Complications of Recognized and Unrecognized Iatrogenic Ureteral Injury at Time of Hysterectomy: A Population Based Analysis

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Purpose: Ureteral injury represents an uncommon but potentially morbid surgical complication. We sought to characterize the complications of iatrogenic ureteral injury and assess the effect of recognized vs delayed recognition on patient outcomes.

Materials and Methods: Patients who underwent hysterectomy were identified in the Healthcare Cost and Utilization Project California State Inpatient Database for 2007 to 2011. Ureteral injuries were identified and categorized as recognized—diagnosed/repaired on the day of hysterectomy and unrecognized—diagnosed/repaired postoperatively. We assessed the outcomes of 90-day hospital readmission as well as 1-year outcomes of nephrostomy tube placement, urinary fistula, acute renal failure, sepsis and overall mortality. The independent effects of recognized and unrecognized ureteral injuries were determined on multivariate analysis.

Results: Ureteral injury occurred in 1,753 of 223,872 patients (0.78%) treated with hysterectomy and it was unrecognized in 1,094 (62.4%). The 90-day readmission rate increased from a baseline of 5.7% to 13.4% and 67.3% after recognized and unrecognized injury, respectively. Nephrostomy tubes were required in 2.3% of recognized and 23.4% of unrecognized ureteral injury cases. Recognized and unrecognized ureteral injuries independently increased the risk of sepsis (aOR 2.0, 95% CI 1.2–3.5 and 11.9, 95% CI 9.9–14.3) and urinary fistula (aOR 5.9, 95% CI 2.2–16 and 124, 95% CI 95.7–160, respectively). During followup unrecognized ureteral injury increased the odds of acute renal insufficiency (aOR 23.8, 95% CI 20.1–28.2) and death (1.4, 95% CI 1.03–1.9, p = 0032).

Conclusions: Iatrogenic ureteral injury increases the risk of hospital readmission and significant, potentially life threatening complications. Unrecognized ureteral injury markedly increases these risks, warranting a high level of suspicion for ureteral injury and a low threshold for diagnostic investigation.

Key Words: ureter, injuries, hysterectomy, intraoperative complications, iatrogenic disease

URETERAL injury represents an uncommon but potentially morbid complication of abdominal and pelvic surgery. Injury can occur as a result of

transection, crush injury, obstruction from inadvertent ligation or thermal injury. Prior reports have noted that gynecologic surgery accounted for

approximately 50% of iatrogenic ureteral injuries, given the proximity of the ureter to the ovary and uterine artery.[1] The rate of injury at hysterectomy ranges from 0.3% to 1.8% of cases.[2-5]

While identifying ureteral injury intraoperatively allows for prompt repair, delayed diagnosis was reported to account for 67% to 87% of ureteral injury cases.[1,6,7] In clinical and legal case series these injuries have been associated with chronic renal insufficiency secondary to obstruction,[6,8] urinoma formation[7] and urinary fistulas.[7,9]

The purpose of this study was to further characterize the long-term complications associated with ureteral injury at hysterectomy and determine the impact of intraoperative recognition vs delayed diagnosis on patient outcomes.

PATIENTS AND METHODS

Data Source
We used the HCUP SID for California, including 2007 to 2011. The development of HCUP SID was sponsored by AHRQ (Agency for Healthcare Research and Quality) to inform health related decisions.[10] HCUP SID includes patient discharge records for all payers with each SID unique to the individual state. Patient data, which are de-identified and protected, include more than 100 clinical and nonclinical variables. Using a unique linkage variable available in the database patients can be followed longitudinally with time and across inpatient admissions.[11]

Patient Selection
To study the long-term sequelae of ureteral injury we chose an index case of hysterectomy. Ureteral injury is a well documented and studied complication of this procedure with an established rate of 0.3% to 1.8% of cases.[2-5] Hysterectomy cases in adults (age 18 years or greater) were identified by the ICD9-CM codes that were previously used in studies of this population.[12] Supplementary table 1 (http://jurology.com/) lists all ICD9-CM codes used in our study.

