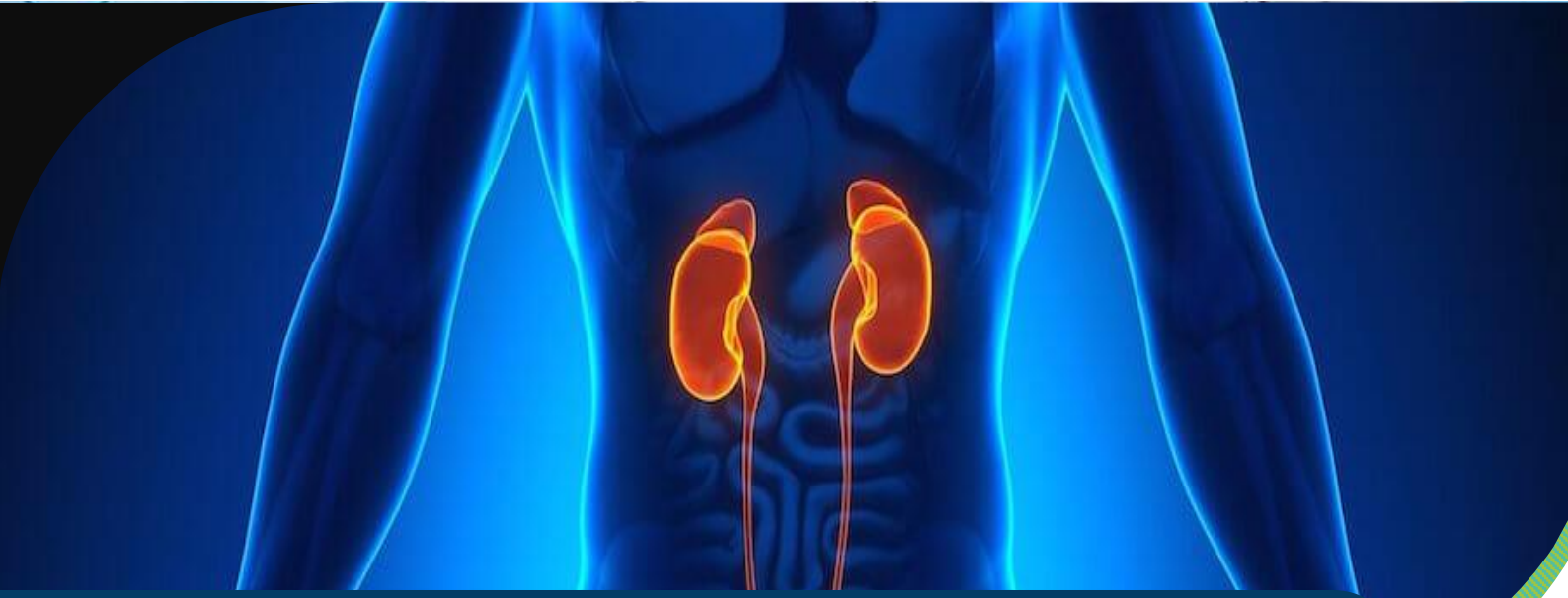

NU Rounds

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "**NU Rounds**" which contains latest and interesting news in the field of Urology.

Inside This Issue:

1. Prostate Cancer androgen deprivation therapy Linked to Lower COVID-19 Infection Risk -2
2. Intratubular Germ Cell Neoplasia In-Situ: Diagnosis and Management -3
3. Predictive Factors of Missed Clinically Significant Prostate Cancers with Negative Magnetic Resonance Imaging -6

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

Prostate Cancer androgen deprivation therapy Linked to Lower COVID-19 Infection Risk

According to a recent study, men who undergo androgen deprivation therapy (ADT) for prostate cancer (PCa) tend to be at lower risk for coronavirus infection which causes COVID-19.

In a study of men with PCa in Veneto, a particularly hard-hit Italian region of COVID-19, only 4 out of 5273 patients receiving ADT were infected with SARS-CoV-2 coronavirus compared to 114 out of 37,161 who did not receive ADT. The no-ADT group had significant 4-fold increased probabilities of positive testing for SARS-CoV-2 compared to the ADT recipients.

