

The risks associated with percutaneous native kidney biopsies: a prospective study

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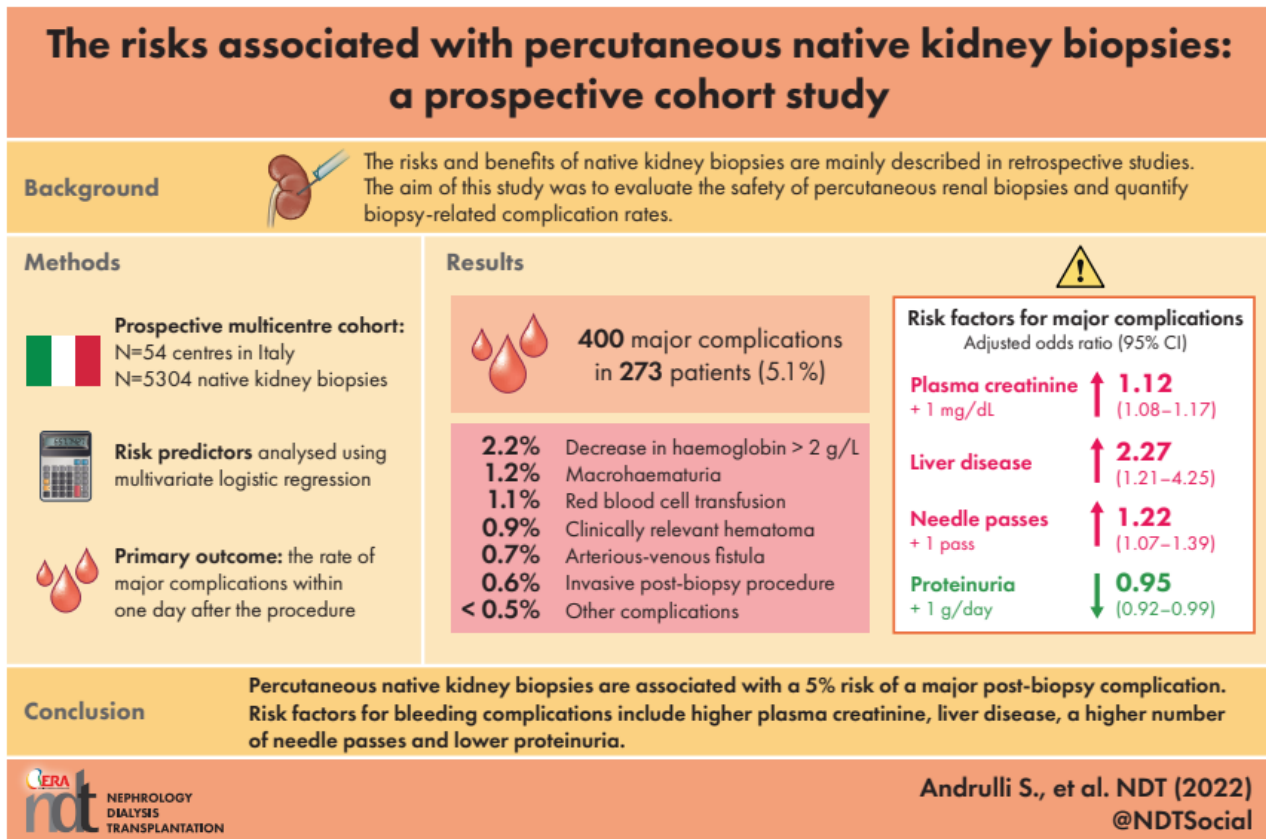
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GRAPHICAL ABSTRACT



ABSTRACT

Background. The known risks and benefits of native kidney biopsies are mainly based on the findings of retrospective studies. The aim of this multicentre prospective study was to evaluate the safety of percutaneous renal biopsies and quantify biopsy-related complication rates in Italy.

Methods. The study examined the results of native kidney biopsies performed in 54 Italian nephrology centres between 2012 and 2020. The primary outcome was the rate of major complications one day after the procedure, or for longer if it was necessary to evaluate the evolution of a complication. Centre and patient risk predictors were analysed using multivariate logistic regression.