Patients who underwent cesarean section on the same day as hysterectomy were also identified. Patients treated with anterior exenteration or pelvic evisceration were excluded from analysis, given the anticipated ureteral manipulation during these procedures. Further, to avoid outcome confounding patients with a present on admission diagnosis of hydronephrosis, hydroureter and/or ureteral stricture at the time of hysterectomy were excluded from analysis. Using the unique patient linkage variable inherent in the data set we identified inpatient readmissions within 1 year following the index hysterectomy admission.

Outcome Measures
Patients were assessed for a new diagnosis of ureteral injury during the index hysterectomy admission or at any subsequent inpatient admission within 1 year postoperatively. Ureteral injury was defined as a new diagnosis of ureteral injury or surgical repair of ureteral injury (eg repair of ureteral laceration, ureteroureterostomy or ureteral reimplantation). Upon followup readmission a new diagnosis of hydroureter, hydronephrosis and/or ureteral obstruction/stricture without a concurrent diagnosis of nephrolithiasis were also included as these entities represent presenting signs of an unrecognized ureteral injury.

Ureteral injuries were further defined as recognized or unrecognized. Recognized ureteral injuries were identified and repaired the same day as hysterectomy was performed. Unrecognized ureteral injuries were identified and/or repaired on a day after hysterectomy was performed, during the same admission or upon readmission. Figure 1 shows the patient population and outcomes assessed in the study.

Patient baseline demographic characteristics and medical comorbidities were assessed (supplementary table 2, http://jurology.com/). The Charlson comorbidity score was calculated for each patient as a measure of overall medical comorbidity. Gynecologic preoperative diagnoses were also determined and grouped as benign, malignant, peripartum hemorrhage or other based on ICD9-CM codes (supplementary table 1, http://jurology.com/).

Additional outcomes specific to ureteral injuries were assessed in the populations with no ureteral injury, recognized ureteral injury and unrecognized ureteral injury. Patients were assessed for readmission within 90 days postoperatively. Additional outcomes assessed within 1 year postoperatively in each group included the identification of patients who required nephrostomy tube placement as well as new diagnoses of acute renal failure, sepsis and urinary tract fistula. Unadjusted mortality rates during year 1 postoperatively were determined.

Statistical Analysis
Descriptive statistics were performed. Continuous variables are reported as the median and IQR. The Wilcoxon rank sum test was performed to assess significance. The chi-square test was used for categorical variables. To determine the independent effects of recognized and unrecognized ureteral injuries on patient outcomes we fit separate multivariable logistic regression models by backward selection using the Akaike information criterion to optimize the model without overfitting and adjusted for confounding conditions. Stata®, version 13 was used for all statistical analysis with p <0.05 considered the threshold for statistical significance.

RESULTS
Between 2007 and 2011 in California 223,872 women underwent hysterectomy (fig. 1). Supplementary table 2 (http://jurology.com/) lists the baseline characteristics of the study population. The women had a median age of 47 years (IQR 42–54), 53.2% were Caucasian and 24.9% were Hispanic. Hysterectomy was performed for benign and malignant gynecologic diagnoses in 81.3% and 13.5% of cases, respectively.

