

# The Association Between Hypertension and Prostate Cancer

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A 2016 meta-analysis documented a possible association between hypertension and prostate cancer. We retrospectively reviewed our 3200 prostate cancer patients that were aged 51 to 76 years to determine the frequency of hypertension. Data was gathered on age, race (African American and white), hypertension, diabetes, and body mass index (BMI). Patients were subdivided into three groups: age 51 to 60 years, age 61 to 70 years, and age 71 to 76 years. Our study population consisted of 1388 (43%) African American patients and 1812 (57%) white patients. Hypertension was found in 1013 (73%) of African American patients and 1290 (72%) of white patients. Diabetes was found in 35% of African American patients and 24% of white patients. BMI over 30 kg/m<sup>2</sup> (obesity) was found in 47% of African American patients and 45% of white patients. We found the frequency of hypertension to be 73% in African American and 72% in white patients, 18% and 44% relatively higher in African American vs white patients, respectively, compared with the general population (62% in African American vs 50% in white patients). The study also found a similar frequency of hypertension among African American and white prostate cancer patients, despite an approximate 12% difference in the general population. Based on these findings, we suggest that prostate cancer and hypertension share a common androgen-mediated mechanism and further prospective studies are recommended to confirm that hypertension is a risk factor for prostate cancer.

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## KEY WORDS

Prostate cancer • Hypertension • Androgen • Risk factor

Prostate cancer is the second leading cause of cancer-related death in American men. In 2016, the American Cancer Society predicted an estimated 180,890 new cases of prostate cancer and 25,120 deaths due to prostate cancer.<sup>1</sup> One in seven US men will be diagnosed with prostate cancer during his lifetime. Nearly 66% of prostate cancer cases are diagnosed in men aged  $\geq 65$  years. If prostate cancer is diagnosed early and treated, it has a 99% 5-year survival rate.<sup>2,3</sup> Early diagnosis of prostate cancer by prostate-specific antigen screening and digital rectal examination has decreased the number of prostate cancer deaths by 40% in the past 2 decades. Identification of risk factors for prostate cancer is important for early detection.<sup>4-6</sup> Well-defined risk factors for prostate cancer include advancing age, African American race, and a family history of prostate cancer. Additional risk factors may include hypertension, obesity, and diabetes.<sup>7</sup>

*Well-defined risk factors for prostate cancer include advancing age, African American race, and a family history of prostate cancer. Additional risk factors may include hypertension, obesity, and diabetes.*

Wallner and colleagues<sup>8</sup> reported a 15-year experience of 2445 white men aged 40 to 79 years and found that hypertensive men were 1.5 times more likely to develop prostate cancer than were nonhypertensive men. In a prospective study of 29,364 Norwegian men, hypertension was associated with increased incidence of prostate cancer.<sup>9</sup> Esposito and colleagues<sup>10</sup> reported a meta-analysis in which hypertension was associated with a 15% greater risk of prostate cancer.

As per a 2016 US Centers for Disease Control and Prevention report, 29% of all US adults (men and women) have hypertension. The prevalence in African American men is 43% and in white men is 34%. The

prevalence of hypertension increases with age. Approximately 52% of men aged 50 to 79 years have hypertension (62% in African American men and 50% in white men).<sup>11</sup> We studied the association between hypertension and prostate cancer stratified by age.

## Materials and Methods

We completed a retrospective analysis of our prostate cancer patients aged 51 to 76 years. We collected data on age, race (African American and white), hypertension, diabetes, and body mass index (BMI) in our 3200 prostate cancer patients during the year 2016. These patients were under the care of Mid-Atlantic Urology Associates and 21st Century Oncology in the Mid-Atlantic, southern, and western US states. Only charts for African American and white men were selected for the study. We excluded other racial groups because age-stratified comparative data on hypertension were not available.

The patient charts of our practice were reviewed and the information was entered in a database. The data were analyzed to determine

the prevalence of hypertension, diabetes, and obesity as stratified by age: men aged 51 to 60 years, aged 61 to 70 years, and aged 71 to 76 years. The prevalence of hypertension in our prostate cancer patients was compared with the prevalence in the population according to the results from the Third National Health and Nutrition Examination Survey (NHANES III), 1988-1991.<sup>12</sup> The NHANES III data provide a breakdown by age and race. Additionally, the NHANES III database provides raw data allowing for statistical comparison.  $\chi^2$  or Fisher's exact tests were used to compare frequencies. All analyses were conducted using the SAS software system (SAS Institute, Cary, NC). The study was approved by the Western Institutional Review Board (study number 1087891).

