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Impact of history of heart failure on diagnostic and prognostic value of BNP: Results from the B-type Natriuretic Peptide for Acute Shortness of Breath Evaluation (BASEL) Study☆

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Abstract

Objectives: This study aimed to examine the influence of history of heart failure (HF) on circulating levels, diagnostic accuracy and prognostic value of B-type natriuretic peptide (BNP) in patients presenting with all cause dyspnea at the emergency department.
Background: BNP has been shown to be very helpful in diagnosis and prognosis of HF. Due to chronically elevated cardiac filling pressures, patients with a history of HF might have higher BNP levels and therefore diagnostic and prognostic properties of BNP may be affected.
Methods: We analyzed circulating levels, diagnostic accuracy and prognostic value of BNP in 388 patients without a previous history of HF and compared these to data to 64 patients with a history of HF included in the B-type Natriuretic Peptide for Acute Shortness of Breath Evaluation (BASEL) Study.
Results: Baseline BNP levels were higher in patients with a history of HF (median 814 pg/ml [353–1300 pg/ml] vs. 216 pg/ml [45–801 pg/ml], $p<0.001$). Diagnostic accuracy of BNP to identify HF was comparable in patients with (AUC=0.804; 95% CI 0.628–0.980) and in patients without history of HF (AUC=0.883; 95% CI 0.848–0.919, $p=0.389$). Prognostic ability of BNP to predict one-year mortality was lower in overall patients with history of HF (AUC=0.458; 95%CI 0.294–0.622) compared to patients without history of HF (AUC=0.710; 95% CI 0.653–0.768, $p<0.05$).
Conclusions: In patients with history of HF, BNP levels retain diagnostic accuracy. Ability to predict one-year mortality was decreased in unselected patients, but not in patients with acute HF-induced dyspnea.

Keywords: History of heart failure; BNP; Diagnostic accuracy; Prognostic value

1. Introduction

HF is a major public health problem that affects nearly 15 million people in North America and Europe, with nearly 1.5 million new cases every year [1–5]. Rapid diagnosis of HF in the emergency department (ED) is crucial for prompt and appropriate treatment but it often poses challenges, particularly in elderly or obese people and when chronic pulmonary or cardiac disease are present [6,7]. Echocardiography, which is considered as the gold standard for the detection of left ventricular dysfunction, is expensive and not ubiquitously

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available [8,9]. Misdiagnosis of HF can be life-threatening and causes increase in time to discharge and treatment costs [4].

B-type natriuretic peptide (BNP) is a marker of cardiac stress, secreted from the ventricles in response to volume expansion and pressure overload [10,11]. BNP has become a widely accepted diagnostic tool in establishing or excluding the diagnosis of HF in patients with acute dyspnea [1,4,12–15]. BNP levels have been shown to be significantly increased in patients with HF and to correlate well with severity of HF, hemodynamic state and patient prognosis [10,16–20].

Several factors such as gender, age, body habitus, cardiac rhythm, renal function, and history of cardiac or pulmonary disease have been shown to affect levels of circulating BNP [2,6,21–25]. A history of HF may be present in 15 to 30% of patients presenting with acute dyspnea to the ED [17]. Little is known regarding the diagnostic and prognostic accuracy of BNP levels in these patients.

The objective of the present study was to evaluate the impact of a history of HF on circulating levels, diagnostic accuracy and prognostic value of BNP in patients presenting with dyspnea.

2. Methods

2.1. Settings and study population

The "*B*NP for *A*cute *S*hortness of Breath *Eval*uation (BASEL)" study [1] was a prospective, randomized, controlled single-blind study, conducted in the University Hospital Basel, Switzerland, from May 2001 to April 2002. Details regarding study design have been published elsewhere [1]. In brief, 452 patients who presented to the ED with shortness of breath as primary symptom and no obvious traumatic cause of dyspnea, were randomly assigned to either a group that used the measurement of BNP levels ($n=225$) in the diagnostic work-up, or a control group that was evaluated with the use of the conventional diagnostic strategy without BNP measurements ($n=227$).

