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Review Article

The fractal and textural analysis of glomeruli in obese and non-obese patients

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ABSTRACT

Background
Fractal dimension is an indirect indicator of signal complexity. The aim was to evaluate the fractal and textural analysis parameters of glomeruli in obese and non-obese patients with glomerular diseases and association of these parameters with clinical features.
Methods
The study included 125 patients mean age 46 ± 15.2 years: obese (BMI ≥ 27 kg/m^2—63 patients) and non-obese (BMI < 27 kg/m^2—62 patients). Serum concentration of creatinine, protein, albumin, cholesterol, trygliceride, and daily proteinuria were measured. Formula Chronic Kidney Disease Epidemiology Colaboration (CKD-EPI) equation was calculated. Fractal (fractal dimension, lacunarity) and textural (angular second moment (ASM), textural correlation (COR), inverse difference moment (IDM), textural contrast (CON), variance) analysis parameters were compared between two groups.
Results
Obese patients had higher mean value of variance (t = 1.867), ASM (t = 1.532) and CON (t = 0.394) but without significant difference ($P > 0.05$) compared to non-obese. Mean value of COR (t = 0.108) and IDM (t = 0.185) were almost the same in two patient groups. Obese patients had higher value of lacunarity (t = 0.499) in comparison with non-obese, the mean value of fractal dimension (t = 0.225) was almost the same in two groups. Significantly positive association between variance and creatinine concentration (r = 0.499, $P < 0.01$), significantly negative association between variance and CKD-EPI (r = -0.448, $P < 0.01$), variance and sex (r = -0.339, $P < 0.05$) were found.
Conclusions
Variance showed significant correlation with serum creatinine concentration, CKD-EPI and sex. CON and IDM were significantly related to sex. Fractal and textural analysis parameters of glomeruli could become a supplement to histopathologic analysis of kidney tissue.

Contents

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Introduction

Obesity is a complex disease involving an excessive amount of body fat. Diabetes mellitus, hypertension, and obesity are the leading causes of chronic renal failure.[1] Obesity increases the progression of pre-existing renal disease. Obesity could lead to obesity related glomerulopathy (ORG).[2] Clinical features of ORG are: proteinuria and degresed estimated glomerular filtration rate (eGFR), histopathologic findings are: glomerulomegalia and progressive glomerulosclerosis.[1,2]

During the last 20 years, there have been many attempts to design image analysis method that could find applicationin medical sciences such as histology and pathology.[3,4] Two mathematical computer-assisted algorithms: fractal and textural methods are found. The fractal analysis parameters are: fractal dimension and lacunarity. Using the method of fractal tissue analysis of changes in the structure of tissues and cells, an attempt was made to assign a 'number'.[3] Textural analysis parameters are mainly parameters of the so-called second-order statistics, where instead of individual values in the analysis of raw data, pairs of values that make up the corresponding mathematical matrix are taken into account.[4]

The aim of this study was to evaluate the fractal and textural analysis parameters of glomeruli in the obese and the non-obese patients with glomerular diseases: minimal change (MCD), focal segmental glomerulosclerosis (FSGS), IgA nephropathy, membranous glomerulonephritis (MGN), membranoproliferative glomerulonephritis (MPGN) and association of these parameters with clinical features.

Methods

Patients

The study included 125 patients mean age 46.92 ± 15.10 years with renal biopsy-proven glomerular diseases: MCD, FSGS, IgA nefropathy, MGN, and MPGN. Indications for the kidney biopsy were: isolated proteinuria, isolated erythrocyturia, and nephrotic syndrome.

Obesity was defined as body mass index (BMI) ≥ 27 kg/m^2.[5] Patients were divided into two groups: obese with BMI ≥ 27kg/m^2 (63 patients) and non-obese BMI < 27kg/m^2 (62 patients). Excluded criteria were: autoimmune and inflamatory diseases, individuals younger than 18 years and older than 85 years. Proteinuria is defined as subnephrotic (<3.5 g/day) and nephrotic (≥3.5 g/day)[6]; proteinuria ≥1 g/day was considered as significant.

