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POLYKYSTOSE RÉNALE AUTOSOMIQUE DOMINANTE: RECOMMANDATIONS KDIGO 2024

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DISCLOSURES

- *Participation à la préparation des KDIGO ADPKD 2024*

BACKGROUND

2014: Controversies Conference on ADPKD

http://www.kidney-international.org meeting report

see commentary on page 14

Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

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2024: First Clinical Practice Guideline For The Evaluation, Management, And Treatment of ADPKD

KDIGO Guidelines on ADPKD

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O Devuyst

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Evidence Review Team
Craig Gordon
Ethan Balk

KDIGO
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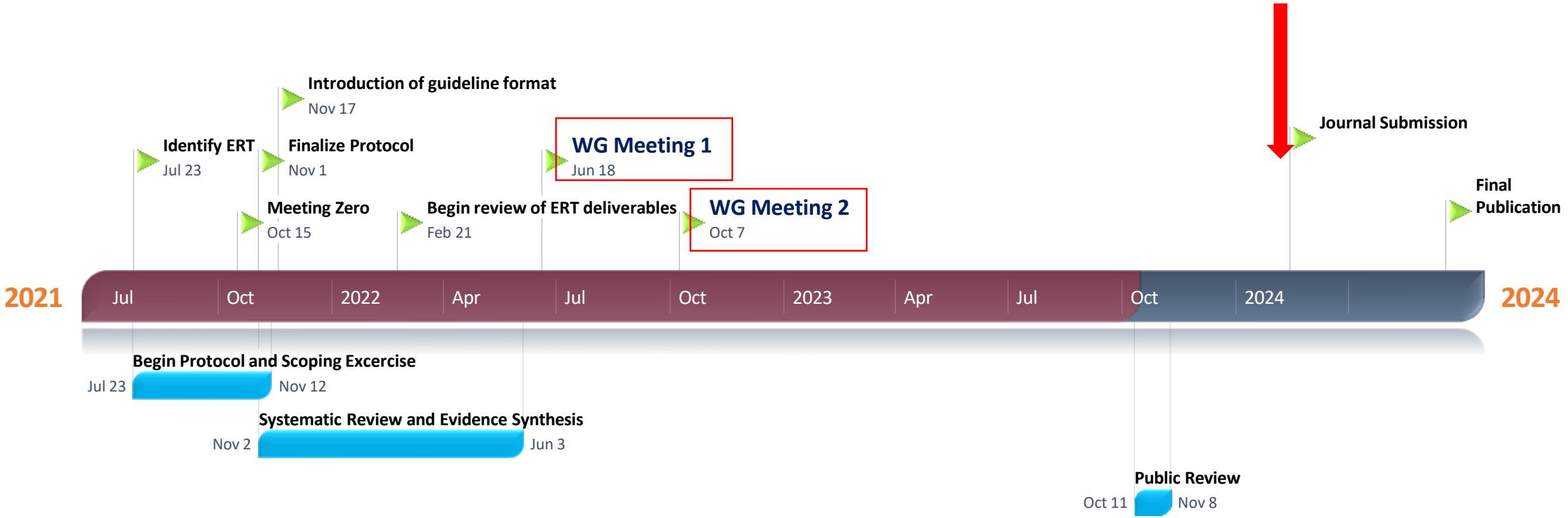
TIMELINE


Introduction of guideline format
Nov 17
Identify ERT
Jul 23
Finalize Protocol
Nov 1
WG Meeting 1
Jun 18
Journal Submission
Meeting Zero
Oct 15
Begin review of ERT deliverables
Feb 21
WG Meeting 2
Oct 7
Final Publication
2021
Jul
Oct
2022
Apr
Jul
Oct
2023
Apr
Jul
Oct
2024
2024
Begin Protocol and Scoping Excercise
Jul 23
Nov 12
Systematic Review and Evidence Synthesis
Nov 2
Jun 3
Public Review
Oct 11
Nov 8

Recommendation versus Practice point

Recommendations will be provided when

- Systematic review was conducted
- Ample evidence is available
- Evidence shows a clear preference for one action over the alternatives
- Consensus statements are supported with evidence and explicit discussion of the balance of benefits and harms, values and preferences will be necessary
- Application of guidance requires explicit discussion of values and preferences or on resource
- Guidance is always actionable
- The guidance is more useful displayed as or requires additional explanation in text

≠

Practice Points are used when

- No systematic review was conducted
- There is insufficient evidence
- Evidence was inconclusive (less evidence than required)
- The alternative option is illogical
- The guidance does not imply action for the physician
- Consensus statements providing guidance and guidance in the absence of evidence may consider benefits and harms but will not be explicitly discussed
- Guidance does not require an explicit discussion of values and preferences or of resource considerations, although is implied that these were considered
- The guidance may be more useful as a table/figure/algorithm

Grading Clinical Recommendations

- Strength of the evidence
  - Level 1: “We recommend ….”
  - Level 2: “We suggest …”

- Quality of the evidence
  - A: High Quality
  - B: Moderate Quality
  - C: Low Quality
  - D: Very Low Quality

KDIGO Guidelines on ADPKD

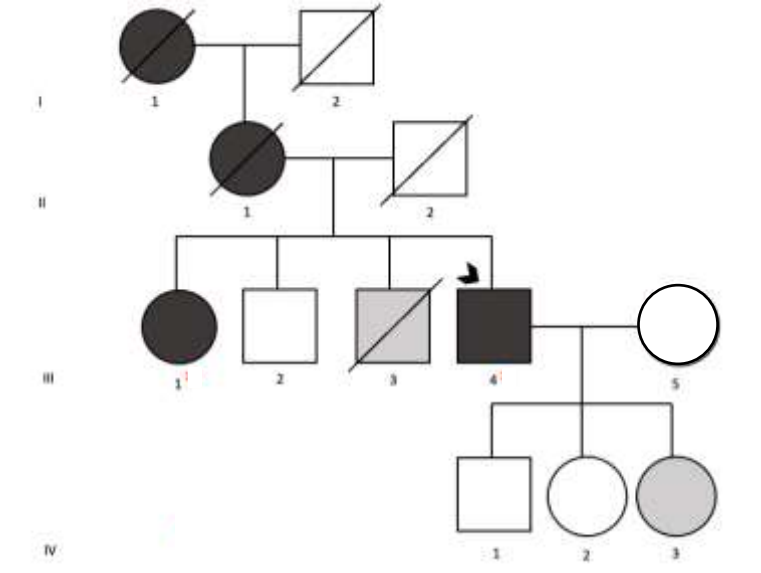
- ✓ Attention, ceci n'est pas la version définitive des recommandations
- ✓ Soumission pour publication fin mai / début juin

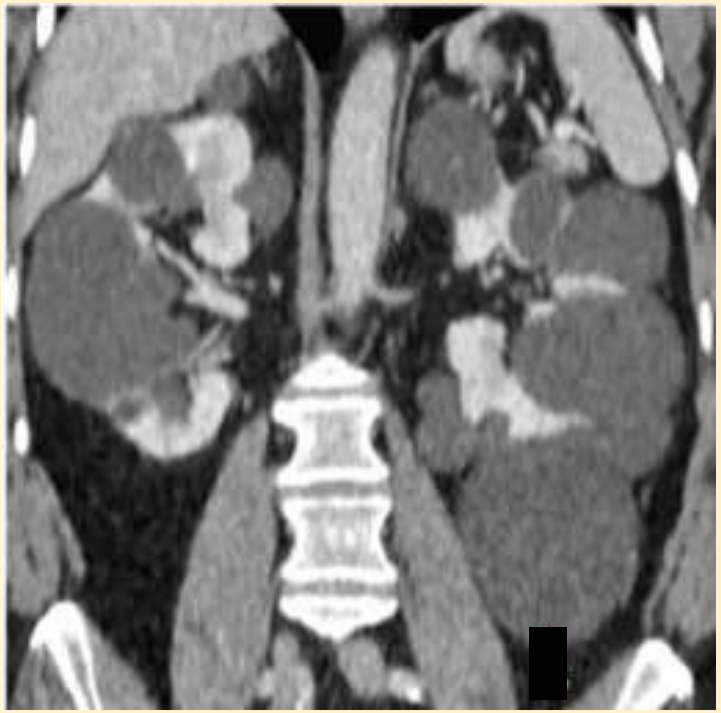
Nomenclature, diagnosis, prognosis and prevalence	Kidney manifestations	CKD progression, Kidney Failure and Kidney Replacement Therapies	Therapies to delay the progression of kidney disease	Polycystic Liver Disease
Intracranial aneurysms & other extrarenal manifestations	Lifestyle and psychosocial aspects	Pregnancy and reproductive issues	Pediatric issues	Approaches to the management of people with ADPKD

- ✓ 10 chapitres
- ✓ 230 pages (hors annexes et références)
- ✓ 35 à 40 recommandations
- ✓ > 230 « practice points »

Vignette Clinique n°1

- ✓ Homme de 65 ans
- ✓ Antécédents familiaux de polykystose
- ✓ DFG 57 ml/min/1.73m²
- ✓ HtTKV = 1336 ml/m





Prescririez-vous une analyse génétique chez ce patient?

