Conspicuity of cribriform prostate cancer on multiparametric magnetic resonance imaging: the jury is still out

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Abbreviations: T2W, T2-weighted imaging; ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; mpMRI, multiparametric magnetic resonance imaging; PI-RADS, Prostate Imaging–Reporting and Data System; PSAD, prostate specific antigen density.

Cribriform, from the Latin for ‘sieve-like,’ describes an aggressive prostate cancer pattern associated with poor prognosis, including biochemical recurrence after prostatectomy [1]. Following progressive integration of multiparametric magnetic resonance imaging (mpMRI) into risk stratification for suspected prostate cancer, there has been understandable concern that particular morphologies (including, intraductal, mucinous and cribriform) may have reduced visibility on mpMRI [2]. If undetected, mpMRI-invisible pathology may avoid biopsy interrogation, resulting in delayed presentation, management, and as such, adverse clinical outcome. However, evidence surrounding mpMRI conspicuity of cribriform disease is contradictory, and given the clinical importance of this phenomenon, warrants discussion.

The radiobiological mechanism of cribriform invisibility on mpMRI is unknown, however, overall reduced tissue density observed in cribriform cancer may partly explain this. Cribriform cancer is typified by numerous punched-out lumina, resulting in loosely-packed architecture and altered gland-to-stroma ratio. As such, lower density may result in less clearly-defined tumours on the anatomic T2-weighted (T2W) sequence. Furthermore, diffusion of water tissue may occur more readily in cribriform disease, resulting in reduced diffusion restriction, and thus, lower signal intensity on diffusion-dependent sequences, including diffusion-weighted imaging (DWI) and the apparent diffusion coefficient (ADC) map.

In a noteworthy study from Truong and colleagues [3], they took a cohort of men with suspected prostate cancer (n = 240) and used a combination of biopsy and whole-mount prostatectomy pathology, correlated to mpMRI phenotype, to assess mpMRI visibility of cribriform disease. They compared cribriform detection by various biopsy approaches (MRI-targeted, systematic, and combined) and also compared lesion presence on mpMRI against prostatectomy, to infer that the majority of cribriform tumours (82.6%) were in fact non-visible to mpMRI.

However, findings from Truong [3] have recently been contradicted by three further studies [4–6]. Using a similar approach, Prendeville and colleagues [4] examined a cohort of men with suspected prostate cancer (n = 154) who underwent pre-biopsy mpMRI followed by targeted and systematic biopsy. In this cohort, cribriform/intraductal cancer was found in 23 cases, of which 96% (22/23) were visible on mpMRI (p < 0.001). Furthermore, they found additional evidence to support conspicuity of cribriform disease, specifically, significant association with high Prostate Imaging-Reporting and Data System v2 (PI-RADS) scores (p = 0.008) and reduced ADC values (p = 0.005). Next, Tonttila and colleagues [5] took another cohort of men with prostate cancer (n = 124) and found that 71% of cases (89/124) contained cribriform or intraductal disease. Again, in contrast to Truong [3], they found that preoperative mpMRI identified 90.5% of tumours (86/95) containing cribriform or intraductal disease [5]. Lastly, Gao and colleagues [6] took a cohort of men with prostate cancer (n = 215) and assessed presence of cribriform disease diagnosed on both biopsy and whole-mount prostatectomy specimens. In their cohort, 51.2% of men (110/215) had cribriform cancer, and when compared to men without cribriform, were noted to have greater levels of tumour mpMRI conspicuity, as denoted by higher PI-RADS v2 scores (p < 0.001), mpMRI lesion size (p < 0.001) and prostate specific antigen density (PSAD; p = 0.001).

Differences in results from Truong [3] and the three subsequent trials [4–6] are considerable, and may be attributable to varied histopathological classification. Truong and colleagues drew attention to ‘pure’ cribriform tumours (that did not contain other patterns) [3], whilst the other investigators considered cribriform disease when mixed other morphologies, including, intraductal carcinoma [4,5], or simply any other cancer pattern [6]. Scientifically, analysis of pure cribriform is commendable, however, the latter approach

(assessing mixed disease) is arguably more pragmatic and representative of clinical practice. Furthermore, both cribriform and intraductal cancer are known to have similar prognostic profiles [1], and as such, may not require discretisation in the manner performed by Truong and colleagues [3].

So, how can this uncertainty be resolved? Two major solutions: generation of new trial data, or statistical summation of extant studies. A trial in which detailed mpMRI-correlated pathology accounted for both cribriform proportion and conspicuity (and the interrelation of these two features) would help bring clarity to this issue, but would have understandable methodological challenges. Alternatively, with an acceptable heterogeneity level, meta-analysis of extant trials would produce an overarching answer to this question, however, the small number of appropriate existing studies might limit this approach.

The majority of evidence now appears to suggest that cribriform cancer is reassuringly conspicuous on prostate mpMRI. However, given a persistent level of uncertainty, it seems prudent to produce a consensus on this issue, with the important diagnostic and treatment implications associated with potential non-detection of this aggressive disease entity.

Conflicts of Interest

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