Efficiency and safety of five procedures for percutaneous native kidney biopsy: a multicentric comparative study.


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Original article

Efficiency and safety of five procedures for percutaneous native kidney biopsy: a multicentric comparative study.

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Stanislas Bataille (1), Laurent Daniel (2), Jean-René Mondain (3), Magali Faure (3), Pierre Gobert (4), Zarih Alcheikh-Hassan (4), Michel Lankester (5), Philippe Giaime (6), Jean Gaudart (7), Yvon Berland (1), Stéphane Burtey (1)

(1) Aix-Marseille Univ, 13284, Marseille, France, APHM, Hôpital de la Conception, Centre de néphrologie et transplantation, 13005, Marseille, France.
(2) Aix-Marseille Univ, 13284, Marseille, France, APHM, Hôpital de la Timone, Laboratoire d'Anatomie Pathologique et Neuropathologie, 13005, Marseille, France.
(3) Service de néphrologie, Hôpital Font Pré, 1208 avenue Colonel Picot BP 1412 Toulon Cedex, France
(4) Service de néphrologie, Hôpital Général Henri Duffaut, Rue Raoul Follereau 84902 Avignon Cedex. France
(5) Service de néphrologie, Clinique La Résidence Du Parc, Rue Gaston Berger 13010 Marseille, France.
(6) Service de néphrologie, Clinique Bouchard, Rue du Docteur Escat, 13006 Marseille, France.
(7) Aix-Marseille Univ, LERTIM EA3283, 13005, Marseille, France; APHM, Hôpital de la Timone, UF Biostatistiques, 13005, Marseille, France.
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Corresponding authors:
Stanislas Bataille, MD
Service de néphrologie
Hôpital de La Conception
147 Boulevard Baille
13005 Marseille, France
Tel : +33 (0)4 91 38 30 42
Email: stanislas.bataille@ap-hm.fr

Stéphane Burtey, MD-PhD
Service de néphrologie
Hôpital de La Conception
147 Boulevard Baille
13005 Marseille, France
Tel : +33 (0)4 91 38 30 42
Email : stephaneb@ap-hm.fr

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Abstract

Background and objectives
Renal biopsy (RB) is necessary for the diagnosis, prognosis, and therapy guidance of native kidney diseases. Few studies have compared outcomes of RB procedures. We compared the efficiency and safety of five biopsy procedures.

Design, setting, participants, and measurements
Number of glomeruli on light microscopy (LM) and on immunofluorescence (IF) and serious adverse events following RB performed in five nephrology units (C1-C5) were retrospectively collected.

C1 performed ultrasound assessment before RB and used a 14-gauge core-cutting needle biopsy gun, C2 ultrasound guidance and a 14-gauge needle, C3 tomodensitometry guidance and a 14-gauge needle, C4 ultrasound guidance and a 16-gauge needle, and C5 tomodensitometry guidance and a 16-gauge needle.

Results
Data from 943 RB performed between January 2006 and July 2010 were collected (C1: 408; C2: 254; C3: 81; C4: 136; C5: 64). On LM, mean number of glomeruli on biopsy core was 14.2±8.6. It was higher in C1 and C2 than in C3, C4, and C5 (p=0.01). At least 10 glomeruli were found in 69% of biopsies. This rate was higher in C1 and C2 than in C3, C4, and C5 (p=0.004). On IF, mean number of glomeruli was 4.4±3.3. It was higher in C1 and C2 than in C3, C4, and C5 (p<0.001). In multivariate analysis, the only factor that influenced number of glomeruli on LM (p=0.004) and IF (p=0.004) was the nephrology unit. Serious adverse events occurred in 1.5% of biopsies. Complication rate was not different between nephrology units.

Conclusions
Efficiency and safety of kidney biopsy

RB is safe but radiological guidance, needle-size, and experience influence the quality of biopsies.

**Keywords:** Renal biopsy; Procedure; Efficiency; Glomerular disease
Efficiency and safety of kidney biopsy

Introduction

Renal biopsy (RB) is necessary for the diagnosis, prognostic assessment, and therapy guidance of various diseases affecting native kidneys or transplants. Percutaneous native kidney RB procedures vary widely among nephrology units according to personal experience and availability of particular techniques (1). The gold-standard procedure should maximize the yield of tissue sampled and minimize the risk of major hemorrhagic complications.

Three techniques are currently used for radiological guidance: real-time ultrasonographic (US) guidance, US assessment before RB, and tomodensitometry. These procedures are respectively used in 67%, 26%, and 6% of the French nephrology units (1). Biopsy-core needle size varies from 12 to 18 gauge; 16 gauge is the most used (58.3% of nephrologists) (1).

