Prevalence and Predictors of Osteoporosis in Advanced Chronic Kidney Disease: A Comparative Analysis of DEXA and Biochemical Markers

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Abstracts

Background: Chronic kidney disease (CKD) is associated with significant disturbances in bone and mineral metabolism, leading to renal osteodystrophy and increased fracture risk. Osteoporosis in advanced CKD remains underdiagnosed, and the utility of biochemical markers as screening tools requires further evaluation.

Objective: To determine the prevalence of osteoporosis using dual-energy X-ray absorptiometry (DEXA) and to identify its predictors, including biochemical markers, in patients with Stage 4 and 5 CKD.

Methods: This cross-sectional observational study was conducted from July 2017 to September 2018 at two tertiary care centers in Bangladesh. A total of 58 diagnosed CKD Stage 4 and 5 patients were enrolled using purposive sampling. All participants underwent clinical evaluation, biochemical testing, and DEXA scanning. Osteoporosis was defined as a T-score ≤ -2.5. Data were analyzed using SPSS version 21.0.

Results: Mean participant age was 46.7±7.7 years (male: female 1:1.1). Osteoporosis prevalence was 51.7% (30/58). Mean T-scores were -2.22±0.62 (lumbar spine), -2.10±0.74 (right femoral neck), and -2.12±0.71 (left femoral neck). Significant differences in calcium (p=0.023), phosphate (p=0.035), and PTH (p=0.004) were observed across BMD categories. Optimal osteoporosis predictors were calcium ≤8.15 mg/dL (sensitivity 67.9%, specificity 50.0%), phosphate ≥4.95 mg/dL (70.0%, 71.4%), and PTH ≥325 pg/mL (70.0%, 67.9%).

Conclusion: Osteoporosis is highly prevalent in advanced CKD, affecting over half of the study population. Biochemical markers, particularly PTH and serum phosphate, demonstrate moderate diagnostic accuracy and may serve as useful adjuncts for osteoporosis risk stratification when DEXA is unavailable.

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Introduction

Chronic kidney disease (CKD) represents a growing global health burden, with its prevalence increasing steadily worldwide. As kidney function declines, a complex array of metabolic disturbances emerges, collectively termed CKD-mineral and bone disorder (CKD-MBD). This syndrome encompasses abnormalities in calcium, phosphate, parathyroid hormone (PTH), and vitamin D metabolism, alterations in bone turnover, mineralization, and volume, as well as vascular or soft-tissue calcification.[1,2] The bone component of CKD-MBD, known as renal osteodystrophy, significantly compromises bone quality and strength through these hormonal and metabolic perturbations.[3] Osteoporosis, characterized by low bone mass and microarchitectural deterioration of bone tissue, has emerged as a particularly concerning complication in the CKD population.[4] Patients with advanced CKD face a substantially elevated fracture risk compared to the general population, with studies demonstrating that the risk of hip fracture is 4.4 times higher in dialysis patients.[5] Furthermore, fractures in this population are associated with greater morbidity and increased mortality, yet fracture incidence rates remain persistently high in end-stage kidney disease even as the general population has experienced a steady decline.[3] The utility of dual-energy X-ray absorptiometry (DEXA) in assessing fracture risk among CKD patients has historically been debated. However, accumulating evidence now indicates that reduced bone mineral density (BMD) is highly predictive of fracture risk in this population, although it cannot distinguish between the underlying causes, such as hyperparathyroidism, adynamic bone disease, or age-related osteoporosis.[6,7] A meta-analysis by Bucur et al. confirmed that BMD measured by DEXA can discriminate fracture status in both predialysis and dialysis-dependent CKD patients.[8] Biochemical markers of bone metabolism offer potential advantages as non-invasive tools for assessing bone health. Parathyroid hormone, while central to mineral metabolism regulation, exhibits considerable variability that limits its utility as a standalone marker.[9] Serum calcium and phosphate, routinely measured in clinical practice, reflect the disturbed mineral homeostasis characteristic of advanced CKD. Studies have demonstrated significant correlations between declining estimated glomerular filtration rate (eGFR) and alterations in these biochemical parameters, as well as with BMD T-scores.[10] The Brazilian Registry of Bone Biopsy (REBRABO) recently reported an elevated prevalence of osteoporosis (44%) in CKD-MBD patients, with dialysis vintage emerging as an independent predictor.[4] Despite growing recognition of osteoporosis as a critical complication in advanced CKD, data from South Asian populations remain limited. Furthermore, the comparative utility of DEXA versus biochemical markers for identifying osteoporosis in Stage 4 and 5 CKD patients requires further elucidation. The present study aimed to determine the prevalence of osteoporosis using DEXA and to evaluate the diagnostic performance of serum calcium, phosphate, and PTH in predicting osteoporosis among Bangladeshi patients with advanced CKD.

