American Journal of Emergency Medicine 35 (2017) 274–280

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

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

Original Contribution

Necessity of hospitalization and stress testing in low risk chest pain patients

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ARTICLE INFO

Article history:
Received 12 May 2016
Received in revised form 10 September 2016
Accepted 28 October 2016

Keywords:
Myocardial infarction
Hospitalization
Discharge
Stress testing
Copeptin

ABSTRACT

Background: Copeptin is a marker of endogenous stress including early myocardial infarction(MI) and has value in early rule out of MI when used with cardiac troponin I(cTnI).
Objectives: The goal of this study was to demonstrate that patients with a normal electrocardiogram and cTnI< 0.040 μg/l and copeptin< 14 pmol/l at presentation and after 2 h may be candidates for early discharge with outpatient follow-up potentially including stress testing.
Methods: This study uses data from the CHOPIN trial which enrolled 2071 patients with acute chest pain. Of those, 475 patients with normal electrocardiogram and normal cTnI(<0.040 μg/l) and copeptin< 14 pmol/l at presentation and after 2 h were considered "low risk" and selected for further analysis.
Results: None of the 475 "low risk" patients were diagnosed with MI during the 180 day follow-up period (including presentation). The negative predictive value of this strategy was 100% (95% confidence interval(CI):99.2%–100.0%). Furthermore no one died during follow up. 287 (60.4%) patients in the low risk group were hospitalized. In the "low risk" group, the only difference in outcomes (MI, death, revascularization, cardiac rehospitalization) was those hospitalized underwent revascularization more often (6.3%[95%CI:3.8%–9.7%] versus 0.5%[95%CI:0.0%–

Abbreviations: CAD, coronary artery disease; Cardrehosp, cardiac rehospitalization events; CI, confidence interval; cTnI, cardiac troponin I; "Low risk" group, denotes those with normal electrocardiogram and normal troponin I (<0.040 μg/l) and copeptin (<14 pmol/l) at presentation and 2 h; MI, myocardial infarction.

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http://dx.doi.org/10.1016/j.ajem.2016.10.072

2.9%], p = .002). The hospitalized patients were tested significantly more via stress testing or angiogram (68.6%[95%CI:62.9%–74.0%] vs 22.9%[95%CI:17.1%–29.6%], p < .001). Those tested had less cardiac rehospitalizations during follow-up (1.7% vs 5.1%, p = .040).

Conclusions: In conclusion, patients with a normal electrocardiogram, troponin and copeptin at presentation and after 2 h are at low risk for MI and death over 180 days. These low risk patients may be candidates for early outpatient testing and cardiology follow-up thereby reducing hospitalization.

1. Introduction

Chest pain is one of the most common presenting symptoms to the emergency department (ED), accounting for 9–10% of visits, which equates to 5.5 million visits a year [1]. One multicenter study estimated that approximately 55% of patients with chest pain are ultimately admitted [2] for monitoring and further testing but under 13% are ultimately diagnosed with acute coronary syndrome [1]. Studies estimate the average cost per hospital day to be as high as $4293 [3,4]. Furthermore, in a 2012 study of Medicare patients, chest pain was the most common reason for short inpatient stays, representing 22.5%, more than the next six reasons combined [5]. During this period, patients are typically monitored clinically and via serial cardiac markers; they often undergo inpatient stress testing while some proceed directly to coronary angiography. Recently, there has been significant interest in early discharge of low risk chest pain patients recognizing the high cost of hospitalization.

Arginine vasopressin is a neurohormone secreted by the posterior pituitary during times of significant stress, including cardiovascular stress [6]. Copeptin is the stable c-terminal part of the vasopressin pro-hormone used as a surrogate for measurement of vasopressin, which has a very short half-life and thus can be difficult to measure [7].

Copeptin has been shown to be elevated early in acute coronary syndrome [8], and it can facilitate early, safe rule out of acute myocardial infarction (MI) in conjunction with troponin [9-15]. Most recently, Möckel et al., completed a study suggesting that a single troponin and copeptin at admission in low to intermediate risk patients with suspected acute coronary syndrome is non-inferior for early rule-out of MI versus the current standard process of serial monitoring of cardiac markers [10]. Currently, many of these low to intermediate patients risk are admitted for stress testing. One study examined the effect of inpatient stress testing and found that although it reduced readmissions, such a strategy was not cost-effective [16].

