

Renal Disease in Madeira Islands: twenty-seven years' experience of native kidney biopsies

Doença Renal na Região Autónoma da Madeira: experiência de vinte e sete anos de biópsias de rim nativo

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■ ABSTRACT

Introduction: Renal biopsy plays an essential role either in the diagnosis or in the prognosis of patients with renal disease. In order to assess its epidemiology and evolution in Madeira Islands, we analysed twenty-seven years of native kidney biopsies. **Methods:** We performed a retrospective analysis of clinical records, including histological revision from 1986 to 2012, totalling 315 native kidney biopsies. They were assessed regarding the temporal evolution both for the quality/indications for renal biopsy and for the patterns of kidney disease. **Results:** A total of 315 native kidney biopsies were analysed. The patients' mean age was of 40.8 ± 18.4 years and 50.5% (n = 159) were males. The most common indications for renal biopsy were nephrotic syndrome (36.2%, n = 114) and acute kidney injury (20.0%, n = 63). Among primary glomerular diseases (41.5%, n = 115) the most common were IgA nephropathy (26.1%, n = 30) and focal-segmental glomerulosclerosis (17.4%, n = 20) and among secondary glomerular diseases (31.4%, n = 87), lupus nephritis (51.7%, n = 45) and amyloidosis (20.7%, n = 18). Statistical analysis revealed significant correlation between gender and major pathological diagnosis (Fisher's exact test, $p < .01$) and between indications for renal biopsy and major pathological diagnosis (χ^2 , $p < .01$). Regarding the temporal evolution, no statistically significant differences were found in the number of renal biopsies (χ^2 , $p = .193$), number of glomeruli per sample (Fisher's exact test, $p = .669$), age (Kruskal-Wallis, $p = .216$), indications for renal biopsy (χ^2 , $p = .106$) or major pathological diagnosis groups (χ^2 , $p = .649$). However, considering the specific clinico-pathological diagnoses and their temporal variation, a statistically significant difference (Fisher's exact test, $p < .05$) was found for lupus nephritis and membranous nephropathy with an increasing incidence and for amyloidosis with an opposite tendency. **Discussion:** The review of the native kidney biopsies from a population with particular characteristics, geographically isolated, such as those from Madeira Islands, showed parallel between epidemiological numbers referring to other European subpopulations, allowing simultaneously a comprehensive approach to our renal biopsy policies.

Key-Words: Epidemiology; glomerulonephritis; nephropathy; renal biopsy; renal disease.

RESUMO

Introdução: A biópsia renal é fundamental na abordagem diagnóstica e no prognóstico de doentes com patologias nefrológicas. No sentido de avaliar a epidemiologia das doenças renais na Região Autónoma da Madeira e a sua evolução, analisou-se as biópsias de rim nativo nos últimos vinte e sete anos. **Métodos:** Procedeu-se à análise retrospectiva dos registos e lâminas histológicas de 1986-2012, com avaliação da evolução temporal na qualidade/indicações para biópsia renal e padrões de patologias nefrológicas. **Resultados:** A amostra compreende 315 biópsias de rim nativo, sendo a idade média dos doentes de 40.8 ± 18.4 anos, sendo 50.5% (n = 159) do sexo masculino. As síndromes nefrológicas mais frequentes foram a síndrome nefrótica (36.2%, n = 114) e lesão renal aguda (20.0%, n = 63). Das patologias nefrológicas mais frequentes, destacam-se no grupo das glomerulopatias primárias (41.5%, n = 115), a nefropatia de IgA (26.1%, n = 30) e a glomeruloesclerose segmentar e focal (17.4%, n = 20) e nas glomerulopatias secundárias (31.4%, n = 87), a nefrite lúpica (51.7%, n = 45) e amiloidose (20.7%, n = 18). Na análise estatística, realça-se a correlação significativa entre sexo e grupos de síndromes nefrológicas (Fisher's exact test, $p < .01$) e entre grupos de síndromes nefrológicas e diagnóstico patológico (χ^2 , $p < .01$). Avaliando a evolução temporal, não se objectivaram diferenças estatisticamente significativas em relação ao número de biópsias renais (χ^2 , $p = .193$), número de glomérulos na amostra (Fisher's exact test, $p = .669$), idade (Kruskal-Wallis, $p = .216$), síndromes nefrológicas (χ^2 , $p = .106$) ou grandes grupos de diagnóstico patológico (χ^2 , $p = .649$). No entanto, considerando os diagnósticos patológicos específicos e a sua variação temporal foram encontradas diferenças significativas (Fisher's exact test, $p < .05$) para nefrite lúpica e nefropatia membranosa com uma incidência crescente e para a amiloidose com uma tendência oposta. **Discussão:** A análise do registo de biópsias renais de uma população com características particulares, isolada geograficamente, permitiu mostrar concordância com outros números epidemiológicos referentes a outras subpopulações europeias, permitindo simultaneamente uma compreensão das directrizes locais sobre biópsias renais.

