Should beta-blockers be used in patients with acute decompensated heart failure?

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ABSTRACT

In the absence of contraindications, beta-blockers are the standard of care for treating patients with chronic heart failure due to systolic dysfunction. Guidelines recommend that beta-blocker therapy be continued for patients hospitalized with acute decompensated heart failure due to left ventricular systolic dysfunction.

Keywords: beta-blockers, acute decompensated heart failure, systolic dysfunction, left ventricular ejection fraction, hospitalization

Beta-blockers are an excellent example of the evolution of medicine. These drugs were historically contraindicated in patients with heart failure due to left ventricular (LV) systolic dysfunction because of their inherent negative inotropic effects. Numerous trials, however, have now shown that beta-blockers improve symptoms, reduce hospitalizations, and prolong survival. Beta-blockers now play an integral role in the treatment of patients with chronic heart failure due to systolic dysfunction and are considered standard of care in the absence of contraindications.

The question now is whether beta-blockers should be continued in patients hospitalized for acute decompensated heart failure due to left ventricular systolic dysfunction. The short answer is, in most patients, yes. The 2009 updated guidelines for the diagnosis and management of heart failure state that continuation of beta-blockers for most patients is well-tolerated and results in better outcomes.[1] This recommendation was made based on data gathered from patient registries and retrospective post-hoc analyses of trials that enrolled large numbers of patients with heart failure. These data from observational analyses and retrospective studies have overwhelmingly shown favorable outcomes when beta-blockers were continued during hospitalizations.

LOOKING AT THE LITERATURE

The OPTIMIZE-HF Program (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) is a hospital-based registry designed to enhance care for patients with heart failure. Data gathered from this registry showed that continuing beta-blocker therapy in patients hospitalized with acute decompensated heart failure was associated with a lower post-discharge mortality risk[2]; however, this was not a randomized trial and most patients were continued on beta-blockers during hospitalization. Of the 1,429 patients on beta-blockers at admission, 1,350 patients remained on therapy and 79 patients had beta-blocker therapy withdrawn. Although the withdrawal of beta-blockers was associated with more severe indicators of heart failure, the mortality benefit remained after adjusting for covariates.

Similar results were found in a post-hoc analysis of COMET (Carvedilol or Metoprolol European Trial).[3] The risk of death was higher in patients when beta-blockers were discontinued or the dose reduced on admission.

> For most patients, beta-blocker therapy during hospitalization is well-tolerated and results in better outcomes.

Again, patients whose beta-blockers were discontinued tended to be sicker (with more severe symptoms and worse LV systolic dysfunction), but the increase in mortality was only partially explained by their worse prognostic profile. Unfortunately, these analyses cannot control for all potentially confounding factors.

The B-CONVINCED trial (**B**eta-blocker **CON**tinuation **V**s. **IN**terruption in patients with **C**ongestive heart failure hospitaliz**ED** for a decompensation episode) was a randomized, controlled, open-label, non-inferiority study that sought to confirm the results of previous observational and retrospective analyses.[4] This trial enrolled patients hospitalized for acute decompensated heart failure who were previously stabilized on beta-blockers for at least one month before admission and whose LV ejection fraction was documented as less than 40% in the previous year. Patients were excluded if they were pregnant, had an acute ST-segment elevation myocardial infarction, atrioventricular

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block (second or third degree), pulse less than 50, or were in the dose escalation process of beta-blocker therapy. Patients who required dobutamine therapy on entry were also excluded; however, use of a phosphodiesterase inhibitor was not a contraindication.

Of the 147 patients in the analysis, 69 were randomized to continue beta-blocker therapy on admission and 78 had their beta-blocker discontinued for at least 3 days. The primary endpoint was the percentage of patients whose dyspnea and general well-being improved at day 3 according to a blinded assessment. Secondary endpoints included the same blinded evaluation at hospitalization day 8 as well as subjective improvement at days 3 and 8 according to the patient; BNP plasma levels at day 3; the duration of hospitalization; the rehospitalization rate at 3 months; the death rate at 3 months; and the proportion of patients receiving a beta-blocker at 3 months.

> Most patients should be continued on beta-blockers unless they have evidence of severe decompensation, such as hypoperfusion that requires inotropic support.

Results revealed that continuing beta-blocker therapy did not affect symptoms at day 3 or day 8 according to both the blinded assessment and patient. Additionally, none of the secondary endpoints were significantly different, with the exception of the proportion of patients receiving a beta-blocker 3 months after hospital discharge. In the group of patients randomized to stop therapy at hospital admission, only 76% were on a beta-blocker 3 months after discharge compared to 90% of patients who were randomized to continue the beta-blocker while hospitalized ($P = 0.04$). This finding is extremely important because the benefits of beta-blocker therapy for chronic heart failure due to systolic dysfunction are well-established.

The finding of no mortality benefit is not surprising given the relatively small number of patients enrolled. Admittedly, this study was not powered to detect differences in death or hospitalization at 3 months. Three deaths occurred during the study, one in the group that continued beta-blockers and two in the group that discontinued beta-blockers. The rehospitalization rate due to heart failure after 3 months was 22% in the "continued" group and 32% in the "discontinued" group ($P = 0.19$). Of the 69 patients randomized to continue beta-blockers, four patients had therapy subsequently stopped during hospitalization: three when dobutamine was required and one due to bronchospasm. This shows the need to continually assess and adjust therapy on an individual basis after hospitalization.

CONCLUSION

In summary, the B-CONVINCED trial showed that continuing beta-blocker therapy during acute decompensated heart failure does not delay clinical improvement when dobutamine is not required. In clinical practice, this translates into continuing beta-blockers in most patients, unless the patient has evidence of severe decompensation (hypoperfusion requiring inotropic support). Of note, for patients admitted with acute decompensated heart failure who are not on chronic beta-blocker therapy, initiation of beta-blockers is usually reserved until the patient is stabilized and close to discharge. **JAAPA**

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