Use of Myeloperoxidase for Risk Stratification in Acute Heart Failure

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BACKGROUND: Myeloperoxidase (MPO) is a biomarker of inflammation and oxidative stress produced by neutrophils, monocytes, and endothelial cells. Concentrations of MPO predict mortality in patients with chronic heart failure. This study sought to investigate the diagnostic accuracy and prognostic value of MPO in patients with acute heart failure (AHF).

METHODS: We prospectively enrolled 667 patients presenting to the emergency department with dyspnea and observed them for 1 year. MPO and B-type natriuretic peptide (BNP) were measured at presentation. Two independent cardiologists adjudicated final discharge diagnoses.

RESULTS: MPO concentrations were similar in patients with AHF (n = 377, median 139 pmol/L) and patients with noncardiac causes of dyspnea (n = 290, median 150 pmol/L, P = 0.26). The diagnostic accuracy of MPO for AHF was limited [area under the ROC curve (AUC) 0.53] and inferior to that of BNP (AUC 0.95, P < 0.001). In patients with AHF, MPO concentrations above the lowest tertile (MPO >99 pmol/L) were associated with significantly increased 1-year mortality (hazard ratio 1.58, P = 0.02). The combination of MPO (<99 vs >99 pmol/L) and BNP (median of ≤847 vs >847 ng/L) improved the prediction of 1-year mortality (hazard ratio 2.80 for both variables increased vs both low, P < 0.001). After adjustment for cardiovascular risk factors in multivariable Cox proportional hazard analysis, increases in MPO contributed significantly toward the prediction of 1-year mortality (hazard ratio 1.51, P = 0.045).

CONCLUSIONS: MPO is an independent predictor of 1-year mortality in AHF, is additive to BNP, and could be helpful in identifying patients with a favorable prognosis despite increased BNP concentrations.

Heart failure is a major and ever-growing public health problem, resulting in enormous numbers of hospital admissions, rehospitalizations, and deaths (1). The high costs associated with the clinical management of heart failure further highlight the need for optimal assessment and risk stratification. Aside from patient history and clinical examination, biomarkers may provide complementary information for appropriate allocation of therapy and patient management (2). Strategies using B-type natriuretic peptide (BNP),4 a marker of myocyte stress, have been shown to improve patient management in the emergency department and risk stratification in patients hospitalized for acute heart failure (AHF) (3, 4). Although it is widely accepted that patients with low BNP concentrations have a good prognosis, low BNP concentrations are rare in AHF patients. Identification and risk stratification in patients who, despite having an increased BNP, still may have a good prognosis would be highly desirable.

Neutrophil activation and inflammation are important in the pathogenesis and progression of many forms of heart failure (5). Myeloperoxidase (MPO) is released from activated neutrophils and monocytes during inflammation (6). The production of MPO has recently been demonstrated in endothelial cells in response to oxidative stress (7). MPO contributes to vascular inflammation by depletion of vascular nitric oxide (NO) with ensuing endothelial dysfunction, as well as by promotion of LDL oxidation (8–10). In patients with acute coronary syndrome, MPO plasma concen-

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4 Nonstandard abbreviations: BNP, B-type natriuretic peptide; AHF, acute heart failure; MPO, myeloperoxidase; NO, nitric oxide; BASEL, Basics in Acute Shortness of Breath Evaluation; eGFR, estimated glomerular filtration rate; IQR, interquartile range; AUC, area under the ROC curve; NYHA, New York Heart Association; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; ADHERE, Acute Decompensated Heart Failure National Registry.
trations were shown to be increased and to predict prognosis (11, 12). Similarly, MPO concentrations were found to be increased in stable chronic heart failure patients (13, 14) and predictive of adverse clinical outcomes (14, 15). The role of MPO in AHF patients is largely unknown. The aim of our study was to investigate the diagnostic accuracy of MPO for AHF and its value for risk stratification in patients with AHF.

