

EDITORIAL COMMENT

Tachycardia After a Heart Failure Hospitalization

Another Piece of the Puzzle?*

Marco Metra, MD

Brescia, Italy

Our evaluation of cardiac patients is still founded on the assessment of 2 major clinical signs: blood pressure and heart rate (HR). The strength of these parameters comes from their relationship with the patients' clinical conditions and the mechanisms causing their symptoms and, likely, their prognosis. Tachycardia predicts a poor prognosis in normal subjects as well as in patients with virtually the entire spectrum of cardiovascular diseases (1–7). The association between tachycardia and increased mortality has also been repeatedly shown in patients with chronic heart failure (HF) (4,6). However, less data are available regarding patients hospitalized for HF.

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In this issue of *JACC: Heart Failure*, Greene et al. (8) analyzed the relationship between resting heart rate and prognosis in 1,947 patients hospitalized for HF and reduced ejection fraction who were enrolled in the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan) trial. After adjustment for baseline characteristics, baseline HR was not predictive of all-cause mortality ($p \geq 0.066$). Also, no prognostic value was found for HR values <70 beats/min assessed at discharge or later. In contrast, HR values ≥ 70 beats/min measured at either 1 or 4 weeks after discharge were independently associated with all-cause mortality, with a 13% ($p = 0.002$) for 1-week HR or 12% ($p = 0.001$) for 4-week HR increase in the risk of death for every 5-beat increase in HR (8).

The results of the study by Greene et al. (8) confirm that there is an association between tachycardia and increased

mortality in patients with a recent hospitalization for HF. The authors also raise 3 lines of inquiry regarding, respectively, the importance of the time of the assessment, the magnitude of the HR increase, and the time dependence of the relation between tachycardia and increased mortality.

Time of Assessment

Major changes occur during the hospitalization of patients with HF (9,10). Acute HF decompensation is associated with massive neurohormonal activation, and this decreases with the improvement in the patient's clinical conditions (10–12). HR, particularly when measured during stress conditions such as maximal exercise or acute HF decompensation, is tightly related to sympathetic activation as well as cardiac beta-adrenergic receptors' sensitivity and density (13). The presence of tachycardia at the time of hospitalization reflects the initial neurohormonal activation of the patient with acute HF and, thus, is related to the severity of the acute event and to short-term outcomes, such as in-hospital mortality (10,14–16), but not with longer-term outcomes (8,17).

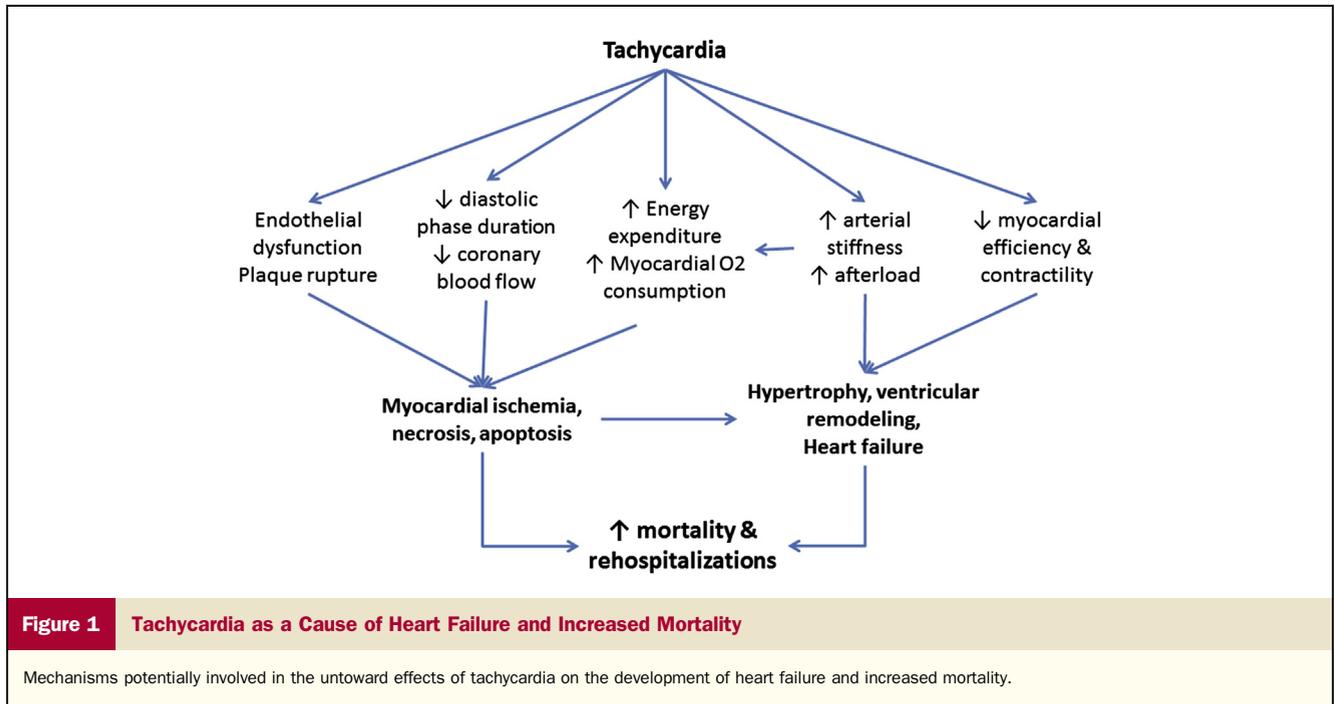
The magnitude of the initial neurohormonal activation is not related to the patient's conditions at the time of discharge (12). For instance, the decrease in the plasma levels of natriuretic peptides during hospitalization and their values before discharge are much more related to prognosis than the values measured at the time of admission (12,18,19). The relation of post-discharge HR, but not baseline HR, with subsequent mortality is consistent with the critical value of the early post-discharge phase for the prediction of the patient's prognosis and the prevention of subsequent events through therapy optimization (9,20).

