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Rare Kidney Disease
Reference Network

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Working Group on Inherited
Kidney Disorders

WELCOME TO

ERKNet
Advanced Webinars on Rare Kidney Disorders

Date: 24 November 2020

Topic: Management of ADPKD - State of the Art

Speaker: Roman Ulrich Müller

Moderator: Francesco Emma

UNIKLINIK KÖLN
Department II of Internal Medicine, Nephrology, Rheumatology, Diabetes and General Internal Medicine
University Hospital of Cologne

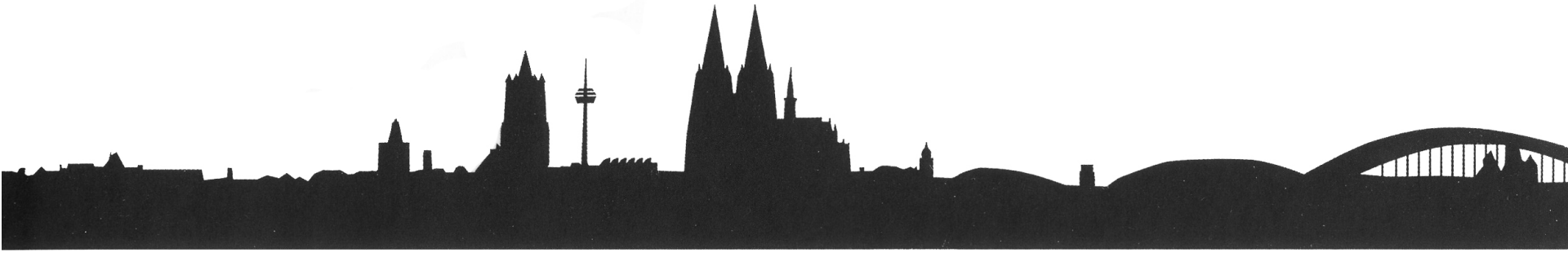
AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

Autosomal dominant polycystic kidney disease

Roman-Ulrich Müller

ERKNet Webinar

24.11.2020



Conflicts of Interest

Research funding, lecturing and consulting activities: Otsuka

Research funding and lecturing: ThermoFisher Scientific

1 Epidemiology and Genetics

2 Diagnostic strategies

3 systemic disease / differential diagnosis

4 Management / therapy

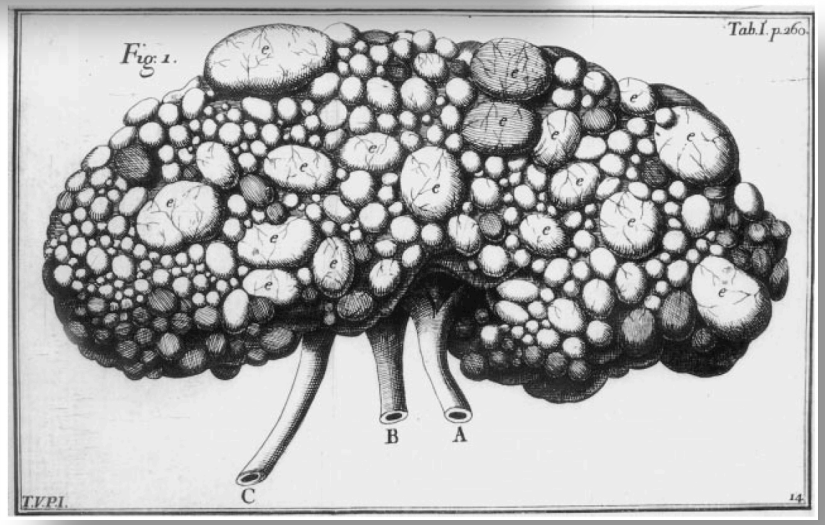
1

Epidemiology and genetics

Autosomal-dominant polycystic kidney disease ADPKD

The most common genetic kidney disease in adults

The most frequent monogenetic cause leading to ESRD



Domenico Gusmano Galeazzi (1757)

Autosomal-dominant polycystic kidney disease ADPKD

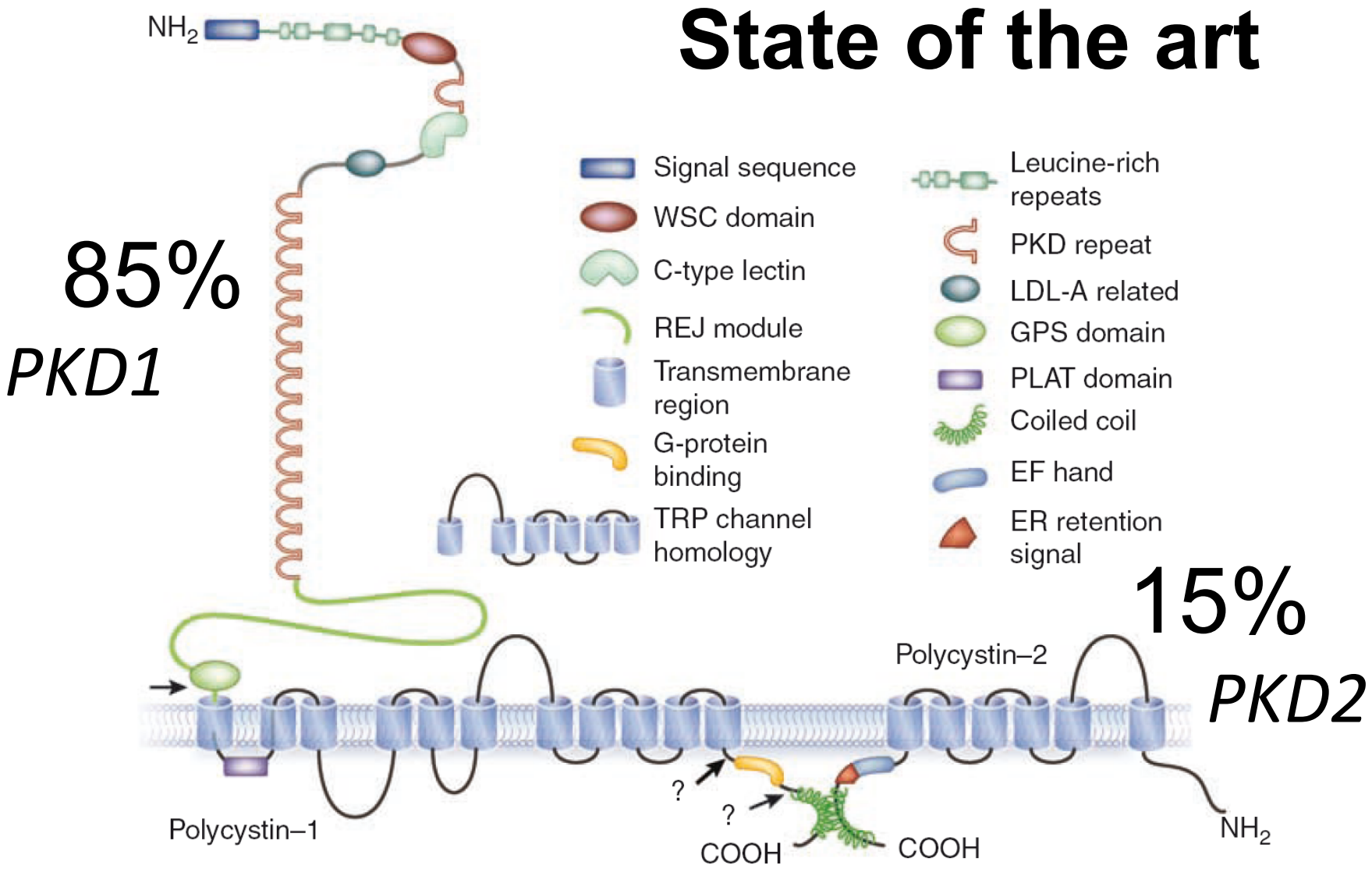
The most common genetic kidney disease in adults

The most frequent monogenetic cause leading to ESRD

Recent data confirm: genetic prevalence 1:1.000
→ ~ 45,000 in the European Union

Lanktree et al. JASN 2018

State of the art



Torres, Harris (2009) *Kidney Int* 76, 149–168

PKD3 ?

ARTICLE

Mutations in *GANAB*, Encoding the Glucosidase IIα Subunit, Cause Autosomal-Dominant Polycystic Kidney and Liver Disease

Binu Porath,[1,16] Vladimir G. Gainullin,[1,16] Emilie Cornec-Le Gall,[1,2,3] Elizabeth K. Dillinger,[4] Christina M. Heyer,[1] Katharina Hopp,[1,5] Marie E. Edwards,[1] Charles D. Madsen,[1] Sarah R. Mauritz,[1] Carly J. Banks,[1] Saurabh Baheti,[6] Bharathi Reddy,[7] José Ignacio Herrero,[8,9,10] Jesús M. Bañales,[11] Marie C. Hogan,[1] Velibor Tasic,[12] Terry J. Watnick,[13] Arlene B. Chapman,[7] Cécile Vigneau,[14] Frédéric Lavainne,[15] Marie-Pierre Audrézet,[2] Claude Ferec,[2] Yannick Le Meur,[3] Vicente E. Torres,[1] Genkyst Study Group, HALT Progression of Polycystic Kidney Disease Group, Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease, and Peter C. Harris[1,4,*]

AJHG

Volume 102, Issue 5, 3 May 2018, Pages 832-844

Article

Monoallelic Mutations to *DNAJB11* Cause Atypical Autosomal-Dominant Polycystic Kidney Disease

Emilie Cornec-Le Gall [1, 4, 5], Rory J. Olson [2], Whitney Besse [6], Christina M. Heyer [1], Vladimir G. Gainullin [1], Jessica M. Smith [1], Marie-Pierre Audrézet [5], Katharina Hopp [7], Binu Porath [1], Beili Shi [8], Saurabh Baheti [3], Sarah R. Senum [1], Jennifer Arroyo [1], Charles D. Madsen [1], Claude Férec [5], Dominique Joly [10], François Jouret [11], Oussamah Fikri-Benbrahim [12] … Peter C. Harris [1, 2]

ALG9 mutation carriers develop kidney and liver cysts

METHODS

Whole Exome Sequencing on 122 genetically unresolved cases of autosomal dominant polycystic kidney and liver disease (ADPKD-NMD and PCLD)

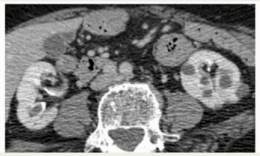
Candidate gene: *ALG9*

Identify *ALG9* mutation carriers in exome sequenced population of 92,000 individuals (n=21; 11 cases with imaging)

In vitro investigation of polycystin-1 maturation

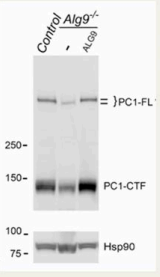
Case versus matched Control analysis of kidney and liver cyst burden

OUTCOME



MC5: *ALG9* het c.1018+1G>A

In *ALG9* mutation carriers over age 50, 88% have at least 4 kidney cysts. Case versus Control analysis (P < 0.0001).



Recessive loss of *ALG9* results in significantly reduced expression level and impaired N-glycosylation of polycystin-1.

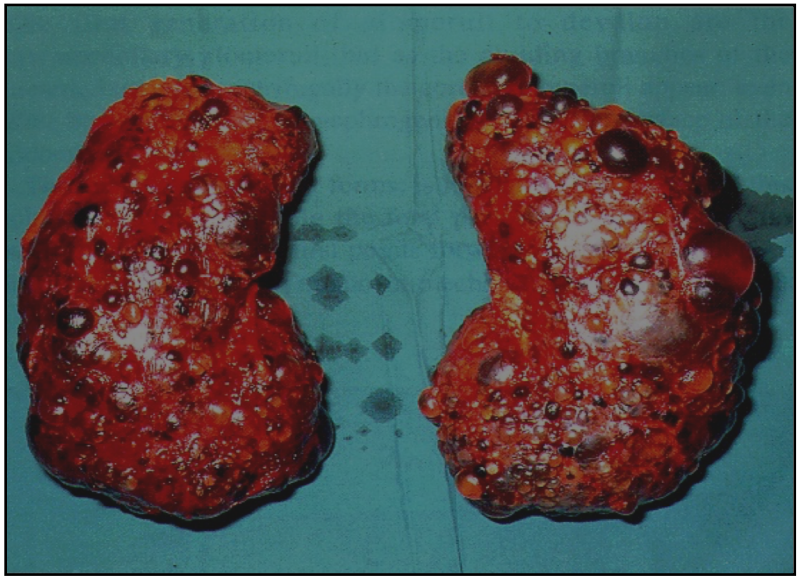
CONCLUSION: *ALG9* is a novel disease gene for the polycystin-1 dosage-dependent spectrum of dominantly inherited polycystic kidney and liver disease spanning the clinical continuum from ADPKD-NMD to PCLD. This study supports the utility of genotype-driven validation and analysis of candidate disease gene phenotypes from genome level sequencing data coupled with the electronic health record in the era of precision medicine.

doi: 10.1681/ASN.2019030298

JASN

→ all rare variants

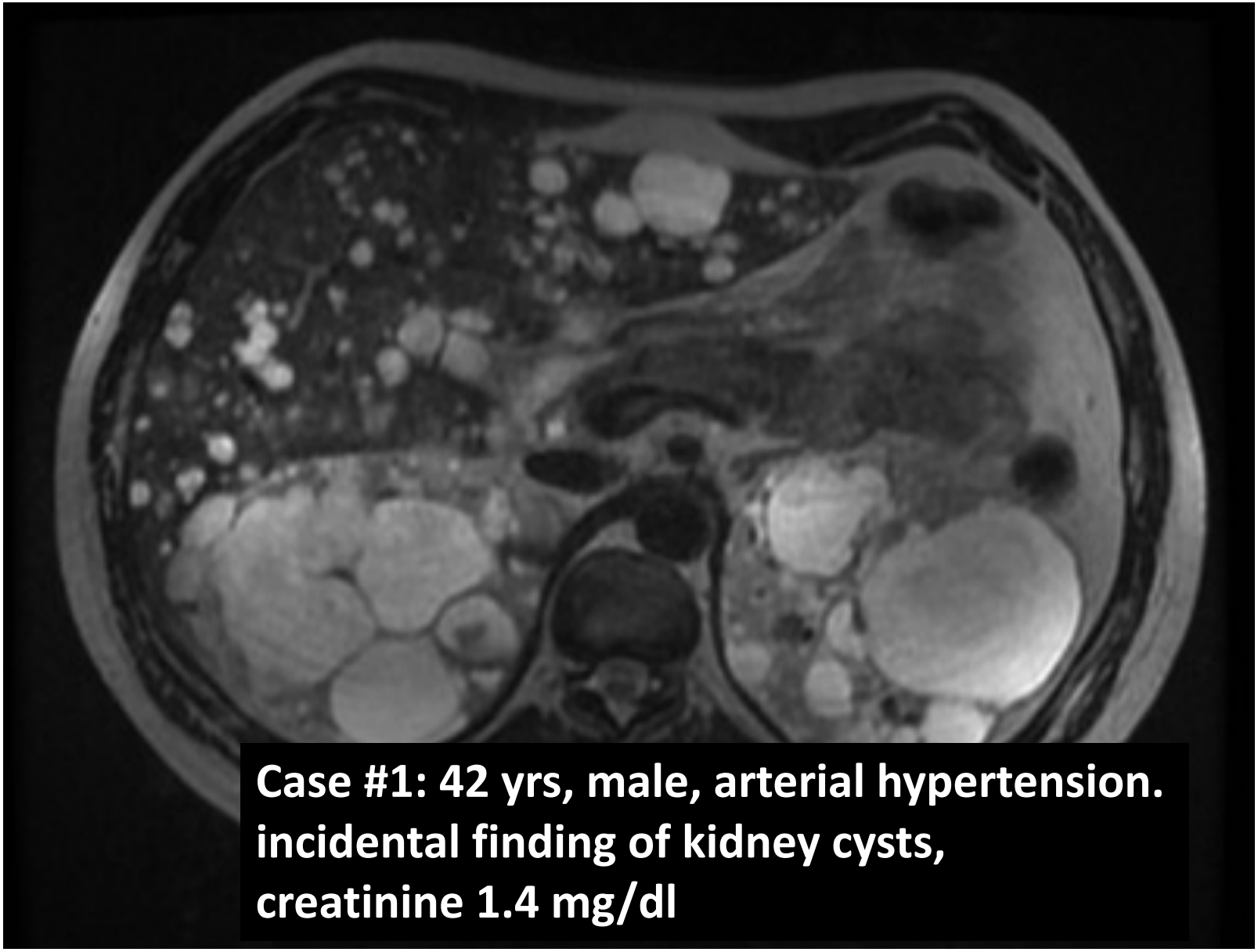
Autosomal-dominant polycystic kidney disease



End-stage renal disease:
at about 50-60 years of age (in 50% of patients)

1 Epidemiology and genetics

2 Diagnostic strategies


Case #1: 42 yrs, male, arterial hypertension.
incidental finding of kidney cysts,
creatinine 1.4 mg/dl

Gen	Protein	Lokalisation an Zilium/ Zentrosom	Renale Symptome
ADPKD			
PKD1	Polycystin-1	+	bds. große Nieren,
PKD2	Polycystin-2	+	ubiquitäre Zysten
ARPKD			
PKHD1	Fibrocystin	+	bds. große Nieren, ubiquitäre Zysten
Nephronophthise			
NPHP1	Nephrozystin-1	+	kleine Nieren,
NPHP2	Inversin	+	(NPHP2: große Nieren)
NPHP3	Nephrozystin-3	+	kortikomedulläre Zysten,
NPHP4	Nephroretinin	+	
NPHP5	Nephrozystin-5	+	
NPHP6	CEP290	+	interstitielle Fibrose,
NPHP7	Glis2	+	Polyurie, Polydyse-
NPHP8	RPGRIP1L	+	
NPHP9	Nek8	+	
NPHP10	?		
NPHP11	TMEM67	+	
MCKD			
MCKD1	?		kortikomedulläre Zysten,
UMOD	Uromodulin	+	Unregelmäßige Basalmembran, interstitielle Fibrose
Von Hippel Lindau Syndrom			
VHL	pVHL	+	große Nieren, RCC
Tuberöse Sklerose			
TSC1	Hamartin		Zysten, Angiomyolipome
TSC2	Tuberin		selten RCC
Meckel Gruber Syndrom			
MKS1	FABB proteome-like protein	+	vergrößerte multizystische Nieren
MKS3	TMEM67	+	NPH-ähnlich bis dysplastisch
MKS4	CEP290	+	
MKS5	RPGRIP1L	+	
MKS6	CC2D2A	+	große, zystische Nieren

Gen	Protein	Lokalisation an Zilium/ Zentrosom	Renale Symptome
Bardet Biedl Syndrom			
BBS1	BBS2-like protein 2	+	NPH-ähnlich
BBS2	BBS2	+	
BBS3	ARL6	+	
BBS4	BBS4	+	
BBS5	BBS5	+	
BBS6	McKusick-Kaufman Syndrom protein	+	
BBS7	BBS2-like	+	
BBS8	tetratricopeat-protein 8	+	
BBS9	PTHB1		
BBS10	C12orf58		
BBS11	TRIM32		
BBS12	C4orf24	+	
BBS13	FABB proteome-like protein	+	
BBS14	CEP290	+	
Alstrom Syndrom			
ALMS1	Alstrom syndrome 1	+	NPH-ähnlich
Orofaziales digitales Syndrom			
OFD1	OFD1	+	normalgroß, polyzystisch

differential diagnosis – polycystic kidneys ?

