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Real-world evidence of the PRIMARY score: an Argentinian experience

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Abstract

Objective:

The PRIMARY score incorporates intraprostatic prostate-specific membrane antigen (PSMA) uptake pattern and intensity to improve the detection of clinically significant prostate cancer. This study evaluated, in an Argentinian real-world cohort, whether intraprostatic maximum standardised uptake value (SUVmax) on [68Ga]Ga-PSMA PET/CT identifies clinically significant prostate cancer, defined as Gleason score ≥ 7 or ISUP grade group ≥ 2.

Methods:

We performed a retrospective observational multicentre study including patients evaluated between 2022 and 2026 who underwent [68Ga]Ga-PSMA PET/CT and had histopathological data available. Age, prostate-specific antigen, SUVmax, Gleason score and referring centre were recorded. Diagnostic performance for an exploratory SUVmax threshold was calculated using histopathology as the reference standard.

Results

Among 273 patients with histologically confirmed prostate cancer, 264 (96.7%) had clinically significant disease and 9 (3.3%) had Gleason 6 disease. All 187 patients with SUVmax ≥ 10.2 had Gleason score ≥ 7. The threshold showed sensitivity of 70.8%, specificity of 100%, positive predictive value of 100%, negative predictive value of 10.5%, diagnostic accuracy of 71.8% and an area under the receiver operating characteristic curve of 0.874. SUVmax differed significantly across ISUP grade groups (Kruskal-Wallis $H = 32.03$; $p < 0.001$).

Conclusions

In this real-world cohort, SUVmax ≥ 10.2 was exclusively associated with clinically significant prostate cancer. These findings support the SUVmax intensity component of the PRIMARY score as a potential non-invasive marker of tumour aggressiveness, requiring prospective validation.

Clinical trial registration

Not applicable this was a retrospective observational study.

Introduction

Prostate cancer has heterogeneous clinical behaviour, and the diagnostic pathway is primarily aimed at distinguishing indolent disease from clinically significant prostate cancer (csPCa). Histological grade remains central to risk stratification, with csPCa commonly defined as Gleason score ≥ 7 or ISUP grade group ≥ 2. Current European guidance supports magnetic resonance imaging-based diagnostic pathways and histological grading according to the ISUP system (1).

Positron emission tomography/computed tomography (PET/CT) with prostate-specific membrane antigen (PSMA) ligands has become an increasingly relevant imaging technique in prostate cancer, particularly for staging higher-risk disease (2). Beyond staging, PSMA PET/CT may provide biologically meaningful information regarding intraprostatic tumour phenotype. Quantitative parameters such as the maximum standardised uptake value (SUVmax) may therefore be associated with tumour aggressiveness.

The PRIMARY trial showed that adding [68Ga]Ga-PSMA PET/CT to multiparametric MRI (mpMRI) improved diagnostic performance for csPCa in men with suspected prostate cancer (3). A subsequent post hoc analysis proposed the five-category PRIMARY score, based on intraprostatic uptake pattern and SUVmax, with PRIMARY score 5 defined by SUVmax ≥ 12 and associated with csPCa in 100% of cases (4). More recent real-world data have further supported the reproducibility and diagnostic accuracy of the PRIMARY score (5).

In Argentina, evidence regarding intraprostatic PSMA uptake and clinically significant prostate cancer remains limited. Bergero et al. reported that SUVmax ≥ 9.5 was associated with csPCa in an Argentinian cohort (6). The present study evaluates whether an SUVmax threshold observed in routine clinical practice can identify csPCa and thereby provide real-world support for the intensity component of the PRIMARY score.

Materials and Methods

Study design and population

This was a retrospective observational multicentre study including patients referred from two healthcare centres who underwent [68Ga]Ga-PSMA PET/CT at a single diagnostic imaging centre. Patients evaluated between 2022 and 2026 were eligible if a PSMA PET/CT report and sufficient clinicopathological data were available for analysis. Patients without histopathological data were excluded.

The study cohort consisted of patients with histologically confirmed prostate cancer. Clinically significant prostate cancer was defined as Gleason score ≥7, corresponding to ISUP grade group 2 or higher.

Imaging and variables

All PET/CT examinations were performed using a United Imaging uMI 550 scanner. The following variables were abstracted from medical reports: age, prostate-specific antigen (PSA) value when available, intraprostatic SUVmax, Gleason score, ISUP grade group when classifiable and referring centre.

Because this was a retrospective report-based study, uptake patterns required to reconstruct the complete PRIMARY score were not consistently available. The analysis therefore focused on the SUVmax intensity component, which is central to the definition of PRIMARY score 5.

