Comparison of two indices to annotate complications after radical nephroureterectomy

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Introduction: The Clavien-Dindo (CD) and Comprehensive Complication Index (CCI) are two grading systems that annotate adverse events following surgical procedures. We compare these two classification systems in a cohort of patients undergoing radical nephroureterectomy (RNU). **Materials and methods:** The charts of 110 consecutive RNU patients were reviewed for complications occurring within 30 days of surgery. Grading by the CD classification system and values for CCI were calculated. Bivariate and multivariate analysis identified associations between perioperative variables and complications, as well as relationship to hospital length of stay.

Results: Sixty-seven men and 43 women with a median age of 71, body mass index of 29, estimated glomerular filtration rate (eGFR) of 64 mL/min/1.73 m², and Charlson score of 4 were included. Seventy-five percent underwent a minimally invasive RNU, 47% had a lymph node

Introduction

Standardized reporting of surgical complications allows us to compare various surgical treatment methods and experiences between institutions, and to identify areas of improvement in our delivery of care.

The Clavien Dindo (CD) classification is the most widely used system for grading severity of a complication.¹ Complications are typically noted as

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Address correspondence to Dr. Jay D. Raman, Division of Urology, c4830, Penn State Health Milton S. Hershey Medical Center, Hershey, PA 17033 USA dissection, and 7% received neoadjuvant chemotherapy. Median hospital length of stay was 4 days (range, 2-22). Overall, 39 patients (35%) experienced a total of 56 complications including 12 major (≥ Clavien III) and 44 minor. Median CCI patients with complications cohort was 20.9 (range, 8.7-100). The upper quartile of $CCI (> 75^{th} \%)$ was associated with higher Charlson score (p = 0.03), lower baseline eGFR (p = 0.005), intraoperative transfusion (p = 0.004), and absence of symptoms at presentation (p = 0.015). Major CD complications were associated with these same variables. On multivariate analysis, only the upper quartile of CCI was associated with length of stay (8.25 versus 5.61 days, p < 0.0001) whilst major CD *complications were not* (7.98 *versus* 6.32, p = 0.211). **Conclusions:** The CCI and CD classification schemes are both associated with similar baseline and perioperative characteristics for RNU patients. However, the cumulative nature of CCI appears to permit more accurate prediction of length of stay following surgery compared to the CD system.

Key Words: risk stratification, urothelial carcinoma, complications, comprehensive complications index

the single most severe complication occurring in a patient after an intervention. What this system does not take into consideration is that the patient may experience multiple complications of various severities, which may collectively contribute to a patient's morbidity. The Comprehensive Complications Index (CCI) was developed to summarize all postoperative complications.² It is the sum of all complications weighted for their severity and is measured on a continuous scale from 0 to 100.

To date, there have been limited comparisons between these two disease processes in non-urologic surgical fields.³ Therefore, our objective was to examine the complications experienced by a cohort of patients who underwent radical nephroureterectomy (RNU) for upper tract urothelial cancer (UTUC). We then compare the CCI and CD classifications with respect to association with baseline and perioperative patient characteristics as well as determine the predictive accuracy of each with respect to measures of convalescence such as length of stay

Materials and methods

The charts of 110 consecutive patients between 2000 and 2014 that underwent RNU were retrospectively reviewed. The patient's age, gender, race, body mass index (BMI), preoperative symptoms, number of comorbidities, American Society of Anesthesiology grade (ASA), Eastern Cooperative Oncology Group performance status (ECOG), Charlson Comorbidity Index, and baseline kidney function as calculated by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) were recorded. Operative data including, surgical approach, estimated blood loss, operating room duration, intraoperative blood transfusion, lymph node dissection, and tumor stage were noted. Length of hospital stay was recorded.

All complications occurring within 30 days of surgery were identified by the Clavien-Dindo classification system. The complications identified were used to calculate values for the Comprehensive Complication Index using the calculator available through AccessSurgery (http://www.assessurgery.com/calculator_single/). Complications were then grouped into major and minor Clavien-Dindo complications, and upper quartile of CCI (>75%). A major complication was considered Clavien Grade III or greater.

Two sample t-test and Spearman correlation was used determine any association between different variables to length of stay. A multivariable linear model was used to adjust the relation between length of stay and the complication groups for the significant covariates found in the bivariate analysis. P values < 0.05 were considered significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

There were 110 RNU patients including 67 (61%) males and 43 (39%) females. Median age was 71 years, BMI was 29, Charlson score was 4, and eGFR was 64 mL/min/1.73 m². Of these patients, 83 (75%) underwent a minimally invasive RNU while 27 (25%) underwent an open approach. Almost 50% of the cohort had a regional lymph node dissection at RNU and under 10% received neoadjuvant chemotherapy. Mean estimated blood loss was 291 mL with a mean operating time of 336 minutes. Fifty-four (49%) of patients were found to have pT2 disease or greater on final pathology. Full descriptive characteristics of our patient cohort noted in Table 1.

TABLE 1. Characteristics of 110 patients undergoing radical nephroureterectomy included in complications analysis

Variable	No. pts (%) n = 110
Age, vrs (median)	70.5
(range)	(39-87)
Gender	
Male	67 (61)
Female	43 (39)
Race	~ /
Non-white	4 (4)
White	106 (96)
Body mass index (median)	29
(range)	(16-62)
Drooportius sumptoms	(10.02)
No.	22 (21)
NO	23 (21) 87 (79)
ies	07 (79)
ASA score	22
1 or 2	32 (29)
3 or 4	78 (71)
ECOG score	
0	70 (64)
1	25 (23)
2 or greater	15 (13)
Charlson index (median)	4
(range)	(0-10)
eGFR (mL/min/1.73 m ²) (median)	64
(range)	(5-121)
Neoadjuvant chemotherapy	
No	103 (94)
Yes	7 (6)
Surgical approach	
MIS	83 (75)
Open	27 (25)
Lymphadenectomy	
No	58 (53)
Yes	52 (47)
OR duration (min) (median)	330
(range)	(188-645)
Estimated blood loss (mL) (modian)	200
(range)	(0.2800)
	(0-2000)
Intraoperative transfusion	
No	95 (87)
	14 (13)
Pathologic stage	
< p12	56 (51)
> p12	54 (49)



Figure 1. Distribution of complications in patients included in study cohort.

Overall, 39 patients (35%) experienced a total of 56 complications including 12 major (\geq Clavien III) and 44 minor, Figure 1. Specifically, 28 patients had one complication, 7 patients had two complications and 4 patients had three or more complications. Of the patients with complications, 12 experienced a major complication with 2 patients having two major complications in addition to two minor complications. Twenty-seven patients experienced only minor complications although several had multiple minor complications (range, 1-3). Most of the minor complications included acute blood loss anemia requiring blood transfusions, postoperative ileus or wound infections. Major complications in our cohort included surgical interventions for bowel obstruction, fascial dehiscence, hematoma, and retained drain, renal failure requiring dialysis, pacemaker placement, and one mortality.

The complications identified were then used to calculate a CCI score for all patients who experienced a complication. The range for CCI was 8.7 to 100, with a

median CCI of 20.9 and upper quartile (>75th percentile) of CCI was 27.6. The upper quartile of CCI (>75th %) (n = 26 patients) was associated with higher Charlson score (p = 0.03), lower baseline eGFR (p = 0.005), intraoperative transfusion (p = 0.004), and absence of symptoms at presentation (p = 0.015). Major CD complications were associated with these same variables in addition to an open surgical approach, Table 2.

The average hospital length of stay was 5.23 days with a median stay of 4 days (range, 2-22). Seven patients were re-admitted. Length of stay was associated with the upper quartile of CCI while it was not associated with major complications. Upper quartile of CCI showed a mean length of stay of 8.25 days with a confidence interval of 6.25 to 10.88 days. Major complications group had a mean length of stay of 7.98 days with a CI of 5.39 to 11.82 days. On multivariate analysis, only the upper quartile of CCI was associated with length of stay (8.25 versus 5.61 days, p < 0.0001) whilst major CD complications were not (7.98 versus 6.32, p = 0.211). Readmissions data was too limited to perform comparative analysis between the two indices.

Discussion

UTUC accounts for 5% of all urothelial cancers and 10% of renal tumors.^{4,5} Standard of care treatment for bulky, high grade, or invasive UTUC is radical nephroureterectomy with bladder cuff excision.⁶ The role of perioperative chemotherapy and regional lymph node dissection continues to be debated. Unfortunately, patients undergoing RNU are typically elderly and comorbid and therefore are at risk for complications. Contemporary work has better sought to objectify this risk.