The study protocol was in conformity with ethical guidelines, approved by School of Medicine, University of Belgrade Ethical comity (number 29/III-9). All patients included in this study signed an informed consent form.

Laboratory methods

The serum concentration of hemoglobin was determined on hematological analyzer The Beckman Coulter HmX. The serum concentration of protein, albumin, cholesterol, and creatinine were determined on biochemical analyzer DCX- 800 Beckman Coulter. The serum concentration of cholesterol and triglyceride were determined on biochemical analyzer ADVIA 1800 (Siemens Healthcare, Clinical Chemistry Analyzer). The serum creatinine was measured according to the Jaffe method. The proteinuria was determined by spectrophotometry with pirogal red (biochemical analyzer DCX- 800 Beckman Coulter). More than 3 red blood cells noticed per high power microscopic field in sterile urine sediments were defined as clinically significant erythrocyturia. The eGFR was determined from serum creatinine concentration according to predictive formula:

CKD-EPI (Chronic Kidney Disease Epidemiology Colaboration equation) [7] (A.1)

$$eGFR = 141 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.993^{age} \times 1.018\ [female] \times 1.159\ [black]$$

Histopathologic analysis

A percutaneous biopsy of the inferior pole of left kidney was done under ultrasound control. The samples were relatively equal in the number of glomeruli and approximately the same size. The tissue samples were stained using Periodic Acid- Schiff method (PAS).

a. Fractal analysis was performed using FracLac (Karperien, 2007) plug in designed for Image J National Institute of Health (NIH, Bethesda, Maryland, USA). Fractal anaysis parameters: fractal dimension and lacunarity were done using differential box count method. Fractal dimension was calculated for each micrograph after creation of a logarithmic graph based on the box count over the object N and scale ε.[8]

1. *Fractal dimension (D)* was calculated according to formula:

$$\boldsymbol{D} = -\lim \frac{\log N\ (\varepsilon)}{log\varepsilon} \tag{A.2}$$

2. *Lacunarity (Λ)* was determined:

$$\boldsymbol{\Lambda} = CV_{\varepsilon,g^2}$$

$$\boldsymbol{\Lambda} = \left(\frac{\delta\ \varepsilon, g}{\mu\ \varepsilon, g}\right)^2 \tag{A.3}$$

where CV is variation coefficient for the micrograph pixel values, μ is the mean for pixels per box at the size ε, σ is the standard deviation in a box count of the orientation g. In this study, fractal dimension was calculated based on the slope of the logarithmic line in the above-mentioned graph.[3]

b. Textural analysis method *Grey Level Cooacurrence Matrix (GLCM)* was used in addition to fractal analysis. This method is based on determining the distribution and mutual relationship of resolution units in the image, and uses the so-called second order statistics by estimating the relationship of resolution units (pixels) in which the units are separated by a defined distance (d = 1). Each resolution unit of a two-dimensional object is assigned a so called 'gray value' and after converting the image to 8-bit format. In this study, for each glomeruli, 5 different parameters were calculated according to the following formulas: [9]

1. *Angular second moment (ASM)*, as a parameter of textural uniformity, was determined:

$$\boldsymbol{ASM} = \sum_{1}\sum_{j}\{p\ (i,j)\}^2 \tag{A.4}$$

i and j are coordinates of the *GLCM*.

2. *Textural correlation* (*COR*)—as a parameter of correlation: Eq. (A.5)

$$\boldsymbol{COR} = \frac{\Sigma_i \Sigma_j (ij)\, p(i,j) - \mu_\chi \mu_\chi}{\delta_\chi \delta_\chi}$$

The correlation can have a value from −1 to +1. When the textural organization of the resolution units is not correlated, it is denoted by 0, while the values of +1 and −1 indicate a perfect positive or negativne correlation.