Results from the study showed that patients with any type of cancer have an increased risk of SARS-CoV-2 infection compared to patients with no cancer diagnosis. For example, of the total male population of Veneto of 2.4 million, 0.2 per cent of cancer patients tested positive for SARS-CoV-2 compared to 0.3 per cent of cancer patients, Dr Alimonti and his colleagues reported.

The authors speculated that the apparent protective effect of ADT might involve inhibition of TMPRSS2, a serine protease involved in multiple physiological and pathological processes including cancer and viral infection. Previous experiments have included TEMPRSS2 as a crucial host cell component for the dissemination of many clinically important viruses, including coronaviruses SARS-CoV and MERS-CoV. TEMPRSS2 is highly expressed in localized and metastatic PCa, with androgen receptors (ARs) regulating its transcription. TMPRSS2 expression in non-prostatic tissue including the lung has been shown to be regulated by ARs. The androgen-dependent regulation of TMPRSS2 expression in the lungs can explain men's increased susceptibility to developing severe SARS-CoV-2 infections compared with women.

They also found that rates of TMPRSS2 are regulated by androgens not only in the prostate but also in the lung, thus put forward the hypothesis that androgen deprivation therapies (ADTs) that protect patients affected by prostate cancer from infections with SARS-CoV-2.

Dr Alimonti and his collaborators noted in a review of research limitations that cancer patients diagnosed with SARS-CoV-2 are treated more frequently than non-cancer patients, and they could have been screened at a higher rate for the coronavirus. This can clarify the elevated incidence of infectious individuals in the cancer patient community. Therefore, PCa patients receiving ADT that practice more social distance than PCa patients who do not receive ADT and cancer patients in general.

Source: Montopoli M, Zumerle S, Vettor R, et al. Androgen-deprivation therapies for prostate cancer and risk of infection by SARS-CoV-2: a population-based study (N = 4532). Ann Oncol. 2020; S0923-7534(20)39797-0.

Intratubular Germ Cell Neoplasia In-Situ: Diagnosis and Management

INTRODUCTION

The malignant counterpart to testicular germ cell tumors is the GERM cell neoplasia in situ, first identified by Skakkebaek in 1972 in a study of 2 infertile patients with atypical intratubular germ cells. GCNIS was originally known as in situ carcinoma and later intratubular germ cell neoplasia or intraepithelial testicular neoplasia, but these terms are considered antiquated as GCNIS is a more accurate description of the neoplastic procedure.

Historical series indicated that GCNIS is present in approximately 5% of all TGCT patients in the contralateral testicles and, if not treated, will progress to an invasive tumor in nearly 50 % of patients within 5 years and 70% within 7 years. The ideal treatment paradigm for patients with GCNIS proven by biopsy, however, is not clearly defined. Although comprehensive literature on the management of solid germ cell tumors is current, there is a shortage of forward-looking evidence to inform the evaluation and care of GCNIS patients. Contra-lateral GCNIS screening guidelines remain ambiguous, with various suggestions in accessible guidance statements. Current treatment options based largely on seminal studies performed in the 1980s include orchiectomy, or testicular radiation therapy, or monitoring. Chemotherapy was also evaluated for GCNIS management, given the use of cisplatin and carboplatin chemotherapy regimens in patients with solid germ cell tumors. While some studies indicate that GCNIS may respond to chemotherapy in part or at least, others have found minimal to no impact. As a consequence, there is currently no agreement about the best strategy for GCNIS patients, so most patients are usually handled according to desires of physicians or clinical practice trends. In this article the authors offer a comprehensive analysis of recent research aimed at improving the diagnosis and care of GCNIS patients.

