Hypertension Artérielle Maligne

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UMR INSERM1034 : biologie des maladies cardiovasculaires, Pessac

DPC HTA 2026

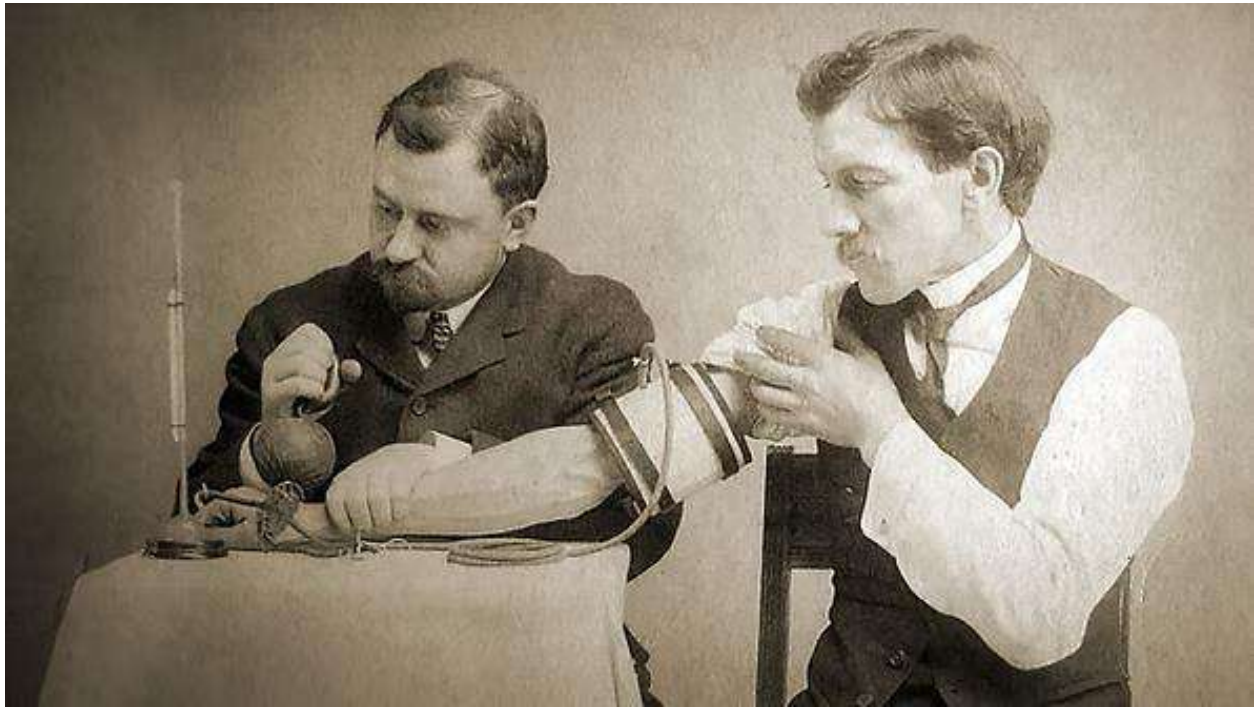
Liens d’intérêts

L’auteur déclare avoir participé à des interventions ponctuelles (essais cliniques, travaux scientifiques, activités de conseil, conférences, colloques) pour les entreprises *Alexion, AstraZeneca, Fresenius, Lilly, Novartis, Servier, Vantive*

www.transparence-sante.gouv.fr

L’importance des outils d’évaluation

1851
Premier ophtalmoscope
Hermann von Helmholtz

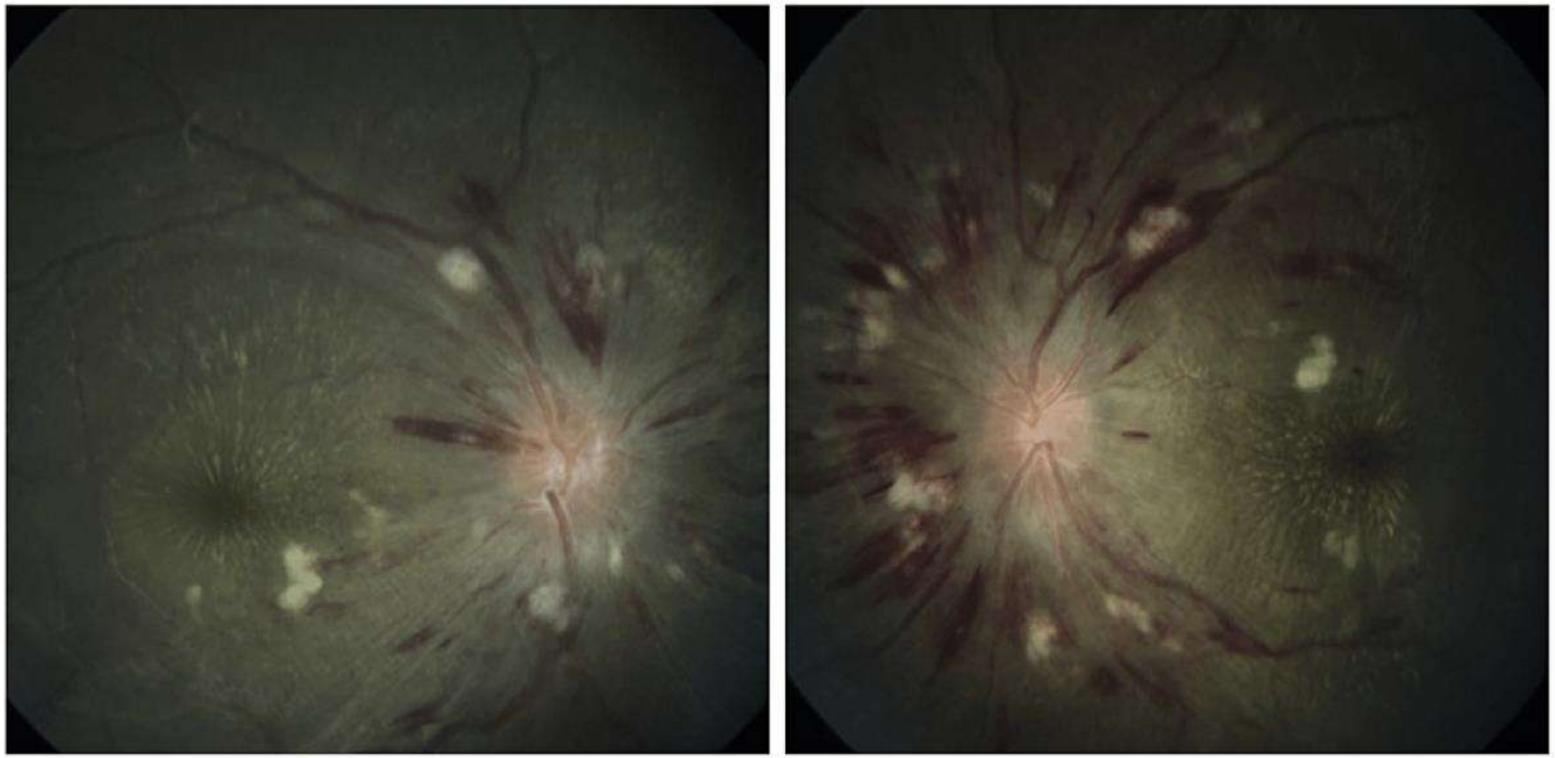


1896 : Riva-Rocci invente la mesure de la PA non invasive
1905 : Nikolai Korotkoff et la PA diastolique

Une forme particulière d'Hypertension Artérielle

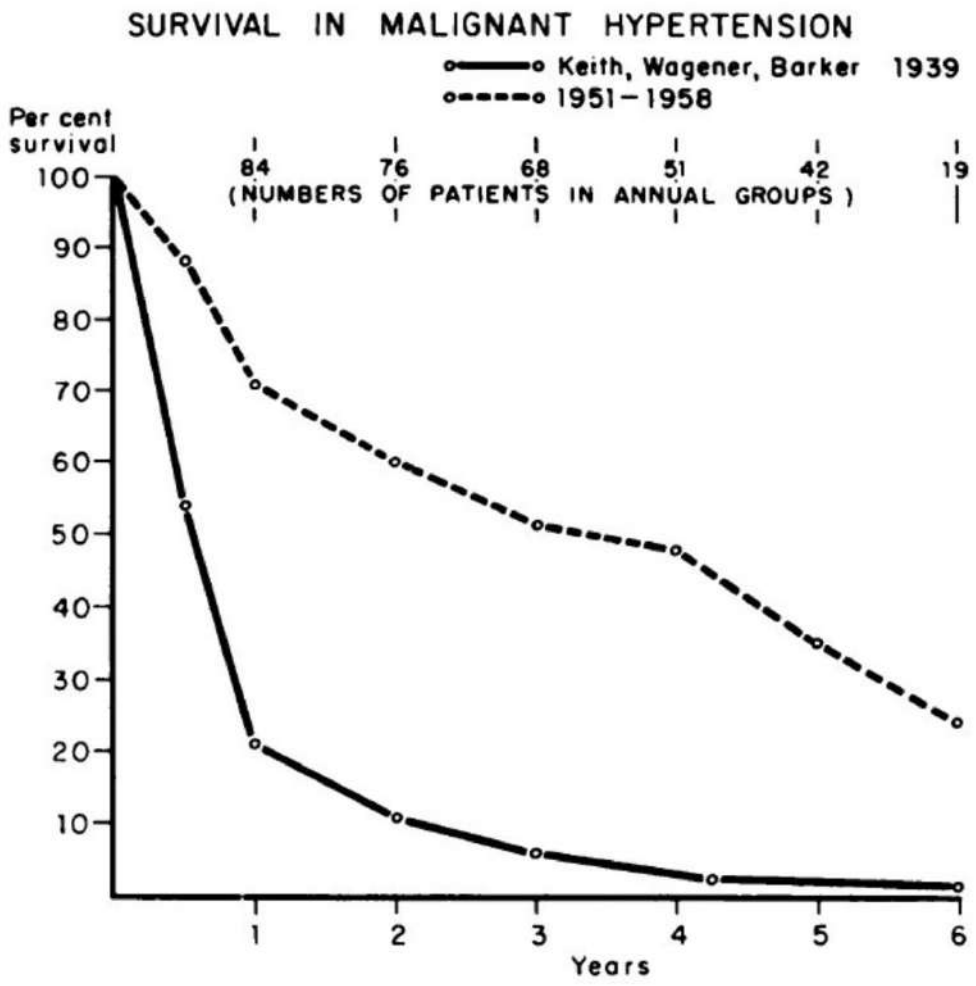
- Rapporté en 1953 par Palmer
- Jeunes patients
- HTA Sévère
- Œdème papillaire
- Mortalité 80% à 1 an

➔ **« HTA Grade 4 »**
➔ **HTA Maligne**



Palmer et al. JAMA 1953

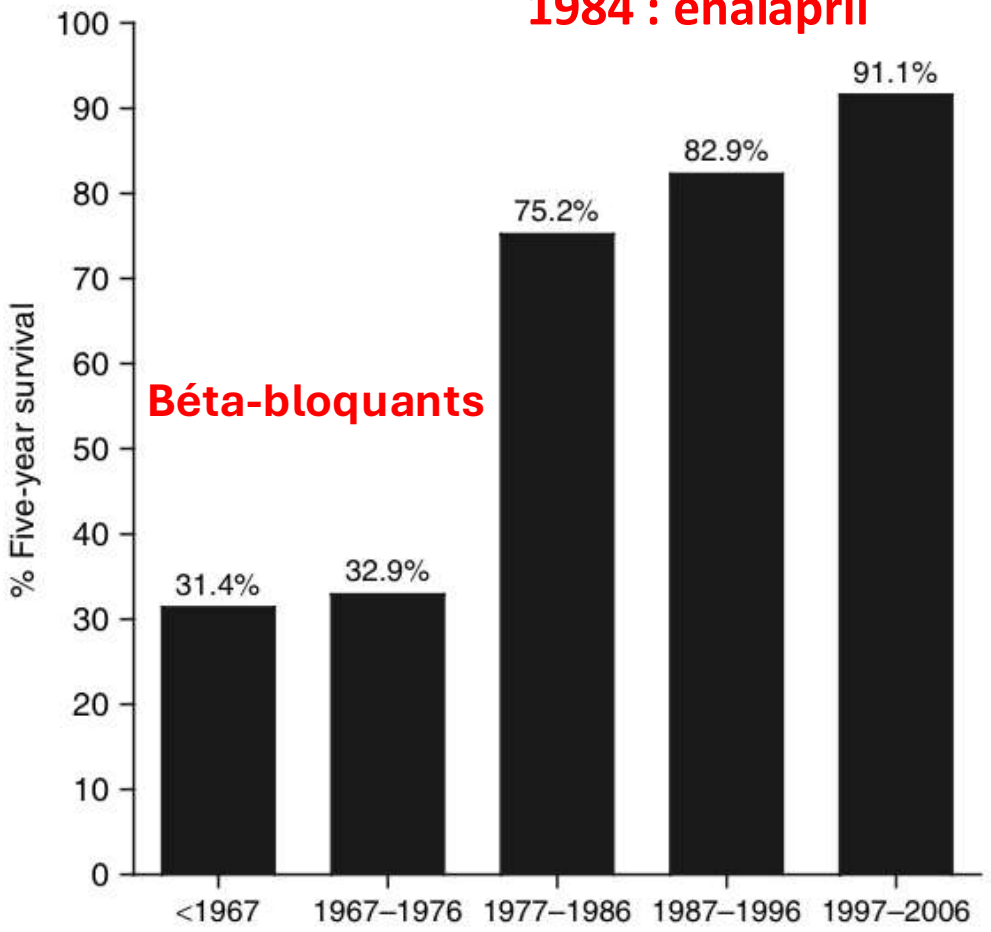
Un nom historique en rapport avec son pronostic