Within 1 year postoperatively 1,753 women (0.78%) were diagnosed with ureteral injury following hysterectomy. Compared to patients without a ureteral
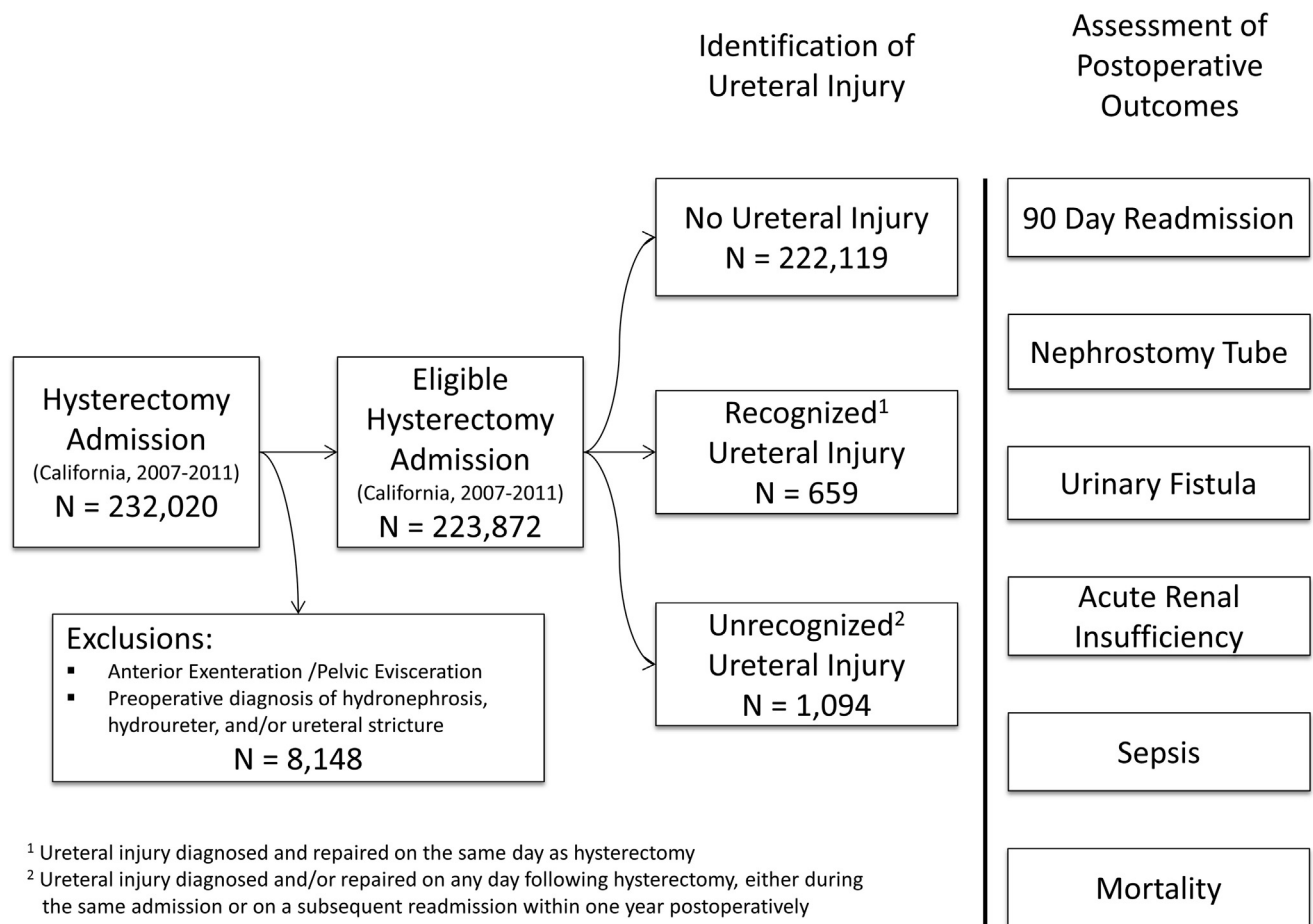
Figure 1. Flow chart of patients included in analysis and outcomes

injury diagnosis those with ureteral injury were more likely to have undergone hysterectomy for a malignant diagnosis (39.2% vs 13.3%, p <0.001). Supplementary table 3 (http://jurology.com/) shows patient characteristics stratified by ureteral injury diagnosis.

