Research Square

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The Impact of the COVID-19 Pandemic on Adverse Pathological Outcomes After Radical Prostatectomy: Pre- and Post-Pandemic Comparison in a Brazilian Public Healthcare Setting

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Abstract

Background

The COVID-19 pandemic severely disrupted healthcare systems, delaying essential oncological treatments. We evaluated how pandemic-related surgical delays affected pathological outcomes—such as staging and grading—in patients undergoing radical prostatectomy (RP) for localized prostate cancer within a Brazilian public university hospital.

Methods

This retrospective, single-center study analyzed 382 patients undergoing RP between 2016 and 2025, divided into pre-pandemic (2016–2019; n = 155) and pandemic/post-pandemic (2020–2025; n = 227) cohorts. We compared clinicopathological variables, including pathological staging, ISUP grade groups, and biopsy-to-surgery intervals, using Mann-Whitney U, Student's t, and Chi-square tests.

Results

The median biopsy-to-surgery interval rose from 245 to 340 days (mean: 245 to 383 days; $p < 0.01$). While baseline PSA remained stable ($p = 0.7$), we observed significant migration toward locally advanced disease (pT2 decreased from 63.2% to 42.3%; pT3a/b increased from 36.8% to 57.7%; $p < 0.01$). ISUP grade 5 tumors nearly doubled (14.2% to 27.7%), and histological upgrading rose from 32.9% to 55.9% ($p < 0.01$). Limitations include the retrospective, single-center design, and lack of long-term biochemical recurrence or survival data.

Conclusions and Clinical Implications: Pandemic-related disruptions were associated with prolonged surgical delays and significantly worse pathological outcomes, strongly supporting the hypothesis of true tumor progression during the waiting period. These findings emphasize the critical need for robust contingency strategies to preserve timely cancer surgery and mitigate long-term oncological harm during future public health crises.

Introduction

The COVID-19 pandemic, caused by SARS-CoV-2, triggered an unprecedented global health crisis that profoundly disrupted healthcare systems worldwide. Brazil emerged as a major epicenter, reporting millions of cases and hundreds of thousands of deaths across successive waves that extended into 2024[1].The scale and rapid progression of the pandemic forced immediate resource reallocation, reorientation of health priorities, and widespread disruption across all facets of medical care, including oncology [2].

The implementation of pandemic-related restrictions, such as lockdowns, limited access to medical facilities, and patient fears of infection, resulted in delays in cancer diagnosis and treatment. Studies have shown that the number of screening and diagnostic tests decreased significantly in many countries

during the pandemic, potentially leading to later cancer detection and negatively affecting patient outcomes [3,4].

Global projections initially suggested a potential rise in cancer mortality in subsequent years, driven by the overwhelming demands on health services and the necessary but often detrimental re-prioritization of healthcare agendas. These disruptions manifested as reductions in diagnostic tests and newly diagnosed cases, interruptions of screening programs, and a significant decline in elective surgeries, consultations, and hospital admissions for cancer patients across multiple countries[5]. The COVID-19 pandemic led to significant delays in cancer diagnosis and treatment which has been confirmed in numerous studies[6,7].

Prostate cancer (PCa) stands as a major health concern among men, being the most common malignancy excluding non-melanoma skin cancer in Brazil[8]. Studies have explored whether treatment delays lead to adverse pathological outcomes, such as higher Gleason scores, positive surgical margins, or extracapsular extension [9]. Patients with ISUP grade group > 2 combined with pT3a, and particularly those with seminal vesicle invasion and/or positive surgical margins, are at high risk of progression, up to 50% at five years[10].

The Brazilian public healthcare system, which provides universal coverage, came under immense strain during the pandemic. Its inherent challenges were further aggravated by COVID-19, leading to the diversion of resources and hospital beds and to the suspension of screening campaigns and elective surgeries[11]. These vulnerabilities and shifts in prioritization disrupted cancer care, particularly in public tertiary hospitals, where patients often present with more advanced disease due to limited access to primary care and screening programs[12].

