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A Randomized Trial of Reminders of Past High BNP to Increase Measurement of LVEF

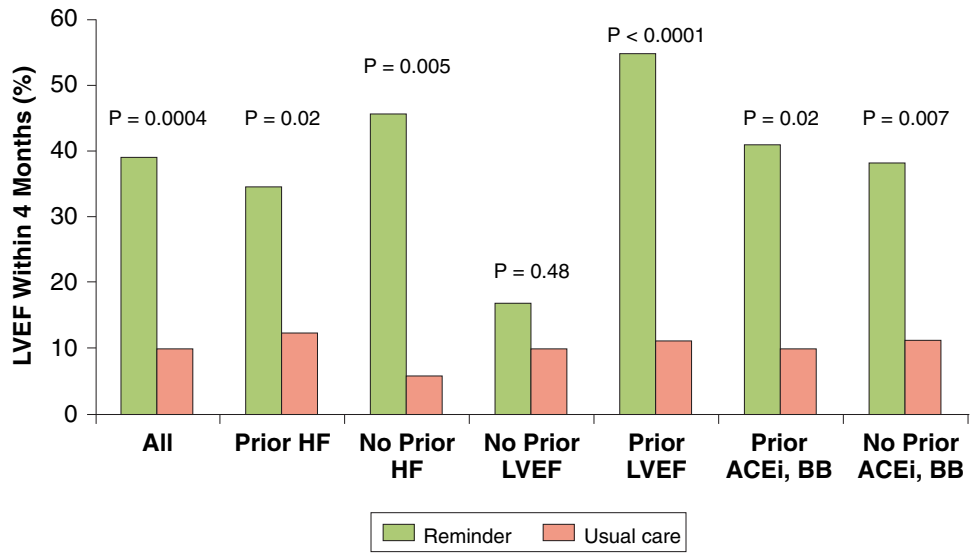
Patients with a high B-type natriuretic peptide (BNP) level have an increased prevalence of a reduced left ventricular ejection fraction (LVEF) (e.g., <40%) and may benefit from life-prolonging therapies (1). However, BNP testing may occasionally go unnoticed by the patient's primary care provider (2). Thus, patients with elevated levels may not have follow-up measurement of LVEFs. Those with depressed LVEFs will not be identified and cannot benefit from several life-prolonging therapies (1). The objective of this study was to determine the impact of a clinical reminder to physicians of patients who have a BNP >200 pg/ml, no previous systolic dysfunction, and no follow-up imaging. We randomized consecutive patients (inpatient or outpatient) from January 1, 2011 to February 15, 2012 with a BNP value of at least 200 pg/ml, with no previous diagnosis of systolic dysfunction (LVEF <40%) and no LVEF measurement recorded in the chart after the BNP measurement for at least 6 months. The primary outcome was measurement of LVEF by any imaging at 4 months after randomization obtained through chart review. A waiver of consent was granted by the Stanford Institutional Review Board.

The mean age of the 115 patients was 77 ± 12 years, 99% were men, 6% were black, and the mean BNP was 485 ± 457 pg/ml. In the 2 years before randomization, 65% had a diagnosis of heart failure, 55% had diabetes, 86% had hypertension, and 55% had ischemic heart disease. A previous LVEF value was known in 61% (mean 55 ± 8%). Overall, 39% of patients were hospitalized in the previous 12 months.

Among the patients randomized to the physician reminder, 39% (22 of 57 patients) had an LVEF measurement within 4 months compared with 10% (6 of 58 patients) of those randomized to usual care ($p = 0.0005$) (**Figure 1**). In another 15 patients in the reminder group, the physician accepted the order for echocardiography, but it was never performed due to patient cancellation (n = 12) or subsequent physician discontinuation (n = 3).

