Dieta con troppe proteine

Dott.ssa Daria Motta

ASL Città di Torino
Ambulatorio di Nefrologia
S.C. Endocrinologia e Malattie Metaboliche

ASL CITTÀ DI TORINO

con il patrocinio di:

AMD Associazione Medici Diabetologi
O.S.D.I. Operatori Sanitari di Diabetologia Italiani
Università di Scienze Gastronomiche di Pollenzo

22 novembre 2025

IN HOC SIGNO VINCES

Strategie culturali-sociali e terapeutiche per la salute metabolica

Bra, Località POLLENZO (CN)

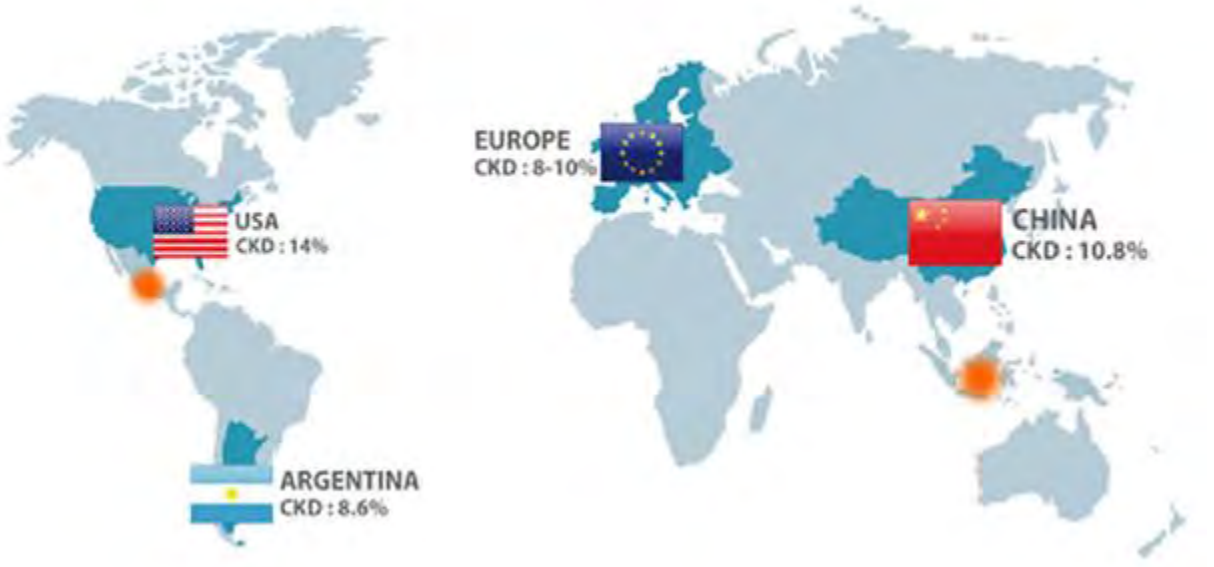
Aula Magna Università degli Studi di Scienze Gastronomiche
Via Amedeo di Savoia, 8

Agenda

- *Cenni epidemiologici*
- *Cenni storici*
- *Linee guida, indicazioni, applicazioni*
- *Conclusioni*

Epidemiologia della Malattia Renale Cronica (MRC)

La malattia renale cronica (MRC), ha una prevalenza a livello planetario, stimata tra il 10% e il 15% della popolazione. Il numero dei pazienti con MRC (il 95% dei quali non ha una malattia che richiede dialisi) nel mondo supera gli 850 milioni, ossia quasi il doppio di quelli affetti da diabete mellito. In Italia è stimata nella popolazione generale una prevalenza del 7% che raggiunge il 17% nella popolazione anziana (>70 anni).



Burden of disease scenarios for 204 countries and territories, 2022–2050: a forecasting analysis for the Global Burden of Disease Study 2021

GBD 2021 Forecasting Collaborators*

B

Leading causes 2022	Leading causes 2050	Mean percentage change in number of deaths	Mean percentage change in all-age death rate	Mean percentage change in age-standardised death rate
1 Ischaemic heart disease	1 Ischaemic heart disease	20·6 (−12·7 to 64)	2·69 (−27 to 44·4)	−44·8 (−64·3 to −15·4)
2 Stroke	2 Stroke	28·5 (7·89 to 51·1)	9·27 (−7·5 to 30·9)	−41·3 (−53·4 to −25·9)
3 COPD	3 COPD	102 (66·1 to 141)	71·8 (40·1 to 113)	−13·7 (−34·3 to 15·6)
4 Lower respiratory infections	4 Alzheimer's disease	173 (124 to 222)	132 (95 to 168)	−3·48 (−5·38 to −1·07)
5 COVID-19	5 Chronic kidney disease	182 (126 to 245)	140 (90·5 to 202)	33·1 (−0·751 to 79)
6 Lung cancer	6 Lower respiratory infections	56·7 (42·3 to 69·5)	33·3 (20·1 to 46·5)	−26·6 (−36·8 to −13·3)
7 Alzheimer's disease	7 Hypertensive heart disease	165 (105 to 232)	126 (74·3 to 192)	17·1 (−16·5 to 61)
8 Neonatal disorders	8 Lung cancer	68·1 (24·5 to 117)	42·7 (8·87 to 80·4)	−17 (−31·9 to 0·776)
9 Diabetes	9 Diabetes	76·2 (43·2 to 115)	49·9 (18·6 to 89·6)	−13·9 (−33·8 to 14·9)
10 Chronic kidney disease	10 Cirrhosis liver	50·7 (34·5 to 67)	28·2 (12·6 to 45·3)	−9·06 (−20·9 to 6·14)
11 Cirrhosis liver	11 Colorectal cancer	103 (41·1 to 177)	72·1 (23·7 to 131)	−3·02 (−24·8 to 23·1)
12 Hypertensive heart disease	12 Falls	113 (82·1 to 146)	81·3 (58·4 to 107)	−5·34 (−10·6 to −0·215)
13 Road injuries	13 Diarrhoeal diseases	30·9 (−0·247 to 68·6)	11·4 (−16·5 to 47·9)	−34 (−54·1 to 0·13)
14 Tuberculosis	14 Road injuries	9·8 (−24·3 to 61·4)	−6·52 (−36·1 to 41·6)	−18·1 (−46·7 to 28·6)
15 Diarrhoeal diseases	15 Pancreatic cancer	140 (72·1 to 219)	104 (50·3 to 169)	18·1 (−6·89 to 46·9)
16 Colorectal cancer	16 Breast cancer	81·8 (36·1 to 137)	54·4 (17·9 to 96·1)	1·42 (−18·9 to 24·8)
17 Stomach cancer	17 Stomach cancer	24·7 (12·6 to 37)	5·99 (−3·94 to 16·1)	−38·1 (−41·6 to −34·4)
18 Falls	18 Atrial fibrillation	229 (177 to 278)	179 (143 to 216)	17·3 (11·9 to 22·5)
19 Self-harm	19 Urinary diseases	203 (176 to 225)	158 (133 to 182)	33·5 (11·4 to 60)
20 Malaria	20 Prostate cancer	145 (86 to 209)	108 (60·6 to 158)	5·51 (−8·93 to 23)
22 Breast cancer	24 Neonatal disorders			
25 Pancreatic cancer	25 Tuberculosis			
27 Prostate cancer	26 Self-harm			
32 Urinary diseases	30 Malaria			
34 Atrial fibrillation	137 COVID-19			

Communicable, maternal, neonatal, and nutritional diseases
Non-communicable diseases
Injuries

Figure 4: Leading 20 Level 3 causes of global DALYs (A) and deaths (B), and percentage change in number of DALYs (A) and deaths (B) and all-age and age-standardised DALY (A) and death (B) rates, 2022–50

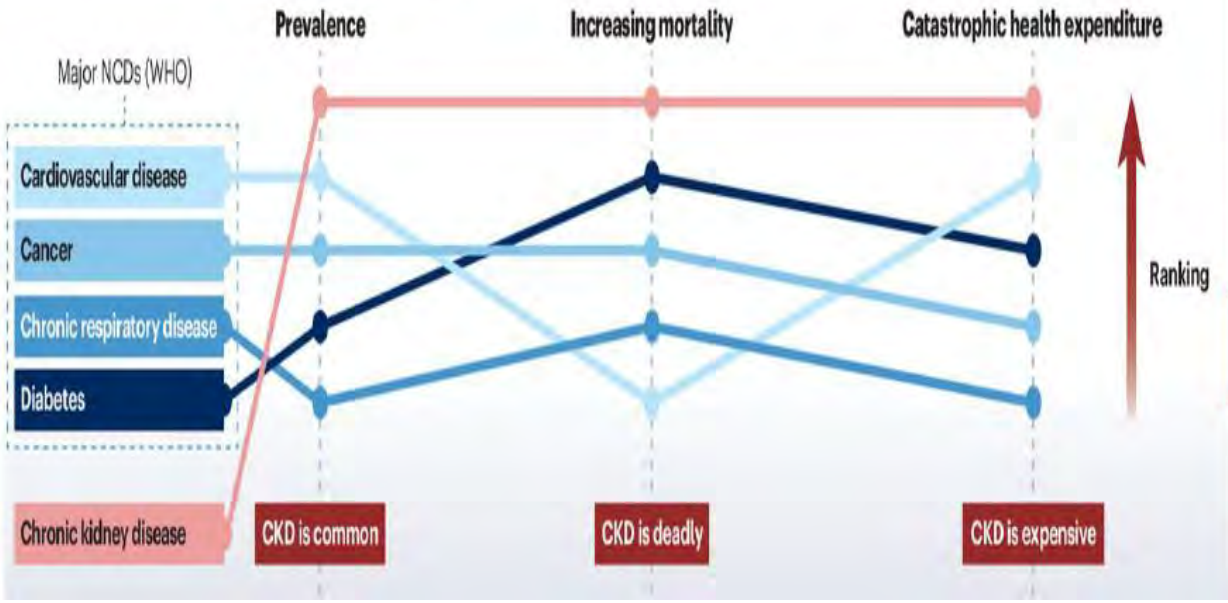
Preserving Kidney Function Instead of Replacing It

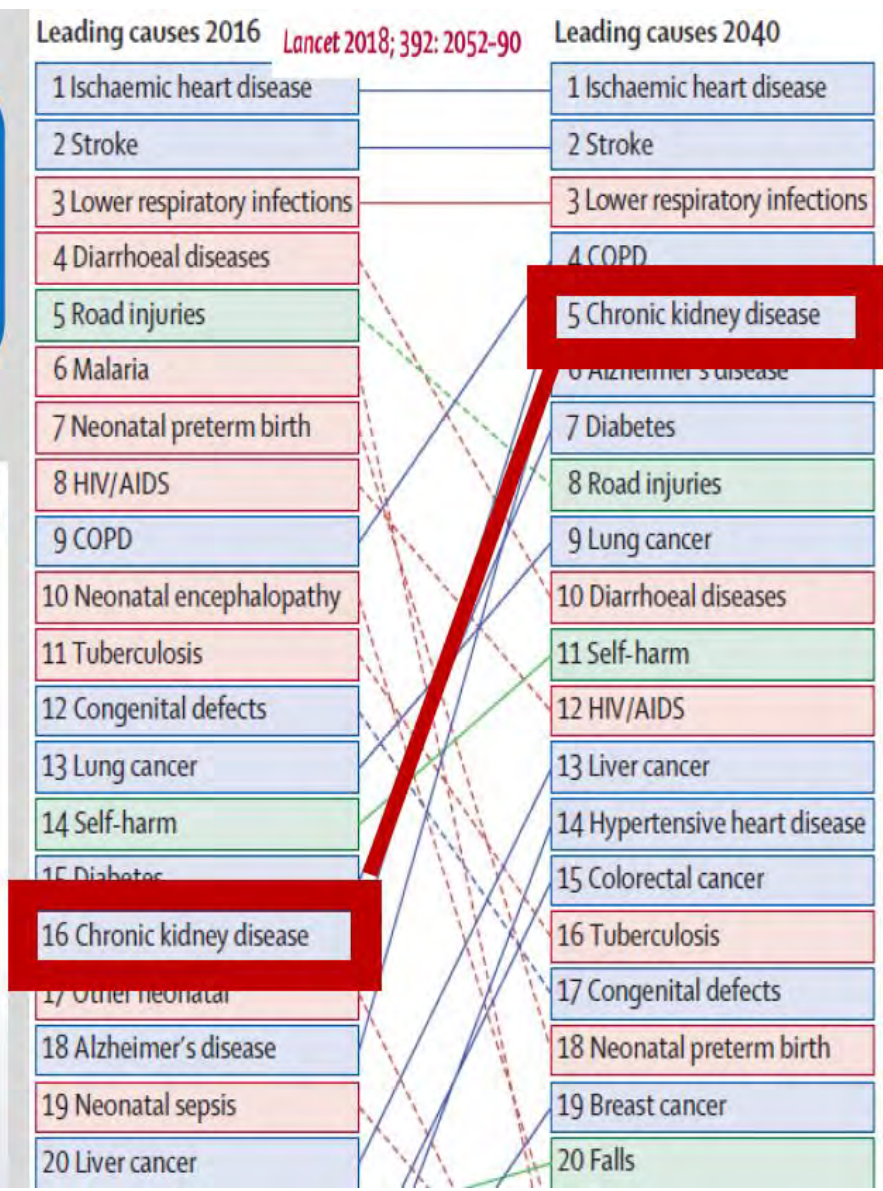
*Alan S. Kliger,[1] and Frank C. Brosius,[2] on behalf of the Diabetic Kidney Disease Task Force of the American Society of Nephrology**

