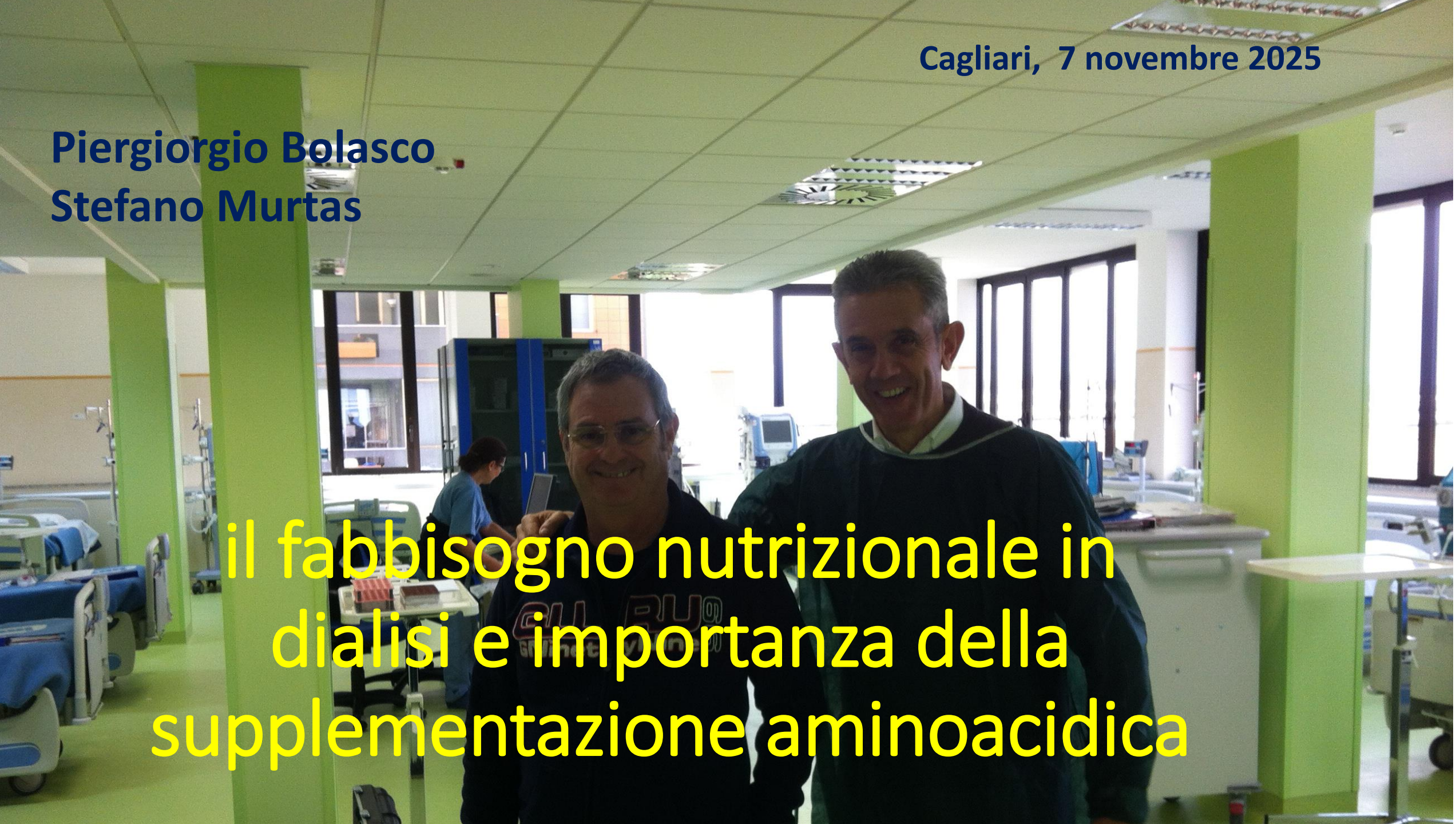
Cagliari, 7 novembre 2025

Piergiorgio Bolasco
Stefano Murtas



il fabbisogno nutrizionale in dialisi e importanza della supplementazione aminoacidica

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

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

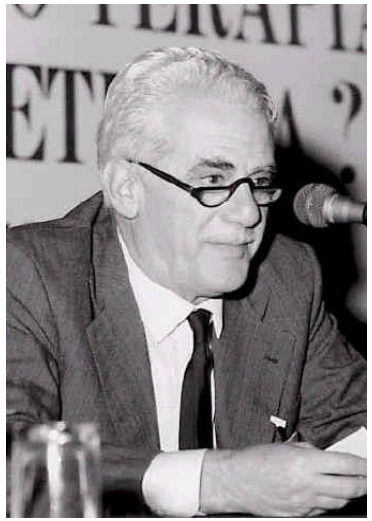
S. GIOVANNETTI
M.D. Pisa
SENIOR LECTURER IN MEDICINE

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-



Sergio Giovannetti

Quirino Maggiore

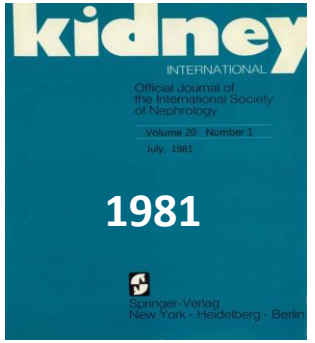
Lancet 1964

Effects on renal function of a low-nitrogen diet supplemented with essential amino acids and ketoanalogues and of hemodialysis and free protein supply in patients with chronic renal failure.
G Barsotti, A Guiducci, F Ciardella, S Giovannetti

Kidney International, Vol. 20 (1981), pp. 122–126

Evaluation of reduced dialysis frequency using nutritional therapy

WILLIAM E. MITCH and DANIEL G. SAPIR



Combined therapy for selected chronic uremic patients: infrequent hemodialysis and nutritional management.
Morelli E, Baldi R, Barsotti G, Ciardella F, Cupisti A, Dani L Mantovanelli A, Giovannetti S.

Ann. Rev. Med. 1984. 35: 249–64

THE INFLUENCE OF THE DIET ON THE PROGRESSION OF RENAL INSUFFICIENCY[1]

1984

William E. Mitch, M.D.

Department of Medicine, Harvard Medical School,
Brigham and Women's Hospital, Boston, Massachusetts 02115

Kidney International, Vol. 40 (1991), pp. 326–341

NEPHROLOGY FORUM

Dietary protein restriction in patients with chronic renal failure

Principal discussant: WILLIAM E. MITCH

Emory University School of Medicine, Atlanta, Georgia

1991

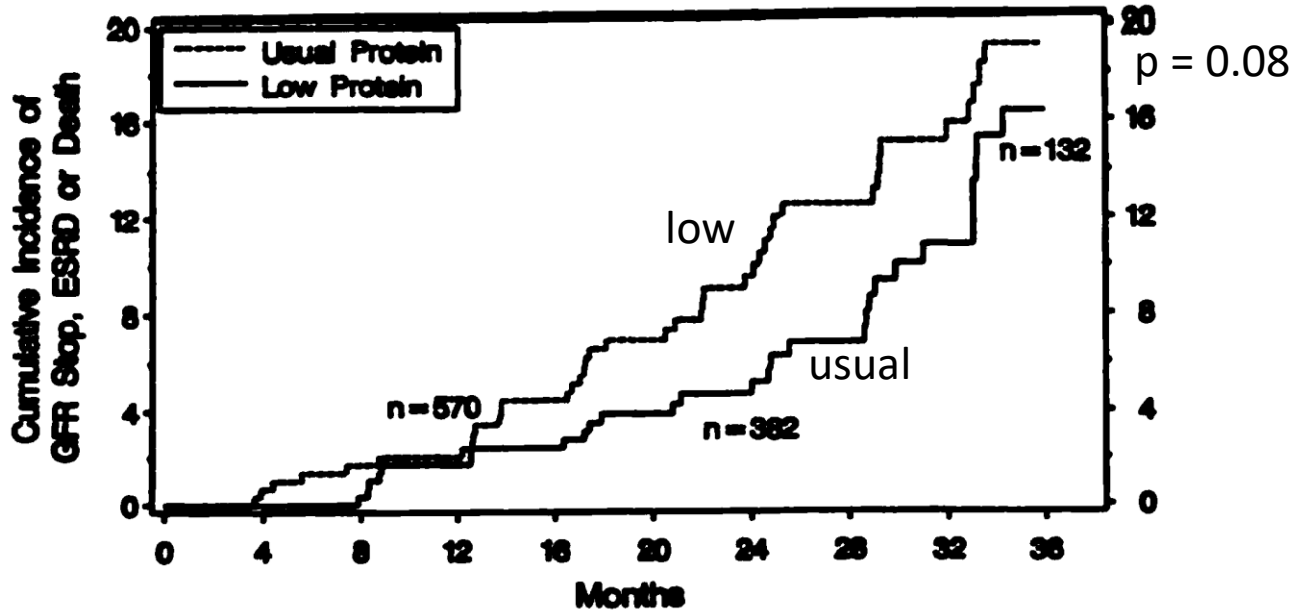
considered a disease by itself, similar to hypertension, which causes progressive destruction of blood vessels and other organs. Although a pathophysiologic basis for the nephrotoxicity of uremia is unknown, a relationship between progressive renal damage and the diet has been suspected for many years because kidney growth is related so closely to the amount of food eaten and because the accumulation of uremic toxins depends on food intake. As early as 1932, available data regarding this association led to the conclusion that, at least in experimental animals, some unidentified factor present in the diet was nephrotoxic (1). After a

[1] Supported by a RCDA (AM 00750) from the National Institutes of Health.

0066–4219/84/0401–0249$02.00

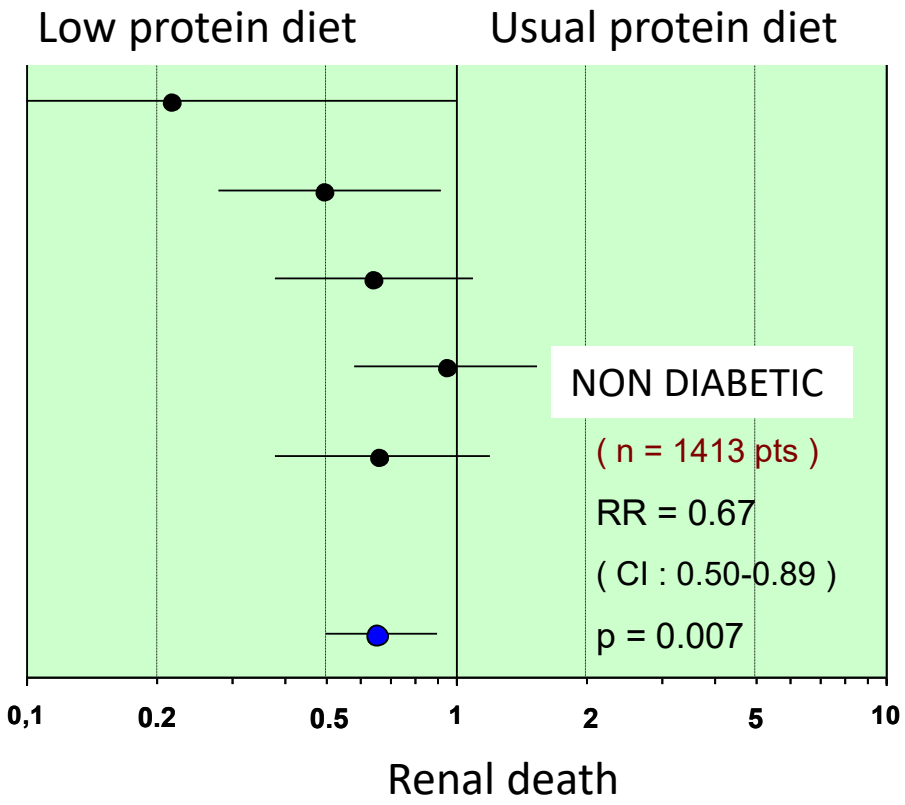
1990's the scenery was finally changing

Effects of Dietary Protein Restriction on the Progression of Moderate Renal Disease in the Modification of Diet in Renal Disease Study
(A.Levey, J. Am. Soc. Nephrol. 1996; 7:2616-2626



After 12 months these data are consistent with a **beneficial effect of the low-protein diet to slow the GFR decline** and to reduce urine protein excretion. These results provide some support for the hypothesis that dietary protein restriction slows the progression of moderate renal disease.

