Syndrome cardio-rénal: gestion par le (la) généraliste

Dr Cambier JF

Introduction

Définition d'une MRC

- Chronicité (> 3 mois)
- eGFR < 60 ml/min/1.73m²
- Anomalies structurelles et/ou fonctionnelles:

- Albuminurie
- Anomalies du sédiment urinaire
- Signes de tubulopathie (Fanconi, diabète insipide, hypoK+…)
- Anomalies histologiques
- Anomalies radiologiques (kystes, dysplasie, SAR…)
- TP rénale

Les stades de MRC

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

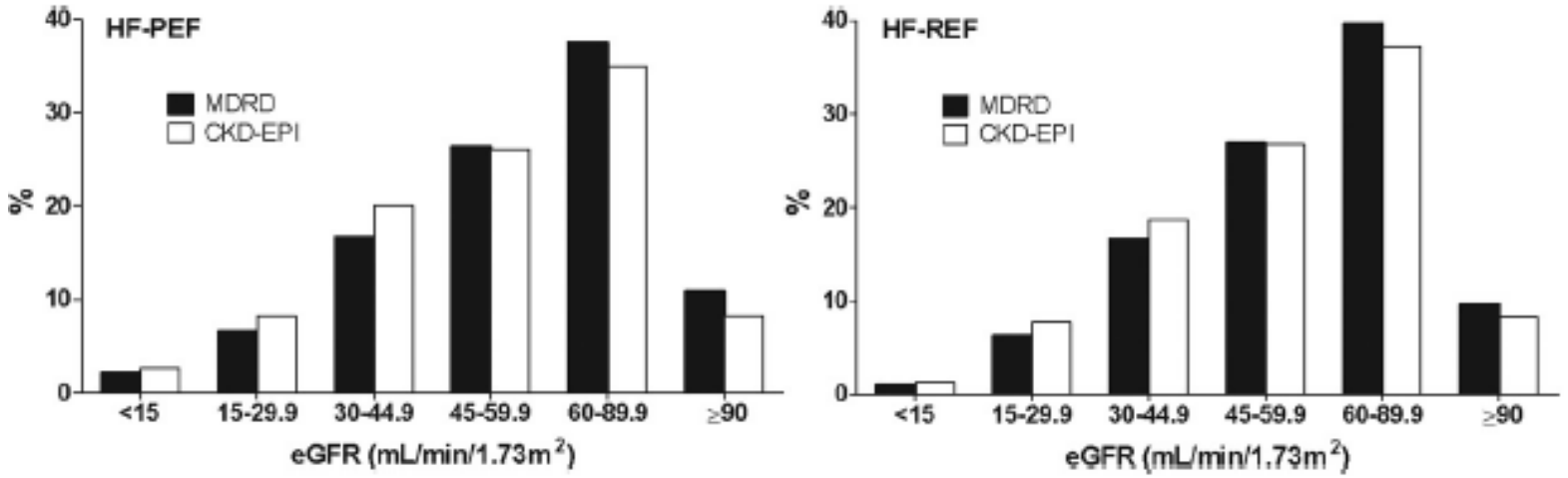
Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Epidémiologie

- IC et IRC: prévalence et incidence ↑.

- Etiologies et facteurs de risque communs: 50% IRT secondaire au diabète ou d'origine vasculaire.

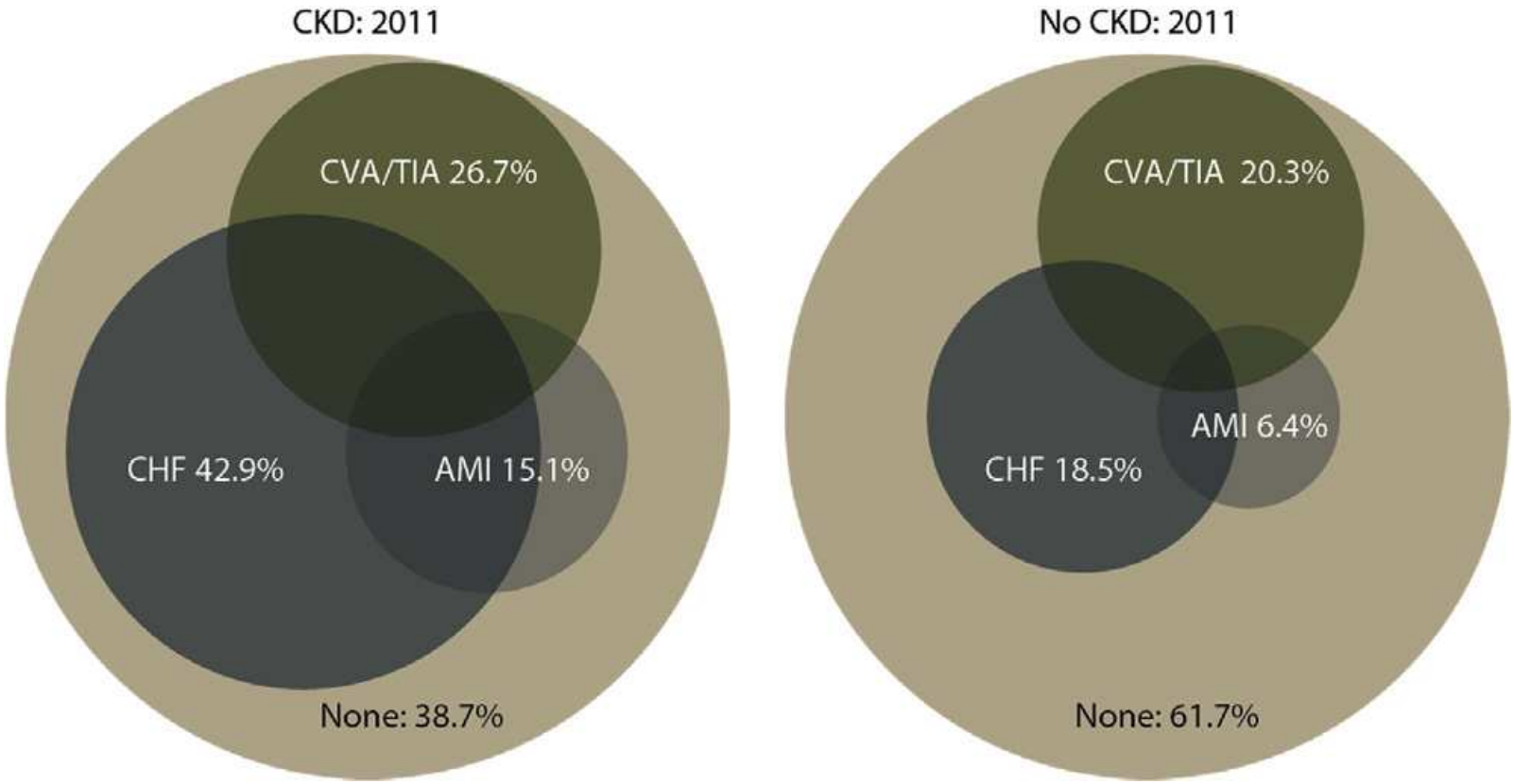
Jusqu'à 50% des patients avec une IC ont une IRC



- 25 études prospectives
- 20 754 patients: 15962 HFrEF et 4792 HFpEF

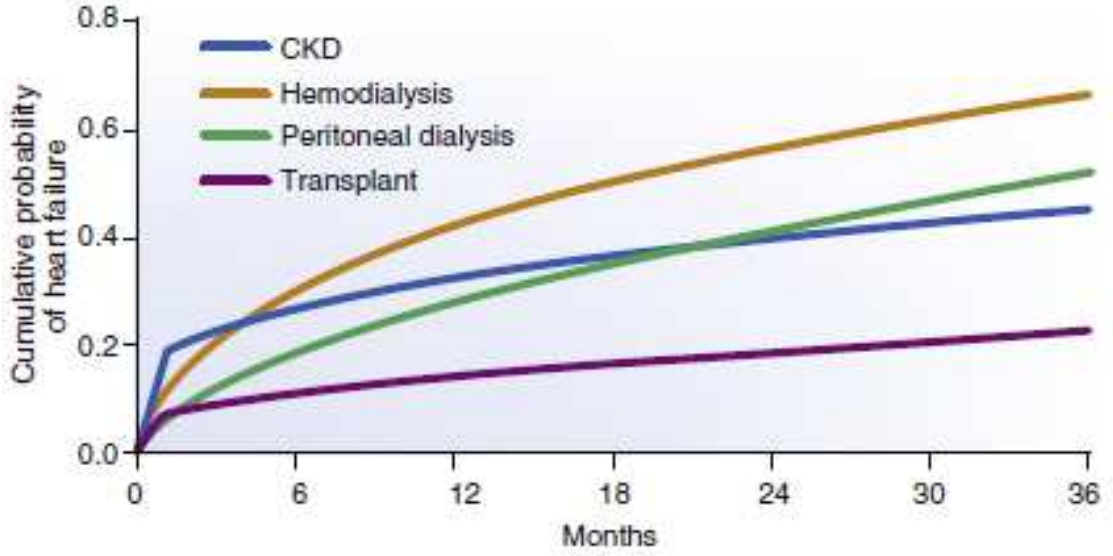
McAlister FA et al, ***Circ Heart Fail,*** 2012

Prévalence de la MCV en cas d'IRC



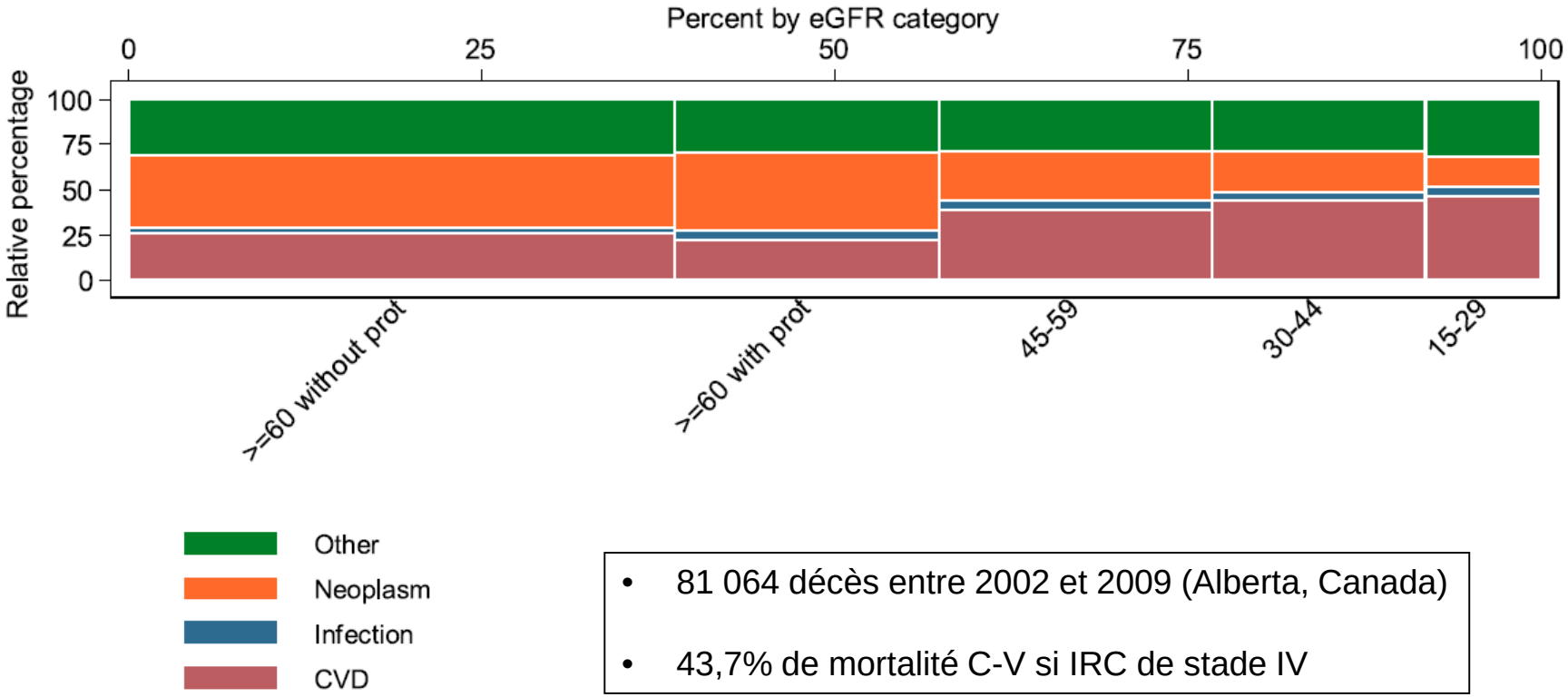
US Renal Data System 2013 Annual Data Report

Incidence de l'IC ↑ au cours du temps en cas d'IRC



Collins AJ et al, ***Am J Kidney Dis,*** 2008

L'IRC augmente la mortalité C-V



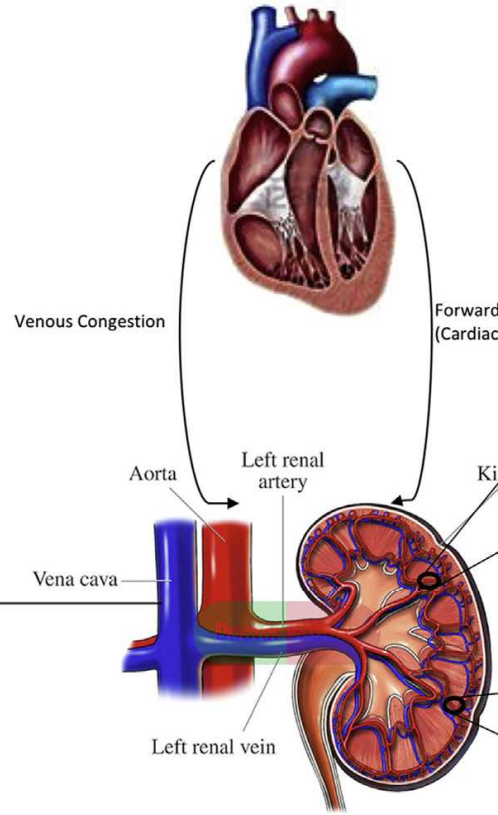
- 81 064 décès entre 2002 et 2009 (Alberta, Canada)
- 43,7% de mortalité C-V si IRC de stade IV

