Prospective studies that have examined associations of lean status and weight loss to risk of mortality from HF.

Chronic HF involves a catabolic state, with the development of wasting (loss of muscle, bone and fat) because of malnutrition from an energy and protein intake that is inadequate to meet energy requirements. However, Cui et al excluded at baseline those subjects with a self-reported history of HF, as well as lung disease and cancer, all of which can cause weight loss. Why, then, was a relationship between lean status and future HF observed?

The study results that only death from HF was evaluated as an endpoint may need careful interpretation. HF, unlike acute myocardial infarction, is a syndrome that develops as a consequence of cardiac disease or various systemic factors. Although death from acute myocardial infarction can occur within a relatively short time after onset, death from HF is usually a terminal event that occurs after a prolonged course from the first onset.
of HF. In previous population-based studies that identified obesity or overweight status as risk factors for HF (particularly the Framingham study), the outcome event was set as the first onset of HF, defined by accurate and detailed diagnostic criteria;1-3 those studies did not investigate death from HF. On the other hand, studies of patients with previous congestive HF have shown opposing results, with obesity or overweight status contributing to a better prognosis;7,8,15 this has become known as the “obesity paradox”. Given these perspectives on outcome evaluation of HF, 2 issues may need to be considered regarding the linkage between body weight parameters and HF death.

First, in the study by Cui et al, subjects who died of HF reached the endpoint after a mean of 11.7 years. The first episode of HF occurred at any point during the follow-up period (prior to death), and thereafter, the prognosis of HF became more likely during a certain period. If body weight at the first episode of HF was less changed from the baseline value, the body mass index (BMI) at baseline would represent an important factor affecting the prognosis of HF (with lower BMI associated with worse prognosis). In this situation, subjects who showed weight loss ≥10 kg from 20 years old displayed the same characteristics as subjects with low BMI at baseline, regardless of the cause of weight loss. Furthermore, because subjects who showed substantial weight loss from 20 years old to baseline were unlikely to display weight gain during follow-up, lean subjects at baseline may also maintain their lean status at the first episode of heart failure. In brief, although obese subjects show better prognosis and therefore less risk of death during follow-up if their first episode of HF occurs relatively early, lean subjects die from HF comparatively early (Figure A). Because the endpoint of the present study was set as death from HF, not the onset of HF, the nature of studies that have investigated the prognosis of patients with HF is likely reflected in the present results.

Second, in the comparison of BMI between subjects at 20 years old and at baseline, the majority of subjects, both men and women, showed less change or tendency of weight gain. Subjects with weight loss ≥10 kg at 20 years old represented a relatively small proportion, comprising 7.6% of men and 5.3% of women. Moreover, a striking feature was that subjects with relatively small proportion, comprising 7.6% of men and 5.3% of women, showed less change or tendency of weight gain. Subsequent poor prognosis in the form of death (Figure B).

Further investigation is needed to appropriately explain the mechanisms underlying the association of preceding lean status and weight loss to increased risk of death from HF. Merging or filling the gaps between the actual clinical course of individual cases and epidemiological findings must contribute to identification of the underlying reasons.

**References**