Vignette Clinique n°1

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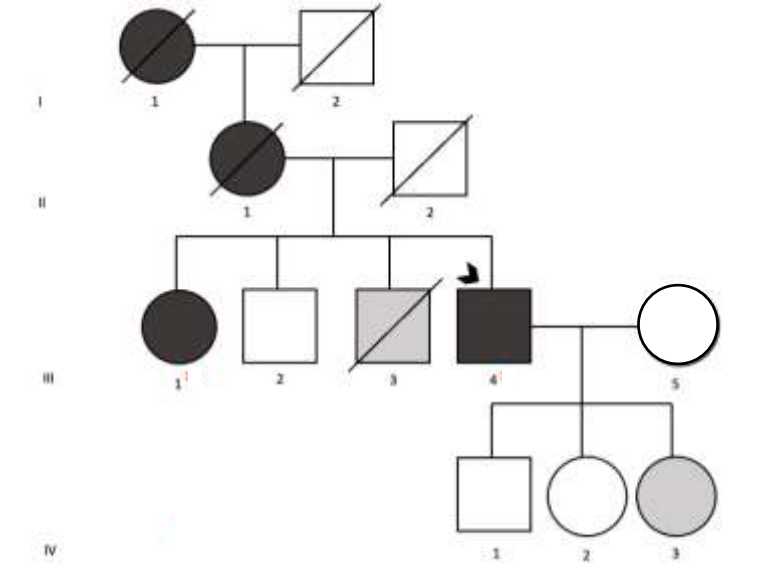

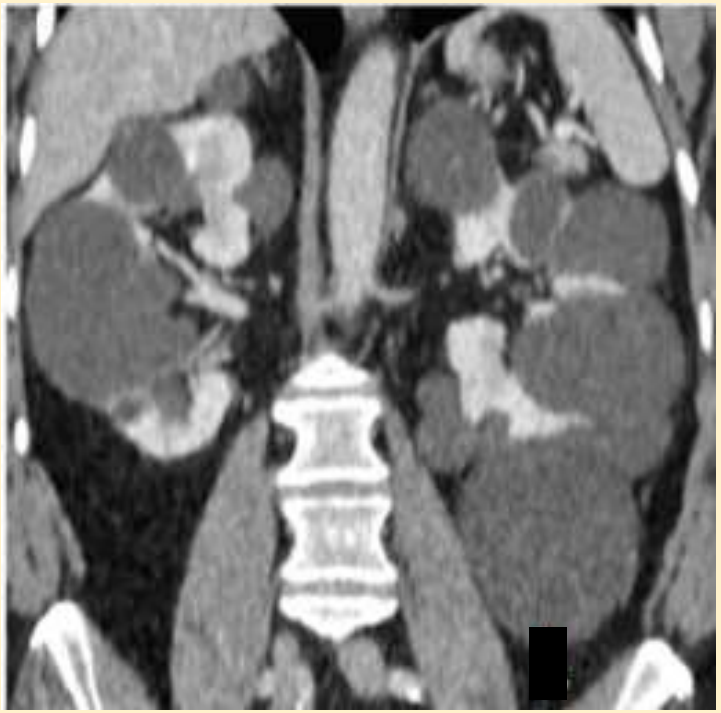

Identification d'un variant pathogène hétérozygote de *IFT140*

NOMENCLATURE

Warning: Unpublished Draft – Content Subject to Change

- Practice Point 1.1.1: In genetically-defined people with ADPKD, a common nomenclature should include the disease name followed by the gene name.

Gene		% of families	Designation
PKD1	Truncating	~48%	ADPKD-*PKD1*
	Non truncating	~19%	
PKD2		15%	ADPKD-*PKD2*
GANAB		0.5%	ADPKD-*GANAB*
DNAJB11		0.5%	ADPKD-*DNAJB11*
ALG9		0.5%	ADPKD-*ALG9*
ALG5		<0.5%	ADPKD-*ALG5*
IFT140		1-2%	ADPKD-*IFT140*
NEK8		<0.5%	ADPKD-*NEK8*
Genetically unresolved		~5% (in case of typical presentation)	ADPKD
ALG6		<0.5%	-
ALG8		~1%	-
PKHD1 (monoallelic)		~1%	-

Minor ADPKD genes with definitive to moderate evidence of disease involvement

Suspected monoallelic genes with limited evidence or not assessed

SITUATIONS WHERE GENETIC TESTING CAN CLARIFY THE DIAGNOSIS AND AID PROGNOSIS

Situation	Genetic findings
Limited number of cysts	Positive result can show a genetic origin (minor gene or hypomorphic allele)
Variable disease severity in a family	Mosaicism or biallelic/digenic disease can explain some extreme variability
Atypical imaging, including asymmetric or unilateral disease	Positive result can show a genetic origin (including mosaicism or minor gene involvement)
Discordance between structural (Mayo Imaging Classification) and functional (GFR) ADPKD severity	Genetic testing may reveal an atypical form of the disease or additional genetic or contributory factors, but non-genetic factors may also be important.
Negative family history	Positive result can show a genetic origin (*de novo* mutation can be proven)
Very early onset (VEO)-ADPKD	Biallelic disease may be found (Chapter 9)
Related living transplant donor (<30 years, especially if a few cysts detected)	Genetic testing can exclude the familial variant and test for other genetic causes
Family planning and preimplantation genetic diagnosis (PGD)	Obtaining a genetic diagnosis can aid family planning and enable PGD (Chapter 8)
All people	Genetics can confirm the diagnosis, identify the responsible gene and variant, and provide prognostic information

Vignette Clinique n°2

- ✓ Une femme de 34 ans est adressée en consultation de néphrologie pour la première fois.
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- ✓ Son DFG est de 92 ml/min/1,73m²

Prescrivez-vous des examens complémentaires à visée d'évaluation pronostique?
Si oui, lequel ou lesquels?

PROGNOSTICS

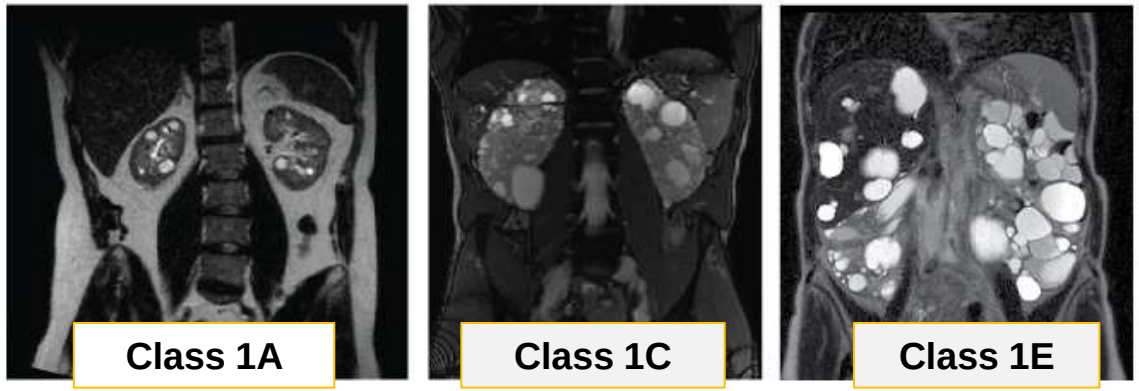
- **Recommendation 1.4.2.1:** We recommend employing the **Mayo Imaging Class (MIC)** to predict future declines in kidney function and the timing of kidney failure (*1B*).

- Practice Point 1.4.2.3: When using the MIC for prognostics, it is important to **exclude people with atypical imaging patterns (Class 2A and 2B)** as the predictions are unreliable in these people.

- Practice Point 1.4.2.4: When using the MIC to predict future kidney function, it is important to **exclude people who have pathogenic variants in genes other than *PKD1* or *PKD2*** as the predictions are unreliable in these people.

- Practice Point 1.4.2.8: The **Predicting Renal Outcome in Polycystic Kidney Disease [PROPKD]** Score can aid the identification of people with rapidly progressive disease.