The primary endpoints of the BASEL study were time to discharge and the total cost of treatment. Secondary endpoints included in-hospital and 30-day mortality. One-year all cause mortality and morbidity, as well as economic data were assessed by telephone interview. All endpoints were assessed in a blinded fashion by physicians who were not involved in patient care, with the use of all medical records pertaining to each patient.

The main goal of the present study was to compare circulating BNP levels, diagnostic accuracy and prognostic value of BNP in patients with and without a history of HF included in the BASEL study.

2.2. Adjudication of HF history

The history of HF was adjudicated by a board-certified specialist in internal medicine not involved in patient care based on all available previous medical records pertaining to each patient, including blood tests, chest radiographs, and transthoracic echocardiography performed prior to the current presentation.

2.3. Adjudication of the final discharge diagnosis

The final discharge diagnosis was based on clinical presentation and standard investigation, and adjudicated by an internal medicine specialist not involved in the ED care on the basis of all available medical records pertaining to the individual patient, including the response to treatment and autopsy data for those patients who died in hospital.

2.4. Measurement and interpretation of BNP levels

During initial evaluation, at the time of venipuncture for routine blood tests, a venous specimen of blood (3 ml) was collected into tubes containing potassium EDTA. BNP was measured using a rapid fluorescence immunoassay (Biosite Diagnostics, La Jolla, Calif) [26].

2.5. Statistical analysis

Statistical analyses were performed using the SPSS/PC software package (version 14.0; SPSS inc., Chicago, IL, USA). Comparisons were made by the *t*-test for normally distributed continuous variables and the Mann–Whitney *U* test for non-normally distributed continuous variables. Receiver-operating characteristic (ROC) curves were drawn to quantify the ability of BNP to diagnose HF as the final diagnosis. Areas under ROC curves were compared using MedCalc software (version 9.2., MedCalc Software, Mariakerke, Belgium). Cumulative survival curves were constructed as time-to-first event plots by Kaplan–Meier survivorship methods, and differences between the curves were tested for significance by the log-rank statistic model. Continuous variables were summarized with medians and quartiles (25th and 75th percentiles), whereas frequency counts or means were given for nominal variables. A *p*-value of less than 0.05 was considered to indicate statistical significance. All hypothesis testing was two-tailed.

3. Results

3.1. Baseline characteristics

Adjudication of HF history allowed the identification of 64 patients (14%) with and 388 patients (86%) without history of HF. The baseline characteristics of the study population in the two groups were well matched and are displayed in Table 1. Patients with history of HF had a higher prevalence of pre-existing coronary artery disease (69% vs. 47%, $p<0.001$) and chronic kidney disease (39% vs. 22%, $p<0.05$). At presentation, patients with history of HF more frequently complained nocturia (44% vs. 28%, $p<0.05$) and shortness of breath at rest (36% vs. 27%, $p<0.05$). Lower-

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Table 1
Main characteristics and outcome in consecutive patients with dyspnea with and without history of heart failure (HF) irrespective of final diagnosis

