PAKISTAN HEART JOURNAL ESTABLISHED 1968

OPEN ACCESS

P: ISSN: 0048-2706
E: ISSN: 2227-9199

Check for updates

DOI: 10.47144/phj.v57i3.2822

Citation: Azam MH, Danish N, Wahab MA, Rehman AU, Naeem S, Muhammad SK. The Relationship between Serum Calcium Levels and Angiographic Severity of Coronary Artery Disease in Patients with Chronic Coronary Syndrome. Pak Heart J. 2024;57(03):194-200.

Corresponding Author:
Dr. Naveed Danish, Fellow Interventional Cardiology, Department of Cardiology, Hayatabad Medical Complex, Peshawar, 25100, Pakistan.
Email: nddanish@yahoo.com

Conflict of interest: Authors declared no conflict of interest.

Funding: The author(s) received no specific funding for this work.

Double blinded peer review history:
Received: July 20, 2024
Review began: July 20, 2024
Revision received: August 15, 2024
Accepted: August 15, 2024

Original Article

The Relationship between Serum Calcium Levels and Angiographic Severity of Coronary Artery Disease in Patients with Chronic Coronary Syndrome

Muhammad Hammad Azam[1], Naveed Danish[1], Muhammad Abdul Wahab[1], Atta ur Rehman[1], Shitba Naeem[2], Shaheer Khan Muhammad[2]

[1]Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan, [2]The National Institute of Cardiovascular Diseases, Karachi, Pakistan

Abstract

Objectives: This study aims to investigate the relationship between serum calcium levels and the angiographic severity of coronary artery disease (CAD) in patients with chronic coronary syndrome (CCS).

Methodology: We conducted an observational study at the Department of Cardiology, Hayatabad Medical Complex, from January 2022 to December 2022, including 150 patients diagnosed with CCS. Serum calcium levels were measured using a colorimetric method, and the severity of CAD was assessed using the SYNTAX score derived from coronary angiography. Statistical analyses were performed using Pearson's correlation coefficient and multivariate logistic regression to account for potential confounding factors such as age, gender, hypertension, diabetes, and dyslipidemia.

Results: The analysis revealed a low negative correlation between serum calcium levels and SYNTAX scores (correlation coefficient: -0.13). Age emerged as a significant predictor of CAD severity ($p<0.001$), whereas serum calcium levels did not demonstrate an independent effect on CAD severity ($p=0.24$). After adjusting for confounding variables, no substantial correlation between serum calcium levels and SYNTAX scores was observed.

Conclusion: While serum calcium levels were not independent predictors of CAD severity after adjusting for other risk factors, a weak negative correlation was observed. Age remained a crucial factor influencing CAD severity. These findings suggest that serum calcium levels alone are insufficient for CAD risk classification but may provide additional value when used in conjunction with other diagnostic methods.

Keywords: Serum calcium, coronary artery disease, SYNTAX score, chronic coronary syndrome, angiographic severity

INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality worldwide. In patients with chronic coronary syndrome (CCS), understanding the factors that contribute to CAD severity is crucial for guiding optimal coronary risk stratification and management. Serum calcium levels have emerged as potential biomarkers for various diseases, including those affecting cardiovascular health, due to their role in several physiological processes and their influence on vascular calcification.

Calcium plays a vital role as an intracellular messenger and is essential for numerous physiological functions, including blood coagulation, muscle contraction, and neurotransmission. Its involvement in cardiovascular research has gained attention because of its impact on vascular calcification—a key feature of atherosclerosis[1]. Coronary artery calcification, which can precede adverse cardiovascular events, is often associated with elevated serum calcium levels.

Recent studies have further explored the relationship between serum calcium levels and CAD severity. For example, some research has indicated that higher serum calcium levels correlate with worse cardiovascular outcomes across various patient populations [1-4]. In a cohort of 3,109 CAD patients, elevated serum calcium levels were linked to reduced mortality rates, suggesting a potentially protective role [5]. Conversely, other studies have investigated the impact of serum calcium levels on outcomes in patients with acute coronary syndrome (ACS), finding that lower admission calcium levels were associated with poorer prognoses [6-9]. This highlights the potential prognostic value of serum calcium concentrations in acute settings.

The association between serum calcium and CAD involves complex biological mechanisms. Calcium is a critical element in the vascular calcification process, where hypercalcemia can lead to the formation of calcium-phosphate complexes, promoting deposition on vessel walls and resulting in arterial stiffening similar to atherosclerotic plaques [10]. Additionally, calcium's role in endothelial function and smooth muscle cell contraction means that disturbances in calcium handling can contribute to endothelial dysfunction and the progression of atherosclerosis [11].

These findings have significant clinical implications. Measuring serum calcium levels could enhance risk stratification for CAD patients. Combining serum calcium measurements with established diagnostic tools, such as coronary artery calcium (CAC) scoring, might improve the accuracy of CAD severity predictions and inform more personalized treatment strategies [12]. Understanding the link between serum calcium levels and CAD severity could thus refine clinical management for patients with CCS, potentially leading to new biomarkers and tailored therapeutic approaches. Further research should focus on exploring how dietary factors, bioactive compounds, and genetic influences affect cardiovascular disease through calcium metabolism, paving the way for precision medicine in cardiology.

METHODOLOGY

Study Design: This cross-sectional study was designed to explore the relationship between serum calcium levels and the severity of coronary artery disease (CAD) in patients with chronic coronary syndrome (CCS). The study was conducted at the Department of Cardiology, Hayatabad Medical Complex (HMC) in Peshawar, with the aim of understanding how variations in serum calcium levels might be associated with the angiographic severity of CAD.

Setting: The research was carried out at Hayatabad Medical Complex, a leading tertiary care hospital in Peshawar, Pakistan. Data collection spanned from January 2022 to December 2022. This setting provided a suitable environment for the evaluation of patients with CCS, leveraging routine cardiological procedures and advanced diagnostic tools available at the facility.

Participants: The study cohort consisted of 150 patients diagnosed with CCS, all of whom underwent coronary angiography during the study period. Participants were selected through a convenience sampling technique. Inclusion criteria required patients to be aged 18 years or older, have a confirmed diagnosis of CCS, and have undergone

coronary angiography within the study timeframe. Those excluded from the study were individuals with known primary hyperparathyroidism, chronic renal disease, or other conditions that could affect calcium metabolism.

Variables: In this study, the primary independent variable was serum calcium levels, measured in milligrams per deciliter (mg/dL). The dependent variable was the severity of CAD, which was quantified using the SYNTAX score derived from coronary angiography. The SYNTAX score reflects the complexity of coronary lesions and helps gauge the severity of CAD.

Data Sources/Measurement: Data collection involved several components: patient interviews, medical record reviews, and laboratory tests. Blood samples were collected in the morning after an overnight fast to measure serum calcium levels. The measurement was performed using the colorimetric method with arsenazo III dye, a standard biochemical assay for determining calcium levels. Coronary angiography was carried out as part of routine clinical care, and the SYNTAX score was utilized to assess the complexity and severity of coronary lesions. The angiographic data were evaluated by two expert cardiologists who were blinded to the patients' serum calcium levels to minimize bias.

Bias: To address potential biases, the study implemented several measures. Cardiologists assessing the angiographic data were blinded to the serum calcium levels to prevent any influence on their evaluation. Additionally, the study used standardized procedures for measuring serum calcium to ensure consistency across all samples. Despite employing a convenience sampling technique, which may limit generalizability, this approach was necessary given the study's logistical constraints.

Study Size: The sample size was determined based on an anticipated correlation coefficient of 0.2 between serum calcium levels and SYNTAX scores, with a desired power of 80% and a significance level of 0.05. This calculation indicated that a minimum of 138 participants was required. To account for potential dropouts and missing data, the study included 150 participants.

Quantitative Variables: Serum calcium levels were quantitatively measured in mg/dL using a colorimetric method. The SYNTAX score, which quantifies the complexity of coronary lesions, was used as a continuous variable to represent the severity of CAD. These measurements were critical in analyzing the association between serum calcium and CAD severity.

Ethics: Ethical approval for the study was granted by the Institutional Review Board of Hayatabad Medical Complex (Approval No. 1025). All participants provided written informed consent before their inclusion in the study, ensuring adherence to ethical standards outlined in the Declaration of Helsinki.

Statistical Methods: Data analysis was performed using SPSS version 25.0. Descriptive statistics summarized the demographic and clinical characteristics of the participants, with categorical variables presented as frequencies and percentages and continuous variables reported as means ± standard deviations (SD). To examine the relationship between serum calcium levels and CAD severity, Pearson's correlation coefficient was used for continuous variables, while the chi-square test was applied to categorical variables. A multivariate logistic regression analysis was conducted to control for potential confounders, including age, gender, hypertension, diabetes, and dyslipidemia. Statistical significance was set at a p-value of less than 0.05.

