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Prostate cancer: A review paper of the evidence in relation to prostate cancer screening in the Irish Defence Forces

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Abstract

The lack of national guidelines for prostate cancer (PCa) screening in Ireland has historically led to ad-hoc screening practices among healthcare providers. This review focuses on evidence for and against prostate cancer screening among military personnel in Ireland, set against the backdrop of evolving guidelines and practices both in Ireland and internationally. A review of published literature was conducted, incorporating data from various studies and guidelines relevant to prostate cancer screening. To assess the risk specific to the Defence Forces Ireland, both civilian and military sources were cited. This included national surveys, landmark trials, and guidelines from the Irish College of General Practitioners (ICGP), the National Cancer Control Programme (NCCP), and international bodies like the UK National Screening Committee (NSC) and the American Urological Association (AUA). Synthesising these numerous, high quality, resources, led to a conclusion that the evidence does not support prostate cancer screening in the Irish military as there is no reduction in overall mortality from this process.

Keywords; Prostate cancer; Mortality; Military; Defence forces; Ireland

1. Introduction

With a 96% male population, discussion on prostate cancer is commonplace when attending for medical assessment within the Irish Defence Forces. While a legitimate concern as prostate cancer is second only to skin cancers for malignancy in men, the mortality is low with this cancer and typically affects males of advanced age. With an average age of 36 years among serving military personnel in Ireland, screening is not usually performed in such a cohort. Due to concerns of personnel and a lack of guiding policy, a review of the evidence in both civilian and miliary populations was performed in order to provide a definitive conclusion on the issue of prostate screening in this cohort.

2. Review of evidence

As recently as 2009[1], doctors in Ireland were criticising the lack of national guidelines for prostate screening and a survey of 1,625 found that the vast majority (79%) would perform a PSA (Prostate Specific Antigen) test in asymptomatic men[1]. This study lamented the "widespread PSA testing of asymptomatic men in primary care" and condemned the combined "clinical experience, poor knowledge and the support of doctors for PSA testing" as the root cause for this ad-hoc testing manner and called for the implementation of national guidelines in relation to Prostate Cancer Screening[1].

In Ireland, the two guidelines now in use are the Irish College of General Practitioners (ICGP) Guidelines (2008)[2] and the National Cancer Control Programme (NCCP) "National Prostate Cancer GP Referral Guideline (2018)[3]. Of note, neither of these documents supports population-based Prostate Cancer (PCa) screening[2,3]. Both guidelines advise an

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individualised approach with "Shared Decision Making" between the patient and their doctor based on individual risk profile[2,3]. They further agree that pre-test counselling of potential negative outcomes should take place and that investigation for PCa should involve both a PSA blood test and a Digital Rectal Examination (DRE) [2,3].

The UK National Screening Committee (NSC) re-examined the case for PCa Screening in 2015[4], based upon the evidence available since the previous reviews performed in 1997 and 2010. This review specifically assessed PCa screening in light of the results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) which published its first findings in 2009[5]. The NSC article did not refute the claim of 21% reduced mortality from PCa in the ERSPC article but found that "The benefits of PSA screening remain unresolved on issues of overdiagnosis and overtreatment of clinically insignificant prostate cancers as well as identifying the optimum treatment for localised prostate cancer." While population-based PCa screening was not supported, the review did endorse an individualised approach to screening of men 50+ with their GP's advice.

"Summary Guidance for GPs" (2009)[6] from the UK Government in relation to PCa Screening concurs with the NSC guidance[5] that an invidualised, rather than population-based, approach best balances the risks and benefits of screening. These two positions further inform the National Institute for Health and Care Excellence (NICE) Guidelines relating to Prostate Cancer[7,8]. Notably, the guidance includes a caution that "GPs should not proactively raise the issue of PSA testing with asymptomatic individuals. Prostate cancer is common and may not cause symptoms or shorten life"[6]. Thus, it can be seen that the guidance in the UK and Ireland is grossly in accord and strongly supports an individual assessment of each patient and their risk factors for PCa, as well as cautioning against the potential risks of unnecessary PCa screening.

In the USA, both the United States Preventive Series Task Force (UPSTF) and the American Cancer Society advise indivualised PCa screening approaches in men aged 50-69 years old[9,10]. Conversely, the American Urological Association does endorse screening via a PSA blood test taken every two years in men aged 55-69 years old, though they caveat this with a similar "Shared Decision Making" to opt-in to screening for this population[11].

Each of the above discussed guidelines or statements in relation to available evidence on the risks and benefits of a population-based approach to Prostate Cancer Screening. The major landmark trials and evidence are examined below.

The European Randomised study of Screening for Prostate Cancer (ERSPC) commenced in 1991 with a randomised, controlled, multi-centre trial[12]. The original study enrolled 182,000 men from seven different European nations aged 50-74 and predefined a core age group of 55–69 year olds, of which there were 162,243[12]. The intervention of the study was randomly assigning men to having a PSA blood test every four years, with the control group not receiving such screening[12]. A "positive" PSA level was set at >3ng/ml. The primary outcome of the trial was death from Prostate Cancer[12]. Prostate Cancer was detected at a higher incidence in the screened group than the control group (8.2% v 4.8%) during the 9 year follow-up period[12]. The Absolute Risk Reduction was 0.71 per 1,000 men[12]. Of note, this study reported a 20% reduction in the rate of death from Prostate Cancer[12] in the screened group – this finding is central to the controversy over PSA based PCa Screening. While this 20% reduction in death from PCa is a tempting headline to endorse population-based PCa Screening, there are caveats within the results. Importantly, there was no difference in all-cause mortality shown between the screening and control groups[12]. Furthermore, the number-needed-to-treat was 48 and 1,410 men would have to be screened to prevent one death from PCa[12]. While this study is large, randomised and of high-quality and shows a reduction in PCa mortality when PSA-based screening is utilised, a high number of patients must be screened and treated (with potential side effects) to prevent any PCa deaths. The period of follow-up to show benefit is of a long duration (9 years)[12] and a follow-up study suggested extending the follow-up even further, to 16 years[13]. Most significantly, no improvement in all-cause mortality was shown[12], indicating that with screening patients may not be dying of PCa have no increased overall survival. This conclusion that PSA-based screening does not affect overall mortality was subsequently supported by systematic review and meta-analysis of five randomised trials examining results of more than 720,000 men over a ten-year period[14].

