

Investigating the Prognostic Utility of Serum Osteocalcin and Osteopontin Levels in Predicting Arthroplasty Outcomes

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Abstract: Background: Arthroplasty is a transformative surgical intervention for treating joint disorders and significantly enhances the quality of healthcare. Recent studies have highlighted the role of vitamin K-dependent proteins, including osteocalcin and osteopontin, in bone remodeling and their potential impact on arthroplasty procedures.

Objectives: This research study investigates the potential of serum osteocalcin and osteopontin levels as predictive biomarkers for the success of total joint replacement surgeries.

Methods: This prospective cohort study involved 50 participants undergoing primary total joint arthroplasty. Patients were divided into two groups based on their arthroplasty outcomes: group A with good outcomes (N=25) and group B with worse outcomes (N=25). Serum osteocalcin and osteopontin levels were measured three months postoperatively, and results were compared between the groups.

Results: Serum osteocalcin concentrations were significantly higher in the good outcome group compared to the worse outcome group (21.34 ± 0.92 ng/ml vs. 14.78 ± 2.22 ng/ml, $p < 0.001$). Conversely, serum osteopontin concentrations were significantly lower in the good outcome group compared to the worse outcome group (28.32 ± 1.08 ng/ml vs. 42.15 ± 7.02 ng/ml, $p < 0.001$). Logistic regression analysis confirmed the effectiveness of these biomarkers, with osteocalcin potentially having the most significant impact.

Conclusion: Higher serum osteocalcin levels and lower serum osteopontin levels are associated with more favorable arthroplasty outcomes. Monitoring these biomarkers may be an optimal strategy for predicting and managing patient outcomes in joint replacement surgeries.

Keywords: Arthroplasty, Joint Replacement, Osteocalcin, Osteopontin, Biomarkers, Bone Remodeling, Serum Levels.

Introduction

Arthroplasty is a transformative surgical intervention that has revolutionized the treatment of joint disorders, such as osteoarthritis and rheumatoid arthritis (Howard et al., 2023; Keller et al., 2023). The continual advancement of arthroplasty techniques, particularly in the shoulder and hip joints, has been driven by the goal of optimizing patient outcomes through improved surgical methods and post-operative rehabilitation protocols (Poursalehian et al., 2023; Gao et al., 2023; Deere et al., 2022).

Surveillance of outcomes of joint replacement surgeries as well will purely be necessary. It provides valuable information that help healthcare providers to develop modern practices and in turn, patient care will change for the better. (Gould et al., 2021; Nogod et al., 2022). Through the observation of long-term outcome and the feedback of the patients, healthcare providers can optimize surgical techniques, develop effective rehabilitation strategies, and most importantly, provide tailor-made care to those undergoing knee replacement (Łukasiewicz et al. 2023; Green et al. 2023; Polisetty et al. 2020).

The role of vitamin K2 in our bone health has garnered significant attention recently after it was discovered that vitamin K2-dependent proteins play an essential role in the building process of minerals in our bones (Merra et al., 2023; Tsugawa et al., 2021). This finding in itself has been vigorously probing to discover how vitamin K2 and its related molecules are connected to the success or failure of arthroplasty procedures (Capozzi et al., 2020, Friedman et al., 2016).

Among these vitamin K-dependent proteins, osteocalcin and osteopontin play a crucial role in the bone remodeling processes; both of them were assigned as key players in this process (Qazi et al., 2023; Dimas et al., 2022). The researchers postulate that the intersect between these proteins and the insertion of prosthetic remnants might hold the secret to forming novel biomarkers that will provide information for predicting surgical success and managing the patient postoperatively (Tu

et al., 2023). The objectives of this research will be illuminated by examining the role of osteocalcin, osteopontin and arthroplasty outcomes that may shed light on a great deal of crucial details that may put improvements in the health care system by guaranteeing increased surgical outcomes.

The proposed research work had mainly two objectives first; i.e to find out if serum concentrations of osteocalcin and osteopontin could be used as indicators of the outcome of the total joint arthroplasty. In particular, we wanted this study to lay the ground for examining the potential of these two bone-related proteins to identify patients with good arthroplasty outcomes from patients with worse outcomes. Exploring the relationship between blood vessel cell specific proteins and the postoperative outcome of joint replacement may give us some new knowledge. The investigation focused on the association between the serum osteocalcin, serum osteopontin and the outcomes that arose after certain arthroplasty procedures. The discovering could be a vital element for a customized risk prediction model and guide treatment-specific interventions and this may significantly contribute to patient's wellbeing after joint replacement surgeries.

