Sidération systémique en hémodialyse

Prof. Thierry Hannedouche
DUTER 2023-24

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Agenda

- Définition
- Sidération myocardique
- Conséquences
- Sidération « systémique » ou multi-organe (intestin, reins, cerveau)
- Prévention
  - Temps x fréquence
  - Préconditionnement
  - Cooling
- Conclusions

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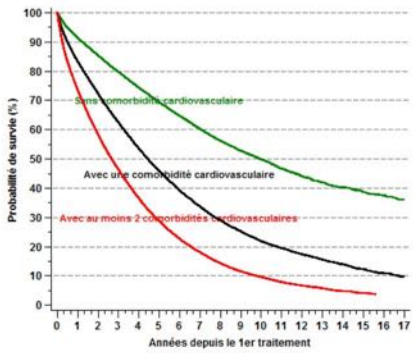
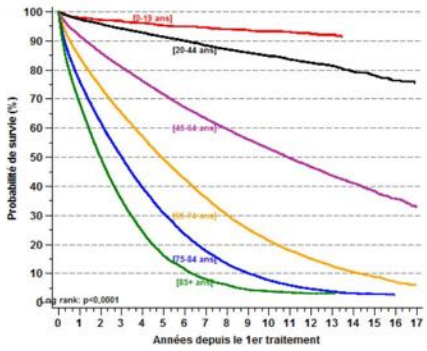
Mortalité en dialyse – registre REIN 2019



Probabilité de survie (IC 95%)

Comorbidité Cardio vasculaire	effectifs	à 1 an	à 3 ans	à 5 ans	à 10 ans	à 15 ans
Sans	43918	91,5 [91,2-91,8]	79,8 [79,4-80,2]	69,3 [68,8-69,8]	49,9 [49,1-50,7]	38,8 [37,3-40,3]
Avec une	35013	83,4 [83,0-83,8]	62,5 [62,0-63,1]	45,8 [45,2-46,4]	21,9 [21,3-22,6]	12,4 [11,5-13,3]
Avec au moins 2	44619	73,6 [73,2-74,0]	46,4 [45,9-46,9]	28,7 [28,2-29,2]	9,6 [9,2-10,1]	4,2 [3,7-4,7]



Probabilité de survie (IC 95%)

Age	effectifs	à 1 an	à 3 ans	à 5 ans	à 10 ans	à 15 ans
00-19	1828	98,0 [97,3-98,6]	96,8 [96,0-97,7]	95,3 [94,2-96,4]	93,3 [91,9-94,7]	91,3 [89,2-93,4]
20-44	13770	97,4 [97,2-97,7]	94,3 [93,8-94,7]	91,4 [90,9-91,9]	84,8 [84,0-85,6]	78,2 [76,8-79,6]
45-64	40559	91,8 [91,5-92,1]	81,0 [80,6-81,4]	71,6 [71,1-72,1]	52,9 [52,3-53,6]	38,4 [37,3-39,5]
65-74	37308	84,4 [84,0-84,8]	65,1 [64,6-65,7]	49,1 [48,5-49,7]	21,2 [20,6-21,9]	8,8 [8,0-9,6]
75-84	42817	76,2 [75,8-76,6]	50,1 [49,5-50,6]	30,7 [30,2-31,3]	7,7 [7,3-8,1]	3,0 [2,5-3,4]
Plus de 85	14221	68,6 [67,8-69,4]	35,3 [34,5-36,2]	16,1 [15,4-16,9]	3,9 [3,3-4,4]	[2,4-3,6]

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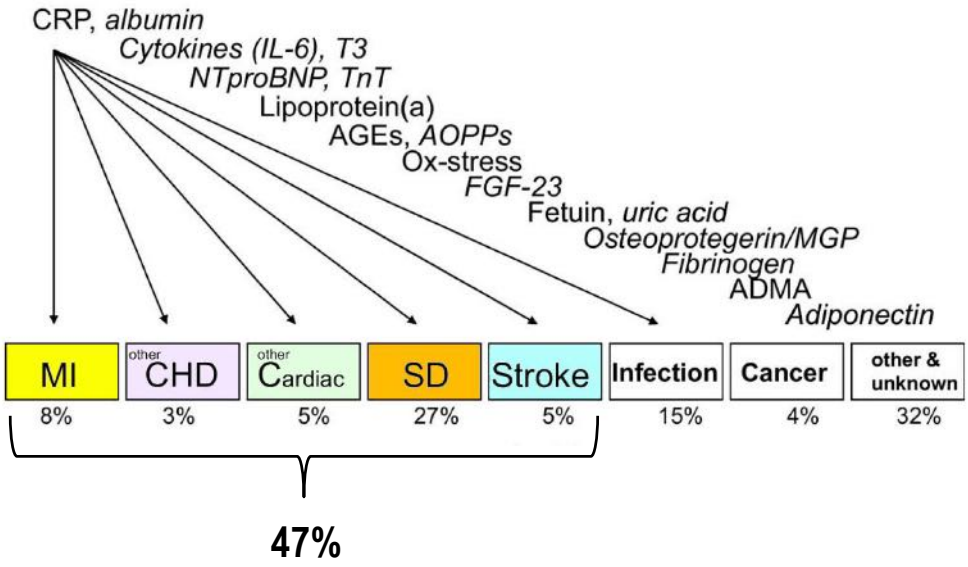
Causes de mortalité en dialyse (études 4D, HEMO)



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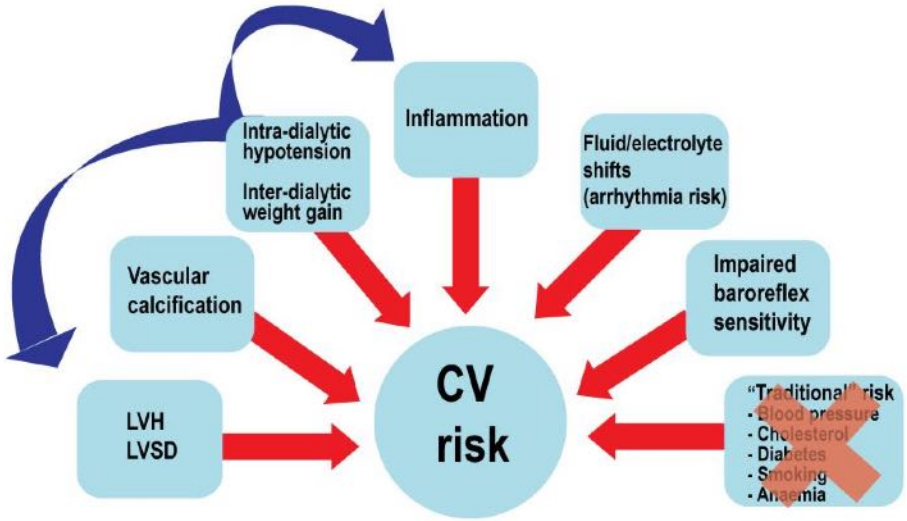
Facteurs de risque cardiaque chez les pts dialysés



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Sidération myocardique ("myocardial stunning")

- Réduction de la fonction myocardique,
  - survenant après un épisode bref et intense d'ischémie myocardique,
  - persistant après la reperfusion, mais réversible avec le temps
  - en l'absence de lésions tissulaire ou de réduction du débit sanguin
- MeSH D017682

