Timing of Albumin Testing Affects Corrected Calcium Levels

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Introduction

- Albumin corrected serum calcium is a proposed clinical performance measure in the Centers for Medicare & Medicaid Services (CMS) End-Stage Renal Disease (ESRD) Quality Incentive Program (QIP) for 2015. In anticipation, the 2014 ESRD QIP final rule requires dialysis providers to monitor patients' serum corrected calcium at least once monthly.[1]
- This policy is motivated by the observation that compared to in-range levels, higher corrected serum calcium is associated with increased morbidity and mortality among dialysis patients.[2]
- While frequency of measurement of calcium and albumin is not standardized, albumin is typically measured less frequently than calcium in contemporary nephrology practice. Changes in circulating albumin levels that occur between albumin measurements may result in erroneous assessment of corrected serum calcium.

Objective

The objective of the current analysis was to measure inter- and intra-patient variability for serum calcium and albumin and to determine the degree to which clinically unobserved changes in serum albumin might bias assessment of serum corrected calcium.

Methods

- In a prospective, observational study of 32 adult, prevalent hemodialysis patients, pre-dialysis serum calcium and albumin were measured for ≤ 12 consecutive sessions/patient. For each serum calcium measurement, corrected serum calcium was calculated using the baseline (CorrCabl) and contemporaneous (CorrCacontemp) serum albumin using the following formula when serum albumin was < 4 g/dL and equal to serum calcium otherwise.

$$CorrCabl = [calcium] + 0.8 \times (4 - [albumin])$$

- Linear regression was used to model bias in CorrCabl (ie, CorrCabl-CorrCacontemp) as function of the time since baseline albumin measurement. The proportion of CorrCabl and CorrCacontemp values > 10.2 mg/dL was examined descriptively. Reported relative change value (RCV) for calcium determinations in hemodialysis patients is 8.2%.[3]

