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Risk management of renal biopsy: 1387 cases over 30 years in a single centre

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Abstract

Background Although renal biopsy is largely employed, even in old patients with systemic diseases, few clinical studies have addressed its risk management. We aimed to obtain a comprehensive assessment of safety/utility ratio of percutaneous renal biopsy.

Patients and methods Retrospective review of all the 1387 patients who consecutively underwent renal biopsy in a single centre over three decades (1973–2002) was made, with calculation of complications, multivariate logistical analyses to evaluate risk factors of complications, and rate of alteration of clinical hypotheses by pathological diagnosis.

Results There were no deaths and five major complications, (0·36%). One nephrectomy (0·07%), two surgical revisions (0·1%) and two arterial-venous fistulae (0·1%). There were also 337 minor bleeding complications (24·2%) (16·4% gross haematuria and 7·8% clinically relevant haematomas needing at least prolonged bed rest). Multivariate analyses demonstrated that the risk for complications was significantly increased by systemic autoimmune diseases with odds ratio (OR) 2·06, 95% confidence interval (CI) = 1·40–3·01, end-stage kidney/acute-tubular necrosis (OR 2·96, 95% CI = 1·19–7·30), and prolonged bleeding time test (BTT) (OR 1·87, 95% CI = 1·17–2·83). Among the 1288 cases in which a clinical hypothesis before renal biopsy was recorded, renal pathology changed previous diagnoses in 423/1,288 (32·8%) of cases.

Conclusions Risk assessment demonstrates that renal biopsy is a useful procedure with a low incidence of serious complications. Platelet function is the only modifiable factor significantly related to bleeding complications, suggesting the need for a more standardized alternative to the BTT. Platelet function should be evaluated to select low-risk patients for renal biopsy as 'a day case procedure', in order to build adequate risk management strategies.

Keywords Bleeding time test, haematomas, haematuria, renal biopsy, renal pathology, risk assessment/risk management.
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Introduction

Prior to the introduction of the percutaneous biopsy technique in the mid-1950s, the diagnostic approach to renal disorders was based on clinical/laboratory data, therapeutic indications were not supported by histological confirmation and prognostic interpretation was limited to clinical/laboratory endpoints.

The introduction of renal biopsy allowed physicians to better understand the pathophysiology of kidney diseases, leading to histological classifications of nephropathies and their correlation with clinical syndromes.

Renal biopsy is now widely recognized as an essential tool for diagnosis, therapy, and prognosis of most nephropathies [1,2].

Many elements would argue in favour of renal biopsy [1]: the awareness that the spectrum of renal diseases underlying urinary abnormalities is indeed quite broad and that long-term evolution into chronic renal failure occurs in a significant proportion of cases [3–7] [2]; the increasing availability of therapies to treat acute immunological nephropathies and to blunt progression in chronic forms [8,9] [3]; the gap between expected diagnosis on the basis of clinical presentation and the biopsy findings in old patients with increased frequency of active nephritis susceptible to therapy [10–12] [4]; the utility of additional pathological information on the degree of end-stage lesions no further reversible.

However, despite technical improvements, renal biopsy is not devoid of morbidity and occasionally even of mortality, with bleeding cited as the main cause of the most serious complications [13,14].

Given this background, every effort should be made to obtain diagnosis and treatment of renal disease based on biopsy, together with risk assessment/management strategies.

The aim of this study was to perform a comprehensive assessment of safety/utility ratio by a retrospective analysis of a very large series of renal biopsies, focusing on complications, risk factors for these complications, and the cases in which renal biopsy changed clinical diagnosis leading to an alteration of therapy.

Patients and methods

All patients undergoing renal biopsy on native kidneys at the Nephrology-Centre of the Molinette-Hospital between 1 January 1967 and 31 December 2002 were included in this study.

Overall, 1542 biopsies were performed. As adequate clinical charts were available from 1973, and some patients performed repeated biopsies, the analysis was restricted to the 1387 who underwent first percutaneous renal biopsy from 1973 to 2002.

Written informed consent was obtained from all the patients, and therapeutic interventions were approved by the appropriate Internal Review Board.

Guidance for percutaneous renal biopsies

Up until 1982 localization of the renal pole was manually achieved by studying a standard abdominal X-ray or pyelography. Since 1983 ultrasound-guided real time visualization has been employed.

