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The Role of procollagen type 1 amino-terminal propertied (P1NP) Cytochrome P450 (CYPs) and Osteoprotegerin (OPG) as Potential Bone function markers in Prostate Cancer Bone Metastasis

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ABSTRACT

Background: Procollagen type I amino-terminal propeptide (PINP) is often present during osteoblast development and could be a biomarker of early bone development. Osteoprotegerin (OPG) may protect tumor cells from apoptosis. Cytochrome P450 enzymes help tumor development and treatment (CYPs). Cytochrome P450 activates and deactivates anticancer drugs and pro-carcinogens.

Objective: The study examined the amounts of a diagnostic marker of bone formation, the amino terminal propeptide of type I procollagen (PINP), Osteoprotegerin (OPG), and P450, in prostate cancer patients at different stages and its ability to detect osteoblastic metastases.

Methods: ELISA was used to measure PINP, OPG, and P450 levels in 30 prostate cancer patients. (n = 32) and healthy men's serum (n = 36).

Results: Prostate cancer patients had higher blood levels of PINP, OPG, and P450 than healthy persons (301.3±134.9, 980±467.2, and 84.2±28.4 pg/mL, respectively). Compared to I+II prostate cancer patients, III+IV patients showed higher serum PINP, OPG, and P450 levels (P 0.001). OPG, P450, and PINP had statistically significant Area under the ROC curve (0.9467, P= 0.0001, 0.91, P= 0.0001, and 0.6977, P= 0.4035) in prostate cancer patients.

Conclusions: Metastatic prostate cancer patients had greater PINP, OPG, and P450 levels, according to our findings. PINP, OPG, and P450 levels may affect prostate cancer progression. These findings imply that serum PINP, OPG, and P450 levels may predict and diagnose prostate cancer.

Keywords: procollagen type 1 amino-terminal property (P1NP), osteoprotegerin (OPG), CYPs, prostate cancer

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INTRODUCTION

The bone metastases of prostate cancer (PCa) produce a general rise in the volume, and remodeling [1]. The most serious consequence of prostate cancer that has spread it usually causes excruciating pain, substantial fatality, and even death [2, 3]. Normal bone turnover is atightly controlled, coupled process wherein the regulated destruction of mineralized extracellular matrix (resorption) is followed by a formative phase. Large multinucleated osteoclasts, which fuse from mononuclear hematopoietic progenitors, are the cells in charge of resorption [4].

The cells that produce new bone, called osteoblasts, interact with osteoclast precursors to control osteoclast genesis and activity [5, 6]. However, the molecular regulators of this relationship were not understood until recently. OPG and RANKL, two proteins expressed by osteoblasts, have been found to directly control osteoclastogenesis and hence bone resorption. Both RANKL and RANK produced on the cell surface of osteoclast progenitors, must interact for the genetic and phenotypic activation of osteoclasts [6, 7]. When compared to OPG, bone cancers such osteoblastomas (large cell bone tumors) were shown to exhibit considerably higher levels of RANKL [8], proving that these proteins may contribute to the bone loss brought on by tumors. [9].

Even while PCa often produces mixed or osteoblastic bone metastases, it is probable that RANKL and OPG have a role in regulating the bone response in PCa bone metastasis. In a study, the biomarker of bone synthesis Procollagen 1 amino-terminal propeptide (P1NP) was shown to be higher in PC patients, indicating the existence of an imaging-confirmed skeletal disease [10, 11].

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Unlike those who have benign prostatic enlargement, de la Piedra et al [10] discovered that P1NP was persistently high in a number of patients with established bone metastatic illness. P1NP performed flawlessly in terms of sensitivity and specificity.

In their investigation, Brasso and classmates discovered a straight link between P1NP concentration and the degree of skeletal illness. These encouraging findings prompted the planned study to include more P1NP testing [12].