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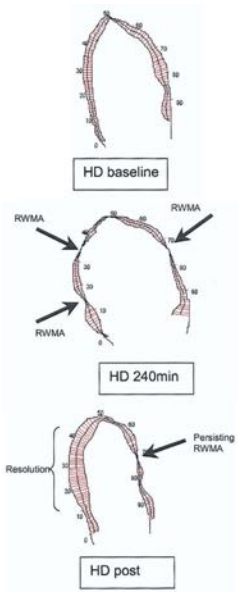
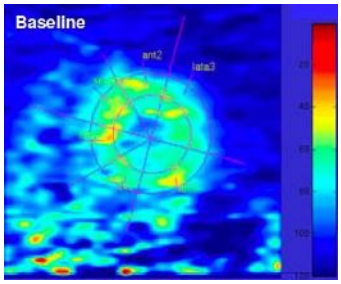
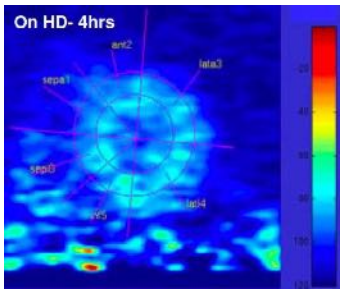
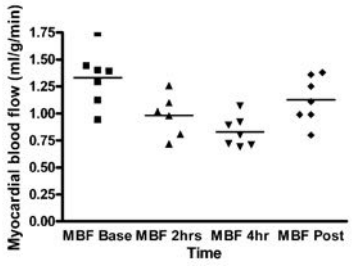
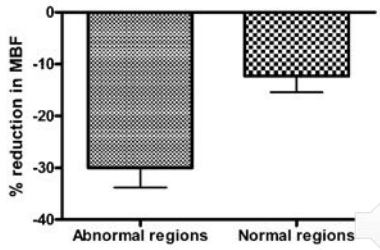
Effets de l'HD sur la perfusion myocardique globale et segmentaire











Selby N, AJKD 2006 – McIntyre CW, Jasn 2008

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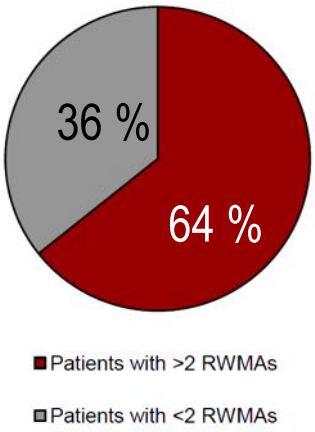
Facteurs associés aux anomalies de cinétique régionales

Facteurs associés au développement de >2 ACR (r^2 = 0,602)



	OR	P
Volume UF 1,0 L /séance	5.1	0,007
Volume UF 1,5 L /séance	11.6	0,007
Volume UF 2,0 L /séance	26.2	0,007
Baisse max de PAS 10 mmHg	1.8	0,002
Baisse max de PAS 20 mmHg	3,3	0,002
Baisse max de PAS 30 mmHg	6,0	0,002
cTnT	1,26	0,004
Age	1,07	0,018

Burton JO & al. Cjasn 2010;4:914

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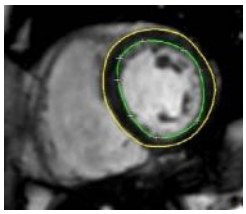
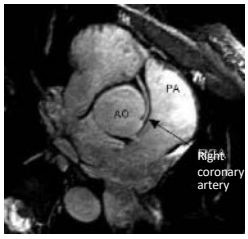
IRM cardiaque pendant l'hémodialyse

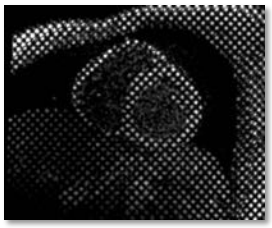
Global function



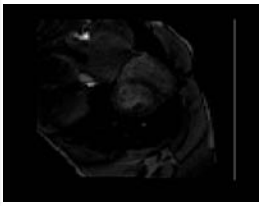
Coronary flow

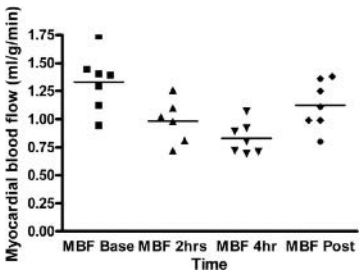


Segmental function

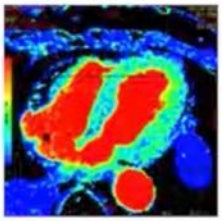


Myocardial perfusion

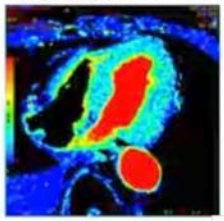




Pre HD



Peak stress



Buchanan C, Jasn 2017;28:1269

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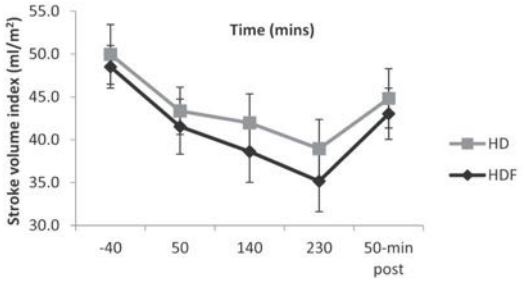
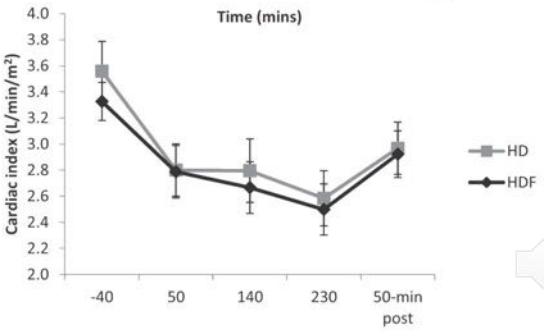
IRM cardiaque intradialytique – VES et débit cardiaque





Buchanan C, Jasn 2017

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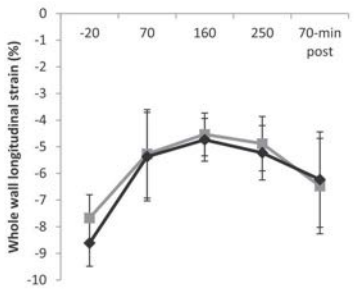
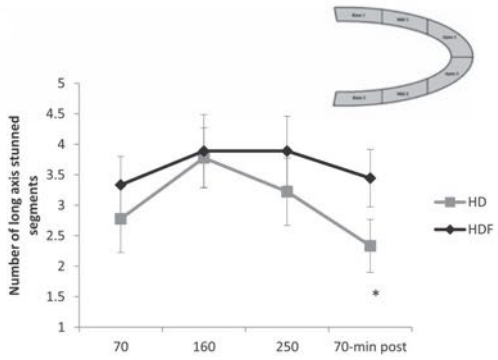
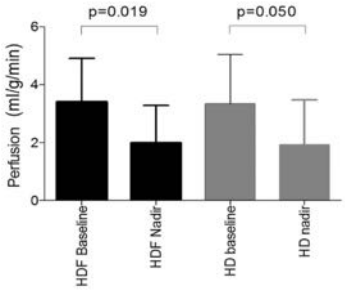
IRM cardiaque intradialytique – VES et débit cardiaque







Déformation longitudinale :
Moins de valeurs négatives
= réduction de la
contractilité globale

Nouvelle ACR en dialyse :
(définie par > 20% de strain longitudinal régional)

