



Urethral complications after holmium laser enucleation of the prostate are more common in patients with smaller prostates

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Background: Holmium laser enucleation of the prostate (HoLEP) is a bladder outlet obstruction procedure used for the treatment of benign prostatic hyperplasia (BPH). While early postoperative complications and outcomes are reported, data regarding the incidence and management of delayed urethral complications (UC), including bladder neck contracture (BNC) and urethral stricture disease (USD) are limited. We aim to define the incidence and outcomes of patients with UC following HoLEP.

Methods: A retrospective chart review was performed for 1,374 patients operated on between 07/2020–12/2023. We defined the occurrence of BNC or USD as requiring surgical treatment postoperatively. Current procedural terminology (CPT) codes were utilized to identify patients who underwent direct vision internal urethrotomy, cystoscopy with urethral dilation, urethroplasty, meatotomy, or incision of BNC. UC patients were compared to available patient metrics from our prospectively maintained database. Mann-Whitney tests, Fisher exact tests, and logistic regression were performed in GraphPad Prism version 10.3.1.

Results: Of 1,374 patients, 20 (1.5%) had a UC postoperatively, including 14 BNC (70%), 3 USD (15%), and 3 who had both BNC and USD (15%). UC patients had significantly lower prostate volumes, surgical specimen weights, lesser enucleation and morcellation times than those without UC ($P < 0.05$), while morcellation and enucleation efficiency were not. Logistic regression resulted in an odds ratio (OR) of 0.987 [95% confidence interval (CI): 0.974–0.997]. Presentation of UC occurred at a mean 148 days (range, 75–205 days) after surgery, with 10 (50%) of patients needing multiple surgical treatments for UC. Fifteen (75%) UC patients had a postoperative urinary tract infection (UTI) defined by presence of positive urinalysis, symptoms, and prescription of antibiotics.

Conclusions: We find that UC after HoLEP occurs with a low incidence of 1.5% and is associated with smaller prostate volume. We also characterize a complicated postoperative course for these patients, marked by high UTI rates and need for multiple UC surgeries. Further investigation into potential pathophysiologic mechanisms driving the association between small prostate volume and UC after HoLEP.

Keywords: Holmium laser enucleation of the prostate (HoLEP); urethral stricture disease (USD); bladder neck contracture (BNC)

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Introduction

Benign prostatic hyperplasia (BPH) increases in prevalence as men age, with proliferative prostate transition zone growth contributing to the development of lower urinary tract symptoms (LUTS) (1). Transurethral resection of the prostate (TURP), remains the most utilized surgical technique to treat BPH, however alternative treatments such as holmium laser enucleation of the prostate (HoLEP) are growing in usage due to better durability and a lower complication rate (2) as well as better outcomes over robot-assisted simple prostatectomy (3,4). Despite the success of newer techniques, complications, such as bladder neck contracture (BNC) and anterior urethral stricture disease (USD), still occur. BNC and USD, which we will collectively term “urethral complications” (UC), are particularly burdensome for the BPH/LUTS patient, as after initial relief from symptoms, UC may cause refractory symptoms and lead to additional unanticipated surgical interventions.

The pathogenesis of UC is poorly understood, and therefore, effective strategies for prevention are limited.

Both physiologic factors, such as variances in urethral anatomy, and inflammatory causes of UC have been proposed. Specific to inflammatory causes, prior histologic studies of urethral strictures demonstrate increased collagen content and altered collagen structure compared to normal tissue (5,6). Inflammation has also been associated with strictures, although depending on stricture etiology, with iatrogenic strictures, such as those that develop after HoLEP, being less likely to display chronic inflammation compared to idiopathic strictures (7). Collagen content and inflammation have been examined previously in surgical TURP BPH/LUTS prostate specimens, with patients with smaller prostates (<75 g) having increased collagen content and decreased inflammation compared to patients with larger prostates (8). Taken together, this suggests that patients with smaller prostates may have more active collagen production, thereby placing them at higher risk for UC after surgical urethral trauma. However, the literature is mixed regarding the relationship between prostate size and post-HoLEP UC risk (9-14). Therefore, we aimed to define the incidence of UC after HoLEP and test the hypothesis that UC is more common in smaller prostates. We present this article in accordance with the STROBE reporting checklist (available at <https://tau.amegroups.com/article/view/10.21037/tau-2025-256/rc>).

