

# Depression Worsens Heart Failure Outcomes

BY BRUCE JANCIN  
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NEW ORLEANS — Depression is common among patients with heart failure and is independently associated with poor outcomes, Dr. Aldo P. Maggioni said at the annual meeting of the American College of Cardiology.

He presented a retrospective study involving 18,623 patients with heart failure over age 60 identified in an administrative health care database covering two regions of Italy. At entry, 13% were being treated for depression.

In a multivariate logistic regression analysis, comorbid depression was independently associated with a highly significant 28% increased risk of all-cause mortality at 1 year, compared with the risk in heart failure patients not treated for depression.

Depression also was associated with an adjusted 36% increased risk of a 1-year composite end point consisting of MI, stroke, or transient ischemic attack, along with an 18% increase in all-cause hospitalization. However, the risk of rehospitalization for heart failure was no greater in patients treated for depression than in those who weren't, according to Dr. Mag-

gioni, a cardiologist at the Mario Negri Research Consortium South, Santa Maria Imbaro, Italy.

He noted that while the adverse effect of comorbid depression on outcomes in patients with coronary artery disease is well established, there is much less evidence regarding the mood disorder's effect in patients with heart failure. Most previous studies have been quite small.

The strength of the new Italian study is its very large numbers. Its weakness is that there was no systematic screening for depression, so it's entirely possible the "nondepressed" comparator group included a fair number of heart failure patients with undiagnosed and untreated depression. Regardless, Dr. Maggioni said, the study conclusion was essentially the same as in the much smaller studies in which heart failure patients were screened for depression by questionnaire or interview: Depression is associated with poor outcomes in heart failure.



The mean age of participants in this study was 78 years. Patients treated for comorbid depression were significantly older than those who weren't. Sixty-nine percent were women, compared with 58% of heart failure patients not treated for depression.

Patients with depression also were significantly more likely to have a baseline history of stroke, transient ischemic attack, cancer, and chronic obstructive pulmonary disease.

Dr. Maggioni offered three potential explanations for the worse clinical outcomes in heart failure patients treated for depression. One possibility is that some antidepressant medications might have adverse effects in this population. Another is that depression exacerbates the underlying pathophysiology of heart failure, which is plausible in light of the fact that both conditions involve increased sympathetic nervous system activity, platelet activation, and systemic inflammation. But the most likely explanation for the associa-

tion, in Dr. Maggioni's view, is that depressed patients have less social support and are less adherent to their cardiovascular therapy.

The big unanswered question is whether treatment of depression improves heart failure outcomes, he said. There are no data, and a definitive randomized clinical trial would need to be very large.

"You need the numbers. If you're testing a new drug, just to see a 15% relative difference in mortality, you need perhaps 7,000 patients," Dr. Maggioni noted in an interview.

Session Chair Douglas P. Zipes called the Italian report linking depression to worse outcomes in heart failure "a very important observation" regarding an issue that doesn't receive sufficient attention from nonpsychiatrists.

"I think we tend to focus on more tangible issues, such as which coronary artery is occluded [and] the warfarin dose. My impression is that issues such as depression, sexual activity, and support groups aren't discussed at length—and they should be," said Dr. Zipes, Distinguished Professor of Medicine, Pharmacology, and Toxicology at Indiana University, Indianapolis. ■

## Transplants OK In Patients in Their Seventies

SAN FRANCISCO — Patients over the age of 70 do almost as well after heart transplants as younger recipients, unless they are infected with hepatitis C, according to a poster presentation by Dr. Jignesh K. Patel at the American Transplant Congress.

In a retrospective analysis, Dr. Patel and colleagues from the University of California, Los Angeles, compared 25 heart recipients aged 70-75 years (mean of 72 years) with 246 younger patients (mean of 56 years).

There were no differences between the groups in early cardiac allograft vasculopathy or in the percentage of patients being treated for rejection during the first year.

The younger patients did have a significantly higher 5-year survival rate than did the older patients—80% vs. 64%. However, when the investigators excluded from the analysis all patients with hepatitis C at the time of transplant and those receiving organs from hepatitis C-positive donors, the difference in 5-year survival failed to reach statistical significance. Three of the nine patients who died in the older age group had hepatitis C prior to transplantation.

Since all the older patients were classified as status 2, indicating relatively low-risk patients who did not require intravenous medications, the investigators selected only status 2 recipients for the control group.

—Robert Finn

## Meta-Analysis Links Renal Dysfunction to ARB Therapy; ACE Inhibitors Should Be First Line

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NEW ORLEANS — Angiotensin receptor blockers were associated with significantly greater risk of worsening renal function than were angiotensin-converting enzyme inhibitors in patients with systolic heart failure in a meta-analysis of all seven head-to-head comparative randomized, controlled, clinical trials, Dr. Rachid Lakhdar reported at the annual meeting of the American College of Cardiology.

"The ARBs are trying to make it as first-line drugs. The most recent guidelines put them as a class IIa indication, allowing them as first-line therapy in patients with mild to moderate heart failure and reduced left ventricular function," he said in an interview.

"Our conclusion from the meta-analysis is maybe that's not such a good idea, and ARBs should continue to be second line, to be used when ACE inhibitors are contraindicated," he continued.

The meta-analysis involved 20,143 systolic dysfunction heart failure patients who were randomized to an ACE inhibitor or ARB. Among the studies they were drawn from were the Valsartan in Acute Myocardial Infarction Trial (VALIANT), the first and second Evalua-

tion of Losartan in the Elderly (ELITE I and II), the Optimal Therapy in Myocardial Infarction With the Angiotensin II Antagonist Losartan (OPTIMAAL) trial, and the Randomized Evaluation of Strategies for Left Ventricular Dysfunction (RESOLVD) study.

Carried out without commercial support, the meta-analysis clearly showed that overall side effects were significantly less frequent with ARBs. Indeed, the combined incidence of cough, angioedema, hyperkalemia, hypotension, and

worsening renal function was 42% less with ARB therapy than with ACE inhibitor therapy in patients with systolic heart failure. However, the relative risk of worsening renal function was 60% greater with angiotensin receptor blockers, according to Dr. Lakhdar, a third-year resident at the Henry Ford Hospital System, Detroit.

The ARB and ACE inhibitor arms were evenly matched in terms of diuretic therapy and other potential confounders.

"This is a new observation that certainly needs more research, including a prospective study to pinpoint the pathophysiology as to why ARBs are more likely to worsen renal function," the physician added.

Discussant Dr. Lynne E. Wagoner pre-

**'Our conclusion from the meta-analysis is [that] ARBs should continue to be second line, to be used when ACE inhibitors are contraindicated.'**

dicted that guideline-writing committees are going to have to pay attention to the new meta-analysis.

"Cough is the major reason ACE inhibitors are discontinued. Often that cough is not severe and certainly is not life threatening," said Dr. Wagoner, medical director of the cardiac transplantation division at the University of Cincinnati.

"However, the risk of worsening renal function is potentially life threatening and therefore should be stressed in guideline recommendations. ARBs should remain second-line therapy behind ACE inhibitors as a result of these findings," he continued. ■

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