Perioperative stroke and myocardial infarction in urologic surgery

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Introduction: *Perioperative stroke and myocardial infarction are uncommon but devastating thromboembolic complications. There is no comprehensive study detailing these complications for urologic procedures. The primary aim of this study is to determine which urologic procedures and patients carry the highest risk of perioperative stroke and myocardial infarction.*

Materials and methods: *The National Surgical Quality Improvement Program data set was reviewed from 2008-2017. Procedures coded under the urology specialty were included and patients who had a perioperative stroke or myocardial infarction were identified. CPTs were stratified into clinically relevant procedure groups. Two multivariable logistic regression analyses were performed to determine preoperative and procedural risk factors for developing perioperative stroke or myocardial infarction. A multivariable logistic regression analysis was performed to determine the association between these complications and 30-day mortality.*

Results: *A total of 281,744 cases were included, identifying 392 strokes (0.14%) and 1,016 myocardial infarctions (0.36%). Age ≥ 70, hypertension, and disseminated cancer were the strongest preoperative risk factors for perioperative stroke or myocardial infarction. Cystectomy was the highest risk urologic procedure (stroke: OR 3.3, 95%CI 2.3-4.8; MI: OR 7.2, 95%CI 5.6-9.1). Thirty-day mortality was dramatically worse for patients who had a perioperative stroke or myocardial infarction.*

Conclusions: *Perioperative stroke and myocardial infarction were confirmed to be uncommon but devastating complications of urologic surgery, with incidence of 0.14% and 0.36%, respectively. Cystectomy was the highest risk urologic procedure. Perioperative stroke and myocardial infarction were strongly associated with age ≥ 70, hypertension, and disseminated cancer.*

Key Words: postoperative complications, stroke, myocardial infarction, urology

Introduction

Perioperative stroke and myocardial infarction (MI) are uncommon but devastating thromboembolic complications that carry significant risk of mortality in the immediate postoperative period.[1,2] Many common urologic conditions have increased incidence in the elderly, often requiring urologists to perform operations on geriatric patients.[3] Additionally, several urologic malignancies are associated with smoking and/or obesity; risk factors that overlap with those of thromboembolic diseases.[4-8] The result is that urologists are frequently operating on patients who are at a significant risk for perioperative stroke and MI.

Despite this fact, there currently is no comprehensive study assessing perioperative stroke and MI risk across a broad spectrum of urologic procedures. There are several published studies regarding stroke and MI risk in non-cardiac, non-neurologic surgeries, but the vast majority of the cases included in these reports are non-urologic.[9-13] A urology-specific assessment would clarify which procedures and patients carry the highest risk,

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potentially facilitating targeted preoperative assessments with the goal of preventing these complications.

The primary aim of this study is to determine which urologic procedures and patients carry the highest risk of perioperative stroke and MI. The secondary aim is to determine the association between perioperative stroke and MI and 30-day mortality.

Materials and methods

NSQIP data set

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database was reviewed from 2008-2017. NSQIP is a validated outcome-based clinical registry of postoperative complications for patients who undergo surgery at over 700 participating hospitals. Ambulatory surgery centers are not included in the data set, but outpatient surgery units within a participating hospital may be sampled. NSQIP collects data on a representative sample of patients undergoing major surgery from member hospitals. Highly trained abstractors collect patient demographics, preoperative risk factors, surgical variables, and morbidity and mortality. The reproducibility of this data abstraction is periodically checked by repeat abstraction of a sample.

Study population

This study was conducted after exemption was granted by the local Institutional Review Board. Procedures coded in NSQIP under the Urology specialty from 2008-2017 were included in the analysis. Patients missing data for the primary CPT code were excluded.

