Renal Ischemia and Functional Outcomes Following Partial Nephrectomy

Joseph R. Zabell, MD, Jitao Wu, MD,
Chalairat Suk-Ouichai, MD, Steven C. Campbell, MD, PhD*

KEYWORDS

• Renal cell carcinoma • Partial nephrectomy • Ischemia • Functional recovery
• Radical nephrectomy

KEY POINTS

- Quantity and quality of preserved renal parenchyma are the most important determinants of functional recovery after partial nephrectomy, with ischemia playing a secondary role.
- Cold ischemia is protective, but recovery from limited warm ischemia also appears to be strong.
- Extended warm ischemia can lead to irreversible ischemic damage and should be avoided, although the threshold at which this occurs has not been well established.
- Surgical techniques to eliminate ischemia during partial nephrectomy have been explored, but a long-term functional benefit has not been unequivocally demonstrated.
- Further work regarding acute renal dysfunction and implications for long-term outcomes is needed.

INTRODUCTION

Renal masses are commonly encountered in urologic practice, with approximately 63,000 new cases diagnosed each year in the United States.[1] Furthermore, the incidental discovery of small renal masses has increased in recent years largely due to expanded utilization of abdominal imaging, including computed tomography (CT) and other modalities.[2] For small, clinically localized renal masses, partial nephrectomy (PN) is the current reference standard according to most commonly used treatment guidelines.[3–5] The driving force behind the use of PN in this setting is the reduced risk of both acute and long-term renal dysfunction with nephron-sparing surgery when compared with radical nephrectomy (RN). However, PN still carries risk of renal insufficiency secondary to the removal of nephrons and/or as a result of ischemic injury induced by vascular clamping. The relative importance of these factors and the long-term clinical implications of renal ischemia remain issues of debate in our field.[6,7] We endeavor to provide an overview of the evidence regarding the relationship between ischemia and functional outcomes following renal surgery, as well as a brief discussion of new developments and ongoing research.

DISCUSSION

Chronic Kidney Disease Following Renal Cancer Surgery

In recent years, the long-term implications of decreased renal function as a result of renal cancer surgery have been increasingly recognized, and various strategies to minimize the incidence

Disclosure Statement: The authors have nothing to disclose.
Glickman Urological and Kidney Institute, Department of Urology, Cleveland Clinic, 9500 Euclid Avenue, Mail Code Q10-1, Cleveland, OH 44195, USA
* Corresponding author. Center for Urologic Oncology, Glickman Urologic and Kidney Institute, Cleveland Clinic, Room Q10-120, 9500 Euclid Avenue, Cleveland, OH 44195.
E-mail address: campbes3@ccf.org

Urol Clin N Am 44 (2017) 243–255
http://dx.doi.org/10.1016/j.ucl.2016.12.010

of chronic kidney disease (CKD) have been explored.[8,9] The significance of CKD was highlighted in a landmark population-based study that identified a direct correlation between degree of CKD and rates of cardiovascular morbidity, hospitalization, and death.[10] This focus on the deleterious implications of CKD has subsequently been applied to renal cancer surgery, although the true effects of renal dysfunction in this setting may not be as clear.

The results of EORTC 30904, a randomized trial comparing PN versus RN[11] provide further insight into this issue. Although PN was associated with better renal function after surgery, there was no significant difference noted in overall survival or incidence of cardiac events between the RN and PN cohorts. Further analysis demonstrated that the rates of severe CKD and renal failure were similar between the groups.[12] This suggests that reduced renal function after renal cancer surgery does not necessarily lead to decreased overall survival, and perhaps not all CKD confers the same adverse long-term consequences. CKD related to medical etiologies (CKD-M) is typically induced by chronic disorders that are ongoing and will continue to adversely impact renal function over time. Conversely, CKD primarily related to surgical removal of nephrons (CKD-S) is the result of an isolated event and further decline in function is less likely once the new baseline glomerular filtration rate (GFR) has been established. Published literature to date has evaluated this hypothesis and, indeed, suggests that CKD-S has a lower rate of functional decline and less impact on survival than CKD-M.[13,14]

The clinical relevance of these findings is germane to this discussion with regard to the significance of CKD after renal cancer surgery. Although certain clinical situations, such as a solitary kidney mandate maximal nephron sparing, one must consider the oncologic potential of larger masses and potential risks of PN against the implications of surgically induced GFR decline when making clinical decisions in patients with a healthy contralateral kidney. The previous discussion notwithstanding, PN remains the recommended treatment modality for small renal masses, and it is certainly preferred in many cohorts, particularly patients with preexisting CKD.[3] Thus, efforts have been made to identify the factors that predict functional outcomes after PN, and to develop surgical strategies to optimize these outcomes.

Renal Function After Partial Nephrectomy

Renal function preservation after PN is of great importance in many patients with localized renal masses, particularly in the setting of a solitary kidney, preexisting CKD, proteinuria,[15] or multiple/bilateral renal masses. Although an important goal of PN is to optimize preservation of renal function, any PN will be associated with some degree of functional decline secondary to loss of vascularized nephron mass and the potential for irreversible ischemic damage. To date, most studies report approximately 10% decline in global GFR after clamped PN for patients with a healthy contralateral kidney,[9] and this average functional loss has been rather consistent in the literature.[16,17] Further work focused on functional recovery specifically within the operated kidney has identified an average recovery of 80% of ipsilateral GFR after PN.[18,19] Thus, the literature in this realm has been consistent in suggesting that the typical clamped PN preserves, on average, 80% of function in the operated kidney and 90% of global GFR.

Regarding the functional loss associated with PN as discussed previously, many investigators have considered the potential role that ischemia may play in this process. Ischemia related to clamped PN has the potential to create injury to nephrons through several hypothesized mechanisms, including vasoconstriction with abnormal endothelial cell compensatory response, tubular obstruction with backflow of urine, and reperfusion injury.[20] More recent study of human kidneys using serum biomarkers and histologic analyses of serial biopsies during clamped PN suggests that the kidney may be more tolerant to ischemia than previously thought.[21] Thus, the degree to which irreversible ischemic injury occurs during PN remains a subject of debate.

One hypothesized method to assess the degree of potential ischemic impact on the operated kidney during clamped PN is to evaluate for atrophy of the preserved renal tissue several months after surgery. Several studies have assessed this through a variety of methods and have reported no substantial atrophy after clamped PN.[22–24] In this context, failure of nonatrophied residual parenchyma to regain function after PN provides an alternate potential explanation for post-PN functional decline. This hypothesis posits that if the percent GFR preserved after PN failed to match the percent parenchymal mass preserved, one would presume a subset of the remaining nephrons failed to recover from the ischemic insult. Several studies have assessed this issue, and have consistently found that most nephrons recover strongly following ischemia during PN with a nearly 1:1 relationship between preservation of parenchymal mass and functional outcomes.[16,25,26] These fundamental findings