Results. Analysis of 5,304 biopsies of patients with a median age of 53.2 years revealed 400 major complication events in 273 patients (5.1%): the most frequent was a ≥ 2 g/dL decrease in hemoglobin levels (2.2%), followed by macrohematuria (1.2%), blood transfusion (1.1%), gross hematoma (0.9%), artero-venous fistula (0.7%), invasive intervention (0.5%), pain (0.5%), symptomatic hypotension (0.3%), a rapid increase in serum creatinine levels (0.1%), and death

(0.02%). The risk factors for major complications were higher plasma creatinine levels (OR 1.12 for each mg/dL increase, 95% CI 1.08-1.17), liver disease (OR 2.27, CI 1.21-4.25), and a higher number of needle passes (OR for each pass 1.22, CI 1.07-1.39), whereas higher proteinuria levels (OR for each g/day increase 0.95, CI 0.92-0.99) were protective.

Conclusions. This is the first multicentre prospective study showing that percutaneous native kidney biopsies are associated with a 5% risk of a major post-biopsy complication. Predictors of increased risk include higher plasma creatinine levels, liver disease, and a higher number of needle passes.

Keywords: kidney biopsy, logistic regression, major complications, prospective cohort study, risk

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KEY LEARNING POINTS

What is already known about this subject?

Until now, the known risks and benefits of native kidney biopsies were mainly based on the findings of retrospective studies.

What this study adds?

This is the first multicentre prospective study showing that percutaneous native kidney biopsies in Italy are associated with a consistent and quantifiable 5% risk of a major post-biopsy complication. Predictors of increased risk include higher plasma creatinine levels, liver disease, a low proteinuria and a higher number of needle passes.

What impact this may have on practice or policy?

The prospective estimated risk of a major post-biopsy complication may be used to improve informed consent procedures. Our findings will be of interest as they could have a very positive clinical impact on the diagnostic work-up and management of patients with a still undefined nephropathy.

INTRODUCTION

Over the last 40 years, the approach to renal biopsies has evolved as a result of the use of ultrasound to examine the kidney [1] before and during the procedure (ultrasound-assisted biopsy) or to guide the biopsy needle (ultrasound-guided biopsy), and automatic core biopsies [2]. However, despite these advances, native kidney biopsies are not devoid of risks [3-6], and no large-scale, multicentre study has provided prospective quantitative data concerning the risk of major complications that would allow nephrologists to give patients more precise information during informed consent procedures.

The aim of this Italian national multicentre study was to collect data concerning the results of native kidney biopsies in Italy that would allow a more accurate evaluation of the risk of major procedure-related complications. The main aim of this study was not the exact timing of major complications, but rather their occurrence in an adequate period of time, focusing on the first 24 h after renal biopsy.

MATERIALS AND METHODS

The invited study centres were not selected *a priori* or restricted to tertiary reference centres in order to ensure the collected data more closely reflected real-world clinical practice. Patient enrolment was competitive until it reached the quorum of 5,000 patients required to make an accurate estimate of the risk of major complications. Data in the Italian Registry of Renal Biopsy (IRRB) [7-8] suggested that reaching this sample size would take five years of active recruitment depending on the commitment of the centres.

As this was an observational study, although the reason for performing the procedure was checked, the enrolment criteria were not questioned. Consequently, all of the consecutive adult and pediatric patients undergoing a native kidney biopsy during the active recruitment period were considered eligible and there were no a priori exclusion criteria.

All of the patients gave their written informed consent; the study protocol was approved by the Ethics Committee of Bari University and implemented in accordance with the principles of the Declaration of Helsinki. The study was registered with ClinicalTrials.gov (No. NCT04948593).

Data collection

Data collection was centralised and made use of an ad hoc web-based database linked to the Italian Renal Biopsy Registry (<http://www.irrb.net/>). The participating centres were required to register and provide all of the data necessary to allow their correct identification and, as this was an observational study, we collected information that was already available and typical of everyday clinical practice. No particular examinations were required. The particular nature of the study was that it allowed the prospective collection of ad hoc data with the greatest possible accuracy and standardisation.