RESULTS

Participants: The study included a total of 150 patients diagnosed with chronic coronary syndrome (CCS). Among these participants, the mean age was 55.4 years, with a standard deviation of 10.2 years and an age range from 35 to 75 years. The cohort comprised 110 males and 40 females. Additionally, 90 participants had hypertension, 70 had diabetes, and 85 had dyslipidemia. The remaining 60, 80, and 65 participants did not have hypertension, diabetes, or dyslipidemia, respectively.

Descriptive Data: Table 1 summarizes the demographic and clinical characteristics of the participants. The mean serum calcium level was 9.2 mg/dL with a standard deviation of 1.1 mg/dL,

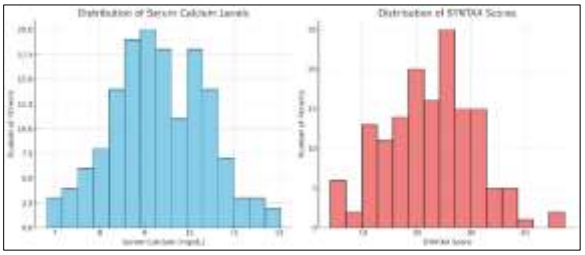
ranging from 7.1 to 11.3 mg/dL. The mean SYNTAX score, which reflects the complexity of coronary lesions, was 22.5 with a standard deviation of 8.4, and ranged between 10 and 45. This table provides a comprehensive overview of the key characteristics relevant to the study.

Table 1: Patient Demographics and Clinical Characteristics

Parameter (N - 50)	Summary	Range
Age (years)	55.4 ± 10.2	35-75
Gender		
Male	110 (73.33%)	
Female	40 (26.67%)	
Comorbidities		
Hypertension	90 (60%)	-
Diabetes	70 (46.67%)	-
Dyslipidemia	85 (56.67%)	-
Labs / Score		
Serum Calcium (mg/dL)	9.2 ± 1.1	7.1-11.3
SYNTAX Score	22.5 ± 8.4	10-45

Outcome Data: The distribution of serum calcium levels and SYNTAX scores is illustrated in Figure 1. This figure depicts the range and variation of these variables among the study participants.

Figure 1: Distribution of Serum Calcium Levels and SYNTAX Scores



The correlation analysis between serum calcium levels and SYNTAX scores revealed a low negative correlation, with a correlation coefficient of -0.13. This indicates a weak inverse relationship between serum calcium levels and the severity of coronary lesions as quantified by the SYNTAX score

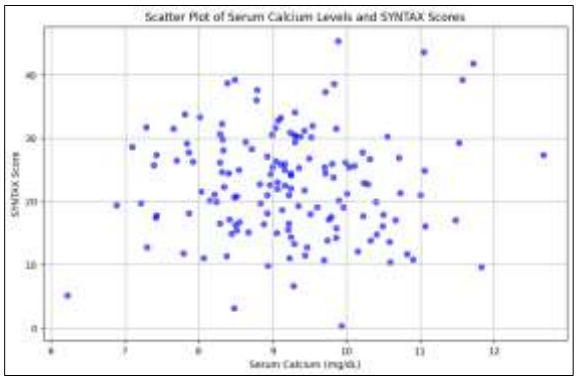
Main Results: Multivariate logistic regression analysis was performed to account for potential confounding variables including age, gender, hypertension, diabetes, and dyslipidemia. The results of this analysis are summarized in Table 2.

The multivariate analysis demonstrated that age was a significant predictor of CAD severity ($p < 0.001$). In contrast, serum calcium levels did not show an independent effect on CAD severity ($p = 0.24$). This suggests that while age plays a crucial role in predicting CAD severity, serum calcium levels alone do not significantly impact the severity of coronary lesions when other variables are considered.

Table 2: Multivariate Logistic Regression Analysis

Variable	Odds Ratio	95% CI	p-value
Age	1.05	1.02-1.08	0.001
Gender (Male)	1.1	0.65-1.85	0.74
Hypertension	1.2	0.70-2.10	0.51
Diabetes	1.3	0.75-2.25	0.36
Dyslipidemia	1.25	0.80-2.00	0.45
Serum Calcium	0.9	0.80-1.10	0.24
SYNTAX Score	1.15	1.10-1.20	<0.001

Figure 2: Scatter Plot of Serum Calcium Levels and SYNTAX Scores



The scatter plot provided in Figure 2 visually represents the relationship between serum calcium levels and SYNTAX scores. The plot illustrates a dispersed distribution of data points, aligning with the numerical correlation coefficient of -0.13, indicating a weak negative correlation. This weak correlation reinforces the finding that while serum calcium levels show some association with the complexity of coronary lesions, it is not strong enough to be a reliable independent marker of CAD severity. Serum calcium levels might offer additional insights when used alongside other diagnostic measures for a more comprehensive evaluation of CAD.