Procurement of tissue

Up until 1982, a Franklin-modified Vim-Silverman needle was used and subsequently replaced with a Travenol Tru-Cut disposable needle gauge-16 until 1992 and from 1993 to the present day a semiautomated spring-loaded core-biopsy gauge-18 needle has been employed. Minimum adequate core material was considered if there were at least seven or eight glomeruli. The provider has found that 16-G-needles commonly yield adequate tissue for diagnosis by one core and one pass. A greater number of cores were required for adequate tissue (two with semiautomated 18-G needles versus one for manual) as did the number of passes (two versus one). Only exceptionally more than two passes have been employed, as our teaching provider's opinion is that a higher number of passes usually means poorer safety.

Providers

Most percutaneous renal biopsies were performed by a single nephrologist and, in the last decade, by a younger nephrologist who had worked under his direct supervision.

Monitoring pre-biopsy

Renal imaging and blood count, functional renal evaluation, prothrombin time, activated partial thromboplastin time (APTT), platelet count, fibrinogen level and bleeding time test (BTT) were checked.

BTT was performed by physicians using the Ivy method making two simultaneous cuts with the manual procedure up to 1991 (normal range ≤ 7 min), and with the automated procedure (Simplate 2R bioMerieux, INC, Box 15969, Durham, North-Carolina 27704–0969, USA) after 1991(normal range ≤ 9·30 min), employed by experienced technicians from the central laboratory of our Hospital, making two simultaneous cuts 5-mm length, 1-mm depth, after 30–60 s of pressure insuffled to 40 mmHg, with a coefficient of variability of 15%.

Only patients with normal plasma coagulation values were biopsied unless prolonged activated partial thromboplastin time was attributable to the presence of lupus anticoagulant, due to the confirmation of a positive mixing time and/or demonstration of antiphospholipid antibodies by immune techniques. Patients who were previously on anticoagulants were shifted to low molecular weight heparin, while antiaggregational therapy was discontinued 1 week before, and the use of any other medication affecting bleeding (such as NSAIDs) was discouraged.

When baseline BTT results exceeded the upper-end of the normal range, renal biopsy was delayed until pharmacological correction was performed. Deamino 8-D-arginine-vasopressin (DDAVP) 0·4 μg kg^{-1} in saline 100 mL was infused intravenously [15–17], and a second BTT was repeated immediately before renal biopsy (real-time BTT). The interval between DDAVP infusion and renal biopsy was < 1 h.

All patients with blood pressure > 140/90 mmHg were given antihypertensive agents and renal biopsy was delayed if control was poor. All patients in whom some level of suspicion was aroused were investigated for the alteration on immunological parameters, depending on what was available at this time (ANA, ENA, anti-DNA, ANCA, complement fraction) and for the presence of myeloproliferative disease (immunoglobulins, cryoglobulins, serum and urine κ and λ measurements and immunofixation).

Monitoring post-biopsy

The patients were hospitalized for 48 h, remained in a prone position for 2 h, and in bed for an additional 22 h. Post-biopsy urines were examined and a blood count was repeated 24 h later. Routine sonography 24 h after biopsy was introduced in 1990, while it was only performed for clinical symptoms (pain/fever) in previous years.

Complications

Major complications were categorized as death, nephrectomy, surgical revision and arterial-venous fistula. Minor complications i.e. all clinically significant outcomes that at least extended the rest period in bed, and hospitalization because of pain/fever/bladder-catheterization/precaution, and required blood transfusions/antibiotics, were recorded. They were categorized as gross haematuria lasting < 24 or > 24 h and peri-renal/subcapsular haematomas with a diameter > 1 cm as, in both cases, extended bed rest and prolonged hospitalization for one night were adopted as a precaution [18,19].

Risk factor variables

Real-time BTT, platelet count and haemoglobin values were used as continuous variables. Renal failure was categorized as absent, mild/moderate or severe if serum urea and creatinine were < 40 mg dL^{-1} and < 1·4 mg dL^{-1}, or ≥ 40 and < 80 mg dL^{-1} and ≥ 1·4 and < 4 mg dL^{-1}, or haemodialysis was needed, respectively. Patient age was categorized as < 30, 30–50, and > 50 years. Blood pressure was categorized as > 140/90 mmHg vs. = 140/90 mmHg.

Clinical diagnosis

Physicians wrote their clinical diagnosis on the chart accompanying biopsy samples. They usually formulated one to three hypotheses depending on the strength of clinical suspicions.

Statistical analysis

Pearson correlation coefficient, a one-way analysis of variance with the Bonferroni/Dunn post hoc correction and non-parametric tests were used when indicated.