Survie à 5 ans

1981 : captopril

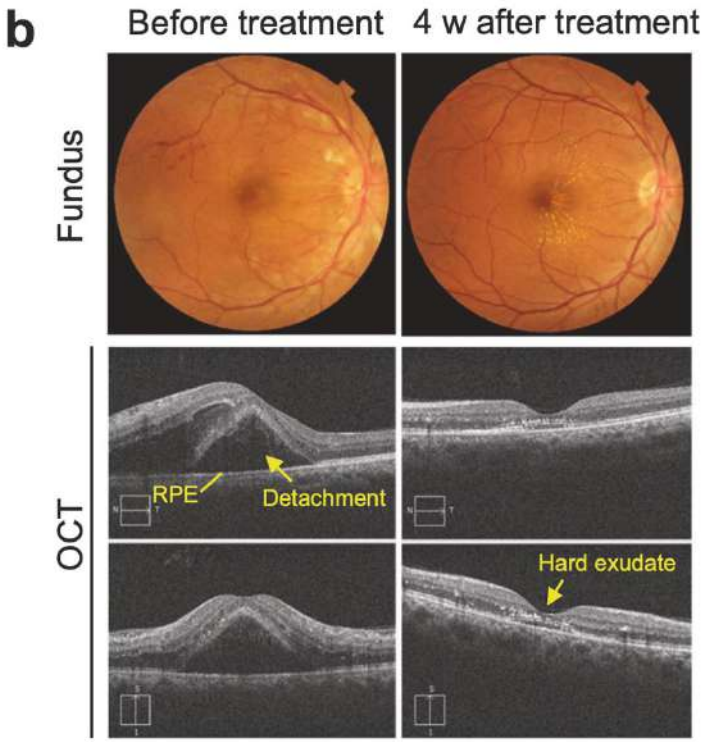
1984 : enalapril

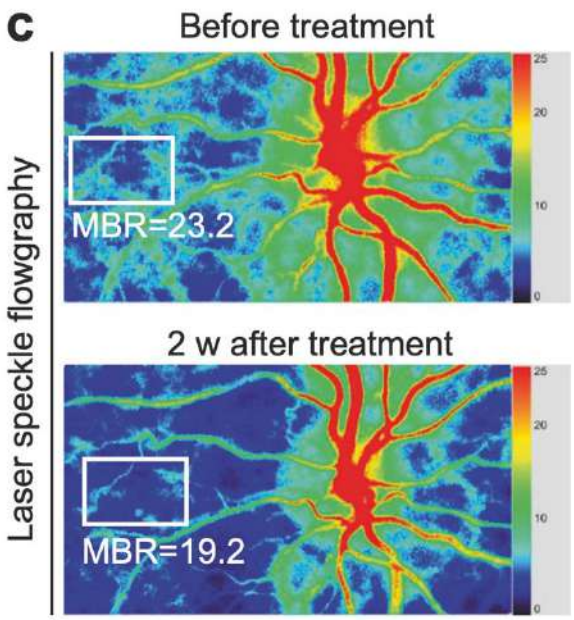


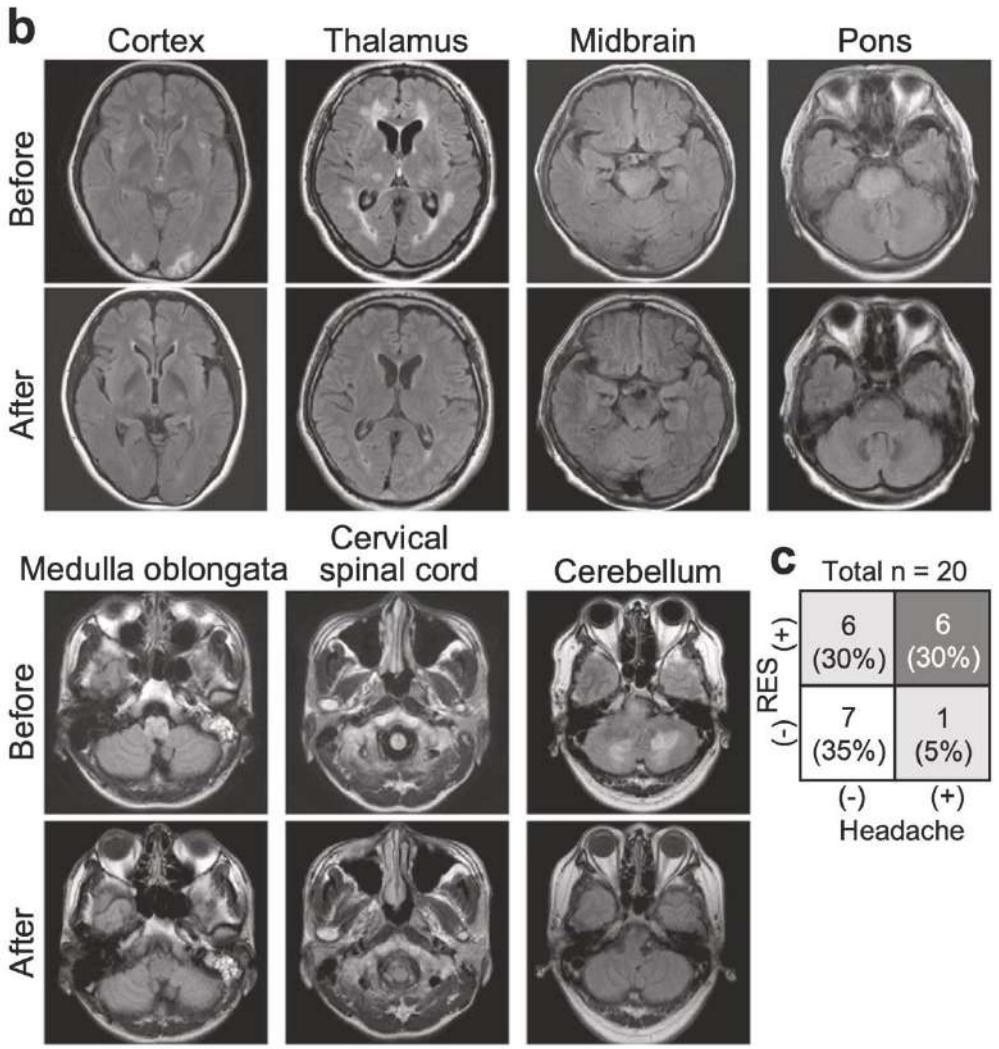
Dustan et al. Circulation 1958

Lip, Am. J. Hypertens.; 2009

Depuis les outils d'évaluations ont transformé le diagnostic / évalution pronostic







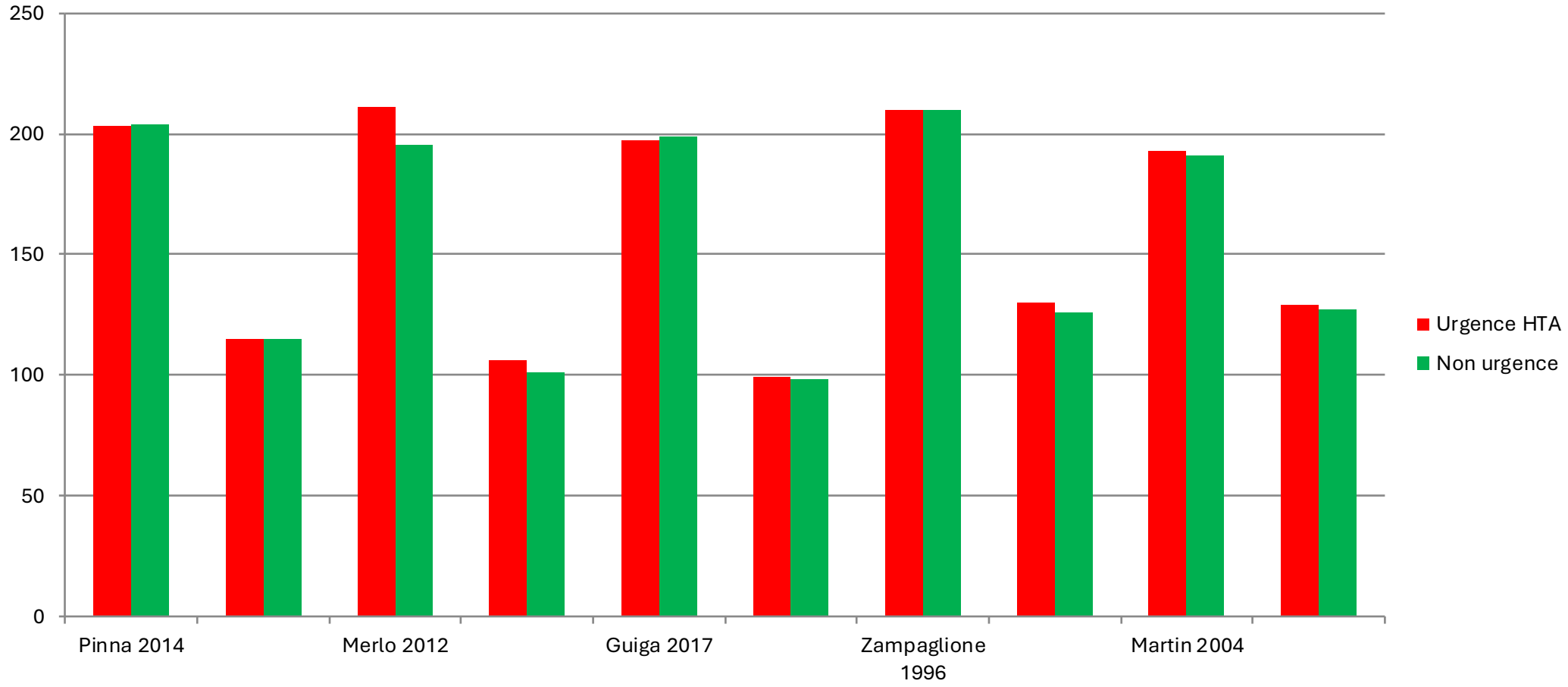
Mishima E et al. Hypertens Res. 2021

Un patient de 41 ans aux urgences

- Homme de 41 ans
- Se présentant aux urgences pour AEG et sensation vertigineuse
- HTA connue depuis 2019. Bilan d'HTA secondaire négatif
  - Poids 55kg
  - Bilan biologique lors du bilan d'HTA secondaire : créatinine : 65 µmol/l, K+ : 3,7 mmol/l
  - Bithérapie fixe (perindopril 8mg/amlodipine 10mg)
- PA : 230/110 mmHg, Poids 49 kg, asthénie, Céphalées, Trouble visuel, Nausées

Comment définir l’HTA Maligne ?

Ce n’est pas le niveau de PA qui diagnostique l’HTA Maligne



Merci Dr Aurelien Lorthioir

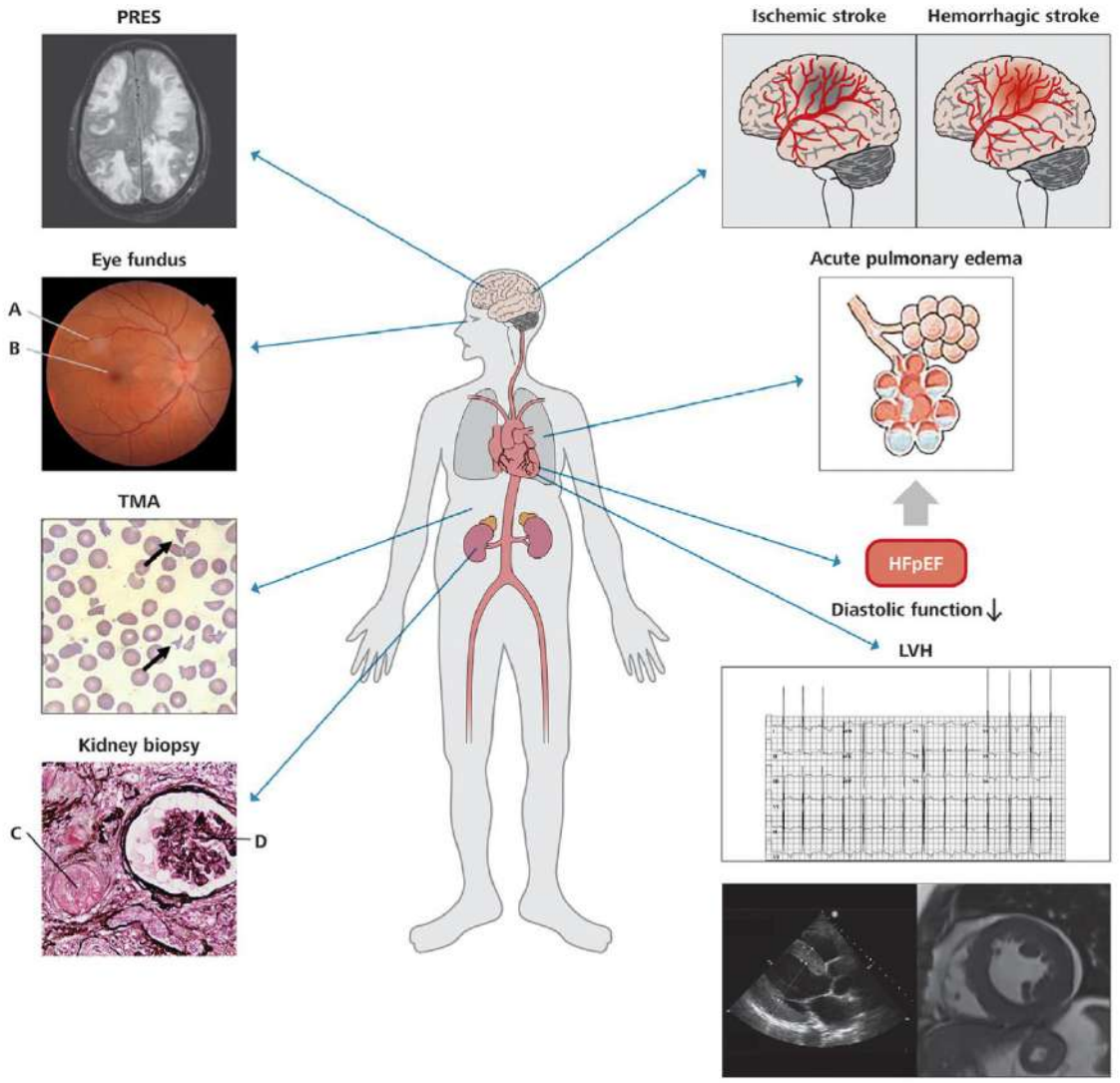
Pinna et al. PLoS One. 2014 - Merlo C et al. Swiss Med Wkly. 2012
Guiga et al. J Clin Hypertens 2017 - Zampaglione et al. Hypertension 1996
Martin et al. Arq Bras Cardiol. 2004