The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial was a USA-based randomised, controlled, multicentre trial designed and funded by the National Cancer Institute (NCI)[15]. The primary goal was to examine the effects of screening on disease-specific mortality[15]. The trial randomised 38,340 men to have both annual PSA blood tests with an annual DRE for four years and paired them with 38,343 controls who were randomised to normal care, which may have included PSA testing[15]. A "positive" PSA level was set at >4ng/ml[15]. While the incidence of detected PCa was 22% higher in the screened group, at 15 year follow-up there were more deaths in the intervention than control arm (255 v 244)[16,17]. This 4% difference was not statistically significant but indicated that there was no reduction in PCa mortality provided by the intervention[16,17]. This finding could possibly be explained by the higher PSA threshold utilised than in the ESRPC trial (>4ng/ml v >3ng/ml)[12,15] as a lower threshold could theoretically be more sensitive and

detect more cancers and at an earlier stage. 56% of the control group had a PSA test in the 4 year period of the trial[15], leading to "PSA contamination", with no effect being shown by intervention in the screening group. In summary, this large, high-quality, randomised, controlled, multicentre showed "no benefit of organized screening versus opportunistic screening"[17].

Part of the controversy surrounding PCa screening centres on the potential for harm to patients. Taking a blood test can result in fainting, bleeding, feeling lightheaded, haematoma formation and is a potential source of infection[18]. False positive PSA results, in which men without PCa are found to have elevated PSA levels, occur at rates up to 66%, resulting in anxiety and psychological harm[9]. 1 in 5 men with a false positive test go on to have a prostate biopsy[19] to aid diagnosis and this procedure has high complication rates[20], potentially leading to pain, infection, haematuria, erectile dysfunction and urinary issues[20]. Current treatment of PCa includes active surveillance, radiotherapy, radical prostatectomy and chemotherapy, each with their own side effects and potential complications[21]. Of great concern is the potential for men who have PCa that may have never caused symptoms or metastasised to other areas, but were detected and led to unnecessary medical intervention[12]. The USPSTF statement summarises this problem succinctly, reporting that "these benefits (of screening) do not outweigh the expected harms"[9].

As both of the Irish PCa screening guidelines previously examined specifically advise a Digital Rectal Examination (DRE), whereby a physician examines the prostate gland by palpation, a review of the evidence is required. Abnormal findings on this exam include; "if the prostate is enlarged, asymmetric, nodular, or tender"[22] but these findings can be subjective and the reliability of findings between physicians is poor[22]. While the Positive Predictive Value (PPV) for PCa with an abnormal DRE range from 18-28%[23,24], the sensitivity of the test is poor[22]. DRE is poorly accepted by patients[25,26,] particularly in the absence of symptoms[25,26], diminishing this examination's utility in screening. While one longitudinal study conducted amongst 36,000 men over 12 years found that the high PPV of an abnormal DRE endorsed its utility as a screening tool[27], another large study of 10,500 men found that those with positive findings on DRE were likely to have an abnormal PSA, making the DRE redundant[28]. This highlights the ongoing controversy and conflicting evidence around even this individual part of PCa screening.

The above guidelines and landmark trials relate to civilian populations. In questioning the appropriate strategy to take in relation to PCa screening within the Defence Forces Ireland, it must be considered that a military population may have a different risk of PCa incidence than the civilian population. The landmark study directly comparing cancer incidence between military and civilian populations was published in the USA by Zhu et al, 2009[29]. This high-powered study compared the incidence of six different cancers (including PCa) from the years 1990-2004 from the United States Dept of Defence database (caring for military populations) with the National Cancer Institute database for civilians[29]. They found that PCa rates in the military were double that of the civilian population (Rate Ratio in white population of 2.12) [29]. Their hypotheses for the cause of this increased risk included access to free medical care and screening identifying more cancers as well as potential incomplete reporting in the civilian database, but also acknowledged military service members are potentially exposed to carcinogens such as depleted uranium[29]. Another high-quality study examined cancer incidence from census data in five Nordic countries from 1961 to 2005[30]. It was found that military personnel had the highest Standardised Incidence Ratio (SIR) of developing PCa amongst all occupations, at 1.97 that of the general population[30]. This correlates well with the result of the study by Zhu et al. Similarly, the authors theorised this increased incidence could potentially be explained by more frequent medical examinations and/or exposure to chemicals that are known to carcinogenic[30]. While these two large studies conducted with long follow-up periods identified an increased incidence of PCa in military populations, they did not examine or identify any increased morbidity or mortality either due to PCa or other causes in their studies. Thus, the same controversy persists; that identifying PCa early by means such as PSA blood test does not conclusively save lives, either in a civilian or military population.

3. Conclusion

A review of the literature surrounding prostate screening in both relevant civilian populations and military personnel indicates that overall mortality is not reduced by screening for prostate cancer. Thus, prostate screening is not recommended within military personnel in Ireland.

Compliance with ethical standards

Disclosure of conflict of interest

The author has no conflict of interest to declare.

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