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## Going Over LEGACY With a Pinch of Salt



Pathak et al. (1) reported that sustained weight loss  $\geq 10\%$  in patients with a body mass index  $\geq 27$  kg/m<sup>2</sup> was associated with a 6-fold reduction of atrial fibrillation (AF) recurrence during a 5-year follow-up, compared to patients without weight loss. The non-randomized design and statistical methods used raise concerns about the extent to which the findings can be considered valid.

The study was based on a post-hoc analysis of 355 patients, allocated to groups for comparison after study completion according to the achieved weight loss. We detected several potential sources of selection bias for these groups. Most importantly, patients with the highest weight loss participated more often in the offered dietician consulting, suggesting generally better lifestyle management and drug

treatment compliance, which could also possibly comprise a better control of other AF relevant comorbidities such as hypertension, obstructive sleep apnea, or diabetes. Indeed, important information on these comorbidities are missing, eliminating the potential to assess their impact on AF: 1) classes and doses of the antihypertensive drugs (rather than their number per patient); 2) changes in apnea-hypopnea index at follow-up; and 3) data on HbA1c at baseline and follow-up (rather than fasting insulin levels that do not inform about longer-term glycemic control). Furthermore, patients with the highest weight loss tended to be older than the control group. More details regarding AF treatment would also be helpful in interpreting the results, since electrocardioversion, number of ablations, and/or use of amiodarone at any time could have influenced the maintenance of sinus rhythm more robustly than sotalol or flecainide use alone. It is not clear whether the outcome was adjusted for these variables.

Another form of bias includes attrition bias: the information on the number and nature of dropouts is missing. Although the authors aimed for a 5-year follow-up, the average follow-up was 48 months for unclear reasons. Dropouts due to death—especially in older subjects (i.e., those with the highest weight loss)—would have affected the outcome. In any study, death can prevent detection of cause-specific nonfatal endpoints. Hence an analysis combining AF recurrence and death is warranted as sensitivity analysis.

In our opinion, evaluating the real effect of weight loss on AF would need a randomized controlled study. Short of this, use of case-mix adjustments, such as the propensity score matching, could provide a better control for confounding.

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