Καρδιονεφρικό μεταβολικό σύνδρομο

Κωνσταντίνος Τσιούφης
Καθηγητής - Διευθυντής Α΄ Καρδιολογικής Κλινικής
ΕΚΠΑ , Ιπποκράτειο ΓΝΑ
Αντιπρόεδρος Ιατρικής Σχολής ΕΚΠΑ

ESH President (2017-19)

Δήλωση σύγκρουσης συμφερόντων

✓ Δεν έχω σύγκρουση συμφερόντων για την συγκεκριμένη ομιλία πέραν της αγάπης μου για τη σχέση καρδιάς-νεφρού


16ο Πανελλήνιο Συμπόσιο
Καρδιαγγειακές Παθήσεις και Νεφρική Δυσλειτουργία 2024
11 - 13 Ιανουαρίου 2024
Ίδρυμα Ευγενίδου, Αθήνα
SAVE THE DATE
www.cardiorenal2024.gr
Διοργάνωση
Ινστιτούτο Μελέτης Έρευνας Εκπαίδευσης & Θεραπείας Νοσημάτων Αγγείων, Καρδιάς, Εγκεφάλου, Νεφρών
Α΄ Πανεπιστημιακή Καρδιολογική Κλινική Γ.Ν.Α. «Ιπποκράτειο»
Υπό την αιγίδα:
Ιατρική Σχολή Πανεπιστημίου Αθηνών
European Society of Hypertension
Οργάνωση - Γραμματεία
The MASTERMIND Group
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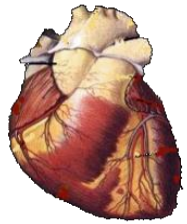
Εθνικόν και Καποδιστριακόν
Πανεπιστήμιον Αθηνών
Πανεπιστημίου 30, 106 79 Αθήνα

ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Εθνικόν και Καποδιστριακόν
Πανεπιστήμιον Αθηνών
ΙΔΡΥΘΕΝ ΤΟ 1837

Αναγόρευση επίτιμου διδάκτορα του Τμήματος Ιατρικής της Σχολής Επιστημών Υγείας του Πανεπιστημίου Αθηνών

George L. Bakris, M.D., Hon. DSc, F.A.S.N., F.A.H.A

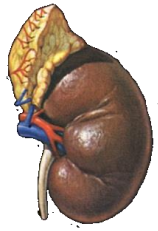
Hearth and Kidney: dangerous liaison



Regulation of perfusion pressure and flow to periphery

Electrical activity depends on electrolytes and acid-base

Hormonal function (ANP - BNP)



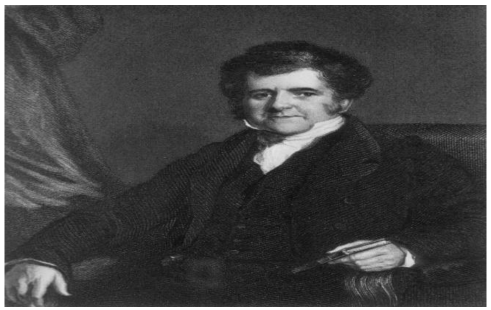
Regulation of volume and BP (Na^+ and H_2O)

Electrolyte and acid-base balance

Hormonal function (Erythropoiesis – Vascular tone)

1836 – Richard Bright

The prevalence of CVD in patients with renal disease was accompanied by the secretion of urinary albumin



1836] *Dr. Bright on Renal Diseases.* 23

CASES AND OBSERVATIONS ILLUSTRATIVE OF RENAL DISEASE, ACCOMPANIED WITH THE SECRETION OF ALBUMINOUS URINE. By *Dr. Bright.*

[Guy's Hospital Reports, No. 2.]

THE importance of the subject, and the ability of the writer, demand a separate article for this report; and, on that account, we have placed it in our REVIEW, instead of PERISCOPIC department. It might be difficult to determine whether the disease in question has become more frequent of late years, or only been better observed and oftener detected. For our own parts, we think that the disease called "mottling," "white degeneration," "contraction," or "granulation," *is* of more common occurrence than formerly, and *is also* better understood, both as to symptoms and pathology. Dr. Bright, who has paid especial attention to this dangerous malady for ten or a dozen years past, is of opinion that 500 people fall victims to it every year in London alone. He thinks there is great reason to believe that the seeds of the disease are often early sown, and that intervals of apparent health produce a false feeling of security.

Hæmaturia is often a precursor of renal disease—and so is scarlatina. Intemperance, however, is its most common source—and exposure to cold the most usual exciting cause. Intemperance in youth generally lays so firm a foundation for the malady, as to bid defiance to remedies afterwards. The history of this disease and its symptoms are nearly as follow:—

"A child, or an adult, is affected with scarlatina, or some other acute disease; or has indulged in the intemperate use of ardent spirits for a series of months or years; he is exposed to some casual cause or habitual source of suppressed perspiration: he finds the secretion of his urine greatly increased, or he discovers that it is tinged with blood; or, without having made any such observation, he awakes in the morning with his face swollen, or his ankles puffy, or his hands œdematous. If he happen, in this condition, to fall under the care of a practitioner who suspects the nature of his disease, it is found, that already his urine contains a notable quantity of albumen: his pulse is full and hard, his skin dry, he has often headache, and sometimes a sense of weight or pain across the loins. Under treatment more or less active, or sometimes without any treatment, the more obvious and distressing of these symptoms disappear; the swelling, whether casual or constant, is no longer observed; the urine ceases to evince any admixture of red particles; and, according to the degree of importance which has been attached to these symptoms, they are gradually lost sight of, or are absolutely forgotten. Nevertheless, from time to time, the countenance becomes bloated; the skin is dry; headaches occur with unusual frequency; or the calls to micturition disturb the night's repose. After a time, the healthy colour of the countenance fades; a sense of weakness or pain in the loins increases; headaches, often accompanied by vomiting, add greatly to the general want of comfort; and a sense of lassitude, of weariness, and of depression, gradually steal over the bodily and mental frame. Again the assistance of medicine is sought. If the nature of the disease is suspected, the urine is carefully tested; and found, in almost every trial, to contain albumen, while the quantity of urea is gradually diminishing. If, in the attempt to give relief to the oppression of the system, blood is drawn, it is often buffed, or the serum is milky and opaque; and nice analysis will frequently detect a great deficiency

1903 – F. Collet

Passive renal congestion because of heart dysfunction

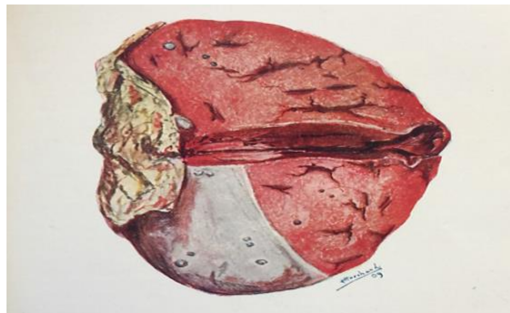


PLANCHE V

Rein cardiaque, avec cicatrices d'infarctus.

CONGESTION RÉNALE 1087

ARTICLE VII

CONGESTION RÉNALE

Le rein est prédisposé aux congestions et aux hémorragies par son abondante vascularisation.

1° Étiologie. — On a coutume de diviser les congestions rénales en actives et passives.

A. — CONGESTION PASSIVE. — La *stase veineuse*, c'est-à-dire la gêne prolongée de la circulation de retour est la principale cause de congestion rénale ; c'est celle qui s'observe dans diverses maladies du cœur, surtout dans les affections mitrales, dans l'insuffisance tricuspidienne, dans l'asystolie, dans la compression de la veine cave inférieure : on la désigne encore sous le nom de congestion passive ou *rein cardiaque*.

B. — CONGESTIONS DITES ACTIVES. — Les autres congestions, dites actives, peuvent se grouper de la façon suivante :

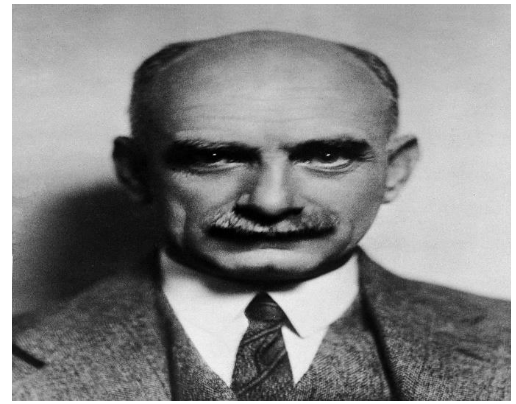
a. *Intoxications.* — Toutes les intoxications peuvent retentir sur le rein. Les poisons s'éliminent, partiellement au moins, par le filtre rénal et le lèsent au passage. L'empoisonnement par la cantharide nous représente le type expérimental de ces congestions, et aussi quelquefois leur type clinique, à la suite de l'application prolongée d'un vésicatoire chez certains sujets particulièrement susceptibles.

b. *Infections.* — Parmi elles, signalons en premier lieu la scarlatine, la pneumonie, la tuberculose, plus rarement la diphtérie et la dothiénentérie, exceptionnellement la syphilis secondaire. L'infection n'agit souvent que par le mécanisme de l'intoxication : les produits solubles de la diphtérie, la tuberculine de Koch, peuvent produire de la dilatation vasculaire, indépendamment de toute action microbienne.

Ces congestions rénales infectieuses, de même que celles d'origine toxique, ne sont généralement que le stade initial d'une néphrite aiguë. On en peut dire autant de la congestion rénale aiguë *a frigore*. — Toutefois, une exception doit être faute pour les fièvres paludéennes pernicieuses à forme hématurique ou hémoglobinurique (KELSCH et KIENER).

c. *Causes nerveuses.* — Le rein a une innervation vaso-motrice spéciale, comme le démontre par exemple la polyurie émotive. Des

1913 – T. Lewis



NOV. 29, 1913.] PAROXYSMAL DYSPNOEA IN CARDIO-RENAL PATIENTS. [THE BRITISH MEDICAL JOURNAL 1417

A Clinical Lecture

ON

PAROXYSMAL DYSPNOEA IN CARDIO-RENAL PATIENTS:

WITH SPECIAL REFERENCE TO "CARDIAC" AND "URAEMIC" ASTHMA.

DELIVERED AT UNIVERSITY COLLEGE HOSPITAL, LONDON, NOVEMBER 12TH, 1913.

BY THOMAS LEWIS, M.D., D.Sc., F.R.C.P.,

ASSISTANT PHYSICIAN AND LECTURER IN CARDIAC PATHOLOGY, UNIVERSITY COLLEGE HOSPITAL; PHYSICIAN TO OUT-PATIENTS, CITY OF LONDON HOSPITAL.

DURING the past few years interest in the question of dyspnoea has awakened very considerably. I propose at the present time to relate some observations made at the hospital during the past twelve months, which, so it seems to me, help us to a fuller understanding of breathlessness in a large group of patients who have evident signs of cardiac disease. I will first direct attention to a special type of breathlessness from which patients suffer, indicate how far we can explain this breathlessness, and how it may be recognized. Finally, I shall briefly discuss the nature and relations of "cardiac" and "uraemic" asthma, so-called, and suggest certain lines of thought and procedure, which may, I think, bring us into closer touch with the realities of disease in these patients.

A SPECIAL FORM OF DYSPNOEA.