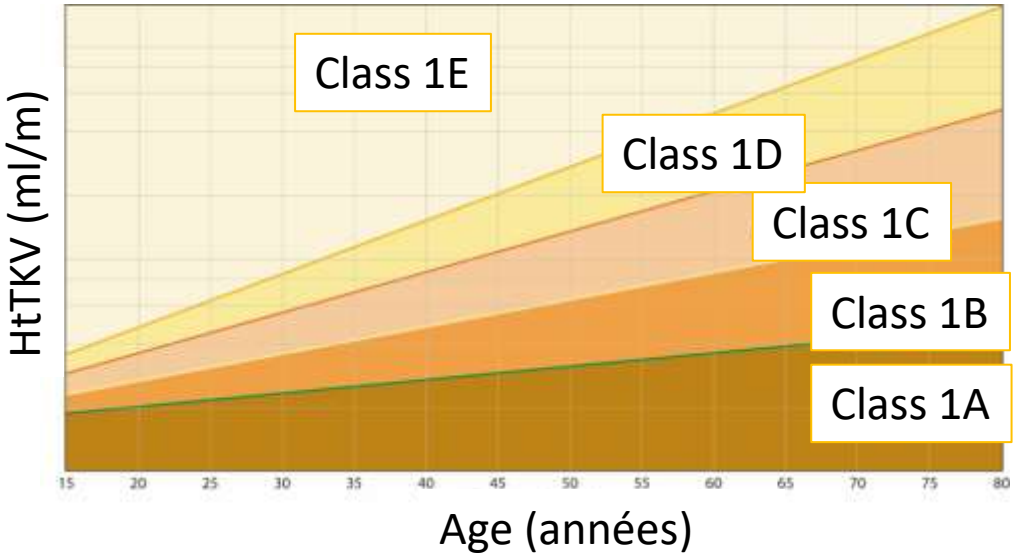
TYPICAL ADPKD : CLASS 1



Class 1A
Male, 33 years
eGFR=97 ml/min/1.73m²
HtTKV 222 ml/m
Class 1A

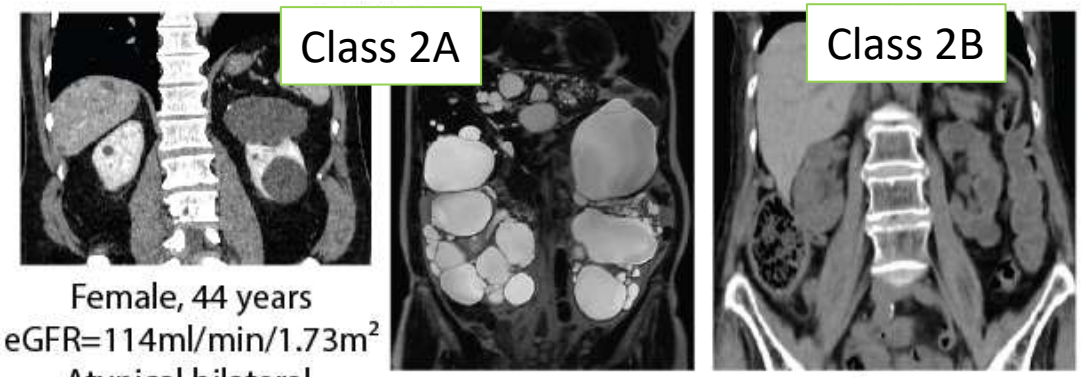
Class 1C
Male, 32 years
eGFR=112 ml/min/1.73m²
HtTKV 452 ml/m
Class 1C

Class 1E
Male, 30 years
eGFR=114 ml/min/1.73m²
HtTKV 1396 ml/m
Class 1E



Mayo Imaging Classification

ATYPICAL ADPKD : CLASS 2



Class 2A
Female, 44 years
eGFR=114ml/min/1.73m²
Atypical bilateral presentation

Female, 65 years
eGFR=55 ml/min/1.73m²
Lopsided kidneys

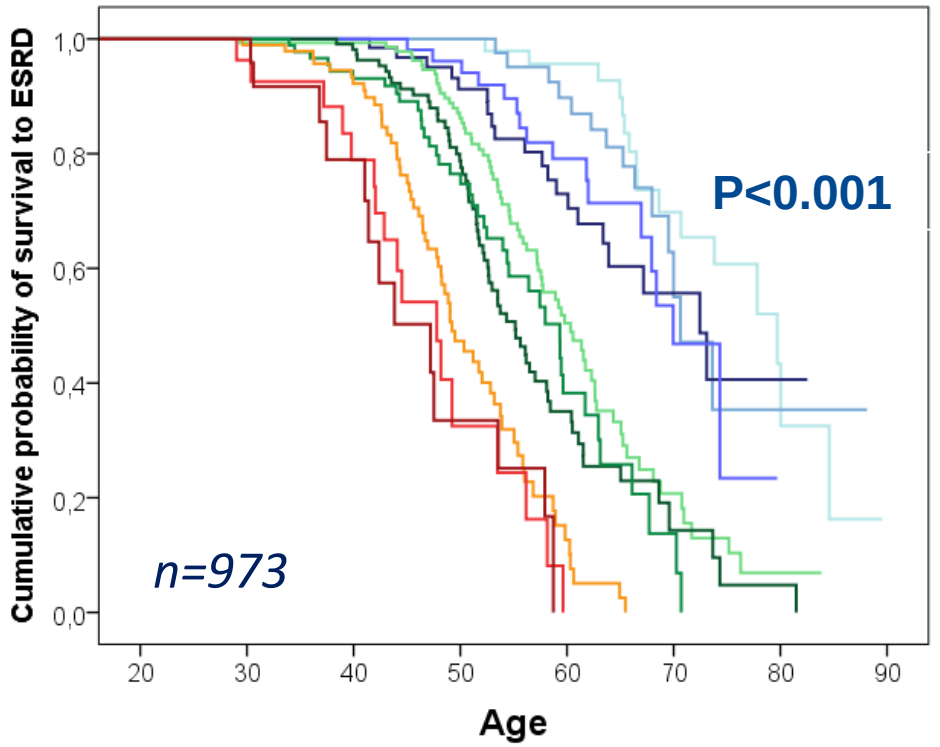
Class 2B
Female, 68 years
eGFR=18 ml/min/1.73m²
Bilateral kidney atrophy

No prognostic value of TKV

Irazabal et al., J Am Soc Nephrol 2015; 26: 160–172
Cornec-Le Gall E, Alam A, Perrone RD, Lancet, 2019, 393: 920

PROGNOSTIC VALUE OF GENETICS IN ADPKD: THE PROPKD SCORE (PREDICTING RENAL OUTCOME IN ADPKD)

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



PROPKD

0 pt
1 pt
2 pts
3 pts
4 pts
5 pts
6 pts
7 pts
8 pts
9 pts

Cornec-Le Gall E et al., J Am Soc Nephrol 2016, Mar;27(3):942-51

Vignette Clinique n°2 - Suite

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- ✓ Sa polykystose a été diagnostiquée à l'âge de 16 ans suite à un première épisode d'hématurie macroscopique.
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- ✓ Son DFG est de 92 ml/min/1,73m²
- ✓ Son HtTKV est à 1005 ml/m correspondant à une classe Mayo 1D
- ✓ Le variant familial est connu, il s'agit d'un variant tronquant dans le gène *PKD1 (PROPKD 7 – HR)*

Mettez-vous en place un traitement pour contrôler sa tension artérielle?
Si oui quelle classe, et pour quelle cible?

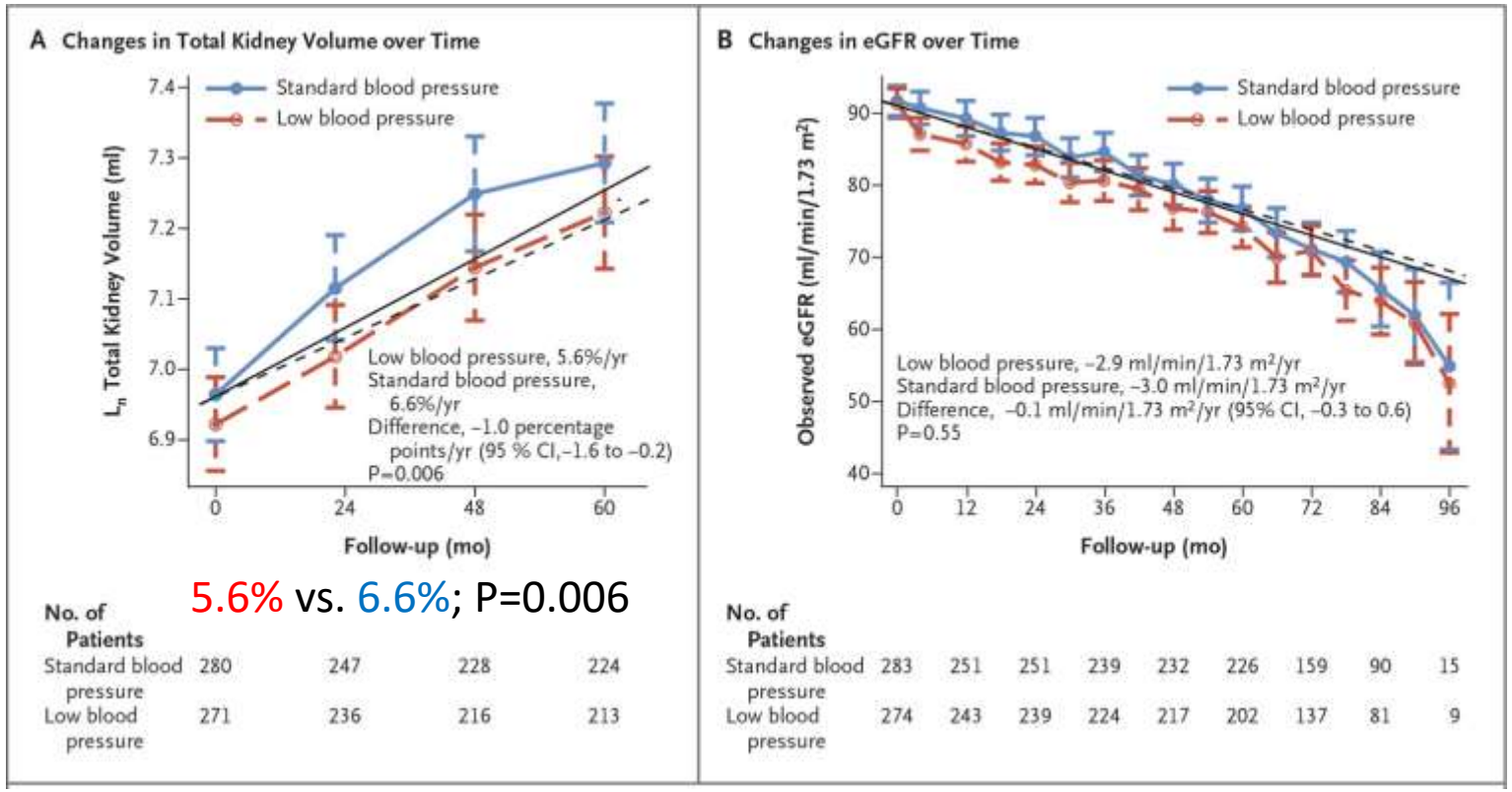
HYPERTENSION

- **Recommendation** 2.1.3 : For people with ADPKD aged **18–49 years with chronic kidney disease (CKD) G1-G2** and high BP (>130/85 mm Hg), we recommend a **target BP ≤110/75 mm Hg** as measured by HBPM, if tolerated **(1D).**