State of the art: polycystic kidneys – more than 100 known genes

No, we do not need to remember all of these. The clinical picture is the first step.

Clinical diagnosis of ADPKD

1. mode of inheritance
2. **imaging – kidney morphology**
3. Renal symptoms
4. Extrarenal manifestations

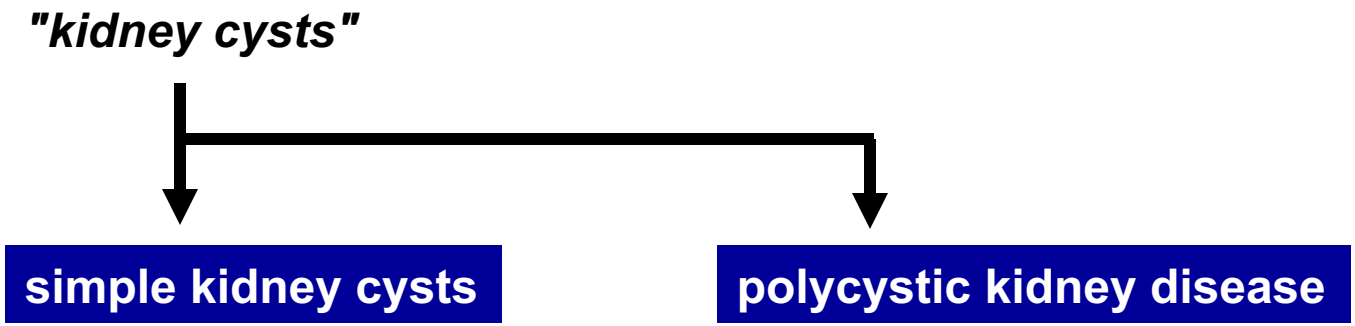
The clinical diagnosis of ADPKD

1 Mode of inheritance

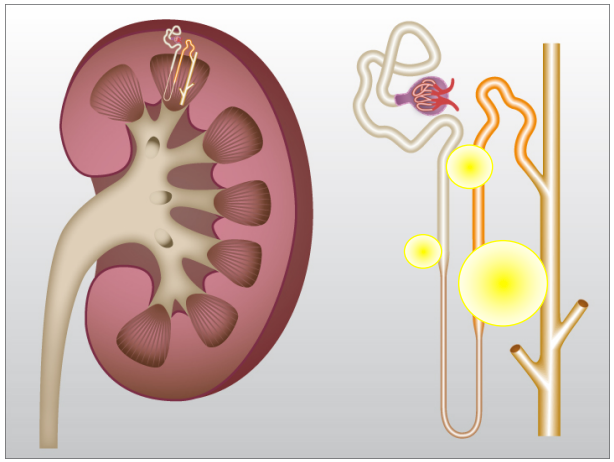
Clinical diagnosis of ADPKD

2 **imaging – kidney morphology**

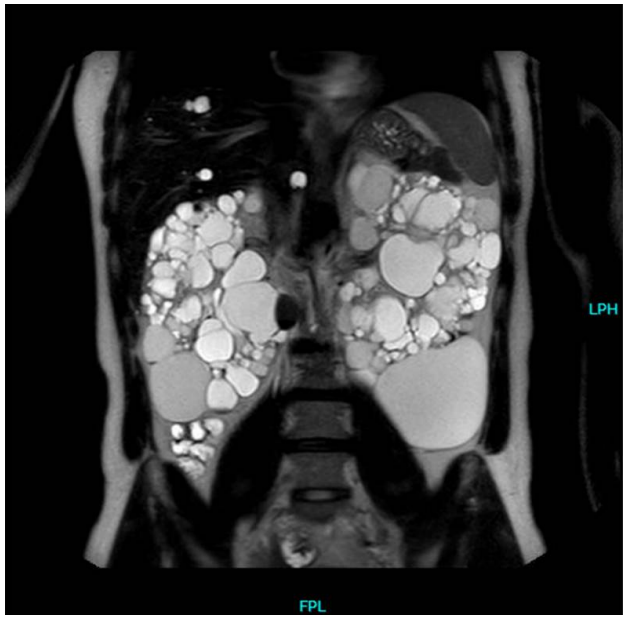
How to diagnose polycystic kidney disease?



Imaging – kidney morphology

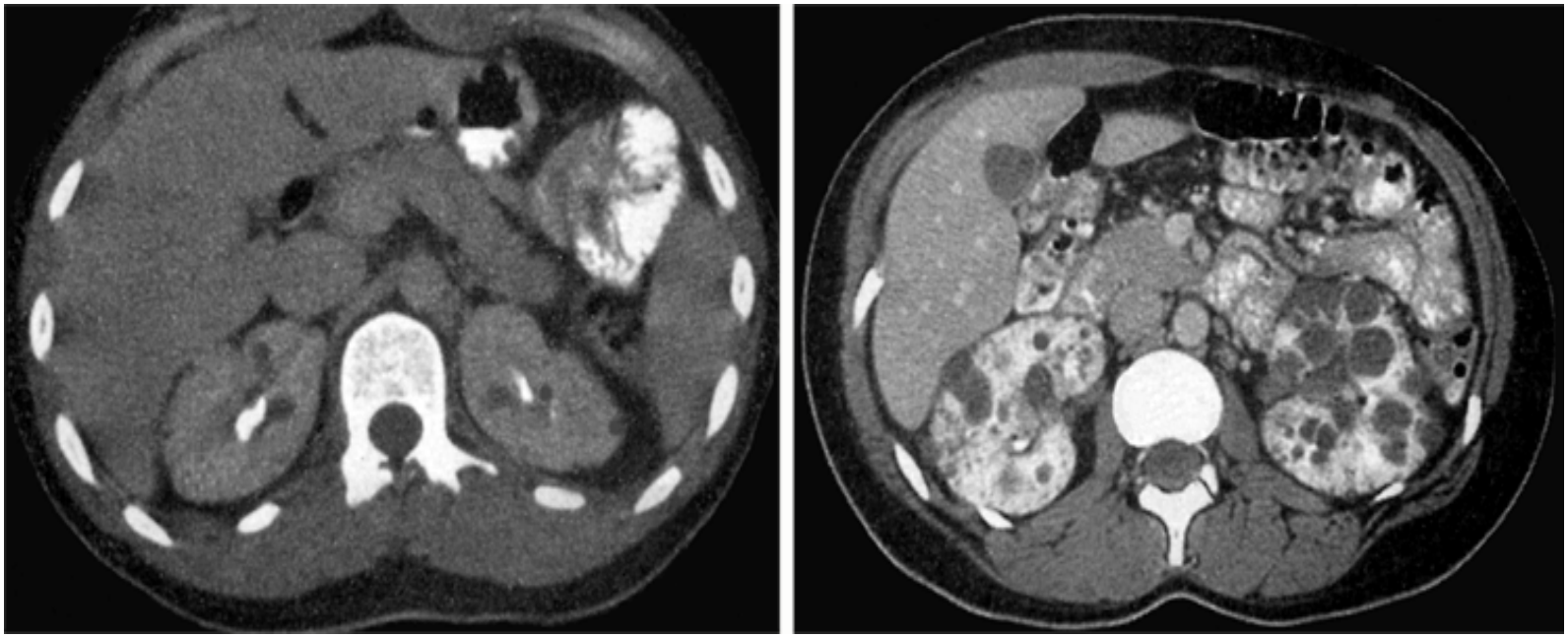


1. number of cysts
2. distribution of cysts
3. kidney size



Therapiehandbuch Innere Medizin
“Genetische Nierenerkrankungen”
(R.-U- Müller)

ADPKD is a slowly progressive disorder



Age: 29 years vs. 40 years

Courtesy of Dr. Y. Pei, University Health Network, Toronto

Toronto Radiologic Imaging Studies of Polycystic Kidney Disease (TRISP)

MRI Diagnostic Performance:

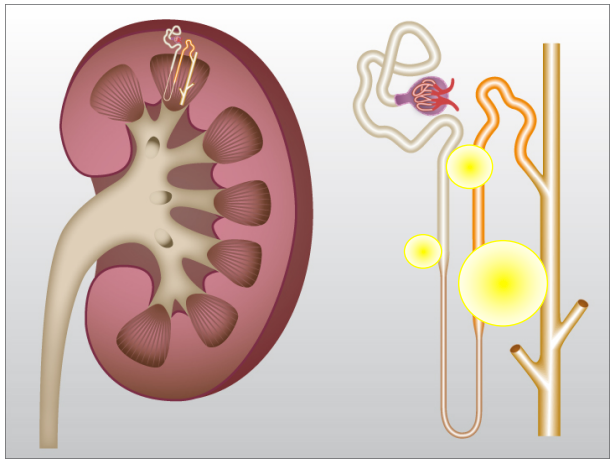
Age group (yr)	Diagnostic criterion	Sensitivity	Specificity	PPV	NPV
16-29	≥1 renal cyst	1.00	0.83	0.79	1.00
	≥2 renal cysts	1.00	0.93	0.90	1.00
	≥3 renal cysts	1.00	0.97	0.95	1.00
	≥5 renal cysts	1.00	0.98	0.97	1.00
	>10 renal cysts	**1.00**	**1.00**	**1.00**	**1.00**
	≥2 cysts in each kidney	1.00	0.98	0.97	1.00
30-40	≥1 renal cyst	1.00	0.77	0.88	1.00
	≥2 renal cysts	1.00	0.82	0.90	1.00
	≥3 renal cysts	1.00	0.95	0.97	1.00
	≥5 renal cysts	1.00	1.00	1.00	1.00
	>10 renal cysts	**1.00**	**1.00**	**1.00**	**1.00**
	≥2 cysts in each kidney	1.00	1.00	1.00	1.00

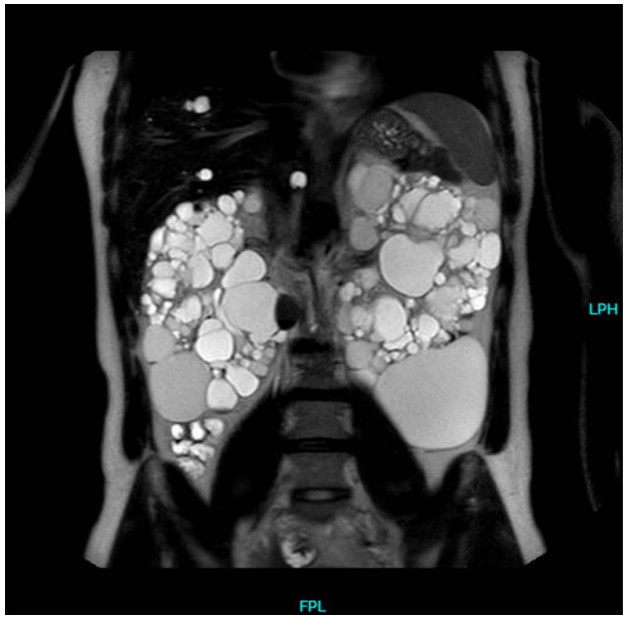
Courtesy of Dr. Y. Pei, University Health Network, Toronto

our approach...

- Detection of 10 cysts and more in patients at risk, specificity and sensitivity 100%
- No cysts at age 30 means no disease (NPV=100%; earlier exclusion by MRI probably possible)
- HR-ultrasound is as good as MRI in the detection of cysts (with some exceptions)

Bildgebung - Nierenmorphologie





Therapiehandbuch Innere Medizin
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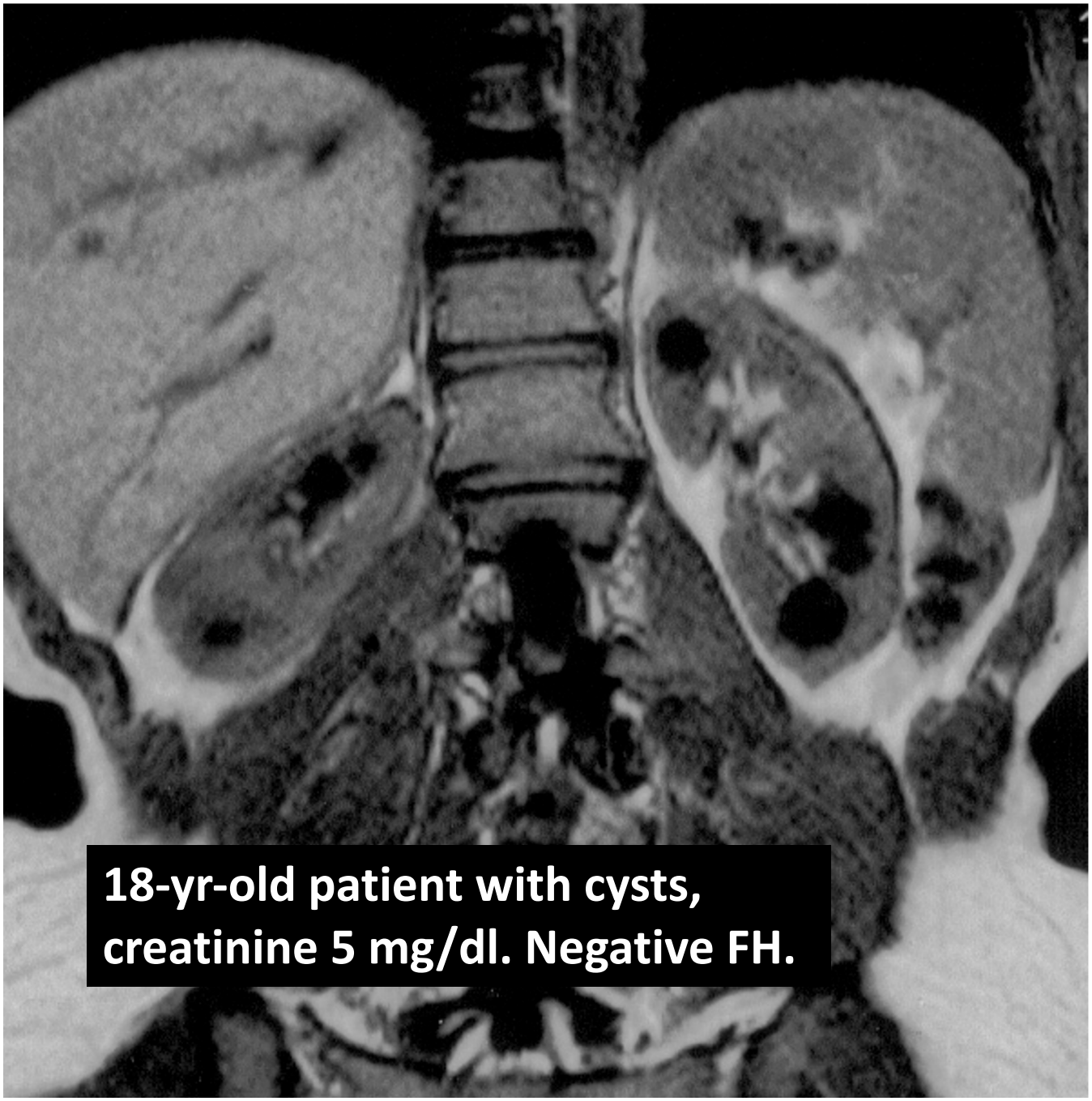
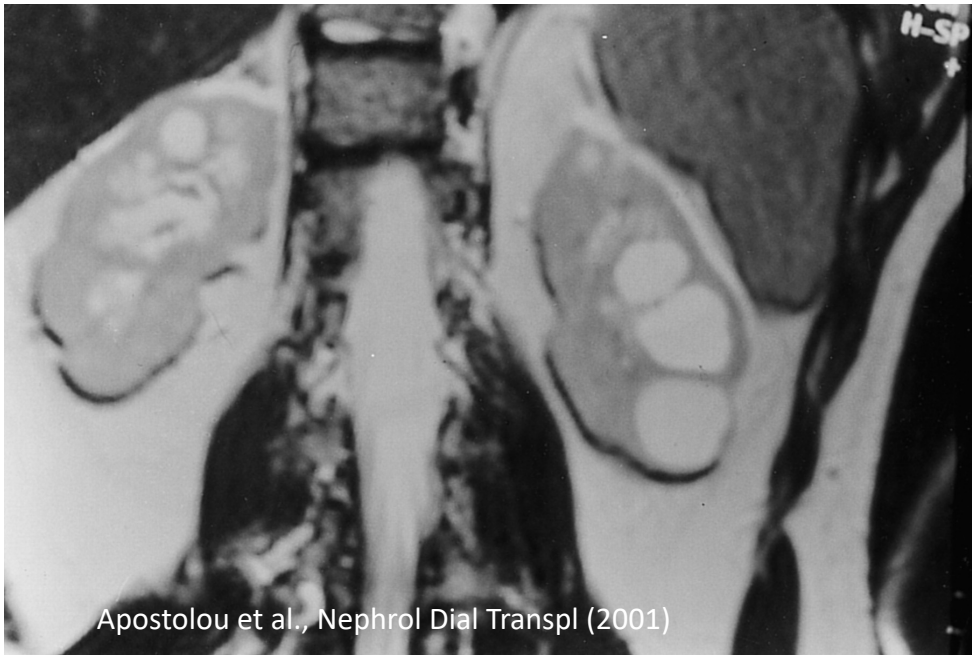
1. number of cysts
2. distribution of cysts
3. kidney size

key words: bilateral, ubiquitous

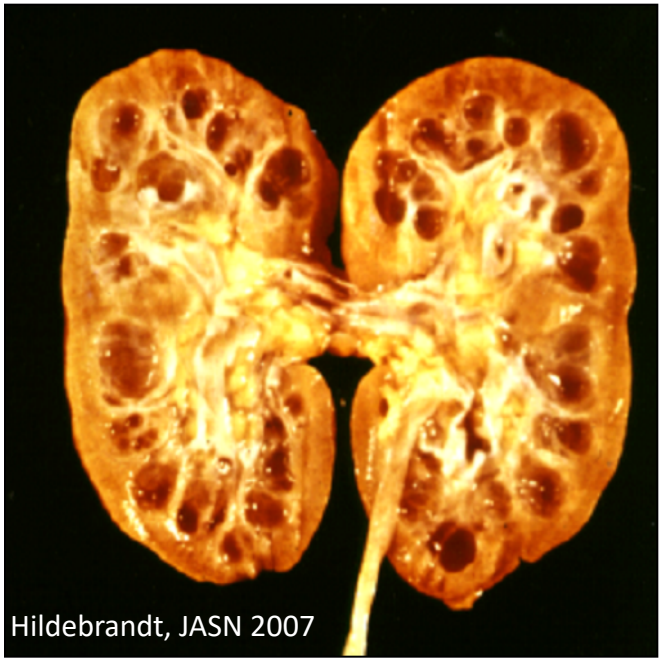

18-yr-old patient with cysts,
creatinine 5 mg/dl. Negative FH.

