

Association Between Comorbidity Burden and Tissue-Adjusted Enucleation Time During HoLEP: A Retrospective Cohort Study

HoLEP Sırasında Komorbidite Yüğü ile Doku Yüğüne Göre Düzeltilmiş Enükleasyon Süresi Arasındaki İlişki: Retrospektif Kohort Çalışması

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ABSTRACT

Objective: To quantify phase-specific operative performance during holmium laser enucleation of the prostate (HoLEP) and evaluate the association between comorbidity burden and tissue-adjusted enucleation performance.

Materials and Methods: This single-center retrospective cohort screened 574 HoLEP procedures performed between January 2023 and June 2025 and included 349 patients. Enucleation efficiency (g/min), morcellation efficiency, and overall extraction efficiency were calculated descriptively. To avoid mathematical coupling, the primary inferential analysis modeled natural log-transformed enucleation time and adjusted for age, log-transformed enucleated tissue weight, prostate-volume stratum, and antithrombotic use. Heteroscedasticity-consistent HC3 standard errors were used.

Results: Median age was 67 years, and 67.9% had at least one comorbidity. Unadjusted enucleation time was similar in patients without and with comorbidity (41.5 vs 42.0 min; $p = 0.337$), whereas enucleation efficiency was lower in those with comorbidity (0.93 vs 1.75 g/min; $p < 0.001$). In the adjusted model, each additional comorbidity was associated with a 9.9% longer enucleation time for a given tissue burden (95% CI: 4.8%-15.2%; $p < 0.001$; adjusted $R^2=0.167$). The association persisted after additional adjustment for operative technique category (8.0%; 95% CI: 4.5%-11.6%; $p < 0.001$). Antithrombotic use was not independently associated with enucleation time.

Conclusion: Comorbidity burden was associated with slower tissue-adjusted enucleation performance despite similar unadjusted enucleation times. Total operating-room occupancy was not assessed. These hypothesis-generating findings require multicenter validation with operator-level, anesthetic, and intraoperative bleeding data before use in scheduling or benchmarking.

Keywords: comorbidity, enucleation, holmium laser enucleation of the prostate, operative time, prostatic hyperplasia

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ÖZET

Amaç: Holmium lazer prostat enükleasyonunda (HoLEP) faza özgü cerrahi verimliliği tanımlamak ve komorbidite yükünün dokuya göre düzeltilmiş enükleasyon performansı ile ilişkisini değerlendirmek.

Gereç ve Yöntemler: Bu tek merkezli retrospektif kohortta Ocak 2023-Haziran 2025 arasında uygulanan 574 HoLEP olgusu tarandı ve 349 hasta analize alındı. Enükleasyon verimliliği (g/dk), morselasyon verimliliği ve toplam ekstraksiyon verimliliği tanımlayıcı olarak hesaplandı. Matematiksel eşleşmeyi önlemek amacıyla birincil çıkarımsal analizde doğal logaritması alınmış enükleasyon süresi sonuç değişkeni olarak modellendi; analiz yaş, logaritmik enükle edilen doku ağırlığı, prostat hacmi kategorisi ve antitrombotik kullanımına göre düzeltildi. Heteroskedastisiteye dayanıklı HC3 standart hataları kullanıldı.

Bulgular: Medyan yaş 67 yıl olup hastaların %67.9'unda en az bir komorbidite vardı. Ham enükleasyon süresi komorbiditesi olmayan ve olan hastalarda benzerdi (41.5 ve 42.0 dk; $p = 0.337$), ancak enükleasyon verimliliği komorbiditesi olanlarda daha düşüktü (0.93 ve 1.75 g/dk; $p < 0.001$). Düzeltilmiş modelde her ek komorbidite, aynı doku yükü için enükleasyon süresinde %9.9 artışla ilişkiliydi (%95 GA: %4.8-%15.2; $p < 0.001$; düzeltilmiş $R^2=0.167$). Cerrahi teknik kategorisini de içeren duyarlılık analizinde ilişki devam etti (%8.0; %95 GA: %4.5-%11.6; $p < 0.001$). Antitrombotik kullanım bağımsız olarak enükleasyon süresiyle ilişkili değildi.

Sonuçlar: Komorbidite yükü, benzer ham enükleasyon sürelerine karşın, doku yüküne göre düzeltilmiş daha yavaş enükleasyon performansı ile ilişkiliydi. Toplam ameliyathane kullanım süresi değerlendirilmedi. Bulguların planlama veya karşılaştırma amacıyla kullanılmasından önce operatör, anestezi ve intraoperatif kanama değişkenlerini içeren çok merkezli çalışmalarla doğrulanması gerekir.

Anahtar Kelimeler: benign prostat hiperplazisi, cerrahi süre, enükleasyon, holmium lazer prostat enükleasyonu, komorbidite

INTRODUCTION

Benign prostatic hyperplasia (BPH) is highly prevalent among aging men and remains a major cause of lower urinary tract symptoms (LUTS) and bladder outlet obstruction. As a guideline-endorsed intervention, endoscopic enucleation offers durable outcomes across a broad spectrum of prostate volumes, with holmium laser enucleation of the prostate (HoLEP) serving as a widely adopted reference technique (1).

Operative efficiency is commonly expressed as tissue removed per unit time during enucleation or morcellation. These metrics are useful for describing technical performance, learning-curve progression, and phase-specific procedural bottlenecks; however, they are also influenced by gland size, tissue characteristics, operative technique, surgeon experience, laser platform and power settings, and morcellator design (2,3).

Although HoLEP is safe and effective in patients with substantial medical comorbidity (4), the contribution of patient-level comorbidity to phase-specific operative performance is less well characterized than anatomical and technical determinants. Medical complexity may coexist with factors that alter operative flow, but observational associations cannot establish mechanisms such as bleeding, impaired visibility, tissue fibrosis, or anesthetic instability unless those variables are directly measured.

We therefore evaluated consecutive HoLEP procedures to quantify phase-specific efficiency metrics and to examine whether cumulative comorbidity burden was associated with tissue-adjusted enucleation performance. The study was designed as a hypothesis-generating analysis rather than a direct test of operating-room resource utilization.