	History of HF	No history of HF	*p*-value
	n=64	*n*=388	
Age (years)	72±11	70±16	0.296
Sex			0.281
Male	41 (64)	221 (57)	
Female	23 (36)	167 (43)	
Medical history			
Coronary artery disease	44 (69)	181 (47)	0.001
Arterial hypertension	38 (59)	199 (51)	0.230
Chronic obstructive lung disease	17 (27)	123 (32)	0.411
Asthma	2 (3)	27 (7)	0.135
Pneumonia	14 (22)	44 (11)	0.057
Pulmonary embolism	4 (6)	27 (7)	0.836
Other pulmonary or pleural disease	11 (17)	35 (9)	0.105
Any pulmonary disease	34 (53)	192 (50)	0.590
Depressive disorder	6 (9)	30 (8)	0.919
Stroke or peripheral vascular disease	17 (27)	72 (19)	0.179
Chronic kidney disease	25 (39)	87 (22)	0.012
Deep vein thrombosis	5 (8)	36 (9)	0.706
Symptoms			
Shortness of breath			0.011
Slight hill	3 (5)	62 (16)	
Level ground	38 (59)	219 (56)	
At rest	23 (36)	103 (27)	
Paroxysmal nocturnal dyspnea	28 (44)	138 (36)	0.209
Nocturia	28 (44)	108 (28)	0.019
Weight gain	11 (17)	40 (10)	0.173
Chest pain	26 (41)	128 (33)	0.233
Coughing	33 (52)	191 (49)	0.730
Expectoration	20 (31)	139 (36)	0.479
Fever	12 (19)	97 (25)	0.249
Vital status			
Systolic blood pressure (mm Hg)	142±32	146±28	0.338
Diastolic blood pressure (mm Hg)	83±19	86±18	0.296
Heart rate (per min)	95±24	98±24	0.357
Temperature (°C)	37.3±1.0	37.4±1.0	0.328
Signs			
Tachypnea (>20/min)	32 (50)	178 (46)	0.541
Elevated jugular venous pressure	14 (22)	50 (13)	0.105
Hepatojugular reflux	9 (14)	40 (10)	0.372
Rales	36 (56)	171 (44)	0.070
Wheezing	12 (19)	88 (23)	0.484
Hyper-resonant percussion	4 (6)	35 (9)	0.466
Dullness	5 (8)	41 (11)	0.501
Lower-extremity edema	32 (50)	124 (32)	0.009
Laboratory tests			
Haemoglobin (g/l)	128±22	136±27	0.004
Serum creatinine (μmol/l)	126±47	113±57	0.002
Serum albumin (g/l)	33±5	34±5	0.255
Troponin I (μg/l)	3.4±9.8	6.7±34.2	0.002
Laboratory tests			
B-type natriuretic peptide (pg/ml)	814 [353–1300]	216 [45–801]	<0.001
Left ventricular ejection fraction (%)[a]	39 [25–54]	50 [35–60]	0.042
Final discharge diagnosis			
Heart failure	54 (84)	169 (44)	<0.001
Obstructive pulmonary disease	4 (6)	72 (19)	0.001
Pulmonary embolism	2 (3)	19 (5)	0.534
Pneumonia	6 (9)	57 (15)	0.197
Anxiety disorder	0 (0)	16 (4)	<0.001
Other disease[b]	2 (3)	56 (14)	<0.001
Unknown cause	2 (3)	17 (4)	0.643
Outcome			
Time to treatment (min)	85 [17–180]	65 [19–177]	0.453
Hospital admission	59 (92)	303 (78)	0.009
Time to discharge (days)	12 [7–18]	9 [1–17]	0.040
Initial treatment cost ($)	5706 [3865–8444]	4784 [1150–8337]	0.346
In-hospital mortality	6 (9.4)	28 (7.2)	0.545
One-year in-hospital days	14 [8–27]	10 [2–21]	0.004
One-year treatment cost ($)	6333 [4332–13829]	5370 [1534–10524]	0.008
One-year mortality	13 (20)	55 (14)	0.076

Data are presented as mean±SD, median [IQR] or number of patients (%).
[a] Available in 217 patients.
[b] Including interstitial lung disease, pleural effusion, anemia, and sepsis.

extremity edema was also found more often in patients with history of HF (50% vs. 32%, $p<0.01$). As anticipated, patients with history of HF had a lower left ventricular ejection fraction (LVEF) (39% [25–54%] vs. 50% [35–60%], $p<0.05$).

3.2. Diagnostic accuracy of BNP

Baseline BNP levels (median 814 pg/ml [353–1300 pg/ml] vs. 216 pg/ml [45–801 pg/ml], $p<0.001$; Fig. 1), as well as creatinine levels (126±47 μmol/l vs. 113±57 μmol/l, $p<0.05$) were significantly higher in patients with history of HF. Area under the receiver operating characteristic (ROC) curves demonstrated a comparable accuracy of BNP measurements to detect acute HF in patients with history of HF (AUC=0.804; 95% CI 0.628–0.980) compared to patients without history of HF (AUC=0.883; 95% CI 0.848–0.919; $p=0.389$) (Fig. 2). Using BNP cut-points of 100 and 500 pg/ml in patients with a history of HF was associated with comparable sensitivity but decreased specificity (Table 2). In this study the optimal BNP cut point to detect HF in patients with a history of HF was 403 pg/ml with a sensitivity of 80% and a specificity of 77%