Magnitude of tachycardia and prognosis. The present study confirms that the relation between HR and outcomes is not continuous, but, rather, there is a threshold with an increase in the risk of death only in patients with an HR ≥ 70 beats/min. Similar data have also been shown in other studies in patients with hypertension (21), coronary artery disease (5), and HF (6). The association of tachycardia with increased mortality may have different causes. Tachycardia is a sign of heightened cardiac sympathetic drive, a major determinant of the progression of HF (13). In addition, tachycardia is associated with increased myocardial oxygen consumption, decreased coronary blood flow and myocardial efficiency, and decreased arterial compliance (Fig. 1) (22,23).

A critical role for tachycardia. In the study by Greene et al. (8), the survival curves of the patients, subdivided according to the HR measured after either 1 or 4 weeks from discharge, started to diverge relatively early, but then continued to diverge during the follow-up (8). These results are consistent with a long-lasting, persistent effect of tachycardia on prognosis and, hence, with its role as a major cause of the patient's prognosis. This causal role is also consistent with the improvement in outcomes observed with pure HR reduction with ivabradine in patients with chronic HF on optimal medical treatment, including beta-blockers, but with

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From the Division of Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University and Civil Hospitals of Brescia, Brescia, Italy. Dr. Metra has reported that he is a consultant to and has received consulting fees from Bayer, Daiichi-Sankyo, Novartis, Servier, and Trevona.



an HR ≥ 70 beats/min in the SHIFT (Systolic Heart Failure treatment with the *If* inhibitor ivabradine Trial) trial (24,25). The present study furthers these results by showing that tachycardia is associated with increased mortality when assessed early after discharge for an HF hospitalization. An HR ≥ 70 beats/min is another extremely simple and extremely important clinical sign that we have to assess early after discharge, in addition to signs of congestion. Its detection should prompt appropriate therapy based on guidelines and current evidence (26).

Based on current results, we can, however, only hypothesize that a strategy of HR reduction, possibly with a selective agent such as ivabradine, would also be beneficial in patients with a recent hospitalization for HF and an HR ≥ 70 beats/min. The usefulness of such an approach, compared with beta-blocker up-titration, with the addition of digoxin, or just with maintenance of ongoing therapy, has not been shown to date (27). When added to congestion, tachycardia might be another major player in the crucial game of patients' outcomes after a hospitalization for HF.

Reprint requests and correspondence: Dr. Marco Metra, Division of Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, c/o Spedali Civili. Piazza spedali Civili 1, Brescia 25123, Italy. E-mail: metramarco@libero.it.

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Key Words: heart failure ■ heart rate ■ hospitalization ■ mortality ■ prognosis.