Thompson S et al, ***J Am Soc Nephrol,*** 2015

Diagnostic du SCR

- Clinique
- ETT
- NT-proBNP (influence de l'IRC)
- Créatinine plasmatique

Physiopathologie



Renal Venous Congestion
- Rowntree, Fitz and Geraghty 1913
- Winton FR: 1937
- Seymour WB et al: 1942
- Blake WD et al: 1949

Reduced GFR
- Warren and Stead: 1947
- Merrill AJ: 1946
- Mokotoff, Ross and Leiter: 1948
- Stead, Warren and Brannon: 1948

Increased urinary sodium re-absorption
- Futcher and Schroeder : 1942
- Borst JG: 1948
- Briggs AP et al: 1948
- Kattus A et al: 1948

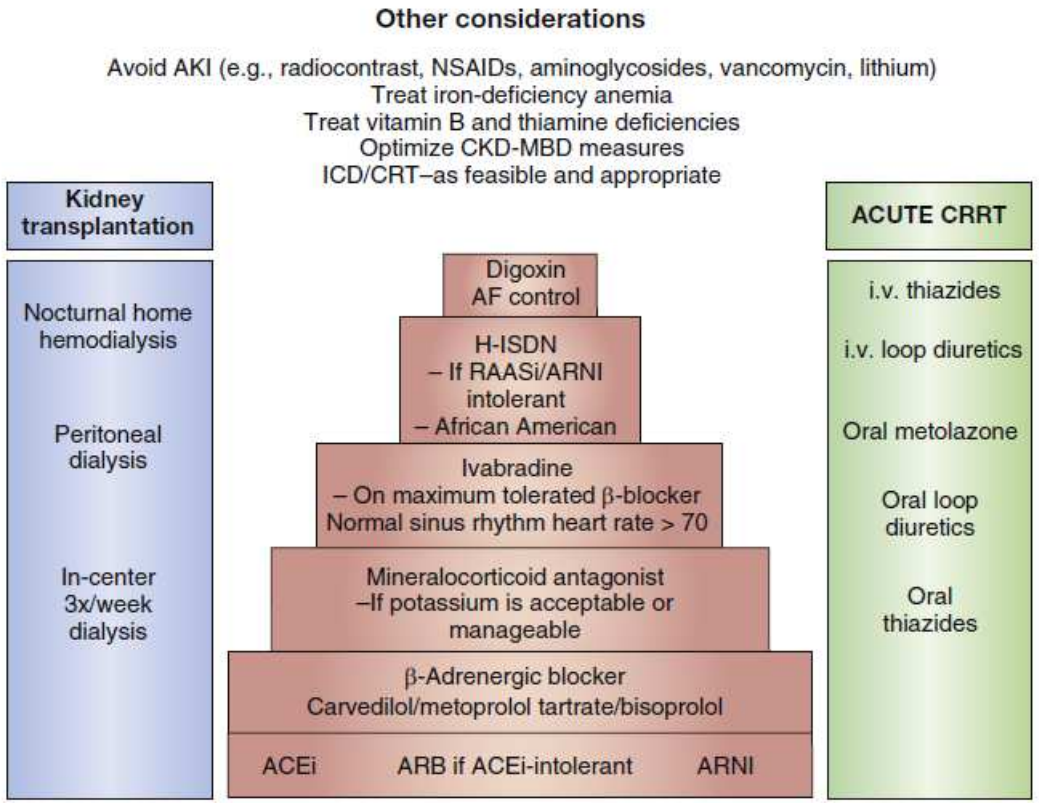
Rangaswami J et al, ***Adv Chronic Kidney Dis,*** 2018

Types de SCR

	Mécanisme initial	Atteinte secondaire
SCR de type 1	IC aiguë	IRA
SCR de type 2	IC chronique	IRC
SCR de type 3	IRA	IC aiguë
SCR de type 4	IRC	IC chronique
SCR de type 5	Maladie systémique (diabète, amylose, sepsis…)	IC et IR

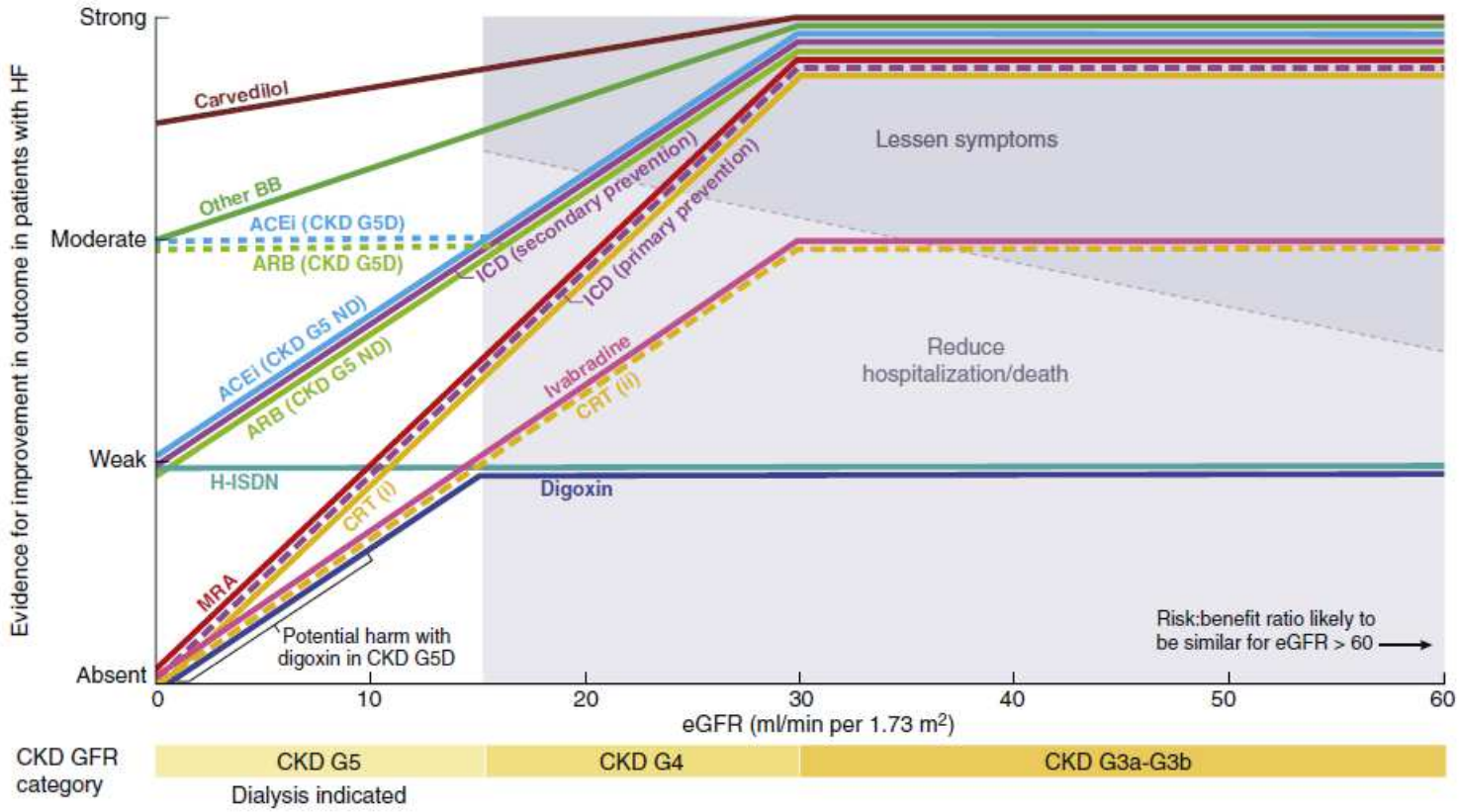
Prise en charge thérapeutique

1. Vue d'ensemble



House AA et al, ***Kidney Int,*** 2019

Niveaux de preuve



CRT (i) = QRS > 120 ms, LBBB QRS morphology, EF ≤ 35%
or QRS > 130 ms, EF ≤ 30%
CRT (ii) = QRS > 150 ms

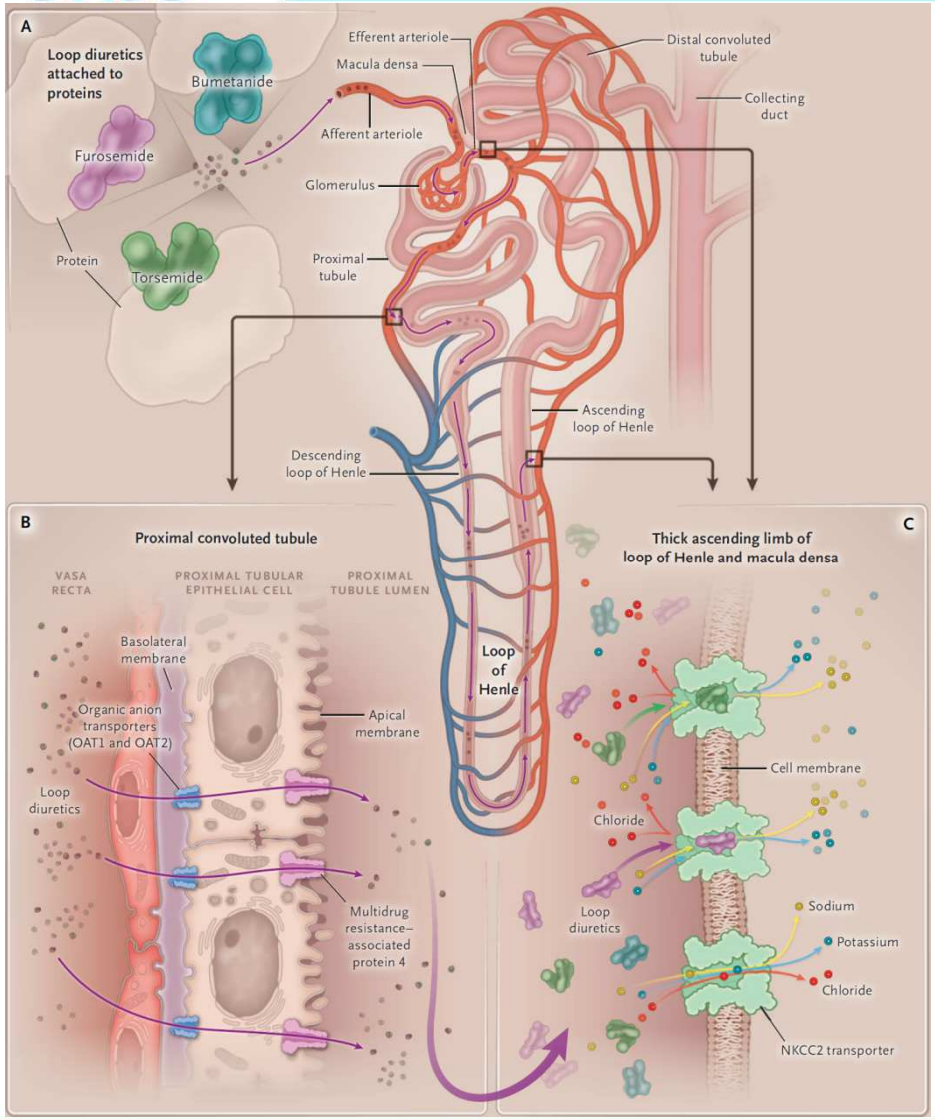
Loop diuretics (p.o./i.v.) (furosemide, bumetanide, torsemide) and thiazide diuretics (metolazone [p.o.], chlorothiazide [i.v.]) = benefit uncertain

House AA et al, ***Kidney Int,*** 2019

2. Education du patient

- Le régime sans sel strict (< 6g NaCl par jour).
  - ⇒ Utilité de la collecte d'urines de 24h: (Natriurèse de 24h/17).
- Suivi du poids: notion de « poids sec ».
- Eviter les néphro(cardio)toxiques: AINS, injection de produit de contraste iodé…

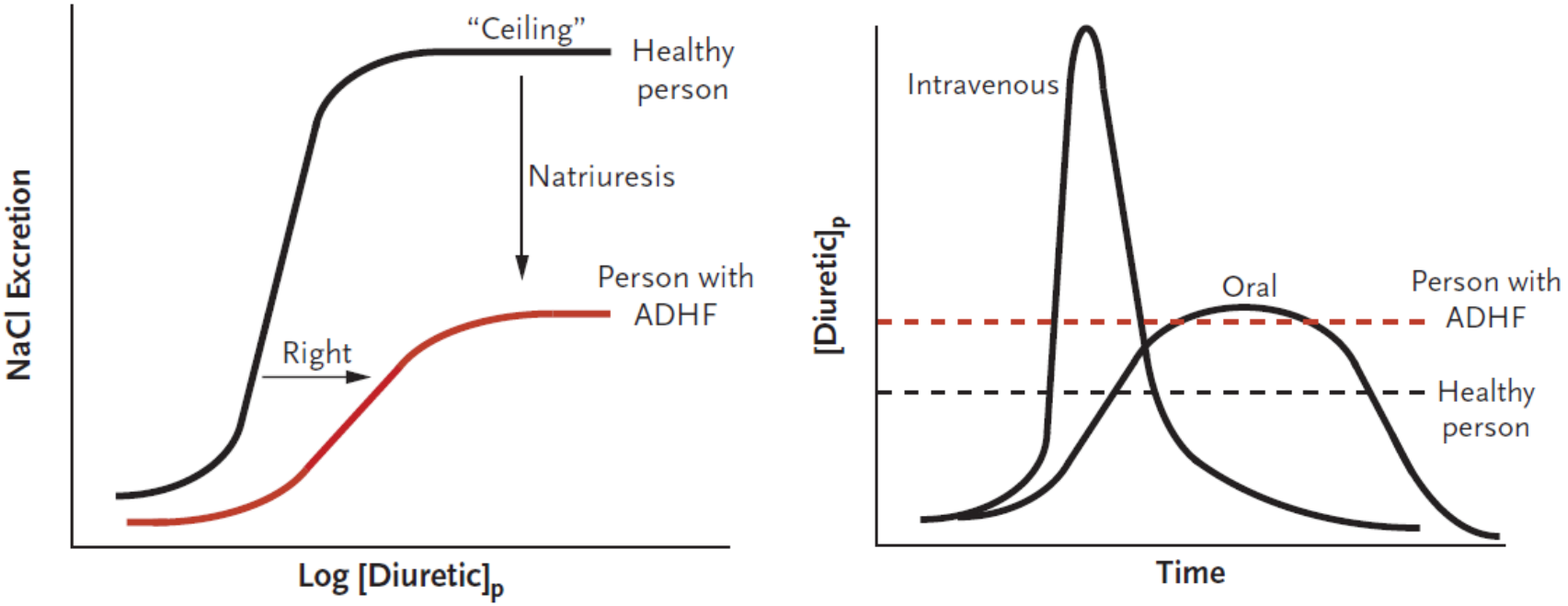
3. Les diurétiques de l'anse



- **Furosémide** (Lasix), **Bumétanide** (Burinex) et **Torasémide** (Torrem).
- **Anions fortement liés aux protéines plasmatiques** (> 90%).
- **Sécrétion tubulaire** (TCP) **via OAT** (attention aux AINS).
- **Blocage des cotransporteurs NKCC (2 et 1).**
- **Biodisponibilité variable:** Bumétanide/Torasémide (> 90%) > Furosémide (+/- 50%).
- **T1/2 courte:** Torasémide (6h) > Furosémide (2,7h) > Bumétanide (1,3h). T1/2↑ si IRC.

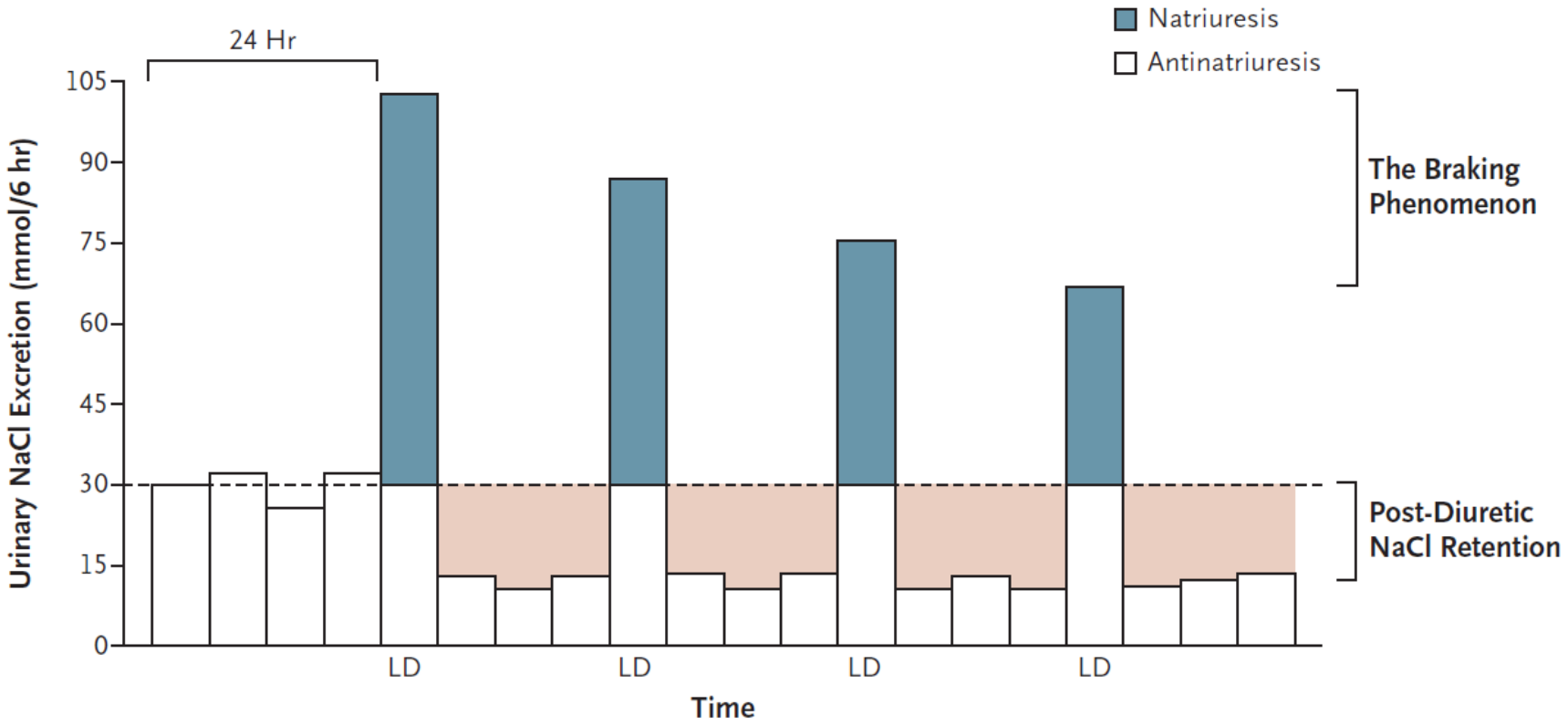
Ellison DH et al, ***N Eng J Med,*** 2017

3.1. Pharmacocinétique



Ellison DH et al, ***N Eng J Med,*** 2017

Objectif = balance sodée négative



Ellison DH et al, ***N Eng J Med,*** 2017

3.2. Résistance aux diurétiques

- Dose insuffisante
- Défaut de compliance: apports sodés, oublis
- Facteurs pharmacocinétiques
  - ↓ absorption digestive (œdème intestinal)
  - ↓ sécrétion tubulaire (IRC, âge, AINS)
- Hypoprotéinémie
- HypoTA

Résistance aux diurétiques

- Syndrome néphrotique
- Agents anti-natriurétiques: AINS
- Baisse du débit sanguin rénal
- Remodelage néphronique
- Activation neuro-hormonale

3.4. Résistance aux diurétiques - quelles solutions?

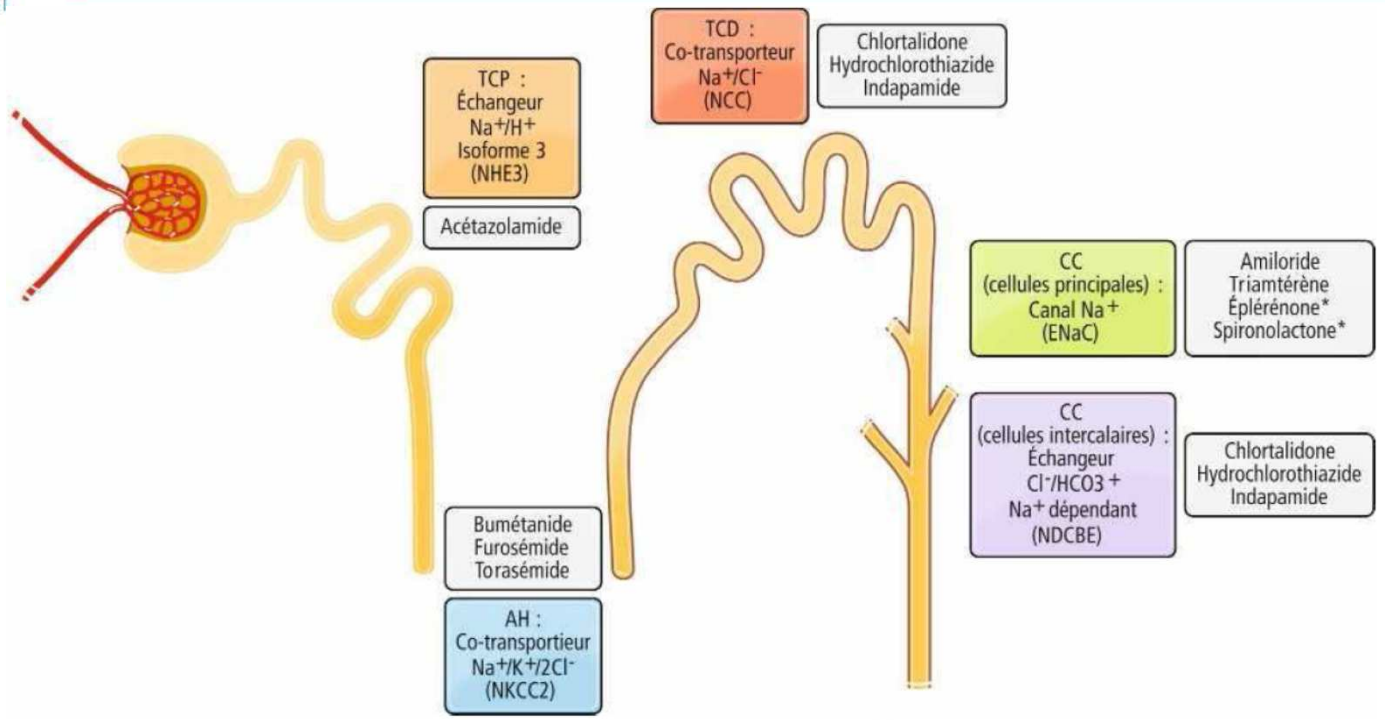
- RSS
- Majorer la dose PO
- Diurétiques à T1/2 plus longue
- Doses plus fréquentes
- Blocage séquentiel du néphron:
  - ⇒ **Thiazidés et apparentés:**
    Chlortalidone (Hygroton), Indapamide (Fludex)
  - ⇒ **Diurétiques d'épargne potassique:**
    Spironolactone (Aldactone), Eplérénone (Inspra)

Résistance aux diurétiques - quelles solutions?

- Passer en IV:
  - ⇒ Approche par étapes
  - ⇒ En bolus ou en continu?

- Ultrafiltration/dialyses.

Blocage séquentiel du néphron



Contrôles fréquents de l'ionogramme

(hypokaliémie, hyponatrémie…)

Lengelé JP et al, ***Traité de Néphrologie,*** Flammarion 2017

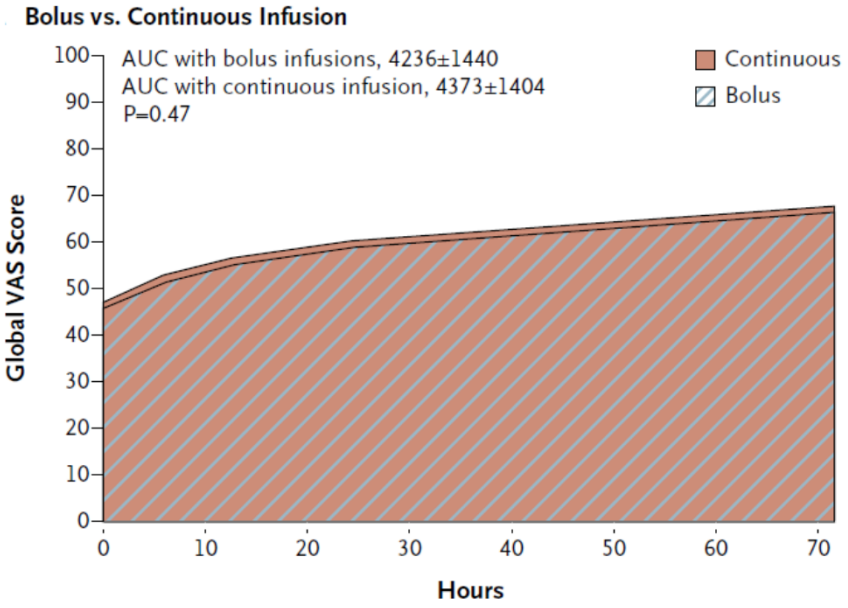
Approche par étapes

Niveau	Furosémide			Chlortalidone
	Dose PO antérieure	**Bolus**	**Perfusion continue**	**Dose PO**
1	≤ 80 mg	40 mg	5 mg/h	/
2	81-160 mg	80 mg	10 mg/h	50 mg 1x
3	161-240 mg	80 mg	20 mg/h	50 mg 2x
4	> 240 mg	80 mg	30 mg/h	50 mg 2x

- **Objectif R/:** DU 3-5L/jour jusqu'à l'euvolémie.
- **Evaluation quotidienne:** changement de niveau selon la DU quotidienne.
- Lasix 40 mg = Burinex 1 mg = Torasémide 20 mg PO.
- **Considérer un support inotrope** en cas d'HFrEF si DU < 3L/jour malgré de hautes doses de diurétiques.