Nephronophthise (NPH)

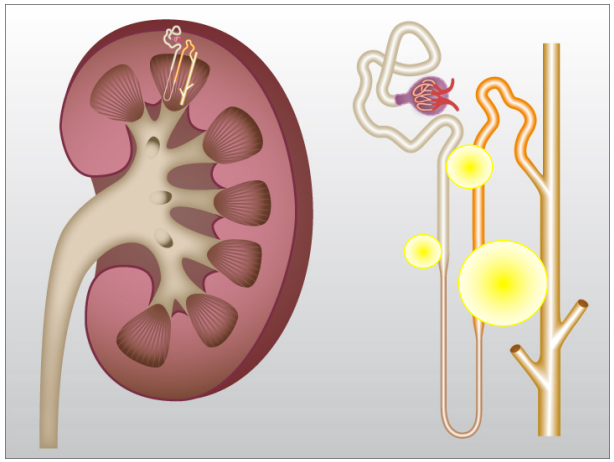
- “kidney shrinkage” or “loss of nephrons”
  νεφρός, grecian: kidney; φθίσις, grecian: shrinkage
- among the most frequent genetic causes of ESRD in children
- autosomal recessive disease
- In Europe approx. 10% of ESRD in childhood
- median age of ESRD: 13 years
- mutations in NPHP1 - NPHP20

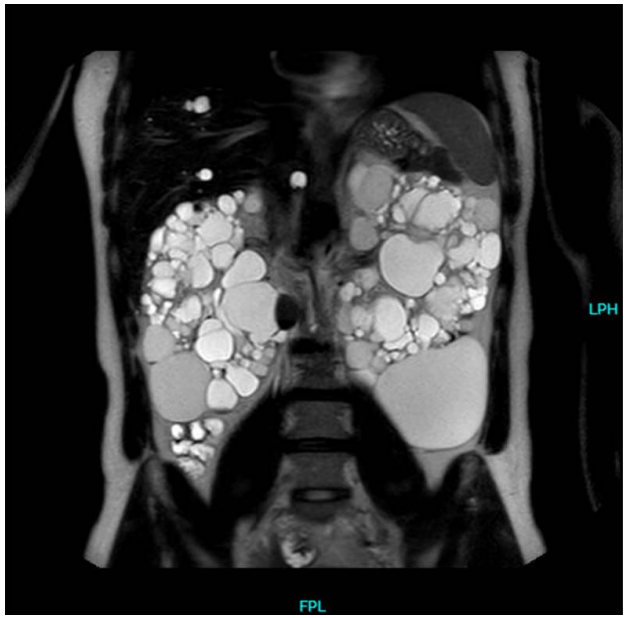


Apostolou et al., Nephrol Dial Transpl (2001)


Hildebrandt, JASN 2007

Imaging – Kidney morphology



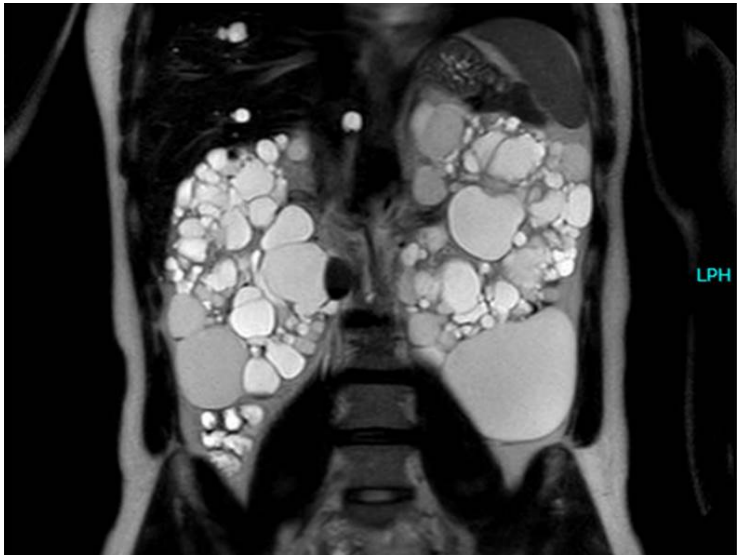


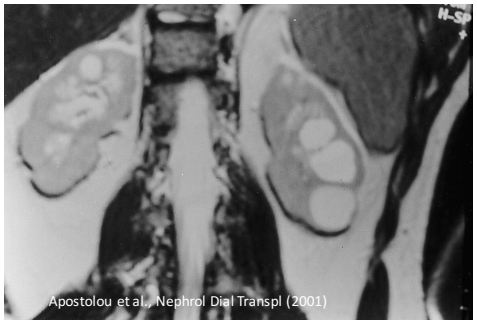
Therapiehandbuch Innere Medizin
“Genetische Nierenerkrankungen”
(R.-U- Müller)

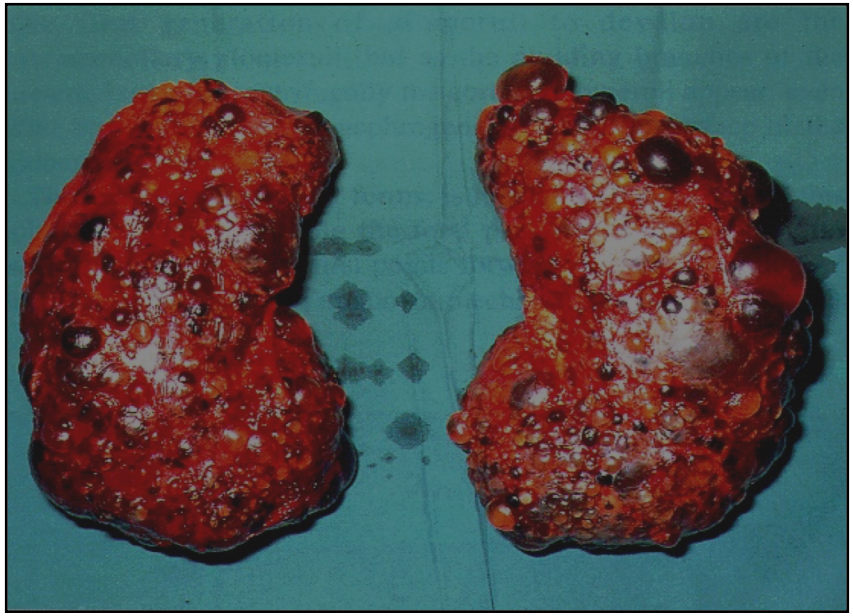
1. number of cysts
2. distribution of cysts
3. kidney size

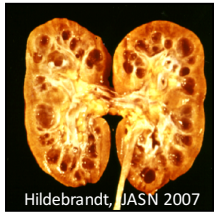
bilateral, ubiquitous, enlarged

Kidney size differs in polycystic kidney disease

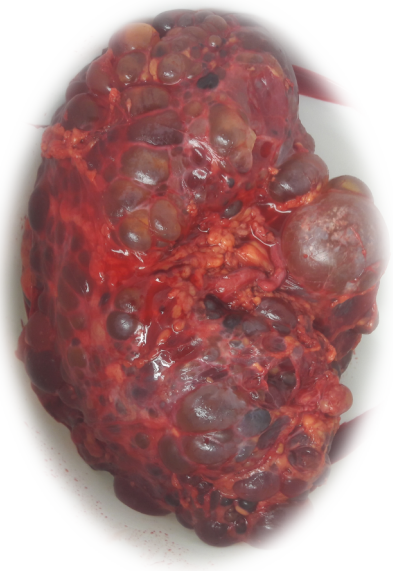




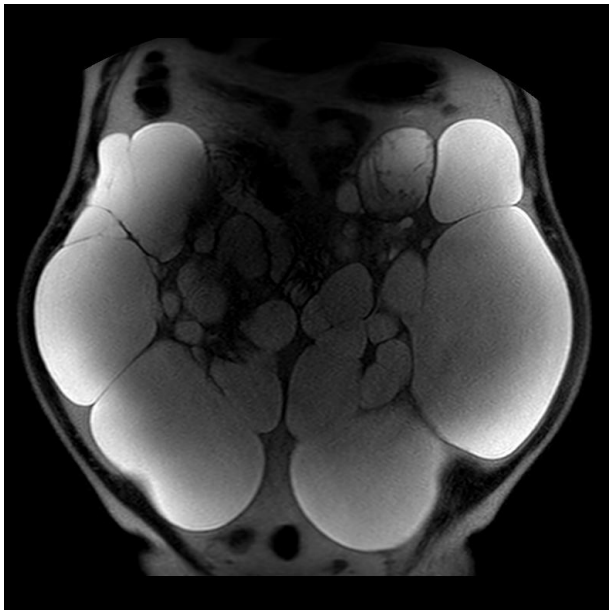


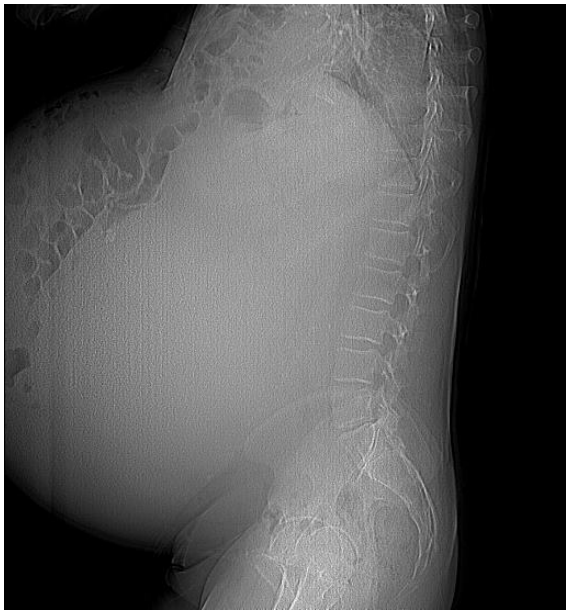


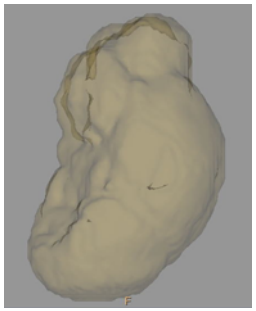
Polycystic kidneys



25 x 18 x 13 cm
2.8 kg





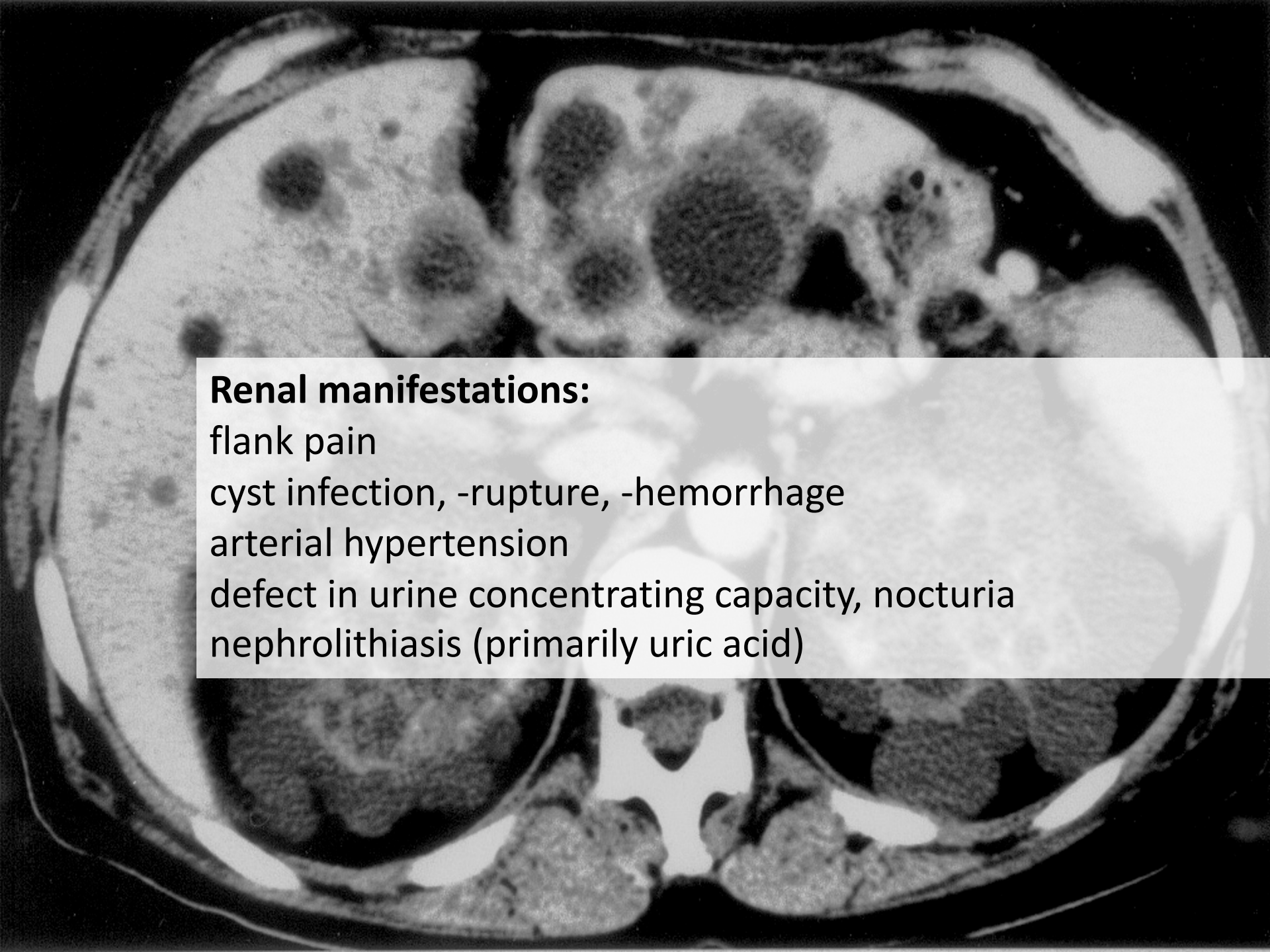


~30 liters total kidney volume

images: PD Dr. Persigehl
Radiologie, UK Köln

The clinical diagnosis of ADPKD

3 Renal symptoms



Renal manifestations:

flank pain

cyst infection, -rupture, -hemorrhage

arterial hypertension

defect in urine concentrating capacity, nocturia

nephrolithiasis (primarily uric acid)