TH 12- *Buchanan C, Jasn 2017*

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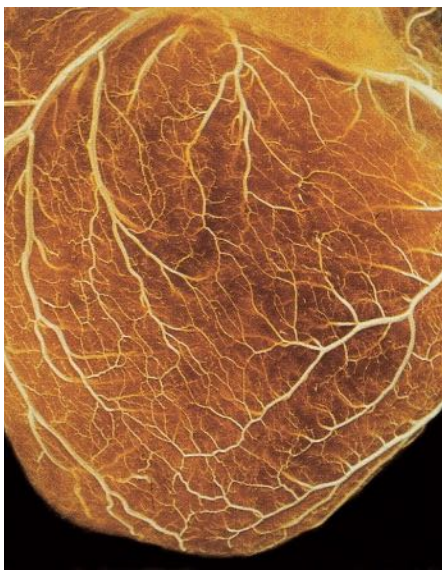
Facteurs favorisant la sidération myocardique en dialyse

- Lésions coronaires macro
- Métabolisme anormal (pyruvate, lactate)
- Hypertrophie du VG
- Fibrose intercardiomyocytaire
- Réduction densité capillaire (mismatch capillaire-myocyte)
- Dysfonction endothéliale
- Réserve coronaire insuffisante
- Orage catécholergique



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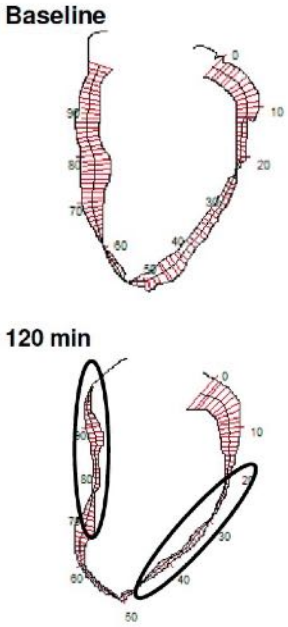
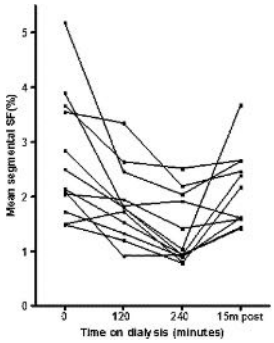
Children on dialysis- Uremia *without* classical CAD



% sidération	11/12
Vol. UF (L)	1.2 ± 0,79
Δ PA (mmHg)	25.5 ± 9
FEVG preHD (%)	55 ± 8,3
FEVG postHD (%)	54,6 ± 7,5



Hothi D & al. Cjasn 2009;4:790

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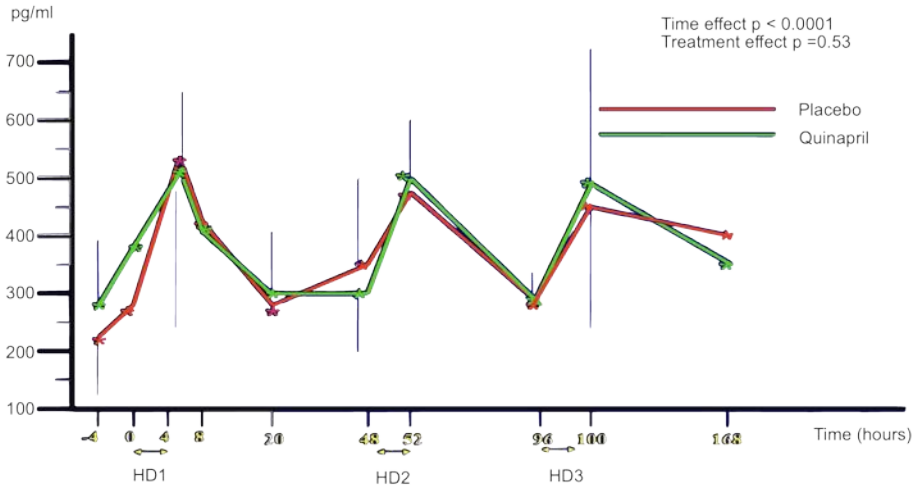
Séance de dialyse, un orage catécholergique ?

Noradrenaline circulante x 1 semaine en HD



London G & al. JHypertens 1998

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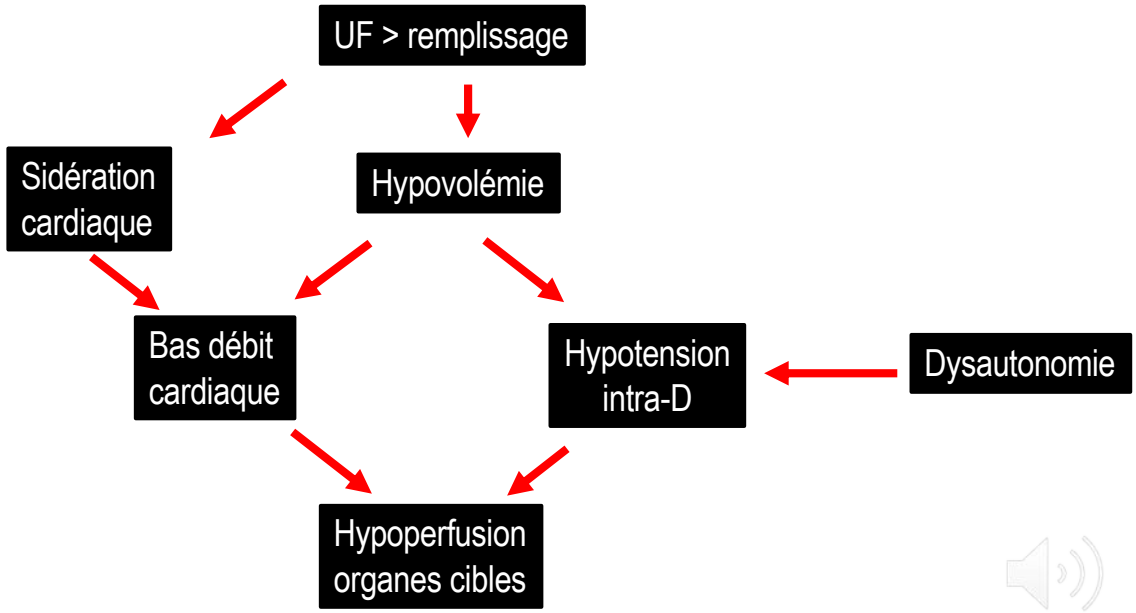
Schéma récapitulatif



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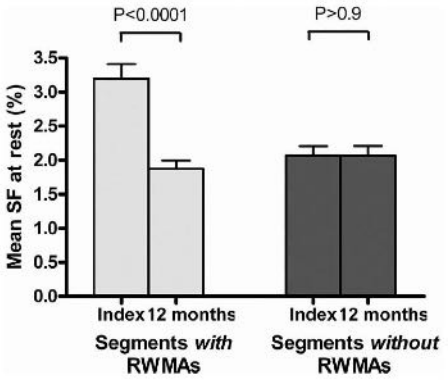
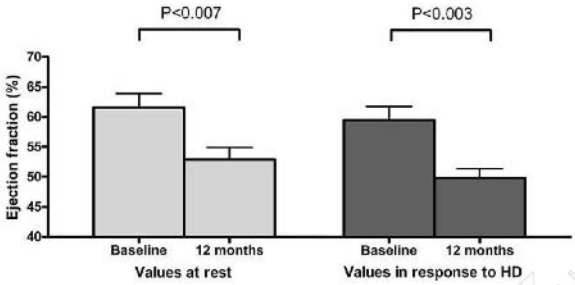
La sidération myocardique en HD induit l'hibernation myocardique et réduit la fonction systolique globale

N = 30 pts, suivi 1 an

Hibernation des segments colocalise avec les ACR induites par le stress

Réduction (absolue) de la FeVG –10%, au repos, au pic de stress en HD





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Burton JO et al. Cjasn 2009;4:914

