

Review Article

Impacts of Prostate Cancer on Bone Health

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ABSTRACT

The patient with prostate cancer shows negative effect on the bone health by both due to emerge of disease as well as its treatment. Androgen deprivation therapy leads to osteoporosis due to pain in bone, fractures, and spinal cord compression. This kind of complications impact of the life of patients as well as lead to boost mortality rate. Maintaining an optimum bone health throughout the natural course is important parameter in the taking of care of patient suffering from prostate cancer. It is need of hour that to discuss the negative effects of the prostate cancer and its associated diagnostic and preventive treatments on the bone health. This article discusses the pathophysiology of the bone metastasis and bone density lowers, that is density of bone decreases because of ADT in the prostate cancer.

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INTRODUCTION

Cancer of prostate gland is one of most causative and shows its presence amongst the cancers that are diagnosed approximately causing 1.5 million cases according to survey present in the research articles. The patients diagnosed with the prostate cancer are now shown positive results in the living of their own life, their long life due to improvement in the treatment strategies and more study about the prostate cancer. The survival of prostate cancer patients has tripled in last few decades almost 80% of people survive and they are living along with cancer about more than ten years. The incline in the rate of survival of the prostate cancer patients is due to advances in the diagnostic strategies, with positive effect in screening and fast diagnosis on death rate (Badri *et al.*, 2019). The patients with cancer of prostate gland have shown that the patients have increased life span to live with cancer and this has helped to identify the effects of cancer treatment on the health condition of bone. Androgen and its associated body parts play a vital character in pathophysiology of prostate cancer. For the surgical methodology is

required for the successful running of ADT, the one more way is also their by using chemicals that is steroidal hormones by using LNRH its agonists and antagonists play important role in the management of prostate cancer. Androgen deprivation therapy is used to treat the prostate cancer patients at various stages, which chronic and severe stages of the prostate cancer. But ADT shows adverse effects are severe which affects on the growth of bones of the patients. ADT have shown adverse effect on mineral density of bone along with this also increases the chances of weakening of bone that is fracture associated with bone. An available study carried out by reputed scientists resulted in outcomes in 50k patients with cancer of prostate gland. Among all of them again survey was carried out which resulted about 20 % of patients shown side effects associated with bone like decreased bone density and increased risk of fracture of bone (Prakash *et al.*, 2013). Also study and survey is available suggesting that the even before imitation of ADT, on the patients who are undergoing through high level infection of cancer of prostate gland

have shown more chances of osteoporosis which ultimately affects bone health (Wang *et al.*, 2015).

In this article, we will mainly discuss about current available treatment and diagnostic strategies for cancer

of prostate gland and also clinical side effects of various therapies available for it.

Table: Treatment of prostate cancer at different stages (Badri *et al.*, 2019)

Stage	Treatment
Localized or Locally-advanced Prostate Cancer	Radical Prostatectomy
	Brachy therapy + ADT
	External Beam Radiotherapy + AD
Biochemical Relapse	Salvage Prostatectomy
	Salvage Radiotherapy + ADT
	ADT alone
	Observation
Metastatic castration sensitive Prostate Cancer	ADT therapy and
	Upfront Docetaxel + prednisolone
	Upfront Abiraterone + prednisolone
Metastatic castration resistant Prostate Cancer	Upfront Radiotherapy
	ADT therapy and
	Enzalutamide
	Abiraterone + prednisolone
	Docetaxel + prednisolone
	Radium-223
Sipuleucel-T	

PATHOPHYSIOLOGY

Prostate Cancer Bone Metastasis

Bone is the major or main site for the metastasis of the prostate cancer. The Bone metastasis is linked with the positive death rate and adverse effect on the life of patients via SREs. Therefore the treatment strategies are designed in such a way that by making slow start of SREs and hence will help maintaining the life quality and keeping the active status of patients suffering from cancer of prostate gland **Error! Reference source not found..** The exact mechanism for progression of bone metastasis in patients suffering from cancer of prostate gland remains unknown and number of research and studies scientist are doing to know the reason. The microenvironment of bone, however, is identified as a main factor for prostate cancer bone unbalanced bone growth and this is regulated by the CXCL16/CXCR6. By the influence of gradient of chemokines that are released from bone marrow circulating tumor cells migrates towards them. The migrated tumor gets infected and parasitizes the hemopoetic cells of bone marrow and become dominant. RANKL is a main regulator for the normal remodeling of bone growth and binds to its protein site RANK osteoclast progenitors on the surface, this result into the differentiation of osteoclast which ultimately leads to resorption of bone (Saad *et al.*, 2017). The spread of cells of cancer of prostate gland increases RANKL expression on osteoblasts by increasing the secretion of parathyroid glands hormone-associated with protein causing to osteoclastogenesis and increment in resorption of bone,

which leads to creation space for cancer cells increase their number in bone marrow.