Methods

This cross-sectional observational study was conducted from July 2017 to September 2018 at the Outpatient Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, and the inpatient Department of Mymensingh Medical College, Mymensingh. A total of 58 patients with diagnosed chronic kidney disease (CKD) were enrolled using a purposive sampling technique.

Inclusion criteria: Patients diagnosed with Stage 4 and 5 CKD, as defined by the KDOQI guidelines, were included in the study.

Exclusion criteria: Patients were excluded if they had a history of malignancy, were currently taking medications known to affect bone metabolism (such as glucocorticoids, immunosuppressive agents, hormone replacement therapy, heparin, or anticoagulants), or had any disease that could cause secondary osteoporosis, including endocrine or gastrointestinal disorders.

Study procedure: Eligible patients who provided informed written consent were enrolled. On the day of recruitment, participants underwent clinical evaluation, including measurement of blood pressure, height, and weight. Blood samples were collected to measure serum calcium, inorganic phosphate, and intact parathyroid hormone levels using standard laboratory procedures; PTH was measured via an immunoradiometric method (Beckman Coulter Unicel DXI 800). Bone mineral density was assessed using dual-energy X-ray absorptiometry (DEXA) at the National Institute of Nuclear Medicine and Allied Sciences, BMU, Dhaka. Osteoporosis was defined as a T-score of -2.5 or below.

Data analysis: Data were collected using a pre-tested, semi-structured questionnaire and analyzed using SPSS version 21.0. Quantitative variables were summarized as means ± standard deviation, while qualitative variables were expressed as frequencies and percentages. Comparative analyses were performed using the chi-square test, t-test, and ANOVA, as appropriate. A p-value of less than 0.05 was considered statistically significant.

Result

A total of 58 patients with Stage 4 and 5 chronic kidney disease (CKD) were enrolled in this cross-sectional study. The mean age of the participants was 46.71±7.73 years, with the majority (70.7%) aged over 40 years. The study population comprised 28 males (48.3%) and 30 females (51.7%). The most common presenting complaints were bone pain, arthralgia, and muscle weakness (98.3%), followed by nausea, vomiting, and bodyache (86.2%). Hypertension (39.7%) and diabetic nephropathy (25.9%) were the predominant primary diseases. Anemia was present in 96.6% of patients, and the mean body mass index was 24.30±2.38 kg/m². According to CKD staging, 30 patients (51.7%) were in Stage 4 (mean eGFR 22.19±3.51 mL/min), and 28 patients (48.3%) were in Stage 5 (mean eGFR 12.72±1.42 mL/min). Biochemical analysis revealed a mean serum calcium of 8.19±0.62 mg/dL, a mean serum phosphate of 5.18±0.64 mg/dL, and a mean parathyroid hormone (PTH) level of 397.38±221.24 pg/mL. Dual-energy X-ray absorptiometry (DEXA) scanning demonstrated mean T-scores of -2.22±0.62 at the lumbar spine, -2.10±0.74 at the right femoral neck, and -2.12±0.71 at the left femoral neck. Based on DEXA criteria, osteoporosis (T-score ≤ -2.5) was diagnosed in 30 patients (51.7%), osteopenia in 21 patients (36.2%), and normal bone mineral density in 7 patients (12.0%). The prevalence of osteoporosis was higher in Stage 5 CKD (60.7%) compared to Stage 4 (43.3%), although this difference did not reach statistical significance (p=0.407). The lumbar spine was the most common site for osteoporosis (39.7%). Significant differences in biochemical markers were observed across the bone mineral density categories. Patients with osteoporosis had significantly lower serum calcium (8.01±0.72 mg/dL) and significantly higher serum phosphate (5.34±0.64 mg/dL) and PTH (473.2±221.8

pg/mL) compared to those with osteopenia and normal BMD (p=0.023, p=0.035, and p=0.004, respectively). However, no significant differences in these biochemical markers were found between CKD Stage 4 and Stage 5 patients. Receiver operating characteristic (ROC) curve analysis identified optimal cut-off values for predicting osteoporosis: serum calcium ≤8.15 mg/dL (sensitivity 67.9%, specificity 50.0%), serum phosphate ≥4.95 mg/dL (sensitivity 70.0%, specificity 71.4%), and PTH ≥325 pg/mL (sensitivity 70.0%, specificity 67.9%). Among the 30 patients diagnosed with osteoporosis by DEXA, abnormal PTH levels were observed in all cases (100.0%), followed by abnormal phosphate (93.3%) and abnormal calcium (86.7%).

Table I: Baseline characteristics of the study population (N=58)

Variable	n	%
Age group (years)		
≤40	17	29.3
41-50	20	34.5
>50	21	36.2
Gender		
Male	28	48.3
Female	30	51.7
Primary disease		
Hypertension	23	39.7
Diabetic nephropathy	15	25.9
Chronic glomerulonephritis	7	12
Polycystic kidney disease	2	3.4
Unknown	11	19

Table II: Biochemical markers and T-scores of the patients

Parameter	Mean ± SD	Min - Max
Serum calcium (mg/dL)	8.19 ± 0.62	5.70 - 9.90
Serum phosphate (mg/dL)	5.18 ± 0.64	3.90 - 6.30
Parathyroid hormone (pg/mL)	397.38 ± 221.24	60.00 - 871.90
T-score (Lumbar Spine)	-2.22 ± 0.62	-3.40 to -0.80
T-score (Right Femoral Neck)	-2.10 ± 0.74	-3.30 to -0.30
T-score (Left Femoral Neck)	-2.12 ± 0.71	-3.20 to -0.20

Table III: Biochemical markers according to BMD category

Biochemical Marker	Osteoporosis (T ≤ -2.5) (n=30)	Osteopenia (n=21)	Normal (n=7)	p-value
Serum Calcium (mg/dL)	8.01 ± 0.72	8.28 ± 0.26	8.67 ± 0.64	0.023
Serum Phosphate (mg/dL)	5.34 ± 0.64	5.12 ± 0.63	4.67 ± 0.29	0.035
PTH (pg/mL)	473.2 ± 221.8	357.6 ± 203.9	192.0 ± 71.4	0.004

Data presented as mean ± SD; ANOVA test was used.

Table IV: Prevalence of osteoporosis by CKD stage

CKD Stage	Osteoporosis	Osteopenia	Normal	p-value
Stage 4 (n=30)	13 (43.3%)	13 (43.3%)	4 (13.4%)	0.407
Stage 5 (n=28)	17 (60.7%)	8 (28.6%)	3 (10.7%)	

Chi-square test was used.

Table V: Diagnostic Accuracy of Biochemical Markers for Osteoporosis

Marker	AUC (95% CI)	p-value	Optimal Cut-off	Sensitivity	Specificity
Serum calcium	0.689 (0.553-0.825)	0.013	≤ 8.15 mg/dL	67.9%	50.0%
Serum phosphate	0.680 (0.537-0.824)	0.018	≥ 4.95 mg/dL	70.0%	71.4%
Parathyroid hormone	0.705 (0.570-0.841)	0.007	≥ 325 pg/mL	70.0%	67.9%

Table VI: Comparison of DEXA and biochemical markers in diagnosing osteoporosis

Diagnostic method	n	%
DEXA scan	30	51.7
Serum calcium	24	41.4
Serum phosphate	29	50
Parathyroid hormone	30	51.7