Outcomes

The primary outcome was any *major* post-native kidney biopsy complication one day after the procedure, or for longer if it was necessary to evaluate the evolution of a complication. All such complications were carefully and prospectively checked, and included clinically relevant cases of hematoma and macrohematuria, a ≥ 2 g/dL decrease in hemoglobin levels after 24 hours, the need for blood transfusion, the presence of a large and persistent artero-venous fistula, post-biopsy anuria, a $>50\%$ increase in serum creatinine levels in the week following the biopsy, the need for an invasive post-biopsy procedure including nephrectomy, and death. A hematoma was considered clinically relevant, during the data cleaning phase, if its greater diameter was >5 cm, if it required longer hospitalisation or a blood transfusion, or if the presence of pain indicated a need for an invasive intervention. Any hematoma with greater diameter less or equal to 5 cm or transient gross hematuria was considered a clinically irrelevant *minor* complication, and so not included in the analysis. During the data collection phase, the attending physician had to fill a form, including the Boolean checks about every major complication and the open-ended text description to better define the clinical outcome. In this way, no subjective judgement could have influenced the accuracy of the main outcome, since redundant information was used for data validation.

Predictive variables

Relevant covariates and factors related to the participating centres or individual patients were prospectively recorded. The information concerning each centre included the number of biopsies performed per year, whether it was a hospital for children or adults, the department in which the biopsy was performed, the place in which the core biopsied tissue was processed, the size of the needle cutting section, whether bleeding time was routinely recorded, whether renal biopsy patients were routinely hospitalised, the number of physicians in the hospital's renal biopsy team, whether there was a specific protocol for overweight patients, the prophylactic use of antibiotics, and the results of routine ultrasound examinations the day after the biopsy.

The information concerning individual patients included their age and gender, co-morbidities, the clinical presentation of their renal disease, the presence of renal failure, pre-biopsy hemoglobin level, platelet count, renal function, dialysis status, blood pressure, body mass index (BMI), position during the biopsy, biopsied side, whether computed tomography (CT) was used to perform the biopsy, the size of the biopsied kidney, the use of anti-platelet agents, the number of needle passes, needle size, pre- and post-biopsy medical treatments, the duration of bed rest, and the use of post-biopsy local ice compression.

Data were collected up to the first day after the biopsy in order to evaluate the possible occurrence of a hematoma 24 hours after the procedure, or for longer if it was necessary to evaluate the evolution of a complication.

Statistical analysis

Normally distributed quantitative variables were analysed using their mean values and standard deviations, and skewed quantitative variables such as the indices of central tendency and variability were analysed using their median values and the 10th and 90th percentiles. Categorical variables were analysed as absolute numbers and percentages.

Multivariate odds ratios (ORs) and the 95% confidence intervals (CIs) of the estimated risk of any major complication associated with the prognostic factors and covariates were calculated using multivariate binary logistic regression. The backward approach was used to simplify the saturated model until finding the best compromise between simplicity (as few factors and covariates as possible) and goodness of fit (the amount of explained variance). The Pin and Pout values were respectively set at 0.1 and 0.05. Given their epidemiological or expected clinical relevance, predictors such as gender, age, and the annual number of native kidney biopsies carried out at each centre were retested in the final model.

All of the analyses were made using the Statistical Package for Social Sciences (SPSS for Windows, version 23.0).

RESULTS

This study involved 160 nephrologists at 54 centres located in 17 of Italy's 20 regions (see Appendix). Enrolment lasted from 3 January 2012 to 4 August 2020, and was most active in three centres (Bari, Eboli, and Bologna). Tables 1 and 2 show the main characteristics of the centres. The centres performed a median of 73 native kidney biopsies (10th and 90th percentiles 10 and 197) over a median of 3.1 years (10th and 90th percentiles 0.5 and 4.6 years); the median number of biopsies per year (25.5) was in line with the expected number. The median length of the needle cutting section was 20 mm. Anti-platelet drugs were discontinued a median of seven days before the procedure (Table 2). The biopsies were most frequently performed in nephrology departments (74%), and the core tissue was most frequently processed by the hospitals' pathology service (65%). Immunofluorescence tests were assured by 96% of the centres, but electronic microscopy was available in only 67%. Bleeding time was routinely recorded by 57% of the centres, and antibiotic prophylaxis was administered by 20%. One-third of the centres had a specific protocol for overweight patients.