3. *Inverse difference moment (IDM)*—parameter of texture homogeneity Eq (A.6):

$$\boldsymbol{IDM} = \sum_{i}\sum_{j} \frac{1}{1 + (i - j)^2} \mathrm{p}\ (\mathrm{i}, \mathrm{j})$$

4. *Textural contrast (CON)*—basically estimates the difference in gray values between two adjacent resolution units. It is inversely proportional to inverse difference moment Eq. (A.7):

$$\boldsymbol{CON} = \sum_{i}\sum_{j} (i - j)^{\boldsymbol{k}} \boldsymbol{P}_d [i,j]^{\boldsymbol{n}}$$

5. *Variance*—depends on the coefficient of variation of gray values of resolution units and is calculated:

$$\boldsymbol{Variance} = \sum_{i}\sum_{j} (i - \mu)^2 p(i,j) \quad \text{(A.8)}$$

The Texture Analyzer subroutine (Cabrera, 2007) of the Image J software was used for analysis. After the kidney tissue samples stained using PAS method, digital tissue micrographs were made, using a ProMicroScan DEM 200 camera (Oplenic Optronic, Hangzhou, CN), mounted on an American Optical Spencer 1036A microscope (Buffalo, NY, USA), magnification 400x. In micrographs, regions of interest for GLCM and fractal analysis were formed with the boundaries along the Bowman's capsule (Fig. 1). For the examined kidney tissue, with the help of special Image J software of the National Institutes of Health (USA), and the above-mentioned integrated subprograms, the mean value of fractal and textural parameters of glomeruli were determined.[4,9]

Statistical analysis

Data are presented as mean values and standard deviation (SD) as well as minimal and maximal values. The Kolmogorov–Smirnov test was used to check the normal distribution of the variables. Data were analyzed using Student's *t* test and Pearson's $\chi 2$ test. Relationships between variables were estimated using Pearson' s parametric correlation method. Statistical analysis is performed using SPSS software 17.0. Statistical significance is defined as the conventional *P*-value with the effects being considered significant at $P < 0.05$.

Results

The study included 125 patients with renal biopsy proven glomerular diseases: 14 MCD (10 obese/4 non-obese), 32 FSGS (15 obese/17 non-obese), 23 IgA nephropathy (9 obese/14 non-obese), 39 MGN (22 obese/17 non-obese), and 17 MPGN (7 obese/10 non-obese) patients mean age 46.93 ± 15.10 years. The patients were divided into two groups: obese (BMI ≥ 27 kg/m^2—63 patients) and non-obese (BMI < 27 kg/m^2—62 patients). There was no significant difference between two patient groups in the number of patients by diagnosis ($\chi^2 = 6.193$, $P > 0.05$).

Table 1 presents that there was no significant difference in indications for the kidney biopsy between obese and non-obese patients ($\chi^2 = 2.531$, $P > 0.05$). Nephrotic syndrome was the major indication for the kidney biopsy (68.3 % obese and 54.8% non-obese patients), while erythrocyturia was the rare one (3.2% obese and 4.8% non-obese patients).

In the obese group were 40 male and 23 female, while in the non-obese group were 37 male and 25 female patients. There was no signifficant difference between the two groups in sex distribution ($\chi^2 = 0.192$, $P > 0.05$). Mean age in obese and non-obese group was not signifficantly different ($t = 2.109$, $P > 0.05$). The youngest patient was 18 years old, the oldest one was 85 years old [Table 2]. In the obese group, 45 patients had arterial hypertension, while in the non-obese group, 31 patients had arterial