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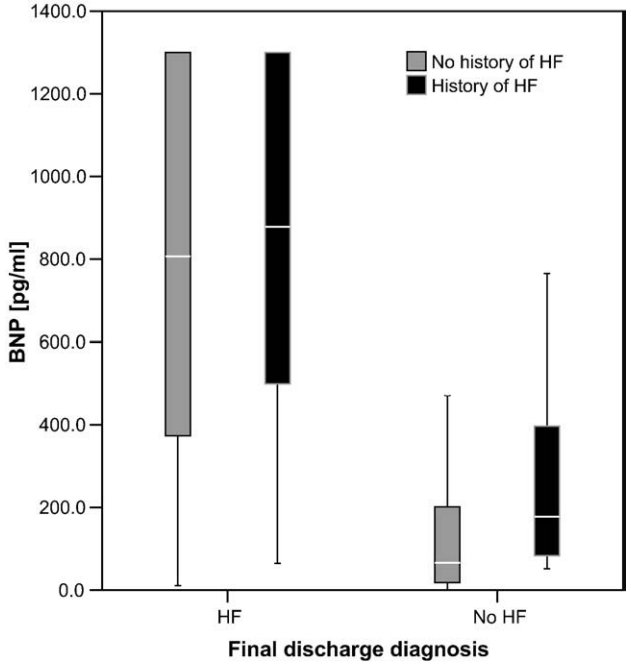

Fig. 1. Box plots showing levels of circulating B-type natriuretic peptide (BNP) among patients with and without history of heart failure stratified by final discharge diagnosis. The lines represent the median, the boxes the interquartile range, and the bars represent the 10th and 90th percentiles.

(positive likelihood ratio PLR: 3.06; negative likelihood ratio NLR: 0.25). In patients without history of HF, a BNP level of 289 pg/ml was best, with a sensitivity of 81% and a specificity of 83% (PLR 4.87; NLR: 0.22).

Table 2
Sensitivity, specificity, positive likelihood ratio and negative likelihood ratio using a BNP cut-level of 100 and 500 pg/ml in patients with and without history of HF

BNP levels [pg/ml]	History of HF	Sensitivity (%)	Specificity (%)	LR+	LR−
100	Yes	96	45	1.72	0.09
100	No	94	59	2.3	0.1
500	Yes	76	77	3.42	0.30
500	No	68	99	7.48	0.35

LR+, positive likelihood ratio; LR−, negative likelihood ratio.

3.3. Prognostic value of BNP

Area under the ROC curves demonstrated a lower accuracy of BNP measurements to predict one-year mortality in patients with a history of HF (AUC=0.458; 95%CI 0.294–0.622) compared to patients without history of HF when the final diagnosis was not considered (AUC=0.710; 95% CI 0.653–0.768, $p<0.05$) (Fig. 3). The optimal BNP cut point to predict one-year mortality in overall patients with history of HF was 1275 pg/ml with a sensitivity of 39% and a specificity of 72% (PLR 1.40; NLR 0.84). In patients without history of HF, the best BNP level to predict one-year mortality was 245 pg/ml with a sensitivity of 71% and a specificity of 60% (PLR 1.79; NLR: 0.47).

In patients with dyspnea due to acute HF ($n=223$, Table 3), accuracy of BNP measurements to predict one-year mortality by ROC curve analysis was similar in patients with a history of HF (AUC=0.502; 95%CI 0.323–0.681) compared to patients without a history of HF (AUC=0.655; 95% CI 0.564–0.747; $p=0.135$).