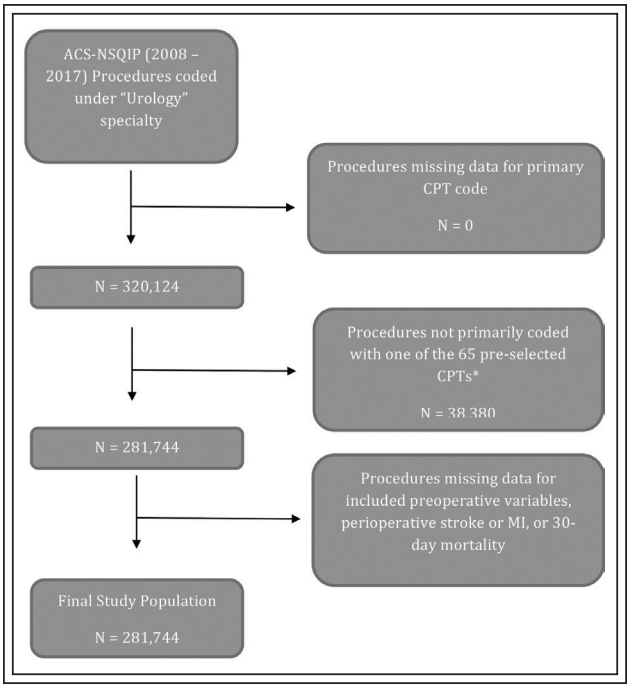

Figure 1. CONSORT diagram.

Patients were included whose primary CPT code matched one of 65 pre-selected CPTs from 11 clinically relevant procedure groups, as detailed in Table 1. Patients missing data for preoperative comorbidities, procedural details, perioperative complications, or perioperative mortality were excluded. The remaining patients were included as the final study population, Figure 1.

TABLE 1. **Included CPT codes for each procedure group**

Procedure group	**CPTs**
Endoscopic prostate	52500, 52601, 52648, 52630, 52649
Endoscopic bladder	52234, 52235, 52240, 52204, 52224
Endoscopic ureter	52344, 52354, 52352, 52353, 52355
Female genital surgery	57288, 57240, 57260, 53500, 53230, 57320
Male genital surgery	53440, 54530, 51040, 55873, 53445, 55040, 54520, 54840, 55530, 55250, 55400, 54900, 54360, 54405, 54440, 53410, 53215
Prostatectomy (laparoscopic)	55866
Prostatectomy (open)	55845, 55842, 55840
Nephrectomy (laparoscopic)	50545, 50543, 50546, 50548, 50547
Nephrectomy (open)	50230, 50240, 50220, 55225, 50234, 50236, 50320
Cystectomy	51595, 51597, 51590, 51596, 51550, 51555, 51570, 51575, 51580, 51585
Retroperitoneal lymph node dissection	38780

Definitions

Perioperative stroke is defined in the NSQIP as "Patient develops an embolic, thrombotic, or hemorrhagic vascular accident or stroke with motor, sensory, or cognitive dysfunction (e.g., hemiplegia, hemiparesis, aphasia, sensory deficit, impaired memory) that persists for 24 or more hours within 30 days of an operation".

Perioperative MI is defined in NSQIP as "An acute MI which occurred intraoperatively or within 30 days following surgery as manifested by one of the following: 1) documentation of ECG changes indicative of acute MI (one or more of the following): ST elevation > 1 mm in two or more contiguous leads; New left bundle branch block; New q-wave in two of more contiguous leads. 2) New elevation in troponin greater than 3 times upper level of the reference range in the setting of suspected myocardial ischemia. 3) Physician diagnosis of MI."

"Days from Operation to Death" is recorded up to 30 days postoperatively; thus, 30-day mortality was defined as any entry in this field from 0 to 30. There is no information regarding the exact cause of death. All preoperative risk factors included in this analysis are coded into the NSQIP data set as described, in a Yes/No manner.

Statistical analyses

Patients were stratified according to who did and did not have a perioperative stroke or MI, and baseline characteristics were described. Baseline patient and procedure characteristics were compared between groups using the Student's t-test, chi-square test, or analysis of variance testing, when appropriate.

Two separate logistic regression multivariable analyses were then performed for the outcomes of perioperative stroke and MI, using the following covariates: age (greater than or less than 70), sex, race, BMI (greater than or less than 30), several preoperative comorbidities (hypertension, COPD, active smoking, diabetes mellitus, disseminated cancer, and heart failure), and procedure group as defined in Table 1. ASA class was not included as a covariate due to significant co-linearity between this variable and the other included preoperative variables.

