Anemia treatment and left ventricular hypertrophy in non-dialysis chronic kidney disease

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To this day, the target hemoglobin level that minimizes cardiovascular risk in chronic kidney disease (CKD) patients remains unclear. When one examines the many randomized trials of epoetin therapy in aggregate, enhanced quality of life provides the most cogent argument for hemoglobin levels above 110 g/L. It remains unclear whether treatment of anemia improves longevity, or even a surrogate marker (such as left ventricular [LV] mass index), especially when applied at earlier phases of CKD.

Studies at earlier phases of CKD, with survival, or validated surrogate markers for survival, such as left ventricular mass index, as outcomes, have the potential to shed light on a difficult therapeutic dilemma. In this regard, the report of Hou and colleagues in the September issue of the Journal of Geriatric Cardiology is timely, because it attempts to address an issue of day-to-day clinical relevance to patients with CKD. An increase in mean hemoglobin levels (from 93.8 to 111.2 g/L) was seen in the epoetin-treated group, and LV mass index dropped in a stepwise manner from 142.6 to 132.4 g/m², in contrast to the untreated anemic and non-anemic patients, in whom LV mass index tended to increase. The apparently beneficial effect of epoetin therapy on LV mass index was not accompanied by an increase in blood pressure, or an increased propensity for renal function to decline. A particularly novel feature of the study was the selection of younger patients with CKD, with an average of only 36.5 years.

It is worth considering briefly some of the design issues. It is unclear how patients were selected to take part in the study, and once in the study, it was unclear how some how anemic patients were selected to receive epoetin therapy. Ideally, questions of therapeutic choice are best assessed with randomized controlled trials, and the more blinding that can be introduced, the better. One of the chief safeguards of this classical design is the natural tendency for equalization of both known and unknown disease-related factors. While non-randomized studies can demonstrate equality of known demographic and etiological factors, as was attempted in this study, they cannot assess the degree of equality of unknown factors between treatments; another great advantage is the tendency for non-study co-interventions to be made equal across study arms. The behavior of the arms that did not receive epoetin therapy was notable; it appeared that rates of change of LV mass index were similar in untreated anemic, and untreated non-anemic groups, suggesting that the progressive rise in mass index seen in both groups was independent of anemia; indirectly, when all three arms are considered, the study suggested that potential benefits of epoetin might be independent of hemoglobin levels achieved, a concept that might be difficult to accept without challenge. All statistical comparisons are made within therapeutic groups, as opposed to between therapeutic groups; the latter, of course, is the gold standard for reporting of clinical trials. Finally, the study was clearly underpowered for examining hard outcomes, like death, cardiovascular events, and end-stage renal disease.

While design issues render may force us to consider them as preliminary, and hypothesis-generating, the findings of the study are provocative. They add a sense of urgency to the need for formal randomized trials of erythropoiesis stimulating agents in younger, healthier populations with anemia and CKD.