Results

- Thirty patients contributed 12 simultaneous calcium and albumin measurements; 1 patient each contributed 6 and 7 contemporaneous measurements. Patient characteristics and baseline calcium, albumin, and corrected albumin levels are presented in Tables 1 and 2, respectively.
- Serum calcium did not change over time (Fig 1a). Serum albumin tended to rise (Fig 1b).
- An upward bias in albumin corrected serum calcium was incrementally associated with a longer time since the baseline albumin measurement was taken (Fig 2).
- For albumin measurements after day 21, only 52.7% baseline albumin corrected serum calcium values were within ± 0.2 mg/dL of contemporaneous albumin corrected calcium (data not shown).
- The proportion baseline albumin corrected serum calcium > 10.2 mg/dL was greater than the proportion of contemporaneous albumin corrected calcium > 10.2 mg/dL at all time points after baseline (Fig 3).
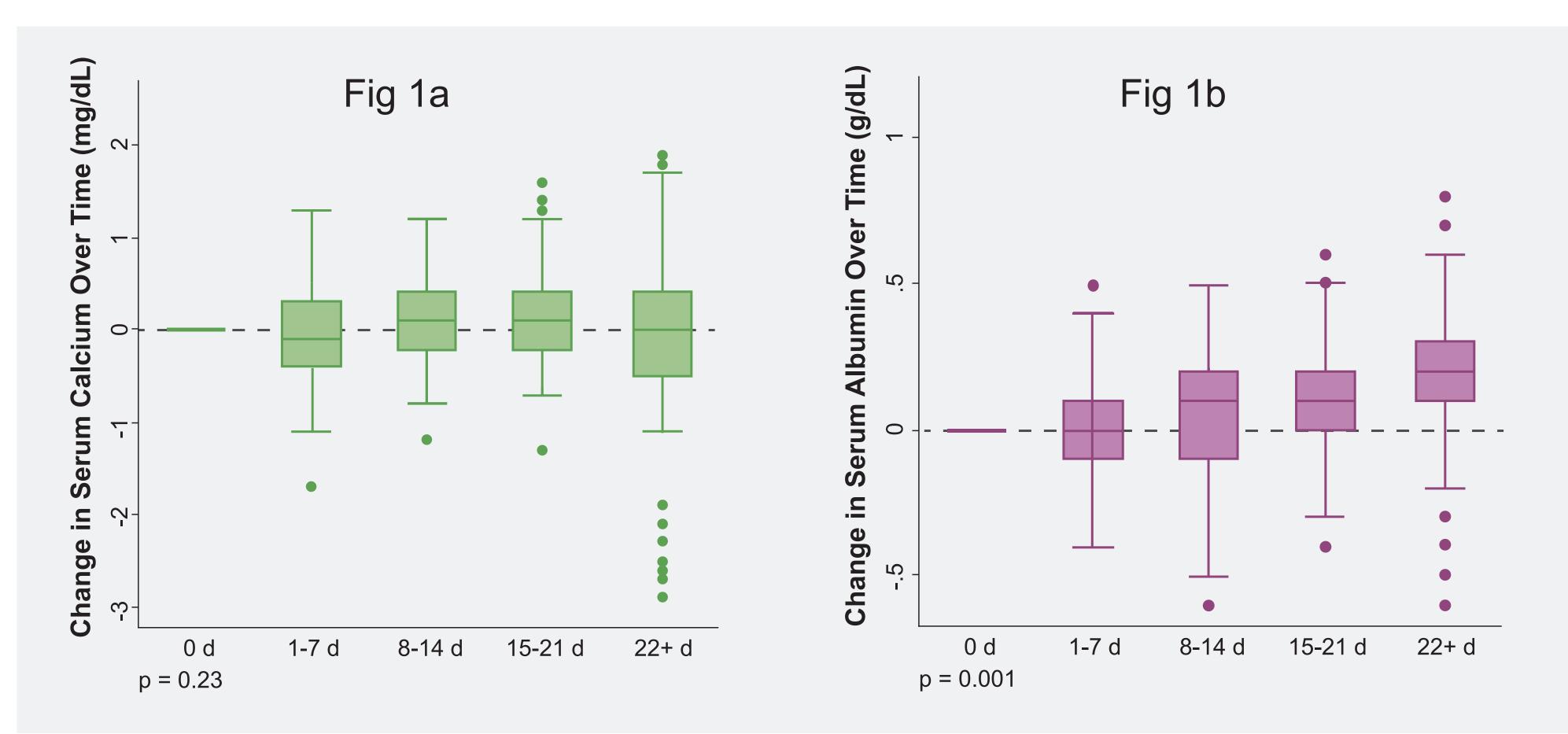
Table 1: Demographic Information

	Mean	Std Dev
N = 32		
Continuous Variables		
Age (years)	55.66	10.94
Vintage (years)	5.17	5.33
Body Mass Index in kg/m²	29.98	7.48
Categorical Variables		
Male	56.3%	
Diabetic	46.9%	
Race/Ethnicity		
African American	84.4%	
Hispanic	6.3%	
Asian, Pacific Islander	0.0%	
Native American	6.3%	
Unknown	0.0%	

Table 2: Distributions for Calcium, Albumin, and Corrected Calcium at Baseline

	Percentile 25%	Percentile 50%	Percentile 75%	Mean	Std Dev
Albumin in g/dL	3.15	3.35	3.60	3.35	0.33
Calcium in mg/dL	8.45	9.25	9.75	9.16	0.90
Corrected Calcium in mg/dL	9.17	9.77	10.13	9.68	0.88

Abbreviations: Std Dev, standard deviation.

Figure 1: Changes in Calcium and Albumin Over Time

Abbreviations: d, day; p, p-value.