Early detection of bone metastases in prostate cancer patients may improve their quality of life and prevent significant issues [13, 14]. In cases of fast bone resorption brought on by metastatic bone disease, the levels of P1NP (the n-terminal property of type I procollagen) and 1CTP (the c-terminal telopeptide of type I collagen) are high [15, 16]. As a result, 1CTP and P1NP measurements can be used to identify those who have bone metastases. Additionally, studies suggest a link between these markers and events relevant to skeletal health, disease development, and survival (SRE)[17, 18] . P1NP has been effectively tested as a marker for the occurrence of osseous metastases in prostate carcinoma [19]. Furthermore, it was demonstrated that type I collagen's metabolic product, 1CTP P450s are enzymes supposed to have a role in the formation of cancer, prevention of cancer and metastasis, according to an increasing number of findings from epidemiological, diagnostic, and clinical research.

The metabolic pathway of taxane anticancer drugs is primarily regulated by enzymes of the cytochrome P450 (CYP) subclass 3A and 2C. The expression of these enzymes in solid tumors may have an impact on the in situ metabolism of drugs, [20] even though their role in the hepatic metabolism of taxanes is well documented. P450 enzymes could be used as particular markers of cancer growth and are thought to be promising targets for focused therapy and prevention. A special class of mixed-function oxidases known as P450 enzymes catalyzes a wide array of biosynthetic and metabolic functions including steroidogenesis and cholesterol metabolism. several publications have discussed how these overexpressed CYP genes can be used as potential drug development targets [21].

METHODS AND MATERIALS

Study population and design

Two main categories are included in this study, 36 healthy people and 62 cases of prostate cancer with clinical and histological diagnosis. The patients' ages ranged from 39 to 71. Early-stage patients (30 cases at stages I and II) and advanced stage patients were separated into two groups (32 cases at stages III and IV). The samples were obtained from the oncology unit at Rizgary Hospital and the Nanakaly Hospital for Blood Diseases and Cancer in Erbil City. Approval for the study was obtained from the Ethics Committee of the Hospital and informed consent has been obtained from the participants.

Collection of Blood Samples

Five to six venous blood samples were drawn for each case, which were placed in gold-top serum separator tubes (SST). The samples were then allowed to stand at room temperature for ten minutes before being centrifuged at 3000 rpm for fifteen minutes. The collected serum samples were immediately transferred to Eppendorf tubes that had already been pre-labeled and coded. For a given test, these samples were frozen at-20°C.

Biochemical Assays

The concentrations of procollagentype I amino-terminal propeptide (PINP), Osteoprotegerin (OPG), cytochromes P450 (CYPs) in serum specimens were estimated by sandwich enzyme-linked immunosorbent assay (ELISA) technique using the kits manufactured by BioVision company.

Statistical analysis

The computer applications utilized for statistical data analysis were GraphPad Prism version 9. Bar graphs and the results of statistical tests were expressed as Mean±SD. The unpaired t-test, also known as the Mann-Whitney U test, was utilized in order to make a comparison of the study parameter means for the two groups that were investigated. Additionally, the receiver operating characteristic curve (ROC) of the research parameters was evaluated.

RESULTS AND DISCUSSION

Serum levels of Procollagen Amino-terminal propertied (P1NP)

Significantly ($P<0.0001$) elevated levels of the serum procollagen Amino-terminal propertied (P1NP) were detected in Patients with prostate carcinoma in comparison to the control group. The mean value of serum P1NP for prostate cancer patients was (545.8± 92.22 pg/mL) and for the control group it was (301.3±134.9 pg/mL) (Table 1).

Prostate cancer that has metastasis to the bone typically has osteoblastic characteristics, which frequently manifest as osteoplastic modifications on plain X-ray

Table 1: Mean SD values of P1NP, OPG, and P450concentration in sera samples of control and patient groups