In the multi-center Copeptin Helps in the Early Detection of Patients with Acute Myocardial Infarction (CHOPIN) trial, "low risk" was defined using a single blood draw strategy of normal troponin and copeptin at presentation alone. In this study, we examine a *more stringent* "low risk" sub-cohort of patients with normal copeptin and troponin I (as well as electrocardiogram) at presentation and 2 h within the CHOPIN trial to determine the rate of adverse cardiac events, subsequent test utilization, and intervention. We sought to demonstrate the low risk nature of this group, making the patients candidates for discharge from the Emergency Department and outpatient follow up rather than hospital admission.

2. Methods

2.1. Study Design and Population

This is a retrospective analysis of data from the Copeptin Helps in the Early Detection of Patients with Acute Myocardial Infarction (CHOPIN) trial, a 16-center prospective study of 2071 patients who presented with non-traumatic chest pain within 6 h of symptom onset. Patients were included in the CHOPIN study if they were over 18 years of age and the ED physician had any suspicion of acute coronary syndrome. Local laboratory values guided patient care. In addition, blood draws were performed at presentation, 2 h, 6 h, and 24 h if the patient was still hospitalized. The blood was centrifuged and stored at −60 °C or below and sent to a core laboratory for analysis. Follow-up was conducted via phone and review of medical records at 30, 90, and 180 days. Institutional review board approval was received at all 16 sites in the CHOPIN trial, and all patients provided written consent. The CHOPIN trial was conducted in compliance with International Conference on Harmonization and Good Clinical Practice regulations.

First, to demonstrate the value of copeptin, in this study, out of 2071 patients with chest pain, we selected 644 patients with normal electrocardiogram and troponin I (<0.040 μg/l) at presentation and 2 h and further subdivided this group into those with normal copeptin (<14 pmol/l) and elevated copeptin (Fig. 1). Outcomes at 180 days (including presentation) were analyzed.

Having demonstrated the value of copeptin, for this study, we defined a "low risk" cohort of patients as those 475 patients with a normal electrocardiogram (including absence of ST segment changes and T wave inversions), cardiac troponin I (cTnI, from core laboratory) under 0.040 μg/l at presentation and after 2 h and copeptin under 14 pmol/l at presentation and after 2 h (Fig. 2). This low risk cohort was evaluated for cardiac events (including MI, death, revascularization, cardiac rehospitalization) at presentation and in the future.

2.2. Final Diagnosis

Two board-certified cardiologists blinded to copeptin data independently determined the patient's final diagnosis based on serial troponins (from the core laboratory) and chart review. Diagnoses were assigned to one of six categories: 1) ST-elevation myocardial infarction, 2) non-ST

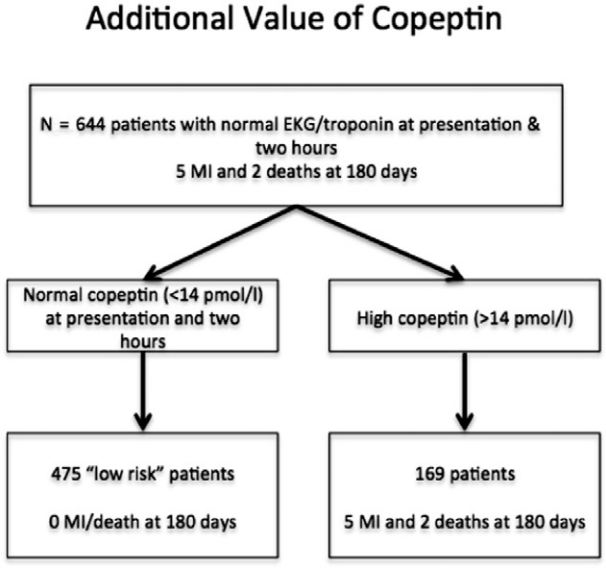

Fig. 1. Additional value of copeptin 644 patients with normal EKG and troponin and presentation and 2 h (out of 2071 patients with acute chest pain) were analyzed to show the additional value of copeptin. They were divided into a group that had normal copeptin (defined as copeptin under 14 pmol/l) at presentation and 2 h, which comprised 475 "low risk" patients and 169 patients with elevated copeptin.