

Prostatic Diseases and Male Voiding Dysfunction

Major Acute Cardiovascular Events After Transurethral Prostate Surgery: A Population-based Analysis



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OBJECTIVE	To test the prevalence and predictors of major acute cardiovascular events (MACE) after transurethral prostate surgery (TPS).
MATERIAL AND METHODS	The American College of Surgeons National Surgical Quality Improvement Program database (2011-2016) was queried for patients who underwent transurethral resection of the prostate, photoselective vaporization, or laser enucleation. MACE included: cerebrovascular events, cardiac arrest, myocardial infarction, deep venous thrombosis requiring therapy, and pulmonary embolism episodes occurred up to 30 days after discharge. Univariable and multivariable logistic regression models tested MACE predictors and effect of MACE on perioperative mortality. Within covariates significant at univariable analyses a stepwise selection, based on Akaike Information Criterion values, was performed to fit the most appropriate multivariable model.
RESULTS	Overall 44,939 patients were included in our analyses. Of these 365 (0.8%) had MACE within 30 days after surgery. The strongest MACE predictors were recent congestive heart failure (odds ratio [OR]: 2.1, 95% confidence interval [CI]: 1.2-3.7, $P = .007$), transfusions (OR: 2.5, 95% CI: 1.5-4.1, $P < .001$) and preoperative Systemic Inflammatory Response Syndrome or sepsis (OR: 2.6, 95% CI: 1.6-4.2, $P < .001$). Similarly, inpatient (OR: 2.0, 95% CI: 1.6-2.5, $P < .001$) and non-elective (OR: 1.5, 95% CI: 1.1-2.1, $P = .012$) patients experienced higher MACE rates. Perioperative mortality rates were statistically significantly higher in MACE patients (OR: 13.1, 95% CI: 8.2-21.0, $P < .001$).
CONCLUSION	Up to 1% of patients undergoing transurethral prostate surgery experience MACE. MACE are burdened by high mortality rates (up to 14% in MACE patients). Proper patient selection and postoperative monitoring are necessary to reduce MACE incidence and mortality rates. UROLOGY 131: 196–203, 2019. © 2019 Elsevier Inc.

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Lower urinary tract symptoms (LUTS) are high prevalent and incident condition in the general population.¹ LUTS may be associated with a wide range of conditions, including bladder outlet obstruction (LUTS/BOO) secondary to benign prostatic hyperplasia (BPH).²

Total incidence of BPH was estimated as 34.4 per 1000 person/year in the United States, with a 4% risk increase with every additional year of age.³ Despite the benign nature of this affection up to 12.6 per 1000 patients will require BPH surgery.⁴

The standard of care in patients with LUTS/BOO refractory to medical treatment is surgery, in both BPH patients and prostate cancer patients as well as other causes (eg, bladder neck contracture).^{5,6} As time goes by, transurethral prostate surgery (TPS) gradually overcome the use of simple prostatectomy.²

Generally considered safe, TPS may be burdened by serious complications such as major acute cardiovascular events (MACE).^{7,8} In highest risk patients, such as those who cannot suspend anticoagulant, some guidelines recommend the use of laser surgeries. However, low grade evidences are available about the best technique in high risk patients and few is known about MACE occurrence after TPS.^{9,10}

As such, we sought to test the rates of MACE and the effect of several possible predictors of perioperative MACE in patients undergoing TPS within a large population-based dataset. We also sought to test the effect of MACE on perioperative mortality. Finally, we aimed to test possible differences in MACE rates according to the different TPS techniques.

MATERIAL AND METHODS

Data Source and Study Population

Within the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) we identified patient who underwent TPS between 2011 and 2016. Patients were identified using Current Procedural Terminology codes for transurethral resection of the prostate (TURP) (52601, 52630), photoselective vaporization (PVP) (52648) and prostate enucleation (52649). Patients with missing information about American Society of Anesthesiologist (ASA) score, principal anesthesia technique, age, and elective surgery status were excluded. Diagnosis was stratified according to the International Classification of Diseases 9 (ICD-9) and ICD-10.

Covariates Definition

Several predictors were tested, namely: age at the time of surgery (≤ 75 , > 75 years), year of surgery (2011-2013, 2014-2016), diagnosis (BPH [ICD-9 codes: 600.xx, ICD-10 codes: N40.xx], Prostate Cancer [ICD-9 codes: 185, ICD-10 codes: C61], Other [codes not directly amenable to a diagnosis of BPH or prostate cancer]), surgical procedure (TURP, PVP, Enucleation), race (Caucasian, African-American, other, and unknown), anesthesia type (general, locoregional, and other), body mass index (underweight, normal, overweight, obese, and unknown), weight loss $> 10\%$, functional status (independent, partially dependent, totally dependent, and unknown), ASA score (≤ 2 , > 2), and current smoker status.

