Letter to the Editor

Human Atrial Natriuretic Peptide, Renal Function, and Cardiac Surgery: Do We All Read the Same?

[Letter regarding "The Efficacy of Human Atrial Natriuretic Peptide in Patients with Renal Dysfunction Undergoing Cardiac Surgery" (Ann Thorac Cardiovasc Surg 2008; 14: 294–302)]

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To the Editor:

I have read with great interest the manuscript by Dr. Kenta Izumi et al. regarding the use of human natriuretic peptide in patients with renal dysfunction undergoing cardiac surgery as a kidney-protecting agent.[1)]

I would like to add some comments to the discussion.

We have all worked extensively trying to find a therapy, drug, or technique that could protect the kidney against additional insults in surgery, and specifically cardiac surgery. To my knowledge that therapy has not yet been scientifically found.[2)]

In this manuscript the authors randomized a group of 18 patients undergoing cardiac surgery to human atrial natriuretic peptide or none. The end points were plasma creatinine and creatinine clearance at different times following surgery.

However, a few problems arise from the study.

(a) The authors studied patients with plasma creatinine of 1.2 mg/dl or higher. They refer to these patients as having renal dysfunction. I disagree. This is a low value to be considered as a marker for renal dysfunction. Most studies concerning these types of patients consider 1.5 mg /dl of plasma creatinine as the cutoff point.[3)] So probably, and according to Table 1, most of the patients had plasma creatinine values within what the literature calls normal values.

(b) Furthermore, the manuscript does not mention a study power analysis. In several previous works on this subject, we find that almost 100 patients in each group are necessary to obtain significant clinical results, positive or negative, when a drug is compared to a kidney-protecting agent, especially if these patients have "normal plasma creatinine values".[4)] Then if this is the case, a much larger number of patients would be needed.

Clinical studies such as this are very important and difficult to implement, but the methodology should be very strict to allow all physicians to read the same facts. In the meantime, the results of this study should be cautiously analyzed.

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Reply:

Thank you for splendid questions, Dr. Guillermo Lema.

We answer your questions.

(a) The definition of chronic kidney disease (CKD) is that in either of the following cases, (1) or (2), or both, it will continue for at least three months: (1) kidney damages obviously exist, as shown from the disorder of

the urine, diagnostic imaging, hemanalysis, and pathology, and/or (2) glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2. Five stages for CKD are categorized.[1,2] Stage 1: GFR ≥ 90 ml/min/1.73 m^2; stage 2: 60–89 ml/min/1.73 m^2 (GFR mild reduction); stage 3: 30–59 ml/min/1.73 m^2 (GFR moderate reduction); stage 4: 15–29 ml/min/1.73 m^2 (GFR extreme reduction); stage 5: < 15 ml/min/1.73 m^2. In stage 3 (moderate deterioration in renal function), estimated GFR (eGFR) 50 ml/min/1.73 m^2 is the borderline stage for introducing a patient to a kidney specialist,[2,3] not estimated eGFR, which is less than 60 ml/min/1.73 m^2. eGFR is calculated as 49.7 ml/min/1.73 m^2 and 36.9 ml/min/1.73 m^2 for a 40-year-old male with creatinine (Cr) 1.2 mg/dl and for a female, respectively {eGFR [ml/min/1.73 m^2] = $0.741 \times 175 \times age^{-0.203} \times Cr^{-1.154}$}; for a female, 0.742 must be multiplied to the calculated eGFR with this formula). In our study, the average ages are 74.7 ± 7.5 for group H and 70.6 ± 12.1 for group N.[4] If we assume that the patient is a 70-year-old male with Cr 1.2 mg/dl, eGFR is 44.4 ml/min/1.73 m^2. Assuming that the patient is a female, it is 32.9 ml/min/1.73 m^2. Therefore we should accept that they have deterioration of renal function or renal dysfunction.

As you have pointed out, when Cr is delimited at 1.5 mg/dl, eGFR ranges from 33.0 to 38.4 ml/min/1.73 m^2 for patients whose ages are from 40 to 85, and the eGFR values fall into CKD stage 3. When Cr is 1.2 mg and patient ages are from 40 to 85, eGFR is 42.6 to 49.7 ml/min/1.73 m^2. That is, both patient populations of Cr 1.2 and Cr 1.5 fall into CKD stage 3. Accordingly, I do not disagree with the opinion that Cr 1.2 mg/dl should be the cutoff point.

(b) Second, I agree with you concerning the small size of the patient population, which we have described in the above article. Currently, the multicenter study has been conducted with the same protocol, and the results will be announced later.

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