Parameters	Healthy controls (Mean ± SD)	Prostate cancer patients (Mean ± SD)	P-Value
Procollagen Amino-terminal propertied (P1NP)(pg/mL)	301.3±134.9	545.8± 92.22	<0.0001
Osteoprotegerin (OPG) (pg/mL)	980±467.2	1994±687.3	<0.0001
P450(pg/mL)	84.2±28.4	120.6±14.38	0.0022

images. Numerous metabolic indicators of bone growth and resorption have been discovered. These indicators were examined to see if they might be helpful for identifying and monitoring bone metastasis in men with prostate carcinoma [22, 23]. It is believed that the type I procollagen carboxy propetides and type I procollagen aminoterminal propeptides, which frequently appear during osteoblast proliferation, are signs of early bone formation. When type I collagen it produced, they are produced as well. Bone turnover biochemical indicators have been found. These indicators, which may influence the osteoblastic activity in bone, could be increased as a result of benign or malignant disease processes [24]. The P1NP, which is a useful indication of metastatic prostate carcinoma since it is mostly osteosclerotic in nature, is a sign of osteoblastic activity. P1NP is a sensitive and accurate indicator of osteoblastic activity [25].The mean P1NP levels in 25 patients with bone metastases and 40 patients without metastases in a sample of prostate cancer patients were 231 ng/ml and 31 ng/ml, respectively. The researchers decided that P1NP is an excellent diagnostic for detecting prostate cancer patients with bone metastases. In another set of studies [10], 67 patients with BPH as well as prostate cancer, with or without metastases, were assessed with average values of 569 ng/ml and 32 ng/ml, respectively. Patients suffering from bone metastases reported significant increased P1NP levels compared to those who did not. Non-metastatic cancer patients did not significantly differ in P1NP. P1NP has a 100 % sensitivity and specificity for bone metastases, according to the scientists, who also noted that this marker might be helpful in identifying metastatic illness. Similar findings were seen in this study. The study revealed that patients with metastases had greater mean P1NP concentrations than patients without metastases.

The increased bone metabolism that bone metastases are known to cause has led to innovative approaches that use specific tumor markers to detect malignant bone turnover. The novel bone formation marker P1NP, a precursor molecule of bone collagen, appears to be a promising predictor of osteoblastic metastases in prostate cancer patients as it is a highly sensitive and specific marker for osteoblastic activity. The current findings suggest that an accurate diagnosis might be made because P1NP levels were elevated in nearly 87 % patients with bone metastases.

Serum levels of Osteoprotegerin (OPG)

Prostate cancer patients had significantly (P<0.0001) high levels of serum osteoprotegerin (OPG) than the control group. The mean value of serum OPG was (1994± 687.3 pg/mL) for prostate cancer patients, while for the control group it was (980± 467.2 pg/mL) (Table 1). According to a study, OPG is produced by prostate cancer cells at levels high enough to inhibit TRAIL-induced apoptosis in vitro [26]. These investigations also revealed that decrease in androgen sensitivity in prostate cancer may be related to higher, constitutive OPG production.

In previous studies where serum OPG levels have been correlated with disease status in prostate cancer, research focused on the activities of OPG as an inhibitor of osteoclastogenesis, elevated levels of concentrations of Osteoprotegerin may therefore be connected with relation to the osteoblastic processes associated to the metastases of prostate cancer. It has been revealed that particularly androgen-resistant prostate carcinoma cell lines produce OPG at physiologically active levels. Bone marrow stromal is well known to produce OPG [27]. OPG is therefore resulting equally from the “seed” and the “soil” in metastatic lesions in the setting of prostate cancer, but the relative significance of each source in terms of disease development remains to be determined.

OPG synthesis in skeletal metastases may have a role in the osteoblastic response observed there, but it may possibly have additional effects. In the case of the latter, our main hypothesis is that OPG may give prostate cancer cells a survival advantage regardless of their surroundings. Recent research employing in vitro-grown prostate cancer cells suggests that OPG is involved in processes other than bone production. In particular, TRAIL, a TNF family member that suppresses apoptosis, uses OPG as a decoy receptor [28]. In particular, OPG blocks interactions between TRAIL and death-inducing receptors on tumor cell surfaces, which are generated in and around tumors by invading monocytes [29, 30].

This activity reveals Osteoprotegerin as a factor directly associated with tumor survival and maybe tumor growth, making it significant in terms of tumor genesis and progression. The existence of more aggressive malignancies, increased Osteoprotegerin levels in the blood of patients suffering from advanced hormone-escaping illness may instantly imply a better likelihood to live after

androgen ablation [31]. Although it is doubtful that androgens directly influence Osteoprotegerin expression, it is unknown that perhaps these data indicate a change from constitutive overexpression in androgen-insensitive cell types to androgen-repressed expression in androgen-sensitive cells. Recent reports on OPG regulatory sequences indicate that they do not seem to include distinctive androgen response elements. It's interesting that OPG expression is induced.

