PREDICTORS OF DISEASE PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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BACKGROUND

• Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic disorder of the kidney, leading to renal failure in most patients. ADPKD has an incidence of 1/1000 and accounts for about 5% of patients with end-stage renal disease requiring replacement therapy. In 86 to 96% of cases, ADPKD is caused by mutations in the *PKD1* gene on chromosome 16, which codes for the protein polycystin 1; most other cases are caused by mutations in the *PKD2* gene on chromosome 4, which codes for polycystin 2. A few familial cases are unrelated to either locus.

• It is difficult to assess the rate of progression and it is very important to identify reliable prognostic factors. By age 75, 50 to 75% of patients with ADPKD require renal replacement therapy (dialysis or transplantation). Predictors of more rapid progression to renal failure include *PKD1* genotype, larger or rapidly increasing kidney size, earlier age at diagnosis, diabetes, high-protein diet, male sex, sickle cell trait, gross hematuria, hypertension, black race, increasing proteinuria, multiple pregnancies.

• The identification of individuals who are at high risk for progression of CKD may be important for prognostic reasons or to target patients who will benefit from specific therapies as they become available. Over the past decade, promising therapies, including vasopressin receptor antagonists, increased fluid intake, maximal inhibition of the renin-angiotensin-aldosterone system, use of mammalian target of rapamycin (mTOR) inhibitors, and rigorous blood pressure control, have been evaluated in ADPKD.

• Total kidney volume measured by magnetic resonance (MR) is a good predictor factor but it is an expensive imagistic technique. Ultrasound does not appear to be sufficiently accurate or reproducible to measure change in kidney volume over a short period of time.
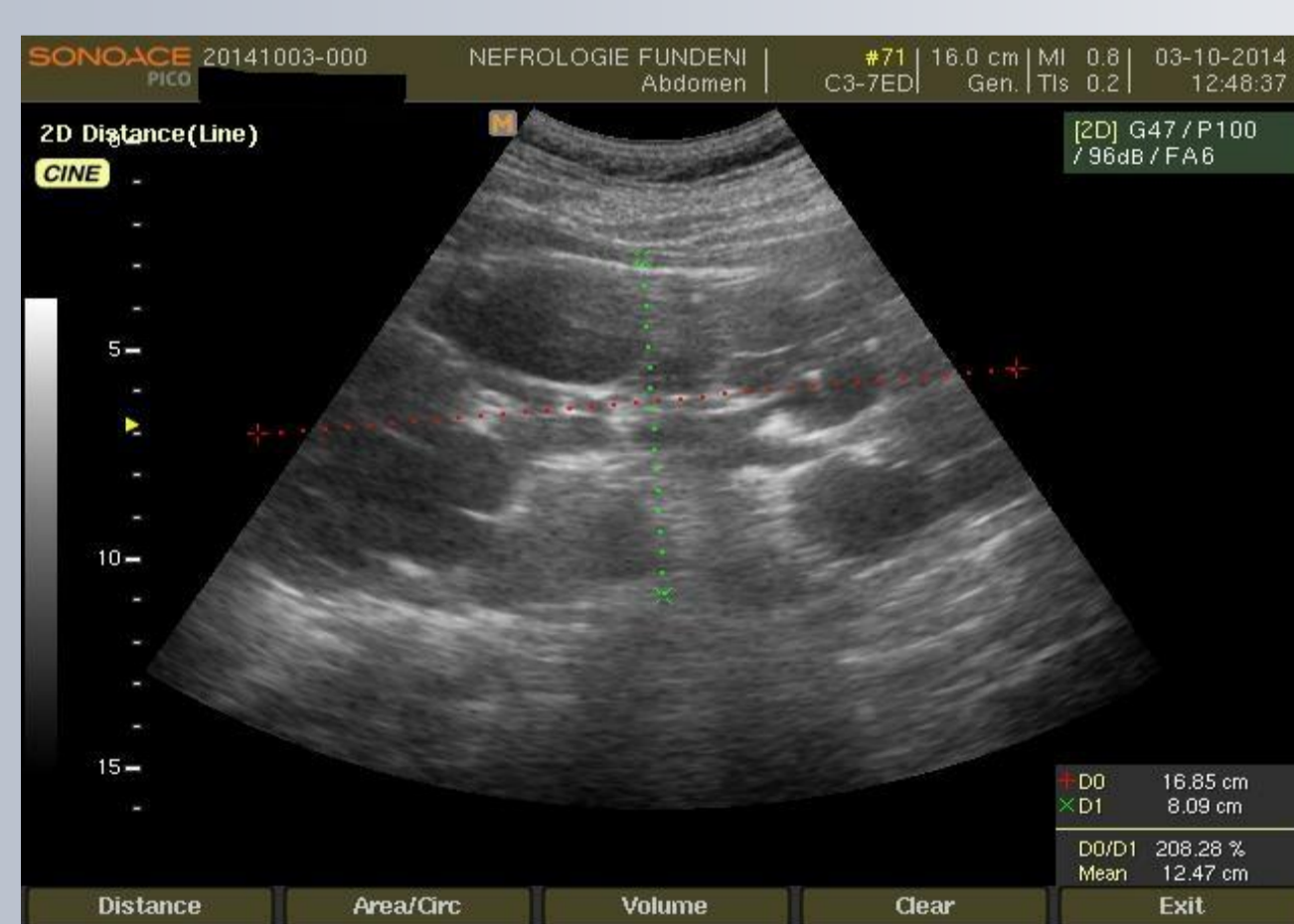
Measurement of the longitudinal axis of a left polycystic kidney by US