Stepwise multivariate logistical regression analyses were employed to evaluate risk factors for bleeding complications. For the last decade, variables of patients who had either haematomas or gross haematuria were compared with those of patients without complications using a multinomial logistical regression model. For most relevant estimates, 95% confidence interval (CI) were reported.

Results

Clinical and histological data

The main characteristics of the 1387 patients are depicted in Table 1. The mean age of patients increased over time ($P < 0·0001$), as well as log-transformed creatinine and urea ($P < 0·0001$).

Baseline BTT values were positively correlated with APTT ($r = 0·113$, P 0·0001), creatinine ($r = 0·137$, P 0·0004), urea ($r = 0·127$, P 0·0019), and negatively with platelet count ($r = –0·103$, P 0·007).

After DDAVP infusion in 98 patients with baseline prolonged BTT, the mean value of real-time BTT (encompassing the 98 corrected and the remaining 1289 non-corrected patients) was 4·3 ± 1·5 min. No side effects or adverse events correlated with DDAVP infusion were recorded.

Outcomes: complications and alteration of pre-biopsy clinical diagnosis

Percutaneous renal biopsies were performed by the same provider in 91·2% of cases. No deaths were recorded (95% upper confidence limit: 0·3%). Five (0·36%) major complications resulted: one nephrectomy (0·07%) on a 40-year-old man with Goodpasture syndrome on dialysis; two surgical revisions of peri-renal haematomas (0·1%), one on a 45-year-old woman with Goodpasture syndrome on dialysis and another on a 65-year-old man with end-stage nephroangiosclerotic kidney; and two arterial-venous fistula (0·1%) (Table 2).

Minor bleeding complications were recorded in 24·2% of cases, including gross haematuria in 16·4% (Table 2). Over the years, the incidence of the most severe form of gross haematuria lasting more than 24 h decreased from 7·1% to 4·5% (χ^2 13,6, $P < 0·001$, OR 0·96, 95% CI 0·95–0·99 for each year from 1982 to 2002).

Clinically relevant haematomas were detected in 7·8% of cases: 15 in the first two decades and 94 in the last one

Table 1 Main clinical and biochemical parameters of the patients who underwent percutaneous renal biopsy during 30 years in a single centre. Values are expressed as mean ± standard deviation, minimum, maximum and percentage are in brackets

Parameters	Overall (1973–2002) $n = 1387$	First decade (1973–82) $n = 422$	Second decade (1983–92) $n = 307$	Third decade (1993–2002) $n = 658$
Sex, M/F	833/554	232/190	193/114	408/250
Age at biopsy, years	40 ± 17 (7–87)	35 ± 14 (7–73)	39 ± 16 (12–78)	46 ± 17* (14–87)
At biopsy:				
Serum creatinine, mg dL^{-1}	1·9 ± 2·2 (0·3–19)	1·5 ± 2·1 (0·4–19)	2·1 ± 2·8 (0·3–17)	2·1 ± 2 (0·4–14·5)
Log transformed		*0·1 ± 0·6*	*0·3 ± 0·8*	*0·5 ± 0·7**
Serum urea, mg dL^{-1}	65 ± 56 (6–399)	54 ± 49 (6–351)	63 ± 58 (15–399)	74 ± 58 (9–336)
Log transformed		*3·7 ± 0·6*	*3·9 ± 0·6*	*4·1 ± 0·6**
Haemodialysis, *n (%)*	105 (7·6)	28 (6·6)	29 (9·4)	48 (7·3)
Haemoglobin, g dL^{-1}	12·6 ± 2 (6·4–18·7)	12·8 ± 2 (7–18·2)	12·9 ± 2 (6·4–18·7)	12·4 ± 2 (7–18·5)
Systolic blood pressure, mmHg	133 ± 16 (87–190)	128 ± 15 (90–180)	135 ± 15 (90–185)	135 ± 16 (87–190)
Diastolic blood pressure, mmHg	83 ± 10 (50–120)	83 ± 10 (50–120)	86 ± 10 (50–110)	82 ± 10 (50–120)
Prothrombin time	–	95% ± 6† (64–103)	95% ± 8† (55–140)	1·02 ± 0·08‡ (0·7-1·71)
APTT, s	31·4 ± 4 (18–56)	31·1 ± 4 (18–49)	30 ± 3 (20–40)	32 ± 4 (23–56)
Fibrinogen, mg dL^{-1}	387 ± 140 (88–1110)	368 ± 140 (100–1000)	405 ± 147 (118–900)	409 ± 135 (88–1110)
ATIII, percentage activity	101 ± 16 (53–297)	104 ± 10 (95–126)	100 ± 13 (55–129)	101 ± 17 (53–297)
Platelet count, $/mm^3$	248 ± 75 (67–767)	250 ± 70 (67–520)	260 ± 73 (112–589)	242 ± 79 (91–767)
Baseline BTT, min	4·8 ± 2 (1–18)	4·4 ± 1·5 (1·3–9·3)	4·0 ± 1·5 (1–14)	5·4 ± 2 (1–18)
Patients who corrected baseline BTT	98(7)	18 (4·3)	7 (2·2)	73 (11·1)
Real-time BTT of all 1387 cases, including results of pharmacological correction	4·3 ± 1·5 (1–9)	4·1 ± 1·3 (1–8)	3·7 ± 1·3 (1·3–9)	4·7 ± 1·6 (1–9)