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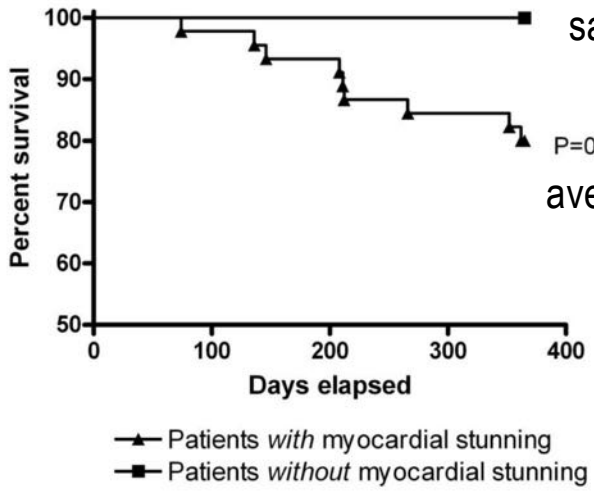
Sidération myocardique et survie en HD et morbi-mortalité

N = 70 pts HD, échoCG séquentielles, suivi 12 mois

Effet de la sidération cardiaque sur la mortalité à 1 an



Burton JO & al. Cjasn 2009;4:914

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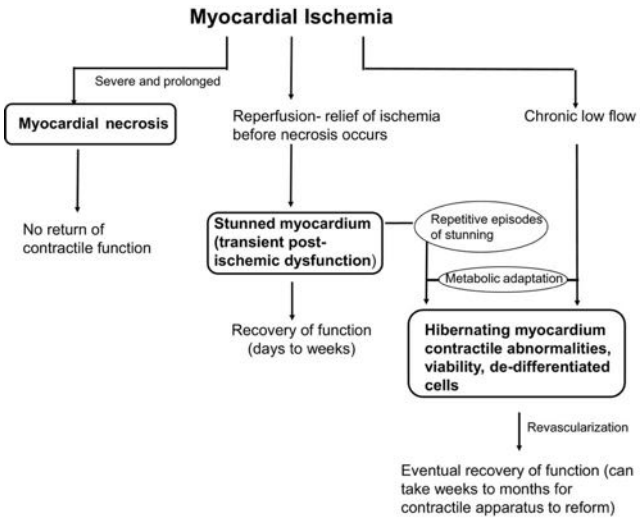
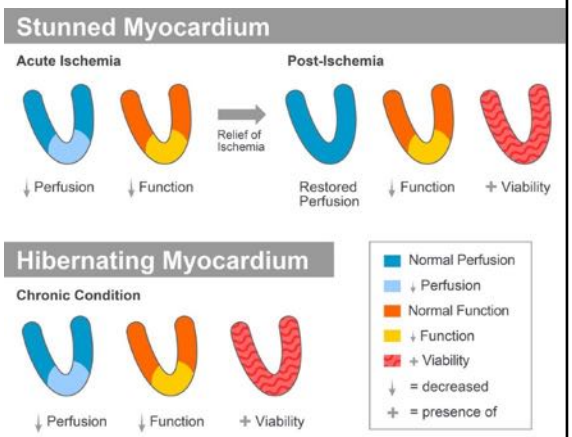
Nécrose vs sidération vs hibernation





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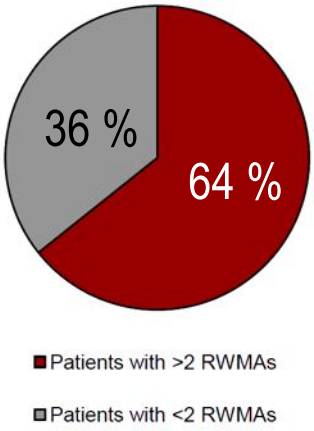
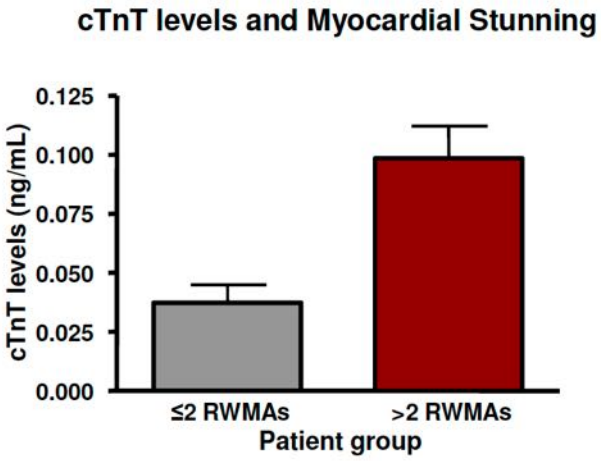
Anomalies cinétique régionale vs troponine c

N = 70 pts hémodialysés chroniques





Burton JO et al. Cjasn 2009;4:914

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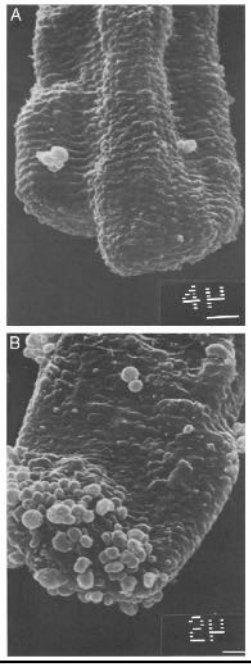
L'élévation de troponine n'est pas toujours un SCA



- Les excroissances (blebs) se développent sur la surface du myocyte
- Ischémie prolongée => rupture des excroissances, nécrose et libération de troponine
- Ischémie de courte durée => libération des excroissances sans rupture, libération transitoire de troponine

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Hickmann et al. Clin Chem Acta 2010

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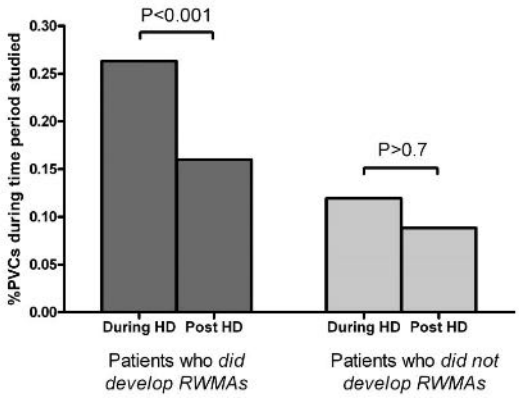
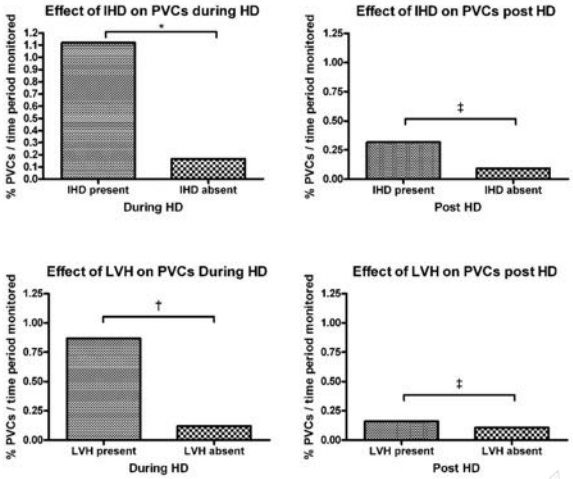
Sidération myocardique en HD et arythmies ventriculaires





