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Post-Renal Biopsy Deglobulization: Risk Factors and Prognosis: A Study of 157 Biopsies

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Abstract

Introduction: Percutaneous renal biopsy (PRB) is the gold standard for the diagnosis of most renal diseases. It is a safe and effective modality for the collection of renal tissue. However, many safety measures are not based on sufficient evidence and therefore vary considerably from a center to another. The aim of this work is to determine the rate of bleeding complications, to identify the risk factors for these complications, and to clarify the post renal biopsy prognosis. **Materials and Methods:** We performed a single-center retrospective observational study in the nephrology department at the University Hospital of Fez, including all patients who underwent percutaneous renal biopsy on native kidney between January 2018 and December 2019. **Results:** Overall, 157 biopsies were performed. Deglobulization was present in 20.4% (40) of patients, the mean age of patients was 41.57 ± 16.11 years [16.78]. The sex ratio M/F: 1.22. Diabetes mellitus was present in four cases (11.1%), arterial hypertension was present in four cases (11.1%). On clinical examination, systolic hypertension was found in 45.7%, diastolic hypertension in 45%, antihypertensive therapy was initiated in all patients with hypertension before. Hyperuremia was present in 29 patients (80.6%), renal failure was present in 77.8%. Anemia was present in 55.6%, thrombocytopenia in six cases (16.7%). Radiologically, the size of the kidneys was reduced in 5 patients (17.2%), differentiation was limited in 5 patients (17.2%). Major complications occurred in 3.8% (6/157). These six patients had a lumbar pain and required blood transfusions. A radiological embolization procedure was indicated in only one patient. Minor complications were seen in 21.6% (34/157). The diagnoses that were retained in patients with deglobulization were: Lupus in 34.71%, pauci-immune vasculitis in 13.79%, membranous glomerulonephritis in 10.34%, focal and segmental hyalinosis in 10.34%, membrano-proliferative glomerulonephritis in 10.34%. In univariate and multivariate analysis, the major risk

factors for deglobulization found in our patients were: hyperuremia 80.6% (p: 0.017), acute renal failure 77.8% (p: 0.04), acute hemodialysis 24.7% (p: 0.02), hyperphosphatemia 63.6% (0.04). **Conclusion:** Renal biopsies are an overall safe procedure with rare major complications. Post-renal biopsy deglobulization is common. Routine post-biopsy ultrasound may not be necessary. Renal biopsies can be performed safely if risk factors are controlled, such as renal failure, hyperuremia, hyperphosphatemia, hemodialysis patients and a diagnosis of lupus nephropathy.

Keywords

Deglobulization, Bleeding, Percutaneous Renal Biopsy, Renal Failure, Lupus, Complications

1. Introduction

Renal biopsy is the gold standard in the diagnosis and management of many diseases. Since its introduction in the 1950s, advances have been made in biopsy technique to improve diagnostic yield while minimizing complications [1]. The contribution of renal biopsy in the diagnosis, therapeutic choice and prognostic evaluation of nephropathies is considerable: it establishes a precise diagnosis, qualifies the degree of damage, guides and adapts the therapy and proposes a prognosis. It includes a morphological and immunohistochemical study. The percutaneous renal biopsy (PRB) is performed with the help of ultrasound (ultrasound guidance or ultrasound detection) which allows the procedure to be performed safely and accurately. PBR is performed in three stages: a preparation phase, an operative phase and a follow-up phase. This PBR technique is an invasive procedure, a risk/benefit assessment must be done in all cases [2]. Physicians must consider the risks of a renal biopsy in the context of the perceived benefit. Anatomic features, such as cysts in the lower renal pole, atrophic kidneys with thin cortices, or horseshoe-shaped kidneys, may contraindicate biopsy in some patients, but alternative biopsy techniques can be considered [3]. Post-biopsy hemorrhagic complications ranged from 13% to 34% and the rate of severe complications from 1.2% to 6.4% [1]. Various studies have identified certain risk factors for bleeding. However, the data in the literature have important limitations as to how best to predict and prevent bleeding complications after renal biopsy. Few studies used only univariate analysis and were not adjusted. More recently a multivariate study analyzed data from prospective and retrospective literature, and determined risk factors (female gender, young age, prolonged activated partial thromboplastin time, decreased GFR, anemia, use of hemodialysis, and a low platelet count) [3].

The aim of this work is to determine the rate of bleeding complications, to identify the risk factors for these complications, and to clarify the post-PRB prognosis.