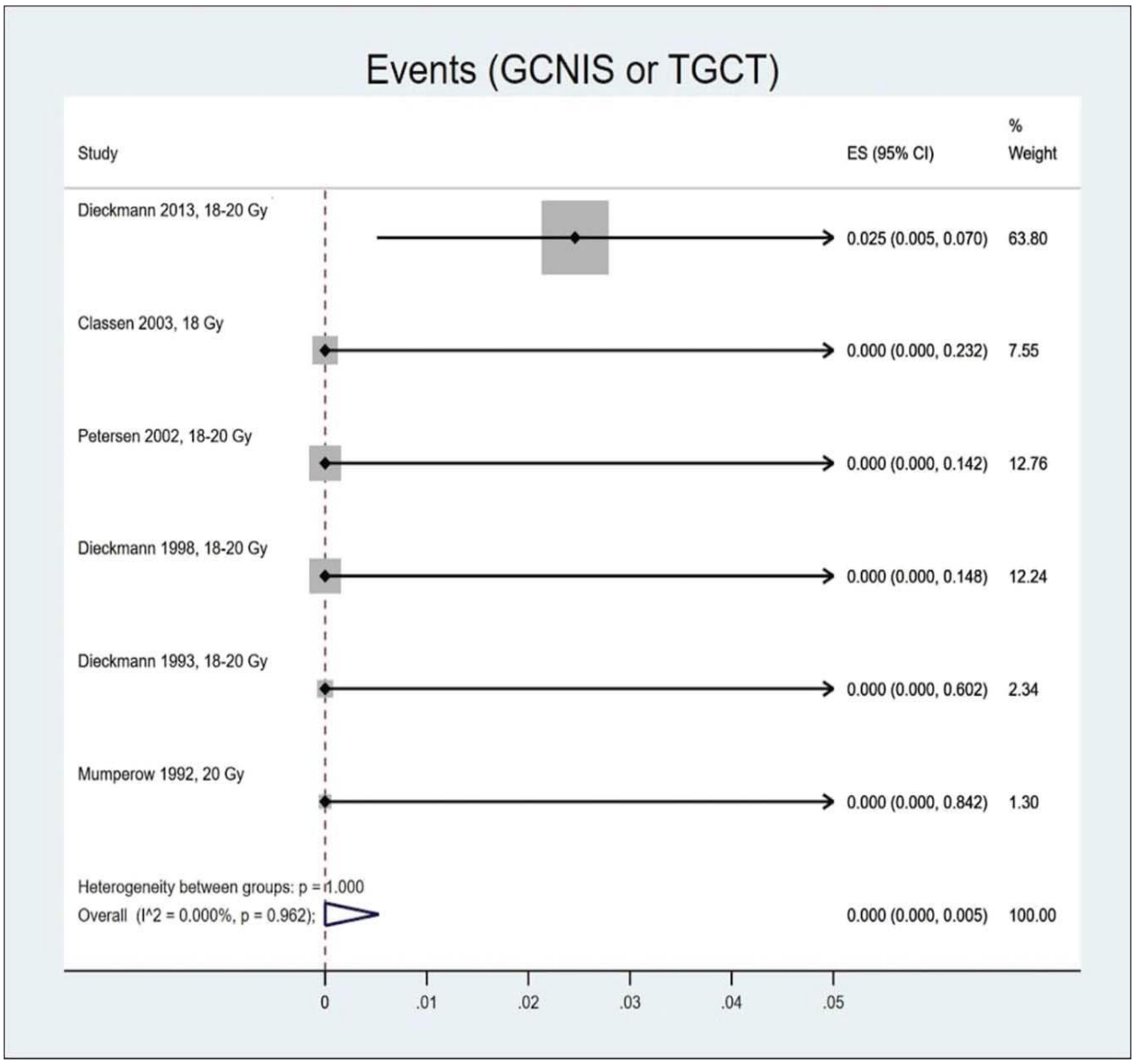
METHODS

Paired investigators independently searched for studies on the diagnosis and management of testicular germ cell neoplasia in situ using PubMed, Embase and the Cochrane Central Register of Controlled Trials from January 1, 1980 through August 2018. The reviewers then extracted data and assessed quality.