## Results

### Patient Characteristics

A total of 3200 prostate cancer patients were reviewed (Table 1). The study population consisted of African American and white men with prostate cancer (1388 African American and 1812 white men); 799 (25%) men were aged 51 to 60 years, 1428 (45%) were aged 61 to 70 years, and 973 (30%) were aged 71 to 76 years. All patients had nonmetastatic, localized prostate cancer.

**TABLE 1**

### Patient Characteristics

Race	Patients (n)	Percentage	
African American	1388	43	
White	1812	57	
Total	3200	100	
Race	Patients (n)	Hypertension (n)	Percentage
African American	1388	1013	73
White	1812	1290	72

**TABLE 2****Prevalence of Hypertension in Prostate Cancer Patients Stratified by Age**

Age (y)	African American Men (n)	Hypertension (n)	Percentage	White Men (n)	Hypertension (n)	Percentage
51-60	404	296	73	395	233	59
61-70	611	445	73	817	593	72
71-76	373	272	73	600	464	77
Total	1388	1013	73	1812	1290	72

**Hypertension Stratified by Age and Race**

There were 1388 African American men (43%) and 1812 white men (57%; Table 2); 1013 African American men (73%) had hypertension and 1290 (72%) white men had hypertension. In those aged 51 to 60 years, 296 African American men (73%) and 233 (59%) white men had hypertension. In those aged 61 to 70 years, 445 (73%) African American men and 593 (72%) white men had hypertension. In those aged 71 to 76 years, 272 (73%) African American men and 464 (77%) white men had hypertension.

**Diabetes Stratified by Age and Race**

Overall, 35% of African American men and 24% of white men had diabetes (Table 3). In African American men aged 51 to 60 years, 61 to 70 years, and 71 to 76 years, 32%, 36%, and 35% had diabetes, respectively. In white men aged 51 to 60 years,

61 to 70 years, and 71 to 76 years, 26%, 24%, and 24% had diabetes, respectively. Both hypertension and diabetes were present in 23% of African American men and 20% of white men. In African American men aged 51 to 60, 61 to 70, and 71 to 76, 20%, 28%, and 20% had hypertension and diabetes, respectively. In white men aged 51 to 60, 61 to 70, and 71 to 76, 22%, 20%, and 19% had hypertension and diabetes, respectively.

**BMI > 30 kg/m<sup>2</sup>**

Obesity was defined as a BMI > 30 kg/m<sup>2</sup> (Table 4). BMI data were available in 2038 patients (67%). A BMI > 30 kg/m<sup>2</sup> was noted in 445 African American men (47%) and 530 white men (45%). In African American men aged 51 to 60, 61 to 70, and 71 to 76, 45%, 52%, and

38% had a BMI > 30 kg/m<sup>2</sup>, respectively. In white men aged 51 to 60, 61 to 70, and 71 to 76, 46%, 46%, and 42% had a BMI > 30 kg/m<sup>2</sup>, respectively. Both hypertension and BMI > 30 kg/m<sup>2</sup> were present in 35% of African American men and 40% of white men. In African American men aged 51 to 60, 61 to 70, and 71 to 76, 32%, 40%, and 29% had hypertension and BMI > 30 kg/m<sup>2</sup>, respectively. In white men aged 51 to 60, 61 to 70, and 71 to 76, 41%, 41%, and 40% had hypertension and BMI > 30 kg/m<sup>2</sup>, respectively.

**Discussion**

In 2016, Liang and associates<sup>13</sup> published a meta-analysis that indicated that hypertension may be associated with an increased risk of prostate cancer. The etiology of

*... hypertension may be associated with an increased risk of prostate cancer. The etiology of this finding is not fully defined, although laboratory and human data suggest a possible association mediated by androgens.*

**TABLE 3****Prevalence of Diabetes in Prostate Cancer Patients Stratified by Age**

Age (y)	African American Men (n)	Diabetes (n)	Percentage	White Men (n)	Diabetes (n)	Percentage
51-60	404	130	32	395	101	26
61-70	611	219	36	817	192	24
71-76	373	130	35	600	144	24
Total	1388	479	35	1812	437	24

**TABLE 4****Prevalence of BMI Over 30 in Prostate Cancer Patients Stratified by Age**

Age (y)	African American Men (n)	BMI > 30 (n)	Percentage	White Men (n)	BMI > 30 (n)	Percentage
51-60	291	131	45	235	109	46
61-70	428	224	52	595	272	46
71-76	234	90	38	355	149	42
Total	953	445	47	1185	530	45

BMI, body mass index.

this finding is not fully defined, although laboratory and human data suggest a possible association mediated by androgens.