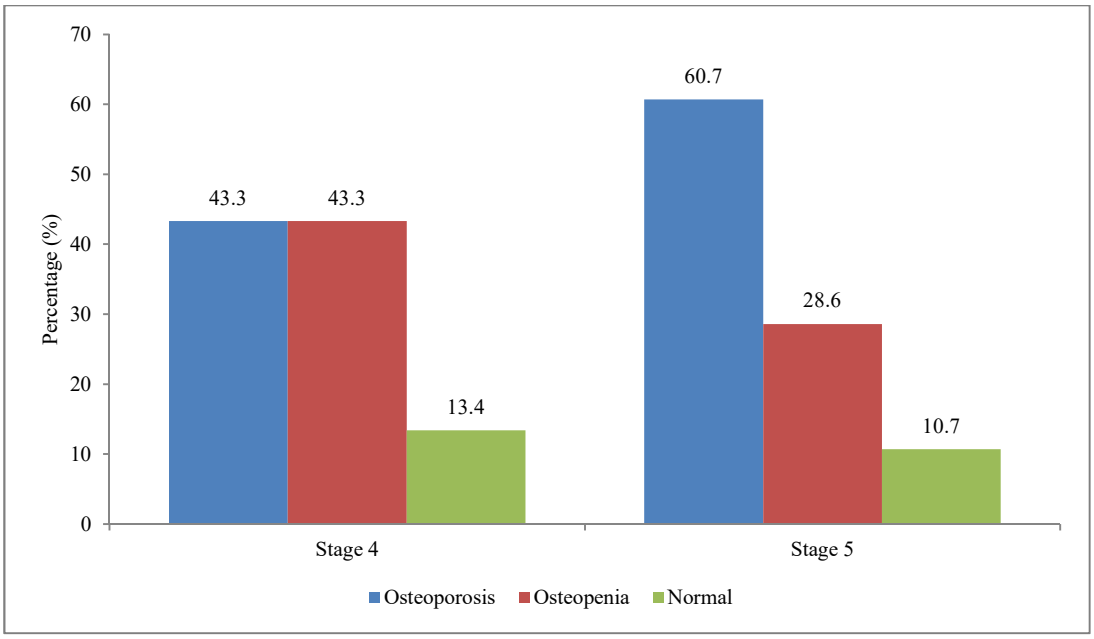

Figure 1. Bar diagram of osteoporosis at different CKD stages

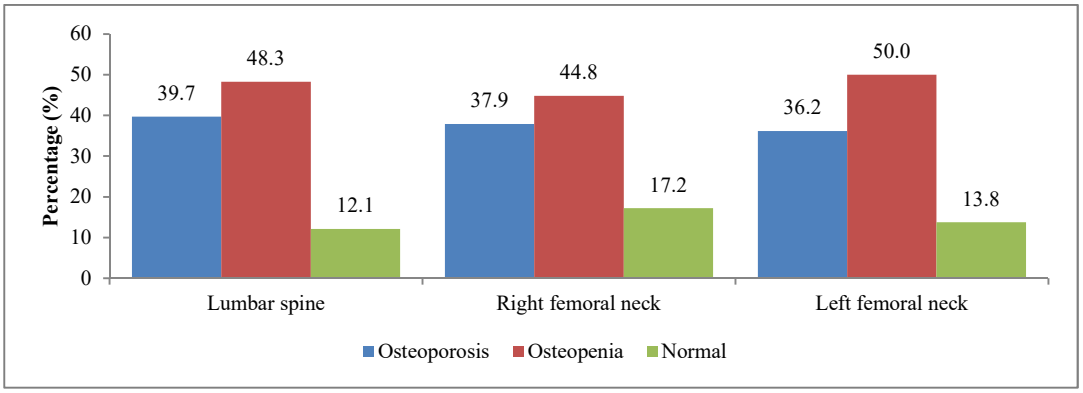

Figure 2. Bar diagram of osteoporosis at different sites

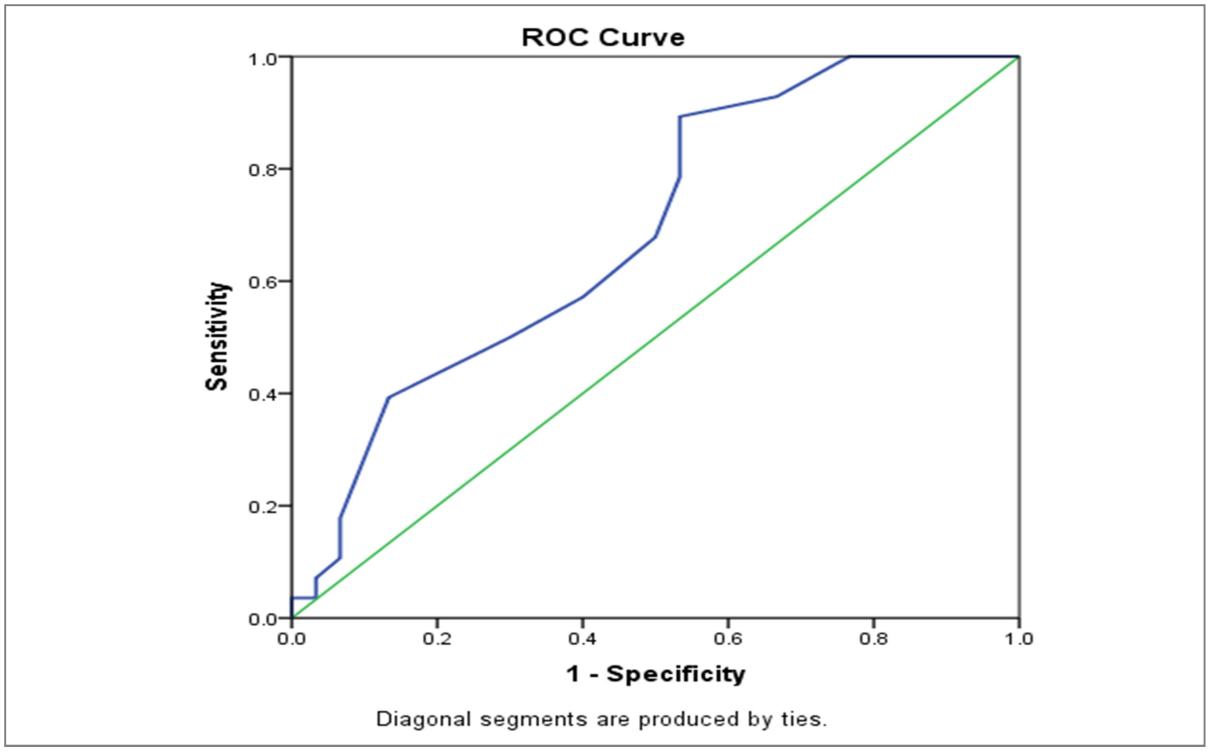

Figure 3. ROC curve for serum calcium in diagnosing osteoporosis

Discussions

The present study demonstrates a high prevalence of osteoporosis (51.7%) among patients with Stage 4 and 5 chronic kidney disease, as determined by DEXA scanning. This finding aligns with the growing recognition of osteoporosis as a major complication in advanced CKD, significantly exceeding the prevalence observed in the general population of a similar age. The reported prevalence is comparable to findings from the Brazilian Registry of Bone Biopsy (REBRABO), which documented osteoporosis in 44% of CKD-MBD patients and higher than the 32.5% prevalence reported in Indian CKD patients.[4, 11] The variation across studies may reflect differences in diagnostic criteria, population characteristics, and CKD stage distribution. The mean T-scores observed in our cohort (-2.22 at lumbar spine, -2.10 and -2.12 at femoral necks) indicate significant bone mineral depletion across all measured sites. The lumbar spine demonstrated the lowest mean T-score and highest frequency of osteoporosis (39.7%), consistent with previous observations that trabecular-rich sites are preferentially affected in CKD-related bone disease.[6,12] This pattern likely reflects the metabolic milieu of secondary hyperparathyroidism, which disproportionately affects cancellous bone. Notably, osteoporosis prevalence was higher in Stage 5 (60.7%) compared to Stage 4 (43.3%) patients, although this difference did not reach statistical significance (p=0.407). The absence of statistical significance may be attributable to the relatively small sample size, as progressive renal dysfunction is expected to exacerbate mineral metabolism disturbances.[10] The significant differences observed in serum calcium, phosphate, and PTH across BMD categories provide important insights into the pathophysiology of osteoporosis in advanced CKD. Patients with osteoporosis exhibited significantly lower serum calcium (8.01±0.72 mg/dL) and significantly higher phosphate (5.34±0.64