DISCUSSION

This study aimed to explore the relationship between serum calcium levels and the angiographic severity of coronary artery disease (CAD) in patients with chronic coronary syndrome (CCS). Our findings revealed a low negative correlation between serum calcium levels and SYNTAX scores, with a correlation coefficient of -

0.13. Additionally, age emerged as a significant predictor of CAD severity ($p < 0.001$). However, serum calcium levels did not demonstrate an independent effect on CAD severity after adjusting for other risk factors ($p = 0.24$).

Our results differ from several previous studies that have explored the relationship between serum calcium levels and cardiovascular outcomes. For instance, Wang et al. (2020) observed that higher serum calcium levels were associated with lower mortality rates among CAD patients, suggesting a potential protective effect [1]. Conversely, Park and Lee (2019) found that borderline high serum calcium levels were linked to arterial stiffness and an increased risk of cardiovascular disease [3]. These discrepancies may be due to differences in study populations, methodologies, or the specific parameters used to assess CAD severity. Our study, focused on a cohort from a single center in Pakistan, may reflect unique demographic and clinical characteristics that differ from those in other populations.

In contrast, Zhang et al. (2020) reported a positive association between higher serum calcium levels and the severity of coronary atherosclerosis in patients undergoing cardiac computed tomography, indicating that elevated calcium levels might contribute to vascular calcification [13]. Narang et al. (2020) also found a significant negative association between serum calcium levels and angiographic CAD severity, which supports our findings [14]. Furthermore, Sun et al. (2020) explored the relationship between serum calcium levels and clinical outcomes in patients with COVID-19, noting that lower calcium levels were associated with worse clinical outcomes. This highlights the complex role of calcium in various disease contexts [15]. Yang et al. (2021) identified a link between elevated serum calcium levels and an increased risk of all-cause and cardiovascular mortality in CAD patients, suggesting a multifaceted relationship between calcium metabolism and cardiovascular health [16].

The low negative correlation between serum calcium levels and SYNTAX scores in our study implies that while there is some association, it is not robust enough to consider serum calcium as a standalone predictor of CAD severity. This finding is consistent with the notion that age remains a crucial factor in determining CAD severity due to the cumulative effects of risk factors and the natural aging of the vasculature. The lack of a significant independent effect of serum calcium levels after adjusting for potential confounders suggests that other factors play a more prominent role in CAD severity among patients with CCS.

While serum calcium levels alone may not be sufficient for CAD risk classification, they could potentially enhance risk stratification when used in conjunction with other diagnostic tools. For example, integrating serum calcium measurements with coronary artery calcium (CAC) scoring could improve the specificity of risk assessment in CCS patients. Further research should focus on validating these findings and exploring the combined use of serum calcium and other biomarkers to enhance CAD assessment and management.

Our study indicates that serum calcium levels are not independent predictors of CAD severity in patients with chronic coronary syndrome. The observed low negative correlation suggests some association, but it is not strong enough to be a primary marker. Age remains a significant factor in CAD severity, underscoring the importance of considering multiple risk factors for comprehensive risk stratification. Future research should aim to validate these findings and investigate the potential benefits of combining serum calcium levels with other diagnostic tools for improved CAD assessment.

Limitations

This study has several limitations that warrant consideration. First, although a sample size of 150 patients is adequate for detecting correlations, it may still be insufficient for generalizing findings to a broader population. The cross-sectional nature of the study restricts the ability to infer causality between serum calcium levels and CAD severity. Furthermore, conducting the study at a single center in Pakistan may limit the external validity of the results, as the demographic and clinical characteristics of the study population might not represent other populations with different attributes. Additionally, the study may be affected by residual confounding factors not

included in the multivariate analysis, such as dietary calcium intake, vitamin D levels, and genetic factors influencing calcium metabolism.

Future Directions

To address these limitations, future research should focus on several key areas. Larger, more diverse populations across multiple centers would enhance the generalizability of the findings. Employing longitudinal study designs could better elucidate causal relationships between serum calcium levels and CAD severity. Additionally, examining other relevant factors, such as dietary calcium intake, vitamin D levels, and genetic predispositions, may provide a more comprehensive understanding of the role of calcium in CAD. Investigating the combined use of serum calcium measurements with advanced biomarkers and imaging techniques, such as coronary artery calcium (CAC) scoring, could offer a more nuanced approach to risk assessment. Future studies should also consider gender-specific analyses, given potential differences in calcium metabolism and cardiovascular health between men and women. Ultimately, these efforts could lead to the identification of novel biomarkers and the development of precision medicine strategies for managing CAD in patients with chronic coronary syndrome.