*$P < 0·0001$ between decades

†as percentage of prothrombin activity; ‡as International Normalized Ratio (INR)

APTT, activated partial thromboplastin time; BTT, bleeding time test; ATIII, antithrombin III.

Table 2 Indications for biopsy and main outcomes of the 1387 patients who underwent percutaneous renal biopsy during 30 years in a single centre. Percentage are in brackets

	Overall (1973–2002) *n* = 1387	First decade (1973–82) *n* = 422	Second decade (1983–92) *n* = 307	Third decade (1993–2002) *n* = 658
Indication for biopsy, *n* (%):				
Urinary abnormalities alone	579 (41·7)	226 (53·5)	109 (35·5)	244 (37)
Nephrotic syndrome	434 (31·2)	102 (24·1)	115 (37·4)	217 (32·9)
Nephritic syndrome	49 (3·5)	16 (3·8)	18 (5·8)	15 (2·3)
Acute renal failure	154 (11·1)	26 (6·2)	36 (11·7)	92 (13·9)
Chronic renal failure	171 (12·3)	52 (12·3)	29 (9·4)	90 (13·7)
Providers N1*, *n* (%)	1265 (91·2)	421 (99·7)	306 (99·7)	538 (82)
Histological diagnosis, *n* (%):				
Primary glomerulonephritis	811 (58·4)	270 (63·9)	198 (64·4)	343 (52·1)
Secondary glomerulonephritis	318 (22·9)	57 (13·5)	61 (19·8)	201 (30·5)
Interstitial nephritis	26 (1·9)	12 (2·8)	5 (1·6)	9 (1·3)
Microangiopathy	17 (1·2)	3 (0·7)	4 (1·3)	10 (1·5)
Nephroangiosclerosis	17 (1·2)	9 (2·1)	3 (0·9)	5 (0·7)
End stage kidney	15 (1·1)	2 (0·4)	3 (0·9)	10 (1·5)
Acute tubular necrosis	7 (0·5)	1 (0·2)	0	6 (0·9)
Inadequate specimen	35 (2·5)	13 (3·1)	8 (2·6)	14 (2·1)
Normal kidney	50 (3·6)	19 (4·5)	8 (2·6)	23 (3·4)
Others	91 (6·6)	35 (8·3)	20 (6·5)	36 (5·4)
Alteration of pre-biopsy clinical diagnosis by biopsy results	423/1288 (32·8)	128/323 (39·6)	113/307 (36·8)	182/658 (27·6)
Major complications, *n* (%):	5 (0·36)			
Nephrectomy	1 (0·07)	1 (0·2)	0	0
Surgical revision	2 (0·1)	1 (0·2)	1 (0·32)	0
Arterial-venous fistula	2 (0·1)	1 (0·2)	1 (0·32)	0
Minor bleeding				
Complications, *n* (%)¶	337 (24·2)	82 (19·4)	68 (22·1)	187 (28·4)
Gross haematuria, total:	228 (16·4)	78 (18·4)	57 (18·5)	93 (14·1)
Lasting < 24 h	148 (10·6)	48 (11·3)	37 (12·0)	63 (9·6)
Lasting > 24 h	80 (5·8)	30 (7·1)	20 (6·5)	30 (4·5)
Clinically significant haematomas:	109 (7·8)	4 (0·9)	11 (3·6)	94 (14·3)§
> 1 cm and < 3 cm	46 (3·3)			46 (6·9)§
> 3 cm and < 5 cm	51 (4·5)	4 (0·9)‡	5 (1·6)‡	42 (6·4)§
> 5 cm	12 (0·9)		6 (1·9)‡	6 (0·9)§

‡detected only in the presence of clinical symptoms
§detected at routine echography at 24 h
¶the two patients with both haematuria and haematomas were considered as having only haematoma (second decade) and only haematuria (third decade)
*Provider N1 = the teaching provider.