PURPOSE

The aim of our study was to identify predictors for renal function in ADPKD which are easy to use in every day practice . These predictors might be useful to better identify patients who are at higher risk for disease progression and thus they mey benefit from more aggressive therapies, including new investigational drugs.

MATERIALS AND METHODS

Type of study
We performed a cross-sectional observational study between 2013-2014.

Inclusion criteria
• Patients with ADPKD diagnosed by imagistic technique prior to inclusion in the present study.
• Age >18 years.
• Informed consent obtained prior to inclusion.

Exclusion criteria
• Other types of herediary or non-hereditary polycystic kidney disease.
• Severe psychiatric diseases.
• Pregnancy or 6 months after a pregnancy.

Prognostic factors analyzed
• Clinical parameters: gender, type of inheritance (mother/father/unlnown), hypertension, age at diagnosis, prior gross hematuria episodes
• Laboratory parameters: serum levels of uric acid, proteinuria.
• Imagistic: nephrolithiasis and kidney size at abdominal ultrasound.

CKD stadialization
The patients were categorized into stages 1 to 5 according to chronic kidney disease (CKD) staging in the NKF-K/DIGO guidelines:

GFR category	GFR (ml/min/1.73 m2)	Terms
G1	≥90	Normal or high
G2	60-89	Mildly decreased
G3	30-59	Mildly to severely decreased
G4	15-29	Severely decreased
G5	<15 or dialysis	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

Statistical analysis
• We used *SPSS v20 (IBM Corporation, USA)*
• For comparative analysis was used ANOVA test or *t* Student, and for correlation analysis was used Pearson coefficients (for variables with normal distribution) and Spearman coefficients (for variables with non-normal distribution).
• Independent prognostic factors for kidney function were identified using multivariate analysis.
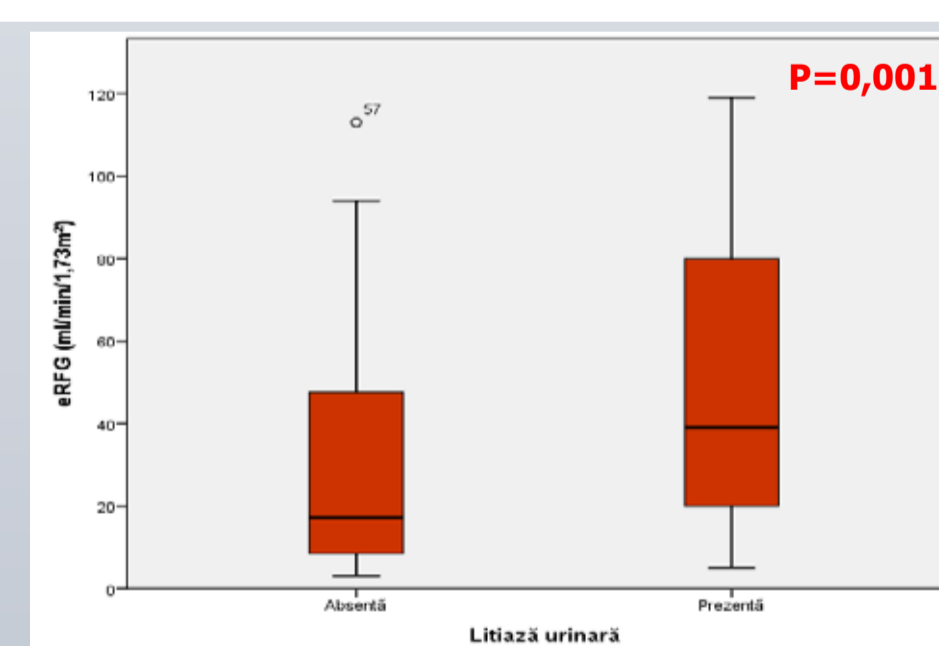
RESULTS

Demographic characteristics
100 patients were included (68 F, 32 M), mean age 52.8±13.0 (22 – 84 years)**.**

Type of inheritance
• The family genetic history was positive for 67 patients: 41 inherited the disease from mother and 26 from father
• No difference was found between the inheritance type and renal function.
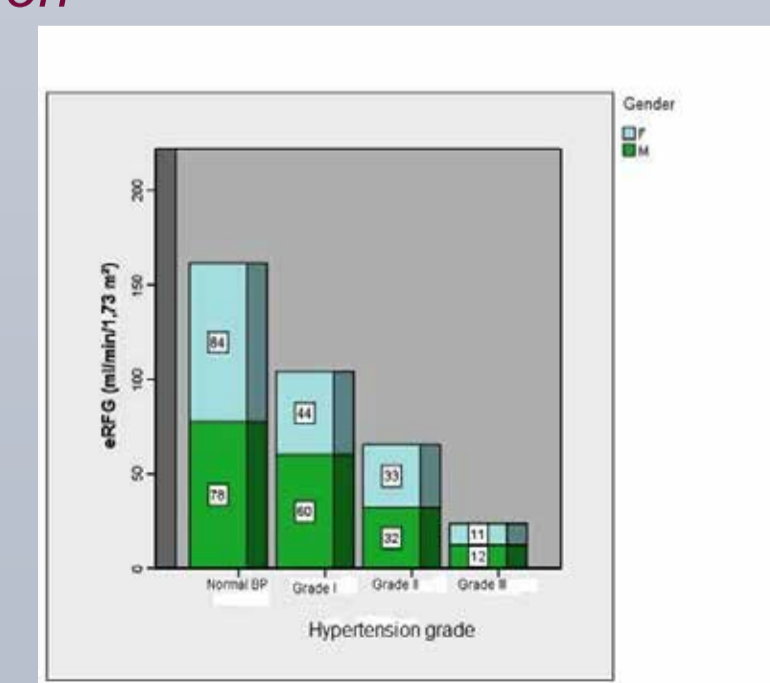
Nephrolithiasis
Patients without nephrolithiasis had a significantly higher mean GFR compared with patients with nephrolithiasis (50.8±35.3 mL/min/1.73 m² vs 29.2±27.1 mL/min/1.73 m², p<0.001)

Nephrolithiasis- negative predictor factor for kidney function
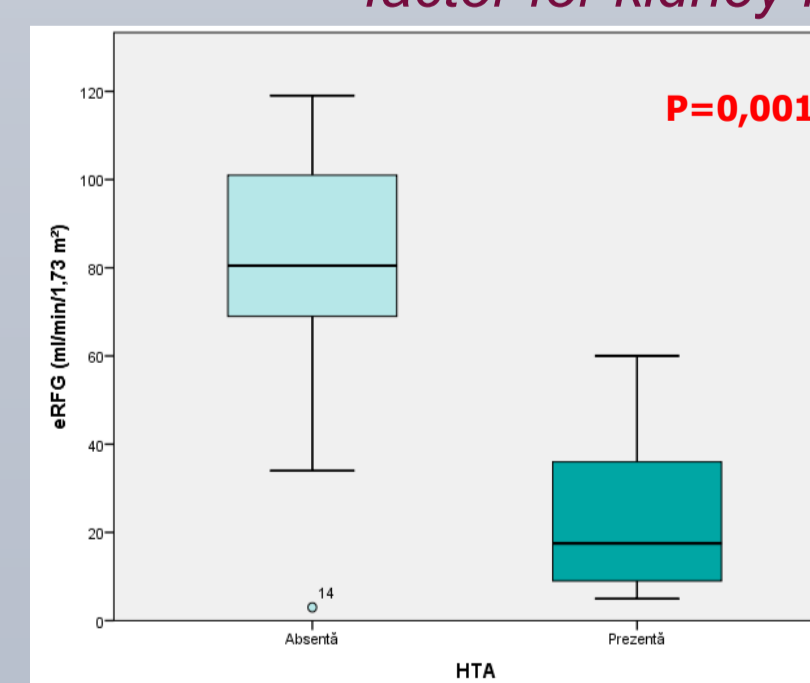
Hypertension- negative predictor factor for kidney function

eGFR variation according to gender and hypertension grade

RESULTS

Hypertension
Arterial hypertension was present in 62 patients. Prevalence of hypertension was increased in more advanced CKD stages: 3.5% in stage 1-2 CKD, 51.2% in stages 3-4 CKD and 96.7% in stage 5 CKD (p<0.01). A negative significant correlation was found between GFR and blood pressure (Pearson coefficient -0.80, p<0.001).