Using Kaplan–Maier survival analysis no difference in one-year mortality in overall patients with a history of HF

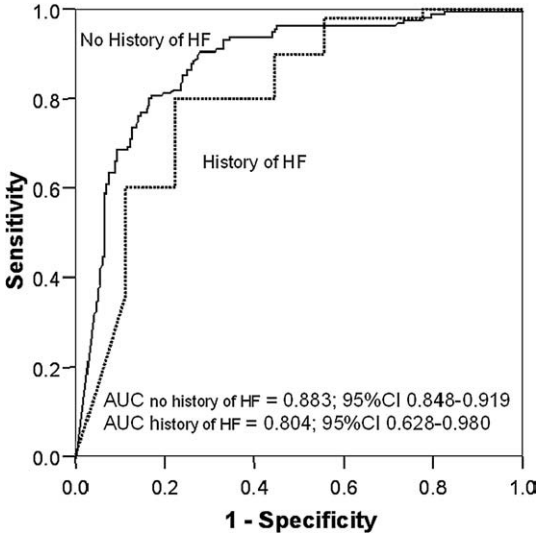

Fig. 2. Receiver-operating characteristic curves analyzing the ability of B-type natriuretic peptide levels to identify heart failure (HF) as final discharge diagnosis in patients with and without history of HF. Areas under the receiver operating characteristic curve (AUC) with 95% confidence intervals are given.

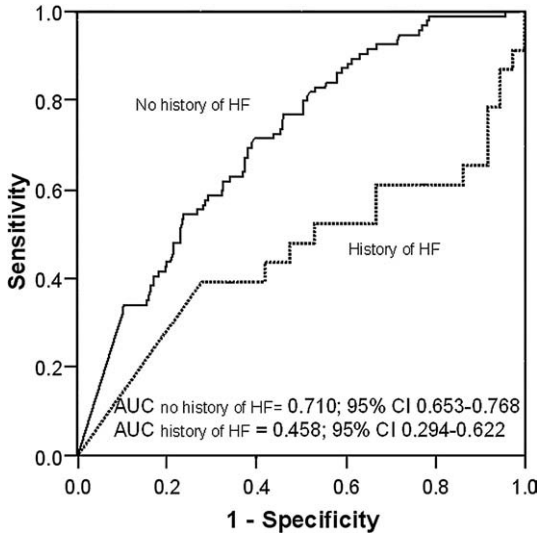

Fig. 3. Receiver-operating characteristic curves analyzing the ability of B-type natriuretic peptide levels to predict one-year mortality in patients with and without history of heart failure (HF). Areas under the receiver operating characteristic curve (AUC) with 95% confidence intervals are given.

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Table 3
Main characteristics and outcome of patients with acute heart failure induced dyspnea, with and without history of heart failure (HF)