A logistic regression multivariable analysis was then performed for the outcome of 30-day mortality, using the following covariates: perioperative stroke, perioperative MI, age (greater than or less than 70), sex, race, BMI (greater than or less than 30), several preoperative comorbidities (hypertension, COPD, active smoking, diabetes mellitus, disseminated cancer, and heart failure), and procedure group as defined in Table 1.

Statistical significance for all analyses was defined as a two-tailed alpha risk of 0.01 or less. Statistical analysis was performed using Stata (version 16.1, StataCorp, College Station, TX, USA).

Results

Study population

A total of 320,124 patients were identified in NSQIP who underwent a urologic procedure from 2008-2017. Zero patients were missing data for primary CPT; 281,744 of the remaining procedures had a primary CPT matching one of the 65 pre-selected CPTs from 11 clinically relevant procedure groups, as detailed in Table 1. Zero patients were missing data for the included preoperative risk factors, perioperative stroke or MI, or 30-day mortality. The remaining 281,744 patients comprised the final study population, Figure 1.

Overall, 392 patients (0.14%) had a perioperative stroke, 1,106 patients (0.36%) had a perioperative MI, and 1,408 patients (0.50%) died within 30 days of their surgery.

Baseline characteristics

On univariable analysis, patients who had a perioperative stroke were older, had a higher ASA classification, and were more likely to have hypertension, COPD, diabetes, disseminated cancer, and heart failure. Patients who had a perioperative MI were more likely to be older, white race, higher ASA classification, and were more likely to have hypertension, COPD, diabetes, disseminated cancer, and heart failure, Table 2.

Patient and procedural risk factors for perioperative stroke and MI

Multivariable logistic regression analysis revealed that the preoperative risk factors most strongly associated with perioperative stroke were age ≥ 70 (OR 2.5, 95% CI 2.0-3.2), hypertension (OR 1.9, 95% CI 1.5-2.5), and disseminated cancer (OR 2.2, 95% CI 1.4-3.3). The preoperative risk factors most strongly associated with perioperative MI were age ≥ 70 (OR 2.2, 95% CI 1.9-2.6), hypertension (OR 2.0, 95% CI 1.7-2.5), disseminated cancer (OR 1.5, 95% CI 1.1-2.0), and heart failure (OR 2.9, 95% CI 2.0-4.4), Table 3.

The procedure groups most strongly associated with perioperative stroke, as compared with endoscopic prostate procedures, were cystectomy (OR 3.3, 95% CI 2.3-4.8), and open nephrectomy (OR 2.8, 95% CI 1.9-4.1). The procedure groups most strongly associated with perioperative MI, as compared with endoscopic prostate procedures, were cystectomy (OR 7.2, 95%

TABLE 2. **Baseline patient and procedural demographics, stratified by perioperative stroke and MI status**

	No stroke (n = 281,352)	Stroke (n = 392)	p value	No MI (n = 280,728)	MI (n = 1,016)	p value
Age (mean, SD)	64.9 (13.3)	72.0 (10.3)	< 0.01	64.9 (13.3)	72.4 (9.9)	< 0.01
Male sex (n, %)	227,687 (81.0)	313 (79.9)	0.58	227,148 (80.9)	852 (83.9)	0.02
Race (n,%)			0.07			< 0.01
White	187,536 (81.0)	268 (82.0)		187,092 (80.9)	712 (89.3)	
Black	20,914 (9.0)	40 (12.2)		20,898 (9.0)	56 (7.0)	
Hispanic	15,663 (6.8)	16 (4.9)		15,669 (6.8)	10 (1.3)	
Other	7,548 (3.3)	3 (0.9)		7,532 (3.3)	19 (2.4)	
BMI (mean, SD)	29.7 (6.2)	29.0 (6.2)	0.02	29.7 (6.2)	29.4 (6.4)	0.13
ASA class (n, %)			< 0.01			< 0.01
1	12,759 (4.5)	3 (0.8)		12,756 (4.6)	6 (0.6)	
2	124,242 (44.3)	82 (20.9)		124,174 (44.3)	150 (14.8)	
3	132,369 (47.1)	248 (63.3)		131,926 (47.1)	691 (68.0)	
4	11,378 (4.1)	59 (15.1)		11,270 (4.0)	167 (16.4)	
5	38 (0.01)	0 (0)		36 (0.01)	2 (0.2)	
Hypertension (n, %)	157,761 (56.1)	305 (77.8)	< 0.01	157,255 (56.0)	811 (79.8)	< 0.01
COPD (n, %)	15,032 (5.3)	36 (9.2)	< 0.01	14,942 (5.3)	126 (12.4)	< 0.01
Smoking (n, %)	44,925 (16.0)	70 (17.9)	0.31	44,818 (16.0)	177 (17.4)	0.21
Diabetes (n, %)	50,871 (18.1)	107 (27.3)	< 0.01	50,652 (18.0)	326 (32.1)	< 0.01
Disseminated cancer (n, %)	6,977 (2.5)	32 (8.2)	< 0.01	6,951 (2.5)	58 (5.7)	< 0.01
Heart failure (n, %)	1,825 (0.7)	8 (2.0)	< 0.01	1,799 (0.6)	34 (3.4)	< 0.01
Procedure group (n, %)			< 0.01			< 0.01
Endoscopic prostate	64,132 (22.8)	84 (21.4)		64,038 (22.8)	178 (17.5)	
Endoscopic bladder	43,846 (15.6)	61 (15.6)		43,783 (15.6)	134 (13.2)	
Endoscopic ureter	4,055 (1.4)	3 (0.8)		4,049 (1.4)	9 (0.9)	
Female genital surgery	13,925 (5.0)	1 (0.3)		13,919 (5.0)	7 (0.7)	
Male genital surgery	24,936 (8.9)	10 (2.6)		24,923 (8.9)	23 (2.3)	
Prostatectomy (laparoscopic)	48,909 (17.4)	41 (10.5)		48,862 (17.4)	88 (8.7)	
Prostatectomy (open)	10,898 (3.9)	11 (2.8)		10,876 (3.9)	33 (3.3)	
Nephrectomy (laparoscopic)	38,366 (13.6)	55 (14.0)		38,246 (13.6)	175 (17.2)	
Nephrectomy (open)	17,909 (6.4)	54 (13.8)		17,814 (6.4)	149 (14.7)	
Cystectomy	13,895 (4.9)	72 (18.4)		13,748 (4.9)	219 (21.6)	
RPLND	471 (0.17)	0 (0)		470 (0.17)	1 (0.10)	

MI = myocardial infarction; BMI = body mass index; ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; RPLND = retroperitoneal lymph node dissection

CI 5.6-9.1), open nephrectomy (OR 5.0, 95% CI 3.8-6.6), and laparoscopic nephrectomy (OR 3.0, 95% CI 2.3-3.9), Table 3.

30-day mortality associations

Patients who had a perioperative stroke or MI had substantially increased risk for death within 30 days of surgery (stroke: OR 16.6, 95% CI 11.9-23.7; MI: OR 12.0, 95% CI 9.4-15.4). Preoperative variables strongly associated with 30-day mortality were age ≥ 70 (OR 3.0, 95% CI 2.6-3.5), disseminated cancer (OR 6.4, 95% CI 5.4-7.4), and heart failure (OR 4.2, 95% CI 3.2-5.6). The procedure groups most strongly associated with 30-day mortality, as compared with endoscopic prostate procedures, were cystectomy (OR 4.1, 95% CI 3.3-5.1), open nephrectomy (OR 3.3, 95% CI 2.6-4.1), and laparoscopic nephrectomy (OR 1.6, 95% CI 1.3-2.0), Table 4.