Urgences hypertensives : symptômes

Presenting symptoms	All patients (N = 670) No. (%)	Hypertensive emergencies (n = 385) No. (%)	Hypertensive urgencies (n = 285) No. (%)	*P* value
Headache	63 (9.4)	10 (2.6)	53 (18.6)	.001
Focal neurologic deficit	152 (22.7)	140 (36.3)	12 (4.2)	.001
Chest pain	77 (11.5)	52 (13.5)	25 (8.8)	.001
Dizziness	83 (12.3)	33 (8.6)	50 (17.5)	.001
Epistaxis	30 (4.5)	1 (0.3)	29 (10.2)	.001
Dyspnea	122 (18.2)	113 (29.3)	9 (3.6)	.001
Others	143 (21.3)	31 (0.8)	122 (42.8)	.001

Guiga et al. J Clin Hypertens 2017

L’HTA maligne : une maladie systémique



Boulestreau et al. JACC 2024

Vous avez éliminé un AVC

- La TDM cérébrale faite ne retrouve pas d'anomalie
- Vous hospitalisez le patient en Soins Intensifs de Néphrologie
- Le patient reconnait ne plus prendre son traitement antihypertenseur depuis plus d'un an.
- Biologie
  - Créatinine : 195 µmol/l, K+ 3,2 mmol/l,
  - Plaquettes 121 000 /mm^2
  - Troponine HS : 921 ng/l (N<14)

HTA maligne, une pathologique systémique moderne

- The Birmingham, Bordeaux and Amsterdam malignant hypertension registries have shown that malignant hypertension is rising in Europe

- Malignant hypertension with or without thrombotic microangiopathy or acute kidney failure **is a hypertensive emergency characterized by small artery fibrinoid necrosis in the kidney, retina and brain. There might be also funduscopic changes** microangiopathy, disseminated intravascular coagulation, encephalopathy (15% of cases) or acute HF.

Hypertension Guideline 2023

European Society of Hypertension

Hypertension-MOD (Multi-organ Damage)

HTA sévère avec 3 atteintes d'organes cibles

ou

HTA sévère avec rétinopathie maligne

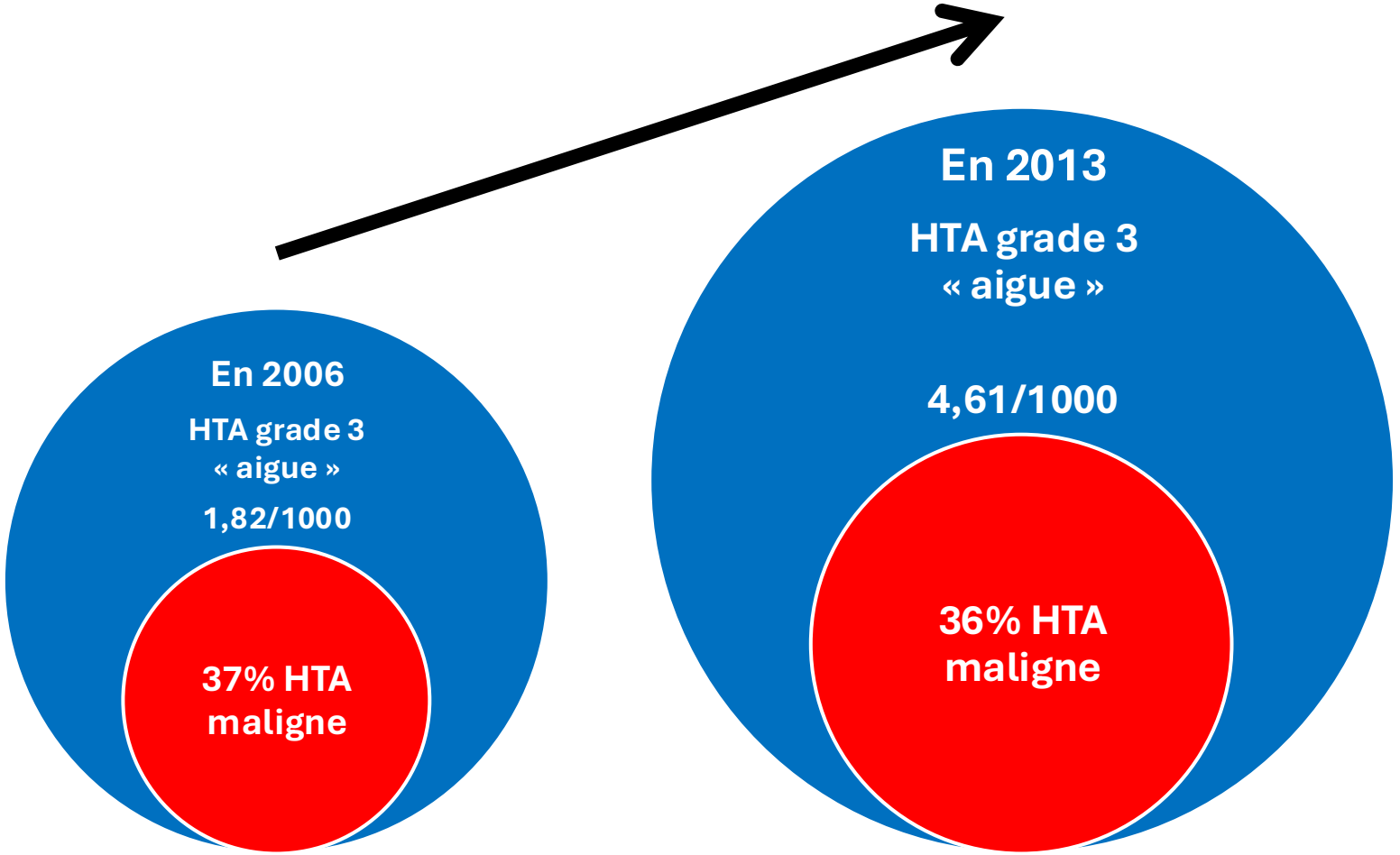
	Criteria
Kidney	Impaired renal function Creatinine elevation >30% with respect to recent assay in the absence of obvious cause Proteinuria (usually modest and non specific)
Heart	Marked LVH Impaired systolic function (especially global longitudinal stain) Abnormalities of repolarization on ECG. Increased troponin
Brain	Ischaemic or haemorrhagic stroke Extensive white matter lesions, microbleeds before 60 years PRES
Microangiopathy	Haemolysis

Rubin et al. J Hypertens 2019

Une maladie pas si rare

HTA sévère : incidence en augmentation

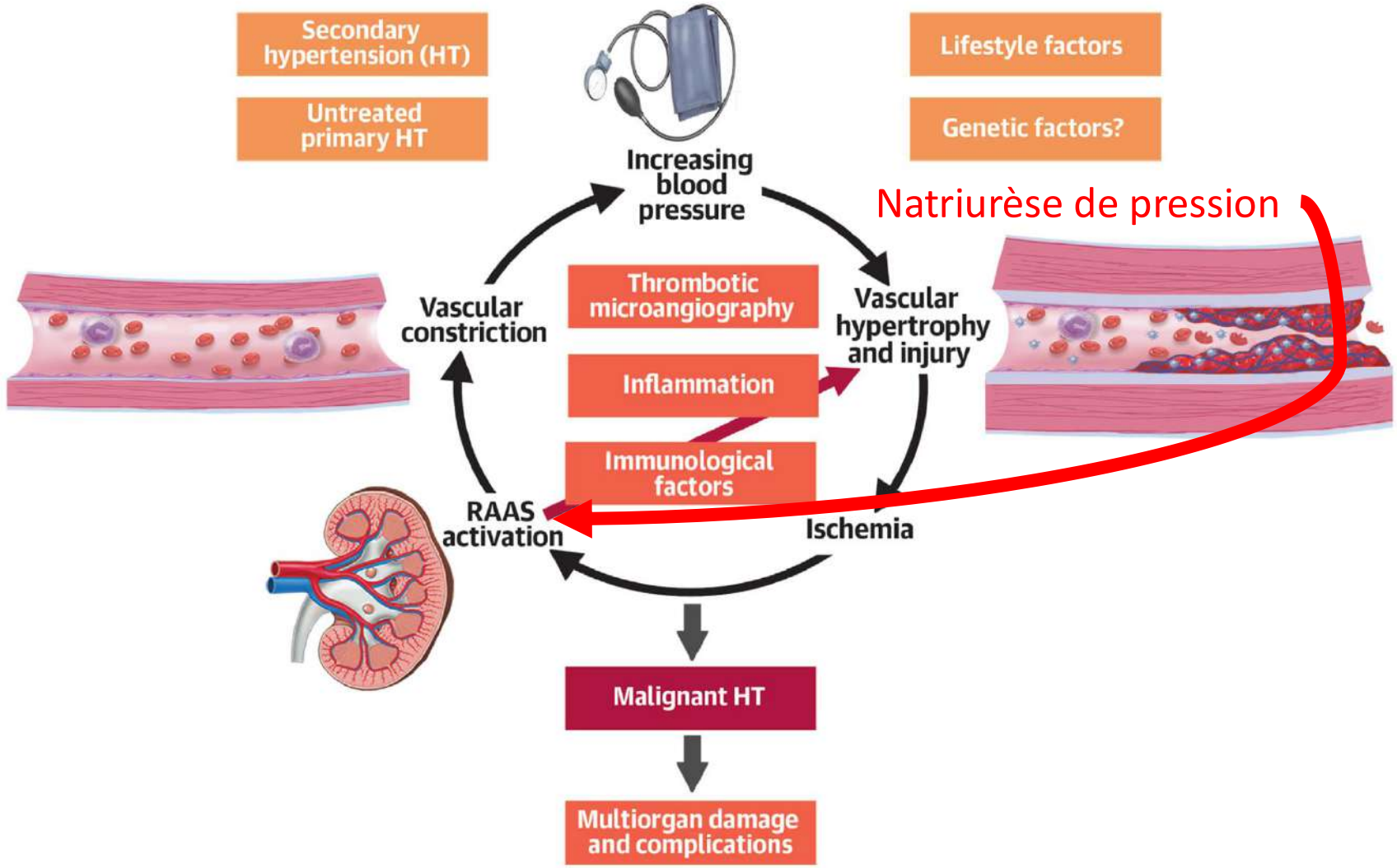
30 états, 947 hôpitaux
809 millions de passages
20% des passages au SAU



Janke et al. J Am Heart Assoc. 2016

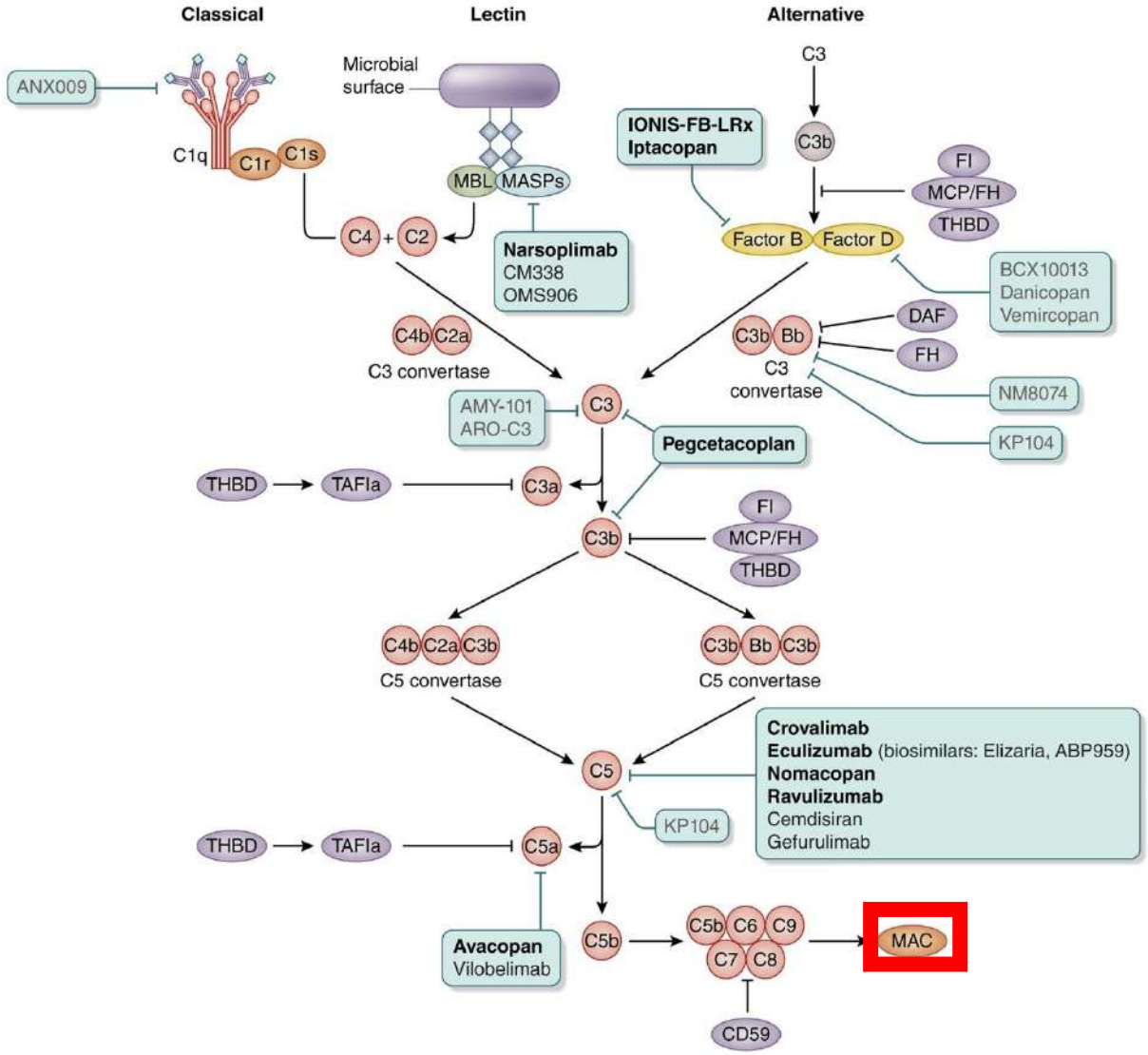
Physiopathologie

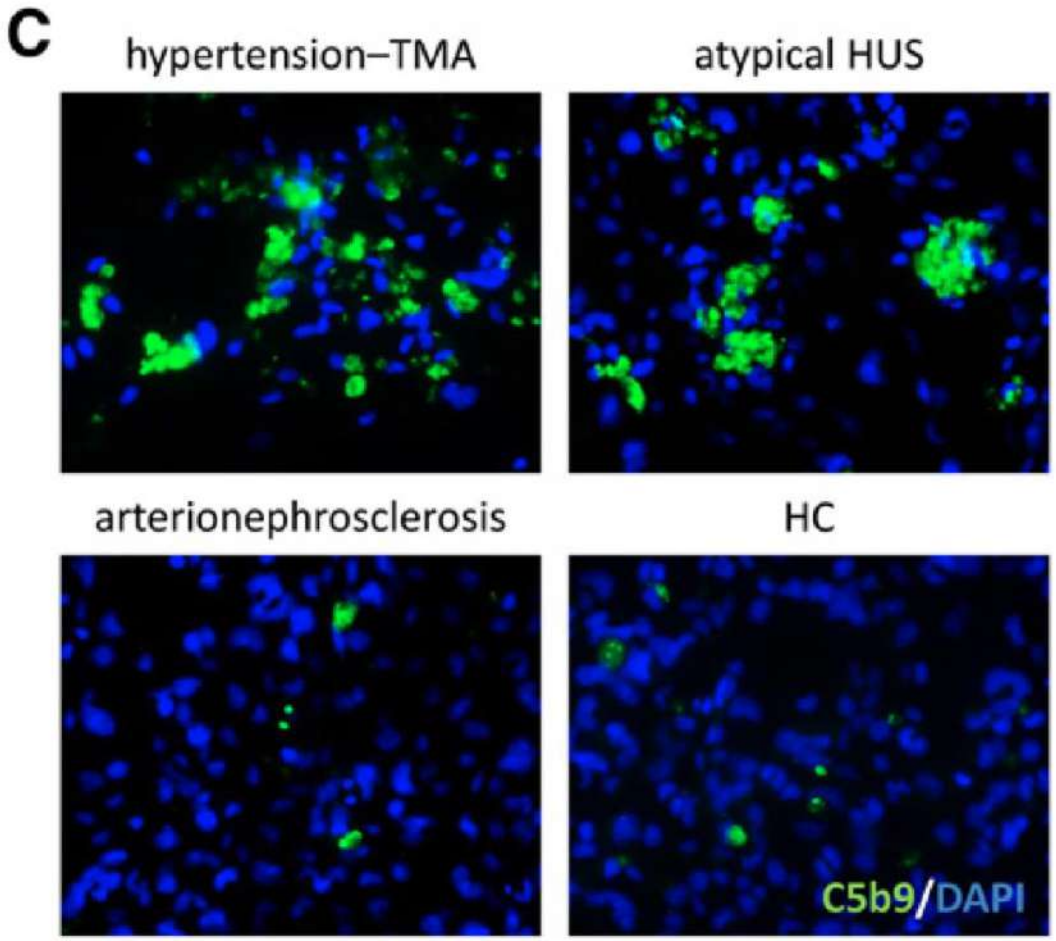
Physiopathologie de l'HTA maligne : ischémie rénale et sécrétion du SRAA



Boulestreau et al. JACC 2024

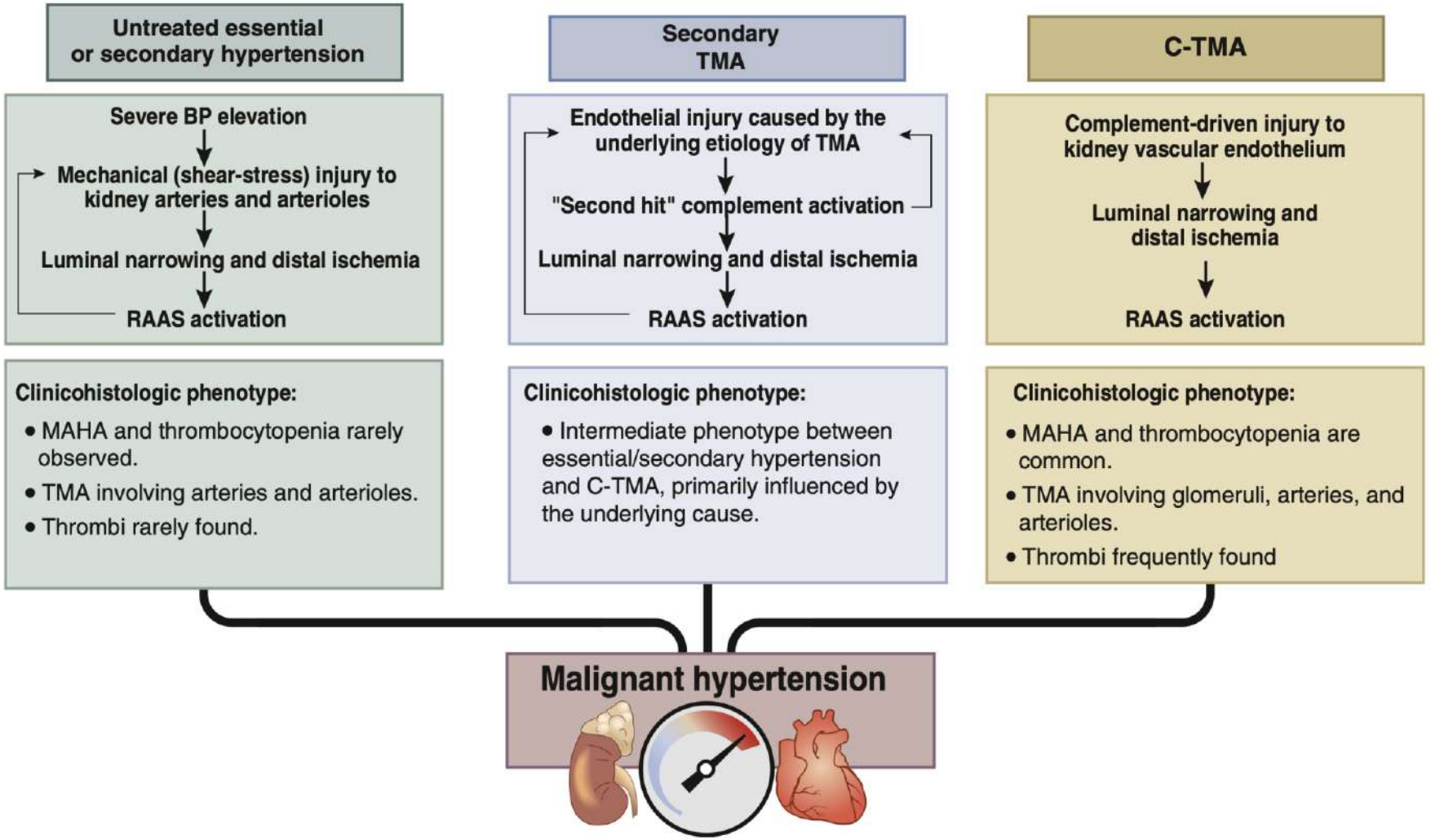
Le complément est activé dans certaines HTA malignes





Timmermans et al JASN 2018
KDIGO, Kidney Int. 2024

HTA maligne : l'activation du SRA le point central de la physiopathologie



Praga et al. Kidney Int. 2026

Etiologies

HTA maligne : étiologies

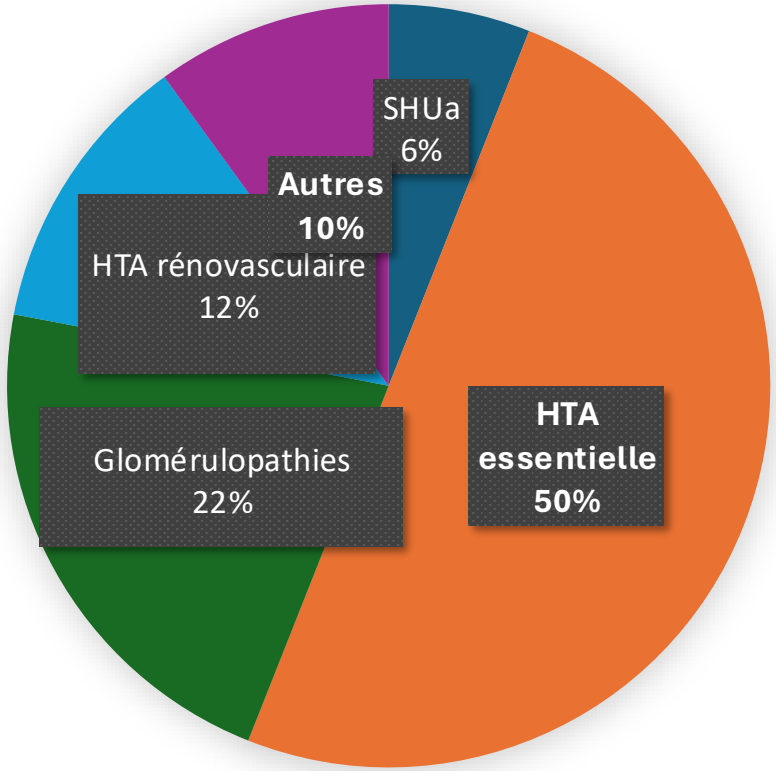
Cohorte Bordelaise`
« très cardiologique »
154 patients

TABLE 4. Causes of hypertension

	n	%
Essential	125	74
Estrogen contraception	18	11
Primary hyperaldosteronism	10	6
Renal artery stenosis	7	4
IgA nephropathy	3	2
Other nephropathy	4	2.5
Pheochromocytoma	1	0.5

Rubin et al. J Hypertens 2019

Cohorte Espagnole
« très néphrologique »
110 patients



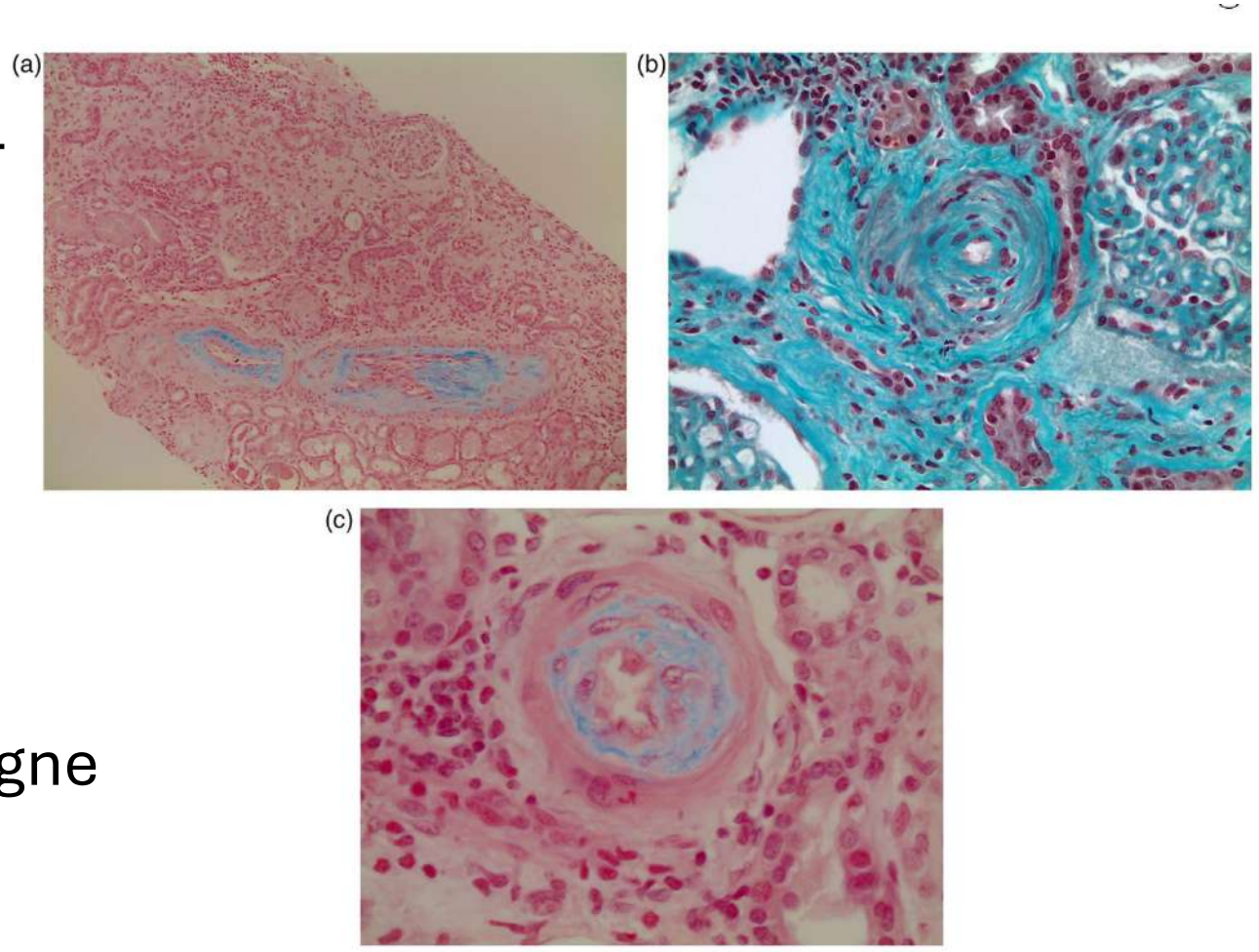
Cavero et al. Nephrol Dial Transplant 2022

A propos d'un cas : Homme de 53 ans

- ATCD : lithiase rénale
- Créatinine connue : 108 µmol/L

(2 ans avant)

- Céphalées brutales
- HTA : 238/127 mmHg
- créatinine 390 µmol/L
- Protéinurie : 1,9 g/g
- BU : hématurie + protéinurie
- Rétinopathie hypertensive maligne
- Masse VG : 167 g/m2
- Troponine : 209 ng/L



Laamecha et al. Blood Pressure 2025

Une crise rénale sclérodermique !