At 4 months of follow-up, a new diagnosis of moderate or greater depressed systolic dysfunction (LVEF <40%) was made in 6 patients: 5 of 57 (9%) patients in the reminder group compared with 1 of 57 (2%) patients in the usual care group ($p = 0.11$). This corresponded to a rate of a low LVEF of 23% (5 of 22 patients) among those who underwent imaging during follow-up. The number needed to remind to

FIGURE 1 Measurement of LVEF



Left ventricular ejection fraction (LVEF) is shown for the reminder and usual care groups, and in 3 subgroups (history of heart failure [HF], previous LVEF measurement, and previous use of angiotensin-converting enzyme inhibitors [ACEi] and guideline recommended beta-blockers [BB]).

identify an additional patient with an LVEF <40% was 15. Among the 6 patients newly diagnosed with a low LVEF, 4 (83%) filled a prescription for a recommended beta-blocker, angiotensin-converting enzyme inhibitor, or angiotensin receptor blocker within 6 months of randomization.

Our study found that an electronic reminder (combined with a draft order for echocardiography) to providers of patients with a high BNP level and an LVEF that was not known to be low increased appropriate follow-up of LVEF measurement. Although our study was not powered to determine a difference in health outcomes, we did find a trend toward a greater diagnosis of depressed LVEF that was subsequently treated appropriately with life-prolonging medications. We estimated that for every 15 reminders sent to providers, 1 additional patient would be diagnosed with an LVEF <40% and potentially benefit from treatment.

Such a reminder is inexpensive to implement and can be automated with electronic medical records. Our study had potential limitations, including the male preponderance of the veteran population. We chose a BNP threshold of 200 pg/ml to identify candidates for follow-up echocardiography. The United Kingdom's Chronic Heart Failure Guideline of the National Institute for Health Care Excellence (3) recommends that patients with suspected heart failure and a BNP level between 100 and 400 pg/ml should have echocardiography and specialist assessment within 6 weeks. Thus, health systems may choose to use the more sensitive threshold of 100 pg/ml, although it is unclear if the impact of the reminder would be as strong as the effect observed in this study.

Paul A. Heidenreich, MD, MS*
Parisa Gholami, MPH
Shoutzu Lin, MS
Anju Sahay, PhD

*Palo Alto VA Health Care System
3801 Miranda Avenue
GRECC 182B
Palo Alto, California 94304
E-mail: heiden@stanford.edu

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Myocardial Infarction With Nonobstructed Coronary Arteries

Impact of CMR Early After Presentation

Seven to 15% of patients with acute coronary syndrome (ACS) have nonobstructed coronary arteries, an entity that is known as myocardial infarction with nonobstructed coronary arteries (MINOCA) (1). In these patients, cardiac magnetic resonance (CMR) can identify different underlying etiologies (2). However, the optimum timing and the impact of CMR on clinical management are unknown. We aimed to evaluate the diagnostic and decision-making implications of CMR timing ("early" ≤2 weeks vs. "late" >2 weeks after presentation) in MINOCA.

A total of 204 consecutive patients (56 ± 17 years; 51% men) with troponin-positive ACS (as per the European Society of Cardiology guidelines for ST-segment elevation [STE] or non-STE ACS and the Third Universal definition of myocardial infarction [MI]) and unobstructed coronary arteries (MINOCA) with unclear final diagnoses were referred for CMR and included in the study from September 2011 to July 2014. Nineteen percent presented with ST-segment elevation on the electrocardiogram (ECG) and the remaining patients presented with non-ST-segment elevation myocardial infarction. The mean troponin level was 640 ng/l (normal <14 ng/l). The study was reviewed and approved by local institutional review board. CMR (1.5-T) was performed using a comprehensive protocol (cines, T2-weighted, and late gadolinium enhancement [LGE] sequences). Myocarditis was diagnosed using the Lake Louise Criteria, MI was diagnosed by territorial subendocardial and/or transmural LGE, and Takotsubo cardiomyopathy was diagnosed by modified Mayo Clinic criteria.

Pre-CMR diagnosis was defined per the referring clinician's suspected diagnosis recorded in the CMR referral, based on a composite of clinical, biomarkers, ECG, and echocardiographic and angiographic