Of the ureteral injuries diagnosed in this study 1,094 (62.4%) were unrecognized. Compared to patients with a recognized ureteral injury, those with an unrecognized ureteral injury had a higher comorbid disease burden (Charlson comorbidity score 2 vs 0, p <0.001) and a malignant diagnosis. Supplementary table 4 (http://jurology.com/) lists the characteristics of patients with ureteral injury stratified by injury recognized vs unrecognized status.

Following hysterectomy the unadjusted 90-day readmission rate in patients without a diagnosed ureteral injury was 5.7%. The readmission rate increased significantly with a ureteral diagnosis whether it was recognized (13.4%) or unrecognized (67.3%). There was more nephrostomy tube placement in unrecognized ureteral injury cases than in recognized and no ureteral injury cases (23.4% vs

2.3% and 0.02%, respectively, table 1). Patients with unrecognized ureteral injury had higher unadjusted rates of sepsis (16.9%), acute renal insufficiency (28.0%) and urinary tract fistula (9.9%) as well as 1-year mortality (8.3%) compared to recognized and no ureteral injury patients (fig. 2). Compared to patients with a recognized ureteral injury that was repaired on the day of hysterectomy, patients with

Table 1. *Outcomes in patients treated with hysterectomy stratified by ureteral injury diagnosis and timing of recognition*

Outcomes	No. Ureteral Injury (%)		
	None	Recognized	Unrecognized
Overall	212,481	659	1,094
90-Day hospital readmission	12,177 (5.7)	85 (13.4)	736 (67.3)
Nephrostomy tube placement	36 (0.02)	15 (2.3)	256 (23.4)
Sepsis	1,499 (0.7)	23 (3.5)	185 (16.9)
Acute renal insufficiency	1,900 (0.9)	22 (3.3)	306 (28.0)
Urinary tract fistula	227 (0.1)	Censored*	108 (9.9)
Death	701 (0.3)	Censored*	91 (8.3)