The clinical diagnosis of ADPKD

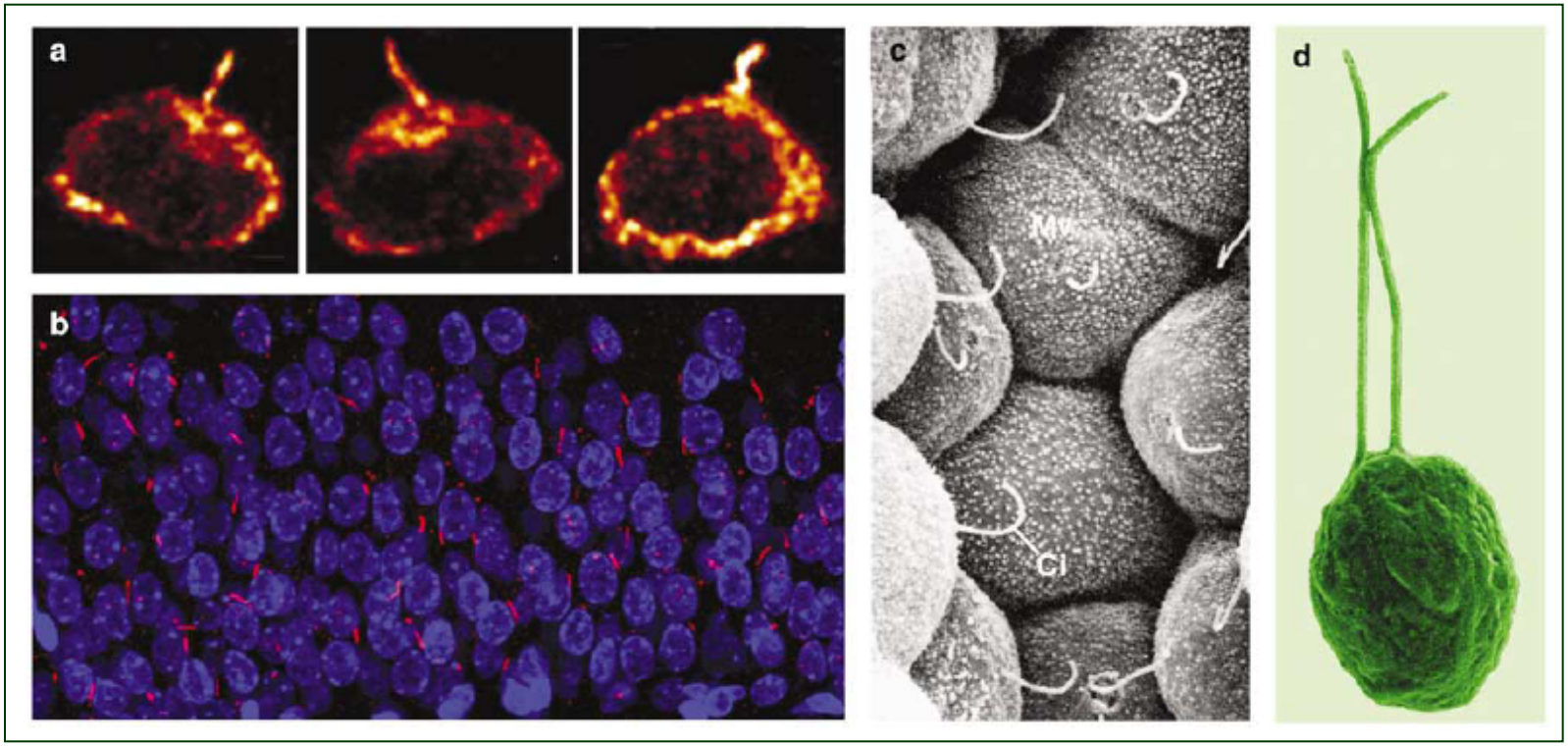
4 Extrarenal manifestations

1 Epidemiology and genetics

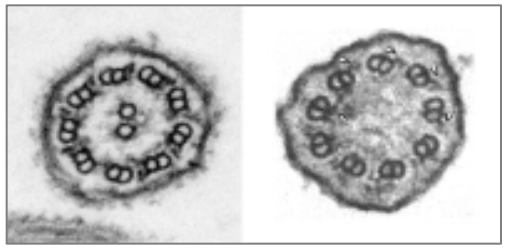
2 Diagnostic strategies

3 Systemic disease / differential diagnosis

Cilia are little organelles that project from almost every cell of the body



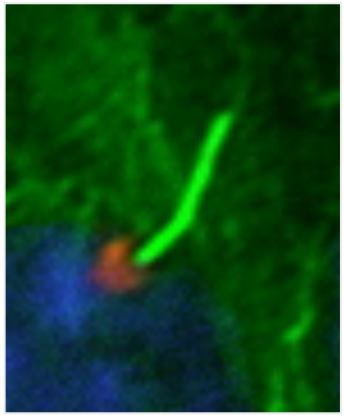
9+2

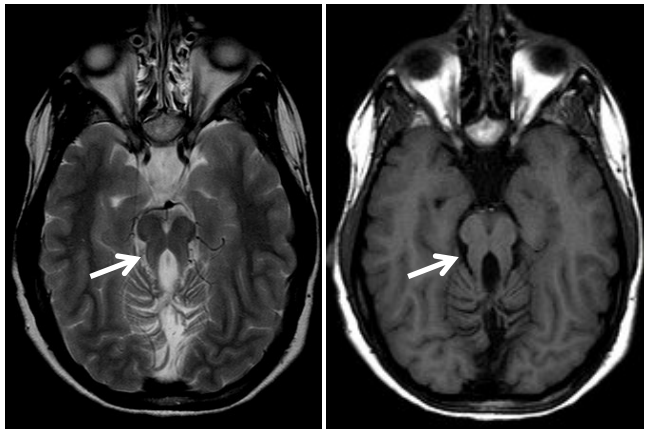


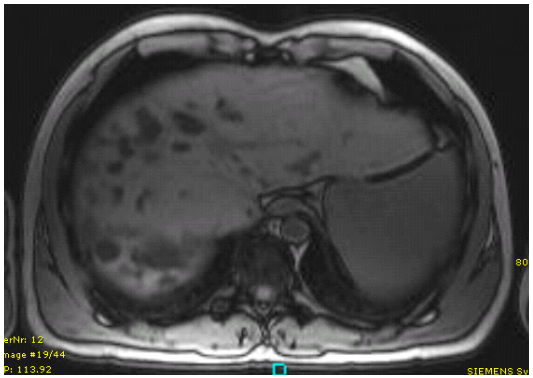
9+0

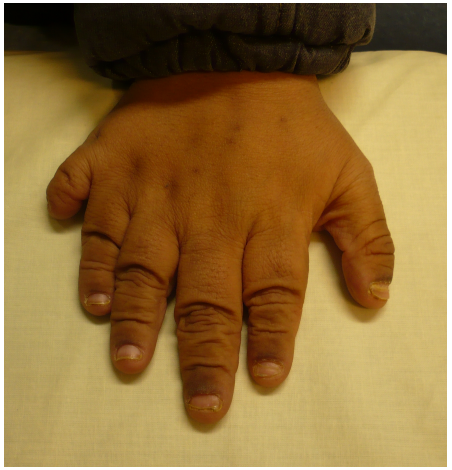
Pan, Lab Invest, 2005

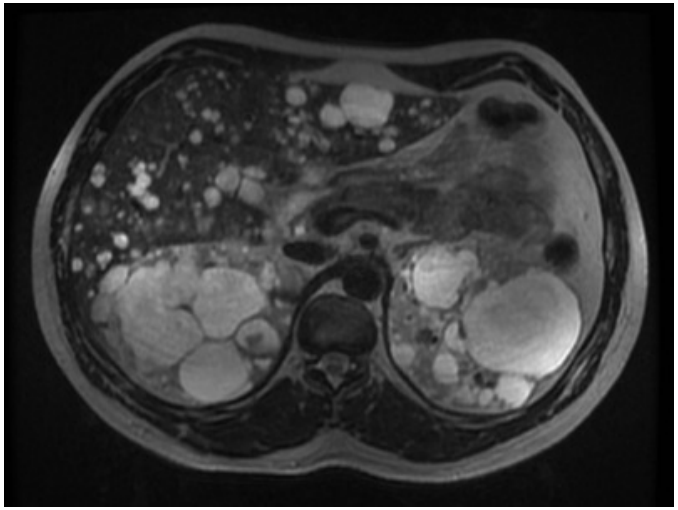
Ciliopathies:
a plethora of phenotypes

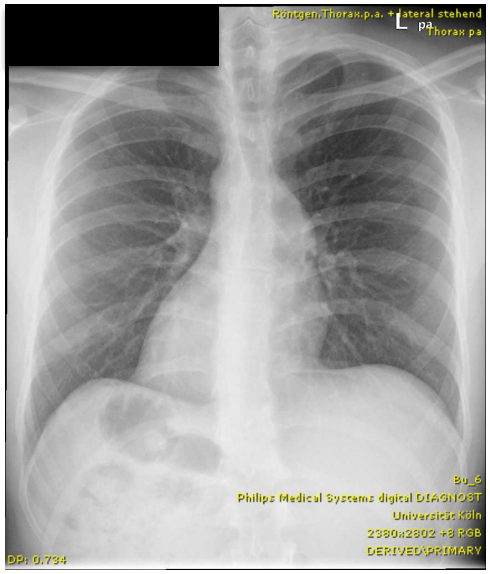












Hildebrandt, Benzing, Katsanis (2011) *N Engl J Med* 364, 1533-1544

ADPKD is multi-system disease

The most important extra-renal manifestations:

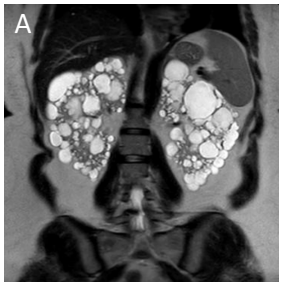
extrarenal cysts

diverticulosis

heart valve defects

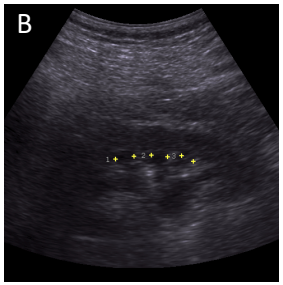
vascular anomalies
(e.g. intracranial aneurysms)

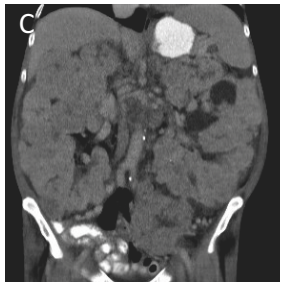
renal manifestations

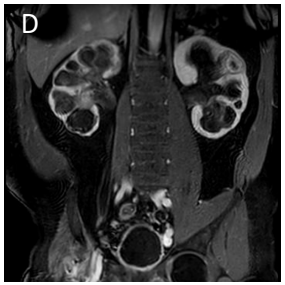


nephrolithiasis, flank pain, hematuria, cyst infection

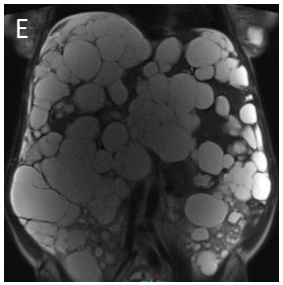
imaging of differential diagnoses of ADPKD

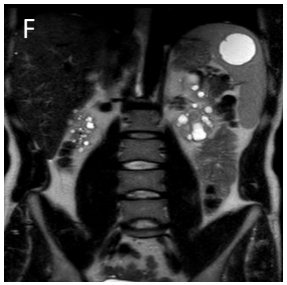


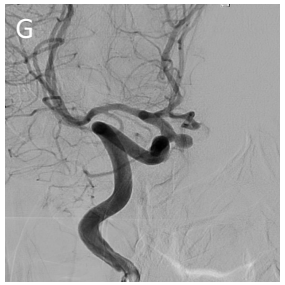


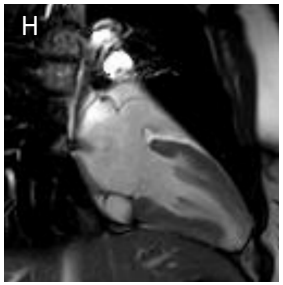


extrarenal manifestations of ADPKD









extrarenal cysts (liver, pancreas, spleen, seminal vesicles, arachnoid…), biliary disease, cardiac valve defects, vascular dissections/aneurysms, pericardial effusion, intracranial aneurysms, hernias, diverticulosis

Müller and Benzing CKJ 2018

our approach...

Diagnostic criteria of ADPKD:
Cysts are ubiquitous and dispersed over the kidneys.
Kidneys grossly enlarged.

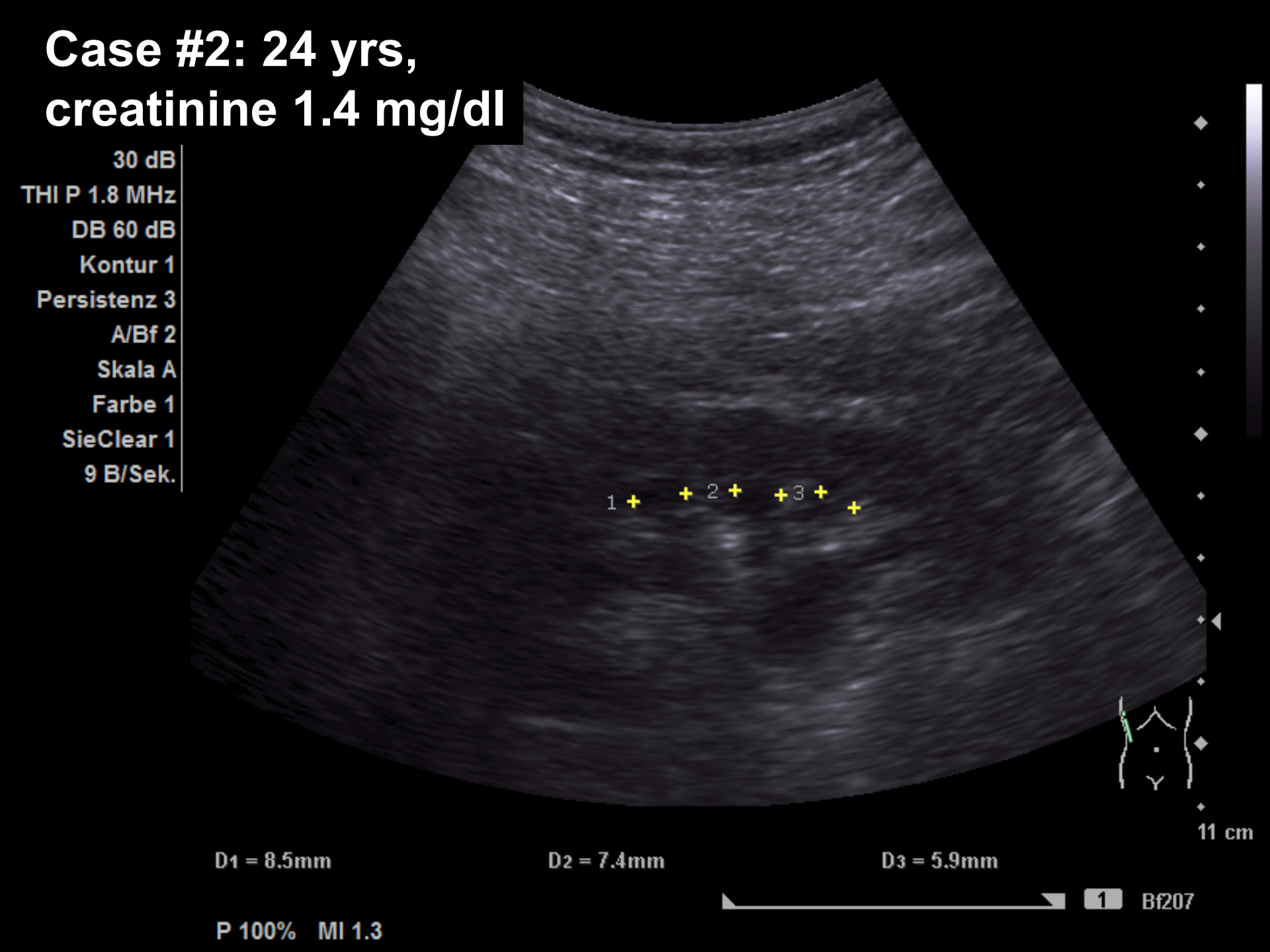
ADPKD classics: extrarenal cysts, cardiac valve defects colon diverticulosis, aneurysms, renal stone disease, flank pain, hypertension, haematuria.

No carcinoma, no angiomyolipoma, no rare extrarenal findings.

Case #2: 24 yrs,
creatinine 1.4 mg/dl

referral from ophthalmology for nephrological assessment

Case #2: 24 yrs, creatinine 1.4 mg/dl



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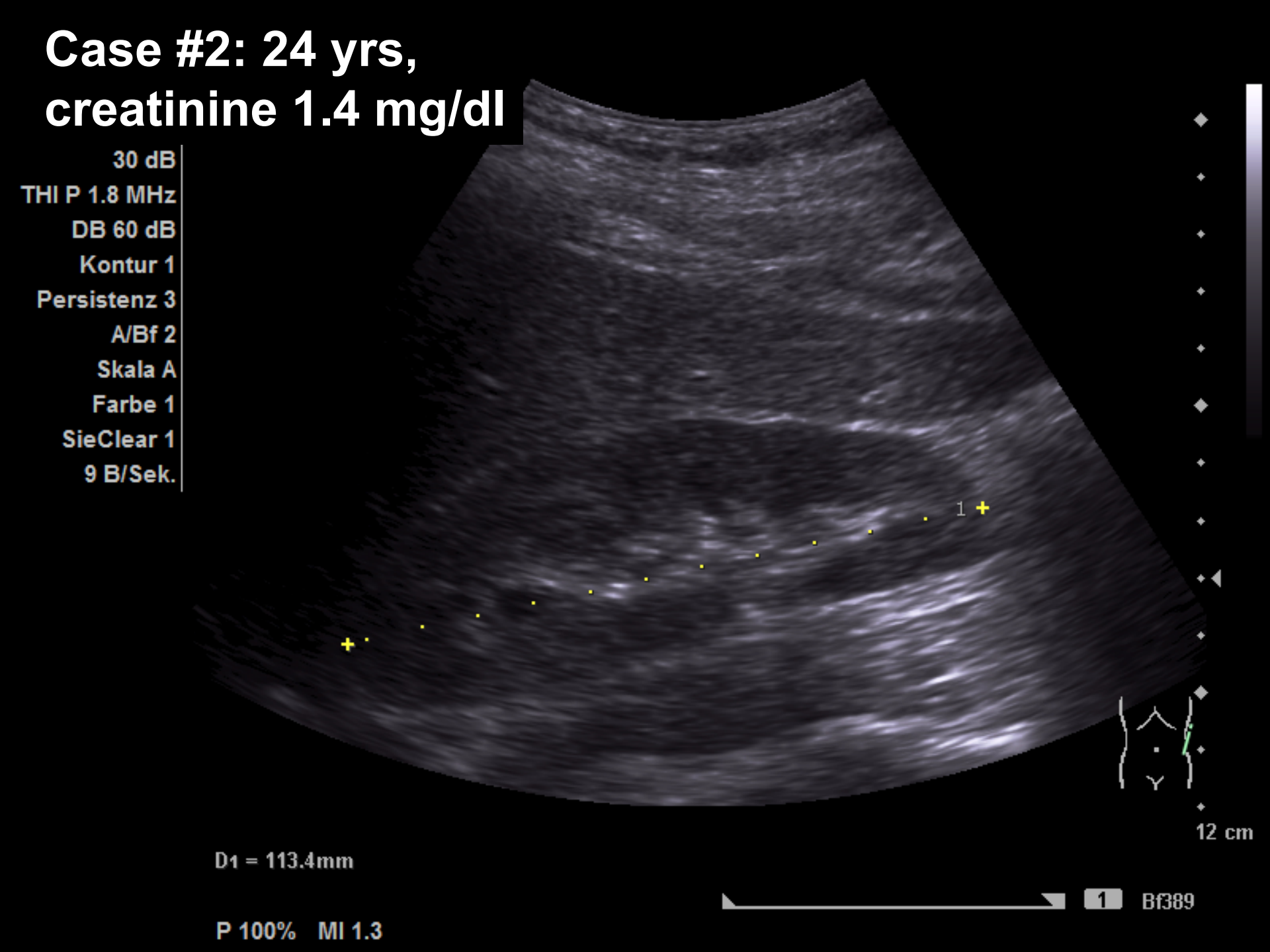
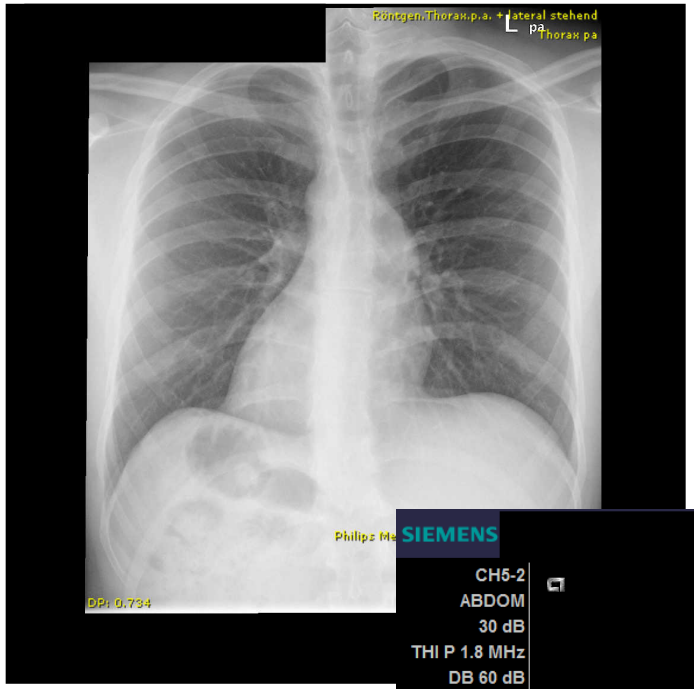
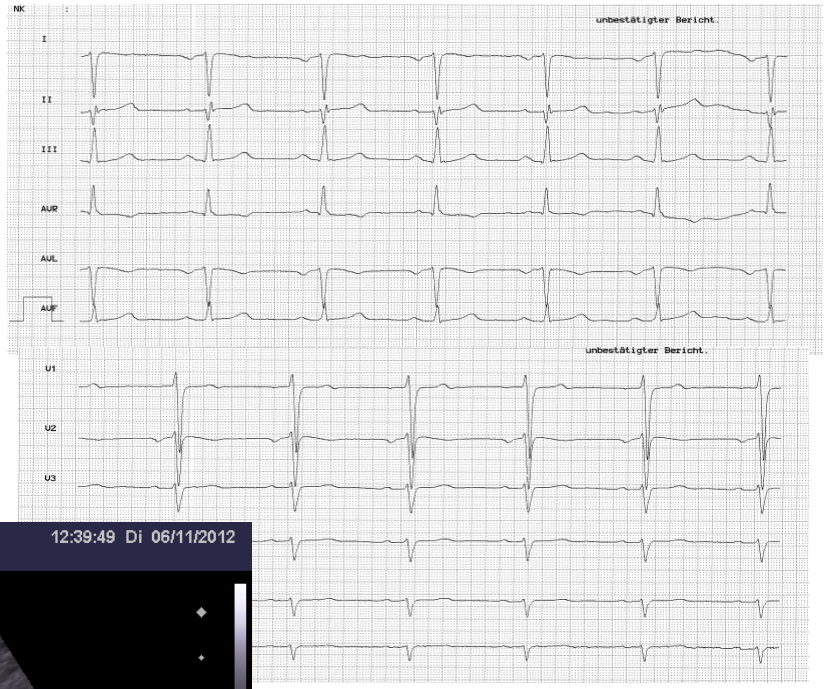
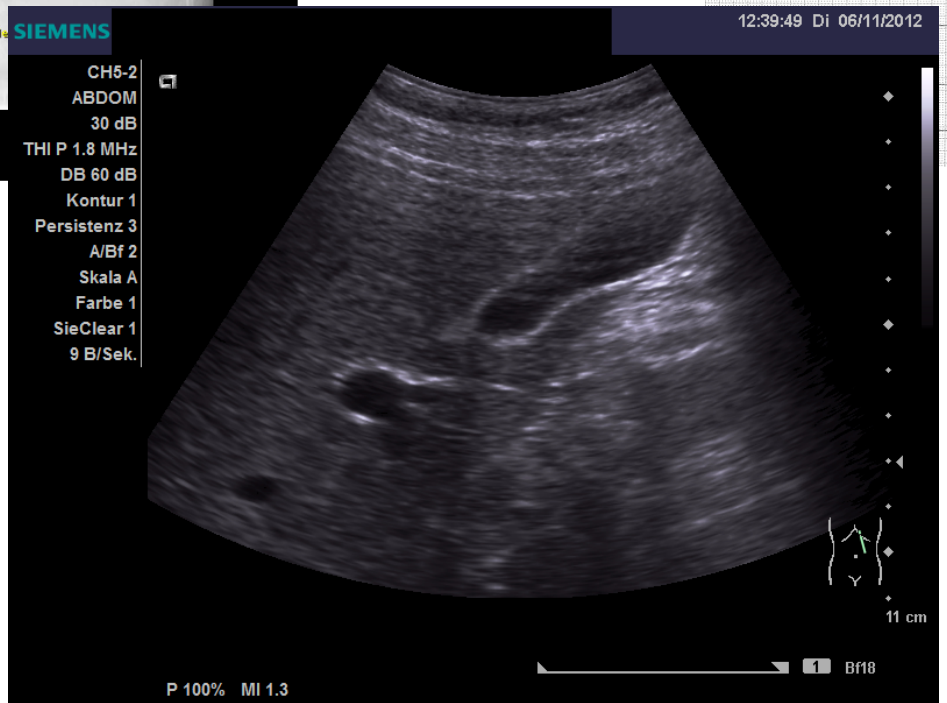
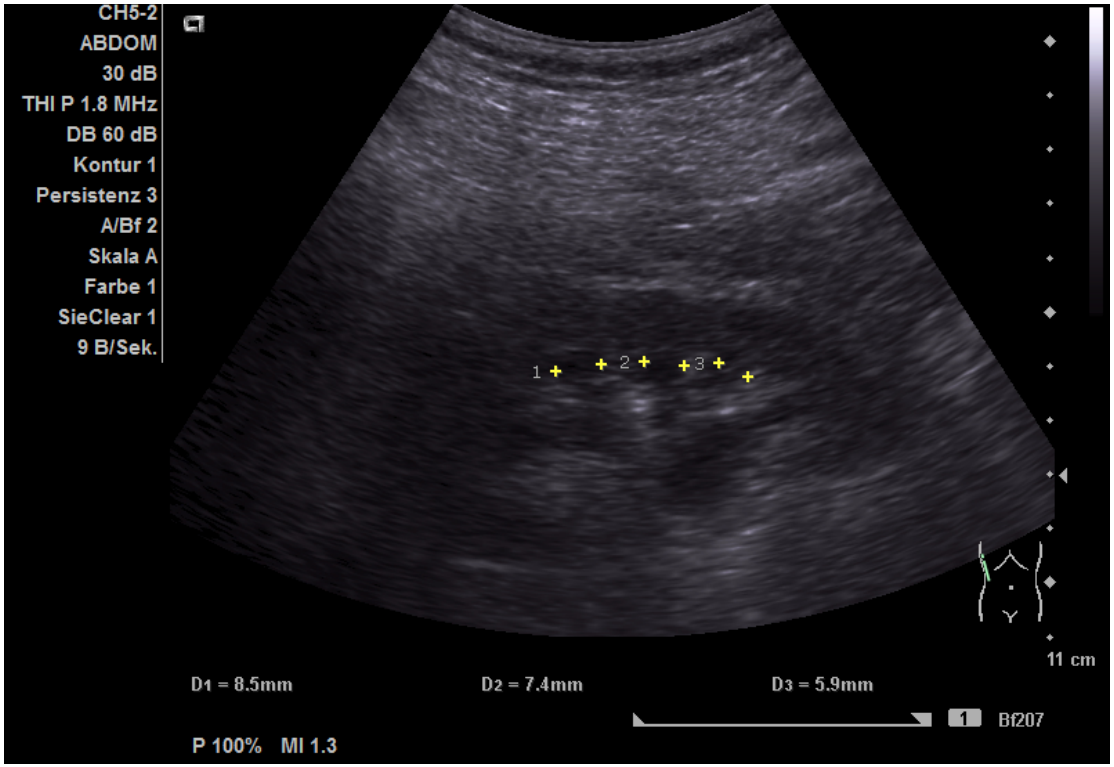