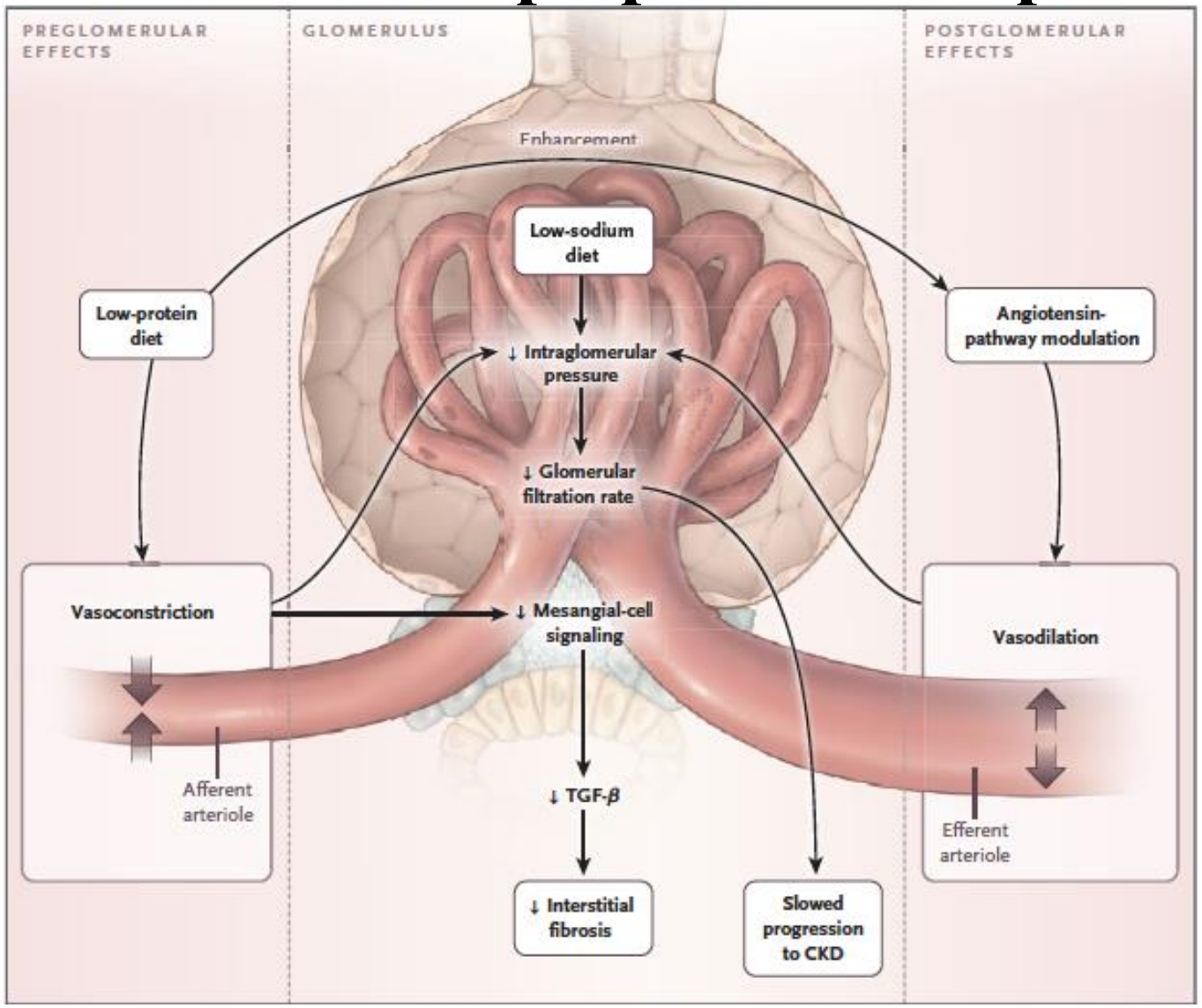
The Effect of Dietary Protein Restriction on the Progression of Diabetic and Nondiabetic Renal Diseases: A Meta-Analysis
Michael T. Pedrini, Ann Intern Med. 1996;124(7):627-632.



Data Synthesis: In five studies of nondiabetic renal disease, a low-protein diet significantly reduced the risk for renal failure or death (relative risk, 0.67)

[95% CI, 0.50 to 0.89]).
Conclusion: Dietary protein restriction effectively slows the progression of renal diseases.

Effetti della dieta ipo-proteica ed ipo-salina



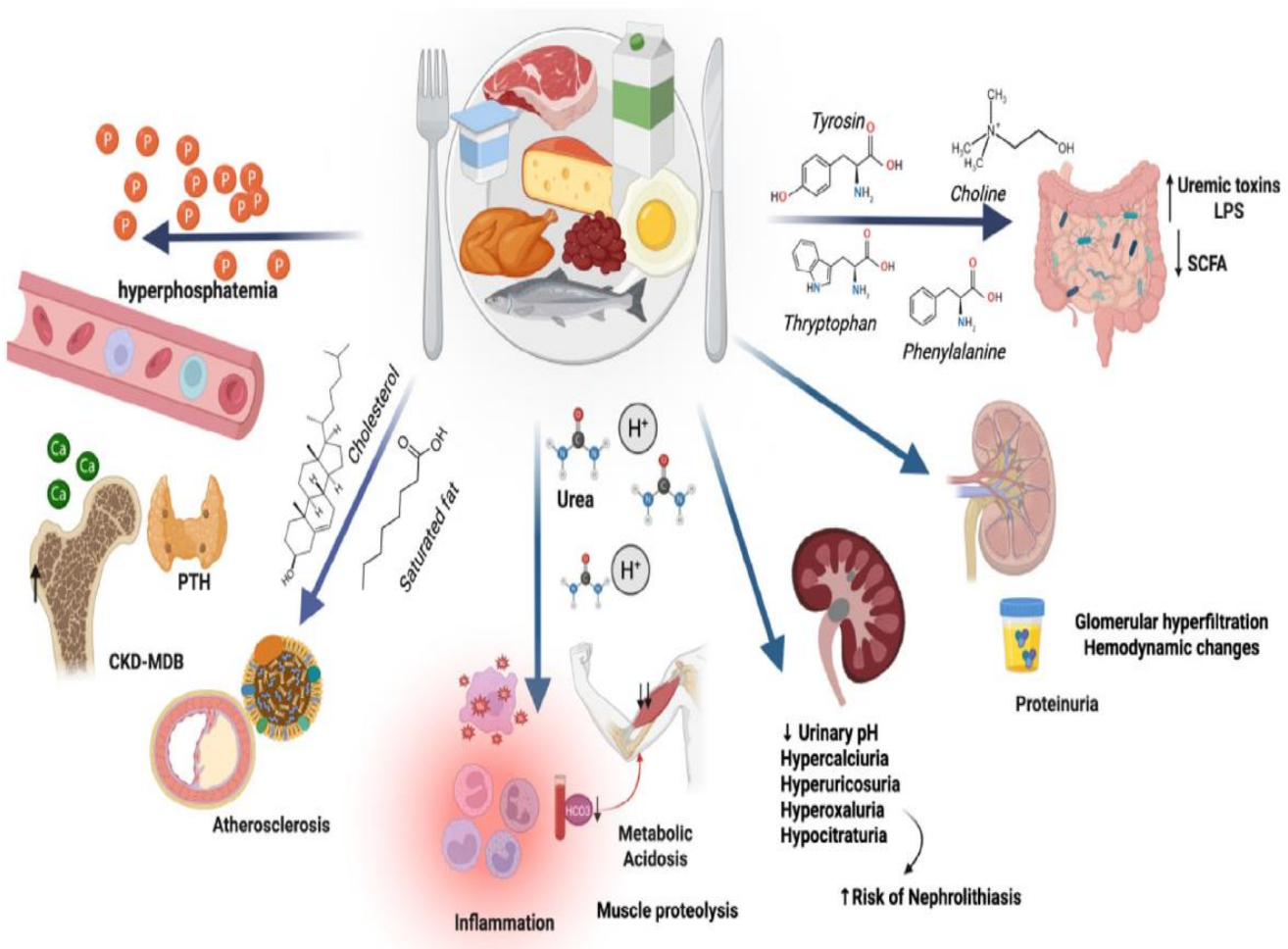
The NEW ENGLAND JOURNAL of MEDICINE

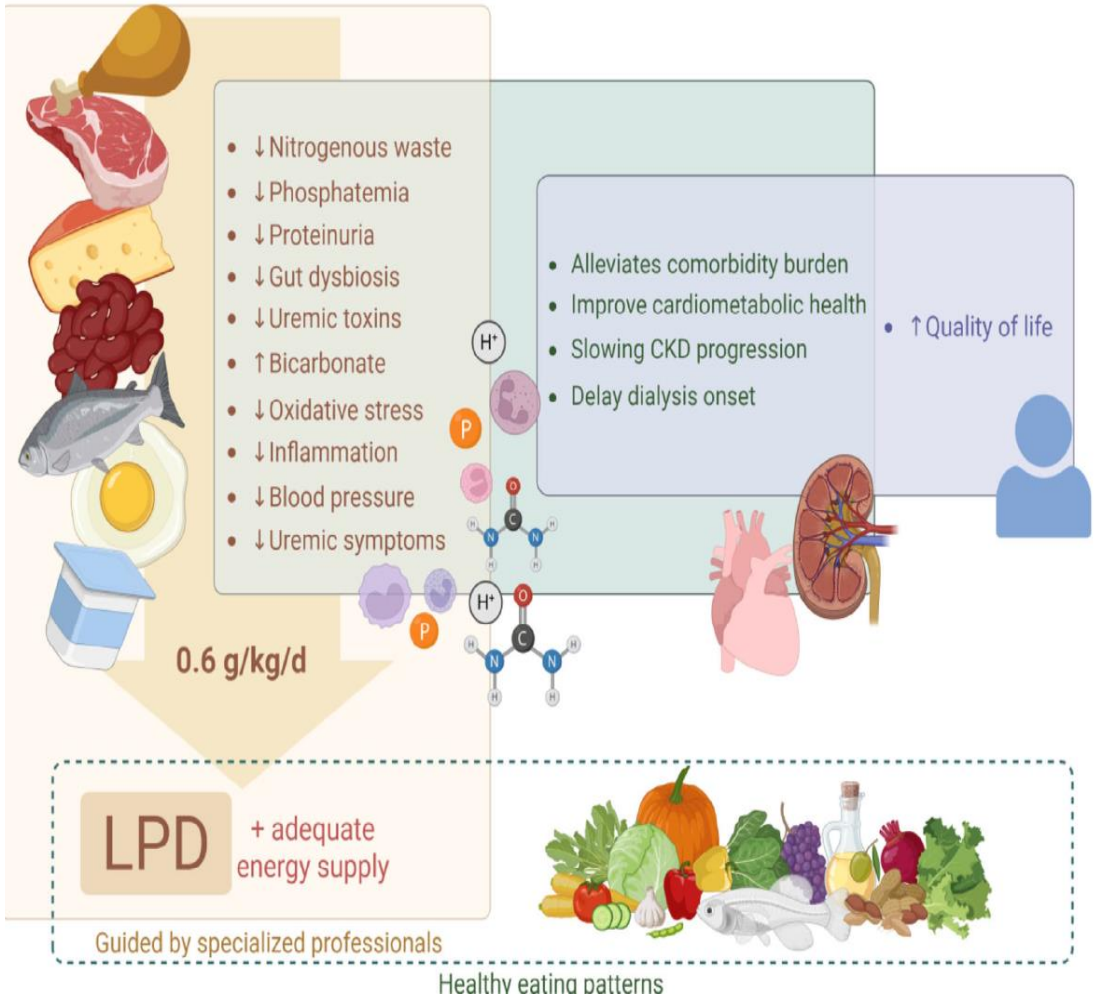
Kamyar Kalantar Zadeh and Denis Foque – November 2017

Low-protein diet for chronic kidney disease: Evidence, controversies, and practical guidelines

JIM LPD for non-dialysis CKD / D. Mafra et al.

