

# A Modified Surgical Technique Using Cyanoacrylate Glue and Parenchymal Restoration Sutures without Tissue Approximation in Patients with Renal Tumors Who Underwent Open Partial Nephrectomy

Açık Parsiyel Nefrektomi Uygulanan Böbrek Tümörlü Hastalarda Doku Yaklaştırılması Yapılmadan Siyanoakrilat Glue ve Prankimal Restorasyon Sütürleri Kullanılarak Yapılan Modifiye Cerrahi Teknik

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## What's known on the subject? and What does the study add?

Modified partial nephrectomy technique by using the cyanoacrylate glue seems to be a very effective technique with low complications rates in nephron-sparing surgery.

## Abstract

**Objective:** To investigate the results of a modified open partial nephrectomy technique by using cyanoacrylate glue after the parenchymal restoration sutures without performing tissue reapproximation and to compare complications between risk groups according to the preoperative aspects and dimensions used for an anatomical (PADUA) classification in 50 patients.

**Materials and Methods:** We performed open partial nephrectomy by using cyanoacrylate glue in 50 patients with a localized tumor and normal contralateral kidney between 2005 and 2012 with a mean follow-up of 40 months. All patients were evaluated by routine biochemical analyses and imaging modalities such as abdominal tomography and magnetic resonance when needed. PADUA scores were assessed according to the computed tomography images.

**Results:** The mean blood loss was higher and the duration of surgery and ischemia was longer in high-risk group than in low-risk group. The difference was statistically significant ( $p=0.001$ ,  $p=0.004$ , and  $p=0.0009$ , respectively). Intraoperative collecting system restoration was performed in 3 (9.9%) low-risk and 10 (50%) high-risk patients. Collecting system fistulization or chronic renal failure was not observed in any patient.

**Conclusion:** Application of cyanoacrylate adhesive in nephron-sparing surgery is safe and effective in patients with a low PADUA risk score. Further randomized and controlled studies in a large series of patients will provide more conclusive results.

**Keywords:** Partial nephrectomy, Cyanoacrylate glue, Renal tumor, Nephron-sparing surgery

## Öz

**Amaç:** Çalışmanın amacı 50 böbrek tümörü olan hastada doku yaklaştırılması uygulanmadan parankimal restorasyon sütürleri sonrası siyanoakrilat glue kullanılarak yapılan modifiye açık parsiyel nefrektomi tekniğinin sonuçlarını araştırmaktır.

**Gereç ve Yöntem:** 2005-2012 yılları arasında böbrekte lokalize tümörü olan ve karşı böbreği normal olan 50 hastaya siyanoakrilat glue hemostatik ve doku yapıştırıcısı kullanılarak modifiye açık parsiyel nefrektomi tekniği uygulandı. Hastaların ortalama takip süreleri 40 ay idi. Hastalara rutin biyokimyasal analiz, bilgisayarlı tomografi ve manyetik rezonans gibi görüntüleme yöntemleri yapıldı. Hastalara Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) skorlaması yapıldı. PADUA skorlaması görüntüleme yöntemlerine göre yapıldı. Hastalar PADUA skorlamasına göre düşük ve yüksek risk olmak üzere 2 gruba ayrıldı.

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**Bulgular:** Ortalama kan kaybı, operasyon süresi ve iskemi süresi istatistiksel açıdan anlamlı olacak şekilde yüksek riskli grupta düşük riskli gruba göre daha yüksek saptandı. Ameliyat sırasında düşük riskli gruptan 3 hastada yüksek riskli gruptan 10 hastada toplayıcı sistem onarımı yapıldı. Ameliyat sonrası takipte hiçbir grupta toplayıcı sistem fistülü ve kronik böbrek yetmezliği görülmedi.

**Sonuç:** Siyanoakrilat glue nefron koruyucu cerrahide düşük PADUA skor riski plan hastalarda daha güvenli ve etkili görülmektedir. Daha güçlü sonuçlar için randomize kontrollü, geniş hasta serili çalışmalara ihtiyaç duyulmaktadır.

**Anahtar Kelimeler:** Parsiyel nefrektomi, Siyanoakrilat glue, Renal tümör, Nefron koruyucu cerrahi

## Introduction

There are a large number of publications including open and laparoscopic partial nephrectomy (LPN) series in the literature but only limited research regarding the use of combination of haemostatic agents (HAs) and tissue glues, is available (1,2). Therefore, in this paper, we present 50 patients who underwent open partial nephrectomy (OPN) using cyanoacrylate glue after applying parenchymal restoration sutures without tissue reapproximation between 2005 and 2012.