Comorbidities of interest were diabetes (no diabetes, insulin dependent, and noninsulin dependent), respiratory disorders, congestive heart failure, chronic steroid use, preoperative transfusions, preoperative Systemic Inflammatory Response Syndrome (SIRS) or sepsis, metastatic cancer, wound infections, hypertension. Patients with an increased risk for bleeding due to an underlying hematologic disorder or chronic anticoagulation were classified as those with bleeding disorders. Patients with respiratory disorders were those with dyspnea at rest or after moderate exertion or ventilator dependent or with a history of chronic obstructive pulmonary disease. Patients who need preoperative dialysis or with acute renal failure were classified as patients with renal disorders. Additional variables of interest were the outpatient status, the elective surgery status and the operation time (≤ 90 minutes, > 90 minutes). Elective patients were those brought from their home or normal living environment on the day of surgery for a nonemergent/nonurgent scheduled surgical procedure.

Outcomes and Complication Definition

Main outcome of interest was the MACE rates. MACE were defined as a composite of cerebrovascular events, cardiac arrest, myocardial infarction, deep venous thrombosis, or pulmonary embolism as defined within the ACS-NSQIP database. Additional outcomes assessed were the need for reintervention (within 30 days) and perioperative mortality.

Complications of interest were as follows: postoperative pneumonia, intubation, acute renal failure, urinary tract infection, intra- and postoperative transfusions, septic shock, and sepsis. Length of stay and prolonged hospital stay (> 30 days) were also examined.

Statistical Analyses

Quantitative variables were reported as either mean or standard deviation (SD). Categorical variables were reported as frequencies and percentages. Patients were stratified according to the occurrence or not of MACE and differences in characteristics of patients among the 2 conditions were tested by Student *t* test and Pearson chi-square test for continuous and categorical variables, respectively.

The main outcome of interest was the occurrence of MACE. Temporal trends were quantified using the annual percentage change with linear regression. Univariable logistic regression model were fitted to evaluate the association of pre- and intraoperative features with MACE occurrence. We relied on penalized logistic regression to model multivariable logistic regression, in order to avoid overfitting. Stepwise regression model in both directions (backward and forward) was performed within the covariates with a statistically significant association with MACE in univariable analyses. In the final multivariable logistic regression model only variables that ensure a model performance improvement, as indicated by the Akaike Information Criterion (AIC), were included.¹¹

Since we included both inpatients and nonelective procedures, we hypothesized a-priori that if inpatients and nonelective patients may be more prone to experience MACE, on the other hand outpatients elective procedure may be burdened by lower MACE rates. For these reasons, we a-priori planned a sensitivity analysis in these 2 groups of patients. In these cohorts all the previous steps to generate multivariable logistic regression models were repeated.

Moreover, univariable logistic regression analyses were applied to evaluate the perioperative mortality risk according to pre- and intraoperative features and postoperative complications. Stepwise regression to fit multivariable models predicting perioperative mortality was performed within the covariates with a statistically significant association in univariable models.

The goodness of the generated models was evaluated according to the Brier Score, defined as the mean squared difference between the predicted probability and the observed outcome. Brier Score may assume values ranging between 0 (perfect prediction) and 1 (worse prediction).¹² Multivariable model was internally validated with 1000 random bootstrap resampling.

All tests were 2-sided, and a level of statistical significance was set at $P < .05$. Analyses were performed using the R software environment for statistical computing and graphics (version 3.5.3; <http://www.r-project.org/>).

RESULTS

Descriptive Characteristics

Overall 44,939 patients were included in our analyses. Of these 365 (0.8%) had MACE within 30 days after surgery. No

statistically significant changes in MACE rates were found over time ($P = .226$) (Supplementary Figure 1). Most of the patients harbored BPH (76.5%), while only the 5.6% harbored prostate cancer. Most were Caucasian (65.9%), obese (30.6%), non-smokers (89.3%), nondiabetic (78.6%) and with functional status classified as independent (95.9%).

Most frequent comorbidities were hypertension (60.6%), respiratory disorders (10.9%) and bleeding disorders (3.6%). Of all, 1.5% of patients harbored metastatic cancer, the 0.8 and 1.0% required transfusion or had SIRS with or without sepsis before surgery, respectively. Most of the patients were classified as ASA score >2 (53.0%).