The impact of the COVID-19 pandemic on cancer-specific mortality remains incompletely understood. In prostate cancer, mortality is typically not an immediate outcome, given the generally indolent natural history of the disease; therefore, analyses with longer follow-up, which are not yet available, are required. As an intermediate approach to assessing potential deterioration in oncologic outcomes, evaluation of the final pathological findings in patients undergoing radical prostatectomy may provide clinically meaningful insight. Accordingly, this study aimed to evaluate the impact of the COVID-19 pandemic on the anatomopathological outcomes of patients undergoing radical prostatectomy, focusing on the five-year period following the pandemic at a public university hospital within the Brazilian Unified Health System (SUS).

Methods

The design, analysis, interpretation of data, drafting, and revisions followed the Helsinki Declaration. The study design was approved by the local independent Research Ethics Committee (approval code: CAAE 83454824.7.0000.5505). The requirement for informed consent was waived by the research ethics committee. All data were anonymized to ensure patient confidentiality and were handled in strict

accordance with ethical guidelines. Ethical approval for the study protocol, including the collection and analysis of retrospective patient data, was duly obtained from the institutional ethics committee of the participating university hospital. This ensured that the research adhered to all relevant regulatory and ethical standards for human subjects research.

This investigation was designed as a retrospective, single-center, observational study, conducted at a university hospital operating within the comprehensive framework of the Brazilian Unified Health System. This study included patients who underwent treatment for non-metastatic PCa with curative intent from January 2016 to January 2026.

Data for this study were extracted from the electronic medical records of all patients who underwent radical prostatectomy for prostate cancer (PCa). The period from January 2016 to December 2019 was defined as the pre-pandemic era, and data from this interval were considered baseline for comparative purposes. In contrast, the interval from January 2020 to January 2026 was designated as the pandemic and post-pandemic period, encompassing the timeframe in which the COVID-19-related public health crisis—and its downstream effects on healthcare access, diagnostic pathways, and surgical backlogs—could plausibly have contributed to shifts in the histopathological profile of patients undergoing radical prostatectomy.

A comprehensive set of variables was collected to provide a detailed pathological profile of the patients. These variables included age at surgery, baseline serum prostate-specific antigen (PSA) level, histological grade according to the International Society of Urological Pathology (ISUP) grading system, and tumor stage as classified by the TNM system.

Statistical Analysis

Statistical analyses compared clinicopathological variables between the pre-pandemic (2016–2019) and pandemic/post-pandemic (2020–2025) periods. Normality of continuous variables was assessed using the Shapiro-Wilk test; the Student's t-test was used for normally distributed data and the Mann-Whitney U test for non-normal data (e.g., PSA). Categorical variables (pT stage, ISUP grade) were analyzed with Pearson's chi-square test, or Fisher's exact test when expected cell frequencies were below five. All tests were two-tailed, with significance set at $p < 0.05$. Analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 382 radical prostatectomy procedures were performed during the study timeframe, with a documented increase in surgical volume from 155 cases in the pre-pandemic baseline (2016–2019) to 227 cases in the pandemic and post-pandemic period (2020–2025). Baseline demographic and clinical characteristics were comparable between the two cohorts, with no statistically significant differences (Table 1). Mean age at surgery was identical across periods (63.6 ± 4.7 vs. 63.6 ± 4.4 years; $p = 0.48$), with median ages of 63.8 years (range, 41–75) and 65.0 years (range, 40–75), respectively. Baseline PSA

levels were also similar between groups, with means of 11.4 ± 7.4 ng/mL and 11.1 ± 5.6 ng/mL, and medians of 7.2 ng/mL and 8.6 ng/mL in the pre-pandemic and pandemic/post-pandemic periods, respectively (p = 0.7).

Table 1
Comparative Analysis of Clinico-Pathological Characteristics. The data are presented as mean ± standard deviation (SD) for continuous variables (age and baseline PSA) and as absolute numbers (n) followed by percentages ($\%$) for categorical variables (pathological staging and ISUP histological grade).