Statistical analysis

Categorical variables were reported as absolute frequencies and percentages. Diagnostic performance of the exploratory SUVmax threshold was evaluated using histopathology as the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy and the area under the receiver operating characteristic curve (AUC) were calculated. Differences in SUVmax across ISUP grade groups were evaluated using the Kruskal-Wallis test. Analyses were performed using R software.

Results

Cohort characteristics

A total of 273 patients with histologically confirmed prostate cancer were included. Mean age was 69 years (range 55-83 years). In the overall cohort, 264 patients (96.7%) had clinically significant prostate cancer, whereas 9 patients (3.3%) had Gleason 6 disease.

Diagnostic performance of SUVmax

All patients with SUVmax ≥10.2 had clinically significant prostate cancer. No Gleason 6 cases had SUVmax equal to or above this value. The diagnostic 2 × 2 matrix is shown in Table 1, and the distribution of SUVmax according to Gleason score is shown in Fig. 1.

At the SUVmax threshold of 10.2, sensitivity was 70.8% (95% CI 64.9-76.2), specificity was 100% (95% CI 66.4-100), PPV was 100% (95% CI 98.0-100), NPV was 10.5% (95% CI 4.9-18.9), diagnostic accuracy was 71.8% and AUC was 0.874.

SUVmax according to ISUP grade group

For the ISUP grade group analysis, 259 classifiable patients were included; 14 cases could not be assigned with certainty and were excluded from this analysis. SUVmax differed significantly across ISUP

groups (Kruskal-Wallis H=32.03; p<0.001). Median SUVmax increased progressively with histological grade, from 5.9 in ISUP 1 to 19.7 in ISUP 5 (Fig. 2).

Discussion

This Argentinian real-world cohort supports an association between intraprostatic PSMA uptake intensity and clinically significant prostate cancer. In this series, an SUVmax threshold of 10.2 identified a subgroup in which all patients had Gleason score ≥7, resulting in an observed PPV and specificity of 100%. Although the NPV was low because clinically significant disease was highly prevalent in the study population, the absence of Gleason 6 cases above the threshold is clinically relevant.

These findings are aligned with the biological rationale of the PRIMARY score. In the original PRIMARY score analysis, very high uptake defined by SUVmax ≥12 corresponded to PRIMARY score 5 and was associated with csPCa in all patients (4). Our threshold of 10.2 is slightly lower than that proposed in the PRIMARY score, but the direction and magnitude of the finding are concordant: high intraprostatic PSMA uptake appears to enrich strongly for clinically significant histology.

The results are also consistent with the Argentinian experience reported by Bergero et al., in which intraprostatic PSMA uptake intensity was associated with clinically significant disease and an SUVmax threshold of 9.5 showed an AUC of 0.73 (6). Together, these data suggest that PSMA uptake intensity may have value as a non-invasive marker of tumour aggressiveness in different clinical settings.

The main strength of this study is that it reflects routine clinical practice across Argentinian referral centres. However, several limitations should be acknowledged. First, the study was retrospective and subject to selection bias. Second, all included patients had histologically confirmed prostate cancer, resulting in a high prevalence of csPCa and limiting estimation of NPV. Third, PET/CT reports did not consistently include uptake-pattern descriptors; therefore, the complete PRIMARY score could not be reconstructed. Fourth, the SUVmax threshold was exploratory and requires external prospective validation before it can be used to modify biopsy indication.

These results should therefore not be interpreted as supporting biopsy omission in current clinical practice. Rather, they generate a hypothesis that the integration of mpMRI, PSMA PET/CT uptake pattern and SUVmax may help define a subgroup of patients with a very high probability of csPCa. Prospective studies using standardised PRIMARY score reporting are needed to determine whether this approach can safely refine diagnostic pathways.

Conclusion

In this Argentinian real-world cohort, intraprostatic SUVmax ≥ 10.2 on [68Ga]Ga-PSMA PET/CT was exclusively associated with clinically significant prostate cancer. SUVmax also increased significantly across ISUP grade groups. These findings support the SUVmax intensity component of the PRIMARY

score as a potential non-invasive marker of tumour aggressiveness. Prospective multicentre validation using complete PRIMARY score reporting is required before clinical implementation.

Declarations

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Competing interests: The authors have no relevant financial or non-financial interests to disclose.

Author contributions: All authors contributed to study conception and design, material preparation, data collection, analysis, manuscript drafting or critical revision, and approved the final manuscript. Individual contributions should be confirmed by all authors before resubmission.