CJASN 15: 129–131, 2020. doi: https://doi.org/10.2215/CJN.07820719

Kidney disease: a global health priority

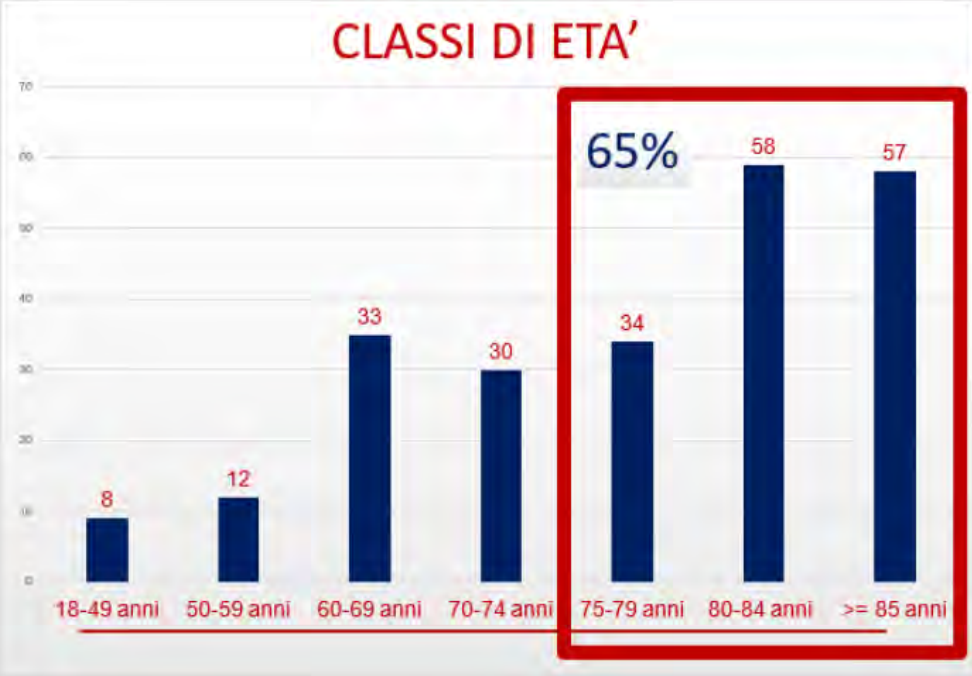
Nature Reviews Nephrology **20**, 421–423 (2024)

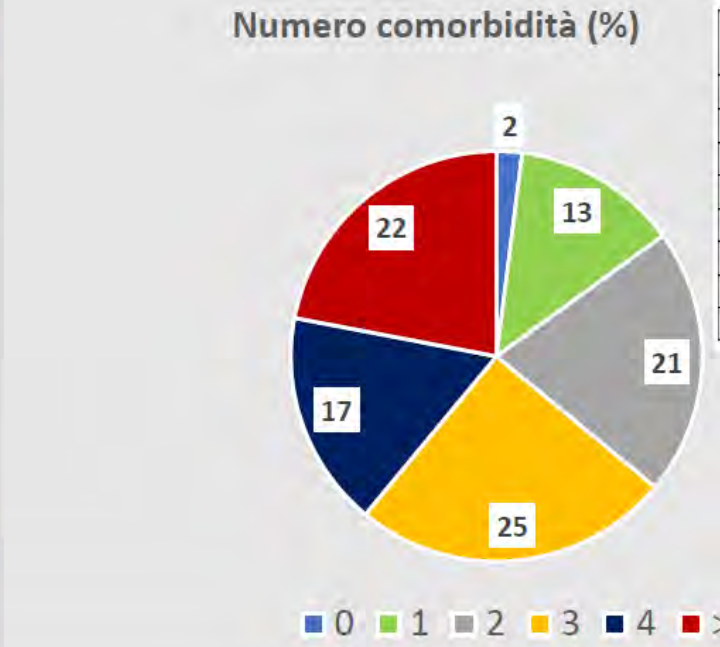




«Il paziente nefropatico costituisce il tipico esempio di cronicità della malattia che richiede un approccio di squadra e una strutturazione dei processi di cura»

Documento di indirizzo per la malattia renale cronica





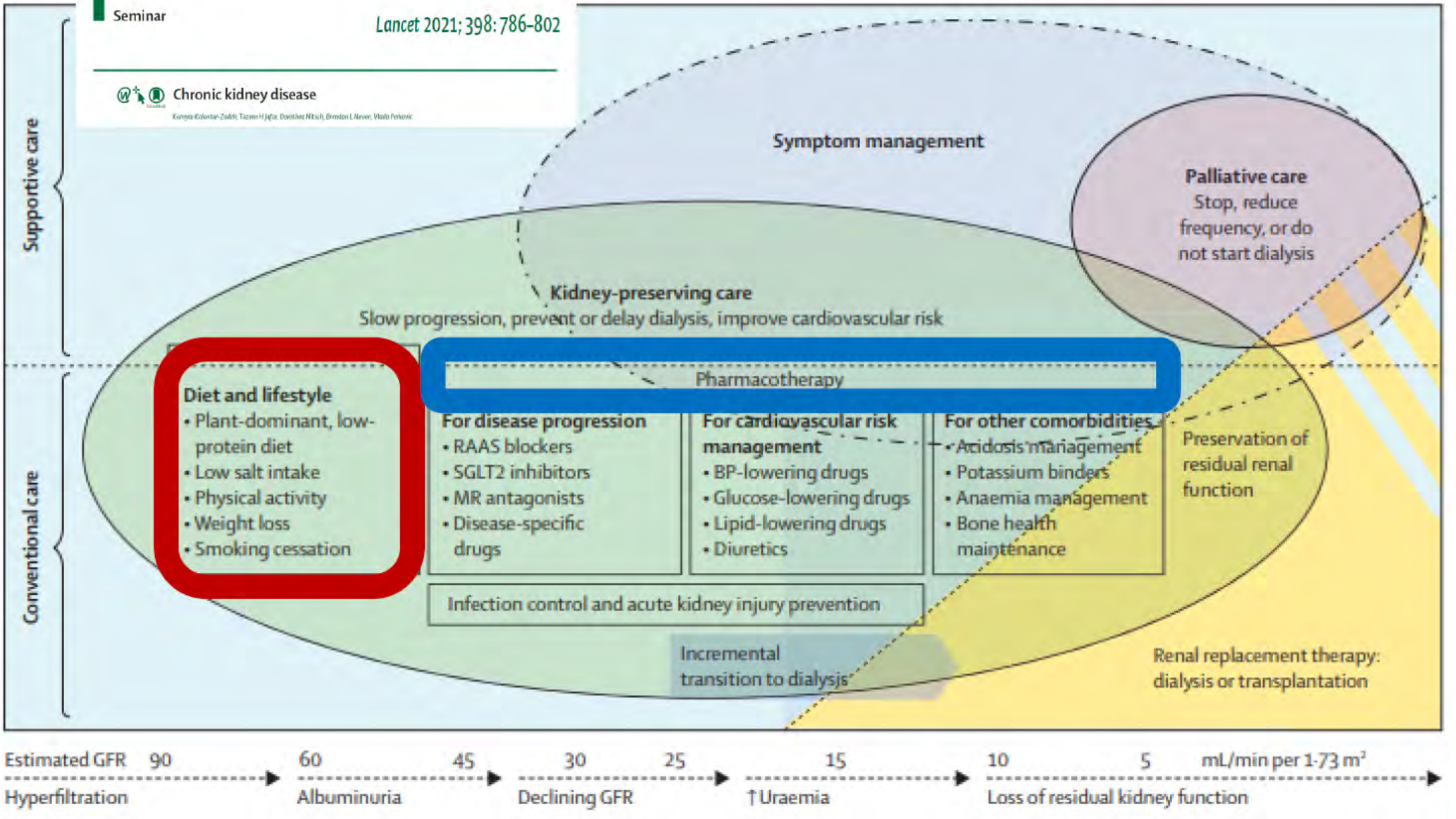
	Numero	Percentuale (%)
Diabete	81	35
Ipertensione arteriosa	212	91
Dislipidemia	108	43
Cardiopatia	127	54
Vasculopatia	92	39
Pneumopatia	34	15
Tireopatia	32	14
Epatopatia	12	5

Seminar

Lancet 2021; 398: 786–802

Chronic kidney disease

Kunyu Yuan-Zuckl, Tuzeen H Jafar, Dorothea Nitsch, Brendon L Neuen, Vlado Perkovic



Una sana alimentazione rappresenta il primo intervento di prevenzione a tutela della salute

….. anche renale.

~~DIETA~~

TERAPIA DIETETICO NUTRIZIONALE (TDN)

It is time for nephrology to embrace a change in paradigm: returning to our traditional focus on pathophysiology and kidney preservation

DIET AND DEATH IN ACUTE UREMIA[1]

By T. ADDIS and W. LEW

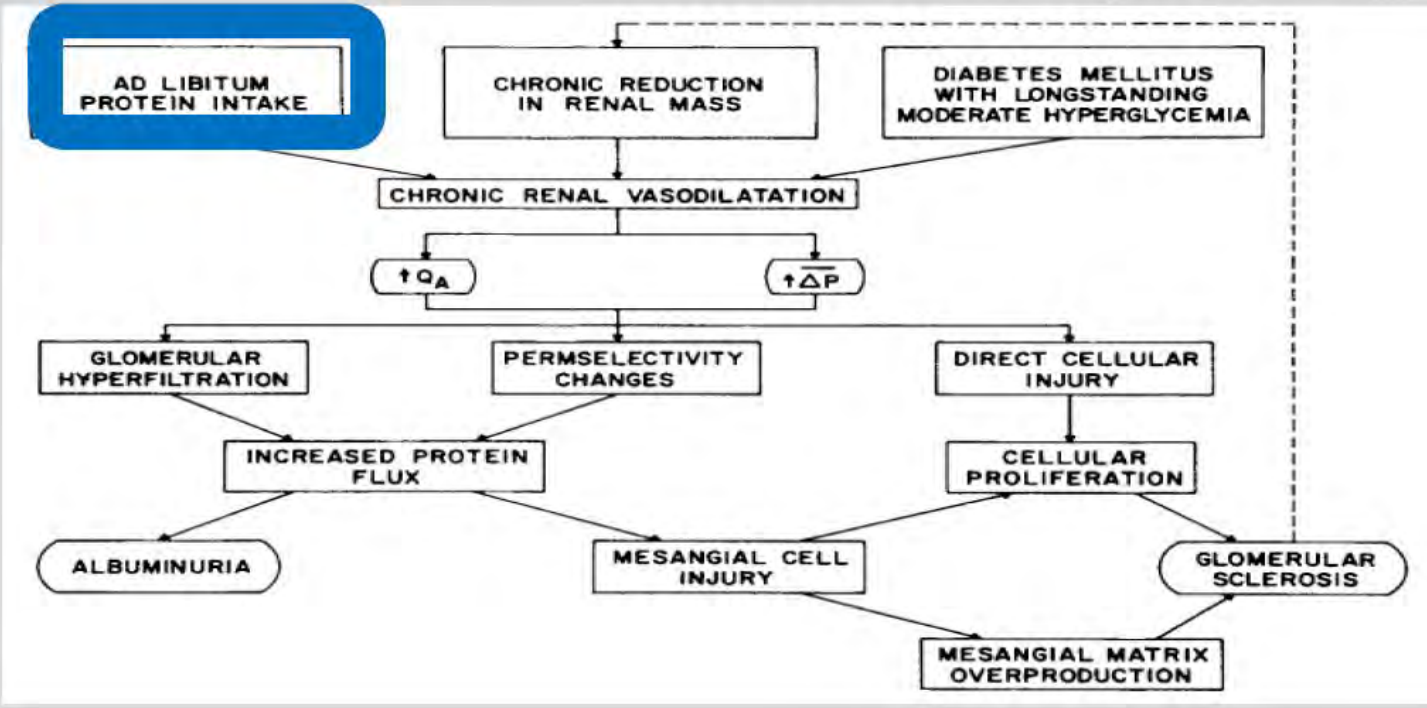
(From the Department of Medicine, Stanford University Medical School, San Francisco)

(Received for publication June 19, 1939)

STRATEGIES FOR INTERRUPTING PROGRESSIVE RENAL DISEASE

The hyperfiltration theory: A paradigm shift in nephrology

Barry M. Brenner, Elizabeth V. Lawler, and Harald S. Mackenzie



1964

A LOW-NITROGEN DIET WITH PROTEINS OF HIGH BIOLOGICAL VALUE FOR SEVERE CHRONIC URÆMIA

S. GIOVANNETTI
M.D. Pisa
SENIOR LECTURER IN MEDICINE

Q. MAGGIORE
M.D. Pisa
LECTURER IN MEDICINE

From the General Medical Department, University of Pisa, Italy

THE diet in chronic uræmia has to fulfil two main and conflicting purposes: to lower the production of protein catabolites, and to prevent wastage of body proteins.

A protein-deficient diet, which could reduce the protein catabolites, is considered unwise because of the protein depletion caused; therefore a high-caloric diet, containing about 0·5 g. of protein per kg. body-weight, is generally advocated as the best compromise between the two opposite requirements (Merrill 1960, Goldman 1962). When renal excretory impairment is severe, however, the admin-

A low-nitrogen diet with protein of high biological value for severe chronic uremia.

Giovannetti S, Maggiore Q: Lancet I:1100:1004,1964

Table 1. Potential Benefits and Challenges of a Low-Protein Diet (LPD) in the Nutritional Management of Chronic Kidney Disease (CKD).*

Measure	Potential Benefits of LPD	Challenges and Risks of LPD	Comments
Ridurre la progressione del danno renale e procrastinare l'avvio della dialisi	Synergistic effect with angiotensin-pathway modulators to lower intraglomerular pressure†	In first several months, slight drop in GFR may be observed, as shown in MDRD study‡	Inconclusive results in MDRD study, but small effect size in meta-analyses§
	Consistent antiproteinuric effect, which may mitigate hypo-albuminemia	LPD is contrary to notion that DPI must be increased to replace urinary protein loss	Some data suggest that even larger effect may be achieved with DPI of <0.6 g/kg/day
	Supported by consistent and biologically plausible data for almost a century	Unlikely to worsen uremia but potential risk of resurfacing or exacerbating PEW	Patients at increased risk for PEW may benefit from supplements (e.g., EAA or KA)
Migliorare l'acidosi ed il metabolismo osseo	H^+ generation decreased in proportion to reduction in DPI, especially with larger proportion of plant-based food	The need for >50% HBV protein may prompt higher intake of non–plant-based foods that are more acidogenic	Although >50% HBV protein is recommended, the remainder can be from plant-based foods
	The lower phosphorus content of LPD improves measures of mineral bone disease, including sHPT and high FGF-23	Higher calcium content in some KA preparations may increase calcium load	Additional improvements in bone health are possible by alleviating acidosis
Migliorare lo stato nutrizionale	Ameliorating hypoalbuminemia in patients with proteinuria may help neutralize circulating inflammatory compounds	Weight loss may occur; the habit of LPD intake may continue after starting thrice-weekly hemodialysis, when higher protein intake is recommended	Half of dietary protein source should be HBV protein; liberalize diet during correction of PEW
Migliorare l'outcome cardiovascolare	Lower protein intake is associated with lower dietary salt and saturated fat intake and may be less atherogenic, given higher proportion of plant-based food	Higher dietary fat intake (to achieve DEI of 30–35 kcal/kg/day) may confound the goal of achieving a heart-healthy diet	Higher proportions of unsaturated fat and complex carbohydrates recommended
Migliorare lo stato nutrizionale	Improvement in insulin resistance is likely	With LPD or VLPD, higher carbohydrate and fat intake (to achieve DEI 30–35 kcal/kg/day) may worsen glycemic control	Given increased insulin half-life and "burnt-out diabetes" with CKD progression, preventing hypoglycemic episodes is prudent
Migliorare la qualità della vita	Enhanced patient-centeredness, given that many patients seek nutritional therapies and dietary advice	Challenges with adherence; diet fatigue, poor palatability, and cravings reported	Recommend creative recipes and strategies to engage patients
Agire in termini di mortalità	There are no convincing data to suggest reduced mortality, although dialysis deferral is a potential mechanism, given high mortality during early dialysis	Increased mortality highly unlikely with DPI of 0.6–0.8 g/kg/day unless severe PEW emerges and is uncorrected	Consider supplements or other corrective strategies whenever PEW is suspected or diagnosed
Migliorare l'outcome cardiovascolare	MDRD and other data suggest improved BP control	Reduction in BP is more likely a result of concomitant lower salt intake than of LPD itself	Higher potassium intake from more plant-based foods may be a potential mechanism
Favorire l'equlibrio del microbiota intestinale	Improved microbiome profile may be achieved through reduced uremic toxin generation	Possibility of promoting unfavorable microbiome milieu cannot be excluded	Uremia itself can lead to unfavorable microbiome

