**Name of journal: *World Journal of Clinical Oncology***

**ESPS Manuscript NO: 16851**

**Columns: EDITORIAL**

**Significant methodologic variations in calculating renal function changes following kidney tumor surgery: A quality reporting issue?**

Blum RD *et al*. Methodologic flaws in renal function calculations after kidney surgery

**Ruth D Blum, Jay D Raman**

**Ruth D Blum, Jay D Raman,** Division of Urology, Penn State Milton S. Hershey Medical Center, Hershey, PA 17033, United States

**Author contributions:** Raman JD designed research;Blum RD performed research; Raman JD analyzed data; Raman JD and Blum RD wrote the paper.

**Conflict-of-interest statement:** There are no conflicts of interest from either author regarding the material provided in this publication.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Correspondence to:** **Jay D Raman, MD, Associate Professor,** Division of Urology, Penn State Milton S. Hershey Medical Center, 500 University Drive, c4830F, Hershey, PA 17033, United States. jraman@hmc.psu.edu

**Telephone:** +1-717-5316969

**Fax:** +1-717-5314475

**Received:** January 31, 2015

**Peer-review started:** February 5, 2015

**First decision:** April 27, 2015

**Revised:** July 3, 2015

**Accepted:** July 29, 2015

**Article in press:**

**Published online:**

**Abstract**

Renal tumor surgery places patients at increased risk for chronic kidney disease (CKD). Accurate quantification of kidney function changes before and after surgery is essential to determine the magnitude of decline attributable to an index procedure. Current literature, however, highlights heterogeneity and inconsistencies in measurement techniques thereby contributing to ambiguity amongst studies. Further efforts are necessary to standardize reporting of kidney function outcomes related to renal surgery.

**Key words:** Radical nephrectomy; Partial nephrectomy; Nephroureterectomy; Glomerular filtration rate; Chronic kidney disease

**© The Author(s) 2015.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Accurate assessment of renal function changes following kidney tumor surgery is essential for quantifying the degree of decline attributable to an index procedure. Current studies, however, demonstrate significant heterogeneity in the timing and calculated formulas used for determining kidney function changes. These variations in methodology significantly confound interpretations regarding the impact of surgical technique on global renal function. Standardization of the reporting process is essential to more accurately characterize and potentially modify aspects of surgical care that can benefit from improvement.

Blum RD, Raman JD. Significant methodologic variations in calculating renal function changes following kidney tumor surgery: A quality reporting issue? *World J Clin Oncol* 2015; In press

**INTRODUCTION**

Studies indicate that kidney tumor surgeries including radical nephrectomy (RN), partial nephrectomy (PN), and radical nephroureterectomy (RNU) place patients at risk for declining renal function. For example, in 2006, Huang and colleagues demonstrated that patients undergoing RN for kidney tumors had a significantly increased risk of developing subsequent chronic kidney disease (CKD)[1]. Furthermore, these authors observed that this risk of CKD following nephrectomy in cancer patients is greater than that for donor nephrectomy and suggested that this may be attributable to baseline kidney dysfunction. Therefore, accurate and reproducible assessment of kidney function before and after kidney tumor surgery is essential to determine the magnitude of decline attributable to an index procedure. In this regard, we suspect that current reporting of kidney function changes following a surgical procedure may be heterogenous and inconsistent in the literature. To better investigate this issue, we reviewed the contemporary literature and evaluated the methodologies currently used and adequacy of reporting.

**LITERATURE STUDY**

The PubMed database was queried to identify studies that evaluated changes in renal function after RN, PN and RNU. We included all articles that evaluated both pre- and post-operative renal function based on estimated glomerular filtration rate (eGFR) and serum creatinine concentration. Data regarding the number of patients included in the study, the time frame for obtaining the pre- and postoperative serum creatinine levels, and the methodology for estimating renal function were collected.

**RESULTS**

Data collected from 99 articles were included in the analysis (Table 1). The mean number of patients included in these studies was 308, ranging from 7 to 2402. In 100% of the studies, there was a single pre-operative creatinine serving as the baseline value, although 88% of the articles failed to specify the timing prior to surgery. Following surgery, 65% of studies reported multiple creatinine measurements at various time points while 17% failed to specify timing of collection. The Modification of Diet in Renal Disease (MDRD) (67%) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) (8%) equations were most commonly used for eGFR calculations. Nonetheless, 20% of studies used other methodologies including renal scintigraphy, Cockroft-Gault equation, Mayo Clinic Quadratic equation, or combinations of these different methods. Five percent of studies did not calculate an eGFR and relied solely on serum creatinine values.