Costanzo MR et al, ***J Am Coll Cardiol HF,*** 2016

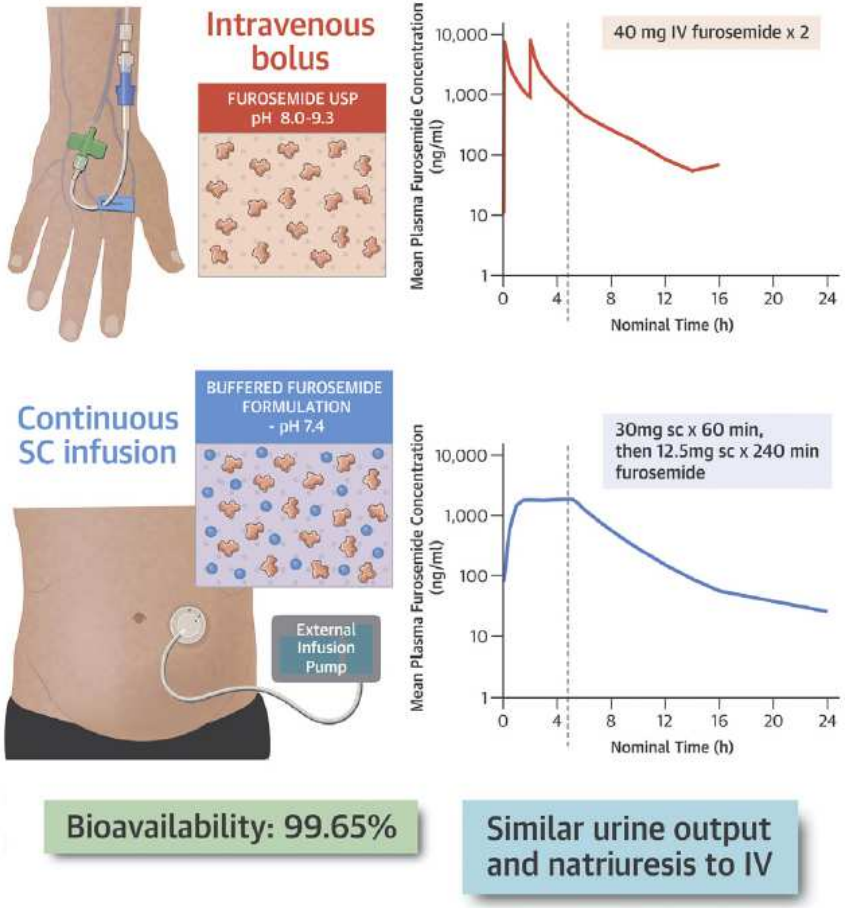
En bolus ou en continu



- **Etude DOSE.**
- **308 patients** avec DC aiguë.
- Double randomisation:
  - Bolus ou continu
  - Dose faible ou élevée
- **Critère d'évaluation primaire** = amélioration des symptômes (AUC) à 72h.

Felker GM et al, ***N Eng J Med,*** 2011

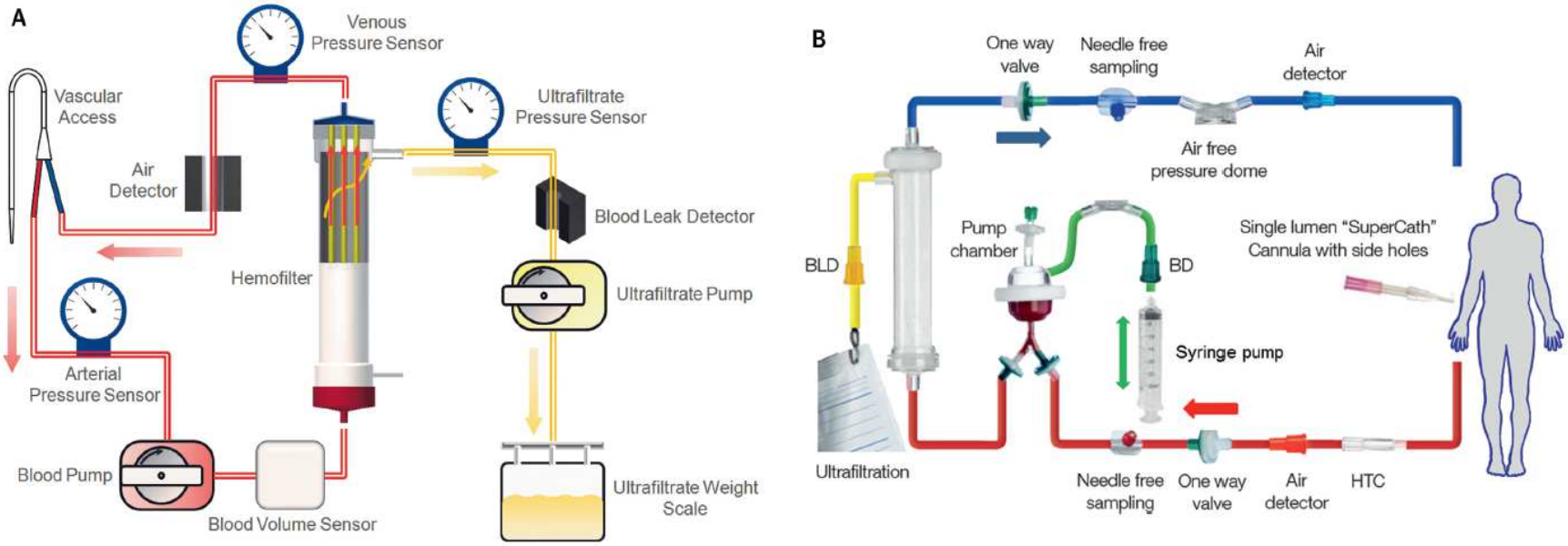
Furosémide SC



- 17 patients.
- Formulation SC avec un pH plus faible, délivrée via une pompe.
- Taux thérapeutiques obtenus endéans les 30 minutes et maintenus jusqu'à 6h.

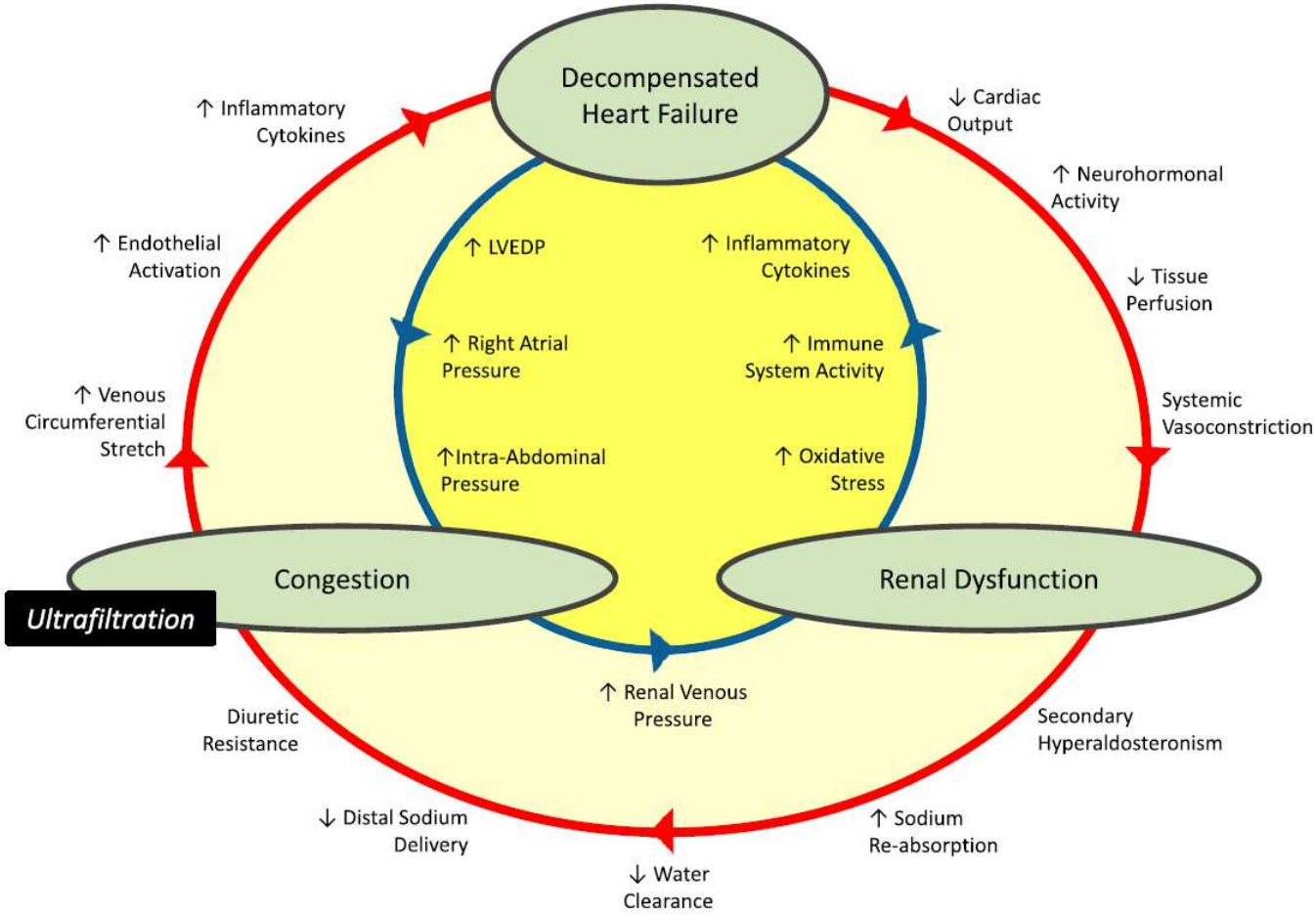
Sica DL et al, ***J Am Coll Cardiol Basic Trans Sci,*** *2018*

Place de l'ultrafiltration?



Costanzo MR et al, ***J Am Coll Cardiol,*** 2017

Rôle de l'ultrafiltration



Kazory A, ***Clin J Am Soc Nephrol,*** 2016

Place de l'ultrafiltration?

Avantages

- ↓ Congestion veineuse rapidement et de manière contrôlée.
- Clearance élevée du Na+.
- ↓ risque de troubles ioniques.
- ↓ risque de réhospitalisation pour DC.
- ↓ durée d'hospitalisation.
- Dispositifs de petite taille.

Inconvénients

- Risque de perte de la fonction rénale résiduelle.
- Pas d'effets sur la mortalité.
- Accès vasculaire.
- Anticoagulation nécessaire.
- Complications d'un circuit extra-corporéel (infections, allergie, embolie gazeuse, hémolyse…).
- Coût élevé.
- Pas de données au long terme.

Kazory A, ***Clin J Am Soc Nephrol,*** 2016

Ultrafiltration – Etudes cliniques

Variables	UNLOAD Trial, 2007	CARRESS-HF Trial, 2012	CUORE Trial, 2014	AVOID-HF Trial, 2016
No. of patients	200 (100 UF, 100 PT)	188 (94 UF, 94 PT)	56 (27 UF, 29 PT)	224 (110 UF, 114 PT)
Study design and protocol	Multicenter; single–session early UF therapy for ADHF (within 24 h)	Multicenter; rescue therapy for patients with both ADHF and WRF	Two centers; one or two early UF treatments for ADHF (within 24 h)	Multicenter; single–session early UF therapy for ADHF (within 24 h)
Primary end point	Weight loss and dyspnea at 48 h (efficacy); changes in renal function and hypotension (safety)	Changes in Scr and weight at 96 h (bivariate)	Rehospitalization rate for HF at 1 yr	Time to first HF event within 90 d after discharge
UF regimen	Duration and rate of UF flexible; maximum UF rate, 500 ml/h; average UF rate, 241 ml/h for 12.3±12 h	Fixed UF rate, 200 ml/h; median duration of UF, 40 h; median duration of 40 h	Duration and rate of UF flexible; maximum UF rate, 500 ml/h; average duration of 19±10 h	Duration and rate of UF flexible; maximum UF rate, 500 ml/h; average UF rate, 138 ml/h for 80±53 h
Medical therapy	Conventional PT (no preplanned algorithm)	Stepped PT (algorithm based)	Conventional PT (no preplanned algorithm)	Adjustable iv loop diuretics (algorithm based)
Baseline renal function	Scr, 1.5 mg/dl; UF, 1.5 mg/dl; PT (Scr>3 mg/dl excluded)	Scr, 1.9 mg/dl; UF, 2.09 mg/dl; PT (Scr>3.5 mg/dl excluded)	Scr, 1.7 mg/dl; UF, 1.9 mg/dl; PT (Scr>3 mg/dl excluded)	Scr, 1.5 mg/dl; UF, 1.6 mg/dl; PT (Scr≥3 mg/dl excluded)
Effect on renal function	No significant difference in renal function between UF and PT	Significant increase in Scr level with UF; no change in Scr for PT	Higher Scr and BUN in the PT group at 6 mo; no difference in eGFR, Scr, and BUN between UF and PT at 1 yr	No significant difference in eGFR, Scr, BUN, and BUN-to-Scr ratio during treatment and ≤90 d between UF and PT
Effect on congestion	Greater weight loss with UF; greater net fluid loss with UF	Weight loss and total amount of fluid removal similar for both groups	Weight loss similar for both groups at discharge; lower body weight for UF at 1 yr	Higher total amount of fluid removed with UF; no difference in weight loss between UF and PT
Other findings	Fewer patients in the UF group rehospitalized at 90 d, with fewer hospitalization days and unscheduled visits; a trend for WRF for UF at 24 and 48 h and discharge (statistically not significant)	Higher rate of serious adverse events in the UF group; enrollment ended prematurely because of a lack of benefit and an excess of adverse events with UF; similar mortality rates for both groups at 60 d	No difference in mortality between UF and PT at 1 yr; UF group had a lower HF readmission and mortality rate (combined) at 1 yr	UF group had fewer patients admitted for HF within 30 d postdischarge and fewer days in the hospital for HF; higher rate of adverse events in the UF group; no difference in mortality at 90 d; trial ended prematurely because of slow recruitment

Kazory A, ***Clin J Am Soc Nephrol,*** 2016

Et la dialyse péritonéale?

CardioRenal Medicine

Cardiorenal Med 2015;5:145–156
DOI: 10.1159/000380915
Published online: March 26, 2015

1664–3828/15/0052–0145$39.50/0
www.karger.com/crm

Review

Peritoneal Dialysis in Patients with Refractory Congestive Heart Failure: A Systematic Review

Renhua Lu[a, b] María-Jimena Muciño-Bermejo[b]
Leonardo Claudino Ribeiro[b] Enrico Tonini[b] Carla Estremadoyro[b]
Sara Samoni[b] Aashish Sharma[b] José de Jesús Zaragoza Galván[b]
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Mitchell H. Rosner[c] Claudio Ronco[b]

Et la dialyse péritonéale?