First I would direct your thoughts to instances of simple cardiac dyspnoea. There are forms of congenital heart disease and of extreme mitral stenosis in which, as you come to the bedside, you immediately recognize a deficiency in the aeration of the arterial blood. The patients I would have you call primarily to mind are those in whom you have seen deep or extreme cyanosis. Some of these patients are very breathless, but it is notable that in many others, especially those who suffer from congenital heart defects, the anxiety of breathing is not severe while they lie at rest. From such observations I argue that if dyspnoea is due to deficiency in the aëration of the arterial blood, cyanosis will be prominent, and, by a comparison of many cases, that urgent dyspnoea, if of the same origin, must be accompanied by extreme discoloration. Next I would point out that a very large proportion of patients who exhibit great anxiety of breathing and have evident signs of cardiac disease, do not exhibit this degree of cyanosis. It is a well-known fact that in heart disease breathlessness and cyanosis are often shown in disproportionate degree, yet the significance of this fact has, I think, escaped attention. Why it has so escaped I shall attempt to explain later. At present let us be content with the observation and the natural conclusions to be drawn from it. If a patient is urgently breathless and an equivalent cyanosis is not found, the dyspnoea is not wholly due to deficient aëration of the blood. You can rarely pass through the wards of this hospital without seeing a number of patients sitting propped up with pillows and in great distress of breathing; examine these cases more closely and you will see that some of them have but little cyanosis. These patients belong to the special group which I shall now describe, and for descriptive purposes I shall give the relevant features of an extreme case.

In the early months of this year I saw a man, aged 57, who for twelve months had experienced failing health. Breathlessness was his chief complaint, and it was periodic in its intensity. For months he would be well, or comparatively so, then for weeks his breathing would be difficult, so that active movement was impossible, and he would lie up. During the periods when he was in bed he was continually breathless, and he dreaded the nights because his breathlessness increased during them; often he was awakened from his sleep by attacks of aggravated breathlessness, in which he feared suffocation; these attacks would last a half-hour or more, and he would relapse into a short sleep to be similarly disturbed. When I saw this patient it was evening, and on the first day of his taking to bed. He was not orthopnoeic, but lay flat in bed; his respirations were deep, noisy, and periodic (Cheyne-Stokes type); he was drowsy, complained of severe headache, and great breathlessness. Yet the mucous membranes of this patient were as pink as those of a child; neither in the lips, tongue, ears, cheeks, or fingers, was there the faintest trace of cyanosis. Upon further examination the heart was found to be a little enlarged, the pulse was at the rate of 92 per minute, occasional extra-systoles interrupted its rhythm, and alternation in the force of the pulse beats was seen. There were no murmurs. The veins pulsated freely and seemed a little engorged, but the liver was not enlarged and there was no dropsy. The blood pressure was 200 mm. Hg. He was passing from 600 to 2,000 c.cm. of urine a day; sometimes a trace of albumin was present, and a few granular casts were found. Over the lungs a few rhonchi were audible.

I take this as a type case and emphasize the following features. The man presented some signs of a degenerate heart muscle, enlargement, and especially pulsus alternans; he presented signs of renal involvement, the urine flow was, as a rule, increased, casts were present, the blood pressure was very high. He had urgent dyspnoea, yet the blood was perfectly aërated. You may say that I am describing a case of so-called "uraemic" dyspnoea; I cannot disagree with you. This patient was one of a series specially investigated for me by my collaborators, Mr. Barcroft, Drs. Ryffel, Cotton, and Wolff. Mr. Barcroft found in him by special methods evidences of a diminished alkalinity of the blood sufficient to account for the dyspnoea and due, not to CO_2, but to non-volatile acids. Having studied a number of cases by these methods, which I will describe briefly later, we were able to isolate a group of symptoms which are specially associated with an altered blood reaction of the kind.

Special Clinical Associations of Relative Acidosis.

The most important feature of these cases is the breathlessness, varying in degree, as Mr. Barcroft has shown, with the reaction of the blood, being of the periodic type known as Cheyne-Stokes respiration, being accompanied when severe by conspicuous restlessness during the periods of hyperpnoea, and lastly becoming exaggerated by the slightest exercise. There is no reserve, the breath cannot be held, and forced breathing is followed by no apnoeic period. Oxygen affords little or no relief, though it alters the type of breathing. Secondly, there is evidence that the blood is well or moderately aërated; there is no cyanosis comparable with the dyspnoea. Thirdly, the dyspnoea is more severe towards evening and in the night, and sleep is broken by exaggerated attacks of breathlessness. Fourthly, the pulse-rate is increased (80–100), and especially towards evening. Fifthly, the temperature is subnormal.

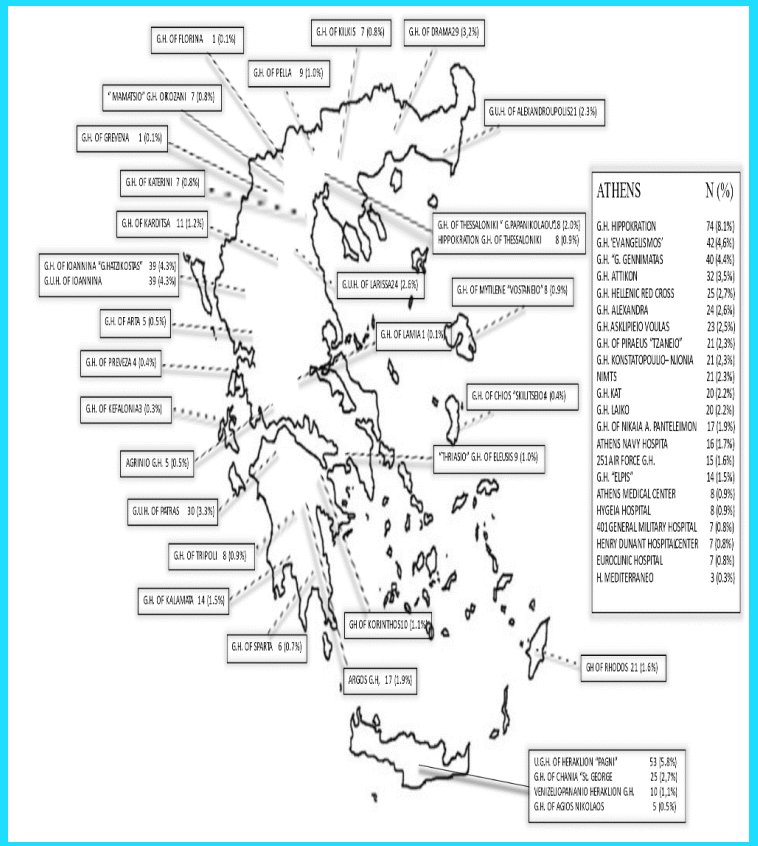
These are almost constant clinical manifestations; but the picture may be modified in a variety of ways, and it is to these modifications that the chief difficulties in diagnosis and the confused pathology of the past are due. Imagine a patient with the symptoms which I have described and take him as a type; add to this symptom group the symptoms and signs of heart disease in its varying forms; add to it also a large number of unquestionable renal manifestations; add to it emphysema and the symptoms of cerebral arterial sclerosis, and you are able to construct all the different types in which this curious form of acidosis is found. The types are protean. Your power of diagnosing acidosis will depend on your ability to discriminate the underlying symptom group which I have detailed. Usually you will have no difficulty; the condition is an extremely common one, and urgent dyspnoea, where there is a want of equivalent cyanosis, is your first guide; really distressed breathing in elderly subjects, accompanied or not by cyanosis, is always open to suspicion; the presence of Cheyne-Stokes breathing, and especially the characteristic nocturnal attacks, are extremely valuable indications. The periodicity of the breathing is often inconspicuous or variable; it may consist merely of slight waxing and waning in the amplitude of the breathing, there may be no true apnoeic periods; it may be present only at night or at the patient's first admission; it is very often overlooked; I have heard its presence denied in patient after patient, and have found it either by immediate close examination or by repeated examination. It should be looked for especially when the patient is quiet or asleep; very small disturbances may abolish it; if you watch your patient when he is unaware that you are watching you may often detect it. But Cheyne-Stokes breathing may not be present; it may be absent in at least two types of case—(1) where the

[2761]

Στιγμιαία αποτύπωση

Καρδιονεφρικής Νοσηρότητας

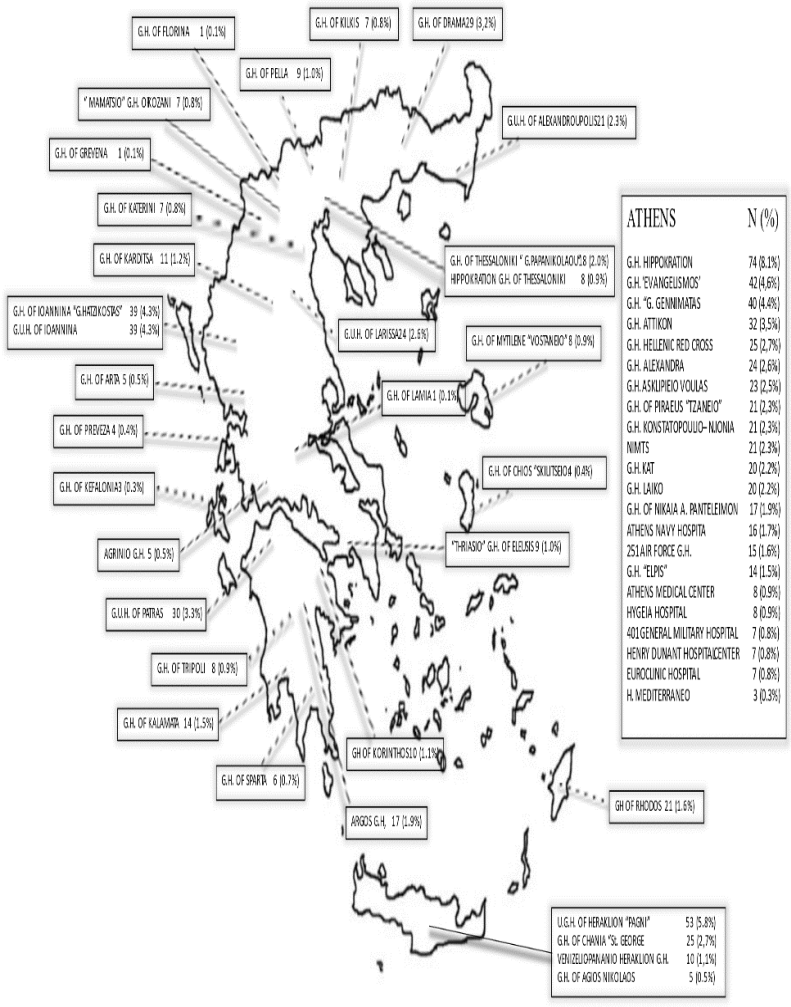
σε Νοσηλευόμενους Καρδιολογικών κλινικών της Ελληνικής Επικράτειας



ATHENS	N (%)
G.H. HIPPOKRATION	74 (8.1%)
G.H. "EVANGELISMOS"	42 (4.6%)
G.H. "G. GENNIMATAS	40 (4.4%)
G.H. ATTIKON	32 (3.5%)
G.H. HELLENIC RED CROSS	25 (2.7%)
G.H. ALEXANDRA	24 (2.6%)
G.H. ASKLIPIEIO VOULAS	23 (2.5%)
G.H. OF PIRAEUS "TZANEIO"	21 (2.3%)
G.H. KONSTATOPOULO– NICONIA	21 (2.3%)
NIMTS	21 (2.3%)
G.H. KAT	20 (2.2%)
G.H. LAIKO	20 (2.2%)
G.H. OF NIKAIA A. PANTELEIMON	17 (1.9%)
ATHENS NAVY HOSPITA	16 (1.7%)
251AIR FORCE G.H.	15 (1.6%)
G.H. "ELPIS"	14 (1.5%)
ATHENS MEDICAL CENTER	8 (0.9%)
HYGEIA HOSPITAL	8 (0.9%)
401GENERAL MILITARY HOSPITAL	7 (0.8%)
HENRY DUNANT HOSPITALCENTER	7 (0.8%)
EUROCLINIC HOSPITAL	7 (0.8%)
H. MEDITERRANEO	3 (0.3%)