Tables 3, 4 and 5 show the clinical characteristics of the 5,304 enrolled patients: 332 aged <18 years and 4,972 aged ≥18 years. The median age of the patients was 53.2 years (10th and 90th percentiles 22.2 and 74.2 years). Most of the patients were male (61%), and the biopsies were most frequently carried out because of urine abnormalities (43%) or nephrotic syndrome (39%). Renal failure was present in 57% of cases (chronic renal failure in 30%, isolated acute renal failure in 16%, and acute renal failure in the context of chronic renal failure in 11%). Serum creatinine values ranged from normal to those typical of severe renal insufficiency (median 1.4 mg/dL; 10th and 90th percentiles 0.7 and 5.2 mg/dL); 5% of the patients were dialysed. Proteinuria levels varied from low pathological values to values compatible with nephrotic syndrome in 38.5% of cases (median 2.4 g/day; 10th and 90th percentiles 0.4 and 9.3 g/day). Median blood pressure was 130/80 mmHg; 10% of the patients had values of more than 150/90 mmHg and BMI values of >32.2 kg/m². Pre-biopsy hemoglobin levels were <9.4 g/dL in 10% of the patients, thus suggesting the presence of pre-biopsy anemia.

The biopsy samples were almost always taken from the left side (95%). The bipolar diameter of the kidney was frequently normal (median 11 cm, 10th and 90th percentiles 9.7 and 12.1 cm), and median parenchymal thickness was 1.6 cm (10th and 90th percentiles 1.0 and 2.0 cm). The median needle gauge was 16 G (10th and 90th percentiles 14 and 18 G). The needles were used for a median

of two passes (10th and 90th percentiles one and three), most frequently with the guide anchored to the probe (82%), and collected a median of 14 glomeruli for optical microscopy (10th and 90th percentiles six and 28). The hematomas arising after 831 biopsies (15.7%) had median greater and smaller diameters of respectively 2.7 cm (10th and 90th percentiles 0.6 and 7.0 cm) and 1.0 cm (10th and 90th percentiles 0.3 and 3.5 cm).

As expected, the most frequent co-morbidity was arterial hypertension (52.3%), followed by diabetes mellitus (14.0%), rheumatic/immunological disease (13.6%), lymphoproliferative disease (6.3%), infectious disease (3.8%), and liver disease (2.3%).

Table 6 shows the histopathological diagnoses: the most frequent was IgA nephropathy (15.6%), followed by idiopathic membranous nephropathy (13%), undefined nephropathy (9.6%), focal segmental glomerulosclerosis (8.7%), minimal change disease (6.9%), and diabetic nephropathy (6.7%). A normal kidney was diagnosed in 1.8% of cases (3.3% in pediatric cases). No rebiopsies of the same patient were included in the study.

Table 7 shows biopsy-related complications. One or more major complications occurred in 273 patients (5.1%, 95% CI 4.5-5.7%), who experienced a total of 400 major events. The most frequent was a ≥ 2 g/dL decrease in hemoglobin levels (2.2%), followed by macrohematuria (1.2%), blood transfusion (1.1%), gross hematoma (0.9%), artero-venous fistula (0.7%), invasive intervention (0.5%), pain (0.5%), symptomatic hypotension (0.3%), and a rapid increase in serum creatinine levels (0.1%). The one procedure-related death (0.02%) was due to massive bleeding in the paravertebral and gluteal muscles after the post-biopsy occurrence of a large peri-renal hematoma measuring 12 x 5 cm in a male aged 67 years. He had a histopathological diagnosis of myeloma cast nephropathy, a pre-biopsy serum creatinine level of 2.5 mg/dL, and was undergoing dialysis to remove light-chain immunoglobulins. No post-biopsy nephrectomies were required.