Anti-ARN Polymerase III : POSITIF

Capillaroscopie : Megacapillaires

Laamecha et al. Blood Pressure 2025

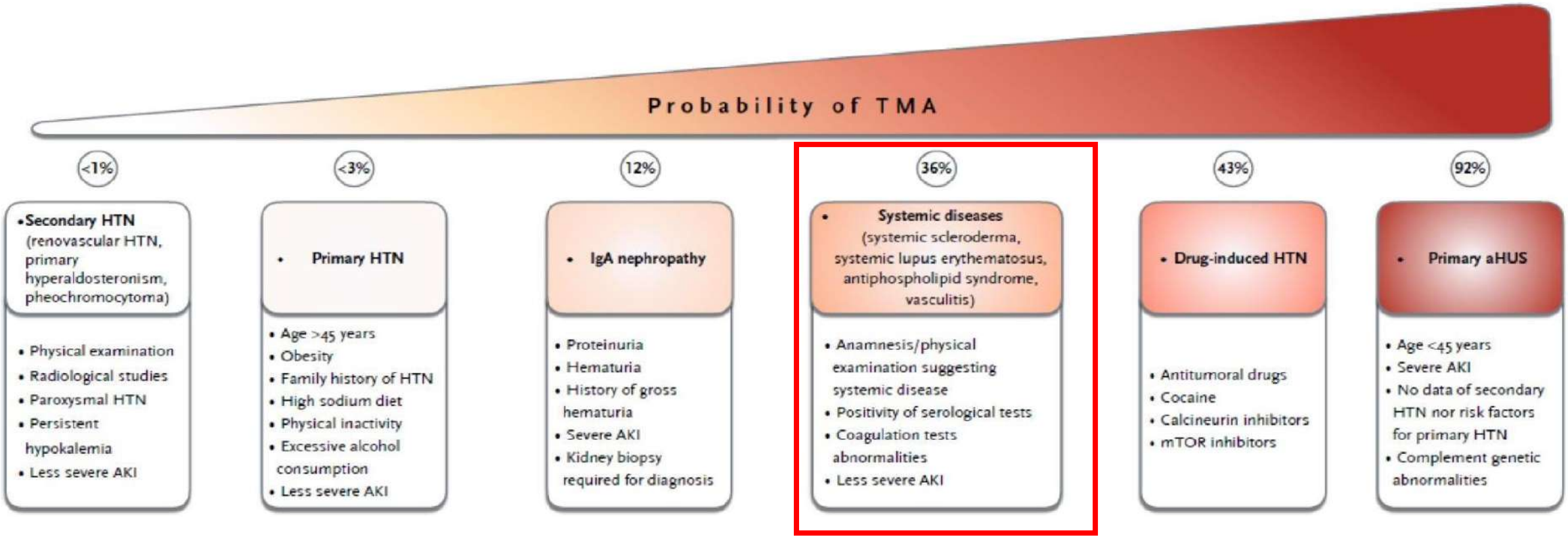
Deux crises rénales sclérodermiques !

Table 1. in-hospital clinico-biological data of patient and last available data for patient 1 and 2.

Case 1	Admission	D4	D9	D15	A5
eGFR (CKD-EPI)	14	11	8	8.5	27
Platelet (G/L)	94	105	149	285	266
Hemoglobin (g/L)	134 g/L	126	110	110	165
Schizocyte	0.3%	0.2%	NA	negative	NA
Haptoglobin (g/L)	< 0.01	< 0.01	NA	NA	NA
LDH UI/L (N < 240)	640	491	NA	212	NA
Proteinuria (g/g)	1.9	NA	NA	0.9	0.3
Blood pressure (mmHg)	224/103	158/114	138/75	134/82	138/76
Case 2	Admission	D4	D9	D15	A5
eGFR (CKD-EPI)	35	20	9.5	11.5	27.5
Platelet (G/L)	185	403	311	658	386
Hemoglobin (g/L)	126	122	117	114	123
Schizocyte	1.1%	1%	NA	negative	NA
Haptoglobin (g/L)	<0.01	NA	NA	NA	NA
LDH UI/L (N < 240)	297	286	NA	215	NA
Proteinuria (g/g)	0.7	NA	NA	0.6	0.1
Blood pressure (mmHg)	206/112	143/99	150/90	148/92	132/81

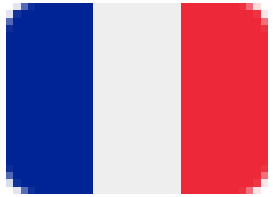
Laamecha et al. Blood Pressure 2025

La découverte d'une hémolyse mécanique rebat les cartes des probabilités étiologiques



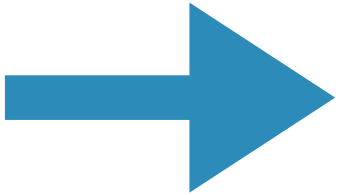
Cavero et al. Nephrol Dial Transplant 2022

La cohorte HAMA

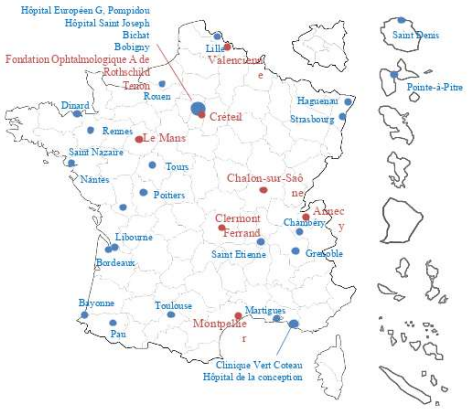


Started in

September 2019



Prospective



Multicentric /

Multidisciplinary

HAMA

Inclusion criteria :

- SBP > 180 ou DPB > 110 mmHg + severe hypertensive retinopathy
- SBP > 180 ou DPB > 110 mmHg + 3 TOD out of 4 = HYP-MOD

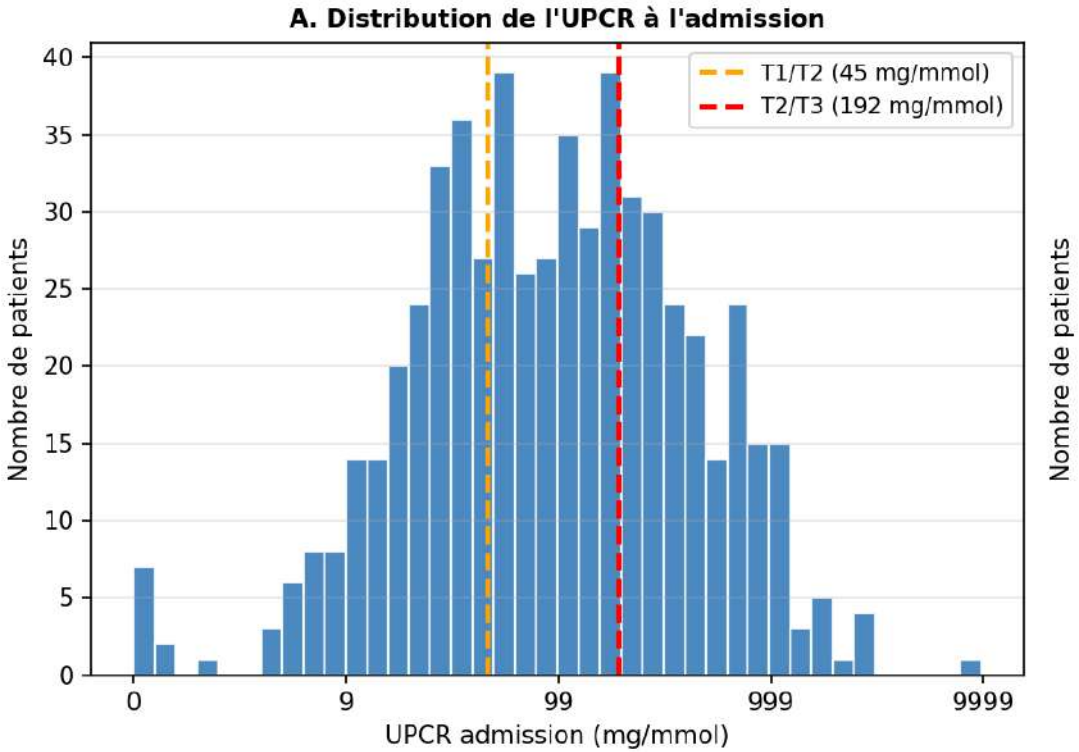
Exclusion criteria : patient's opposition, age below 18 y.o, guardianship

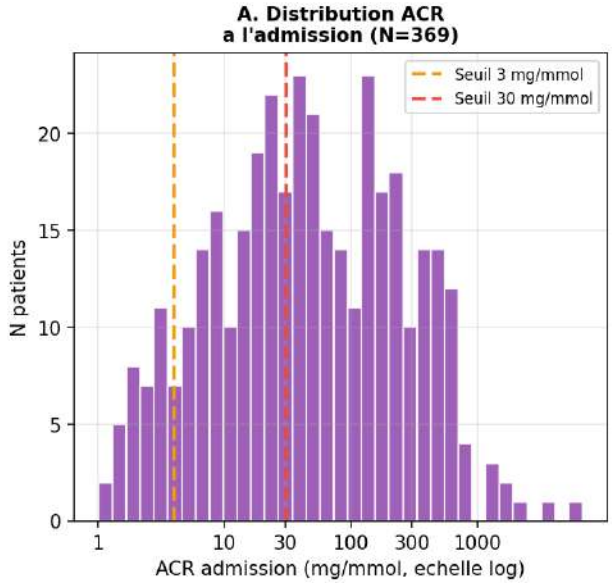
HAMA : patients à l'inclusion

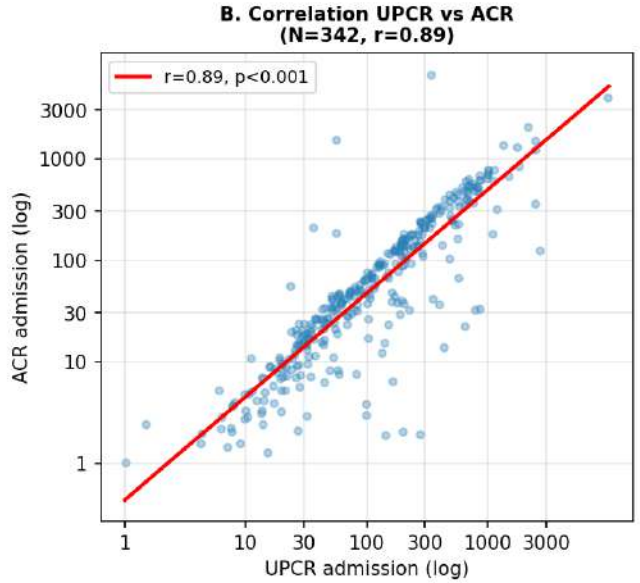
Variable	HAMA	BIRMINGHAM	MADRID	AMSTERDAM	BORDEAUX
Period	2019-2023	1964-2006	1974-2007	1992-2010	1995-2017
N	364	446	227	120	153
Nb/year	91	11	7	7	7
Age (years)	48±14.	48±13	49±13	44±12	46±12
Male,n (%)	185 (68%)	292(65.5)	144(63%)	83(69%)	104(68%)
BMI	27.8±6.5	NA	29.7±6.6	NA	NA
Smokers	102 (37%)	225(53.2%)	77(34%)	39(33%)	44(29%)
African origin	55 (20%)	20%	NA	NA	NA
Previous known Hypertension	174(64%)	117 (27%)	145(64%)	65(54%)	90(59%)
Secondary cause of hypertension	42 % of 139	204 (46%)	NA	25(21%)	52(34%)
Mean baseline SBP (mmHg)	217±27	229.3±29.5	207.8±32.4	230±23	211±33
Mean baseline DBP (mmHg)	128±23	142.2±19.2	125.3±21.4	145±17	118±20
Retinopathy papiloedema	117 (43%)	310(69.5%)		66(55%)	77(50%)

Les atteintes d’organes

Protéinurie dans la cohorte HAMA

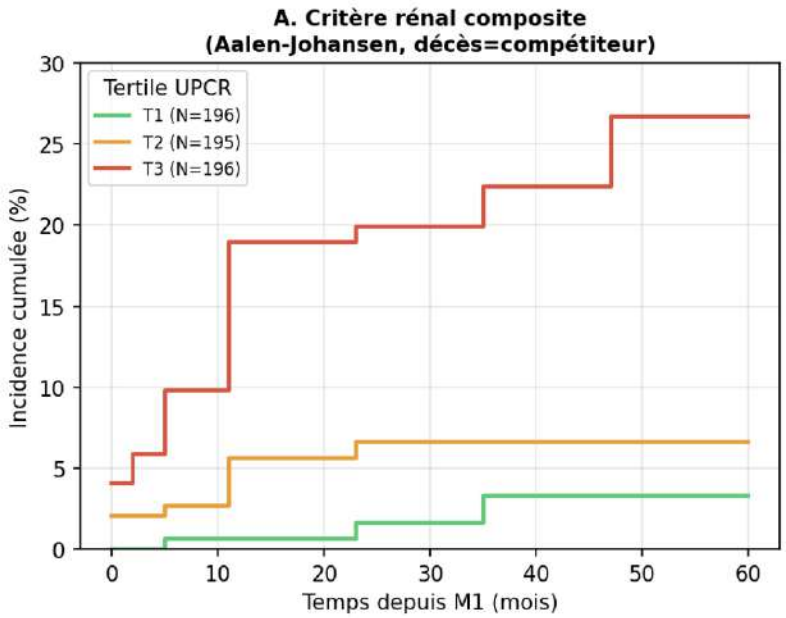






Unpublished data, Thèse Gwillerm Collet

Impact de la protéinurie sur les risques rénaux



Univariable and multivariable Cox proportional-hazards analysis of factors associated with renal composite outcome (n = 493).