- **Recommendation** 2.1.4: For people with ADPKD **≥50 years** of age with all CKD stages, we suggest a **target mean systolic blood pressure (SBP) <120 mm Hg**, if tolerated, using standardized office blood pressure BP measurement **(2C).**

- **Recommendation** 2.1.5: For people with ADPKD and high BP, we recommend using **renin-angiotensin system inhibitors (RASi)** (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin II receptor blocker [ARB]) as primary treatment to achieve the recommended target BP **(1C).**

BLOOD PRESSURE TARGET – HALT PKD STUDY A



5.6% vs. 6.6%; P=0.006

- ✓ Greater decline in LVMI
- ✓ Reduced urinary albumin excretion rate
- ✓ Safe and tolerable

- ✓ A post-hoc analysis showed a larger effect in participants with more severe disease (Mayo 1D 1E) including a significant reduction of the eGFR decline

18-49 y, eGFR> 60 ml/min/1.73m²

N= 558

Standard blood-pressure target (120/70 to 130/80 mm Hg) - HBPM

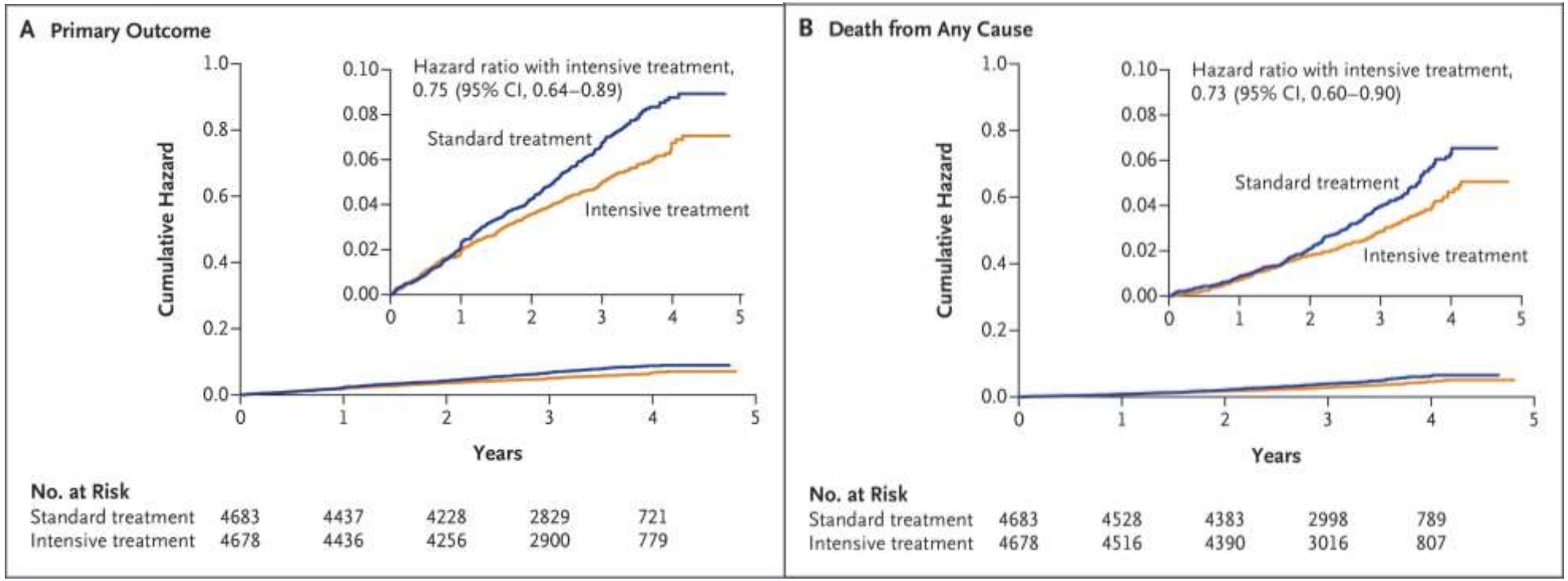
Low blood-pressure target (95/60 to 110/75 mm Hg) - HBPM

< 50y with CKD Stage G1-G2
BP target: 110/75
1D

Schrier et al., NEJM, 2014: 371: 2255–66

Irazabal M et al, Nephrol Dial Transplant 2017 Nov 1;32(11):1857-1865

BLOOD PRESSURE TARGET – SPRINT TRIAL



Primary outcome:
Composite outcome of myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes

>50 y, TAS 130-180, increased cardiovascular risk, eGFR (MDRD) 20-60

Exclusion of ADPKD patients

N= 9361

Standard blood-pressure target (TAS<140 mmHg – standardized office BP)

Low blood-pressure target (TAS<120 mmHg – standardized office BP)

> 50y or CKD Stage G3-G5
BP target < 120
2C

NEJM 2015; 373:2103-2016

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- ✓ Le variant familial est connu, il s'agit d'un variant tronquant dans le gène *PKD1 (PROPKD 7 – HR)*

- ✓ *Vous avez introduit un traitement ARA2 – elle revient 3 mois plus tard*
  - ✓ *AMT = 110/75, bien toléré*
  - ✓ *DFG 88 ml/min/1,73m²*

Proposez-vous d'autres mesures thérapeutiques chez cette patiente?

TOLVAPTAN

Warning: Unpublished Draft – Content Subject to Change

- **Recommendation** 4.1.1.1: We recommend initiating tolvaptan treatment in patients with ADPKD aged **18-55 years** with an estimated glomerular filtration rate (eGFR) **≥25 ml/min/1.73 m²** who are at risk for rapidly progressive disease (Figure 25) (1B).

- Practice Point 4.1.1.2: **Shared and individualized decision-making** should be undertaken when deciding to initiate tolvaptan in **people >55 years old .**

Initiation of tolvaptan should be offered to adults with ADPKD and:
eGFR ≥25 ml/min per 1.73 m²

AND

Risk of rapid disease progression as indicated by either:
Mayo class 1C to 1E
OR
Historical rate of eGFR decline (≥3 ml/min per 1.73 m² per year)

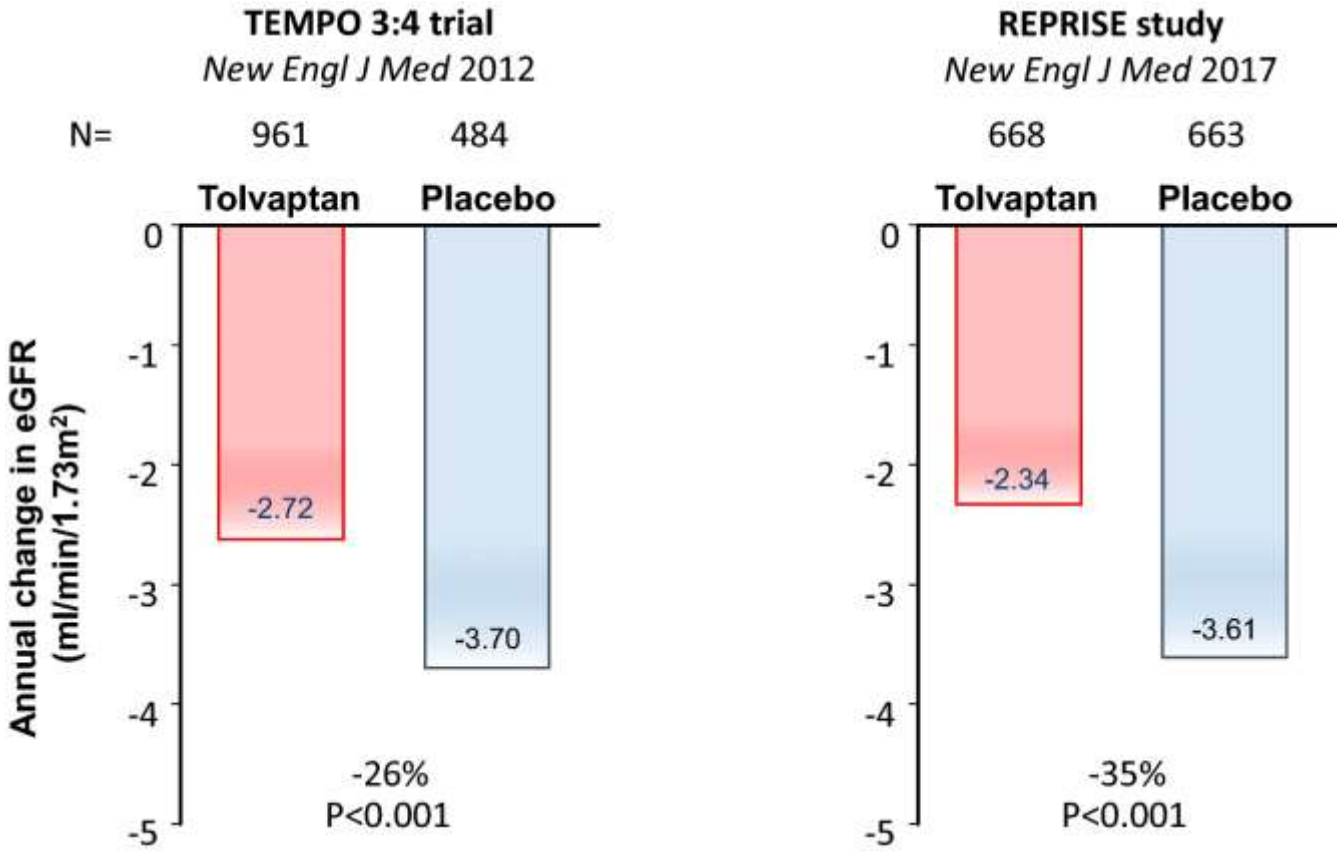
Because some individuals with Mayo 1C may not progress, consider also other indicators for risk of rapid progression:
- ✓ *PROPKD >6*
- ✓ *Family history with onset of KRT <60 years in ≥2 first-line family members*

