European Journal of Internal Medicine 22 (2011) 495–500

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original article

Systolic blood pressure at Emergency Department presentation and 1-year mortality in acute chest pain patients ☆

Affan Irfan [a,1], Philip Haaf [a,1], Julia Meissner [a], Raphael Twerenbold [a], Miriam Reiter [a], Tobias Reichlin [a,b], Nora Schaub [a], Anina Zbinden [a], Corinna Heinisch [a], Beatrice Drexler [a], Katrin Winkler [c,d], Christian Mueller [a,b,*]

[a] Department of Internal Medicine, University Hospital, Basel, Switzerland
[b] Department of Cardiology, University Hospital, Basel, Switzerland
[c] Servicio de Pneumologia, Hospital del Mar — IMIM, UPF, CIBERES, ISC III, Barcelona, Spain
[d] Servicio de Urgencias, Hospital del Mar — IMIM, Barcelona, Spain

ARTICLE INFO

Article history:
Received 30 December 2010
Received in revised form 9 June 2011
Accepted 10 June 2011
Available online 2 August 2011

Keywords:
High blood pressure
1-year mortality
Chest pain
Risk stratification

ABSTRACT

Background: High blood pressure at rest has been an established risk factor for cardiovascular disease. However the relationship between Systolic Blood Pressure (SBP) and 1-year-mortality among acute chest pain patients presenting to Emergency Department (ED); and effects of preexisting renal insufficiency, hemodynamic stress — as quantified by Brain Natriuretic Peptide (BNP) and chest pain duration, on this relationship is unknown.

Methods: Data was used from APACE (Advantageous Predictors of Acute Coronary Syndrome Evaluation), a prospective observational multicenter study of 1240 ED chest pain patients. SBP at presentation was categorized into quartiles: Q1 ≤ 127 mm Hg; Q2 128–142 mm Hg; Q3 143–160 mm Hg; Q4 ≥ 161 mm Hg.

Results: 60 deaths occurred during 1-year. One-year-mortality-rate showed lower Hazard Ratios for Q2, Q3 and Q4 vs Q1 (HR [95% CI]; 0.39 (0.19–0.78), 0.34 (0.17–0.70), 0.35 (0.17–0.72); $p<0.01$ respectively). Cox model adjusted for various demographic and treatment variables showed that participants in Q3 and Q4 had better prognoses than Q1. Patients showed progressively better prognosis from Q2 through Q4 vs Q1 only in patients who presented to ED with for more than 12 h of chest pain duration. Patients with renal insufficiency had lower SBP at presentation than others ($p=0.001$). There was no association between the outcome and interaction variable of SBP quartiles and BNP ($p=0.27$).

Conclusion: Acute chest pain patients presenting to ED exhibit an inverse association between SBP at presentation and 1-year-mortality; a relationship which appears stronger in those who present with chest pain of greater than 12 h duration.

1. Introduction

About 6 million patients in United States present to Emergency Department (ED) annually for evaluation of chest pain [1], incurring 8–10 billion dollars for hospital stays [2]. However, only a small proportion of patients are diagnosed with life-threatening conditions and the majority (55–60%) has no worrisome cause and could be safely discharged [3]. Despite many advances in innovations, contemporary risk stratification models for Acute Coronary Syndrome (ACS) patients' remains suboptimal [4] and an important unmet clinical need. More accurate and prompt identification of low risk patients would help avoid the delay and uncertainty faced by clinicians in the management and discharge of patients with chest pain.

High blood pressure at rest has been an established risk factor for cardiovascular disease [5,6]. However, interestingly recent findings show that higher Systolic Blood Pressure (SBP) during stressful conditions carries a better prognosis [7–10]. Stenestrand et al. evaluated supine SBP at admission as a predictor of 1 year mortality in Swedish Intensive Care Units (ICU) patients with acute chest pain. This large cohort found that there was an inverse association between supine SBP and 1-year mortality rate [7]. However unlike other studies which evaluated SBP in association with in-hospital mortality among ACS patients [9,10], Stenestrand et al. did not evaluate renal insufficiency and time since onset of chest pain.

☆ Grant support: The study was supported by research grants from the Swiss National Science Foundation (PP00B-102853), the Swiss Heart Foundation, Abbott, Roche, Siemens, and the Department of Internal Medicine, University Hospital Basel.

* Corresponding author at: Department of Internal Medicine, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland. Tel.: +41 61 265 5826; fax: +41 61 265 5353.
E-mail address: chmueller@uhbs.ch (C. Mueller).

[1] Drs. Irfan and Haaf contributed equally to this article and should both be considered first authors.

0953-6205/$ – see front matter
doi:10.1016/j.ejim.2011.06.009

Furthermore, as the vast majority of patients with acute chest pain are triaged in the ED and not the ICU, we sought to determine the ability of SBP to predict 1-year mortality among acute chest pain patients presenting to the ED. We were also particularly interested in the effects, if any, of preexisting renal insufficiency, hemodynamic stress — as quantified by Brain Natriuretic Peptide (BNP) [11–13] and the time since onset of chest pain on the association between SBP and mortality.

