Author's response to reviews

Title: Comparison of Amyloid Deposition in Human Kidney Biopsies as Predictor of Poor Patient Outcome.

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Author's response to reviews:

New Haven, December 8, 2014

Dear Madame or Sir:

We would like to re-submit our original article “Comparison of Amyloid Deposition in Human Kidney Biopsies as Predictor of Poor Patient Outcome” to your prestigious journal. We are grateful for the positive critique by the reviewers and have answered their questions accordingly. Below, please our answers to their questions.

Reviewer #1:

1. The amyloid types diagnosed in this series are limited to AL and AA with AA being diagnosed rather frequently. What is the reason for the high percentage of AA amyloidosis in this study?

The higher percentage of AA amyloidosis was due the population being studied, which consisted predominantly of an indigenous, inner city population with a higher incidence of chronic infections, such as tuberculosis and osteomyelitis.

2. Please provide the information for the treatment of these patients and the rate of response, if available.

Unfortunately treatment information could not be rigorously analyzed. This is due to the fact that many cases were older and the treatment information could not be retrieved from the respective hospitals or clinicians. Moreover, all patients with glomerular amyloidosis were dead at the time of review, supporting our conclusion that glomerular amyloidosis has a worse outcome compared to other localizations.

Reviewer #2:

1. Were any other types of Amyloid identified in these patients?

This is a retrospective study in which all patients showed either AA or AL
amyloidosis. No other types of amyloid were identified. AA and AL amyloidosis constitute over 98% of all amyloid cases in the US.

2. Why does glomerular involvement correlate better with degree of impaired renal function than interstitial amyloid?

We conclude that the strong effect of glomerular amyloidosis on renal function, compared to the limited effect of interstitial amyloid, is due to the disproportionally larger amount of amyloid being deposited in glomerular sites compared to the rather small amount of interstitial amyloid. Moreover, the glomerular amyloid deposits involved entire glomeruli, while interstitial amyloid was mostly very focal. Therefore the detrimental effect of glomerular amyloid on renal function was disproportionally larger.

3. Please indicate “arterial/arteriolar” involvement instead of vascular involvement.

We disagree with the reviewer that vascular involvement should be replaced by “arteriolar” involvement. We believe that amyloid deposits in the vessels outside the glomerular capillary tuft are adequately described as vascular amyloid.

We have corrected the references to make them uniform and have reviewed and corrected grammatical errors.

We conclude from the findings of our study that in kidneys affected by amyloidosis, the amyloid protein is predominantly deposited along vessels, especially the small vessels including glomerular capillary loops. The severity of glomerular amyloid deposition enhances the risk of developing ESRD and increases the risk for premature death.

We believe that our study has led to new insights, which are important for the management and prediction of outcome in this patient population. We hope you agree that our study is worthy of publication and hope to hear from you favorably.

Sincerely,

Gilbert Moeckel, MD, PhD
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