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Imaging of PSMA-targeted Radiotracers for the Detection of Prostate Cancer Biochemical Recurrence After Definitive Therapy: A Systematic Review and Meta-analysis.

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CONTEXT: Prostate-specific membrane antigen (PSMA)-targeted radiotracers are promising agents for imaging patients with biochemical recurrence of prostate cancer after definitive therapy.

OBJECTIVE: To report the results stratified by PSA levels of a systematic review and meta-analysis for detection of biochemical recurrence after definitive therapy for prostate cancer using PSMA-targeted radiotracers.

METHODS: Following the Preferred Reporting Items for Systematic reviews and Meta-Analysis Diagnostic Test Accuracy (PRISMA-DTA) guidelines, our systematic review searched for articles in PubMed and EMBASE databases from 2012 to July 2018. Studies evaluating men with prostate cancer biochemical recurrence after definitive therapy, without known metastatic disease, who underwent PSMA PET/CT for detection of recurrent disease were included. The risk of bias and applicability concerns were assessed using QUADAS-2. Statistical heterogeneity was assessed with Cochrane Q and an I2 estimate. The reference standard was pathology, follow-up imaging, or PSA decline after salvage treatment. We calculated the pooled estimates and 95% confidence intervals around the prevalence of a positive exam in the study population using a random effects model.

RESULTS: A total of 5113 patients from 43 studies were included in this systematic review. Fifteen (34.8%) of the studies were prospective. Three (6.9%) were multi-institutional and remainder were single centered. Eighteen (41.8 %) were in subjects post-RP, 2 (4.6%) were in subjects post-RT, and 23 (53.5%) were in subjects who were both post-RP and post-RT. The median PSA was 1.6 ng/ml (IQR 0.7-4.4) and the median age was 68 years (IQR 67-70). 33/43 (76.7%) of the studies evaluated 68Ga PSMA-11 (Ga-HBED-CC) PET/CT. The pooled detection rate was 70.2% (95% CI

65.0-75.4%) for the entire cohort. For PSA <0.5 ng/ml, 0.5-0.9 ng/ml, 1-1.9 ng/ml and ≥ 2 ng/ml, the pooled detection rates were 44.9% (36.0-53.9%), 61.3% (95% CI 52.3-70.3%), 78.2% (95% CI 70.8-85.6%), and 93.9% (95% CI 92.0-95.8%). A reference standard was confirmed positive in 684/715 (95.7%) of the patients. There were significant study heterogeneity and publication bias (p<0.01).

DISCUSSION: PSMA-targeted radiotracers are likely effective for the detection of biochemically recurrent prostate cancer at low PSA levels. However, existing studies are limited by retrospective designs, limited reference standards, publication bias, and lack of inter-agent comparison.

KEYWORDS: Biochemical recurrence; F-18 DCFBC; F-18 DCFPyL; F-18 PSMA-1007; Ga-68 HBED-CC; Ga-68 PSMA I&T; Ga-68 PSMA-11; Imaging; Meta-analysis; PET; PSMA; Positron imaging; Prostate recurrence; Prostate-specific membrane antigen; biochemical failure; prostate cancer; radiotracers

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