Variable	Pre-pandemic Era (2016–2019)	Pandemic/Post-pandemic Period (2020–2025)	p-value
Total Procedures (n)	155	227	-
Age (years)	Mean: 63.6 (± 4.7) Median: 63.8 (41–75)	Mean: 63.6 (± 4.4) Median: 65.0 (40–75)	0.48
Baseline PSA ± SD (ng/mL)	Mean: 11.4 (± 7.4) Median: 7.2	Mean: 11.1 (± 5.6) Median: 8.6	0.7
Pathological Staging (T) (n, %)	pT2: 98 (63.2%) pT3a: 35 (22.6%) pT3b: 22 (14.2%)	pT2: 96 (42.3%) pT3a: 88 (38.8%) pT3b: 43 (18.9%)	< 0.01
Histological Grade (ISUP) (n, %)	ISUP 1: 9 (5.8%) ISUP 2: 89 (57.4%) ISUP 3: 31 (20.0%) ISUP 4: 4 (2.6%) ISUP 5: 22 (14.2%)	ISUP 1: 4 (1.8%) ISUP 2: 77 (33.9%) ISUP 3: 79 (34.8%) ISUP 4: 4 (1.8%) ISUP 5: 63 (27.7%)	< 0.01
Positive Surgical Margins (n, %)	82 (52.9%)	126 (55.5%)	0.44
Upgrading (n, %)	51 (32.9%)	127 (55.95%)	< 0.01
Time from biopsy to surgery, days	Mean ± SD: 245 ± 134.8 Median: 245 (11-1306)	Mean ± SD: 383.2 ± 172.4 Median: 340 (42-1905)	< 0.01

Regarding pathological staging, a significant stage migration toward more advanced disease was observed between the two periods (p < 0.01) (Fig. 1). The proportion of patients with organ-confined

disease (pT2) decreased from 63.2% (n = 98) in the pre-pandemic era to 42.3% (n = 96) in the pandemic/post-pandemic period, whereas locally advanced tumors became more prevalent, with pT3a increasing from 22.6% (n = 35) to 38.8% (n = 88) and pT3b rising from 14.2% (n = 22) to 18.9% (n = 43).

Histological evaluation using the ISUP grading system revealed a significant shift toward higher-grade disease between the two periods ($p < 0.01$) (Fig. 2). The proportion of ISUP grade 2 tumors, which constituted the majority in the pre-pandemic era, decreased from 57.4% (n = 89) to 33.9% (n = 77), whereas ISUP grade 3 tumors increased from 20.0% (n = 31) to 34.8% (n = 79). The prevalence of ISUP grade 5 tumors nearly doubled, rising from 14.2% (n = 22) to 27.7% (n = 63), while ISUP grades 1 and 4 remained uncommon and comparable between periods (5.8% vs. 1.8% and 2.6% vs. 1.8%, respectively).

Analysis of surgical outcomes revealed a persistently high rate of positive surgical margins in both periods, with no statistically significant difference between groups ($p = 0.44$). Positive surgical margins were observed in 82 cases (52.9%) in the pre-pandemic era and in 126 cases (55.5%) in the pandemic/post-pandemic period.

Regarding the concordance between biopsy and definitive pathological Gleason grading, a significant shift was observed between the two periods. In the pre-pandemic era (2016–2019), upgrading occurred in 51 of 155 patients (32.9%), while the grade remained stable in 73 patients (47.1%) and downgrading was observed in 31 patients (20.0%). In the pandemic/post-pandemic period (2020–2025), the upgrading rate increased markedly to 127 of 227 patients (55.9%), whereas the proportion of stable grades decreased to 78 patients (34.4%) and downgrading declined to 22 patients (9.7%). Overall, across the entire cohort of 382 patients, upgrading was documented in 178 cases (46.6%), stable grading in 151 cases (39.5%), and downgrading in 53 cases (13.9%).

The time interval from diagnostic biopsy to radical prostatectomy increased significantly between the two periods ($p < 0.01$). The mean interval rose from 245 ± 134.8 days in the pre-pandemic era to 383.2 ± 172.4 days in the pandemic/post-pandemic period, with the median increasing from 245 days (range, 11–1306) to 340 days (range, 42–1905), respectively.