Procedures might influence renal core size, which is critical for diagnosis. Clearly, having many tissues and glomeruli is diagnostically useful (2). To our knowledge, few studies have been published on the efficiency of RB procedures in adults (3, 4, 5). The gold standard for RB procedures remains to be defined.

As an invasive procedure, RB also incurs potential bleeding complications of variable severity from transitory gross hematuria or pauci symptomatic hematoma to massive bleeding requiring nephrectomy and, very rarely, death (6, 7, 8). Although several studies have revealed risk factors associated with bleeding (9, 10, 11), it remains unknown which procedure best prevents complications.

Our study compares the efficiency and safety of five native kidney percutaneous biopsy procedures in five nephrology units.

Materials and Methods

Patients
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Data from percutaneous native kidney biopsies performed between January 2006 and July 2010 in five nephrology units in the south of France were retrospectively collected. We recorded age at biopsy, gender, number of glomeruli on light microscopy (LM), number of glomeruli on immunofluorescence (IF), histopathological diagnosis, and the occurrence of any serious adverse event following renal biopsy. A serious adverse event was defined as bleeding requiring transfusion (hematoma or hematuria), arteriovenous fistula requiring embolization, pneumoperitoneum or urinoma, nephrectomy for bleeding or death.

Renal biopsy procedures

The five nephrology units named C1 to C5 consisted of one teaching hospital (C1), two public general hospitals, and two private centers. The RB procedures of these units are reported in table 1. All the units gave the patients oral and written information on the procedure and risks of the RB. Only one of the five units did not require written consent.

In C1, oral and written information and consent was collected. Assessment of hemorrhagic risk factors before RB consisted of oral questioning about personal bleeding history, blood cell count, coagulation tests, and bleeding time. Nephrologists did not perform biopsy if systolic blood pressure was higher than 150 mmHg or if diastolic blood pressure was higher than 90 mmHg. No sterile urinalysis was required. The biopsy was performed by a senior or junior nephrologist. Radiological guidance was performed with ultrasound assessment before RB. Two biopsy cores were taken with a 14-gauge core-cutting needle automated side-notch biopsy gun. Patients were monitored during 24 h in hospital lying in bed.

In C2, assessment of hemorrhagic risk factors was the same as in C1 except that blood pressure control required was less stringent, i.e. \( \leq 160/95 \) mmHg. C2 was the only unit in which radiologists but not the nephrologists performed the kidney biopsy. The sampling was performed with US guidance: US was performed during the biopsy. As in C1, two fragments
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were taken with a 14-gauge core-cutting needle automated biopsy gun and patients were monitored during 24 h lying in bed.

In C3, the same hemorrhagic risk factors were assessed except bleeding time, which was not required. Blood pressure control was ≤140/90 mmHg. Kidney biopsies were performed by the nephrologists with tomodensitometry guidance. Two fragments were taken with a 14-gauge needle automated biopsy gun. Patients were monitored 24 h in hospital after biopsy as in all other units.

In C4, nephrologists performed biopsy with US guidance like the radiologist in C2. The automatic biopsy gun needle was 16 gauge, which is smaller than in C1, C2, and C3. Two fragments were systematically taken: one for light microscopy and one for immunofluorescence. Only coagulation tests and oral bleeding history were checked but not blood cell count, urinalysis, or bleeding time. Blood pressure was required to be ≤140/90 mmHg before biopsy and patients stayed in bed for 24 h hospital monitoring.

In C5 as in C3, the nephrologists performed kidney biopsy under tomodensitometry guidance. Two fragments were taken with a 16-gauge needle automatic biopsy gun as in C4. Blood cell count, coagulation tests, and bleeding time were performed before biopsy and blood pressure ≤150/90 mmHg was required. C5 was the only unit requiring urinalysis before biopsy. As in all the previous units, patient stayed in bed for 24 h in hospital.