2. Patients and Methods

2.1. Study Population

We performed a single-center, retrospective, observational study in the nephrology department at the University Hospital of Fez, including all patients who underwent percutaneous renal biopsy on native kidney between January 2018 and December 2019.

All patients older than 16 years were included. The indication for biopsy was made for the first time in these patients. We compared two groups, patients with deglobulization defined as a decrease in hemoglobin of more than 1 g/dl within 03 days after the procedure, and patients without deglobulization.

2.2. Definitions

Post biopsy bleeding complications: minor complications included gross hematuria and/or subcapsular perinephric hematoma that spontaneously resolved without need for further intervention. Major complications were defined as those that required an intervention for resolution, either the transfusion of blood products or an invasive procedure (angiography, surgery), or death.

2.3. Biopsy Procedure

All biopsies were performed by a nephrologist or conventional radiologist. As safety thresholds for biopsy, blood pressure < 140/90 mm Hg, INR < 1.4, and platelet count ≥ 120.000 g/L were used, antiplatelet agents were stopped 1 week before the procedure, all patients had hemoglobin > 8 g/dl. All biopsies were performed on prone position, guided or detected by ultrasound, with 16G automatic trocars. Following the biopsy, patients lay in bed on their backs for a 24-hour observation time. During this time, clinical (gross hematuria, flank pain, hypotension), control blood count, and ultrasound evaluations were performed to identify those patients with bleeding complications.

2.4. Data Collection

Data were collected through a data collection form completed using patient's charts. The data collected were: demographic data (sex, age), history (diabetes, hypertension, comorbidities…), baseline systolic and diastolic blood pressure, laboratory findings (serum creatinine; hemoglobin; baseline coagulation parameters: prothrombin time, partial thromboplastin time, 24-hour prebiopsy urinary protein excretion, calcemia, phosphatemia, protidemia, immunological assessment…), indication for renal biopsy, histopathological results, information regarding any postbiopsy bleeding complications (gross hematuria, haematoma, arteriovenous fistula), intervention (transfusion of blood products or an invasive procedure radiological embolization, nephrectomy), and death.

2.5. Statistical Analysis

The data were entered into an excel sheet and analyzed using SPSS software

package V20. In the descriptive part of the analysis, quantitative variables were expressed as mean ± standard deviation and/or, and qualitative variables as percentages. The comparison of proportions was performed using the Chi-square test. Significant independent predictors of post biopsy bleeding were determined by linear regression and multiple logistic regression analysis. The level of significance adopted was 0.05.

3. Results

We collected 157 patients. Indications for renal biopsy in all patients were rapidly progressive glomerulonephritis in 15%, impure nephrotic syndrome in 54%, pure nephrotic syndrome in 13.72%, positive proteinuria without renal failure in 5.8% and proteinuria with renal failure in 11.48%.

40 patients presented with deglobulization; the mean age was 41.57 ± 16.11 years [16.78]. The sex ratio M/F: 1.22. Alcohol and tobacco intoxication was present in 3 (8.3%) patients, diabetes was present in 4 (11.1%) cases, arterial hypertension was present in 4 (11.1%) cases, heart disease was found in 2 (5.6%) cases, a history of tuberculosis was found in 3 (8.3%) cases.

On clinical examination, systolic hypertension was found in 16 (45.7%) patients, diastolic hypertension in 13 (45%) patients, and reduced diuresis in 7 (37.1%) cases, antihypertensive therapy was initiated in all patients with hypertension before. Hyper uremia was present in 29 (80.6%) patients, renal failure was present in 12 (77.8%) patients with an average GFR(MDRD) of 30 ± 10.5 ml/min/1.73 m^2 [58 - 2]. Anemia was present in 22 (55.6%) cases, an average hemoglobin of 9.21 ± 1.43 g/dl [8 - 10.4], thrombocytopenia in 6 (16.7%) cases with an average of 142000 ± 3386 elements/mm^3 [120,000 - 144,000], phosphoremia was increased in 21 (63.6%) patients with an average of 70.12 ± 28.75 mg/l [46 - 138]. Table 1 summarize all the biological tests in patient with deglobulization.

Table 1. Biological characteristics of the group with deglobulization.