Fibrin was first used as a HA by Bergel in 1909 (3). Human fibrinogen and thrombin were obtained as a result of separation of plasma in 1938, and the first fibrin glue was developed in 1944. Cronkite et al. (4) used combined fibrinogen and thrombin in 1944 to prolong the life of skin grafts and increase the adhesion of graft in severe burn cases. After these developments, Gelfoam® and Oxygel® were introduced in 1945, followed by Surgicel® in 1960. In 1972, Matras combined cryoprecipitate with pure bovine thrombin to obtain the first modern fibrin glue (5).

In this study, we also classified patients as high- and low-risk groups according to the preoperative aspects and dimensions used for an anatomical (PADUA) classification and compared the laboratory findings, intraoperative results, and complications between the two groups (6).

## Materials and Methods

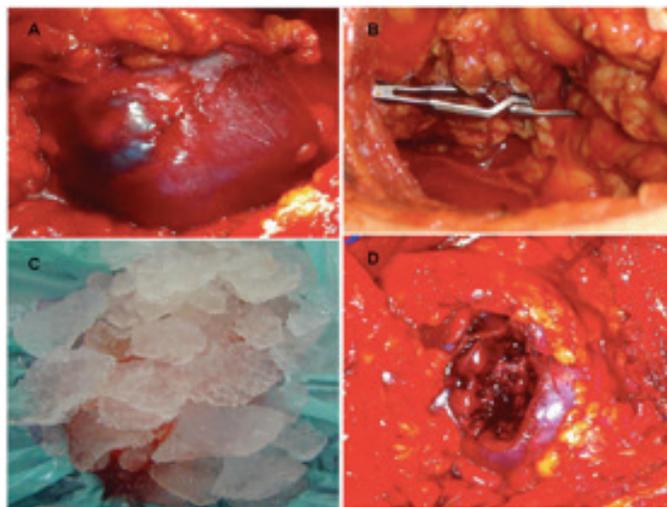
We performed OPN in 50 patients (27 male, 23 female) with localized tumours and a normal contralateral kidney between April 2005 and March 2012 with a mean follow-up of 40 months. The mean age of the patients was 58.4 ( $\pm$ 9.43) years. Patients with bilateral renal tumours, spinal problems or accompanying system tumours, those over 80 years of age, and those having more than one mass in one kidney were excluded. All patients were evaluated by routine biochemical analyses and imaging modalities, such as abdominal computed tomography and magnetic resonance imaging when needed. The PADUA scoring system was employed based on the computed tomography images as defined before. The patients with a PADUA score of 6-7 were placed in the low-risk group and those with a PADUA

score of  $\geq$ 8 in the high-risk group. The study were approved by the Ankara Atatürk Training and Research Hospital of Local Ethics Committee (protocol number: 2012/İK-04). Consent form was filled out by all participants.

## Surgical Technique

All patients were operated on using subcostal flank incision including rib resection (rib bed incision). The 11<sup>th</sup> rib was resected in 50 patients. After applying the standard extraperitoneal approach, the renal artery was clamped from the posterior approach for warm ischemia, and ice was used for cold ischemia (Figure 1).

After achieving warm ischemia, mannitol infusion was commenced. The standardized partial nephrectomy technique was performed following 10 minutes of cold ischemia. Having finished resection, restoration sutures were used for controlling bleeding and closing the collecting system. After releasing the arterial clamp, additional bleeding areas were closed and the collecting system was checked using methylene blue through the ureteral catheter. Following these procedures, cyanoacrylate glue (Glubran®; General Enterprise Marketing, Viareggio, Lucca, Italy) was applied to the floor of the resection area (Figure 2). Having achieved complete control, Gerota's fascia was attached to the tumour bed. No approximation sutures were used



**Figure 1.** A) Image of the lower pole tumor of the right kidney, B) Clamping of the renal artery, C) Application of ice for cold ischemia, D) Image of the kidney after the tumor resection

between the edges of the parenchyma, such as over absorbable bolsters (Figure 2).

Duration of the surgery, renal ischemia time, amount of blood loss, and transfusion demand were also recorded and compared between the high- and low-risk groups. Postoperative complications were also evaluated and compared. The detailed analysis of the results will be presented in another publication. In the present study, only the complications and perioperative parameters pertinent to the technique are discussed and compared.

### Statistical Analysis

All data were analysed using Statistical Package for Social Sciences software, v. 16.0 (SPSS Inc., Chicago, IL, USA). Parametric continuous variables were given as the mean plus or minus standard deviation and categorised according to the median value. Statistical comparison was performed between the high- and low-risk groups. The independent samples t-test was used to compare the variables. A p value of less than 0.05 was considered statistically significant.