Burton JO & al. Ren Fail 2008;30:701

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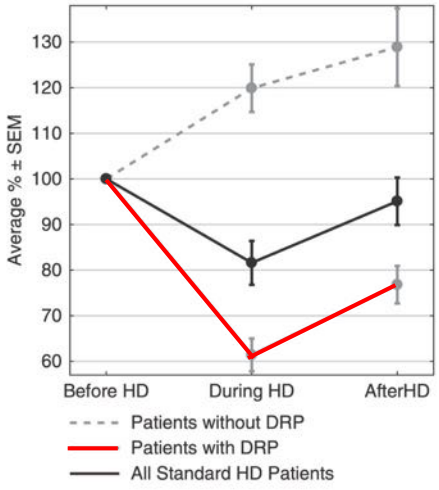
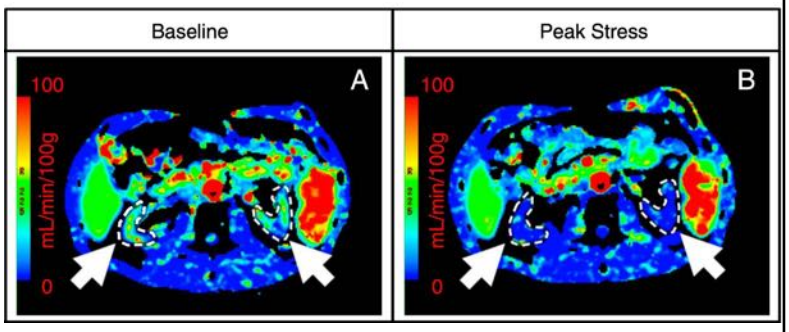
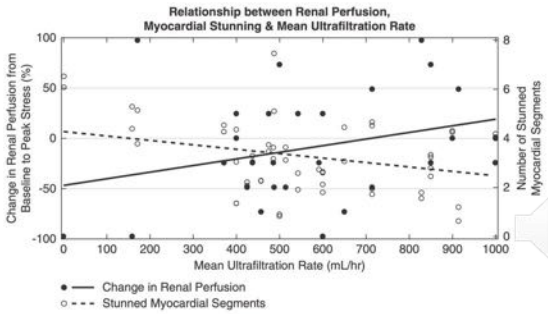
La sidération « rénale », une forme récurrente d'IRA induite par l'HD







 Marants R, Jasn 2019;30:1086

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Lésions cérébrales associées à l'hémodialyse

- Diminution aiguë du débit cérébral (en HD)
- **Déclin cognitif significatif** (test CBS)
- Directement proportionnel aux lésions morphologiques de la substance blanche
- Lésions morphologiques **universelles** (tous les individus en HD), et **progressives** (d'aspects similaires à celles post-AVC)
- Indépendamment associées à l'instabilité hémodynamique

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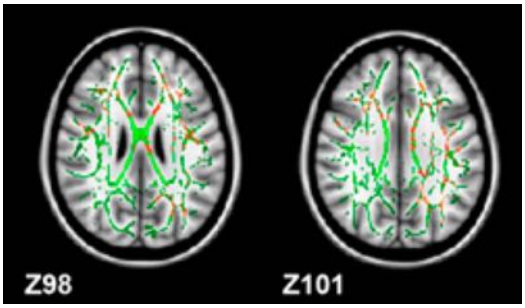
Les lésions cérébrales (MB) sont progressives et dépendent de la variabilité tensionnelle



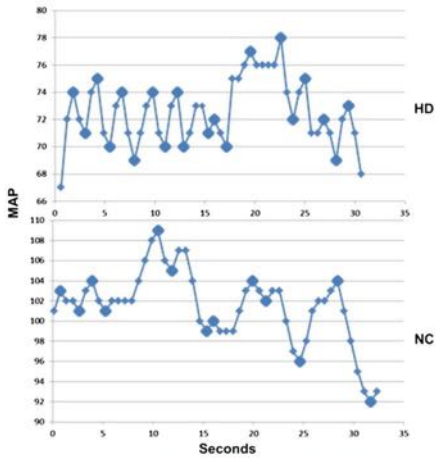


Figure 1 A 30 seconds sample demonstrating extrema points of Mean Arterial Blood Pressure (MAP) in a haemodialysis patient during haemodialysis (HD) and in a normal control (NC) during exercise.

Eldehni MT, Jasn 2015 – Eldehni MT, TBMM 2013

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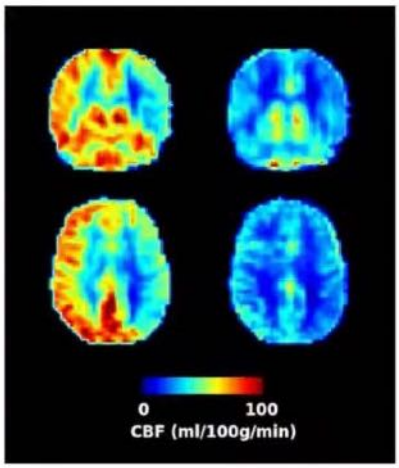
Effets aigus de l'HD (imagerie TEP-IRM)



ClinicalTrials.gov Identifier: NCT03342183

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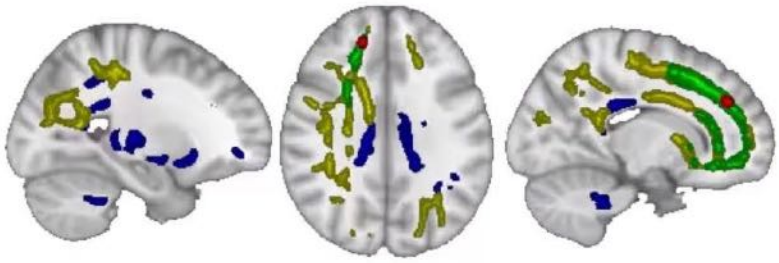
La séance d'HD induit des lésions cérébrales aiguës



Regions where fractional anisotropy (blue), axial (yellow), radial (red), and mean (green) diffusivity increase at peak stress during hemodialysis

Significant (P<0.05) by tract-based spatial statistics with threshold-free contrast enhancement

Darcey M, Anazado U, McIntyre CW. ASN 2019

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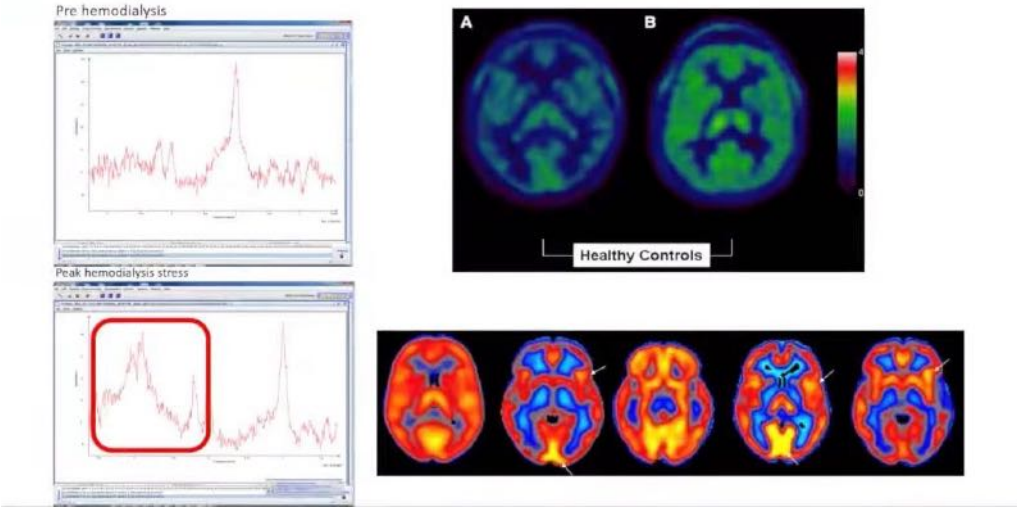
Inflammation cérébrale en HD (IRMS et TEP FEPPA^{18})