Osteoprotegerin has been demonstrated to be created by prostate carcinoma cells, but other cell types may also produce OPG, which can accumulate in the bloodstream and decrease tumor apoptosis in people with elevated OPG levels. OPG has been found to be widely distributed in bone marrow stromal cells [32] and may be detected in the blood of individuals with osteoblastic prostate cancer metastases. In the initial phases of metastasis, when few tumor cells are striving to survive, the availability of bone-derived OPG may influence the selection of bone marrow as the preferred location for prostate carcinoma metastasis.

The presence of osteoblastic lesions and the proliferation of osteoblasts is indicative of prostate carcinoma metastasis to the bone. Woven bone is produced in excess, which compromises bone health and leads to pathological fractures and compressions. In this preliminary stage of metastasis, there is already a rise in bone reabsorption, which destroys the framework of preexisting bone. The resorptive process in normal adult bone is regulated by the master controllers RANK, RANKL, and OPG [33]. We anticipated that since Osteoprotegerin is a released protein, patients with prostate cancer bone metastases would have higher blood Osteoprotegerin levels. Previous research has revealed that metastasizing prostate carcinoma cells express considerably higher levels of Osteoprotegerin than initial prostate cancer cells [34].

Our research demonstrates that individuals with progressed prostate cancer had greater circulating Osteoprotegerin levels than those who had lower prostatic disease stages. Prostate carcinoma cells activate human and rat osteoblasts, according to in vitro studies [35]. Therefore, greater osteoblastic activity in response to prostate cancer cells present in the bone microenvironment and higher Osteoprotegerin expression by prostate carcinoma cells in bone metastases may both contribute to the observed elevation in serum Osteoprotegerin levels [27].

Serum levels of cytochromes P450 (CYPs) enzymes

Significantly (P=0.0022) elevated levels of the serum cytochromes P450 (CYPs) enzymes were observed in prostate cancer patients with respect to the control group. The mean value of Serum P450 for prostate cancer patients was (120.6±14.38 pg/mL) and for the control group, it was (84.2±28.4 pg/mL) (Table 1).

The cytochromes P450 are crucial enzymes in the development and therapy of cancer. The inactivation and activation of anticancer medications, as well as the metabolic activation of several precarcinogens is facilitated by cytochromes P450. Since CYPs play a vital role in the metabolic activation of precarcinogens, several studies have been reported to identify genetic variations that may predispose to particular cancer types [36]. This is largely due to inadequate control of confounding factors, the numerous cases and controls required to obtain relatively small risk factors, the small differences in function between the variant alleles investigated, the P450 reaction in issue only partially contributing to the development of cancer, and the important environmental influences [37].

Key enzymes implicated in the development of cancer include CYP enzymes [38]. Numerous procarcinogens are metabolically activated by them [36]. Therefore, monitoring alterations in cytochromes P450 enzyme activity would be helpful for identifying potential risk factors for cancer as well as designing individualized cancer treatments, because cancer might be accompanied by a variety of physiological issues.

Seven CYPs were examined by Yan et al [39] in tumors taken from 26 individuals with hepatocellular carcinoma. The results demonstrate that, in comparison to peri carcinomatous HLMs and control HLMs, the activity of these seven cytochromes P450 isoforms was declined in tumor human liver microsomes (HLMs). Although cirrhosis was identified in the peri carcinomatous tissues, the illness history of the donors of the control pooled HLMs remained unclear. Another comparable study [40] described the CYP3A4 activity in the hepatocellular carcinoma tumors of 18 individuals. Controls included pooled male liver microsomes and liver microsomes from nearby non-cancerous tissue. The unique variance of CYP activity in healthy liver tissue was not discussed in either of these two reports.