Ethics approval and consent to participate: This retrospective observational multicentre study was approved by the Comité de Bioética del Centro Diagnóstico Imaxe, Buenos Aires, Argentina (RENIS registration code CE000365; approval reference No. 73; approval date 1 May 2026). The approval included the Servicio de Urología, Hospital General de Agudos Dr. Carlos G. Durand and Imaxe as participating centres. The study was performed in accordance with the principles of the Declaration of Helsinki. The requirement for individual informed consent was waived by the Ethics Committee because the study involved only review of pre-existing clinical and paraclinical records, with no direct intervention or additional patient contact, and data were anonymized/de-identified prior to analysis.

Consent for publication: Not applicable.

Data availability: The datasets analysed during the current study are not publicly available because they contain sensitive clinical data and are subject to institutional confidentiality restrictions. De-identified data may be available from the corresponding author upon reasonable request and subject to approval by the relevant ethics committee and participating institutions.

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Table

Table 1 Diagnostic 2 × 2 matrix for SUVmax ≥10.2 and clinically significant prostate cancer

SUVmax	Gleason ≥7	Gleason <7	Total
≥10.2	187	0	187
<10.2	77	9	86
Total	264	9	273

Figures

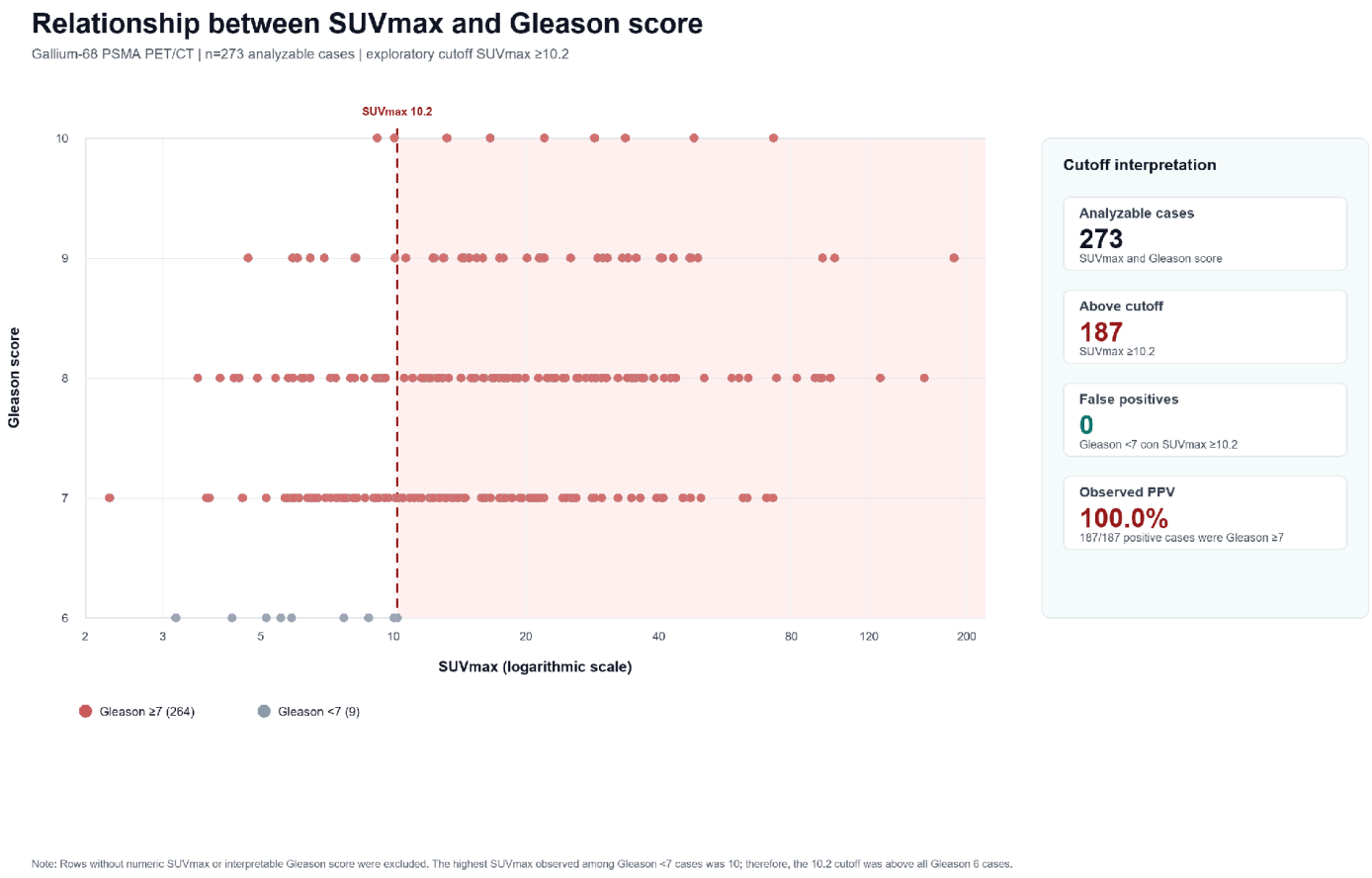


Figure 1

Relationship between intraprostatic SUVmax and Gleason score. The vertical dashed line indicates the exploratory SUVmax threshold of 10.2; all cases above this threshold had Gleason score ≥7. Grey points denote Gleason <7 and red points denote Gleason ≥7.