HECMOS

HELLENIC CARDIORENAL MORBIDITY SNAPSHOT



HECMOS

HELLENIC CARDIORENAL MORBIDITY SNAPSHOT

168 (18.2%) combined

3/4 comorbidities

HF + AF commonest combo - 20.6%

NATION-WIDE SURVEY

923

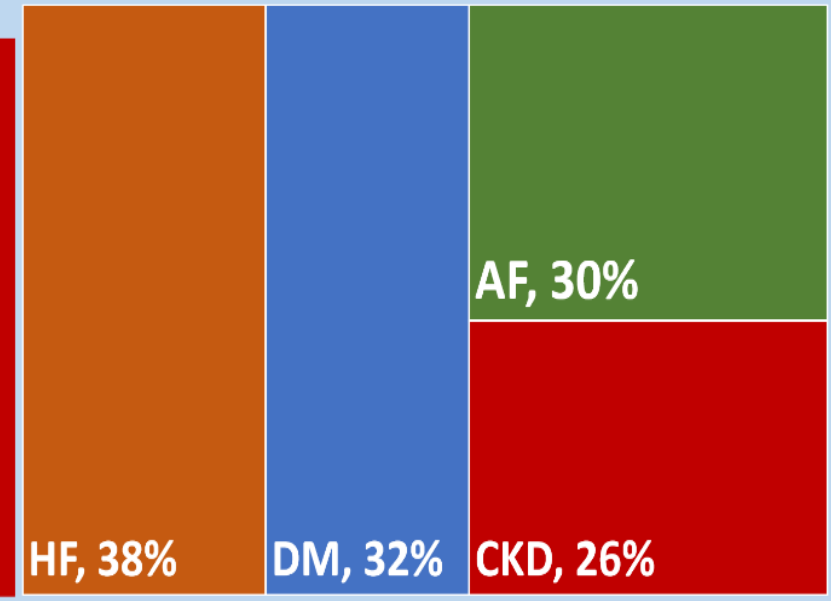
CARDIOLOGY INPATIENTS

68.4% ♂

73±14.8 years old

Smokers 24.9%

HTN 66%

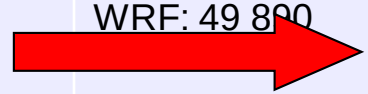


Leontsinis,….,Tsioufis HJC 2023

Epidemiological perspectives

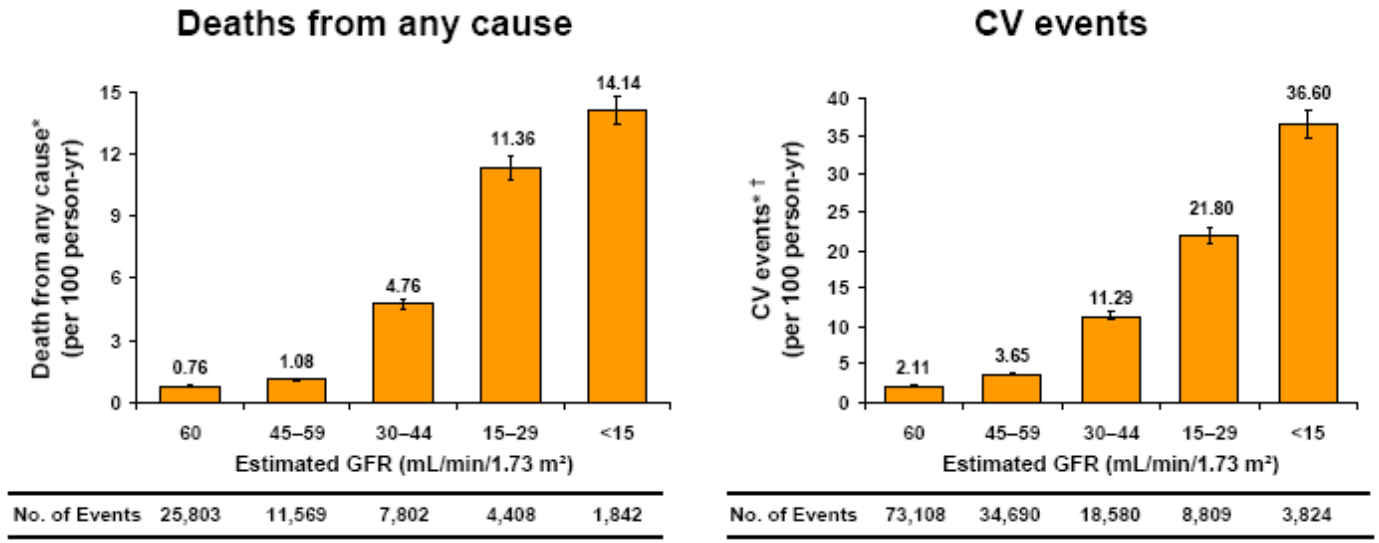
Renal impairment in HF

Author	Year	Population	Total n	Main results
Smith	2006	Acute and chronic HF	CKD: 80 098 WRF: 12 634	CKD present in 63% of patients Baseline CKD associated with mortality: HR 1.56 (1.53-1.60) WRF associated with mortality: HR 1.47 (1.26-1.72)
Tonelli	2006	CV disease, including chronic HF	Total: 1 371 990 HF: 78 272	CKD present in 33% of patients Baseline CK associated with mortality: HR 1.78 (1.57-2.01)
Damman	2007	Acute and chronic HF	HF: 18 634	WRF occurred in 25% of patients WRF associated with mortality: OR 1.62 (1.45-1.82) WRF associated with HF hospitalizations: OR 1.30 (1.04-1.62)
Clark	2014	Chronic HF patients included in RAAS-inhibitor trials	HF: 20 573	WRF occurred in 13 and 9.6% with RAAS inhibitors and placebo, respectively WRF associated with mortality RR: 1.36 (1.25-1.48), in both treatment groups
Damman	2014	Acute and chronic HF	CKD: 1 076 104 WRF: 49 800	CKD present in 32% of patients Baseline CKD associated with mortality: OR 2.34 (2.20-2.50) WRF associated with mortality: OR 1.81 (1.55-2.12) Evidence of publication bias for studies on WRF



Damman k, et al. Eur Heart J 2015;36:1437-1444

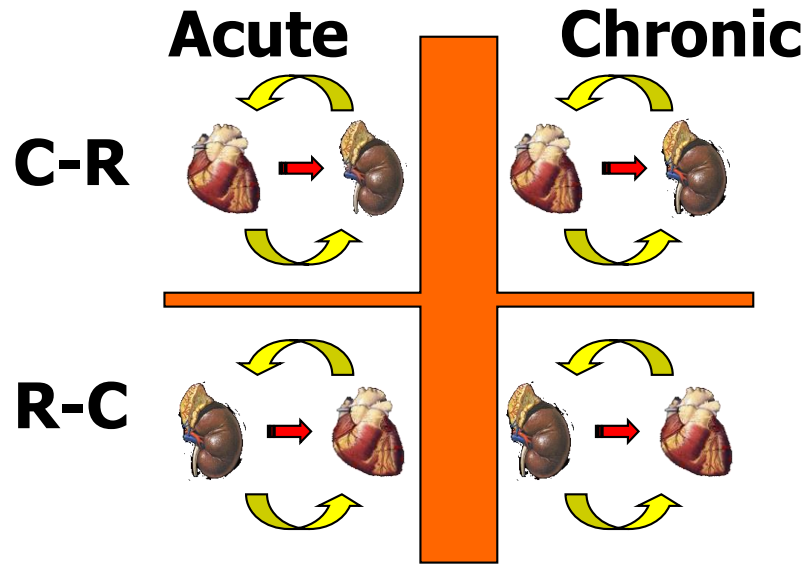
Independent Effect of CKD on CVD Morbidity / Mortality



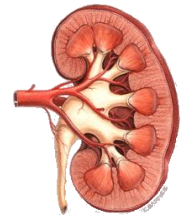
N=1,120,295 adults
***Age-standardized rates**
†Cardiovascular event defined as hospitalization for coronary heart disease, heart failure, ischemic stroke, and peripheral
arterial disease per 100 person-years
Independent Effect of CKD on CVD Morbidity / Mortality

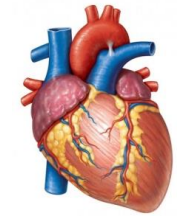
Go AS et al. N Engl J Med 2004;351:1296–305.

CRS: bidirectionality and time window



The need for a consensus classification and definition that describes all the clinical conditions together with the bidirectional nature of the organ cross-talk and the time frame of the insult and sequelae emerges clearly.





Clinical cardiorenal syndrome

Pre-clinical cardiorenal syndrome

CKD

CHF

Microalbuminuria, slight decrease in GFR

LVH, LA enlargement, Diastolic dysfunction, reduced CFR

Clinical disease

Organ damage

Asymptomatic stage

Hypertension, Diabetes, Obesity, Elderly, Smoking

Risk Factors

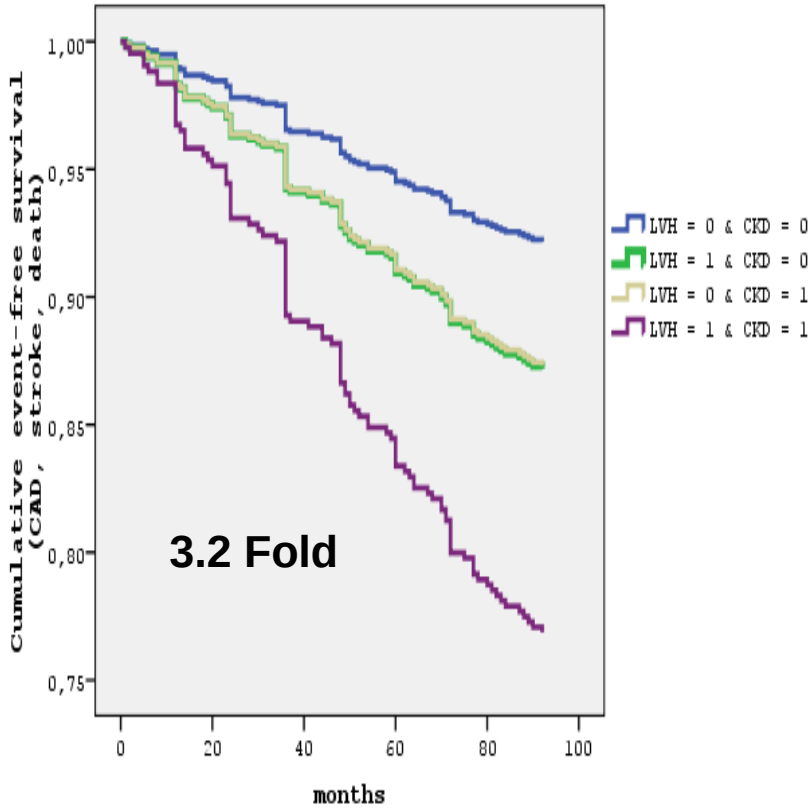
Tsioufis et al, Cardiorenal Medicine 2013

Microalbuminuria in hypertension: Index of difuge vascular damage beyond the glomelurus ….our experience