Comparison of Serum Procollagen Amino-terminal propertied levels between the four stages of the disease

When disease stages are compared, it can be seen that serum amino-terminal property levels rise rather gradually from stage I and stage II to stage III to stage IV of the

illness. Additionally, as the stages progress from III, IV, to V, the serum levels of amino-terminal propertied proteins are often significantly elevated (P=0.0001) (Figure 4). De la Piedra et al [18] examined the levels of numerous indicators of the bone turnover in males with and without bone involvement of prostate carcinoma, including amino-terminal propertied, procollagen type 1 aminoterminal telopeptide and specific alkaline phosphatase.

All tested bone markers were found to be considerably higher in patients with bone metastases. They discovered 100% sensitivity and specificity for type I procollagen aminoterminal propeptides. Similar P1NP values for this question were discovered in a prior study by Horas et al. Specificity and sensitivity in their investigation were both 100 % [41]. In cases with bone involvement, Merlo et al. similarly reported significantly increased P1NP values compared to the group without bone metastases as a control [42]. According to the investigations, there were increased serum P1NP concentrations. Koizumi M et al [25] discovered that type I procollagen aminoterminal propeptides is a reliable marker for expressing the number of bone metastases that really are present in response to the question of whether it is helpful in determining the extent of bone involvement. This study thus confirms their conclusions. In our investigation, we also discovered that substantial bone involvement was associated with the highest type I procollagen aminoterminal propeptides concentrations. An additional finding was that patients with significant metastases other than bone had higher P1NP serum levels, as well. These results might corroborate with research by Jensen et al. that found a link between high P1NP levels and an aggressive cancer illness. Jensen et al. were able to explain in their research that high P1NP levels are linked to a rapid illness development.

As depicted in Figure 1, we think that P1NP, a marker of bone production, may be useful but may not always reflect the degree of bone degradation. Several studies have found a strong link between indicators of bone remodeling and the stage of cancer. When compared to stage I disease, myeloma stage II/II had greater serum levels of type I collagen's C-terminal cross- linking telopeptide [25, 43]. Advanced myeloma stage and abnormally high urinary levels of the type I collagen C-terminal cross-linking telopeptide were also associated [25].

Comparison of Serum Osteoprotegerin levels between the four stages of the disease

The comparison of disease stages shows a reasonably gradual increase of sera Osteoprotegerin levels in stage I and stage II through stage III to stage IV of the disease, and generally, the Osteoprotegerin serum levels are significantly increased (P<0.0001) as the stages go up from III, IV, to V (Figure 2). OPG is essential for the formation of bone disease. Patients with metastases prostate carcinoma have been shown to have serum Osteoprotegerin concentrations that are considerably higher than those with early-stage cancer [44]. In a different study, individuals with prostate carcinoma who had bone metastases had significantly lower OPG serum levels than patients with non-metastatic disease, benign hyperplasia, and healthy controls.

Metastases of bone typically cause significant pain and advanced prostate cancer patients' morbidity while also inducing variety of bone remodeling processes. Indirectly or directly, metastatic prostate cancer cells frequently have an impact on bone metabolism, including the processes of bone production and resorption [45].Their impact is manifested, however, as lesions of the bone that are mostly osteoblastic. The importance of the RANKL, OPG, and RANK axis in bone turnover and the emergence