2. Methods

2.1. Study design and population

From April 2006 to March 2010, consecutive patients were enrolled in the APACE study (Advantageous Predictors of Acute Coronary Syndrome Evaluation), an ongoing prospective observational multicenter study, coordinated by the University Hospital of Basel, Switzerland. These patients presented to the ED with symptoms suggestive of Acute Myocardial Infarction (AMI) such as chest pain and angina pectoris. Criteria for inclusion were patients with new onset or peak of chest pain within the last 12 h. Patients with acute trauma, those requiring dialysis and those with pulse pressure of less than 9 mm Hg were excluded. One year all-cause mortality was assessed by telephone interview.

All centers followed standard protocol developed by the University Hospital of Basel, thus allowing for consistent and uniform data collection. The study was approved by the institutional ethics committee of the participating centers. Written informed consent was obtained from all included patients.

2.2. Outcome of interest

The primary outcome of interest was time from presentation to all-cause 1-year-mortality.

2.3. Methods of measurement

All patients underwent an initial clinical assessment that included history taking, a physical examination including the standardized noninvasive measurement of supine arterial blood pressure using a dedicated automatic blood pressure monitor and an appropriate sized cuff, 12-lead ECG, continuous ECG-monitoring, pulse oximetry, standard blood tests and chest radiography at the time of presentation to the ED. Cardiac Troponin I or T, Creatinine Kinase-MB and myoglobin were measured at presentation and 6 to 9 h after presentation or as long as clinically indicated. The precise timing of clinical post-baseline measurements and the treatment of patients were left to the discretion of the attending physician.

2.4. Adjudicated final diagnosis

To determine the final diagnosis for each patient, two independent cardiologists reviewed all available medical records – the clinical history, findings on physical examination and results of laboratory tests, radiologic testing, ECG, echocardiography, cardiac exercise test, coronary angiography – from the time of the patient's arrival in the ED to the end of the 60-day follow-up period. When there was disagreement about the diagnosis, cases were reviewed and adjudicated in conjunction with a third cardiologist. The details of the predefined criteria for diagnosis have been mentioned elsewhere [14].

2.5. Statistical analysis

The data is presented as proportions, mean (range) and in case of non-normal distribution, median with InterQuartile Range [IQR]. For all analyses baseline SBP was categorized in quartiles and were compared with the referent group, first quartile (Q1). Since all the data included in analyses were non-normally distributed, variables were compared by the Mann–Whitney U, Chi-square and Kruskal–Wallis tests. There were no missing data on the primary outcome of interest or the baseline variables used in this study. For univariate analysis, Kaplan–Meier analysis was used to assess all-cause mortality and baseline SBP quartiles with comparisons by logrank test. Association between SBP and long term mortality was assessed by Hazard Ratios derived from Cox regression analyses. All clinical variables (probability for entry 0·05; probability for removal 0·10) were considered, and three prognostic models were developed to adjust for medications use on admission and discharge (Model 1), significant risk factors for long term mortality, excluding (Model 2) and including (Model 3) preexisting Renal insufficiency (based on patients' history). All models were also adjusted according to age, gender and baseline diastolic blood pressure. Receiver operator characteristic (ROC) curves were also performed and to calculate ability of SBP to predict 1-year mortality. The comparison of areas under the ROC curves (AUC) was performed as recommended by DeLong [15]. The variables were used to check for possible interactions due to the possibility that independent variables, particularly BNP, could combine and have more than an additive effect on 1 year all-cause-mortality. For all tests on the whole cohort a p value of ≤ 0.05 (two-sided) was considered significant. All statistical analyses were performed with the use of SPSS for Windows version 15.0 (SPSS), and MedCalc software version 9.6.4.0 (MedCalc). This study is being reported as per STROBE guidelines for the reporting of observational studies [16].

3. Results

3.1. Characteristics of patients (Table 1)

Of the 1247 consecutive patients enrolled in this study, 7 patients were excluded because their pulse pressure was less than 9 mm Hg. The baseline characteristics of the remaining 1240 patients are shown by quartile and of entire cohort in Table 1.

AMI was the adjudicated final diagnosis in 196 (16%) of patients. Other adjudicated diagnoses included unstable angina in 173 (14%), cardiac symptoms from causes other than Coronary Artery Disease in 160 (13%), non-cardiac causes in 602 (48%) and symptoms of unknown origin in 109 (9%) patients.

SBP at presentation was categorized into quartiles as follows: first quartile (Q1) $\leq$ 127 mm Hg; second quartile (Q2) 128–142 mm Hg, third quartile (Q3) 143–160 mm Hg, and fourth quartile (Q4) $\geq$ 161 mm Hg.

3.2. Univariate analysis

A total of 60 deaths occurred during one year follow-up. The median follow-up was 493 days. There was a significant association between quartiles of SBP and 1-year mortality, with the highest mortality in patients with a SBP in the lowest quartile (logrank test $p = 0.001$; Fig. 1). Using the Q1 as reference, the HR for the Q2 was 0.39 (95% CI 0.19–0.78) ($p = 0.007$); for the Q3 it was 0.34 (95% CI 0.17–0.70) ($p = 0.004$); and for the Q4 it was 0.35 (95% CI 0.17–0.72) ($p = 0.005$).

Out of 60 deaths, 33 (55%) occurred among those with AMI as final diagnosis. The mortality rate among patients with SBP in the lowest quartile was higher than those with SBP in higher quartiles among AMI ($p = 0.04$) and non AMI patients ($p = 0.07$).

3.3. Multivariate analysis (Table 2)

Model 1 was developed to account for age, gender, diastolic blood pressure, use of antihypertensive medications and nitroglycerin on admission and discharge and use of statin, Aspirin and warfarin on