined in a scoring rule to optimize the discharge diagnosis of these patients. This score should be validated in other populations before its use in clinical practice can be recommended.

Previous studies in acute heart failure patients presenting at the emergency department, found a BNP < 100 pg/ml in only 10% of the patients. However, in a more stable outpatient heart failure population from another study, a BNP < 100 pg/ml was found in as many as 21% of the patients. Therefore, we aimed to investigate the prevalence and characteristics of stabilized patients with BNP < 100 pg/ml before discharge after admission for heart failure. In chapter 7 we showed that in our study population consisting of clinically stable patients with a recent admission for heart failure, only 10% had BNP levels below 100 pg/ml. These patients with low BNP levels seemed to have less severe heart failure and more frequently had preserved systolic function compared to patients with BNP levels ≥ 100 pg/ml.

In chapter 8 we discussed whether different BNP and NT-proBNP cut-off values should be used in different populations, since natriuretic peptides are not only influenced by the severity of heart failure, but by several other factors as well (this thesis). On the other hand, it would be very unpractical to use many different cut-off levels for each group of patients. This means that each outcome level of BNP or NT-proBNP should be interpreted in the light of the other factors that might have influenced this value.

We also discussed the issues of whether we should use either BNP or NT-proBNP in clinical practice, and in which settings these natriuretic peptides can be used. Finally we made several recommendations for future clinically applied research on BNP and NT-proBNP in patients with heart failure.

In conclusion, BNP and NT-proBNP have important benefits in the daily management of patients with possible or established heart failure, including, as shown in this thesis, those patients discharged from hospital after admission for suspected heart failure. Besides the benefits, however, our studies also revealed important limitations that should be taken into consideration in the decision to assess BNP/ NT-proBNP levels and in the interpretation of