Hypertension and gender
Arterial hypertension was more prevalent in female patients, who also had lower GFRs compared with males with the same hypertension stage.

Uric acid
Patients with abnormal uric acid had significant lower GFR compared with those with normal levels (33±24 mL/min/1.73 m² vs 45±35 mL/min/1.73 m², p<0.01) and also higher blood pressure (118±17 mmHg vs 116±19 mmHg, p<0.05).

Hypertension and gender
Arterial hypertension was more prevalent in female patients, who also had lower GFRs compared with males with the same hypertension stage.

Kidney size measured by US
The mean value of the longitudinal kidney diameter was higher in patients with advanced CKD stages (18.3±3.2 cm in stage 5 CKD vs 17.9 ± 3.5 cm in stage 3 CKD, p=0.04). **Kidney size measured by US was the only independent prognostic factor for kidney function in multivariate analysis.**
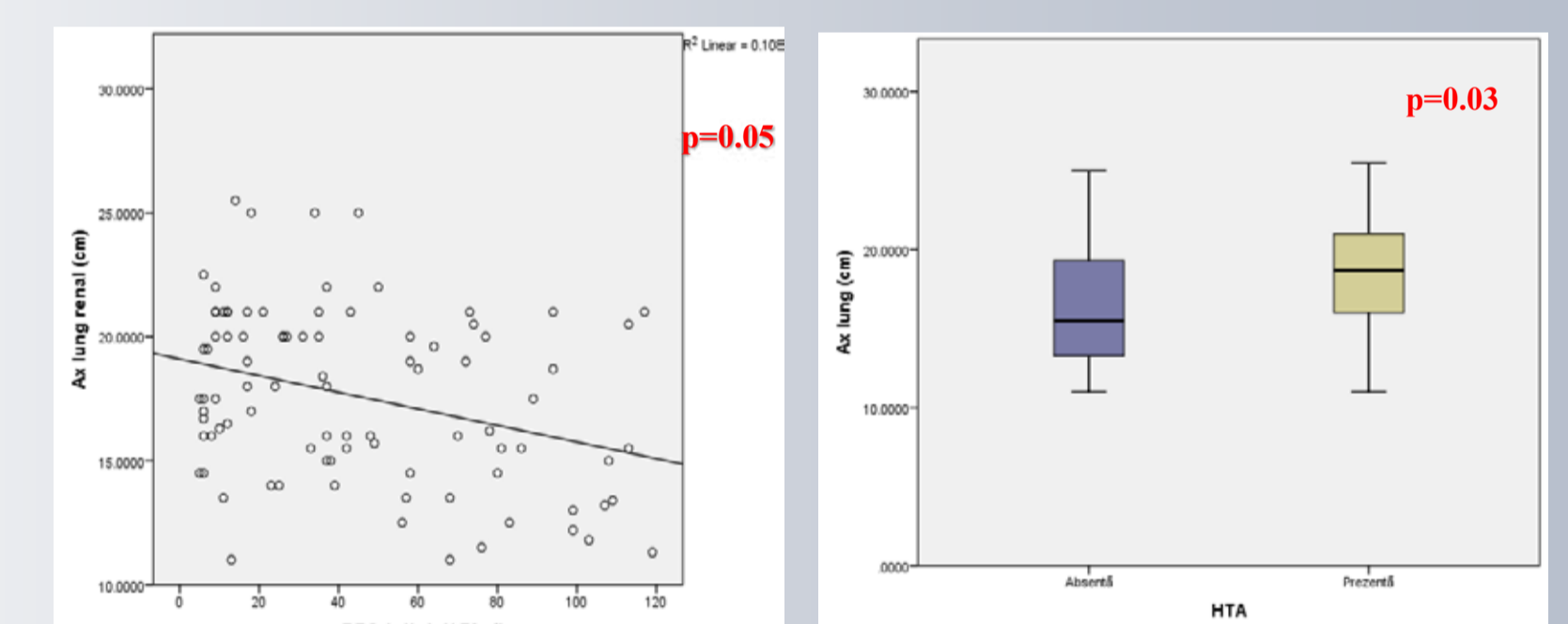
Negative correlation between kidney size and eGR

Kidney size- negative predictor factor for severity of hyertension

CONCLUSIONS

• This study identifies longitudinal kidney diameter measured by US as an independent prognostic factor for renal function in ADPKD.

• US is much cheaper and easier to use in every day practice compared to MR and may be a useful tool in assessing risk for progression in ADPKD.

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