The Use of Tissue Adhesive for Tumor Bed Closure during Partial Nephrectomy is Associated with Reduced Devascularized Functional Volume Loss

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Abstract

Objectives: To quantitatively compare the functional renal volume loss, following nephron sparing surgery (NSS) between patients in whom tumor bed closure was done by biological tissue adhesive and those who were managed by standard suture technique. Methods: From our institutional NSS database we retrospectively collected patients who had two sequential quantitative single-photon emission computed tomography of 99mTc-dimercaptosuccinic acid uptake studies, the first study immediately before surgery and the second one 3–6 months following surgery. The study group included 69 patients: 26 (37.7%) patients in the sealant group (BioGlue®) and 43 (62.3%) patients in the standard suture group. Results: No statistically significant differences were noted in the baseline clinical and pathological characteristics of the studied groups. However, there were several statistically significant differences in operative variables: patients in the suture group had larger amount of blood loss (3-fold), longer ischemia time (26.6 vs. 21 minutes,) and slightly longer operation time. Patients in whom tumor bed was closed by sutures had nearly 3-fold higher parenchymal loss compared to patients managed by sealant (26.28 vs. 8.92 ml, p = 0.048). Conclusions: The use of tissue sealant during tumor bed reconstruction is associated with reduced devascularized parenchymal mass loss and should be considered among modifiable surgical factors during NSS.
Materials and Methods

From our institutional NSS database and after our institutional review board approval, we retrospectively collected patients who had two sequential quantitative single-photon emission computed tomography (SPECT) of 99mTc-dimercaptosuccinic acid (DMSA) (QDMSA) uptake studies (between 1995 and 2014), the first study immediately before surgery and the second one 3–6 months following surgery. The study group included 69 patients: 26 (37.7%) patients in the sealant group (BioGlue®) and 43 (62.3%) patients in the standard suture group.

Surgical Technique

An extraperitoneal, extrapleural supra-11th rib incision was done on the operated side. After complete mobilization of the kidney within Gerota’s fascia, the ureter and vascular pedicle were identified and isolated on a vascular loop. Mannitol with 0.5 g/kg was given intravenously before clamping the renal vasculature, with subsequent in-situ hypothermia by cooling the kidney surface with ice-slush. Enucleation of the tumor was done with circumferential incision followed by blunt dissection between the fibrous pseudocapsule and the renal parenchyma. Attention was made to remove a minimal rim of normal tissue. Samples from the remaining renal parenchyma at the tumor base were sent for intraoperative frozen section analysis to verify a tumor-free margin. Open blood vessels or collecting system were sutured using monocryl 4/0 continuous sutures; argon beam coagulator was used to seal the exposed renal parenchyma. Renorrhaphy was done by either large sutures (1/0 vicryl with blunt-end liver needle) to approximate the edges of the parenchymal defect, or by using 2–10 ml of tissue adhesive (BioGlue® CryoLife, Atlanta, Ga) to fill the tumor bed (fig. 1). The decision how to close tumor bed was mainly based on the availability of the BioGlue® tissue adhesive but also was related to the ability to completely control major blood vessels. Pedicle clamping was then removed, clamp ischemia time was determined, and the kidney was inspected for bleeding or urinary leakage. All surgical procedures were made by a single surgeon (O.N.).

QDMSA Scan

QDMSA uptake by the kidney was done as described previously [7, 8]: SPECT scintigraphy of the kidneys was performed 4 h after intravenous injection of 148 MBq (4 mCi) 99mTc-DMSA using either single- or double-head rotating cameras with all-purpose parallel-hole collimators (Apex 415-ECT, Elscint, Haifa, Israel). Data were accumulated from 120 projections 38 apart; the process lasted for about 20 minutes. Raw data were reconstructed by filtered back projections with a Hann filter (cutoff point: 0.5 cycle/cm). Following reconstruction each image was sectioned at 1-pixel (0.68 cm) intervals in transaxial, coronal, and sagittal planes by using a 64 × 64 byte matrix. Kidney volumes and radioactive concentration measurements were calculated on the reconstructed data by using the threshold method with a 43% threshold value that is known to best fit the target to non-target ratio of DMSA in the kidney [9]. Data analysis was automated and operator-independent; the operator chose the slice that best defined the kidney and drew a region of interest around it. Functional volume measurement was calculated by the sum of pixels in all sections multiplied by slice thickness.

