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Short Communication

Persistent Prostate-Specific Antigen Levels after Radical Prostatectomy: An Important Indicator for Monitoring

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INTRODUCTION

Radical Prostatectomy (RP) is the primary treatment modality for localized Prostate Cancer (PC), demonstrating long-term efficacy and a favorable prognosis [1]. Postoperative PSA value monitoring is currently the best indicator for PC. The European Association of Urology guidelines for the diagnosis and treatment of PC suggest that A PSA value of ≥ 0.1 ng/ml defined as persistent PSA for 4-8 weeks following PSA [2]. Therefore, the prognostic and predictive value of persistent PSA status after RP is debatable.

DESCRIPTION

PSA has a half-life of 3.15 days and is expected to decline to undetectable levels within 4 weeks following RP in patients with complete pathological resection [3]. The emergence of PSA Persistence provides clinicians with a new indicator for determining the poor prognosis. And intervention can be prioritized for this subset of patients to ensure a better prognosis.

PSA persistence has been identified as an independent risk factor for the development of systemic metastases and poor survival in almost all published studies [4-7]. Biochemical Recurrence (BCR), occurrence of metastasis and death are the more commonly used indicators to assess patient prognosis. Most studies have compared Recurrence-Free Survival (RFS), Metastasis-Free Survival (MFS), Overall Survival (OS), and Cancer-Specific Survival (CSS) and confirmed that there is indeed a difference in survival between the PSA Persistence group and the no-PSA Persistence group. Preisser scholars determined that there were statistically significant differences in MFS, OS, and CSS between PSA Persistence and no PSA Persistence groups in a study of 11,604 patients with 15 years of long-term follow-up. A multifactorial COX regression analysis found that PSA Persistence was an independent predictor of the occurrence of metastasis, death and cancer-specific mortality in patients [4]. Milonas scholars further categorized prostate cancer patients into low, intermediate and high risk groups. The significance of PSA Persistence was found to be negligible in low-risk groups. In intermediate risk patients, PSA Persistence only predicted biochemical recurrence. It has the greatest prognostic impact in high-risk PCa patients and can be used as an independent predictor of poorer long-term prognosis in high-risk PCa patients [7].

PSA Persistence can help physicians make better clinical decisions. Salvage radiotherapy and a more accurate counseling follow-up program could help this group of patients achieve clinical prognostic benefit. Studies have found that salvage radiotherapy can benefit patients with positive lymph nodes from adjuvant therapy [8-11]. More precise treatment and follow-up programs need to be further confirmed by clinical studies.

What factors contribute to the development of PSA Persistence need to be considered in terms of 1) Incomplete surgical resection of the tumor, 2) Residual benign prostate and 3) The presence of distant tumor micrometastases. Different clinical features preoperatively, intraoperatively, and postoperatively have been associated with the development of Persistent PSA Persistence. Three existing clinical studies have confirmed that different clinical indicators are associated with the occurrence of PSA Persistence [4,12,13].

More advanced prostate cancer is associated with the development of PSA Persistence, which includes later pathological staging, higher Gleason score, larger tumor lesions and the presence of regional lymph node metastases. Different studies have confirmed that both clinical T-stage ≥ T2a and pathologic T-stage ≥ T3a are associated with the development of PSA Persistence [4,12,13]. Puncture pathology Gleason ≥ 2 and postoperative pathology Gleason ≥ 3 have been associated with the development of PSA Persistence [4]. Guo's study noted tPSA at diagnosis >49.73 ng/mL and fPSA at diagnosis >2.07 ng/mL, further confirming the association between high tumor load and

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the the occurrence of Persistent PSA Persistence [12]. More advanced prostate cancer may have tumor micrometastases that are difficult to detect on imaging, which substantially increases the chance of PSA Persistence after RP. Another explanation for this phenomenon is that the tumor load itself is heavy, and although the half-life of PSA is 3.15 days, it is still difficult to fall to less than 0.1 ng/mL in a short period of time.

The relationship between positive surgical margins and PSA Persistence remains to be further explored. Positive surgical margins represent the possibility of surgical residue, but another issue that also deserves our consideration is the residue of benign prostatic body, which is related to the qualification and clinical experience of the operator, the more qualified surgeon can remove the prostate completely. However, for the clinically inexperienced surgeon, there is also residual benign prostatic tissue along with the residual tumor tissue [5]. Residual benign glandular tissue can also lead to PSA Persistence. And only one study by Preisser found that positive postoperative pathologic margins were associated with PSA Persistence, and further studies are needed to confirm this observation.

Scholar Preisser's study concluded that the closer the year of surgery, the lower the risk of PSA persistence [4]. After the diagnosis of prostate cancer by puncture biopsy, the shorter the interval between the RP surgery and the tumor invasion of the gland and the occurrence of distant micrometastases will be drastically reduced, the lower the risk of PSA persistence. This conclusion remains to be confirmed by further research. This indicator was not included in Guo's study [12].

It is well known that ADT combined with antiandrogen therapy is an effective modality for the treatment of prostate cancer. Patients treated with ADT have postoperative PSA values that are lower to varying degrees than those without ADT. Therefore, patients who experienced preoperative and postoperative ADT need to be excluded from this study to minimize the influence of other factors on the findings [14,15]. This is a great limitation of the Guo study.

It has been found that older age is associated with a lower risk of persistent PSA [16,17]. Previous studies have confirmed that advanced age patients have more aggressive tumors and worse prognosis than younger prostate cancer patients, with a higher risk of biochemical recurrence, distant metastasis and tumor-specific death after surgery [5,6]. However, this study reached a contradictory conclusion and more studies are still needed to confirm the relationship between age and persistent PSA [18,19].

CONCLUSION

The percentage of patients who developed persistent PSA after RP still varies among studies. This includes the 3 available studies on risk factors 8.8%, 33.02% and 15.01% and other studies reported 26.0%, 9.2%, etc. The fluctuation in the percentage of patients with persistent PSA represents differences in treatment modalities and operator levels across study centers. Therefore, larger multicenter studies or meta-analyses are needed to further explore the relationship between preoperative intraoperative and postoperative clinical factors and the occurrence of persistent PSA, pending better clinical decisions for clinicians.

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