Extrarenal symptoms – key to diagnosis









Senior Løken Syndrome

- Nephronophthisis
- Retinitis pigmentosa
- Situs inversus

ADPKD is multi-system disease

The most important extra-renal manifestations:

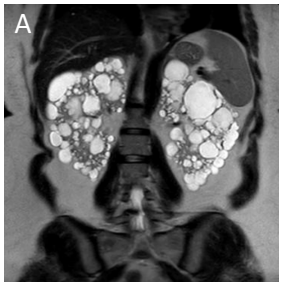
extrarenal cysts

diverticulosis

heart valve defects

vascular anomalies
(e.g. intracranial aneurysms)

renal manifestations



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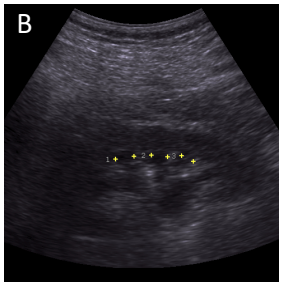
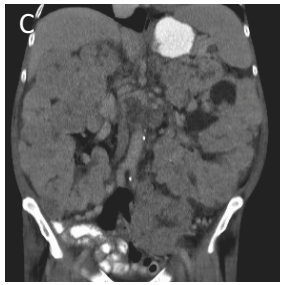
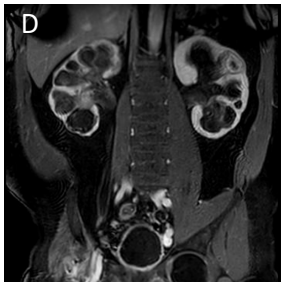
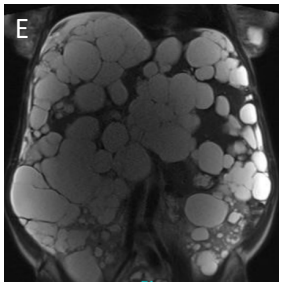
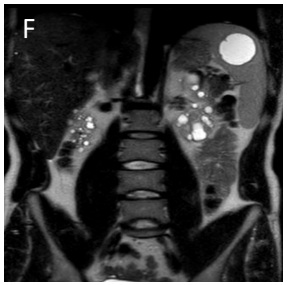


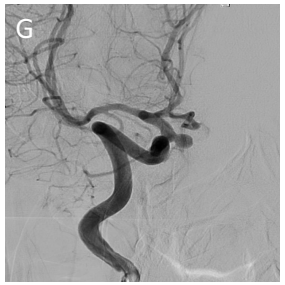


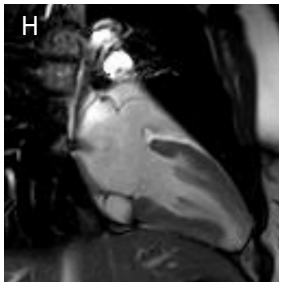


extrarenal manifestations of ADPKD









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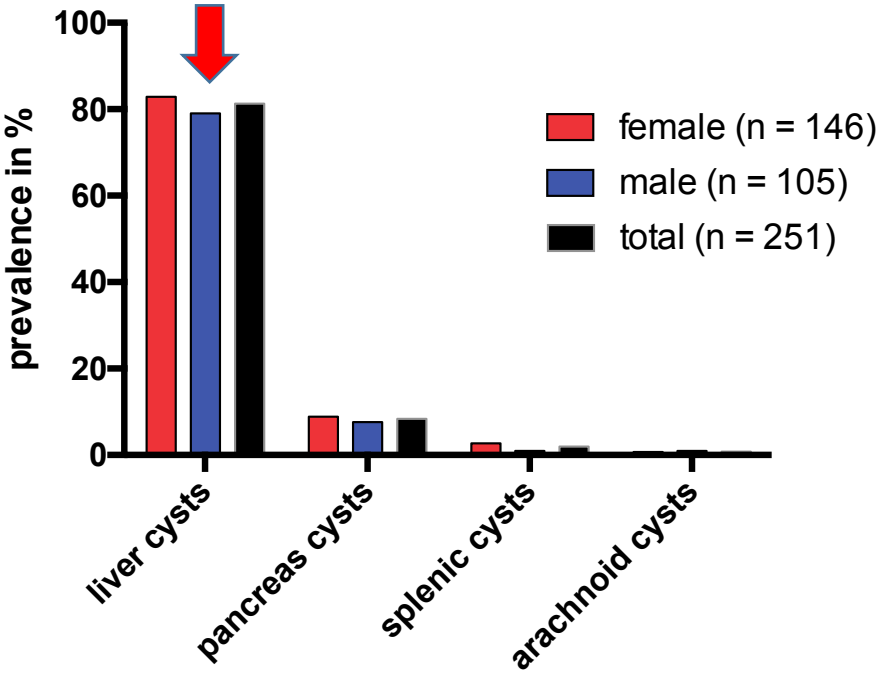
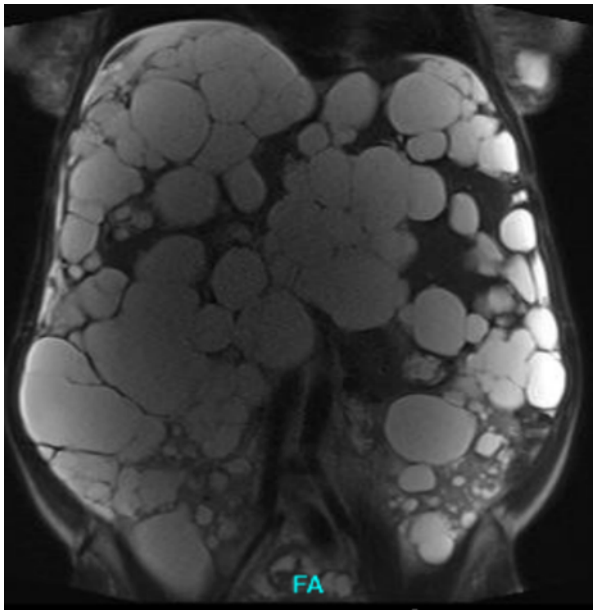
Müller and Benzing CKJ 2018

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

extrarenal cysts



Polycystic liver disease

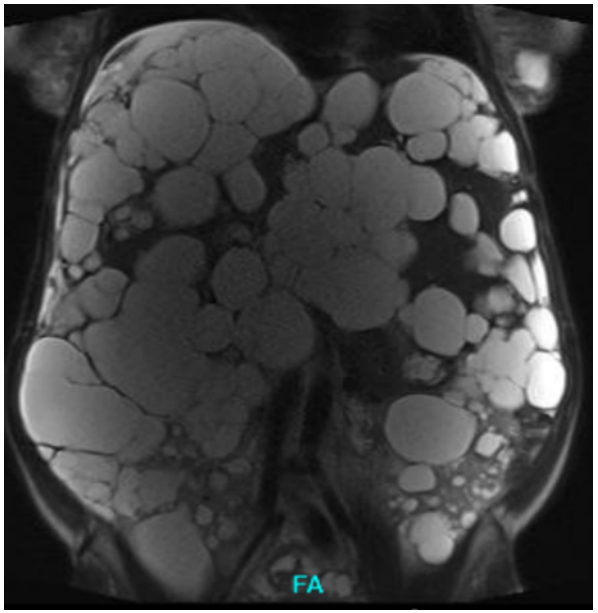


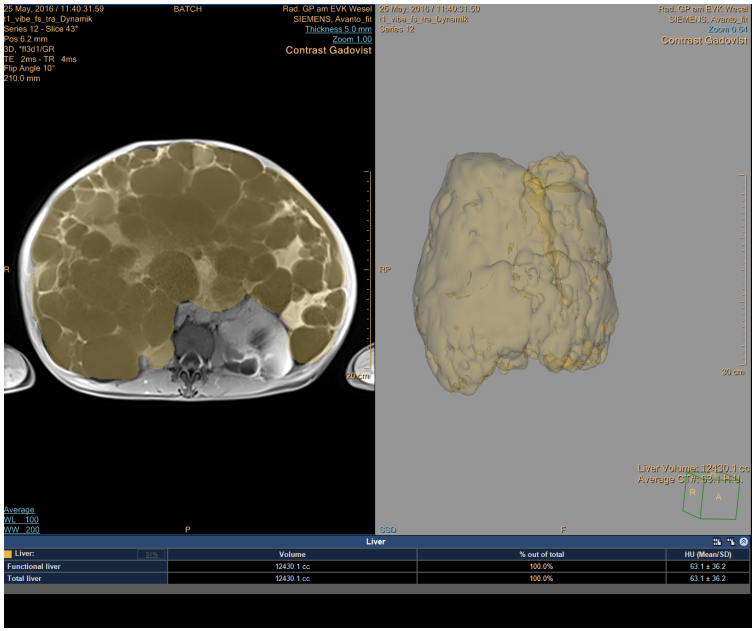
Bilder: T. Persigehl, Radiologie, Uniklinik Köln

young woman, 34 years
massive PLD with compression of heart, lung and inferior vena cava

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

Polycystic liver disease



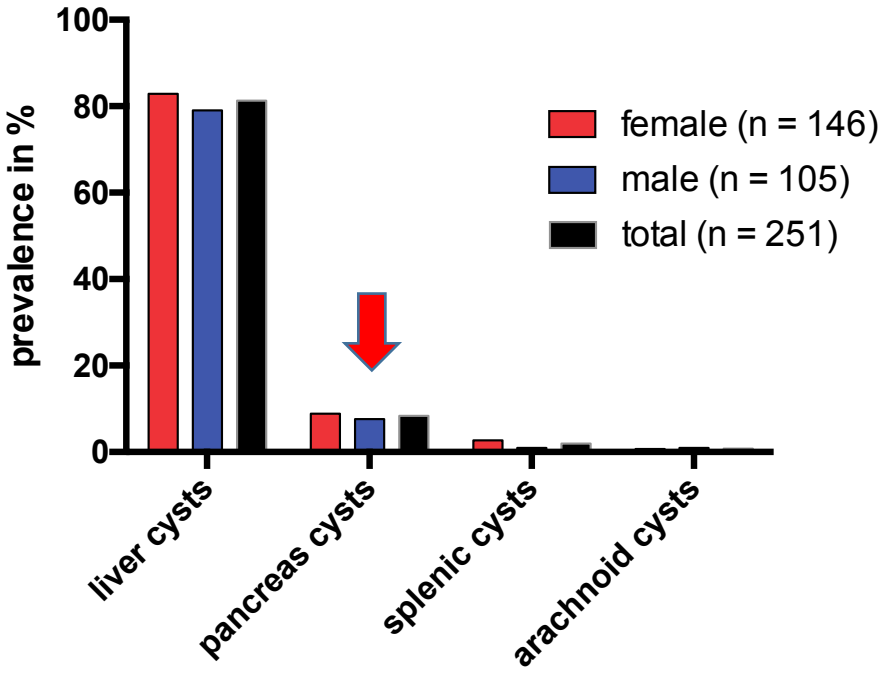


- liver volume 12 liters!
  (normal: appr. 1.5 liters)

images: T. Persigehl, Radiologie, Uniklinik Köln

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

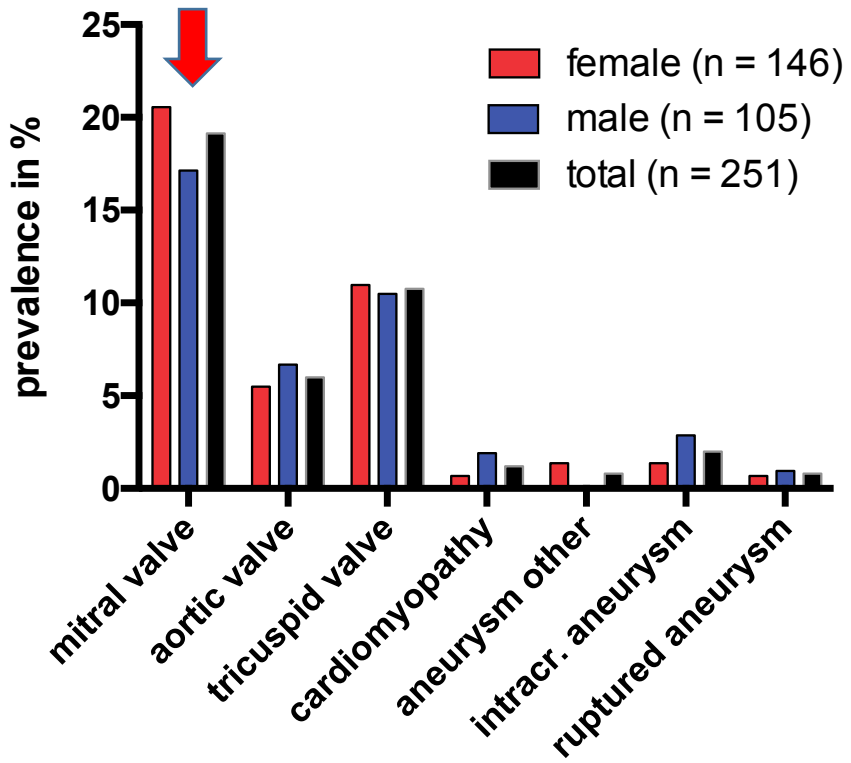
extrarenal cysts



usually pancreatic cysts are an uncomplicated manifestation of ADPKD

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

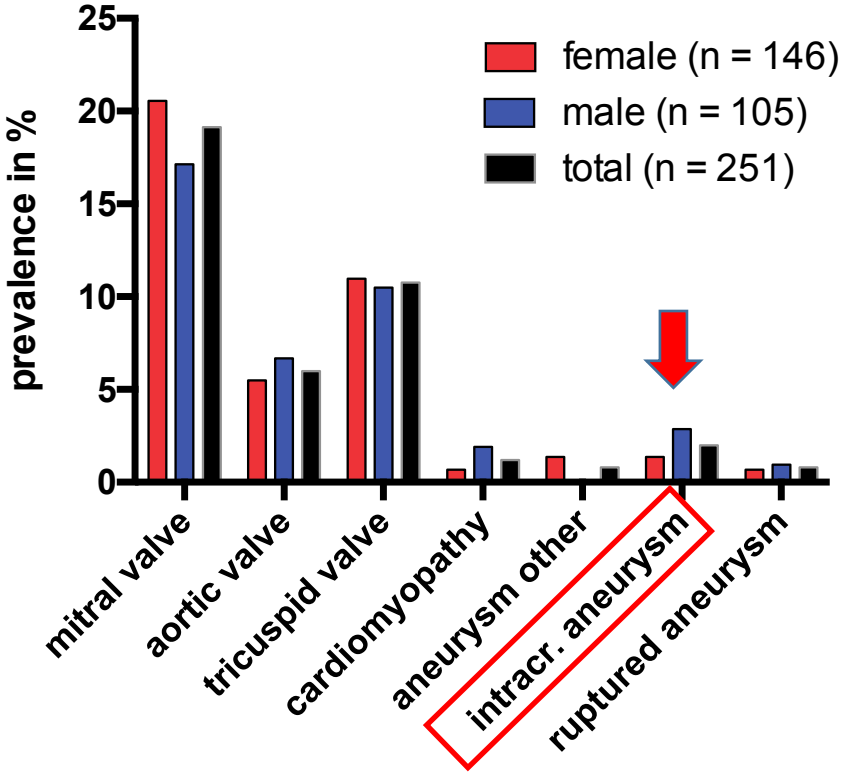
cardiovascular manifestations



1 in 2-3 patients has a cardiac valve defect → echocardiography

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

cardiovascular manifestations



in cohorts with general screening prevalence approximately 10 %, Sanchis et al. CJASN 2019

The risk of intracranial aneurysms (ICA):

We generally offer, although do not necessarily recommend, screening to adult ADPKD patients and discuss with them potential risks of screening versus the risks of rupture of an undetected aneurysm.

