Hypoalbuminemia: a biological expression of frailty

La albúmina: una expresión biológica de la fragilidad

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In the study conducted by Garmendia et al. (1) the objective was to determine the prevalence of hypoalbuminemia and its clinical impact in patients with severe aortic stenosis treated with TAVI. This was a single-center, retrospective study where the baseline characteristics were analyzed based on the presence or absence of hypoalbuminemia (albumin levels < 3.5 g/dL) plus an overall survival study using the Kaplan-Meier estimator.

Albumin discrimination abilities to predict overall mortality using the ROC curve and its area were studied. The prevalence of hypoalbuminemia was 18.3%. A very important piece of information in this study is the higher overall mortality rate in patients with hypoalbuminemia (25.5% vs 6.0%; P = .002). Albumin showed modest discrimination abilities of 0.715% regarding the overall mortality rate and a greater discrimination cut-off value of 3.81 g/dL.

Currently, we use well-established surgical risk scores in candidates eligible for TAVI to stratify such risk in patients with severe aortic stenosis like the European System for Cardiac Operative Risk Evaluation (EuroSCORE 1 and 2) and the Society of Thoracic Surgeons (STS) (2,3). Both these scores were developed to predict the procedural mortality and morbidity rates of patients referred for cardiac surgery.

The capacity of these scores to predict disease progression is limited because they don't include frailty.

How can frailty be defined? It is defined as a reduced capacity to recover in pathological or iatrogenic situations due to the weakness associated with old age (4). This concept of frailty is very important because it can be applied to all invasive procedures where the disease progression of frail patients is poor (5).

Most in-hospital reports of TAVI confirm procedural successes in over 95% of the cases. However, 2 out of 5 patients from the PARTNER I (Placement of AoRTic traNscathetER valve trial), and early studies with CoreValve revealed a low quality of life or a low 1-year mortality rate (6).

Regarding TAVI, it seems obvious that frailty damages patient progression significantly (7,8). To complement the risk scores, the Valve Academic Research Consortium (VARC) 2 established that we should use other anatomical and biological tools to assess risk and disease progression, being frailty one of the most important ones. The other one recommended is albumin as a biological marker (9).

In a former study conducted by Segev et al., in isolation, albumin has predictive value regarding prognostic assessments within the same TAVI procedure. (10)

In the following study conducted by the same group (1), researchers added albumin to the STS and EuroSCORE-2 to predict mortality in 426 patients treated with TAVI and studied retrospectively. Patients were divided into 4 groups based on their levels of albumin (4 g/dL), STS score (4.5%), and EuroSCORE-2 (3.45%) (high vs low). Patients with hypoalbuminemia had a higher mortality rate. However, those with hypoalbuminemia and high STS or EuroSCORE had higher mortality rates. In conclusion, adding albumin to conventional risk scores improved their predictive value to assess 1-year mortality. After adjusting the scores, hypoalbuminemia remained a strong independent predictive factor of 1-year mortality. Even patients with elevated albumin levels had better prognoses regardless of the results of their early risk scores. Mortality difference starts immediately after the procedure and grows progressively within the first 4 months after TAVI.

Based on these data, the objective assessment of frailty to optimize patient selection is strongly advised. However, there is no strong consensus on how to assess frailty. At the same time, this lack of consensus is the reason why it is not assessed in the routine daily practice. Walking speed is one of the methods most widely used. However, using this resource alone undermines the specificity needed to discriminate complex patients who will have poor disease progression after TAVI (12,13).

The Frailty-AVR trial (14) compared the predictive value of 7 different scales as predictors of poor disease progression after TAVI or surgical aortic valve replacement. One of these methods is the Essential Frailty Toolset (EFT) that basically assessed the muscle strength of lower limbs, cognitive impairment, and anemia with the following cut-off values: 13 g/dL for men, and 12 g/dL for women. The albumin cut-off value was 3.5 g/dL. The endpoints were all-cause mortality and 1-year disability after the procedure. This prospective study was conducted in 14 centers from 3 different countries and included 1020 patients with a mean age of 82 years. Depending on the scale used, frailty went from 26% up to 68%. The most powerful predictor of 1-year mortality was the EFT. As a matter of fact, it was the strongest predictor of worsening disability and 30-day mortality. This is the largest comparative study of frailty scores in the TAVI or surgical aortic valve replacement setting. Although the possibility of success of both procedures was very high, the rate of 1-year functional impairment was 35% for all patients and > 50% for those considered frail. Inflammatory markers are elevated in these patients, which is indicative of a biological connection between inflammation and frailty (15).

In conclusion, this study conducted by Garmendia et al. shows how important it is to assess albumin prior to perform TAVI. Also, it replicates former studies conducted in our setting as a good expression of the scientific method. There is no doubt that hypoalbuminemia is an expression of frailty, which is a huge risk factor for disability and mortality.

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