	History of HF	No history of HF	*p*-value
	n=54	*n*=169	
Age (years)	73±11	76±11	0.093
Sex			0.434
Male	33 (61)	88 (52)	
Female	21 (39)	81 (48)	
Medical history			
Coronary artery disease	38 (70)	118 (70)	0.939
Arterial hypertension	33 (61)	109 (65)	0.653
Chronic obstructive lung disease	10 (18)	42 (25)	0.339
Asthma	1 (2)	3 (2)	0.971
Pneumonia	12 (22)	15 (9)	0.009
Pulmonary embolism	2 (4)	5 (3)	0.785
Other pulmonary or pleural disease	9 (17)	6 (4)	0.001
Any pulmonary disease	27 (50)	62 (37)	0.083
Depressive disorder	5 (9)	9 (5)	0.301
Stroke or peripheral vascular disease	14 (26)	47 (28)	0.787
Chronic kidney disease	24 (44)	63 (37)	0.348
Deep vein thrombosis	4 (7)	12 (7)	0.307
Symptoms			
Shortness of breath			0.151
Slight hill	2 (4)	24 (14)	
Level ground	33 (61)	95 (56)	
At rest	19 (35)	48 (28)	
Paroxysmal nocturnal dyspnea	25 (46)	79 (47)	0.954
Nocturia	22 (41)	67 (40)	0.886
Weight gain	10 (18)	29 (17)	0.819
Chest pain	21 (39)	66 (39)	0.983
Coughing	30 (56)	64 (38)	0.022
Expectoration	16 (30)	44 (26)	0.605
Fever	9 (17)	25 (15)	0.739
Vital status			
Systolic blood pressure (mm Hg)	136±33	147±31	0.208
Diastolic blood pressure (mm Hg)	86±20	90±21	0.162
Heart rate (per min)	95±25	94±26	0.916
Temperature (°C)	37.1±1.0	37.2±1.0	0.606
Signs			
Tachypnea (>20 per min)	26 (48)	74 (44)	0.576
Elevated jugular venous pressure	14 (26)	36 (21)	0.479
Hepatojugular reflux	8 (15)	28 (17)	0.761
Rales	32 (60)	102 (60)	0.886
Wheezing	8 (15)	23 (14)	0.824
Hyper-resonant percussion	4 (7)	13 (8)	0.945
Dullness	5 (9)	19 (11)	0.683
Lower-extremity edema	27 (50)	176 (45)	0.520
Laboratory tests			
Haemoglobin (g/l)	123±22	131±23	0.068
Serum creatinine (μmol/l)	130±50	117±71	0.478
Serum albumin (g/l)	34±5	33±6	0.666
Troponin I (μg/l)	3.8±10.5	7±24.7	0.140
Laboratory tests			
B-type natriuretic peptide (pg/ml)	878 [495–1300]	807 [372–1300]	0.360
Left ventricular ejection fraction (%)[a]	35 [25–49]	40 [30–55]	0.213
Outcome			
Time to treatment (min)	84 [19–156]	54 [18–172]	0.856
Hospital admission	49 (91)	148 (88)	0.529
Time to discharge (days)	11.5 [7–17]	11 [4–19.5]	0.856
Initial treatment cost ($)	5614 [3971–7485]	5940 [3257–9516]	0.676
In-hospital mortality	5 (9.3)	14 (8.3)	0.824
One-year in-hospital days	26 [10–44]	16 [6–31]	0.016
One-year treatment cost ($)	12024 [5982–21918]	8182 [4517–15509]	0.050
One-year mortality	19 (35)	50 (30)	0.439

Data are presented as mean±SD, median [IQR] or number of patients (%).
[a]Available in 150 patients.

could be demonstrated, when patients were stratified by tertiles of admission BNP levels ($p=0.878$ in patients with a history of HF and $p<0.0001$ in patients without a history of HF; Figs. 4 and 5).

3.4. Medical and economic outcome

The final discharge diagnosis was considerably different between the two patient groups. HF was more frequently diagnosed (84% vs. 44%, $p<0.001$) in patients with history of HF, whereas other disease including obstructive pulmonary disease (6% vs. 19%, $p<0.05$), anxiety disorder (0% vs. 4%, $p<0.001$) and anemia (14% vs. 3%. $p<0.001$) were more frequent in patients without history of HF. History of HF was associated with more frequent hospitalizations (92% vs. 78%, $p<0.01$) and prolonged initial hospitalizations (12 [7–18] days vs. 9 [1–17] days, $p<0.05$). Days in hospital at one year (14 [8–27] vs.10 [2–21], $p<0.01$) as well as total treatment costs at one year were higher in patients with history of HF (6333 USD [4332–13829] vs. 5370 [1534–10524], $p<0.01$). One-year mortality tended to be higher in patients with a history of HF (38% in patients with a history of HF vs. 26%; $p=0.053$).

4. Discussion

In this study we evaluated the diagnostic accuracy and prognostic value of BNP in patients presenting with dyspnea and a history of HF at the ED. We report following major findings. First, a total of 64 patients (14%) had a history of HF. This rate is lower than reported in the Breathing Not Property Study (14% vs. 33%)4. The discrepancy in the prevalence of history of HF in these series of consecutive