Multivariate analysis

Multivariate logistic regression analysis (Table 8) showed that the risk factors for at least one major complication were a high plasma creatinine level (OR 1.12 for each increase of 1 mg/dL, CI 1.08-1.17; P <0.001), concomitant liver disease (OR 2.27, CI 1.21-4.25; P=0.010), and a high number of needle passes (OR 1.22 for each additional pass, CI 1.07-1.39; P=0.003). High proteinuria levels (OR 0.95 for each additional 1 g/day, CI 0.92-0.99; P=0.009] and ultrasound-guided vs ultrasound-assisted biopsy (OR 0.68, CI 0.49-0.95; P=0.022) were protective factors. Dialysed patients were also associated with an increased risk of major post-biopsy complications (OR 2.18, CI 1.42-3.36; P <0.001), but this association lost its significance (OR 1.33, CI 0.80-2.19; P=0.268) when plasma creatinine level was included in the model. No differences were found in the rate of major

complications according to the department in which biopsies were carried out ($P=0.253$), to the pre-biopsy systolic and diastolic blood pressure values ($P=0.694$ and 0.699 , respectively) and to the haemoglobin values (OR 0.97 for each increase of 1 g/dL, CI 0.91-1.05; $P=0.466$).

Patient age at the time of biopsy was not associated with the risk of a major complication either as a continuous variable per year (OR 1.004, CI 0.997-1.012; $P=0.238$) or as a categorical variable considering the three age groups of <18 years, ≥ 18 but <65 years, or ≥ 65 years ($P=0.828$).

Males seemed to be at a slightly lower risk of post-biopsy complications than females, but the difference was not statistically significant (OR 0.78, CI 0.60-1.02; $P=0.066$).

Other factors more unexpectedly not associated with the risk of biopsy complications included the annual number of biopsies performed at a centre (OR 0.999 for each additional biopsy/year, CI 0.995-1.003; $P=0.59$); bipolar kidney diameter (OR 0.91 for each additional cm, CI 0.80-1.04; $P=0.159$); and needle gauge (OR 0.958 for each additional gauge, CI 0.852-1.077; $P=0.473$), although only 30% of centres used differently sized needles depending on the patients' characteristics. Finally, unlike some specific diagnoses such as Anti-Glomerular Basement Membrane (GBM) disease (OR 6.13, CI 1.75-21.45; $P=0.005$) or ANCA associated vasculitis (OR 4.20, CI 1.53-11.56; $P=0.005$), the post-biopsy histological diagnoses did not seem to be associated with an increased risk of complications ($P=0.222$),

The final model correctly distinguished patients experiencing major complications with 49.2% sensitivity, 66.6% specificity, 65.7% overall accuracy, a 7.3% positive predictive value, and a 96.1% negative predictive value.

DISCUSSION

The main finding of this planned, prospective study involving many nephrology centres throughout Italy over the last decade is that a native kidney biopsy is associated with a 5.1% point-estimated risk of experiencing at least one major complication, a uniquely valuable finding obtained by checking all clinically relevant events using ultrasound and colour Doppler imaging one day after the procedure. The study also provides data about individual complications: for example, post-biopsy red blood cell transfusions and invasive interventions were required in respectively 1.1% and 0.5% of cases, which is similar to the rates described in some other studies [5-6,9], but less than those in some population-based studies [3-4], and more than those in some registry-based studies [10]. However, the findings of the large-scale, American retrospective population-based study of more than 118,000 hospital admissions for native kidney biopsies by Al Turk *et al.* [3] cannot be entirely attributed to kidney biopsy complications as the patients often had co-morbidities (49% anemia, 14% heart failure, 15% chronic pulmonary disease, and 11% coagulopathy), the mortality rate was high (1.8%) and there was a very high incidence of red blood transfusions (26%);

furthermore, the French population-based study [4] over-estimated the risks of red blood cell transfusions and death as not all of the events were attributable to kidney biopsies. The results of the meta-analysis by Poggio *et al.* [6] are similar to our findings probably because the point-estimates of the American study [3] were counter-balanced by the under-estimates of major post-biopsy events typical of many small retrospective studies. Similarly, the under-reported complication rates in the retrospective registry-based study of Tondel *et al.* (0.9% of the patients required blood transfusions and 0.2% underwent surgery or catheterisation) can be explained by its retrospective registry-based design [10].