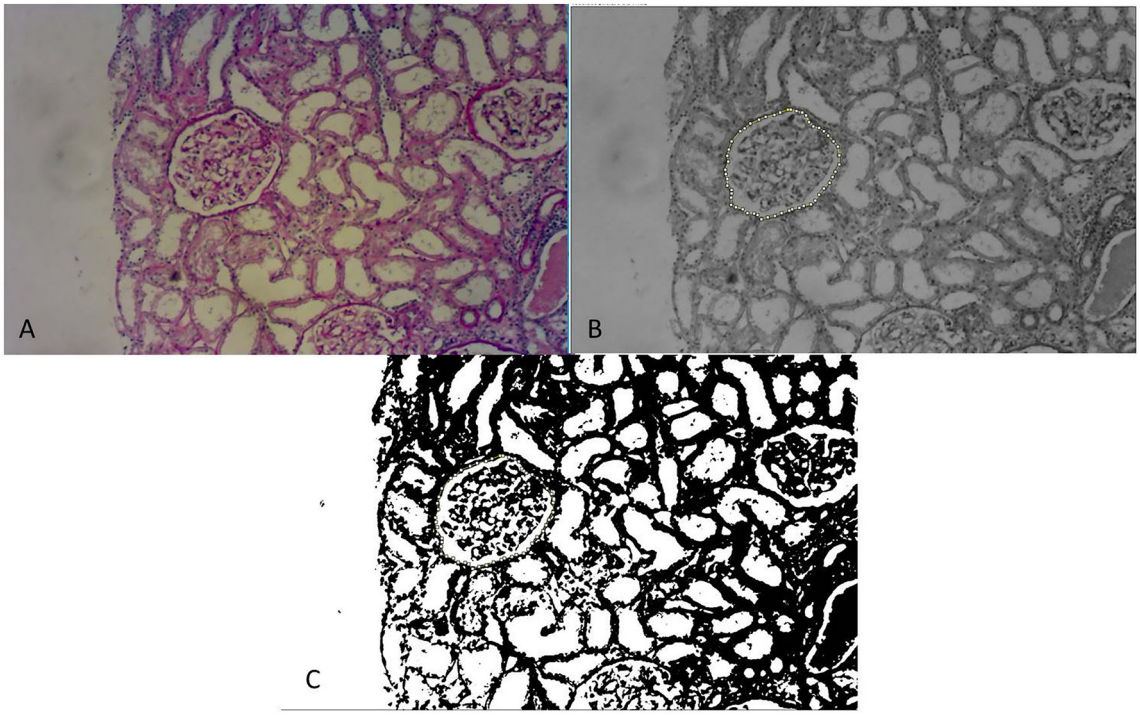

Fig. 1. Regions of interest for fractal and GLCM analysis were made in ImageJ software (NIH, Bethesda, MD) using the so-called polygonal selection (A). For GLCM analysis, the micrographs were converted to 8-bit grayscale format (B). For fractal analysis, the micrographs were automatically binarized in FracLac software.

Table 1
Indications for the kidney biopsy in two patient groups.

Groups	Erythrocyturia		Proteinuria		Erythrocyturia and proteinuria		Nephrotic syndrome	
	N	%	N	%	N	%	N	%
Obese	2	3.2%	9	14.3%	9	14.3%	43	68.3 %
Non-obese	3	4.8%	11	17.7%	14	22.6%	34	54.8%
Total	5	4.0%	20	16.0 %	23	18.4%	77	61.6%

$P = 0.470$.

hypertension ($\chi^2 = 6.020$, $P < 0.05$). The vast majority of obese patients (50) had diabetes mellitus type 2, while only 16 non-obese patients had diabetes mellitus type 2 ($\chi^2 = 35.967$, $P < 0.01$).

At the time of kidney biopsy, the obese had significantly higher serum creatinine concentration (z = 1.988, $P < 0.05$), daily proteinuria (z = 2.469, $P < 0.05$) and serum triglyceride concentration (z = 2.131, $P < 0.05$) in comparison with the non-obese. There was significant difference in eGFR calculated by CKD-EPI formula (z = 2.661, $P < 0.01$) between two groups. In other measured parameters: serum hemoglobin ($t = 1.012$), protein ($t = 0.935$), albumin ($t = 0.928$), and cholesterol ($t = 0.456$), there were no significant difference between two groups ($P > 0.05$) [Table 2].