Palavras-chave: Biópsia renal; doença renal; epidemiologia; glomerulonefrite; nefropatia.

INTRODUCTION

Renal biopsy was introduced into regular clinical practice in the early 1950s and, since then, it has become an essential tool in assessing the diagnosis, providing information of prognostic value and guiding the treatment of patients with renal disease¹. However, given its invasive nature and despite the advances in the renal biopsy technique with the development and utilization of real-time ultrasound guidance and automated biopsy needles² there are still inherent risks and one must balance the pros and cons considering each patient. In a broader perspective, reviewing the epidemiology of renal diseases besides assessing its incidence, prevalence and trends may help to identify environmental or genetic factors contributing towards disease development and other relevant demographical, clinical and histological features, as well as the influence from single-centre biopsy policies.

Given the particular characteristics of the Madeira Islands, an archipelago geographically isolated in the North Atlantic Ocean comprising about 250,000 inhabitants, a virtually self-contained community with only one major medical provider facility makes it exceptionally suited for these observational studies. Therefore, we reviewed twenty-seven years' experience of native kidney biopsies in order to assess its renal disease epidemiology and evolution.

SUBJECTS AND METHODS

This retrospective study identified all patients for whom a native kidney biopsy was performed, between January 1986 and December 2012, in the Nephrology Department of Hospital Central do Funchal, the single referral nephrology centre for Madeira Islands. During

this time period, a total of 315 native kidney biopsies were performed, including children (< 16 years) and adult patients (≥ 16 years).

The renal biopsy technique in our centre has evolved during the time period the study refers to. In the beginning, the technique used was by computerized tomography marking and then the biopsy itself was accomplished using a 14G Vim Silverman needle. Since 1995, we started using a standard real-time ultrasound-guided technique with an automated spring-fired biopsy gun and a 14G disposable needle (Bard Biopsy Systems®, Bard, UK). All renal biopsy specimens were then dispatched along with the clinical information (medical history, physical examination and laboratory data) and analysed at a Renal Pathology Laboratory in Curry Cabral Hospital, Lisbon. All biopsy specimens were evaluated by optical microscopy and immunofluorescence (IF) whenever possible, using standard procedures. Electron microscopy was available only for selected cases. The renal biopsies were studied by means of routine staining: haematoxylin-eosin, periodic acid-Schiff, Masson's trichrome and methenamine silver and, in selected cases, with other histochemical stains. For cases without adequate frozen tissue for IF, the formalin-fixed, paraffin-embedded renal tissue was used for IF.