The second major finding of our study concerns the predictors of major events. It was expected that the annual number of biopsies performed out at a centre would affect the occurrence of complications [10], but the fact this was not confirmed (OR 1.002, CI 0.997-1.007; P=0.548) suggests that the risk of complications is not higher in less experienced centres. Furthermore, unlike Doyle *et al.* [11], we found that the risk of major complications was not related to the gauge of the needle (P=0.473), which is probably more closely associated with centre practices than patient characteristics as 70% of the centres used the same type of needle for all of their patients.

On the other hand, unlike Tondel *et al.* [10], we found a direct association between the number of needle passes and the risk of major complications (OR 1.22, CI 1.07-1.39; P= 0.003), with a 22% increased risk for each additional pass. This suggests that obtaining an additional research biopsy core may have a negative impact, as has been found in the ongoing prospective TRIDENT observational study [12].

High proteinuria levels were associated with a lower risk of complications (OR 0.95 for each additional 1 g/day, CI 0.92-0.99; P=0.009), thus increasing the benefit/risk ratio in highly proteinuric adult patients who are more likely to undergo a renal biopsy. Furthermore, in line with the suggestion of Gigante *et al.* [13], we speculate that the thrombophilic status of patients with nephrotic syndrome can reduce the risk of post-biopsy bleeding.

Unlike other retrospective [14] and prospective studies [15] indicating that younger patients are at greater risk of post-biopsy complications, we found no significant association with age (OR 1.004, CI 0.997-1.012; P=0.238). This discrepancy may be because the retrospective study [14] involved *outpatients*, and the prospective study [15] mainly analysed more frequent *minor* complications (34%) rather than rarer major complications (6/471 biopsies, 1.2%), thus underlining the difficulty of comparing studies with different endpoints.

Another finding relates to renal function. In line with other studies [5,10,16], we found that the independent effect of renal function was highly significant (OR 1.12, CI 1.08-1.17; P <0.001), with the risk of complications increasing by 12% with each mg/dL increase in pre-biopsy plasma

creatinine levels. Dialysed patients were also associated with an increased risk of major post-biopsy complications (OR 2.18, CI 1.42-3.36; $P < 0.001$), but this association lost its significance (OR 1.33, CI 0.80-2.19; $P = 0.268$) when plasma creatinine level was included in the model.

The information given to patients when obtaining their informed consent to a native kidney biopsy is often inadequate because it is based on the findings of retrospective studies [17] conducted by a single centre [18,19] and characterised by a small sample size [18] or poorly standardised primary outcomes [3,4,9,15], or comes from heterogeneous populations of locally specific elective patients [20], registry data [10], or national population databases [3,4,9]. Even meta-analyses may be affected by the same limitations as their sources, and as they are based on aggregate data [5-6], cannot make individual-based multivariate analyses of the role of putative predictors. It is interesting to consider the two putative predictors of needle gauge and the number of biopsy passes: Corapi *et al.* [5] found that 14-gauge needles were associated with higher transfusion rates than smaller 16- and 18-gauge needles (2.1% vs 0.5%; $P = 0.009$) and, although they did not infer any associated risk, their patients underwent a mean number of two passes, whereas Poggio *et al.* [6] found that the risk of transfusion was much higher with an 18- than a 16-gauge needle (16.1% vs 5.7%; $P = 0.06$) and did not draw any descriptive or inferential conclusions concerning the number of passes. In contrast, our findings indicate that the number of passes *on an individual basis* can affect biopsy-related complication rates.

Our mean point estimate of a 5.1% risk of a major complication is valid for the analysed biopsies as a whole, but even a multivariate approach leads to uncertainty concerning individual risk. The *a priori* risk is about 5.1%, but the contribution of *a posteriori* data increases the estimate's positive predictive value only to 7.3%, thus indicating greater individual variability.

Although the voluntary collaboration of the participating centres may have had a negative impact on the quality of the data, we believe that the strengths of this study counterbalance this drawback properly. Indeed, it focused on a largely under-investigated subject, it has a prospective design, an adequate sample size, a virtually national coverage, and a systematic search for any major post-biopsy complication, while performing an analysis of the data at individual patient level.