### Results

Tumours were localised on the right in 21 patients (42%) and on the left in 29 (58%). The mean tumour diameter was  $3.61 \pm 1.3$  cm. The diameter was  $\leq 4$  cm in 34 patients and varied between 4.1 and 7 cm in 16 patients. Tumour distribution according to the PADUA scoring system is given in Table 1 and Figure 2. Thirty patients (60%) were categorized as having low risk and 20 (40%) as having high risk. Diabetes mellitus type 2, hypertension and hypercholesterolemia were diagnosed in 10 (20%), 23 (46%)

and eight (16%) patients, respectively. Twenty-nine of the 52 patients (48%) were heavy smokers.

At least one of the symptoms of lumbar pain, macroscopic haematuria and weight loss was found in 32 patients (64%). Clinical and pathological characteristics are also summarised in Table 1.

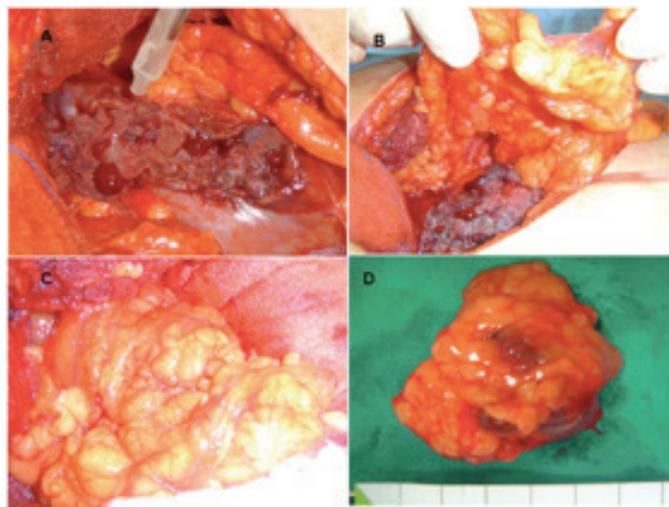
The mean blood loss was higher and the duration of the surgery and ischemia was found to be longer in the high-risk group than in the low-risk group (Table 2A). The differences between the two groups were statistically significant ( $p=0.001$ ,  $p=0.004$  and  $p=0.0009$ , respectively) (Table 2A). Intraoperative collecting system restoration was performed in three (9.9%) low-risk and 10 (50%) high-risk patients with a statistically significant difference ( $p=0.0001$ ) (Table 2A). Collecting system fistulisation was not observed in any of the patients.

Blood transfusion was needed in three patients intraoperatively. Although a higher rate of transfusion requirement was observed in the high-risk group, there was no statistically significant difference between the two groups (Table 2B). The rate of pleural damage was higher and the length of hospital stay was longer in the high-risk group. Acute renal failure developed in three patients in each group. Chronic renal failure was not observed in any patient.

**Table 1. The clinical and pathological features of patients**

Average age (year) (mean +/- SD)	58.44±9.43
Female, n (%)	27 (54%)
Male, n (%)	23 (46%)
Tumor of the right kidney n (%)	21 (42%)
Tumor of the left kidney n (%)	29 (58%)
The mean tumor size (mm) (mean +/- SD)	36.1±13.1
Upper pole tumor n (%)	14 (28%)
Middle pole tumor n (%)	12 (24%)
Lower pole tumor n (%)	24 (48%)
≥50% exophytic tumor n (%)	37 (74%)
<50% exophytic tumor n (%)	8 (16%)
Completely endophytic tumor n (%)	5 (10%)
Lateral tumor n (%)	43 (86%)
Medial tumor n (%)	7 (14%)
Connected with renal sinus n (%)	9 (18%)
Nonconnected with renal sinus n (%)	41 (82%)
Connected with collecting system n (%)	8 (16%)
Nonconnected with collecting system n (%)	42 (84%)
Tumor size $\leq 4$ cm n (%)	34 (68%)
Tumor size 4.1-7 cm n (%)	16 (34%)
Low-risk patient in the PADUA score system	30 (60%)
High-risk patient in the PADUA score system	20 (40%)

PADUA: Preoperative aspects and dimensions used for an anatomical



**Figure 2.** A) Application of the glubran on the resection area, B) Gerotal tissue closure over the area of resection, C) Image of the right kidney after the gerotal tissue closure, D) Image of the tumor and surrounding tissues after the resection

**Table 2A. Comparison of the intraoperative results between preoperative aspects and dimensions used for an anatomical risk groups**

PADUA risk group	Patient (n-%)	Average blood loss (mL)	Average operation time (minimum)	Average ischemia time (minimum)	Collecting system repairing (n-%)
Low	30	200±133,9	178.5±22.3	26.3±3.85	3 (9.9%)
High	20	315±87.5	212±20.15	34.05±3.37	10 (50%)
p*	-	0.001	0.0004	0.0009	0.001

PADUA: Preoperative aspects and dimensions used for an anatomical, \*Independent-sample t-test