TABLE 3. **Two separate logistic regression multivariable analyses for perioperative stroke or MI**

	Stroke		MI	
	OR (95% CI)	**p value**	**OR (95% CI)**	**p value**
Age ≥ 70	2.5 (2.0-3.2)	< 0.01	2.2 (1.9-2.6)	< 0.01
Male sex	0.9 (0.7-1.2)	0.38	1.5 (1.2-1.8)	< 0.01
Race				
White	Ref		Ref	
Black	1.5 (1.1-2.1)	0.02	0.8 (0.6-1.0)	0.05
Hispanic	0.9 (0.5-1.4)	0.56	0.2 (0.1-0.4)	< 0.01
Other	0.3 (0.1-0.8)	0.03	0.7 (0.4-1.1)	0.12
BMI ≥ 30	0.75 (0.6-0.9)	0.02	0.9 (0.8-1.1)	0.33
Hypertension	1.9 (1.5-2.5)	< 0.01	2.0 (1.7-2.5)	< 0.01
COPD	1.2 (0.8-1.8)	0.31	1.5 (1.2-1.9)	< 0.01
Smoking	1.3 (0.9-1.7)	0.14	1.1 (0.9-1.4)	0.2
Diabetes	1.3 (0.9-1.6)	0.07	1.7 (1.5-2.0)	< 0.01
Disseminated cancer	2.2 (1.4-3.3)	< 0.01	1.5 (1.1-2.0)	< 0.01
Heart failure	1.9 (0.9-4.1)	0.09	2.9 (2.0-4.4)	< 0.01
Procedure group				
Endoscopic prostate	Ref		Ref	
Endoscopic bladder	1.0 (0.7-1.4)	0.9	1.3 (1.0-1.7)	0.03
Endoscopic ureter	0.6 (0.2-1.9)	0.4	1.3 (0.7-2.6)	0.45
Female genital surgery	0.1 (0.1-0.7)	0.03	0.4 (0.2-1.2)	0.1
Male genital surgery	0.4 (0.2-0.9)	0.03	0.7 (0.4-1.1)	0.16
Prostatectomy (laparoscopic)	1.0 (0.7-1.6)	0.9	1.4 (1.0-1.9)	0.03
Prostatectomy (open)	1.0 (0.5-2.4)	0.9	2.3 (1.4-3.7)	< 0.01
Nephrectomy (laparoscopic)	1.2 (0.8-1.8)	0.3	3.0 (2.3-3.9)	< 0.01
Nephrectomy (open)	2.8 (1.9-4.1)	< 0.01	5.0 (3.8-6.6)	< 0.01
Cystectomy	3.3 (2.3-4.8)	< 0.01	7.2 (5.6-9.1)	< 0.01
RPLND	N/A	N/A	2.8 (0.4-20.6)	0.3

MI = myocardial infarction; BMI = body mass index; COPD = chronic obstructive pulmonary disease; RPLND = retroperitoneal lymph node dissection

Discussion

For urologic procedures, the perioperative incidence of stroke and MI were 0.14% and 0.36%, respectively. Cystectomy, open nephrectomy, and laparoscopic nephrectomy were the procedure groups with the highest risk of these complications. Patients with preoperative age ≥ 70, hypertension, and disseminated cancer were at the highest risk. Perioperative stroke and MI were confirmed to be devastating events, carrying a 17-fold and 12-fold increased odds of death within 30 days of surgery, respectively, on multivariable analysis.

The overall incidence of perioperative stroke for urologic procedures (0.14%) was identical to that reported for other non-cardiac procedures in NSQIP.[10] The incidence of perioperative MI for urologic procedures (0.36%) is lower than that reported for a NSQIP cohort of non-cardiac procedures that excluded "low-risk" procedures (1.10%).[9] These incidence rates are sensitive to the proportion of high-risk procedures in the cohort studied. The low incidence of perioperative MI in this study is influenced by the relatively low proportion of the highest risk procedure, cystectomy, in the data set (13,967 cystectomies, 5.0% of procedures).

The risk of perioperative stroke and MI has been previously described for radical cystectomy.[14,15] Sathianathen et al in 2018 described that the risk of MI is significantly higher in smokers undergoing radical cystectomy than for non-smokers (2.0% versus 0.4%, respectively, p < 0.001), while the risk of stroke was not

TABLE 4. **Multivariable logistic regression analysis for 30-day postoperative mortality**