Methodology:

From 50 orthopaedic surgery cases treated in our treatment center, we drew our experience. We divided them into two groups, on the basis of successful and unsuccessful surgeries.

The 25 patients in the first group had good outcomes. Their operations were performed properly, no further planned treatments or check-ups in the next two years after.

Another 25 patients had worse outcomes. These patients experienced significant problems with their joint function and needed additional medical or surgical treatments.

Serum Biomarker Measurements: Blood samples from all participants were taken 3 months after the surgery in the follow-up. The next part was to let the blood samples clot naturally at room temperature for 30 minutes, while the separated serum was collected under the centrifugal force at 3,000 rpm for 10 minutes. The serum samples were divided in aliquots and kept at -80°C until analysis.

Serum Osteocalcin Measurement: The human serum levels of osteocalcin were determined utilizing the commercially available enzyme-linked immunosorbent assay (ELISA). Firstly, the serum samples were thawed and diluted according to the kit instructions. The prepared samples were poured into the test tubes which were consecrated by Osteocalcin Standards followed by the addition of 50 μL of the provided standard controls. The plate was incubated for one hour, following the kit guidelines, to enable osteocalcin in the samples to react with the immobilized antibodies. After that, the plate was washed and a horseradish peroxidase (HRP)-conjugated detection antibody was added. Lastly, the plate was incubated for the required time. After being incubated for 30 minutes and left at room temperature, the dish was then ready for the next step.

The enzymatic reaction was initiated by adding the substrate solution after which the plate was left to incubate in the dark for 15 minutes. The process was then brought to halt by adding the stop solution, and the absorbance measurement was done with the microplate reader at 450 nm. The serum samples' osteocalcin concentrations were obtained by literary interpolation of the sample absorbance values with the standard curve and the results were later presented in ng/mL .

Serum Osteopontin Measurement: Osteopontin serum's concentration was measured by an appropriate ELISA kit. The procedure was similar to the osteocalcin assay, with the following modifications: Firstly, the serum samples were diluted as per the kit instruction, and then incubated for 2 hours at room temperature, with capture antibody-coated plate. The HRP-conjugated detection antibody was incubated for 1 hour, and the substrate reaction was allowed to develop for 30 minutes before stopping the reaction. The absorbance was measured at 450 nm, and the osteopontin concentrations were calculated from the standard curve, with the results expressed in ng/mL .

All serum biomarker measurements were performed in duplicate, and the mean values were used for the statistical analyses. The laboratory personnel performing the ELISA assays were blinded to the patient grouping (good outcome vs. worse outcome) to minimize any potential bias.

Arthroplasty Outcome Assessment: Clinical and functional assessments were performed at regular intervals to evaluate the arthroplasty outcomes. The good outcome group was defined as patients who met the following criteria during the 2-year follow-up period: (1) no need for any major medical or surgical interventions, such as revision surgery, (2) maintenance of joint function with a minimum score of 80 on a validated patient-reported outcome measure (e.g., Oxford Hip Score or Knee Society Score), (3) absence of any significant pain or disability that interfered with daily activities. The worse outcome group included patients who experienced any of the following: (1) the need for major interventions, such as revision surgery, (2) a decrease in joint function with a patient-reported outcome measure score below 60, (3) persistent pain or disability that significantly impacted the patient's quality of life.

Data Analysis: The concentration of serum osteocalcin and osteopontin was compared between the good outcome and worse outcome groups at each time with the appropriate statistical tests, such as ttests or Chi-squares tests, depending on the distribution the data. Data distribution test methods have been used, depending on the nature of data. Furthermore, logistic regression models were developed in order to investigate the prognostic value of the serum biomarkers independently from other clinical and demographic factors.

Results

Table 1 Table 1: Comparison of Arthroplasty Outcomes between Good and Worse Outcome Groups

Item	Good outcomes group (n=25)	Worse outcomes group (n=25)	Pvalue
Age (mean+/-SD)	45+/-6.28	44.8+/-5.5	0.452
Male gender n(%)	12/25 (48%)	13/24(52%)	0.777
Osteocalcin levels ng/ml (mean+/-SD)	21.34+/-0.92	14.78+/-2.22	<0.001
Osteopontin levels ng/ml (mean+/-SD)	28.32+/-1.08	42.15+/-7.02	<0.001