Parameter	Studies, n	Studies used, %	Weights used, %	Pre-PD	Post-PD	Δ	p value
Weight (kg)	12	57.14	58.89	73.37	69.71	−3.66	0.0006
Diuretics (mg/day)	5	23.81	25.56	246.28	252.60	6.33	0.7387
GFR (ml/min)	8	38.10	40.56	29.93	24.90	−5.03	0.0118
GFR, only non-CKD5D (ml/min)	6	28.57	30.56	24.89	21.88	−3.01	0.1065
LVEF (%)	13	61.90	63.33	34.78	38.86	4.08	0.0013
NYHA	15	71.43	70.55	3.53	2.17	−1.37	0.0000
Hospital days/year	14	66.67	67.78	6.30	1.22	−5.08	0.0001

Lu R et al, ***Cardiorenal Med,*** 2015

Recommandations des sociétés savantes

American College of Cardiology/American Heart Association (2013) (49)

- Ultrafiltration may be considered for patients with obvious volume overload to alleviate congestive symptoms and fluid weight (level of evidence: B)
- Ultrafiltration may be considered for patients with refractory congestion not responding to medical therapy (level of evidence: C)
- Consultation with a nephrologist is appropriate before initiating ultrafiltration, especially in circumstances where the non-nephrology provider does not have sufficient experience with ultrafiltration

Canadian Cardiovascular Society (2012) (50)

- Venovenous ultrafiltration may be of benefit in relieving congestion, particularly in patients who are diuretic resistant
- Patients with persistent congestion despite diuretic therapy with or without impaired renal function may, under experienced supervision, receive continuous venovenous ultrafiltration

European Society of Cardiology (2012) (51)

- Venovenous isolated ultrafiltration is sometimes used to remove fluid in patients with heart failure, although it is usually reserved for those unresponsive or resistant to diuretics
- If doubling the dose of loop diuretics and infusion of dopamine do not result in an adequate diuresis and the patient remains in pulmonary edema, venovenous isolated ultrafiltration should be considered

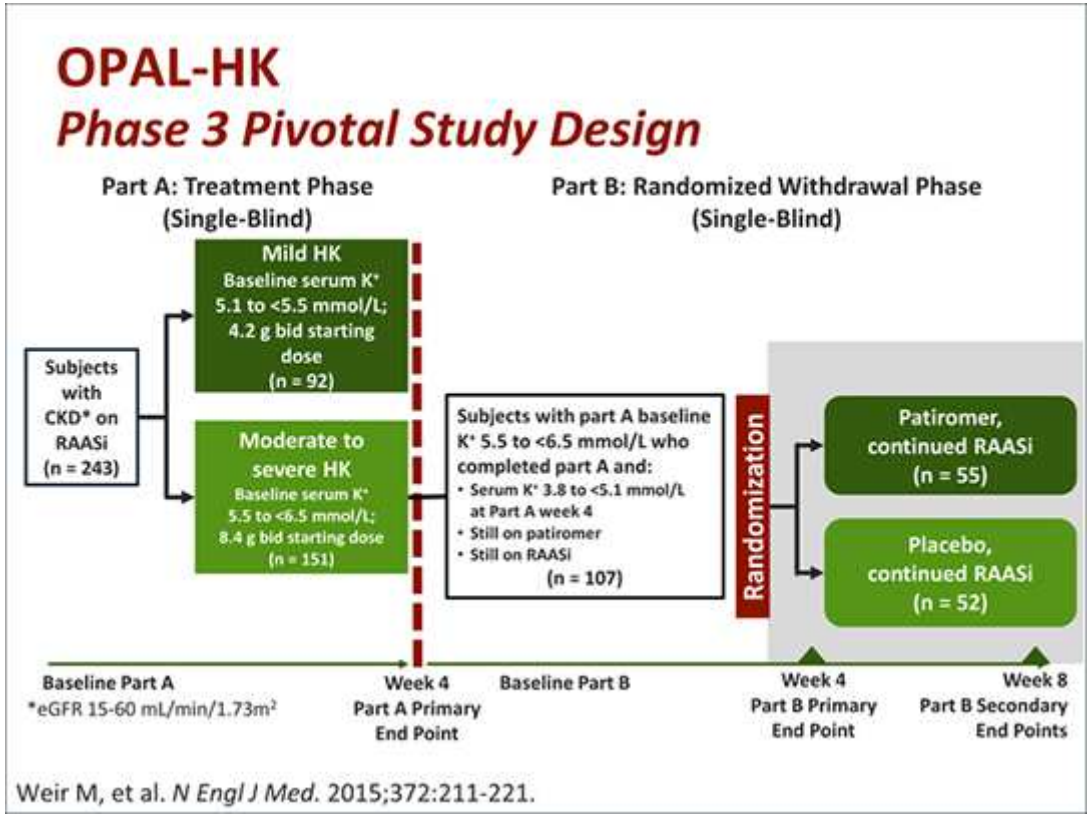
Heart Failure Society of America (2010) (52)

- It is recommended that patients admitted with ADHF and evidence of fluid overload be treated initially with loop diuretics; ultrafiltration may be considered *in lieu* of diuretics (strength of evidence: B)
- When congestion fails to improve response to diuretic therapy, ultrafiltration may be considered (strength of evidence: C)

4. Gestion de l'hyperkaliémie

- Nombreux facteurs favorisants:
  - IC
  - IRC
  - Diabète
  - Médicaments: IECA-ARA2, Entresto, diurétiques d'épargne potassique…
- Traitements actuellement disponibles:
  - Mesures hygiéno-diététiques
  - Polystyrène sulfonate de calcium (Sorbisterit®, Kayexalate calcique®) ou de sodium (Kayexalate sodique®)
  - Patiromer (Veltassa®)

Patiromer - étude princeps



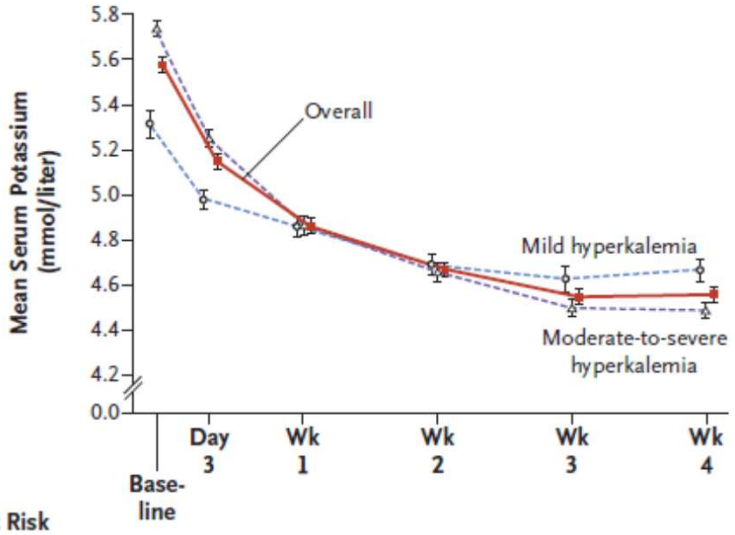
Weir M, et al. *N Engl J Med.* 2015;372:211-221.

OPAL-HK

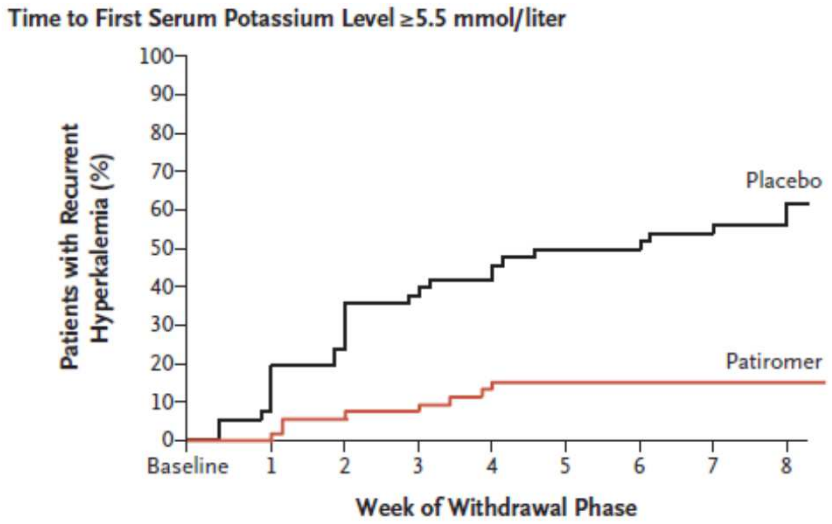
Characteristic	Initial Treatment Phase	Randomized Withdrawal Phase	
	Overall (N=243)	Placebo (N=52)	Patiromer (N=55)
Male sex — no. (%)	140 (58)	30 (58)	28 (51)
Age — yr	64.2±10.5	65.0±9.1	65.5±9.4
White race — no. (%)†	239 (98)	52 (100)	55 (100)
Type 2 diabetes — no. (%)	139 (57)	33 (63)	34 (62)
Heart failure — no. (%)	102 (42)	22 (42)	27 (49)
Myocardial infarction — no. (%)	60 (25)	14 (27)	18 (33)
Hypertension — no. (%)	236 (97)	50 (96)	54 (98)
Serum potassium — mmol/liter	5.6±0.5	5.9±0.4	5.9±0.6
Estimated GFR — ml/min/1.73 m^2‡	35.4±16.2	39.0±20.4	38.6±20.7
RAAS-inhibitor use — no. (%)‡	243 (100)	52 (100)	55 (100)
ACE inhibitor	170 (70)	38 (73)	37 (67)
Angiotensin II–receptor blocker	92 (38)	16 (31)	24 (44)
Aldosterone antagonist	22 (9)	4 (8)	4 (7)
Renin inhibitor	2 (1)	0	0
Dual RAAS blockade§	41 (17)	6 (12)	10 (18)
Receiving maximal dose¶	106 (44)	21 (40)	21 (38)
Non–RAAS-inhibitor diuretic use — no. (%)‡	132 (54)	27 (52)	28 (51)
Thiazide	70 (29)	11 (21)	16 (29)
Loop	77 (32)	20 (38)	16 (29)

Weir MR et al, ***N Eng J Med,*** 2014

Résultats d'OPAL-HK



No. at Risk						
Overall	243	217	237	228	221	219
Mild hyperkalemia	92	80	90	87	85	85
Moderate-to-severe hyperkalemia	151	137	147	141	136	134



No. at Risk									
Placebo	52	46	38	31	29	25	25	23	15
Patiromer	55	53	49	48	45	43	42	42	32

Weir MR et al, ***N Eng J Med,*** 2014

Patiromer – E2

- Constipation (6%)
- Diarrhées (3%)
- Douleurs adbominales (3%)
- Hypomagnésémie (5%)
- Hypokaliémie (3%)

Veltassa® – Conditions de remboursement

II – Eléments à attester par un médecin spécialiste en néphrologie:

Je soussigné, docteur en médecine, médecin spécialiste en médecine interne, porteur du titre professionnel en néphrologie, certifie que le patient mentionné ci-dessus est âgé d'au moins 18 ans, est atteint d'hyperkaliémie chronique à cause du traitement d'inhibiteur RAAS qui est cliniquement nécessaire et remplit simultanément toutes les conditions figurant au point a) du § 9580000 du chapitre IV de l'A.R. du 1er février 2018:

Conditions relatives de la pathologie comme définit au point a) 1 du § 9580000:

⊔ Diabète, ET/OU

⊔ Insuffisance cardiaque, ET/OU

⊔ Protéinurie >1g/24h,

ET

⊔ Maladie rénale chronique stade 3 ou 4 avec un eGFR entre 15 et 60 ml/min/1,73m²

ET

⊔ Hyperkaliémie récidivante de >5,1mEq/l depuis le traitement avec un inhibiteur RAAS, malgré le régime à faible teneur en potassium et la correction d'une éventuelle acidose métabolique,

ET

⊔ Un effet insuffisant lors de l'utilisation d'un diurétique de l'anse si cliniquement indiqué,

ET

⊔ La posologie d'inhibiteur RAAS qui est cliniquement nécessaire chez le bénéficiaire ne peut pas être administrée suite à une hyperkaliémie récidivante

Inhibiteur RAAS actuel : .....

Date de début du traitement : ⊔⊔/⊔⊔/⊔⊔⊔⊔

Posologie actuelle : .....

Posologie souhaitée qui est cliniquement nécessaire : .....