Of all, the 66.4, 28.6 and 5.0% respectively underwent TURP, PVP, and Enucleation. Most of the surgical procedures were performed under general anesthesia (76.5%), in election (92.9%) and in outpatient regimen (62.7%). Most of the surgical procedures lasted ≤ 90 minutes.

Main Characteristics of MACE vs No-MACE Patients

Patients who experienced MACE were more frequently older than 75 years (odds ratio [OR]: 1.9, 95% confidence interval [CI]: 1.5-2.3, $P < .001$). Similarly, surgery for prostate cancer (OR: 1.7, 95% CI: 1.1-2.5, $P = .010$) and other causes (OR: 1.8, 95% CI: 1.4-2.2, $P < .001$) was associated with higher rates of MACE than surgery for BPH. In addition, functional status in MACE patients was more frequently classified as partially dependent (OR: 2.7, 95% CI: 1.7-4.0, $P < .001$) or totally dependent (OR: 3.5, 95% CI: 1.2-7.7, $P = .006$). Furthermore, a history of several chronic conditions was associated with MACE (Table 1). Interestingly, the inpatient status (OR: 2.6, 95% CI: 2.1-3.2, $P < .001$) and non-elective surgeries (OR: 3.8, 95% CI: 2.9-4.8, $P < .001$) were also associated with higher MACE rates (Table 1). Conversely, PVP was associated with lower MACE rates than TURP (OR: 0.7, 95% CI: 0.6-0.9, $P = .017$).

In multivariable logistic regression models the strongest predictor of MACE were recent congestive heart failure (OR: 2.1, 95% CI: 1.2-3.7, $P = .007$), transfusions (OR: 2.5, 95% CI: 1.5-4.1, $P < .001$), and preoperative SIRS or sepsis (OR: 2.6, 95% CI: 1.6-4.2, $P < .001$; Fig. 1). Multivariable model was internally validated with 1000 random bootstrap resampling and showed good accuracy of probabilistic predictions according to Brier score (0.008, 95% CI: 0.007-0.009).

Sensitivity Analyses

In multivariable logistic regression model, patients classified as inpatients experienced higher MACE rates compared to those classified as outpatients (OR: 2.0, 95% CI: 1.6-2.5, $P < .001$). Similarly, nonelective patients experienced higher MACE rates compared to their elective counterpart (OR: 1.5, 95% CI: 1.1-2.1, $P = .012$) even after multivariable adjustment. In consequence, we repeated the stepwise regression selection in the highest risk patients ($n = 2871$, MACE rates = 2.8%, Supplementary Table 1), defined as those that were both inpatients and nonelective, and in their outpatients elective counterpart ($n = 27,864$, MACE rates = 0.5%, Supplementary Table 2). Within the highest risk patients cohort, preoperative transfusion (OR: 3.0, 95% CI: 1.8-5.0, $P < .001$) and SIRS or sepsis (OR: 2.5, 95% CI: 1.5-4.2, $P < .001$) maintained virtually the same effect on MACE rates (Fig. 2a). Interestingly, patients who underwent PVP surgery experienced lower MACE rates (OR: 0.4, 95% CI: 0.2-1.0, $P = .051$; Fig. 2a). Multivariable model was internally validated with 1000 random bootstrap resampling and

showed good accuracy of probabilistic predictions according to Brier score (0.026, 95% CI: 0.019-0.034).

Similarly, among lowest risk patients preoperative SIRS or sepsis (OR: 5.7, 95% CI: 1.4-24.1, $P = .017$) maintained its predictor value on MACE rates. However, the surgery type did not add any further accuracy to the model and similarly to the overall cohort was not included in the final multivariable logistic regression (Fig. 2b). Multivariable model was internally validated with 1000 random bootstrap resampling and showed good accuracy of probabilistic predictions according to Brier score (0.005, 95% CI: 0.004-0.006).

Main Surgical Outcomes, Complications and Mortality

Overall, patients who experienced MACE required longer length of stay (5.6 ± 9.2 vs 1.7 ± 5.2 days, $P < .001$). Moreover, MACE patients had higher reoperation rates (12.6 vs 1.9%, $P < .001$) and readmission rates (51.2 vs 5.4%, $P < .001$). In addition, MACE patients usually experience more frequently all the examined complications (Table 2). In particular, MACE patients showed meaningful higher rates of urinary tract infections (13.4 vs 4.8%, $P < .001$), intra- and postoperative transfusions (11.5 vs 1.5%, $P < .001$) and sepsis (5.5 vs 0.8%, $P < .001$) or septic shock (7.1 vs 0.2%, $P < .001$; Table 2). Perioperative mortality rates were statistically significant higher in MACE patients (14.2 vs 0.3%, $P < .001$), even after multivariable adjustment (OR: 13.1, 95% CI: 8.2-21.0, $P < .001$, Brier test: 0.003, 95% CI: 0.002-0.004).

