Analysis of Atrophy After Clamped Partial Nephrectomy and Potential Impact of Ischemia

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OBJECTIVE Ischemia is a potential contributor to decline of function after partial nephrectomy (PN), although loss of parenchymal mass related to excision and reconstruction appears to be a more significant factor. However, loss of parenchymal mass could also be due to global effects of ischemia leading to parenchymal atrophy. In this study, we evaluated parenchymal volumes in regions away from the operated site to assess for atrophy.

MATERIALS AND METHODS A total of 164 patients undergoing PN for whom detailed analysis of function and parenchymal mass within the operated kidney could be performed were assessed for opposite pole volume (OPV) before and 4-12 months after surgery. Tumor location was required to be $\geq$2 cm away from the opposite polar line to exclude local effects related to excision or reconstruction. OPV was estimated by software analysis, and the ratio of the estimates (OPV ratio = postoperative OPV to preoperative OPV) was used to assess for atrophy.

RESULTS Patient demographics and tumor characteristics were representative of conventional PN populations, and warm ischemia (n = 101; median, 21 minutes) and cold ischemia (n = 63; median, 26 minutes) were applied by surgeon discretion. OPVs before and after PN were 63.2 and 62.5 cm^3, respectively (P = .76). The median OPV ratio was 0.99 suggesting that significant atrophy did not occur. OPV ratio was 0.99 for warm ischemia cases and 0.99 for cold ischemia cases (P = .95).

CONCLUSION Limited warm ischemia or hypothermia was not associated with significant parenchymal atrophy after PN, which suggests that parenchymal volume loss in this setting is primarily due to excision or reconstruction. UROLOGY 85: 1417−1423, 2015. © 2015 Elsevier Inc.

One of the main objectives of partial nephrectomy (PN) is to preserve as much renal function as possible and such efforts should be intensified for patients with pre-existing chronic kidney disease.[1,2] Recent studies[3] suggest that the new baseline level of renal function after PN also has important implications with respect to stability of renal function and overall survival, particularly if it falls below 40-45 mL/min/1.73 m^2. Most studies suggest that loss of parenchymal mass related to tumor excision and reconstruction is the primary driver of functional decline after PN,[4-9] whereas ischemic injury plays a secondary role as long as limited warm ischemia or hypothermia have been applied.[10] However, loss of parenchymal mass could also be due to global effects of ischemia leading to parenchymal atrophy, and this has not been well studied to date. Chronic ischemia, as seen with renal artery stenosis, can lead to renal atrophy, but can limited duration of ischemia during PN also lead to significant parenchymal atrophy, as some have proposed?[11-14]

The limited number of studies that have evaluated parenchymal atrophy after clamped PN have shown only minimal changes, particularly when extended warm ischemia has been avoided. In the article by Simmons et al,[11] atrophic changes in the parenchyma were estimated to be 0%-2% as long as the warm ischemia time was <40 minutes and only 4% when more than this threshold. Choi et al[15] reported only 3% parenchymal mass decline in a relatively small series of PN, although more impressive changes were observed when ischemia time was >35 minutes. However, independent confirmation of these findings has not been published, ideally with a novel and more stringent methodology to provide more informative assessment of this important issue. In

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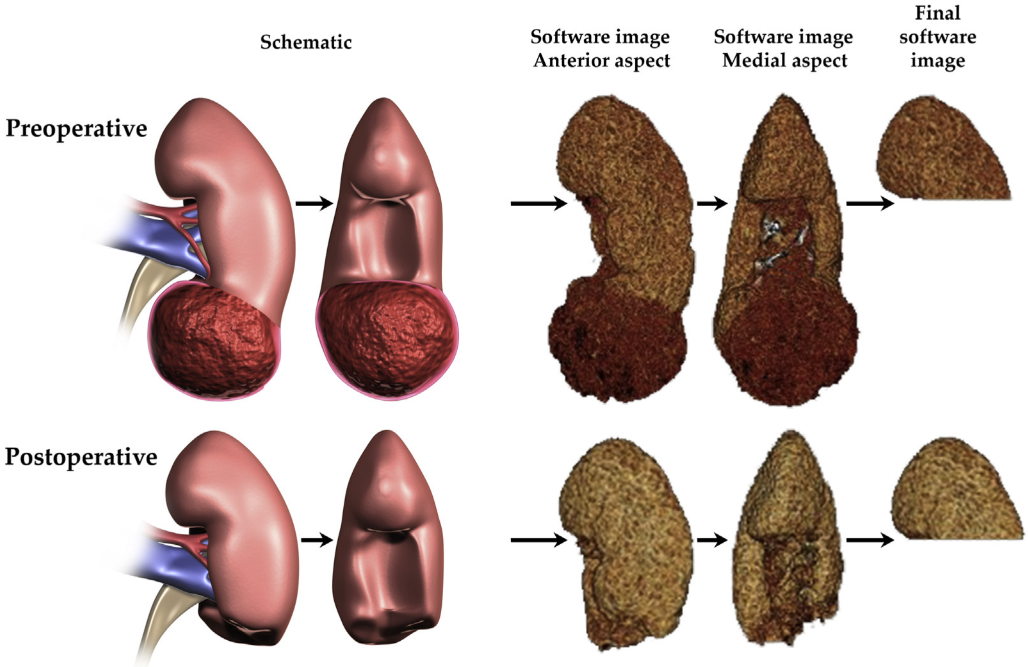