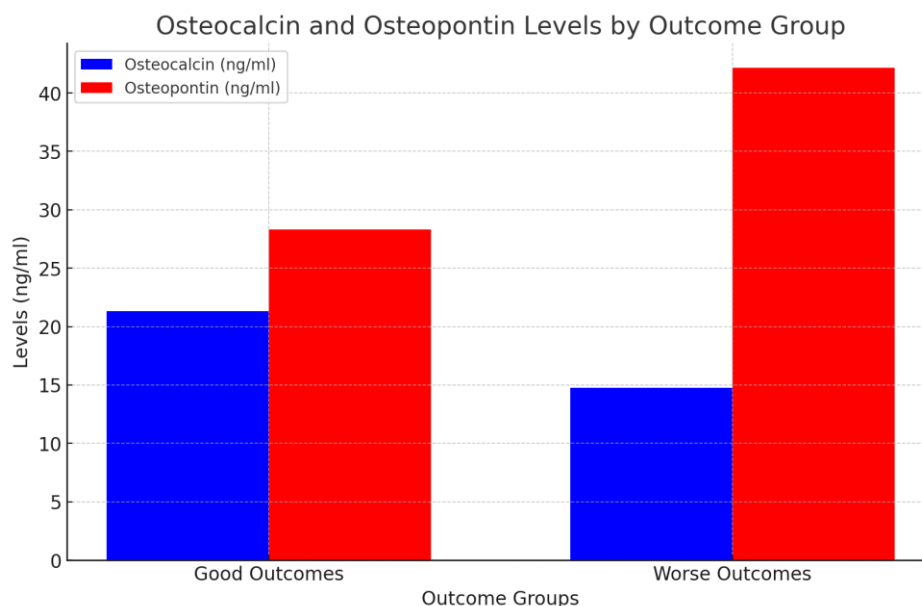


Figure 1: Osteocalcin and osteopontin levels in both study groups

This table compares key parameters between patients with good and worse outcomes after arthroplasty surgery. The average age was similar, around 45 years, in both the good outcome group (45.0 ± 6.28 years) and the worse outcome group (44.8 ± 5.5 years). The gender distribution was also comparable, with roughly half of the patients being male in each group.

However, there was a significant difference in serum osteocalcin levels. Patients in the good outcome group had notably higher osteocalcin levels (21.34 ± 0.92 ng/ml) compared to those in the worse outcome group (14.78 ± 2.22 ng/ml). A difference that was statistically significant ($p < 0.001$) was observed.

This test revealed that patients who did well in terms of post-operative arthroplasty outcomes had less levels of the particular protein osteopontin in their blood (28.32 ± 1.08 ng/ml) compared to patients who had poor outcomes (42.15 ± 7.02 ng/ml, $p < 0.001$). Interestingly, better outcomes have been reported in individuals with higher levels of the protein osteocalcin. The positive evidence relates that the higher level of osteocalcin and the lower levels of osteopontin are associated with better arthroplasty postoperative results.

Table: 2 Logistic Regression Analysis of Serum Biomarkers and Arthroplasty Outcomes

ANOVA Significance F	ANOVA F	Observations	Standard Error	Adjusted R Square	R Square	Multiple R	Biomarker
5.99E-13	94.83222	50	0.29583	0.65694	0.663941	0.814826	Osteopontin
4.50E-18	184.6999	50	0.23177	0.789428	0.793726	0.890913	Osteocalcin

The results obtained demonstrated that those who had better results after the arthroplasty surgery had low level of osteopontin in their blood (28.32 ± 1.08 ng/ml) than those who had worse results (42.15 ± 7.02 ng/ml; $p < 0.001$). However, for the patients with more favorable outcomes the level of osteocalcin protein was higher. The above evidence represents the fact that osteocalcin level increase together with corresponding osteopontin decrease are markers of better arthroplasty results.

In this table, the findings from a statistical analysis of logistic regression regarding the role of serum biomarkers in the outcomes of arthroplasty are highlighted.

For serum osteopontin, the result clearly indicated a high correlation with arthroplasty outcomes as there is a multiple R of 0.814826. Thus, 66.39% of the variability in arthroplasty outcomes is due to the serum osteopontin level which is implied by the adjusted R-squared value of 0.663941.

The ANOVA analysis of the osteopontin regression model was highly significant, with F-statistics of 94.83222 and the p-value of 5.99E-13. This endorses the characteristic feature of the model's statistical significance.

Osteopontin level regression coefficient was -0.04799; the p-value was 5.99e-13. This is an evidence of an inverse and almost significant relationship between the osteopontin levels and the arthroplasty outcomes.