Discussion

This study provides a comprehensive analysis of the impact of theCOVID-19 pandemic on the pathological outcomes of patients undergoing radical prostatectomy at a Brazilian public tertiary teaching hospital. Our findings reveal four major observations: a significant stage migration toward more advanced pathological stages (pT3) in the post-pandemic period; a substantial increase in histological aggressiveness, with ISUP grade 5 tumors more than doubling; a persistently high rate of positive surgical margins, exceeding those reported in the contemporary literature; and a significant prolongation of the interval between diagnosis and definitive local treatment with radical prostatectomy[10,13].

The marked increase in locally advanced disease(pT3a/pT3b) from 36.8% to 57.7% and the rise in ISUP grade 4 and 5 tumors from16.8% to 29.5% represent the most striking findings of this analysis. These

results align with a growing body of international evidence documenting the collateral oncological damage of the pandemic[12]. This finding is not merely descriptive, but also prognostically relevant, since pathological upstaging beyond organ-confined disease is consistently associated with more adverse oncological outcomes after radical prostatectomy [14,15]. In particular, extraprostatic extension (pT3a) and, even more importantly, seminal vesicle invasion (pT3b) have been linked to a higher risk of biochemical recurrence, a greater probability of requiring adjuvant or salvage treatment, and worse long-term cancer control [16,17]. Therefore, the marked increase in pT3 disease in our series suggests that the delays and barriers to timely diagnosis and treatment during the pandemic may have had a direct impact not only on pathological severity, but also on the subsequent prognosis of these patients. A population-based study in Northern Italy reported a significant increase in advanced prostate cancer diagnoses following pandemic-related disruptions in screening and diagnostic pathways[18]. Similarly, Gouveia et al. demonstrated a national reduction of approximately 29%in radical prostatectomy procedures in Brazil during the pandemic period, suggesting that thousands of patients did not receive timely curative treatment[5].

The stability of baseline PSA (mean 11.4 vs. 11.1 ng/mL; p = 0.7) despite significant increases in pathological stage and ISUP grade is a notable paradox, suggesting that surgical delay may have allowed progression of more aggressive clones that do not express PSA proportionally[19]. The median interval from biopsy to surgery rose from 245 to 340 days, and many patients lacked updated PSA before surgery, potentially underestimating disease burden.

The upgrading rate observed in our cohort demonstrated a substantial increase between the two study periods, rising from 32.9% in the pre-pandemic era to 55.9% in the pandemic/post-pandemic period. A comprehensive systematic review and meta-analysis by Wang et al. (2023), encompassing 26 studies and 18,745 patients, reported a pooled upgrading rate of 38.3% across contemporary radical prostatectomy series[20]. Our pre-pandemic rate of 32.9% was actually below this benchmark, suggesting that the diagnostic accuracy during that period was relatively satisfactory within the constraints of the public health system. However, the post-pandemic upgrading rate of 55.9% substantially exceeds both the meta-analysis average and the upper range of most reported cohorts. Several factors may explain this. First, pandemic-related diagnostic bottlenecks may have created selection bias, enriching the surgical cohort for patients with more clinically evident, inherently aggressive disease. Second, the prolonged interval between diagnosis and surgery may have allowed true histological progression, consistent with the parallel rise in pT3 staging. Third, the limited availability of mpMRI and fusion biopsy within the SUS likely contributed to underestimation of tumor grade at initial biopsy, as these technologies reduce upgrading rates were routinely employed[21]. The combination of pandemic-related delays and limited preoperative diagnostic accuracy likely acted synergistically to produce the exceptionally high upgrading rate in the post-pandemic cohort.

