FP377 **NOVEL RISK-BASED THRESHOLDS FOR BONE MINERAL BIOMARKERS IN ADVANCED CKD**

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INTRODUCTION AND AIMS: Current laboratory reference ranges for bone mineral biomarkers (BMB) are drawn from normal population values, and have limited utility in advanced CKD. Current guidelines offer little to facilitate the interpretation of BMB results, which may contribute to therapeutic nihilism. We aimed to describe expected values of parathyroid hormone (PTH), fibroblast growth factor 23 (FGF23), 1,25-dihydroxyvitamin D (1,25D3), and 25-hydroxyvitamin D3 (25D3) with decreasing eGFR, and to establish risk-based thresholds for each biomarker within specific eGFR intervals.

METHODS: Using data from a prospective cohort study of 1812 patient with advanced CKD in Canada under the care of nephrologists between 2008-2013, we measured intact PTH, FGF23, 1,25D3, and 25D3 in a central laboratory using sensitive DiaSorin assays. Adjudicated cardiovascular (ischaemic heart disease, congestive heart failure, stroke and sudden cardiac death) and renal outcomes (40% decrease in eGFR or initiation of renal replacement therapy) were recorded over 5 years of follow-up. We describe the expected distribution of BMBs as a function of eGFR, and determine risk-based thresholds by eGFR level using a robust computational methodology (Contal and O'Quigle).

RESULTS: The mean age was 68.9, 62% were male and 45% were diabetic. The mean eGFR was 28.9 $\pm$10 ml/min per 1.73m^2 with 19.4%, 40.3% and 40.3% with eGFR $<$20, 20-29 and $>$30 ml/min per 1.73m^2 respectively. The median follow up of the cohort was 52 months. Within each category of eGFR, there were statistically significant differences in PTH, FGF23, 25D3 and 1,25D3 levels (see Table). For each of the BMBs, a high proportion of the cohort had values outside the laboratory reference range, and these proportions were higher at lower levels of eGFR. Risk-based thresholds differed by eGFR level and identified significantly different proportions of patients at risk. For example, advanced CKD patients with PTH above the laboratory reference range, but below the risk-based threshold, did not have significantly higher risk of cardiovascular events. However, patients with PTH above the risk-based threshold had significantly higher risk of events compared with patients above the laboratory reference range but below the risk-based threshold (eGFR 20-30 ml/min: HR=1.78, 95% CI: 1.17-2.72; eGFR $<$ 20ml/min: HR=1.86, 95% CI: 1.19-2.89).

CONCLUSIONS: The majority of patients with advanced CKD have values of BMB that are outside the laboratory reference range. Furthermore, the distributions of BMB vary at different levels of eGFR. We propose that employing risk-based thresholds of BMB may serve to inform clinicians of 'expected values' of BMB within eGFR ranges, and eGFR-specific values that confer increased risk of hard outcomes. Further studies are needed to validate these findings, and to determine the clinical utility of this novel approach.

Biomarker	All	GFR <20mL/min	GFR 20-30mL/min	GFR >30mL/min	P value
PTH1-84 (pg/mL)	49.1 (31.7-77.4)	78.6 (47.2-124)	53.4 (35.1-83.3)	38.5 (24.8-55.3)	<0.0001
FGF-23 (intact) (pg/mL)	162 (114-240)	291 (179-469)	172 (130-249)	126 (97-168)	<0.0001
25D3 (ng/mL)	27.0 (19.7-35.1)	22.1 (15.1-29.3)	26.5 (19.5-33.5)	30.3 (22.5-38.3)	0.0126
1,25D3 (pg/mL)	25.2 (17.7-32.8)	24.2 (16.5-32.3)	24.3 (17.0-32.4)	36.3 (19.1-33.6)	<0.0001
% Patients Outside of Normal Laboratory Values					
PTH1-84 > 39.4 pg/mL	62%	83%	66%	48%	0.0001
25D3 < 20.0 ng/mL	32%	36%	34%	27%	0.0011
1,25D3 < 15.0 pg/mL	12%	24%	12%	7%	<0.0001
% Patients Outside of Risk-based Cut-point					
PTH1-84 (pg/mL)	28%	> 134.3 pg/mL 22%	> 104.6 pg/mL 15%	> 42.5 pg/mL 43%	0.0001
25D3 (ng/mL)	46%	< 37 ng/mL 85%	< 26 ng/mL 55%	< 17 ng/mL 18%	0.0011
1,25D3 (pg/mL)	64%	< 20 pg/mL 41%	< 30 pg/mL 65%	< 38 pg/mL 74%	<0.0001