La terapia dietetica nutrizionale nella gestione del paziente con Malattia Renale Cronica in fase avanzata per ritardare l'inizio e ridurre la frequenza della dialisi, e per il programma di trapianto pre-emptive

Consensus Document

Adamasco Cupisti[1], Giuliano Brunori[2], Biagio Raffaele Di Iorio[3], Claudia D'Alessandro[1 4], Franca Pasticci[4 5], Carmela Cosola[6], Vincenzo Bellizzi[7], Piergiorgio Bolasco[8], Alessandro Capitanini[9], Anna Laura Fantuzzi[10], Annalisa Gennari[4 11], Giorgina Barbara Piccoli[12], Giuseppe Quintaliani[13], Mario Salomone[14], Massimo Sandrini[11], Domenico Santoro[15], Patrizia Babini[16], Enrico Fiaccadori[17], Giovanni Gambaro[18], Giacomo Garibotto[19], Mariacristina Gregorini[20], Marcora Mandreoli[21], Roberto Minutolo[22], Giovanni Cancarini[11], Giuseppe Conte[22], Francesco Locatelli[23], Loreto Gesualdo[6]

Adamasco Cupisti

La TDN comprende la modulazione dell'apporto proteico, l'adeguatezza dell'apporto calorico, il controllo dell'apporto di sodio e di potassio e la riduzione dell'apporto di fosforo. Per tutte le terapie dietetico-nutrizionali, ed in particolare quelle mirate al paziente con insufficienza renale cronica, l'aderenza del paziente allo schema dietetico-nutrizionale è un elemento fondamentale per il successo e la sicurezza della TDN. Questa può essere favorita da un approccio interdisciplinare e multi-professionale di informazione, educazione, prescrizione dietetica e follow-up. Questo documento di consenso, che definisce 20 punti essenziali dell'approccio nutrizionale al paziente con insufficienza renale cronica avanzata, è stato preparato, discusso e condiviso dai nefrologi italiani insieme con i rappresentati dei dietisti (ANDID) e dei pazienti (ANED).

Giornale Italiano di Nefrologia, Vol. 5, Anno 35, Settembre Ottobre 2018

1. **Nel paziente con MRC 4-5, una dieta non controllata nell'apporto di calorie, proteine, sale e fosforo anticipa e aggrava le alterazioni clinico metaboliche proprie dell'insufficienza renale cronica avanzata**

9. **La terapia dietetica nutrizionale nella MRC 4-5 deve essere gestita con le fasi ed i criteri di una qualsiasi altra terapia farmacologica:**

- **indicazioni**
- **controindicazioni**
- **effetti collaterali**
- **modifiche della posologia**
- **verifica dei risultati**
- **follow-up**

17. **È necessario implementare modelli organizzativi per una più efficace e più agevole gestione clinica della malattia renale cronica avanzata: integrare diverse figure professionali**

19. **L'aderenza alle prescrizioni dietetiche è una criticità così come nelle terapie farmacologiche. La condivisione del programma dietetico mediante una corretta informazione ed educazione rimane alla base di una corretta gestione della cronicità da parte del paziente**

KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE
National Kidney Foundation

eat right® Academy of Nutrition and Dietetics

KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN CKD: 2020 UPDATE

T. Alp Ikizler, Jerrilynn D. Burrowes, Laura D. Byham-Gray, Katrina L. Campbell, Juan-Jesus Carrero, Winnie Chan, Denis Fouque, Allon N. Friedman, Sana Ghaddar, D. Jordi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple, Daniel Teta, Angela Yee-Moon Wang, and Lilian Cuppari

Restrizione proteica

Apporto calorico

Contenuto di calcio
Contenuto di fosforo
Contenuto di potassio
Contenuto di sodio

Quale tipo di proteine

COSA CI DICONO LE LINEE GUIDA KDOQI 2020

AJKD Vol 76 | Iss 3 | Suppl 1 | September 2020

Restrizione proteica

Negli adulti con malattia renale cronica (MRC) di grado 3-5 metabolicamente stabili, raccomandiamo, sotto stretta supervisione clinica, una restrizione proteica con o senza chetoacidi analoghi

- per ridurre il rischio di malattia renale allo stadio terminale (ESKD)/morte (1A)
- per migliorare la qualità della vita QoL) (2C):

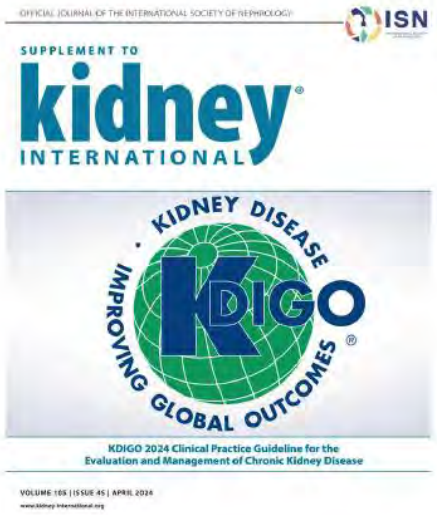
- una dieta ipoproteica che fornisca 0,55-0,60 g di proteine alimentari/kg di peso corporeo/giorno, oppure
- una dieta molto ipoproteica che fornisca 0,28-0,43 g di proteine alimentari/kg di peso corporeo/giorno con ulteriori chetoacidi/analoghi di amminoacidi per soddisfare il fabbisogno proteico (0,55-0,60 g /kg di peso corporeo/giorno)

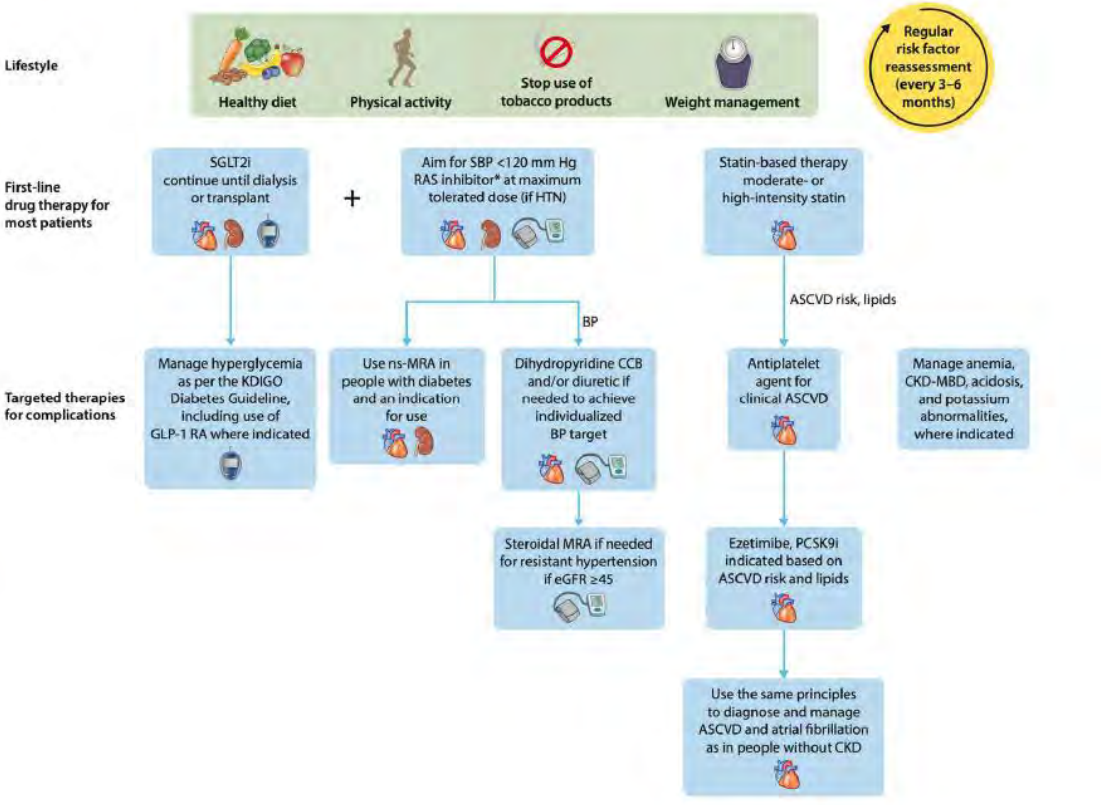
Le linee guida del 2020 della K-DOQI suggeriscono un inizio precoce della restrizione proteica

La restrizione proteica (livello di evidenza: 1A) è raccomandata non solo per ridurre il rischio di insufficienza renale terminale ma anche quello di morte

2024

Holistic approach to chronic kidney disease (CKD) treatment and risk modification.





Nel Diabete

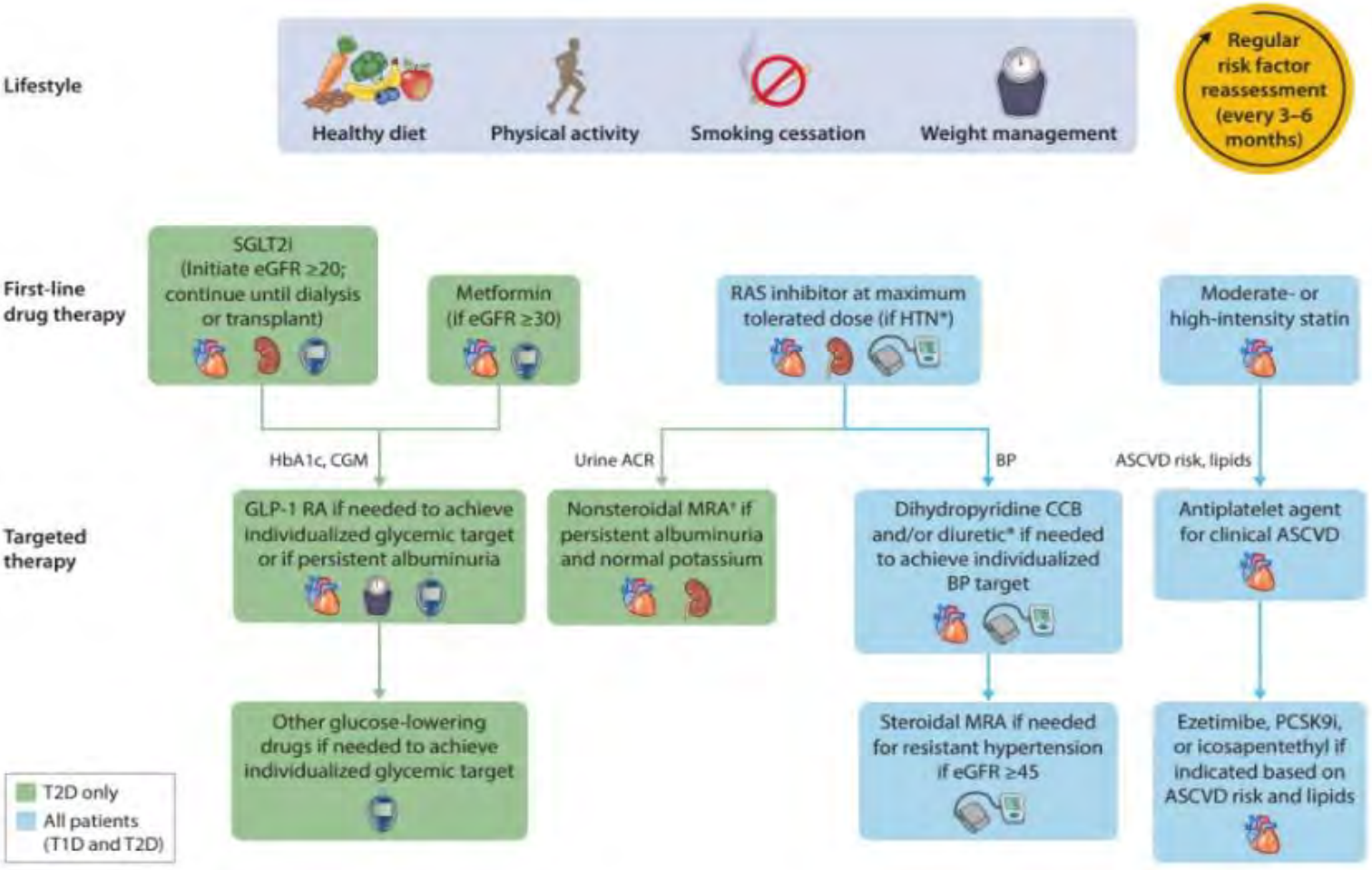
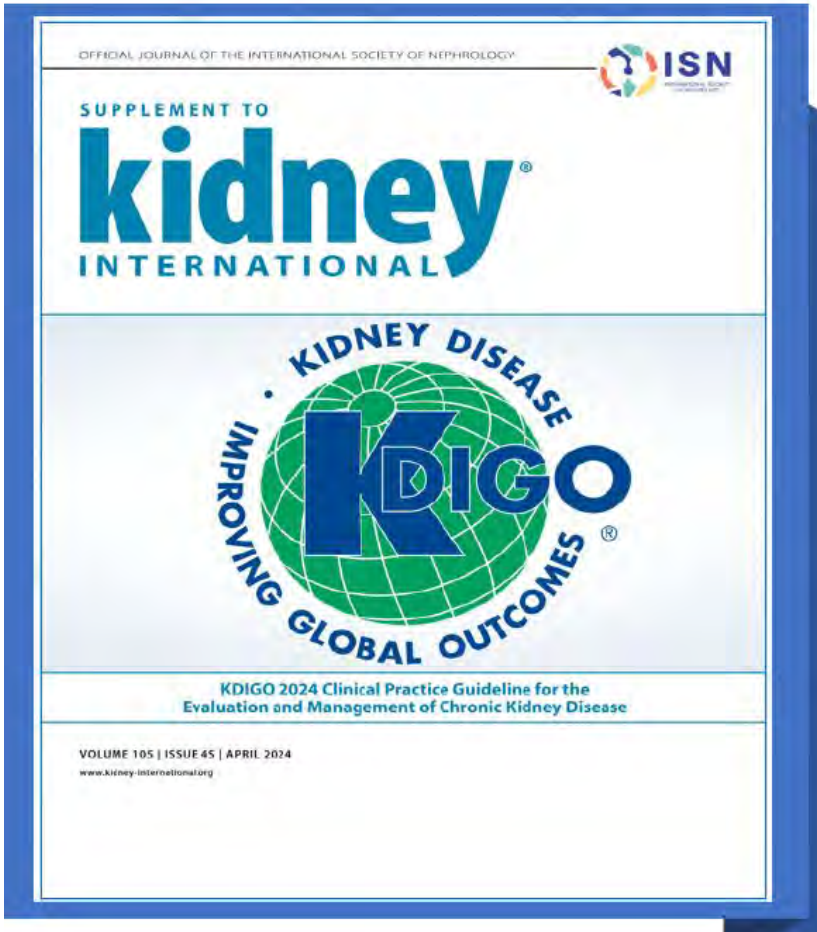


Figura 1. Linee guida per il trattamento dei pazienti diabetici con malattia renale (11)



DIET

Consigliare alle persone affette da malattia renale cronica di adottare diete sane e diversificate, con un maggiore consumo di alimenti di origine vegetale rispetto a quelli di origine animale ed un minore consumo di alimenti ultra-processati.