Positive surgical margins (PSMs) were high in both periods (52.9% vs. 55.5%) with no significant difference between groups. These rates exceed those commonly reported in contemporary series

(approximately 11%–38%), although higher rates may occur in locally advanced disease [22–24]. Therefore, the elevated frequency of PSMs in our cohort is unlikely to reflect the isolated effect of the pandemic alone, but rather the combined influence of a more complex oncological case mix, particularly the increased proportion of pT3 tumors in the post-pandemic period, together with the characteristics of a teaching institution, where procedures are performed with resident and fellow participation under supervision and surgical training is an integral component of clinical practice[22].

Another important aspect is the median interval from diagnostic biopsy to radical prostatectomy, which rose substantially from 245 days pre-pandemic to 383 days in the pandemic/post-pandemic period. This prolongation reflects a direct consequence of the pandemic, as the suspension of elective procedures and reallocation of hospital resources during successive waves postponed definitive surgical treatment. Nevertheless, the oncological consequences of surgical delay for localized prostate cancer remain debated [25,26]. In a cohort of 32,184 patients from the US National Cancer Database, Xia et al. found that delays of up to 180 days did not increase adverse pathological features or mortality in high-risk disease, concluding that surgery could be safely postponed for up to six months[27]. Similarly, van den Bergh et al. reported no harm from delays of several months in low-risk patients, though delays of 2.5–9 months may adversely affect non-low-risk disease[28]. Nguyen et al. likewise deemed delays of up to three months safe for all localized prostate cancer, with worse outcomes reported only beyond six to nine months[29]. Importantly, the mean waiting interval in our post-pandemic cohort (383 days, ~ 12.6 months) far exceeds these thresholds. This temporal association, coinciding with the shift toward non-organ-confined disease and higher ISUP grades, supports the hypothesis that pandemic-related delays permitted true tumor progression, although the retrospective design precludes definitive causal inference.

This study has limitations. Its retrospective, single-center design and modest sample size limit generalizability. Restricting analysis to patients who underwent surgery introduced selection bias, excluding those with the longest delays or progression. The observational design precludes causal inference, and unmeasured confounders (referral patterns, limited MRI/fusion biopsy availability, case-mix shifts) may explain the findings. Pathological outcomes served as surrogates, as follow-up was insufficient to assess biochemical recurrence, metastasis, or cancer-specific survival. Finally, the heterogeneous pandemic and recovery phases and unrecorded reasons for delay limit interpretation. Nonetheless, the marked deterioration in outcomes warrants attention and reinforces the need to preserve timely cancer care in future crises.

Conclusion

The COVID-19 pandemic profoundly disrupted prostate cancer care in the Brazilian public healthcare system, with consequences extending beyond the acute crisis. Our findings show a significant deterioration in pathological outcomes after radical prostatectomy, most likely driven by prolonged delays between diagnosis and surgery. These results underscore the vulnerability of oncological care

during health emergencies and the urgent need for contingency strategies to mitigate the long-term harm of treatment delays in future crises.

Declarations

Clinical trial number: not applicable.

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The authors have no conflict of interest to declare.

Human Ethics and Consent to Participate declarations: this study was approved by the Research Ethics Committee of the Federal University of São Paulo (Universidade Federal de São Paulo – UNIFESP), São Paulo, Brazil (**CAAE: 83454824.7.0000.5505**). The study was conducted in accordance with the Declaration of Helsinki. As this was a retrospective study using de-identified data obtained from medical records, the requirement for individual informed consent was waived by the Ethics Committee.