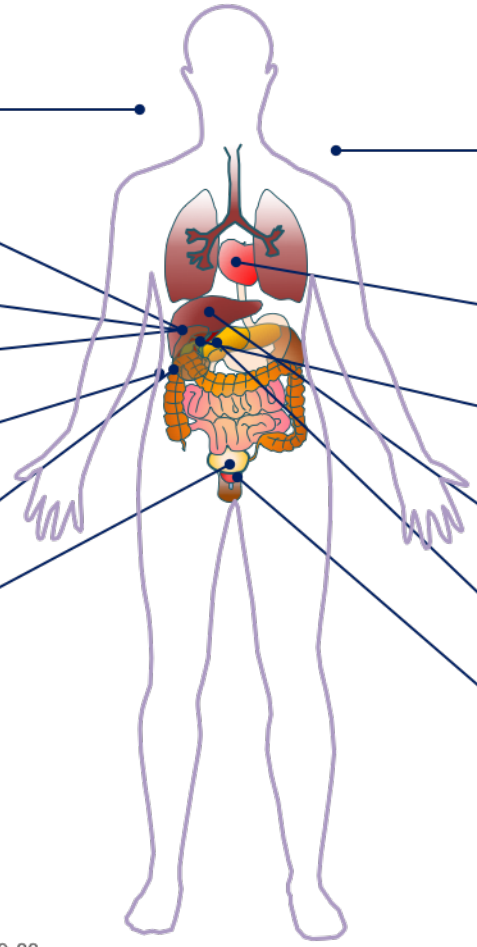
Screening is recommended in high risk patients:

1) Warning symptoms (headache)
2) **Previous rupture, positive family history**
3) High-risk occupation in which loss of consciousness would place the patient or others at extreme risk
4) patient preference
5) Prior to major surgery

ADPKD is a multisystem disease

Renal Manifestations

- Hypertension
- Haematuria
- Polyuria
- Nocturia
- Palpable kidneys
- Kidney stones
- Abdominal/flank pain
- Hernia
- Renal artery/vein occlusions
- Recurrent UTIs



Extra-renal Manifestations

- Intra-cranial aneurysms
- Seminal vesicle, dura, arachnoid cysts
- Vascular dissections
- Valvular heart disease
- Dilated cardiomyopathy
- Pericardial infusion
- Bile duct dilation
- Diverticulosis
- Hepatic cysts
- Pancreatic cysts
- Intraductal papillary mucinous neoplasms
- Male infertility

1. Halvorson CR *et al.* (2010). *Int J Nephrol Renovasc Dis*. 3: 69-83.
2. Torres VE *et al.* (2009). *Kidney Int*. 76(2): 149-68.
3. Luciano RL *et al.* (2014). *Nephrol Dial Transplant*. 29(2): 247-54.

1 Epidemiology and genetics

2 Diagnostic strategies

3 systemic disease / differential diagnosis

4 Management / therapy

Management of ADPKD – state of the art

- sufficient fluid intake (urine volume > 3 l/d)
- limit salt intake (max. 5-7g /d)
- healthy diet (e.g. mediterranean diet)
- physical activity, avoid overweight
- blood pressure control ! (HALT-PKD trial, Schrier NEJM 2014) (our approach: < 120 / 80 mmHg in young patients with maintained eGFR)

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- **moderate coffee consumption, no smoking**

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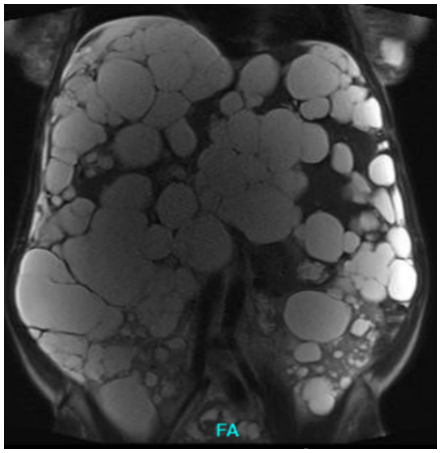
- **estrogen-free/-limited contraception**



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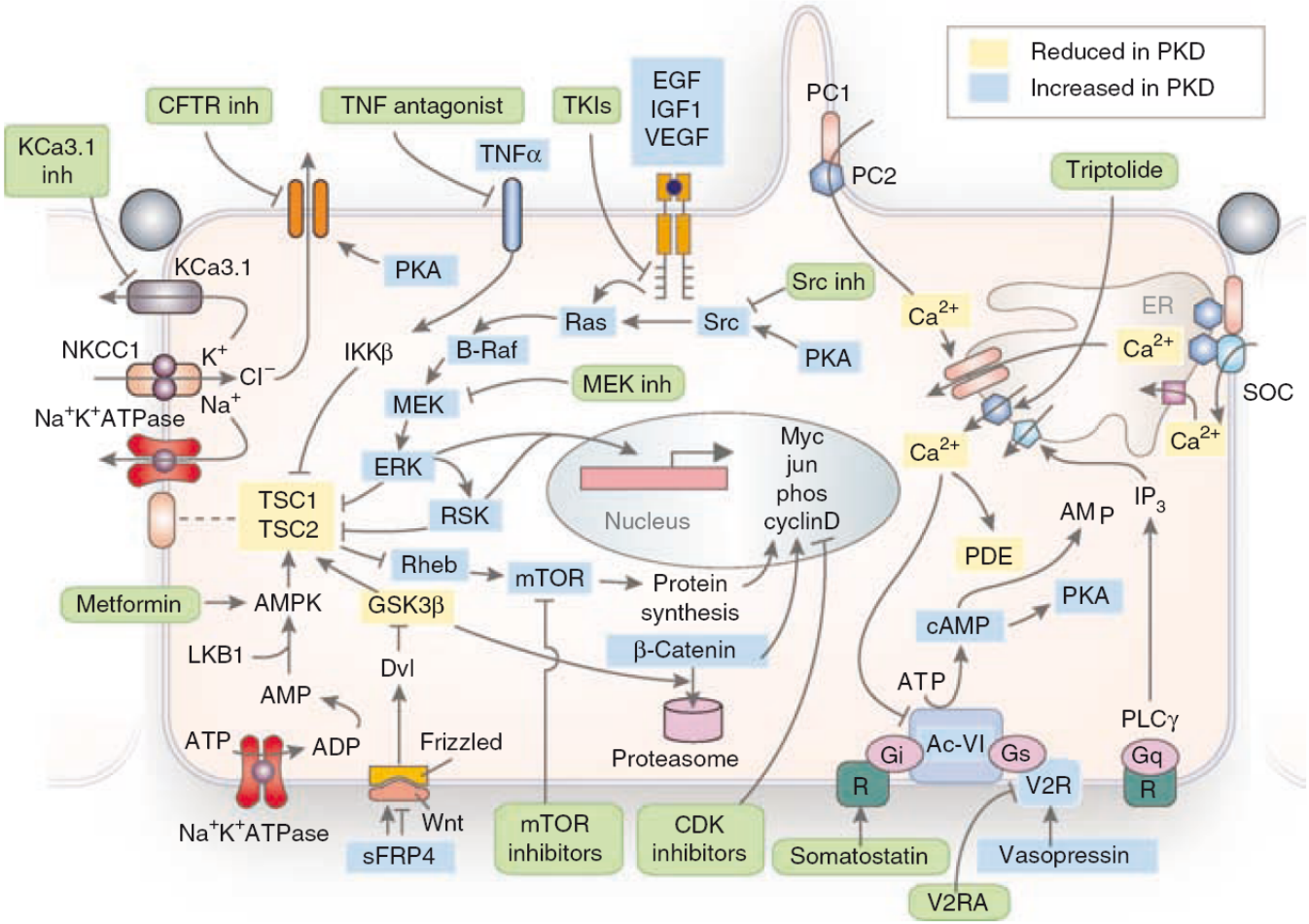
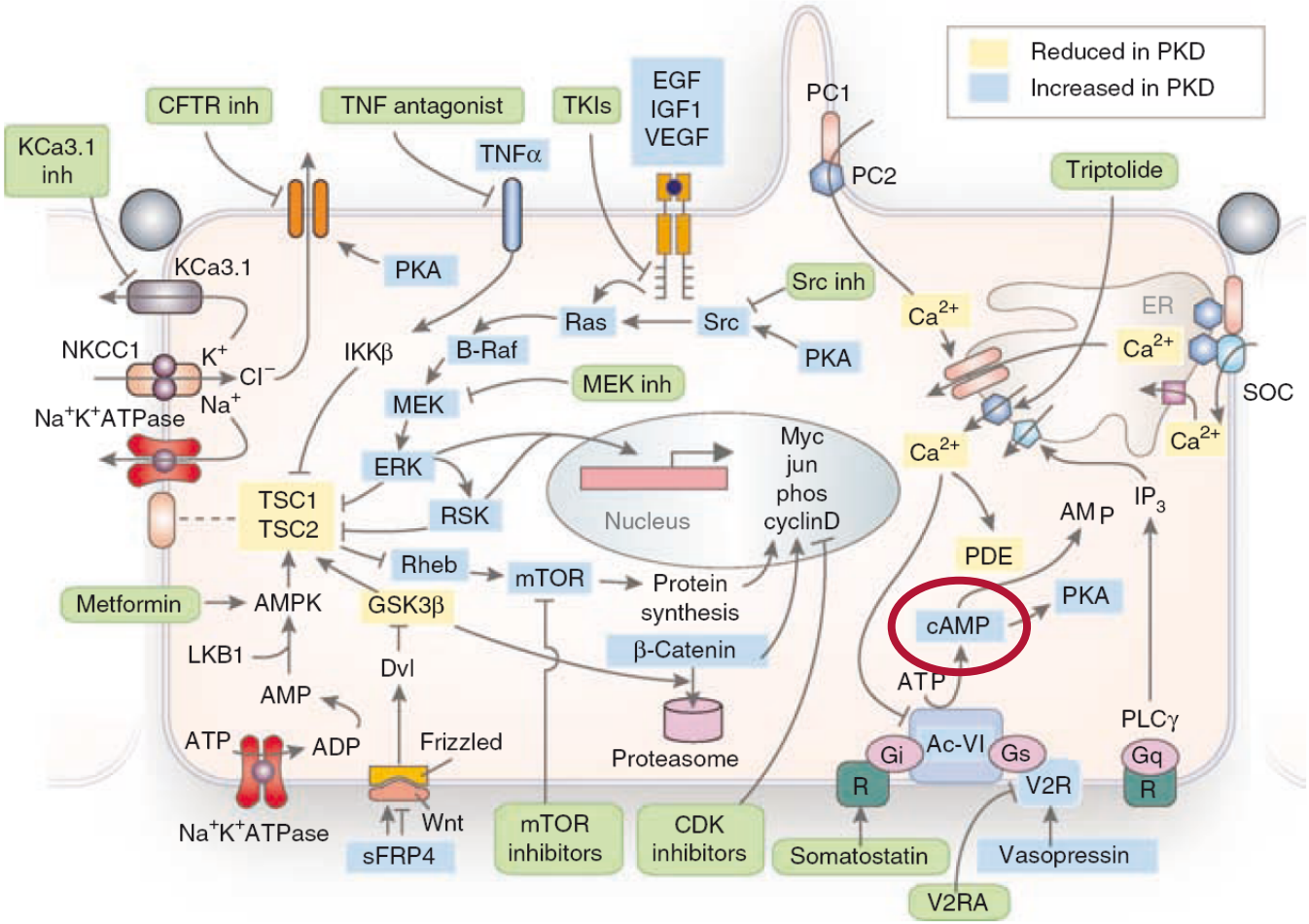
Targeted therapies ?



Torres, Harris, Kidney Int. 2009; 76,149–168



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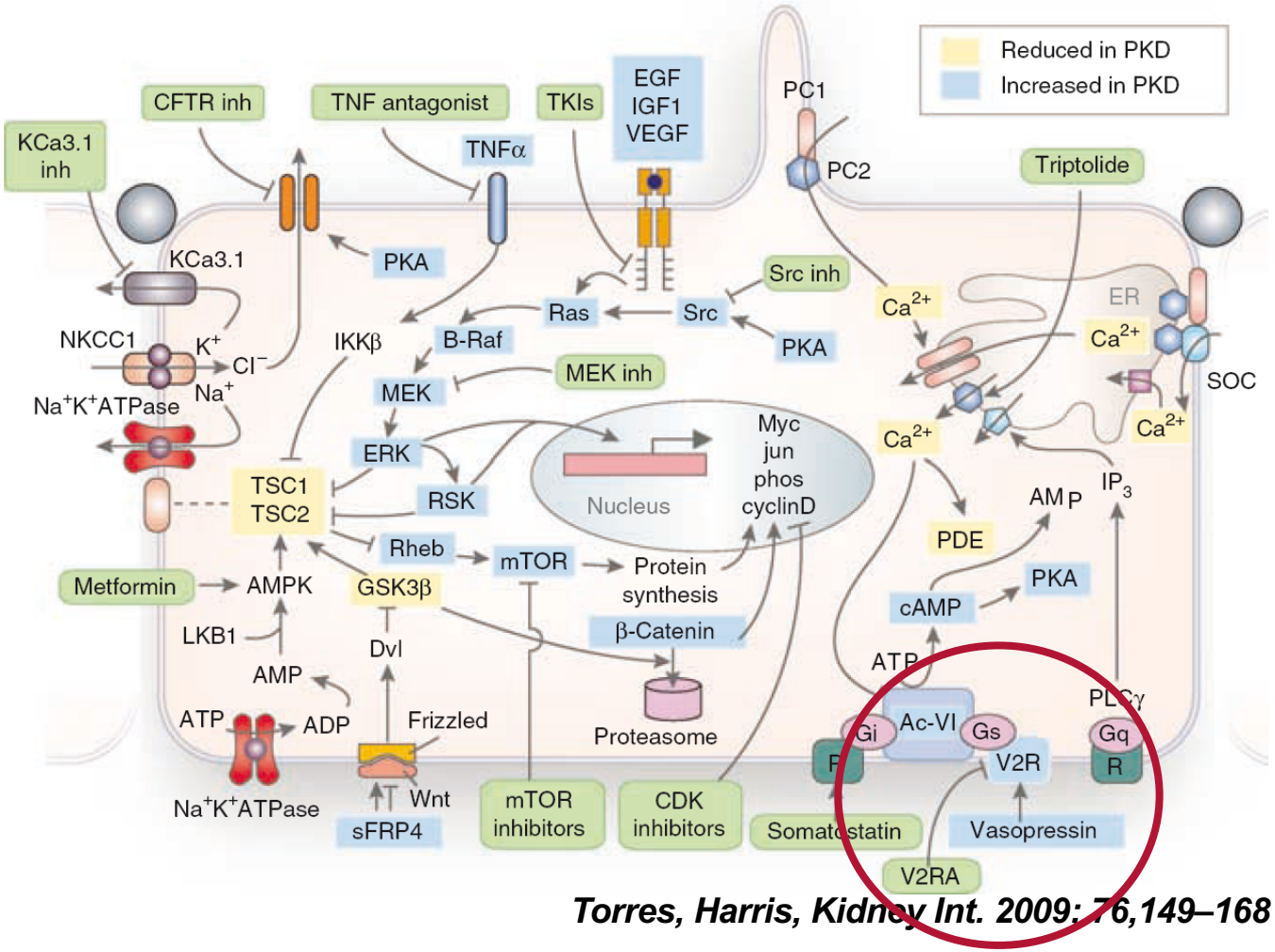


Torres, Harris, Kidney Int. 2009; 76,149–168

The NEW ENGLAND JOURNAL of MEDICINE

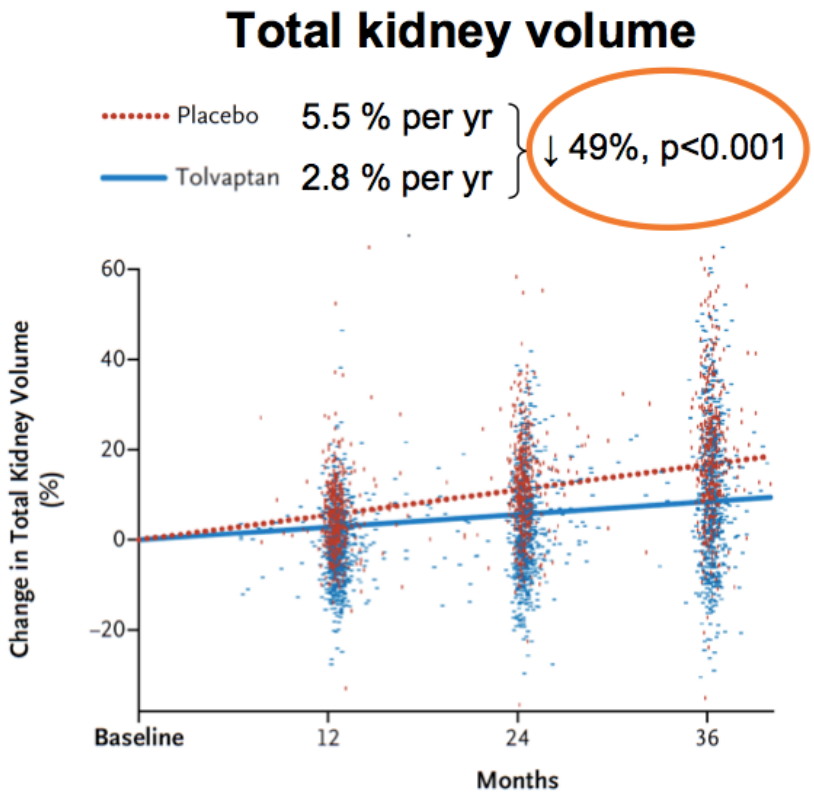
ORIGINAL ARTICLE

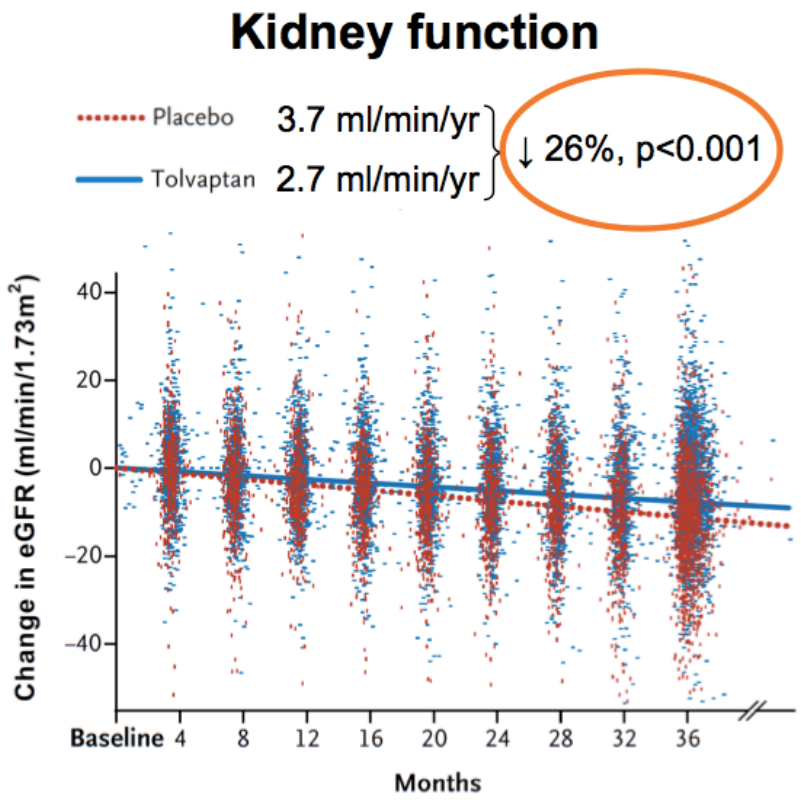
Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease

Vicente E. Torres, M.D., Ph.D., Arlene B. Chapman, M.D.,
Olivier Devuyst, M.D., Ph.D., Ron T. Gansevoort, M.D., Ph.D.,
Jared J. Grantham, M.D., Eiji Higashihara, M.D., Ph.D., Ronald D. Perrone, M.D.,
Holly B. Krasa, M.S., John Ouyang, Ph.D., and Frank S. Czerwiec, M.D., Ph.D.,
for the TEMPO 3:4 Trial Investigators*

Torres et al., N Engl J Med. 2012; 367, 2407-18

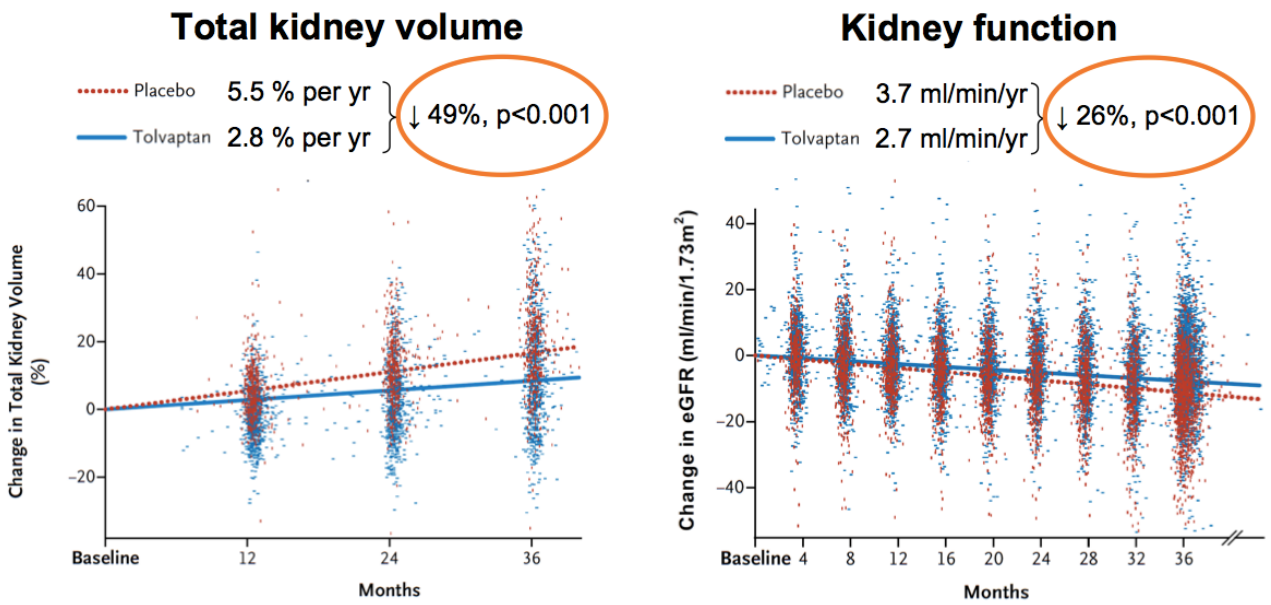
TEMPO 3:4 trial – state of the art





Torres et al. (2012) N Engl J Med, 363, 20;367, 2407-18

TEMPO 3:4 Trial
State of the art

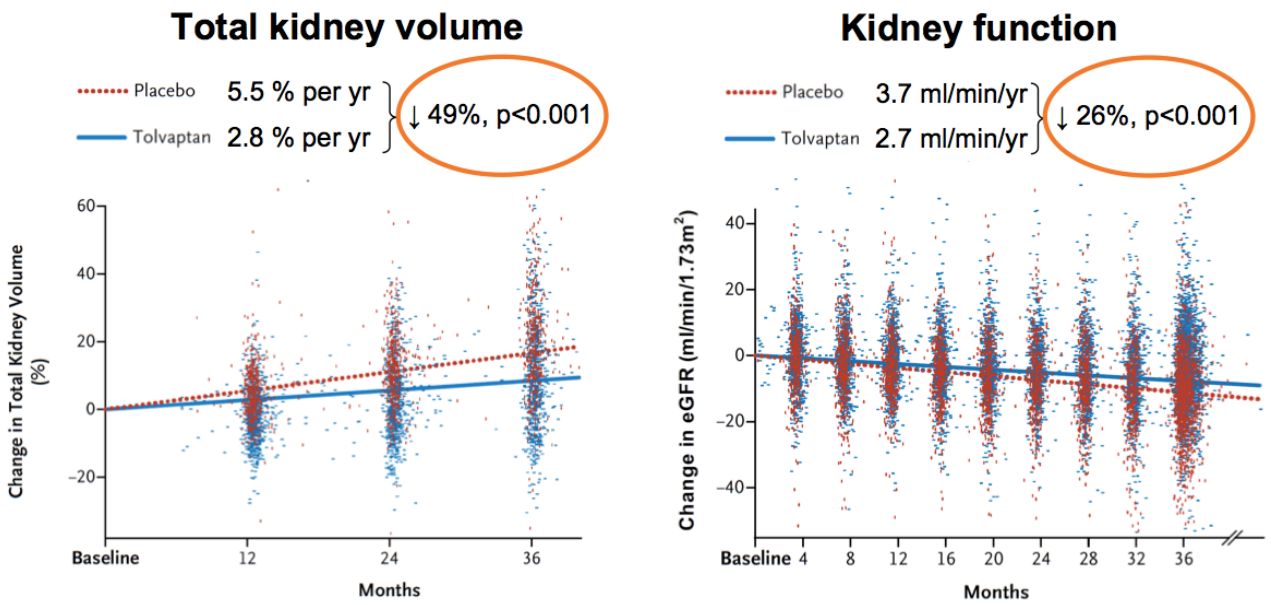


Torres et al. (2012) N Engl J Med, 363, 20;367, 2407-18

REPRISE confirms efficacy in later-stage disease (up to 55 yrs und CKD stage G4)

Torres et al. N Engl J Med. 2017 Nov 16;377(20):1930-1942.

TEMPO 3:4 Trial
State of the art



Torres et al. (2012) N Engl J Med, 363, 20;367, 2407-18

EMA: Tolvaptan is approved for an initiation of treatment in CKD stages 1-4 with evidence of rapidly progressing disease.

How can we judge disease progression in individual patients?

indicators of rapid disease progression

genotype

early urological symptoms

eGFR loss

TKV

family history

early arterial hypertension

indicators of rapid disease progression

genotype

early urological symptoms

eGFR loss

TKV

family history

early arterial hypertension

Pro-PKD Score ...

973 PKD patients from the Genkyst Cohort

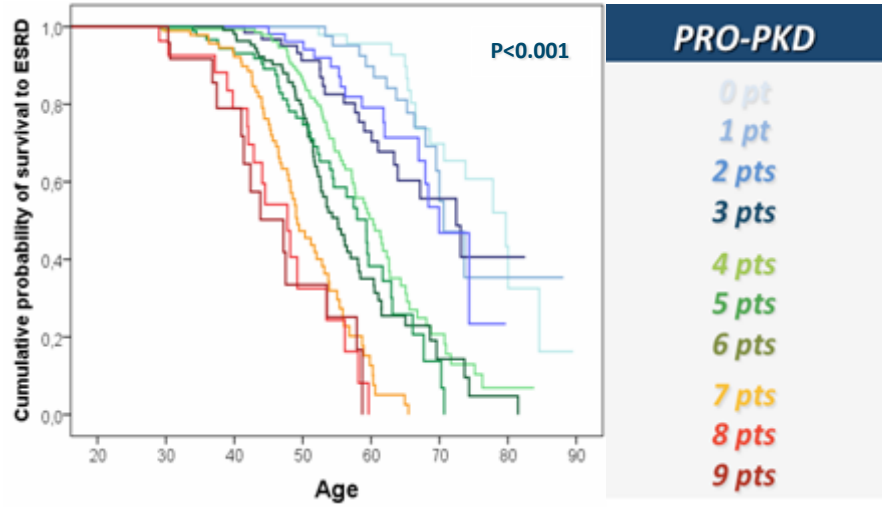
1- Multivariate analysis

Variable	Category	N	HR	0.95 CI	P Value
Gender	*Female*	541			
	Male	432	**1.55**	1.25-1.88	<0,001
Hypertension < 35 yrs	*No*	679			
	Yes	214	**2.11**	1.71-2.61	<0,001
At least one urological complication < 35 yrs	*No*	734			
	Yes	239	**1.73**	1.38-2.18	<0.001
Mutation	*PKD2*	186			
	PKD1/Non-Truncating	239	**2.27**	1.57-3.28	0.002
	PKD1/Truncating	548	**4.75**	3.41-6.60	<0.001

2- The PRO-PKD score

Variable	Category	Pts
Gender	*Female*	**0**
	Male	**1**
Hypertension < 35 yrs	*No*	**0**
	Yes	**2**
At least one urological complication < 35 yrs	*No*	**0**
	Yes	**2**
Mutation	*PKD2*	**0**
	PKD1/Non-Truncating	**2**
	PKD1/Truncating	**4**
TOTAL		**0 to 9 points**

3- Renal survival according to PRO-PKD score



4- Internal validation:

- Bootstrap resampling analysis
- Cross-validation

Cornec-Le Gall E *et al. J Am Soc Nephrol* 2015 doi:10.1681/ASN.2015010016.

indicators of rapid disease progression

genotype

early urological symptoms

eGFR loss

TKV

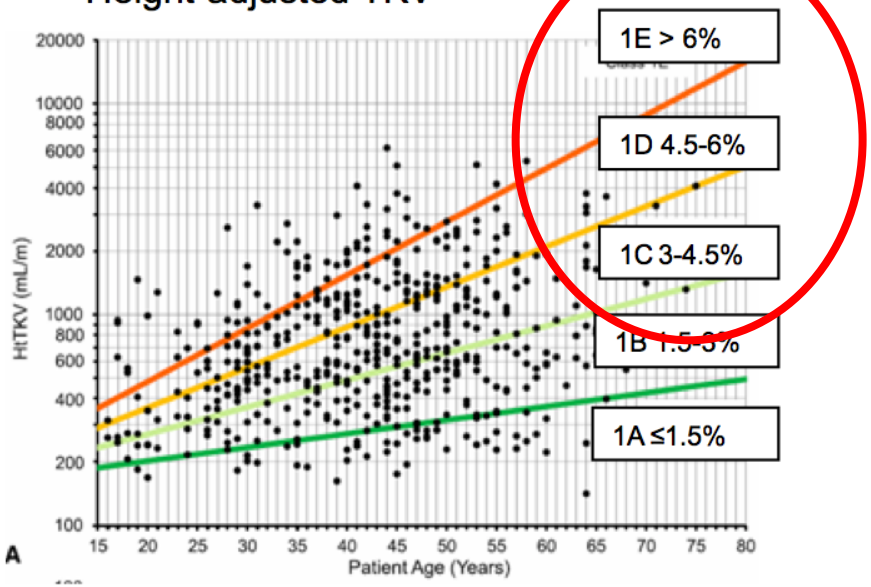
family history

early arterial hypertension

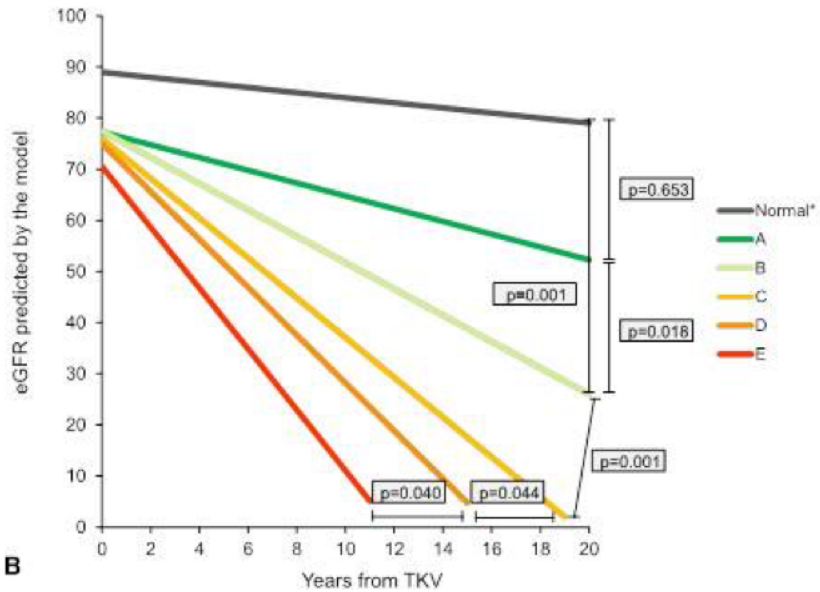
The Mayo Classification...

2- Stratification of the patients according to estimated kidney growth rate:

- Theoretical starting HtTKV of 150ml/m
- Height-adjusted TKV



3- multivariable longitudinal linear mixed-effects model based on:
sex, age, HtTKV, eGFR



Irazabal MV *et al. J Am Soc Nephrol* 2015;26:160–72.

https://www.mayo.edu/research/documents/pkd-center-adpkd-classification/doc-20094754

Ellipsoid equation is sufficient for the clinical determination of total kidney volume

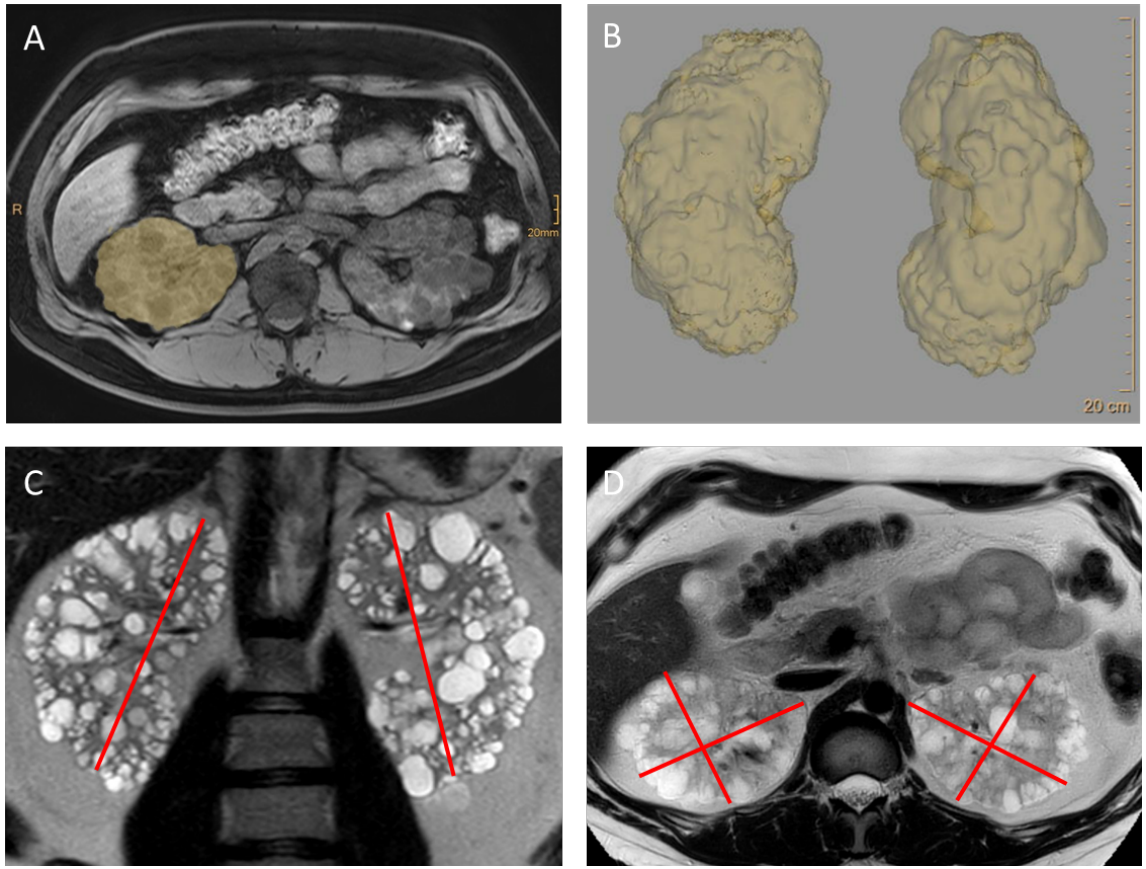
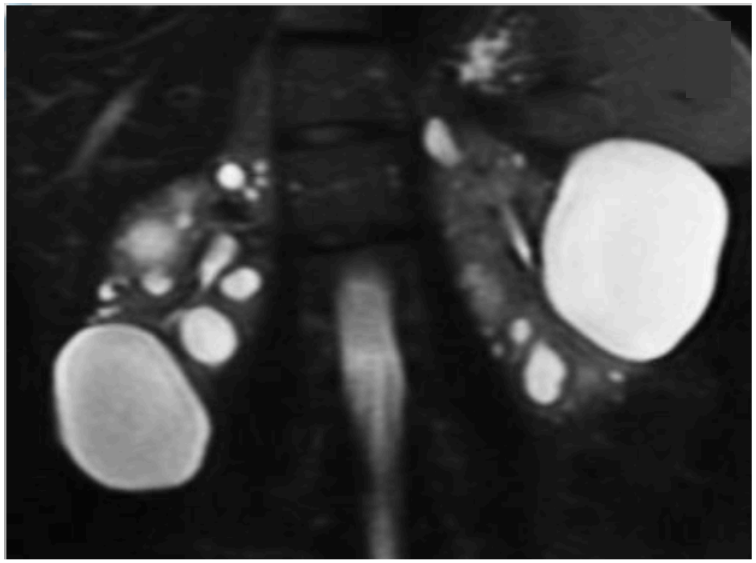


image from Müller et al. CKJ 2017

Irazabal et al. JASN 2015; 26: 160-72

But: mere volumetry is not enough, every image needs to be looked at by an ADPKD expert

Mayo Class 2



Irazabal et al. JASN 2015; 26: 160-72

What‘s important for patients taking tolvaptan?

side effects?

2 important points:
Polyuria and **potential hepatotoxicity**

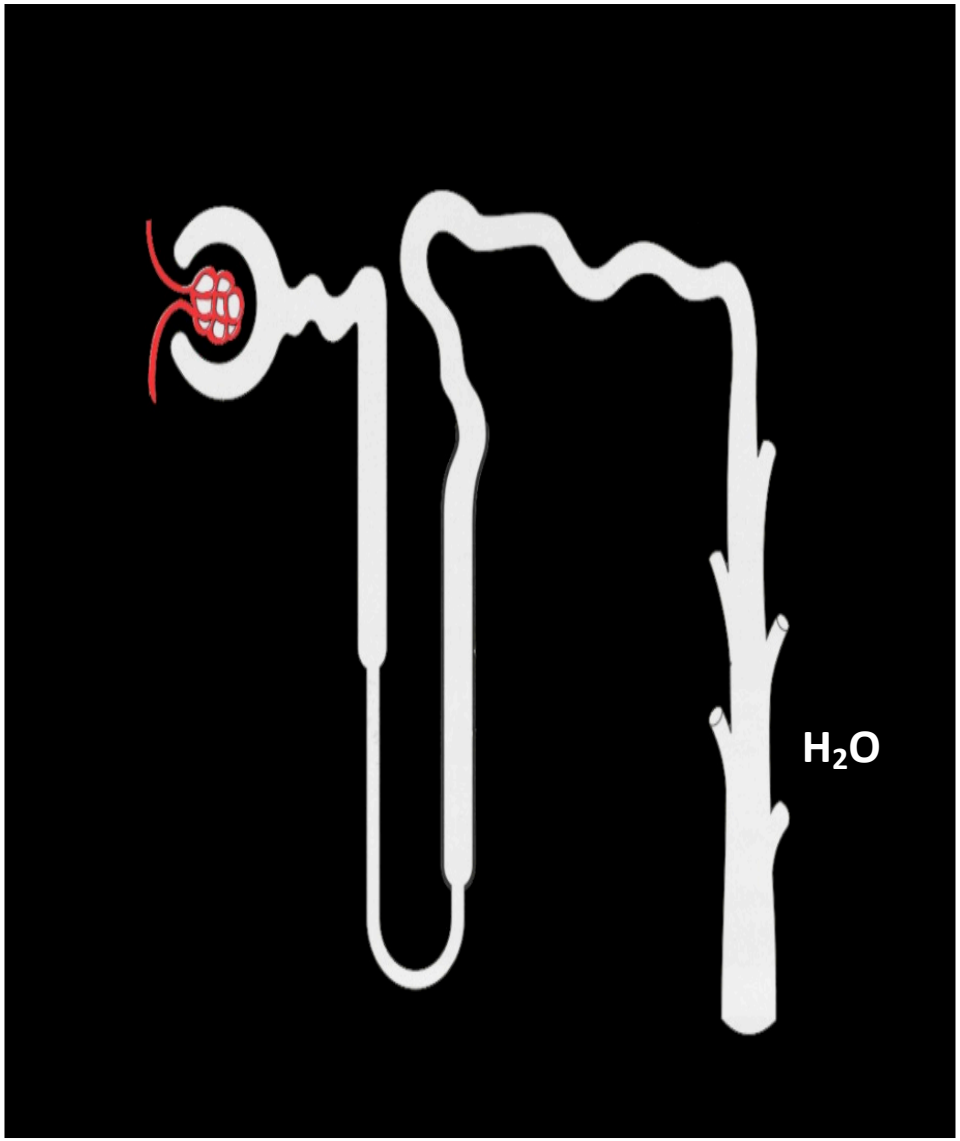
monitoring: liver enzymes 1x/month in the first 18 months; afterwards every 3 months

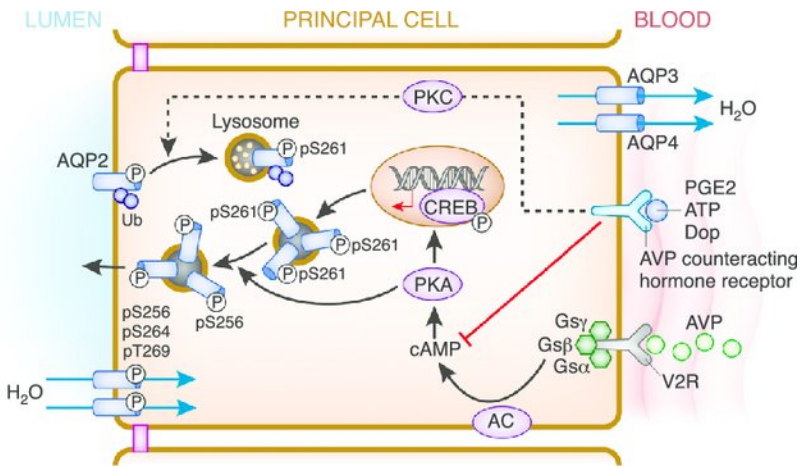
What‘s important for patients taking tolvaptan?

side effects?

2 important points:
Polyuria and potential hepatotoxicity

Vasopressin (ADH)-Signaling





Pearce et al. CJASN 2014

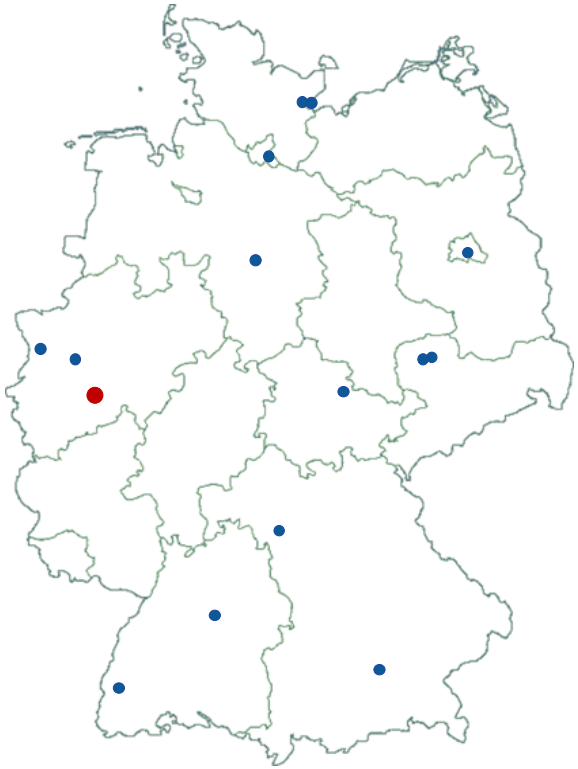
What‘s important for patients taking tolvaptan?

- regular water intake is absolutely essential:
  always carry along a bottle of water
  do not wait too long until getting thirsty
  stop Tolvaptan in cases of dehydration,
  diarrhoe, vomitting, lacking access to water ...

- to be discussed with the patient:
  do not compensate the water deficit with
  calory-rich drinks (milk, soft drinks)

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

Participating centers



- Uniklinik Jena
- Praxisgem. Peschel Leipzig
- Uniklinik Leipzig
- Uniklinik Schleswig-Holstein
- RBK Stuttgart
- Uniklinik Würzburg
- Medizinische Hochschule Hannover
- Nierenzentrum und Dialyse Lübeck
- FGM Bad Krozingen

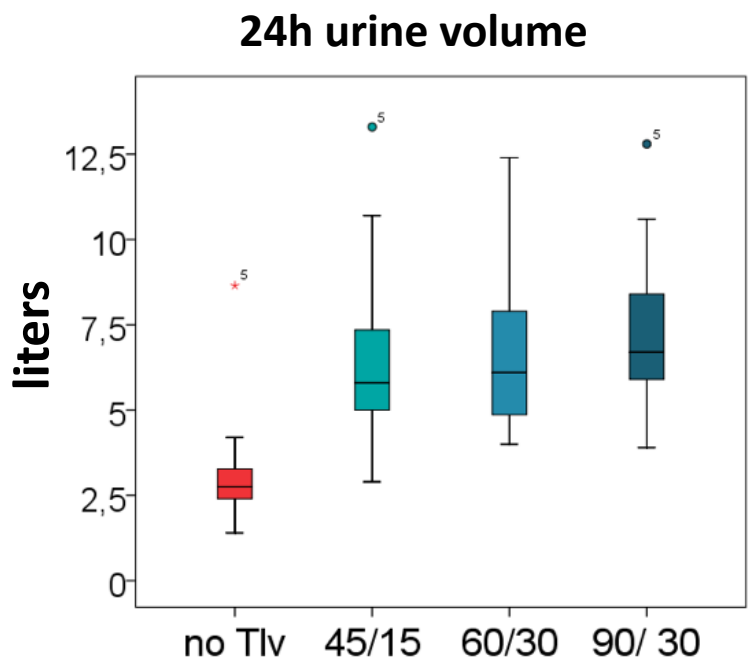
n = 771 (Stand August 2020)

Real-life urine volume...

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

Real-life urine volume...

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie



- 5-8 Liter urine volume in the majority of patients

unpublished data Uniklinik Köln

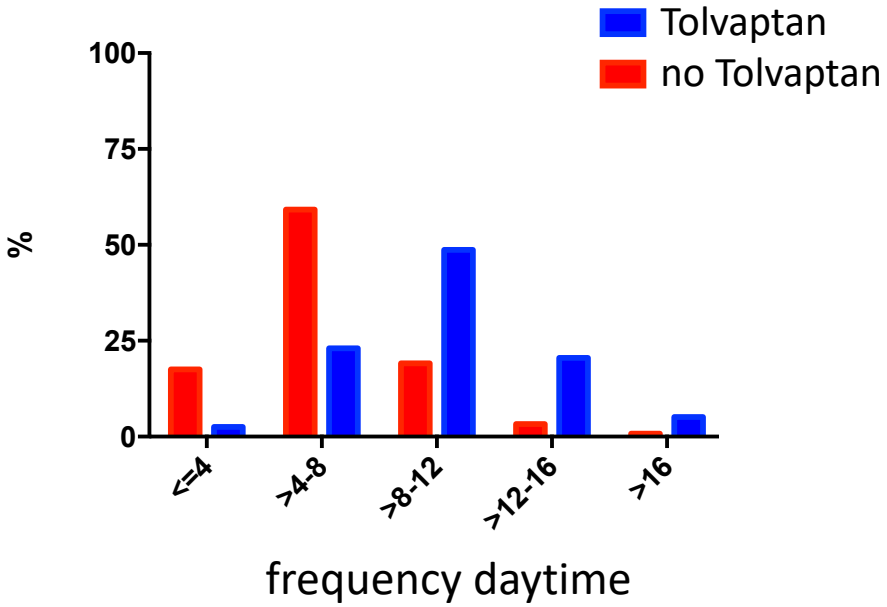
BUT: what does this mean for the patient?

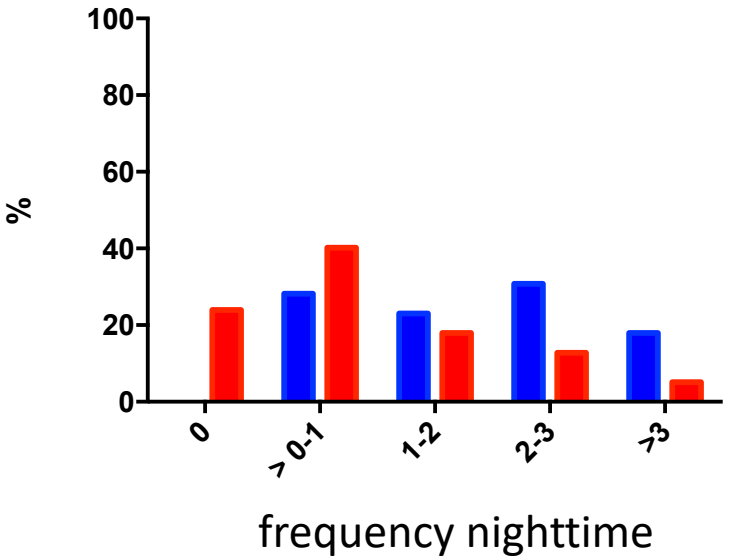
AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

BUT: what does this mean for the patient?

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

How many times do I have to go to the toilet ?





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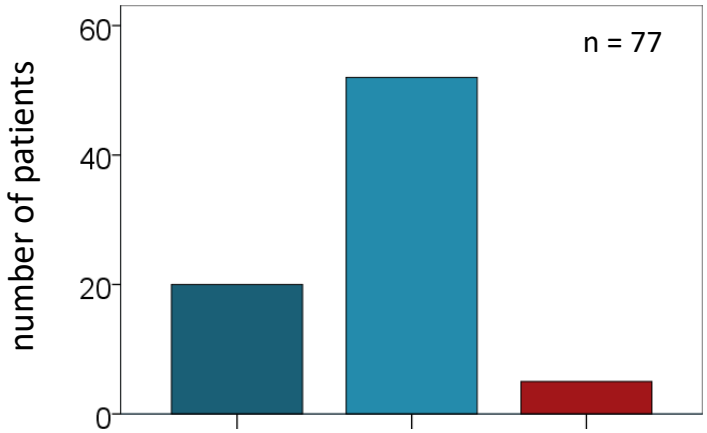
Feasibility in real life?

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

What would you tell to other patients?



Die treatment….

is no problem at all

is well feasible, but
requires some adaptation

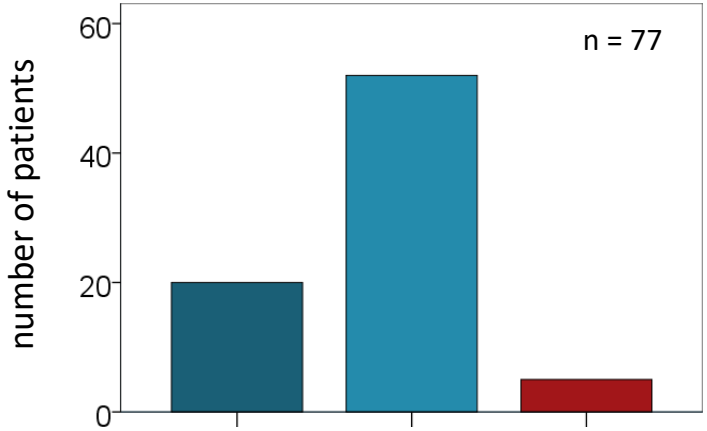
has a significant impact on everyday life

unpublished data Uniklinik Köln

Feasibility in real life?

AD(H)PKD
Zystennieren: Diagnose, Forschung, Therapie

What would you tell to other patients?



None of the participants would tell others not to try the treatment.

Die treatment….

is no problem at all

is well feasible, but requires some adaptation

has a significant impact on everyday life

unpublished data Uniklinik Köln

Update Kidney Week 2019

Quality of Life and Tolerability of Tolvaptan in Swiss ADPKD Patients
Abstract Kidney Week 2019 Anderegg et al.

- 28 patients on tolvaptan
- 1 year after start both mental and physical QoL were not influenced by tolvaptan

Kidney Medicine Original Research

Quality of Life in Autosomal Dominant Polycystic Kidney Disease Patients Treated With Tolvaptan

Manuel A. Anderegg, Nasser A. Dhayat, Grit Sommer, Mariam Semmo, Uyen Huynh-Do, Bruno Vogt, and Daniel G. Fuster

Conclusion for the real-life setting:

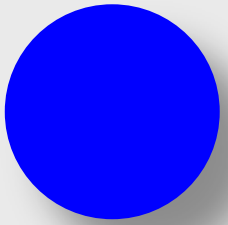
Tolvaptan ...

- **urine volume is as high as expected**
  → 1x per hour to the bathroom during the day
  → 2-3 x nocturia

- **however, the therapy is feasible in the real-life setting**
  → ~70 % continuation in the longer term

- **uptitration to 90/30 mg can (and should) be performed without a major increase in urine vol.**

Conclusion for the real-life setting:



Tolvaptan is the first targeted therapy...

BUT:

→ ADPKD is a multisystem disease!

→ Tolvaptan only slows down the loss of kidney function.

Conclusion:

1) **Supportive measures are still important**
2) **New therapies urgently needed**

AD(H)PKD

Zystennieren: Diagnose, Forschung, Therapie

ADPKD – new targeted approaches

- **combination therapies**, e.g. somatostatin analogs and –vaptans
- **repurposing of drugs**: **statins, metformin,** TKI, CFTR correctors, **glucosylceramide synthase inhibition, bardoxolone**….
- **dietary interventions**: e.g. **ketogenic diets,** limiting oxalate / phosphate intake, citrate supplementation….
- **Metabolic reprogramming**: 2-DG…
- phosphodiesterases and PKA as drug targets (to lower cAMP)
- niacinamide, vitamin K3....

ADPKD – new targeted approaches

2021

- **combination therapies**, e.g. somatostatin analogs and –vaptans
- **repurposing of drugs**: **statins, metformin,** TKI, CFTR correctors, **glucosylceramide synthase inhibition, bardoxolone**….
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- **Metabolic reprogramming**: 2-DG…
- phosphodiesterases and PKA as drug targets (to lower cAMP)
- niacinamide, vitamin K3....

end of 2023
STAGED-PKD
FALCON

several pilot
trials running,
first results
2021-2022

Question of a participant:

What's the role for treatments on the level of genes?

PKD
Familiäre Zystennieren e.V.

CRISPR/Cas9?


WHAT IS GENE
THERAPY
Lorem ipsum dolor sit amet, consectetur adipiscing elit. Sed sit amet tempor lorem
Lorem ipsum dolor sit amet, consectetur adipiscing elit. Sed sit amet tempor lorem

CRISPR/Cas9?

- highly important approach for basic research, BUT: still many open questions, e.g.:
- side effects not clear yet (off-targets)
- targeted treatment of the kidney not established yet

Questions?

- questions about PKD ?
- therapy with tolvaptan ?
- ongoing trials ?

telephone: 0221-478-3439
Email: nephrologie-adpkd@uk-koeln.de

Next Webinars

ESPN/ERKNet Educational Webinars on Pediatric Nephrology & Rare Kidney Diseases

Date: **01 Dec 2020**

Speaker: **Olivia Boyer**

Topic: **Congenital Nephrotic Syndrome**

ERKNet/ERA-EDTA Advanced Webinars on Rare Kidney Disorders

Date: **15 Dec 2020**

Speaker: **Pierre Ronco**

Topic**: Membranous Nephropathy**

Subscribe the ERKNet and IPNA Newsletter and don‘t miss Webinars!