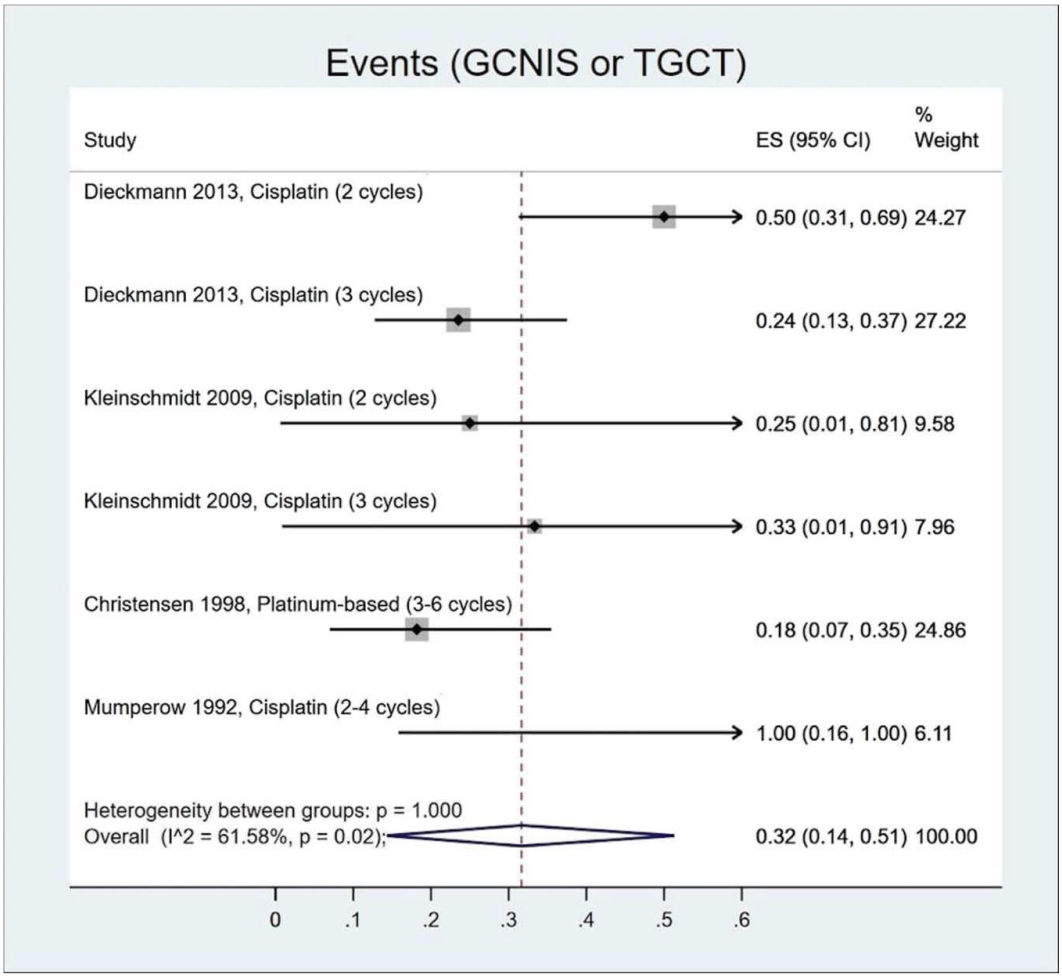
RESULTS

Eighteen studies met inclusion criteria. Among patients with a testicular germ cell tumor the prevalence of contralateral germ cell neoplasia in situ was 4.0% to 8.1%. No significant difference in the risk of metachronous malignancy was identified between unscreened groups vs those with routine contralateral testicular screening (cumulative incidence 1.9% vs 3.1%, $p<0.097$, respectively). Patients who presented with a history of testicular atrophy, age less than 40 years or cryptorchidism had an elevated risk of germ cell neoplasia in situ.

In patients with germ cell neoplasia in situ the use of 18 to 20 Gy radiation therapy demonstrated the lowest rate of disease on follow-up biopsies (0% to 2.5%), compared to a median of 30% on biopsies in patients treated with cisplatin based chemotherapy. Carboplatin based treatment regimens demonstrated positive disease in 66% to 75% on repeat biopsies. Rates of treatment related hypogonadism were 30.8% to 38.5% and 13% to 20% for patients treated with 18 to 20 Gy and cisplatin based chemotherapy, respectively.



Lowest rates of GCNIS on subsequent biopsy at least 3 to 6 months following RT. ES, effect size.



Use of chemotherapy for eradication of GCNIS. ES, effect size.

CONCLUSIONS

In patients with a testicular germ cell tumor, the probability of developing in situ contralateral germ cell neoplasia is 4% to 8%, with greater incidence of patients with testicular atrophy, cryptorchidism, or age below 40 years. The risk for in situ germ cell neoplasia is high enough to support the use of contralateral testicular biopsy in patients with these risk factors.