Chi-square test for categorical variables and Kruskal-Wallis test for continuous variables all p <0.001.
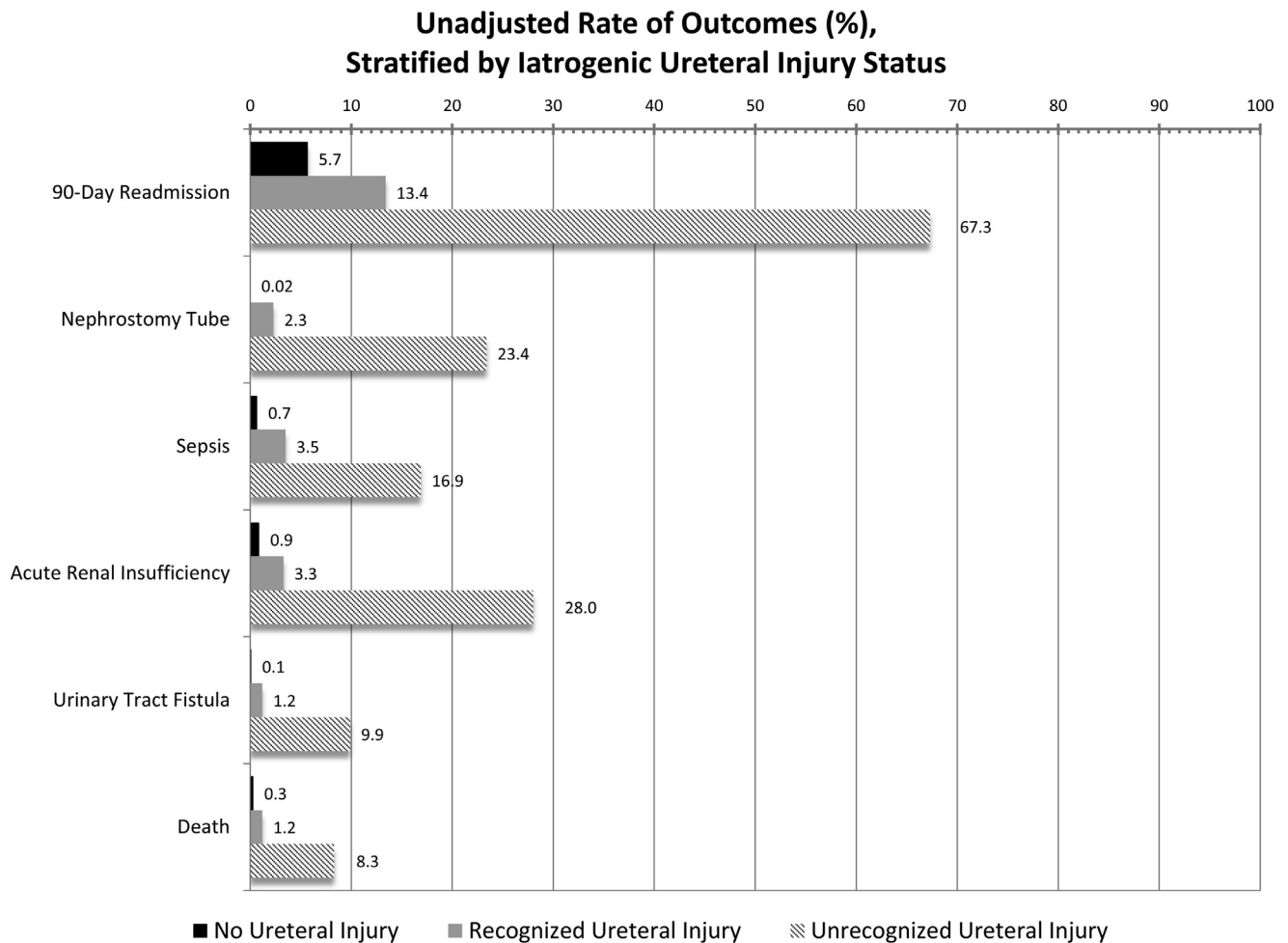* Absolute number censored due to data use restrictions prohibiting data reporting on 10 or fewer patients.

Unadjusted Rate of Outcomes (%), Stratified by Iatrogenic Ureteral Injury Status

Figure 2. Unadjusted rate of outcomes stratified by iatrogenic ureteral injury status

an unrecognized ureteral injury did not undergo definitive repair for a median 84 days (IQR 45–158) after hysterectomy.

On multivariate analysis the independent effect of ureteral injury status on the patient outcome was determined after controlling for patient factors, comorbidities, gynecologic diagnoses and surgical approaches (table 2). While recognized and unrecognized ureteral injuries increased the odds of postoperative complications following hysterectomy, this effect was more pronounced in cases of unrecognized injury. The odds of hospital 90-day readmission increased 1.5-fold and 24.2-fold for recognized and unrecognized ureteral injuries, respectively. Further, for recognized and unrecognized injuries there were increased odds of sepsis (aOR 2.0, 95% CI 1.2–3.5 and 11.9, 95% CI 9.9–14.3) and urinary fistula (aOR 5.9, 95% CI 2.2–16.0 and 124, 95% CI 95.7–160, respectively). Unrecognized ureteral injury increased the odds of acute renal insufficiency (aOR 23.8, 95% CI 20.1–28.2) as well as 1-year mortality (aOR 1.4, 95% CI 1.03–1.9, p = 0.032).

It is important to note that this risk was present with the model adjusted for the outcomes of sepsis and acute renal failure, which appeared to be the primary drivers of mortality in this population. These outcomes are known independent risk factors for mortality.