CONCLUSION

Our study concluded that serum calcium levels do not serve as independent predictors of coronary artery disease (CAD) severity in patients with chronic coronary syndrome (CCS). Although a weak negative correlation between serum calcium levels and SYNTAX scores was identified, suggesting a minor association, the relationship is not strong enough to establish serum calcium as a standalone marker for CAD severity. Age emerged as a significant determinant of CAD severity, reinforcing the need to consider multiple risk factors in a comprehensive risk assessment. While serum calcium levels alone are insufficient for CAD risk classification, they may offer added value when used in conjunction with other diagnostic tools. Future research should aim to validate these findings and explore the integration of serum calcium levels with other diagnostic modalities for more effective CAD assessment.

AUTHORS' CONTRIBUTION

MSA, GI and ZM: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. FQ, MA, SAS, and AM: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Acknowledgment: None.

REFERENCES

1. Wang M, Yan S, Peng Y, Shi Y, Tsauo J-Y, Chen M. serum calcium levels correlates with coronary artery disease outcomes. Open Med. 2020;15:1128-36.
2. Wang H, Li W, Du F, Tian J. Correlation of serum calcium with cardiovascular outcome in patients with acute coronary syndrome. Iran Red Crescent Med J. 2021;23(2):e676.
3. Park B, Lee Y. borderline high serum calcium levels are associated with arterial stiffness and 10-year cardiovascular disease risk determined by framingham risk score. J Clin Hypertens. 2019;21:668-73.
4. Ismail A, Abdeltawab A, Roshdy A. echocardiography calcium score as predictive tools of severity of coronary artery disease. QJM An Int J Med. 2021;114. https://doi.org/10.1093/qjmed/hcab090.011.
5. Liaquat A, Khan A, Ullah Shah S, Iqbal H, Iqbal S, Rana AI, et al. evaluating the use of coronary artery calcium scoring as a tool for coronary artery disease (cad) risk stratification and its association with coronary stenosis and cad risk factors: a single-centre, retrospective, cross-sectional study at a tertiary cent. BMJ Open. 2022;12:e057703.
6. Shreya D, Zamora DI, Patel GS, Grossmann I, Rodriguez K, Soni M, et al. Coronary Artery Calcium Score - A Reliable Indicator of Coronary Artery Disease? Cureus. 2021;13(12):e20149.
7. Umer M, Qamar A, Shehzadi N, Aslam MU, Noor S, Maryam S, et al. frequency of coronary artery disease using calcium scoring by 640 slice ct. J Heal Med Nurs. 2020.
8. Patel M, Agrawal S, Acharya S, Kumar S. serum calcium levels and its association with coronary artery disease. J Sci Soc. 2022;49:256.
9. Noshin TF, Ali MR, Banik S. increased oxidative stress and altered serum macro-minerals and trace elements levels are associated with coronary artery disease. J Trace Elem Med Biol. 2021;64:126707.
10. Kai R, Murtala B, Zainuddin AA, Amin M, Ilyas M. correlation between serum calcium and phosphate with coronary artery calcium scores on cardiac msct examination. Saintika Med. 2019;15:120.
11. Pathakota SR, Durgaprasad R, Velam V, AY L, Kasala L. correlation of coronary artery calcium score and carotid artery intima-media thickness with severity of coronary artery disease. J Cardiovasc Thorac Res. 2020;12:78-83.
12. Shabbir A, Virk ST, Malik J, Kausar S, Nazir TB, Javed A. coronary artery calcium score: assessment of syntax score and prediction of coronary artery disease. Cureus. 2021;13(1):e12704
13. Zhang C, Bangming CA, Huang X, Jian GU, Ming XI, Xiangjun YA, Hongxia LI. Association between serum calcium and first incident

acute myocardial infarction: a cross-sectional study. Iran J Public Health. 2020 Jul;49(7):1278.
14. Narang R, Ridout D, Nonis C, Kooner JS. serum calcium, phosphorus and albumin levels in relation to the angiographic severity of coronary artery disease. Int J Cardiol. 1997;60:73-9.
15. Sun J-K, Zhang W-H, Zou L, Liu Y, Li J-J, Kan X-H, et al. serum calcium as a biomarker of clinical severity and prognosis in patients with coronavirus disease 2019. Aging (Albany NY) 2020;12:11287-95.
16. Zhang J-F, Meng X, Jing J, Pan Y, Wang Y-L, Zhao X-Q, et al. serum calcium and long-term outcome after ischemic stroke: results from the china national stroke registry iii. Atherosclerosis. 2021;325:24-9.