Published in final edited form as:
Cancer Epidemiol Biomarkers Prev. 2013 April ; 22(4): 589–596. doi:10.1158/1055-9965.EPI-12-0944.

Relationship of Early Onset Baldness to Prostate Cancer in African-American Men

Charnita Zeigler-Johnson[1], **Knashawn H. Morales**[1], **Elaine Spangler**[1], **Bao-Li Chang**[1], and **Timothy R. Rebbeck**[1]

[1]Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, PA 19104

Abstract

Background—Early onset baldness has been linked to prostate cancer (CaP), however, little is known about this relationship in African Americans (AA) who are at elevated CaP risk.

Methods—We recruited 219 AA controls and 318 AA CaP cases. We determined age-stratified associations of baldness with CaP occurrence and severity defined by high stage (T3/T4) or high grade (Gleason 7+.) Associations of androgen metabolism genotypes (CYP3A4, CYP3A5, CYP3A43, AR-CAG, SRD5A2 A49T, and SRD5A2 V89L), family history, alcohol intake, and smoking were examined by baldness status and age group by using multivariable logistic regression models.

Results—Baldness was associated with odds of CaP (OR=1.69, 95% CI=1.05–2.74). Frontal baldness was associated with high stage (OR=2.61, 95% CI=1.10–6.18) and high grade (OR=2.20, 95% CI=1.05–4.61) tumors. For men diagnosed less than age 60, frontal baldness was associated with high stage (OR=6.51, 95% CI=2.11–20.06) and high grade (OR=4.23, 95% CI=1.47–12.14). We also observed a suggestion of an interaction among smoking, median age and any baldness (p=0.02).

Conclusions—We observed significant associations between early onset baldness and CaP in AA men. Interactions with age and smoking were suggested in these associations. Studies are needed to investigate the mechanisms influencing the relationship between baldness and CaP in AA.

Impact—AA men present with unique risk factors including baldness patterns that may contribute to CaP disparities.

Keywords

Prostate Cancer; African Americans; Baldness; Genotypes; Smoking

INTRODUCTION

Few definitive prostate cancer (CaP) risk factors have been identified, but those that are clearly associated with CaP risk include advancing age, family history of CaP, and African American (AA) race. (1, 2) Among AA men, prostate cancer (CaP) has the highest incidence of any non-cutaneous tumor and is a leading cause of cancer-related mortality.(3) AA men

Corresponding Author: Charnita Zeigler-Johnson, Ph.D., Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, 220 Blockley Hall, 423 Guardian Drive, Philadelphia, PA 19104-6021, Telephone: 215-573-5264, Fax: 215-573-1050, czj@mail.med.upenn.edu.

There are no conflicts of interest to disclose by any of the authors responsible for this study.

suffer from among the highest rates of CaP in the world, with an age-adjusted incidence of 233.8 per 100,000. This rate is substantially higher than that in European Americans (EA; age-adjusted incidence of 149.5 per 100,000).(4) AA men also present with more advanced disease at initial diagnosis and have a worse prognosis than EA men.(5–7) Studies to date have not completely determined the reasons for these apparent ethnic disparities, but it is likely that they are multifactorial and complex.

Baldness has been investigated for a number of years as a potential risk factor for CaP etiology. Also known as androgenetic alopecia, this age-dependent genetic disorder is characterized by patterned permanent hair loss. (8, 9) Baldness affects about 50–70% of men during their lifetime. (10, 11) Though the incidence of both CaP and baldness increases with age and both have been connected to androgen metabolism, the association between the two remains unclear. Genes involved in androgen metabolism have been suggested to be associated with the etiology of both baldness and CaP. While studies have shown a null relationship (9, 10) and others suggest that an inverse relationship (12, 13), some have reported a positive association between CaP and baldness. (10, 11, 14)

To date, little is known about the relationship of baldness, CaP, and androgen metabolism genotypes in AA men. The aim of this study was to conduct a case-control study to examine the relationship between early-onset baldness and CaP in AA men. This study also included measures of polymorphic variation in candidate androgen metabolism genes to assess differences in baldness association with CaP by genotype.

MATERIALS AND METHODS

Study Participants and Data Collection

We identified a sample of 219 AA male controls (ages 33–93) and 318 AA CaP cases (ages 39–86) with baldness data through the University of Pennsylvania Health System (UPHS) and Philadelphia VA Hospital recruited to the Study of Clinical Outcomes, Risk and Ethnicity (SCORE) between 1998 and 2010. SCORE is a hospital-based prostate cancer case-control study to examine genetic and other risk factor associations for prostate cancer etiology and progression in a diverse population of patients from the Philadelphia, PA region. Cases were histologically confirmed CaP patients from UPHS and VA urology clinics. Controls were ascertained through UPHS primary care facilities. The participation rate was 98% for cases and controls approached to participate in the SCORE study. Case and control status was confirmed by medical records review using a standardized abstraction form. Participants were excluded from this analysis if they reported having exposure to finasteride (for treatment of baldness or prostate-related issues) at the time of their CaP diagnosis. Participants with a prior diagnosis of cancer at any site other than the prostate were also excluded.