J Intern Med. 2025





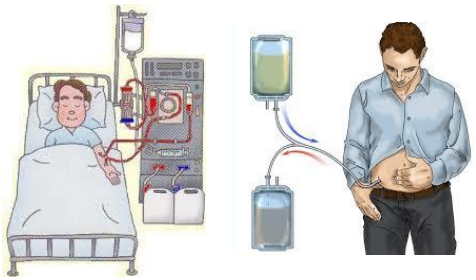
low molecular weight	Protein Bound Toxins	middle molecules
Asymmetric dimethylarginine	3-Deoxyglucosone	Adrenomedullin
Benzylalcohol	CMPF*	Atrial natriuretic peptide
ß-Guanidinopropionic acid	Fructoselysine	$ß_2$-Microglobulin
ß-Lipotropin	Glyoxal	ß-Endorphin
Creatinine	Hippuric acid	Cholecystokinin
Cytidine	Homocysteine	Clara cell protein
Guanidine	Hydroquinone	Complement factor D
Guanidinoacetic acid	Indole-3-acetic acid	Cystatin C
Guanidinosuccinic acid	Indoxyl sulfate	Degranulation inhibiting protein I
Hypoxanthine	Kinurenine	Delta-sleep-inducing peptide
Malondialdehyde	Kynurenic acid	Endothelin
Methylguanidine	Methylglyoxal	Hyaluronic acid
Myoinositol	N-carboxymethyllysine	Interleukin 1ß
Orotic acid	P-cresol	Interleukin 6
Orotidine	Pentosidine	Kappa-Ig light chain
Oxalate	Phenol	Lambda-Ig light chain
Pseudouridine	P-OHhippuric acid	Leptin
Symmetric dimethylarginine	Quinolinic acid	Methionine-enkepahlin
Urea	Spermidine	Neuropeptide Y
Uric acid	Spermine	Parathyroid hormone
Xanthine		Retinol binding protein
Tumor necrosis factor alpha		

...and phosphates!

EUTox
European Uremic Toxin Work Group of the ESAO

Vanholder R. et al., *Kidney Int.* 2003

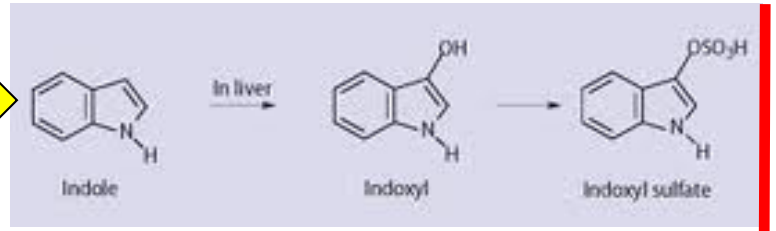
Protein Bound Uremic Toxins : PBUTS



Migliori metodiche emodialitiche
Dialisi peritoneale

Eliminazione
30-40%

INDOXYL SULPHATE

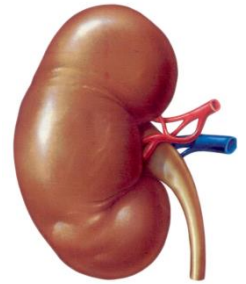


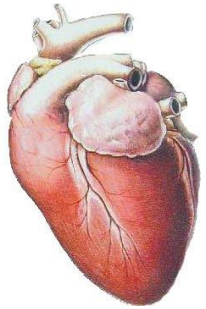
P-CRESOLO

Diuresi

Eliminazione
60-70%

Main Targets





per il Nutrizionista «renale»

CKD Stage 5D

a. Riduzione dell' l'intake di sale (specie in caso di ipertensione arteriosa);

a. Limitare il consumo di frutta e tutti i vegetali compatibilmente con i livelli di potassiemia;
b. Considerare perdita di peso in caso di over weight;
c. Ridurre l'introduzione di grassi saturi;
d. Privilegiare i migliori grassi insaturi;
e. Prescrizione proteica 0,4 - 1,2 g/kg/die;
f. Limitazione alimenti fosforici;
g. Assicurare un'intake calorico minimo di 25-30 Kcal/kg/die
h. Obbligatorio l'utilizzo di supplementi a base di aminoacidi

FLESSIBILITA' PERSONALIZZATA!

Trattamento sostitutivo da considerare con G.F.R. 5 -10 mL/min/1,73 m^2

Il piano terapeutico va personalizzato secondo la frequenza delle sedute di emodialisi, la RKF (funzione renale residua), l'antropometria del paziente……

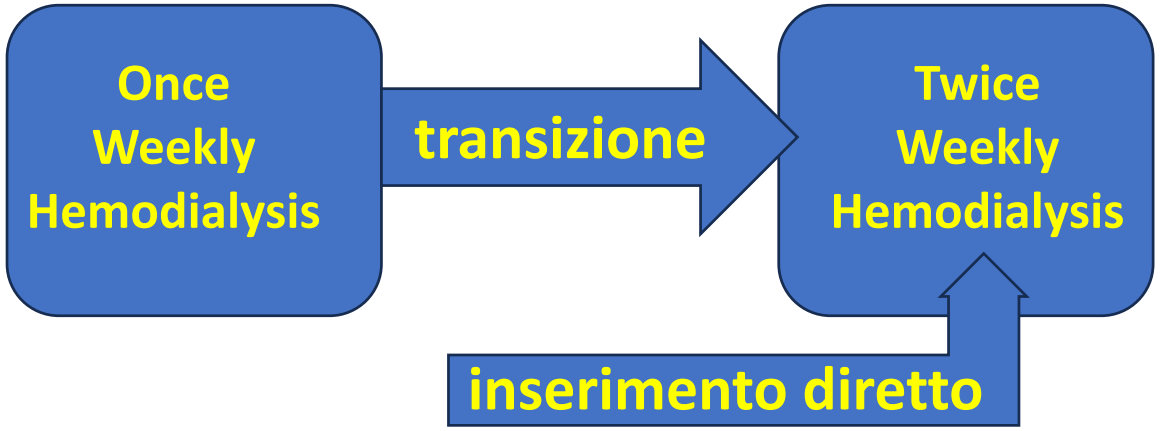
Questi concetti devono essere sostenuti anche dall'infermiere di sala dialisi

NUTRIZIONE E DIALISI INCREMENTALE

Questi programmi sono indicati nei pazienti che provengono dall'ambulatorio pre-dialisi e/o in pazienti selezionati che assicurano una ottima collaborazione ed aderenza duratura alla dieta ipoproteica

+

L'EMODIALISI INCREMENTALE (IH)



CPE Dietary Management of Incremental Transition to Dialysis Therapy: Once-Weekly Hemodialysis Combined With Low-Protein Diet

Piergiorgio Bolasco, MD, Adamasco Cupisti, MD,† Francesco Locatelli, MD, PhD,‡ Stefania Caria, MD,* and Kamyar Kalantar-Zadeh, MD, MPH, PhD§*

Journal of Renal Nutrition, Vol 26, No 6 (November), 2016: pp 352-359

Table 1. Different Feature Recommendations Between Twice-Weekly Dialysis and CDDP

Twice-Weekly Dialysis [21]	CDDP
1) Residual kidney function 5-10 mL/min/1.73 urine output >0.5 L/	1) Residual kidney function 5-10 mL/min/1.73 and urine output >0.8-1.0 L/day
2) No signs of water retention or responsive to diuretic therapy; fluid interdialytic gain <5% of ideal dry weight	2) No signs of water retention or responsive to diuretic therapy; fluid interdialytic gain <5% of ideal dry weight
3) Limited or readily manageable cardiovascular or pulmonary symptom	3) Limited or readily manageable cardiovascular or pulmonary symptoms
4) Suitable larger body size relative to residual kidney function	4) Excluded patients with BMI >35
5) Infrequent and readily manageable hyperkalemia (>5.5 mEq/L) and/or hyperphosphatemia (P > 5.5 mg/dL)	5) Infrequent and readily manageable hyperkalemia (>5.5 mEq/L) and/or hyperphosphatemia (P > 5.5 mg/dL)
6) Good nutritional status without florid hypercatabolism	6) Good nutritional status without any signs of hypercatabolism; adherence to nutritional therapy: low-protein (0.6 g/kg/day), low-phosphorus, high energy diet
7) Lack of profound anemia (Hb > 8) and appropriate responsiveness to anemia therapy	7) Mild anemia (Hb > 9-10) and appropriate responsiveness to anemia therapy
8) Infrequent hospitalization and easily manageable comorbid conditions	8) Infrequent hospitalization and easily manageable comorbid conditions
9) Satisfactory health-related quality of life	9) Satisfactory health-related quality of life
	10) Good dialytic adequacy: eqKt/V ≥ 1.2, session duration ≥ 4 hrs
Implementation Strategies	**Implementation Strategies**
To initiate and maintain 2xW/HD, the patient should meet first criteria plus 5 of 9 of other criteria	To initiate and maintain 1xW/HD, the patient should meet all criteria
Examine these criteria every months	Checking these criteria every week; twice-monthly calculating urea nitrogen appearance
Consider transition from 2X/w to 3X/W HD regimen in case of oligoanuria, malnutrition signs, and deteriorating general health	Consider immediately transition from 1X/W to 2-3X/W HD regimen in case of oligoanuria or malnutrition signs or general health deterioration
	Free acetate dialysate, synthetic membranes

BMI, body mass index; CDDP, Combined Diet Dialysis Program.

3-5 mL/min/1.73 m^2

Urine output >500-800 L/die

mandatory amino acids supplement

Mantain good dialytic adequacy

Biocompatible membranes

nutrients

MDPI

Review

Incremental Hemodialysis: Review of Clinical Trials Focused on Patients Undergoing Once-Weekly Hemodialysis

Piergiorgio Bolasco

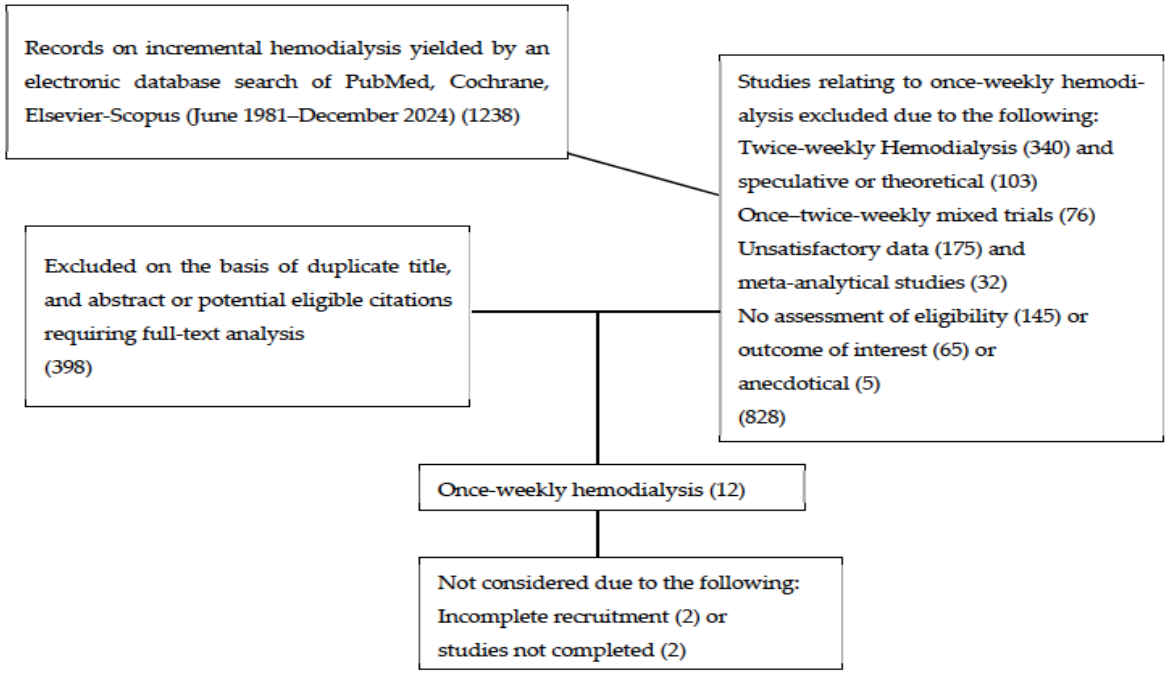


Figure 1. Flowchart of selected studies assessed to identify once-weekly hemodialysis trials.