For each case, final diagnosis was then established concerning the correlation between both clinical and histological investigations. The reports were then forwarded back to the referring nephrologist and the renal biopsy specimens were stored in case future revision was needed. From the clinical information provided, an indication for biopsy was determined, according to the following clinical syndromes³:

1. Nephrotic syndrome (NS): defined as proteinuria > 3.5 g/d with hypoalbuminemia (serum albumin < 2.5 g/dl) with or without peripheral oedema;
2. Nephritic syndrome (NiS): defined as haematuria, hypertension, oedema and reduced glomerular filtration rate (GFR);
3. Asymptomatic urinary abnormalities (AUA): proteinuria < 3.5 g/d and/or haematuria with more than 3 red blood cells per field without clinical manifestations;

4. Acute kidney injury (AKI): rapid deterioration of GFR, including "acute on chronic", with or without oligoanuria or rapidly progressive renal failure;
5. Chronic kidney disease (CKD): decline in renal function less severe and/or less abrupt than defined for AKI, with or without proteinuria and/or haematuria. (Patients with NS and chronic-progressive kidney injury were categorized under NS)

The histological findings were classified as follows, using a modified classification scheme of World Health Organization recommendations⁴⁻⁶:

1. Primary glomerulonephritis (GN): minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), IgA nephropathy (IgAN), mesangioproliferative GN other than IgAN (MesGN), crescentic GN (CrGN)(not fulfilling the criteria for systemic disease), membranoproliferative GN (MPGN) and proliferative endocapillary GN (PEGN);
2. Secondary GN: lupus nephritis (LN), systemic vasculitis (VAS), anti-glomerular basement membrane disease (antiGBM), Henoch-Schönlein purpura (HSP), renal amyloidosis and GN caused by dysgammaglobulinaemia or paraproteinaemia, such as light-chain deposit disease (LCDD), myeloma kidney (MM), essential cryoglobulinaemia and Waldenström's macroglobulinaemia, diabetic nephropathy (DN), GN associated with infectious diseases (non-streptococcal GN, endocarditis, shunt GN and others) and hereditary GN;
3. Tubulointerstitial diseases, including acute and chronic tubulointerstitial nephritis and acute tubular necrosis;
4. Vascular diseases, including benign and malignant nephroangiosclerosis (NAS), thrombotic microangiopathy and cortical necrosis;
5. Other findings including end-stage renal disease (ESRD) of undetermined cause, unclassified nephropathies, others such as pregnancy related nephropathies, rare nephropathies and normal renal tissue samples.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS, version 17.0 (SPSS, Chicago, IL), considering three inclusive 9-year time frames: 1986–1994, 1995–2003 and 2004–2012. Chi-square test and Fisher's exact test were used for categorical variables, and Kruskal-Wallis test for ordinal variables. *P*-values <.05 were considered statistically significant.

RESULTS

Over the 27 year study, a total of 315 renal biopsies were performed, totalling 295 patients given that 20 records were identified as re-biopsy, with 10 of these carried out due to inadequate sampling during the first biopsy, and 10 for therapeutic/diagnostic reasons at different time points of follow-up (range 6–118 months). The incidence of renal biopsies, considering the 9-year time frames varied between 53.3 per million population (p.m.p.)/year in 1986–1994 to 42.6 p.m.p./year in 1995–2003 and to 44.0 p.m.p./year in 2004–2012, though there were no statistically significant differences (χ^2 , *p* =.193). In what concerns sampling adequacy, renal tissue was obtained in 277 renal biopsies (87,9%) and in spite of the changing renal biopsy technique, no statistical differences were found concerning the number of glomeruli per sample (Fisher's exact test, *p* =.669). Regarding the demographic variables, the patients' mean age was of 40.8 ± 18.4 years and 50.5% (*n* = 159) were male, including children < 16 years (*n* = 17, 5.4%). The patients' mean age was

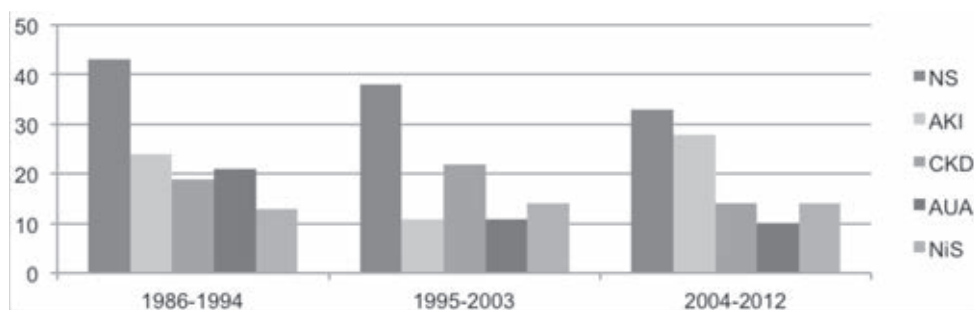
compared according to the previously established time-frames, but no significant variability was found (Kruskal-Wallis, *p* =.216).

The most common indications for a biopsy were NS (*n* = 114, 36.2%) and AKI (*n* = 63, 20.0%) followed by CKD (*n* = 55, 17.5%), AUA (*n* = 42, 13.3%) and NiS (*n* = 41, 13.0%) and once more the time-framed analysis showed no statistically significant differences (χ^2 , *p* =.106) (Fig. 1).

The frequency of the clinico-histological diagnoses is shown in Table I. Overall, among the major pathological groups, primary GN was the most common diagnosis (41.5%), followed by secondary GN (31.4%), tubulointerstitial diseases (7.6%), vascular diseases (3.6%) and other findings (15.9%). Considering the specific diagnosis, the most common type of primary GN were IgAN (*n* = 30, 26.1%), FSGS (*n* = 20, 17.4%) and MCD (*n* = 19, 16.5%) and amid the secondary GN the most common were LN (*n* = 45, 51.7%), amyloidosis (*n* = 18, 20.7%) and DN (*n* = 11, 12.6%). In view of the temporal evolution, according to the time-frames previously established, no statistically significant differences were found regarding the major pathological groups (χ^2 , *p* =.649). Considering the specific clinico-pathological diagnoses, its distribution according to temporal evolution is shown in Fig. 2 and taking into account the statistical analysis of the most common types of specific diagnoses, the temporal evolution shows a statistically significant difference (Fisher's exact test, *p* <.05) only for LN and MN with an increasing incidence and for amyloidosis with an opposite tendency. For informational purposes we have subdivided LN and amyloidosis according

Figure 1

Indications for biopsy according to 9-year time frames



NS nephritic syndrome; AKI acute kidney injury; CKD chronic kidney disease; AUA asymptomatic urinary abnormalities; NiS nephritic syndrome

Table 1

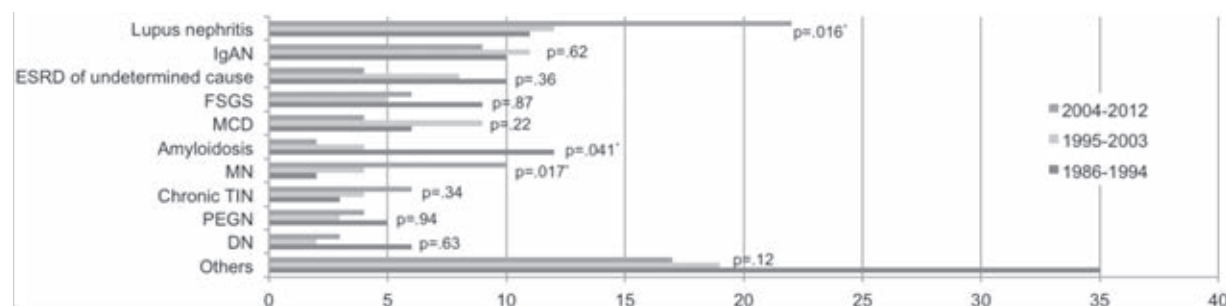
Clinico-histological diagnoses (major pathological groups and specific diagnosis) by age group