MATERIALS AND METHODS

Study Design and Participants

All patients who underwent HoLEP at a tertiary referral center between January 2023 and June 2025 were screened for eligibility for this single-center retrospective cohort study (n = 574). Eligibility required reliable perioperative data for enucleated tissue weight and phase-specific time stamps. Exclusions were concomitant or staged procedures during the same anesthetic session (n = 97), prior prostate surgery that could alter dissection planes (n = 64), reoperation or salvage HoLEP (n = 11), and incomplete or unreliable perioperative documentation (n = 53). The final analytic cohort comprised 349 unique patients (Figure 1).

Surgical Team, Technique, and Equipment

Procedures were performed by one of four endourologists. Before the study period, each surgeon had completed at least 50 HoLEP procedures and was considered to have passed the initial learning-curve phase. Operator identity and a reliable chronological case sequence were not retained in the de-identified analytic dataset; therefore, surgeon-level adjustment and formal learning-curve analyses were not possible. Three operative technique categories were documented, but technique selection was not protocolized and depended on prostate morphology and surgeon preference; technique category was therefore evaluated only in sensitivity analysis.

All procedures used a 28-Fr continuous-flow endoscopic resectoscope with isotonic saline irrigation. Enucleation and morcellation were performed using a single integrated holmium:yttrium aluminum garnet (Ho:YAG) platform (MultiPulse HoPLUS 150; Jena Surgical, Jena, Germany) with a built-in morcellation module; no standalone morcellator was used. A 550- μ m laser fiber was used in all cases. Laser settings were standardized at 2.0 J and 40 Hz (80 W) in short-pulse mode for enucleation and 2.0 J and 35 Hz (70 W) in long-pulse mode for coagulation. Morcellation was performed at high aspiration, 2,000 rpm rotation speed, and 3.0 Hz oscillation frequency.

Perioperative Antithrombotic Management

In the analytic cohort, antiplatelet and anticoagulant medications were discontinued five days before surgery following preoperative consultation with the relevant specialty. When bridging was considered clinically necessary, enoxaparin was administered at the dose recommended by the consulting physician.

Data Collection and Definitions

Clinical variables were retrieved from electronic medical records and operative reports and included age, prostate-specific antigen (PSA), estimated prostate volume (PV), antiplatelet use, anticoagulant use, transrectal ultrasound-guided biopsy history, preoperative urethral catheterization, and medical therapy for BPH. PSA density was calculated as PSA divided by PV. Prostate volume was categorized a priori as <80 g, 80–120 g, or >120 g.

Comorbidity burden was defined as the unweighted count of eight prespecified conditions: hypertension, diabetes mellitus, coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease (COPD) or asthma, prior prostate cancer, non-urollogic malignancy, and neurovascular or neurodegenerative disease. Rather than utilizing a validated anesthetic risk score, a simple comorbidity count was employed as an intuitive metric to reflect cumulative documented disease burden. Notably, established risk stratifiers and operative parameters—such as the American Society of Anesthesiologists (ASA) physical status classification, Charlson Comorbidity Index, intraoperative blood pressure, irrigation pressure, and tissue consistency—could not be evaluated due to their absence in the analytic dataset.

Operative Outcomes

Enucleation time was defined as the interval from initiation of laser enucleation to completion of adenoma enucleation. Morcellation time was defined as the interval from morcellator activation to completion of tissue retrieval. Total

extraction time was the sum of enucleation and morcellation times and should not be interpreted as anesthesia time or total operating-room occupancy. Enucleated tissue weight was obtained from the specimen weight documented for histopathology. Descriptive efficiency metrics were calculated as enucleated tissue weight divided by enucleation time, morcellation time, or total extraction time.

The descriptive primary performance metric was enucleation efficiency. Because including tissue weight as both a component of an efficiency ratio and a regression predictor creates mathematical coupling, the primary inferential outcome was natural log-transformed enucleation time modeled conditional on tissue burden. Morcellation time and total extraction time were secondary inferential outcomes.

Statistical Analysis

Continuous variables are presented as median and interquartile range (IQR), and categorical variables as number and percentage. Comparisons between two groups used the Mann-Whitney *U* test, with rank-biserial correlation reported as an effect-size measure. Comparisons across PV strata used the Kruskal-Wallis test followed, when significant, by Dunn tests with Bonferroni adjustment. No clinically meaningful threshold for phase time or efficiency was prespecified; therefore, absolute median differences and effect sizes were interpreted alongside *p* values.

Multivariable ordinary least-squares models used natural log-transformed phase times. The primary model included cumulative comorbidity count, age, log-transformed enucleated tissue weight, PV stratum, and any preoperative antithrombotic use. Heteroscedasticity-consistent HC3 standard errors were used. Coefficients were converted to percentage change as $(e^{\beta}-1) \times 100$ and are reported with 95% confidence intervals. Model R^2 and adjusted R^2 are provided. Sensitivity analyses replaced any antithrombotic use with separate antiplatelet and anticoagulant indicators and additionally adjusted for operative technique category.

Individual comorbidities were evaluated in separate exploratory models that also included the number of other comorbidities. Benjamini-Hochberg false-discovery-rate adjustment was applied across the eight condition-specific tests for each outcome. For subgroups with fewer than 10 patients, 5,000 nonparametric bootstrap resamples were used as a sparse-data sensitivity analysis. Condition-specific morcellation findings were treated as exploratory regardless of nominal significance.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA), with additional syntax-based procedures used for heteroscedasticity-consistent standard errors, false-discovery-rate adjustment, and bootstrap analyses.

Ethics Approval

The study protocol was approved by the Local Ethics Committee of Dr. Lütfi Kırdar Kartal City Hospital (Decision No. 2025/010.99/23/21; December 30, 2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. Since the study was retrospective and based on anonymized data, the requirement for informed consent was waived.

RESULTS

Cohort Characteristics

Of 574 screened procedures, 349 unique patients were included (Figure 1). The median age was 67 years (IQR: 62–73), and median preoperative PV was 84 g (IQR: 60–127). Any antithrombotic medication was recorded in 104 patients (29.8%): 66 received antiplatelet therapy, 42 received anticoagulant therapy, and 4 received both. Detailed baseline characteristics are shown in Table 1.

