# Real-World Evidence of the PRIMARY Score: An Argentinian Experience

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## Abstract

**Introduction.** We evaluated whether intraprostatic maximum standardised uptake value (SUVmax), the intensity component of the PRIMARY score, identifies clinically significant prostate cancer.

**Methods.** This retrospective multicentre study included patients evaluated from 2022 to 2026 with [$^{68}$Ga] Ga-PSMA-11 PET/CT and histopathology. We used Gleason score ≥7 to define clinically significant disease and evaluated an exploratory SUVmax threshold.

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

**Conclusion.** In this cohort, intraprostatic SUVmax ≥10.2 was associated with clinically significant disease. The exploratory threshold requires prospective validation.

**Keywords:** Glutamate Carboxypeptidase II; Prostatic Neoplasms/diagnostic imaging; Positron Emission Tomography Computed Tomography; Sensitivity and Specificity

## 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. 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 [$^{68}$Ga] 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.

## Methods

### Study design and population

This was a retrospective observational multicentre study including patients referred from two healthcare centres who underwent [$^{68}$Ga]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

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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 administered activity of [$^{68}$Ga]Ga-PSMA-11 was 1.8–2.2 MBq/kg. PET/CT acquisition began 50 minutes after administration. PET images were reconstructed using ordered-subsets expectation maximisation (OSEM).

Three readers reviewed each PET/CT examination and jointly agreed on the intraprostatic SUVmax recorded for analysis. SUV was normalised to total body weight. Variables abstracted from medical reports included 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.

### 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. The committee approved the study under the protocol title “Intraprostatic SUVmax on PSMA-PET as a Biomarker for Clinically Significant Prostate Cancer”.

### Statistical analysis

Categorical variables were reported as absolute frequencies and percentages. The exploratory SUVmax threshold was selected post hoc as the lowest observed value above the highest SUVmax among patients with Gleason score <7. PET/CT results were classified as positive at or above this threshold. Performance at the threshold was estimated in the same cohort, 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. Table 1 shows the diagnostic 2 × 2 matrix. Fig. 1 shows the receiver operating characteristic (ROC) curve, and Fig. 2 shows the distribution of SUVmax by Gleason score.

**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 |

SUVmax, maximum standardised uptake value.

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. 3).

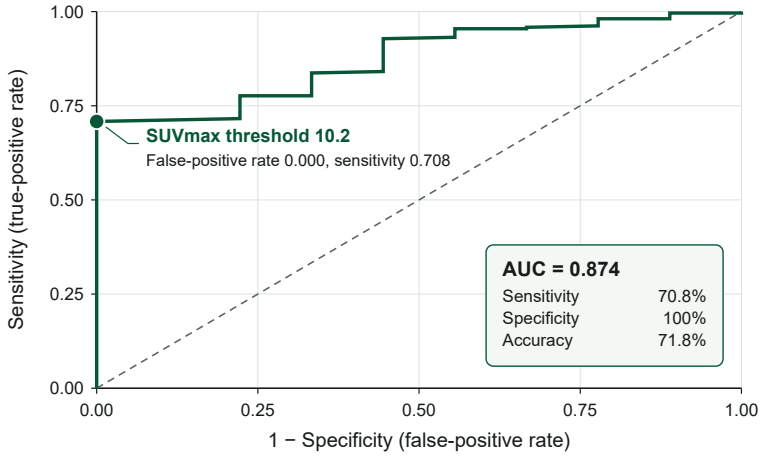



**Figure 1 -** Receiver operating characteristic (ROC) curve for intraprostatic SUVmax in detecting Gleason score ≥7. The marker indicates the exploratory threshold of 10.2. The dashed diagonal indicates chance discrimination. AUC, area under the curve.

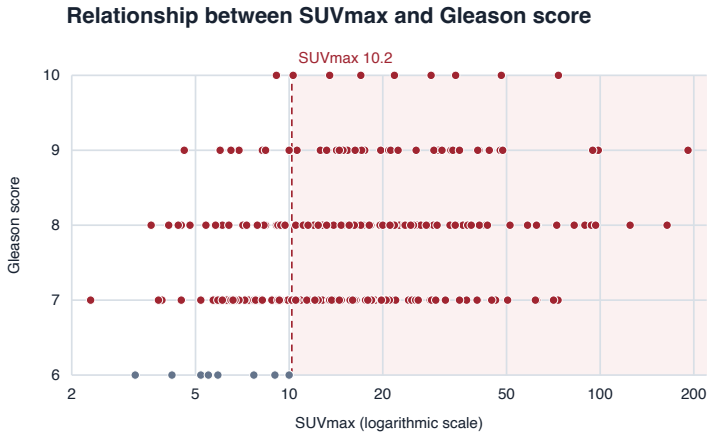



**Figure 2 -** Relationship between intraprostatic SUVmax and Gleason score. The vertical dashed line indicates the exploratory SUVmax threshold of 10.2; all cases at or above this threshold had Gleason score ≥7. Grey points denote Gleason <7 and red points denote Gleason ≥7.

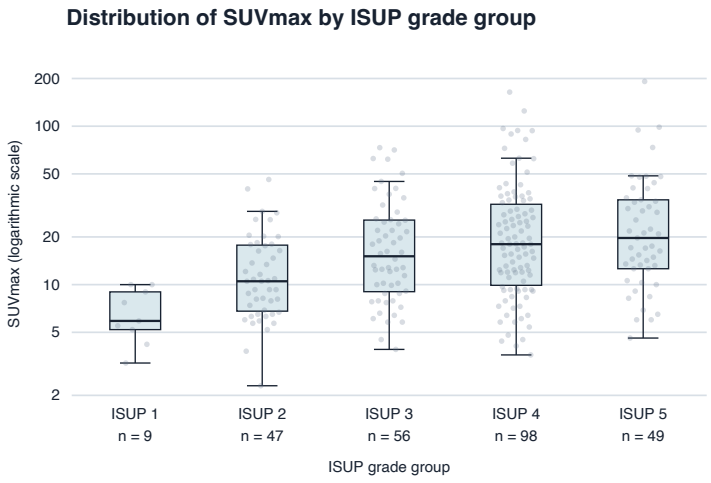



**Figure 3 -** Distribution of intraprostatic SUVmax by ISUP grade group. Boxplots show median and interquartile range; whiskers represent the most extreme values within 1.5 times the interquartile range. Fourteen cases not classifiable by ISUP grade group were excluded.

## 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 [$^{68}$Ga]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.

## Learning Points

- Among 273 patients with histologically confirmed prostate cancer, all 187 patients with intraprostatic SUVmax ≥10.2 had a Gleason score of at least 7.
- The exploratory threshold was selected and evaluated in the same cohort, which included only nine Gleason 6 cases. It needs external validation before it can inform biopsy decisions.


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## Ethical Disclosures

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## Contributorship Statement

SC: Contributed to data collection and wrote the initial draft.
DB, RC, DM, RM and WDB: Contributed to data collection and manuscript preparation and review
All authors contributed to this work, approved the final version of the manuscript for publication, and agree to be accountable for all aspects of the work, ensuring the accuracy and integrity of the data presented.

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