	total	% of the major group	adults n = 262 (83.2%)			children n = 17 (5.4%)			elder (age ≥ 65 yrs) n=36 (11.4%)		
			subtotal	m	f	subtotal	m	f	subtotal	m	f
Primary GN	115 (41.5)		n = 92	54 (58.7)	38 (41.3)	n = 10	7 (70.0)	3 (30.0)	n = 13	7 (53.8)	6 (46.2)
IgAN	30 (10.8)	26.1	27	19	8	2	1	1	1	1	0
FSGS	20 (7.2)	17.4	16	11	5	3	1	2	1	0	1
MCD	19 (6.9)	16.5	14	4	10	2	2	0	3	1	2
MN	16 (5.8)	13.9	12	7	5	1	1	0	3	1	2
PEGN	12 (4.4)	10.4	9	6	3	1	1	0	2	2	0
MPGN	7 (2.5)	6.1	6	1	5	-	-	-	1	1	0
MesGN	7 (2.5)	6.1	6	5	1	1	1	0	-	-	-
CrGN	4 (1.4)	3.5	2	1	1	-	-	-	2	1	1
Secondary GN	87 (31.4)		n = 76	17 (22.4)	59 (77.6)	n = 1	1 (100.0)	0 (0.0)	n = 10	4 (40.0)	6 (60.0)
Lupus nephritis	45 (16.2)	51.7	44	4	40	1	1	0	-	-	-
Amyloidosis	18 (6.5)	20.7	12	4	8	-	-	-	6	2	4
Diabetic nephropathy	11 (4.0)	12.6	8	3	5	-	-	-	3	1	2
Systemic vasculitis	4 (1.4)	4.6	3	0	3	-	-	-	1	1	0
HSP	2 (0.7)	2.3	2	1	1	-	-	-	-	-	-
Cryoglobulinaemic GN	1 (0.4)	1.2	1	0	1	-	-	-	-	-	-
Other	6 (2.2)	6.9	6	5	1	-	-	-	-	-	-
Tubulointerstitial diseases	21 (7.6)		n = 14	8 (57.1)	6 (42.9)	n = 0	-	-	n = 7	5 (71.4)	2 (28.6)
Chronic tubulointerstitial nephritis	13 (4.7)	61.9	10	5	5	-	-	-	3	3	0
Acute tubulointerstitial nephritis	5 (1.8)	23.8	3	2	1	-	-	-	2	1	1
Acute tubular necrosis	3 (1.1)	14.3	1	1	0	-	-	-	2	1	1
Vascular diseases	10 (3.6)		n = 9	4 (44.4)	5 (55.6)	n = 0	-	-	n = 1	0 (0.0)	1 (100.0)
Hypertensive nephroangiosclerosis	8 (2.9)	80.0	7	4	3	-	-	-	1	0	1
Thrombotic microangiopathy	2 (0.7)	20.0	2	0	2	-	-	-	-	-	-
Other	44 (15.9)		n = 39	27 (69.2)	12 (30.8)	n = 3	-	-	n = 2	2 (100.0)	0 (0.0)
ESRD (undetermined cause)	22 (7.9)	50.0	20	15	5	-	-	-	2	2	0
Unclassified nephropathies	5 (1.8)	11.4	5	4	1						
Normal renal tissue	17 (6.2)	38.6	14	8	6	3	1	2			
(no kidney sample)	38		32			3			3		

GN glomerulonephritis; IgAN IgA nephropathy; FSGS focal segmental glomerulosclerosis; MCD minimal change disease; MN membranous nephropathy; PEGN proliferative endocapillary GN; MPGN membranoproliferative GN; MesGN mesangioproliferative GN other than IgAN; CrGN crescentic GN; LN Lupus nephritis; HSP Henoch-Schönlein purpura.

Figure 2

Specific clinico-pathological diagnoses according to 9-year time frames.



*(p<.05)

IgAN IgA nephropathy; ESRD end-stage renal disease; FSGS focal segmental glomerulosclerosis; MCD minimal change disease; MN membranous nephropathy; TIN tubulointerstitial nephropathy; PEGN proliferative endocapillary glomerulonephritis; DN diabetic nephropathy

Table II

Correlations between gender, indications for renal biopsy and clinico-histological diagnoses

Gender	Indications for renal biopsy ($\chi^2, p = .908$)					
	NS	NiS	AUA	AKI	CKD	total
male	56	21	19	33	30	159
female	58	20	23	30	25	156
total	114	41	42	63	55	315
Gender	Major pathological diagnosis (Fisher's exact test, $p < .01$)					
	primary GN	secondary GN	Tl diseases	Vasc diseases	Other	total
male	68	20	13	4	31	136
female	47	67	8	5	14	141
total	115	87	21	9	45	277
Indications for renal biopsy	Major pathological diagnosis ($\chi^2, p < .01$) ^a					
	primary GN	Secondary GN	Tl diseases	Vasc diseases	Other	total
NS	61	32	2	1	11	107
NiS	14	6	4	4	5	33
AUA	20	7	0	0	8	35
AKI	17	22	8	1	5	53
CKD	3	20	7	3	16	49
	115	87	21	9	45	277

^a Tl/Vasc diseases were not considered for statistical analysis due to small sized sample

to classes and subtypes, respectively. Among LN, the histopathological classes most found were class IV (51.1%), class II (26.7%) and class III (17.8%) and as amyloidosis is referred AA subtype (66.7%) and AL (22.2%) were the most frequent. Once we had established a decreasing incidence of amyloidosis, we analysed the subset of AA, AL and other amyloidosis for temporal variation having found no statistically significant differences ($p = .14$, $p = .74$ and $p = .34$, respectively). Correlations between gender, indications for renal biopsy and clinico-histological diagnoses are shown in Table II and, as one can observe, statistically significant differences were found between gender and major pathological diagnoses (Fisher's exact test, $p < .01$) and between indications for renal biopsy and major pathological diagnosis ($\chi^2, p < .01$).

DISCUSSION

This retrospective study enables a comprehensive approach to our centre biopsy policies and their adjustments in the past twenty-seven years. According to the demographical and clinical analysis, we found no statistically significant differences in what concerns number

of biopsies performed, sampling adequacy and indications for biopsy. This may suggest, on one hand, a stable approach and workup for nephropathies and, acknowledged the indispensable evolution in the kidney biopsy technique, that the sampling adequacy kept the same standards. On the other hand, given the small sized sample the detection of any underlying statistically significant differences may be underpowered. Regarding the renal biopsy rate in our study, the numbers are quite similar to those described in almost all European registries (48 p.m.p./year in Spain⁷, 34 p.m.p./year in Italy⁶, 16.3–20.1 p.m.p./year in France⁸, 44.1–69.3 p.m.p./year in the Czech Republic⁹, 40 p.m.p./year in Denmark¹⁰ and to those of our own national registry, 61.4 p.m.p./year in 2011–2012) apart from some registries whose numbers are somewhat uneven due to particular reasons (10.8 p.m.p./year in Serbia¹¹, 10.7–12.8 p.m.p./year in Romania¹², 126.3 p.m.p./year in Scotland¹³ and 176 p.m.p./year in Finland¹⁴). Whereas indications for biopsy are concerned, NS was our most frequent clinical presentation as in some other registries (7, 9, 11, 12), however we found some divergences with other registries as the AUA came responsible only for 13.3% while in many other studies it imposed itself as a more frequent indication for biopsy (24.3–38.7%) (6, 7, 9, 11, 14). This may foretell a somewhat conservative approach

at our centre in terms of kidney biopsy as the workup for these clinical presentations or, as Okpechi suggests, it may reflect healthcare investment¹⁵. Our report shows that, among the major pathological groups, primary GN stands as the most common (41.5%), followed by secondary GN (31.4%) what mirrors other registries' results where primary GN varies between 51.5-64.1%(6-9, 11, 12) and secondary GN between 20.4-26.4%(6, 7, 9, 11, 12). Addressing the specific diagnosis analysis we recognized IgAN (26.1%) as the most common primary GN, as in other European subpopulations (6-9, 14), and LN (51.7%) as the most frequent among the secondary GN going in line not only with European subpopulations, but also with worldwide biopsy-proven glomerular diseases¹⁶, both of which go according to our own national registry.