Conditions relatives de la pathologie comme définit au point a) 2, a)3 et a)4 du § 9580000:

⊔ Il n'y a pas des antécédents d'occlusion intestinale ou d'intervention chirurgicale gastro-intestinale majeure, d'affections gastro-intestinales graves ou de troubles de la déglutition,

⊔ Le taux sérique de potassium ne dépasse pas le 6,5 mEq/l au début du traitement,

⊔ Le taux sérique de magnésium sera surveillé pendant au moins 1 mois après le début du traitement,

5. Gestion de l’hyponatrémie

- Bilanter
- Tovaptan?
- Restriction hydrique
- Privilégier les diurétiques de l’anse et éviter les thiazidés

Efficacité relative

Current Management of Hyponatremia in Acute Heart Failure: A Report From the Hyponatremia Registry for Patients With Euvolemic and Hypervolemic Hyponatremia (HN Registry)

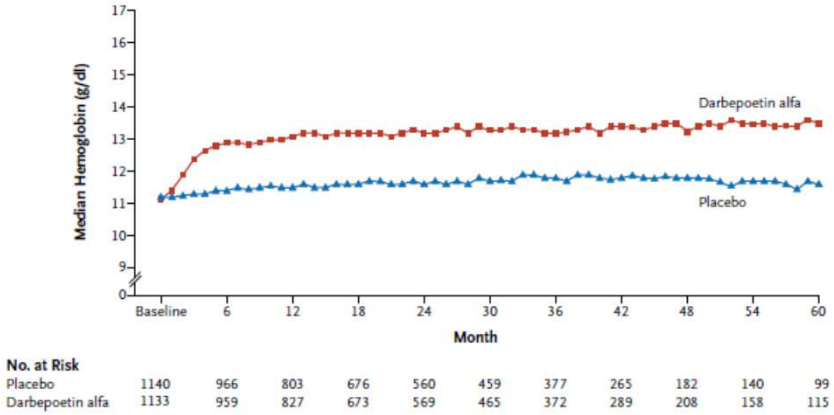
Mark E. Dunlap, MD; Paul J. Hauptman, MD; Alpesh N. Amin, MD; Sandra L. Chase, PharmD; Joseph A. Chiodo, III, PharmD; Jun R. Chiong, MD; Joseph F. Dasta, MSc

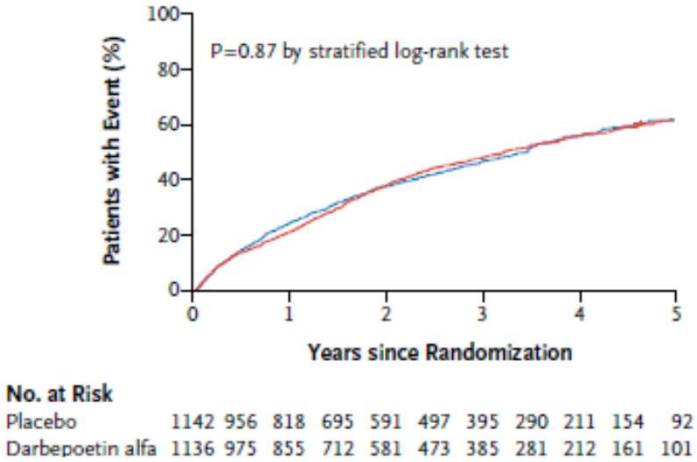
Background—Hyponatremia (HN) occurs commonly in patients with acute heart failure and confers a worse prognosis. Current HN treatment varies widely, with no consensus. This study recorded treatment practices currently used for patients hospitalized with acute heart failure and HN.

Methods and Results—Data were collected prospectively from 146 US sites on patients hospitalized with acute heart failure and HN (serum sodium concentration [Na^+] ≤130 mEq/L) present at admission or developing in the hospital. Baseline variables, HN treatment, and laboratory values were recorded. Of 762 patients, median [Na^+] was 126 mEq/L (interquartile range, 7) at baseline and increased to 130 mEq/L at discharge. Fluid restriction was the most commonly prescribed therapy (44%), followed by no specific HN treatment beyond therapy for congestion (23%), isotonic saline (5%), tolvaptan (4%), and hypertonic saline (2%). Median rate of change in [Na^+] varied by treatment (0.5 [interquartile range, 1.0] to 2.3 [8.0] mEq/L/d) and median treatment duration ranged from 1 (interquartile range, 1) to 6 (5) days. Fluid restriction and no specific HN treatment resulted in similar changes in [Na^+], and were least effective in correcting HN. Few patients (19%) had [Na^+] ≥135 mEq/L at discharge.

Conclusions—The most commonly used treatment approaches for HN (fluid restriction and no specific treatment) in acute heart failure increased [Na^+] minimally, and most patients remained hyponatremic at discharge. (***J Am Heart Assoc.*** **2017;6:e005261. DOI: 10.1161/JAHA.116.005261.)**

6. Gestion de l'anémie





- **Etude RED-HF:** 2278 patients avec IC et anémie (9-12 g/dl)
- Darbepoetin alpha (Aranesp) ou placebo
- Critère d'évaluation primaire (mortalité, hospitalisation pour DC)
- **E2 thrombo-emboliques plus fréquents**

Swedberg K et al, ***N Eng J Med,*** 2013

Correction de la carence martiale

	FER-CARS-01	FAIR-HF	EFFICACY-HF	CONFIRM-HF
Patient population	Ambulatory, optimally treated, systolic CHF with ID, NYHA class II/III, eGFR < 60 mL/min/1.73 m^2	Ambulatory, optimally treated, systolic CHF with ID, NYHA class II/III	Ambulatory, optimally treated, systolic CHF with ID, NYHA class II/III	Ambulatory, optimally treated, systolic CHF with ID, NYHA class II/III
Randomisation	2:2:1 (FCM:IS:placebo)	2:1 (FCM:placebo)	1:1 (FCM:placebo)	1:1 (FCM:placebo)
Patients, *n* (FAS) FCM/placebo	30/27[a]/15	304/155	20/14[b]	150/151
Comparator	i.v. FCM vs. IS vs. placebo[c]	i.v. FCM vs. placebo[c]	i.v. FCM vs. placebo[c]	i.v. FCM vs. placebo[c]
Study duration	12 weeks	24 weeks	24 weeks	52 weeks
Calculation of iron repletion dose	Ganzoni formula using the mean of two baseline Hb values	Ganzoni formula using the mean of two baseline Hb values	Ganzoni formula using the mean of two baseline Hb values	Determined by baseline Hb values and screening body weight
Correction phase duration (i.e. until iron repletion)	Weekly i.v. injections for minimally 3, maximally 9 weeks	Weekly i.v. injections for maximally 4 weeks	Weekly i.v. injections for minimally 3, maximally 9 weeks	Maximally two i.v. injections over a 6-week period
Correction phase dosing regimen (i.e. until iron repletion)	200 mg/100 mg iron: FCM or placebo	200 mg/100 mg iron: FCM or placebo	200 mg/100 mg iron: FCM or placebo	500 mg/1000 mg iron: FCM or placebo
Maintenance phase	4-weekly 200 mg iron i.v. injection (FCM/placebo) up to 24 weeks after randomisation	4-weekly 200 mg iron i.v. injection (FCM/placebo) up to 12 weeks after randomisation	4-weekly 200 mg iron i.v. injection (FCM/placebo) up to 24 weeks after randomisation	3-monthly 500 mg iron i.v. injection (FCM/placebo) up to 36 weeks after randomisation, if ID still present
Primary endpoint(s)	PGA at week 12 and NYHA class from baseline to week 12	PGA at week 24 and NYHA class from baseline to week 24	Change in 6MWT and NYHA class from baseline to week 24	Change in 6MWT from baseline to week 24

6MWT, 6-minute walk test; CHF, chronic heart failure; eGFR, estimated glomerular filtration rate; FAS, full analysis set; FCM, ferric carboxymaltose; Hb, haemoglobin; ID, iron deficiency; IS, iron sucrose; NYHA, New York Heart Association; PGA, patient global assessment.
Ganzoni formula of total iron deficit [mg]: body weight [kg] × (150 − actual Hb [g/L]) × 0.24 + 500 [mg]. Iron repletion dose, correction of iron deficiency.
[a]Patients randomised to i.v. IS ($n = 27$) were not included in this meta-analysis.
[b]EFFICACY-HF was discontinued as a result of recruitment issues.
[c]Placebo, i.v. normal saline.

Anker SD et al, ***Eur J Heart Fail,*** 2018

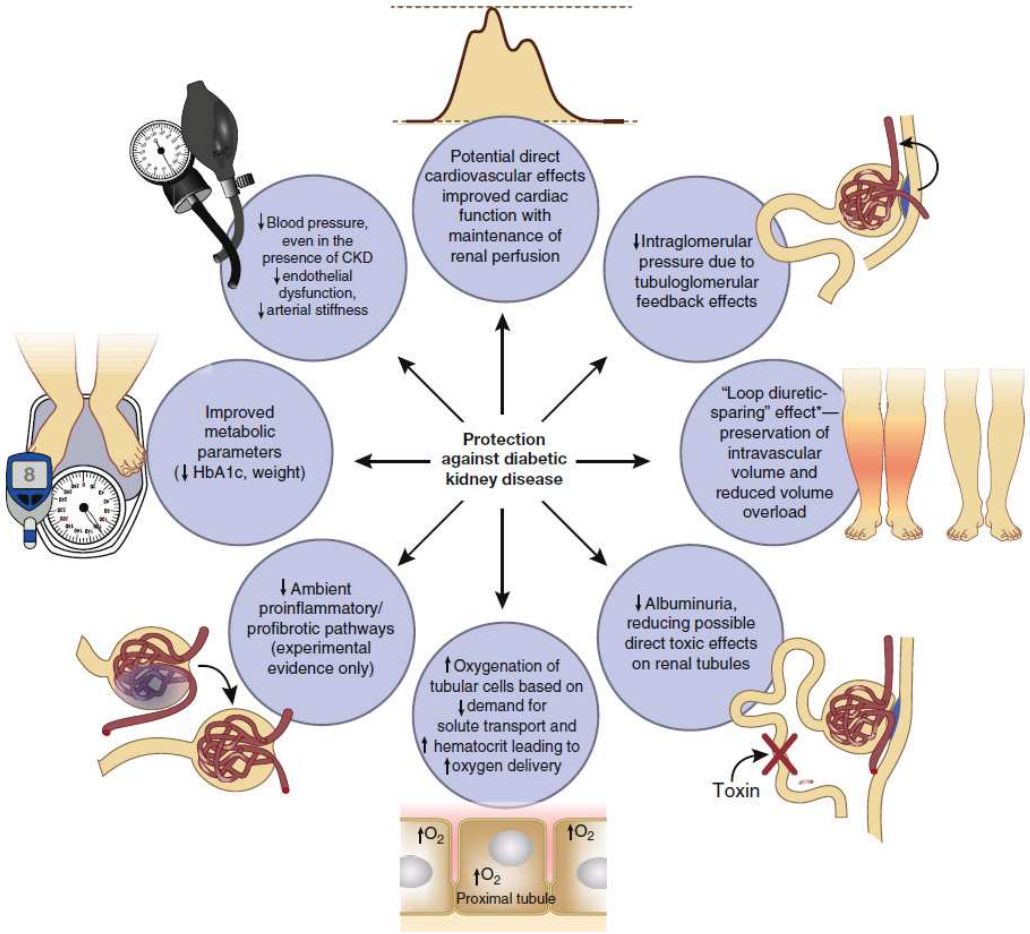
Correction de la carence martiale

Outcomes	Total events, *n* (incidence per 100 patient-years of follow-up)		RR (95% CI)	*P*-value
	FCM pool (*n* = 504)	Placebo pool (*n* = 335)		
CV hospitalisations and CV mortality	69 (23.0)	92 (40.9)	0.59 (0.40–0.88)	0.009
HF hospitalisations and CV mortality	39 (13.0)	60 (26.7)	0.53 (0.33–0.86)	0.011
CV hospitalisations and all-cause mortality	71 (23.7)	94 (41.8)	0.60 (0.41–0.88)	0.009
HF hospitalisations and all-cause mortality	41 (13.7)	62 (27.6)	0.54 (0.34–0.87)	0.011
All-cause hospitalisations and all-cause mortality	108 (36.1)	118 (52.5)	0.73 (0.52–1.01)	0.060
HF hospitalisations	22 (7.3)	43 (19.1)	0.41 (0.23–0.73)	0.003
CV hospitalisations	52 (17.4)	75 (33.3)	0.54 (0.36–0.83)	0.004
All-cause hospitalisations	89 (29.7)	99 (44.0)	0.71 (0.50–1.01)	0.056

- **Ferritine 100 à 300 µg/L**
- **Saturation de la transferrine > 20%**

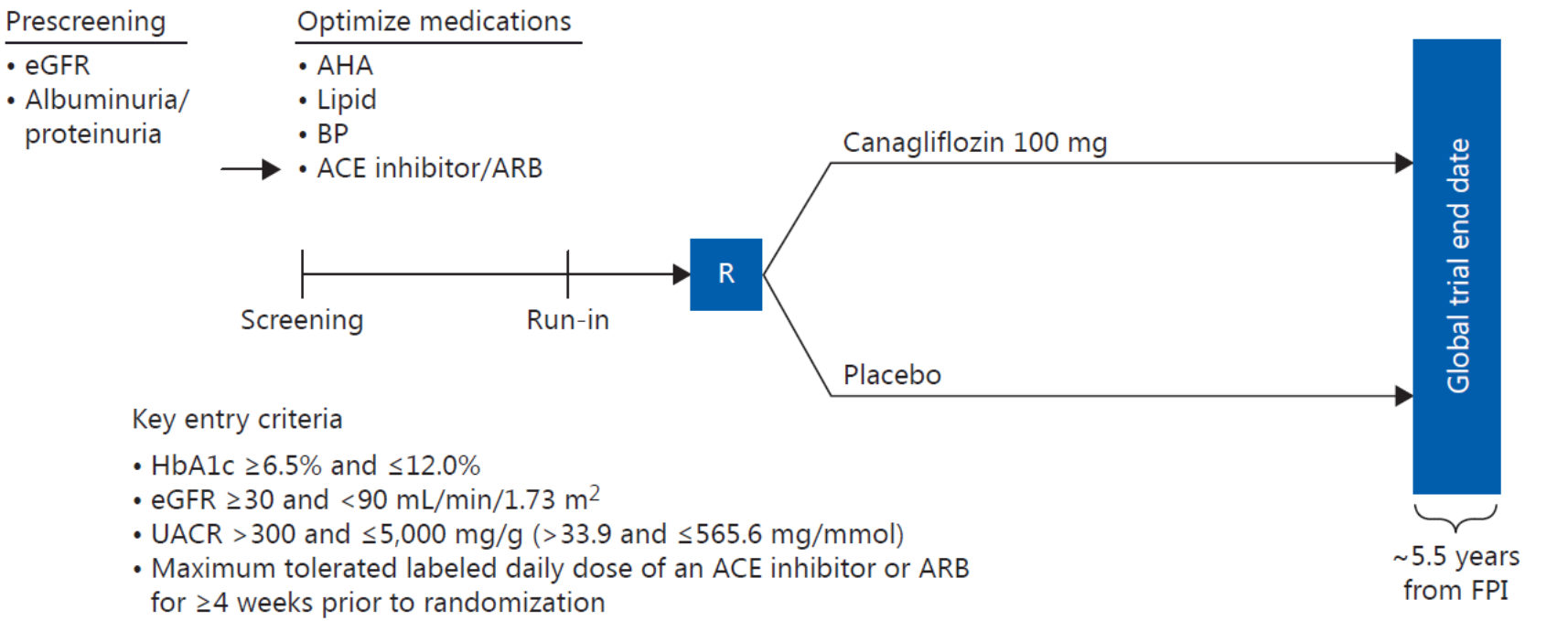
Anker SD et al, ***Eur J Heart Fail,*** 2018

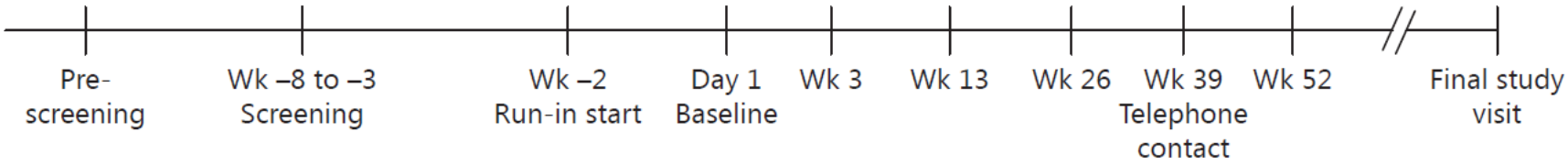
7. Place des glifozines?