Highlight box

Key findings

- Urethral complications after holmium laser enucleation of the prostate (HoLEP) occur with a low incidence of 1.5% and are associated with smaller prostate volumes.
- Resectoscope sheath size was not associated with development of post-HoLEP urethral complications.

What is known and what is new?

- Although prostate size has been correlated in the past to urethral complications after HoLEP, the literature on this is mixed, reporting no, inverse, and direct relationships between prostate size and development of urethral complications after HoLEP.
- We report that those who developed urethral complications had significantly smaller preoperative prostate volumes and compare this finding to prior literature that both supports and contradicts our results; we also comment on possible pathophysiologic explanations for this finding.

What is the implication, and what should change now?

- Given the wide variety of surgical options available to treat benign prostatic hyperplasia (BPH), our data may improve patient selection for BPH surgery—particularly for those with small prostate volumes that may have the greatest amount of surgical treatment options.
- We suggest further research into pathophysiologic mechanisms driving the association of smaller prostate glands and increased risk for post-HoLEP urethral complications.

Methods

Following institutional review board approval, we performed a retrospective cohort study from our prospectively maintained institutional database of 1,374 patients (age ≥ 18 years) who underwent HoLEP between July 2020 and December of 2023 at the University of Wisconsin. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the institutional review board of the University of Wisconsin (IRB00003739) and individual consent for this retrospective analysis was waived. Surgery was performed by five urologists in a two-lobe technique with a 26 French Wolf resectoscope (Richard Wolf Knittlingen, Germany) or 28 French Storz resectoscope (Karl Storz Tuttlingen, Germany), using a 550-micron Lumenis pulse 120H holmium laser fiber (Boston Scientific, Marlborough, MA, USA). Both resectoscope size selection and meatus dilation via Van Buren sounds up to 30Fr were dependent on surgeon preference. Prophylactic bladder neck and/or urethral incisions were not utilized in any cases. The Wolf Piranha morcellator was used to morcellate prostate tissue

in all cases. Surgical specimen weight was measured in the operating room by the surgeon prior to submission for pathologic analysis.

Our primary outcome was the incidence of UC after HoLEP, defined as USD or bladder neck BNC requiring procedural treatment. Patients with UC were identified by cross-referencing HoLEP patients with current procedural terminology (CPT) codes for direct vision internal urethrotomy (52276), cystoscopy with urethral dilation (52281), urethroplasty (53410 or 53400 or 53415 or 53420 or 53450 or 54326 or 53405 or 53010), meatotomy (53020), or incision of BNC (52640) that occurred following HoLEP. This captures both scheduled procedural treatments performed in the operating room or clinic and unplanned surgical interventions that occurred due to presentation at the emergency department at our institution. Demographic, preoperative characteristics, surgical details, and postoperative outcomes were collected for all patients from the electronic medical record if available. Preoperative prostate volume estimations were made using either three-dimensional (3D) magnetic resonance imaging (MRI), ellipsoid estimation MRI, ellipsoid estimation computed tomography (CT), or transrectal ultrasound (TRUS) imaging, utilized in preferential order.

Statistical analysis

Patients with and without UC were compared to identify preoperative risk factors for UC and differences in surgical outcomes. Mann-Whitney tests, Fisher exact tests, and logistic regression were performed in GraphPad Prism version 10.4.0. Differences were considered significant if $P < 0.05$.

Results

Preoperative characteristics

Of 1,374 consecutive HoLEP patients, 20 (1.5%) had a UC postoperatively, including 14 BNC (70%), 3 USD (15%), and 3 patients who had both BNC and USD (15%). Average prostate size was 103.1 ± 60.8 g; body mass index (BMI), age, international prostatic symptom score (IPSS) total, IPSS quality of life (QoL), history of prior outlet procedure, preoperative catheter dependency status, and PVR were similar between UC and non-UC groups (*Table 1*). No UC patients had a history of pelvic radiotherapy. UC patients

had significantly smaller preoperative prostate volume (72.6 ± 33.9 vs. 103.9 ± 61.2 g; $P = 0.01$) and PSA (2.80 ± 2.62 vs. 5.89 ± 13.5 ng/mL; $P = 0.01$) compared to non-UC patients but were otherwise similar with respect to preoperative clinical characteristics. Logistic regression found that preoperative prostate volume was significantly associated with the occurrence of UC [odds ratio (OR) = 0.987, 95% confidence interval (CI): 0.974–0.997; $P < 0.01$].