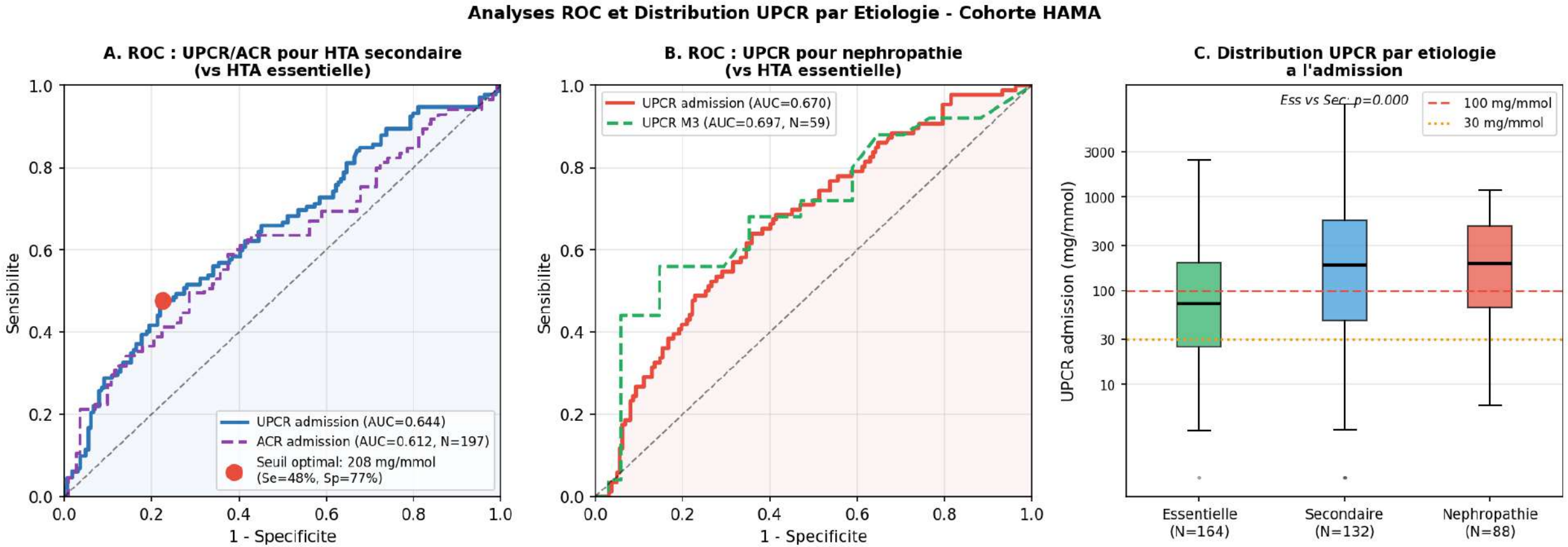
Variable	N	Unadjusted HR [95% CI]	p	Adjusted HR [95% CI]	p
log(UPCR) at admission	493	1.66 [1.33–2.09]	**<0.001**	1.19 [0.90–1.59]	0.225
eGFR at admission (per mL/min)	493	0.96 [0.94–0.98]	**<0.001**	0.97 [0.95–0.98]	**0.001**
Known CKD	493	3.53 [1.79–6.94]	**<0.001**	1.81 [0.85–3.86]	0.123
Diabetes	493	2.33 [1.05–5.14]	**0.036**	1.96 [0.74–5.18]	0.173
Age (per year)	493	1.00 [0.98–1.03]	0.778	1.00 [0.97–1.02]	0.702
Male sex	493	1.10 [0.53–2.30]	0.795	1.13 [0.54–2.38]	0.742
UPCR, time-updated (LMM) [a]	490	—	—	1.55 [1.02–2.37]	**0.040**

HR, hazard ratio; CI, confidence interval; UPCR, urine protein-to-creatinine ratio; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; LMM, linear mixed model. P-values in bold are statistically significant ($p < 0.05$).

[a] UPCR modelled as a time-updated covariate through a joint longitudinal–survival (linear mixed) model; baseline admission UPCR is shown separately in the first row. Adjusted estimate only.

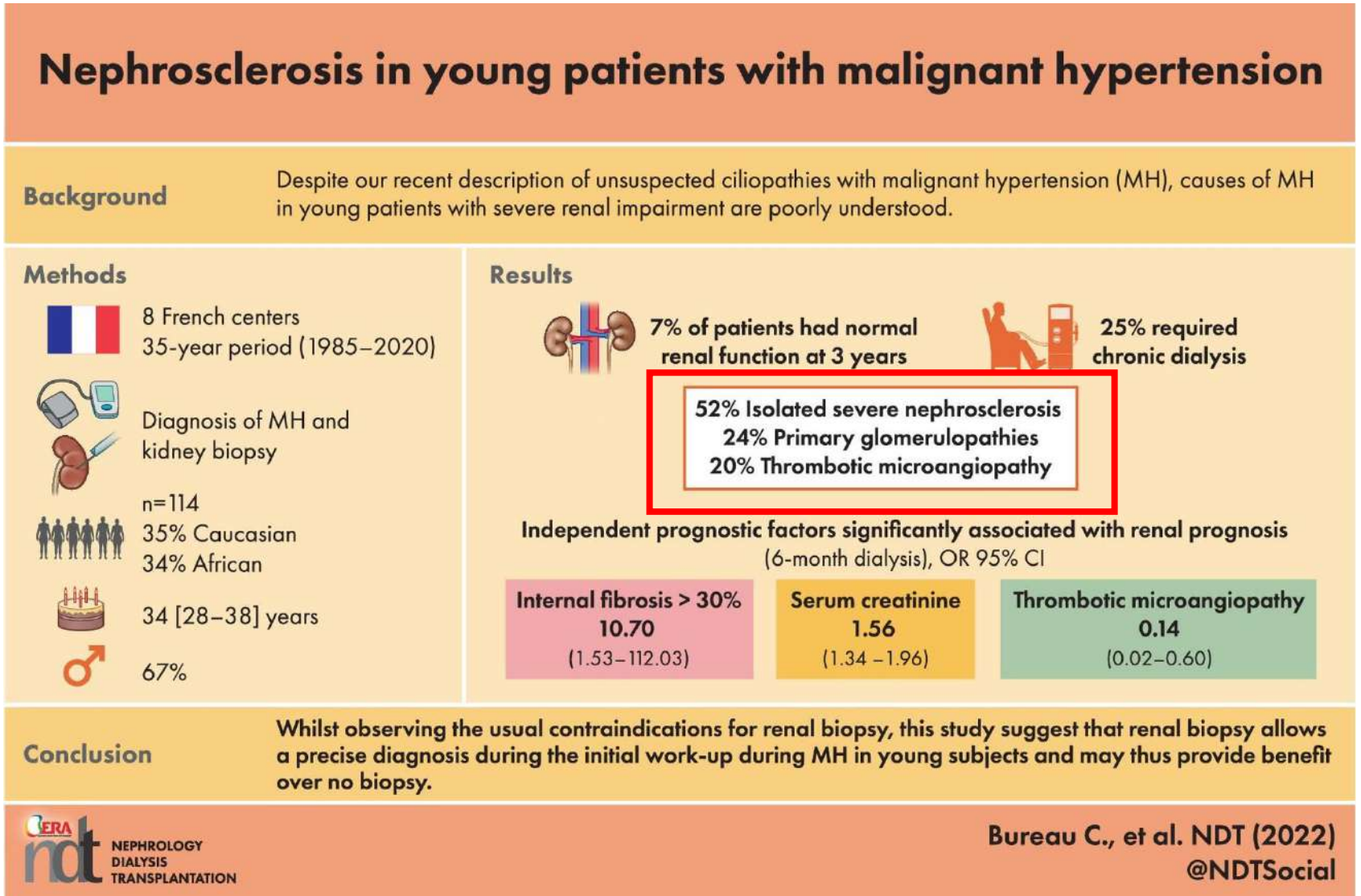
Unpublished data, Thèse Gwillerm Collet

Impact prédictif de la protéinurie pour l'étiologie de l'HTA



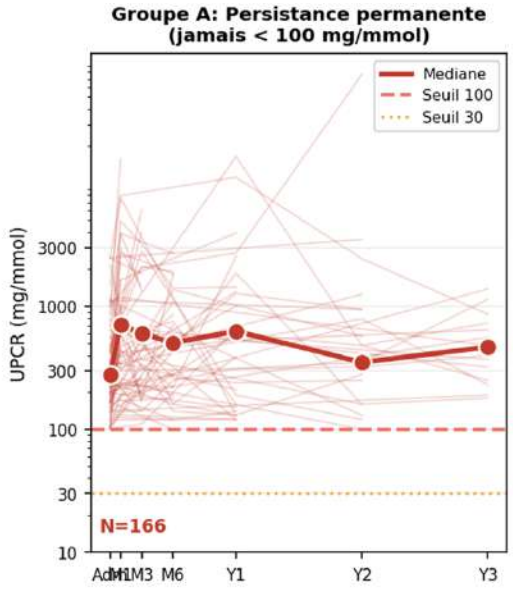
Unpublished data, Thèse Gwillerm Collet

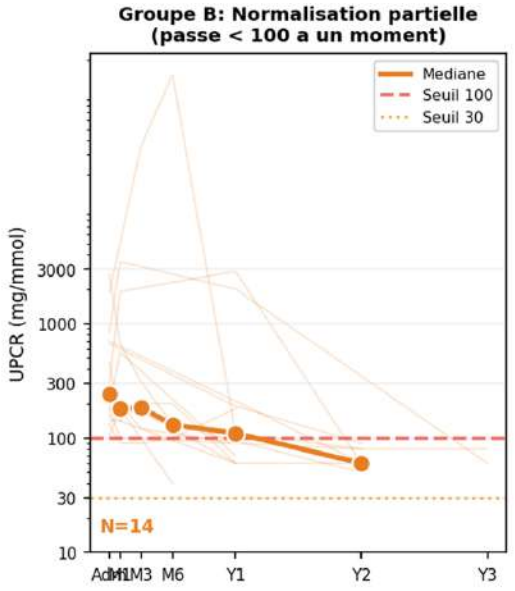
Faut-il biopsier la protéinurie persistante après une HTA maligne ?

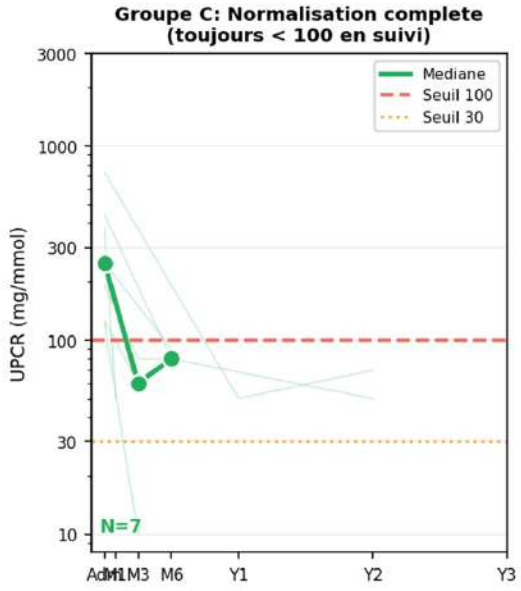


Quand biopsier le patient ? La protéinurie de M3 donne l'information

Visite	% >= 100	VPP vs Y1
M1 (1 mois)	98%	84%
M3 (3 mois)	95%	90%
M6 (6 mois)	95%	92%
Y1 (12 mois)	92%	--







Unpublished data, Thèse Gwillerm Collet

HTA maligne et biopsie rénale : méta analyse systématique

Renal histology findings in Malignant hypertension a systematic review

American Heart Association. Hypertension
Journal of the American Heart Association

PubMed, Embase, Cochrane Library, and Web of Science

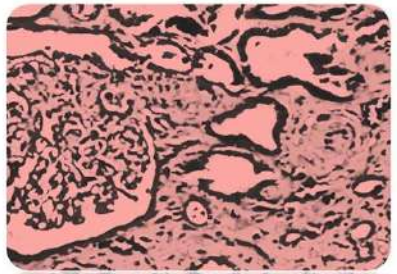
Original data on malignant hypertension and kidney histology in adult patients

14,003 identified studies
144 met inclusion criteria

1,781 patients

Men : 67%
Age : 38.4 years
Creatinine : 588 [511-664] µmol/L
Proteinuria : 4.3 [2.8-5.8] g/g
Sub-Saharan origin : 2.1%

Hematological TMA : 72.8%
Renal TMA : 95.2%
Increasing rates in recent decades



Nephrosclerosis: 68.4%
IgA nephropathy: 11.8%
FSGS: 6.9%
aHUS: 4.1%

Maisons et al, 2025

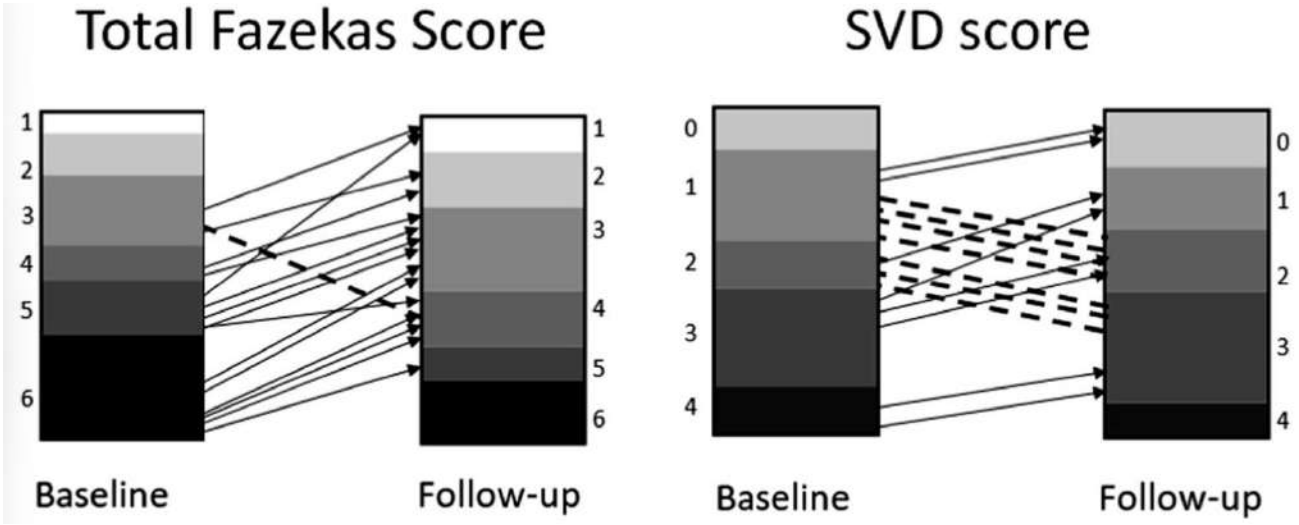
CONCLUSION
A third of patients with MH have other lesions than nephrosclerosis and that hematological and renal TMA are present in two-thirds and almost all of patients.

