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Original article

Validation of lactate level as a predictor of early mortality in acute decompensated heart failure patients who entered intensive care unit

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ABSTRACT

Background: The significance of routine measurement of lactate level is unclear in patients with critical acute decompensated heart failure (ADHF).
Methods and results: Consecutive 754 patients who were admitted to the intensive care unit (ICU) in our hospital from January 2007 to March 2012 and given a diagnosis of ADHF were eligible for retrospective entry into the registry. Lactate level was measured on admission from routine arterial blood sample and we investigated by comparing the lactate level and parameters of conventional in-hospital mortality predictors. Among the patients, 88 (12%) died during hospitalization. The lactate level had great power to predict in-hospital mortality, as suggested by the *c*-statistics of 0.71. The occurrence of in-hospital death was more pronounced in patients with high levels of lactate (>3.2 mmol/l) and the tendency was observed in patients in both the acute coronary syndrome (ACS) group and non-ACS group. In multivariate analysis, elevated lactate levels remained an independent predictor of in-hospital death (odds ratio, 2.14; 95% confidence interval, 1.10–4.21; $p = 0.03$).
Conclusions: Elevated levels of arterial lactate on admission were related to worse in-hospital mortality in patients with ADHF either with or without ACS, suggesting that the presence of high lactate in patients who enter the ICU with ADHF could help stratify the initial risk of early mortality.

Introduction

Heart failure has emerged over the past few decades as a major public health problem, with rising prevalence [1]. Among heart failure patients, visits to the emergency room are reportedly a common occurrence and the majority of patients who present to the emergency room with acute decompensated heart failure (ADHF) syndrome are admitted to hospital [2,3]. Better understanding of the pathophysiology and more evidence of risk stratification in patients with ADHF are required.

In patients with ADHF, evaluation of the degree of decompensation, especially the adequacy of tissue perfusion, is important [4]. In extreme cases, a marked tissue hypoperfusion due to low cardiac output leads to impaired tissue oxygenation and elevation of lactate. The use of lactate level for risk assessment has been evaluated for acute myocardial infarction [5,6], but the significance of lactate level in the setting of ADHF has not been adequately addressed. We investigated whether lactate level on admission in patients with ADHF is related to early outcomes.

Methods

Eight hundred consecutive patients who were admitted to the intensive care unit (ICU) in our hospital from January 2007 to March 2012 and given a diagnosis of ADHF were eligible for retrospective entry into the registry. ADHF was diagnosed according to the Framingham criteria [7]. Patients were excluded if blood gas analysis on admission was not available ($n = 35$) or if cardiopulmonary arrest occurred on admission ($n = 11$) (Fig. 1).

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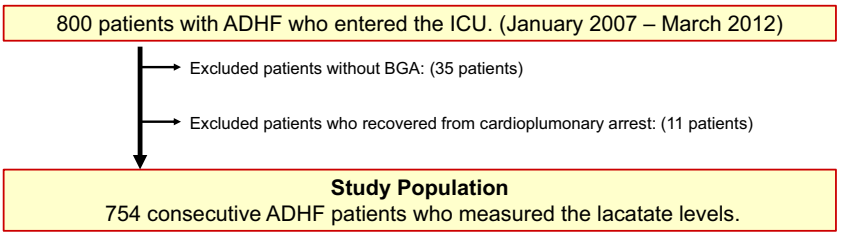

Fig. 1. Patient flowchart for the present study. ADHF, acute decompensated heart failure; ICU, intensive care unit; BGA, blood gas analysis.

This left a total of 754 patients for inclusion, and their patient demographics, medical history, clinical presentation, laboratory results, treatment course, and clinical outcomes data were collected by chart review. The study method was reviewed and approved by the institute research ethics committee.