TOLVAPTAN

Absolute and Relative contraindications

Absolute - Planning pregnancy, pregnancy, or breastfeeding - Medical conditions associated with or at high risk of volume depletion - Inability to respond or perceive thirst - Uncorrected baseline hypernatremia - Urinary tract obstruction - Strong CYP3A inhibitors* — e.g. ketoconazole, itraconazole, clarithromycin, lopinavir, ritonavir, and indinavir - Significant liver disease unless due to PLD
Relative - eGFR at initiation <25 ml/min per 1.73 m^2 - History of gout, hyperuricemia, and/or known uric acid nephrolithiasis - Moderate CYP3A inhibitors†, P-gp inhibitors‡, grapefruit juice - Urinary incontinence

TOLVAPTAN: THE TEMPO 3:4 AND REPRISE TRIALS



18-50y eCrCl > 60ml/min
AND TKV > 750 ml
N=1445

18-55y with eGFR 25-65
OR 56-65y with eGFR 25-45
N=1390

Torres VE et al NEJM 2012;367:2407-18 - Torres VE et al NEJM 2017; 377:1930-42 – Bais T et al, Drugs 2022; 82:1095–1115

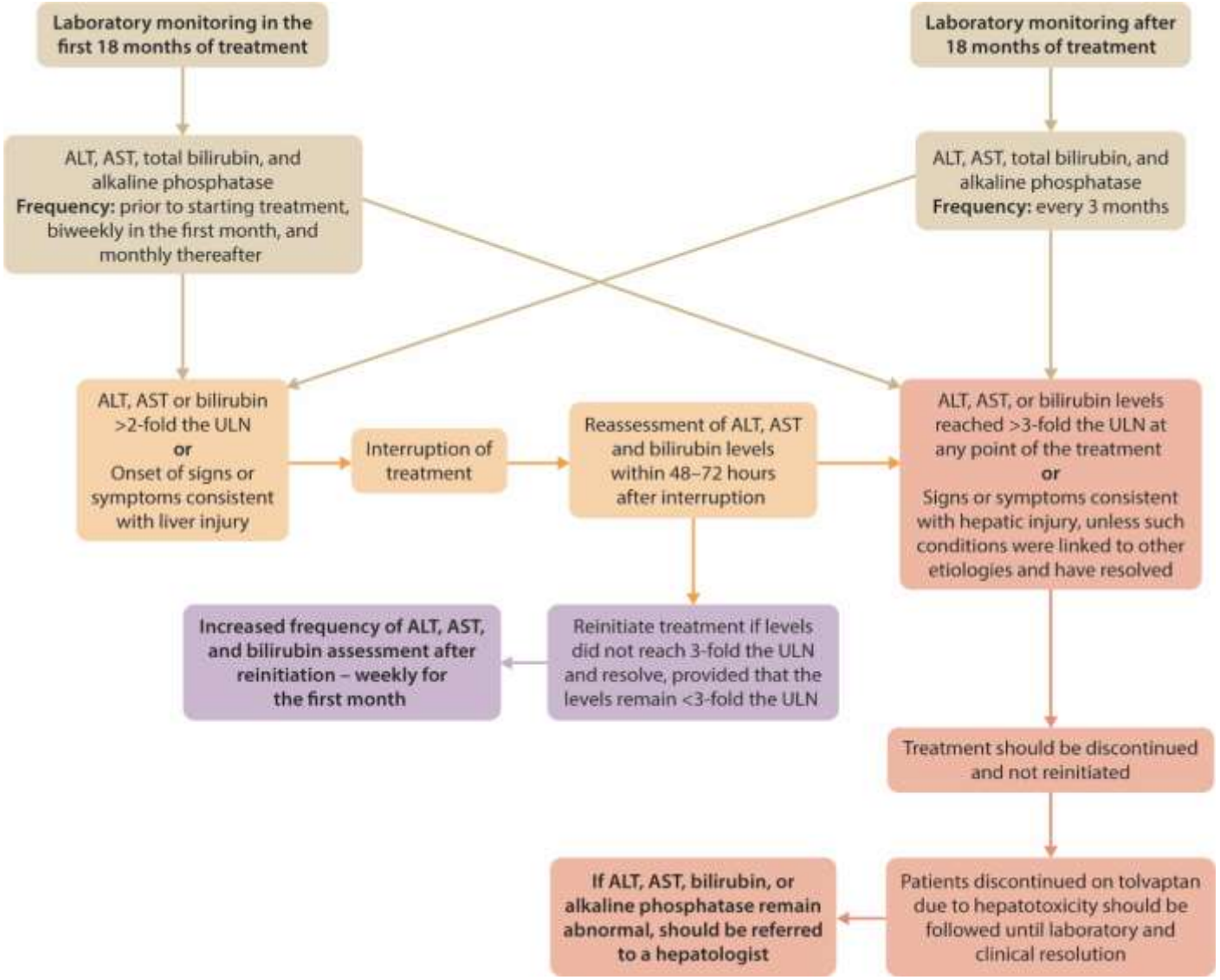
HARMS, BENEFITS, AND UNCERTAINTIES REGARDING LONG-TERM TREATMENT WITH TOLVAPTAN

Benefits
- Reduces eGFR decline (–1.3 ml/min per 1.73 m^2/year)
- Reduces increase in total kidney volume (greatest in first year of treatment)
- Reduction in acute pain events (stone and urinary tract infection)

Harms
- Aquaretic side effects (polyuria, polydipsia, thirst)
- Risk of drug-induced hepatoxicity
- Requirement for lifelong blood tests to monitor liver function tests (monthly for first 18 months and then 3 monthly)
- Drug interactions
- Cost

Uncertainties
1. Can tolvaptan delay onset of kidney failure?
2. What is the long-term tolerability of tolvaptan?

TOLVAPTAN: LIVER ENZYMES MONITORING



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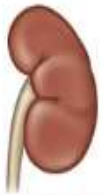
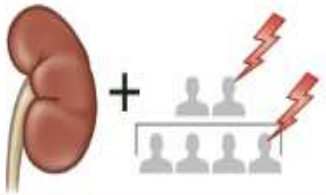
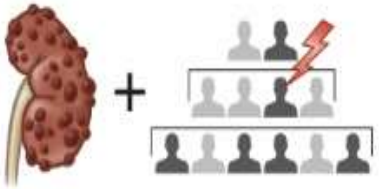
- ✓ Son DFG est de 92 ml/min/1,73m²
- ✓ Son HtTKV mesuré en IRM est à 1005 ml/m correspondant à une classe Mayo 1D
- ✓ Le variant familial est connu, il s'agit d'un variant tronquant dans le gène *PKD1 (PROPKD 7 – HR)*
- ✓ Elle est traitée par ARA2 et Tolvaptan depuis 6 mois, le traitement est bien toléré.
- ✓ Reprenant son histoire, vous réalisez que vous n'avez pas discuté du dépistage des anévrysmes intracrâniens

Elle fume 3 cigarettes par jour. Elle n'a pas notion d'anévrysme ni chez son père, ni sa tante, son oncle et sa grand-mère.

Recommandez-vous un dépistage? Si oui selon quelles modalités?
Si non, l'informez-vous du surrisque de développer un anévrysme quand on est atteint de PKRAD?