- Microalbuminuria and aortic stiffness *Tsioufis et al. Am J Cardiol 2000; 86: 797-801*

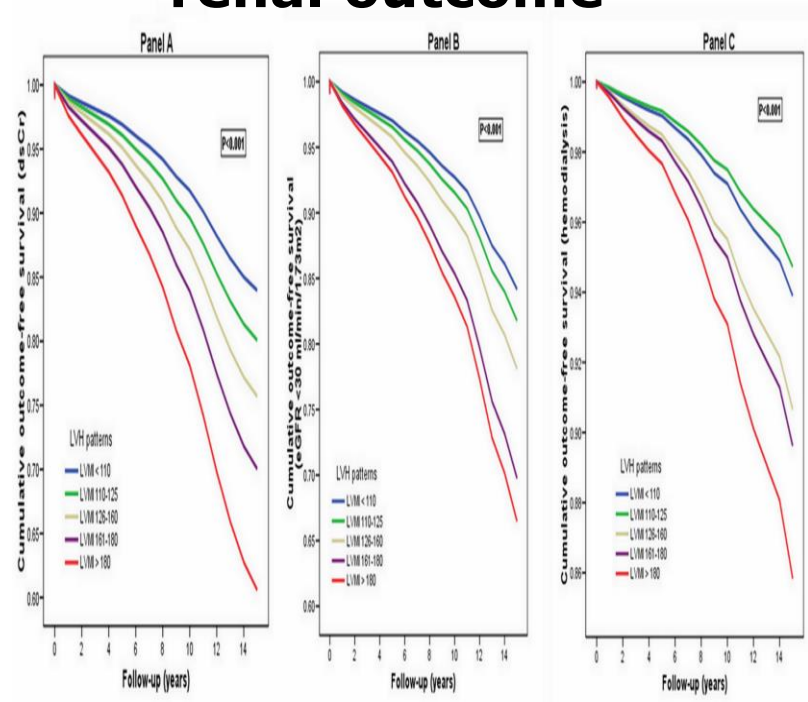
  Tsioufis, et al. Nephron Clin Pract 2003; 93: 106-111
- Microalbuminuria and concentric LVH *Tsioufis et al. J HH 2002; 16: 249-254*
- Microalbuminuria and exaggerated BP response during exercise *Tsioufis et al. Am J Med 2008; 19: 211-7*
- Microalbuminuria and uric acid *Tsioufis et al. J HH 2005; 19: 211-7*
- Microalbuminuria and ↑ hsCRP and adiponektin levels *Tsioufis, et al. Am J Cardiol 2005*
- Microalbuminuria and CD40L and IL-18 *Tsioufis C, et al. Am J Hypertens 2006*
- Microalbuminuria and ADMA *Tsioufis et al. Am J Kidney Dis 2009*
- Microalbuminuria and resistin *Tsioufis, et al. Am J Hypertens 2009*
- *Microalbuminuria and impaired coronary microcirculation Tsioufis et al, Am J Cardiol 2012*

LVH vs CKD as predictors of CV events in hypertension: a Greek 6-year-follow-up study



Tsioufis C, et al. J Hypertension 2009

Severity of LVH and renal outcome



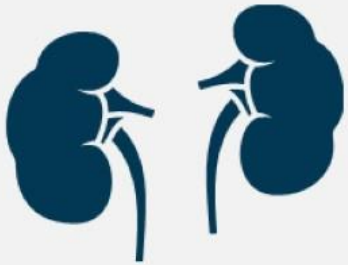
Tsioufis C, et al. J Hypertension 2011

CKD in Patients With T2D

Epidemiological Situation and Human Economic Burden

Of the ~34 million North Americans with T2D, **~40%** have CKD[a]

Diabetes is the **#1 cause of kidney failure**[a,b]



CKD associated with T2D increases the risk for CV events **2-3 fold**[c]

More than **1 in 7** North-American adults are estimated to have CKD;

that is about **37 million** people![d]

In 2017, treating Medicare beneficiaries with CKD cost more than **$84 billion**, and treating people with ESKD cost an additional **$36 billion**[d]

CKD, chronic kidney disease; CV, cardiovascular; ESKD, end stage kidney disease; T2D, type 2 diabetes.

a. https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf; b. https://www.kidney.org/news/newsroom/factsheets/Diabetes-And-CKD; c. Chen SC and Tseng CH. Rev Diabet Stud. 2013;10:88-100; d. CDC. Updated March 4, 2021. https://www.cdc.gov/kidneydisease/prevention-risk/CKD-common-serious-costly.html

A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association

Health disorder caused by **interaction among cardiovascular disease (CVD), chronic kidney disease (CKD) and metabolic risk factors** (e.g. diabetes, hypertension, obesity).

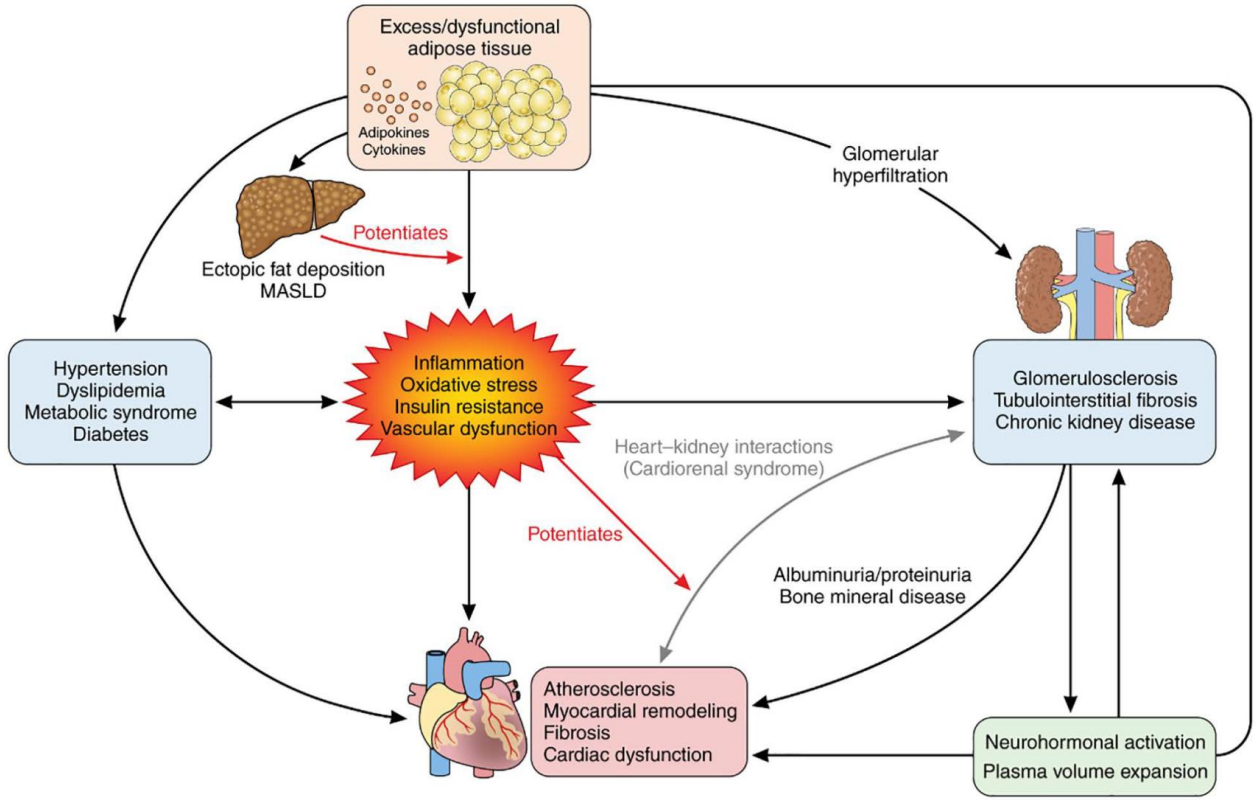
It can lead to **development or progression of CVD.**

Patients with **established CVD** are also involved.

Chiadi E. Ndumele, MD, PhD, FAHA etc

Circulation. 2023;148:00–00. DOI: 10.1161

Cardiovascular-kidney-metabolic (CKM) syndrome



Ndumele CE et al, Circulation 2023 Nov 14;148(20):1636-1664

Multidisciplinary team approach is essential for holistic care of patients with CKM syndrome.

Ndumele CE et al, Circulation 2023 Nov 14;148(20):1636-1664
Larkin H JAMA 2023 Dec 5;330(21):2042-2043

Cardiovascular-Kidney-Metabolic (CKM) Syndrome

Screening

- Screening for **all key CKM risk factors** (hypertension, diabetes, dyslipidemia, obesity).
- Screening for **kidney impairment** (eGFR, UACR).
- Need for development of a **risk calculator,** especially for the assessment of high-risk subjects.

Optimal age for **early life screening** has not been determined in clinical trials.

Ndumele CE et al, Circulation 2023 Nov 14;148(20):1636-1664
Larkin H JAMA 2023 Dec 5;330(21):2042-2043

Cardiovascular-Kidney-Metabolic (CKM) Syndrome

Prevention-treatment

- Stage 1: **prevention** of metabolic risk factor development (weight loss-adjunctive pharmacotherapies and surgical approaches, e.g. bariatric surgery).
- Stage 2: focus on **CVD prevention** (treatment of hypertension, hyperlipidemia, diabetes mellitus or CKD according to established guidelines).
- Stage 3: preventive therapies for **patients with subclinical CVD/HF** (CAC scoring for possible statin use for patients with borderline/intermediate ASCVD risk, ACE inh., β-blockers in subclinical systolic dysfunction, SGLT2inh. in HFpEF).
- Stage 4: management of **patients with CVD overlapping with CKM risk factors** [aspirin or P2Y12i + high-intensity statin +- additional LDL-C-lowering agents, GDMT for HF (ARNi, β-blockers, MRAs, SGLT2i)].

Ndumele CE et al, Circulation 2023 Nov 14;148(20):1636-1664

Cardiovascular-Kidney-Metabolic (CKM) Syndrome

Gaps in knowledge (1)

- **Heterogeneity** of patients with CKM syndrome (regarding the presence of **risk factors/speed and extent of progression** across CKM stages).
- Mechanisms of arrhythmias in CKM syndrome.
- **Heart failure subtypes** most linked to CKM syndrome.
- Insufficient data regarding **the age for screening** for CKM syndrome.