Patient measures and definition

The primary endpoint in this study was in-hospital death. All patients underwent an initial clinical assessment that included taking a clinical history, a physical examination, 12-lead electrocardiogram (ECG), continuous ECG monitoring, pulse oximetry, standard blood measurements, echocardiography, and chest radiography. A routine arterial blood sample was also obtained immediately on presentation to the emergency room, and lactate level was measured in the same specimen. Lactate was measured within 5 min on an ABL 800 series analyzer (Radiometer, Copenhagen, Denmark) with a lower detection limit of 0.1 mmol/l. Left ventricular ejection fraction (LVEF) was measured at the time of admission via trans-thoracic echocardiography using the Simpson method. Duration of both ICU stay and hospital stay were recorded in days. Mechanical ventilation and mechanical circulatory support were also recorded. To determine the etiology of heart failure for each patient, all the available medical records (the clinical history, findings on physical examination, and results of laboratory tests, radiologic studies, ECG, echocardiography, cardiac stress testing, coronary computed tomography angiogram, and coronary angiography) were reviewed. An acute myocardial infarction (AMI) was defined in accordance with current guidelines [8]. In brief, an AMI was diagnosed when there was evidence of myocardial necrosis in association with clinical signs of myocardial ischemia with at least one of the following: symptoms typical for ischemia, new ECG change indicative of new ischemia, and/or imaging evidence of new regional wall motion abnormality. Necrosis was diagnosed on the basis of the cardiac troponin level, with at least one value above the 99th percentile. Among AMI patients, those with Killip classification I were not included. All the cases diagnosed as ACS were confirmed by coronary angiogram. Renal failure was defined as estimated glomerular filtration rate (eGFR) < 30 ml/min per 1.73 m^2 according to the Modification of Diet in Renal Disease study equation modified for Japanese patients [9]. Positive inotropic therapy included continuous intravenous administration of catecholamine or phosphodiesterase III inhibitor, and digitalis use was not included.

Statistical analysis

Categorical variables are presented as counts and/or percentages in Tables 1–3 and were compared using the chi square test. Continuous variables are expressed as mean ± standard deviation unless otherwise indicated, and were compared using the Student *t*-test or Wilcoxon rank sum test on the basis of their distributions. Receiver operating characteristic (ROC) curves were constructed to assess the cut off point of lactate levels obtained at presentation and we inferred their ability to predict the outcomes. Mortality after the initial admission including death events that occurred after discharge was analyzed using the Kaplan–Meier method and the log-rank test. We used the logistic regression model to make adjusted comparisons with and without elevation of lactate levels for in-hospital death. All the variables in Table 3 were dichotomized by clinically meaningful thresholds using ROC curves for death and were used as potential risk-adjusting variables, and we selected those variables with a univariate p-value <0.05 for the multivariate model. Because B-type natriuretic peptide (BNP) and troponin-I had missing values that cannot be ignored, these factors were separately analyzed in subanalyses.

All the reported p-values are two-sided and p-values <0.05 were regarded as statistically significant. We conducted all the statistical analyses using JMP version 10.0 software (SAS Institute, Inc., Cary, NC, USA).

Results

Patient characteristics

Patient characteristics are presented in Table 1. Among the total study population, 388 (52%) were ACS patients and 368 (48%) were non-ACS patients. Among non-ACS patients, 170 (46%) had chronic coronary artery disease, 70 (19%) had hypertensive heart disease, 55 (15%) had arrythmogenic heart disease, 35 (10%) had valvular heart disease, and 28 (8%) had cardiomyopathy; the remaining patients (3%) were considered to have other causes of decompensated heart failure (Table 1).

Of the 754 patients, 88 (12%) died during hospitalization. Cardiac death occurred in 53 patients (60%) and non-cardiac death occurred in 35 patients (40%; including 14 renal failure, 10 pneumonia, 8 sepsis, and 3 cerebrovascular events) (Table 2).

The clinical characteristics of the patients are presented in Table 3. The non-survivor group was older, had a lower body mass index (BMI), lower systolic blood pressure (SBP) on admission, and a higher prevalence of renal failure and previous myocardial

Table 1
Etiology of the patients in the study.

Variable	*n* (%)
Overall	*n* = 754
In-hospital death	88 (12)
ACS patients who underwent primary PCI	388 (52)
Etiology of non-ACS group	*n* = 366
Ischemic heart disease	170 (46)
Hypertensive heart disease	70 (19)
Arrythmogenic heart disease	55 (15)
Valvular heart disease	35 (10)
Cardiomyopathy	28 (8)
Other	8 (3)

Data are number (percentage). ACS, acute coronary syndrome; PCI, percutaneous coronary intervention.