	Percentage %	Mean ± SD Range
Anemia (g/dl)	55.6	9.21 ± 1.43 [8 - 10.4]
Thrombocytopenia (element/mm^3)	16.7	142,000 ± 3386 [120,000 - 144,000]
GFR ml/min/1.73m^2 (MDRD)	78.8	30 ± 10.5 [58 - 2]
Hyperuremia (g/l)	80.6	1.44 ± 0.92 [0.54 - 4.25]
Elevated CRP (mg/l)	47.2	51.6 ± 84 [11 - 320]
Low blood calcium (mg/l)	58.8	75.55 ± 7.29 [61 - 83]
Hyperphosphatemia (mg/L)	63.6	70.12 ± 28.75 [46 - 138]
Hyperuricemia (mg/l)	78.1	84.13 ± 22.64 [52 - 157]
Hypercholesterolemia (g/l)	52	2.75 ± 0.78 [4.15 - 2.03]

Only one patient (2.8%) had a low TP of 60%, the activated partial thromboplastin time (APTT) was iso. Proteinuria was glomerular in 18 cases (62.1%), it was tubulointerstitial in 37.9%. Leukocyturia was positive in 75% of patients, hematuria was positive in 72.5% of patients.

Radiologically, the size of the kidneys was reduced in 5 patients (17.2%), differentiation was limited in 5 patients (17.2%). The diagnoses that were retained in patients with deglobulization were Lupus in 35%, pauci-immune vasculitis in 14%, membranous glomerulonephritis in 10%, focal and segmental hyalinosis in 10%, membrano-proliferative glomerulonephritis in 10%, minimal glomerular lesions in 7%, chronic glomerulonephritis in 7%, IgA nephropathy in 4% and diabetic glomerulonephritis in 3% (Figure 1).

Post biopsy deglobulization occurred in 25.4% (40/157) of the study cohort. Major complications occurred in 3.8% (6/157) in whom four patients presented with gross hematuria, and hematoma in five patients. No cases of renal arteriovenous fistula have been detected. All subjects with major complications had a lumbar pain and required blood transfusions. One patient underwent angiographic evaluation of the bleeding and gel-foam trans arterial catheter embolization of the lesion, this patient had membranoproliferative glomerulonephritis, the evolution was marqued by the development of hemorrhagic shock and death.

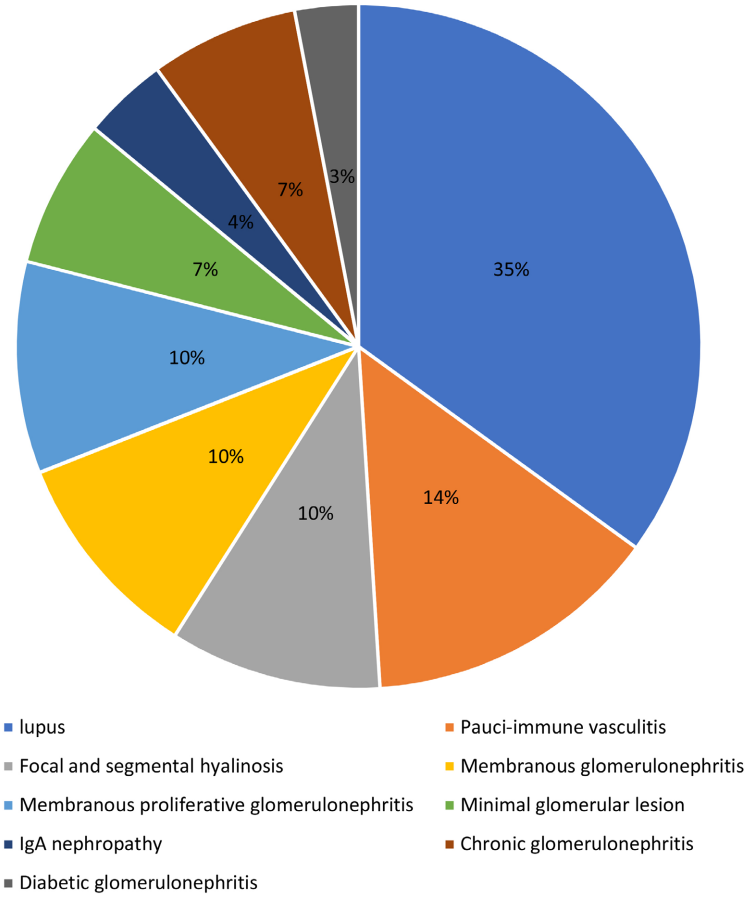

Figure 1. Diagnosis patients withdeglobulization.