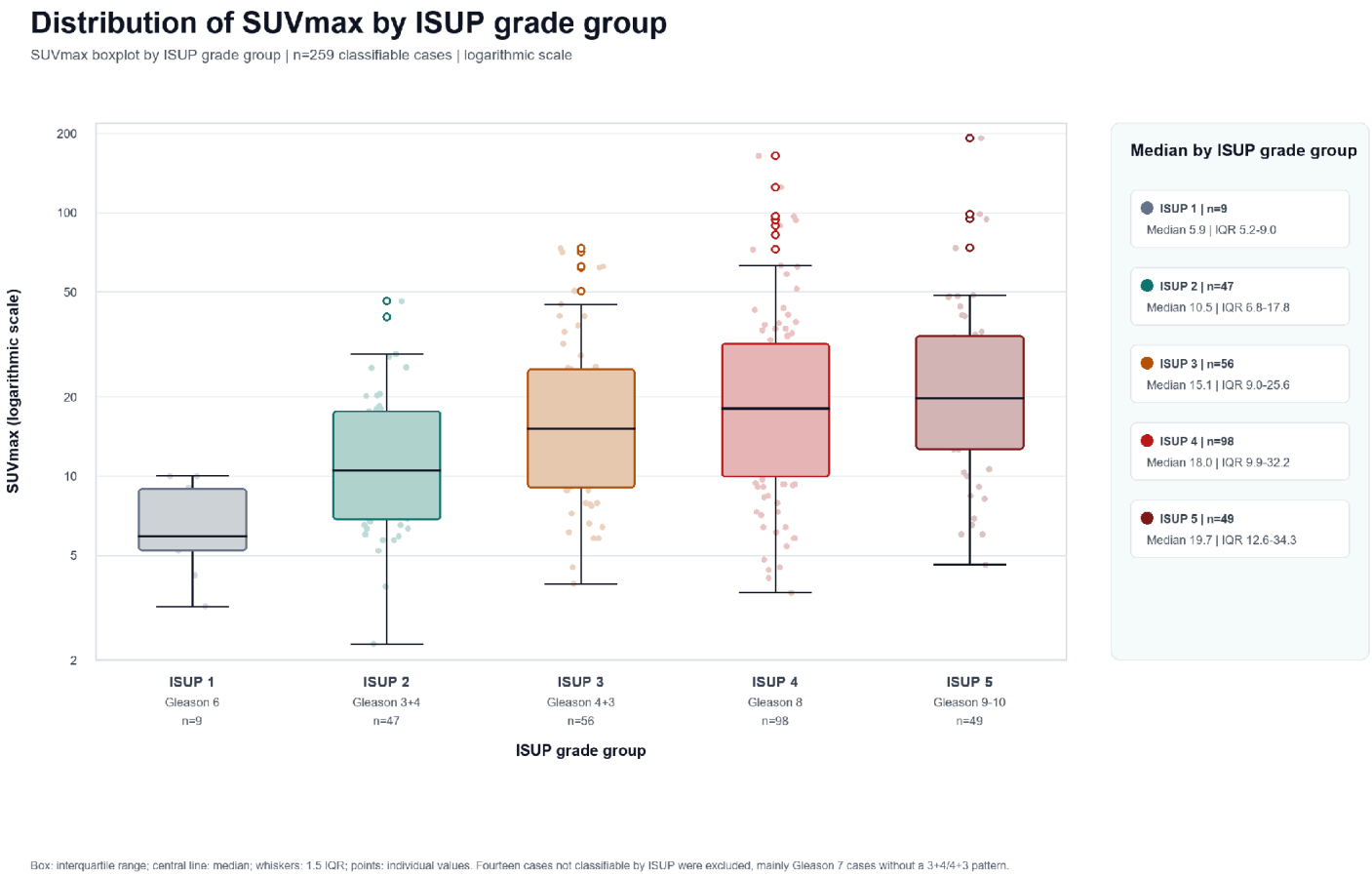


Figure 2

Distribution of intraprostatic SUVmax by ISUP grade group. Boxplots show median and interquartile range; whiskers represent 1.5 × IQR. Fourteen cases not classifiable by ISUP grade group were excluded.