(Table 2). Gross haematuria and haematomas appeared to be two distinct and separate complications. Only two patients had both haematuria and haematomas: one in the second decade with haematuria lasting < 24 h and haematomas > 3 cm and < 5 cm, was counted as having only haematoma, and one in the third decade, with haematuria lasting > 24 h and haematoma > 1 < 3 cm, was counted as having only haematuria.

A decline of more than 10% in haemoglobin values at 24 h was recorded in 53 out of 1397 patients (3·8%). Twelve transfusions were performed (0·86%), eight for gross haematuria and four for haematomas, five in the first decade, three in the second and four in the third.

Timing of complications

Except for arterial-venous fistulae, evidence of complications occurred by < 6 h for gross haematuria and by < or = 24 h for haematomas.

Risk factors for complications in the overall period

Multivariate logistical regression analyses demonstrated that only some histological categories and BTT were significant risk factors for bleeding complications, namely end stage kidney and acute tubular necrosis (OR 2·96, 95% CI

Table 3 Multivariate logistical regression analysis evaluating risk factors for major and minor bleeding complications among the 1387 patients who underwent percutaneous renal biopsy over three decades between 1972 and 2002 in a single centre. The two cases with arterial-venous fistula are not included, as this is not a bleeding complication

		No bleeding complications $n = 1045$		Major and minor bleeding complications* $n = 340$					
		n	%	n	%	$\times^2$	P	OR	95% CI
Age (years)	< 30	346	33	126	37	2·845	0·24	1	–
	30–49	387	37	108	32			0·77	0·56–1·04
	> 49	314	30	106	31			0·75	0·39–1·02
Gender	Female	429	41	132	39	0·193	0·791	1	–
	Male	618	59	208	61			1·08	0·82–1·41
Platelets, mm^3	–	–	–	–	–	–	–	0·88	0·43–1·81
Hb ($g\ dL^{-1}L$)	–	–	–	–	–	–	–	1·25	0·78–2·02
Real-time BTT (min)	–	–	–	–	–	–	–	1·87	1·17–2·83
Blood pressure (mmHg)	≤ 140/90	764	73	224	66	4·394	0·036	1	–
	> 140/90	283	27	116	34			1·15	0·78–1·70
Renal dysfunction	Absent	503	48	150	44	1·617	0·445	1	–
	Mild/moderate	460	44	159	47			1·12	0·75–1·67
	Severe	84	8	31	9			1·15	0·52–2·52
Renal histology	All the others	932	89	276	81	14·88	< 0·001	1	–
	Autoimmune systemic diseases (Vasculitis/SLE/ CRYO/Goodpasture)	95	9	51	15			2·06	1·40–3·01
	End-stage kidney/ATN	20	2	13	4			2·96	1·19–7·30

Major and minor bleeding complications include:
1 nephrectomy, 2 surgical revisions, 228 patients with gross haematuria and 109 with > 1 cm haematomas;
The two patients with both haematuria and haematomas were considered as having only haematoma (second decade) and only haematuria (third decade).
SLE, systemic lupus erythematosus; CRYO, cryoglobulinaemia; ATN, acute tubular necrosis; BTT, bleeding time test; Hb, haemoglobin.

1·19–7·30), and systemic autoimmune diseases including vasculitis, systemic lupus erythematosus, cryoglobulinaemia, Goodpasture syndrome (OR 2·06, 95% CI 1·40–3·01). Real-time BTT was a significant risk factor (OR 1·82, 95% CI 1·17–2·83), as was baseline BTT before any correction (OR 1·78, 95% CI 1·089–3·051) (Table 3).

Risk factors for complications only in the last decade

As routine sonography was only adopted in the last decade, a separate analysis was performed.

Multinomial logistical regression analysis demonstrated that real-time BTT significantly increased the occurrence of haematomas by 21% for each minute, but not the risk of haematuria (Table 4). The histological renal category of Systemic Autoimmune Diseases was a significant risk factor for haematomas (OR 2·08, 95% CI 1·11–3·91), but not for haematuria.