The other patients were monitored, the evolution was marked by the resorption of the hematoma and the stabilization of the hemoglobin. Minor complications were seen in 21.6% (34/157), 22 patients presented with lumbar pain, ultrasound showed a subcapsular hematoma in all patients. Hematuria was seen in 12 patients, it was associated with lumbar pain in 4 of the subjects, ultrasound showed a hematoma in 2 cases. The evolution was marqued by resolution of the clinical symptoms and stabilization of hemoglobin. Hemodialysis within 3 days of biopsy was indicated in 4 patients, of which one had a major complication.

Distribution of potential predictors of bleeding in patients who did or did not present with postbiopsy bleeding complications is reported in **Table 2**. In univariate analysis, the major risk factors for deglobulization found in our patients were: hyperuremia 80.6% (p: 0.017), acute renal failure 77.8% (p: 0.04), acute hemodialysis 24.7% (p: 0.02), hyperphosphatemia 63.6% (p: 0.04). In the multivariate analysis, the risk factor related to deglobulization the need of acute hemodialysis p = 0.023, OR = 3.738, confidence intervals (1.196 - 11.684).

4. Discussion

We listed 157 renal biopsies over a period of one year, this incidence is comparable to studies performed by Belarbia *et al.*, but it is lower than that reported by European studies [4] [5]. The mean age of these patients is 37.68 ± 31 years, which is comparable to the results of two other studies [2] [6]. For renal manifestations, high blood pressure was found in 41.13% and reduced dieresis in 11.39%, nephrotic syndrome is the most frequent mode of presentation in our patients, it presents the first indication for renal biopsy with a frequency of 65.18%, this result is comparable to the study conducted in Oujda [7], this frequency is higher than the study conducted in Spain [8]. The presence of acute renal failure was the second indication for PRB with a frequency of 14.55%.

All of our biopsies were performed with 16G trocars, according to the literature the yield with the 16G trocar was higher and the major complication rate was lower than with older tools. The use of 14-gauge needles was associated with higher transfusion rates (2.1%) compared with 16-gauge (0.4%) and 18-gauge (0.6%) needles [9]-[14].

The literature reports that major complications occur in 1.2% to 6.7% of renal biopsies [1] [3]. In our study, major complications occurred in 3.8% of cases. Embolization techniques have greatly reduced the need for hemostasis nephrectomy [1] [3].

In the literature, several factors related to post-biopsy bleeding have been identified, including female gender, young age, prolonged activated partial thromboplastin time, decreased GFR, anemia, use of hemodialysis, and a platelet count below 140,000 elements/mm^3 [3] [15] [16] [17]. In our study, there was no significant difference between genders, age, diabetic, high blood pressure and thrombocytopenic patients. The presence of anemia was not considered a factor in deglobulization as well. The univariate analysis, identified renal failure, hyper

Table 2. Distribution of potential predictors of bleeding in patients who did or did not present with post biopsy bleeding complications (univariate analysis).

Item	Patients with deglobulization % (n)	Patients without deglobulization % (n)	P
Number	25.4 (40)	74.5 (117)	
- Average age (years)	41.57 ± 16.11	37.25 ± 16.11	
- Sex ratio M/F	1.22	1.34	0.7
- Alcohol and tobacco intoxication	8.3 (3)	5.1 (6)	
- History of hypertension	11.1 (4)	14.5 (17)	0.782
- History of diabetes	11.1 (4)	8.5 (10)	0.742
- Heart disease	5.6 (2)	2.6 (3)	0.336
- History of tuberculosis	8.3 (3)	6.8 (8)	0.721
- Nephrotoxic plant	2.8 (1)	7.7 (9)	0.454
- Systolic hypertension	45.7 (16)	39.7 (46)	0.560
- Diastolic hypertension	37.1 (13)	28.4 (33)	0.402
- Reduced diuresis	19.4 (7)	9.4 (11)	0.341
- Hyperuremia	80.6 (29)	56.9 (66)	0.017
- acute kidney injury	77.8 (12)	49.6 (58)	0.04
- Leukocyturia	82.5 (33)	52.99 (62)	0.819
- Hematuria	78.8 (26)	76.4 (81)	0.516
- Hyperferritinemia	23.8 (5)	13.1 (8)	
- Hypoferritinemia	28.6 (6)	52.5 (32)	
- Increased CRP	47.2 (17)	33.6 (38)	0.167
- Anemia	55.6 (20)	46.6 (54)	0.446
- Hyperleukocytosis	37.1 (13)	29.3 (32)	0.888
- Leukopenia	8.6 (6)	11.2 (13)	0.690
- Thrombocytopenia	16.7 (6)	7.8 (9)	0.197
- TP	2.8 (1)	6 (7)	0.681
- Hypoalbuminemia	91.4 (32)	92.8 (103)	1
- Hypocalcemia	58.8 (6)	66.3 (67)	0.535
- Hyperphosphatemia	63.6 (21)	42.7 (38)	0.04
- Hyperparathormonemia	80.8 (21)	71.8 (34)	0.441
- Hyperuricemia	78.1 (25)	70.4 (4)	0.487
- Hypercholesterolemia	52 (13)	46.7% (35)	0.818
- Complementary C3 consumed	29 (9)	33.7 (34)	0.669