Heerspink HJL et al, ***Kidney Int,*** 2018

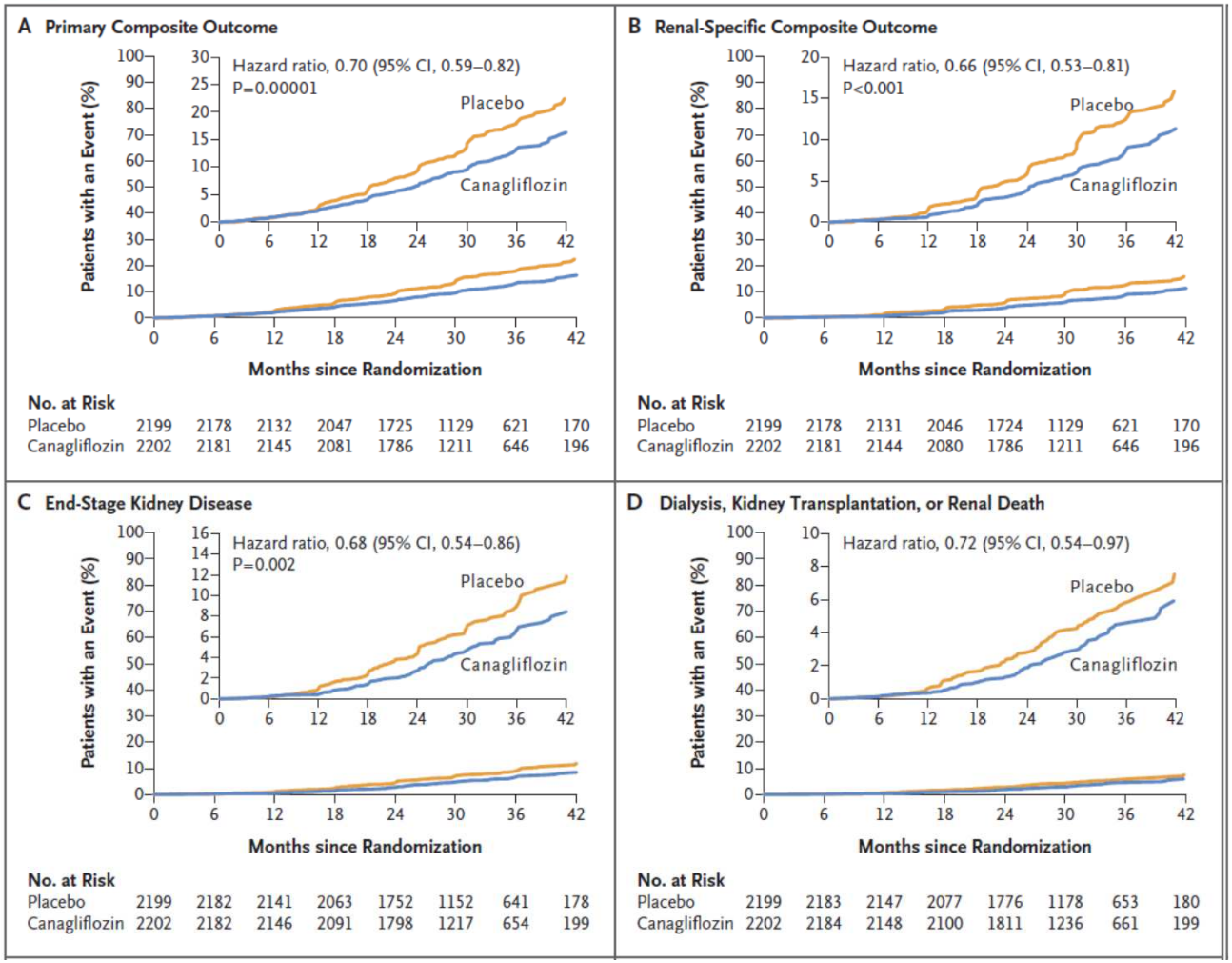
Néphroprotection - CREDENCE





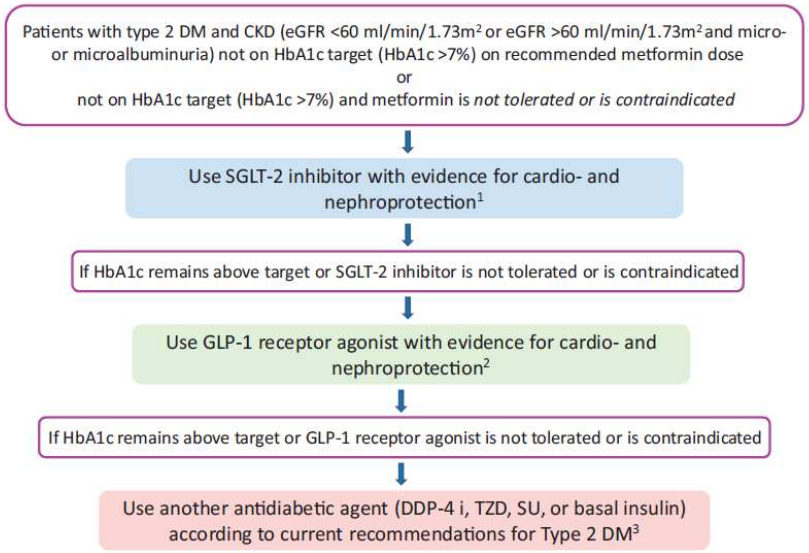
Jardine MJ et al, ***Am J Nephrol,*** 2017

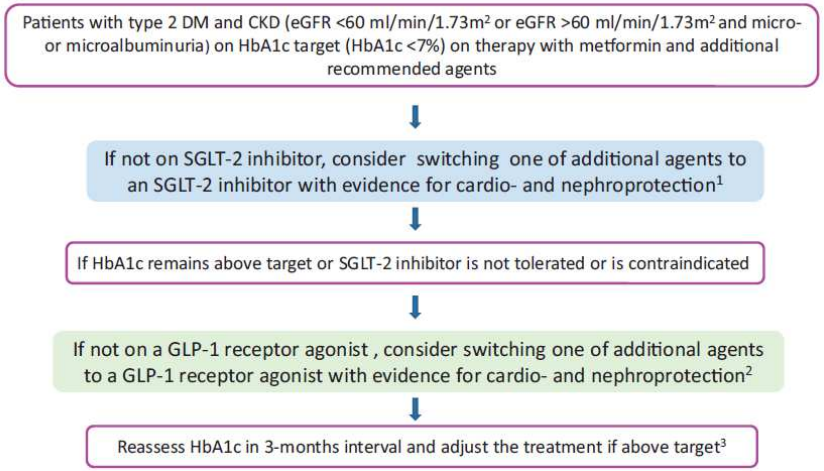
CREDENCE – résultats



Perkovic V et al, ***N Eng J Med,*** 2019

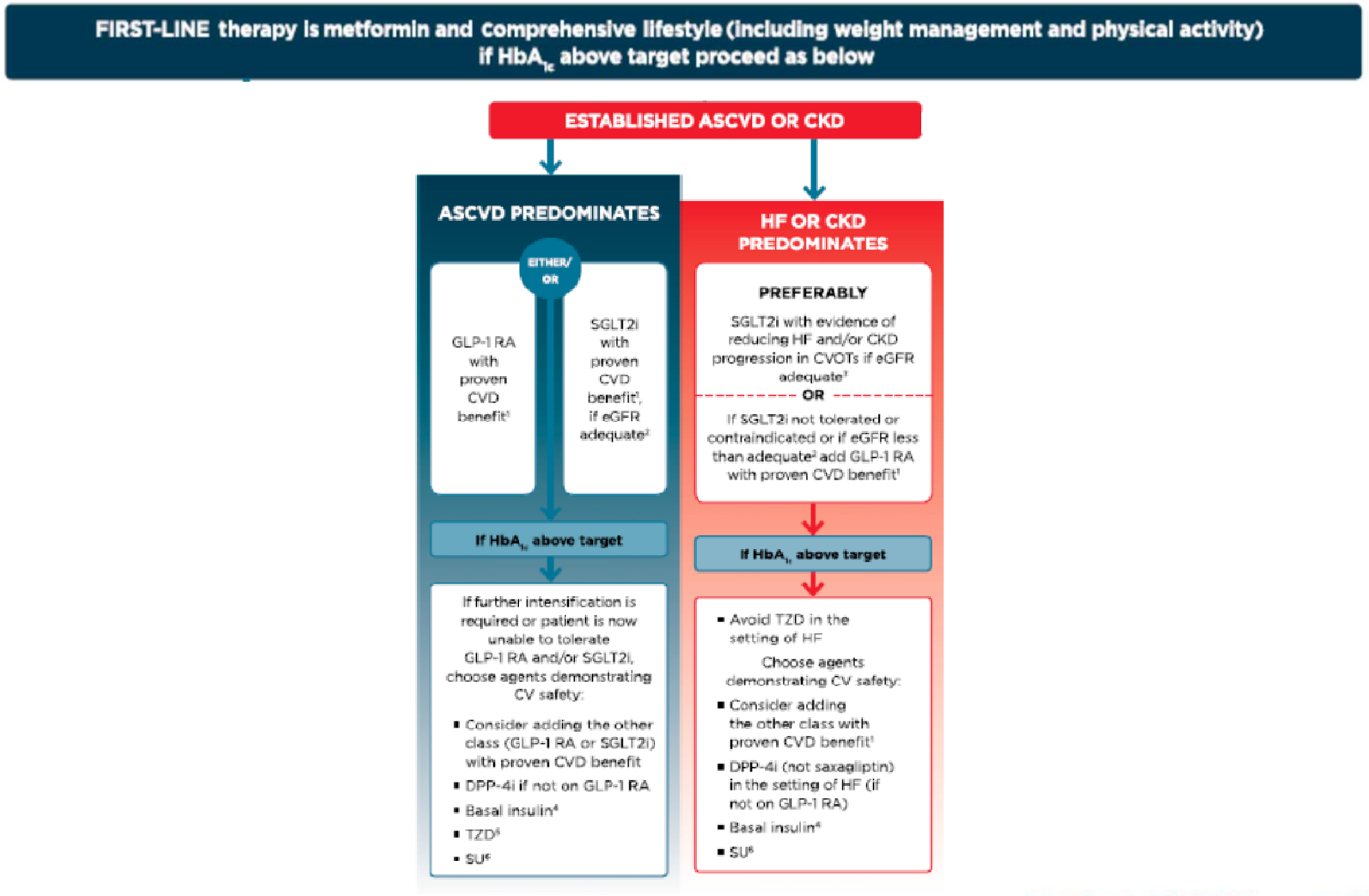
Recommandations ERA-EDTA





Sarafidis P et al, ***Nephrol Dial Transplant,*** 2019

Recommandations ADA



Conclusions

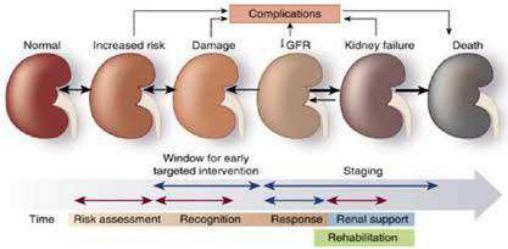
Travaillons ensemble

- Eduquer le patient
- Suivi régulier (clinique, biologique)
- Ajustement des diurétiques
- Ne pas être iatrogène (produit de contraste iodé, AINS)

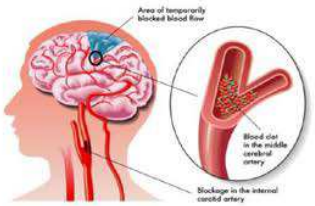
Futures études

Major Adverse Renal and Cardiac Events (MARCE)