When both haematomas and haematuria were grouped together, the effects of BTT were at the limits of the statistical significance (Table 4).

Additional studies

The 98 patients with baseline prolonged BTT over all the periods were not significantly different from the others as far as age, sex, arterial pressure, INR, APTT, fibrinogen, histological renal categories and provider. They showed significantly increased serum urea (94 ± 72 vs. 72 ± 56 mg dL^{-1}, P 0·0027) and creatinine ($2·9 \pm 2·5$ vs. $2·0 \pm 1·9$, $P < 0·0001$), and decreased platelet count (235 ± 63 vs. 249 ± 76, P 0·01). Figure 1 shows that risks of bleeding complications follow a continuously increasing trend both in corrected and non-corrected people. The risk shifts towards a lower, though still parallel risk, in corrected patients eventually leading to a difference from 3·20 to 2·01 and 4·73–2·97 for real-time BTT values of six and eight min, respectively [OR = e(0·1943 ⋆ BTT –0·4656 ⋆ treatment), where: BTT = real time BTT, in minutes; treatment = 0 if not, 1 if yes].

Alterations of pre-biopsy clinical diagnosis

Disagreement between clinical hypothesis and histological diagnosis was valuable in 1288 cases, formulated as a single hypothesis in 370 cases, two hypotheses in 479 cases, and three hypotheses in 439 cases. Globally, alteration in pre-biopsy diagnosis was observed in 32·8% of cases, 39·5% in single hypothesis, 31·6% in two hypotheses, 28·8% in three hypotheses (Table 2), and disagreement significantly decreased over the time (χ^2 18·35, $P < 0·005$) [Fig. 2].

Alteration in pre-biopsy diagnoses was mainly observed in end stage renal kidney (78%), interstitial nephritis (60%)

Table 4 Multinomial logistical regression analysis evaluating risk factors for major and minor bleeding complications and separately, only for gross haematuria and for haematomas among the 658 patients who underwent percutaneous renal biopsy in the last decade (1992–2002) in a single centre

		No bleeding complications $n = 71$		Major and minor bleeding complications* $n = 187$		Only gross haematuria $n = 93$				Only haematomas > 1 cm $n = 94$			
		n	%	OR	95% CI	*n*	%	OR	95% CI	*n*	%	OR	95% CI
Age (years)	< 30	98	21	1	–	26	28	1	–	21	22	1	–
	30–49	162	34	0·93	0·58–1·48	31	33	0·80	0·44–1·45	39	42	1·09	0·59–2·02
	> 49	211	45	0·63	0·39–1·02	36	39	0·67	0·37–1·24	34	36	0·60	0·31–1·16
Gender	Female	159	36	1	–	38	41	1	–	43	46	1	–
	Male	302	64	0·81	0·56–1·17	55	59	0·96	0·59–1·56	51	54	0·68	0·42–1·11
Platelets, mm^3	–	–	–	0·96	0·46–2·04	–	–	0·70	0·23–2·10	–	–	1·24	0·50–3·04
Hb ($g\ dL^{-1}L$)	–	–	–	1·26	0·78–2·05	–	–	1·47	0·80–2·72	–	–	1·09	0·57–2·05
Real-time BTT (min)	–	–	–	1·09	0·99–1·21	–	–	0·98	0·87–1·12	–	–	1·21	1·07–1·39
Blood pressure (mmHg)	≤ 140/90	318	67	1	–	64	69	1	–	57	61	1	–
	> 140/90	153	32	1·15	0·78–1·70	29	31	1·02	0·61–1·70	37	39	1·31	0·79–2·15
Renal dysfunction	Absent	179	38	1	–	40	43	1	–	27	29	1	–
	Mild/moderate	261	55	1·12	0·75–1·67	43	46	0·75	0·45–1·27	60	64	1·69	0·98–2·92
	Severe	31	7	1·15	0·52–2·52	10	11	1·03	0·39–2·69	7	7	1·27	0·43–3·80
Renal histology	All the others	413	88	1	–	74	80	1	–	72	77	1	–
	Autoimmune systemic diseases (Vasculitis/SLE/CRYO/Goodpasture)	49	10	1·82	1·10–3·02	15	16	1·59	0·81–3·10	19	20	2·08	1·11–3·91
	End stage kidney/ATN	9	2	1·66	0·55–5·02	4	4	1·91	0·50–7·31	3	3	1·49	0·34–6·34

*One patient with both gross haematuria and haematoma > 1 < 3 cm was considered only in the subgroup of gross haematuria

Abbreviations. SLE, Systemic Lupus Erythematosus; CRYO, Cryoglobulinaemia; ATN, Acute tubular necrosis; BTT, Bleeding time test.