ANEURYSMS AND ADPKD: EPIDEMIOLOGY

Warning: Unpublished Draft – Content Subject to Change

				
Prevalence of ICA (95% CI)	3.2% (1.9–5.2)	4% (2.6–5.8)[a] 11% (9–14)[b]	13% (10.7–15.3)	18% (13–24)[c] 22% (14–31)[d]

Nb: median age at rupture 41 in ADPKD vs 52 in the general population

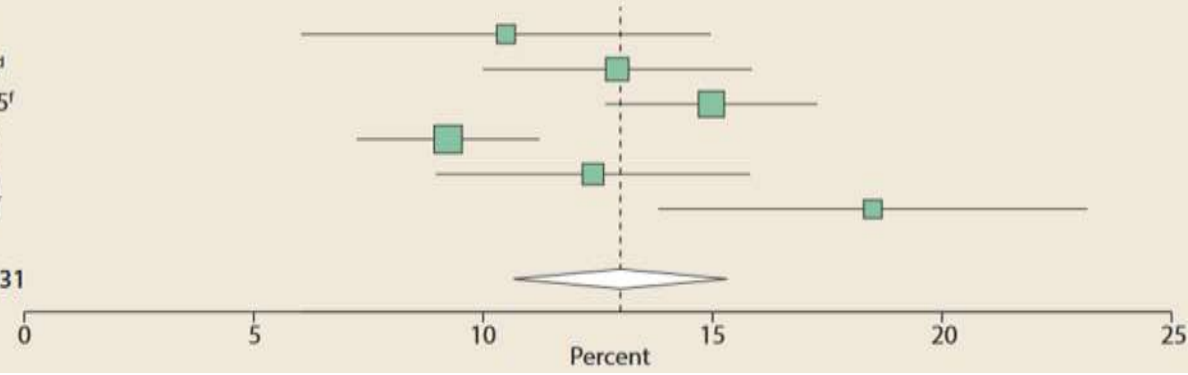
Vlak et al, Lancet Neurol 2011
Rinkel Ruigrok Int J of Stroke 2022
Sanchis et al CJASN 2022
Xu et al Stroke 2011
Etminan JAMA Neurology 2019
Wilkinson et al, Neurosurgery 2019

Flahaut et al, Kidney Int 2018
Kataoka et al, Sci Rep 2022
Lee et al, Cerebrovasc Dis 2021
Yoshida et al, Acta Neurochir 2017
Jiang et al, Eur J Radiol 2013

ANEURYSMS AND ADPKD: EPIDEMIOLOGY

Prevalence of ICA
(95% CI)

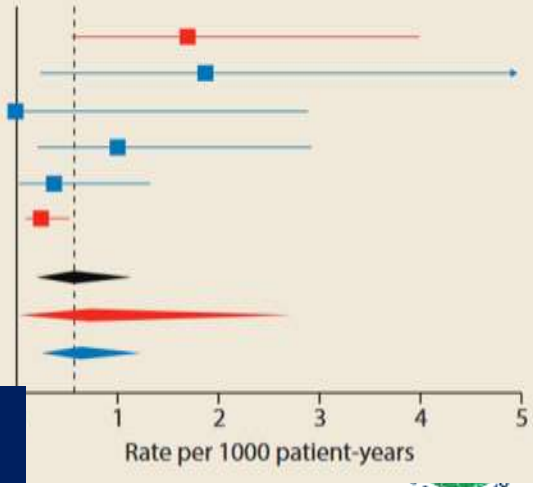
Studies	% imaged[a]	Percent (95% CI)	n/N
Flahault 2018[b]	37%	10.5 (6.0, 15.0)	19/181
Kataoka 2022[c]	88%	12.9 (10.0, 15.9)	65/503[d]
Lee 2021[e]	55%	15.0 (12.7, 17.3)	137/915[f]
Sanchis 2019[g]	29%	9.2 (7.2, 11.2)	75/812
Xu 2011[c]	94%	12.4 (9.0, 15.8)	44/355
Yoshida 2017[c]	78%	18.5 (13.8, 23.2)	49/265[f]
Overall (I^2=70%)		12.9 (10.4, 15.4)	389/3031



Prevalence:12.9%

Incidence rates of SAH
(per 1000 person-years, 95% CI)

Studies	Country (years)	Imaging, %	n/N	F/up, yr	Pt-Yr	Rate (95% CI), per 1000 pt-yr	Population*
Flahault 2018	France (2008–15)	37	5/495	5.9[†]	2921	1.71 (0.56, 3.99)	All patients
		37	2/181	5.9	1068	1.87 (0.23, 6.75)	Imaging
Jiang 2013	China (2007–08)	94	0/355	3.6	1278	0 (0, 2.88)	Imaging
Kataoka 2022	Japan (2003–19)	89	3/503	6.0	3008	1.00 (0.21, 2.91)	Imaging
Sanchis 2019	US (1989–2017)	27	2/812	6.7	5451	0.37 (0.04, 1.32)	Imaging
Wilkinson 2019	US (2004–14)		6/9110	2.8	25,408	0.24 (0.09, 0.51)	All patients
All patients or imaging (I^2=57%)[‡]			16/11,275		38,066	0.57 (0.19, 1.14)	
All patients (only) (I^2=NA)			11/9605		28,329	0.72 (<0.01, 2.73)	
Imaging (only) (I^2=5%)			4/1851		10,805	0.64 (0.24, 1.23)	



Incidence: 0.57 per 1000 person-year = 1 in 1754 patients per year

ANEURYSMS AND ADPKD: RISK FACTORS

	Predictors for prevalent ICA or rupture of ICA and strength of the association
Evidence for association with ICA/SAH in ADPKD population	• Family history of SAH or ICA (stronger association when first-degree relative) – *Strong* • Personal history of SAH or ICA – *Strong* • Tobacco smoking (especially >20 pack-years) - *Strong* • Female sex – *Moderate* • *PKD1* genotype - *Moderate* • Uncontrolled hypertension - *Moderate* • Early onset hypertension (<35y) - *Moderate* • Severity of ADPKD – *Weak*
Evidence in non-ADPKD population	• Japanese or Finnish ancestry – *Weak* • Alcohol in large quantity (risk factor for ICA rupture) – *Weak*

The Importance of Providing Detailed Information

We recommend informing adults with ADPKD about increased risk for intracranial aneurysms (ICA) and subarachnoid hemorrhage (*1C*)

- All people with ADPKD should be educated to recognize **thunderclap headache** which should prompt immediate medical attention.

- A **detailed personal history** of SAH and a **family history** of ICA, SAH, and unexplained sudden death should be obtained to identify people with ADPKD at higher risk for ICA.

- Because **tobacco smoking** is a strong modifiable factor for ICA development and rupture, clinicians should ask all people with ADPKD about their tobacco use, advise them to stop using tobacco, and provide behavioral interventions and approved pharmacotherapy for cessation, if needed.

- Because **uncontrolled hypertension** is a strong modifiable factor for ICA development and rupture, early diagnosis and adequate treatment of hypertension is indicated in people at risk of or diagnosed with ADPKD, particularly in those at an increased risk for ICA.

The Importance of Providing Detailed Information

People should be informed of the **implications** of ICA screening

May **allow adequate intervention** if an ICA at risk of rupture is identified, allowing **to prevent death or significant comorbidity**.

May allow **adequate imaging follow-up if an ICA with low risk of rupture** is identified

May **reduce anxiety and provide reassurance** when no ICA is detected

May lead **to the identification of an ICA with very low risk of rupture** (≤5 mm/anterior circulation) and which do not require intervention but long-term follow-up

May **lead to procedures with possible treatment failure or complications**, including death or significant comorbidities.

Does **not exclude the risk of de novo ICA development** and rupture after screening

May **limit access to life insurance, loans, driving licenses, work opportunities**

May **cause anxiety** when an ICA is identified

-> Also discuss the implications in term **of cascade screening** if an ICA is detected, and mention the possibility of **incidental findings**

RECOMMENDATIONS FOR ICA SCREENING

We recommend screening for ICA in people with a **personal history of SAH or a positive family history of ICA, SAH, or unexplained sudden death** if the person will be **eligible for treatment** and have **good life expectancy (1D)**

➢Screening for unruptured ICA may also be discussed in people with **de novo ADPKD**, those with **unknown familial history or small number of ADPKD-affected relatives**, and in those with **personal or familial history of extracerebral vascular phenotype.**

➢Screening for unruptured ICA may also be discussed in specific clinical settings, such as in the **context of evaluation for kidney and/or liver transplantation or before major elective surgery.**

➢People with ADPKD who are not considered at increased risk for ICA and who, after comprehensive information, **prefer being screened for ICA should be given access to screening.**

➢In **women** with ADPKD and either a **family history of ICA, SAH, or unexplained sudden death; *de novo* ADPKD**; unknown familial history; or a small number of ADPKD-affected relatives, screening for unruptured ICA should **precede pregnancy planning.**

Nb : Screening before adulthood is usually not advised

Strategies For Screening and Therapeutic decision making

- **Time-of-flight (TOF) magnetic resonance angiography (MRA) without gadolinium** enhancement should be the method of imaging when screening is to be pursued for ICA in people with ADPKD. High-resolution computed tomography angiography (CTA) can be an alternative.

- If the screening is negative in people with high-risk of ICA, timing of rescreening should be **individualized**, **possibly every 5–10 years, based on risk factors, age, and life expectancy.**
  - ✓ *Despite repeated screening and preventive treatment of unruptured ICAs, not all episodes of SAH can be prevented*

- When one or several ICAs are identified, treatment options, such as conservative management and microvascular or endovascular repair, should be assessed within a **multidisciplinary setting at centers of expertise with high ICA case volumes.**

A PROPOSED ADPKD CARE PATHWAY.