Su 1238 studi, considerando come key di ricerca il termine “Incremental Hemodialysis”, solo 8 studi hanno sviluppato e completato il trial.

Once-weekly-hemodialysis: completed studies – 1981-2016

Study and location, methodology	recruited patients (M/F)	age of recruited patients, years	Residual Kiney Function at start, mL/min/1.73m^2	Average daily urine volume at start, mL	Average daily urine volume at the end, mL	Method for GFR measurement	Prescribed hypoproteic diet, nutritional supplement	duration of study, months	Prescribed Kt/V	Total drop-out, %	mortality, n. %	Cumulative survival at the end of the study	advantages and/or disadvantages
Mitch WE et Al - 1981 USA Cross-over	**7** (5/2)	45	3.43 ± 0.98	n.r.	n.r.	average urea/creatinine clearances	0.4 g/kg + 10 g/day EAAs	**3**	n.r.	28%	n.r.	71.4%	n.r.
Morelli E et Al. - 1987 Italy Prospective	**17** (14/3)	48.5±11.8	2.0	1529±420 (mediana: 1450)	682±426 (mediana: 500)	average creatinine clearances	0,3 g/kg + EAAs and keto-analogues	18.2±17.7 **(mediana:11)**	n.r.	76,6%	5,90%	17.5%	- reduction of TAC of urea, phosphate and serum methylguanidine - lower costs
Locatelli F. et Al - 1994,1998 Italy Prospective	**69**	61±3	2,46±0,9	n.r.	n.r.	average urea/creatinine clearances	0.4 g/kg + EAAs and/or ketoanalogs	**24**	spKt/V 1.2	66,60%	n.r.	24.6%	sintomi di malnutrizione ed uremia
1WHD *Caria S et Al.* - 2014 *Bolasco et Al.* - 2016 Italy Prospective	**38** (25/13)	64.5±13.2	7,8±1,9 (median: 6.2)	1983±651	1875±315	average urea/creatinine clearances	0,6g/kg + EAAs+NEAAs. free diet on the dialysis day	**24**	eqKt/V > 1,2	41,90%	3 (7.9%) cardiac events	49.8%	**ONLY IN ONCE-WEEKLY-HD** - manteinance good nutritional condition - reduction EPO dosage - reduction of phosphate binders dosage - reduction of calciomimetic drugs - decrease of C-Reactive Protein - better psychological adaptation - slowing RKF decline - 50% cost saving
3WHD	**30** (19/11)	65.2±11	9.2±4.2 (median: 6.8)	1472±133	<200 at 6th month	average urea/creatinine clearances	1,2 g/kg/day		eqKt/V>1.2	none	10,40%	86.8%	

Once-weekly-hemodialysis: completed studies – 2018-2025

Study and location, methodology	recruited patients (M/F)	age of recruited patients, years	Residual Kiney Function at start, mL/min/1.73m^2	Average daily urine volume at start, mL	Average daily urine volume at the end, mL	Method for GFR measurement	Prescribed hypoproteic diet, nutritional supplement	duration of study, months	Prescribed Kt/V	Total drop-out, %	mortality, n. %	Cumulative technical survival at the end of the study	advantages and/or disadvantages
Nakao et Al. - 2018 Japan Prospective	**112** (80/32)	(median: 63)	3.8±0,8	n.r.	n.r.	creatinine clearances	0,6 g/kg salt intake 6 g/day	**24**	spKt/V 1.2-1.4	75,9%	11,6%	12.5%	
Takkavatakarn - 2021 Thailand Prospective	**11** (7/4)	64.4±15.1	5,1±4,0	n.r.	n.r.	average urea clearance	inter-dialysis days 0.6-0.8 g/kg/day dialysis day 1.2 g/kg/day	**9,7**+6,9	spKt/V≥1,2	75,40%	n.r.	n.r.	better quality of life
1WHD *Torreggiani M et Al.* - 2022 France	**30** (17/13)	69.3±14.2 (mediana: 67.5)	9.1±6.2 (median: 8)	1800±706 (median: 1850)	(median: 1825)	CKD-EPI	0.6-0.8 g/Kg/d	**17.2**±10.8 (median:14)	spKt/V≥1,2	53,20%	2 /6.6%)	43.2%	saving costs on 1WHD
3WHD	**67** (38/29)	(65.9±13.2) (median:67)	9.8±3.9 (median:5.85)	937 ± 641 (median: 900)	(median: 100)		n.r	**24.2**±14.9 (median: 28.5)	n.r.	88%	13,40%	0%	
1WHD *Praditpornsilpa K. et Al* - 2024 *Kittiskulnam et Al.* 2025 Thailand. open-label, randomized controlled	**15**	58±19.3	6.9±1.4	2226±743	1738±744	CKD-EPI	Interdialytic day 0,6 g/kg + ketoanalogues 1.0-1.2 dialysis day	**12**	spKt/V≥ 1.2	33.3%	none	33.3%	n.r.
2WHD	**15**	61.9±16.8	6.2±1.9	1690±986	878±464		1.0-1.2 g/kg			none	none	100%	- slowing RKF decline in once-weekly haemodialysis compared to twice-weekly haemodialysis - saving costs

si può notare dal 2014 il progressivo abbandono, nella Once-Weekly-Hemodialysis, della Very-Low-Protein-Diet (0,4/kg/die) verso la Low Protein Diet (0,6g/kg/die).

Caria et al. BMC Nephrology 2014, 15:172
http://www.biomedcentral.com/1471-2369/15/172

BMC Nephrology

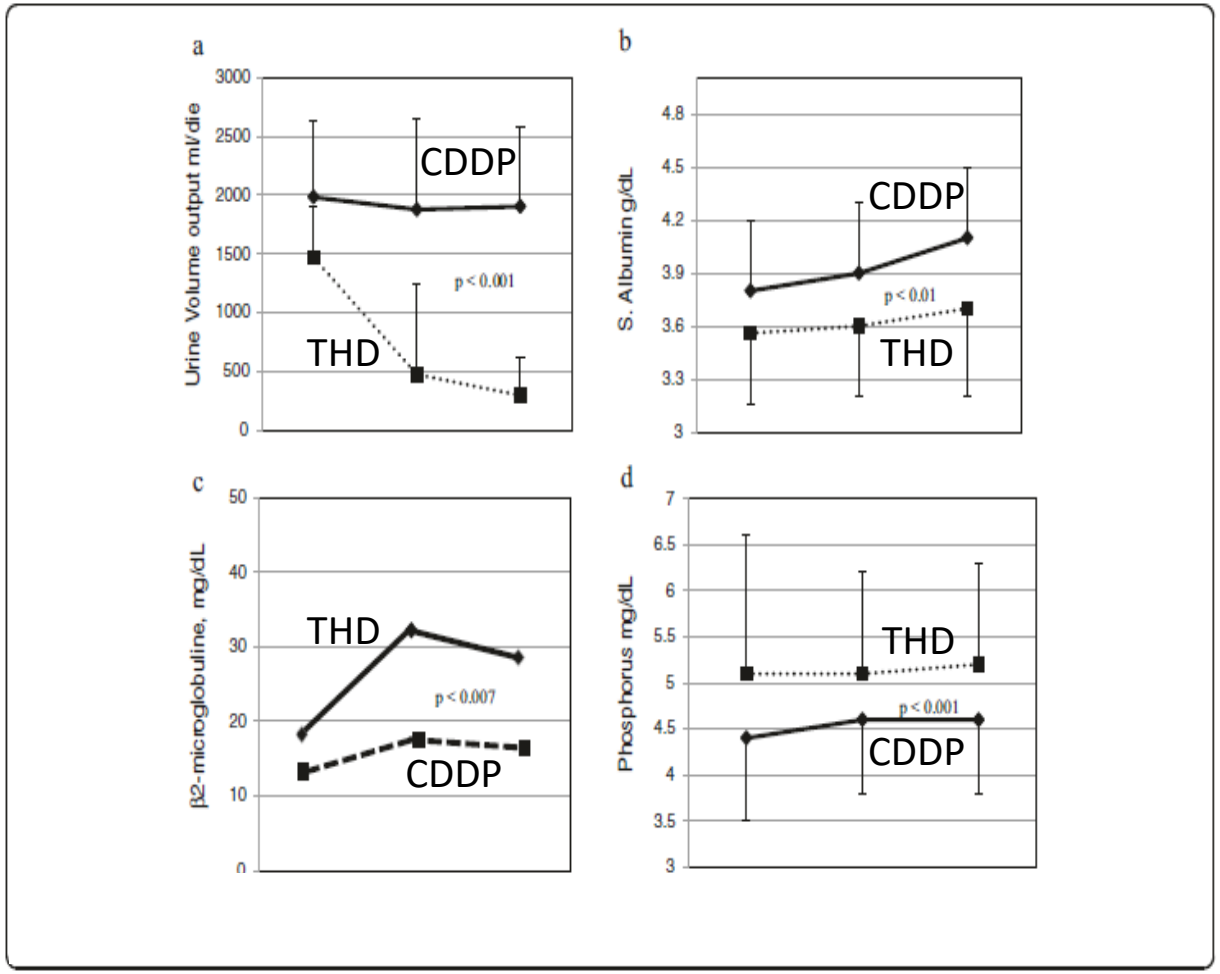
RESEARCH ARTICLE Open Access

The incremental treatment of ESRD: a low-protein diet combined with weekly hemodialysis may be beneficial for selected patients

Stefania Caria[1*], Adamasco Cupisti[2], Giovanna Sau[3] and Piergiorgio Bolasco[1]

Table 1 Baseline characteristics of the studied groups

	CDDP group (n = 38)	THD group (n = 30)	p
Male/females	25/13	19/11	
Age, years	64.5 ± 13.2	65.2 ± 11	*0.82*
Body weight (kg)	65.5 ± 15.1	66.2 ± 11.9	*0.73*
BMI (kg/m^2)	23.7 ± 4.0	25.6 ± 4.13	*0.03*
Urine volume output (mL/24 h)	1983 ± 651	1472.6 ± 433	*<0.001*
GFR (mL/min × 1.73 mq b.s)	7.8 ± 1.9	9.2 ± 4.2	*<0.01*
EPO (IU/kg/week)	104 ± 108	184 ± 84	*<0.001*
CRP <5 mg/dl, %	89	66.6	*<0.01*
iPTH, >300 pg/mL, %	31.5	50	*<0.01*
Charlson comorbidity index score	5.5 ± 2.5	3.8 ± 2.5	*0.004*
Charlson comorbidity index score >4, %	62.5	33.3	*<0.01*

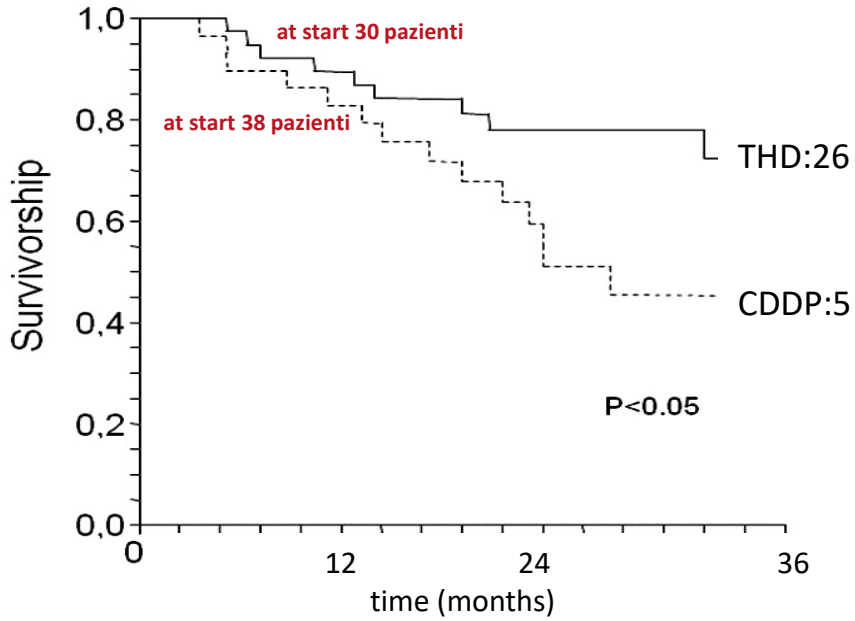


THD: patients on thrice weekly conventional hemodialysis. - CDDP: Combined Diet Dialysis Programme on Once-Weekly Hemodialysis

CPE Dietary Management of Incremental Transition to Dialysis Therapy: Once-Weekly Hemodialysis Combined With Low-Protein Diet

Piergiorgio Bolasco, MD, Adamasco Cupisti, MD,† Francesco Locatelli, MD, PhD,‡ Stefania Caria, MD,* and Kamyar Kalantar-Zadeh, MD, MPH, PhD§*

Journal of Renal Nutrition, Vol 26, No 6 (November), 2016: pp 352-359



3 kidney tranplant; 15 decline of RKF –> twice-thrice; 5 no diet adherence; 2 excess interdialytic weight; 2 high blood pressure recurring; 3 died; 3 recovery of RRF

Stepwise Incremental Hemodialysis and Low-Protein Diet Supplemented with Keto-Analogues Preserve Residual Kidney Function: A Randomized Controlled Trial †

nutrients

Kittskulman P et al. July 2025 (Thailand)

ESKD patients with an eGFR of 5–10 mL/min/1.73 m^2 and urine output of ≥800 mL/day were randomly assigned to receive either once-weekly HD (1-WHD) or twice-weekly HD (2-WHD) for 12 months. Patients in the 1-WHD group were prescribed once-weekly HD combined with low-protein diet (0.6 g/kg/day) supplemented with keto-analogues (KAs) 0.12 g/kg/day. In the 2-WHD group, patients received twice-weekly HD with a regular-protein diet. Primary outcomes were changes in RKF by renal clearance and urine volume.

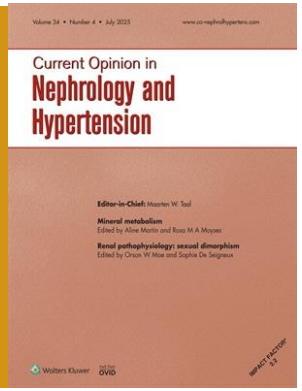
Completed study 15 patients in once-weekly-HD and 15 patients in twice-weekly-HD

	Month 3			Month 6			Month 9			Month 12		
	1-WHD Group	2-WHD Group	*p*	1-WHD: Group	2-WHD Group	*p*	1-WHD: Group	2-WHD Group	*p*	1-WHD: Group	2-WHD Group	*p*
Urine CUrea (mL/min)	3.8 ± 2.9	2.2 ± 1.0	0.06	3.2 ± 2.3	1.7 ± 1.0	0.03	2.9 ± 2.3	1.5 ± 0.6	0.03	3.3 ± 2.3	1.5 ± 1.0	0.01
Urine CCr (mL/min)	7.6 ± 6.4	6.1 ± 5.1	0.48	5.9 ± 3.6	3.8 ± 1.4	0.04	4.4 ± 1.8	3.1 ± 1.1	0.03	4.6 ± 1.9	2.5 ± 1.2	0.01
Urine volume (mL/day)	1921 ± 767	1305 ± 599	0.02	1859 ± 775	918 ± 468	<0.01	1645 ± 652	926 ± 411	<0.01	1738 ± 744	878 ± 464	<0.01
nPCR (g/kg/day)	0.89 ± 0.22	1.08 ± 0.27	0.04	0.83 ± 0.22	1.09 ± 0.25	0.01	0.90 ± 0.24	1.05 ± 0.31	0.15	0.86 ± 0.20	1.10 ± 0.23	0.01

Twice-weekly-hemodialysis

Precision Medicine in End-Stage Kidney Disease and Personalized Renal Replacement Therapy
Hamid Moradi, MD, and Kamyar Kalantar-Zadeh, MD, MPH, PhD, Guest Editors
July 2018 Volume 38 - Issue 4p315-432

Incremental hemodialysis transition in veterans and nonveterans with kidney failure
Rhee, Connie, M. Kovesdy, Csaba P., Unruh, Mark; Crowley, Susan; Geller, David; Goldfarb, David S.; Kraut, Jeffrey; Rastegar, Mandana; Rifkin, Ian R.; Kalantar-Zadeh, Kamyar
Current Opinion in Nephrology and Hypertension 34(1):p 33-40, January 2025.



Ten criteria:
1. daily urine volume ≥ 600;
2. (Kru) of at least 3 ml/min;
3. intradialytic weight gain 2,5 Kg
4. stable cardiovascular status;
5. infrequent hospitalization;
6. satisfactory health-related QoL;
7. small to normal body size;
8. good nutritional status;
9. absence of hyperkalemia, and hyperphosphatemia
10. profound anemia

Murea, Mariana; Kalantar-Zadeh, Kamyar – cJASN – 2021

North Carolina, California

La dialisi bi-settimanale conserva il vantaggio di preservare la funzione renale residua (RKF)

- ✓ **Riduzione della mortalità**: tassi di mortalità più bassi, sia per cause cardiovascolari che per tutte le cause.
- ✓ **Miglior protezione cardiovascolare:** livelli più bassi di biomarcatori cardiaci come NT-proBNP e troponina T, indicando una migliore funzione cardiaca e una minore ipertrofia ventricolare sinistra, riduzione delle resistenze periferiche
- ✓ **Equilibrio elettrolitico:** livelli più stabili di potassio, sodio, calcio e fosfati, riducendo il rischio di iperfosfatemia e iperkaliemia. Diminuzione FGF-23
- ✓ **Controllo dell'idratazione:** prevenzione e minor incidenza sul sovraccarico di liquidi, migliorando il bilancio idrico e riducendo episodi di ipotensione durante le sessioni di emodialisi.
- ✓ **Miglior stato nutrizionale:** migliore massa magra e indice di massa magra
- ✓ **Gestione dell'anemia:** minor utilizzo di agenti stimolanti l'eritropoiesi.
- ✓ **Riduzione dell'infiammazione:** più bassi di marcatori infiammatori
- ✓ **Riduzione β2-microglobulina**: all'outup medio HD/HDF sia in one week and two weeks-HD si aggiunge l'output urine.

Se a questo si aggiunge una dieta ipoproteica si ottengono ulteriori vantaggi:

- ❑ **Protezione del GFR**: I pazienti che seguono una dieta a basso contenuto proteico hanno mostrato un rallentamento della velocità di progressione della RKF (MD = 1,37 ml/min; 95% CI: 0,18–2,55).
- ❑ **Effetto maggiore nei pazienti con GFR iniziale basso**: I pazienti con un GFR di base inferiore a 4 ml/min hanno beneficiato maggiormente, con una riduzione più lenta del declino della funzione renale.

Numerosi autori hanno confermato queste osservazioni:

- *Murea M. et Al. KI – 2025 – (comprehensive recommendations with RKF)*
- *Belcher J et Al. Kidney360 – 2025 (BISTRO trial)*
- *Campo A et Al. J Nephrol – 2025 (and save money)*
- *Aoun M. et Al. BMC Nephrology 2025 (twice = thrice survival)*
- *Torreggiani et Al. J Nephrol 2022 – (Le Mans Style)*
- *Garofalo et A. J Nephrology 2018 – (review on 12 patients in twice HD)*
- *…….*

L'importanza di preservare la RKF e una buona diuresi in once/twice-weekly-hemodialysis protocol: PBUTs e fosfati.

Anche l'eliminazione delle Protein-Bound Uremic Toxins nei pazienti in emodialisi è maggiormente garantita dalla Funzione Renale Residua/diuresi ed è scarsamente implementata dall'emodialisi con un non significativo implemento utilizzando metodiche emodialitiche che privilegiano il trasporto convettivo (HDF-post ad alti flussi, emofiltrazione on-line);

van Gelder KM et Al - Toxins – 2020; **PBUTs**

Phosphates

Hemodialysis sessions/week	phosphate intake, g/week (seven days)	average output HD, weekly sessions	phospate binder adsorption (-25%), g/week	phosphaturia, g/week	posphate balance, g/week
Thrice-weekly High Efficiency	9.38	2.30 ± 0.36	7.03	-	**+ 4.73**
Thrice-weekly post-HDF	9.38	2.47 ± 1.05	7.03	-	**+ 4.66**
Thrice-weekly post-HDF	9.38	3.06 ± 1.10	7.03	-	**+ 3.97**
Twice-weekly (°°)	5.82	3.6 (°)	4.37	1.14 (°°)	**- 0.37**
Once-weekly	4.8	1.8 (°)	3.6	2.18 (°°°)	**- 0.38**

Bolasco P, Murtas S. Panminerva Med. 2017 Jun;59(2):133-138.

Schematic Differences Between the Combined Diet Dialysis Program (CDDP) undergoing once-weekly-hemodialysis and the twice-and thrice Weekly Hemodialysis schedule Relative Level of Impact on the Item: **+ Low, ++ Middle, +++ High**			
	once a week	**twice a week**	**thrice a week**
Nutritional protein support	**0.6**	**0.8**	**≥1.2**
Protein intake (g/kg/day	30-35	30-35	30-35
Energy Intake Kcal/kg/day	+	++	+++
Vascular Access stress	**+**	**++**	**+++**
Protection of Residual Kidney Function	+++	++/+	+
Phophatemia Control	+++	++	+
Accomodation of dialysis schedule	+++	++	+
Clinical involvement: doctors, nursess	**+++**	**++**	**++**
Evaluation of weekly depurative efficacy	**+++**	**++**	**++**
Cost burden	**+++**	**++**	**+**
Protein Bound Uremic Toxins output	+++	++	+
Amino Acids Loss	+	++	+++

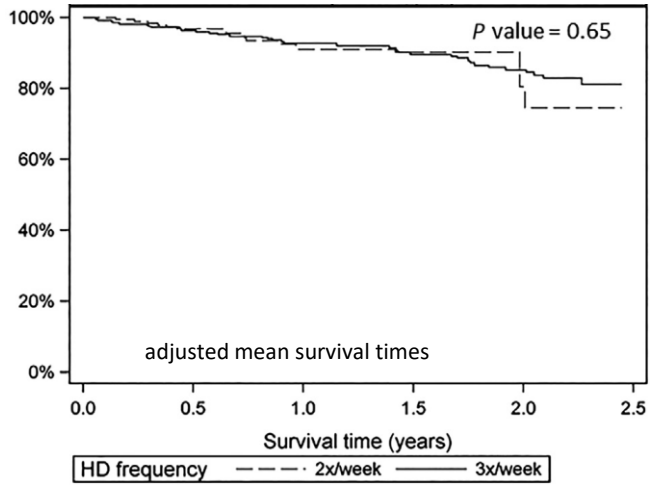
KI REPORTS
KIReports.org

Twice-Weekly Hemodialysis and Clinical Outcomes in the China Dialysis Outcomes and Practice Patterns Study

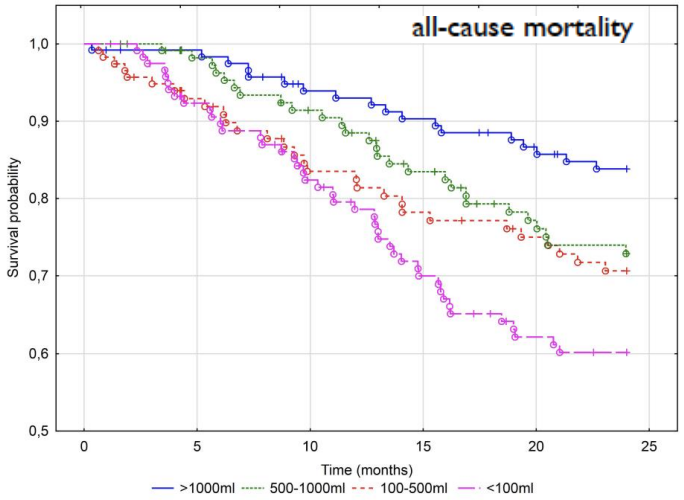
Yan Y et Al – Shangai - 2018

Il 25% di pazienti in HD in China effettuano la Twice-weekly-hemodialysis

Twice-HD: 133/1265 senza RKF (10,5%);
Thrice-HD 893/1265 senza RKF ; (71%);
nPCR: 06-07 g/kg/die
Dieta: iposalina,ed ipoproteica non specificate

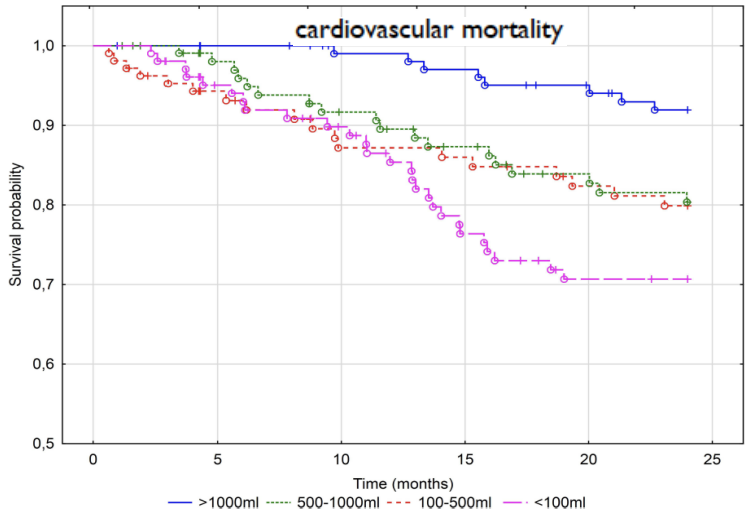


Ma uno degli elementi fondamentali per la sopravvivenza è il mantenimento il più a lungo possibile della RKF



485 pazienti

2023

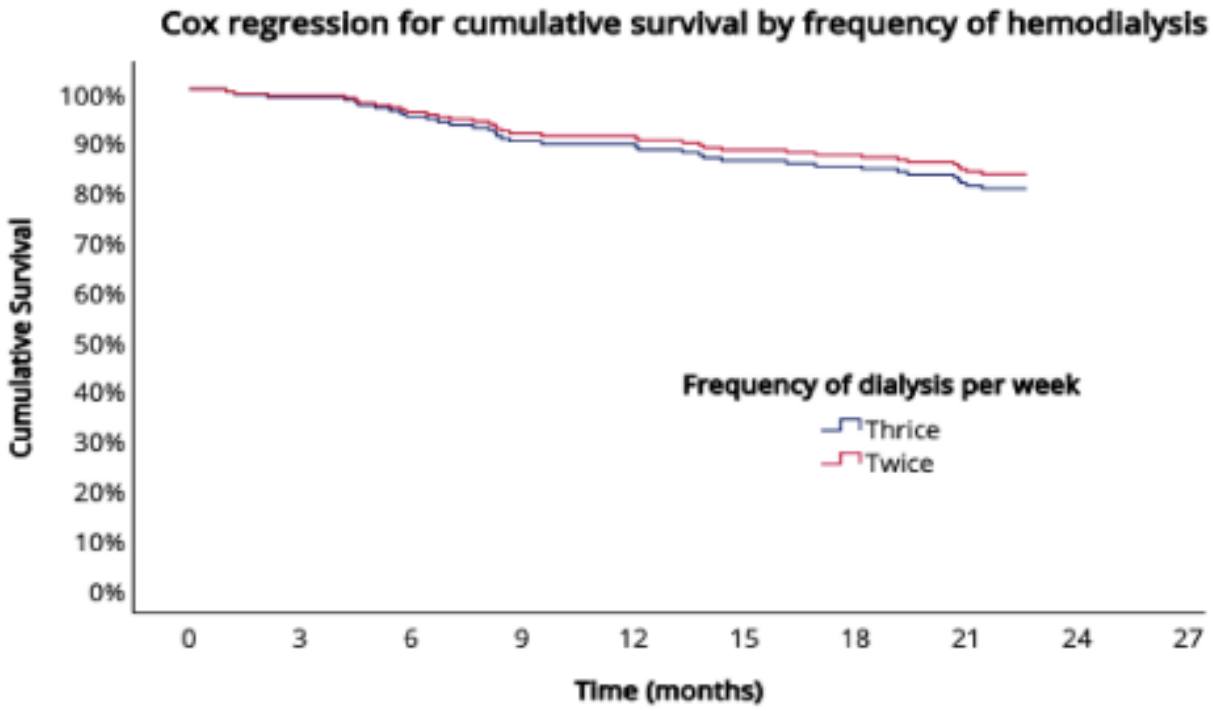


La RKF è stata calcolata dalla media della (KrCrs + KBUN)

International Journal of Nephrology and Renovascular Disease 2023:16

Dopierala M et Al. – Poland – International Journal of Nephrology and Renovascular Disease 2023

Twice against thrice-weekly hemodialysis (TATH): a multicenter nonrandomized trial



Number at risk

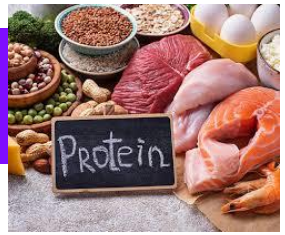
Twice	71	71	70	68	65	56
Thrice	132	130	129	123	114	101
Months	0	1	3	6	12	24

Maggiore richiesta di Epo in twice. Nessun dato su sintomatologia, nessuna indicazione nutrizionale

Aoun M. et Al – BMC Nephrology - 2025


AMINOACIDI

La necessità di una supplementazione aminoacidica nell'insufficienza renale cronica in terapia conservativa



- La necessità di aminoacidi indispensabili **(IAAs)** è di **0.184 g/kg/die**
- Nei pazienti in emodialisi convenzionale: in una prescrizione di proteine di 1.2 g/kg/die la quantità acquisita di amino acidi soprattutto essenziali è > 69%;

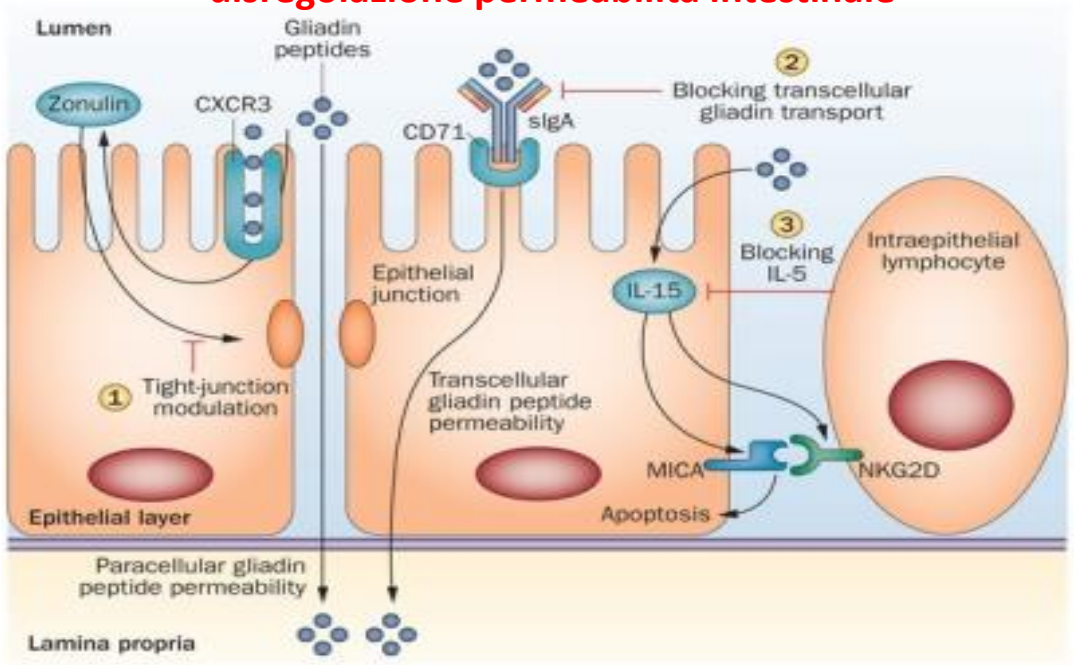
  - con dieta ipoproteica di **0.6 g/kg/die si riduce al 27-30%;**

  - con una dieta di 0.4 g/kg/die si riduce al 18%:

- Uomo 70 kg: con **dieta 0.6 g/kg/die = intake IAAS 4.9 g/kg/die (deficit circa 8 g/kg/die)**; **dieta 0.4 g/kg/die = intake IAAs 3.3 g/kg/die (deficit di circa - 9.0-10.0 g/die)**;
- Ma si aggiungono altri numerosi fattori che riducono l'assorbimento e l'utilizzazione ottimale degli IAAs: insufficiente apporto calorico, ridotta digeribilità (DIAAs), ridotto assorbimento intestinale, microbiota uremico, acidosi metabolica, riduzione dell'efficacia dell'insulina…. (*Wolf RR-Nutr Rev 2016*)
- **Nella once-weekly-hemodialysis l'alimentazione ipoproteica aiuta a ridurre la progressione della Residual Kidney Function (*Takkavatakarn K -Int J Artif Organs. 2021*)**
- Oltre al deficit aminoacidico esistono fattori dialisi dipendenti……

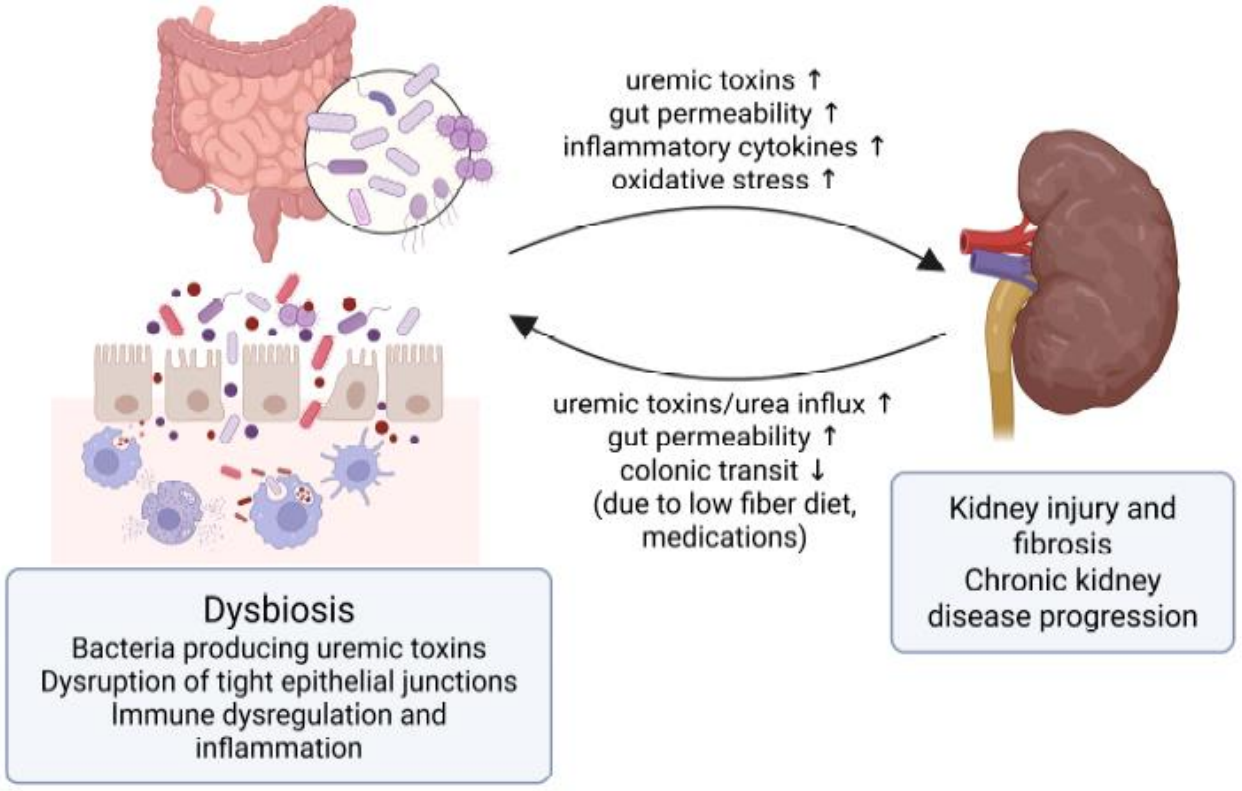
Microbiota uremico

Aumento della Zonulina fecale
= disregolazione permeabilità intestinale



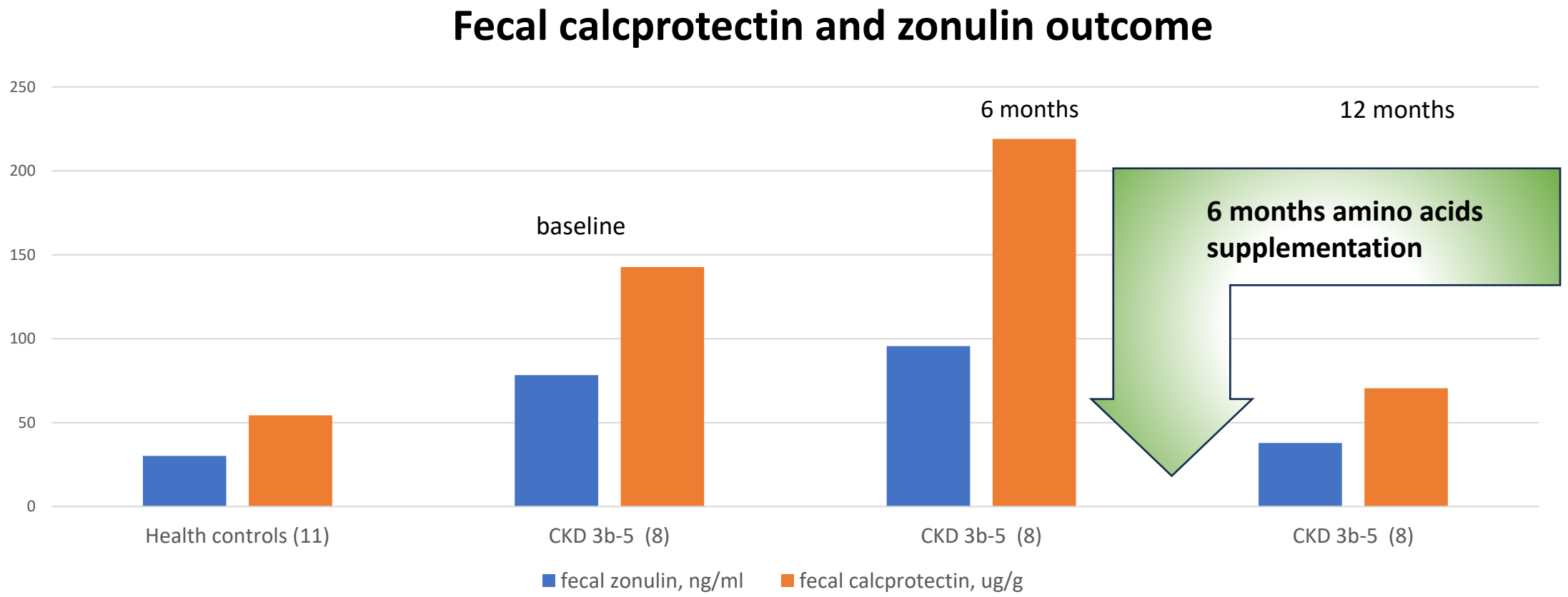
Per studiare l'impatto di numerose patologie sul microbiota viene misurata la **zonulina fecale**, una pre-proteina dell'aptoglobina2, secreta dalle cellule epiteliali intestinali in risposta a fattori che inducono stress, principalmente a causa dell'aumento di patobionti che si verifica in patologie come neoplasie, patologie intestinali di vario genere malattie autoimmuni, dieta chetogeniga, celiachia, LES……*(Fasano -Physiol Review – 2011/Buttler et Al – Gut Microbes 2025)*

In CKD, both serum and **fecal calcprotectin** (FC) serve as clinically relevant markers. Recent longitudinal studies have demonstrated that serum calprotectin independently predicts cardiovascular outcomes in CKD patients, with elevated levels associated with increased mortality risk over 5–10 years of follow-up



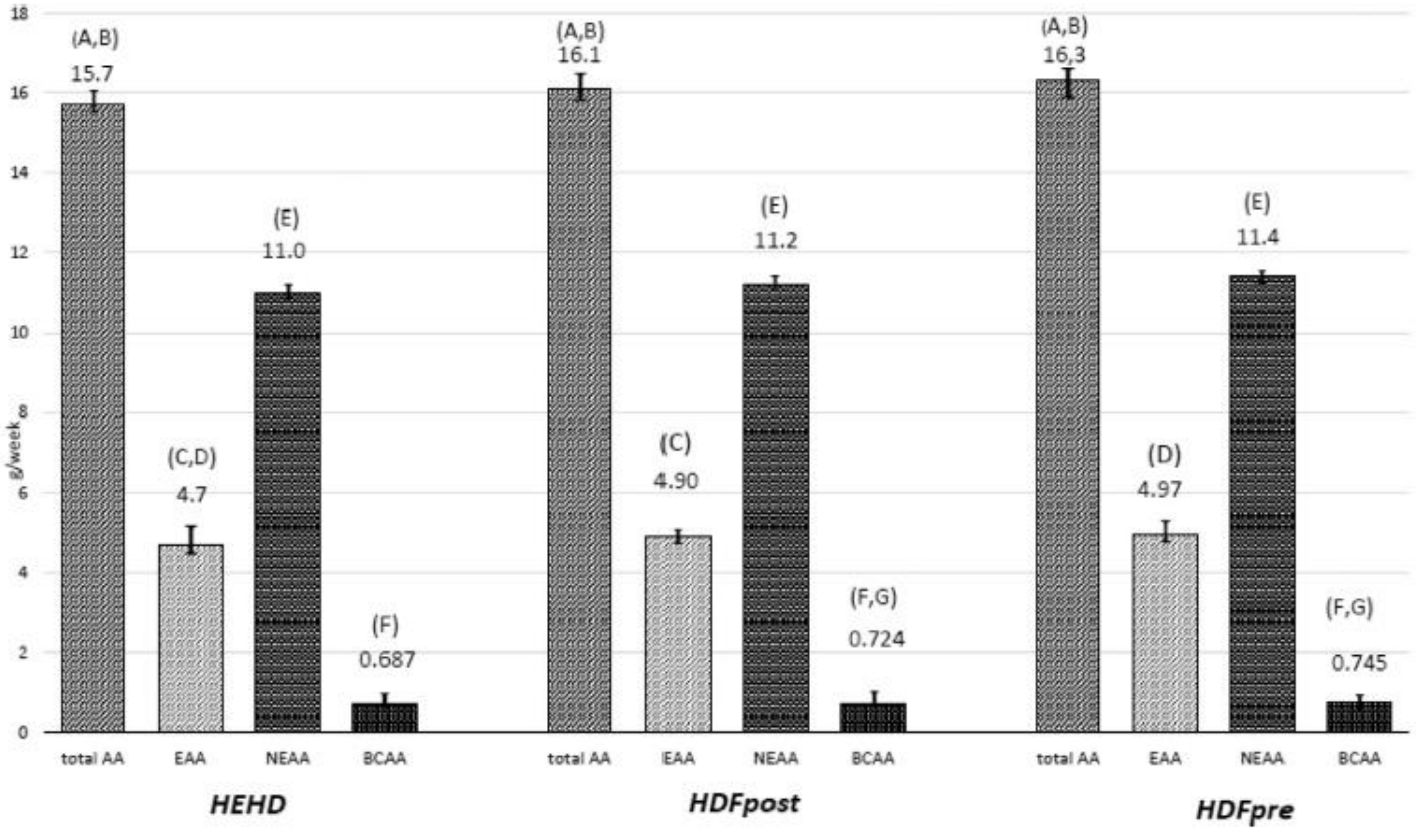
Lee SY – Biomolecules 2025 (Korea)

Intestinal mucosa inflammation (calcprotectin, μg/g) and permeability (zonulin, ηg/ml) of eight Chronic Kidney Disease (CKD3b-5) patients at baseline and after 6 months of amino-acids oral supplementation.



Aquilani R , Bolasco P, Murtas S. Metabolites - 2022
Bolasco P , Aquilani R, Murtas S – Clinical Nutr ESPEN - 2023

Loss of Amino Acids from extra-corporeal treatments



Sequence randomized methods in 10 patients

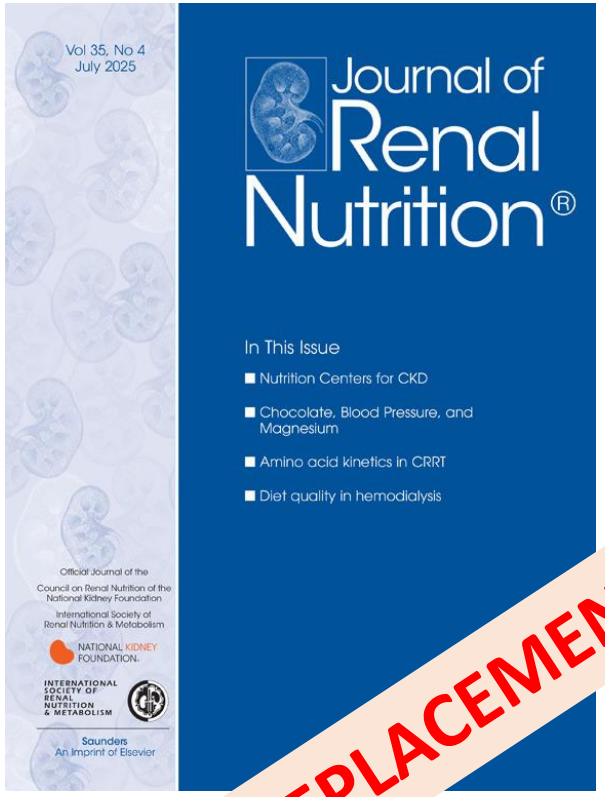
Average loss of aminoacids

Once-weekly-HD: **5.3 g**/week
= **279 g**/year

Twice-weekly-HD: **10.6 g**/week
= **558 g**/year

Thrice-weekly-HD: **15.9 g**/week
= **805 g**/year

Murtas S. et Al. Cagliari – Journal of Renal Nutrition - 2019



MANDATORY REPLACEMENT!!!

Amino acid and protein losses in adult patients receiving maintenance dialysis: a literature review

Bruno Mafrici et Al. August 2025 (Nottingham – UK)

- **Twenty-nine eligible records were identified (14 HD/15 PD). Amino acid losses ranged from 9.3±2.9g to 12.0±2.0g per four-hour HD session; conventional thrice HD ≥ 1,4 Kg/year**
- **Amino acid losses 0.314g to 0.522g/day in PD;**
- **Albumin loss ranged from 0.448 g to 3.99 g per HD/HDF session and 4.23g to 6.12g/day in PD.**
- **Albumin losses were higher with post-dilution HDF compared to HD.**

Come effettuare un rimpiazzo di aminoacidi?
Alcune tipologie di miscele amino acidiche commercializzate in Italia

Contenuto per una bustina o compressa

Miscela A	Miscela B	Miscela C	Miscela D
Alfa-chetoleucina, 101 mg	L-Leucina 1250 mg	L-leucina 560 mg	L-leucina 1200 mg
D,L-lisina acetato 75 mg	L-Lisina 650 mg	L-lisina 480 mg	L-lisina 900 mg
Alfa-chetoisoleucina 67 mg	L-Isoleucina 625 mg	L-isoleucina 400 mg	L-isoleucina 600 mg
Alfa-chetovalina 86 mg	L-Valina 625 mg	L-valina 400 mg	L-valina 600 mg
L-treonina: 53 mg	L-Treonina 350 mg	L-treonina 360 mg	L-treonina 700 mg
L-istidina: 38 mg	L-Cistina 150 mg	L-cistina 340 mg	L-cistina 150 mg
Alfa-chetofenilalanina 68 mg	L-Istidina 150 mg,	L-istidina 480 mg	L-istidina 150 mg
D,L-Alfa-idrossimetionina 59 mg	L-Fenilalanina 100 mg	L-fenilalanina 320 mg	L-fenilalanina 100 mg
L-tirosina: 30 mg	Metionina 50 mg	L-metionina 180 mg	L-metionina 50 mg
L-triptofano: 23 mg	L-Tirosina 30 mg	L- tirosina 240 mg	L-triptofano 50 mg
	L-Triptofano 20 mg	L-triptofano 140 mg	L-ornitina 100 mg
		L-ornitina 100 mg	
		L-serina 100 mg	
Totale amino acidi: 0.6 g	**Totale amino acidi: 4 g**	**Totale amino acidi: 4.1 g**	**Totale amino acidi: 4.6 g**