Laboratory biopsy analysis

One fragment was taken for light microscopy (LM) and the other for immunofluorescence (IF). For LM, tissue was fixed in 2.5% glutaraldehyde for 12 h and embedded in araldite. Serial sections of 2 and 0.25 µm were stained respectively with Masson’s trichrome and Jones staining. Glomeruli were counted only if the whole glomerulus was present on the specimen. Material for IF was fixed in Michel’s liquid for 24-48 h and then frozen in -80°C isopentane.
Sections of 5µm were used for IF with fluorescein-conjugated antibodies specific for human IgG, IgM, IgA, C3, C1q, and kappa and lambda light chains. Glomeruli on frozen sections were counted excluding sclerosed glomeruli. During the study, all biopsies were read by the same pathologist. When no glomeruli were available, the biopsy was considered to have failed. In most glomerulopathy classifications, at least 10 glomeruli are required to consider the core biopsy representative and the diagnosis accurate (12, 13, 14). Thus, on LM analysis, biopsies were separated into three groups according to the number of glomeruli on tissue fragments: 0 glomeruli, 1 to 9 glomeruli, and 10 glomeruli or more. On IF analysis, because the number of glomeruli is less critical, biopsies were separated into only two groups: those with glomeruli and those with no glomeruli.

**Statistical Analysis**

For univariate analysis, mean comparisons were tested using analysis of variance (or Kruskall Wallis test if necessary). Relationships between qualitative variables were assessed using Pearson Khi² (or Fisher exact test if necessary). Relationships between quantitative variables were assessed using Pearson correlation coefficient (or Spearman approach if necessary). For multivariate analysis, logistic regression assessed covariates associated to LM and IF. P-values were interpreted with a risk $\alpha=0.05$. The PASW® 17.0.2 (SPSS Inc.) software was used for statistical analysis.

**Results**

**Efficiency of renal biopsy procedures**

Data from 943 native kidney RB were collected (C1: 408; C2: 254; C3: 81; C4: 136; C5: 64). Of them, 534 (57%) were men. Sex ratio was not different between the five nephrology units
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(p=0.053). Mean age at biopsy was 52.8±19.7 (mean ±SD) years old (Table 2). It was statistically higher in C2 (57.2 ±20.0 years old) than in the other units (p<0.001).

On LM, mean number of glomeruli on biopsy core was 14.2 ±8.6 (mean ±SD). It was statistically higher in C1 (15.1 ±9.1) and C2 (14.3 ±8.3) than in C3 (12.3 ±9.5), C4 (12.7 ±7.3), and C5 (13.3 ±7.4) (p=0.01). The number of biopsies with at least 10 glomeruli on LM was 651/943 (69%). It was higher in C1 (72%) and C2 (71%) than in C3 (57%), C4 (63%), and C5 (67%) (p=0.004) (Figure 1A).

On IF, mean number of glomeruli on biopsy core was 4.4 ±3.3 (mean ±SD). As for LM, mean number of glomeruli was higher in C1 (5.2 ±3.8) and C2 (4.4 ±2.9) than in C3 (2.7 ±2.9), C4 (3.6 ±2.4), and C5 (3.6 ±2.7) (p<0.001) (Figure 1B).

Number of failed biopsies was 48/943 (5%) on LM. This rate was higher in C1 (8%) and C3 (9%) than in the other units (p<0.001). Number of failed biopsies on IF was 99/943 (10%). It was higher in C3 (33%) than in the other nephrology units (p<0.001). Causes of failure are classified in two categories: medullary core with no glomeruli or no kidney core (Table 3).

Renal diseases were nephroangiosclerosis (14%), IgA nephropathy (10%), minimal change nephropathy (9%), extracapillary glomerulonephritis (9%), lupus nephropathy (9%), focal and segmental glomerular sclerosis (8%), membranous glomerulonephritis (8%), interstitial nephritis (6%), diabetic nephropathy (4%), amyloidosis (3%), membranoproliferative glomerulonephritis (2%), others (14%), and no diagnosis (4%). Histology influenced the mean number of glomeruli on LM (p=0.001) and IF (p=0.015) in univariate analysis, but this effect was not found in multivariate analysis (p=0.4 and p=0.3).

In univariate analysis, the numbers of glomeruli on LM analysis and on IF analysis were correlated with a correlation coefficient (CC) of 0.306 (p<0.001). Age was inversely correlated to number of glomeruli on LM (CC= -0.107; p=0.001) and to number of glomeruli in IF (CC= -0.086; p=0.005). Number of glomeruli on LM was higher in women (15.5+/−9.0;
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mean ±SD) than in men (13.2±8.2) (p<0.001). On IF analysis, gender did not affect number of glomeruli, which was identical (4.4+/−3.3) in men and in women (p=0.8).

In multivariate analysis, the only factor that significantly influenced number of failed biopsies on LM (p=0.004) and IF (p=0.004) was the nephrology unit.

