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#### Platinum Priority – Collaborative Review – Kidney Cancer Editorial by XXX on pp. x-y of this issue

### Collaborative Review of Risk Benefit Trade-offs Between Partial and Radical Nephrectomy in the Management of Anatomically Complex Renal Masses

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#### Article info

Article history: Accepted November 29, 2016

*Associate Editor:* Stephen Boorjian

Keywords:

Partial nephrectomy Radical nephrectomy Renal cell carcinoma Renal masses Surgery

#### Abstract

**Background:** While partial nephrectomy (PN) is the recommended treatment for many small renal masses, anatomically complex tumors necessitate a clear understanding of the potential risks and benefits of PN and radical nephrectomy (RN).

**Objective:** To critically review the comparative effectiveness evidence of PN versus RN; to describe key trade-offs involved in this treatment decision; and to highlight gaps in the current literature.

*Evidence acquisition:* A collaborative critical review of the medical literature was conducted.

*Evidence synthesis:* Patients who undergo PN for an anatomically complex or large mass may be exposed to perioperative and potential oncologic risks that could be avoided if RN were performed, while patients who undergo RN may forgo long-term benefits of renal preservation. Decision-making regarding the optimal treatment with PN or RN among patients with anatomically complex or large renal mass is highly nuanced and must balance the risks and benefits of each approach. Currently, high-quality evidence on comparative effectiveness is sparse. Retrospective comparisons are plagued by selection biases, while the one existing prospective randomized trial, albeit imperfect, suggests that nephron-sparing surgery may not benefit all patients.

**Conclusions:** For anatomically complex tumors, PN preserves renal parenchyma but may expose patients to higher perioperative risks than RN. The risks and benefits of each surgical approach must be better objectified for identification of patients most suitable for complex PN. A prospective randomized trial is warranted and would help in directing patient counseling.

**Patient summary:** Treatment decisions for complex renal masses require shared decision-making regarding the risk trade-offs between partial and radical nephrectomy.

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http://dx.doi.org/10.1016/j.eururo.2016.11.038

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Please cite this article in press as: Kim SP, et al. Collaborative Review of Risk Benefit Trade-offs Between Partial and Radical Nephrectomy in the Management of Anatomically Complex Renal Masses. Eur Urol (2016), http://dx.doi.org/10.1016/ j.eururo.2016.11.038 ARTICLE IN PRESS

#### 1. Introduction

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More than 60 000 patients in the USA and >100 000 patients in Europe are diagnosed annually with kidney cancer [1,2]. With cross-sectional imaging now ubiquitous, the incidence of localized renal masses is increasing [3,4]. The majority of patients who currently present with stage I renal cell carcinoma (RCC)-clinical T1a (<4 cm) or T1b (4-7 cm)are surgically treated with partial nephrectomy (PN) or radical nephrectomy (RN) [5]. Clinical practice guidelines recommend PN for T1 tumors that are amenable to nephronsparing surgery (NSS) with the goal of preserving healthy renal parenchyma without compromising cancer control [6–9]. These guidelines are based on a growing number of observational studies that suggest better overall survival (OS) and renal function for patients who undergo PN [9]. As a result, several population-based studies have demonstrated that the clinical paradigm has shifted towards higher utilization of PN in the surgical management of localized renal tumors [10–12].

While little controversy exists regarding the utility and prudence of PN for patients with small and anatomically simple renal tumors, patients who undergo complex NSS for large and/or anatomically complex masses may be exposed to perioperative and potential oncologic risks that would be avoided if RN were performed. Issues of additional surgical complexity are especially salient in the elderly and patients with comorbidities, while oncologic safety is crucial for all, particularly the young and robust individuals. Thus, decision-making regarding the optimal treatment with PN or RN among patients with large and/or anatomically complex renal masses is highly nuanced and must balance the risks and benefits of each approach. Risk trade-offs in this space are particularly complex given that advanced treatment technologies have evolved to include a variety of surgical approaches, ranging from conventional open surgery to minimally invasive surgery via laparoscopy or robotics using both transperitoneal and retroperitoneal approaches [13–18]. In this collaborative review, we critically evaluate the key elements of decision-making for patients presenting with large/anatomically complex, localized renal masses. We highlight gaps in the current literature and outline the clinical challenge of determining which mass in which patient is most appropriate for PN versus RN.

#### 2. Evidence acquisition

MEDLINE, EMBASE, and Scopus were used to search the English literature from inception to January 2016 using the following terms: "renal mass/tumor", "partial nephrectomy", "radical nephrectomy", and "nephron-sparing surgery" in conjunction with "large", "complex", "complications", "renal function", or "survival". The authors further reviewed the reference lists of relevant articles identified by this search. The full text of selected studies that focused on pertinent topics for this manuscript was reviewed by the first and senior authors. Co-authors then added or removed articles via consensus as part of draft revisions. After reaching agreement regarding the structure of the manuscript, an initial draft was written and circulated by the first and senior authors. After a number of iterations, consensus regarding the content of the manuscript was reached among the authors. In the process of writing this critical review, the most recent pertinent studies were also added as references.

#### 3. Evidence synthesis

#### 3.1. Quantification of the anatomic complexity or renal masses

A strong argument can be made, with some data providing support, that PN for a small peripheral renal mass is associated with similar perioperative risks as RN [19]. Nevertheless, risks associated with PN increase with tumor size and anatomic complexity [20]. Indeed, tumor anatomic complexity is one of the key predictors of risk associated with PN. Tumor excision and reconstruction are inherently more challenging for larger, endophytic, central, and hilar tumors when compared to smaller, peripheral, polar lesions [20]. Several validated scoring systems have been developed to quantitate the anatomic complexity of localized renal tumors to facilitate objective reporting, allow meaningful comparisons between series, and help objectify surgical decision-making [21-24]. These scoring systems for anatomic complexity, now often collectively termed "nephrometry", quantitate renal mass attributes such as tumor size, endophytic versus exophytic location, nearness to the collecting system, centrality, proximity to the hilar vessels, and renal contact surface area [25,26].

The literature contains many reports from numerous institutions demonstrating that higher tumor complexity scores are associated with greater perioperative risks among patients undergoing cancer-directed renal surgery [27]. Importantly, there is evidence that tumor anatomic complexity correlates with more aggressive renal tumor biology [28]. Figure 1 highlights several examples of large, endophytic, and/or central masses, with some in challenging locations, that most renal surgeons would consider complex for resection using PN. Although many nephrometry scoring systems offer low, intermediate, and high groupings for anatomic complexity score, the score cutoffs are admittedly arbitrary. Thus, thresholds for how tumor anatomic complexity affects risk balance and clinical decision-making continue to depend on a surgeon's skill and opinion.

#### 3.2. Potential benefits of PN over RN

Recommendations for PN for localized renal tumors in current clinical practice guidelines are largely predicated on the growing number of observational studies suggesting better outcomes with respect to renal function and OS compared to other treatment options, in particular RN [6–8]. PN was first introduced as a surgical treatment for renal masses with imperative indications such as a solitary kidney, bilateral renal masses, or pre-existing chronic kidney disease (CKD) because of the deleterious impact on quality of life and mortality of worsening renal function

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