Operative and postoperative characteristics

Patients with UC had shorter enucleation times (39.4 ± 15.3 & 52.9 ± 26.9 min; $P = 0.01$), shorter morcellation times (7.80 ± 8.50 & 11.8 ± 11.5 min; $P = 0.02$), and lower surgical specimen weights (40.2 ± 33.4 & 61.2 ± 45.9 g; $P = 0.02$) compared to non-UC patients (*Table 2*). A graphical comparison of specimen weight and preoperative gland sizes for UC and non-UC can be seen in *Figure 1*. Enucleation efficiency (1.12 ± 1.09 & 1.23 ± 0.88 g/min), morcellation efficiency (7.10 ± 4.39 & 6.51 ± 3.07 g/min), size of resectoscope sheath utilized (45.0% vs. 45.6% 26-French & 55% vs. 54.4% 28-French) and the percentage tissue removed ($51.8\% \pm 22.8\%$ & $56.7\% \pm 23.9\%$) were similar between UC and non-UC groups, respectively (*Table 2*; $P > 0.05$). Patients with UC had higher postoperative IPSS scores (14.8 ± 7.90 & 7.92 ± 6.19 ; $P < 0.001$) and longer average follow up (26.7 ± 13.5 & 16.5 ± 12.2 months; $P < 0.001$) but were otherwise similar with regard to postoperative outcomes (*Table 3*).

UC characteristics

Of 20 UC patients, a single patient who developed a postoperative BNC had a history of USD, which did not require prior surgical intervention (*Table 4*). Presentation of UC occurred at a mean 148 days (range, 75–205 days) after surgery, with 10 (50%) of patients needing multiple surgical treatments for UC. For USD patients, location of stricture included one meatal, three fossa navicularis, and two bulbar urethral strictures. Surgical intervention occurred at a mean 216 days after surgery (range, 49–277 days). The most common surgical interventions for UC were urethral dilation and incision of BNC, with additional information on surgical interventions found in *Table 4*. Fifteen (75%) UC patients had a postoperative urinary tract infection (UTI) defined by presence of positive urinalysis, symptoms, and prescription of antibiotics.

Table 1 Preoperative characteristics of patients with and without urethral complications

Variable	Urethral complications (N=20)	No urethral complication population (N=1,354)	P value
BMI (kg/m ²)	28.6±6.97	28.8±5.29	0.56
Preoperative IPSS total	20.3±6.7	19.4±7.36	0.65
Preoperative IPSS QoL	3.83±0.94	3.91±1.37	0.71
Prior outlet procedure			0.73
Yes	3 (15.0)	115 (12.7)	
No	17 (85.0)	789 (87.3)	
History of prostatic artery embolization			0.99
Yes	0	7 (1.1)	
No	20 (100.0)	633 (98.9)	
Age at time of surgery (years)	67.4±9.09	71.5±8.25	0.060
PSA (ng/mL)	2.80±2.62	5.89±13.5	0.01
Preop catheter status			0.24
Catheter dependent	4 (20.0)	310 (34.4)	
Catheter independent	16 (80.0)	591 (65.6)	
PVR (mL)	288.6±506.0	230.7±288.1	0.56
Preoperative prostate size (g)	72.6±33.9	103.9±61.2	0.01
Preoperative 5-ARI status			0.23
Current	3 (15.0)	275 (30.1)	
Former	1 (5.0)	124 (13.6)	
Never	16 (80.0)	514 (56.3)	
Transition zone index	0.61±0.19	0.66±0.16	0.35
Transition zone size (g)	48.3±43.1	68.0±49.8	0.17

Data are presented as mean ± SD or n (%). 5-ARI, 5-alpha reductase inhibitors; BMI, body mass index; IPSS, international prostatic symptom score; PSA, prostate-specific antigen; PVR, post-void residual; QoL, quality of Life; SD, standard deviation.