As analysed by means of regression, there was a tight correlation between serum osteocalcin levels and the effectiveness of arthroplasty on a person's arthritis. The multiple R value was obtained as 0.890913 and the R-squared value was 0.793726, thus suggesting that 79.37% of the variation in arthroplasty outcomes can be explained by the assessment of serum osteocalcin levels.

Osteocalcin regression model ANOVA output has shown the statistical significance of the model, and has yielded a highly significant F-statistic of 184.6999 and a p-value of 4.50E-18.

The regression coefficient of serum osteocalcin was 0.120995, with a p-value of 4.50E-18, which was associated with quite a significant and positive relationship between osteocalcin levels and arthroplasty outcomes.

The highlighted results point out that the diagnostic utility of serum osteopontin and osteocalcin in forecasting prosthetic surgical outcomes is very high, and osteocalcin is more efficient than osteopontin in differentiating these surgical procedures

Discussion

This study was chiefly focused on attempts of checking the serum levels of osteocalcin and osteopontin and predicting in a positive way the success of total joint arthroplasty. The objective of the research is to measure these 2 bone proteins and use their results as criterion to distinguish patients either in the good or bad arthroplasty outcome group.

The research indicates that the participants with a better prognosis had much higher levels of osteocalcin in their serum as against those with a poorer prognosis (21.34 ± 0.92 ng/ml vs. 14.78 ± 2.22 ng/ml, $p < 0.001$) (Table 1). On the other hand, those with better outcomes had significantly lower levels of serum osteopontin than the worse outcome group (28.32 ± 1.08 ng/ml vs. 42.15 ± 7.02 ng/ml, $p < 0.001$) (Table 1).

The logistic regression analysis further confirmed the strong predictive ability of these biomarkers. For serum osteopontin, the regression analysis showed a multiple R of 0.814826, indicating a strong correlation with arthroplasty outcomes, with 66.39% of the variation in outcomes explained by osteopontin levels (Table 2). Similarly, serum osteocalcin demonstrated an even stronger correlation, with a multiple R of 0.890913 and 79.37% of the variation in outcomes explained by osteocalcin levels (Table 2).

The findings of the present study highlight the usefulness of measuring the levels of serum osteocalcin and osteopontin to predict how patients will do after having a total joint replacement surgery. These results align with growing research that shows bone metabolism markers are important in the context of orthopedic procedures, particularly joint replacement surgeries.

Our study found that patients with higher serum osteocalcin levels were much more likely to have better outcomes from their joint replacement surgery. This matches what was seen in a previous study, where hip replacement led to increased osteocalcin levels which correlated with improved function in patients with bone death in the hip (Li, 2020). Apart from the previous study, another research also showed that the medication zoledronic acid decreased the level of osteocalcin in patients of a particular type of hip replacement in which the rate of bone metabolism was reduced. Thus, it could be used as a metabolic marker which helps in the prevention of bone deterioration and the new joint surface might function better as a result (Hsu et al., 20

On the contrary, the results of the investigation suggested that the lesser amount of the osteopontin in the blood was linked with the better prognosis of the patients at the joint replacement surgery. The researchers observed that the markers for inflammation including the osteopontin levels were high in COVID-19 patients, who had bad outcomes, making the researchers speculate that the inflammation that is linked to osteopontin probably also applies to recovery in patients after joint replacement (Hayek et al., 2021).

The fact that osteocalcin and osteopontin could potentially predict joint replacement outcomes is part of the bigger picture that is about osteocalcin and osteopontin relation to health in different situations. For instance, a study reported significant associations between these markers and bone health in women with diabetes, suggesting that they could help to provide adjunct treatment beyond joint replacement (Roomi et al, 2022). Moreover, studies have revealed osteocalcin has functions in controlling glucose and muscle function and could affect the post-surgery recovery period (Lin et al., 2018).

Conclusion:

The outcomes of this research imply an interesting prospect of introducing these serum markers as important predictive indicators used before total joint replacement surgery. The observed significantly higher osteocalcin and lower osteopontin levels in patients with a good outcome combined with good indication suggest that these markers could be excellent prognostic factors of surgery success.

Such results bring knowledge on the impact of bone metabolism on orthopaedic operations, mainly joint replacements, to the forefront of the expanding body of work on the field. Through the identification of the linkage between these biomarkers and the results of arthroplasty, physicians can modify their strategies and provide individualized care to their patients.

After the validation of our initial findings in larger patient populations, we need then to explore the practicality of employing osteocalcin and osteopontin into clinical decision-making. Ultimately, doctors as well as patients will be empowered to obtain the insights they need to strive for outcomes that are most favorable from such surgeries.

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