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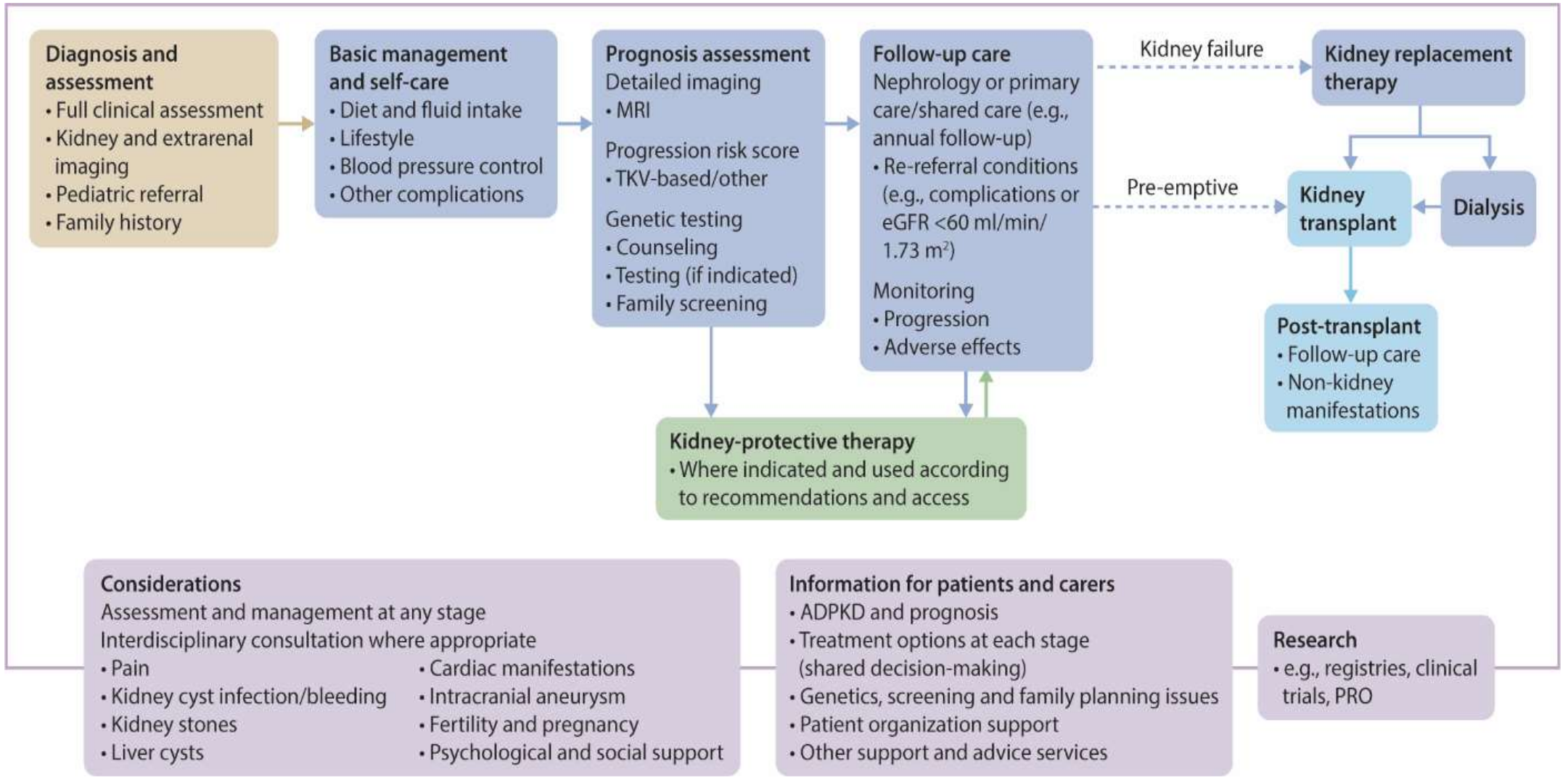

KDIGO Guidelines on ADPKD

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Journée scientifique MARHEA

Polykystose rénale autosomique dominante (PKRAD)

Vendredi 13 septembre 2024

Brest

Marina du Château
Quai Eric Tabarly
29200 Brest

Matinée patients et familles

MARHEA

Polykystose rénale autosomique dominante (PKRAD)

Samedi 14 septembre 2024

Format hybride

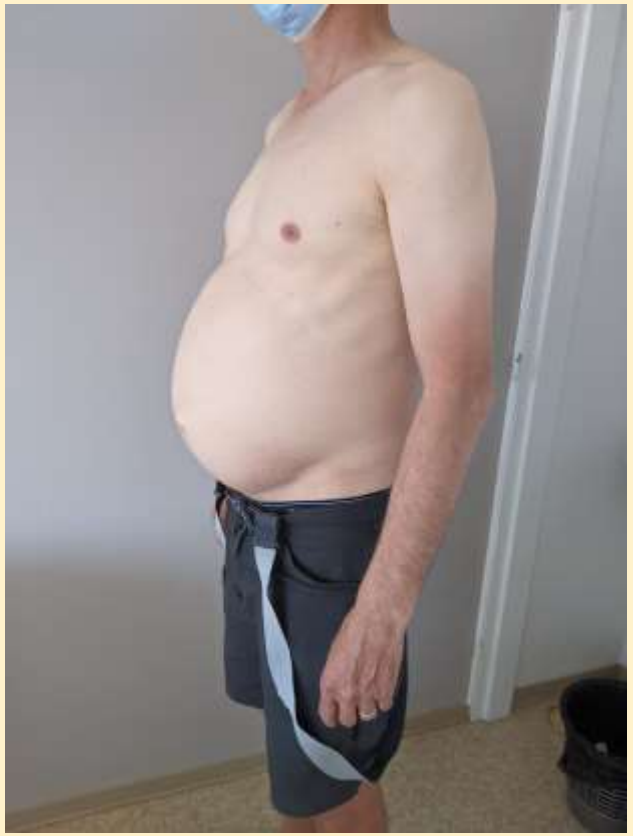
Faculté de médecine
22 Rue Camille Desmoulins,
29238 Brest

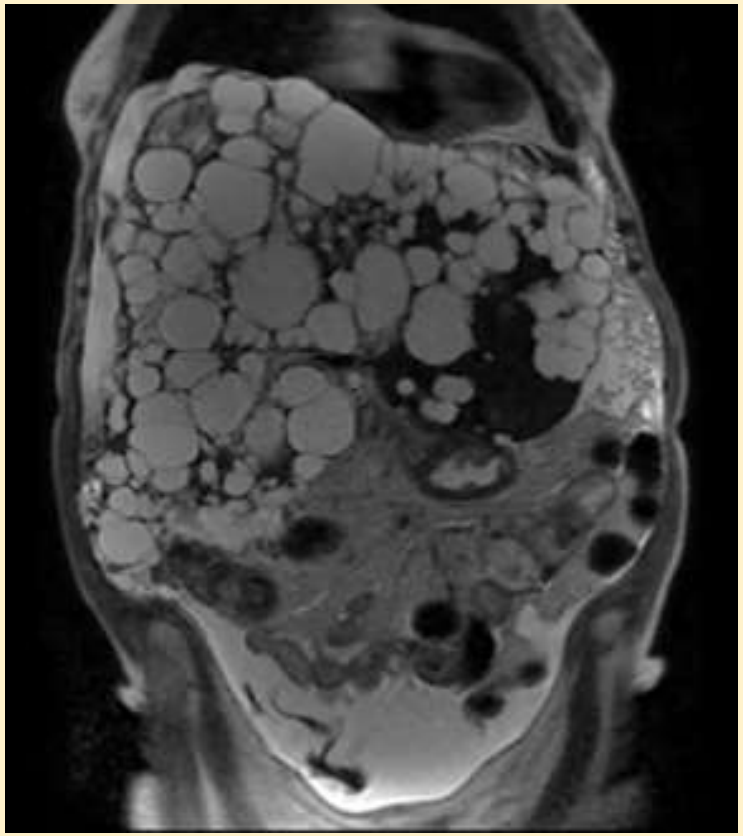
Le lien de connexion sera envoyé **après l'inscription** et **juste avant le jour** de l'événement

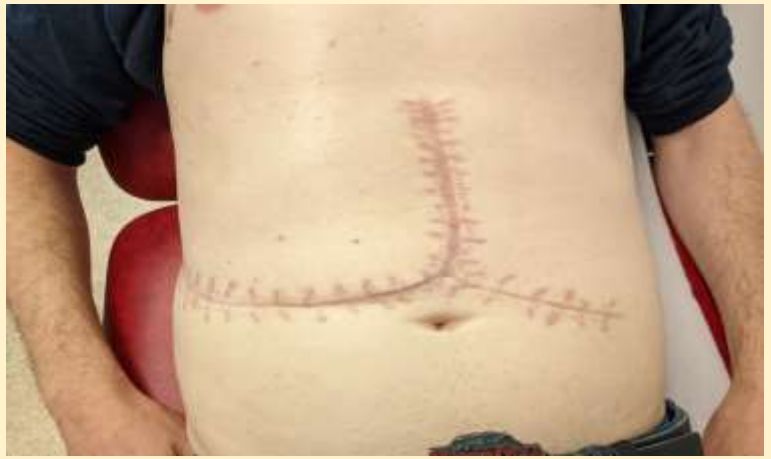
Inscription **gratuite** mais **obligatoire**

https://www.eventbrite.com/e/852122480277?aff=oddtdtcreator

Polykystose hépatique







Patient de 44 ans. eGFR= 55ml/min/1,73m², traité par Tolvaptan depuis 2 ans.