Rivolgersi a dietisti renali o a nutrizionisti accreditati per educare le persone con malattia renale cronica sugli adattamenti dietetici riguardanti l'assunzione di sodio, fosforo, potassio e proteine, in base alle loro esigenze individuali e alla gravità della malattia renale cronica e di altre comorbilità.

DIET – PROTEIN INTAKE

Suggeriamo di mantenere un apporto proteico di 0,8 g/kg di peso corporeo/giorno negli adulti con malattia renale cronica G3–G5 (2C).

Evitare un elevato apporto proteico (>1,3 g/kg di peso corporeo/giorno) negli adulti con CKD a rischio di progressione.

Weight (kg)	35	40	50	55	60	65	70	75	80	85	90	95	100
Grams of protein per day (wt × 0.8 g/kg)	28	32	40	44	48	52	56	60	64	68	72	76	80

DIET – PROTEIN INTAKE

Negli adulti con malattia renale cronica che sono disposti ed in grado di farlo e che sono a rischio di insufficienza renale, si consideri la prescrizione, sotto stretta supervisione, di una dieta a bassissimo contenuto proteico (0,3-0,4 g/kg di peso corporeo/die) integrata con amminoacidi essenziali o analoghi chetoacidi

Non prescrivere diete a basso o bassissimo contenuto proteico a persone con malattia renale cronica (MRC) metabolicamente instabili.

Animal proteins

Meat, poultry, fish, seafood, eggs:
28 g (1 oz) = 6–8 g protein
1 egg = 6–8 g protein

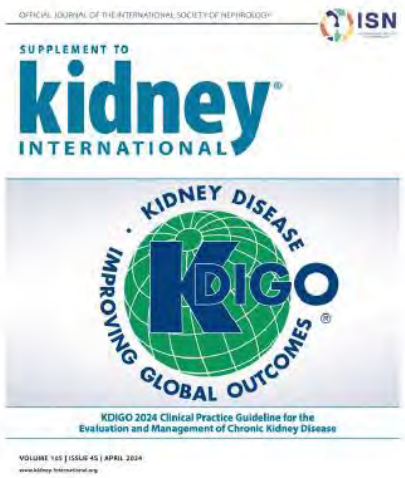
Dairy, milk, yogurt, cheese:
250 ml (8 oz) = 8–10 g protein
28 g (1 oz) cheese = 6–8 g protein

Plant proteins

Legumes, dried beans, nuts, seeds:
100 g (0.5 cup) cooked = 7–10 g protein

Whole grains, cereals:
100 g (0.5 cup) cooked = 3–6 g protein

Starchy vegetables, breads:
2–4 g protein



This heterogeneity in phenotype makes it more difficult to implement the recommendations of current guidelines, which are mainly based on early trials that generally enrolled younger patients with normal BMI.

JAMA Network Open

JAMA Netw Open
Published Online: August 7, 2024
2024;7;(8):e242657

Original Investigation | Nutrition, Obesity, and Exercise

Protein Intake and Mortality in Older Adults With Chronic Kidney Disease

Adrián Carballo-Casla, PhD; Carla Maria Avesani, PhD; Giorgi Beridze, MD; Rosario Ortolá, MD, PhD; Esther García-Esquinas, MD, PhD; Esther Lopez-Garcia, PhD; Lu Dai, MD, PhD; Michelle M. Dunk, PhD; Peter Stenvinkel, MD, PhD; Bengt Lindholm, MD, PhD; Juan Jesús Carrero, PhD; Fernando Rodríguez-Artalejo, MD, PhD; Davide Liborio Vetrano, MD, PhD; Amaia Calderón-Larrañaga, PhD

In questo studio multicoorte, un maggiore apporto di proteine totali, animali e vegetali è stato associato a una minore mortalità negli anziani con malattia renale cronica.

Nei pazienti con malattia renale cronica (MRC), un aumento dell'apporto proteico superiore a 0,80 g/kg/die era associato a un minor rischio di mortalità, con una riduzione del rischio di circa l'8% per ogni aumento di 0,20 g/kg/die nell'apporto proteico (HR 0,92; IC al 95% 0,86-0,98).

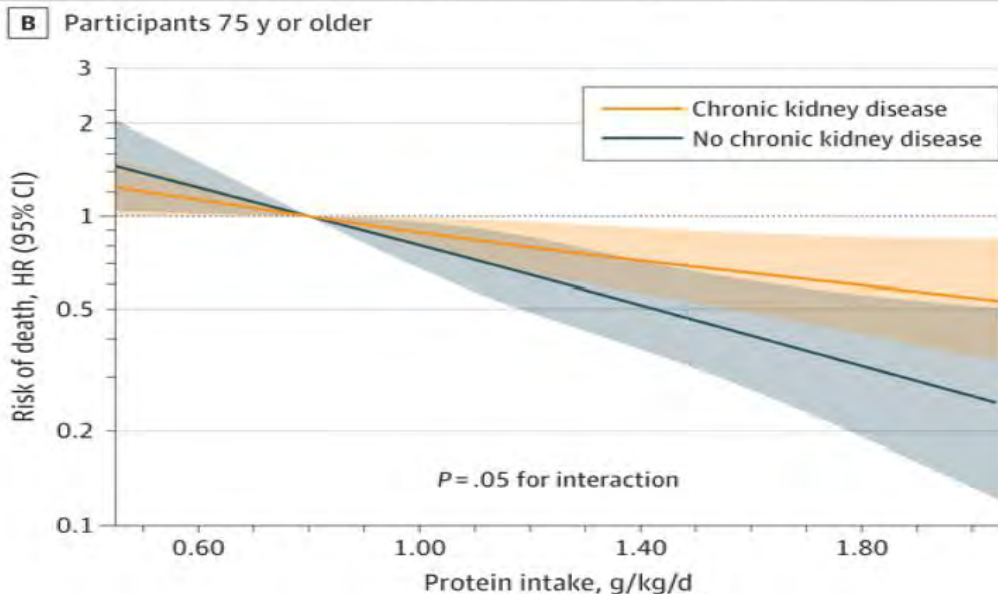


Table 1. Characteristics of the Participant Observations, Stratified by CKD

Characteristic	Participant group[a] With CKD (n = 4789)	Without CKD (n = 9610)
Sociodemographic		
Sex		
Male	2063 (43.1)	4352 (45.3)
Female	2726 (56.9)	5258 (54.7)
Age, mean (SD), y	78.0 (7.20)	70.0 (5.8)
Chronic kidney disease stage		
1	49 (1.0)	NA
2	726 (15.2)	NA
3A	3323 (69.4)	NA
3B	691 (14.4)	NA

Non leggete per contraddire e confutare, né per credere e accettar per concesso ma per pesare e valutare.

Francis Bacon

Lo studio si è basato su due questionari per la valutazione dell'assunzione dietetica

Sono state registrate comorbilità come il diabete, ma non sono state fornite informazioni ad esempio sul dato dell'albuminuria

Lo studio non ha inoltre valutato il rischio cardiovascolare né classificato la mortalità in base alla causa

I pazienti con un maggiore consumo di proteine potrebbero avere un appetito meglio preservato, meno comorbilità o altre caratteristiche

Revisiting Protein Restriction in Early CKD: Did We Get it Wrong?

AJKD Vol 85 | Iss 5 | May 2025

Biruh T. Workeneh, Linda W. Moore, and William E. Mitch

Commentary on: *Carballo-Casla A, Avesani CM, Beridze G, et al. Protein intake and mortality in older adults with chronic kidney disease. JAMA Netw Open. 2024;7(8):e2426577. doi:10.1001/jamanetworkopen.2024.26577*

One size fits all?

Nonostante i limiti dello studio, i risultati suggeriscono che:

- potrebbe essere necessario un **approccio più personalizzato** alle raccomandazioni dietetiche nella gestione della malattia renale cronica (MRC).
- **l'approccio "taglia unica"**, in particolare per gli anziani con malattia renale più lieve o per le persone con MRC lentamente progressiva con stadio IRC IIIa, potrebbe non essere applicabile.

Con i nuovi farmaci per controllare la progressione del danno renale, tra cui le glifozine ed i GLP 1, sarà importante collocare la restrizione proteica nel contesto di queste terapie per valutare se vi sia un beneficio incrementale o sinergico.

Le prescrizioni dietetiche devono essere adattate a ciascun individuo e non esiste un unico piano dietetico che vada bene per tutti, poiché ogni persona che convive con la MRC è unica e ha le proprie esigenze e preferenze.

il piano dietetico per la MRC deve essere considerato nel suo complesso, trovando un equilibrio tra evitare carenze, raggiungere il risultato previsto di ritardare la progressione della MRC e la necessità di dialisi e rispettare le abitudini alimentari del paziente e il suo background socioeconomico e culturale.

la gestione dietetica della MRC richiede una collaborazione multidisciplinare

nutrients

MDPI

Review

Dos and Don'ts in Kidney Nutrition: Practical Considerations of a Panel of Experts on Protein Restriction and Plant-Based Diets for Patients Living with Chronic Kidney Disease

Massimo Torreggiani [1,*], Carla Maria Avesani [2], Barbara Contzen [3], Adamasco Cupisti [4], Sylwia Czaja-Stolc [5], Claudia D'Alessandro [4], Liliana Garneata [6], Abril Gutiérrez [7], Françoise Lippi [1], Carmen Antonia Mocanu [6], Alice Sabatino [2] and Giorgina Barbara Piccoli [1] on behalf of the European Renal Nutrition (ERN) Working Group of the European Renal Association (ERA)

Cosa fare e cosa non fare

Dos ✓	Don'ts ✗
Animal vs. vegetal proteins	
Prescribe a plant-based diet in all CKD stages; regularly check nutritional status; periodically check for intake of all essential amino acids in the same meal (ideally) or at least in the same day, in particular in vegan diets. Consider occasionally including unrestricted meals. Consider supplementation with essential ketoacids and amino acids in vegan diets, both for simplifying management (0.6 g/kg/day diets) and making it possible to use VLPDs.	Do not limit prescription for fear of PEW. Do not prescribe a plant-based (vegan) or a VLPD without a detailed monitoring plan.
Potassium	
Prescribe plant-based diets in all CKD stages with regular checks of potassium and bicarbonate levels. Add potassium binders, provided that food sources are controlled (readily absorbed potassium salts are ubiquitous additives in ultra-processed food; they are not necessarily disclosed on food labels).	Do not limit prescription of plant-based diets in the case of high potassium levels, or fear of causing them. Do not prescribe a plant-based (vegan) or a VLPD without preparing a strict monitoring plan.
Phosphorus	
Keep in mind that a plant-based diet is a source of phosphorus whose bioavailability is lower than animal-based diets. Beware of ultra-processed foods, as readily absorbed phosphate salts are ubiquitous additives in ultra-processed food and they are not necessarily disclosed on food labels.	Do not limit prescription of plant-based diets in the case of high phosphate levels, or fear of causing them.
Ideal body weight	
Consider each person living with CKD's body composition, weight trajectory and perspectives when approaching the issue of real or ideal body weight. Consider real body weight at least below a BMI of 30 kg/m^2. Evaluate obese people living with CKD individually and review prescriptions in case of modifications of body weight.	Do not use a formula to calculate ideal or adjusted body weight without a previous critical appraisal of the individual person living with CKD.

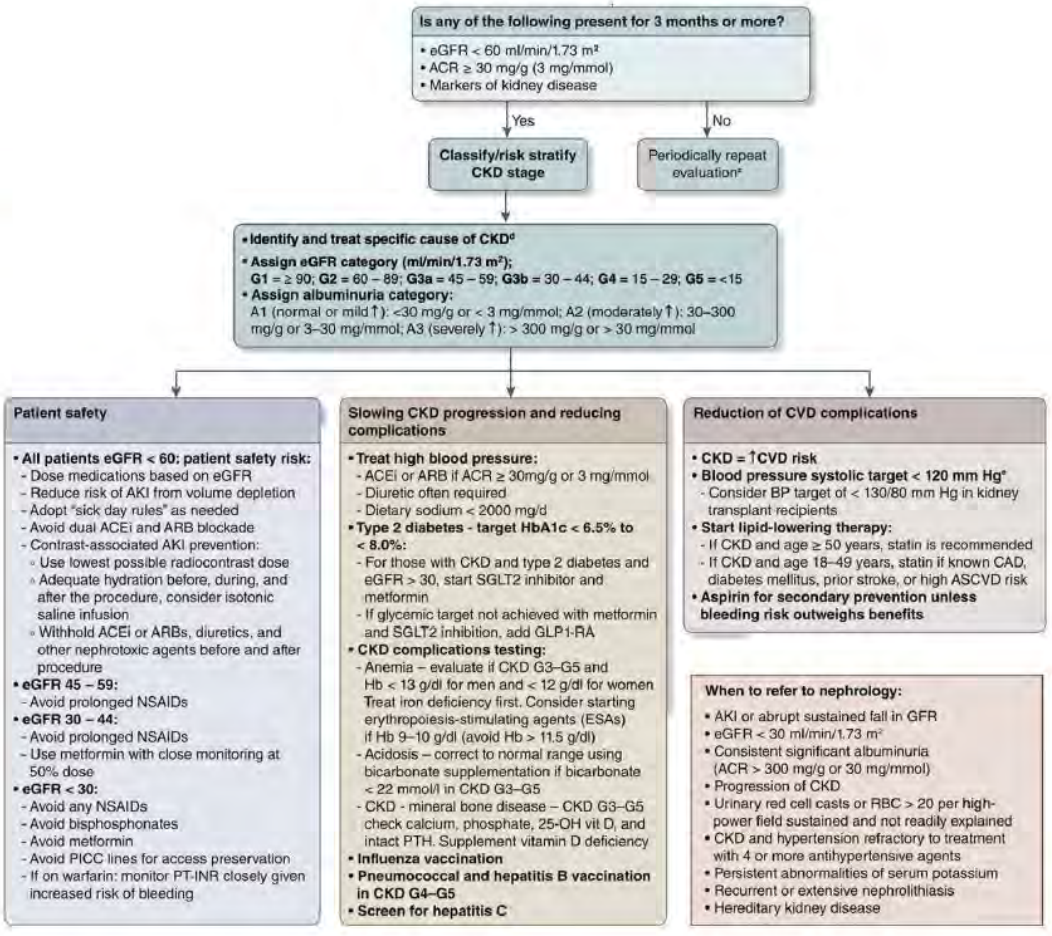
KDIGO executive conclusions www.kidney-international.org

The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

Michael G. Shlipak[1,2], Sri Lekha Tummalapalli[1,2], L. Ebony Boulware[3], Morgan E. Grams[4,5], Joachim H. Ix[6,7,8], Vivekanand Jha[9,10,11], Andre-Pascal Kengne[12,13], Magdalena Madero[14], Borislava Mihaylova[15,16], Navdeep Tangri[17], Michael Cheung[18], Michel Jadoul[19], Wolfgang C. Winkelmayer[20] and Sophia Zoungas[21,22]; for Conference Participants[23]

OPEN

Identifying and treating CKD at the earliest stages is an equity imperative!