Figure 2: Bias in Calcium Corrected for Baseline Albumin Over Time

Values >0 indicate that calcium corrected for historical albumin > than calcium corrected for on concurrent albumin
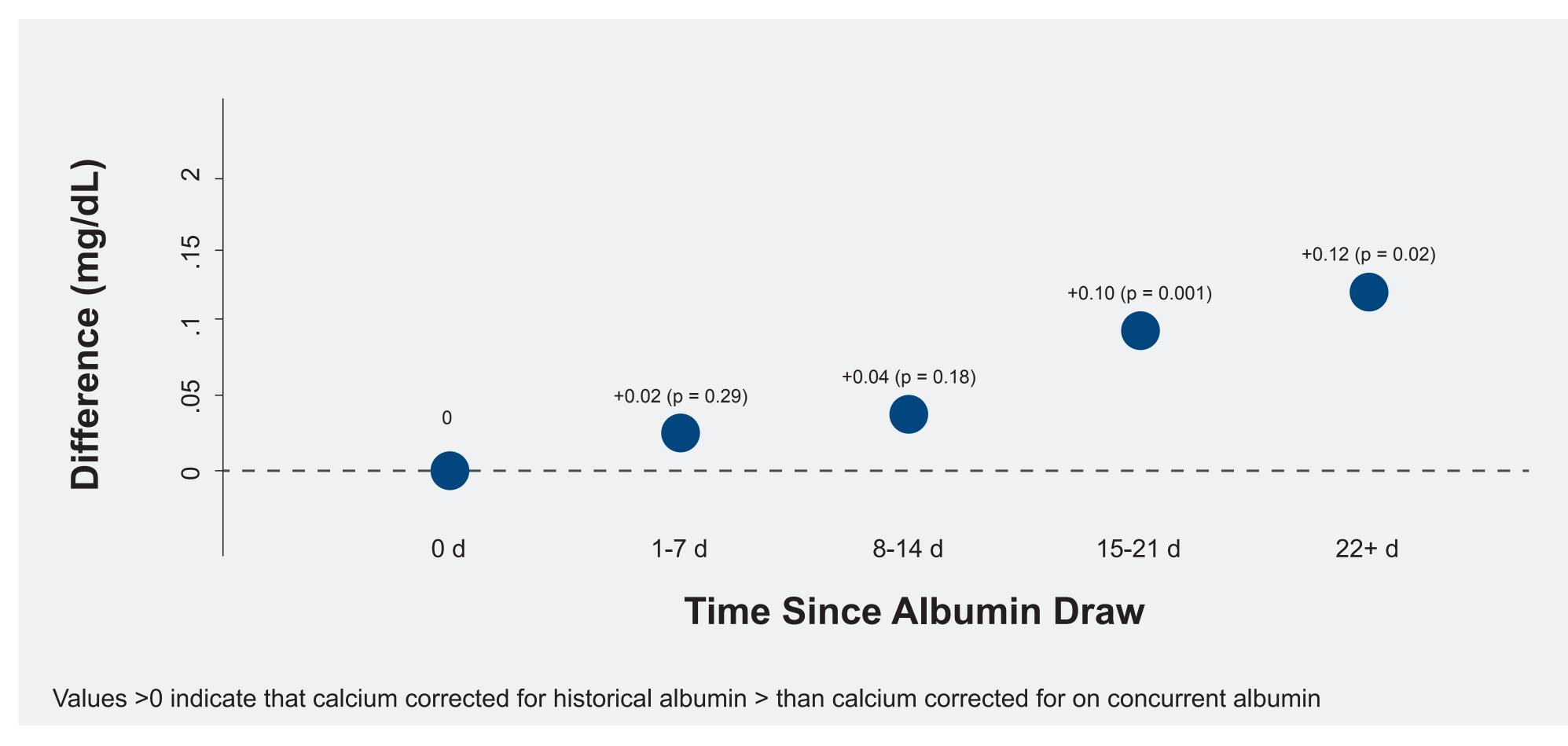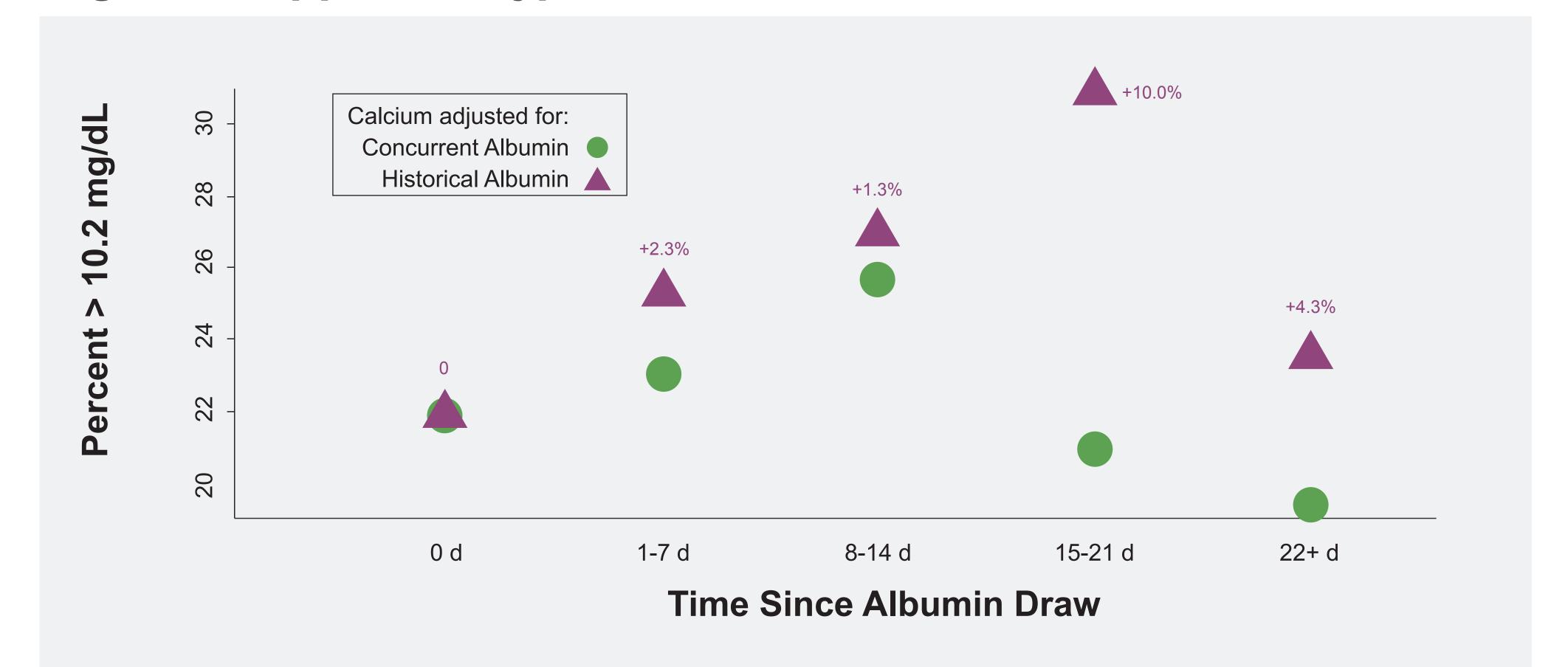
Figure 3: Apparent Hypercalcemia Over Time

Conclusions

- Compared to albumin measured contemporaneously, the use of historical albumin values creates an upward bias in corrected serum calcium that likely increases the QIP-reported rate of hypercalcemia.
- Current revisions to the CMS policy around albumin and corrected calcium is consistent with the findings of this analysis.

References

1. Centers for Medicare & Medicaid Services (CMS), HHS. Medicare program; end-stage renal disease prospective payment system, quality incentive program, and bad debt reductions for all Medicare providers. Final rule. Fed Regist. 2012;77(218):67450-531.
2. Phelan PJ, O'Kelly P, Walshe JJ, Conlon PJ. The importance of serum albumin and phosphorous as predictors of mortality in ESRD patients. Ren Fail. 2008;30(4):423-9.
3. Gardham C, Stevens PE, Delaney MP, et al. Variability of parathyroid hormone and other markers of bone mineral metabolism in patients receiving hemodialysis. Clin J Am Soc Nephrol. 2010;5:1261–1267.

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