mg/dL) and PTH (473.2±221.8 pg/mL) compared to those with normal BMD. These findings corroborate previous research demonstrating significant correlations between bone turnover markers and eGFR in pre-dialysis CKD patients.[9] The progressive elevation of PTH with declining BMD underscores the central role of secondary hyperparathyroidism in mediating bone loss, as sustained PTH excess promotes cortical bone resorption and trabecular thinning.[3] The absence of significant differences in biochemical markers between CKD Stage 4 and Stage 5 patients was unexpected, given the expected progression of mineral disturbances with declining renal function. Several explanations may account for this observation. First, the cross-sectional design captures a single time point, whereas mineral metabolism parameters exhibit considerable temporal variability.[13] Second, therapeutic interventions such as phosphate binders or vitamin D analogs, although not documented in this study, may have modulated these parameters. Third, the relatively modest sample size may have limited statistical power to detect between-stage differences. The ROC curve analysis identified optimal cut-off values with moderate diagnostic accuracy for predicting osteoporosis. The PTH cut-off of ≥325 pg/mL demonstrated the best overall performance (AUC 0.705, sensitivity 70.0%, specificity 67.9%), consistent with its central role in bone metabolism regulation. The serum phosphate cut-off of ≥4.95 mg/dL (AUC 0.680, sensitivity 70.0%, specificity 71.4%) also showed acceptable discriminatory capacity. These findings support the potential utility of biochemical markers as screening tools, particularly in resource-limited settings where DEXA accessibility is restricted. Among patients with DEXA-confirmed osteoporosis, abnormal PTH was present in 100% of cases, abnormal phosphate in 93.3%, and abnormal calcium in 86.7%, highlighting the pervasive nature of mineral metabolism disturbances in this population. The clinical presentation of our cohort merits consideration. Bone pain, arthralgia, and muscle weakness were nearly universal (98.3%), reflecting the symptomatic burden of CKD-MBD. Hypertension (39.7%) and diabetic nephropathy (25.9%) predominated as primary etiologies, consistent with the global epidemiology of CKD.[14] The high prevalence of anemia (96.6%) reflects the advanced stage of kidney disease and its hematological consequences. Several limitations warrant acknowledgment. The relatively small sample size (n=58) limits generalizability and statistical power for subgroup analyses. The cross-sectional design precludes assessment of temporal relationships between biochemical disturbances and bone loss. The absence of bone turnover markers (e.g., bone-specific alkaline phosphatase, cross-linked telopeptide) and vitamin D levels limits comprehensive characterization of renal osteodystrophy subtypes. Additionally, data on medications affecting bone metabolism, such as phosphate binders or calcimimetics, were not systematically collected. Finally, the single-center design with purposive sampling may introduce selection bias. Despite these limitations, this study provides valuable data on osteoporosis prevalence and biochemical correlates in South Asian CKD patients, a population underrepresented in the literature. The findings reinforce the importance of osteoporosis screening in advanced CKD and suggest that readily available biochemical markers may aid in risk stratification when DEXA is unavailable. Future research should focus on larger, prospective cohorts with longitudinal follow-up to establish temporal relationships between biochemical disturbances and bone loss. Incorporation of bone turnover markers and advanced imaging modalities would enhance the characterization of underlying bone pathology. Validation of the identified cut-off values in independent

populations is essential before clinical implementation. Ultimately, randomized controlled trials are needed to determine whether biochemical marker-guided interventions can reduce fracture risk in this vulnerable population.[15,16]

Conclusion

Osteoporosis is highly prevalent, affecting over half of patients with advanced CKD. Significant associations exist between BMD and serum calcium, phosphate, and PTH levels. Biochemical markers demonstrate moderate diagnostic accuracy for predicting osteoporosis, with optimal cut-off values identified. These readily available tests may serve as useful screening tools when DEXA is unavailable. Routine osteoporosis assessment should be integrated into advanced CKD management to reduce fracture risk.

Limitations

The small sample size (n=58) limits generalizability. The cross-sectional design precludes causal inferences, and the absence of bone turnover markers and medication data restricts comprehensive characterization of renal osteodystrophy subtypes. Single-center recruitment with purposive sampling may introduce selection bias.

Recommendation

Routine osteoporosis screening using DEXA should be considered for all Stage 4-5 CKD patients. Biochemical markers, particularly PTH and phosphate, may guide initial risk stratification where DEXA is inaccessible. Larger prospective studies are needed to validate optimal cut-off values and evaluate intervention strategies.

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