Continued

-	Complementary C4 consumed	22.6 (7)	22.6 (21)	1
-	Anti-nuclear antibodies	33.3 (8)	40 (28)	0.632
-	Anti DNA antibodies	27.3 (6)	31.7 (20)	0.792
-	ANCA	33.3 (4)	20 (6)	0.433
-	Reduced kidney size	17.2 (5)	10.5 (9)	0.513
-	Limited differentiation	17.2 (5)	16.3 (14)	0.554
-	Nephroprotective	65.7 (23)	61.4 (70)	0.694
-	Acute hemodialysis	24.7 (23)	78 (8)	0.02
-	Hemodialysis after PRB	11.4 (4)	6.5 (7)	0.465

uremia, hyperphosphatemia, and use of acute hemodialysis as risk factors of deglobulization. In the multivariate analysis, the only factor correlated to deglobulization was the need of acute hemodialysis which intercorrelated with the other factors.

In a recent study, amyloidosis found to be a risk factor for post RPB bleeding [15]. Contrary to our study; where 34% of patients who presented with deglobulization had a lupus nephropathy without being statistically significant.

The risk of deglobulization in patients with renal failure is probably explained by uremic thrombopathy. Hyperphosphatemia and acute hemodialysis are correlated with renal failure, so one factor could confound with the other. The effect of blood pressure appeared to be insignificant because not all biopsies were performed, if arterial pressures were not lowered. Few biopsies were performed with a platelet count < 145.000 elements/mm^3, which could explain that thrombocytopenia was not a risk factor for bleeding in our study. Overall, our safety margins for renal biopsies (platelets greater than 120,000 elements/mm^3) seem reasonable.

Zhang W.J. *et al.*, showed that renal parenchymal thickness is a significant predictor of presence of hematoma evident on post-biopsy ultrasound evaluation, which would be used in the early prevent the complications of percutaneous renal biopsy [18].

A major conclusion of our study is that renal biopsies can be performed safely as long as the factors studied are well controlled, and even as an outpatient procedure, an observation period post-procedure is recommended. The use of acute hemodialysis after the procedure can be performed without fear. It seems reasonable to establish a score to differentiate between patients with a high risk of deglobulization or not, justifying a close and different monitoring.

Based on our study, we propose a flowchart to help decide whether an ambulatory biopsy is feasible and to identify patients at increased risk for deglobulization (**Figure 2**).