A non-parametric check, necessary due to the huge SD, confirmed the result of the *t*-test.

Obese patients had higher mean value of variance ($t = 1.867$), ASM ($t = 1.532$) and CON ($t = 0.394$) but without significant difference ($P > 0.05$) compared to non-obese. Mean value of COR ($t = 0.108$) and IDM ($t = 0.185$) were almost the same in the two patient groups. Fractal analysis of glomeruli showed that obese patients had higher value of lacunarity ($t = 0.499$) in comparison with non-obese, the mean value of fractal dimension ($t = 0.225$) was almost the same in two groups. There was no significant difference in mean value textural and fractal analysis parameters of glomeruli between the two patient groups ($P > 0.05$) [Table 3].

Table 4 presents association between textural analysis parameters: ASM, CON, COR, and IDM with measured parameters at the time of the kidney biopsy. Significantly negative association between sex and CON ($r = -0.310$, $P < 0.05$) and significantly positive association between sex and IDM ($r = 0.277$, $P < 0.05$) were found. In other measured textural analysis parameters of glomeruli there were no significant difference ($P > 0.05$) [Table 4].

Table 5 shows significantly positive association between variance and serum creatinine concentration ($r = 0.499$, $P < 0.01$), significantly negative association between variance and eGFR ($r = -0.448$, $P < 0.01$) and significantly negative association between variance and sex ($r = -0.339$,

Table 2
Demographic characteristics, clinical and laboratory data in two patient groups.

Variable	Group	Mean ± SD	Minimal value	Maximal value	*P*
Age (years)	Obese	50.1 ± 15.1	21	80	0.575
	Non-obese	44.1 ± 14.5	18	72	
BMI (kg/m^2)	Obese	30.17 ± 3.40	26.60	36.40	0.000**
	Non-obese	22.90 ± 2.16	20.70	26.40	
Hemoglobin (g/ l)	Obese	131.14 ± 19.59	92.00	182.00	0.313
	Non-obese	134.72 ± 19.97	96.00	184.00	
Serum protein (g/l)	Obese	52.66 ± 12.66	30.00	79.00	0.352
	Non-obese	54.79 ± 12.74	33.00	82.00	
Serum albumin (g/l)	Obese	31.53 ± 9.52	15.00	46.00	0.355
	Non-obese	33.12 ± 9.63	15.00	50.00	
Cholesterol (mmol/l)	Obese	7.02 ± 2.36	3.36	12.70	0.649
	Non-obese	6.85 ± 2.25	3.08	12.36	
Triglyceride (mmol/l)	Obese	2.76 ± 1.39	1.10	8.87	0.049*
	Non-obese	2.20 ± 1.30	0.45	6.50	
Serum creatinine (μmol/l)	Obese	122.14 ± 87.56	32.00	540.00	0.022*
	Non-obese	93.66 ± 41.40	40.00	232.00	
CKD-EPI† (ml/min/1.73 m^2)	Obese	71.52 ± 31.15	8.80	132.50	0.006**
	Non-obese	86.36 ± 27.63	23.90	135.00	
Proteinuria (g/day)	Obese	6.11 ± 4.94	0.61	27.60	0.048*
	Non-obese	4.47 ± 4.95	0.15	33.00	

*$P < 0.05$, ** $P < 0.01$.
Abbreviations: $^{\text{Ŧ}}$BMI-body mass index, †CKD-EPI-Chronic Kidney Disease Epidemiology Colaboration equation.

Table 3
Textural and fractal analysis parameters in two patient groups.