We used the Hamilton-Norwood Hair Baldness Patterns scale arranged according to “No Baldness (stages I and II), Frontal Baldness (stages IIa, III, IIIa, IVa) and any Vertex Baldness (stages III, IV, vertex-V, V, Va, VI, VII)” categories.(15) These were categories similar to those used in studies by Faydaci, et al. and Demark-Wahnefried, et al. (9, 16) All baldness data were self-reported. Patients were asked to recall their hair pattern at age 30.

Risk factor, medical history, and CaP diagnostic information were obtained by using a standardized questionnaire and review of medical records. Information collected included personal history of previous cancer diagnoses, demographic information, CaP screening history, tumor characteristics at diagnosis, and cancer treatments. All study participants provided written informed consent for participation in this research with guarantees of

confidentiality under a protocol approved by the Committee for Studies Involving Human Subjects at the University of Pennsylvania.

Biosample Collection and Genotype Analysis

Genomic DNA for the present study was self-collected by each study participant using sterile cheek swabs (Cyto-Pak Cytosoft Brush, Medical Packaging Corporation, Camarillo, CA), and processed using either a protocol modified from Richards et al. (17) as described previously (18), or using a modified protocol on the Qiagen 9604 robot with the QIAamp 96 DNA Buccal Swab Biorobot Kit (Valencia, CA). The methods used to determine each of the genotypes have been reported previously.(19–21)

Statistical Methods

This study investigated the relationship between male pattern baldness and odds of developing CaP. We considered the presence of any baldness and well as type of baldness. Type of baldness was defined as ‘frontal only’ or ‘any vertex’ (either vertex only or frontal with vertex.) To compare demographics by CaP case-control status, we computed frequency tables and chi-square statistics for categorical variables. The Wilcoxon rank sum test was used to test for significant case-control differences in median age and median BMI.

For age stratified associations which were also adjusted for age, we calculated odds ratios to determine the relationship between type of baldness and CaP severity compared to controls in the same baldness and age category. CaP severity was defined by higher tumor stage (T1/T2 vs. T3/T4) or Gleason score (<7 vs. 7+) at diagnosis. The median age at diagnosis among cases (age 60 years) was used as the point of age stratification.

Additional analyses considered risk factors that have been reported in previous studies of baldness and CaP (family history, alcohol use, smoking history, and prostate specific antigen) and genotypes associated with testosterone metabolism.(9, 14, 22, 23) Patient knowledge of any family history of CaP (first degree or second degree relatives diagnosed with prostate cancer), any weekly alcohol intake in the year prior to study entry, and ever smoking status were all categorized as ‘positive’ or ‘negative’ for these analyses. Prostate specific antigen (PSA) was grouped as high (≥ 10 ng/ml) and low (<10 ng/ml) among cases. The median number of repeats for our sample was used as a cutpoint for the AR repeat polymorphism to optimize the sample size in the comparisons. For genotype analyses, we coded genotypes according to phenotypically relevant groups based on previous reports in the literature. For AR-CAG, we compared more than 21 repeats to 21 or less repeats.(21, 24) We also coded the other genotypes by presence of the known variant (homozygote or heterozygote): CYP3A43 *3, CYP3A4 *1B, CYP3A5 *1, SRD5A2 A49T (T), and SRD5A2 V89L (L). (19, 20) Each risk factor was modeled in a separate logistic regression model adjusting for age at diagnosis for cases and age at study entry for controls. We explored age as an effect modifier by testing for interactions between age group (age 60 cut-point) and all risk factors of interest (family history, alcohol use, smoking history and genotypes) in baldness-stratified analyses. Statistical heterogeneity among groups was tested using the Mantel-Haenszel Test of Independence.

Analyses were performed in STATA version 11.0 (STATA Corporation, College Station, TX). A two-sided p-value of 0.05 or less was considered statistically significant. We corrected for multiple testing by controlling the false discovery rate in the analysis of risk factors.

RESULTS

Table 1 reports the demographics for our sample. Median age at study entry for controls was 57 years and for CaP patients was 60 years (p=0.001). Cases were significantly more likely to report a family history of CaP (36% vs. 27%; p=0.033) and more likely to report any baldness (20% vs. 13%, p=0.038) based upon findings from the Hamilton-Norwood Hair Baldness Patterns Scale (baldness reference age 30.) There were no significant differences in completion of high school education, median Body Mass Index (BMI), ever smoking, any weekly alcohol intake or type of baldness (Table 1).

Associations with CaP severity by baldness and age group are presented in Table 2. In most cases, baldness was associated with an increased risk of CaP. Significant associations were observed for men with any balding and all CaP (OR=1.69, 95% CI=1.05–2.74) and low grade cancer (OR=1.82, 95% CI=1.07–3.10). Frontal baldness was associated with high stage (OR=2.61, 95% CI=1.10–6.18) and high grade cancer (OR=2.20, 95% CI=1.05–4.61). Any vertex balding was associated with low grade CaP (OR=1.45, 95% CI=1.01–2.07).

Among younger men (men under age 60 years), baldness was associated only with more severe disease. Men with any balding had more than 3 times the odds of being diagnosed with high stage cancer (OR=3.43, 95% CI=1.37–8.61) and more than twice the odds of being diagnosed with high grade CaP (OR=2.33, 95% CI=1.03–5.28). Frontal baldness particularly increased the odds of severe disease. The odds ratio associated with frontal baldness was 6.51 (95% CI=2.11–20.06) for high stage and 4.23 (95% CI=1.47–12.14) for high grade disease.