In a review, Reckelhoff<sup>14</sup> documented that male rats have higher blood pressure compared with female rats, which may be related to increased levels of androgens in males. Castration of spontaneously hypertensive rats (SHRs) decreases the blood pressure whereas administration of testosterone in ovariectomized female SHRs resulted in increased blood pressure. These data suggest that androgen may have an effect on sodium reabsorption, as androgen receptors are located in the nephron's proximal tubule. Hypertensive rats have an exaggerated response to androgens that normotensive rats do not. Blood pressure increases with chronic androgen supplements in normotensive rats. Male SHRs have a 27% higher renin-angiotensin system compared with female SHRs, but castrated male SHRs have a decreased renin-angiotensin system as measured by decreased plasma renin activity.

Androgens can increase sodium reabsorption via angiotensin II- or androgen-mediated increases in aldosterone. Clinically, Miller and colleagues<sup>15</sup> have documented higher aldosterone and higher blood pressure, respectively, in men

compared with women. Schunkert and associates<sup>16</sup> found a positive correlation between dehydroepiandrosterone sulfate (a metabolite of testosterone), aldosterone levels, and blood pressure in a population of hypertensive men.

Combined, these animal and human data indicate that androgen may have a possible causative effect on hypertension. It is also well known that decreasing androgen levels by orchiectomy or by chemical means slows the progression of prostate cancer. These findings suggest that androgens may have a causative role in prostate cancer and hypertension.

*... an androgen-mediated mechanism may be responsible for both prostate cancer and hypertension. The study suggests that hypertension may be a risk factor for prostate cancer.*

In the current study consisting of 3200 prostate cancer patients, we found that hypertension was present in 73% of African American men and in 72% of white men. To our knowledge, this is the largest study investigating the role of hypertension in US prostate cancer patients. The result is significant because it shows a higher prevalence of hypertension in prostate cancer patients compared with the general population, when stratified by age (62% in African American vs 50% in white men). This translates to

an 18% relative increase in African American men and a 44% relative increase in white men (based on a comparison with the Third National Health and Nutrition Examination Survey data; Table 5).

In the general population, African American men have a 12% higher prevalence of hypertension compared with white men. We found a similar percentage of hypertension among African American men and white men with prostate cancer (72% vs 73%). This suggests that an androgen-mediated mechanism may be responsible for both prostate cancer and hypertension. The study suggests

that hypertension may be a risk factor for prostate cancer. We believe that a prospective study is needed to validate that hypertension is a risk factor for prostate cancer.

## Conclusions

The study of our 3200 US patients with prostate cancer showed that hypertension was present in 73% of African American men and 72% of white men. This indicates that patients with prostate cancer have a

**TABLE 5****Prevalence of Hypertension in the Population of NHANES III Compared With the Present Study**

Prevalence of HTN in Men (NHANES)			Prevalence of HTN in PCa Patients (Present Study)						
Age (y)	African American Men (%)	White Men (%)	Age (y)	African American Men (%)	P Value	Relative Increase (%)	White Men (%)	P Value	Relative Increase (%)
51-60	55	40	51-60	73	.0002	33	59	< .001	48
61-70	62	51	61-70	73	.0070	18	72	< .001	41
71-76	69	60	71-76	73	.4313	6	77	< .001	28

HTN, hypertension; NHANES, Third National Health and Nutrition Examination Survey; PCa, prostate cancer.

significantly higher prevalence of hypertension compared with that of the general population, when stratified by age and race (62% African American vs 50% white). The study also found a similar frequency of hypertension among African American men (73%) and white (72%) prostate cancer patients, despite a 12% difference in the general population. Based on these findings, we postulate that both hypertension and prostate cancer are possibly mediated by an androgen-based mechanism, and that

hypertension is a risk factor in the causation of prostate cancer. Further prospective studies are needed to validate that hypertension is a risk factor for prostate cancer. ■

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### MAIN POINTS

- Well-defined risk factors for prostate cancer include advancing age, African American race, and a family history of prostate cancer. Additional risk factors may include hypertension, obesity, and diabetes.
- Several studies have concluded that hypertension is associated with increased incidence of prostate cancer. The etiology of this finding is not fully defined, although laboratory and human data suggest a possible association mediated by androgens.
- It is also well known that decreasing androgen levels by orchiectomy or by chemical means slows the progression of prostate cancer.
- Our study of 3200 US patients with prostate cancer showed that hypertension was present in 73% of African American men and 72% of white men. This indicates that patients with prostate cancer have a significantly higher prevalence of hypertension compared with that of the general population when stratified by age and race. The study also found a similar frequency of hypertension among African American (73%) and white (72%) prostate cancer patients. Based on these findings, we postulate that both hypertension and prostate cancer are possibly mediated by an androgen-based mechanism, and that hypertension is a risk factor in the causation of prostate cancer.

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