Variable	Group	Mean ± SD	Minimal value	Maximal value	*P*
Angular second moment	Obese	0.069 ± 0.098	0.02	0.40	0.133
	Non-obese	0.038 ± 0.027	0.02	0.15	
Textural correlation	Obese	0.960 ± 0.033	0.82	0.98	0.914
	Non-obese	0.960 ± 0.015	0.900	0.980	
Inverse difference moment	Obese	0.725 ± 0.078	0.64	0.94	0.854
	Non-obese	0.722 ± 0.057	0.640	0.870	
Textural contrast	Obese	1.07 ± 0.43	0.11	1.87	0.695
	Non-obese	1.029 ± 0.377	0.27	1.69	
Variance	Obese	68.86 ± 25.19	19.96	107.19	0.069
	Non-obese	56.98 ± 17.40	19.99	83.66	
Fractal dimension	Obese	1.49 ± 0.127	1.24	1.70	0.823
	Non-obese	1.50 ± 0.11	1.21	1.72	
Lacunarity	Obese	0.558 ± 0.134	0.30	0.75	0.620
	Non-obese	0.540 ± 0.118	0.310	0.760	

Table 4
Correlation between textural analysis parameters and measured parameters at the time of kidney biopsy.

	ASM‡		CON§		COR¶		IDM*	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Age	0.169	0.261	0.023	0.879	-0.183	0.223	0.011	0.940
BMI₸	0.063	0.685	0.078	0.615	0.083	0.593	-0.011	0.946
Sex	0.151	0.315	-0.310	0.036*	0.022	0.883	0.277	0.050*
Serum creatinine	-0.168	0.264	0.219	0.143	0.194	0.195	-0.203	0.176
CKD-EPI†	0.118	0.447	-0.234	0.126	-0.124	0.422	0.229	0.135
Proteinuria (g/day)	0.072	0.636	0.003	0.987	-0.012	0.935	0.082	0.587

∗$P < 0.05$.
Abbreviations: †CKD-EPI-Chronic Kidney Disease Epidemiology Colaboration equation, ‡ASM-angular second moment, §CON-textural contrast, ¶COR-textural correlation,*IDM-inverse difference moment, ₸BMI-body mass index.

Table 5
Correlation between variance, fractal analysis parameters and measured parameters at the time of kidney biopsy.

	Variance		Fractal dimension		Lacunarity	
	r	*P*	*r*	*P*	*r*	*P*
Age	0.076	0.622	0.067	0.657	0.133	0.380
BMI₸	0.231	0.137	-0.098	0.527	0.023	0.882
Sex	-0.339	0.023*	-0.205	0.172	0.223	0.136
Serum creatinine	0.499	0.000**	0.093	0.538	-0.195	0.194
CKD-EPI†	-0.448	0.003**	-0.056	0.716	0.075	0.630
Proteinuria 24 h (g/day)	0.220	0.146	0.172	0.253	0.147	0.329

∗$P < 0.05$, ** $P < 0.01$
Abbreviations: ₸BMI-body mass index, †CKD-EPI-Chronic Kidney Disease Epidemiology Colaboration equation.

$P < 0.05$). There was no significant correlation between fractal analysis parameters and measured parameters at the time of kidney biopsy ($P > 0.05$) [Table 5].

Discussion

Fractal analysis, as a software mathematical algorithm, is one of the first methods that managed to assign a "number" to changes in tissue and cell structure. In the last 20 years, many researchers have tried to apply fractal analysis in biomedical sciences such as histology, pathology, and physiology with variable success. The application of this software model has found importance in medicine in: connective tissue infiltration, inflammation, carcinogenesis, and trauma which is confirmed in findings of Azemina et al.,[10] Di Ieva et al.,[11] Gaudio et al.,[12] and Hotta et al.[13] Most papers studying fractal analysis have been published in the field of neuroscience.[14]

Textural analysis is a mathematical method for estimating the structure of two-dimensional objects such as images and micrographs (Castellanos et al.,[15] Galavis et al.,[16] Harrison et al.[17], Mayerhoefer et al.[18], and Linder et al.[19]).