Prostate cancer treatment against induced bone loss:

The sex steroid plays important role in bone and extensive studies have been done regarding the influence of sex steroids on bone growth and development. The signaling of the androgen receptor from osteoblasts is accountable for the protective action of androgen trabecular bone mass, which ultimately leads to a decrease in number of osteoclast and also lead to decrease bone resorption. The oestrogens that are produced by the aromatization of the androgen from men helps to protect the endocortical resorptions in the stromal cells (Wang *et al.*, 2015). Common proof from number of interventional and observational studies of human being states the theory that estrogen plays a significant role in regulation of metabolism of bone in men than testosterone (Siegel *et al.*, 2019). After the starting of ADT the hormonal amount of testosterone and estrogen falls down leading to the disruption of the bone activity. The available statically study indicated the decrease in the mineral density of bone is most significant in first 1 year after the start of ADT; hence the importance of early initiation of preventive measures is essential. It also resulted in rate of loss of bone cells in patients of prostate gland cancer initiating androgen therapy was 10 times higher than in either healthy men with prostate gland cancer with normal hormone levels (Sottnik *et al.*, 2013).

Glucocorticoids the pregnans are also important drug component in the treatment strategies of cancer of prostate gland with metastatic growth. Mainly they are

used with combination with chemotherapeutic agents or sometimes also used as low dose mono therapeutic agents. Studies regarding this combination and their effect on bone growth, bone density are also necessary. A novel oral androgen signaling inhibitor, now singled green for use in patients with metastatic prostate cancer called Enzalutamide have shown changes on the growth of bone and bone density (Vignani *et al.*, 2016).

Prevention and treatment

Systemic anticancer therapies as well as bone-targeted agents such as zoledronic acid, denosumab and radium-223 have proven effective for the prevention of skeletal-related events associated with prostate cancer (Wang *et al.*, 2015). **Awareness and Education**

Various available surveys highlights that patients suffering from prostate gland cancer have no information about risk associated with prostate cancer and treatment strategies and preventive measures. So it is important to create the public awareness regarding prostate cancer will helps to diagnose the cancer in its primary stage (Mohamad *et al.*, 2016).

Lifestyle Modification

The most common adverse effects of cancer of prostate gland are Osteoporosis and osteopenia. Study of patients with prostate gland cancer have shown result that it affects the health of bone, including higher BMI, exercise avoid use of alcohol and smoking as well, high administration calcium may help to overcome these side effects. The supplementation of calcium and vitamin D plays potential role in the pathogenesis of prostate cancer but it has been a topic to study (Prakash *et al.*, 2013). However, not a single clinical trial resulted in that the intakes of calcium supplements have decreased risk in patients undergoing androgen therapy. Also the other significant disadvantage of exposure to androgen therapy is the sarcopenia; it is non generative loss of mass of muscle that is associated with increased falls risk and frailty as well (Saad *et al.*, 2017). Parameters like muscle exercise and maintaining healthy diet with proper protein intake have been estimated and shown help amend the risk of sarcopenia and its negative impacts on ADT undergoing prostate gland cancer patients.

Bone-Targeted Agents (Siegel *et al.*, 2019)

Bisphosphonates-The role of biophosphonates in bone mass and density loss during prostate cancer is studied extensively. Their results confirmed the profit along with bisphosphonates in decrease in BMD loss in patients with cancer of prostate gland on ADT.

Endocrine Agents-The impact of specified estrogen receptor enhancers such as toremifene and raloxifene in avoiding loss of BMD in patients undergoing ADT has also been detected given the growing identification of the character of estrogen in metabolism of bone in patients of prostate gland cancer.

CONCLUSION AND FUTURE PROSPECTIVE

Due to availability of several lines of therapies the patients with cancer of prostate gland cancer have shown positive impact on life, they are living now long life, advancement in treatment strategy and those available therapies have made a significant impact on bone growth of patients with prostate gland cancer over large period of years. Early detection and improvement of prostate and bone health is fruitful in the treatment of prostate gland cancer. A number of new chemicals have been discovered and licensed for treating cancer of prostate gland I last few years, and large group of chemicals are in pipeline of development, like apalutamide, which will make more options available for treatment of cancer of prostate gland. There is also need of public awareness among the patients regarding the risks of prostate cancer as well as a developmental model for physician to assist which will help them to which sticks to the standard guidelines for diagnosis and prevention strategies.

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CONSENT STATEMENT/ETHICAL APPROVAL

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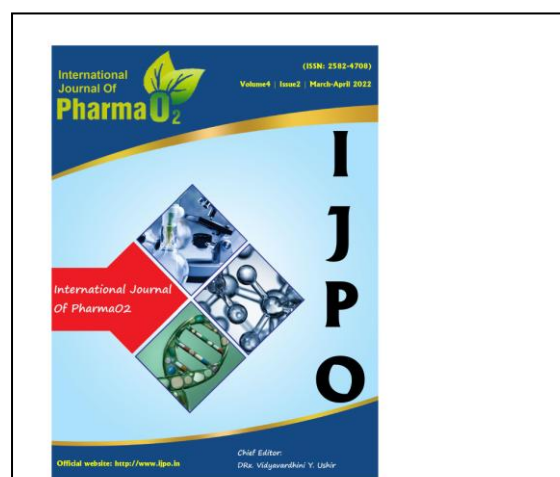
CONFLICT OF INTEREST

The authors declare no conflict of interest

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