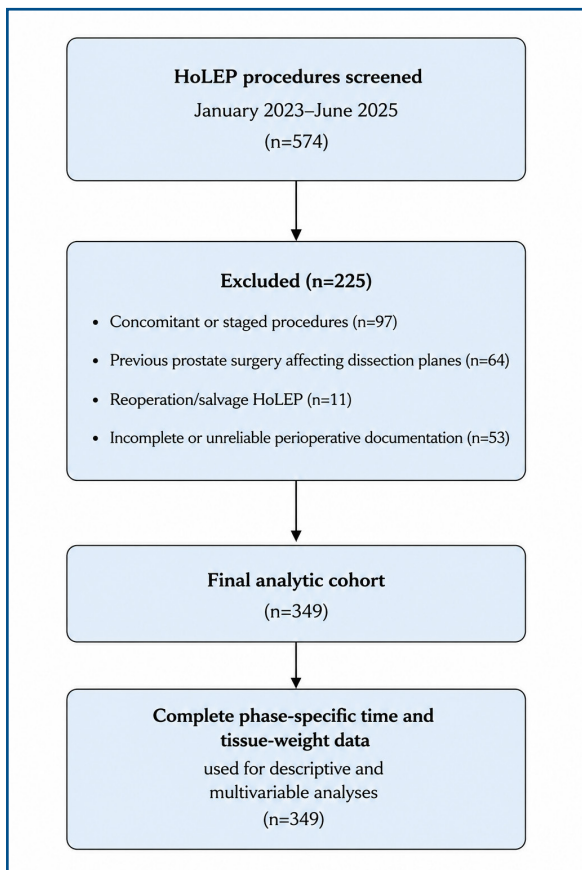


Figure 1. Patient flow through screening, exclusion, and final analysis.

Flow diagram showing 574 screened HoLEP procedures, the four recorded exclusion categories totaling 225 procedures, and the final analytic cohort of 349 unique patients.

At least one comorbidity was documented in 237 patients (67.9%). Comorbidity counts were 0 in 112 patients (32.1%), 1 in 117 (33.5%), 2 in 100 (28.7%), 3 in 16 (4.6%), and 4 in 4 (1.1%). Hypertension was the most common condition (47.6%), followed by coronary artery disease (22.6%) and diabetes mellitus (15.5%).

Operative and Efficiency Outcomes

Median enucleated tissue weight was 53.0 g (IQR: 32.0–70.0). Median enucleation, morcellation, and total extraction times were 42.0, 9.0, and 51.0 minutes, respectively. Median enucleation efficiency was 1.12 g/min, morcellation efficiency was 7.00 g/min, and overall extraction efficiency was 0.96 g/min (Table 2).

Effect of Prostate Volume

Enucleation time did not differ across PV strata ($p = 0.386$), whereas enucleation efficiency increased from 0.86 g/min in prostates <80 g to 1.75 g/min in prostates >120 g ($p < 0.001$). Morcellation time differed statistically across strata (9, 7, and 9 min; $p = 0.001$), but the pattern was non-linear and the absolute median differences were small. Detailed post hoc comparisons are presented in Table 3.

Unadjusted Comparisons by Comorbidity Status

Unadjusted enucleation time was similar in patients without and with at least one comorbidity (41.5 vs 42.0 min; absolute median difference, 0.5 min; $p = 0.337$; rank-biserial correlation=0.064). Morcellation time was 9.0 vs 8.0 minutes (absolute difference, –1.0 min; $p = 0.013$; rank-biserial correlation=–0.164), a statistically significant but small difference. Total extraction time did not differ (51.5 vs 49.0 min; $p = 0.480$). In contrast, enucleation efficiency was lower among patients with comorbidity (0.93 vs 1.75 g/min; $p < 0.001$; rank-biserial correlation=–0.498) (Table 4).

Table 1. Baseline demographic and clinical characteristics and comorbidity profile (n=349).

Variable	Category	Value
Age, years		67 (62-73)
Preoperative PSA, ng/mL		3.26 (2.00-4.90)
Preoperative prostate volume, g		84 (60-127)
PSA density, ng/mL/g		0.037 (0.023-0.072)
TRUS-guided biopsy history		144 (41.3)
Preoperative urethral catheter		88 (25.2)
Antithrombotic therapy	Any antithrombotic	104 (29.8)
	Antiplatelet	66 (18.9)
	Anticoagulant	42 (12.0)
	Both	4 (1.1)
Preoperative medical therapy	None	20 (5.7)
	Alpha-blocker	138 (39.5)
	Combination (alpha-blocker + 5-ARI)	191 (54.7)
Prostate-volume stratum	<80 g	157 (45.0)
	80-120 g	98 (28.1)
	>120 g	94 (26.9)
Comorbidity count	0	112 (32.1)
	1	117 (33.5)
	2	100 (28.7)
	3	16 (4.6)
	4	4 (1.1)
Comorbidity	Any comorbidity	237 (67.9)
	Hypertension	166 (47.6)
	Diabetes mellitus	54 (15.5)
	Coronary artery disease	79 (22.6)
	Chronic kidney disease	26 (7.4)
	COPD or asthma	32 (9.2)
	Prior prostate cancer	8 (2.3)
	Non-urollogic malignancy	8 (2.3)
	Neurovascular or neurodegenerative disease*	8 (2.3)

Data are median (IQR) or n (%). *Includes cerebrovascular disease, Alzheimer disease, and other dementias.

IQR: interquartile range; COPD: chronic obstructive pulmonary disease; TRUS: transrectal ultrasound; 5-ARI: 5-alpha-reductase inhibitor.

Adjusted Association Between Cumulative Comorbidity Burden and Phase Time

In the primary log-time model, each additional comorbidity was associated with a 9.9% longer enucleation time conditional on tissue weight, age, PV stratum, and antithrombotic use (95% CI: 4.8%-15.2%; $p < 0.001$; $R^2=0.181$; adjusted $R^2=0.167$) (Table 5). Any antithrombotic use was not independently associated with enucleation time (−6.1%; 95% CI: −15.2% to 4.1%; $p = 0.232$).

Table 2. Operative time components and efficiency outcomes (n=349).

Operative metric	Median (IQR)
Enucleated tissue weight, g	53.0 (32.0-70.0)
Enucleation time, min	42.0 (32.0-63.0)
Morcellation time, min	9.0 (5.0-10.0)
Total extraction time, min	51.0 (41.0-76.0)
Enucleation efficiency, g/min	1.12 (0.68-1.81)
Morcellation efficiency, g/min	7.00 (4.00-9.57)
Overall extraction efficiency, g/min	0.96 (0.57-1.43)

Data are presented as median (interquartile range, IQR).

Table 3. Operative outcomes stratified by prostate volume (n=349).

