Partial Nephrectomy for T1b Renal Cell Carcinoma: A Safe and Superior Treatment Option

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In recent decades, rapid advances in the surgical management of localized renal cell carcinoma (RCC) have taken place. Partial nephrectomy (PN) has supplanted radical nephrectomy (RN) as the treatment of choice for T1a renal masses with comparable oncological outcomes and the added benefits of renal preservation.[1-3] Although initially reserved for these small renal masses and for imperative indications, PN has been successfully extended to T1b and larger renal masses.

When undergoing treatment for RCC, most patients have three main goals: (1) to be cured from cancer; (2) to have minimal risk of complications; and (3) if at all possible, to have their surgery performed via minimally invasive strategies. The first goal, achieving long-term cancer control, is usually the most pressing concern. For T1b renal masses, PN has been shown to be equivalent to RN in terms of cancer specific outcomes.[4-9] In the largest published study to date, Badalato and colleagues used the Surveillance, Epidemiology, and End Results (SEER) database to retrospectively compare PN and RN for T1b renal masses.[4] They included 11 256 patients (1047 who underwent PN) with a median follow-up of close to 3 years. When controlling for several clinical factors, no difference was found in cancer specific survival (CSS) or overall survival (OS) between treatment groups. This finding held true even when stratifying by tumour size and patient age. Similarly, in a recent 15-year systematic review performed by El-Ghazaly and Rendon investigating survival rates among patients undergoing PN and RN for renal masses >4 cm, the predicted 5-year CSS rates for those with T1b renal masses were 97% and 90%, respectively.[10] From these studies, among others, it is clear that PN is an effective treatment for T1b renal masses with no sacrifice in cancer specific outcomes when compared with RN.

Limiting the morbidity associated with undergoing treatment is the second most important goal among patients with RCC. When considering the preservation of renal function, PN provides significant advantages over RN. Decreased renal function is associated with an increased risk of several disease states, including metabolic derangements, anemia and cardiovascular disease and it is independently associated with an increased risk of all cause mortality.[11-15] Therefore, when treating RCC, the preservation of renal function becomes paramount. Several studies have shown that PN results in a smaller decrease in renal function and a decreased risk of developing chronic renal failure when compared with RN.[8,16-20] In a study by Huang and colleagues including 647 patients (385 who underwent PN), only 2.9% who underwent PN had new-onset of glomerular filtration rate (GFR) <45 mL/min/1.73 m^2 postoperatively compared with 35.8% who underwent RN.[16] This amounted to a hazard ratio (HR) of 11.8 for the development of GFR <45 mL/min/1.73 m^2 even after controlling for age, comorbidities and preoperative GFR. Although this study looked specifically at T1a renal masses, this association remains when considering only T1b renal masses. In a study by Weight and colleagues, a postoperative decline in GFR of 16.6% and 23.5% was observed in 212 and 298 patients undergoing PN and RN for T1b renal masses, respectively.[17]

Unsurprisingly, the preservation of renal function associated with PN has resulted in decreased long-term morbidity and mortality. In a study by Huang and colleagues, including 3659 patients undergoing RN and 556 undergoing PN for T1a renal masses, the incidence of cardiac events during follow-up was 40% greater among patients undergoing RN.[21] There was also an increased risk of all-cause mortality among those undergoing RN (HR 1.38, $p < 0.001$). Again, this finding has been extended to T1b renal masses. In the above mentioned study by Weight and colleagues, including only T1b renal masses, the excess loss of renal function attributed to RN was associated with a 25% increased risk of cardiac death and a 17% increased risk of all-cause mortality, although CSS was equivalent among PN and RN groups.[17]

Although PN results in decreased long-term morbidity when compared with RN, the incidence of perioperative complications may be slightly higher. In a prospective, randomized trial by van Poppel and colleagues, there was an increased incidence of hemmorhage (3.1% vs. 1.2%), urinary fistulae (4.4% vs. 0%) and re-operation (4.4% vs. 2.4%) in patients who underwent PN compared to those who underwent RN.[22] This remains an area for significant debate, as other authors have found no difference in perioperative complication rates. In a 2007 meta-analysis by Lesage and colleagues, a trend towards increased perioperative complication rates in those undergoing PN was identified, but it did not reach statistical significance.[23] Nonetheless, the overall risk of suffering a severe perioperative complication remains low regardless of treatment type and will likely decrease further with the refinement of surgical techniques.

The third major goal among patients undergoing treatment for RCC is to have their procedure performed with minimally invasive techniques. Fortunately, recent studies have reported favourable outcomes when treating T1b renal masses with laparoscopic and robotic strategies.[8,24,25] For example, in a study by Lifshitz and colleagues comparing laparoscopic PN for T1a and T1b renal masses, no difference was found in operative time, warm ischemia time, blood loss or intraoperative complications, although postoperative complication rates were higher in the T1b group.[25] The nephron-sparing benefits of PN have also been shown when using minimally invasive techniques for T1b tumours. Comparing laparoscopic PN to RN for T1b renal masses, Deklaj and colleagues found a postoperative decline in GFR of 12.5% and 29.3%, respectively.[8] Thus, it appears that minimally invasive PN is safe and beneficial in the treatment of T1b renal masses. As experience grows and surgical training programs place a greater focus on minimally invasive approaches, the benefits of minimally invasive PN will likely continue to increase.

Although the bulk of existing evidence suggests that PN is an effective and advantageous treatment for all T1 renal masses, there is a small body of evidence suggesting that patients undergoing PN have a slightly increased risk of all-cause mortality compared with those undergoing RN. In the above mentioned randomized trial by van Poppel and colleagues, 10-year OS was greater for patients undergoing RN compared with PN (81.1% vs 75.7%, $p = 0.03$).[26] In the subgroup of patients with proven RCC, however, this result did not maintain statistical significance and RN and PN provided excellent oncological outcomes, with only 12 RCC-related deaths in the entire study population. Furthermore, the planned accrual for this study was over 1300 patients, but only 541 patients were actually enrolled. It is hypothesized that many patients refused to partake in this trial and only a subset of eligible patients was included, imparting a selection bias. Finally, during this study period it was believed that the thickness of the surgical margin was correlated with oncological outcomes. Therefore, it is likely that more renal parenchyma was removed than would be today, reducing the nephron-sparing benefits of PN.

In the modern treatment of RCC, the weight of evidence shows clear advantages to performing PN for T1b renal masses. It results in superb oncological outcomes which are comparable to those achieved with RN and can be safely performed through open and minimally invasive approaches. Although there may be a small increase in perioperative complications associated with PN, this is outweighed by the significant long-term gains provided by the preservation of renal function. When treating T1b renal masses, PN should be the preferred treatment option.

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