Materials and Methods

SETTING AND STUDY POPULATION
The Basics in Acute Shortness of Breath Evaluation (BASEL) V study was a prospective observational study enrolling unselected patients presenting to the emergency department of the University Hospital of Basel, Switzerland, with a chief complaint of acute dyspnea. From April 2006 to March 2008, 684 patients were enrolled prospectively (of 762 patients screened). Exclusion criteria included age <18 years, an obvious traumatic cause of dyspnea, cardiogenic shock, severe renal disease defined by hemodialysis, and request for an early transfer to another hospital. Of the 684 patients, 667 had complete MPO data on admission and made up the study population. We carried out the study according to the principles of the Declaration of Helsinki, and it was approved by the local ethics committee. Written informed consent was obtained from all participating patients.

ADJUDICATION OF THE FINAL DISCHARGE DIAGNOSIS
Two independent cardiologists who were blinded to concentrations of MPO made an adjudicated final discharge diagnosis using all available medical records pertaining to the patient (including results of standard investigations, response to therapy, and autopsy data in those patients who died during their hospital stay). The diagnosis of AHF followed the guidelines of the European Society of Cardiology (16).

BLOOD SAMPLING AND LABORATORY METHODS
Upon each patient’s presentation to the emergency department, blood samples were collected into tubes containing potassium EDTA. Samples were immediately centrifuged and kept frozen at −80 °C until their analysis in a single batch. We measured MPO using a 2-step chemiluminescent microparticle immunoassay on the Architect system (Abbott Laboratories). The detection limit as reported by the manufacturer was 20 pmol/L, and the assay was linear to 10 000 pmol/L. Expected values were determined through a reference interval study conducted in 400 apparently healthy individuals (200 men and 200 women, 44% of whom were >40 years of age). Mean (SD) concentrations of MPO were 128.5 (85.5) pmol/L [135 (103) pmol/L in men, 122 (64) pmol/L in women]. The 95th and 99th percentiles of MPO concentrations in healthy individuals were 286 and 527 pmol/L, respectively. Accuracy in spike/recovery experiments ranged from 92.4% to 111.8%. Intra- and interday CVs were found to be in the ranges of 1.7%–7.6% and 3.1%–9.8%, respectively (17). We measured the concentration of BNP in EDTA plasma using the AxSYM BNP assay (Abbott Laboratories). The analytical measurement range as reported by the manufacturer extends from 15 to 20 000 ng/L for the AxSYM assay. We calculated the estimated glomerular filtration rate (eGFR) using the abbreviated 4-variable Modification of Diet in Renal Disease study equation (18).

ENDPOINTS AND FOLLOW-UP
All-cause mortality during 12 months of follow-up was the primary endpoint. Patients were contacted for a telephone interview regarding vital status and recurrent hospitalizations performed by trained researchers blinded to the results of laboratory testing. In case of uncertainties regarding vital status, we contacted referring physicians and administrative databases of the patients’ places of residence.

STATISTICAL ANALYSIS
Categorical variables are expressed as number (percentage) and continuous variables as mean (SD) or median (interquartile range [IQR]). We made comparisons between groups using the Student t-test, χ2 test, Mann–Whitney U-test, Wilcoxon test, and Kruskal–Wallis test as appropriate. We assessed correlations using Spearman rank-correlation coefficients. We calculated ROC curves for MPO and BNP in the diagnosis of AHF performed and comparison of areas under the ROC curves (AUCs) as recommended by DeLong et al. (19). We performed Kaplan–Meier analysis for survival and used log-rank values to assess statistical significance. We used Cox proportional hazard models to calculate hazard ratios and 95% CIs of predictors of 1-year mortality. We adjusted the initial model for MPO and BNP; in a second step, we further adjusted for cardiovascular risk factors (age, sex, body mass index, hypertension, diabetes mellitus, smoking status, coronary artery disease, previous MI, and history of heart failure) as well as for New York Heart Association (NYHA) classification at admission. The final model was also adjusted for eGFR, urea nitrogen, and uric acid, all of which have been shown to predict outcome in patients with AHF (20, 21). All hypothesis testing was 2-tailed, and a P value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS/PC version 15.0 (SPSS) and MedCalc 9.6.4.0 (MedCalc Software).
Results

VALUE OF MPO AT PRESENTATION FOR THE DIAGNOSIS OF AHF
Baseline characteristics of 667 patients with acute dyspnea are presented in Table 1. AHF was the adjudicated discharge diagnosis in 377 patients (57%). Among the noncardiac causes of dyspnea, an exacerbation of chronic obstructive pulmonary disease (COPD) or asthma was present in 15% of patients, pneumonia or bronchitis in 11%, pulmonary embolism in 3%, anxiety disorders in 3%, and other causes such as malignancy, interstitial lung disease, or anemia in 11%.

At presentation, median MPO concentration was 143 pmol/L (IQR 88–233 pmol/L). No statistically significant differences were found in median concentrations of MPO with respect to the adjudicated diagnosis [AHF, median 139 pmol/L (IQR 87–225 pmol/L) vs noncardiac causes of dyspnea, median 150 pmol/L (IQR 90–266 pmol/L), P = 0.26]. Consequently, the diagnostic accuracy for the diagnosis of AHF as assessed by ROC curve analysis was poor for MPO (AUC 0.53) and inferior to that for BNP (AUC 0.95, P < 0.001 for comparison).

CORRELATES OF MPO AT PRESENTATION IN AHF
Median MPO concentrations were higher in women compared with men [152 pmol/L (IQR 95–247 pmol/L) vs 121 pmol/L (IQR 91–177 pmol/L), P = 0.03]. No differences were observed in median MPO concentrations between patients with known coronary artery disease (CAD) compared to those without CAD [121 pmol/L (IQR 83–212 pmol/L) vs 148 pmol/L (IQR 91–232 pmol/L), P = 0.15] and between patients in NYHA classes II [138 pmol/L (IQR 75–229 pmol/L)], III [140 pmol/L (IQR 91–221 pmol/L)], and IV [135 pmol/L (IQR 87–233 pmol/L), P = 0.32]. Concentrations of MPO were lower in diabetic patients than in nondiabetic individuals [120 pmol/L (IQR 78–206 pmol/L) vs 149 pmol/L (IQR 91–233 pmol/L), P = 0.04]. Concentrations of MPO were significantly associated with total leukocyte count (r = 0.36, P < 0.001), absolute and relative neutrophil count (r = 0.32, P < 0.001 and r = 0.18, P < 0.001), C-reactive protein concentration (r = 0.30, P < 0.001), and BNP concentration (r = −0.15, P = 0.005). Conversely, no significant correlations were found with age (r = 0.09, P = 0.07), body mass index (r = 0, P = 0.96), or renal function as estimated by eGFR (r = −0.05, P = 0.32).

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Table 1. Baseline characteristics of the patients.a

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>AHF</th>
<th>No AHF</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>667</td>
<td>377</td>
<td>290</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>76 (64–83)</td>
<td>79 (72–84)</td>
<td>69 (56–78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>353 (53)</td>
<td>200 (53)</td>
<td>153 (53)</td>
<td>0.94</td>
</tr>
<tr>
<td>History</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>452 (68)</td>
<td>282 (75)</td>
<td>170 (59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>151 (23)</td>
<td>110 (29)</td>
<td>41 (14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoking</td>
<td>152 (23)</td>
<td>71 (19)</td>
<td>81 (28)</td>
<td>0.005</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>212 (32)</td>
<td>166 (44)</td>
<td>46 (16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>111 (17)</td>
<td>87 (23)</td>
<td>24 (8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>202 (30)</td>
<td>171 (45)</td>
<td>31 (11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA classification</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Class II</td>
<td>85 (13)</td>
<td>27 (7)</td>
<td>58 (20)</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>279 (42)</td>
<td>163 (43)</td>
<td>116 (40)</td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>303 (45)</td>
<td>187 (50)</td>
<td>290 (40)</td>
<td></td>
</tr>
<tr>
<td>Vital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>91 (76–107)</td>
<td>90 (72–110)</td>
<td>92 (80–105)</td>
<td>0.55</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>140 (123–160)</td>
<td>137 (118–157)</td>
<td>142 (126–162)</td>
<td>0.006</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>84 (72–96)</td>
<td>83 (71–96)</td>
<td>85 (75–95)</td>
<td>0.24</td>
</tr>
<tr>
<td>Body mass index</td>
<td>25.4 (22.2–29.4)</td>
<td>25.6 (23.0–29.4)</td>
<td>24.9 (21.2–29.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73m²</td>
<td>72 (48–96)</td>
<td>58 (39–82)</td>
<td>86 (66–117)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