Ndumele CE et al, Circulation 2023 Nov 14;148(20):1636-1664

Cardiovascular-Kidney-Metabolic (CKM) Syndrome

Gaps in knowledge (2)

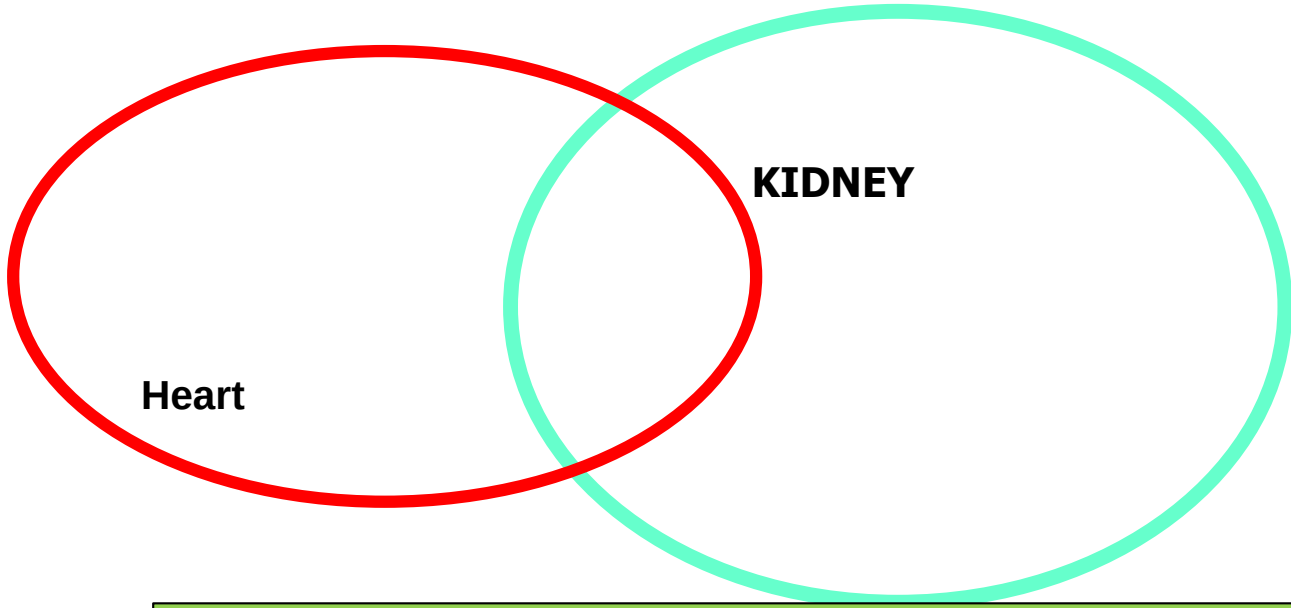
- Limited data regarding the frequency of **use of cardiac biomarkers** in patients with CKM syndrome.

- Limited data regarding **screening of high-risk subjects,** prevention and management of CKM syndrome.

Patients with CKM syndrome and subjects with advanced CKD are underrepresented in clinical studies.

Ndumele CE et al, Circulation 2023 Nov 14;148(20):1636-1664

Καρδιά και Νεφρός
Παθοφυσιολογική Θεώρηση-Θεραπευτικές Εφαρμογές

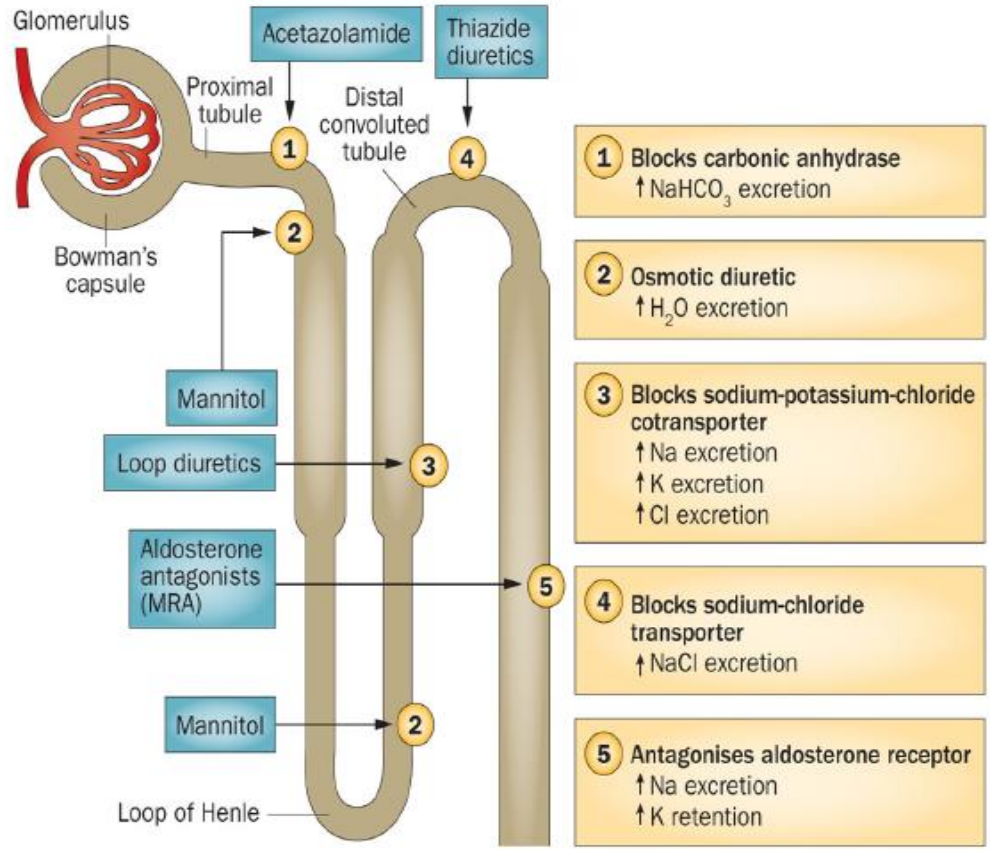


Kidney as basis of CV therapies

(DRUGS; Diuretic, RAAS blockers, SGL2I,

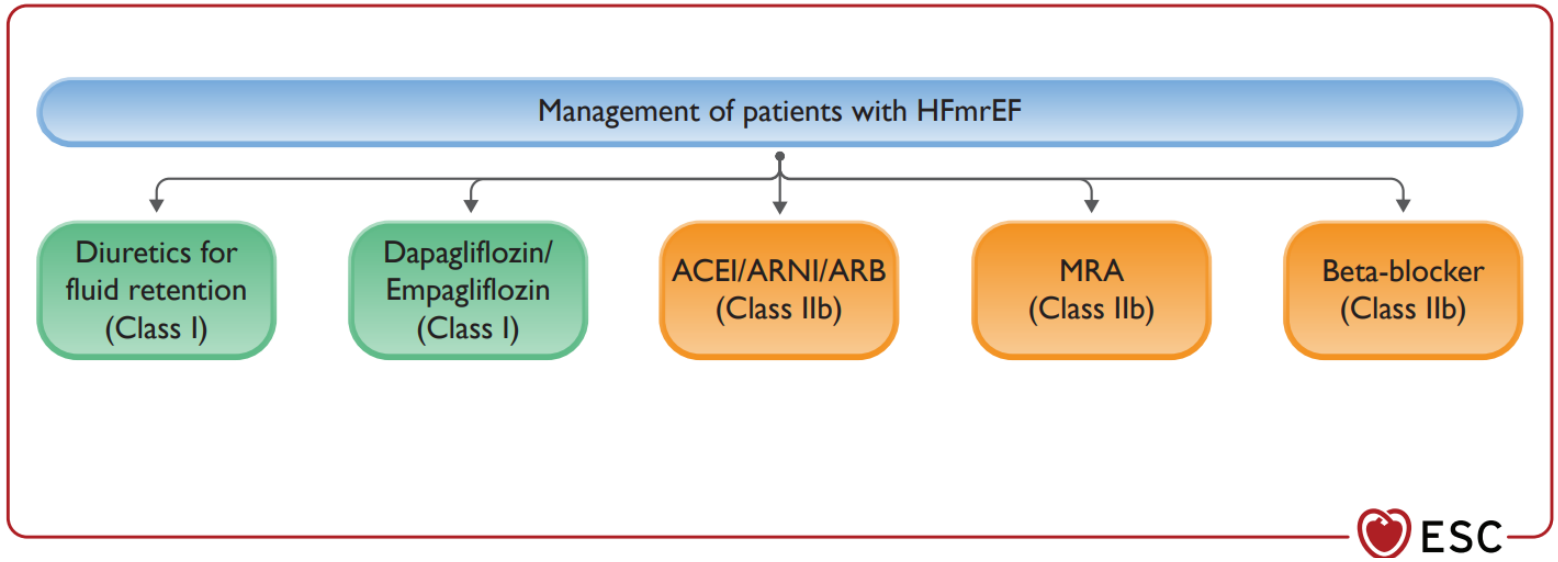
Interventions; Renal artery stenting, RDN)

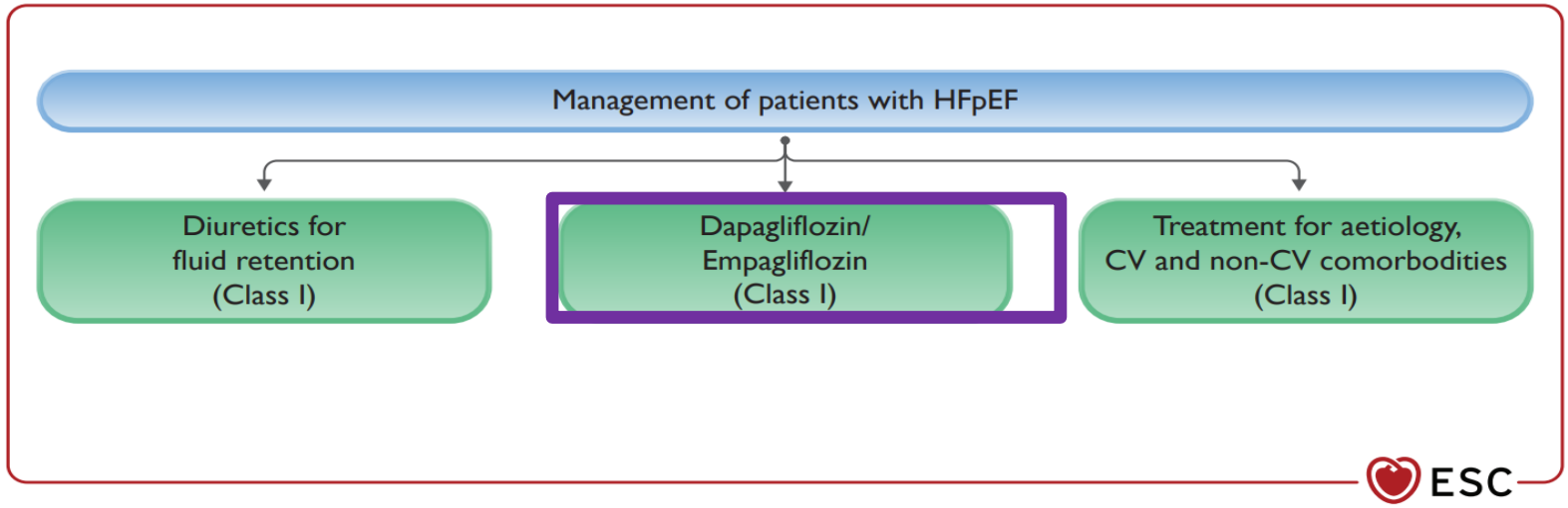
Diuretic therapy



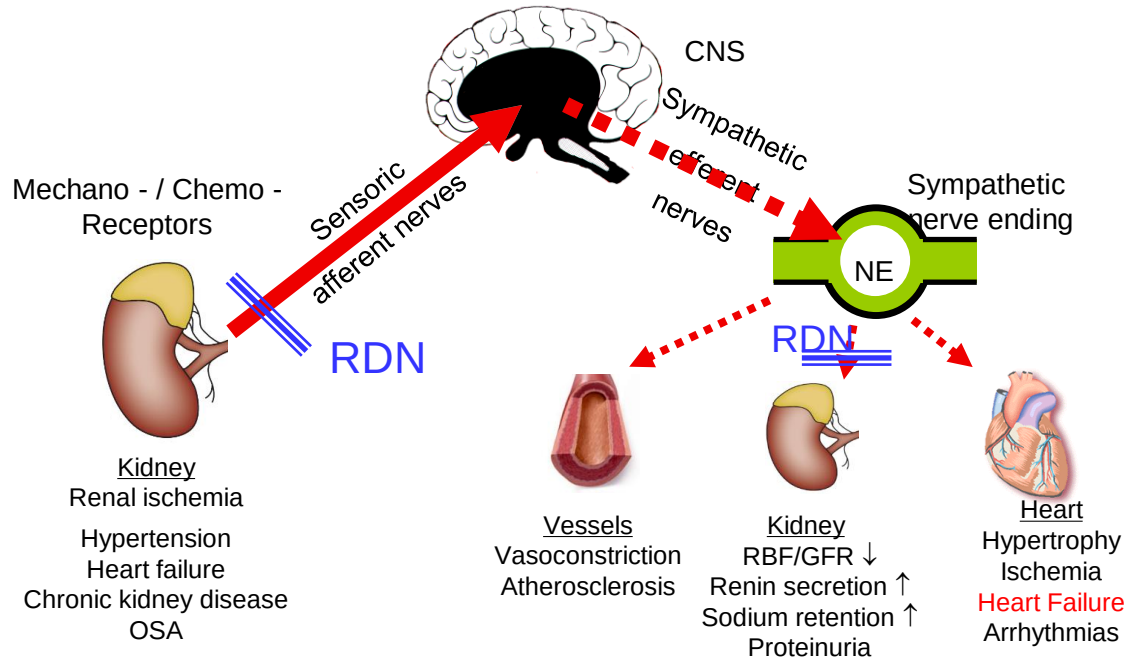
ter Maaten, J. M. *et al.* (2014) Diuretic response in acute heart failure—pathophysiology, evaluation, and therapy
Nat. Rev. Cardiol. doi:10.1038/nrcardio.2014.215

