



Nutritional gap

**Mind The
Gap**

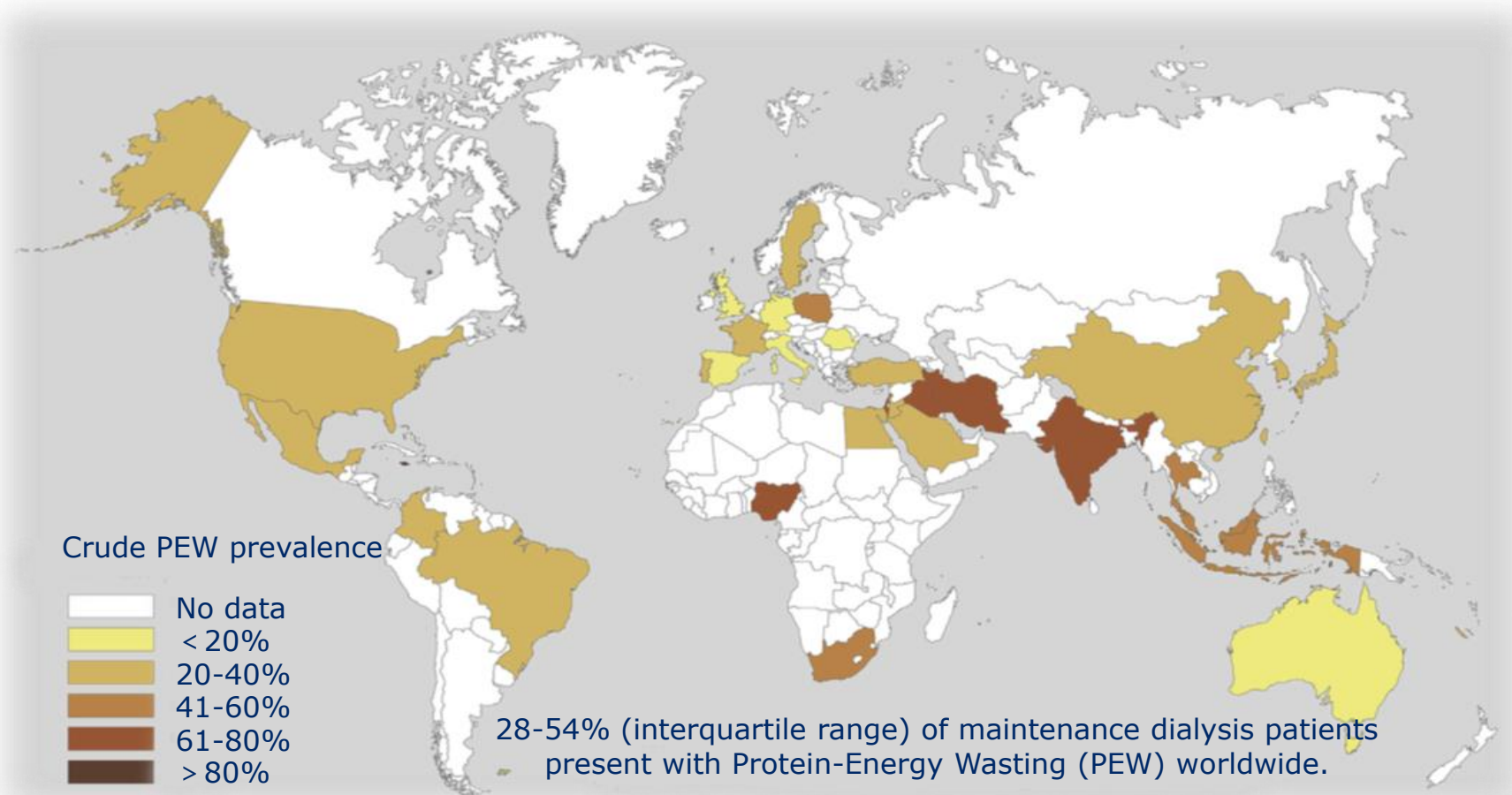
Benefit of PN in Patients on Hemodialysis

