Author’s response to reviews

Title: Evaluation of Prophylactic Dosages of Enoxaparin in Non-Surgical Elderly Patients with Renal Impairment

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Dear Dr. Al-Sallami,

Thank you for your review and comments. Please find below my response and amendments to the manuscript. Many thanks again for your input and comments. Looking forward to hearing from you.
Author’s Reply to Editor's Comments

1. Figure 3 has gone wonky (and now spans 2 pages). Can you please upload it again?
   • Absolutely. Figure 3 has been uploaded again.

2. Re CLcr, can you please specify what measure of body size was used in the C-G equation (total body weight, ideal body weight, adjusted body weight, fat-free mass, etc)?
   • Thank you for your question about the weight. Please find below the definition that we used during the study. We added the following to the methods section:P.6, lines 118-121
     • To calculate the CrCl, the actual body was used if actual body weight was less than ideal body weight. If actual body weight was greater than ideal body weight (IBW) by more than 20%, adjusted body weight was used. Adjusted body weight = IBW + 0.4(actual body weight - IBW).

3. Also, the use of 35 mL/min as a cut-off point requires clarification. Your explanation (that CLcr in this patient group fluctuates more than other groups) is not biologically plausible. Could be that your institution does this because clinicians suspect the calculated CLcr to overpredict GFR in this patient group? This is possible due to the correlation between age and body composition (less muscle mass in older age means less serum creatinine and a potential overprediction of creatinine clearance)?
   • Yes, thank you for the clarification. Yes, this is based on the concern that the CrCl may over predict GFR in this patient group due to physiologic changes in elderly patients as well as the fact that we also had patients with acute kidney injury. Please see addition to the discussion.
     • P.13 lines 269-276, we added the CrCl cut off as a limitation and added the following text and references:
       • We acknowledge the limitations to our study namely the small sample size, short duration of follow up and the use of a CrCl cut off of ≤35ml/min instead of <30ml/min. This less stringent cut off was adopted based on the concern that CrCl may over predict the GFR. (Fernandez-Prado R, Castillo-Rodriguez E, Velez-Arribas FJ et al. Creatinine Clearance Is Not Equal to Glomerular Filtration Rate and Cockcroft-Gault Equation Is Not Equal to CKD-EPI Collaboration Equation. Am J Med, 2016. 129(12):1259-1263.) Although dosing references recommend the CrCl as calculated by the Cockcroft-Gault formula for medication dose adjustments, clinical judgment is recommended to account for the physiologic changes in elderly patients in order to optimize risk versus benefit.( Manzano-Fernández S, Andreu-Cayuelas JM, Marín F et al. Comparison of estimated glomerular filtration rate equations for dosing new oral anticoagulants in patients with atrial fibrillation. Rev Esp Cardiol (Engl Ed), 2015. 68(6):497-