ESC Update 2023 on HFpEF GDLs





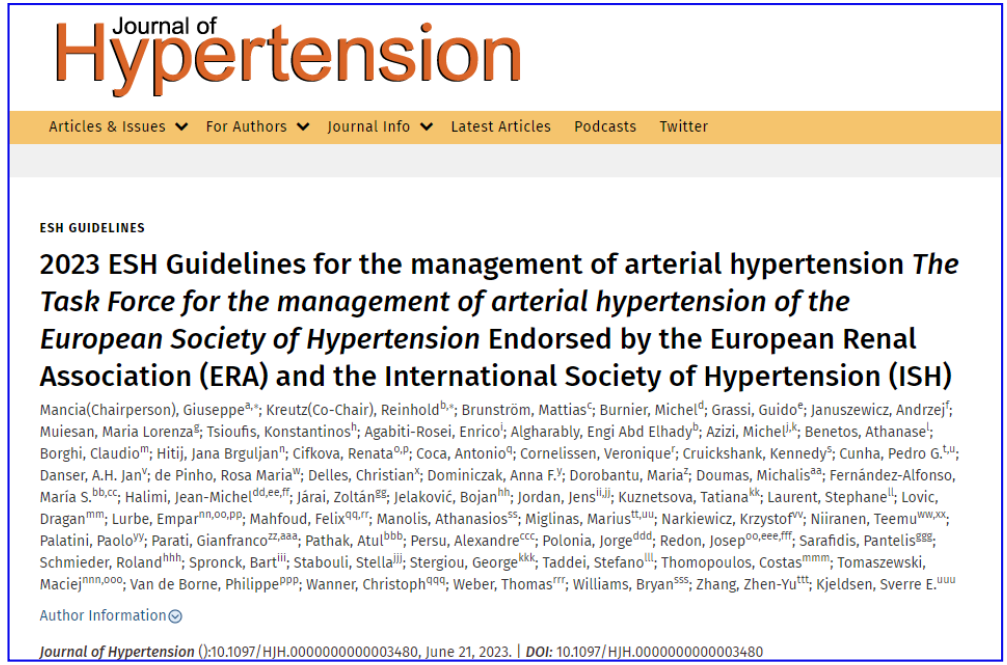
Possible effects by targeting the sympathetic renal fibers



Papademetriou V, Tsioufis C, Doumas M. Circulation 2014

2023 ESH guidelines recommend RDN as a safe and effective adjunctive treatment option in uncontrolled hypertension

New guidelines *endorsed* by ERA and ISH*



Journal of Hypertension

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ESH GUIDELINES

2023 ESH Guidelines for the management of arterial hypertension *The Task Force for the management of arterial hypertension of the European Society of Hypertension* Endorsed by the European Renal Association (ERA) and the International Society of Hypertension (ISH)

Mancia(Chairperson), Giuseppe[a,*]; Kreutz(Co-Chair), Reinhold[b,*]; Brunström, Mattias[c]; Burnier, Michel[d]; Grassi, Guido[e]; Januszewicz, Andrzej[f]; Muiesan, Maria Lorenza[g]; Tsioufis, Konstantinos[h]; Agabiti-Rosei, Enrico[i]; Algharably, Engi Abd Elhady[b]; Azizi, Michel[j,k]; Benetos, Athanase[l]; Borghi, Claudio[m]; Hitij, Jana Brguljan[n]; Cifkova, Renata[o,p]; Coca, Antonio[q]; Cornelissen, Veronique[r]; Cruickshank, Kennedy[s]; Cunha, Pedro G.[t,u]; Danser, A.H. Jan[v]; de Pinho, Rosa Maria[w]; Delles, Christian[x]; Dominiczak, Anna F.[y]; Dorobantu, Maria[z]; Doumas, Michalis[aa]; Fernández-Alfonso, María S.[bb,cc]; Halimi, Jean-Michel[dd,ee,ff]; Járai, Zoltán[gg]; Jelaković, Bojan[hh]; Jordan, Jens[ii,jj]; Kuznetsova, Tatiana[kk]; Laurent, Stephane[ll]; Lovic, Dragan[mm]; Lurbe, Empar[nn,oo,pp]; Mahfoud, Felix[qq,rr]; Manolis, Athanasios[ss]; Miglinas, Marius[tt,uu]; Narkiewicz, Krzystof[vv]; Niiranen, Teemu[ww,xx]; Palatini, Paolo[yy]; Parati, Gianfranco[zz,aaa]; Pathak, Atul[bbb]; Persu, Alexandre[ccc]; Polonia, Jorge[ddd]; Redon, Josep[oo,eee,fff]; Sarafidis, Pantelis[ggg]; Schmieder, Roland[hhh]; Spronck, Bart[iii]; Stabouli, Stella[jjj]; Stergiou, George[kkk]; Taddei, Stefano[lll]; Thomopoulos, Costas[mmm]; Tomaszewski, Maciej[nnn,ooo]; Van de Borne, Philippe[ppp]; Wanner, Christoph[qqq]; Weber, Thomas[rrr]; Williams, Bryan[sss]; Zhang, Zhen-Yu[ttt]; Kjeldsen, Sverre E.[uuu]

Author Information

Journal of Hypertension ():10.1097/HJH.0000000000003480, June 21, 2023. | **DOI:** 10.1097/HJH.0000000000003480

LoE [2]	Definition
A	• **RCT or meta-analysis of RCTs with CVD outcomes** • Single trial enough if sufficient power and without important limitations
B	• RCT with surrogate measures • Observational studies with CVD outcomes and no major limitations • Meta-analysis including the above study types
C	• Observational studies of surrogate measures • Any study type may be downgraded to level C due to limitations • Expert opinion (EO)

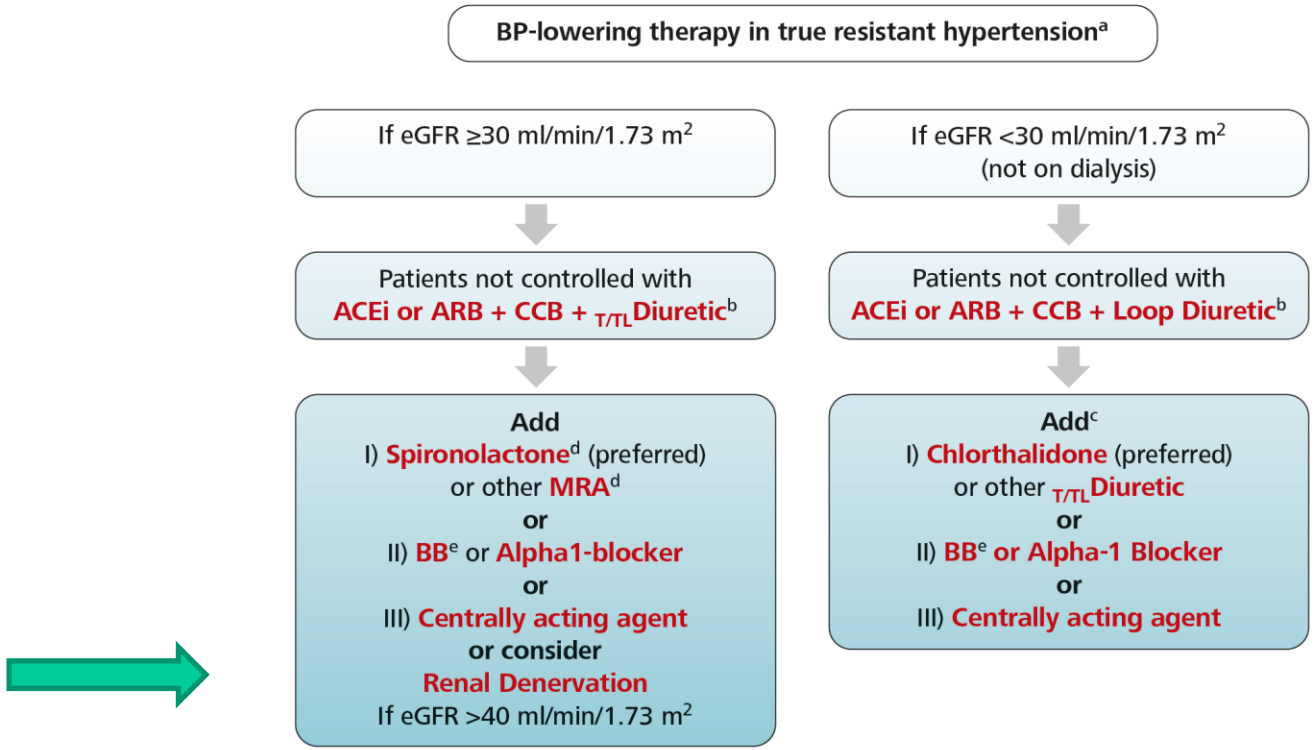
*Endorsed also by AHA after publication https://www.ahajournals.org/doi/abs/10.1161/HYPERTENSIONAHA.123.21592

Mancia G. et al. Journal of Hypertension 2023, 41:000–000 DOI:10.1097/HJH.0000000000003480

New 2023 ESH guidelines

European Society of Hypertension

Treatment Resistant Hypertension



New 2023 ESH guidelines

European Society of Hypertension

Use of renal denervation

Recommendations and statements	CoR*	LoE*
RDN can be considered as a treatment option in patients with an eGFR >40/ml/min/1.73m^2 who have **uncontrolled BP** despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	**II**	**B**
RDN can be considered as an additional treatment option in patients with **resistant hypertension** if eGFR is >40 ml/min/1.73m^2	**II**	**B**
Selection of patients to whom RDN is offered should be done **in a shared decision-making process** after objective and complete patient's information.	**I**	**C**
Renal denervation should only be performed in **experienced specialized centers** to guarantee appropriate selection of eligible patients and completeness of the denervation procedure.	**I**	**C**

* CoR Class of Recommendation, LoE Level of Evidence

- ESC Council on Hypertension and the European Association of Cardiovascular Intervention (EAPCI)

Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

Emanuele Barbato[1], MD, PhD; Michel Azizi[2,3], MD; Roland E. Schmieder[4], MD; Lucas Lauder[5], MD; Michael Böhm[5], MD; Sofie Brouwers[6], MD , PhD; Rosa Maria Bruno[2,7], MD, PhD; Dariusz Dudek[8], MD, PhD; Thomas Kahan[9], MD, PhD; David E. Kandzari[10], MD; Thomas F. Lüscher[11], MD; Gianfranco Parati[12], MD; Atul Pathak[13], MD, PhD; Flavio L. Ribichini[14], MD; Markus P. Schlaich[15], MD; Andrew S.P. Sharp[16], MD; Isabella Sudano[17], MD, PhD; Massimo Volpe[18], MD; Costas Tsioufis[19], MD; William Wijns[20,21], MD, PhD; Felix Mahfoud[5]*, MD, MA

RDN may be used

- In adult patients with uncontrolled resistant hypertension
  - OBP ≥140/≥90 mmHg
  - confirmed by 24-hr ambulatory SBP ≥130 or daytime SBP ≥135 mmHg
- Treated with ≥3 antihypertensive drugs
- And eGFR ≥40 ml/min/1.73 m^2

RDN may be a possible treatment option for

- Patients unable to tolerate antihypertensive drugs in the long term
- Patients who express a preference to undergo RDN in a tailored, shared decision-making process.