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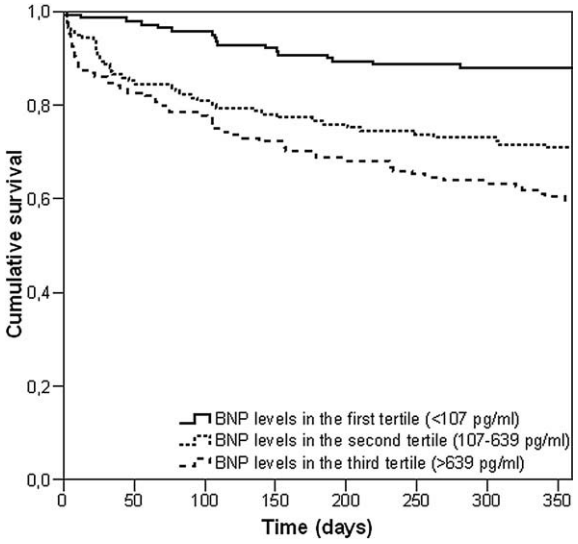

Fig. 4. Kaplan–Maier analysis showing one-year mortality in patients without a history of heart failure stratified by tertiles of admission B-type natriuretic peptide (BNP) levels ($p<0.0001$).

patients presenting with acute dyspnea, highlights the diagnostic dilemma of HF prior to the use of BNP. Second, despite similar age, patients with a history of HF had significantly higher BNP levels compared to patients without a history of HF. The accuracy of BNP measurements to identify HF by ROC curve analysis was comparable in patients with and without history of HF. Third, BNP levels were less able to predict one-year mortality in patients with a history of HF when the final diagnosis was not considered. However, in the group of patients with dyspnea due to acute HF, there was no significant difference in the ability of BNP to predict one-year mortality between those with and those without a history of HF. Fourth, patients with a history of HF represent a high-risk patient group with increased renal and cardiovascular co-morbidities. Fifth, a history of HF significantly impacts on the distribution of final discharge diagnosis. HF is the predominate cause (84%) of acute dyspnea in these patients. Sixth, patients with history of HF have significantly increased morbidity, increased mortality and increased total cost of treatment.

Given the increasing incidence of HF in western countries and the difficulty of rapidly and accurately identifying the cause of dyspnea, these findings are of considerable clinical importance. The population of patients with history of HF in this study was highly representative for the elderly population currently presenting to the ED [2,4,14]. Co-morbidity in this population was extensive and included coronary artery disease in nearly 70%, arterial hypertension in 60%, chronic kidney disease in 39%, and pulmonary disease in almost half.

The proportion of patients classified as having a history of HF in our study, is different than in other comparable studies. Januzzi et al. in the PRIDE and ICON studies examined data from 600 and 1256 patients respectively presenting to the ED with dyspnea [27,28]. In PRIDE and ICON, 25% and 33% of patients respectively had a history of HF, whereas only 14% of our patients did. As mentioned above, this discrepancy emphasizes difficulties in the diagnosis of HF prior to the introduction of BNP testing.

In our study, 84% of patients with a history of HF had a final discharge diagnosis of acute HF after presenting with an episode of dyspnea, whereas only 44% of patients without a history of HF were classified as having acute HF. In a post-hoc analysis of the Breathing Not Properly Multinational Study comparable results could be demonstrated [17]. In this study, 67% of patients with a history of HF had HF as the primary complaint vs. 45% without history of HF ($p<0.05$). Chung et al. reported 80% of patients with a HF history were subsequently diagnosed with HF compared with 28% of patients without a history of HF ($p<0.001$) [29]. These data confirm the strong predictive character of history of HF on the final diagnosis of acute HF.

In recent years, several studies have demonstrated to what extent patient prognosis is affected by HF [30,31]. Our data corroborate and extend these important findings, demonstrating higher hospitalization rates and longer initial hospital stay in patients with a history of HF. Despite major improvements in medical therapy for HF during the past decade, patients with a history of HF in our study spent more days in hospital at one year and accumulated significantly higher treatment costs. There was also a strong trend to a higher one-year-mortality in patients with a history of HF, underlining the negative impact of history of HF on patient outcome.