Table 2 Operative detail comparison of patients with and without urethral complications

Variable	Urethral complications (N=20)	No urethral complication population (N=1,354)	P value
Enucleation time (min)	39.4±15.3	52.9±26.9	0.01
Morcellation time (min)	7.80±8.50	11.8±11.5	0.02
Specimen weight (g)	40.2±33.4	61.2±45.9	0.02
Enucleation efficiency (g/min)	1.12±1.09	1.23±0.88	0.18
Morcellation efficiency (g/min)	7.10±4.39	6.51±3.07	0.86
Percent tissue removed (%)	51.8±22.8	56.7±23.9	0.52
Resectoscope sheath size utilized			>0.99
26-French	9 (45.0)	618 (45.6)	
28-French	11 (55.0)	736 (54.4)	

Data are presented as mean ± standard deviation or n (%).

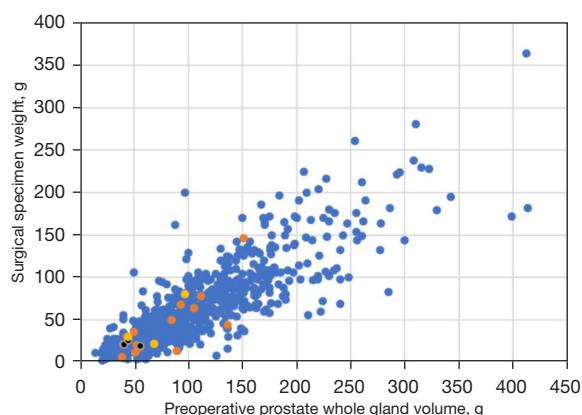


Figure 1 Comparison of preoperative prostate gland volume and surgical specimen, distinguished by postoperative UC status. Patients with a postoperative UC had significantly smaller preoperative prostate volumes ($P<0.05$). Logistic regression revealed an OR of 0.987 (95% CI: 0.974–0.996). CI, confidence interval; OR, odds ratio; UC, urethral complication.

Discussion

Overall, we found a 1.5% incidence of procedurally managed UC after HoLEP. While UC are rare in modern series, they pose a significant burden to patients who experience recurrent/worsening symptoms, possible UTI, and require additional unexpected surgeries. Our data support these points, with UC patients reporting higher postoperative IPSS totals than their non-UC counterparts, half of UC patients needing multiple surgical interventions to treat UC, and 75% of UC patients having a UTI post-HoLEP. Notably, those who developed UC had significantly smaller preoperative prostate volumes, which yielded a small but significant risk on univariate analysis (OR =0.987; 95% CI: 0.974–0.997; $P=0.01$). As the number of surgical BPH treatment options expands, understanding differential risk of specific complications, including UC, is key to improving patient selection—especially in patients

Table 3 Postoperative characteristic comparison of patients with and without urethral complications

Variable	Urethral complications (N=20)	No urethral complication population (N=1,354)	P value
Length of stay (days)	0.20±0.52	0.39±0.82	0.20
Catheter duration (days)	2.83±2.96	2.6±2.3	0.95
PCa	8 (40.0)	343 (25.0)	0.19
Postop PSA (ng/mL)	0.97±0.94	7.85±58.1	0.58
Postop 5-ARI status			>0.99
Current	0	24 (3.7)	
Former	0	0	
Never	20 (100.0)	630 (96.3)	
Postop IPSS total	14.8±7.90	7.92±6.19	<0.001
Postop IPSS QoL	2.94±1.81	2.51±1.82	0.26
Catheter status			>0.99
Catheter dependent	0	16 (2.5)	
Catheter independent	20 (100.0)	633 (97.5)	
Length of follow-up (months)	26.7±13.5	16.5±12.2	<0.001
PVR (mL)	122.9±257.9	53.0±125.3	0.78

Data are presented as mean ± standard deviation or n (%). 5-ARI, 5-alpha reductase inhibitors; IPSS, international prostatic symptom score; PCa, prostate cancer on pathology specimen; PSA, prostate-specific antigen; PVR, post-void residual; QoL, quality of life; SD, standard deviation.