a Data are median (IQR) or n (%).
Information from 1-year follow up was available in 98.4% of AHF patients, with a 1-year mortality rate of 35% (130 deaths). As shown in Fig. 1, higher mortality rates were observed when MPO concentrations at presentation were in the second (99–190 pmol/L, 37% mortality) and third (>190 pmol/L, 39% mortality) tertiles of MPO compared with the first tertile (≤99 pmol/L, 28% mortality, \(P = 0.058\) by log-rank test). In univariate Cox regression analysis, the calculated hazard ratio for patients in the second and third tertiles of MPO was 1.58 (95% CI 1.08–2.31, \(P = 0.02\)) compared with patients in the first tertile.

BNP similarly predicted 1-year mortality, with a hazard ratio of 2.03 (95% CI 1.43–2.87, \(P < 0.001\)) for patients with BNP concentrations above the median (847 ng/L) at presentation compared with patients below the median. The combination of MPO (≤99 pmol/L vs >99 pmol/L) and BNP (≤847 vs >847 ng/L) improved the prediction of 1-year mortality, which was 53.4% in patients with increased values of both BNP and MPO compared with 25.5% in patients with low concentrations of both BNP and MPO (hazard ratio 2.80, \(P < 0.001\)) (Fig. 2). In bivariable analysis, both markers were independent predictors of 1-year mortality (Table 2). Within the first year after presentation, there were 59 heart failure hospitalizations, resulting in a combined endpoint of death or heart failure hospitalization in 169 patients (45%) after 1 year. Rates for the combined endpoint showed a non-significant increase from 42% in the first tertile to 45% in the second and 48% in the third tertile of MPO (\(P = 0.47\)).

**Value of MPO and BNP in Prediction of 1-Year Mortality in AHF**

After multivariable adjustments for cardiovascular risk factors (age, sex, body mass index, hypertension, diabetes mellitus, smoking status, coronary artery disease, previous myocardial infarction, and history of heart failure) as well as for NYHA class at admission, increases in MPO remained a significant predictor of 1-year mortality (hazard ratio 1.52, 95% CI 1.03–2.24, \(P = 0.035\)) (Table 2). In a third model adjusted further for eGFR, urea nitrogen, and uric acid, increases in MPO invariably remained an independent predictor of 1-year mortality (hazard ratio 1.51, 95% CI 1.01–2.26, \(P = 0.045\)) (Table 2).

In the subgroup of patients with CAD, the increase in risk of death in patients in the upper 2 tertiles of MPO was not statistically significant, with a hazard ratio of 1.24 (95% CI 0.74–2.07, \(P = 0.42\)), whereas the risk of death was significantly increased in the top 2 MPO tertiles of patients with AHF but without known CAD (hazard ratio 2.08, 95% CI 1.16–3.72, \(P = 0.01\)).

**Discussion**

The initial assessment and risk stratification of patients with AHF and, more generally, patients with acute dys-
pnea is of great importance in the emergency department to guide subsequent implementation of the optimal patient management and medical treatment regimen. This prospective study examined the value of MPO for diagnosis and risk stratification in AHF. We report 2 major findings. First, because MPO concentrations were found to be similar in patients with AHF and patients with noncardiac causes of dyspnea, MPO was not helpful in the diagnosis of AHF. Second, MPO concentrations were found to independently predict 1-year mortality in patients with AHF and to improve the risk stratification provided by BNP through identification of patients with a good prognosis despite increased BNP concentrations.