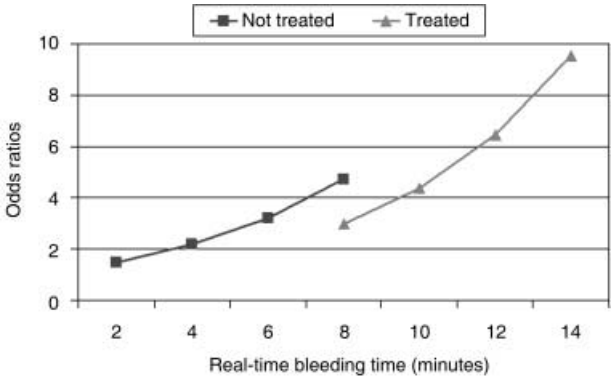

Figure 1 Estimated ORs for bleeding complications in treated with DDAVP and untreated patients, by baseline BT before percutaneous renal biopsy. OR = e(0·1943 ⋆ Baseline BT –0·4656 ⋆ treatment), where: BBT = Baseline BT, in minutes; treatment = 0 if not, 1 if yes.

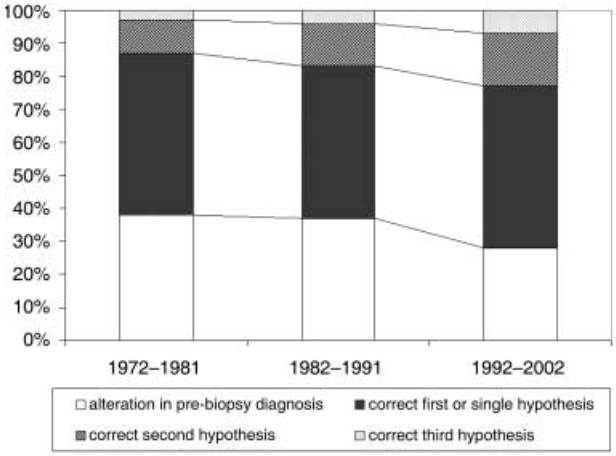

Figure 2 Change in alterations in pre-biopsy diagnosis over time was available among the 1288 patients in whom pre-biopsy clinical diagnosis was available.

membranous-proliferative glomerulonephritis (56%), followed by nephrosclerosis (38%), cryoglobulinaemia (30%), paraproteinaemia including amylodosis (25%), membranous nephropathy/IgA-glomerulonephritis (15%) and lupus nephritis (10%), while complete agreement was found in cases of acute tubular necrosis and cast nephropathy (Fig. 3).

Discussion

No series as large as the current one are available among clinical studies on percutaneous biopsies and performed mostly by the same operator, thus avoiding the amount of variability connected with different operators, and appearing as the ideal setting to evaluate the predictive ability of other variables.

Our outcomes of no death, 0·36% major complications and 24·2% minor complications are similar (0·1% nephrectomy, 0·18% infection, 0·3% surgical revision, 15·3% gross haematuria) [13,14,20], or better than others previously published (death 0·05%–0·1%, haematomas 37·8%–44%, overall complications up to 34·1%) [18,19,21–23]. Furthermore, a significant reduction in the occurrence of haematuria has been demonstrated (–4% for each year from 1982 to 2002) with a drop of severe form lasting more than 24 h from 7·1% to 4·5% in the last decade, when the role of core sampling with ultrasound guidance and smaller gauge-needle is cumulative.

On the other hand, knowledge of renal histology altered our patient management in more than 30% of cases, under-