This is the first multicentre prospective study showing that percutaneous native kidney biopsies in Italy have been associated with a consistent, prospectively recorded and quantifiable 5.1% risk of a major post-biopsy complication over the last ten years, and that the predictors of this risk include the level of renal function, liver disease, the number of needle passes, and a low proteinuria level.

PATIENT CONSENT

Informed consent was obtained from all of the enrolled patients or their parents/legal guardians.

AUTHORS' CONTRIBUTIONS

Simeone Andrulli designed the study, wrote the study protocol, analysed the data, and wrote the first draft of the paper. Umberto Venere and Domenico Roselli participated in data collection. Umberto Venere, Domenico Roselli and Simeone Andrulli participated in data quality control. Sandro Feriozzi, Francesca Bruno and Michele Rossini contributed to classifying the histopathological findings. All of the authors assisted in the preparation of the final manuscript.

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This was an independent study without any direct sponsorship, and so there was no financial conditioning that may have affected the analyses.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

The results presented in this paper have not been published previously in whole or part, except in abstract format.

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APPENDIX

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Table 1. Characteristics of the 54 participating centres (categorical variables).

	%
Department in which biopsies were carried out (Nephrology/Radiology/Other)	74/19/7
Place of core processing (Local/Pathology Service/Other)	9/65/26
Immunofluorescence	96
Electron microscopy	67
Diagnostic report (Nephrologist/Nephrologist and Pathologist /Pathologist)	9/39/50
Scheduled meetings	67
Bleeding time measured/recorded	57
Dedicated procedure for obese subjects	32
Antibiotic prophylaxis before biopsy	20
Post-biopsy ultrasound check	91

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Table 2. Characteristics of participating centres (quantitative variables).

	No.		Percentiles				
	Centres	Missing	10 th	25 th	50 th	75 th	90 th
Number of biopsies per centre	54	0	10.0	33.3	73.0	125.8	196.5
Number of event-free biopsies per centre	54	0	9.0	32.0	69.5	116.8	189.5
Number of biopsies per centre followed by a major event	54	0	0.0	1.0	4.0	7.0	13.5
Event frequency per centre (%)	54	0	0.0	2.3	5.2	8.8	13.9
Recruitment duration per centre (years)	54	0	0.5	1.2	3.1	4.0	4.6
Expected number of biopsies per year	51	3	9.2	13.0	25.0	40.0	86.2
Actual number of biopsies per year	54	0	12.4	18.9	25.5	40.1	68.4
Needle cutting section (mm)	49	5	15	16	20	22	23
Pre-biopsy anti-platelet drug discontinuation (days)	53	1	5	7	7	7	10
Number of physicians in renal biopsy team	53	1	2	2	2	2	3

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Table 3. Patient and biopsy related characteristics (quantitative variables)

	No.		Percentiles				
	Valid	Missing	10 th	25 th	50 th	75 th	90 th
Age (years)	5296	8	22.2	38.0	53.2	66.2	74.2
Creatinine (mg/dL)	5304	0	0.7	0.9	1.4	2.6	5.2
Proteinuria (g/day)	5304	0	0.4	1.0	2.4	5.2	9.3
Systolic blood pressure (mmHg)	5286	18	110	120	130	140	150
Diastolic blood pressure (mmHg)	5286	18	60	70	80	80	90
Body weight (kg)	4765	539	53.4	62.4	72.0	83.0	95.0
Body Mass Index (BMI)	3999	1305	20.2	22.6	25.3	28.4	32.2
Hemoglobin (g/dL)	5299	5	9.4	10.7	12.2	13.8	15.0
Platelet count (x 1000)	2705	2599	156	190	236	290	350
INR	2705	2599	0.90	0.95	1.00	1.06	1.14
Bipolar kidney diameter (cm)	4167	1137	9.7	10.1	11.0	11.6	12.1
Parenchymal thickness (cm)	3881	1423	1.0	1.3	1.6	1.9	2.0
Needle gauge	5255	49	14	16	16	16	18
Biopsy passes (n)	4929	375	1	2	2	2	3
Biopsy cores (n)	5116	188	1	2	2	2	3
Glomeruli (n)	5136	168	6	10	14	20	28
Bed rest (hours)	5103	201	12	22	24	24	24
Hematoma (greater diameter, cm)	831		0.6	1.2	2.7	4.5	7.0
Hematoma (smaller diameter, cm)	765		0.3	0.6	1.0	2.0	3.5