Consent to Publish declaration: not applicable

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Figures

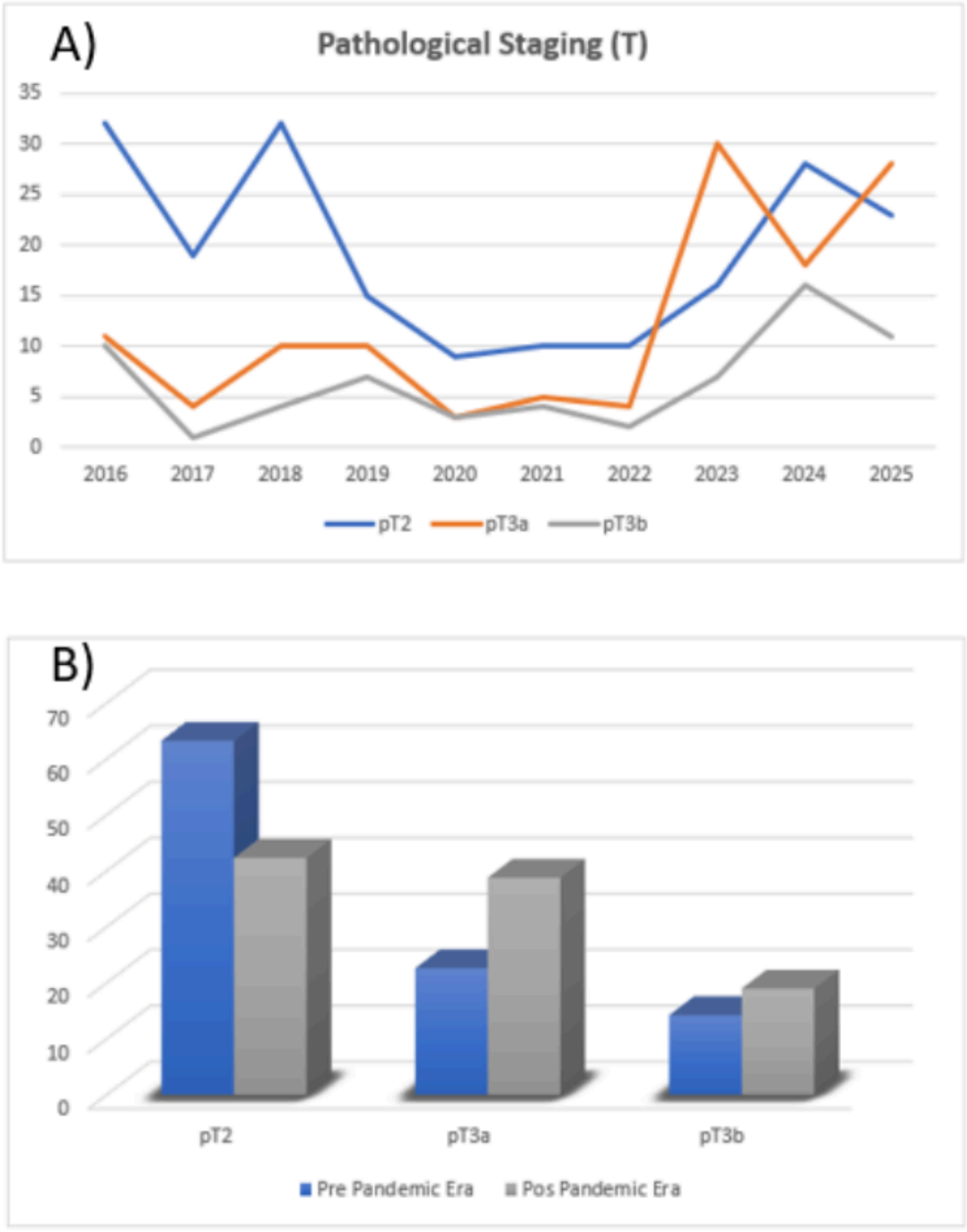


Figure 1

a) Distribution of Pathological Staging (pT) Between Study Periods. The chart illustrates the percentage distribution of pathological T staging for patients undergoing radical prostatectomy. A significant stage migration is observed, characterized by a reduction in organ-confined disease (pT2) and a concomitant

increase in locally advanced disease (pT3a and pT3b) when comparing the pre-pandemic baseline (2016–2019) to the pandemic/post-pandemic period (2020–2025). B) Distribution of pathological tumor stage (pT) among patients undergoing radical prostatectomy, comparing the pre-pandemic (2016–2019) and pandemic/post-pandemic (2020–2025) periods. A significant stage migration toward more advanced disease was observed in the pandemic/post-pandemic period, with a decrease in pT2 tumors and a corresponding increase in pT3a and pT3b tumors ($p < 0.01$).