DISCUSSION

To our knowledge this is the first report of the multiple postoperative sequelae of iatrogenic ureteral injury in a population based analysis. Further, we assessed the effect of recognizing ureteral injury, demonstrating the magnitude of impact of an unrecognized ureteral injury on patient outcomes. Ureteral injury affected 1 in 128 patients who underwent hysterectomy in this study, consistent with prior reports in the literature.[2–5]

A diagnosis of ureteral injury contributed to an increased risk of several clinically significant outcomes, including postoperative 90-day readmission as well as postoperative outcomes during year 1

Table 2. *Analysis of outcomes following ureteral injury*

	Recognized Ureteral Injury		Unrecognized Ureteral Injury	
	OR (95% CI)	p Value	OR (95% CI)	p Value
90-Day hospital readmission:				
Unadjusted	2.0 (1.6—2.6)	<0.001	35.6 (31.4—40.4)	<0.001
Adjusted	1.5 (1.2—2.0)	0.002	24.2 (21.1—27.6)	<0.001
Sepsis:				
Unadjusted	3.6 (2.1—6.0)	<0.001	30.6 (26.0—36.1)	<0.001
Adjusted	2.0 (1.2—3.5)	0.009	11.9 (9.9—14.3)	<0.001
Acute renal failure:				
Unadjusted	2.6 (1.5—4.5)	<0.001	45.2 (39.3—51.8)	<0.001
Adjusted	1.3 (0.8—2.4)	0.3	23.8 (20.1—28.2)	<0.001
Nephrostomy tube placement:				
Unadjusted	67.1 (29.8—151.1)	<0.001	1,851 (1,304—2,628)	<0.001
Adjusted	66.0 (29.2—148.9)	<0.001	1,792 (1,244—2,591)	<0.001
Urinary tract fistula:				
Unadjusted	6.2 (2.3—16.8)	<0.001	109 (85.9—137)	<0.001
Adjusted	5.9 (2.2—16.0)	<0.001	124 (95.7—160)	<0.001
Death:				
Unadjusted	2.5 (1.04—6.1)	0.041	28.9 (23.1—36.2)	<0.001
Adjusted	0.8 (0.3—2.1)	0.6	1.4 (1.03—1.9)	0.032

Unadjusted logistic regression models show odds of each outcome for recognized and unrecognized ureteral injury vs patients without documented injury, and adjusted logistic regression models show odds of each outcome for recognized and unrecognized ureteral injuries vs patients without documented ureteral injury with models created by backward selection using Akaike Information Criterion to avoid overfitting.

such as nephrostomy tube placement, urinary tract fistula, acute renal insufficiency and sepsis even when recognized and repaired intraoperatively. The risk of each of these complications was markedly increased when ureteral injury went unrecognized.

Unrecognized ureteral injury is a morbid complication which occurred in 62.4% of all ureteral injury cases in our study. Estimates of delayed ureteral injury range from 67% to 87% of ureteral injury cases.[1,6,7] Patients with an unrecognized injury experienced a 67% 90-day readmission rate as well as severe medical conditions, including sepsis in 16.9% and acute renal failure in 28.0%. Patients also experienced increased rates of nephrostomy tube placement and urinary fistula (23.4% and 9.9%, respectively).

Given that intraoperative detection allowed for immediate repair with significantly lower complication rates (fig. 2), the implication of this work is that every effort should be made to detect these injuries prior to leaving the operating room. Two techniques that have been investigated to that end have been preoperative ureteral stent placement and postoperative cystoscopy.

To date preoperative ureteral stenting has not been associated with a significant reduction in the ureteral injury rate. In a prospective study by Chou et al 3,141 women undergoing gynecologic surgery were randomized to bilateral ureteral catheters or usual care with no difference in the overall rate of ureteral injury between the groups (1.2% vs 1.09%, p = 0.774).[13] However, it is interesting that injuries in the stented group were recognized when they were less severe, resulting in a lower rate of major repair needed in stented vs unstented patients (47% vs 76%, p = 0.01). This result is consistent with other established literature, suggesting that while prophylactic stenting does not prevent injury, it is useful for improving early recognition and immediate repair.[14,15]