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Table 4. Patient and biopsy related characteristics (categorical variables)

	%
Gender (M/F)	61/39
Frequency of biopsied patients on dialysis	5
Biopsy side (left/right)	95/5
Ultrasound approach (guided / assisted)	82/16
Needle gauge (14/16/18)	16/70/14
Biopsy passes (1/2/3/4+)	17/60/18/5
Type of imaging used in biopsy procedure (CT / ultrasound)	1/99

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Table 5. Co-morbidities

	%
Arterial hypertension	52.3
Diabetes mellitus	14.0
Rheumatic/immunological disease	13.6
Infectious disease	3.8
Lymphoproliferative disease	6.3
Liver disease	2.3
Others	30.4

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Table 6. Histopathological diagnoses of 5304 native kidney biopsies.

	No.	%
IgA nephropathy	826	15.6
Membranous nephropathy	690	13.0
Undefined nephropathy	507	9.6
Focal segmental glomerulosclerosis	460	8.7
Minimal change disease	367	6.9
Diabetic nephropathy	353	6.7
Lupus nephritis	333	6.3
Hypertension and ischemic renal injury	328	6.2
ANCA associated vasculitis	305	5.8
Tubulo-interstitial disease	283	5.3
Amyloidosis	184	3.5
Normal kidney	93	1.8
Membranoproliferative glomerulonephritis	83	1.6
Myeloma cast nephropathy	82	1.5
Light chain deposition disease	63	1.2
C3 nephropathy	63	1.2
Henoch Schoenlein purpura	62	1.2
Hereditary glomerulopathies	55	1.0
Acute post-infection glomerulonephritis	42	0.8
Thrombotic micro-angiopathy	37	0.7
Anti-Glomerular Basement Membrane (GBM) disease	30	0.6
Cryoglobulinemic glomerulonephritis	20	0.4
Immunotactoid / fibrillary nephropathy	17	0.3
Storage disease	9	0.2
Other	7	0.1
Inadequate material	5	0.1

Table 7. Major post-biopsy events

	No.	%
Decrease in hemoglobin level of ≥ 2 g/dL	115	2.2
Clinically relevant macrohematuria	65	1.2
Red blood cell transfusion	60	1.1
Clinically relevant hematoma	50	0.9
Arterious-venous fistula	37	0.7
Invasive post-biopsy procedure	29	0.5
Clinically relevant colic pain	26	0.5
Symptomatic hypotension	14	0.3
Rapid, >50% increase in creatinine level in post-biopsy week	3	0.1
Death	1	0.02

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Table 8. Multivariate logistic regression analysis of the predictors of the risk of experiencing at least one major post-biopsy complication.

	B	SE	Wald	P value	OR	OR 95% CI
Gender (M vs F)	-0.246	0.134	3.380	0.066	0.782	0.602-1.016
Age (years)	0.004	0.004	1.391	0.238	1.004	0.997-1.012
Creatinine (for each increase of 1 mg/dL)	0.117	0.021	30.951	<0.001	1.124	1.079-1.171
Proteinuria (for each increase of 1 g/day)	-0.049	0.019	6.771	0.009	0.952	0.918-0.988
Biopsy passes (for each additional pass)	0.198	0.067	8.721	0.003	1.219	1.069-1.391
Ultrasound-guided vs ultrasound-assisted biopsy	-0.383	0.167	5.281	0.022	0.682	0.492-0.945
Liver disease (yes vs no)	0.821	0.320	6.594	0.010	2.272	1.214-4.252
Year of biopsy (for each year after 2012)	-0.068	0.035	3.826	0.050	0.935	0.873-1.000
Systolic blood pressure (mmHg)	-0.002	0.005	0.155	0.694	0.998	0.988-1.008
Diastolic blood pressure (mmHg)	0.003	0.008	0.149	0.699	1.003	0.987-1.019

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