基隆長庚腎臟科 林祐誠醫師

2024.04.21

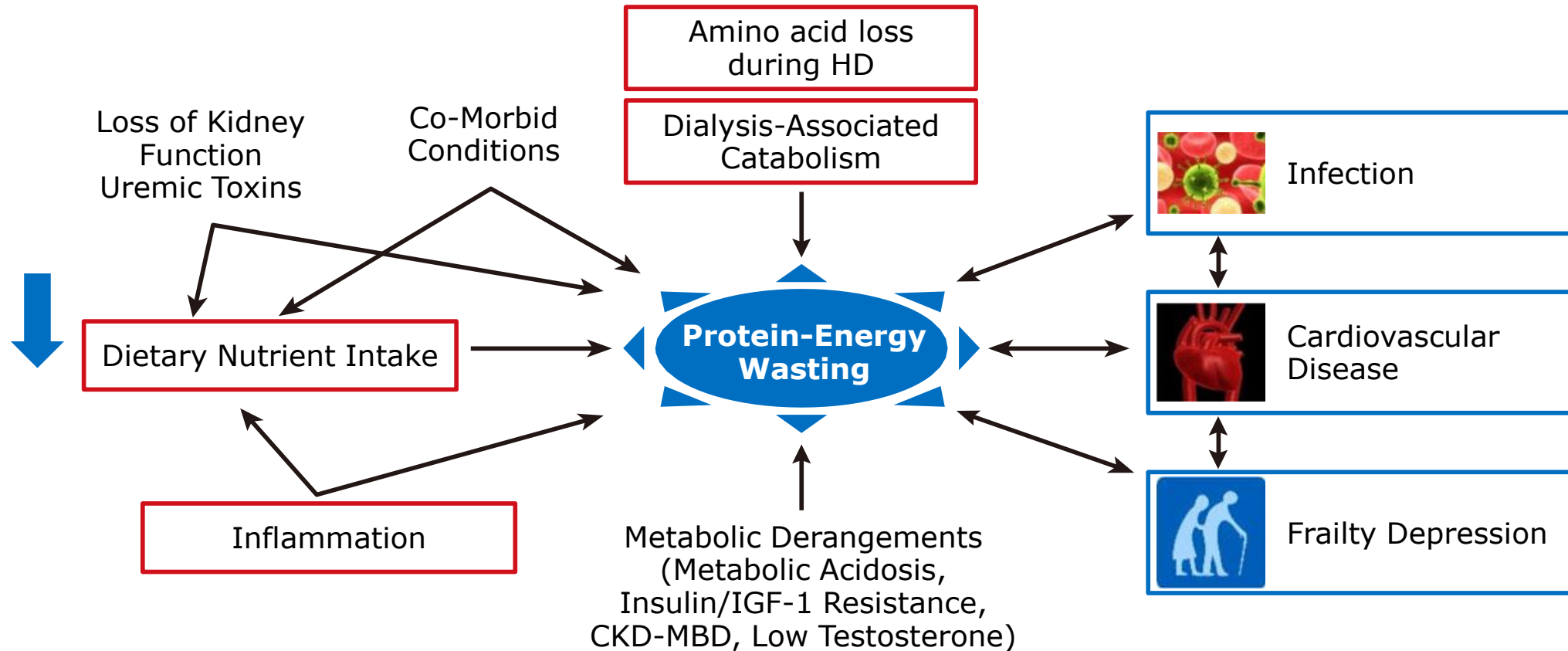
PEW (protein energy wasting) 盛行率

- Approximately **28-54%** of patients undergoing dialysis are **affected by PEW**.