DISCUSSION

We sought to test MACE rates and predictors of perioperative MACE in patients undergoing TPS, with a specific focus on possible differences in MACE rates according to the different TPS technique. We also sought to test the effect of MACE on perioperative mortality. We relied on ACS-NSQIP database, which include 44,939 patients in whom TPS was performed in a contemporary era (2011-2016). Our analyses showed several important results.

First, MACE are relatively uncommon complications ($<1\%$) after TPS, that remain a safe and reliable treatment choice in patients with LUTS/BOO. Furthermore, no changes in MACE rates over time were shown in our analyses. However, considering the high prevalence and incidence of LUTS/BOO and the large number of TPS performed per year, MACE may be a life-threatening condition for hundreds of patients every year. Indeed, in the United States approximately the 15% of the population age is over 65 years old.¹³ Considering that, according to different casuistry, the prevalence of BPH/LUTS is around 50% in these patients,¹⁴ up to 13,000 men may be at risk of MACE after a TPS. Obviously, not all the patients with LUTS should undergo surgery,¹⁵ however, this relatively uncommon complication is of importance considering the high prevalence of BOO/LUTS surgically treated in the United States and Europe. Furthermore, MACE is associated with a clinically meaningful increase of perioperative mortality and may result in higher disability and care demand.¹⁶ Thus, physicians and patients should consider these aspects and risks when surgery is planned, in particular because TPS are more often indicated for

Table 1. Descriptive pre- and intraoperative characteristics of patients undergoing transurethral surgery of the prostate stratified according to Major Acute Cardiovascular Events (MACE) occurrence. Data are reported as frequencies (%). Univariable logistic regression odds ratios (OR) with 95% confidence interval and p-values are also shown

Features, n (%)	No MACE n = 44574	MACE n = 365	OR (95% CI)	P Value	Features	No MACE n = 44574	MACE n = 365	OR (95% CI)	P Value
Age (>75 years)	15,958 (35.8)	188 (51.5)	1.9 (1.5-2.3)	<0.001	Diabetes				
Year of surgery					No	35080 (78.7)	263 (72.1)	Reference	
2011-2013	15,569 (34.9)	140 (38.4)	Reference		Insulin dependent	2808 (6.3)	38 (10.4)	1.1 (0.8-1.4)	0.484
2014-2016	29,005 (65.1)	225 (61.6)	0.9 (0.7-1.1)	0.172	Noninsulin dependent	6686 (15.0)	64 (17.5)	1.3 (1.0-1.7)	0.081
Diagnosis					Functional status				
BPH	34,126 (76.6)	238 (65.2)	Reference		Independent	42774 (96.0)	331 (90.7)	Reference	
Other	7952 (17.8)	98 (26.8)	1.8 (1.4-2.2)	<0.001	Partially dependent	1200 (2.7)	25 (6.8)	2.7 (1.7-4.0)	<0.001
Prostate Cancer	2496 (5.6)	29 (7.9)	1.7 (1.1-2.5)	0.010	Totally dependent	185 (0.4)	5 (1.4)	3.5 (1.2-7.7)	0.006
Surgical procedure					Unknow	415 (0.9)	4 (1.1)	1.2 (0.4-2.9)	0.664
TURP	29,588 (66.4)	266 (72.9)	Reference		Respiratory disorders	4826 (10.8)	68 (18.6)	1.9 (1.4-2.5)	<0.001
PVP	12,737 (28.6)	85 (23.3)	0.7 (0.6-0.9)	0.017	Recent congestive heart failure	414 (0.9)	15 (4.1)	4.6 (2.6-7.5)	<0.001
Enucleation	2249 (5.0)	14 (3.8)	0.7 (0.4-1.1)	0.181	Chronic steroid use	1164 (2.6)	21 (5.8)	2.3 (0.3-3.5)	<0.001
Race					Weight loss (>10%)	280 (0.6)	3 (0.8)	1.3 (0.3-3.5)	0.642
Caucasian	29370 (65.9)	230 (63)	Reference		Bleeding disorders	1606 (3.6)	29 (7.9)	2.3 (1.5-3.3)	<0.001
African-American	2461 (5.5)	26 (7.1)	1.3 (0.9-2.0)	0.150	Transfusions	337 (0.8)	24 (6.6)	9.2 (5.9-13.9)	<0.001
Other	1520 (3.4)	11 (3.0)	0.9 (0.5-1.6)	0.799	SIRS or sepsis	407 (0.9)	23 (6.3)	7.3 (4.7-11.3)	<0.001
Unknow	11,223 (25.2)	98 (26.8)	1.1 (0.9-1.4)	0.369	Metastatic cancer	677 (1.5)	19 (5.2)	3.6 (2.2-5.5)	<0.001
Anesthesia					Renal disorders	370 (0.8)	11 (3.0)	3.7 (2.0-6.8)	<0.001
General	34,125 (76.6)	273 (74.8)	Reference		Wound infections	308 (0.7)	9 (2.5)	3.6 (1.7-6.7)	<0.001
Locoregional	9500 (21.3)	83 (22.7)	1.1 (0.8-1.4)	0.484	Operation Time (min)				
Other	949 (2.1)	9 (2.5)	1.2 (0.6-2.2)	0.617	≤90	38212 (85.7)	291 (79.7)	Reference	
Body mass index					>90	6362 (14.3)	74 (20.3)	1.5 (1.2-2.0)	0.001
Normal	11,426 (25.6)	103 (28.2)	Reference		Smoking history	4765 (10.7)	44 (12.1)	1.1 (0.8-1.6)	0.401
Underweight	429 (1.0)	3 (0.8)	0.8 (0.2-2.1)	0.666	Hypertension	26962 (60.5)	256 (70.1)	1.5 (1.2-1.9)	<0.001
Overweight	18,422 (41.3)	150 (41.1)	0.9 (0.7-1.2)	0.429	Inpatients status	16552 (37.1)	220 (60.3)	2.6 (2.1-3.2)	<0.001
Obese	13,637 (30.6)	102 (27.9)	0.8 (0.6-1.1)	0.183	Nonelective surgery	3094 (6.9)	80 (21.9)	3.8 (2.9-4.8)	<0.001
Unknown	660 (1.5)	7 (1.9)	1.2 (0.5-2.4)	0.679	ASA score (>2)	23543 (52.8)	257 (70.4)	2.1 (1.7-2.7)	<0.001