La modulazione dell'apporto proteico nel paziente con CKD

Keto Acid Therapy in Predialysis Chronic Kidney Disease Patients: Final Consensus

Michel Aparicio, MD, Vincenzo Bellizzi, MD, PhD,† Philippe Chauveau, MD,‡§ Adamasco Cupisti, MD, PhD,¶ Tevfik Ecder, MD,** Denis Fouque, MD, PhD,†† Liliana Gameata, MD, PhD,‡‡ Shanyan Lin, MD,§§ William E. Mitch,¶¶ Vladimír Teplan, MD, PhD, DSc,*** Gábor Zakar, MD,‡‡‡ and Xueqing Yu, MD, PhD§§§*

J Ren Nutr 2012;22:S22-S24

Stadio CKD	GFR (ml/min/1,73 m²)	Apporto proteico giornaliero
I	>90	0,8 – 1,0 g/kg/p.c.
II	60-89	Apporto proteico = RDA: 0,8 g/kg/p.c.
IIIa	45-59	Controllo / Restrizione proteica: a. 0.8 g/kg/p.c.
IIIb	44-30	b. 0,7 g/kg/p.c. c. 0,6 g/kg/p.c.
IV	15-29	Restrizione proteica: a. 0,6 g/kg/p.c. b. 0,3-0,4 g/kg/p.c. + AAE e KA
V	< 15 non in dialisi	Restrizione proteica: a. 0,6 g/kg/p.c. b. 0,3-0,4 g/kg/p.c. + AAE e KA

Normalizzazione / Riduzione del carico dietetico di Sodio - Fosforo - Proteine

1) *Controllo di CKD-MBD*
2) *Riduzione della Pressione Arteriosa*
3) *Riduzione della Proteinuria*

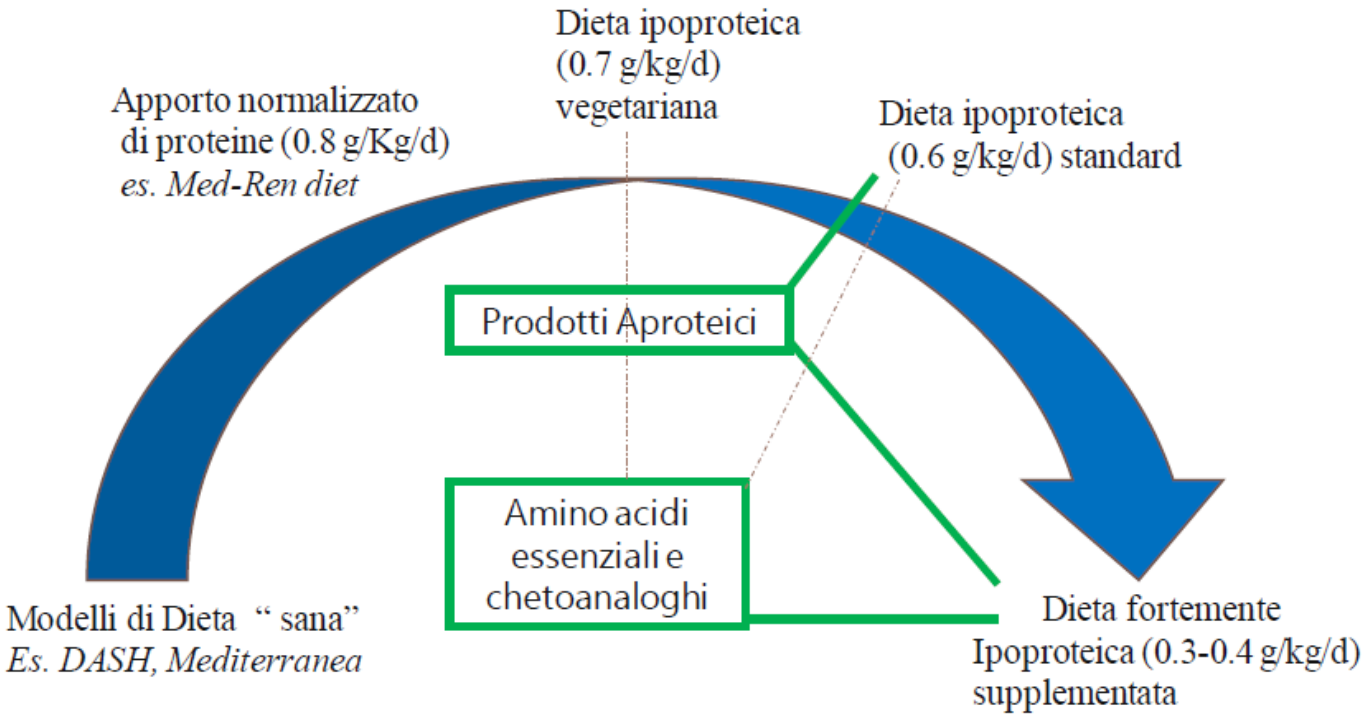
Rallentamento della progressione della CKD

Restrizione dell'apporto dietetico di Sodio - Fosforo - Proteine Elevato Apporto calorico

1) *Riduzione dell'intossicazione uremica*
2) *Correzione dei sintomi e segni della IRC*
3) *Prevenzione della Malnutrizione*

Allontanamento dell'inizio della Dialisi

IL CONTINUUM DEL SUPPORTO NUTRIZIONALE NELLA MALATTIA RENALE CRONICA



Inflammation and Progression of CKD: The CRIC Study

Richard L. Amdur, Harold I. Feldman, Jayanta Gupta, Wei Yang, Peter Kanetsky, Michael Shlipak, Mahboob Rahman, James P. Lash, Raymond R. Townsend, Akinlolu Ojo, Akshay Roy-Chaudhury, Alan S. Go, Marshall Joffe, Jiang He, Vaidyanathapuram S. Balakrishnan, Paul L. Kimmel, John W. Kusek, Dominic S. Raj, and the CRIC Study Investigators

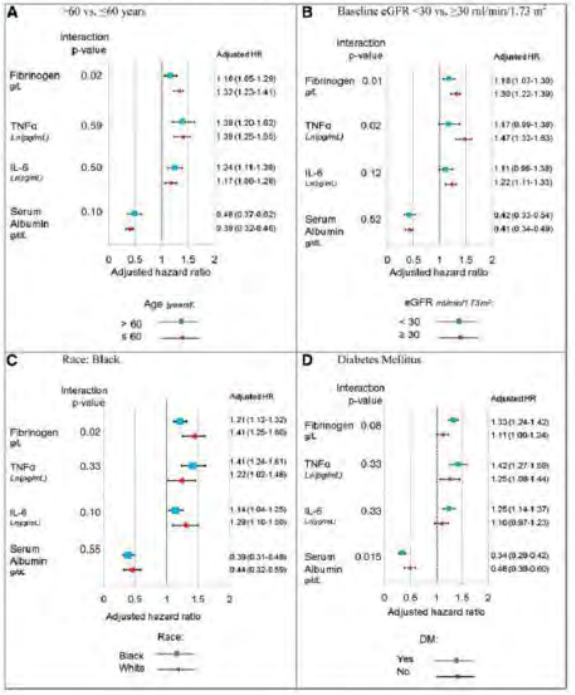
Clin J Am Soc Nephrol 11: 1546–1556, 2016.

Biomarker	*N* with Composite Outcome (%)	Chi-Squared *P* Value	Model 1 Hazard Ratio (95% CI)	*P* Value	Model 2 Hazard Ratio (95% CI)	*P* Value
Fibrinogen, g/L		<0.001		<0.001		<0.001
Quartile 1, <3.39	126 (14.6)		Reference group		Reference group	
Quartile 2, 3.39 to <4.04	171 (19.4)		1.38 (1.10 to 1.74)		1.05 (0.84 to 1.33)	
Quartile 3, 4.04 to <4.80	247 (28.2)		2.11 (1.71 to 2.62)		1.41 (1.13 to 1.76)	
Quartile 4, ≥4.80	355 (43.9)		4.04 (3.30 to 4.95)		2.05 (1.64 to 2.55)	
IL-1β,[a] pg/ml		<0.001		<0.001		0.66
Quartiles 1 and 2, <0.21	383 (22.0)		Reference group		Reference group	
Quartile 3, 0.21 to <1.29	235 (27.7)		1.33 (1.13 to 1.56)		1.01 (0.86 to 1.19)	
Quartile 4, ≥1.29	281 (33.4)		1.81 (1.55 to 2.11)		1.07 (0.92 to 1.26)	
IL-1RA, pg/ml		0.002		0.001		0.93
Quartile 1, <390.00	196 (22.5)		Reference group		Reference group	
Quartile 2, 390.00 to <715.70	207 (24.5)		1.09 (0.90 to 1.33)		0.98 (0.81 to 1.20)	
Quartile 3, 715.70 to <1551.00	252 (29.1)		1.32 (1.10 to 1.60)		0.97 (0.80 to 1.17)	
Quartile 4, ≥1551.00	244 (28.9)		1.39 (1.15 to 1.68)		0.94 (0.78 to 1.14)	
IL-6, pg/ml		<0.001		<0.001		0.008
Quartile 1, <1.17	147 (16.4)		Reference group		Reference group	
Quartile 2, 1.17 to <1.90	227 (25.8)		1.74 (1.41 to 2.14)		1.26 (1.02 to 1.56)	
Quartile 3, 1.90 to <3.15	255 (29.9)		2.13 (1.74 to 2.61)		1.32 (1.07 to 1.63)	
Quartile 4, ≥3.15	270 (33.8)		2.57 (2.10 to 3.14)		1.44 (1.17 to 1.77)	
TNF-α, pg/ml		<0.001		<0.001		<0.001
Quartile 1, <1.50	91 (11.1)		Reference group		Reference group	
Quartile 2, 1.50 to <2.20	180 (21.0)		2.05 (1.59 to 2.64)		1.22 (0.95 to 1.58)	
Quartile 3, 2.20 to <3.20	276 (31.9)		3.53 (2.79 to 4.48)		1.57 (1.23 to 2.01)	
Quartile 4, ≥3.20	352 (39.7)		4.99 (3.96 to 6.29)		1.94 (1.52 to 2.47)	
Serum albumin, g/dl		<0.001		<0.001		<0.001
Quartile 1, <3.70	375 (49.9)		4.72 (3.93 to 5.67)		3.48 (2.88 to 4.21)	
Quartile 2, 3.70 to <4.00	224 (27.0)		1.99 (1.63 to 2.44)		1.81 (1.48 to 2.22)	
Quartile 3, 4.00 to <4.20	120 (18.5)		1.34 (1.06 to 1.69)		1.35 (1.07 to 1.71)	
Quartile 4, ≥4.20	167 (14.5)		Reference group		Reference group	

Elevated plasma levels of fibrinogen and TNF-α and decreased serum albumin are associated with rapid loss of kidney function in patients with CKD.

3430 participants (eGFR 20-70 ml/min)
Follow-up time of 6.3 years
Primary outcomes:

1. Occurrence of ≥50% decline in GFR from baseline or onset of ESRD
2. Slope of eGFR over time



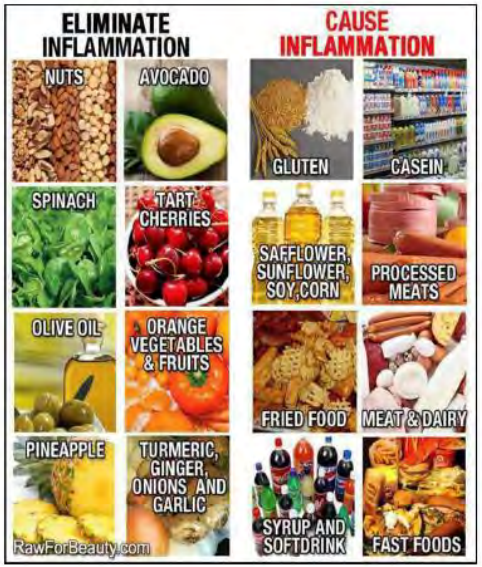


Table 1 | Acute inflammation versus systemic chronic inflammation

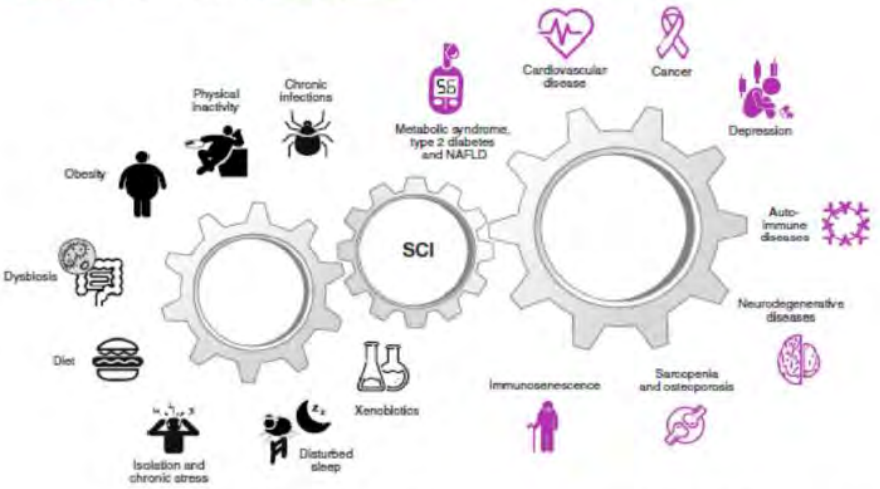
	Acute inflammation	Systemic chronic inflammation
Trigger	PAMPs (infection), DAMPs (cellular stress, trauma)	DAMPs ('exposome', metabolic dysfunction, tissue damage)
Duration	Short-term	Persistent, non-resolving
Magnitude	High-grade	Low-grade
Outcome(s)	Healing, trigger removal, tissue repair	Collateral damage
Age-related	No	Yes
Biomarkers	IL-6, TNF-α, IL-1β, CRP	Silent—no canonical standard biomarkers

DAMP, damage-associated molecular pattern; PAMP, pathogen-associated molecular pattern.

Chronic inflammation in the etiology of disease across the life span

David Furman[1,2,3,4*], Judith Campisi[1,5], Eric Verdin[1], Pedro Carrera-Bastos[6], Sasha Targ[4,7], Claudio Franceschi[8,9], Luigi Ferrucci[10], Derek W. Gilroy[11], Alessio Fasano[12], Gary W. Miller[13], Andrew H. Miller[14], Alberto Mantovani[15,16,17], Cornelia M. Weyand[18], Nir Barzilai[19], Jorg J. Goronzy[20], Thomas A. Rando[20,21,22], Rita B. Effros[23], Alejandro Lucia[24,25], Nicole Kleinstreuer[26,27] and George M. Slavich[28]

NATURE MEDICINE | VOL 25 | DECEMBER 2019 | 1822–1832 |



Recent research has revealed that certain social, environmental and lifestyle factors can promote systemic chronic inflammation that can lead to severa diseases that collectively represent the leading causes of disability and mortality worldwide, such as cardiovascular disease, cancer, diabetes mellitus, **chronic kidney disease**, non-alcoholic fatty liver disease and autoimmune and neurodegenerative disorders.

Potenziali benefici renali

ORIGINAL RESEARCH

Dietary Protein Sources and Risk for Incident Chronic Kidney Disease: Results From the Atherosclerosis Risk in Communities (ARIC) Study

Bernhard Haring, MD, MPH, Elizabeth Selvin, PhD, MPH,†‡ Menglu Liang, ScM, MPH,†‡ Josef Coresh, MD, PhD, MHS,†‡ Morgan E. Grams, MD, PhD, MHS,†§ Natalia Petruski-Ivleva, MS,¶ Lyn M. Steffen, PhD, MPH, RD,** and Casey M. Rebholz, PhD, MS, MPH†‡*

J Ren Nutr. 2017 July ; 27(4): 233–242. doi:10.1053/j.jrn.2016.11.004.

11,952 adults aged 44-66 years, free of diabetes mellitus, cardiovascular disease and eGFR ≥60 ml/min/1.73 m²

Follow-up period of 23 years.
2,632 incident CKD cases.

↑ 23% risk of CKD

↑ 42% risk of CKD

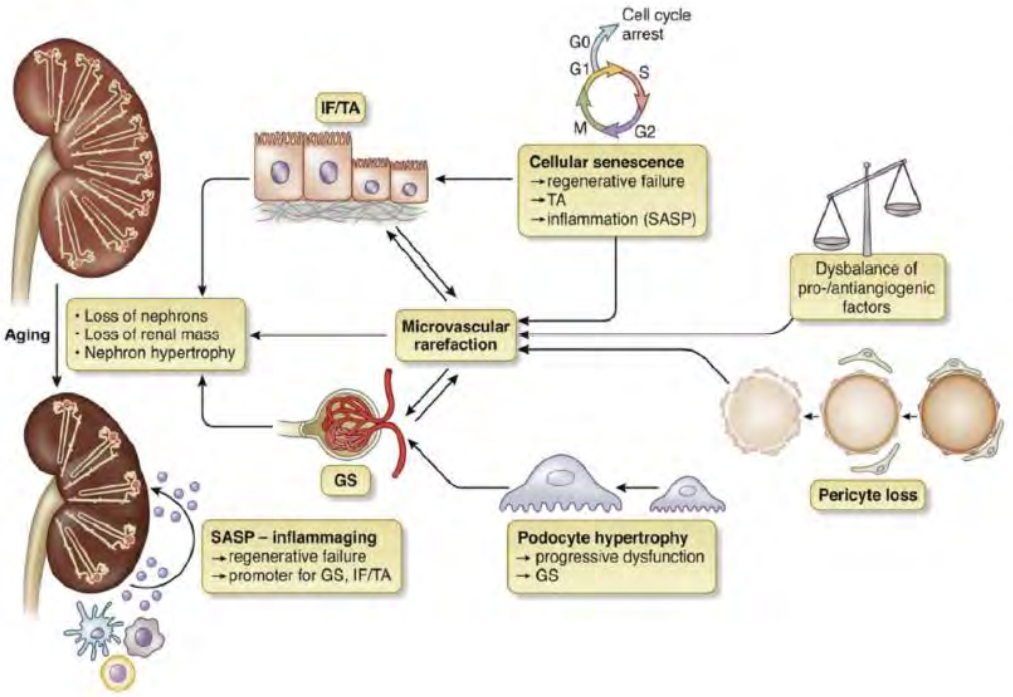
↓ 17% risk of CKD

↓ 19% risk of CKD

Molecular mechanisms of renal aging

Roland Schmitt[1] and Anette Melk[2]

Kidney International (2017) **92,** 569–579



Inflammation plays a critical role in the initiation and progression of renal fibrosis.

Proinflammatory and profibrotic cytokines and inflammatory cells which include immune cells from bone marrow and locally damaged resident renal cells constitute the inflammatory microenvironment.

Strategie non farmacologiche

PRACTICAL ASPECTS

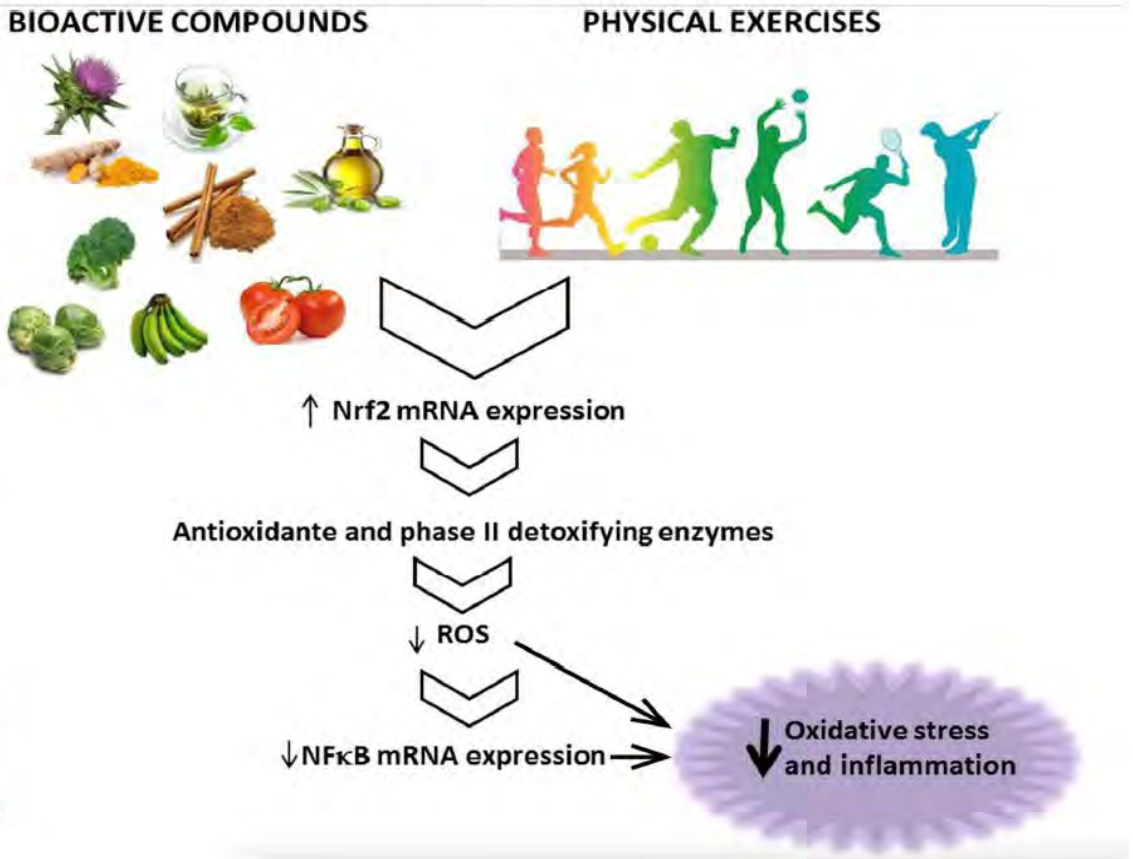
Nonpharmacologic Strategies to Modulate Nuclear Factor Erythroid 2–related Factor 2 Pathway in Chronic Kidney Disease

Marta Esgalhado, MSc, Peter Stenvinkel, MD, PhD,† and Denise Mafra, PhD**

J Ren Nutr. 2017 Jul;27(4):282-291

Nuclear factor erythroid 2-related factor 2 (Nrf2) is a transcription factor with a high sensitivity to oxidative stress, which regulates the expression of detoxifying enzymes, besides that, can also control antioxidant and anti-inflammatory cellular responses. Therefore, the modulation of this transcription factor can be a new therapeutic approach to reduce complications in chronic kidney disease (CKD) patients, like oxidative stress and inflammation, which leads to increased risk of developing cardiovascular disease, the major cause of death in these patients. Recent studies have shown that nutritional components and physical exercises can regulate the activation of Nrf2.

Nrf2-interacting natural compounds:
tocotrienols, curcumin, epigallocatechin gallate, quercetin, genistein, resveratrol, silybin, phenethyl isothiocyanate, sulforaphane, triptolide, allicin, berberine, piperlongumine, fisetin and phloretin




La terapia dietetico-nutriziale deve **anticipare** ed **integrarsi** con le terapie farmacologiche.

La dieta come farmaco

A. Types and Dosages of Low Protein Diet
- Conventional LPD, supplying 0.55 to 0.60 g/kg b.w./day of mixed proteins, at least 50% of high biological value.
- Vegan LPD, supplying 0.6–0.7 g/kg b.w./day of plant origin proteins using a special combination of cereal and legumes, and/or soy.
- Very low protein diet to patients with CKD and without diabetes: 0.28 to 0.43 g/kg b.w./day with additional keto acid/amino acids to meet protein requirement of 0.55 to 0.60 g/kg b.w./day, usually 1 tablet every 5 kg b.w.
- Mostly vegetarian diets supplying 0.7–0.8 g/kg b.w.d of unselected proteins, supplemented or not with essential amino acids and ketoacids (usually 1 tablet every 10 kg b.w).
B. Mechanisms of Action of Low Protein Diet
- Reduced production of protein-derived waste products
- Reduced retention of protein-derived toxins and fixed acids
- Reduced phosphate load, with lesser stimulation of parathyroid hormone production
- Reduced single-nephron glomerular hyperfiltration
- Reduced urine protein excretion
C. Indications to a Low-Protein Diet
- Prevention and treatment of metabolic and electrolyte abnormalities, signs and symptoms of chronic renal insufficiency
- Prevention of protein-energy wasting
- Delay the start of renal replacement therapy
- Management of proteinuria, hypertension, or progressing chronic kidney disease

Cupisti A et al. J. Clin. Med. ***2020, 9, 3644***

La dieta come farmaco

D. Contraindications to a Low-Protein Diet
Absolute
- Protein energy wasting
- Hypercatabolic state (acute or chronic)
- Anorexia and eating disorders
- End of life care management
Relative
- Poor attitude to dietary modifications
- Psychiatric / psychological disorders
- Logistic barriers (economic, cultural, lack of support)
- Poorly controlled diabetes
- Chronic steroid treatment
- Intestinal diseases including chewing disorders
- Short life-expectancy
E. Unwanted Side Effects of LPD
- Weight loss due to reduced energy intake
- Loss of muscle mass due to inadequate protein and energy intake
- Depression, relational problems, psychological discomfort

Cupisti A et al. J. Clin. Med. ***2020, 9, 3644***

Giornale Italiano di Nefrologia

La terapia dietetica nutrizionale nella gestione del paziente con Malattia Renale Cronica in fase avanzata per ritardare l'inizio e ridurre la frequenza della dialisi, e per il programma di trapianto pre-emptive

Consensus Document

Adamasco Cupisti[1], Giuliano Brunori[2], Biagio Raffaele Di Iorio[3], Claudia D'Alessandro[1 4], Franca Pasticci[4 5], Carmela Cosola[6], Vincenzo Bellizzi[7], Piergiorgio Bolasco[8], Alessandro Capitanini[9], Anna Laura Fantuzzi[10], Annalisa Gennari[4 11], Giorgina Barbara Piccoli[12], Giuseppe Quintaliani[13], Mario Salomone[14], Massimo Sandrini[11], Domenico Santoro[15], Patrizia Babini[16], Enrico Fiaccadori[17], Giovanni Gambaro[18], Giacomo Garibotto[19], Mariacristina Gregorini[20], Marcora Mandreoli[21], Roberto Minutolo[22], Giovanni Cancarini[11], Giuseppe Conte[22], Francesco Locatelli[23], Loreto Gesualdo[6]

Adamasco Cupisti

2. Nel paziente con MRC 4-5, una dieta non controllata nell'apporto di calorie, proteine, sale e fosforo, può ridurre l'efficacia della terapia farmacologica o richiederne l'aumento di posologia.

Un eccessivo apporto calorico può contribuire all'obesità e alla dislipidemia e aggrava la resistenza all'insulina; limita l'efficacia delle terapia antidiabetiche ed ipolipemizzanti e ne richiede l'aumento della posologia.

Un elevato apporto di sale riduce l'efficacia delle terapie antipertensive e antiproteinuriche (in particolare degli SRAA) con aumento del rischio di progressione della MRC e del consumo di farmaci, in particolare dei diuretici.

Un elevato carico dietetico di fosforo riduce l'efficacia dei chelanti e ne richiede un aumento della posologia. Contribuisce inoltre ad un peggior controllo dell'iperPTH secondario riducendo la sicurezza dell'uso di preparati a base di vitamina D attiva. Inoltre, un peggior controllo della fosforemia e del PTH si associa ad una ridotta risposta agli ESA e agli ACEi.

Un elevato apporto di acidi fissi, associato al consumo di proteine animali, rende arduo prevenire l'acidosi metabolica e obbliga all'uso di maggiori quantità di sodio bicarbonato per la sua correzione.

Mind pathophysiology

when treat patients

glomerular hyperfiltration as a therapeutic target for CKD

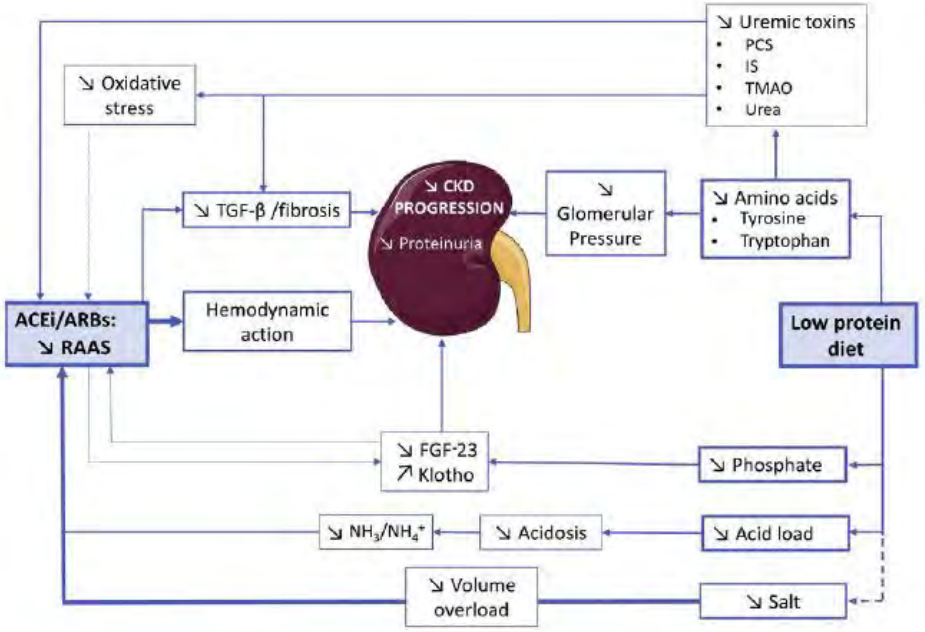
chronic inflammation as a therapeutic target for CKD

Interazione dieta - farmaci

..... nella terza decade degli anni 2000.... I vecchi RAASi

Le azioni antipertensive e antiproteinuriche del RAASi sono attenuate dall'assunzione incontrollata di proteine e sale.

Mentre l'associazione di una dieta a basso contenuto proteico e a base vegetale, una dieta a basso contenuto di sodio aumenta l'efficacia del RAASi sulla proteinuria e sulla pressione arteriosa con maggiori possibilità di protezione renale (e CV)



: Koppe L, Fouque D. AJKD 2019; 73:2

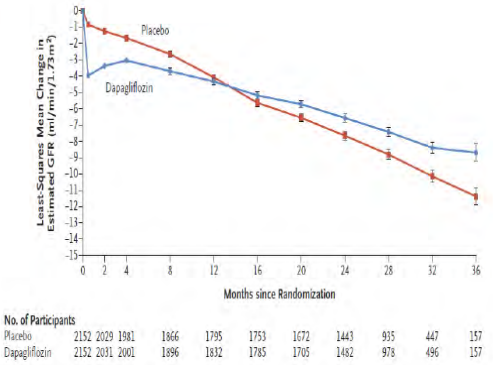
Interazione dieta - farmaci

..... nella terza decade degli anni 2000.... l'era SGLT2i

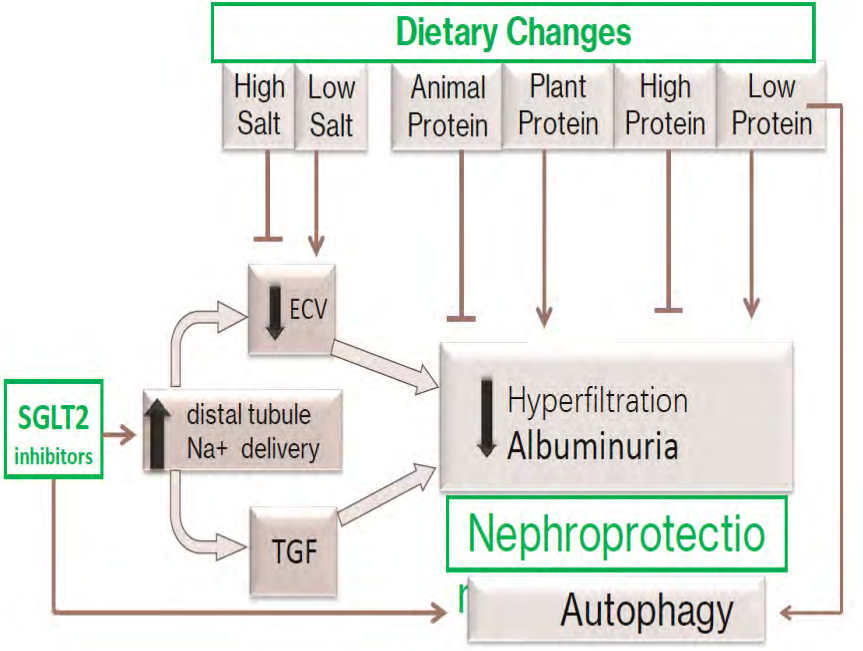
SGLT2i aumenta il rilascio distale di sodio, con l'attivazione del feedback tubulo-glomerulare

Questo modula le resistenze glomerulari principalmente attraverso la vasocostrizione afferente e meno attraverso la vasodilatazione efferente

L'effetto anti-iperfiltrazione (e anti-proteinurico) è evidente dall'improvviso calo di GFR che si verifica dopo l'inizio di SGLT2i,e questo rappresenta il principale meccanismo di nefroprotezione nel lungo periodo.....

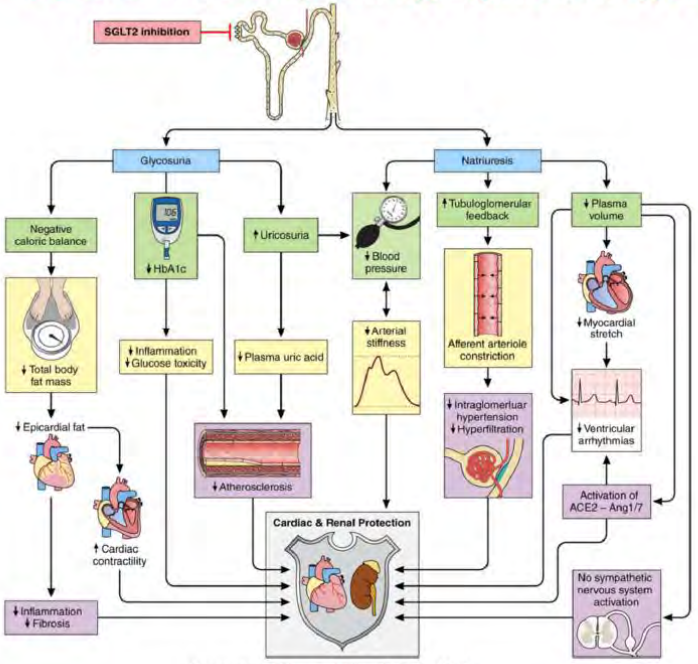


Heerspink H.J.L. et al. N Engl J Med 2020;383:1436-46.



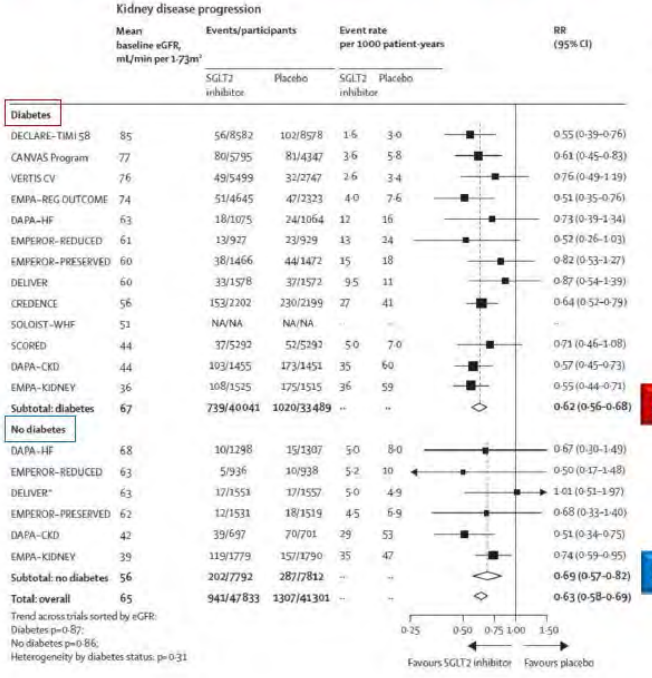
Cupisti A et al. Front Med 2020; 7:62259

SGLT2-i: not only anti-hyperfiltration effect!



Heerspink HJL et al Circulation 2016

Effect of SGLT2-i on kidney disease progression by DM status



Kidney disease progression as composite of:

- *sustained eGFR decrease ≥50%,*
- *end-stage kidney disease (ie, start of dialysis or receipt of a kidney transplant),*
- *sustained low eGFR (<15 mL/min/1.73 m² or <10 mL/min/1.73 m²)*
- *death from kidney failure*

Patients with diabetes: risk reduction 38%

Patients without diabetes: risk reduction 31%

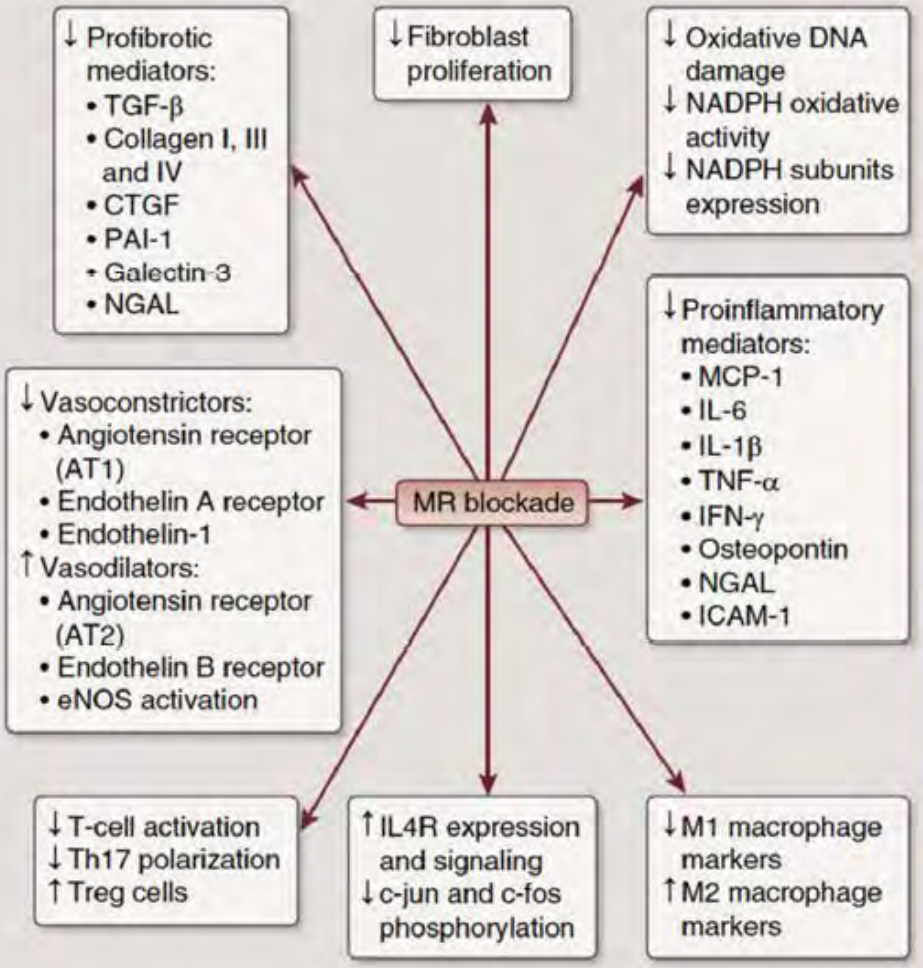
Lancet 2022; 400: 1788–801

Differential MR binding of steroidal MRAs vs finerenone

Trial FIDELIO
Trial FIGARO
Studio FIDELITY

	Aldosterone antagonists		Finerenone
			
Structural properties	Flat (steroidal)	Flat (steroidal)	Bulky (nonsteroidal)[1,5]
Potency to MR	High[4,10]	Moderate[1,4,10]	High[1,2,10]
Selectivity to MR	Low[4,10]	Moderate[4,10]	High[1,2,10]
Half-life	>20 hours*	4–6 hours*	2–3 hours#
Active metabolites	++	–	–
CNS penetration	Yes	Yes	No based on preclinical data[3]
Gynecomastia	Yes[4]	Less than spironolactone[4]	No signal in phase II studies[7-9]
Hyperkalaemia	Yes[4]	Yes[4]	Moderately increased*,[7-9]
Indication (SmPC)	Congestive HF[2]	HF and LVEF ≤40% or ≤30%[3]	CKD with albuminuria, associated with T2D[4]

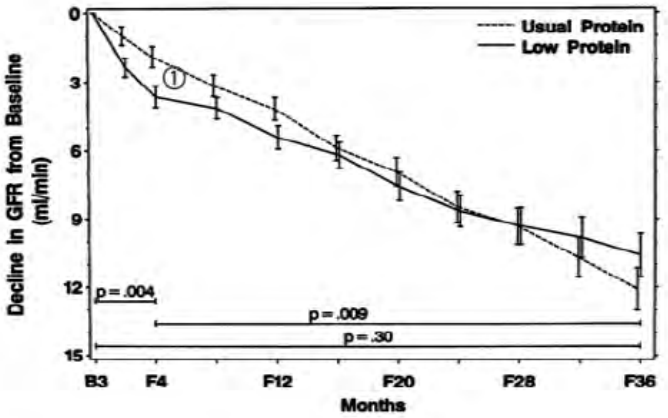
Renal cell types	Tissue effects	Mode of action of MR antagonists	Clinical settings	Clinical effects
Distal tubular cells	↓ Tubular injury		Situations with risk of IRI: • cardiac surgery • kidney transplantation • other?	IRI prevention
	↓ Fibrosis			Prevention of AKI to CKD transition
Endothelial cells SMC	↓ Glomerulosclerosis		Hypertension	Antihypertensive
	↓ Podocyte injury			
Podocytes Mesangial cells Fibroblasts	↓ Inflammation		Diabetes	Antiproteinuric
	↓ Vasoconstriction		Glomerulonephritis	Prevention of CV outcomes
Macrophages T cells	↓ Vascular injury		CKD–fibrosis	Prevention of CKD progression
	↓ Mesangium expansion		Kidney transplantation	Prevention of CNI toxicity



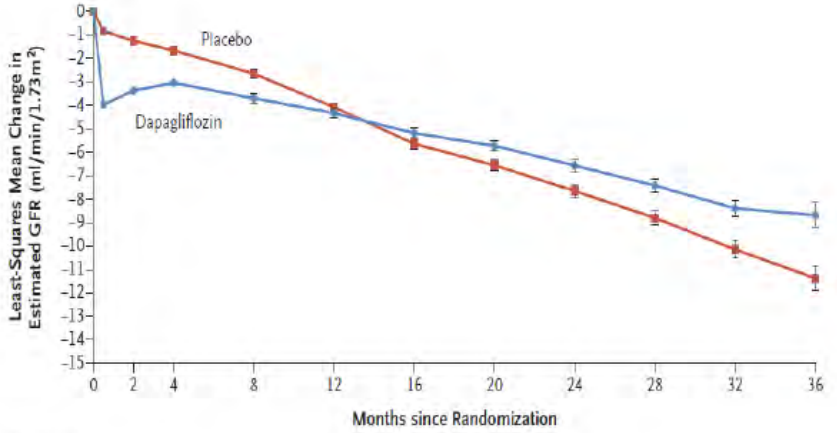
Barrera-Chimal Jet al., Kidney Int. - 2019

Interazione dieta - farmaci

...questa curva è molto simile a quanto riportato dallo studio MDRD degli anni '90, quando l'azione anti-iperfiltrazione e anti-proteinurica veniva ottenuta mediante restrizione proteica



Klahr S, et al. N Engl J Med 1994



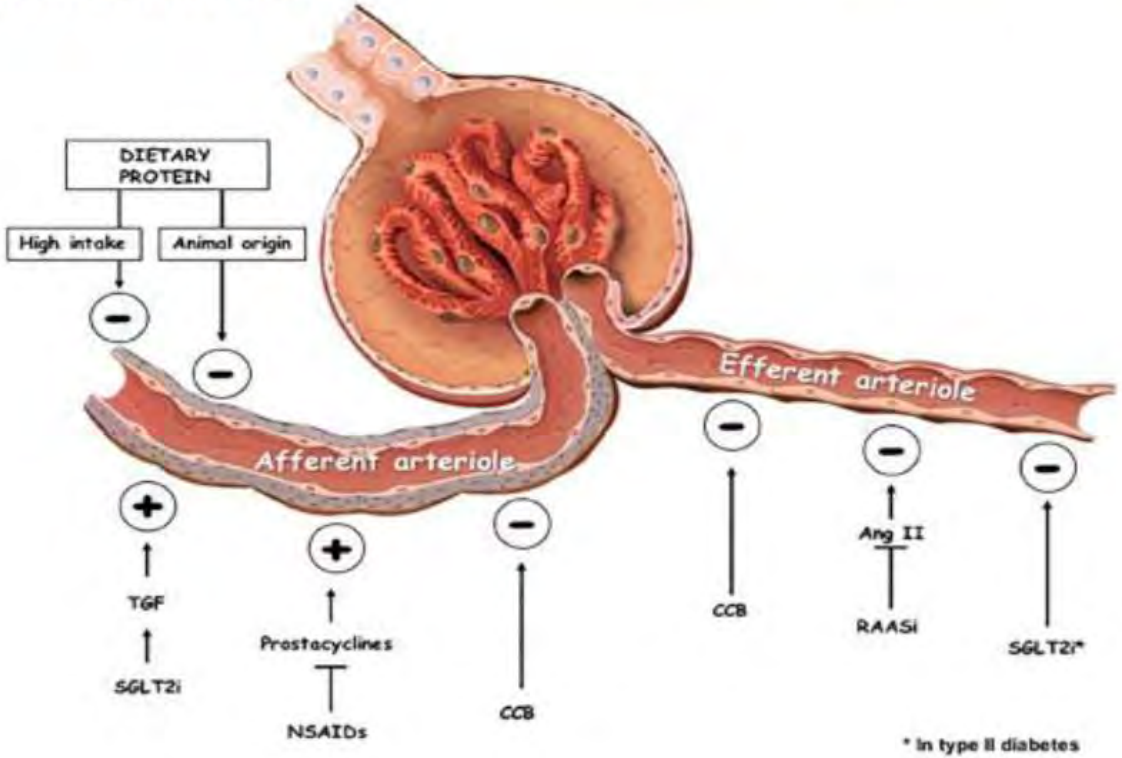
No. of Participants

Placebo	2152	2029	1981	1866	1795	1753	1672	1443	935	447	157
Dapagliflozin	2152	2031	2001	1896	1832	1785	1705	1482	978	496	157

Heerspink H.J.L. et al. N Engl J Med 2020;383:1436-46.

Interazione dieta - farmaci

SIA I FARMACI CHE GLI INTERVENTI DIETETICI SONO IN GRADO DI MODULARE L'EMODINAMICA GLOMERULARE MEDIANTE CAMBIAMENTI DEL TONO VASCOLARE

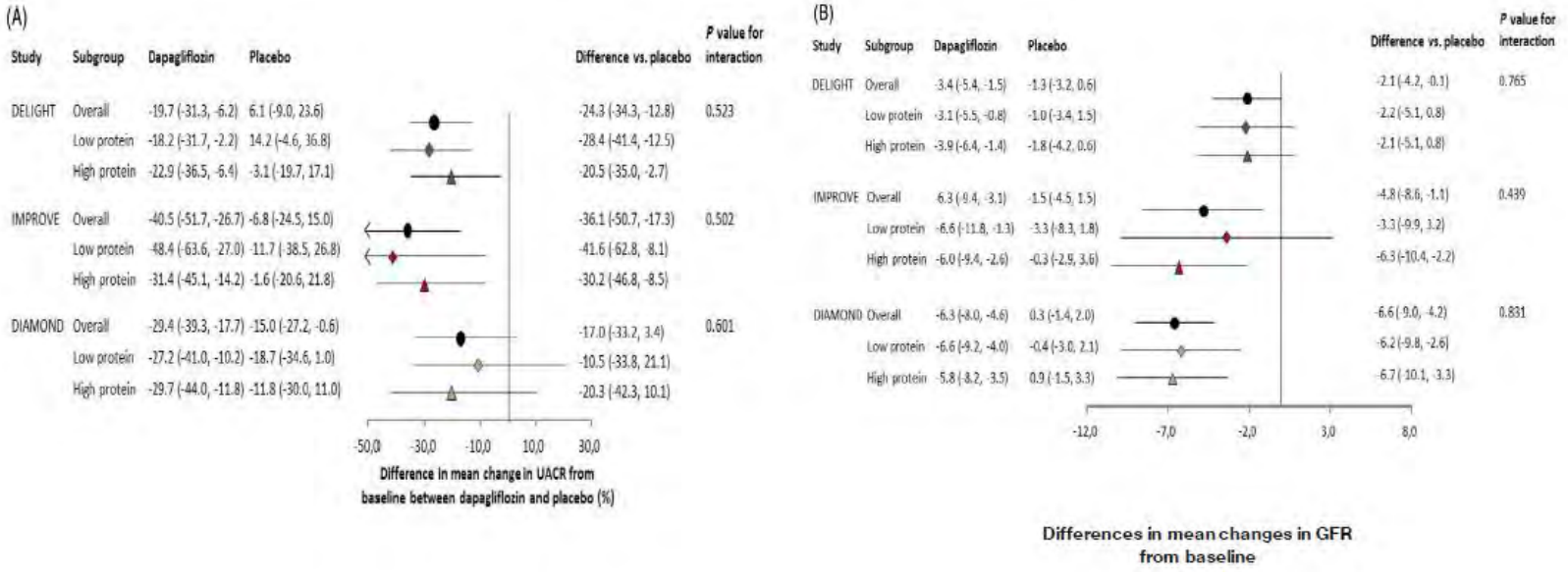


Cupisti A et al. Front Med 2020; 7:622593

Interazione dieta - farmaci

un'analisi post-hoc di tre studi randomizzati e controllati suggerisce che
la risposta emodinamica renale al SGLT2-i non dipende dall'assunzione di proteine

Risposte non differenti tra i pazienti a basso o ad alto apporto proteico, a seguito di SGLT2i



van der Aart-van der Beek AB et al. Diabetes Obes Metab. 2021;23:1961–1967.

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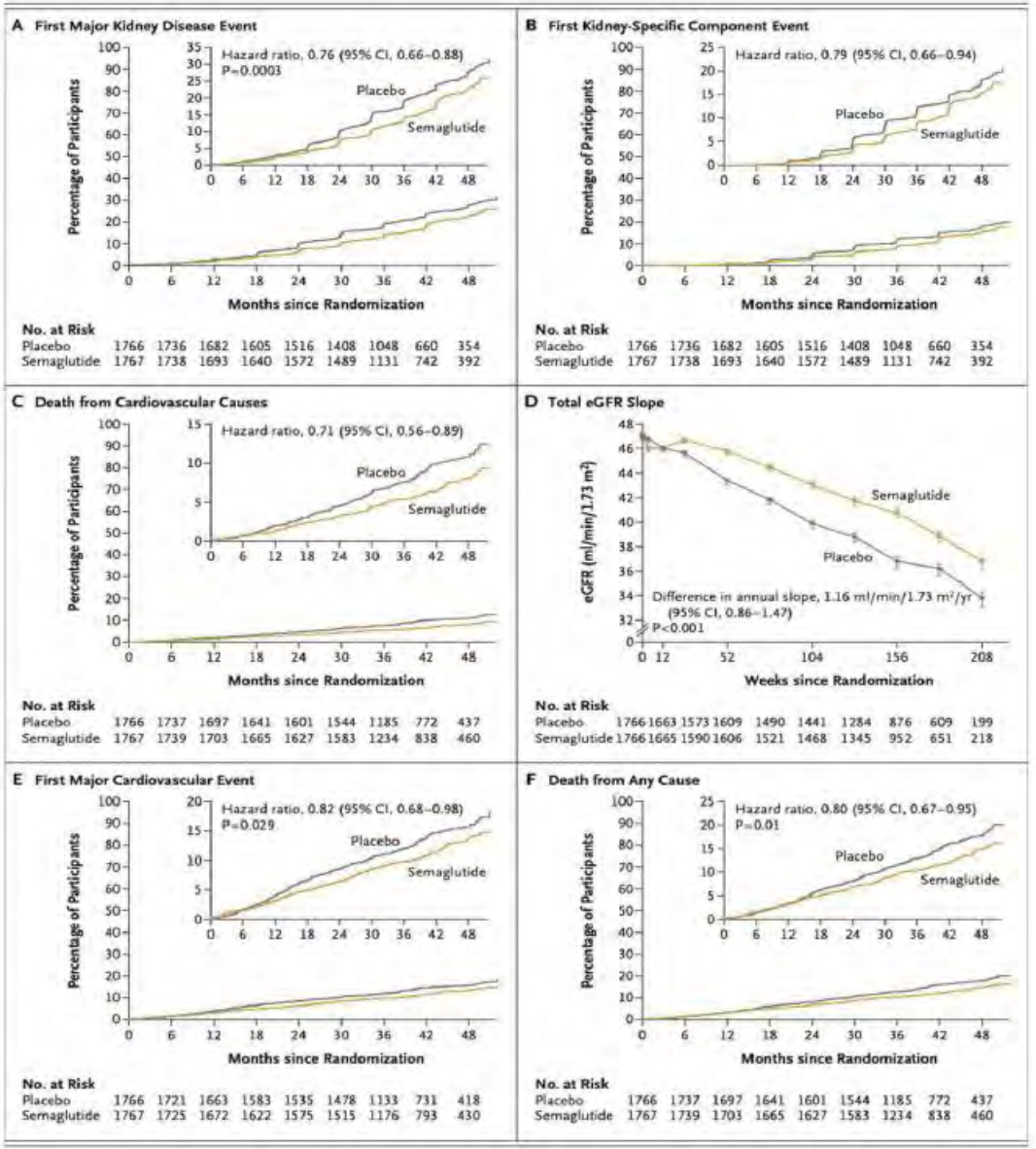
Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

Vlado Perkovic, M.B., B.S., Ph.D., Katherine R. Tuttle, M.D., Peter Rossing, M.D., D.M.Sc., Kenneth W. Mahaffey, M.D., Johannes F.E. Mann, M.D., George Bakris, M.D., Florian M.M. Baeres, M.D., Thomas Idorn, M.D., Ph.D., Heidrun Bosch-Traberg, M.D., Nanna Leonora Lausvig, M.Sc., and Richard Pratley, M.D., for the FLOW Trial Committees and Investigators*

GLP1 RA

3533 patients with type 2 diabetes, BMI 32, and CKD (eGFR of 50 to 75 ml/min/1.73 m2 and a uACR of >300 and <5000 mg/g) randomized to receive subcutaneous semaglutide at a dose of 1.0 mg weekly or placebo.

Primary outcome: major kidney disease events, a composite of the onset of kidney failure (dialysis, transplantation, or an eGFR of <15 ml/min/1.73 m2), at least a 50% reduction in the eGFR from baseline, or death from kidney-related or cardiovascular causes.



GLP1-RA

Pathway		GLP-1 RAs	Low-protein diet (LPD/VLPD)
Glomerular hemodynamics		Vasodilatory effects; ↓ inflammation	↓ nitrogen load; ↓ hyperfiltration
Albuminuria		Moderate ↓ albuminuria	↓ albuminuria in some trials (esp. VLPD +KAs)
Fibrosis / inflammation		Anti-inflammatory, anti-fibrotic (GLP-1R, NLRP3)	↓ profibrotic signaling; ↑ autophagy may help
CKD progression		Moderate evidence in diabetic CKD	Supportive evidence: slower CKD if balanced

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CKD progression		Moderate evidence in diabetic CKD	Supportive evidence: slower CKD if balanced
Clinical concerns		**GI side effects; sarcopenia risk**	**needs renal dietitian and close follow-up**

Take home messages

Renal diet and SGLT2-i may interact to improve renal hemodynamics, metabolism, electrolyte and fluid balance, and control of proteinuria, diabetes, and blood pressure.

As second line agents in diabetic CKD, nsMRAs and long-acting GLP1-RAs can be added to SGLT2-i or be an alternative option when SGLT2-i are controindicated or not tolerated.

A diet-drug integrated, synergistic approach, may be a good opportunity to maximize the metabolic and hemodynamic renal benefits of the two interventations.

Atena (Ἀθηνᾶ)o **Pallade Atena** (Παλλάς Ἀθηνᾶ): dea greca della sapienza, delle arti e della strategia in battaglia

Grazie per l'attenzione!