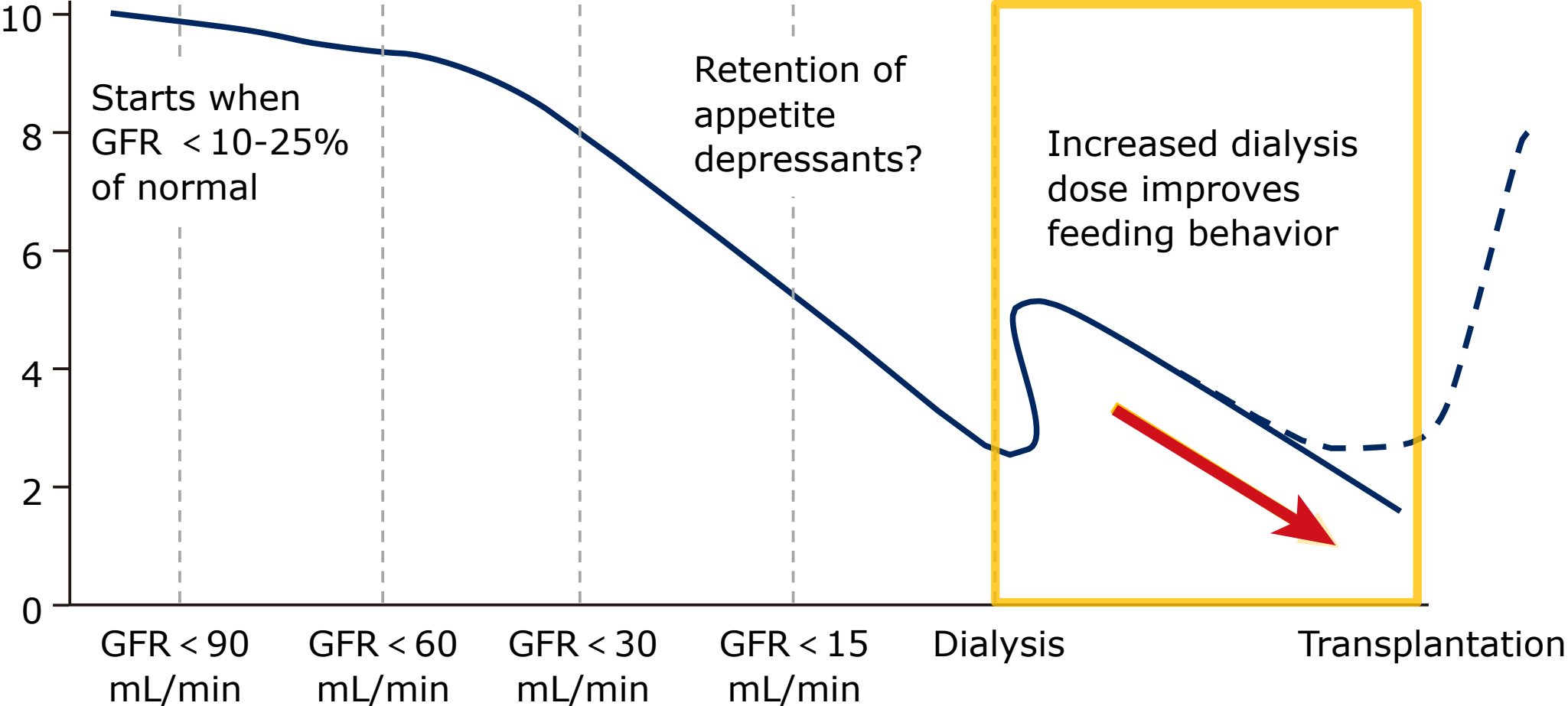


PEW 的原因與危害

- **PEW** is defined as a pathological state where there is a continuous **decrease/wasting** of **both protein deposits and energy reserves**.