No significant associations between baldness and CaP severity were observed for older men (age 60+ years) in this sample.

Controlling the false discovery rate in Table 3, we analyzed risk factor associations with CaP by presence of baldness. We observed a significant relationship between positive family history of CaP in men with no baldness (OR=1.74, 95% CI=1.14–2.67). There was also an inverse relationship between the presence of CYP3A43 *3 and CaP in men with no baldness (OR=0.32, 0.15–0.70). No associations with CaP were observed for men with any baldness.

Table 3 also presents these associations stratified by age group. we observed effects for younger men with no baldness for 3 variables. Younger men with a CaP family history were twice as likely to develop CaP (OR=2.04, 95% CI=1.14–3.65). Younger men who ever smoked (OR=0.37, 95% CI=0.20–0.69) or carried the CYP3A43*3 variant (OR=0.21, 95% CI=0.07–0.63) had a significantly lower odds of developing CaP. There was also a suggestion of an interaction between smoking, median age and any baldness (p=0.02). However, tests of heterogeneity demonstrated no significant differences between estimates by baldness group.

We also determined associations of baldness and prostate cancer by high and low prostate specific antigen (PSA) at prostate cancer diagnosis (results not shown.) The results showed an association of any baldness with prostate cancer in younger men (diagnosed before age 60) among cases with high PSA at diagnosis (≥ 10 ng/ml, OR=3.08, 95% CI= 1.28–7.40, p<0.001) For men with frontal only baldness, the association with prostate cancer in younger men among cases with high PSA was even stronger (OR=5.29, 95% CI= 1.70–16.53, p<0.001) These multivariable models were adjusted for age. No significant associations were observed for cases with lower PSA at diagnosis (<10 ng/ml), nor for models including any vertex or older men stratified by PSA group.

DISCUSSION

Key Finding

This study aimed to determine the association between early onset baldness, CaP risk factors and CaP occurrence in a sample of AA men. We observed a greater prevalence of early onset baldness among CaP cases with no significant difference in the type of baldness (frontal only vs. any vertex.) We also observed positive associations between baldness and CaP occurrence. The greatest odds and most severe disease occurred in men with frontal only baldness and those younger than age 60 with frontal only baldness.

Baldness Prevalence

The prevalence of baldness, especially vertex and frontal with vertex baldness, increases with age. (8, 12, 25) In the Washington State SEER registry, the frequency of any hair loss by age 30 was reported in 20% of CaP cases and 25% of controls (p=0.005). 55% of cases and controls reported hair loss in their 50s, while 66% of cases and 74% of controls ages 65+ reported any hair loss. The prevalence of frontal baldness was 47% in controls and 32% in CaP cases. (12) The prevalence of frontal baldness was also 33% in Australian men ages 40–69 (8). We observed 13% of controls and 20% of cases with any baldness, while 7 % for controls and 13 % for cases in our sample suffered from frontal baldness only.

Our results are opposite of the Washington State SEER data and other reports which suggest that the prevalence of baldness is greater among controls compared to cases.(12–14) Although most studies show some variability in prevalence depending on age, ethnic composition of the sample and study design (population-based vs. hospital-based and reference age for baldness), our results are similar to several other studies that support an increased prevalence of early onset baldness among prostate cancer cases and an association of baldness with early onset prostate cancer. (10, 16, 26) Unfortunately, the prevalence of early pattern baldness types among African-American prostate cancer cases and controls has not been documented.

Our prevalence of baldness was expected to be lower for an AA sample and is similar (11, 12) or slightly higher (27) to rates described previously for African-Americans. Results from the NHANES and Washington State SEER and hospital-based Washington, D.C. studies describe an increased prevalence of baldness among Caucasian prostate cancer patients compared to African-Americans.(11, 12, 27) According to our calculations using data provided in the report of Washington State SEER data (12), prevalence rates of any hair loss at age 30 are higher for Caucasian cases (Caucasian: 21%; African-American: 15%, p=0.112) compared to controls (Caucasians: 26%; African-Americans: 16%, p=0.033) in the population-based study.

Associations between Baldness and CaP

Male patterned baldness was associated with CaP in Black men in the NHANES cohort (RR=2.10, 95% CI=1.04–4.25) and non-Blacks (RR=1.42, 95% CI=1.01–1.98). (11) In NHANES, men with baldness were at higher risk for CaP in all age strata, but only significantly so for men in the oldest stratum when CaP was most common for this cohort study (ages 65–74 years, RR=1.69, 95% CI=1.14–2.46). This differs from our case-control study as we had similar number of cases in both the older and younger age groups. This enabled us to capture differences that may only occur in a younger age group, because we had a sufficient sample size in to detect significant differences in our age-group analyses. A case-control study of 669 subjects in France also found a positive association between CaP and baldness at age 20 (OR=2.01, 95% CI=1.07–3.79). Interestingly, this trend was lost when baldness at ages 30 and 40 was recalled. (10) The authors suggested that it may be

more difficult to see effects of baldness in older men as baldness prevalence increases similarly in cases and controls with aging. Contrary to their findings, a recent large prospective study of 9,448 Australian men found that baldness at age 40 rather than age 20 was predictive of early onset prostate cancer.(26) It has been suggested that age 20 may be too early to observe associations of baldness on prostate cancer, as many men that will experience early onset baldness have not yet begun balding by that age. An age range between 30–40 seems more appropriate as a reference point to avoid misclassification of early pattern baldness and is also a closer timepoint to prostate cancer diagnosis and related processes. Type of baldness has also been investigated for differential associations with CaP risk. An Australian study showed that only vertex baldness was positively associated with CaP occurrence (OR=1.54, 95% CI=1.19–2.00). (14) Additional studies from Washington state and the Netherlands found protective effects of baldness on CaP risk, particularly for men with a combination of early onset frontal-vertex balding. (12, 13) We noted no significant inverse associations in this AA sample of patients, or significant effects related to vertex baldness. It remains unclear if there are differences in the biological significance of type of baldness as it relates to CaP and if different patterns of baldness reflect genetic predisposition to hormonal milieu that might alter risk for disease. However, frontal baldness clearly is more significant for our sample of AA patients and is particularly relevant for severe disease.

It remains unclear why men bald differently (frontal vs. vertex) and how the mechanisms that influence baldness type contribute differentially to prostate cancer onset. This is the first study to report the association of frontal baldness with aggressive disease in younger prostate cancer cases. However, it is also the first study to examine these associations stratified by age group and baldness type in an all African-American sample. This study is unique in that respect and cannot be easily compared to previous studies. These results will have to be validated using similar methods in a similar sample of patients. Given that CaP outcomes are worse for AA men than other ethnic groups, future confirmatory studies may suggest frontal baldness by age 30 as an important risk factor for early diagnosis of this high risk group.

There are also limited data concerning the effect of PSA values on baldness and prostate cancer associations. We found significant associations of any baldness and frontal baldness with early prostate cancer among men with high PSA levels (PSA ≥ 10 ng/ml.) However, a study by Yassa, et al. demonstrated no associated on early pattern baldness (by age 40) in French prostate cancer cases with a much higher PSA cutpoint of > 20 ng/ml (p=0.63) (10)

Baldness and prostate cancer are linked by their relationship to androgen metabolism. (22) There are differences in the prevalence of genotypes that metabolize testosterone and influence dihydrotestosterone (DHT) levels. (19, 20) High DHT levels have been associated with both early pattern baldness and prostate cancer processes, including increases in PSA levels. Perhaps the underlying mechanisms that influence these associations by race are genetically determined. Genetic studies to date have found genes associated with early onset baldness that are also involved in pathways of androgen metabolism, hair development / hair cycling and neurodegenerative diseases that increase with aging. (28–30) However, little is known about the associations of many of these pathways in men of African descent. Interestingly, not all studies with predominately Caucasian samples show consistent effects of baldness on prostate cancer, so there is heterogeneity in the reports that have been published in recent years. Much more research in this area is needed to confirm our results and the previous results of other investigators.

Smoking

While only alcohol intake and not smoking has been previously associated with baldness (8), we observed no association of alcohol intake with CaP in the context of baldness. However, we were surprised to find an association that others had not reported with smoking. By extending our analytical design to examine smoking results stratified by age group and baldness type, we observed significant protective smoking effects for particular subgroups of AA men. We also observed in our study significant interactions of smoking, median age and baldness. Although smoking has not been a consistent risk factor in CaP, recent studies have shown significant positive associations for CaP incidence, CaP mortality and risk of biochemical recurrence in CaP patients. (31, 32) While smoking may have a direct biological consequence on promoting carcinogenesis and increasing CaP risk and progression (33), for individuals with particular predisposition, smoking may yield a protective effect for cancer (34), similar to what we observed in certain subgroups of our sample.

Both ever smoking and the CYP3A43 *3 genotype in particular showed protective effects with CaP in young men with no balding at age 30. This could suggest that hypoandrogenism, mediated by the combination of smoking and the expression of CYP3A43 *3, may lower risk of disease for hormonally-driven cancers. It is unclear what the mechanisms might be that invoke such protection in this subgroup of men or if the mechanism for smoking and CYP3A43 may be connected in some way. Little is known about the interplay of these variables and how they may jointly contribute to CaP risk.

This “phenotype-limited” pattern of association (i.e., where the genetic association is only observed on the background of a specific phenotype) is consistent with other studies evaluating genotype and phenotype associations simultaneously. For example, Kanetsky et al., observed that MC1R genotypes only affect risk of melanoma among individuals with “low-risk” phenotypes (i.e., dark hair color).(35) Similarly, we observe here that genotypes have their primary effect in men with a “low risk” prostate cancer phenotype (i.e., no baldness). To better understand the etiology of common diseases, it may be necessary to explore the phenotype-limited effects of susceptibility genotypes.

However, it is important to note that our sample sizes for the individual baldness groups by smoking and genotype were small and may thus have been underpowered to detect some associations. We computed tests of heterogeneity and determined that there were no significant differences in the estimates that were obtained for these risk factors by baldness status. Therefore, we must view these results with caution, as there may be little difference in the smoking and genotype effects on prostate cancer in men with and without baldness. It is also clear that the health risks of smoking far outweigh any interesting biological “benefits” that may occur for a subset of patients in this particular context. In general, it appears that more research is needed in this area before we can conclude what the true relationships among baldness, smoking and androgen genotypes may be. This study suggests that we take a closer look at these variables in other populations before we discount them, especially among younger prostate cancer patients.

Study Limitations and Strengths

Our study lacked power to study associations with frontal-vertex / vertex baldness, a pattern shown to be a predictive factor in some other studies. However, this pattern appears to be less common among AAs, so it may not be an important risk factor for this population. There may also have been recall bias in remembering baldness pattern at a younger age accurately. However, this is unlikely, as most men would likely remember when they developed alopecia due to psychosocial effects that it might have on the individual patient.

(10, 36) Aside from finasteride, we did not ask about other treatments for baldness, such as Rogaine. Future studies may also take a more thorough look at exposure to smoking.

A strength of our study is that we were able to analyze genotypes, PSA and other risk factors with baldness in an understudied high risk population of men, AAs. All of the studies reported in the literature, except for NHANES (11), either were homogenous samples, did not correct for race, or adjusted for race without reporting results for AAs separately. There is tremendous variation in associations of early onset baldness and prostate cancer by race, but it is very difficult to compare studies because of differing methodology. Study designs vary by age groups, sample populations, community-based vs. hospital-based, and differing assessment of baldness with varying age of reference and categories of baldness type. Early onset baldness also has been associated with several cardiovascular risk factors for which African-Americans are at increased risk, including diabetes and central adiposity. (37–39) Our ability to observe stronger associations in our sample may also be linked to underlying biology and higher prevalence of risk factors that place African-Americans at increased risk for a variety of chronic diseases involving disturbances in androgen metabolism. Although we have a limited number of patients in our analyses, our results are thought-provoking and provide evidence for building larger follow-up studies that examine interactions among genotypes, lifestyle factors, baldness, and CaP.

CONCLUSIONS

The mechanistic relationship between baldness, genotypes, smoking and CaP etiology/severity is not yet well-defined. However, our findings support the need to study these interactions and their effects on the underlying hormones that impact CaP risk.

Given the high prevalence of CaP in AAs, early onset baldness may be a particularly relevant indicator of risk that deserves attention in future studies as we seek to advance our knowledge about high risk populations. Future studies examining magnitude of risk and consistency compared to other risk factors may suggest whether early onset baldness is an important predictor of early onset CaP. Furthermore, knowledge of both CYP3A43 genotype and baldness pattern may provide predictive information about the risk of CaP in AA men.

Acknowledgments

We would like to thank Saarene Panossian and Amy Walker for providing laboratory analysis for this project.

This study was supported by grants from the Department of Defense and the Public Health Service (W81XWH-09-1-0576 to CZJ; P50-CA105641 and R01-CA85074 to TRR)

References

1. Silverberg E, Lubera J. Cancer Statistics-1989. Ca A Cancer J for Clinicians. 1989; 39:3–20.
2. Ernster V, Winkelstein W, Selvin S. Cohort mortality for prostatic cancer among non-whites. Science. 1978; 200(4346):1165–6. [PubMed: 653361]
3. Altekruse, S.; Kosary, C.; Krapcho, M.; Neyman, N.; Aminou, R.; Waldron, W., et al. SEER Cancer Statistics Review, 1975–2007. Bethesda, MD: 2010. Available from: http://seer.cancer.gov/csr/1975_2007/
4. Howlader, N.; Noone, A.; Krapcho, M.; Neyman, N.; Aminou, R.; Waldron, W., et al. SEER Cancer Statistics Review, 1975–2008. National Cancer Institute; Bethesda, MD: 2011. http://seer.cancer.gov/csr/1975_2008/based on November 2010 SEER data submission]
5. Powell I, Heilbrun L, Sakr W, Grignon D, Montie J, Novallo M, et al. The predictive value of race as a clinical prognostic facotr among patients with clinically localized prostate cancer: a

multivariate analysis of positive surgical margins. Urology. 1997; 49(5):726–31. [PubMed: 9145978]

6. Moul J, Douglas T, McCarthy W, McLeod D. Black race is adverse prognostic factor for prostate cancer recurrence following radical prostatectomy in an equal access health care setting. J Urol. 1996; 155(5):1667–73. [PubMed: 8627850]
7. Chornokur G, Dalton K, Borysova M, Kumar N. Disparities at presentation, diagnosis, treatment, and survival in African American men affected by prostate cancer. The Prostate. 2011; 71:985–97. [PubMed: 21541975]
8. Severi G, Sinclair R, Hopper J, English D, McCredie M, Boyle P, et al. Androgenetic alopecia in men aged 40–69 years: prevalence and risk factors. British Journal of Dermatology. 2003; 149:1207–13. [PubMed: 14674898]
9. Faydaci G, Bilal E, Necmettin P, Fatih T, Asuman O, Ugur K. Baldness, benign prostate hyperplasia prostate cancer and androgen levels. The Aging Male. 2008; 11(4):189–92. [PubMed: 19172550]
10. Yassa M, Saliou M, De Rycke Y, Hemery C, Henni M, Bachaud J, et al. Male pattern baldness and the risk of prostate cancer. Annals of Oncology. 2011; 22:1824–7. [PubMed: 21324955]
11. Hawk E, Breslow R, Graubard B. Male pattern baldness and clinical prostate cancer in the epidemiologic follow-up of the first National Health and Nutrition Examination Survey. Cancer Epidemiology, Biomarkers and Prevention. 2000; 9:523–7.
12. Wright J, Page S, Lin D, Stanford J. Male pattern baldness and prostate cancer risk in a population-based case-control study. Cancer Epidemiology. 2010; 34:131–5. [PubMed: 20206591]
13. Cremers R, Abeb K, Vermeulen S, den Heijer M, van Oort I, Kiemeney L. Androgenic alopecia is not useful as an indicator of men at high risk of prostate cancer. European Journal of Cancer. 2010; 2010:3294–9. [PubMed: 20561779]
14. Giles G, Severi G, Sinclair R, English D, McCredie M, Johnson W, et al. Androgenetic alopecia and prostate cancer: Findings from an Australian case-control study. Cancer Epidemiology, Biomarkers and Prevention. 2002; 11:549–53.
15. Norwood O. Male pattern baldness: Classification and incidence. Southern Medical Journal. 1975; 68(11):1359–65. [PubMed: 1188424]
16. Demark-Wahnefried W, Schildkraut J, Thompson D, Lesko S, McIntyre L, Schwingl P, et al. Early onset baldness and prostate cancer risk. Cancer Epidemiol Biomarkers Prev. 2000; 9:325–8. [PubMed: 10750672]
17. Richards B, Skoletsky J, Shuber A, Balfour R, Stern R, Dorkin H, et al. Multiplex PCR amplification from the CFTR gene using DNA prepared from buccal brushes/swabs. Hum Mol Genet. 1993; 2(2):159–63. [PubMed: 7684637]
18. Walker A, Najarian D, White D, Jaffe J, Kanetsky P, Rebbeck T. Collection of genomic DNA by buccal swabs for polymerase chain reaction-based biomarker assays. Environ Health Perspect. 1999; 107(7):517–20. [PubMed: 10378997]
19. Zeigler-Johnson C, Walker A, Mancke B, Spangler E, Jalloh M, McBride S, et al. Ethnic differences in the frequency of prostate cancer susceptibility alleles at *SRD5A2* and *CYP3A4*. Human Heredity. 2002; 54:13–21. [PubMed: 12446983]
20. Zeigler-Johnson C, Friebel T, Walker A, Wang Y, Spangler E, Panossian S, et al. CYP3A4, CYP3A5, CYP3A43, genotypes and haplotypes in the etiology and severity of prostate cancer. Cancer Research. 2004; 64:8461–7. [PubMed: 15548719]
21. Zeigler-Johnson C, Weber A, Spangler E, Panossian S, Rebbeck T, Malkowicz S. Relationship of obesity, Androgen Receptor genotypes and biochemical failure after radical prostatectomy. Prostate. 2011 Epub Oct 24.
22. Demark-Wahnefried W, Lesko S, Conaway M, Robertson C, Clark R, Lobaugh B, et al. Serum androgens: Associations with prostate cancer risk and hair patterning. Journal of Andrology. 1997; 18(5):495–500. [PubMed: 9349747]
23. Hsieh C, Thanos A, Mitropoulos D, Deliveliotis C, Mantzoros C, Trichopoulos D. Risk factors for prostate cancer: A case-control study in Greece. Int J Cancer. 1999; 80:699–703. [PubMed: 10048970]

24. Lange E, Sarma A, Ray A, Wang Y, Ho L, Anderson S, et al. The androgen receptor CAG and GGN repeat polymorphisms and prostate cancer susceptibility in African-American men: results from the Flint Health Study. J Hum Genet. 2008; 53(3):220–6. [PubMed: 18217192]
25. Ellis J, Scurrah K, Cobb J, Zaloumis S, Duncan A, Harrap S. Baldness and the androgen receptor: The AR polyglycine repeat polymorphism does not confer susceptibility to androgenetic alopecia. Hum Genet. 2007; 121:451–7. [PubMed: 17256155]
26. Muller D, Giles G, Sinclair R, Hopper J, English D, Severi G. Age dependent associations between androgenetic alopecia and prostate cancer risk. Cancer Epidemiology, Biomarkers and Prevention. 2012 Epub October 16, 2012.
27. Setty L. Hair patterns of the scalp of white and Negro males. Am J Phys Anthrop. 1970; 33:49–56. [PubMed: 5431486]
28. Heilmann, S.; Kiefer, A.; Kluck, N.; Drichel, D.; Hillmer, A.; Herold, C., et al. Androgenetic alopecia: identification of four new genetic loci and evidence for the contribution of WNT-signaling to its etiology. 2012. Epub http://www.ashg.org/2012meeting/abstracts/fulltext/f120120402.htm
29. Li R, Brockschmidt FF, Kiefer AK, Stefansson H, Nyholt DR, Song K, et al. Six novel susceptibility Loci for early-onset androgenetic alopecia and their unexpected association with common diseases. PLoS Genet. 2012 May.8(5):e1002746. [PubMed: 22693459]
30. Brockschmidt F, Heilmann S, Ellis J, Eigelshoven S, Hanneken S, Herold C, et al. Susceptibility variants on chromosome 7p21.1 suggest *HDAC9* as a new candidate gene for male-pattern baldness. British Journal of Dermatology. 2011; 165(6):1293–302. [PubMed: 22032556]
31. Huncharek M, Haddock S, Reid R, Kupelnick B. Smoking as a risk factor for prostate cancer: A meta-analysis of 24 prospective cohort studies. American Journal of Public Health. 2010; 100(4): 693–701. [PubMed: 19608952]
32. Kenfield S, Stampfer M, Chan J, Giovannucci E. Smoking and prostate cancer survival and recurrence. JAMA. 2011; 305(24):2548–55. [PubMed: 21693743]
33. Chen R-J, Chang L, Lin P, Wang Y-J. Epigenetic effects and molecular mechanisms of tumorigenesis induced by cigarette smoke: An overview. Journal of Oncology. 2011; 2011
34. Colilla S, Kantoff P, Neuhausen S, Godwin A, Daly M, Narod S, et al. The joint effect of smoking and A1B1 on breast cancer risk in BRCA1 mutation carriers. Carcinogenesis. 2006; 27(3):599–605. [PubMed: 16244359]
35. Kanetsky P, Panossian S, Elder D, Guerry D, Ming M, Schuchter L, et al. Does MC1R genotype convey information about melanoma risk beyond risk phenotypes? Cancer. 2010; 116(10):2416–28. [PubMed: 20301115]
36. Ellis J, Sinclair R, Harrap S. Androgenetic alopecia: pathogenesis and potential for therapy. Expert Reviews in Molecular Medicine. 2002; 4(22):1–11.
37. Bruce M, Sims M, Miller S, Elliott V, Ladipo M. One size fits all? Race, gender, and body mass index among U.S. adults. Journal of the National Medical Association. 2007; 99(10):1152–8. [PubMed: 17987919]
38. Hirsso P, Rajala U, Hiltunen L, Jokelainen J, Keinanen-Kiukaanniemi S, Nayha S. Obesity and low-grade inflammation among young Finnish men with early-onset alopecia. Dermatology. 2006; 214:125–9. [PubMed: 17341860]
39. Arias-Santiago S, Gutierrez-Salmeron M, Buendia-Eisman A, Giron-Prieto M, Naranjo-Sintes R. Sex hormone-binding glubulin and risk of hyperglycemia in patients with androgenetic alopecia. J Am Acad Dermatol. 2010; 65(1):48–53. [PubMed: 21511365]

Table 1

Demographics of AA SCORE sample

Variables	Controls (N=219)	Cases (N=318)	p-value
Median Age (years)	57	60	0.001
% High School Education	80%	84%	0.196
Median Body Mass Index (BMI)	29	27.8	0.215
% Ever Smokers	68.0%	63.6%	0.290
% family history CaP	27%	36%	0.033
% any weekly alcohol intake	31%	39%	0.078
% Any Baldness at age 30	13%	20%	0.038
% Frontal Baldness only at age 30	7%	13%	0.053
% any Vertex Baldness at age 30	7%	10%	0.283
% High Gleason (7–10)	---	40%	---
% High Stage (III/IV)	---	22%	---

Table 2

CaP Case-Control Associations of Baldness with CaP by Age Group – adjusted for age

Reference Group N=219			All CaP (N=318)		Low Stage (N=231)		High Stage (N=63)[a]		Low Grade (N=182)		High Grade (N=122)[b]	
	Baldness Type at age 30	**Controls (n)**	**Cases (n)**	**OR (95% CI)**	**Cases (n)**	**OR (95% CI)**	**Cases (n)**	**OR (95% CI)**	**Cases (n)**	**OR (95% CI)**	**Cases (n)**	**OR (95% CI)**
All Ages	No balding	190 (87%)	254 (80%)	1.00	187 (81%)	1.00	49 (78%)	1.00	143 (79%)	1.00	100 (82%)	1.00
	Any Balding	29 (13%)	64 (20%)	**1.69 (1.05–2.74)**	44 (19%)	1.60 (0.95–2.67)	14 (22%)	1.93 (0.94–3.95)	39 (21%)	**1.82 (1.07–3.10)**	22 (18%)	1.15 (0.82–2.79)
	Frontal only	15 (7%)	37 (12%)	1.86 (0.99–3.51)	24 (10%)	1.63 (0.82–3.22)	10 (16%)	**2.61 (1.10–6.18)**	18 (10%)	1.57 (0.77–3.25)	17 (14%)	**2.20 (1.05–4.61)**
	Any Vertex	14 (6%)	27 (8%)	1.23 (0.88–1.73)	20 (9%)	1.25 (0.87–1.80)	4 (6%)	1.10 (0.61–1.96)	21 (12%)	**1.45 (1.01–2.07)**	5 (4%)	0.87 (0.51–1.48)
Age <60	No balding	116 (87%)	117 (80%)	1.00	82 (82%)	1.00	20 (67%)	1.00	64 (87%)	1.00	44 (75%)	1.00
	Any balding	17 (13%)	29 (20%)	1.79 (0.90–3.55)	18 (18%)	1.69 (0.77–3.70)	10 (33%)	**3.43 (1.37–8.61)**	14 (18%)	1.68 (0.75–3.78)	15 (25%)	**2.33 (1.03–5.28)**
	Frontal only	7 (5%)	17 (12%)	2.60 (1.00–6.79)	9 (9%)	2.12 (0.70–6.44)	8 (27%)	**6.51 (2.11–20.06)**	6 (8%)	1.76 (0.54–5.76)	11 (19%)	**4.23 (1.47–12.14)**
	Any Vertex	10 (8%)	12 (8%)	1.10 (0.69–1.75)	9 (9%)	1.18 (0.70–1.98)	2 (7%)	1.09 (0.49–2.42)	8 (10%)	1.28 (0.76–2.14)	4 (7%)	1.00 (0.53–1.89)
Age 60+	No balding	74 (86%)	137 (80%)	1.00	105 (80%)	1.00	29 (88%)	1.00	79 (76%)	1.00	56 (89%)	1.00
	Any balding	12 (14%)	35 (20 %)	1.23 (0.58–2.57)	26 (20%)	1.19 (0.55–2.59)	4 (12%)	0.68 (0.19–2.37)	25 (24%)	1.53 (0.70–3.38)	7 (11%)	0.59 (0.21–1.65)
	Frontal Only	8 (9%)	20 (12%)	1.07 (0.43–2.63)	15 (11%)	1.05 (0.41–2.69)	2 (6%)	0.51 (0.10–2.68)	12 (12%)	1.12 (0.41–3.03)	6 (10%)	0.78 (0.24–2.51)
	Any Vertex	4 (5%)	15 (9%)	1.25 (0.70–2.22)	11 (8%)	1.23 (0.67–2.24)	2 (6%)	1.01 (0.41–2.45)	13 (13%)	1.53 (0.85–2.78)	1 (2%)	0.49 (0.16–1.51)

[a] 16 cases missing stage

[b] 16 cases missing grade

Cancer Epidemiol Biomarkers Prev. Author manuscript; available in PMC 2014 April 01.

Cancer Epidemiol Biomarkers Prev. Author manuscript; available in PMC 2014 April 01.

Table 3

Risk Factor Associations with CaP by Baldness Pattern in AA Men – adjusted for age

Age Group	Variables of Interest	No Baldness at age 30		Any Baldness at age 30	
		N	OR (95% CI)	N	OR (95% CI)
All ages	CaP Family history	430	**1.74 (1.14–2.67)**[a]	87	1.26 (0.48–3.35)
	Alcohol (any weekly intake)	426	1.42 (0.94–2.13)	78	1.52 (0.56–4.09)
	Ever Smokers	439	0.80 (0.53–1.21)	93	0.80 (0.32–1.99)
	AR-CAG (≤21 repeats)	193	1.42 (0.77–2.62)	45	2.31 (0.41–12.93)
	SRD5A2 A49T (any T)	165	1.34 (0.13–13.43)	36	---
	SRD5A2 V89L (any L)	187	1.09 (0.58–2.04)	41	0.83 (0.16–4.30)
	CYP3A43 (*3)	163	**0.32 (0.15–0.70)**[a]	36	0.38 (0.04–3.97)
	CYP3A4 (any *1B)	126	0.44 (0.17–1.20)	28	0.17 (0.02–1.70)
	CYP3A5 (any *1)	136	0.64 (0.26–1.58)	31	2.52 (0.33–19.02)
< Age 60 years	CaP Family history	226	**2.04 (1.14–3.65)**[a]	43	1.26 (0.32–4.97)
	Alcohol (any weekly intake)	223	1.56 (0.88–2.76)	39	1.06 (0.27–4.14)
	Ever Smokers	230	**0.37 (0.20–0.69)** [a]	46	2.51 (0.66–9.57)
	AR-CAG (≤21 repeats)	91	1.14 (0.46–2.82)	22	1.45 (0.10–22.02)
	SRD5A2 A49T (any T)	---	---	---	---
	SRD5A2 V89L (any L)	94	1.79 (0.70–4.58)	19	0.17 (0.01–4.25)
	CYP3A43 (*3)	80	**0.21 (0.07–0.63)**[a]	---	---
	CYP3A4 (any *1B)	74	0.56 (0.18–1.78)	12	0.95 (0.05–17.36)
	CYP3A5 (any *1)	80	0.57 (0.19–1.70)	13	2.39(0.14–39.95)
≥ Age 60 years	CaP Family history	204	1.36 (0.68–2.73)	44	2.82 (0.46–17.31)
	Alcohol (any weekly intake)	203	1.05 (0.56–1.99)	39	2.08 (0.35–12.25)
	Ever Smokers	209	1.30 (0.68–2.49)	47	0.12 (0.02–0.80)
	AR-CAG (≤21 repeats)	102	2.34 (0.92–5.96)	23	3.04 (0.21–43.42)
	SRD5A2 A49T (any T)	---	---	---	---
	SRD5A2 V89L (any L)	93	0.72 (0.27–1.88)	22	1.39 (0.11–16.84)
	CYP3A43 (*3)	83	0.65 (0.20–2.09)	20	0.54 (0.04–6.54)

Age Group	Variables of Interest	No Baldness at age 30		Any Baldness at age 30	
		N	OR (95% CI)	N	OR (95% CI)
	CYP3A4 (any *1B)	52	0.11 (0.01–1.40)	---	---
	CYP3A5 (any *1)	56	0.87 (0.11–6.70)	18	2.37 (0.10–55.07)

Significance levels:

[a]=adjusted p ≤0.05 controlling the false discovery rate

Tests of heterogeneity of estimates showed no significant differences by baldness group.