Routine screening is not recommended though. 18 to 20 Gy radiation therapy was associated with far better eradication of in situ germ cell neoplasia than with chemotherapy. Chemotherapy will remove in situ germ cell neoplasia in up to two-thirds of patients undergoing chemotherapy as an adjuvant to a main germ cell tumor.

REFERENCE

Gupta M, Cheaib JG, Patel HD, et al. Diagnosis and Management of Intratubular Germ Cell Neoplasia In Situ: A Systematic Review. J Urol. 2020;204(1):33-41.

Predictive Factors of Missed Clinically Significant Prostate Cancers with Negative Magnetic Resonance Imaging

INTRODUCTION

A significant concern in screening and early identification of prostate cancer is over treatment and over managing indolent illness. At present, prostate MRI is transforming the pathway for diagnosing prostate cancer. Several studies have provided strong evidence that MRI use improves clinically significant prostate cancer diagnosis. MRI has excellent negative predictive value in excluding csPCa. MRI has also shown the potential to reduce the diagnosis of is PCa. Performing MRI before any prostate biopsy is widely recommended. Results of the PRECISION trial, where prostate biopsies were avoided in cases of prebiopsy negative MRI, suggest that MRI could be used as a triage test for prostate biopsy. Nonetheless, such findings need to be viewed in the sense of the MRI-FIRST test performance, in which guided biopsy skipped several csPCa. NMRI accounts for 20 to 30% of all cancer naiive communities and early screening helps to improve the amount.

It is controversial to advise about biopsy if the prebiopsy MRI is negative (PI-RADS 1-2). NMRI patients may avoid prostate biopsy but may miss 5 to 15 per cent of csPCa. Recent recommendations say that men can safely escape prostate biopsy if MRI is negative, especially "if PSA density (PSAD) is small and PSA evaluation is acceptable" or "clinical presumption of prostate cancer is small on the basis of joint patient decision taking."

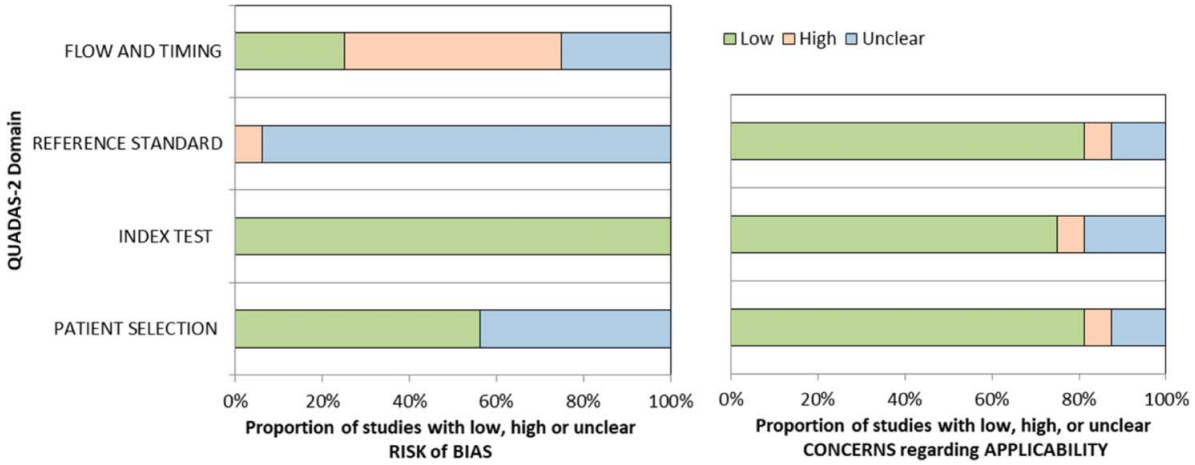
Digital rectal tests are part of PCa's diagnostic process. In PRECISION and MRI-FIRST trials, respectively, 15 per cent and 30 % of patients had an irregular DRE total. It is still not known how to identify patients with nMRI and a high risk of csPCa. Associating MRI with predictive factors can increase MRI NPV and decrease the number of prostate biopsies in men who have a low risk of csPCa. In this work they systematically reviewed the literature on predictive factors for csPCa in patients with nMRI who are naive with prostate cancer.