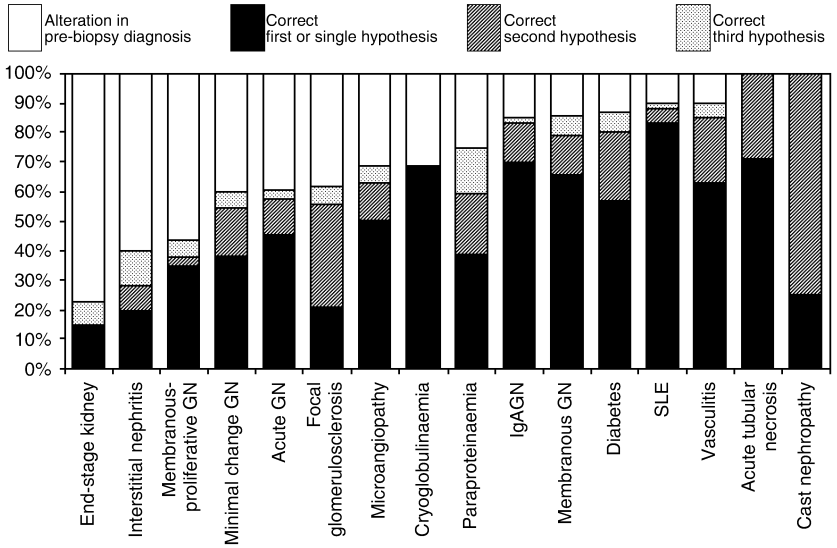

Figure 3 Frequency of alteration in pre-biopsy diagnosis in different subsets of renal disease among the 1288 patients in whom pre-biopsy clinical diagnosis was available. Abbreviations: GN, glomerulonephritis; IgAGN, glomerulonephritis with IgA deposition; SLE, systemic lupus erythematosus.

scoring that renal biopsy remains an essential diagnostic tool, as previously reported with a large variability of results (disagreement ranging from 3% in cases of isolated haematuria to 86% in cases of nephrotic range proteinuria) [12,24,25].

The increased risk in some subsets of renal diseases confirms previous data, indicating that renal parenchyma offers less resistance in the presence of fibrous or inflammatory processes interfering with the contraction of small vessels crossed by the needle [10,13,14,26].

On the contrary, the role of prolonged BTT is controversial at best. Previous studies on renal biopsy did not demonstrate a firm relationship between BTT and bleeding complications in some studies [23,27,28], unlike others [29,30].

BTT is a poor predictor of bleeding after surgical intervention [31–33], but this should not apply to percutaneous procedures, when the surgical techniques able to stop directly visualized small haemorrhages cannot be applied, and the first phase of haemostasis (explored by BTT) has to be guaranteed for bleeding to stop [34,35].

Furthermore, BTT has been defined as the best predictor of haemorrhagic risk in patients with kidney diseases [36–38] and our patients with prolonged BTT have some renal dysfunctions. The significant relationships we have found between baseline BTT and urea, creatinine, APTT and platelet values may explain why, in our analysis, these factors are not related to bleeding complications as in previous studies [19,21,23,39], as they look as surrogate variables potentially blunted by BTT. Renal failure might be a risk factor for bleeding complications via platelet dysfunction, and BTT a predictor of haemorrhagic risk due to uraemic platelet dysfunction.

Lastly, our not significant increased risk of bleeding for blood pressure > 140/90 mmHg unlike other studies [13–15,39] might be explained by our habit of postponing renal biopsy for values ≥ 160/100 mmHg.

The key demonstration of our study is the relationship between in-vivo platelet function and biopsy outcomes, as the former is a potentially modifiable factor. The BTT has been claimed to be a non-sensitive, non-specific test with low reproducibility, and the 15% reproducibility of our centre may look insufficient, but the 1387 BTT were always performed in duplicate by skilled people in our centre who paid particular attention to this problem. Certainly, more standardized alternative tests than BTT should be looked for to evaluate platelet function, mainly in patients with kidney disease, on which physicians could base decisions such as who, or who not, to pre-treat with pharmacological approaches, or who shift towards laparoscopic or transvenous-transjugular renal biopsy for high risk of bleeding [38,40]. We cannot know the outcomes of the 98 patients with prolonged baseline BTT without correction, but they still have an increased risk after correction, as shown in Fig. 1.

The major bias of this study is that it has all the limits of retrospective studies carried out over a prolonged time period: all the variables adopted in this study did change. Furthermore, it does not address BTT's overall ranges, as renal biopsy was not performed in the presence of BTT still prolonged after correction. Third, DDAVP is potentially not without side effects [17]. Lastly, the clinical significance might be debatable in the case of small haematomas. However, no side effects were observed in the patients treated with DDAVP, and fatal complications reported in the literature often started from small haematomas.

We conclude that in expert hands and with appropriate precautions, renal biopsy can be considered safe and useful in the native kidney, as it has been demonstrated also in transplanted kidneys [41]. Platelet function should be evaluated to select low-risk patients for renal biopsy as 'a day case procedure', in order to build risk management strategies including 'risk abatement' as the process of combining complication prevention or control to minimize a risk.

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