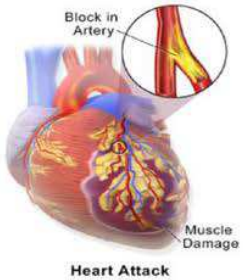
Acute Kidney Injury



Stroke

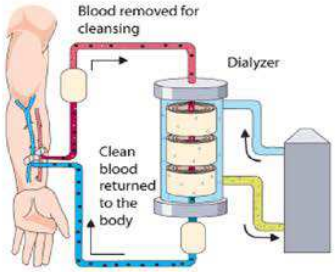


Myocardial Infarction

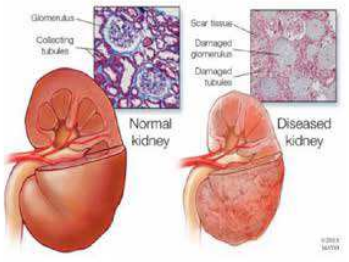


Hospitalization

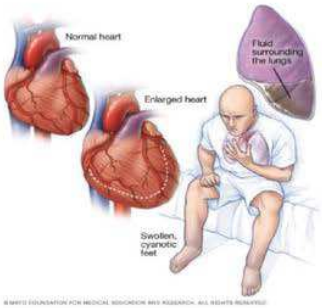
Renal Replacement Therapy (Dialysis)



Progression of Chronic Kidney Disease

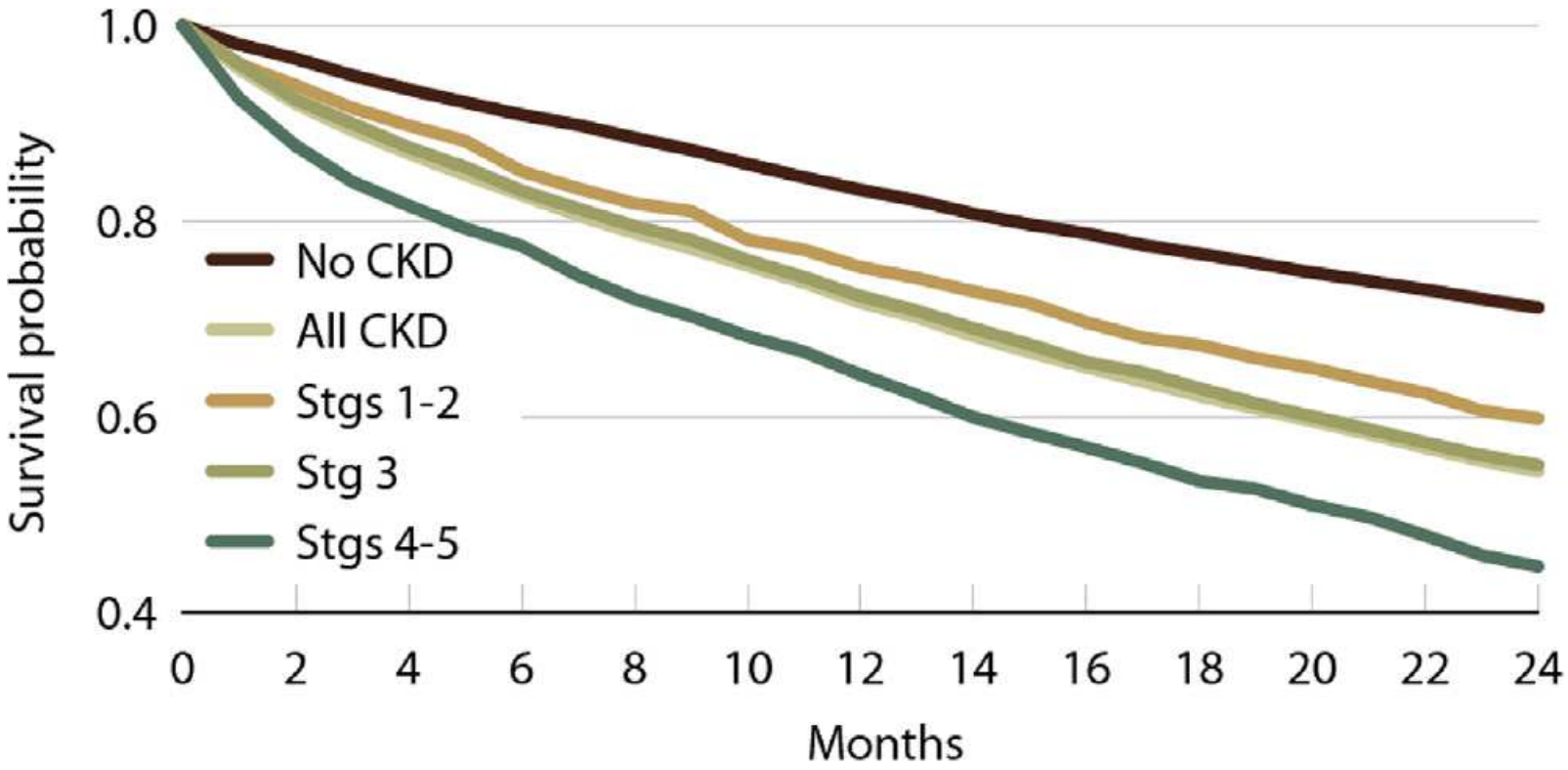


Heart Failure



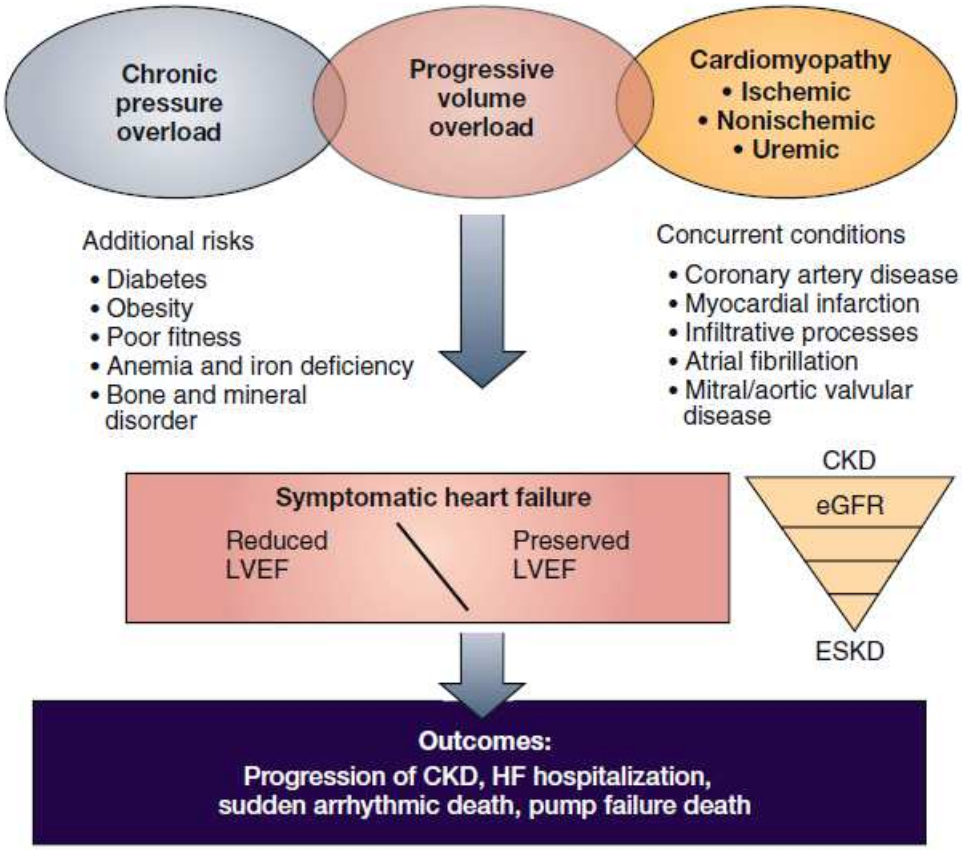
Death

En cas d'IC, l'IRC augmente la mortalité



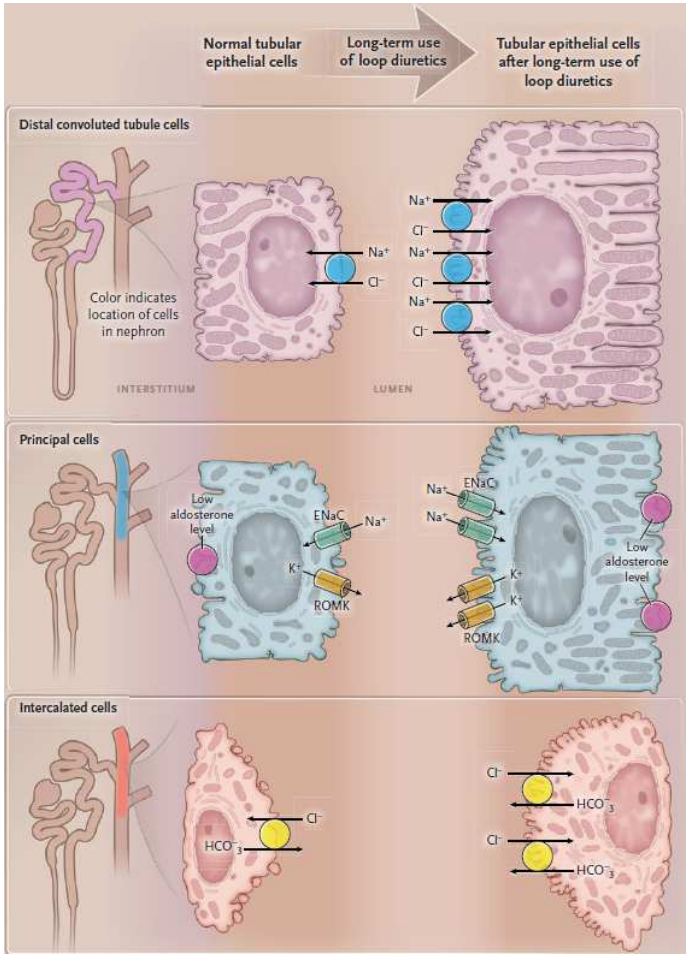
US Renal Data System 2013 Annual Data Report

Physiopathologie du SCR de type 4



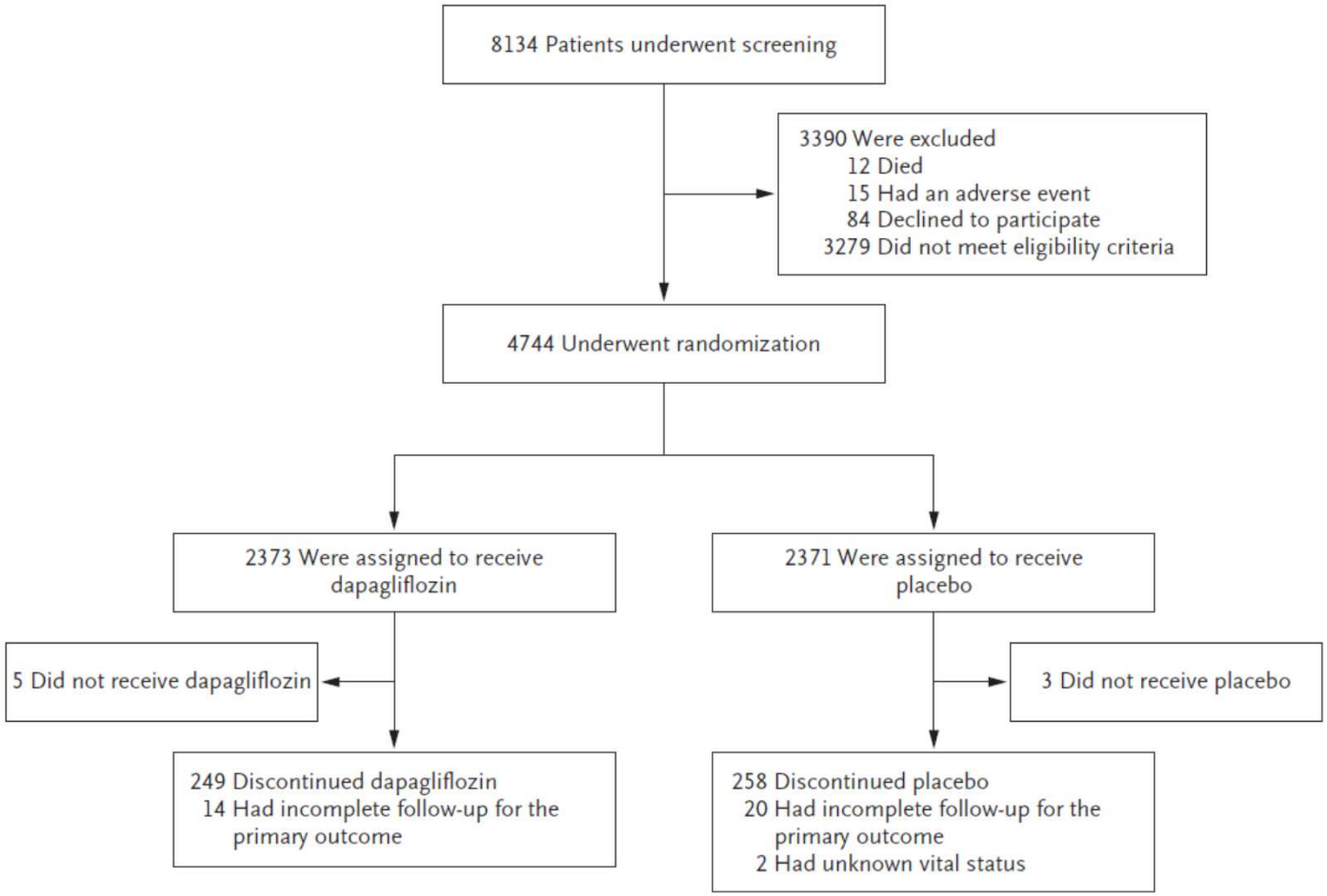
House AA et al, ***Kidney Int,*** 2019

Remodelage néphronique



Ellison DH et al, ***N Eng J Med,*** 2017

Cardioprotection – DAPA-HF



McMurray JJV et al, ***N Eng J Med,*** 2019

Cardioprotection – DAPA-HF