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ABSTRACT N. PO18

# "DOES MUSCLE MASS MATTER? APPENDICULAR LEAN MASS AS A DETERMINANT OF ANTI-XA ACTIVITY IN ELDERLY PATIENTES".

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**INTRODUCTION:**
Direct oral anticoagulants (DOACs) are first-line treatments for venous thromboembolism (VTE) and stroke prevention in non-valvular atrial fibrillation (NVAF). Dosing is currently based on age, body weight, and glomerular filtration rate (GFR). However, aging alters body composition, notably reducing lean mass, which is not detectable by body weight and may affect DOAC pharmacokinetics.

**AIMS:**
This study investigates whether appendicular lean mass (ALM) influences anti-Xa activity in older patients on DOACs, independently of age, sex, weight, and GFR.

**METHODS:**
We enrolled consecutive patients over 65 years on direct factor Xa inhibitors for atrial fibrillation at steady state (after at least 14 days from the initiation of anticoagulation). Data collection included medical history, anthropometric and lab measurements, physical performance, appendicular lean mass and fat mass evaluated by dual-energy X-ray absorptiometry (DEXA). Plasma anti-Xa activity was assessed at trough and peak levels through two blood samples. These data were analyzed using a generalized linear model adjusted by sex, age, dose, albumin, GFR.

**RESULTS:**
Seventy-seven patients (42% male, median age 85 year, IR 11) undergoing treatment anti-Xa inhibitors were enrolled: apixaban (n=16, 21%), edoxaban (n=33, 42%), and rivaroxaban (n=29, 37%). Mean body weight was 68.4 (± 15.4) kg; median ALM and mean fat mass were 17.4 (IR 8.4) Kg and 20.6 (± 7.2) Kg, respectively. Median GFR (Cockcroft-Gault) was 48.3 (IR 26.4) ml/min; serum albumin 40.0 (IR 4.0) g/L. Time between trough and peak samples was 2.2 ± 0.3 hours.
Peak anti-Xa activity was associated with ALM for all DOACs, in particular positively for edoxaban ($p<0.01$; $R^2=0.804$, fig. 1a), negatively for apixaban ($p<0.001$; $R^2=0.714$, fig. 1b) and rivaroxaban ($p<0.001$; $R^2=0.004$, fig. 1c), no association was found with body weight. Peak levels were also positively associated with albumin for rivaroxaban ($p=0.01$) and edoxaban ($p=0.042$); male sex for rivaroxaban ($p<0.001$) and apixaban ($p=0.027$); and age for rivaroxaban ($p=0.019$).
Trough anti-Xa activity was associated with ALM only for apixaban ($p=0.005$), but not with body weight. Trough levels were associated with reduced dose for edoxaban ($p=0.049$) and apixaban ($p=0.042$); male sex for rivaroxaban ($p=0.019$) and edoxaban ($p=0.001$); and age for rivaroxaban ($p=0.029$).

**CONCLUSIONS:**
ALM may influence the anti-Xa pharmacodynamics of all the DOACs analyzed. This effect appears to be more relevant for edoxaban and apixaban. This finding suggests that ALM could be used as a novel parameter in prescribing anti-Xa factors in elderly people, given the lack of correlation between anti-Xa activity and body weight. However, this finding requires confirmation with a larger sample size and further evaluation of adverse events (minor/major bleeding, ischemic events, mortality) in a longitudinal or clinical trial study.

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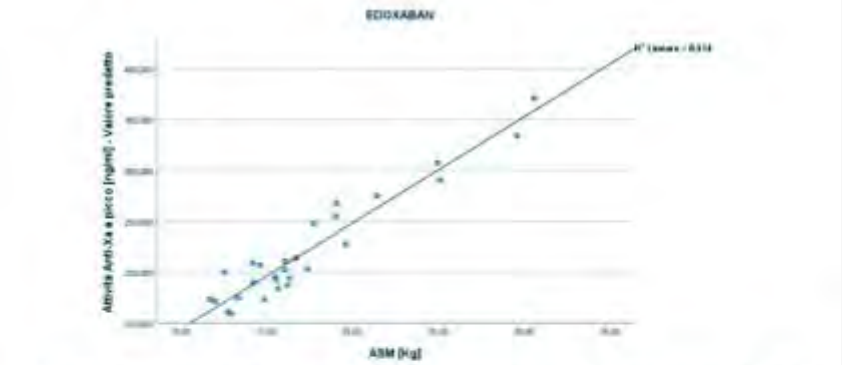
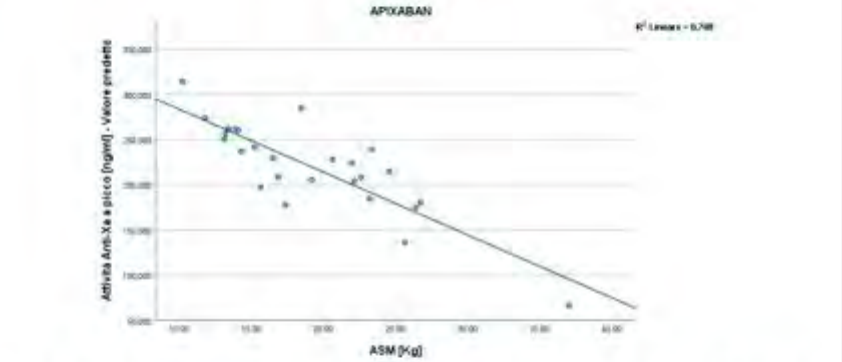
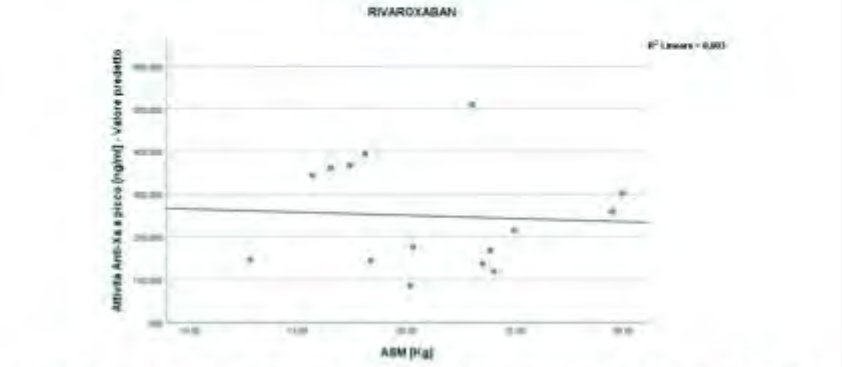



a Positive linear association between lean appendicular mass (ALM) and apixaban, $R^2$=0.804




b Negative linear association between lean appendicular mass (ALM) and edoxaban, $R^2$=0.714




c Negative linear association between lean appendicular mass (ALM) and rivaroxaban, $R^2$=0.004