Safety of renal biopsy procedures

Serious adverse events occurred in 14/943 (1.5%) of biopsies (Table 4). No nephrectomy or death was reported. Complication rate did not differ with nephrology unit (p=0.7), age (p=0.3), or gender (p=1).

Discussion

Most nephrologists perform renal biopsy by a standard technique developed in the early 1990s with an automated biopsy device and radiological guidance (15). Its superiority over previous techniques has been validated (5). Many options remain possible for radiological guidance techniques, and core-cutting needle size may vary between 14 and 18 gauge. Moreover, the precautions taken before and after biopsy vary according to nephrology units (16). In our retrospective study of 943 kidney biopsies comparing five different practices, we found no difference concerning severe complications according to biopsy procedure, but the choice of the procedure may affect biopsy efficiency.

The practices in our study are representative of daily practices in nephrology units in France (1). Within the five nephrology units, all gave oral and written information prior to biopsy concerning indication, technique, monitoring, and recommended post-procedure precautions or potential complications. Four out of five units obtained written consent for RB. Bollée et al. reported 56% of units in France gave oral and written information and only 44% of units obtained written consent (1). Assessment of hemorrhagic risk factors before RB included oral
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questioning about personal history of bleeding, blood cell count, and coagulation tests (prothrombin time and activated partial prothrombin time) in all units, but none obtained written questioning about personal history of bleeding. Differences appeared regarding bleeding time, which was recorded in only two units, and in platelet function analyzer (PFA100), recorded in one unit. Two units reported neither bleeding time nor platelet function analyzer. In all of France, 100% of nephrologists perform coagulation tests, 98% blood cell count, 76% oral questioning about personal history of bleeding, 57% bleeding time, and 11% PFA100 (1). Units C3 and C4 were stringent with hypertension whereas C2 tolerated hypertension of 160/95. In the literature, it remains controversial whether hypertension increases hemorrhagic risk (7, 9, 17). All of our patients were hospitalized for 24 h after biopsy. Whittier et al. reported a 33% risk of bleeding occurring 8 h after biopsy and an 11% risk of bleeding more than 24 h after biopsy (17).

When minimal precautions are taken (blood cell count, coagulation test, no uncontrolled hypertension), RB is safe whatever the procedure used. In our “real-life practices” study, we found an overall serious adverse event rate of 1.5%, which is consistent with previously reported rates (7, 16). In the literature, serious complication following renal biopsy ranges from 0 to 7.7% (18). This rate is higher using Tru-Cut device instead of automated biopsy gun (19, 20), which explains why Tru-Cut is now abandoned. In a retrospective study of 5832 renal biopsies, Atwell et al. reported an overall complication rate of 0.6%, which did not differ whether the patient was treated by aspirin or not at biopsy (21). Similarly, in our study, no difference was found between nephrology units. Thus, RB complication remains rare and technical procedure does not affect the rate of serious complications. Nevertheless, techniques might influence the efficiency of the kidney biopsy.
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Number of glomeruli is critical for interpretation and classification of nephropathy in numerous international classifications. At least 10 glomeruli are recommended to provide an accurate diagnosis and prognosis based on RB (12, 13, 14). According to the literature, mean numbers of glomeruli on biopsies vary between 9 and 33 (18) according to needle size (19, 20). In C1 and C2, the mean number of glomeruli and the proportion of kidney biopsies with more than 10 glomeruli were higher than in the other units. Two explanations can be given. First, C1 and C2 used 14-gauge core-cutting needles. In the literature, size of the needle influences the mean number of glomeruli on biopsies (2) and logically, 14-gauge needles provide more glomeruli on biopsy. Nevertheless, C3 also used 14-gauge needles, but had the lowest number of glomeruli on biopsies. The second explanation is that the two units (C1 and C2) who had the highest number of glomeruli on renal core on LM and IF are the two units performing the most biopsies. Thus, experience of biopsy may be critical for RB efficiency. Interestingly, C1 had a high mean number of glomeruli and successful biopsies but also a high rate of failed biopsies.

In our overall population, biopsy failed on LM and IF in respectively 5 and 10% of biopsies. Reported rates of failed biopsy range between 0 and 6% (22, 18, 6). Scheckner et al. reported a 10.7% rate of inconclusive renal biopsies, including 1.5% with no kidney core available in a pediatric population (23). In our study, the number of failed biopsies was higher in C1 and C3. What is remarkable in these two units is that failed biopsies are mainly due to the absence of renal core and not to medullar sampling. The absence of kidney sample is certainly due to imprecise kidney localization. Thus, practices could be improved, especially in C1 where radiological guidance technique is US assessment before RB and not real-time guidance. This is supported by the findings of Maya et al., who showed that US guidance was more efficient than US previous assessment before RB (5). The high rate of failure in C1 might also be explained by a lack of experience, since it is a teaching nephrology unit.
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Limitations of this study are retrospective data recording, lack of report of minor (but frequently not clinically relevant) complications, and absence of one-day procedure comparison. However, for native kidney, full hospitalization is the main procedure in France and worldwide (1). The 24 h follow up after procedure is important regarding the 20% rate of complications occurring between the 8th and the 24th hour following RB (17).