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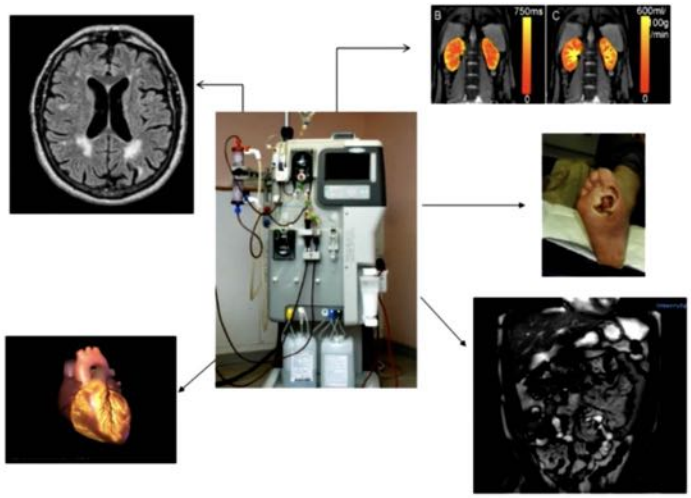
Comment réduire la sidération systémique en hémodialyse ?



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Facteurs associés aux anomalies de cinétique régionales

Facteurs associés au développement de > 2 ACR (r^2 = 0,602)

	OR	P
Volume UF 1,0 L /séance	5.1	0,007
Volume UF 1,5 L /séance	11.6	0,007
Volume UF 2,0 L /séance	26.2	0,007
Baisse max de PAS 10 mmHg	1.8	0,002
Baisse max de PAS 20 mmHg	3,3	0,002
Baisse max de PAS 30 mmHg	6,0	0,002
cTnT	1,26	0,004
Age	1,07	0,018

Burton JO & al. Cjasn 2010;4:914

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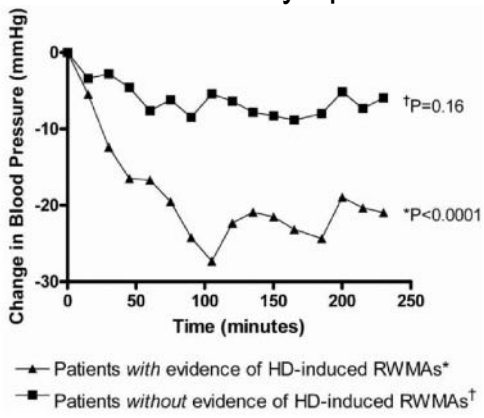
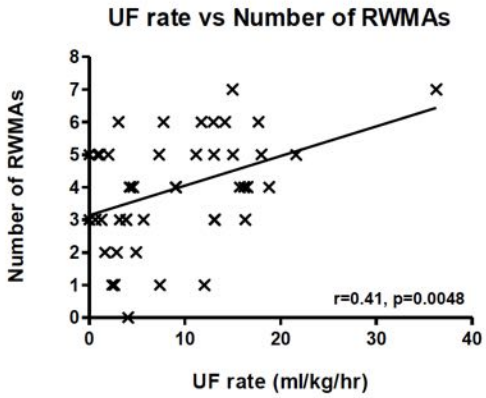
HID, UF horaire et sidération

PA intradialytique



UF horaire



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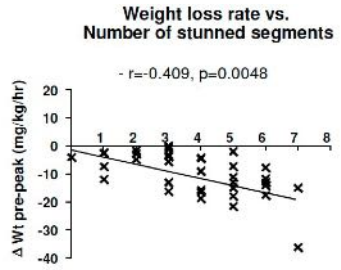
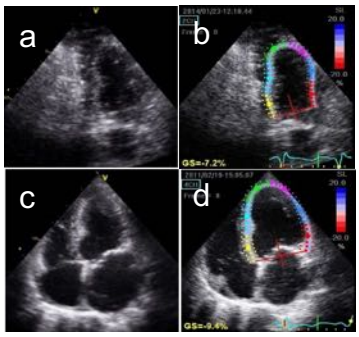
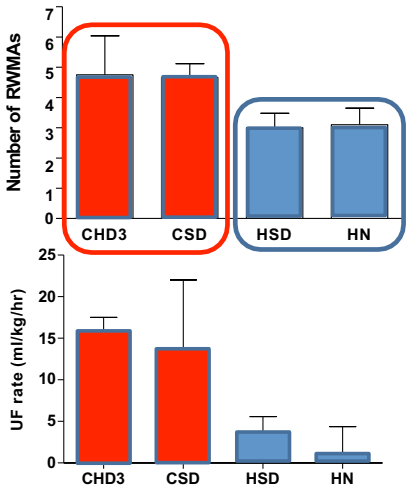
Impact de la dialyse fréquente sur la sidération cardiaque





CHD3 : 3 x 4h en centre
CSD, HSD : 5 x 2-3h centre (C) ou domicile (H)
HN : 5 x 6-8h nocturne à domicile



Jefferies H & al. Cjasn 2011;6:1326

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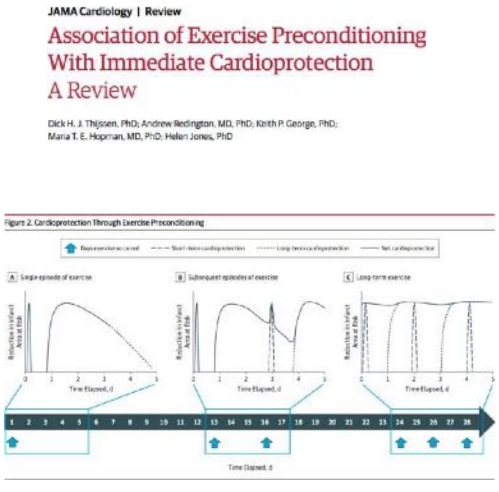
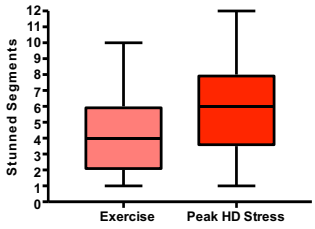
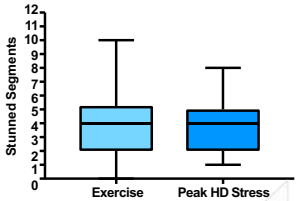
Pré-conditionnement par l'exercice pour prévenir la sidération cardiaque


JAMA Cardiology | Review

Association of Exercise Preconditioning With Immediate Cardioprotection
A Review

Dick H. J. Thijssen, PhD; Andrew Redington, MD, PhD; Keith P. George, PhD; Maria T. E. Hopman, MD, PhD; Helen Jones, PhD





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Thijssen DH & al. Jama Cardiol 2017 - Penny J, & al. NDT 2019

