Who suffers most in a low level PSA screening system? A comparison of prostate cancer cohorts from New Zealand and USA

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AIM

The current assessment is to understand the variability of detecting high-risk prostate cancer (PC) in a New Zealand (NZ) cohort (with low scale prostate-specific antigen [PSA] screening [16-35%] [1,2]) in comparison to a cohort from the US (that had better organised PSA screening [40-70%] until 2012[3,4]).

INTRODUCTION

Use of the PSA biomarker for PC screening is currently being debated world over[5]. According to the NZ Prostate Cancer Taskforce consideration in 2013, there was no clear evidence to support organised national screening for PC with the PSA marker to outweigh the harms of over-diagnosis and over-treatment[6]. Previously we have recorded that the PSA levels have a genetic association with the *aldo-keto reductase 1C3* (*AKR1C3*) rs12529 single nucleotide polymorphism (SNP) compounded by tobacco smoking[7].

METHOD

The NZ cohort from Auckland University study consisted of 95% Caucasians while that of the US cohort from the National Cancer Institute consisted of 47% African Americans (AA) and 53% European Americans (EA). Recruitment was carried out with informed consent and was restricted to the ages 40-90 years. Age, PSA level, disease stage and grade at diagnosis were collected from the hospital databases. Disease stage grouping followed the criteria defined by the 7th edition of the American Joint Committee on Cancer using the tumor–node–metastasis (TNM) system and a stage IIB and beyond were considered as high-risk disease.

At recruitment ethnicity and tobacco smoking status were collected, in addition to a blood sample for DNA extraction. Patients were genotyped for the *AKR1C3* rs12529 SNP. A total of 376, 202 and 232 NZ, AA and EA men respectively were included in the final analysis. Cumulative frequencies of high-risk PC were plotted against PSA class intervals and compared between the three groups with and without additional stratifications based on tobacco smoking status and genotype. Statistical testing was based on the Kolmogorov-Smirnov (KS) test with significance set at 0.05.

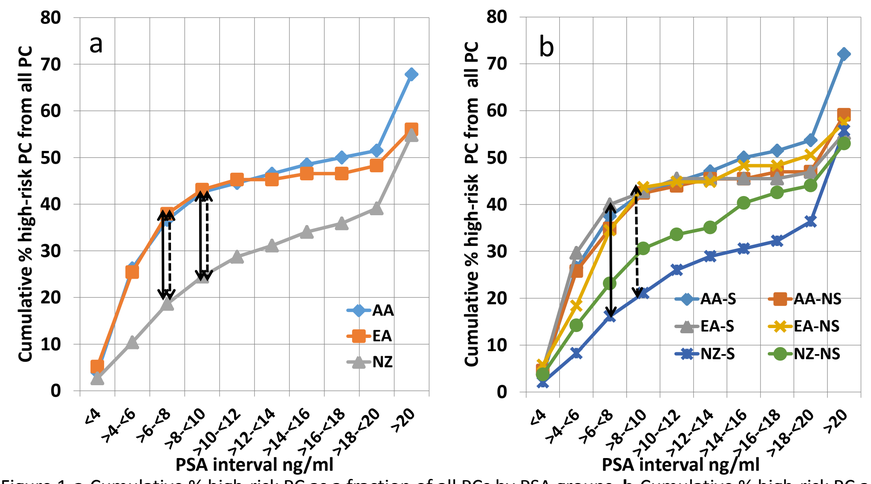

Figure 1-**a**-Cumulative % high-risk PC as a fraction of all PCs by PSA groups. **b**-Cumulative % high-risk PC as a fraction of all PCs by PSA groups stratified by tobacco smoking. (AA=African American ,EA= Caucasian American , NZ= New Zealanders. Points of significant differences are shown according to the KS test results. Full double headed arrow=maximum difference between EA and NZ. Dashed double headed arrow =maximum difference between AA and NZ, S=Ever smoker, NS=Never smoker).

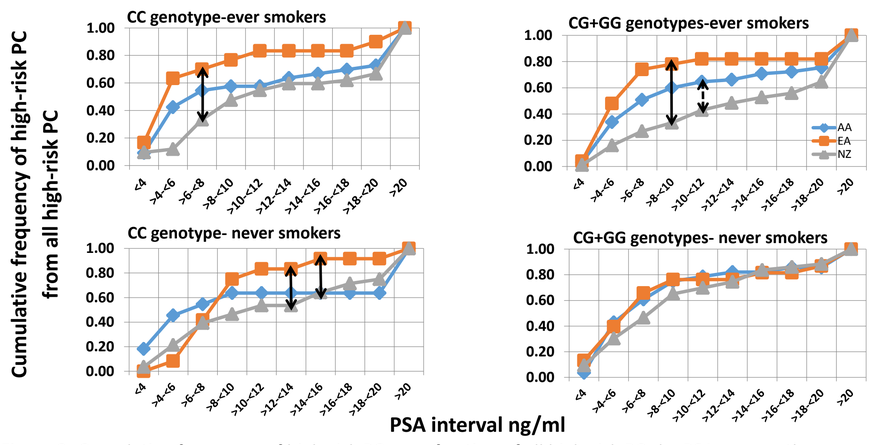

Figure 2- Cumulative frequency of high-risk PCs as a fraction of all high-risk PCs by PSA groups, the AKR1C3 rs12529 genotype and tobacco smoking status. (AA=African Americans, EA= Caucasian Americans, NZ= New Zealanders ,S= ever smokers ,NS= never smokers. Points of significant differences are shown according to the KS test results. Full double headed arrow=maximum difference between EA and NZ. Dashed double headed arrow =maximum difference between AA and NZ).

RESULTS

NZ cohort has been diagnosed at significantly higher mean age [NZ= 66.7y ±(8.0) compared to AA=62.6y ±(8.1) and EA=64.8y ±8.60], PSA level (NZ=8.9ng/ml compared to AA=6.9ng/ml and EA=5.8ng/ml) and Gleason sum (NZ=7 compared to AA=7 and EA=6). Similar tobacco smoking rates and genotype frequencies were observed between all groups. However, the cumulative high-risk PC detection rates by PSA groups show that the NZ cohort records delayed diagnoses compared to US groups (Fig 1a), which is further compounded by tobacco smoking status (Fig 1b) and tobacco smoking status interacting with genetics (Fig 2).

CONCLUSION

Lower level PSA screening affects delayed diagnosis of high-risk PC in NZ which is worsened among ever smokers. This situation is further aggravated among ever smokers when interacting with the *AKR1C3* rs12529 G allele. Current care gap in NZ among those found with increased PSA levels[2] could also be compounding this variability. Lifestyle and genetics based PSA testing could be a way forward for screening for significant PC in the future.

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