

Mental health

Does BPH raise the risk of dementia?

Men with benign prostatic hyperplasia (BPH) may be at increased risk of developing Alzheimer's disease and other dementias, the findings of a Danish population-based cohort study suggest.

The BPH cohort comprised all men with a secondary care diagnosis of BPH and/or a history of TURP and/or at least one prescription for alpha-receptor blockers or 5-alpha reductase inhibitors from 1996 to 2016. Those with dementia or mild cognitive impairment prior to BPH diagnosis were excluded.

Data were obtained from national registers of hospital activity and dispensed prescriptions.

The comparison cohort was assembled from a national register of Danish residents; up to four age-matched men were selected for each BPH patient.

A total of 297,026 men with BPH and 1,107,176 controls were included in the study. Follow-up started one year after BPH diagnosis, TURP or a BPH-related prescription to avoid dementia diagnoses detected as part of a diagnostic work-up for BPH. The median age at the start of follow-up was 67.5 years; the median follow-up period was 6.9 years for the BPH cohort and 6.4 years for the comparison group.

The results were adjusted for sociodemographic factors, cardiovascular disease, metabolic syndrome, COPD and the use of antihypertensive drugs, NSAIDs and testosterone.

During 1-10 years of follow-up, the cumulative risk of Alzheimer's disease was 1.15% (95% CI: 1.11-1.20%) in the BPH cohort and 1.00% (95% CI: 0.98-1.02%)

in the comparison cohort. The adjusted hazard ratios were 1.16 (95% CI: 1.10-1.21) for Alzheimer's disease and 1.21 (95% CI: 1.17-1.25) for all-cause dementia. The increased risk persisted throughout 21 years of follow-up.

The authors postulate that the increased risk of Alzheimer's disease and other dementias was mediated by nocturia, leading to sleep fragmentation and sleep deprivation.

There is increasing evidence to suggest that disturbed sleep or lack of sleep is a risk factor for Alzheimer's disease: a meta-analysis found that individuals with sleep problems had a 1.55 times greater risk of developing Alzheimer's disease.¹

The mechanism may involve the glymphatic system: during NREM sleep the brain glial cells shrink by up to 60%, enlarging the interstitial space and allowing convective influx of CSF which then drains along the perivenous space to the cervical lymphatic system. This washes beta-amyloid and other toxic substances out of the brain.²

The authors acknowledge that a weakness of their study was the lack of information regarding lower urinary tract symptoms. Consequently, it was not possible to investigate whether dementia risk was related to severity of nocturia, and inclusion of BPH patients who did not have nocturia may have reduced the risk estimate.

The results are also likely to have been affected by unmeasured confounders such as smoking and anticholinergic drug use.

The authors conclude that 'the diagnosis of BPH may present an opportunity to reduce dementia risk in men by treatments (apart from anticholinergic drugs) that reduce sleep-disruptive symptoms.'

Such treatments may include sleep CBT, reduction of alcohol and fluid intake before bedtime, earlier administration of diuretics and evening leg elevation. I would also suggest the following interventions: exercising more (but not in the late evening), avoiding caffeine after 3 pm (it inhibits the sleep regulator adenosine and exacerbates nocturia), and not looking at LED screens 1-2 hours before bedtime (blue light delays the rise in melatonin).³

Public Health England (PHE) is asking GPs through NHS Health Checks to provide midlife patients with information about risk factors for dementia and encourage them to adopt healthier lifestyles.⁴ Perhaps PHE should consider adding

improving sleep hygiene to their list of recommended lifestyle changes.

DR PHILLIP BLAND

Nørgaard M, Horváth-Puhó E, Corraini P et al. Sleep disruption and Alzheimer's disease risk: inferences from men with benign prostatic hyperplasia. *EclinicalMedicine* 2021;32:100740

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