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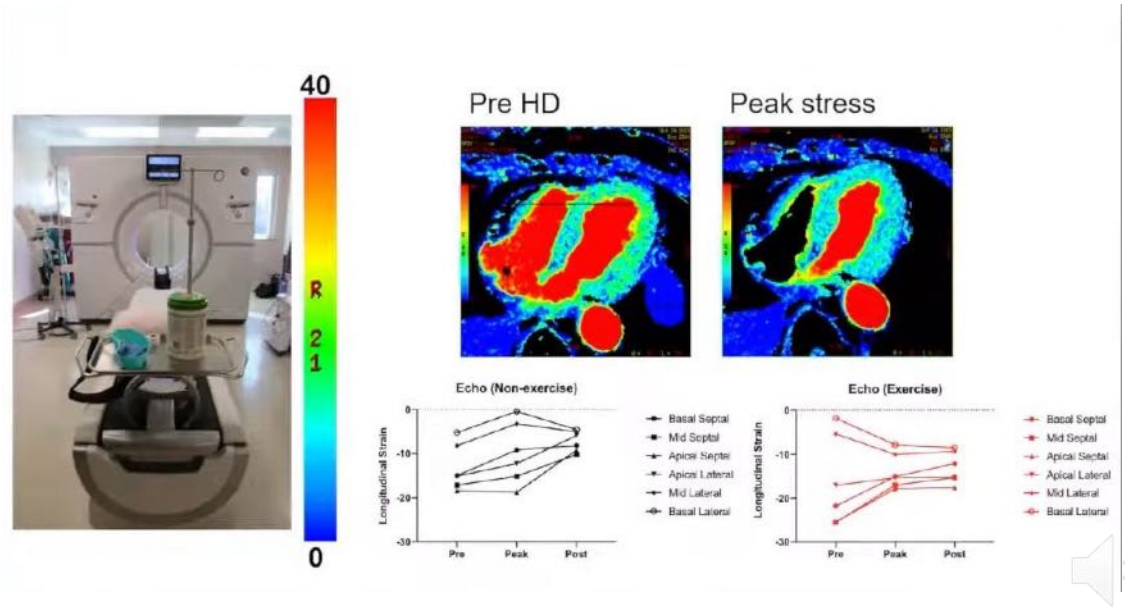
Effet de l'exercice intra-D sur le débit myocardique



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Dialysat froid « cooling » et protection cardiovasculaire

Original Paper

Blood Purification

Individualised Dialysate Temperature Improves Intradialytic Haemodynamics and Abrogates Haemodialysis-Induced Myocardial Stunning, without Compromising Tolerability

Helen J. Jefferies[a] James O. Burton[a] Christopher W. McIntyre[a, b]

[a]Department of Renal Medicine, Royal Derby Hospital, and [b]School of Graduate Entry Medicine and Health, University of Nottingham, Nottingham, UK

Randomized Controlled Trial of Individualized Dialysate Cooling for Cardiac Protection in Hemodialysis Patients

Aghogho Odudu[a–c] Mohamed Tarek Eldehni[a, c] Gary P. McCann[d] and Christopher W. McIntyre[a]

Abstract

Background and objectives Cardiovascular disease is the most common cause of death in patients on hemodialysis (HD). HD-associated cardiomyopathy is appreciated to be driven by exposure to recurrent and cumulative ischemic insults resulting from hemodynamic instability of conventionally performed intermittent HD treatment itself. Cooled dialysate reduces HD-induced recurrent ischemic injury, but whether this confers long-term protection of the heart in terms of cardiac structure and function is not known.

Design, setting, participants, & measurements Between September 2009 and January 2013, 73 incident HD patients were randomly assigned to a dialysate temperature of 37°C (control) or individualized cooling at 0.5°C below body temperature (intervention) for 12 months. Cardiac structure, function, and aortic distensibility were assessed by cardiac magnetic resonance imaging. Mean between-group difference in delivered dialysate temperature was 1.2°C ± 0.3°C. Treatment effects were determined by the interaction of treatment group with time in linear mixed models.

Results There was no between-group difference in the primary outcome of left ventricular ejection fraction (1.5%; 95% confidence interval, −4.3% to 7.3%). However, left ventricular function assessed by peak systolic strain was preserved by the intervention (−3.3%; 95% confidence interval, −6.5% to −0.2%) as was diastolic function (measured as peak diastolic strain rate, 0.38 s^{-1}; 95% confidence interval, 0.02 to 0.76 s^{-1}). Reduction of left ventricular dilation was demonstrated by significant reduction in left ventricular end-diastolic volume (−23.0 ml; 95% confidence interval, −44.7 to −2.9 ml). The intervention was associated with reduced left ventricular mass (−15.6 g; 95% confidence interval, −29.4 to −1.9 g). Aortic distensibility was preserved in the intervention group (1.8 mm^{2}kg^{-1}×10^{-3}; 95% confidence interval, 0.1 to 3.6 mm^{2}kg^{-1}×10^{-3}). There were no intervention-related withdrawals or adverse events.

Conclusions In patients new to HD, individualized cooled dialysate did not alter the primary outcome but was well tolerated and slowed the progression of HD-associated cardiomyopathy. Because cooler dialysate is universally applicable at no cost, the intervention warrants wider adoption or confirmation of these findings in a larger trial.

Clin J Am Soc Nephrol 10: ■■■–■■■, 2015. doi: 10.2215/CJN.00200115

Randomized Clinical Trial of Dialysate Cooling and Effects on Brain White Matter

Mohamed T. Eldehni, Aghogho Odudu, and Christopher W. McIntyre

Division of Medical Sciences and Graduate Entry Medicine, School of Medicine, University of Nottingham, Nottingham, United Kingdom

ABSTRACT

Hemodialysis is associated with significant circulatory stress that could produce recurrent and cumulative ischemic insults to multiple organs, such as the brain. We aimed to characterize hemodialysis-induced brain injury by longitudinally studying the effects of hemodialysis on brain white matter microstructure and further examine if the use of cooled dialysate could provide protection against hemodialysis-associated brain injury. In total, 73 patients on incident hemodialysis starting within 6 months were randomized to dialyze with a dialysate temperature of either 37°C or 0.5°C below the core body temperature and followed up for 1 year. Brain white matter microstructure was studied by diffusion tensor magnetic resonance imaging at baseline and follow-up (38 patients available for paired analysis). Intradialytic hemodynamic stress was quantified using the extreme points analysis model. Patients on hemodialysis exhibited a pattern of ischemic brain injury (increased fractional anisotropy and reduced radial diffusivity). Cooled dialysate improved hemodynamic tolerability, and changes in brain white matter were associated with hemodynamic instability (higher mean arterial pressure extrema points frequencies were associated with higher fractional anisotropy (peak r=0.443, P<0.03) and lower radial diffusivity (peak r=−0.439, P<0.02)). Patients who dialyzed at 0.5°C below core body temperature exhibited complete protection against white matter changes at 1 year. Our data suggest that hemodialysis results in significant brain injury and that improvement in hemodynamic tolerability achieved by using cooled dialysate is effective at abrogating these effects. This intervention can be delivered without additional cost and is universally applicable.

J Am Soc Nephrol 26: ■■■–■■■, 2015. doi: 10.1681/ASN.2013105086

Nephrol Dial Transplant
doi: 10.1093/ndt/gfl126

Original Artic

A systematic review of the clinical effects of reducing dialysate fluid temperature

Nicholas M. Selby[1] and Christopher W. McIntyre[1,2]

Hemodialysis International 2009; 13:189–196

Cool dialysate reduces asymptomatic intradialytic hypotension and increases baroreflex variability

Lindsay J. CHESTERTON,[1] Nicholas M. SELBY,[1] James O. BURTON,[1] Chris W. McINTYRE[1,2]

[1]*Department of Renal Medicine, Derby City General Hospital, Derby, UK;* [2]*School of Graduate Entry Medicine and Health, University of Nottingham, Derby, UK*