**Table 2B. Comparison of the complications between preoperative aspects and dimensions used for an anatomical risk groups in postoperatively**

PADUA risk group	Patient (n-%)	Postoperative transfusion (n-%)	Postoperative damage of pleura (n-%)	Postoperative acute renal failure (n-%)	Average hospitalization time (date)	Postoperative urine leak
Low	30	1 (3.33%)	2 (6.6%)	3 (9.9%)	3.86±1.25	0
High	20	2 (10%)	7 (35%)	3 (15%)	4.7±1.65	0
p*	-	0.082	0.01	0.6	0.034	-

PADUA: Preoperative aspects and dimensions used for an anatomical, \*Independent- Sample t-test

## Discussion

There is only limited information about the use of HAs and glues in the literature. Recent studies reported the potential efficacy of these materials in reducing haemorrhage and urinary leakage in LPN series (7). In this paper, we presented a series of 50 patients who underwent modified OPN, in whom we used cyanoacrylate glue after parenchymal restoration sutures without tissue reapproximation. Tissue sealants and glues as renal HAs have been used for many years and shown to improve haemostasis and aid in collecting system repair with fewer complications (7). There are many types of HAs and glues, such as gelatine matrix thrombin tissue sealant (FloSeal; Baxter Healthcare, Deerfield, IL, USA), fibrin glue (Tisseel; Baxter), bovine serum albumin-based adhesive (BioGlue; CryoLife, Keensaw, GA, USA), and cyanoacrylate glue (Glubran; General Enterprise Marketing, Viareggio, Lucca, Italy). The limited number of publications comparing the features of these agents in partial nephrectomy series including small tumours reported them to be effective (8). Glubran constitutes a thin resistant membrane when applied to the tissue through a polymerization mechanism in 1-2 s. It prevents fluid permeability by reaching the maximal solidification process in 60-90 s. To the best of our knowledge, our study described the only OPN series in which glubran was used as a single agent over the resection area after achieving bleeding control and collecting system closure without performing any approximation sutures between the edges of the parenchyma, such as over absorbable bolsters. In a previous multicentric study, different HAs were used in 1.041 patients who underwent LPN, and in 34 of these patients, glubran was applied over surgical using parenchymal approximation sutures (7).

In a survey study including 1347 patients who underwent LPN, the overall rates of haemorrhage requiring transfusion and urine leakage in cases for whom HAs and/or glues were used were 2.6% and 19%, respectively (7). These percentages were lower compared to previous series in which no sealant or glue was used. In another study including 1.118 partial nephrectomy patients, the fistulisation percentage was found to be 4.4% (9). Minervini et al. (10) reported fistulisation in 3% of 200 patients who had undergone OPN. In our series, urine leakage was not observed in any patient postoperatively. Although it is very difficult to reach conclusive results in a limited number of patients, it was very interesting not to have encountered any urinary leakage especially in high-risk patients. This was probably due to our modification to the surgical technique explained in the related section. Furthermore, we used cold (ice) and warm ischemia concordantly in our technique and gained an important time advantage by refraining from using parenchymal approximation sutures. It is well known that ischemia duration is very important in partial nephrectomy series. The mean cold ischemia time was previously reported as 45 minutes in an OPN series of 238 patients and 52 minutes in an LPN series (11,12). However, the mean ischemia duration was found to be shorter in our series compared to the literature, especially for the high PADUA risk group, but chronic renal failure was not observed in any of our patients. To the best of our knowledge, there is no other study in the literature reporting OPN series using the cold and warm ischemia techniques concomitantly.

We found that the mean blood loss was higher and the duration of surgery and ischemia was longer in the high PADUA risk group than in the low-risk group. Although more transfusion

requirement was observed in the high-risk group, there was no statistically significant difference between the two groups. Ficarra et al. (6) reported high intraoperative complication rate in 119 partial nephrectomy patients classified as having high risk. In another series, similar results were obtained from 62 patients who had undergone robotic partial nephrectomy (13).

### Study Limitations

The prominent limitation of the study is the fact that the patients who underwent partial nephrectomy had not been compared with the patients who underwent classical renography.

### Conclusion

Application of cyanoacrylate glue is safe and effective in nephron-sparing surgery in patients with a low PADUA risk score. It is necessary to perform randomised and controlled studies in a large series of patients to reach more conclusive results.

### Ethics

**Ethics Committee Approval:** The study were approved by the Ankara Ataturk Training and Research Hospital of Local Ethics Committee (protocol number: 2012/İK-04).

**Informed Consent:** Consent form was filled out by all participants.

**Peer-review:** Externally peer-reviewed.

### Authors Contrubious

Concept: E.I., Design: Ö.K., Data Collection and/or Processing: E.I., Analysis and/or Interpretation: E.O.

Literature Research: E.I., Writing: Ö.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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