Statistical Analysis

The functional volume change of QDMSA in the operated kidney (the dependent variable) was calculated as the percent change of the value obtained after surgery, considering the preoperative functional volume as 100%. Samples were analyzed using mean and standard error of the mean. Fisher’s exact test was used to evaluate the correlation between categorical variables. Student
p value of less than 0.05 was considered statistically significant.

Table 1. Clinical, surgical and pathological characteristics of both study groups stratified by the tumor bed closure technique

| Variable                  | Suture group (n = 43) | Sealant group (n = 26) | p     |
|---------------------------|-----------------------|------------------------|-------|
| Age, years                | 60.6 (29–85)          | 59.88 (31–84)          | 0.8   |
| Gender, n (%)             |                       |                        | 0.46  |
| Male                      | 26 (60.5%)            | 13 (50%)               |       |
| Female                    | 17 (39.5%)            | 13 (50%)               |       |
| Single kidney, n (%)      | 4 (9.3%)              | 5 (19.2%)              | 0.28  |
| Tumor size, cm            | 3.92 ± 0.23           | 3.48 ± 0.24            | 0.18  |
| Side, n (%)               |                       |                        | 0.8   |
| Right                     | 18 (41.8%)            | 12 (46.1%)             |       |
| Left                      | 25 (58.2%)            | 14 (53.9%)             |       |
| R.E.N.A.L score           | 7.12 ± 0.25           | 6.96 ± 0.39            | 0.73  |
| Closure of collecting duct| 53.4%                 | 52%                    | 0.55  |
| Estimated blood loss, ml  | 289.42 ± 88.21        | 86.73 ± 41.73          | 0.04  |
| Serum creatinine, mg/dl   | 1.17 ± 0.07           | 1.1 ± 0.07             | 0.47  |
| eGFR, ml/min/1.73m²       | 66.77 ± 2.98          | 70.62 ± 4.84           | 0.5   |
| Pathology, n (%)          |                       |                        | 0.38  |
| Benign                    | 12 (27.91%)           | 4 (15.38%)             |       |
| Malignant                 | 31 (62.09%)           | 22 (84.62%)            |       |
| Ischemic time, minutes    | 26.58 ± 2.07          | 20.96 ± 2.05           | 0.058 |
| Operation time, minutes   | 151.26 ± 7.72         | 124.71 ± 6.92          | 0.01  |

The t-test was used to evaluate significant differences between continuous variables in the same group and between the 2 groups. A p value of less than 0.05 was considered statistically significant.

Results

The entire cohort included 69 patients: the suture group included 43 patients (62.3%) while the sealant group included 26 patients (37.7%). Table 1 presents clinical, surgical and pathological variables of both study groups. No statistically significant differences in the analyzed baseline variables were noted. However, there were several statistically significant differences in operative factors. Namely, patients in the suture group had larger amount of blood loss (3-fold), longer ischemia time (26.6 vs. 21 minutes, p = 0.058) and slightly longer operation time (151.26 vs. 124.71 minutes, p = 0.01).

The mean functional volume decrease of the operated kidney after the surgical procedure was measured by QDMSA. Our analysis revealed that patients managed by sutures had nearly threefold higher parenchymal loss compared to patients managed by sealant (26.28 vs. 8.92 ml, p = 0.048). This was translated into 4.0% kidney volume loss in the sealant group compared to 11.95% of kidney volume in the sutures group (p = 0.05) (table 2). As expected, no significant change in functional renal volume was noted in the contralateral, non-operated renal unit (table 2).

Table 2. Functional volume decrease of the operated and contralateral kidney, stratified by tumor bed closure method

| Variable                  | Group  | Mean  | SEM  | p     |
|---------------------------|--------|-------|------|-------|
| Operated kidney           |        |       |      |       |
| Functional volume         | glue   | 8.92  | 6.51 | 0.048 |
| Change, ml               | suture | 26.29 | 5.59 |       |
| Functional volume         | glue   | 4.00  | 3.11 | 0.05  |
| Change, %                | suture | 11.95 | 2.46 |       |
| Contralateral kidney      |        |       |      |       |
| Functional volume         | glue   | 1.52  | 2.56 | 0.8   |
| Change, ml               | suture | 2.73  | 3.88 |       |
| Functional volume         | glue   | 0.67  | 1.3  | 0.66  |
| Change, %                | suture | 1.66  | 1.79 |       |

Discussion

The main advantage of NSS over radical nephrectomy relates to better renal function preservation and reduced rate of long-term chronic kidney disease, with no oncological compromises. Recent studies suggested that new post-NSS glomerular filtration rate (GFR) is an important predictor of long-term renal function and overall survival [10–12].