L’atteinte cérébrale en IRM dans l’HTA Maligne

Variable	No FU brain MRI $n = 57$	At least 1 FU brain MRI $n = 47$	p
Age (years)	47.9 (12.4)	48.2 (10.8)	0.88[a]
Sex (female/male)	21/35	13/34	0.36[b]
Diabetes mellitus	3 (5.3%)	5 (10.6%)	0.46[d]
Hypercholesterolemia	7 (12.3%)	10 (21.3%)	0.22[b]
Active smoker	24 (42.1%)	17 (36.2%)	0.54[b]
Hypertension and Target Organ damage			
SBP at admission (mmHg)	215.7 (33.2)	211.3 (24.5)	0.46[a]
DBP at admission (mmHg)	119.2 (19.7)	118.4 (18.6)	0.83[a]
Severe Hypertensive retinopathy	44 (78.5%)	31 (66%)	0.20[b]
Creatinin level (µmol/l)	124 (95 – 180)	106 (84–172)	0.12[c]
eGFR (ml/min/1.73 m²)	54.3 (28.6)	63.7 (30.1)	0.10[a]
Cardiac damage	50 (89.3%)	40 (85.1%)	0.53[b]
TMA stigmata	8 (14.0%)	12 (25.5%)	0.14[b]
Neurological manifestations upon admission			
Neurologic symptoms at admission	22 (38.6%)	22 (46.8%)	0.39[b]
Acute brain injury	22 (38.6%)	27 (57.4%)	0.055[b]
Ischemic stroke	9 (15.8%)	10 (21.3%)	0.44[b]
Cerebral Hemorrhage	7 (12.3%)	9 (19.1%)	0.31[b]
PRES	7 (12.3%)	12 (25.5%)	0.082[b]
Mean SVD score	1.6 (1.1)	1.9 (1.2)	0.17[a]

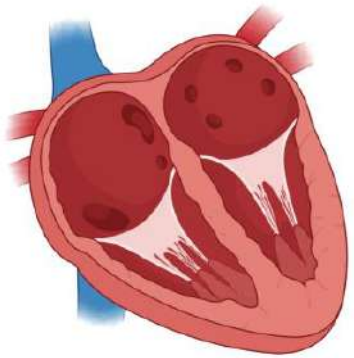
- **SVD** = score global de microangiopathie (0 à 4)
- **Fazekas** = score spécifique des lésions de substance blanche (0 à 6)

7,5 mois médian de suivi



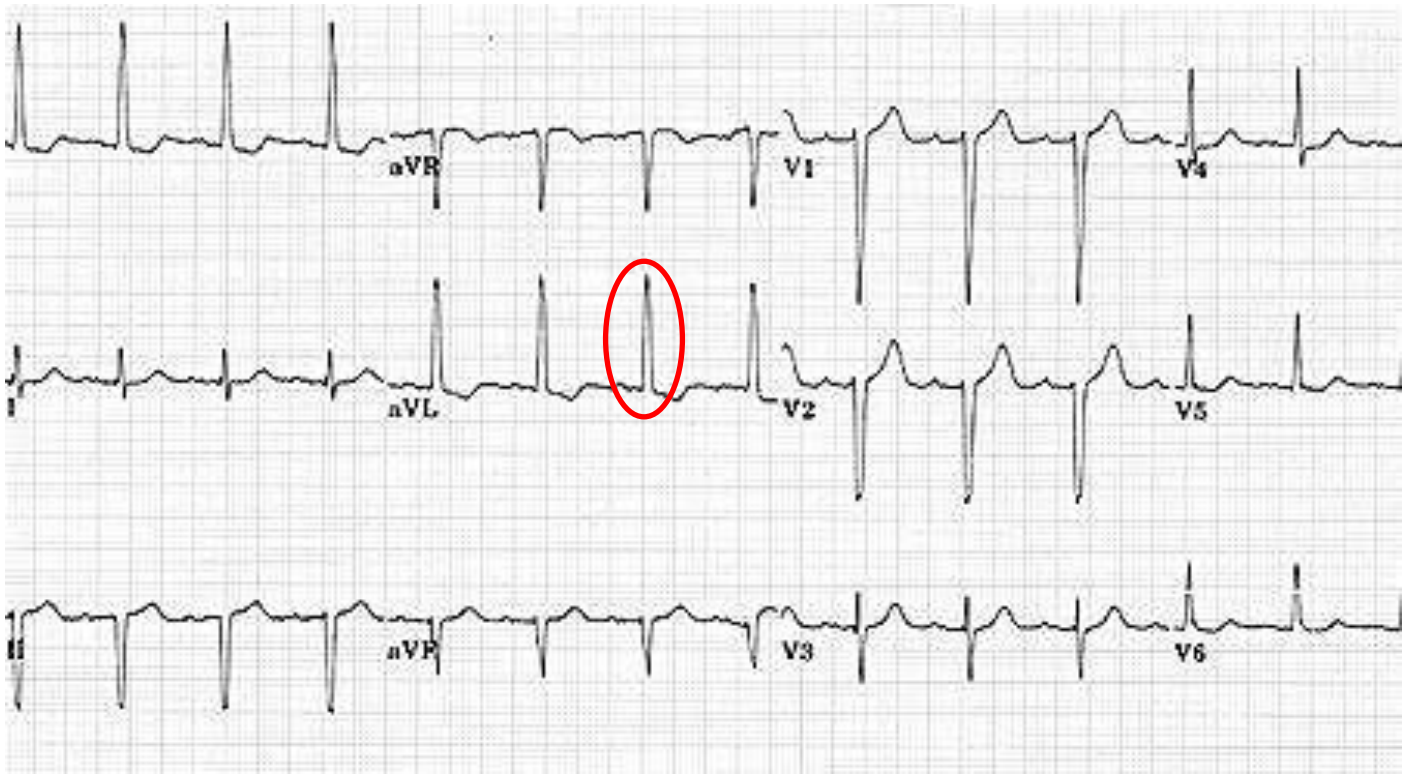
Liegey et al. J Hum Hypertens 2025

L’ECG l’outil simple et immédiat dans l’HTA Maligne



Septum(diastolic) : 13.7 ± 4 mm
LVEF 52.7% ± 12.1
Global longitudinal Strain : 13.6 ± 4.4 %

R aVL > 10 mm dans 97%



Rubin et al. J. Hypertens. 2019

Evaluation initiale

Quelle stratégie d’évaluation initiale proposons nous ?

1. Fond d'œil
2. ETT /ECG : hypertrophie ventriculaire gauche ?
3. Troponine / BNP : lésion microvasculaire cardiaque ?
4. Créatinine, rapport albumine/créatinine/ECBU: atteinte rénale ?
5. LDH, d'haptoglobine, de schizocytes, d'hémoglobine et les numérations plaquettaires : **MAT ?**
6. IRM cérébrale
7. La recherche HTA secondaire doit être effectué après la gestion de la crise aiguë

HTA Maligne : bilan étiologique, a adapter en fonction du profil du patient

Condition	Diagnosis
Hematologic TMA	Complete blood count, LDH, peripheral blood smear, Coombs test, and serum haptoglobin
TTP	ADAMTS-13 activity and PLASMIC score
STEC-TMA	Stool culture for STEC and PCR for Shiga toxin type 2/type 1
Secondary TMA	
Infection	
Streptococcus pneumoniae	Blood or pleural cultures, PCR for streptococcal antigen, and Thomsen-Friedenreich antigen
Other infections (Klebsiella pneumoniae, HIV, SARS-CoV2, EBV, CMV, influenza, and parvovirus B19)	Specific PCR/serology
Drug-induced	Careful review of medications and illicit-drugs consumption. Urine screening for cocaine and other illicit drugs
Cancer	Patients with solid organ (lung, breast, prostate, gastric, and ovarian) cancer or hematologic malignancies
Transplantation	Solid organ (kidney and lung). Hematopoietic stem cell transplant
Autoimmune systemic diseases	
Systemic sclerosis, scleroderma renal crisis Antiphospholipid syndrome Lupus nephritis Vasculitis	ANA, anti-dsDNA, Anti-Scl70, anticentromere and anti-RNA polymerase III antibodies, anticardiolipin and anti-ß2 glycoprotein antibodies, and ANCA
Glomerulonephritis (mainly IgA nephropathy)	Kidney biopsy
Pancreatitis	Pancreatic enzymes
Cobalamin C deficiency	Homocysteine plasma levels
Secondary hypertension	
Diagnostic workup to identify etiology (renovascular hypertension, pheochromocytoma, and primary hyperaldosteronism) and to assess hypertension-induced organ damage	Complete physical examination; electrocardiogram, echocardiography, kidney/Doppler ultrasound, abdominal CT angiography, brain CT or MRI (if neurological symptoms), aldosterone-to-renin ratio, adrenal glands CT (suspicion of primary hyperaldosteronism), and plasma and urine catecholamines (suspicion of pheochromocytoma)
Other tests	Coagulation tests, serum and urine electrophoresis, iron profile, and thyroid hormones

Praga et al. Kidney Int. 2026

Le traitement

HTA Maligne : traitement

Acute Target-Organ Damage	Timing for Acute BP Reduction†	Preferred Intravenous Drugs‡
Diffuse microvascular injury ("malignant hypertension")§	Decrease BP by 20–25% during first hr and to 160/100 mm Hg by 2–6 hr	Labetalol, nicardipine, nitroprusside
Hypertensive encephalopathy	Decrease BP by 20–25% during first hr and to 160/100 mm Hg by 2–6 hr	Labetalol, nicardipine, nitroprusside; avoid hydralazine

Peixoto N Engl J Med 2019

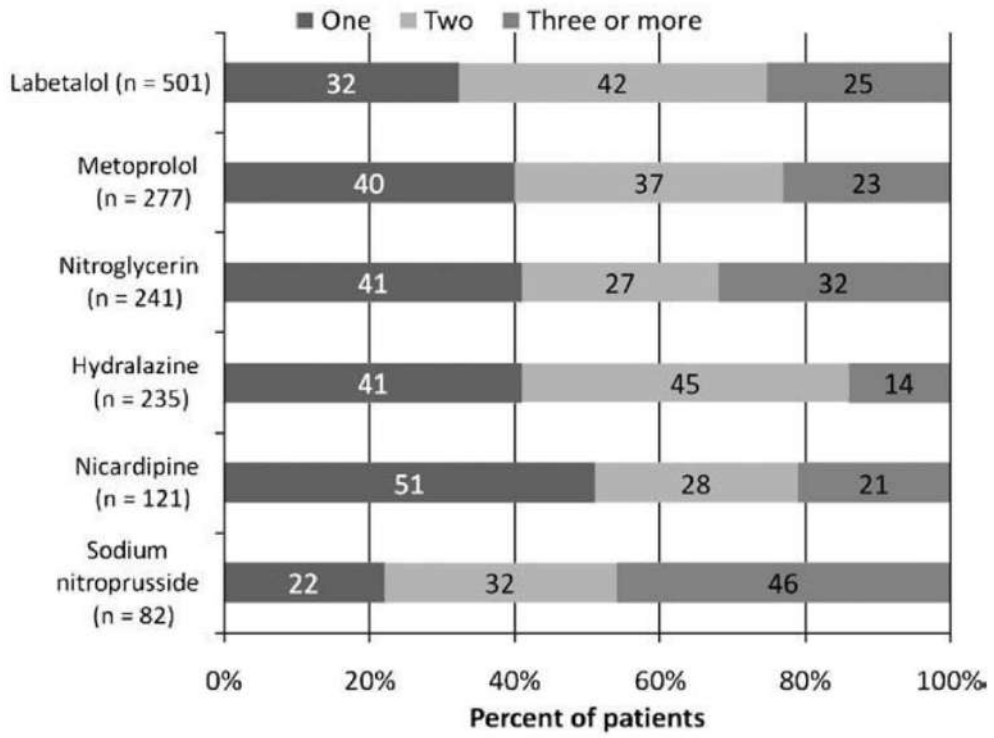
Clinical presentation	Time line and target BP	1st line treatment	Alternative
Malignant hypertension with or without TMA or acute renal failure	Several hours, MAP -20% to -25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediate, MAP -20% to -25%	Labetalol Nicardipine	Nitroprusside