	OR (95% CI)	p value
Age ≥ 70	3.0 (2.6 - 3.5)	< 0.01
Male sex	1.0 (0.9-1.2)	0.63
Race		
White	Ref	
Black	1.4 (1.1-1.7)	< 0.01
Hispanic	1.0 (0.8-1.4)	0.86
Other	1.1 (0.8-1.5)	0.74
BMI ≥ 30	0.8 (0.7-0.9)	< 0.01
Hypertension	1.2 (1.0-1.3)	0.03
COPD	1.8 (1.5-2.1)	< 0.01
Smoking	1.2 (1.0-1.4)	0.03
Diabetes	1.2 (1.0-1.3)	0.03
Disseminated cancer	6.4 (5.4-7.4)	< 0.01
Heart failure	4.2 (3.2-5.6)	< 0.01
Procedure group		
Endoscopic prostate	Ref	
Endoscopic bladder	1.9 (1.6-2.3)	< 0.01
Endoscopic ureter	1.3 (0.9-2.1)	0.3
Female genital surgery	0.3 (0.1-0.6)	< 0.01
Male genital surgery	1.0 (0.8-1.4)	0.8
Prostatectomy (laparoscopic)	0.6 (0.4-0.8)	< 0.01
Prostatectomy (open)	1.4 (0.9-2.3)	0.12
Nephrectomy (laparoscopic)	1.6 (1.3-2.0)	< 0.01
Nephrectomy (open)	3.3 (2.6-4.1)	< 0.01
Cystectomy	4.1 (3.3-5.1)	< 0.01
RPLND	1.8 (0.4-7.2)	0.43
Stroke	16.8 (11.9-23.7)	< 0.01
MI	12.0 (9.4-15.4)	< 0.01

BMI = body mass index; COPD = chronic obstructive pulmonary disease; RPLND = retroperitoneal lymph node dissection; MI = myocardial infarction

affected by smoking status.[14] Yu et al in 2020 described a 14.1% risk of myocardial injury in a cohort of high-risk patients undergoing radical cystectomy in Korea.[15] Though the perioperative morbidity of cystectomy has been well described, assessing the risk of these complications within the context of other urologic procedures highlights the importance of targeting these patients for more extensive preoperative assessment and optimization. Patients who underwent a cystectomy had 3.3-fold higher odds of a perioperative stroke and 7.2-fold higher odds of a perioperative MI, as compared with the endoscopic prostate procedure group.

In addition to stroke and MI, venous thromboembolism represents a potentially life-threatening perioperative complication that cystectomy patients are at an relatively high risk of experiencing.[16] In 2014, VanDlac et al described that patients undergoing radical cystectomy were at a 6% risk of venous thromboembolism, and those patients were subsequently at a 6% risk of 30-day mortality.[16] The present study was not designed to assess perioperative venous thromboembolism.

Consistent with prior reports of non-cardiac surgery, urologic patients with advanced age, hypertension, disseminated cancer, and heart failure were at the highest risk of perioperative stroke and MI.[9-13] Knowledge that a patient is high-risk for one of these complications can guide additional preoperative assessments such as carotid duplex ultrasound or cardiac stress testing, especially if they are scheduled to undergo a high-risk procedure.

A limitation to this analysis is that NSQIP collects data on a selection of procedures and does not track every procedure performed by participating hospitals, resulting in a distribution of procedures in the data set that may not reflect the actual distribution of procedures nationally. For example, common urologic procedures such as circumcision and most lithotripsy/lithotomy cases are not captured in NSQIP. Additionally, NSQIP does not track perioperative outcomes beyond 30 days, potentially missing complications that occur beyond this timeframe. Given the retrospective nature of this study, the analysis is limited to the data points available in NSQIP. For example, data regarding atrial fibrillation and anticoagulation status would contribute significantly to the perioperative stroke analysis, and knowledge of preoperative angina or prior cardiac events would contribute to the MI analysis. Additionally, NSQIP only captures clinically apparent complications, and would not identify subclinical cardiac or neurologic ischemic events. Finally, the 30-day mortality figures do not include details regarding the exact cause of death.

Conclusions

The incidence of perioperative stroke and MI was 0.14% and 0.36%, respectively. Cystectomy and open nephrectomy were found to be the highest risk urologic procedures for these complications. Patients with baseline age ≥ 70, hypertension, disseminated cancer, and heart failure are at the highest risk for perioperative stroke and MI. The risk of 30-day mortality is dramatically increased for patients who have a perioperative stroke or MI. □

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