ASA, American Society of Anesthesiologists; BPH, Benign prostatic hyperplasia; PVP, photoselective vaporization of the prostate; SIRS, Systemic inflammatory response syndrome; TURP, Transurethral resection of the prostate.

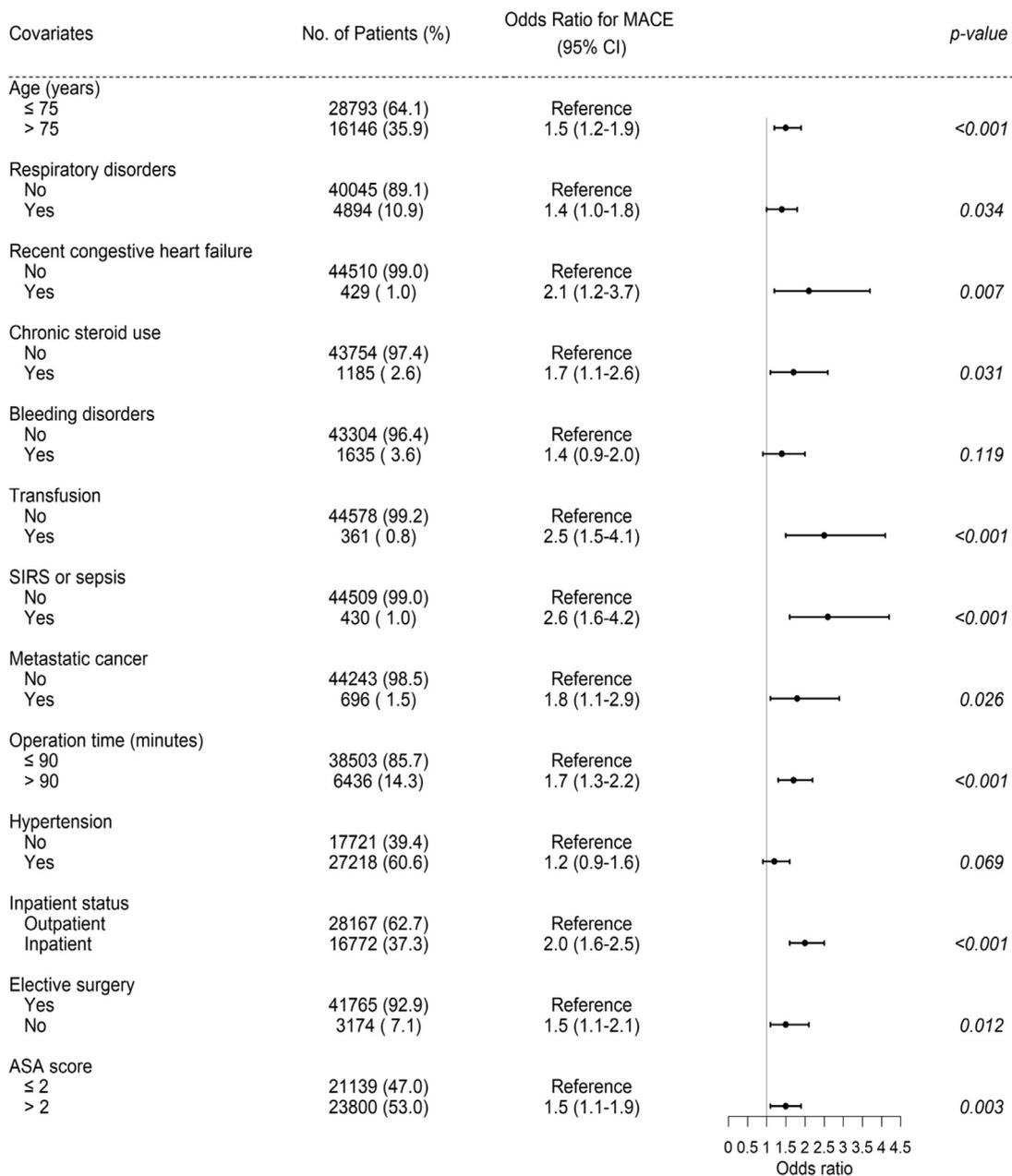


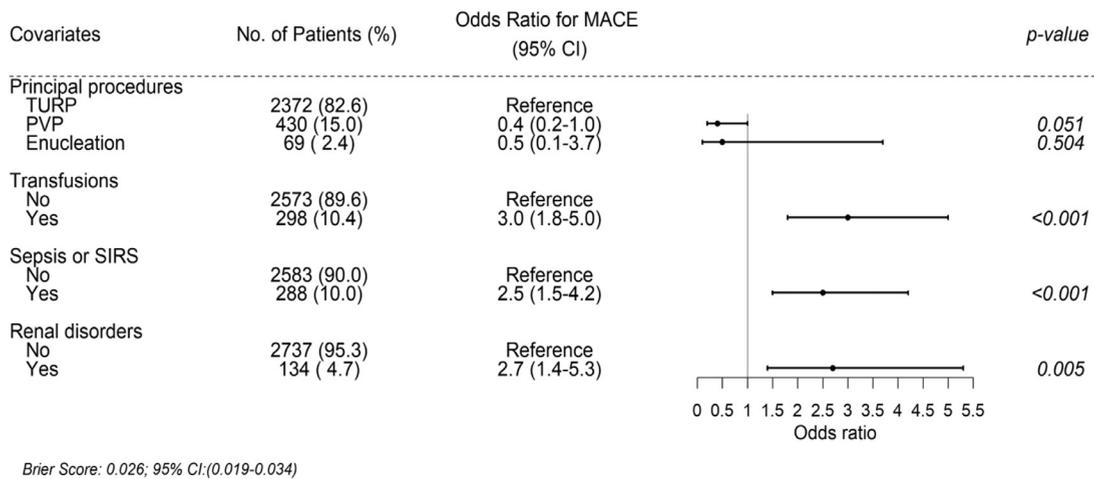
Figure 1. Forest plot depicting odds ratios (95% CI) derived from multivariable logistic regression models. Covariates selection relied on stepwise regression models. Within statistically significant variables at univariable logistic regression models in the overall population, only those that ensured an improvement in model performance, as indicated by the Akaike Information Criterion, were included. The Brier score after random sample bootstrapping tested the goodness of the generated model.

non-life-threatening conditions, to relief BOO bothersome symptoms. In selected patients other alternatives may be appealing.¹⁷

Second, our analyses showed that TPS are performed in almost one third of the cases to relief BOO in prostate cancer patients or with other-cause BOO (not directly conducive to BPH). This is of interest because previous analyses, differently from ours, did not test the effect of different diagnoses on the outcomes within the ACS-NSQIP.¹⁸⁻²² Remarkably, in univariable analyses prostate cancer and other causes patients experience higher

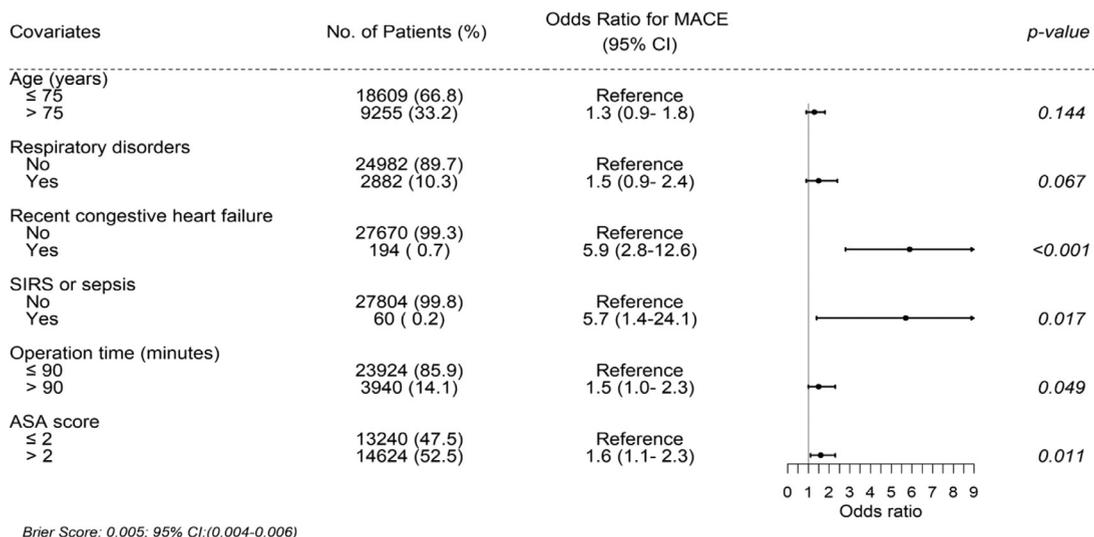
MACE rates. However, postoperative diagnosis does not add any further predictive value to the multivariable model according to AIC and its effect is not significant in multivariable models. This is important, since corroborate previous analyses investigating the safety and feasibility of TPS in prostate cancer patients.⁶

Third, MACE rates vary also according to operative variables, namely operation time and surgical procedure type. Our results corroborate those by Riedinger et al that also relied on ACS-NSQIP (2006-2016), but tested the effect of surgical duration only within TURP patients.²²



(a)

Figure 2a. Forest plot depicting odds ratios (95% CI) derived from multivariable logistic regression models within the group of inpatients undergoing non-elective transurethral surgery. Covariates selection relied on stepwise regression models. Within statistically significant variables at univariable logistic regression models in the overall population, only those that ensured an improvement in model performance, as indicated by the Akaike Information Criterion, were included. The Brier score after random sample bootstrapping tested the goodness of the generated model.



(b)

Figure 2b. Forest plot depicting odds ratios (95% CI) derived from multivariable logistic regression models within the group of outpatients undergoing elective transurethral surgery. Covariates selection relied on stepwise regression models. Within statistically significant variables at univariable logistic regression models in the overall population, only those that ensured an improvement in model performance, as indicated by the Akaike Information Criterion, were included. The Brier score after random sample bootstrapping tested the goodness of the generated model.

Authors showed that the increase of surgical duration had a detrimental effect on complications rates after TURP.²² Interestingly, these findings do not apply only to TURP, but to all the TPS procedures. Several hypotheses were formulated to explain MACE after TPS. For instance, Bell et al showed a catecholamine-mediated hypercoagulable prothrombotic state after TURP as a physiological response to stress.²³ Actually, fluid absorption during

TPS²⁴⁻²⁶ may lead to circulatory system overload and to hemodilution, which could be a coagulation system trigger. However, several pathways may concur in MACE occurrence. Different TPS types may be associated with different stress types and physiological responses. However, due to the dataset retrospective nature, we are not able to specifically determine the weight of patient selection¹⁸ vs body stress responses to fully explain MACE

Table 2. Descriptive postoperative outcomes and complications in patients who underwent transurethral surgery of the prostate stratified according to Major Acute Cardiovascular Events (MACE) occurrence. Data are reported as frequencies (%) and mean \pm standard deviation (SD).

Features, n (%)	No MACE n = 44,574	MACE n = 365	P Value Chi-Square Test
Length of stay (days), mean \pm SD	1.7 \pm 5.2	5.6 \pm 9.2	<0.001*
Postoperative pneumonia	146 (0.3)	30 (8.2)	<0.001
Intubation	49 (0.1)	42 (11.5)	<0.001
Acute renal failure	56 (0.1)	9 (2.5)	<0.001
Urinary tract infection	2158 (4.8)	49 (13.4)	<0.001
Intra- and postoperative transfusions	660 (1.5)	42 (11.5)	<0.001
Sepsis	368 (0.8)	20 (5.5)	<0.001
Septic shock	85 (0.2)	26 (7.1)	<0.001
Still in hospital >30 days			<0.001
No	40,956 (91.9)	330 (90.4)	
Yes	65 (0.1)	7 (1.9)	
Unknown	3553 (8.0)	28 (7.7)	
Reoperation	852 (1.9)	46 (12.6)	<0.001
Readmission	2411 (5.4)	187 (51.2)	<0.001
Death	141 (0.3)	52 (14.2)	<0.001

* Student t test for unpaired data MACE vs No MACE.

rates differences according to TPS type shown in the overall and sensitivity analyses. Thus, as NICE guidelines suggested, prospective studies should be planned.⁹ However, to the best of our knowledge none of the available prospective randomized trial comparing different TPS included the cardiovascular safety as primary outcome. Moreover, population-based studies may be the only analyses powered enough to test MACE predictors.

Fourth, the ACS-NSQIP TPS population is heterogeneous. Indeed, metastatic cancer patients as well as patients who need transfusion or had SIRS or sepsis were deemed eligible to TPS. Furthermore, a proportion of patients underwent nonelective surgery. This is surprising, since the main indication of TPS is to relieve bothersome BOO/LUTS. In those patients MACE rates are invariably higher, even after stepwise selection and multivariable adjustment. These findings and others, namely the higher MACE rates in older patients as well as in those with preoperative chronic and acute conditions, corroborate the considerations by Deveraux et al about preoperative, intraoperative, and postoperative factors associated with perioperative MACE in patients undergoing major non-cardiac surgery.²⁷ Similarly, more demanding surgical procedures (>90 minutes) are also associated with higher MACE rates. Although MACE are uncommon, it is fundamental at the time of patient selection to include only those patients in whom a TPS may led to a great benefit in terms of quality of life and avoid surgery in highest risk patients, when it could be postponed. Moreover, careful monitoring after surgery, in particular for those at highest risk, and a prompt MACE management are mandatory.²⁷

Despite, the goodness of our models was tested according to Brier test²⁸ and internally validated, the present study is not devoid of limitations. First, MACE definition varies across different studies, and no clear consensus is available.²⁹ Despite the use of an aggregate endpoint is debated, we relied on such primary outcome definition

with the purpose to evaluate the potential utility and hazardousness of TPS in several patients' settings. With this view, our definition of MACE clearly define those that are at immediate risk of serious events, even death, in whom perform this kind of surgical procedure should be avoided in absence of mandatory indications. Second, ACS-NSQIP population may not represent all TPS candidates. Indeed, the ACS-NSQIP hospitals are large teaching hospitals with more quality-related accreditations and financial resources.³⁰ The impact of hospital volume is well known and differences may exist according to caseload or teaching status.³¹ Third, both Current Procedural Terminology codes and the data collection within the datasets may be subjected to coding errors.²⁰ Moreover, it is plausible that some of complications happened outside the ACS-NSQIP participating centers may not be reported. Fourth, we have no information about the reasons why patients were treated with one of the included TPS instead of another, or even why patients were considered eligible to TPS. In particular we have no information about previous treatment for prostate cancer patients (eg, radiotherapy, androgen deprivation therapy, active surveillance, or watchful waiting). Fifth, preoperative prostate gland size, PSA level, symptom score, and other clinically important variables are not available in the dataset. Sixth, details regarding the type of laser used or the type of TURP performed are also lacking. Finally, only patients who underwent a procedure were included and no comparison with those who did not accept the risk of surgery is possible.²⁸

In conclusion, up to 1% of patients undergoing TPS experience MACE. MACE is burdened by high mortality rates (up to 14% in MACE patients) and longer length of stay. Proper patient selection and postoperative monitoring are deemed necessary to reduce MACE incidence and mortality rates. Moreover, surgical technique used, especially in high risk patients, may have an effect on MACE rates. Thus, future prospective studies are necessary to investigate

the possible advantage of laser surgeries in this specific patients' subset.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.urology.2019.05.014>.

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