Table 4 Postoperative urethral complication patient details

Variable	Urethral complication patients (N=20)
Type of urethral complication	
BNC	14 (70.0)
USD	3 (15.0)
Both	3 (15.0)
Positive for history of stones	8 (40.0)
History of USD or BNC	1 (5.0)
Prior surgical treatment for USD or BNC	0
Postop UTI	15 (75.0)
UTI before or after UC diagnosis	
Before	7 (46.7)
After	6 (40.0)
Same day	2 (13.3)
Time between HoLEP and UC symptom presentation (days)	148 [75–205]
Time between HoLEP to UC diagnosis (days)	182 [87–227]
Time between HoLEP and UC surgery (days)	216 [49–277]
UC surgical intervention	
DVIU	5 (12.0)
Cystoscopy with urethral dilation	15 (35.7)
Incision of bladder neck contracture	15 (35.7)
Urethroplasty	3 (7.1)
Meatotomy	3 (7.1)
Other	1 (2.4)
Total number of treatments	42
Multiple surgeries necessary for UC	
Yes	10 (50.0)
No	10 (50.0)

Data are presented as n (%), mean [range] or number. BNC, bladder neck contracture; DVIU, direct vision internal urethrotomy; HoLEP, holmium laser enucleation of the prostate; UC, urethral complication; UTI, urinary tract infection; USD, urethral stricture disease.

with smaller prostate volumes where the most treatment options exist.

We report a rate of 0.4% USD and 1.3% BNC after HoLEP, which is at the lower end of ranges reported previously in the literature: 0–4% for BNC and 1–8% for USD post-HoLEP (11,12,15). The range in reported incidence may be attributed to variation in UC definition, with some studies including only those UC requiring surgical intervention and other omitting definitions altogether. Further, average length of follow-up varies in these studies, which also impacts the measurement of UC incidence. Despite these factors, BNC and USD post-HoLEP are generally lower compared to other outlet obstruction procedures, such as Bipolar TURP, wherein rates range from 0–4% for BNC and 0–8% for USD postoperatively (15). Taken together, this suggests that both patient and surgical factors play a role in the pathogenesis of UC following BPH surgery.

Prior research has investigated the impact of comorbidities on the likelihood of BNC or USD after bladder outlet obstruction surgery. Longer operative time, increased sheath size, and longer postoperative catheter duration have been associated with the development of postoperative BNC or USD after HoLEP (9,10). Similarly, after TURP, longer operative time, re-catheterization, repeat infection, and mucosa rupture were risk factors for USD or BNC (13,16). While overall operative time was not analyzed in this study, we report a significantly shorter duration for morcellation and enucleation within the UC group versus the non-UC group ($P<0.05$). However, this is likely due to the co-linear relationship of enucleation and morcellation time with prostate volume. This is supported by a lack of significant difference between enucleation efficiency, morcellation efficiency, and percent tissue in UC and non-UC groups. Regarding resectoscope sheath size and UC risk, literature is mixed. Elsaqa *et al.* reported that significantly more UC in cases utilizing a 28-French sheath when compared to those utilizing a 26-French sheath in a retrospective study of 566 HoLEP patients (10). Conversely, in a retrospective study of 502 HoLEP patients, Thai *et al.* reported no significant difference in sheath size utilization between UC and non-UC groups (17). Similar to the Thai *et al.* study, we found no significant difference

between UC and non-UC groups in resectoscope size usage ($P < 0.05$). Beyond the mixed literature on technical and perioperative factors association with post-HoLEP UC, our report stimulates interest in the role of prostate volume in postoperative UC development.

Like our series, prior HoLEP studies have found that UC is more common in smaller prostates (9,11,12). For example, in a cohort of 206 HoLEP patients with an overall mean prostate volume of 68.2 g, Kuo *et al.* found an overall BNC incidence of 3.9% and that patients with BNC had lower prostate volumes (28.8 *vs.* 69.8 g) (11). Ibrahim *et al.* found in their cohort of 1,476 patients with an overall average prostate volume of 92.3 g BNC only developed in those with glands less than 55 g, with a BNC rate of 2.0% and USD of 1.4% (12). In our series, we have a higher average prostate volume of 103 g but note a similar association with small effect size. However, a positive association between prostate volume and incidence of UC has also been reported in the literature. Shah *et al.* found a higher incidence of USD in those with >100 g gland (4.8%) compared to those with 60–100 g (2.6%) and <60 g (1.3%) (14). Yet importantly, cohort sizes were unequal and larger glands were comparatively under-represented, with 235 patients <60 g, 77 patients 60–100 g, and 42 patients >100 g glands. In a comparison study of 107 HoLEP and 101 TURP patients, Elsaqa *et al.* reported upon multivariate regression that “larger prostate volume” [hazard ratio (HR) = 1.222, 95% CI: 1.057–1.411, $P < 0.05$] was associated with increased risk of USD and BNC, but did not specify whether this considered prostate volume as continuous or categorical and combined TURP and HoLEP patients in analysis (13). Conversely, in a HoLEP-only study including 566 patients, Elsaqa *et al.* found no significant difference in preoperative gland size between those with and without UC, with an overall rate of 4.9% (10). This suggests inclusion of TURP patients may have impacted the analysis, although association of UC with smaller gland size in TURP patients has been reported previously (18). Overall, these data suggest that post HoLEP UC is generally more common in smaller prostates, but that this relationship is complex.

Despite primarily congruent data pointing to a possible link between UC risk and smaller prostates, a potential pathophysiologic mechanism has not been identified. One possibility is that the local environment modulates UC risk, as many urethral strictures are known to have significant inflammation and a modified collagen environment (5–7). Prior literature focusing on BPH patients treated via TURP or open-simple prostatectomy showed generally decreased

histologic inflammation and increased fibrosis (collagen content) in smaller prostates (less than 75 g) compared to larger prostates (more than 75 g) (8). Therefore, it could be hypothesized that increased fibroblast activation in smaller glands predisposes patients to development of UC after surgical urethral trauma. In the current study, 8 (40%) patients who developed UC had preoperative gland sizes over 75 g, however, their individual collagen content and/or inflammation parameters were not assessed. Additional research is necessary to assess the interplay of prostate size, inflammatory environment, and UC risk.

We also suggest consideration of prostate features outside of overall gland size in consideration of UC risk or in relation to the pathophysiologic environment of the prostate. In the limited literature available, while prostate transition zone index (the ratio of transition zone volume to whole gland volume) was not ($P = 0.06$), transition zone size was significantly smaller in TURP patients who developed a UC (16). In our cohort with available transition zone measurements of seven patients (35%) we did not find a significant correlation between transition zone volume and UC, however, we plan to investigate this further. Further research on the relationship between infrequently utilized prostate imaging metrics, the inflammatory environment within the prostate, and UC risk is suggested, with the overall aim of improved patient counseling.

Besides the inherent limitations of a surgical retrospective study design, there are other limitations that should be acknowledged. Firstly, we utilized CPT codes to determine our rate of UC, which may miss patients who were coded incorrectly or presented to outside clinics for treatment of UC. Secondly, we only reported those who underwent surgical intervention, underestimating the extent of UC due to excluding those who may have been diagnosed on cystoscopy, but not treated surgically. Thirdly, we utilized a combination of imaging types, but preferentially utilized MRI, CT, then TRUS if available. The variety of imaging modalities may impact the accuracy of reported preoperative gland sizes. Fourth, a multivariate model was not performed due to low event rate, which possibly limits the analysis of our data: a multi-center study in the future is recommended to address this. Despite these limitations, our research offers a greater understanding of the incidence of and postoperative journey for those with UC after HoLEP.

Conclusions

We report a 1.5% UC incidence after HoLEP, with those

experiencing an UC having an average gland size of 72.6 ± 33.9 g—significantly smaller than the non-UC group. While we did not characterize the extent of inflammation or collagen in our cohort, smaller prostates have been associated with increased collagen content in literature, offering a potential pathophysiologic mechanism. Additionally, we suggest further research on prostate imaging metrics beyond the whole gland volume in assessment of UC risk. In the future, patient counseling for surgical treatment of BPH/LUTS may become increasingly individualized based on a combination of prostate imaging metrics and both the inflammatory and collagen environment of the prostate, ideally improving both treatment selection and operative.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://tau.amegroups.com/article/view/10.21037/tau-2025-256/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was

conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the institutional review board of the University of Wisconsin (IRB00003739) and individual consent for this retrospective analysis was waived.

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