Non sono elencati vitamine , micronutrienti, attivatori mitocondriali

Nella nostra esperienza, aumentando il numero di bustine e/o pillole, il paziente abbandona in pochi mesi la supplementazione aminoacidica poiché già esasperato dalla numerosità di farmaci che deve già obbligatoriamente assumere;

nutrients

MDPI

Article

Effects of a Novel Amino Acid Formula on Nutritional and Metabolic Status, Anemia and Myocardial Function in Thrice-Weekly Hemodialysis Patients: Results of a Six-Month Randomized Double-Blind Placebo-Controlled Pilot Study

Stefano Murtas [1], Roberto Aquilani [2], Gianmarco Fiori [3], Roberto Maestri [4], Paolo Iadarola [5], Cristina Graccione [1], Rita Contu [1], Maria Luisa Deiana [1], Fabrizio Macis [1], Romina Secci [1], Antonella Serra [1], Mariella Cadeddu [1], Maura D'Amato [5], Paola Putzu [1], Mirella Marongiu [1] and Piergiorgio Bolasco [6,*]

Parameters	Placebo Group at Start of the Study	Placebo Group after 6 Months	Treatment Group at Start of the Study	Treatment Group after 6 Months	Placebo Group—δ Variation over 6 Months	Treatment Group—δ Variation over 6 Months
Hb, g/dL	11.12 ± 0.72	11.28 ± 0.73	11.49 ± 0.86	11.64 ± 0.81	0.14 ± 0.68	0.16 ± 1.10
Blood Iron, µg /dL	48.91 ± 19.08	57.27 ± 25.08	48.73 ± 22.85	52.27 ± 11.94	3.55 ± 26.38	8.36 ± 23.72
Ferritin, ng/dL	414.0 ± 285.7	428.8 ± 219.2	444.5 ± 180.9	469.7 ± 239.2	25.2 ± 169.3	14.8 ± 258.3
Transferrin, mg/dL	188.1 ± 66.3	176.8 ± 29.6	179.0 ± 29.9	169.3 ± 27.5	−9.7 ± 37.8	−11.3 ± 72.9
Lymphocytes, mm^3	1518 ± 678	1380 ± 247	1053 ± 569	934 ± 607	−138 ± 644	−120 ± 522
Parenteral Iron administration (i.v), mg/week	198.9 ± 228.5	278.9 ± 204.7	194.9 ± 232.1	319.1 ± 114.8	124.2 ± 304.7	80.1 ± 193.3
Erythropoietin, U.I./week	14373 ± 7337	15459 ± 4425	13205 ± 5838 $^{\Delta}$	8444 ± 3547 $^{\Delta}$	+4761 ± 4169 $^{\blacklozenge}$	−1086 ± 7112 $^{\blacklozenge}$
ERI, EPO IU/week/Kg/g/dL	19.44 ± 9.73	20.97 ± 5.79	19.37 ± 9.69 $^{\#}$	12.64 ± 6.96 $^{\#}$	−6.73 ± 4.64 $^{\theta}$	1.53 ± 7.47 $^{\theta}$

Parameters	Placebo Group at Start of the Study	Placebo Group after 6 Months	Treatment Group at Start of the Study	Treatment Group after 6 Months	Placebo Group—δ Variation over 6 Months	Treatment Group—δ Variation over 6 Months
Phase Angle, degree	4.20 ± 0.99	3.99 ± 0.98	4.36 ± 1.13	4.53 ± 1.16	−0.21 ± 0.50 $^{\Delta}$	0.16 ± 0.36 $^{\Delta}$
Total Body Water, %	55.88 ± 5.44	56.47 ± 5.51	54.29 ± 9.48	55.15 ± 8.41	0.59 ± 5.03	0.85 ± 6.00
Extracellular Water, %	56.30 ± 7.27	58.12 ± 7.65	53.94 ± 9.52	57.69 ± 5.80	1.82 ± 5.85	3.75 ± 11.57
Intracellular Water, %	42.23 ± 7.27	40.78 ± 8.45	45.83 ± 9.04	42.10 ± 5.78	−1.45 ± 5.46	−3.73 ± 11.03
Fat Free Mass, %	70.44 ± 7.83	71.27 ± 7.00	69.82 ± 12.85	71.28 ± 11.49	0.84 ± 6.45	1.47 ± 6.96
Body Cellular Mass, %	40.78 ± 7.66	40.24 ± 8.07	44.64 ± 9.73	39.98 ± 6.42	−0.55 ± 6.01	−4.65 ± 11.90
Muscle Mass, %	38.72 ± 7.36	37.70 ± 7.77	39.82 ± 8.68	41.25 ± 8.09	−1.02 ± 5.32 $^{\Delta}$	1.44 ± 3.31 $^{\Delta}$
Fat Mass, %	29.36 ± 7.72	29.05 ± 7.04	32.70 ± 8.95	28.74 ± 11.50	−0.32 ± 6.20	−3.96 ± 7.31
Resting Energy Expenditure, Kcal/kg	20.74 ± 2.93	20.25 ± 3.25	22.67 ± 2.66	22.95 ± 2.41	−0.48 ± 1.57	0.28 ± 2.90
Body Mass Index, Kg/m^2	23.75 ± 4.74	23.98 ± 5.27	24.96 ± 6.40	24.92 ± 6.27	0.24 ± 1.22	−0.05 ± 1.12

Inter-Study Group variation δ: Δ: $p < 0.05$.

2022

Hb stabile, senza
- nessuna variazione nella somministrazione di ferro,
- importante riduzione nei dosaggi di eritropoietina,
- riduzione degli indici di resistenza (ERI) all'eritropoietina

Miglioramento della performance cardiaca

Miglioramento della massa muscolare e dell'angolo di fase

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

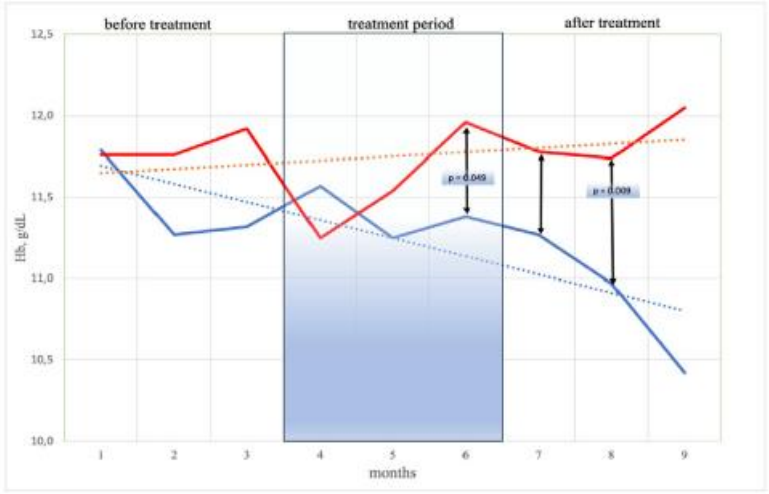
Replacement of the massive amino acid losses induced by hemodialysis: A new treatment option proposal for a largely underestimated issue

Stefano Murtas [a], Giorgio Reggiardo [b], Rita Contu [a], Mariella Cadeddu [a], Romina Secci [a], Paola Putzu [a], Cristina Mocco [a], Marco Leoni [a], Vita Gigante Maria [a], Cesarina Marras [a], Fedia Moro [a], Mirella Marongiu [a], Marco Meleddu [a], Piergiorgio Bolasco [c, *]

2024

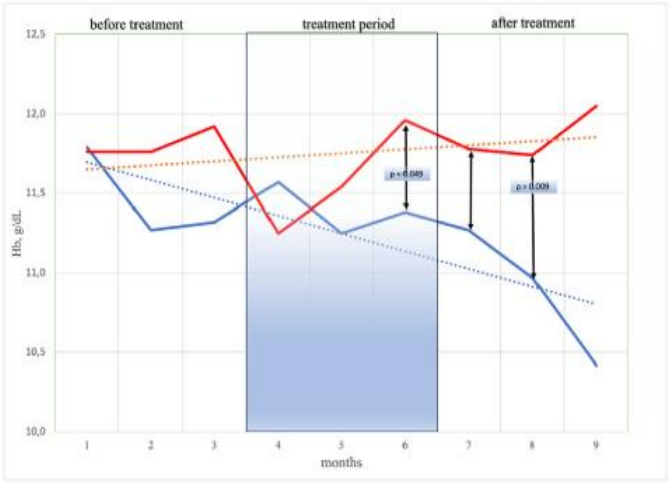
Randomized prospective study: 15 pazienti trattati (in rosso), 15 pazienti di controllo non trattati (in blu)

Δ difference values of Hb for three months before, during and after Study Period



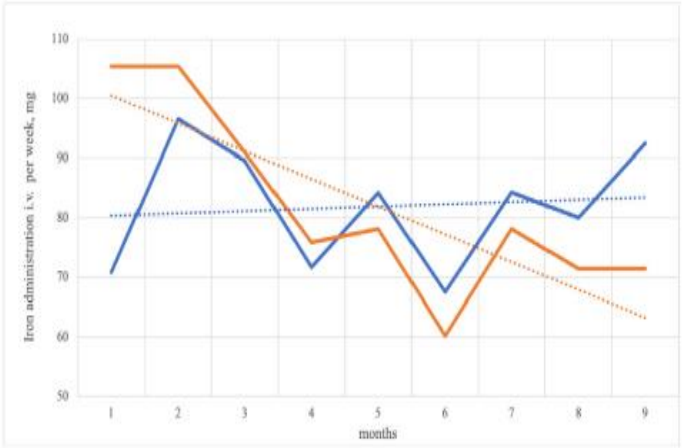
Hb

Δ difference values of Erythropoietin dosage before during and after Study Period



Dose eritropoietina

Δ difference values of Iron dosage i.v. before during and after Study Period



Terapia marziale

La maggior frequenza delle sessioni emodialitiche killer della diuresi e della Funzione Renale Residua;

- L'infermiere di sala dialisi deve applicare una accurata gestione dell'UFR per evitare ipotensioni arteriose; nei pazienti in once-weekly-HD che arrivano alla HD successiva sotto il peso secco stimato vanno reintegrati gradatamente.
- L'aumento dell'incremento ponderale conduce ad progressivo utilizzo dell'UFR; l'UFR correla con la perdita della diuresi e della RKF (*Yu-Ji Lee et Al - J Kidney Dis – 2021)*
- Gli effetti dello stress emodinamico dovuto ad un maggior numero sedute extra-corporee produce una forte attivazione sui monociti pro-infiammatori CD14+CD16+ (*Bolasco P, La Nasa et Al –Blood Purif -2019)* conducendo ad una cascata ematica di tossine come durante TNF-α, IL-6, IL-1 che agiscono negativamente sul sistema endoteliale, cardiaco e sulla RKF ;
- I pazienti inseriti in emodialisi convenzionale trisettimanale perdono la diuresi mediamente in 6-8 mesi;

CONCLUSIONI

- Oggi l'emodialisi Incrementale (IH) è una realtà **da tenere sempre in considerazione negli ambulatori pre-dialisi**;

- La once-weekly-hemodialysis può essere iniziati solo **in pazienti selezionati**, sicuramente e decisamente collaboranti con le caratteristiche precedentemente elencate;

- La once-weekly-hemodialysis deve essere iniziata e condotta da **personale infermieristico e medico adeguatamente formato e rigoroso sulle procedure**; non bisogna farsi sfuggire, quando esistono segnali di fattibilità, l'occasione di effettuare un passo verso la terapia conservativa anche se momentaneo;

- **La scelta più frequente** nei centri di Nefrologia di tutto il mondo è la **twice-weekly-hemodialysis** senza farsi sfuggire, quando esistono segnali di fattibilità, **l'occasione di effettuare un passo decrementale;**

- Occorrerebbe **creare un gruppo nazionale e/o internazionale** per **redigere delle procedure precise** per la dialisi bisettimanale e soprattutto per la dialisi mono-settimanale; mancano studi randomizzati di numerosità;

- Fenomeno non trascurabile la significativa riduzione dei costi diretti ed indiretti in once- e twice-weekly-hemodialysis

- Comunque la once e la twice hemodialysis **sono periodo bridge** dell'inevitabile passaggio verso l'emodialisi convenzionale: