The factors associated with BCH are not entirely understood. For example, Henry et al found no association between BCH and age while Anim et al found the prevalence of BCH to increase with aging.[4,6] Conversely, Thorson et al found an association between BCH and younger age which agrees with our findings.[3] Other patient factors such as race, BMI, PSA levels, DRE, prostate volume, and geographic region were not associated with BCH. Similar results were obtained by Henry et al who found no correlation between BCH and PSA levels, prostate volume, medical treatments, or comorbidities.[4] However, in our study BCH was associated with more histological prostate atrophy and acute inflammation and less chronic inflammation. Contrariwise, Thorson et al, found BCH to be associated with lymphocytic (chronic) inflammatory infiltrate in most cases.[3] Given the conflicting results on the factors associated with BCH, further studies evaluating the potential causes of BCH are warranted.

The relationship of BCH in prostate biopsies with LUTS and prostatitis-related symptoms is unknown. Yang et al postulated that basal cell proliferation was present in almost all subjects who underwent surgery for BPH/LUTS while Henry et al found BCH in only 13 subjects of the 141 prostate TURP and open prostatectomy specimens evaluated.[4,12] In our study, we found no association between BCH in the peripheral zone with prostate volume or IPSS score. This suggests that BCH found in the peripheral zone is not associated with BPH or LUTS while BCH in the transitional zone may be associated with BPH and LUTS, though this requires further study.

Previous studies have suggested BCH could be a metaplastic reaction to injury and in some cases may progress to basal cell carcinoma.[13,14] However, this hypothesis has been contested in multiple studies. For example, Thorson et al demonstrated that the presence of BCH in peripheral zone was associated with lower PCa risk.[3] In addition, they did not find any topographical association between BCH and PCa in prostate specimens. Similarly, a study by Benett et al failed to demonstrate PCa development in patients diagnosed with BCH.[14] In our study, PCa at the 2-year repeat biopsy was unrelated to baseline BCH. Thus, although it seems that BCH is unrelated to PCa, further studies evaluating the molecular changes associated with BCH and how they correlated with prostate carcinogenesis are needed.

Our study has several strengths including its large, multicentric sample with central pathology review by 2 independent pathologists. Nonetheless, it has some limitations. First, subjects with severe LUTS (IPPS >= 25 or 20 among those on alpha-blocker) and prostate volume >80 cm^3 were excluded and only men with baseline PSA values between 2.5 and 10 ng/dl were included. Second, those with atypical small acinar proliferation, HGPIN, or previous prostate surgery were also excluded. Third, we did not evaluate subtypes of BCH, including typical and atypical. Finally, the prevalence of BCH was low, which reduced our statistical power.

CONCLUSION

Among men undergoing repeat prostate biopsy, BCH was associated with more histological atrophy and less chronic prostatitis. BCH was not associated with LUTS/BPH, clinical prostatitis or PCa. Thus, given the limited clinical relevance of BCH, it may be excluded from routine prostate biopsy pathology reports.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.02.034.

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EDITORIAL COMMENT

Repeat biopsies in prostate disease are notoriously difficult to acquire, but provide a wealth of data linking phenotype with disease progression.

The REDUCE trial is a rare longitudinal clinical trial that performed prostate biopsy at baseline and again at 2 and 4 years to determine the effect of dutasteride on prostate cancer

prevention.[1] The authors performed a retrospective analysis of peripheral zone needle biopsies from 6471 men enrolled in the REDUCE trial to determine the association between baseline basal cell hyperplasia (BCH) and the risk of (1) prostate cancer, (2) benign prostatic hyperplasia with lower urinary tract symptoms, or (3) prostatitis. In short, BCH was not predictive of any clinically meaningful disease progression at 2 years, prompting the suggestion that this rare phenotype should not even be noted by pathologists.

It is important to document these negative results, but with several caveats noted. The incidence of BCH in needle biopsies from this REDUCE cohort was extremely low (1.3%), with other cohorts demonstrating an incidence of 3.1% in needle biopsies to 23% in whole mounts.[2] Our own study of BCH in transition zone tissue from patients with BPH/LUTS undergoing TURP or simple prostatectomy tissue showed an incidence of 8%, but the total volume of BCH foci was highly variable between patients.[3] The low incidence and sporadic appearance of BCH foci in the peripheral zone may make its random detection in biopsies an underestimate, and the relatively short 2-year follow-up may be insufficient to detect clinically meaningful differences in relation to prostate cancer progression. On this point, it is unclear why the biopsies from the 4-year follow-up in the REDUCE trial were not used instead. It is also difficult to extrapolate the relationship between BCH detected by biopsy in the peripheral zone and symptoms due to transition zone BPH. However, the conclusion that BCH is not related to age, prostate volume, LUTS, or prostatitis does largely agree with our own study performed on larger specimens from the transition zone.[3]

Based on a transcriptional profile of basal cells from patients with BCH compared to basal cells from patients without BCH, we established that BCH is likely a metaplastic event.[3] This study suggests that the BCH phenotype is clinically meaningless and should be ignored. Perhaps future studies with a higher incidence and longer follow-up will alter this opinion, but it an important observation nonetheless.

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AUTHOR REPLY

Several nonmalignant histological prostate findings have been shown to be of clinical relevance. For example, we and others have shown chronic histological prostate inflammation in needle biopsies is associated with worsening prostatitis- and benign prostate hyperplasia (BPH)-related symptoms over time.[1,2] While basal cell hyperplasia (BCH) in the transitional zone has been associated with BPH in prior studies, the clinical significance of BCH in needle biopsies of the peripheral zone has not been previously studied in earnest.[3,4] Although limited by a low prevalence of BCH (1.3%), the current study is one of the largest analysis of BCH and it was unable to identify any association between BCH and prostate cancer, BPH or prostatitis-related symptoms. The lower BCH prevalence in our study likely stem from the fact that: (1) our biopsies targeted the peripheral zone only, and (2) subjects with very large prostates and/or severe urinary symptoms were excluded. Moreover, data from the 4-year repeat prostate biopsies were indeed analyzed but not included in the final manuscript given the results were similar to the ones obtained using 2-year biopsy data. While it is conceivable that future studies with larger BCH samples may identify correlations between BCH and clinically meaningful outcomes, the current relevance of BCH seems to rely solely on being a differential diagnosis for high-grade prostatic intraepithelial neoplasia and prostate adenocarcinoma and, as such, may be omitted from routine pathological prostate needle biopsy reports.

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