In 2013, Lin and colleagues noted that 38% of patients will develop a complication following RNU with one-fifth of these being major complications.⁷

	Major CD complications			CCI > 75 th %		
Variable	Odds ratio	95% CI	, p value	Odds ratio	95% CI	p value
Charlson (per 1 unit increase)	1.73	1.23-2.45	0.002	1.30	1.02-1.65	0.031
eGFR (per 10 mL/min/1.73 m ²)	1.52	1.12-2.04	0.007	1.35	1.1-1.67	0.005
Preoperative symptoms	4.76	1.11-20.0	0.017	3.45	1.27-9.09	0.015
Open surgical approach	8.10	1.93-40.77	0.001	3.12	1.21-8.06	0.019
Intraoperative transfusion	4.26	0.80-19.85	0.047	5.58	1.49-22.25	0.004

TABLE 2. Associations of perioperative variables with complications (CCI and CD) following RNU

Similar observations have been noted in other series although the rates are significantly higher for single institution tertiary care centers when compared to population based administrative datasets.⁸ Likely explanations for these observations include case mix index as well as the ability to annotate more carefully at an individual center versus that which is extracted form a larger database.

Beyond simply noting that complications after RNU occur, there are two avenues of further investigation that merit consideration. First, it would be beneficial to identify patients at risk for a complication to better guide the preoperative discussion and decision making process. In that regard, in 2017, Raman et al. published on a preoperative nomogram to predict complications following RNU.⁹ This analysis was based on over 700 patients undergoing RNU with close to 40% having complications. The second avenue that requires better delineation is objectifying the impact of complications following RNU to guide clinical care pathways.

The focus of the presented analysis seeks to better define the optimal complications scheme that yields information for RNU patients. Indeed the Clavien Dindo grading system is quite well known with clearly annotated descriptions for classifying complications after index procedures. The challenges of the CD system are two-fold however. Firstly, the system categorizes data in a purely categorical system (I to V). Secondly, as a result, the cumulative impact of multiple complications in the same patient will not be fully recognized. Due to these considerations, the CCI has been introduced with the hope that the cumulative and continuous nature of this index will be more accurate than the CD system.

Early data from the general surgical literature implicates superiority of CCI over CD.³ Indeed, experience in urology is far more limited. Here, we appreciate that the upper quartile of the CCI and major CD events are associated with similar perioperative and demographic factors. Conversely, when consideration was made of specific metrics of recovery or convalescence such as length of stay, the CCI was superior. Our practice has now been to use the CCI as a guide to engage our care coordination team to therefore engage home services to potentially blunt the impact of length of stay and/or hospital readmission. Although we suspect that readmission can be predicted by CCI, our current dataset presented here was too small to determine an association.

There are several limitations to our study. First, the study is a relatively small sample size owing to the rare nature of UTUC. The comparison for major complications to the upper quartile was somewhat arbitrary and based on publications criteria in the general surgical literature. Secondly, this was a retrospective study. We had to rely on electronic medical records, and may have missed complications as patients may have sought treatment at other facilities after hospital discharge. Nonetheless, these data are compelling and we are presenting investigating the CCI and CD in a larger multicenter consortium to determine if similar effects are noted.

Conclusions

The CCI is another approach to classify complications as opposed to the CD system. The cumulative nature of CCI may be superior to better quantify surgical morbidity and hospital length of stay. Continuing to studying complications of our surgical interventions will aid us to identify those with increased risk of postoperative complications for appropriate counseling as well as target areas of improvement in our management of these patients.

References

- 1. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240(2):205-213.
- Slankamenac K, Graf R, Barkun J et al. The comprehensive complication index: A novel continuous scale to measure surgical morbidity. *Ann Surg* 2013;258(1):1-7.
- 3. Kim TH, Suy US. Huy YJ et al. The comprehensive complication index (CCI) is a more sensitive complication index than the conventional Clavien-Dindo classification in radical gastric cancer surgery. *Gastric Cancer* 2017 [Epub ahead of print].
- 4. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin* 2015;65(1):5-29.
- Munoz JJ, Ellison LM. Upper tract urothelial neoplasms: incidence and survival during the last 2 decades. J Urol 2000;164(5):1523-1525.
- 6. Margulis V, Shariat SF, Matin SF et al. Outcomes of radical nephroureterectomy: a series from the upper tract urotheliasl carcinoma collaboration. *Cancer* 2009;115(6):1224-1233.
- Lin YK, Deliere A, Lehman K et al. Critical analysis of 30 day complications following radical nephroureterectomy for upper tract urothelial carcinoma. *Can J Urol* 2014;21(4):7369-7373.
- 8. Raman JD, Jafri SM. Complications following radical nephroureterectomy *Curr Urol Rep* 2016;17(5):36.
- 9. Raman JD, Lin YK, Shariat SF et al. Preoperative nomogram to predict the likelihood of complications after radical nephroureterectomy. *BJU Int* 2017;119(2):268-275.