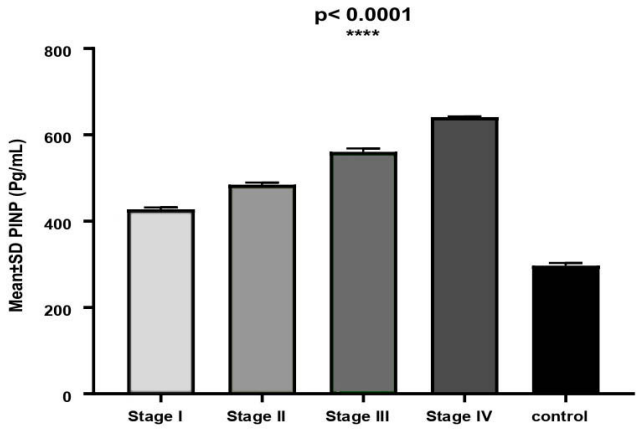

Fig. 1. P1NP serum levels in relation to prostate cancer stages

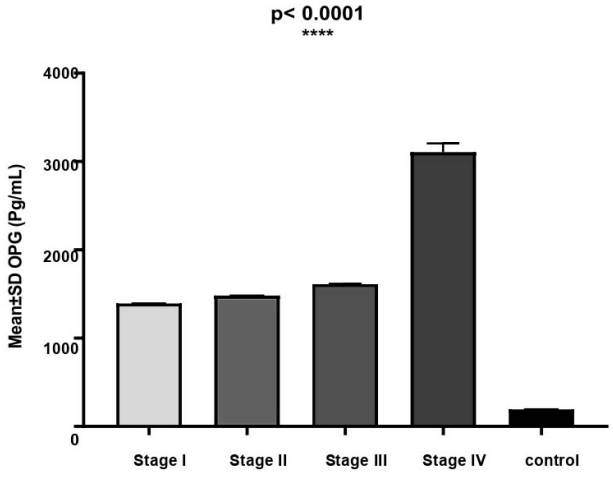

Fig. 2. Serum Osteoprotegerin levels in relation to prostate cancer stages

of bone metastases has also been discussed in prior research [46, 47]. While mature osteoblasts, certain stromal bone marrow cells, and some lymphocytes in lymph nodes have been shown to express RANKL and Osteoprotegerin, RANK and RANKL are expressed by mature osteoclasts and their progenitors. OPG levels in the present study were statistically significantly elevated in PCa patients, while higher values were present in the serum of patients with metastatic bone disease, which may indicate that OPG expression is linked to the advancement of prostate carcinoma to the bone. In addition to bone marrow stromal cells, prostate carcinoma cell lines also generate Osteoprotegerin, which in turn stimulate osteoblasts in vitro [26, 48]. As a result, higher Osteoprotegerin concentrations in patients with metastatic prostate carcinoma may be observed because prostate carcinoma cells have a predominately osteoblastic stimulation in the bone microenvironment [49]. Patients with advanced prostate carcinoma and bone metastases have greater serum levels of Osteoprotegerin, according to previous clinical research. Additionally, patients with greater bone metastatic dissemination were shown to have higher Osteoprotegerin values in our study. Indeed, elevated serum OPG expression, according to Phillips et al [50] represents the severity of PCa metastatic bone disease and predicts biochemical failure. Additionally, Kamiya et al [51] noted that „circulating level of Osteoprotegerin could be an independent predictive factor for prostate cancer-related death". According to our data, higher blood levels of Osteoprotegerin may be a good indicator of metastatic bone metastasis in patients with prostate carcinoma and may play a vital role in the ongoing care of affected individuals with advanced metastatic malignancy.

Comparison of serum P450 levels between the four stages of the disease

The comparison of disease stages shows a reasonably gradual increase of sera P450 levels in stage I and stage II through stage III to stage IV of the disease, and generally, the P450 serum levels are significantly increased (P<0.0001) as the stages go up from III, IV, to V (Figure 3).

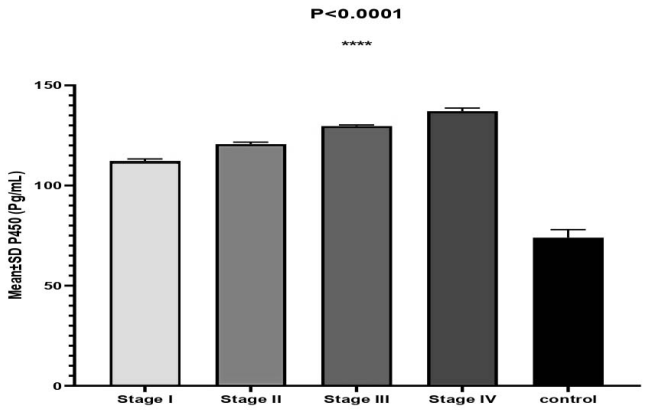

Fig. 3. Serum P450 levels in relation to prostate cancer stages

A significant portion of fatalities associated with malignant development are caused by metastasis, however this component of cancer biology is still remaining unclear.

Metastas research makes rapid progress in understanding the molecular mechanisms that underlie its spread and metastatic output. Malignant growth cell nature is starting to become clearer [52]. Due to different epoxygenases, their effects on the development of cancer, and their diverse expression patterns, the P450s are associated with possible cancer treatments. In many malignancies, EET therapy greatly elevated the gene expression patterns associated with migration, invasion and prometastatic behavior. Arachidonic acid is transformed into four Regio isomeric epoxyeicosatrienoic acids (REA) by P450 epoxygenases [53]. Different biological reactions are elicited by these enzymes in various systems. Numerous investigations discovered CYP2J2 epoxygenase upregulation in human cancer cells.

Because there is little genetic data linking the CYP AA epoxygenase enzymes to the growth or oncogenesis of specific tumor types, it is unknown how these enzymes participate in the carcinogenesis process as either drivers or passengers. Research utilizing genetic studies has shown that arachidonic acid Cytochrome P450 (CYP) epoxygenases enzymes are involved in cancer [54]. The stimulation of arachidonic acid Cytochrome P450 (CYP) epoxygenases enzymes and release from dormancy, both contribute to the growth and spread of primary tumors [55]. Mammary tumor engraftment is inhibited by decreasing cancer cell-intrinsic CYP3A4 [56]. The findings from genetic methods demonstrate the facilitating function of arachidonic acid Cytochrome P450 (CYP) epoxygenases enzymes in the formation development and spread of malignancies, which can be a key tactic in the treatment of cancer.

Receiver operating characteristic (ROC) curves for Assessing the diagnostic performance of Osteoprotegerin and procollagen type 1 amino-terminal propeptide

According to the area under the Receiver operating characteristic curve, the diagnostic values of serum P1NP, OPG, and P450 were compared using the Receiver operating characteristic curve analysis in the current investigation (AUC). A better diagnostic test has a higher AUC. Serum levels of OPG showed a significant AUC (0.9467), (P=0.0001), as shown in Figure 4.

As illustrated in Figure 5, serum levels of P450 showed a significant AUC (0.9157), (P<0.0001).

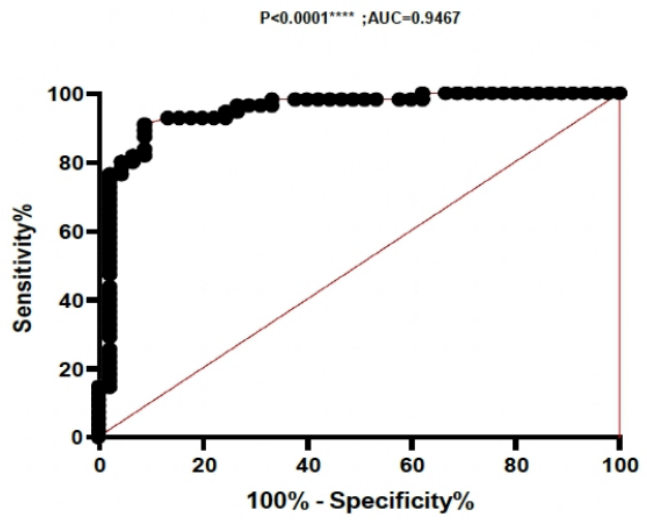

Fig. 4. Receiver operating characteristic curves for osteoprotegerin (OPG)