**DISCUSSION**

This analysis highlights that there exist significant methodological variations in calculating renal function related to kidney surgery in the contemporary literature. In particular, there is poor reporting of timing of serum creatinine collections as well as variability in methods used to estimate renal function. Serum creatinine concentration alone is a poor estimate of kidney function because it is affected by several factors including age, gender, ethnicity, muscle mass, creatinine secretion, and extrarenal excretion[2]. Furthermore, these factors can be affected by medications, hydration status, diet, certain disease states, and exercise[3]. Thus, there is a relatively wide range of normal serum creatinine levels as well as individual variability and these characteristics render it a poor predictor of early decline in renal function. Moreover, there is concomitant loss of both renal function and muscle mass in the elderly, so serum creatinine level may give the impression of normal renal function when the GFR is in fact low[2]. Many patients undergoing surgery for renal tumors are generally older and accordingly are an especially poor population for using serum creatinine level alone for estimating renal function.

Kidney function is better approximated using the estimated GFR, which is determined using the serum creatinine concentration and several other variables such as age, gender, and race. The two equations used most commonly in the contemporary literature are the MDRD study equation and the CKD-EPI equation. The MDRD study equation has been shown to be more accurate and precise than the Cockroft-Gault equation for those with a GFR less than approximately 90 mL/min per 1.73 m2. However, there are questions about its validity for persons without renal disease, persons > 70 years old, and patients with serious comorbid conditions[1,4]. The CKD-EPI equation was developed to overcome some of the shortcomings of the MDRD equation and be more applicable to the general population. It was found to be more accurate than the MDRD Study equation and have lower bias, especially in persons with an eGFR greater than 60 mL/min per 1.73 m2, thus reducing that rate of false-positive diagnoses of stage 3 CKD[5]. This was further highlighted by a study by Clark *et al*[6], where it was found that for patients with two functioning kidneys who underwent PN, the CKD-EPI equation provides slightly higher eGFRs compared to the MDRD equation at baseline and follow-up. However, there was no significant difference between the two equations when calculating the percent change of eGFR pre- and post-operatively[6].

This study highlights the methodological variation in the contemporary literature for determining renal function related to kidney surgery. The collection of serum creatinine levels was nonhomogeneous between studies, with variable numbers of measurements and poorly reported time frames. Additionally, there is utilization of multiple methods for estimating renal function, further confounding interpretation of the data. Such ambiguity amongst studies renders comparison of outcomes highly problematic. Further investigation is warranted to better standardize the reporting of kidney function outcomes related to renal surgery.

**REFERENCES**

1 **Huang WC**, Levey AS, Serio AM, Snyder M, Vickers AJ, Raj GV, Scardino PT, Russo P. Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol* 2006; **7**: 735-740 [PMID: 16945768 DOI: 10.1016/S1470-2045(06)70803-8]

2 **Levey AS**, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med* 2003; **139**: 137-147 [PMID: 12859163 DOI: 10.7326/0003-4819-139-2-200307150-00013]

3 **Perrone RD**, Madias NE, Levey AS. Serum creatinine as an index of renal function: new insights into old concepts. *Clin Chem* 1992; **38**: 1933-1953 [PMID: 1394976 DOI: 10.1146/annurev.me.39.020188.002341]

4 **Levey AS**, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999; **130**: 461-470 [PMID: 10075613 DOI: 10.7326/0003-4819-130-6-199903160-00002]

5 **Levey AS**, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; **150**: 604-612 [PMID: 19414839 DOI: 10.7326/0003-4819-150-9-200905050-00006]

6 **Clark MA**, Shikanov S, Raman JD, Smith B, Kaag M, Russo P, Wheat JC, Wolf JS, Matin SF, Huang WC, Shalhav AL, Eggener SE. Chronic kidney disease before and after partial nephrectomy. *J Urol* 2011; **185**: 43-48 [PMID: 21074205 DOI: 10.1016/j.juro.2010.09.019]

**P-Reviewer:** Amin AR, Kupeli S **S-Editor:** Tian YL

**L-Editor: E-Editor:**

**Table 1** **Data from the 99 studies in contemporary literature reporting renal function outcomes related to renal surgery *n* (%)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No. Patients per study** | | | | | |
| Mean | 308 | | | | |
| Range | 7-2402 | | | | |
| **Preoperative serum Cr collection – months prior to surgery** | | | | | |
|  | < 1 mo | 1-2 mo | Unspecified | | |
| Studies | 11 (11) | 1 (1) | 87 (88) | | |
| **Postoperative serum Cr collection – months after surgery** | | | | | |
|  | < 3 mo | * 1. Mo | > 12 mo | Unspecified | Multiple |
| Studies | 5 (5) | 9 (9) | 4 (4) | 17 (17) | 64 (65) |
| **Method for estimating renal function** | | | | | |
|  | MDRD | CKD-EPI | Other | None | |
| Studies | 66 (67) | 8 (8) | 20 (20) | 5 (5) | |

MDRD: Modification of Diet in Renal Disease; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration.