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Stratifying risk for progression in IgA nephropathy: how to predict the future?

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KEY WORDS

estimated glomerular filtration rate, glomerulonephritis, IgA nephropathy, Oxford classification, proteinuria

ABSTRACT

INTRODUCTION IgA nephropathy (IgAN) is characterized by a highly heterogeneous clinical course, which results in controversies regarding the assessment of individual prognosis and establishing the optimal treatment approach.

OBJECTIVES The aim of the present study was to define risk factors for IgAN progression. We evaluated histopathological features derived from the Oxford classification of IgAN and additional, non-Oxford biopsy findings, as well as baseline and follow-up clinical data.

PATIENTS AND METHODS We conducted a single-center retrospective study on 52 patients with biopsy-proven IgAN. The endpoint was an increase in serum creatinine levels of 50% from baseline.

RESULTS Eight subjects (12%) reached the endpoint. Poor renal outcome was independently related to time-average proteinuria (TA-P) exceeding 2.0 g/d ($P = 0.047$), estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 m^2 ($P = 0.01$), history of tonsillectomy ($P = 0.01$), and crescent lesions in renal biopsy ($P = 0.03$). High global sclerosis index (GSI) ($P = 0.009$), TA-P ($P = 0.03$), and the presence of microscopic hematuria ($P = 0.03$) were independent predictors of a more rapid rate of renal function loss, assessed by the velocity of eGFR decline. Of the variables included in the Oxford classification, only interstitial fibrosis and tubular atrophy proved to have prognostic value, as revealed by a univariate, but not multivariate Cox regression analysis.

CONCLUSIONS The extent of proteinuria during follow-up and impaired renal function at the time of diagnosis remain the most significant clinical prognostic factors in IgAN. We also report additional, non-Oxford histopathological features that can be used for risk stratification in IgAN, including the GSI and the presence of crescents.

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INTRODUCTION IgA nephropathy (IgAN) is the most common form of primary glomerulonephritis. The clinical spectrum is wide, ranging from indolent to rapidly progressive forms. Within 10 to 20 years of diagnosis, about 15% to 40% of the patients developd end-stage renal disease (ESRD).[1] Known factors explain only about 50% of the variations in the observed outcome, resulting in controversies while assessing individual prognosis and establishing an optimal approach to treatment.[2]

The factors most consistently linked with progressive IgAN include persistent proteinuria, poorly controlled hypertension, and impaired renal function at the time of diagnosis.[3] The prognostic role of other parameters, such as hematuria, hyperuricemia, hypoalbuminemia, anemia, and hypertriglyceridemia, is not widely recognized.[1,4,5] Therefore, the identification of other predictors of IgAN progression continues to attract more and more interest. Several scoring systems based on renal biopsy data, including the most recent Oxford classification, have been developed to assess the outcome in IgAN.[6] Although it has proved to be a powerful tool for risk stratification, the prognostic value of some variables is questioned, and, at the same time, there is a rising concern that substantial histopathological parameters have not been included.[7]

TABLE 1 Baseline clinical and histopathological characteristics of the patients

Variables			n
male sex		30 (57.7)	52
age, y		32.5 ±11.7	52
eGFR, ml/min/1.73 m^2		74.7 ±28.3	52
SBP, mmHg		130 (120–140)	46
DBP, mmHg		80 (70–84)	46
MAP, mmHg		97 (88–103)	46
Hb, g/dl		13.5 ±1.6	52
serum uric acid, mg/dl		6.0 ±1.3	48
serum albumin, mg/dl		3.6 ±0.9	52
TG, mg/dl		165.8 ±97.0	48
TC, mg/dl		248.1 ±73.0	49
proteinuria, g/d		1.35 (0.6–2.0)	43
hematuria, RBC per mf		18 (6–30)	52
history of tonsillectomy		11 (21.2)	52
upper respiratory tract symptoms		17 (32.7)	52
number of glomeruli		13 (11–16)	42
globally sclerotized glomeruli, %		13.4 (0–29.4)	42
mesangial hypercellularity, %		58.2 ±35.3	39
crescents	0/1/2[a]	35/6/1 (83.3/14.3/2.4)	42
interstitial fibrosis	0/1/2[a]	38/3/1 (90.5/7.1/2.4)	42
tubular atrophy	0/1[a]	40/2 (95.2/4.8)	42
interstitial inflammation	0/1[a]	7/35 (16.7/83.3)	42
WHO class	III/IV/V	13/18/1 (40.6/56.3/3.1)	32

Data are presented as means ± standard deviations, medians (interquartile range), or numbers (with percentages) where appropriate.

a for categories, see the **PATIENTS AND METHODS** section: **Histopathological data**

Conversion factors to SI units are as follows: for Hb, 10; uric acid, 59.48; albumin, 10; TG, 0.0114; and TC, 0.02586.

Abbreviations: BMI – body mass index, DBP – diastolic blood pressure, eGFR – estimated glomerular filtration rate, Hb – hemoglobin, MAP – mean arterial pressure, RBC per mf – red blood cells per microscopic field, SBP – systolic blood pressure, TC – total cholesterol, TG – triglycerides, WHO – World Health Organization

In this retrospective study of adult patients with biopsy-proven IgAN, we sought to identify clinical markers allowing to discriminate between individuals with a progressive and non-progressive course. We also tested the applicability of the Oxford classification for assessing prognosis in the population from our institution and evaluated additional, non-Oxford kidney biopsy findings.

PATIENTS AND METHODS

Patients We enrolled consecutive patients with biopsy-proven IgAN admitted to the Department of Nephrology and Transplantation Medicine of the Wroclaw Medical University, Poland, between May 2008 and February 2014. The inclusion criteria were as follows: age at diagnosis over 18 years and estimated glomerular filtration rate (eGFR) higher than 15 ml/min/1.73 m^2. Patients with postbiopsy follow-up period shorter than 6 months or with insufficient medical records were excluded. The final study population consisted of 52 subjects.

Clinical and laboratory data Demographic, clinical, and laboratory data obtained at the time of biopsy and during follow-up were derived from patients' medical records. The variables included sex, age, urinary protein excretion, systolic and diastolic blood pressures (SBP and DBP, respectively), degree of hematuria, serum creatinine, albumin, and uric acid levels, hemoglobin (Hb) concentration, serum lipid levels, use of medications, history of tonsillectomy, and concomitant diseases. Proteinuria was estimated by measuring the protein concentration in a 24-hour urine sample or by the protein-to-creatinine ratio of the first morning spot urine. Arterial hypertension was defined as an SBP of 140 mmHg and higher or DBP of 90 mmHg and higher or the use of antihypertensive therapy; anemia as Hb levels lower than 13.5 g/dl in men and lower than 12 g/dl in women; hypoalbuminemia as serum albumin levels lower than 3 mg/dl; hyperuricemia as serum uric acid levels exceeding 7.5 mg/dl in men and 5.7 mg/dl in women; hypertriglyceridemia as serum triglyceride (TG) levels exceeding 150 mg/dl; and hypercholesterolemia as serum total cholesterol (TC) levels exceeding 200 mg/dl. Poorly controlled arterial hypertension was considered as an SBP of 140 mmHg and higher or DBP of 90 mmHg and higher. A history of tonsillectomy as well as the records of frequent or chronic infections of the upper respiratory tract were considered as upper respiratory tract disorders.

GFR was estimated using the abbreviated Modification of Diet in Renal Disease equation. The mean arterial pressure (MAP) was defined as DBP plus one-third of SBP. Time-weighted averages were calculated for MAP and proteinuria from the area under the curve (AUC) of all measurements during follow-up. Time-average MAP (TA-MAP) was defined as the ratio of the AUC of the MAP to the duration of follow-up. Time-average proteinuria (TA-P) was determined using the same method as that for TA-MAP.

The rate of renal function decline was expressed as the velocity of eGFR decline, which was obtained by fitting a straight line through the values of eGFR measured at every visit during follow-up using linear regression and the principle of the least squares. These values were plotted and examined for each patient.

The follow-up started on the day of kidney biopsy. The endpoint was defined as an increase of serum creatinine levels by 50%.

Histopathological data Histopathological data were obtained from the recorded biopsy results, which were available for 42 of the 52 patients. All samples had been examined in the course of routine diagnostic workup.

The biopsy results were examined for 7 histopathological features, of which 4 were derived from the Oxford classification, 3 were estimated according to the following criteria: mesangial hypercellularity score (M; M0 ≤0.5; M1 >0.5),

TABLE 2 Clinical and histopathological predictors of IgA nephropathy progression by Cox proportional hazard models

Clinical predictors	Univariate models				Multivariate model (n = 47)		
	HR	95% CI	*P*	n	HR	95% CI	*P*
TA-P, g/d	2.0	1.2–3.1	0.004	47	–		
TA-P >2.0 g/d, yes vs. no	6.2	1.03–37.3	0.047	47	26.3	1.5–473.7	0.03
history of tonsillectomy, yes vs. no	6.9	1.5–31.9	0.01	52	10.5	1.04–105.3	0.046
eGFR <60 ml/min/1.73 m^2, yes vs. no	7.8	1.6–39.3	0.01	52	32.1	1.2–855.5	0.04
poorly controlled arterial hypertension, yes vs. no	5.6	1.1–29.2	0.04	52	–		
Histopathological predictors	**Univariate models**				**Multivariate model (n = 42)**		
	HR	95% CI	*P*	n	HR	95% CI	*P*
GSI, %	133.7	1.5–11972.7	0.03	42	3.6	0.001–10891.7	NS
C, C0–C2	12.8	1.3–123.2	0.03	42	20.3	1.3–327.01	0.03
TA, TA0–TA1	22.9	1.3–390.0	0.03	42	1.1	0.04–31.9	NS
IF, IF0–IF2	5.5	1.6–18.9	0.01	42	7.7	0.6–104.2	NS

Abbreviations: C – crescents, CI – confidence interval, GSI – global sclerosis, HR – hazard ratio, IF – interstitial fibrosis, NS – nonsignificant, TA – tubular atrophy, TA-P – time-average proteinuria, others – see TABLE 1

endocapillary hypercellularity (E; E0 when absent; E1 when present), and segmental sclerosis (S; S0 or S1 analogically to E). The assessment of the fourth Oxford parameter, tubular atrophy/interstitial fibrosis ratio (T), was modified to the semiquantitative categorization of both tubular atrophy (TA) and interstitial fibrosis (IF) separately according to the extent of the affected interstitium (TA: TA0 for 0%–25%; TA1 for >25%; IF: IF0 for 0%–25%; IF1 for >25%–50%; IF2 for >50%). Three additional, non-Oxford features were incorporated, including the global sclerosis index (GSI), expressed as the percentage of glomeruli showing global sclerosis; crescent index (C; C0 for 0%; C1 for >0%–25%; C2 for >25%), and the presence of interstitial inflammation (I; I0 when absent; I1 when present).

Statistical analysis Normally distributed continuous variables were expressed as means with standard deviations, and their intergroup differences were tested using the *t* test. The remaining continuous variables had a skewed distribution, and were expressed as medians with lower and upper quartiles; the intergroup differences were tested using the Mann–Whitney test. Categorical variables were expressed as numbers with percentages, and their intergroup differences were tested using the χ^2 test with Yates' correction for continuity. A bivariate correlation analysis was performed using the Pearson's correlation coefficient.

The associations between the analyzed variables and event-free survival were established using Cox proportional hazards models (both univariate and multivariate), and Kaplan–Meier curves were constructed for factors determined by the multivariate model. Differences in event-free survival rates were tested using the log-rank test.

To establish clinical and histopathological determinants of the velocity of eGFR decline, a univariate followed by multivariate linear regression model was used. Variables with a significant univariate association with the slope (P <0.1) and clinically relevant parameters were entered in a stepwise backward multivariate model based on the strength of their univariate association.

Since there were patients with incomplete data for single clinical parameters, statistical analyses for those variables were performed after exclusion of those subjects. Therefore, the exact number of the analyzed patients is given for every variable.

A P value of less than 0.05 was considered statistically significant. All statistical analyses were performed using the Statistica 10 software (StatSoft Inc., Tulsa, Oklahoma, United States).

RESULTS

Baseline clinical parameters The baseline clinical characteristics of the study cohort are shown in TABLE 1. Throughout the follow-up period, the study population demonstrated the mean TA-P level of 1.2 ±1.0 g/d (n = 47) and mean TA-MAP values of 95 ±7 mmHg (n = 49).

Survival analysis The median follow-up period of the entire cohort of 52 patients was 14 months (8–42 months). Eight subjects (15.4%) reached the endpoint. The clinical factors predictive of an increase in serum creatinine levels by 50% in univariate Cox proportional regression models are presented in TABLE 2. These included TA-P, baseline eGFR of less than 60 ml/min/1.73 m^2, and a history of tonsillectomy. Arterial hypertension demonstrated the prognostic value when poorly controlled; however, in other cases, it did not affect the renal outcome. The baseline proteinuria level was significant in this analysis. In the multivariate Cox model (χ^2 = 13.6, P = 0.003), TA-P exceeding 2.0 g/d, a history of tonsillectomy, and eGFR of less than 60 ml/min/1.73 m^2 proved to be independent prognostic factors. Kaplan–Meier event-free survival curves for these 3 features are shown in FIGURE 1.

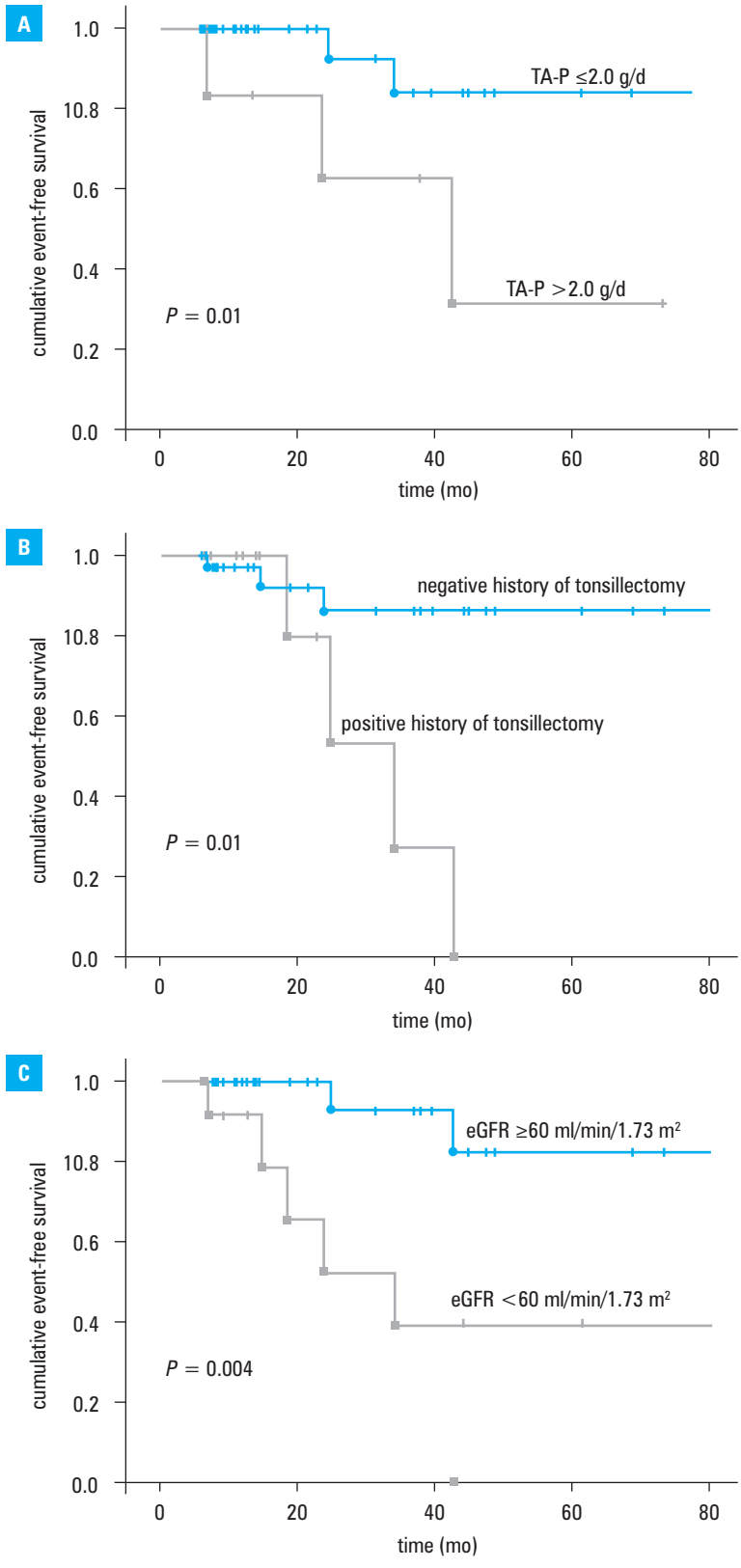

FIGURE 1 Kaplan–Meier curves reflecting the difference in event-free survival (an increase in serum creatinine levels of >50% from baseline) between patients with time-average proteinuria (TA-P) >2.0 g/d and ≤2.0 g/d (**A**), patients with a positive and negative history of tonsillectomy (**B**), and patients with the baseline estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m² and ≥60 ml/min/1.73 m² (**C**)

More patients with TA-P exceeding 2.0 g/d met the endpoint compared with those with lower TA-P values (42.9% vs. 7.5%; $P = 0.047$; n = 47). IgAN progression was observed significantly more often in patients with the baseline eGFR of less than 60 ml/min/1.73m² than in those with higher eGFR values (75.0% vs. 27.3%; $P = 0.03$; n = 52). Patients who reached the endpoint differed from those who did not in terms of TA-P (1.0 ±0.7 g/d vs. 3.1 ±2.7 g/d; $P < 0.001$; n = 47), serum creatinine level (1.9 ±1.1 mg/dl vs. 1.1 ±0.4 mg/dl; $P = 0.001$; n = 52), DBP (87.5 ±7.6 mmHg vs. 77.7 ±9.9 mmHg; $P = 0.03$; n = 46), MAP (103.3 ±9.1 mmHg vs. 93.8 ±10.5 mmHg; $P = 0.04$; n = 46), and the prevalence of poorly controlled arterial hypertension (62.5% vs. 20.5%; $P = 0.04$; n = 52).

Renal impairment Clinical variables were tested for associations with the velocity of eGFR decline. The associations are shown in TABLE 3. The multivariate model was highly significant ($r^2 = 0.3$, $P < 0.01$). A correlation between TA-P and the velocity of eGFR decline is shown in FIGURE 2A.

Baseline histopathological parameters Baseline histopathological features of the examined cohort are presented in TABLE 1. The median number of glomeruli in biopsies was 13 (11–16; n = 42).

Survival analysis Five of 42 patients (11.9%) whose biopsy data were analyzed reached the study endpoint. Four histopathological parameters—GSI, C, TA, and IF—predicted renal survival in the univariate Cox regression model (TABLE 2). The independent prognostic value of C was confirmed in the multivariate Cox regression model ($\chi^2 = 12.9$, $P = 0.01$) (TABLE 2).

Renal impairment Similarly to clinical parameters, histopathological findings were examined for the relationship with the velocity of eGFR decline (TABLE 3). GSI and I correlated with a more rapid filtration loss in the univariate regression analysis. Of these 2 factors, GSI proved to be an independent determinant of the velocity of eGFR decline in the multivariate model ($r^2 = 0.3$, $P < 0.001$). The positive correlation between GSI and the annual rate of renal function decline is shown in FIGURE 2B.

DISCUSSION In this study, we tested a set of clinicopathological parameters to detect predictors of the IgAN progression, and thus to identify patients who are likely to benefit from close monitoring and an earlier or more aggressive therapy.

Significant clinical factors revealed by the multivariate Cox regression analysis include: baseline impairment of renal function, a history of tonsillectomy, and TA-P exceeding 2 g/d, the latter representing the average level of proteinuria throughout the follow-up period.

The strength of our study lies in collecting several clinical and laboratory data at every follow-up visit. TA-P was independently related to renal outcome, while the baseline level of proteinuria had no prognostic value. Additionally, we demonstrated a positive correlation of TA-P with the rate of renal function decline. These findings confirm that achieving clinical remission by reducing

TABLE 3 Clinical and histopathological factors affecting the velocity of eGFR decline (ml/min/1.73 m² per year) by regression analysis

Clinical variables, units	Univariate models			Multivariate models (n = 41)	
	standardized β	*P*	n	standardized β	*P*
TA-P, g/d	0.35	0.02	45	0.34	0.03
TA-P >0.5 g/d, yes vs. no	0.29	0.049	45	–	
TA-P >2.0 g/d, yes vs. no	0.47	0.00	45	–	
DBP, mmHg	0.37	0.01	45	0.22	NS
upper respiratory tract disorders, yes vs. no	0.23	0.10	50	0.13	NS
hyperuricemia, yes vs. no	0.30	0.04	46	–	
hematuria of ≥5 RBC per mf, yes vs. no	0.27	0.05	50	0.32	0.03
Histopathological variables, units	**Univariate models**			**Multivariate models (n = 42)**	
	standardized β	*P*	n	standardized β	*P*
GSI, %	0.49	0.001	42	0.41	0.01
I, yes vs. no	0.39	0.01	42	0.25	NS

Abbreviations: I – interstitial inflammation, others – see **TABLES 1** and **2**

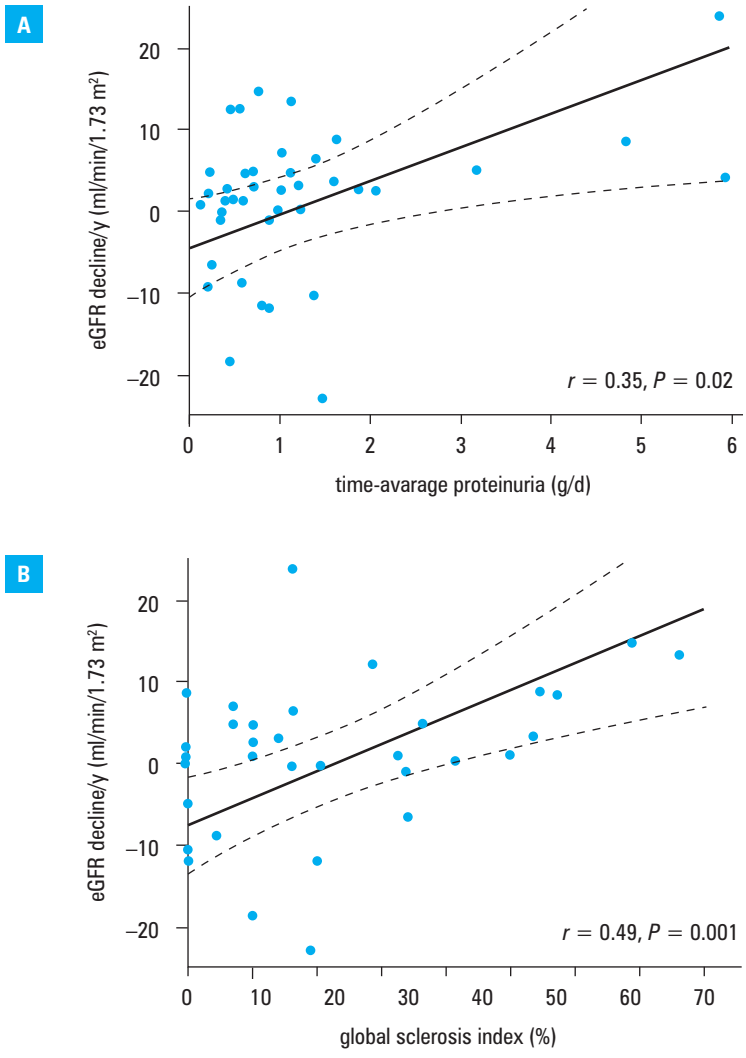

FIGURE 2 Correlations between the velocity of estimated glomerular filtration rate (eGFR) decline and time-average proteinuria (**A**) and global sclerosis index (**B**)

urinary protein excretion over time below a certain threshold value is crucial for securing a favorable renal outcome, regardless of the baseline urinary protein excretion.[8] The cut-off point of TA-P was set at 1 g/d or even 0.5 g/d in a few large long-term studies.[4,9] Our analysis was probably underpowered to detect the significance of such small values owing to the modest sample size.

Renal impairment at diagnosis is a well-documented predictor for progression of IgAN.[10,11] In the present study, baseline eGFR of less than 60 ml/min/1.73 m² was the strongest marker for progression, associated with an almost 8-fold increase in the risk of reaching the endpoint.

There is an ongoing debate over the curative value of tonsillectomy in IgAN. Some reports from Japan have suggested that tonsillectomy has beneficial effects on clinical remission (disappearance of urine abnormalities) and delayed renal deterioration, especially when combined with steroid treatment. However, these studies failed to demonstrate that tonsillectomy alone could affect the development of ESRD.[12-14] Two European research groups addressed this issue and found that tonsillectomy did not prevent progression of IgAN to advanced renal disease.[15,16] Finally, a recent meta-analysis found that tonsillectomy alone did not improve clinical outcomes compared with those obtained with general treatment.[17] Unlike in many Japanese centers, tonsillectomy is not regarded as a routine adjuvant treatment for IgAN in our center and was performed for indications voiced solely by otolaryngologists. Therefore, the surgery was not accompanied by corticosteroid treatment, which was suggested to be the crucial determinant of therapy effectiveness. The possible explanation for the association between a history of tonsillectomy and an unfavorable renal outcome in the present study is the more severe initial symptomatology of renal disease in patients with IgAN scheduled for this procedure.

In the current study, the presence of microscopic hematuria accelerated the rate of eGFR decline. Previously reported findings are inconsistent. The association of hematuria with IgAN progression was observed in 2 studies performed in patients at an early stage of renal disease.[18,19] It was hypothesized that a rising number of urinary erythrocytes might indicate a high degree of glomerular inflammation in the initial course of renal impairment.[18,19] However, our cohort included patients in a more advanced stage of chronic

kidney disease compared with the above studies. In addition, other reports did not show the prognostic value of hematuria.[10,11] Therefore, although our results suggest that microscopic hematuria negatively affects the course of IgAN, it needs to be confirmed in further research.

Even though hyperuricemia was reported as an independent marker for IgAN progression in some studies, we found a relationship between this feature and a higher velocity of eGFR decline only in the univariate model.[4,5] Our results do not support the concept that other recently suggested parameters including anemia, hypoalbuminemia, dyslipidemia, and the presence of urinary casts could be used to predict renal outcome in IgAN.

Apart from evaluating the clinical risk factors for IgAN progression, our study was also designed to test the applicability of the Oxford classification in the cohort from our institution. The Oxford classification identifies 4 histopathological features as predictors for renal outcome in IgAN, including mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S), and tubular atrophy/interstitial fibrosis ratio (T). In the original paper, the Cox regression analysis showed a significant association for M and T and the endpoint of an increase in serum creatinine levels by 50%.[6,20] In the present study, we used the same endpoint and found that, of the 2 above variables, only T (interpreted in a modified manner, as described in the Methods section) proved to have prognostic relevance. We also demonstrated that patients with I displayed an increased velocity of eGFR decline in the multivariate model. Our findings are in line with the results of other researchers that interstitial lesions are better prognostic indicators for renal outcome than glomerular lesions. It is believed that tubulointerstitial changes are the most reliable marker of chronic and irreversible renal damage in glomerulopathies.[18,21]

We reported additional, non-Oxford histopathological features that predict the risk for progression of IgAN, including the GSI and the presence of crescents. For the GSI, a positive correlation with the velocity of eGFR decline was demonstrated (r = 0.511). A similarly strong correlation (r = 0.53) was also reported in other studies.[22] GSI is simple to assess and shows excellent intraobserver reproducibility.[20] It directly reflects the loss of functioning nephrons and is associated with established chronic kidney injury. Patients with high GSI are likely to have reached the so called point of no return, beyond which the self-perpetuating renal injury inevitably leads to the development of ESRD.[23] The issue of crescents was not addressed in the Oxford study owing to the low prevalence of these lesions. In our validation population, more crescents were observed since patients with rapidly progressive glomerulonephritis who are most likely to display extracapillary proliferation were not excluded. Therefore, we could demonstrate that crescent formation was an independent negative predictor of poor renal outcome. Our results are supported by a recent meta-analysis of 16 retrospective cohort studies, which concluded that crescents (along with M, S, and T lesions) strongly correlate with progression to kidney failure. Furthermore, the authors suggested that E lesions should be excluded from the Oxford classification because they did not prove to be significant predictors of disease progression. In addition, no interaction with immunosuppressive therapy was confirmed. This was the main reason why those features were included in the score in the first place. The role of E lesions is expected to be clarified by the ongoing European Validation Study of the Oxford Classification of IgAN (VALIGA).[7]

Our study has several limitations. First, it was a retrospective, observational study in a single center. Secondly, the investigated cohort was relatively small, which affected the statistical power.

In conclusion, our study provides an insight into both clinical and histopathological markers that should be useful in risk stratification, outcome prediction, and planning of therapeutic interventions in patients with IgAN. We demonstrated that the extent of proteinuria during follow-up and impaired renal function at diagnosis remain the most significant prognostic factors for the progression of IgAN. As for the Oxford classification, only T proved to be of prognostic significance in our study. As for additional, non-Oxford histopathological features that predict the risk for progression of IgAN, GSI and the presence of crescents should be mentioned.

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Stratyfikacja ryzyka progresji nefropatii IgA – jak przewidzieć przyszłość?

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SŁOWA KLUCZOWE

białkomocz, klasyfikacja oksfordzka, kłębuszkowe zapalenie nerek, nefropatia IgA, szacunkowy współczynnik filtracji kłębuszkowej

STRESZCZENIE

WPROWADZENIE Nefropatię IgA (IgAN) cechuje wybitnie heterogenny przebieg kliniczny, co skutkuje kontrowersjami dotyczącymi oceny indywidualnego rokowania i określenia optymalnego podejścia do terapii.
CELE Celem badania było zdefiniowanie czynników ryzyka progresji IgAN. Analizowano cechy histopatologiczne zaczerpnięte z oksfordzkiej klasyfikacji IgAN i dodatkowe, nie-oksfordzkie parametry biopsyjne, a także dane kliniczne w momencie rozpoznania i z całego okresu obserwacji.
PACJENCI I METODY Przeprowadzono jednoośrodkowe retrospektywne badanie, w którym wzięło udział 52 kolejnych pacjentów z potwierdzoną biopsyjnie IgAN. Punkt końcowy stanowił 50% wzrost poziomu kreatyniny w surowicy krwi w stosunku do wartości wyjściowej.
WYNIKI Ośmiu (12%) pacjentów osiągnęło punkt końcowy. Znaczne pogorszenie funkcji nerek było związane ze średnią proteinurią w okresie obserwacji (*time-average proteinuria* – TA-P) >2,0 g/dobę ($p = 0,047$), szacunkowym współczynnikiem filtracji kłębuszkowej (*estimated glomerular filtration rate* – eGFR) <60 ml/min/1,73 m^2 ($p = 0,01$), tonsillektomią w wywiadzie ($p = 0,01$) i półksiężycami w materiale biopsyjnym ($p = 0,03$). Indeks całkowicie zeszkliwiałych kłębuszków (*high global sclerosis index* – GSI) ($p = 0,009$), TA-P ($p = 0,03$) i obecność krwinkomoczu ($p = 0,03$) prognozowały szybszą utratę funkcji nerek, co oceniono za pomocą analizy krzywej spadku eGFR. Spośród parametrów klasyfikacji oksfordzkiej, jedynie włóknienie śródmiąższowe i zanik cewek wykazały istotną wartość predykcyjną, co zaprezentowano w modelu proporcjonalnego hazardu Coxa przy uwzględnieniu jednej, ale nie wielu zmiennych.
WNIOSKI Zakres białkomoczu podczas okresu obserwacji oraz upośledzona funkcja nerek w momencie postawienia diagnozy pozostają czynnikami o największym znaczeniu prognostycznym w IgAN. Wykazaliśmy także dodatkowe, nie-oksfordzkie cechy histopatologiczne, które mogą być użyteczne w stratyfikacji ryzyka progresji w IgAN, takie jak GSI i obecność półksiężyców.

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