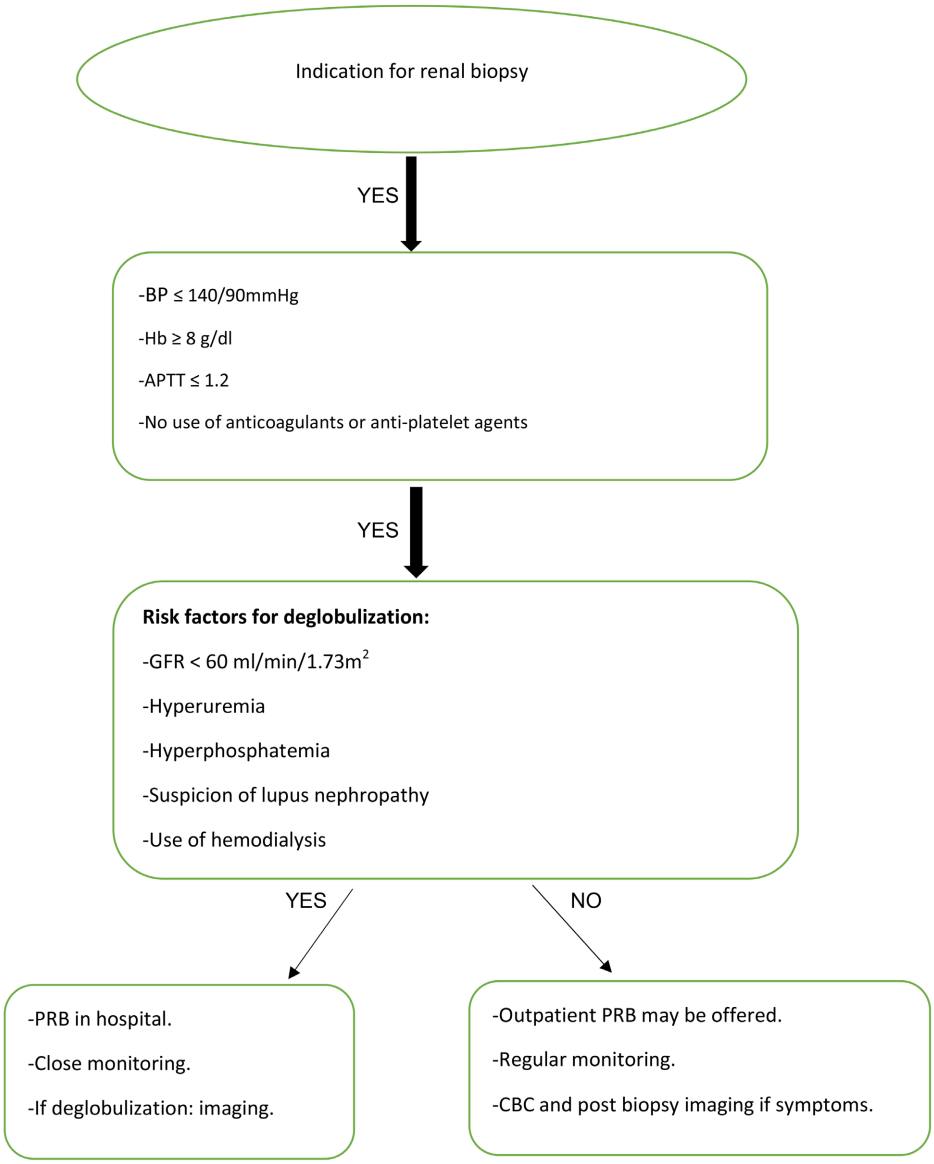

Figure 2. Flow chart for identifying patients at risk of deglobulization. BP: Blood Pressure; Hb: Hemoglobin; GFR: Glomerular Filtration Rate; CBC: Cell Blood Count, the Activated Partial Thromboplastin Time (APTT).

5. Conclusion

Renal biopsies are an overall safe procedure with rare major complications. Post-renal biopsy deglobulization is common. Routine post-biopsy ultrasound may not be necessary. Renal biopsies can be performed safely if risk factors are controlled, such as renal failure, hyperuremia, hyperphosphatemia, hemodialysis patients and a diagnosis of lupus nephropathy.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Data Collection Form

Name:
Date of hospitalization:
Age:
Sexe
History:
Diabetes mellitus: Yes No
High blood pressure: Yes No
Cardiopathy: Yes No
Tobacco consumption: Yes No
Alcohol consumption: Yes No
Tuberculosis: Yes No
Other medication or plant consumption: Yes No
Anti coagulant therapy: Yes No
Anti platelet therapy: Yes No
Angiotensin inhibitors: Yes No
Clinic examination:
High blood pressure: Yes No
Systolic
Diastolic
Lumb oedema: Yes No
Urinary dipstick:
Proteinuria Hematuria Diuresis
Laboratory examination:
Urea Creatinin glomerular filtration rate (MDRD)
Urinary cytobacteriological examination Leucocyturia Hematuria
Hemoglobin before biopsy Hemoglobine Day 1
Hémoglobine Day 2 Hemoglobine Day 3
ferritin WBC platelet TP TCA CRP
Protidemia albumin proteinuria/day
Natremia Kaliemia Calcemia phosphatemia
Uric acid Parathormonemia
Total Cholesterol LDL-C HDL-C Triglycrid
Complement C3 Complement C4
Antinuclear antibodies
Anti-DNA antibodies
Anti ssA, anti ssB antibodies
Centromeres antibodies
ANCA MPO/PR3
Anti-MBG antibodies
Anti PLA2R antibodies
***Imaging*:**
Right kidney size Left kidney size Cortico-medullary differentiation

B*iopsy date*:		
Biopsy results:		
Hemodialysis:		
Acute Dialysis:	Yes	No
Dialysis after biopsy (3 days):	Yes	No
Complications after renal biopsy:		
Hematuria:	Yes	No
Pain:	Yes	No
Hematoma:	Yes	No
Need for transfusion:	Yes	No
Embolization:	Yes	No
Nephrectomy:	Yes	No