

CLINICAL LABORATORY STRATEGIES

Mastering Change in Laboratory Practice

Relating Albumin to Heart Failure Outcome

Low Levels Associated with Mortality

By Phil Kibak

Although hypoalbuminemia is common in patients with heart failure, its ability to predict outcomes in this population is not well known. In chronic disease states, such as end-stage renal disease, hypoalbuminemia is associated with poor outcomes. This issue of Strategies examines results of a new study suggesting that low serum albumin is associated with increased risk of all-cause mortality, as well as progression of heart failure resulting in death or an urgent need for transplantation.

Synthesis of the hepatic protein albumin is affected by nutritional intake and other factors like systemic inflammation. However, inflammatory processes—such as infection, trauma, and surgery—are known to decrease plasma albumin levels. Hypoalbuminemia has been shown to be the strongest predictor of death in patients on dialysis, but the importance of low levels of this protein as a predictor of outcome in systolic heart failure has been uncertain. Now results of a new study published in the *American Heart Journal* suggest that hypoalbuminemia is an independent predictor of survival in patients with advanced systolic heart failure (*Am Heart J* 2008; 155: 883–889).

A Measure of Nutritional Status

“Albumin determination is part of a complete metabolic panel that helps us assess a heart failure patient’s liver function, and we use it to see if he has problems that might preclude heart transplantation,” noted Tamara Horwich, MD, Assistant Professor of Medicine at the David Geffen School of Medicine at UCLA, and lead researcher of the study. “It’s also a gross measure of a patient’s nutritional status. So if hypoalbuminemia is present, it indicates that the patient may need to improve his nutritional status to be able to withstand a serious intervention like a transplant.”

Horwich and her colleagues analyzed albumin levels in 1,726 patients with systolic heart failure who were followed in a comprehensive management program at an academic medical center. Patients were divided into quartiles based on serum albumin: Q1, ≤ 3.4 g/dL; Q2, 3.5–3.8 g/dL; Q3, ≥ 3.9 –4.2 g/dL; and Q4, ≥ 4.3 g/dL. The primary endpoint for the study was all-cause mortality, and secondary outcomes included sudden death, death from heart failure, and a combined end point of death plus urgent heart transplant.

Lower Levels Equal Worse Survival

At the 1-year follow-up, 314 patients had died—according to the published report 147 were from progressive heart failure, 91 from sudden death, six from MI, and 59 from other causes. During that first year, 422 patients also had transplant surgery. At the 5-year mark the number of deaths increased to 591 and the number of transplants rose to 634. Worse 1-year survival was apparent in Q1 patients versus those from other quartiles: 66% of Q1 patients survived compared with 83% of those from other quartiles. At the 5-year follow-up, low albumin levels remained associated with significantly worse survival (38% versus 56%). After adjusting for multiple risk factors, the researchers determined that low albumin was an independent predictor of all-cause mortality. When they subdivided the cohort by albumin quartiles, 1-year survival rose from 66% in Q1 to 88% for Q4. At 1-year, patients with hypoalbuminemia were about 2.5 times more likely to die from any cause than patients with albumin levels greater than 3.4 g/dL. At 5 years, patients with hypoalbuminemia were twice as likely to die from any cause compared with patients whose albumin levels were higher than 3.4 g/dL.

“We had expected that low albumin levels would correlate with mortality, but we did have one surprising finding,” remarked Horwich. “We had expected that body mass would correlate with albumin levels; that is, we assumed that heavier patients with higher body mass index would have higher albumin levels. However, we did not see a clear-cut correlation between body mass and albumin levels. This suggests that the determinants of albumin level are more complex and not just related to how well a patient is eating, but that other factors like inflammation are acting to drive down plasma levels of this protein.”

Horwich and her colleagues also noted that heart failure patients with low albumin may have a higher rate of comorbidities, such as cancer or pulmonary disease, that contribute to their increased mortality rates. They also postulated that normal levels of albumin may have direct protective effects, such as antiapoptotic and antioxidant activity.

A New Use for a Common Test

What the study shows, Horwich added, is that this simple, very inexpensive test that is performed routinely on every patient who enters a hospital or gets a complete metabolic panel can be used as a powerful indicator of heart failure prognosis. “The importance of albumin was just one of those things that was never really acknowledged or studied before, but now we know that it requires even further assessment,” she said.

Sharon Hunt, MD, Professor of Cardiovascular Medicine at Stanford University School of Medicine (Palo Alto, Calif.) agreed. “This won’t change clinical practice in the short term but it’s a good, solid, observational study that correlates a common lab finding with prognosis, and opens up questions and avenues for further research,” she remarked.

Standardization Could Be An Issue

Brad Karon, MD, PhD, Director of Hospital Clinical Laboratories at the Mayo Clinic (Rochester, Minn.) said the findings were not unusual but it was something no one had shown before. “Albumin is commonly performed but in many instances ignored. It is used as a nutritional assessment, but this would be a new application for a test that’s incredibly common and inexpensive. And it would help because heart failure is such a huge problem.”

Of course, he added, as far as labs and clinicians are concerned, the finding that albumin can be used as an independent risk marker for heart failure needs to be confirmed in larger studies, but if that's done then there's another challenge.

"Albumin tests in labs are not well standardized," he said. "There are different ways of measuring it so it would depend on which test a particular lab is using in terms of picking a cutoff and predicting outcome. So, if future research does confirm this finding, we'll have to determine whether all labs could use the same cut-off or whether further standardization of the assay is necessary."