HtTKV 1,7L/m Mayo 1D - Volume hépatique 13,1 L. (soit volume rein + foie = 16,2 L)

Depuis un an, douleurs abdominales de plus en plus invalidantes - Changement de travail – puis arrêt longue durée

Hospitalisations pour infections de kystes x 2 en 6 mois - Reflux – anorexie - Perte de poids – essoufflement au moindre effort

Polycystic Liver Disease

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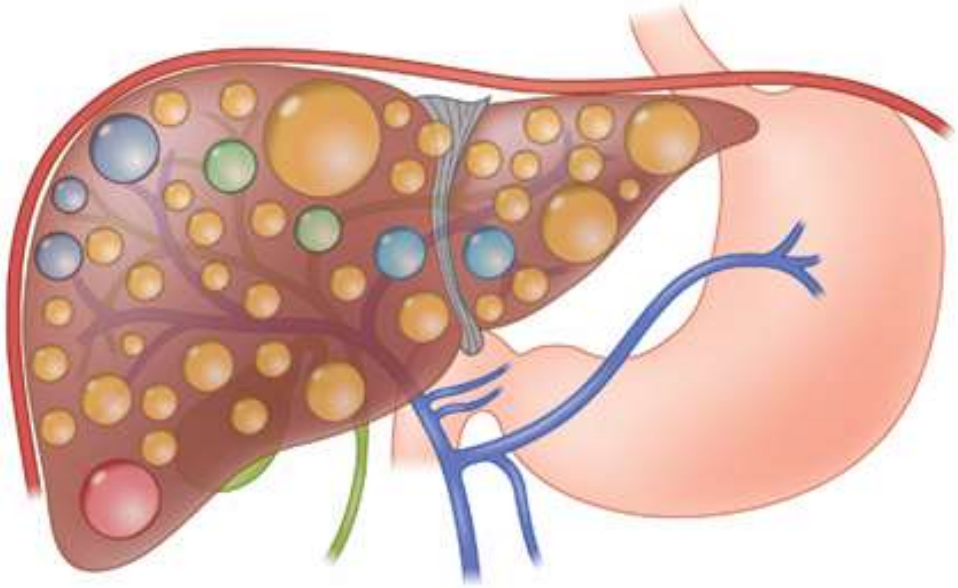
- Practice Point 5.1.4: Symptoms of PLD should be captured with the disease-specific symptom questionnaires **Polycystic Liver Disease Questionnaire** (PLD-Q) and **Polycystic Liver Disease Complaint-specific Assessment** (POLCA).

Pressure against diaphragm and lungs
1. Shortness of breath
2. Fatigue

Overall liver size
1. Abdominal fullness
2. Limited mobility
3. Fatigue
4. Anxiety
5. Concern or dissatisfaction with abdomen size
6. Problems with intercourse
7. Mechanical back pain



Pressure against the stomach
1. Lack of appetite or early satiety
2. Acid reflux
3. Nausea and vomiting
4. Involuntary weight loss

Cyst complications
1. Intracystic
   a. Recurrent cyst infection
   b. Recurrent cyst hemorrhage
2. Extracystic
   a. Jaundice
   b. Hepatic venous outflow obstruction and portal hypertension

- Practice Point 5.2.1.1: Women with ADPKD, particularly those with PLD, should be counseled about the benefits and potential harms of **sex hormone therapy.**

Polycystic Liver Disease

- Practice Point 5.3.3.1: Treatment for PLD should be performed in **centers of expertise.**

- Practice Point 5.2.3.2: People with ADPKD and PLD **should receive treatment (i.e., medical and/or surgical including minimally invasive treatments) if they experience cyst-related symptoms or complications that negatively impact their quality of life (QoL).** Determination of treatment type should be based on symptoms, liver cyst characteristics, total liver volume (TLV), and treatment availability.

- **Recommendation** 5.3.3.1: We suggest prescribing **long-acting somatostatin analogues in people** with ADPKD and PLD with volume related symptoms (2B).

- Practice Point 5.3.3.3: When long-acting somatostatin analogues are prescribed, the effect on symptom burden and/or volume of polycystic liver and kidneys should be evaluated **after 6 months.** When beneficial effects of therapy are not observed, somatostatin analogues should be discontinued.

Polycystic Liver Disease – Somatostatin Analogs

- Four RCTs assessed the effect of SSA on PLD with a follow-up of ≥1 year :
  - SSA reduce TLV in people with ADPKD and ADPLD compared to placebo (Moderate evidence)

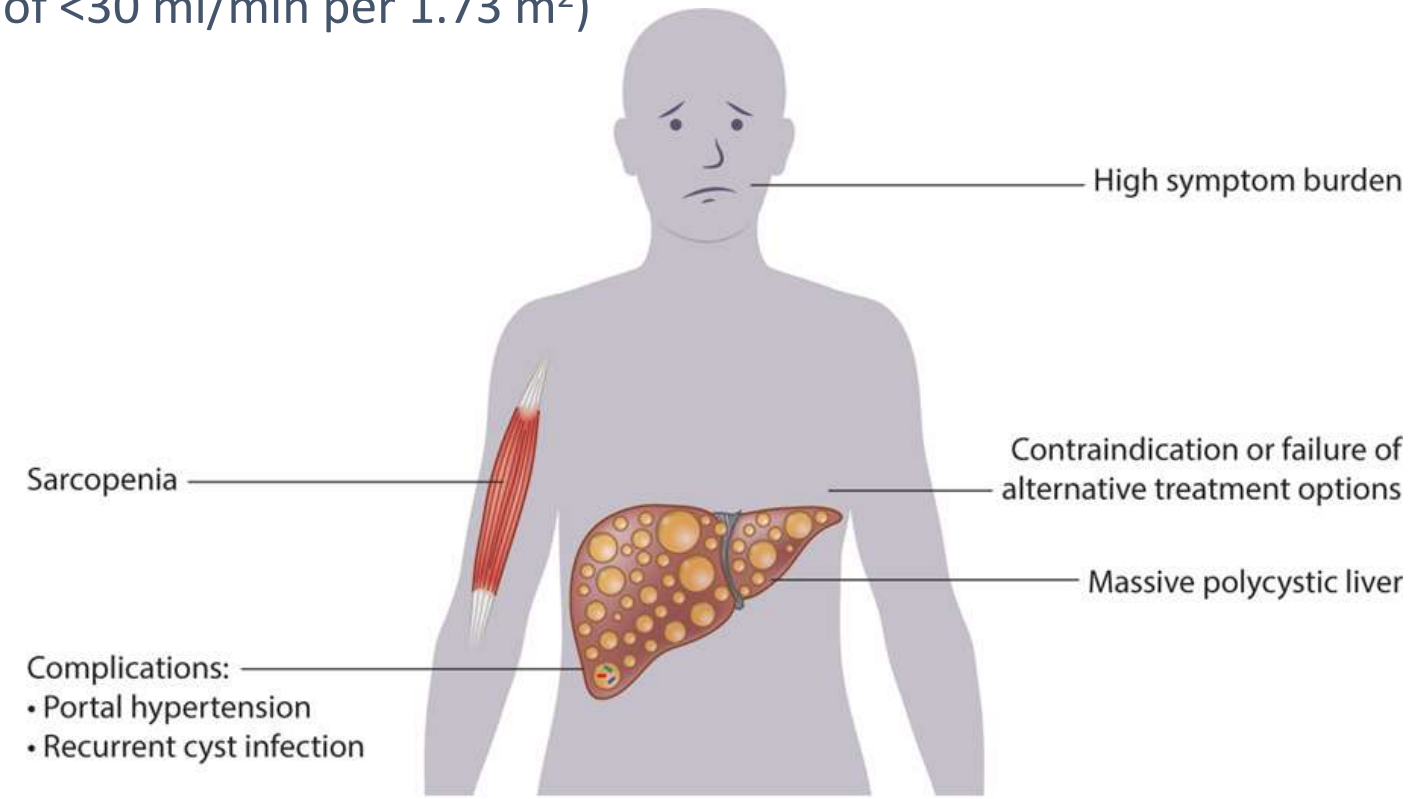
- Adverse events include mild gastrointestinal symptoms, cholelithiasis, hypo- and hyperglycemia, and alopecia. Hyperglycemia and diabetes are more common with pasireotide compared to lanreotide and octreotide.

- Values and preference: A special emphasis was also placed on preventing liver transplantation. Consequently, the Work Group deems SSA to be a beneficial treatment modality in people with symptomatic PLD and large polycystic livers. The expected beneficial effects and side effects of this therapy should be discussed with the person before treatment is initiated.

van Aerts RMM et al, Gastroenterology 2019
Hogan MC et al, CJASN 2020
Hogan MC et al, JASN 2010
Pisani A et al, Clin Gastroenterol Hepatol 2016

Evaluation For Liver Transplantation

- Practice Point 5.3.3.7: People with PLD should be referred for liver transplantation in the event of massive PLD in the absence of contraindications or alternative treatment options.
- Practice Point 5.3.3.8: People with PLD should be referred for combined kidney-liver transplantation when there is an indication for liver transplantation and the person has a severely impaired kidney function (eGFR of <30 ml/min per 1.73 m^2)



Reproductive Options

- Practice Point 8.2.3: People with ADPKD at reproductive age should be offered all available reproductive options