These patients may, therefore, be on fewer than 3 drugs at the time of their selection for RDN due to their prior drug intolerance.

Barbato, et al. *European Heart Journal*, 15 February 2023, https://doi.org/10.1093/eurheartj/ehad054

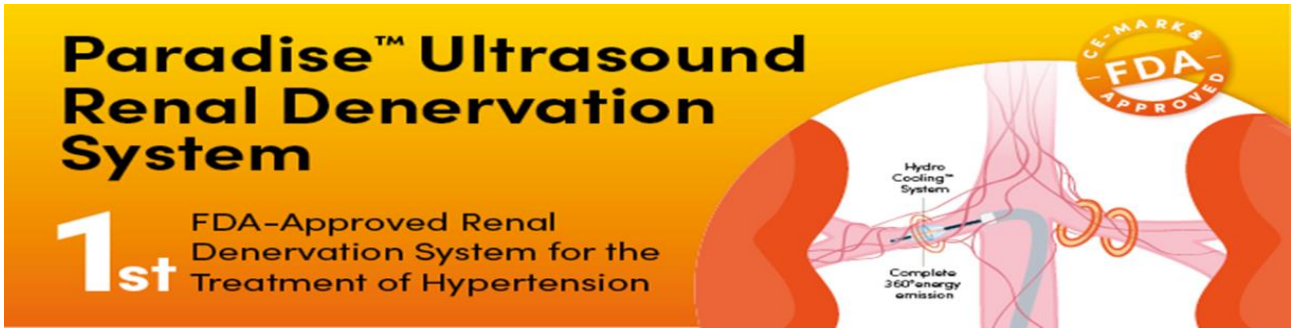
Indications of RDN in the 2023 ESH guidelines vs. other international

Indication	ESH 2023	SCAI 2023	ESC 2022	NL 2022	SCAI/ NKF 2021	Spain 2021	Italy 2020
Uncontrolled hypertension	+*	+			+	+	+
Resistant hypertension	+	+**	+	+	+	+	+
Intolerant to drugs	+	+	+	+	+	+	+
Non-adherent to drugs		+	+		+	+	+
High CV risk / severe HMOD		+	+		+	+	+

* Despite antihypertensive drug combination therapy

** defined by blood pressure >130/80 mm Hg despite being on 3 medications with maximally tolerated doses from classes with outcomes data (angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, calcium channel blockers, thiazide diuretics, and beta blockers)

FDA Approval



indicated to reduce blood pressure as an adjunctive treatment in hypertension patients in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure.

Medtronic Symplicity Spyral™ RDN system approved by U.S. FDA

The Symplicity Spyral renal denervation system is indicated

to reduce blood pressure as an adjunctive treatment in patients with hypertension in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure.

Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

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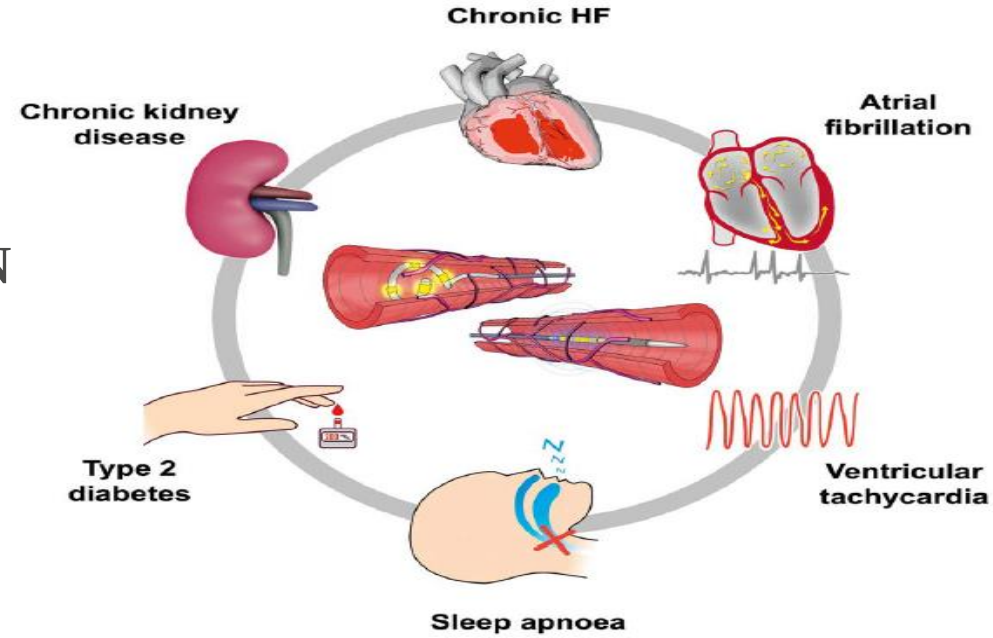
EAPCI

EUROPEAN SOCIETY OF CARDIOLOGY®

Potential future indications for RDN beyond hypertension

(currently under investigation).



Η επίδραση της νεφρικής απονεύρωσης στην αρτηριακή πίεση σε ασθενείς με χρόνια νεφρική νόσο και μη ελεγχόμενη υπέρταση (CKD-RDN)

Inclusion criteria

50 pts (out of about 20 will be randomized)

>18 y.o

uncontrolled HTN (SOBP ≥ 140mmHg and 24h-SBP >130mmHg)

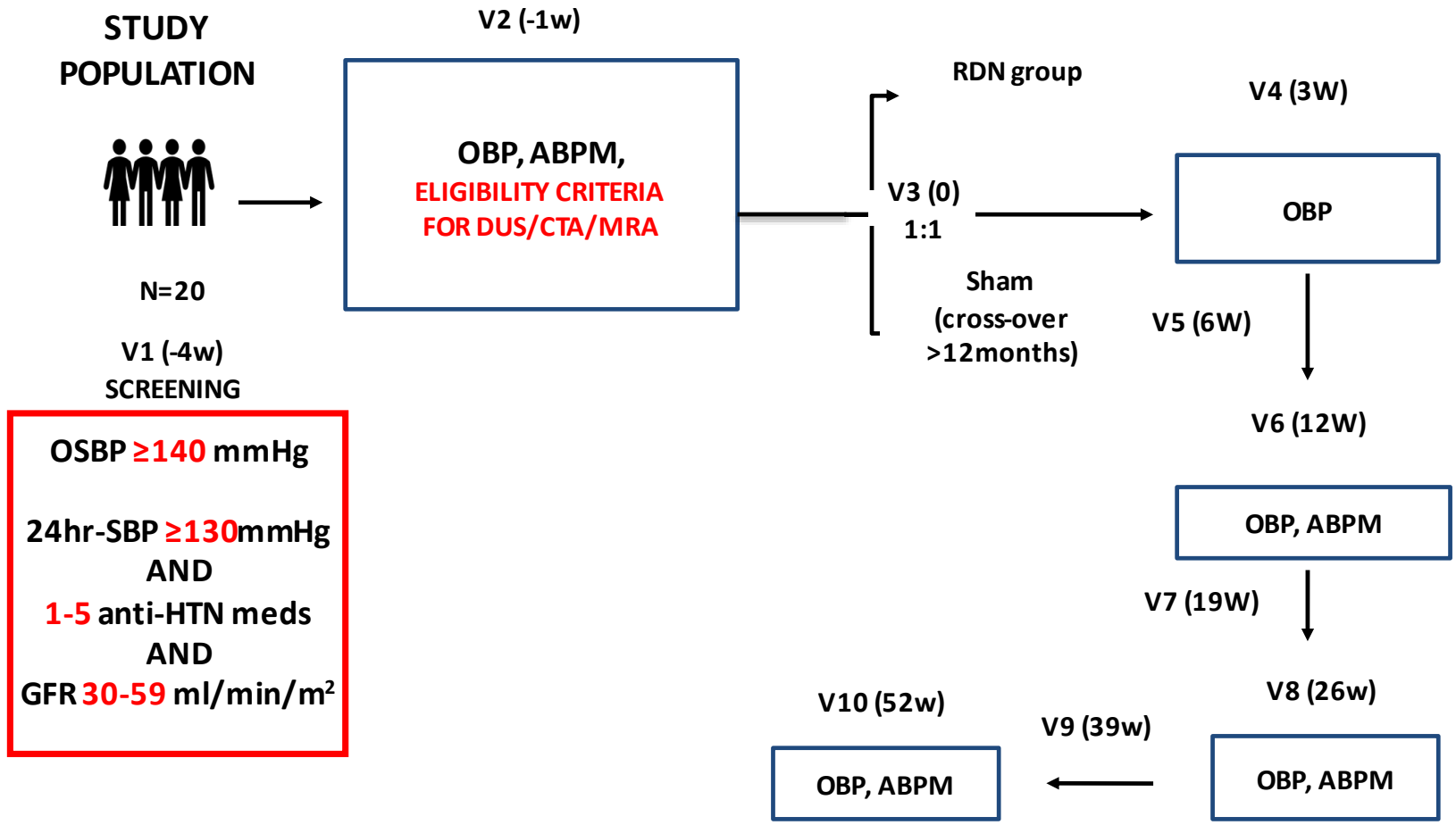
1-5 anti-HTN drugs (ARB among these) and stable antihypertensive medication for at least 4weeks

GFR 30-59 ml/min/1.73m^2 (MDRD, CKD-EPI)

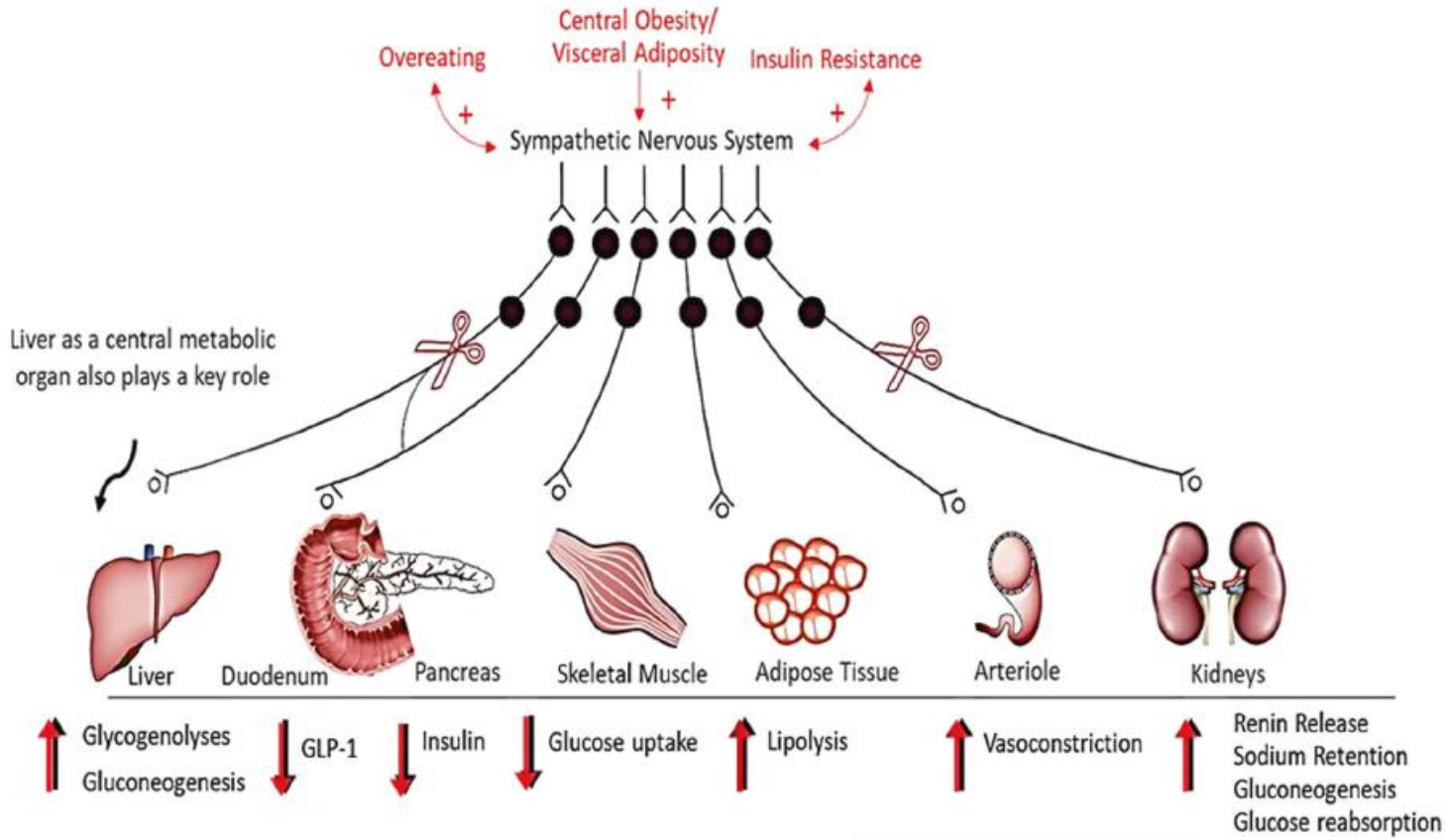
Exclusion criteria

a. Ανατομικά σημαντική ανωμαλία νεφρικής αρτηρίας
b. Άλλη αιτία υπέρτασης που μπορεί να αντιμετωπιστεί με παρέμβαση/χειρουργική επέμβαση (e.g. αιμοδυναμικά σχετική στένωση νεφρικής αρτηρίας, λειτουργικό αδένωμα επινεφριδίων)
c. Προηγούμενη επέμβαση νεφρικής απονεύρωσης
d. ΑΠ Ιατρείου ≥180 mmHg συστολική και/ή ≥110 mmHg διαστολική
e. 24ωρη περιπατητική ΑΠ ≥160 mmHg συστολική
f. Ανατομικός ή λειτουργικός μονήρης νεφρός, μεταμόσχευση νεφρού
g. Έλλειψη καταγραφής των επιπέδων κρεατινίνης ορού στο παρελθόν
h. Σακχαρώδης διαβήτης τύπου 1
i. Νεφρωσικό σύνδρομο
j. Αντένδειξη για μαγνητική τομογραφία (MRI)
k. Οξύ έμφραγμα του μυοκαρδίου, ασταθή στηθάγχη ή εγκεφαλοαγγειακό ατύχημα εντός 3 μηνών από την επίσκεψη αρχικής αξιολόγησης
l. Οξύ επεισόδιο νεφρικής νόσου που απαιτεί προς τα άνω τιτλοποίηση οποιουδήποτε σχήματος ανοσοκατασταλτικού φαρμάκου εντός των τελευταίων 3 μηνών
m. Ασθενής έγκυος, που θηλάζει ή σκοπεύει να μείνει έγκυος
n. Συμμετοχή σε άλλο πρωτόκολλο παρεμβατικής έρευνας
o. Οποιαδήποτε κατάσταση που, κατά την κρίση του ερευνητή, θα απέκλειε τη συμμετοχή στη μελέτη (π.χ. μη συμμόρφωση)

Flowchart of CKD-RDN

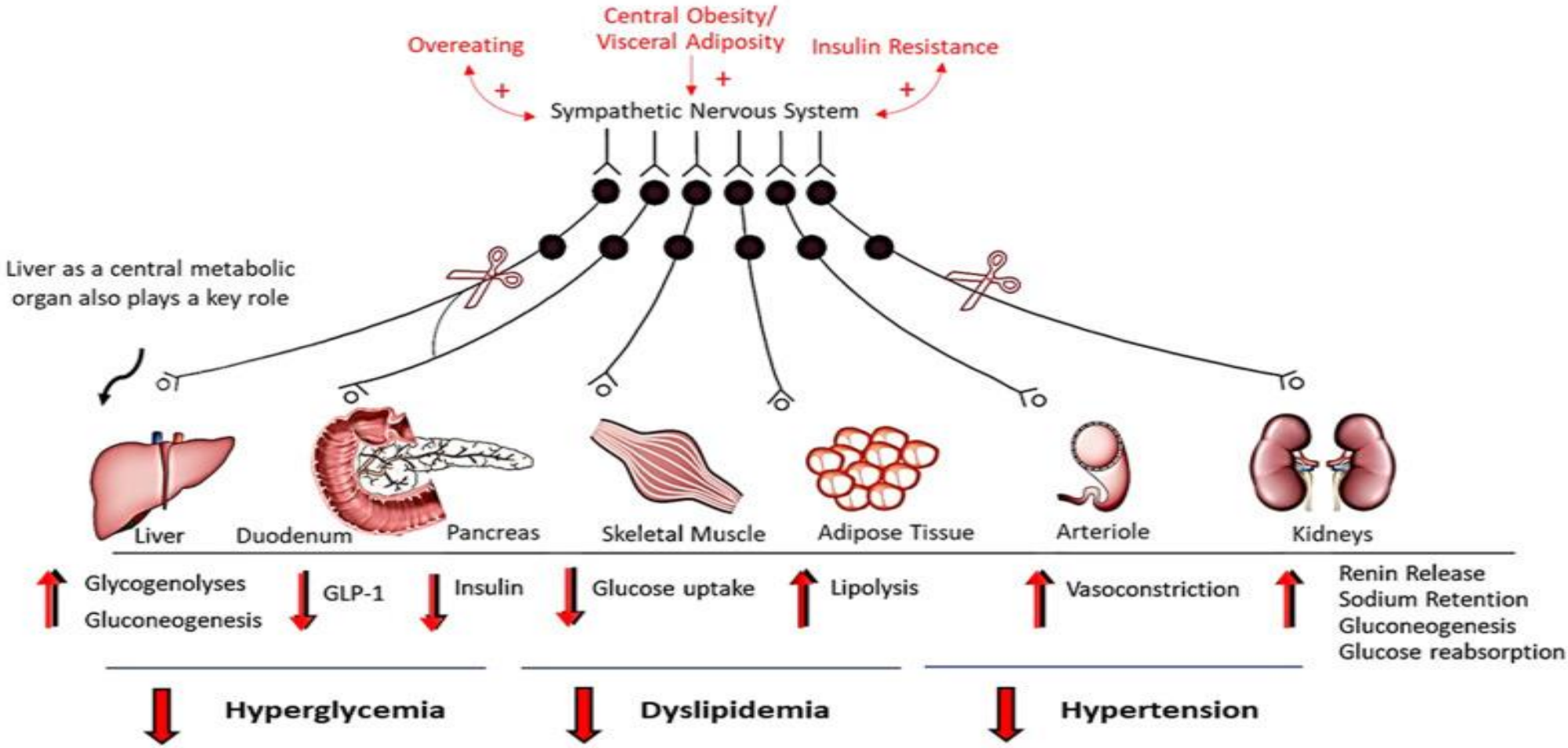


Cardiometabolic effects of sympathetic overdrive



M G Kiuchi et al, Hypertens Res. 2023 Jul;46(7):1747-1758

Multi-organ denervation to interfere with several key SNS signaling pathways



Hypertension Research (2023) 46:1747–1758

The ideal patient for RDN

Resistant

Damage

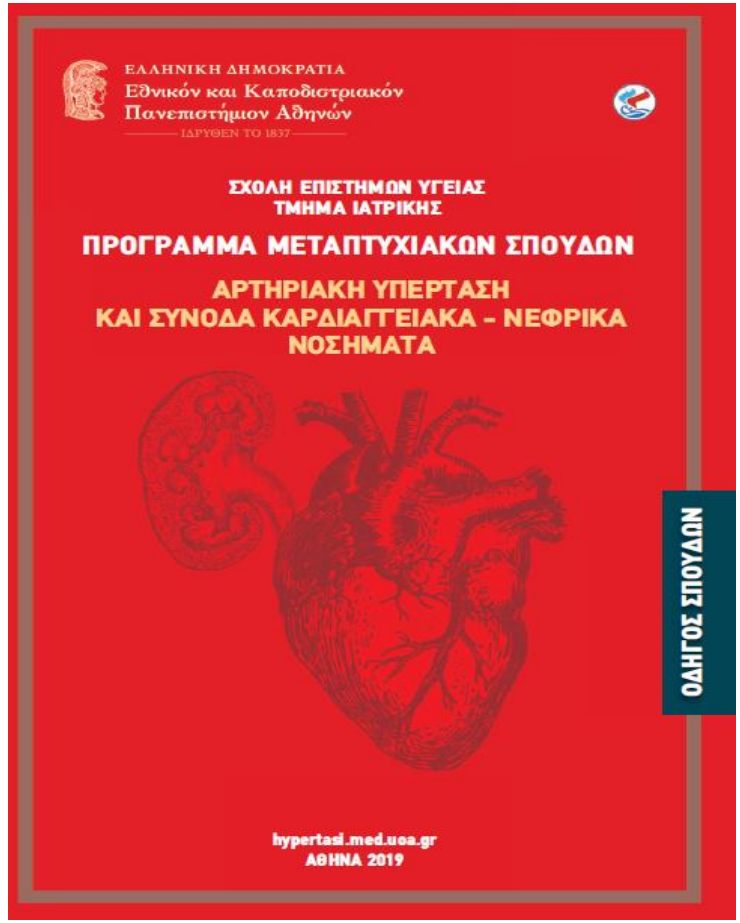
Non-adherent

The ideal patients for MDN

Metabolic

Damage

Non-adherent


ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Εθνικόν και Καποδιστριακόν Πανεπιστήμιον Αθηνών
ΙΔΡΥΘΕΝ ΤΟ 1837
ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ
ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ
ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
ΑΡΤΗΡΙΑΚΗ ΥΠΕΡΤΑΣΗ
ΚΑΙ ΣΥΝΟΔΑ ΚΑΡΔΙΑΓΓΕΙΑΚΑ – ΝΕΦΡΙΚΑ
ΝΟΣΗΜΑΤΑ
ΟΔΗΓΟΣ ΣΠΟΥΔΩΝ
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