Van den Born et al. Eur Heart J 2018

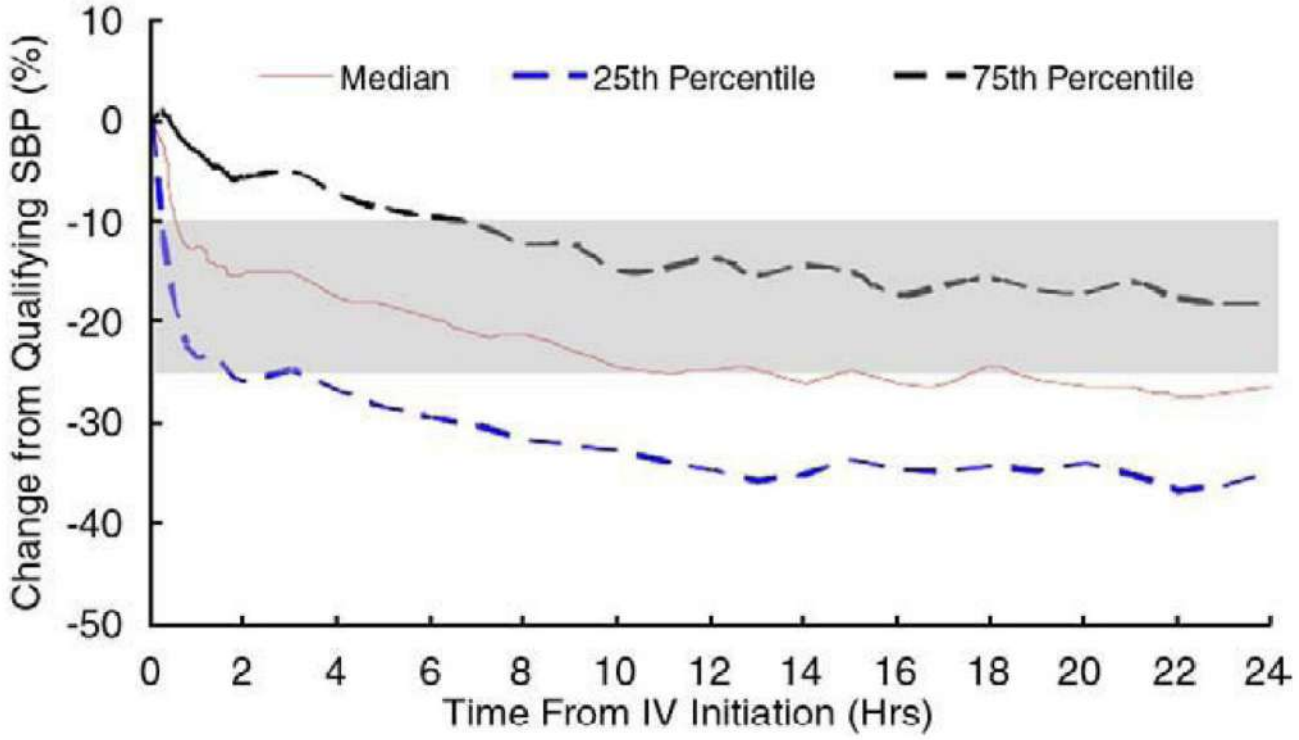
Stratégie IV : les leçons du registre STAT

1588 patients
HTA >180/110 mmHg

Nombre de molécules IV utilisé



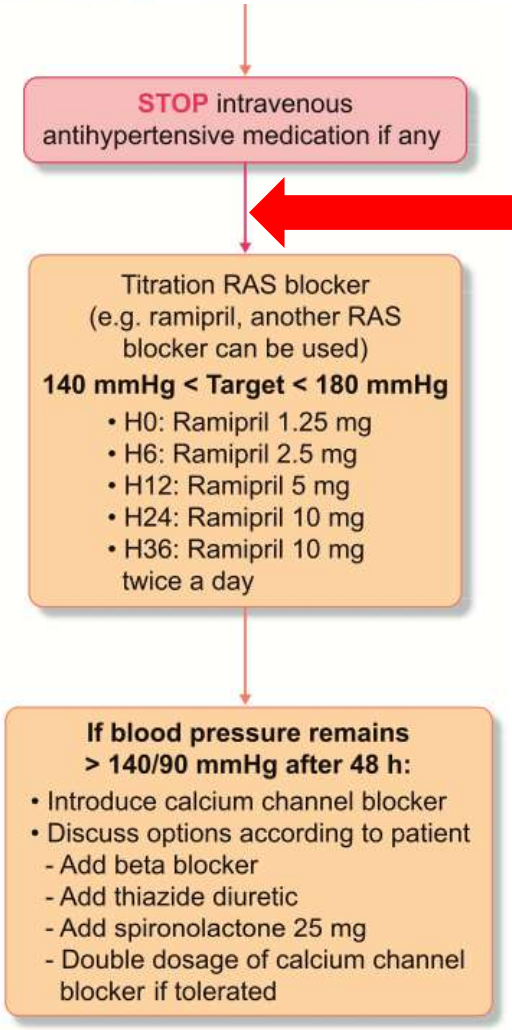
Variation de la PA



Katz JN, et al. Am Heart J. 2009

A plea for renin–angiotensin system blockers as first-line treatment in cases of severe acute hypertension

Sébastien Rubin [1,2], Romain Boulestreau[3], Philippe Gosse[4] and Christian Combe [1,5]

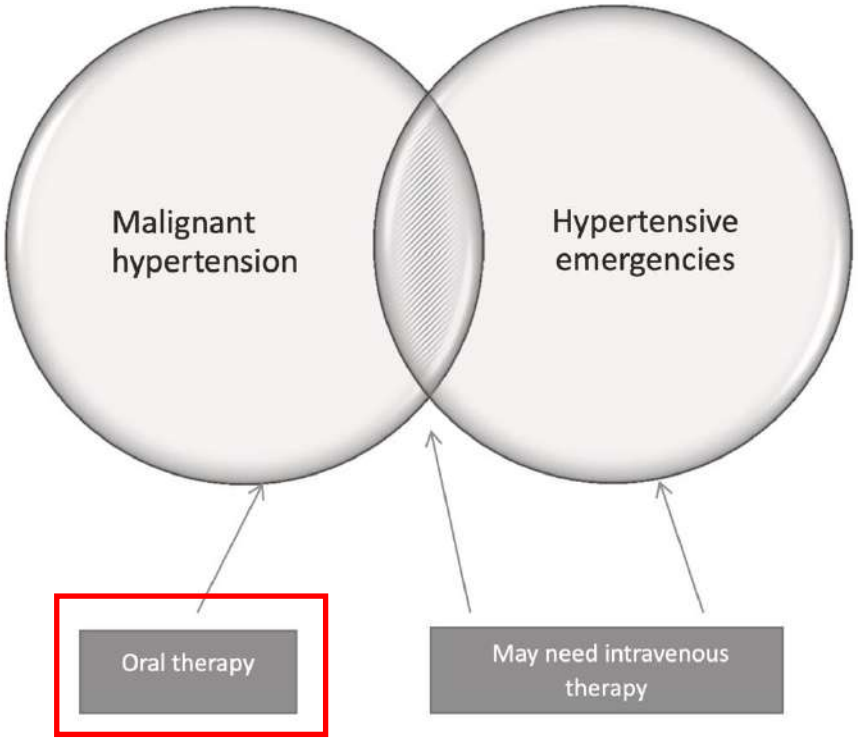


Expansion volémique

HAMA

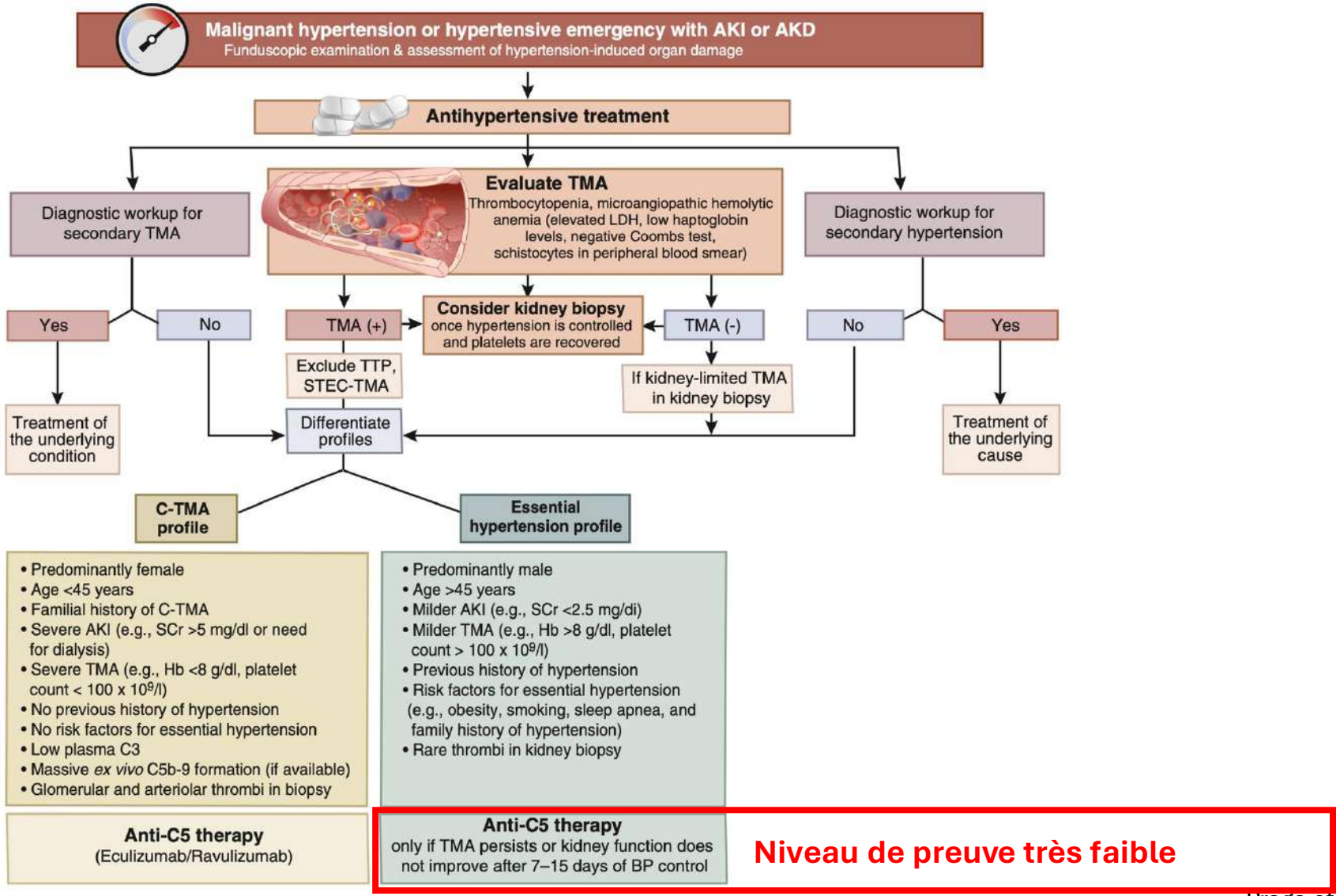
Initial treatment	
IV initial treatment	234 (77%)
Urapidil IV	87(29%)
Calcium Antagonist IV	148 (49%)
Oral ACEI	68 (23%)

British and Irish Society of hypertension 2022



Rubin et al. N Engl J Med 2020
Rubin et al. Nephro Dial Transplant 20
British and Irish Society Position 2022

La place du traitement spécifique : anti C5



Niveau de preuve très faible

Praga et al. Kidney Int. 2026

HTA maligne : quand y penser ?

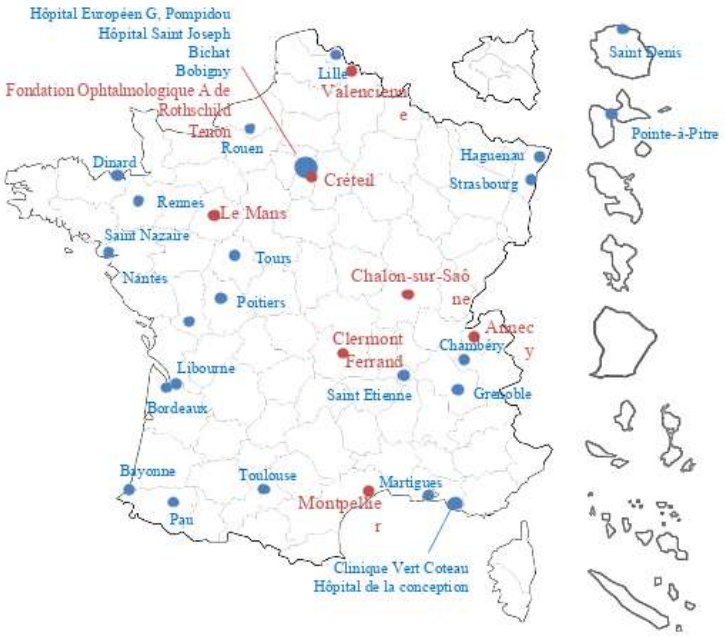
- Profil à haut risque
  - Âge : 30-60 ans, homme
  - Origine africaine, conditions de vie défavorisées
  - Non-adhérence thérapeutique
- Caractéristiques de l'HTA
  - Céphalées et troubles visuels
  - Hypokaliémie ± Insuffisance rénale aigüe
  - Micro-Angiopathie Thrombotiques
  - Insuffisance rénale aigüe associée à une HTA sévère
  - Hypertrophie ventriculaire gauche disproportionnée (évaluation échocardiographique / électrocardiographique)

Conclusion

- L’HTA maligne est un syndrome clinique : HTA sévère + atteinte aigue des organes cibles
- L’HTA maligne présente de multiples étiologies
- Elle nécessite
  - Un traitement ciblé sur le SRAA et la Pression Artérielle
  - Une IRM cérébrale : évaluation de la cSVD
  - Une recherche étiologique
  - Un suivi de ces patients
- Confier au néphrologue les patients proteinuriques à 1 mois
- Penser à la recherche d’hémolyse mécanique
  - LDH/Haptoglobine/Schizocytes

HAMA : la première cohorte prospective mondiale d'HTA maligne

PI : Dr Romain Boulestreau



- Étape 1 : Preuve de concept, la cohorte prospective multicentrique française HAMA, une cohorte de science ouverte et collaborative
- Étape 2 : Établissement de sous-études HAMA pour répondre aux objectifs du programme HAMA (études IVAMA et HAMCOG)
- Étape 3 : Extension de la cohorte HAMA aux centres européens
- Étape 4 : Mise en place d'une biobanque (génomique, peptidomique urinaire, métabolomique et transcriptomique à partir des cellules rénales)
- Étape 5 : Établissement d'un modèle murin d'hypertension maligne afin de valider les hypothèses de pathogenèse / options thérapeutiques

Remerciements

Conseil Scientifique HAMA

Investigateurs HAMA

Inserm
La science pour la santé
From science to health

HTA
Société Française d'HyperTension Artérielle

ESH European Society of Hypertension

HYPERTENSION
FONDATION DE RECHERCHE SUR L'HYPERTENSION ARTERIELLE

Fédération Française de Cardiologie

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