In accordance with other studies [16,29,32], patients with a history of HF in our cohort presented with significantly higher circulating levels of BNP compared to patients without a history of HF. This finding can be explained by

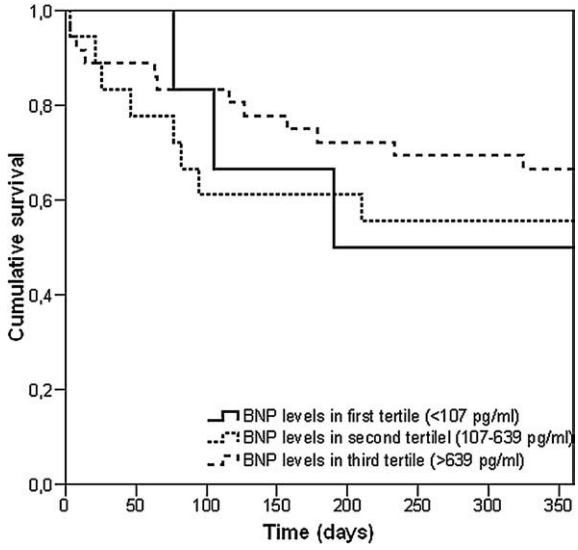

Fig. 5. Kaplan–Maier analysis showing one-year mortality in patients with a history of heart failure stratified by tertiles of admission B-type natriuretic peptide (BNP) levels ($p=0.878$).

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chronically elevated cardiac filling pressures and consequent higher "dry BNP levels" in this patient group. This presumption is supported by a reduced LVEF demonstrated in patients with a history of HF in our cohort (39% vs. 50%; $p<0.05$). Chronically elevated levels of BNP may lead to a false positive diagnosis of HF in patients presenting with dyspnea of non-cardiac origin, particularly when co-morbidities such as chronic pulmonary disease are present. Chung and colleagues analyzed data from 143 patients with or without a history of HF presenting to the ED with dyspnea [29]. In this study the accuracy of BNP to predict HF was substantially impaired in patients with a history of HF. Area under the ROC curves for BNP to predict HF was 0.74 for patients with a history of HF and 0.94 for patients without a history of HF ($p<0.01$). In our study, the difference between the AUC was not statistically significant, but a trend towards a lower AUC was present. The likeliest explanation for this finding is the difference between the proportions of patients classified as having a history of HF in the two studies (14% in our study vs. 56% in Chang et al.'s study.) [4,13,19]. A more rigorous adjudication of prior HF diagnosis may have been performed in our study. Of course regional and seasonal differences in patient recruitment and the smaller number of included patients in our study may also have contributed to this finding.

BNP levels at the time of admission to hospital have been demonstrated to be a powerful predictor of death in patients presenting with acute dyspnea, irrespective of the final discharge diagnosis [33]. The present study demonstrated that admission BNP levels are less able to predict one-year mortality in patients with a history of HF compared to patients without history of HF, when the final diagnosis was not considered. However, in patients admitted with dyspnea due to acute HF, BNP predicted outcome similarly in patients with or without a history of HF. One possible explanation for the lower ability of admission BNP levels to predict one-year mortality in overall patients with history of HF, might be related to the independently of the existence of acute HF, chronically elevated levels of natriuretic peptides in this patient group [32].

Accordingly, further studies are needed to assess the role of new biomarkers either alone or in combination with BNP to predict outcome in patients admitted in the ED with dyspnea and a history of HF. Noteworthy, BNP levels do retain prognostic significance when they are determined during the stable phase of HF [34].

5. Limitations

Several limitations to our study need to be mentioned. First, this is a post hoc analysis of a randomized, controlled trial. Second, BNP levels were available for the final discharge diagnosis in 50% of the patients. Therefore, our analysis might slightly overestimate the accuracy of BNP to diagnose HF in 50% of patients. However, this bias should have equally affected patients with and without history of HF. Therefore the comparison between the two patient groups is still valid.

6. Conclusions

Patients with acute dyspnea and a history of HF represent a high-risk patient group with extensive renal and cardio-vascular co-morbidity, a very high rate of HF as the discharge diagnosis, and increased one-year morbidity and mortality. In patients with a history of HF, BNP levels retain diagnostic accuracy. Ability to predict one-year mortality was diminished in unselected patients, but not in patients with dyspnea due to acute HF.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [35].

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