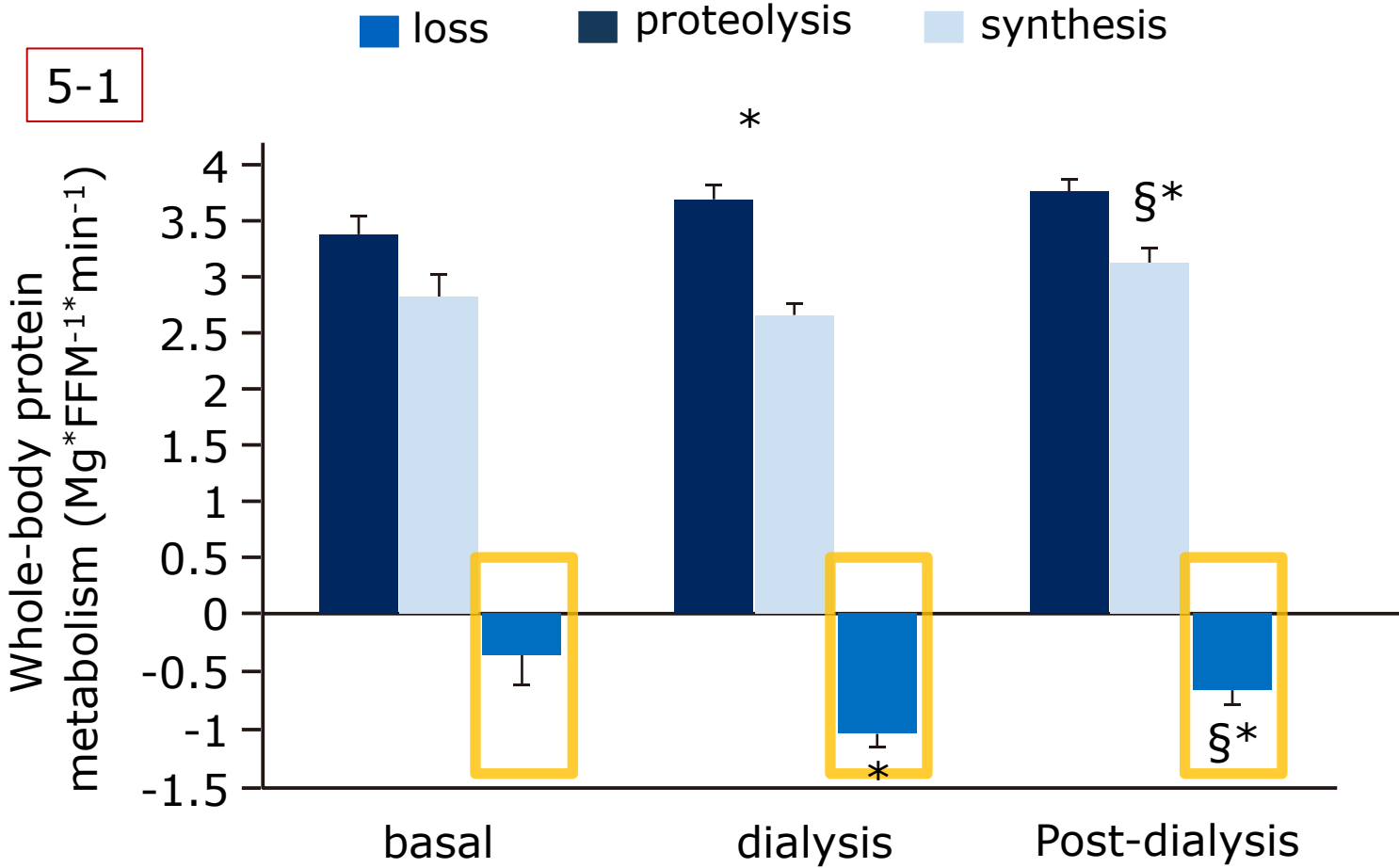


透析病友：胃口逐漸變差、厭食



J Ren Nutr 2009 Jan;19(1):10-5.