Functional recovery after NSS is mainly related to the renal tissue preservation, which depend on the amount of excised normal parenchyma surrounding the tumor and degree of devascularized kidney loss during tumor bed closure [13, 14]. The advantage of tumor enucleation over standard partial nephrectomy has already been proven and this technique is used by us routinely in all cases of the current study [15]. The sutures commonly placed during NSS to close the tumor bed in order to decrease the risk of postoperative bleeding and urine extravasation were shown to cause devascularization of the normal parenchyma and thus to be a source of functional tissue loss [16].

What is the potential functional benefit of omitting sutures for tumor bed closure is less defined and is the main aim of the current study. The major finding of our project indicate that the use of standard suture technique for reconstruction of the cavity left after tumor enucleation is associated with 3-fold increase in the amount of devascularized functional parenchyma loss compared with the use of tissue adhesives. The average percent devascularized functional volume loss in the suture and
sealant groups were 11.95 and 4% that represent 12.51 and 4.17% of the total preoperative mass of the operated kidney respectively.

Some investigators have hypothesized that the reconstructive phase of NSS is the main source of nephron mass loss and is much more important for functional outcomes after NSS than the excised parenchyma or irreversible loss of function related to ischemic injury [17, 18]. A recent study by Bahler et al. [19], in which they evaluated the functional implications of renorrhaphy, found that the step of tumor bed closure may lead to decreased nephron mass preservation and thus to compromised functional outcomes. In their study, the median volume loss was 17 ml for those managed by renorrhaphy versus 9 ml for the non-renorrhaphy group (p = 0.003). The functional advantage of using sealant rather than sutures was previously reported by Hidas et al. [20]. However, unlike the current project this study evaluated differential overall renal function and not ipsilateral functioning parenchyma of the operated kidney. The QDMSA method is a quantitative and differential technique that has been used for evaluation of the adaptive modifications occurring in functioning kidneys after nephrectomy and NSS. This method was found to be reproducible with minimal variates [8, 21–23]. The parameters determined included functional kidney volume and the concentration of the cortical agent (99m Tc-DMSA) per gram of tissue. The total kidney 99mTc-DMSA uptake obtained by multiplying these 2 parameters is an index of renal function and has been shown to correlate with effective renal plasma flow, GFR, and creatinine clearance [21, 24, 25].

Other studies have used volumetric analyses for assessment of the remaining renal parenchyma. Such analysis is usually obtained from abdominal axial CT scan or MRI for both pre- and post-operative studies. Special software (for example TeraRecon iNtuition, TeraRecon, Foster City, CA) is used to evaluate the imaging studies, with freehand approximation performed at each 3 mm interval to define the lesion and the kidney. The sum of these areas is then calculated to estimate the total renal parenchyma and tumor; the tumor alone and the final postoperative parenchymal volume. This method may be limited by inclusion of non-functioning renal structures such as renal sinus fat, collecting system, and renal cysts or scars. Moreover, estimation of parenchymal mass preserved can be subjected to measurement errors [18].

The limitations of this study include its retrospective nature, a relatively small cohort, and the lack of randomization. Furthermore, the decision to use sealant over sutures was done solely by the surgeon discretion, and the possibility of selection bias cannot be ruled out.

It is likely that the use of tissue adhesive will preferentially benefit patients with a solitary kidney or those with pre-existing chronic kidney disease, where in small and exophytic lesions the advantage of the method presented might be clinically less important.

Conclusions

Our data suggest the use of tissue sealant rather than standard sutures during tumor bed reconstruction is associated with reduced devascularized parenchymal mass loss. This may be translated into better functional outcome and should be considered among modifiable surgical factors during NSS. Large prospective study is needed to further evaluate the relative importance of this technique in different settings.

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