

Statins in Heart Failure**Estatinas en la insuficiencia cardiaca****To the Editor,**

We have read with the utmost interest the letter by Ramirez et al,¹ published in *Revista Española de Cardiología*. In their report, the authors retrospectively evaluate the prognostic effect of lipophilic statins in 270 patients admitted to a single center for acute heart failure. After multivariable analysis, which included at least 10 covariates, they conclude that lipophilic statins were not associated with cardiovascular mortality risk (odds ratio = 1.12; 95% confidence interval, 0.22-5.64; $P = .88$) or all-cause mortality (odds ratio = 4.94; 95% confidence interval, 0.90-27.11; $P = .06$), or with readmissions for cardiovascular causes (odds ratio = 0.91; 95% confidence interval, 0.63-1.34; $P = .66$) or all-cause readmissions (odds ratio = 1.06; 95% confidence interval, 0.82-1.38; $P = .61$).

First, we appreciate the publication of reports of this type that attempt to clarify the role of statins in the treatment of heart failure, which continues to arouse strong debate.

With respect to the findings presented here, we would like to discuss certain issues, mostly methodological, which we feel should be taken into account in the interpretation of the reported results:

1. The text does not provide the absolute number of adverse events recorded, the length of follow-up, or the multivariable model performance measures.²
2. Although we do not know the length of follow-up, we understand that, in analyses of the time to the first event, as in this case, the use of a Cox regression model would be much more appropriate than logistic regression,² especially with irregular follow-ups, which are very common in studies of this type.
3. Although the total number of events is not reported, we understand that, being a small study, the accuracy of the risk estimates is vague (demonstrated very clearly by the width of the confidence interval for the odds ratio corresponding to all-cause mortality). Moreover, the probability of overfitting of the multivariable model is quite high (because of the inclusion of more than 10 covariates). The latter aspect is particularly important, as it has a highly significant effect on the external validation of the results.²
4. The prediction of the time to the first readmission requires the use of survival analyses that take into account competing adverse events.³ In the case of heart failure, adjustment for mortality as a competing adverse event appears to be necessary, given the high rate of mortality following hospital admission. It is well-known that standard techniques for survival analysis overestimate the risk of interim adverse events, such as readmissions, in contexts with a high mortality rate.³

5. Given that hospital admissions are usually recurrent, limiting the analysis to the time of the first readmission is a simplification that impedes a more detailed analysis of the disease course. In this respect, in recent years, a number of professionals have argued in favor of replacing analyses of time to first readmission with longitudinal analyses that include all the events that occurred during follow-up.⁴ A clear example is the case of statins in heart failure. The randomized clinical trial, CORONA, which evaluated the impact of rosuvastatin on prognosis in patients with heart failure and systolic dysfunction, demonstrated that the drug had a discrete protective effect, bordering on statistical significance, on the first readmission for heart failure (hazard ratio = 0.91; 95% confidence interval, 0.82-1.02; $P = .105$); however, a post hoc analysis taking into account repeated hospitalizations demonstrated that rosuvastatin was associated with a greater reduction (from 14%-18%, depending on the type of statistical method employed) that was statistically significant ($P < .05$ for all the comparisons) in the risk of repeated hospital admission.⁵
6. The lack of data on natriuretic peptides and the inflammatory status makes it impossible to define the clinical profile of the study population in greater detail.

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Statins in Heart Failure. Response**Estatinas en la insuficiencia cardiaca. Respuesta****To the Editor,**

We have read with interest the comments by Núñez et al, which contribute to the interpretation of the results of our work, published in *Revista Española de Cardiología*.¹ We acknowledge

the inherent limitations due to our not using Cox proportional hazards regression or Cox regression. With an absolute number of 34 cardiovascular deaths and 113 readmissions for heart failure, in the absence of follow-up time, the study design did not permit calculation of the incidence of events. For this reason, we decided on multivariable logistic regression for the analysis. To include the confounding variables and effect modifiers when building the logistic regression model, we first performed an analysis to identify those that could have an influence on the final event. We agree