# Metabolic Alterations, Vascular Disease and Advanced Prostate Cancer: New Players for Metastatic Advanced Prostate Cancer?

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**Abstract:** *Introduction*: Epidemiologic studies have implicated metabolic imbalance in prostate cancer (PCa) aggressiveness, nevertheless no clear consensus has been reached. The aim of the research was to investigate the association of hypertension, hypercholesterolemia and vascular disease in advanced PCa with and without bone metastases.

*Methods*: Retrospective analysis of 66 patients with diagnosis of advanced PCa between 2005 and 2009 was conducted. We examined hypertension, hypercholesterolemia and vascular disease in 25 patients with advanced PCa and bone metastases versus 41 patients with advanced non-metastatic PCa. Men with incomplete data available, history of hormone therapy or chemotherapy, vascular surgery or other anticancer therapies were excluded.

*Results*: Hypertension was significantly linked to advanced PCa with bone metastases (OR 4.5, p = 0.01). Hypercholesterolemia also was significantly associated with aggressive metastatic PCa (OR 3.28, p = 0.01). A significant association was noted between metastatic PCa and vascular disease (OR 3.8, p = 0.04).

*Conclusions*: In our study, hypertension, hypercholesterolemia and vascular disease were significantly related to advanced metastatic PCa. Further research should elucidate these relations in larger samples to confirm these associations and to stabilize future prevention strategies.

**Keywords:** Prostate Cancer, bone metastases, hypertension, dyslipidaemia, vascular disease.

## 1. INTRODUCTION

Clinical studies have related metabolic imbalance with prostate cancer (PCa) development and aggressiveness with conflicting results [1-12].

Indeed, while the relationship between metabolic alterations as diabetes mellitus (DM), obesity and PCa has been heavily examined, the influence of factors as hypertension, dyslipidaemia and vascular disease on metastatic PCa has been poorly studied, despite the frequent co-existence of these disorders in prostate cancer [13].

The aim of the research was to evaluate the association of hypertension, dyslipidaemia and vascular disease in advanced metastatic PCa.

## 2. METHODS

Retrospective analysis of 66 patients with diagnosis of advanced PCa (locally advanced or poorly differentiated cancer; stage T3-4 and/or GS 7-10) between 2005 and 2009 was conducted. We examined arterial hypertension (arterial blood pressure > 130/85), dyslipidaemia and vascular disease (carotid vascular disease and/or symptomatic coronary artery disease) in 25 patients with advanced PCa with diagnosed bone metastases (Group 1) versus 41 patients with advanced non-metastatic PCa (Group 2).

We have considered in our study as hypercholesterolemia high levels of Total Cholesterol and LDL-C. Each patient was considered to be the average of at least 3 measurements at the same hospital laboratory at 8 am.

Men with incomplete data available, history of hormone therapy or chemotherapy, urological or vascular surgery or other anticancer therapies were excluded.

Differences in the distribution of continuous variables between study groups were described as median or media ± standard deviation (SD) and assessed for statistical significance with Mann-Whitney Rank Sum Test or t-test. Differences in distributions for categorical variables were expressed as number of patients (frequencies and percentage) and evaluated using Chi-square testing of independence; however, when low cell counts were found, Fisher's exact testing was utilized. A P value <.05 was considered statistically significant.

## 3. RESULTS

Cases and controls were age-matched (68 years vs 67 years, respectively, p=0,423). Baseline

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**Table 1: Baseline Characteristics in Patients with Advanced Non-Metastatic PCa (Group 1) Versus Patients with Advanced Metastatic PCa (Group 2)**

| | Group 1<br>Advanced Non-Metastatic PCa | Group 2<br>Advanced Metastatic PCa |
|---|---|---|
| Age at diagnosis (media ± SD) | 67 ± 9.54 | 68 ± 6.43 |
| Systolic Blood Pressure (media ± SD) | 130± 10.2 | 140± 9.8 |
| Diastolic Blood Pressure (media ± SD) | 80± 4.2 | 85± 5.4 |
| LDL-C mg/dl (media ± SD) | 128± 10.2 | 149 ± 12.6 |
| Total Cholesterol mg/dl (media ± SD) | 180± 12.8 | 200 ± 11.3 |

characteristics at initial diagnosis were shown in Table **1**.

Hypertension was significantly linked to advanced metastatic PCa (OR 4.5, p = 0.01). Hypercholesterolemia, particularly high levels of Total Cholesterol and LDL-C, also was significantly associated with aggressive metastatic PCa (OR 3.28, p = 0.01). A significant association was noted between advanced PCa with bone metastases and vascular disease (OR 3.8, p = 0.04).

## 4. DISCUSSION

More than 30% of men with PCa die of cardiovascular disease, which constitutes one of the most common causes of death in this patient population [14-16].

Aggressive PCa spreading to the bone, is a fatal disease requiring early diagnosis and effective treatment [17].

The aim of this study was to examine in a retrospective analysis of 66 patients with diagnosis of advanced PCa the association between hypertension, hypercholesterolemia and vascular disease with advanced PCa with bone metastases.

In recent studies hypertension, hypercholesterolemia, atherosclerosis and a composite score of metabolic factors were associated with advanced PCa, biochemical recurrence and an increased risk of death from PCa [5, 18-25].

In our study firstly we found a significant association between arterial hypertension, particularly systolic blood pressure, hypercholesterolemia and vascular disease with advanced PCa with bone metastases.

If confirmed in other larger studies, our results suggested that these alterations could be considered new players in metastatic advanced PCa and suggests common shared etiologies.

A study of Thysel and al. studied metabolites associated with PCa metastases and particularly identified high levels of cholesterol in PCa bone metastases. The authors proposed that tumor epithelial cells in PCa bone metastases synthesize cholesterol de novo as well the influx of this metabolite from the surroundings was implicated [17].

The pathogenic mechanisms potentially linking hypertension, hypercholesterolemia and vascular disease to PCa aggressiveness are complex. The chronic pro inflammatory state and oxidative stress associated with metabolic factors and vascular injury could contribute to progression in advanced metastatic PCa.

The results of the current study also will add some further motivation to control metabolic factors to decrease the risk of cardiovascular disease and PCa aggressiveness.

## CONCLUSIONS

In our study, hypertension, hypercholesterolemia and vascular disease were significantly related to advanced metastatic PCa.

The metabolic derangements may increase oxidative stress and cause a permanent pro inflammatory state that predisposes to metastatic PCa. Further research should elucidate these relations in larger samples to confirm these associations and to stabilize future prevention strategies.

## CONFLICT OF INTEREST STATEMENT

We have no conflict of interest and no source of funding.

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