Outcome	PV <80 g (n=157)	PV 80-120 g (n=98)	PV >120 g (n=94)	p
Enucleation time, min	40.0 (35.0-55.0)	44.0 (25.0-57.0)	45.0 (35.0-65.0)	0.386
Enucleation efficiency, g/min	0.86 ^a (0.50-1.22)	1.03 ^b (0.80-1.84)	1.75 ^c (1.25-2.30)	<0.001
Morcellation time, min	9.0 ^{ab} (5.0-10.0)	7.0 ^a (5.0-10.0)	9.0 ^b (6.5-10.8)	0.001
Morcellation efficiency, g/min	5.91 ^a (3.00-8.12)	7.14 ^b (4.56-9.57)	7.60 ^b (5.62-11.67)	<0.001
Overall extraction efficiency, g/min	0.75 ^a (0.43-1.14)	0.93 ^b (0.71-1.36)	1.40 ^c (1.07-1.75)	<0.001

Data are median (IQR). Overall comparisons used the Kruskal-Wallis test; significant tests were followed by Dunn-Bonferroni pairwise comparisons. Values sharing a superscript letter are not significantly different.

PV: prostate volume.

Table 4. Unadjusted operative outcomes by comorbidity status (n=349).

Outcome	No comorbidity (n=112)	Any comorbidity (n=237)	Absolute median difference	p	Rank-biserial correlation
Enucleation time, min	41.5 (30.0-56.0)	42.0 (33.0-66.0)	0.5	0.337	0.064
Morcellation time, min	9.0 (5.0-12.0)	8.0 (5.0-10.0)	-1.0	0.013	-0.164
Total extraction time, min	51.5 (39.0-68.5)	49.0 (42.0-80.0)	-2.5	0.480	0.047
Enucleation efficiency, g/min	1.75 (1.19-2.18)	0.93 (0.60-1.37)	-0.82	<0.001	-0.498
Morcellation efficiency, g/min	8.00 (5.20-11.67)	6.00 (3.33-8.83)	-2.00	<0.001	-0.247
Overall extraction efficiency, g/min	1.38 (0.95-1.73)	0.79 (0.50-1.17)	-0.59	<0.001	-0.491

Data are median (IQR). The absolute median difference is any comorbidity minus no comorbidity. Rank-biserial correlation values farther from zero indicate larger distributional separation.

Table 5. Primary multivariable associations between cumulative comorbidity burden and phase-specific time outcomes.

Outcome	Adjusted % change per additional comorbidity	95% CI	p	R ²	Adjusted R ²
Enucleation time	9.9	4.8 to 15.2	<0.001	0.181	0.167
Morcellation time	-8.3	-15.2 to -0.8	0.031	0.197	0.183
Total extraction time	7.2	2.6 to 12.1	0.002	0.232	0.219

Outcomes were natural log-transformed. Models were adjusted for age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use and used HC3 robust standard errors. Positive values indicate longer phase time; negative values indicate shorter phase time. Total extraction time is enucleation plus morcellation time and is not total operating-room occupancy.

Each additional comorbidity was associated with an 8.3% shorter morcellation time (95% CI: –15.2% to –0.8%; $p = 0.031$) and a 7.2% longer total extraction time (95% CI: 2.6%-12.1%; $p = 0.002$). The morcellation association was considered exploratory and should not be interpreted as a beneficial biological effect. Total extraction time represents only enucleation plus morcellation and not total operating-room occupancy.

The association with enucleation time was materially unchanged when antiplatelet and anticoagulant use were entered separately (9.7%; 95% CI: 4.6%-15.1%; $p < 0.001$) and when operative technique category was additionally included (8.0%; 95% CI: 4.5%-11.6%; $p < 0.001$; adjusted $R^2 = 0.523$) (Supplementary Table S1). Standardized predictions increased from 43.0 minutes at zero comorbidities to 62.7 minutes at four comorbidities, with wider uncertainty in the highest-burden category because only four patients had four conditions (Figure 2).

Table 6. Exploratory condition-specific associations with enucleation time.

Condition	n	Adjusted % change	95% CI	p	FDR-adjusted q value
Hypertension	166	28.1	18.0 to 39.0	<0.001	<0.001
Diabetes mellitus	54	-6.4	-16.3 to 4.6	0.244	0.390
Coronary artery disease	79	1.7	-8.3 to 12.9	0.743	0.743
Chronic kidney disease	26	2.9	-12.7 to 21.4	0.731	0.743
COPD or asthma	32	-2.6	-14.4 to 10.9	0.695	0.743
Prior prostate cancer*	8	84.1	64.3 to 106.3	<0.001	<0.001
Non-urolologic malignancy*	8	32.0	11.6 to 56.2	0.001	0.003
Neurovascular/ neurodegenerative disease*	8	42.6	0.3 to 102.9	0.048	0.096

Each model included the condition of interest, number of other comorbidities, age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use, with HC3 robust standard errors.

*Sparse subgroups; 5,000-resample bootstrap 95% CIs were 64.3%-105.9%, 13.4%-57.8%, and 2.2%-105.6%, respectively. These estimates are exploratory.

FDR: false discovery rate.

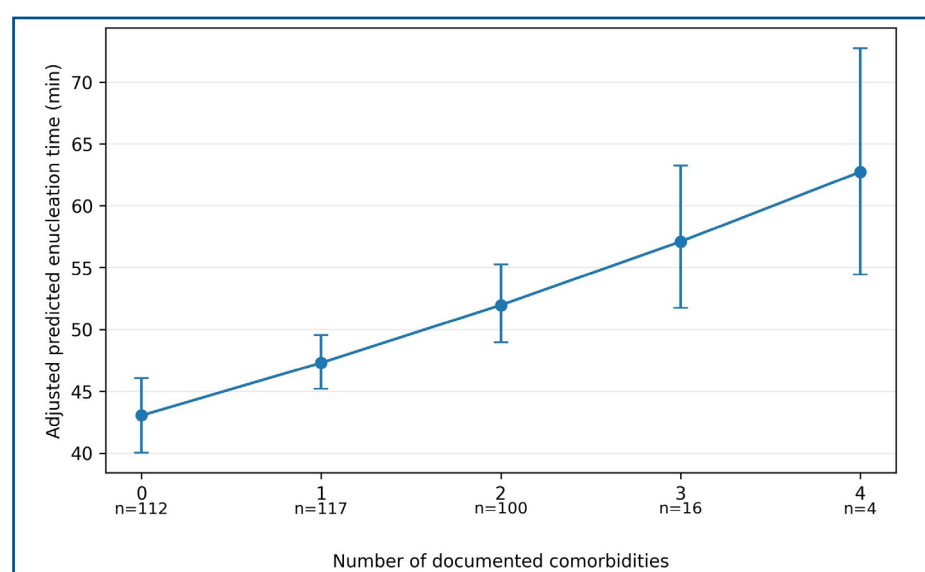


Figure 2. Adjusted predicted enucleation time according to cumulative comorbidity burden.