GLCM algorithm estimates these 5 parameters: ASM, COR, IDM, CON, and variance. These are mainly the parameters of the so-called second-order statistics, where instead of individual values in the analysis of raw data, pairs of values that make up the corresponding mathematical matrix are taken into account. The potential application of this model in the biological sciences has not yet been sufficiently explored. Although it has been shown that the change in cellular angular moment exists during some physiological processes (apoptosis, aging), not every cell will experience one of the physiological processes by changing this parameter.[3]

In the present study, fractal and textural glomerular analysis in all patients showed that the obese patients had higher mean values of variance, ASM, CON, and lacunarity in comparison with the non-obese. Also, mean values of COR, IDM, and fractal dimension were almost the same in both patient groups.

Swiss researchers Losa and Castelli [14,20] showed on breast cancer tumor cells that fractal characteristics of chromatin change after exposure to a proapoptotic chemical. This suggests that this method can be used to detect the early stage of programmed cell death. Lacunarity is a fractal analysis parameter that determines the heterogeneity of fractal structure.[21] The number and size of empty fields (regions without structure), after image binarization, directly affect the value of this parameter.[21–23] Pantic et al.[24] studied lacunarity and showed that this parameter possesses a relatively high degree of sensitivity in the detection of early changes in the cell nucleus during programmed cell death. Lacunarity detected apoptosis earlier compared to fluorometric methods. The results of this study indicate that lacunarity is an important parameter in cell physiology and molecular biology. This parameter can be used to identify discrete changes that are not visible by standard microscopy. This method may be helpful in reaching a valid conclusion in scoring of biopsy samples. Lacunarity, fractal dimension, and textural analysis parameters may be used together to create a unique so-called scoring system in histopathologic evaluation of altered tissues and cells.[3] Also, fractal and textural analysis could be use in some morphological sciences.[25]

On the other hand, there are some disadvantages of fractal analysis such as the fact that the focus is on a two-dimensional object, i.e., tissue micrograph. The quality of a micrograph depend on a large number of factors: light exposure, use of an appropriate lens (magnification), type of microscope, type of camera, filter, and characteristics of the condenser on the microscope. It has been demonstrated that imaging of a tissue at different light intensities (dark room versus lighted room) results in different values for fractal dimension.[24,26] A group of authors recommend another solution that the image is always made in the same place in the tissue, e.g., photographing the same cells before and after the exposition of a harmful factor.[24,26,27]Another limitation of fractal analysis is in the tissue itself being analyzed. Normal tissues in physiological conditions have parts that are more homogeneous (filled with cells) and more heterogeneous (filled with connective tissue). If the image is made in an area that has more detail (cells), it is expected that the fractal dimension will have a higher value. On the other hand, by imaging areas with few cellular or other elements, the fractal dimension is expected to have a lower value. In order to overcome this problem in pathology and histology, it is recommended to make a sample from a large number of images and calculate the mean and standard deviation for fractal parameters before reaching a definitive conclusion about the complexity of cytoarchitecture. The third limitation of fractal analysis is the fact that images are binary for its performance and during the binary process most of the information may be lost.

A potential addition to conventional GLCM analysis is the discrete wavelet transform, usually based on Harr wavelets. This method allows one to further assess heterogeneity of a texture and can be used to quantify various additional features such as wavelet coefficient energies. Indicators obtained through wavelet analysis could provide additional insight in the reasons behind the changes in GLCM angular second moment, inverse difference moment, and textural contrast. Also, it is possible this technique could in the future be used to supplement fractal method in terms of explaining changes in fractal dimension and lacunarity.[28,29] Other methods such as Fourier Transform Infrared (FTIR) micro-spectroscopy can be applied for tissue analysis, but it also has limitations caused due to different tissue preparation methods (Zhodi et al.[30]).