Postoperatively cystoscopy with observation for ureteral efflux can be performed to assess ureteral patency with or without intravenous dye (eg indigo carmine or sodium fluorescein[16]) to improve ureteral jet visualization. Two prospective studies of universal cystoscopy with intravenous dye at hysterectomy revealed similar findings.[2,5] In the study by Vakili et al routine cystoscopy at the time of hysterectomy was prospectively performed in 471 women and it detected ureteral injury in 8 (1.7%).[2] Prior to cystoscopy only 1 ureteral injury (12.5%) was detected and reported as ureteral kinking while cystoscopy ultimately led to the detection and treatment of 4 transected ureters, 2 ligated ureters and 1 crushed ureter. Similarly in a prospective trial of universal cystoscopy at hysterectomy performed by Ibeanu et al ureteral injury was detected in 15 of 839 patients (1.8%).[5] Only 1 injury (6.7%) was detected visually prior to cystoscopy. In each report no unrecognized ureteral injury was noted.

Taken together, universal cystoscopy appears to be an effective way to detect otherwise unrecognized ureteral injury. Reliance on only a high level of suspicion for ureteral injury may be an inadequate metric to use to initiate further diagnostic intervention.

While universal cystoscopy could be considered the gold standard for diagnosing otherwise unrecognized ureteral injury, this may be an unattainable goal. Requiring a consultant urologist to perform cystoscopy at the completion of every abdominal/pelvic procedure would be an unrealistic burden while allowing gynecologists and surgeons to perform cystoscopy would require training and credentialing in a technique not currently universally performed in residency training.[17] A more reasonable approach may be to determine the risk of ureteral injury for a particular surgeon and/or approach and use cystoscopy selectively when the ureteral injury risk exceeds a predetermined threshold.

Visco et al constructed a decision analysis model to determine the cost-effectiveness of cystoscopy at hysterectomy.[18] With a 1.5% to 2.0% threshold rate of ureteral injury cystoscopy became a cost saving procedure to the hospital system per ureteral injury diagnosed. As such, when considering cost alone, a hospital, procedure or surgeon specific

determination could be made on whether cystoscopy is warranted based on the established rate of ureteral injury in that setting.

Limitations to the current study warrant discussion. Foremost is that the validity of the analysis relied on the accuracy of the billing coding from which these data were derived. To ensure that we accurately identified our study population treated with hysterectomy we used codes that have been used in prior work.[12] Because to our knowledge ureteral injury identification was not studied previously in this fashion, it was performed using any ICD9-CM code for a ureteral injury diagnosis or repair during the index admission. For followup analysis identification codes also included any new diagnosis of hydronephrosis or ureteral stricture in the absence of a stone diagnosis, given the possibility and the risk of silent ureteral obstruction.

Longitudinal analysis was limited to patients who underwent followup care in California. Any conditions that were diagnosed and treated outside California left our data subject to underestimation.

The analysis was also limited by the ability to investigate urological interventions (eg cystoscopy and ureteral stents) to prevent and/or detect ureteral injury. While these procedures can be identified as having been performed, a limitation of the data set is determining the timing and rationale for additional interventions on the same day. As such, while patients could be identified in whom a ureteral stent or stents were placed, it is unclear whether stents were placed preoperatively for identification purposes or after ureteral injury was detected. Similarly it is unclear when or why cystoscopy was performed in this population or who performed it.

Finally, the results of this study pertain to women who underwent hysterectomy. Results may not be generalizable to patients who undergo other surgical procedures.

CONCLUSIONS

Iatrogenic ureteral injury at hysterectomy increases the risk of hospital readmission and significant, potentially life threatening complications. Unrecognized ureteral injuries markedly increase these risks, warranting a high level of suspicion for ureteral injury and a low threshold for diagnostic investigation. Future work should focus on techniques and/or protocols that are time effective and cost-effective, and minimize the risk of unrecognized ureteral injury.

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