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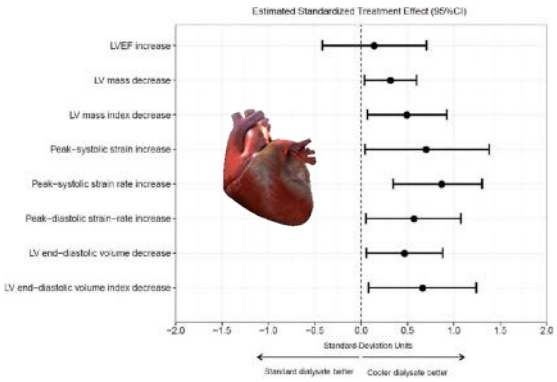
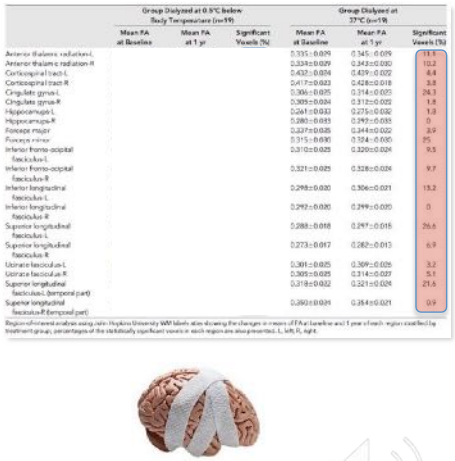
Protection cardiaque et neurologique par le « cooling"





Odudu A, & al. Cjasn 2015

Eldehni MT, & al. Jasn 2014

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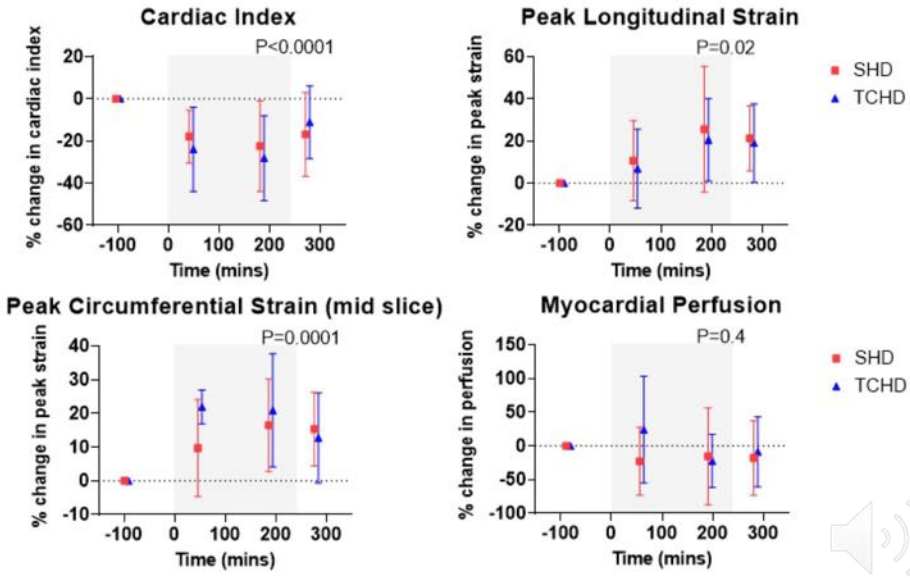
HD thermorégulée vs HD standard à 37°

n = 11
crossover
IRM multiparamétrique



Gullapudi VR, NDT 2023

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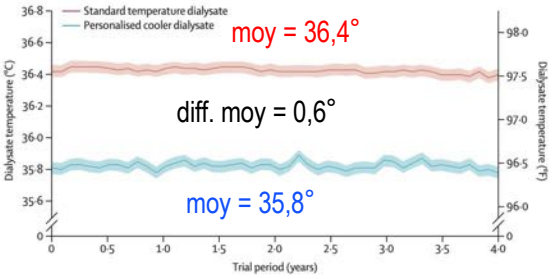
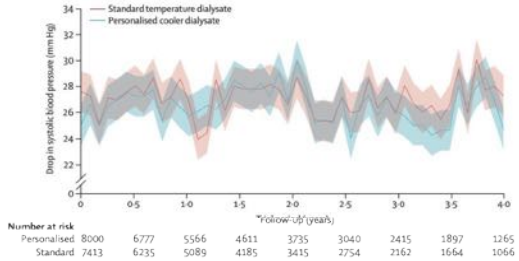
Etude randomisée « MY TEMP »



Intradialytic Hypotension



C1	Personnalisé (n = 8000)	Temp » « standard » (n = 7413)	HR
C1 CV*	1711 (21,4%)	1658 (22,4%)	1,00
Mortalité toute cause	2962 (37,0%)	2848 (38,4%)	1,03

* combinaison mortalité CV + hospit pour SCA, AVC, ICC (= MACE 4 pts)

myTemp, Lancet 2022

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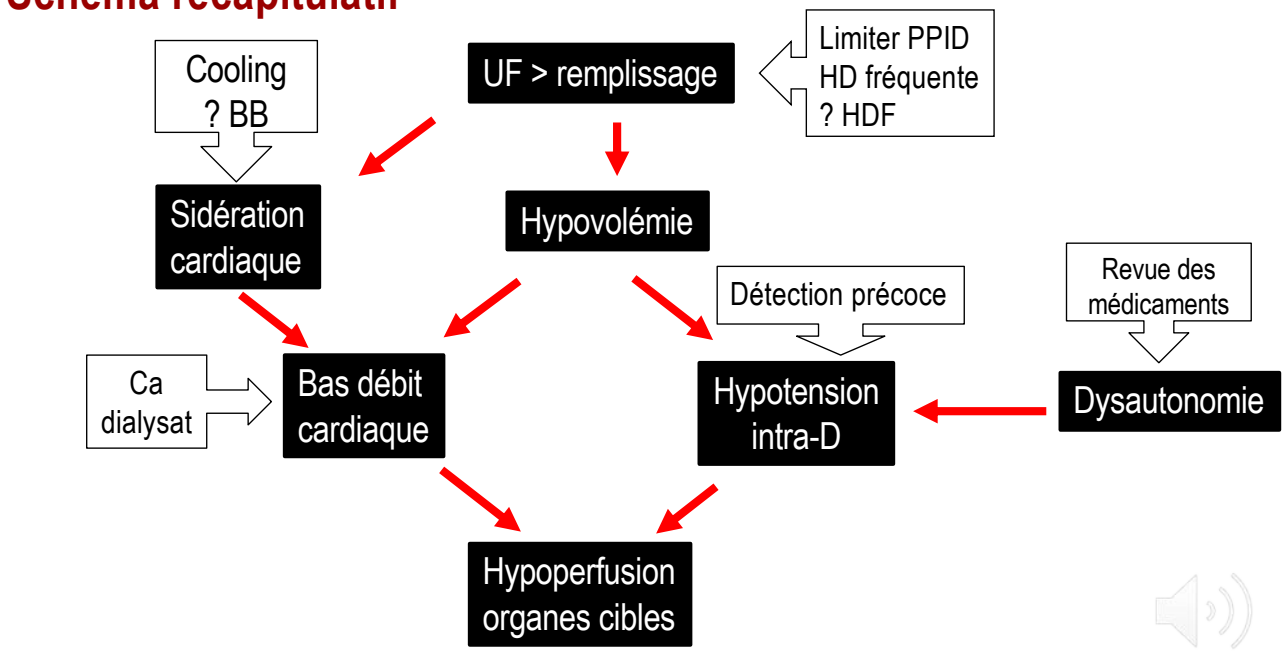
Schéma récapitulatif



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Que retenir ?




- La sidération multi-organe est un nouveau mécanisme **d'aggressions ischémiques répétées** survenant, et déclenchée, pendant la séance d'HD/UF
- Les cq à termes de la sidération myocardique sont la **perte permanente de la fonction VG** (= ins. cardiaque), et les **troubles du rythme** (mort subite)
- Les effets délétères de la sidération sont **synergiques avec ceux de l'HID**
- Les mesures préventives connues sont d'efficacité limitée et associent la **réduction de l'UF**, le **pré-conditionnement** et le **cooling**.

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