Figure 1. Methodology for measuring opposite pole volume before and after partial nephrectomy. Schematic illustrates principle of measurement of the volume of the opposite pole beyond the polar line (arrows) within a region that would not be directly affected by excision and reconstruction, yet still exposed to the global effects of ischemia. Polar lines are illustrated for analysis of the volume of the upper pole for a patient with a lower pole tumor requiring heminephrectomy. Medial and anterior aspects are shown. Software is used to line up the images of the kidneys along the vertical axis, the polar line is identified, and the volume above this level is then isolated and measured. (Color version available online.)

this study, we directly measure the volume of the parenchyma away from the site of tumor excision and reconstruction to evaluate for atrophic changes that could be related to global ischemia. In addition, we assess the potential impact of the type and duration of ischemia.

MATERIALS AND METHODS

Patient Population

With institutional review board approval, we reviewed all 2101 PNs performed at our institution between 2007 and 2014 and identified 186 patients for whom glomerular filtration rate (GFR) and parenchymal volume specifically within the operative kidney could be established both before and after surgery. Inclusion required availability of necessary preoperative and postoperative imaging, functional studies, clinical and demographic parameters, and mercaptoacetyltriglycine nuclear renal scans for patients with 2 kidneys, all within defined timeframes. All such eligible patients were included in this analysis. Choice between open and minimally invasive approach to PN and use of warm ischemia vs hypothermia were made by the treating surgeon based on individual tumor and patient characteristics. PN techniques used at our institution have been described previously.[16-19] Mannitol was routinely administered and resection began immediately after clamping in all cases. The artery was always occluded, whereas the vein was clamped selectively per surgeon discretion.

All serum creatinine measurements were made at a single clinical reference laboratory, and GFR was estimated using the Modification of Diet in Renal Disease 2 equation.[20] In patients with a contralateral kidney, GFR was estimated specifically in each kidney by preoperative and postoperative mercaptoacetyltriglycine nuclear renal scans. Venous phase of computed tomography scans were used for parenchymal volume estimates before and after surgery as outlined before.[16] All measurements were made <2 months before surgery and 4 and 12 months postoperatively.

Measurement of Atrophy

To avoid local effects related to tumor excision and reconstruction, cases with tumor located within 2 cm of the opposite polar line were excluded (n = 22), leaving 164 cases in our cohort for analysis of atrophy. The polar line, which is illustrated in Figure 1, was defined by Kutikov and Uzzo[21] in their landmark study describing the RENAL nephrometry system, which has been widely adopted in the field. Opposite pole volume (OPV) was defined as the volume beyond this line in the portion of the kidney remote from the resection site. The iNtuition software (TeraRecon, Foster City, CA) was used to measure OPV before and after surgery using computed tomography images as shown in Figure 1. Briefly, the software captures parenchyma and tumor and creates images that illustrate these structures from both the anterior and the medial aspects. The captured images were then aligned in the vertical dimension to correct for any postoperative rotation, and the parenchyma volume beyond the polar line was isolated and measured in both the preoperative and postoperative states. The OPV ratio was defined as the postoperative OPV to preoperative OPV and was taken as an estimate of potential atrophy. Each measurement was blinded and performed 3 times, and the average OPV and standard error were recorded. For the first 20 cases, 2 different observers performed each analysis, and intraobserver and