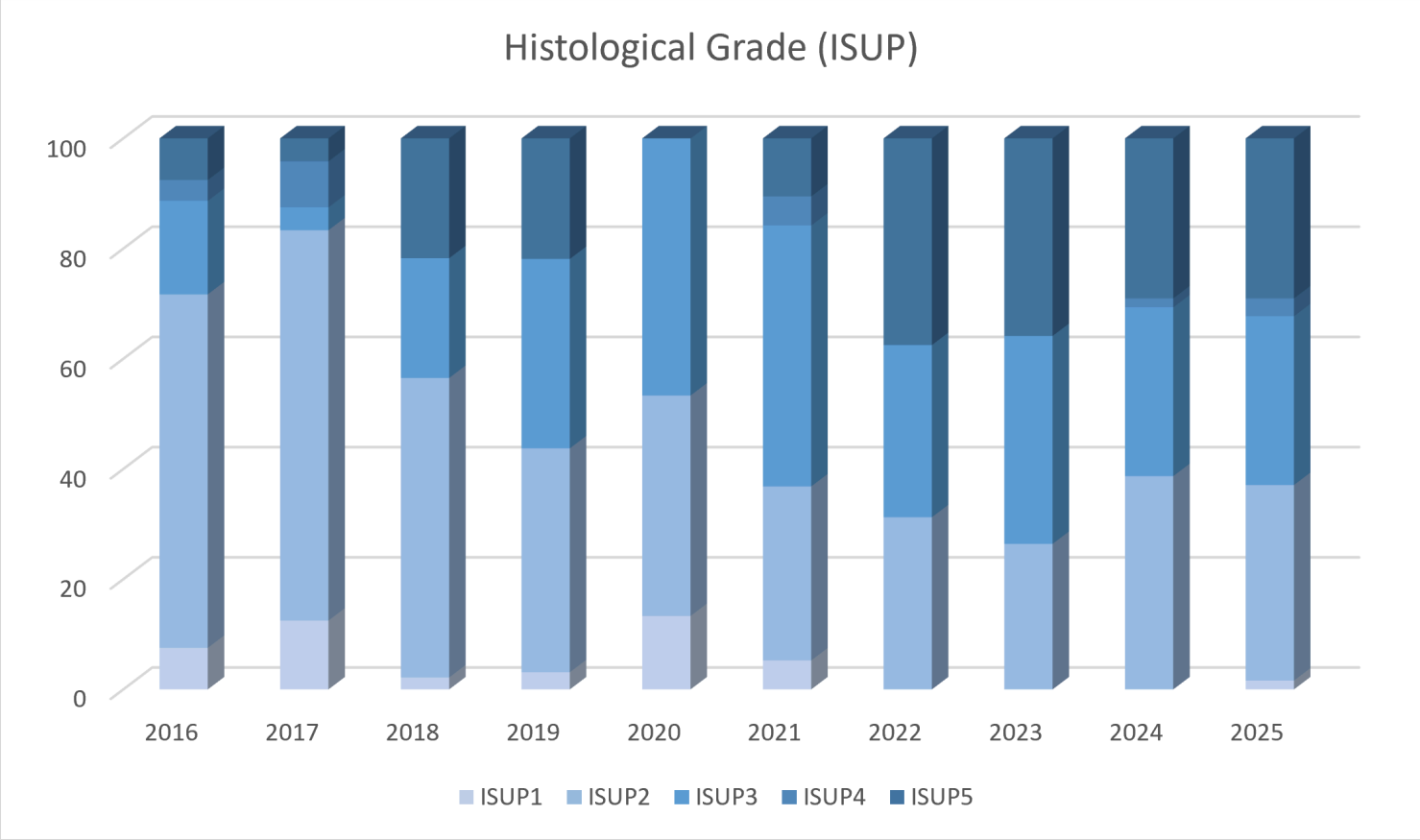


Figure 2

Comparison of Histological Grade Groups (ISUP). This figure demonstrates the shift in histological aggressiveness according to the ISUP grading system. Notable findings include a decrease in the prevalence of lower-grade tumors (ISUP 1–2) and a substantial rise in high-grade malignancies, particularly ISUP grade 5, indicating a trend toward more biologically aggressive disease in the post-pandemic era.