These findings are of great importance, as they complement and corroborate current knowledge on the role of MPO in heart failure and may lead to better understanding of its interpretation in heart failure patients. A growing amount of evidence suggests mechanistic links between MPO, inflammation, and adverse cardiac effects (8, 11, 12, 14, 15). The sources of MPO in acute cardiac conditions such as acute heart failure are poorly known. Although MPO was known to be released from activated neutrophils and monocytes during inflammation, it has recently been shown that MPO is also produced directly in endothelial cells in response to oxidative stress (7). The detrimental effects of MPO in heart failure may be manifold—among other effects, MPO has been shown to deplete endothelial-derived NO, resulting in endothelial dysfunction (8, 9, 22, 23), and in experiments using MPO knockout mice, MPO-generated toxic oxidants directly promoted adverse ventricular remodeling after myocardial infarction (24, 25).

In several clinical studies including patients with heart failure, activation of polymorphonuclear cells with increases in plasma concentrations of MPO as well as markers of oxidative stress have been shown (13, 14, 26, 27). MPO has received growing interest after the observation that concentrations of MPO predict event-free survival in chronic heart failure patients (14, 15) as well as developing heart failure in healthy subjects (28, 29). These findings were challenged recently by the study of Shah et al. (30), who investigated patients with acute dyspnea and found a lack of diagnostic and prognostic utility of MPO concentrations at admission in patients with and without AHF.

**Table 2. Predictors of 1-year mortality in patients with acute heart failure: multivariable Cox proportional hazard analysis (significant predictors only).**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: MPO and BNP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BNP, divided by median</td>
<td>2.24</td>
<td>1.58–3.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MPO, higher tertiles vs first tertile</td>
<td>1.60</td>
<td>1.09–2.34</td>
<td>0.017</td>
</tr>
<tr>
<td>Model 2: additionally adjusted for cardiovascular risk factors&lt;sup&gt;a&lt;/sup&gt; and NYHA classification at admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, per year</td>
<td>1.05</td>
<td>1.03–1.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA classification, per class</td>
<td>1.75</td>
<td>1.28–2.39</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index, per increase of 1 unit</td>
<td>0.94</td>
<td>0.90–0.98</td>
<td>0.003</td>
</tr>
<tr>
<td>Sex, female</td>
<td>0.59</td>
<td>0.41–0.85</td>
<td>0.005</td>
</tr>
<tr>
<td>BNP, divided by median</td>
<td>1.65</td>
<td>1.15–2.37</td>
<td>0.007</td>
</tr>
<tr>
<td>MPO, higher tertiles vs first tertile</td>
<td>1.52</td>
<td>1.03–2.24</td>
<td>0.035</td>
</tr>
<tr>
<td>Model 3: additionally adjusted for eGFR, urea nitrogen, and uric acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, per year</td>
<td>1.04</td>
<td>1.02–1.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA classification, per class</td>
<td>1.70</td>
<td>1.24–2.33</td>
<td>0.001</td>
</tr>
<tr>
<td>Body mass index, per increase of 1 unit</td>
<td>0.93</td>
<td>0.89–0.97</td>
<td>0.002</td>
</tr>
<tr>
<td>Sex, female</td>
<td>0.56</td>
<td>0.39–0.81</td>
<td>0.002</td>
</tr>
<tr>
<td>EGFR, &lt;60 mL/min/1.73m²</td>
<td>1.65</td>
<td>1.05–2.61</td>
<td>0.031</td>
</tr>
<tr>
<td>MPO, higher tertiles vs first tertile</td>
<td>1.51</td>
<td>1.01–2.26</td>
<td>0.045</td>
</tr>
</tbody>
</table>

<sup>a</sup> Cardiovascular risk factors incorporated in models 2 and 3 included age, sex, body mass index, hypertension, diabetes mellitus, smoking status, coronary artery disease, previous MI, and history of heart failure.
In the present study, patients with acute dyspnea presenting to the emergency department regardless of the presence of AHF or a noncardiac cause of dyspnea had no differences in MPO concentrations. This finding is well in line with those of Shah et al. (30) for patients with acute dyspnea. Among non-AHF patients, COPD, asthma, pneumonia, and bronchitis are the most common causes of dyspnea, all of which have been associated with increases in MPO (31–33). Because these disorders are all associated with acute shortness of breath and the release of MPO, this biomarker may not be best suited to aid in the diagnosis of AHF.