In conclusion, renal biopsy is safe, with an overall serious adverse event rate of 1.5% whatever the procedure used. The quality of biopsies is influenced by radiological guidance, core-cutting needle-size, and experience. We propose that real time US guidance, a 14-gauge core-cutting needle automatic biopsy device, and good operator experience should be considered as the gold standard for native kidney biopsy.
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References


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Tables and figures

Table 1: Kidney biopsy protocols in each of the nephrology units.

Table 2: Demographic data, efficiency and complications of renal biopsies.

Table 3: Number of renal biopsy failures on light microscopy and immunofluorescence according to the cause of failure.

Table 4: Serious adverse events following renal biopsies according to nephrology unit.

Figure 1: Number of glomeruli in biopsy core on light microscopy (LM) and immunofluorescence (IF) according to nephrology unit.
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### Table 1: Kidney biopsy protocols in each of the nephrology units.

BH: Bleeding personal history. * Coagulation test includes prothrombin time and activated partial prothrombin time.
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<td>254</td>
<td>81</td>
<td>136</td>
<td>64</td>
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<tr>
<td>Number of men</td>
<td>534 (57%)</td>
<td>217 (53%)</td>
<td>146 (58%)</td>
<td>41 (51%)</td>
<td>87 (64%)</td>
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<td>Age at biopsy in years (mean ±SD)</td>
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<td>50.3 ±13.3</td>
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<td>Mean number of glomeruli on LM (mean ±SD)</td>
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<td>15.1 ±9.1</td>
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<td>Mean number of glomeruli on IF (mean ±SD)</td>
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<td>0 glomeruli</td>
<td>48 (5%)</td>
<td>32 (8%)</td>
<td>3 (1%)</td>
<td>7 (9%)</td>
<td>4 (3%)</td>
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<td>1 to 9 glomeruli</td>
<td>244 (26%)</td>
<td>81 (20%)</td>
<td>70 (28%)</td>
<td>28 (34%)</td>
<td>46 (34%)</td>
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<td>≥ 10 glomeruli</td>
<td>651 (69%)</td>
<td>295 (72%)</td>
<td>181 (71%)</td>
<td>46 (57%)</td>
<td>86 (63%)</td>
<td>43 (67%)</td>
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<td>Number of biopsies with serious adverse events</td>
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Table 2: Demographic data, efficiency and complications of renal biopsies. SD: standard deviation. LM: light microscopy. IF: immunofluorescence.
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<td>33 (69%)</td>
<td>26 (81%)</td>
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<td>3</td>
<td>7</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td><strong>Immunofluorescence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No kidney core*</td>
<td>44 (44%)</td>
<td>22 (59%)</td>
<td>4 (25%)</td>
<td>15 (55%)</td>
<td>0 (0%)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Medullary</td>
<td>55 (56%)</td>
<td>15 (41%)</td>
<td>12 (75%)</td>
<td>12 (45%)</td>
<td>13 (100%)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Total</td>
<td>99</td>
<td>37</td>
<td>16</td>
<td>27</td>
<td>13</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 3: Number of renal biopsy failures on light microscopy and immunofluorescence according to the cause of failure. * No kidney core includes no core available for histopathology or extra-renal tissue.
## Efficiency and safety of kidney biopsy

<table>
<thead>
<tr>
<th></th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>3 Arteriovenous fistula with embolization, 4 Hematoma with transfusion</td>
</tr>
<tr>
<td>C2</td>
<td>2 Arteriovenous fistula with embolization, 1 Hematoma with transfusion</td>
</tr>
<tr>
<td>C3</td>
<td>1 Hematoma with transfusion</td>
</tr>
<tr>
<td>C4</td>
<td>1 Arteriovenous fistula with embolization</td>
</tr>
<tr>
<td>C5</td>
<td>1 Pneumoperitonitis, 1 Urinoma</td>
</tr>
</tbody>
</table>

**Table 4: Serious adverse events following renal biopsies according to nephrology unit.**