Deliberately, we have revised the Canary Islands' Registry of renal biopsies (17, 18) separately, since it somehow presents with similar characteristics to those of our own. As a result, we found parallel epidemiological data among pathological groups, with primary GN attaining top place with 39.8%, and its subset of specific diagnosis showing also similar distribution with IgAN being the most frequent (36.6%), followed by MCD (18.1%) and FSGS (17.1%), with the latter two assuming an inverse order when compared to our data. However, we would like to draw attention to the differences found in the prevalence of certain glomerulopathies among different provinces in the Canary Islands, mainly as FSGS is concerned, what seems to be related to a different genetic load on each province and set the authors in search of genetic mutations¹⁷.

Examining the results of the epidemiological analysis in relation to temporal variation we found no significant differences in the major pathological diagnoses, nonetheless, considering the most common specific diagnoses and assessing their variation along the time periods we found, on the one hand, statistically significant increasing incidence in biopsy-proven LN and MN and, on the other, decreasing incidence among amyloidosis. Focusing on the absence of temporal variation of IgAN's incidence, as shown in other series¹⁹, this may reflect once more the conservative biopsy policies. Then again, LN's raise is probably due to both low nephrology referral in the early period the study refers to and re-biopsying relapses for therapeutic purposes, while the increasing incidence in MN is somewhat similar to that described in other registries (6, 7). Taking into consideration the decreasing incidence

of amyloidosis, the subset analysis for amyloidosis (AA, AL and others) despite not having found statistical significance among them, demonstrated a higher tendency ($p = .14$) for amyloidosis AA as being the reason for the decline for amyloidosis. This decline in the incidence of amyloidosis contrasts with the results of the Italian Registry²⁰ but goes along with those from Spain²¹. In our study, the decrease is mainly justified by the AA form, what previous studies(21, 22) suggest being due to advances in the treatment of chronic infections and autoimmune inflammatory diseases, thus reflecting an increasing healthcare investment and leaving the aforementioned AUA's low prevalence as indication for kidney biopsy as probably resulting from a conservative approach at our centre. In the course of the subset analysis of amyloidosis, the recognition of four cases of AL amyloidosis caught our eye as none of "myeloma kidney" or cast nephropathy was diagnosed. Such result discloses that the true prevalences of different kidney diseases are not always represented by biopsy rates, once cast nephropathy is considered the most common renal pathology in myeloma patients²³. However, one must bear in mind that in the case of myeloma patients with cast nephropathy their common clinical contraindications and sometimes presumptive diagnosis avert the definitive diagnosis made by renal biopsy, justifying the discrepancy by one side with necropsy results (11% cases of AL amyloidosis vs. 32% cases of cast nephropathy)²⁴ that reflect more truthful prevalences in opposition to renal biopsy database's revision results (68% cases of AL amyloidosis vs. 17% cases of cast nephropathy)²⁵.

Another finding that drew our attention was that of two cases of TI nephritis presenting with NS (Table II). Although the histological analysis revealed no more than tubular and interstitial changes, the NS suggests the presence of glomerular pathology, thus we thought further individual consideration on these two cases was imperative. Considering the first of the two, an acute interstitial nephritis was clinically interpreted as a case of NSAID's nephropathy, thus justifying the association with NS as in patients who develop both AIN and minimal change disease(26-28). These cases usually conceal extensive foot process effacement only revealed by electron microscopy that was not performed in this particular situation justifying, therefore, the non-description of glomerular changes by optical microscopy²⁶. The latter was histologically characterized as a chronic interstitial nephritis but no aetiology was clinically plain. In this case, we can only consider

a possible sampling bias as only 4 glomerulus were present, what might withhold the finding of glomerular sclerosis in the context of CIN.

Although a broader analysis could enhance our epidemiology knowledge of this geographical region, in view of such a small sample an in depth analysis of temporal evolution, covering all clinico-histological diagnoses rendered itself unattainable.

CONCLUSION

This study allowed us, on the one hand, to acknowledge comprehensively our centre biopsy policies and on other to render information that, despite the geographical isolation of Madeira Islands, showed that the demographical and clinical data of renal diseases is in many aspects similar to that from other European subpopulations. However, as in other similar regions it may conceal some endemic mutations.

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Conflict of interest statement: None declared

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