Similar to observations in patients with stable chronic heart failure (14, 15), however, MPO was found to be a significant predictor of 1-year mortality in the 377 AHF patients in the present study, independent of other cardiovascular risk factors. Because various stimuli may cause elevations of MPO, the incremental value of MPO is in the identification of patients at low risk (MPO in the lowest tertile) despite having other risk factors such as increased BNP concentrations. Interestingly, the information provided by MPO seems to differ from many other biomarkers, in that risk stratification of mortality seems to differ between the first tertile and the higher tertiles, a finding that was also observed in chronic heart failure patients (15). Therefore, the association between the underlying pathophysiological processes quantified by MPO concentrations and mortality do not seem to be continuous. Although this observation is not of concern for the use of MPO in the risk stratification of AHF patients, it may make difficult the potential therapeutic interventions targeting the underlying pathophysiological mechanisms. Interestingly, statin therapy resulted in a significant reduction of MPO concentrations in a randomized study conducted in stable chronic heart failure patients (34).

There are 4 potential explanations for the discrepancy of the major finding of this study compared to the aforementioned study by Shah et al. (30) in patients with acute dyspnea that found no prognostic role for MPO in patients with AHF. First, the baseline characteristics of the studied populations differed substantially. Patients in the study of Shah et al. were younger (mean age 61 years) and 57% were African American with a strong dominance of hypertensive heart disease, factors which are markedly different from our study or large registries of AHF patients such as the Acute Decompensated Heart Failure National Registry (ADHERE) (35) or the EuroHeart Failure survey program (36). Second, the AHF cohort studied in the present study was more than 2 times larger (n = 377 vs 147), and the mortality rate after 1 year was markedly higher (35% vs 12%), resulting in a much higher statistical power to detect a real prognostic role of MPO in AHF patients. Third, the noncontinuous relationship between MPO and mortality observed in the chronic heart failure population (15) as well as in our AHF population suggests that comparison of tertiles might be more appropriate than analysis according to continuous MPO concentrations or MPO concentrations divided by the median. Fourth, the assays used in the 2 studies were different (Abbott Architect MPO vs Siemens Dimension RxL), which might have contributed at least in part to the different results. It is critical to note that both assays are immunoassays that measure MPO values in EDTA plasma, and both were developed on the basis of the former PrognostiX CardioMPO assay (37).

Potential limitations of the current study merit consideration. First, data derived from a single-center study always need to be replicated in larger multicenter studies. However, because our patient demographics were highly comparable to recent multicenter studies enrolling patients with acute dyspnea (38, 39), as well as to large registries of AHF patients (35, 36), we consider our results to be representative. Second, we assessed all-cause mortality because classification of death in clinical practice can sometimes be difficult and unreliable (40). However, exact numbers of all different causes of death could have provided interesting insights into the pathophysiological role of MPO. Third, we do not have subsequent MPO concentrations in our patients following recompensation. The serial changes of MPO over time in patients with stable chronic heart failure as well as in acute decompensation of heart failure should be assessed in future studies to learn more about the intraindividual variability of MPO in HF patients.

In conclusion, our study showed that MPO plasma concentrations at presentation were similar in patients with AHF and patients with noncardiac causes of dyspnea. In patients with AHF, MPO provided independent and incremental prognostic information. This information could be particularly helpful in the identification of patients with a favorable prognosis despite increased BNP concentrations.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.
Myeloperoxidase in Acute Heart Failure

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