METHODS

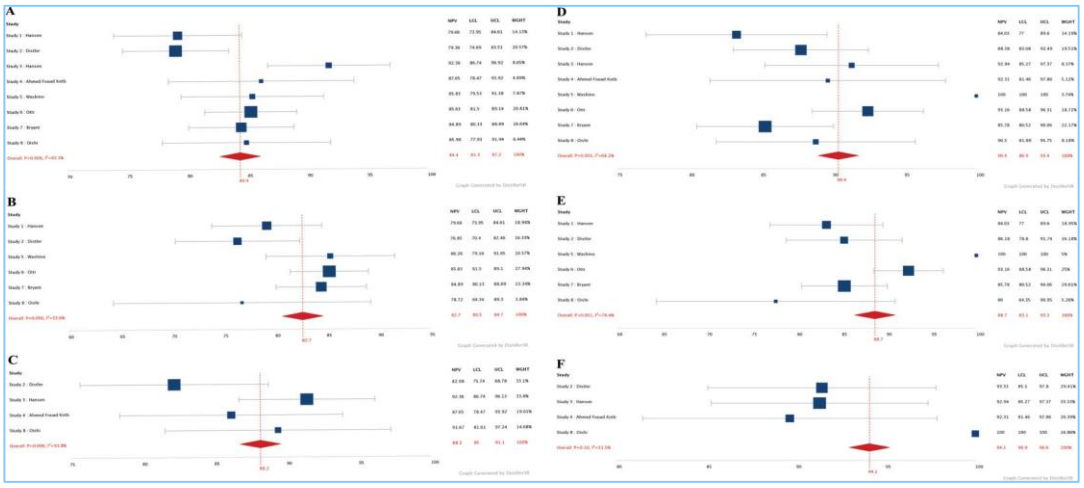
The MEDLINE and Scopus databases were searched up to March 2019. The review protocol was published in the PROSPERO database (CRD42019125549). The clinical factors and markers studied were age, prostate specific antigen, prostate specific antigen isoforms, prostate specific antigen density, PCA3, prostate volume, family history, ethnicity and risk calculators. The primary objective was to determine their predictive ability for clinically significant prostate cancer diagnosis. Secondary objectives included meta-analysis of the negative predictive value of prebiopsy negative magnetic resonance imaging when combined with these predictive factors.

RESULTS

A total of 16 studies were eligible for inclusion. Few studies reported negative predictive value of magnetic resonance imaging combined with a marker. Prostate specific antigen density was the best studied and the strongest predictor of clinically significant prostate cancer in men with prebiopsy negative magnetic resonance imaging. There were 8 studies (1,015 patients) eligible for meta-analysis of the added value of prostate specific antigen density less than 0.15 ng/ml/ml to magnetic resonance imaging in reducing the risk of missing clinically significant prostate cancer. When combined with prostate specific antigen density, overall magnetic resonance imaging negative predictive value increased from 84.4% to 90.4% in cancer naive patients. The increase was from 82.7% to 88.7% in biopsy naive and from 88.2% to 94.1% in previous negative biopsy subgroups.



Risk of bias with QUADAS-2, with assessment of RoB for included studies (A) and RoB summary graph (B)



Forest plots showing NPV of MRI alone in cancer na€ıve (A), BN (B) and PNB (C) cases, and with PSAD less than 0.15 ng/ml/ml in PCa naive (D), BN (E) and PNB (F) cases. LCL, lower confidence limit. UCL, upper confidence limit. WGHT, study weight.

CONCLUSION

The most well studied and reliable negative predictor factor for clinically relevant diagnosis of prostate cancer was PSAD of less than 0.15 ng / ml / ml. The authos consider using PSAD less than 0.15 ng / ml / ml in conjunction with unfavorable MRI tests to avoid biopsy suggestion in patients who are naive to cancer.

REFERENCE

Pagniez MA, Kasivisvanathan V, Puech P, et al. Predictive Factors of Missed Clinically Significant Prostate Cancers in Men with Negative Magnetic Resonance Imaging: A Systematic Review and Meta-Analysis. J Urol. 2020;204(1):24-32.