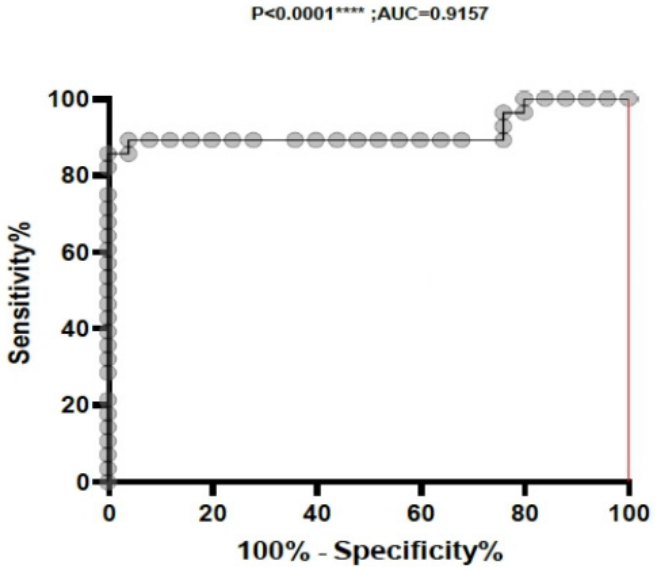

Fig. 5. Receiver operating characteristic curves for P450

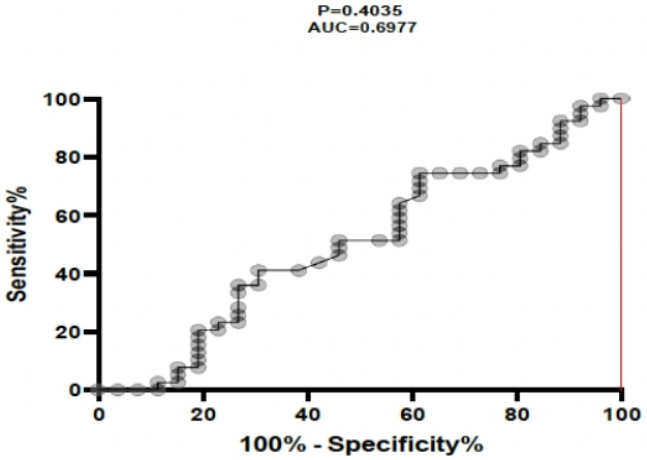

Fig. 6. Receiver operating characteristic curves for P1NP

As illustrated in Figure 6, serum levels of P1NP presented a significant AUC (0.6977), (P=0.4035).

ROC curves were created and are displayed in Figures 4-6. The AUC measures the test's diagnostic precision. OPG collagen had the highest AUC (0.9467) among the individual markers, followed by P450 (0.9157) and P1NP (0.6977).

The ROC curve's sensitivity/specificity diagram is the most important factor for tumor markers. The clinical usefulness of a tumor marker is evaluated according to the area under the ROC curve, and a bigger area under the curve suggests a more beneficial tumor marker [57, 58].

CONCLUSIONS

According to the data, P1NP, a marker for bone development, is a dependable indicator of bone involvement in males with prostate carcinoma. Given that significantly raised procollagen type I amino-terminal propeptide levels are remarkably related with the existence of Osteolytic metastases in individuals with prostate cancer, P1NP appears to be helpful for treating and diagnosing these patients. A study focused on treatment would demonstrate the value of P1NP even more as a future area of study. OPG seems to be a distinctive indicator that is detected in advanced prostate carcinoma patients' serum at increased levels. Regardless of the osteoblastic microenvironment in the setting of progression or its responsiveness to androgen control, OPG exhibits anti-osteoclastogenic capabilities in malignant bone disease,

In addition to possibly improving survival for prostate cancer in vivo. This suggests that circulating concentration of Osteoprotegerin may not only serve as an indicator for disease progression but also serve as a direct indicator of a tumor's ability to survive and the potential for associated disease progression. In the interim, more research is needed to confirm a novel predictive indicator for prostate cancer patients is serum OPG testing. A potentially helpful new biomarker for the peritoneal metastasis of prostate cancer is the serum P450 level.

ABBREVIATIONS

PCa – Prostate Cancer

PINP – Procollagen type 1 amino terminal propeptide

CYPS – Cytochromes P450

OPG – Osteo protegrin

ELISA – Enzyme-linked immunoassay

CAP – Community-acquired pneumonia

1CTP –1 Cytidine 5′-triphosphate

ROC –Receiver operating characteristic curve

TNF – Tumor necrosis factor

TRAIL –Tumor necrosis factor-related apoptosis-inducing ligand

RANK –Receptor activator of nuclear factor κ B

RANKL –Receptor activator of nuclear factor kappa-B ligand

AUC–Area Under the Curve

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AUTHORS' CONTRIBUTION

Authors declare equal contribution in all regards.

CONFLICT OF INTEREST

The authors declare that they have no competing interests. This paper received no funding.

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