Average marginal predictions were derived from the primary log-time model and standardized over the observed covariate distribution. Error bars represent 5,000-resample bootstrap 95% confidence intervals. The number of patients with 0, 1, 2, 3, and 4 comorbidities was 112, 117, 100, 16, and 4, respectively.

Exploratory Condition-Specific Analyses

After adjustment for the number of other comorbidities and false-discovery-rate correction, hypertension was associated with 28.1% longer enucleation time (95% CI: 18.0%-39.0%; $q < 0.001$), whereas coronary artery disease was not associated with enucleation time (1.7%; 95% CI: -8.3% to 12.9%; $q = 0.743$). Condition-specific estimates are summarized in Table 6 and visualized in Supplementary Figure S1. Prior prostate cancer and non-urologic malignancy were associated with longer enucleation time, but each subgroup included only eight patients; these estimates remained similar in 5,000-resample bootstrap analyses and are considered exploratory because of sparse data (Supplementary Table S2). Condition-specific morcellation results were inconsistent in direction and are reported only in Supplementary Table S3.

DISCUSSION

In this contemporary single-center HoLEP cohort of 349 patients, phase-specific operative performance was evaluated using both conventional efficiency metrics and tissue-adjusted time models. Three principal findings emerged. First, median enucleation and morcellation efficiencies were 1.12 g/min and 7.00 g/min, respectively, with substantial interpatient variability despite the use of a standardized laser platform and institutional workflow (Table 2). Second, enucleation efficiency increased across prostate-volume strata, whereas the relationship between prostate volume and morcellation time was non-linear and characterized by relatively small absolute differences (Table 3). Third, and most importantly, the presence of comorbidity was associated with a lower unadjusted tissue-removal rate, although raw enucleation time was nearly identical in patients without and with comorbidity. After accounting for tissue burden and relevant covariates, each additional comorbidity was associated with a 9.9% longer enucleation time for a given amount of enucleated tissue (Table 5). Accordingly, the principal finding should be interpreted as an association between comorbidity burden and slower tissue-adjusted enucleation performance, rather than evidence that patients with comorbidity necessarily require longer unadjusted enucleation or total operative time.

Operative efficiency in HoLEP has increasingly been used as a pragmatic descriptor of technical performance, learning-curve progression, and phase-specific procedural throughput. Early comparative work reported enucleation efficiencies of approximately 0.6–0.7 g/min and morcellation efficiencies of approximately 3–4 g/min, while also demonstrating considerable variation between institutions and across prostate sizes (5). Subsequent high-volume experience showed that cumulative case exposure and refinement of operative technique can produce substantial gains in enucleation efficiency, particularly in larger glands (6). Randomized comparisons with transurethral resection of the prostate (TURP) in patients with large prostates further demonstrated that operative duration alone may not adequately represent procedural performance, because HoLEP can remove a greater tissue volume while providing durable functional outcomes and shorter catheterization and hospitalization (7). Previous studies in medically complex populations have focused predominantly on perioperative safety, anesthetic risk, antithrombotic exposure, and conventional postoperative outcomes (8–11), whereas large contemporary series have supported the reproducibility and size-independent applicability of HoLEP across broad clinical case mixes (12–14). In the present cohort, procedures were performed by four endourologists, each of whom had completed at least 50 HoLEP cases before the study period and was considered to have passed the initial learning-curve phase. This reduces the likelihood that the findings were driven solely by novice performance; nevertheless, operator identity and chronological case sequence were unavailable for model-level adjustment, and residual variation related to individual technique, case selection, or continued refinement cannot be excluded.

Comorbidity was common in the present cohort, with 67.9% of patients having at least one documented condition and hypertension being the most prevalent diagnosis. In the unadjusted comparison, median enucleation time differed by only 0.5 minutes between patients without and with comorbidity—41.5 and 42.0 minutes, respectively—and this difference was not statistically significant ($p = 0.337$) (Table 4). By contrast, median enucleation efficiency was substantially lower in patients with comorbidity, at 0.93 versus 1.75 g/min. These apparently divergent findings

reflect the influence of tissue burden on ratio-based efficiency measures and underline the need to distinguish raw procedural time from tissue-adjusted performance. In the primary inferential model, each additional comorbidity was associated with a 9.9% longer enucleation time conditional on enucleated tissue weight, age, prostate-volume stratum, and antithrombotic use. The association remained present after additional adjustment for operative technique category, with an estimated 8.0% increase per additional comorbidity. Standardized model predictions increased from approximately 43.0 minutes in patients with no comorbidity to 62.7 minutes in those with four conditions; however, this upper estimate was based on only four patients and had correspondingly greater uncertainty (Figure 2). These findings demonstrate a graded statistical association, but they do not establish a causal effect of comorbidity or define a clinically validated threshold for scheduling or performance benchmarking.

Condition-specific analyses also require cautious interpretation. Hypertension was associated with a 28.1% longer tissue-adjusted enucleation time, whereas coronary artery disease was not independently associated with the outcome (Table 6). This discordance argues against interpreting the findings as a simple consequence of generalized “poor vascular health.” Hypertension should not be considered a direct surrogate for intraoperative bleeding, impaired visibility, or increased hemostatic requirements because treated hypertensive patients may be normotensive during surgery, and intraoperative blood pressure is actively managed by the anesthesia team. In addition, anesthetic technique, hypertensive or hypotensive episodes, irrigation pressure, hemostasis time, and the frequency of coagulation maneuvers were not recorded. Coronary artery disease was also captured as a heterogeneous binary diagnosis without distinction among stable coronary disease, previous myocardial infarction, coronary stenting, heart failure, disease severity, or associated antithrombotic exposure. Prior HoLEP literature has primarily examined perioperative risk, predictors of enucleation time, and the safety of surgery in patients receiving antiplatelet or anticoagulant therapy rather than the independent relationship between these diagnoses and tissue-adjusted enucleation performance (8–11). In the present analysis, antithrombotic use was not independently associated with enucleation time. However, in the analytic cohort, antiplatelet and anticoagulant agents were discontinued five days before surgery, and selective enoxaparin bridging was used when recommended by the relevant specialty. Therefore, the absence of an independent association should be interpreted within this perioperative management strategy and should not be extrapolated to HoLEP performed under uninterrupted antithrombotic therapy. Prior prostate cancer and non-urolologic malignancy were also associated with longer enucleation time, but each subgroup included only eight patients. Although bootstrap sensitivity analyses produced similar estimates, these findings remain exploratory and may reflect sparse-data instability, unmeasured tissue characteristics, previous diagnostic interventions, or other clinical factors rather than reproducible condition-specific effects.

The morcellation phase demonstrated a less coherent relationship with comorbidity burden. Patients with comorbidity had a median morcellation time of 8 minutes compared with 9 minutes in those without comorbidity, representing an absolute difference of only one minute and a small rank-biserial effect size despite statistical significance (Table 4). Similarly, median morcellation times across prostate-volume strata were 9, 7, and 9 minutes, which does not suggest a simple linear or clinically intuitive size-dependent pattern (Table 3). In the adjusted analysis, each additional comorbidity was associated with an 8.3% shorter morcellation time; however, this direction is not biologically persuasive and should not be interpreted as evidence that comorbidity improves morcellation performance. Condition-specific morcellation estimates were also inconsistent and were particularly pronounced in some small subgroups. Morcellation efficiency is likely to be determined more directly by adenoma consistency, tissue fragmentation, intravesical visibility, blade engagement, morcellator performance, and operator technique than by systemic comorbidity itself. Comparative evidence indicates that morcellator design can substantially affect tissue retrieval speed (15), while predictor analyses have emphasized the roles of tissue burden, procedural characteristics, and surgeon experience in determining morcellation time and efficiency (16). The relationship between prostate size and morcellation performance may also become non-linear at different gland-size thresholds, further limiting

simple between-group interpretation (17). For these reasons, the morcellation findings in the present study should be regarded as secondary, exploratory observations rather than confirmatory evidence of a comorbidity-related effect.

From an implementation perspective, separating enucleation and morcellation outcomes remains useful for identifying where procedural variation occurs; however, the present findings do not establish that comorbidity-based scheduling or risk-adjusted benchmarking is ready for direct clinical application. Total extraction time in this study represented only enucleation plus morcellation time and did not include anesthesia induction, positioning, endoscopic access, hemostasis outside the recorded phase, emergence from anesthesia, turnover time, or total operating-room occupancy. Similarly, American Society of Anesthesiologists (ASA) physical status classification, Charlson Comorbidity Index, postoperative complications, intensive care requirement, length of hospital stay, and perioperative resource utilization were not analyzed. Consequently, the observed association with tissue-adjusted enucleation performance cannot be assumed to translate into longer operating-room occupancy, greater complication risk, or increased hospital resource use. Phase-specific metrics may nevertheless provide a useful research framework for distinguishing enucleation-related bottlenecks from morcellation-related limitations, particularly when interpreted alongside device and technique characteristics (15,16). Laser power and energy source must also be considered when comparing operative performance. Both high-power and low-power HoLEP approaches have been reported to provide acceptable safety and functional outcomes, although perioperative parameters and efficiency benchmarks may vary according to the equipment and settings used (18,19). In a prospective multicenter randomized trial, HoLEP and thulium laser enucleation of the prostate showed similar operative time, enucleated tissue weight, catheterization time, hospital stay, and follow-up functional outcomes, whereas thulium laser enucleation was associated with a smaller postoperative hemoglobin decrease and fewer early episodes of acute urinary retention and stress urinary incontinence (20). Because all procedures in the present cohort were performed using a single high-power Ho:YAG platform with standardized fiber and laser settings, the observed performance estimates should be interpreted within this specific technological context and should not be directly generalized to other laser systems.

Several methodological features strengthen the interpretability of the present findings. Phase-specific time stamps and tissue weights were available for all included patients, equipment and laser parameters were standardized, all participating surgeons had completed the initial HoLEP learning curve, and absolute time differences and effect-size measures were considered alongside p values. The primary inferential model used enucleation time conditional on tissue weight rather than entering tissue weight as a predictor of an outcome ratio containing the same variable, thereby avoiding mathematical coupling. Heteroscedasticity-consistent standard errors, model-fit statistics, false-discovery-rate correction, bootstrap sensitivity analyses for rare subgroups, and additional adjustment for operative technique were also incorporated.

Limitations

Nevertheless, several limitations remain. The retrospective single-center design limits causal inference and external validity. Of the 574 screened procedures, 225 were excluded, and detailed baseline comparisons between included and excluded patients could not be performed because complete analytic variables were not available for all excluded cases; selection bias therefore remains possible. Although the four surgeons had each performed at least 50 HoLEP procedures before the study period, surgeon identity, calendar period, and chronological case number were not retained, precluding operator-level or learning-curve adjustment. Detailed intraoperative measurements of blood loss, visibility, hemostasis time, blood-pressure variability, anesthesia type, irrigation pressure, tissue consistency, fibrosis, and capsular-plane difficulty were unavailable. Comorbidity burden was represented by an unweighted count in which conditions with different clinical severity and perioperative implications contributed equally; ASA physical status classification and the Charlson Comorbidity Index were not available for comparison. Several condition-specific subgroups were small, and multiplicity adjustment and bootstrap analyses cannot completely eliminate sparse-data

bias or false-positive findings. Finally, the adjusted R^2 of the primary model was 0.167, indicating that most variation in enucleation time remained unexplained by the measured variables.

In summary, the present study extends the HoLEP efficiency literature by showing that cumulative comorbidity burden was associated with slower tissue-adjusted enucleation performance after accounting for tissue weight, prostate-volume stratum, age, and antithrombotic use. This association should not be interpreted as evidence that patients with comorbidity necessarily have longer raw enucleation time, longer total operating-room occupancy, or greater perioperative resource requirements. The condition-specific findings, particularly those obtained from rare subgroups, remain exploratory, and the underlying mechanisms cannot be determined from the available data. These results should therefore be regarded as hypothesis-generating and require validation in multicenter cohorts incorporating operator identity, chronological case sequence, validated comorbidity indices, anesthesia variables, intraoperative bleeding and visibility measures, and complete operating-room utilization data before being applied to scheduling or benchmarking.

CONCLUSION

Higher comorbidity burden was associated with longer enucleation time after accounting for tissue burden, age, prostate-volume stratum, and perioperative antithrombotic use. This association reflects slower tissue-adjusted enucleation performance rather than a demonstrated increase in unadjusted operative time or total operating-room occupancy. The findings are hypothesis-generating and should be validated in multicenter cohorts with operator-level, anesthetic, hemostatic, and perioperative resource data.

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Ethics Approval: The study protocol was approved by the local ethics committee (Decision No: 2025/010.99/23/21; 30 December 2025) and was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee because of the retrospective and de-identified nature of the study.

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Availability of Data and Materials: The datasets generated and analyzed during the current study are not publicly available because they contain clinical information subject to institutional and ethical restrictions. De-identified data may be made available by the corresponding author upon reasonable request and subject to approval by the relevant institution and ethics committee.

REFERENCES

1. Lerner LB, McVary KT, Barry MJ, Bixler BR, Dahm P, et al. Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline Part II—Surgical Evaluation and Treatment. *J Urol*. 2021;206(4):818–826. <https://doi.org/10.1097/JU.0000000000002184>
2. Bae J, Oh SJ, Paick JS. The learning curve for holmium laser enucleation of the prostate: a single-center experience. *Korean J Urol*. 2010;51(10):688–693. <https://doi.org/10.4111/kju.2010.51.10.688>
3. Anıl H, Güzel A, Yıldız A, Akdemir S, Karamık K, et al. Predictive factors affecting morcellation efficiency in holmium laser enucleation of the prostate. *Investig Clin Urol*. 2023;64(4):388–394. <https://doi.org/10.4111/icu.20220361>
4. Di Maida F, Grosso AA, Tellini R, Nardoni S, Giudici S, et al. Holmium laser enucleation of the prostate (HoLEP) is safe and effective in patients with high comorbidity burden. *Int Braz J Urol*. 2023;49(3):341–350. <https://doi.org/10.1590/S1677-5538.IBJU.2022.0174>
5. Kim SC, Matlaga BR, Kuo RL, Watkins SL, Kennett KM, et al. Holmium laser enucleation of the prostate: a comparison of efficiency measures at two institutions. *J Endourol*. 2005;19(5):555–558. <https://doi.org/10.1089/end.2005.19.555>
6. Dusing MW, Krambeck AE, Terry C, Matlaga BR, Miller NL, et al. Holmium laser enucleation of the prostate: efficiency gained by experience and operative technique. *J Urol*. 2010;184(2):635–640. <https://doi.org/10.1016/j.juro.2010.03.130>
7. Tan AHH, Gilling PJ, Kennett KM, Frampton C, Westenberg AM, et al. A randomized trial comparing holmium laser enucleation of the prostate with transurethral resection of the prostate for the treatment of bladder outlet obstruction secondary to benign prostatic hyperplasia in large glands (40 to 200 grams). *J Urol*. 2003;170(4 Pt 1):1270–1274. <https://doi.org/10.1097/01.ju.0000086948.55973.00>
8. Soyster ME, Agarwal D, Slade A, Sahm E, Large T, et al. Impact of American Society of Anesthesiologists score on postoperative holmium enucleation of the prostate outcomes and complications. *Prostate*. 2023;83(4):316–322. <https://doi.org/10.1002/pros.24463>
9. Lin CH, Wu WJ, Li CC, Wen SC. Preoperative predictors of enucleation time during en bloc ‘no-touch’ holmium laser enucleation of the prostate. *BMC Urol*. 2020;20:185. <https://doi.org/10.1186/s12894-020-00758-4>
10. Sun J, Shi A, Tong Z, Xue W. Safety and feasibility study of holmium laser enucleation of the prostate (HoLEP) on patients receiving dual antiplatelet therapy (DAPT). *World J Urol*. 2018;36(2):271–276. <https://doi.org/10.1007/s00345-017-2129-y>
11. Xu P, Dean NS, Tsai K, Ganesh M, Khondakar N, et al. To Hold or Continue Blood Thinners? A Retrospective Analysis on Outcomes of Holmium Laser Enucleation of the Prostate in Patients Who Either Held or Continued Antiplatelet/Anticoagulation Therapy. *Urology*. 2025;195:4–12. <https://doi.org/10.1016/j.urology.2024.08.050>
12. Krambeck AE, Handa SE, Lingeman JE. Experience with more than 1,000 holmium laser prostate enucleations for benign prostatic hyperplasia. *J Urol*. 2013;189(1 Suppl):S141–S145. <https://doi.org/10.1016/j.juro.2012.11.027>
13. Yalçın S, Yılmaz S, Gazel E, Kaya E, Aydoğan TB, et al. Holmium laser enucleation of the prostate for the treatment of size-independent BPH: a single-center experience of 600 cases. *Turk J Urol*. 2020;46(3):219–225. <https://doi.org/10.5152/tud.2020.19235>
14. Elzayat EA, Elhilali MM. Holmium laser enucleation of the prostate (HoLEP): the endourologic alternative to open prostatectomy. *Eur Urol*. 2006;49(1):87–91. <https://doi.org/10.1016/j.eururo.2005.08.015>
15. McAdams S, Nunez-Nateras R, Martin CJ, Cha S, Humphreys MR. Morcellation efficiency in holmium laser enucleation of the prostate: oscillating morcellator outperforms reciprocating morcellator with no apparent

learning curve. Urology. 2017;106:173–177. <https://doi.org/10.1016/j.urology.2017.05.018>

16. Monn MF, El Tayeb M, Bhojani N, Mellon MJ, Sloan JC, et al. Predictors of enucleation and morcellation time during holmium laser enucleation of the prostate. Urology. 2015;86(2):338–342. <https://doi.org/10.1016/j.urology.2015.04.028>
17. Ahmed MS, Nkwam N. Morcellation efficiency across prostate size categories in holmium laser enucleation of the prostate (HoLEP): a complete-case analysis of 255 consecutive procedures at a UK tertiary centre. Cureus. 2025;17:e92533. <https://doi.org/10.7759/cureus.92533>
18. Yıldız A, Akdemir S, Anıl H, Arslan M. Watt matters: safety and efficacy of using a 140-W high-powered holmium laser for enucleation of the prostate (HoLEP). Turk J Urol. 2021;47(2):131–136. <https://doi.org/10.5152/tud.2021.20558>
19. Suh J, Choo MS, Oh SJ. Efficacy and safety of low power holmium laser enucleation of the prostate: a prospective short- and medium-term single-blind randomized trial. Investig Clin Urol. 2023;64(5):480–488. <https://doi.org/10.4111/icu.20230017>
20. Bozzini G, Berti L, Aydoğan TB, Maltagliati M, Roche JB, et al. A prospective multicenter randomized comparison between Holmium Laser Enucleation of the Prostate (HoLEP) and Thulium Laser Enucleation of the Prostate (ThuLEP). World J Urol. 2021;39(7):2375–2382. <https://doi.org/10.1007/s00345-020-03468-6>

SUPPLEMENTARY TABLES

Supplementary Table S1. Sensitivity analyses for cumulative comorbidity burden and enucleation time

Model	Antithrombotic adjustment	Additional adjustment	Adjusted % change per additional comorbidity	95% CI	p value	R ²	Adjusted R ²
Primary model	Any antithrombotic use	None	9.9	4.8 to 15.2	<0.001	0.181	0.167
Sensitivity model 1	Antiplatelet and anticoagulant entered separately	None	9.7	4.6 to 15.1	<0.001	0.182	0.166
Sensitivity model 2	Antiplatelet and anticoagulant entered separately	Operative technique category	8.0	4.5 to 11.6	<0.001	0.535	0.523

All outcomes were natural log-transformed enucleation time. All models adjusted for age, log-transformed enucleated tissue weight, and prostate-volume stratum and used HC3 robust standard errors.

Supplementary Table S2. Sparse-subgroup bootstrap sensitivity analyses for enucleation time

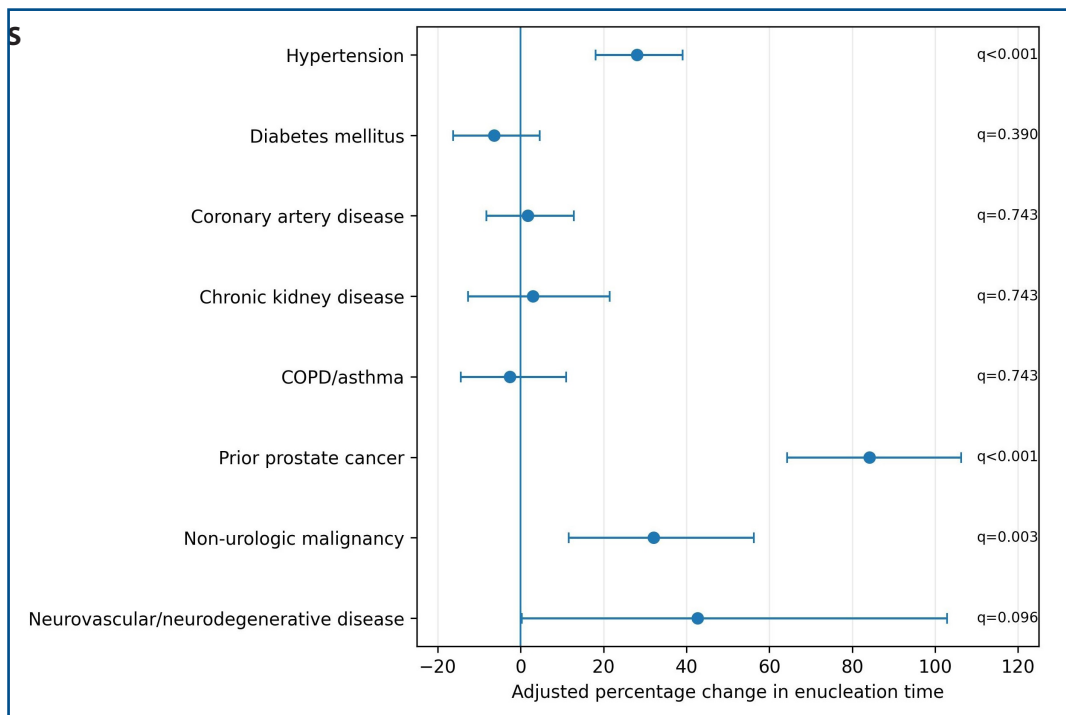
Condition	n	Adjusted % change	HC3 robust 95% CI	5,000-resample bootstrap 95% CI	Interpretive status
Prior prostate cancer	8	84.1	64.3 to 106.3	64.3 to 105.9	Exploratory
Non-urolologic malignancy	8	32.0	11.6 to 56.2	13.4 to 57.8	Exploratory
Neurovascular/neurodegenerative disease	8	42.6	0.3 to 102.9	2.2 to 105.6	Exploratory

Bootstrap analyses resampled patients with replacement and refitted the same adjusted condition-specific model. Wide intervals and small subgroup sizes preclude confirmatory interpretation.

Supplementary Table S3. Exploratory condition-specific associations with morcellation time

Condition	n	Adjusted % change	95% CI	p value	FDR-adjusted q value	Interpretation
Hypertension	166	8.8	-7.1 to 27.5	0.296	0.395	Not significant
Diabetes mellitus	54	12.6	-7.2 to 36.7	0.230	0.368	Not significant
Coronary artery disease	79	-3.2	-19.0 to 15.7	0.721	0.721	Not significant
Chronic kidney disease	26	-37.3	-52.5 to -17.1	0.001	0.006	Exploratory shorter time
COPD or asthma	32	-35.8	-51.1 to -15.6	0.001	0.006	Exploratory shorter time
Prior prostate cancer	8	-17.4	-31.5 to -0.4	0.046	0.122	Not FDR-significant
Non-urolologic malignancy	8	11.2	-19.0 to 52.8	0.512	0.585	Not significant
Neurovascular/neurodegenerative disease	8	-39.3	-71.7 to 30.1	0.199	0.368	Not significant

Each model included the condition of interest, number of other comorbidities, age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use, with HC3 robust standard errors. Negative values indicate shorter morcellation time. These analyses are exploratory because morcellation is strongly influenced by unmeasured tissue, visibility, device, and technical factors. FDR: false discovery rate.



Supplementary Figure S1. Adjusted condition-specific associations with enucleation time

Forest plot showing percentage change in enucleation time with 95% confidence intervals from exploratory condition-specific log-time models. Each model adjusted for the number of other comorbidities, age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use, with HC3 robust standard errors. Positive values indicate longer enucleation time. False-discovery-rate-adjusted q values are reported in Table 6. Rare-subgroup findings are exploratory.