Fractal and textural analysis parameters could be apply in the study of age-related changes in the renal parenchyma in an animal model of mice.[8] The study is in agreement with the view that tissue complexity in biological structures decreases with aging. In the present study, approximately, the same fractal dimension values were obtained in the obese and the non-obese patients. No statistically significant difference in age between the two patient groups was found. So patients age did not signifficantly differ and the age did not affect the results of fractal dimension. Standard digital micrographs, in all analyzed organs, blood vessels,

and connective tissue generally have a lower fractal dimension value compared to regions where functional cells are more present.[8,31]

This is the first study to examine the fractal and textural analysis parameters of glomeruli between obese and non-obese patients and require further investigations. In the present study, significantly positive association between variance and serum creatinine concentration, significantly negative association between variance and eGFR calculated by formula CKD-EPI and significantly negative association between variance and sex were found. These obtained associations can not be interpreted and compared because there are no available data in the literature on the fractal and textural analysis of glomeruli in patients with diferent value of BMI. Nigro et al.[32] found that fractal dimension of tubules and the density of tubules have significant positive correlation with eGFR calculated by CKD-EPI formula. When they separate patients into groups: hypertensive, diabetic nephropathy, FSGS, and IgA nephropathy, they showed that fractal dimension had the best correlation in hypertensive patients. In this sudy, fractal and textural parameters were not compare separatly in each bioptied group. The present investigation was focused only on diferences between two groups obese and non-obese patients.

During the last few years, there has been a growing interest in using fractal and textural analysis indicators in artificial intelligence. Both GLCM and fractal methods provide quantifications that can be used for training of different machine learning models for prediction and classification of biological phenomena. The examples of such models could include support vector machines, random forest, and decision trees, principal component analysis, as well as the models based on binomial logistic regression. Particularly interesting is the potential application for training and testing artificial neural networks. These range from simple perceptrons to more complex recurrent and convolutional neural networks. All these models could in the future increase the potential diagnostic sensitivity and accuracy of computational methods such as GLCM in pathology and related fields.[33,34]

Conclusions

Textural analysis parameter variance showed significant correlation with sex and some clinical parameters (serum creatinine concentration, eGFR calculated by formula CKD-EPI). Also, CON and IDM were significantly related to sex. The results of this study indicate that these two glomerular analyses could become a supplement to histopathologic analysis of kidney tissue and other diagnostic procedures in everyday clinical practice.

Conflicts of interest

The authors declare no conflict of interests.

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Declaration of interests

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Appendix A. Appendices

CKD-EPI (Chronic Kidney Disease Epidemiology Colaboration equation) [7] (A.1)

$$eGFR = 141 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.993^{age} \times 1.018\ [female] \times 1.159\ [black]$$

$$\boldsymbol{D} = -\lim \frac{\log N(\varepsilon)}{log\ \varepsilon} \tag{A.2}$$

$$\boldsymbol{\Lambda} = CV_{\varepsilon,g^2}$$

$$\boldsymbol{\Lambda} = \left(\frac{\delta\,\varepsilon, g}{\mu\,\varepsilon, g}\right)^2 \tag{A.3}$$

$$\boldsymbol{ASM} = \sum_{I}\sum_{j}\{p(i,j)\}^2 \tag{A.4}$$

$$\boldsymbol{COR} = \frac{\Sigma_i\Sigma_j(ij)\,p(i,j) - \mu_\chi\,\mu_\chi}{\delta_\chi\delta_\chi} \tag{A.5}$$

$$\boldsymbol{IDM} = \sum_{i}\sum_{j}\frac{1}{1+(i-j)^2}\mathrm{p}(i,j) \tag{A.6}$$

$$\boldsymbol{CON} = \sum_{\mathbf{i}}\sum_{\mathbf{j}}(i-j)^{\boldsymbol{k}}\boldsymbol{P}_d[i,j]^{\boldsymbol{n}} \quad \text{(A.7)}$$

$$\boldsymbol{Variance} = \sum_{\mathbf{i}}\sum_{\mathbf{j}}(i-\mu)^{\mathbf{2}}p(i,j) \quad \text{(A.8)}$$

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