ISUP: International Society of Urological Pathology.

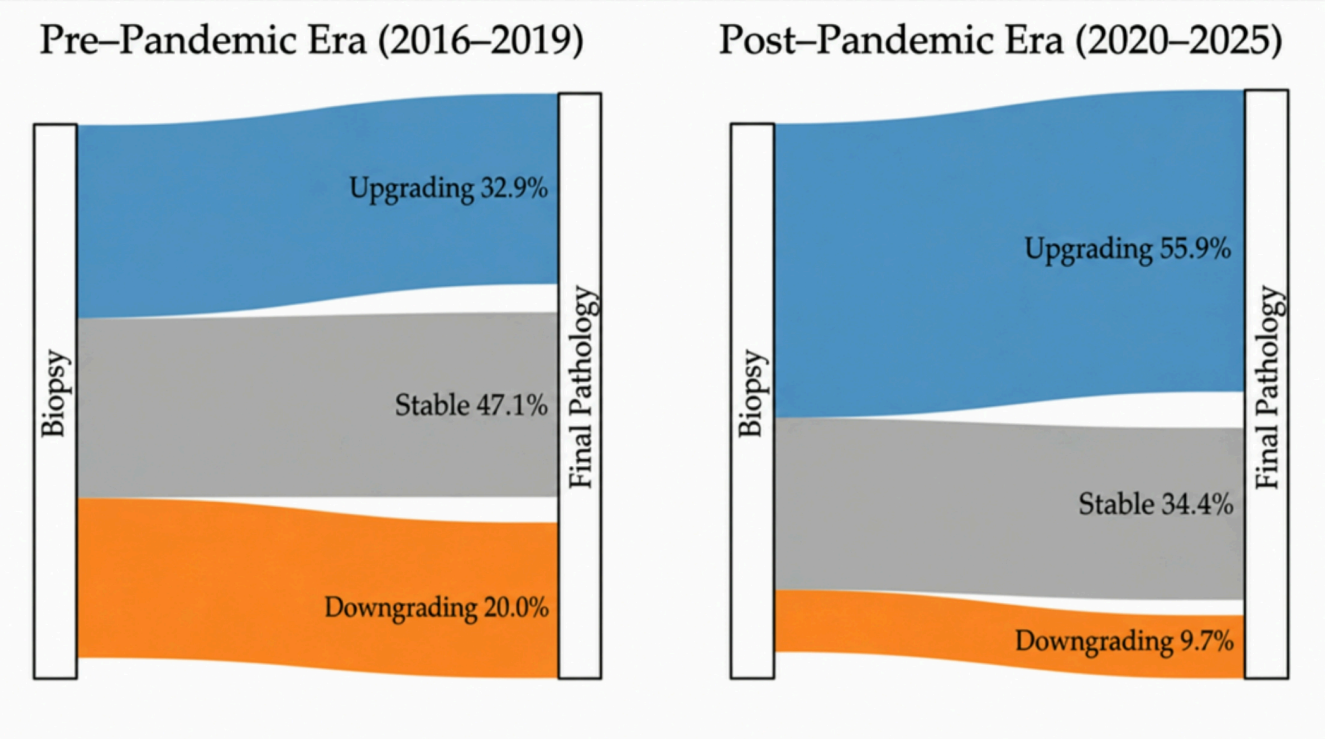


Figure 3

Concordance between biopsy and radical prostatectomy Gleason grading, categorized into 'Upgrading', 'Stable', and 'Downgrading' groups. Pre-Pandemic Era (2016–2019): Characterized by a predominant stability (47.1%), with a secondary emphasis on upgrading (32.9%) and a marginal downgrade rate (20.0%). Post-Pandemic Era (2020–2025): Demonstrates a robust expansion in the 'Upgrading' sector (reaching 55.9%), correlating with a marked reduction in both 'Stable' (34.4%) and 'Downgrading' (9.7%) metrics.