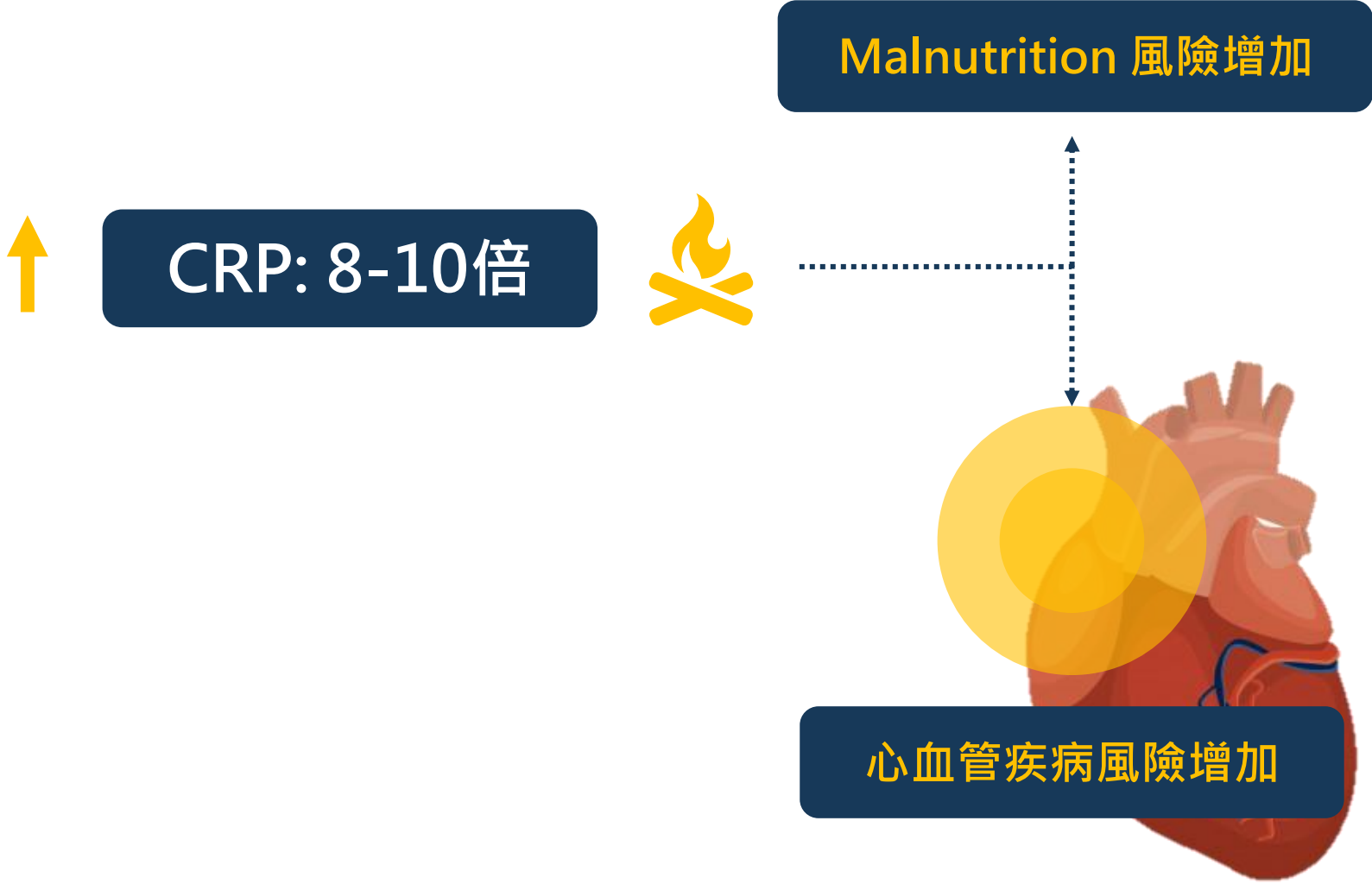
透析病友：透析造成分解增加、營養流失



每次透析損失: 8-12g 胺基酸，
一年流失 1-2公斤

1. Am J Physiol Endocrinol Metab 2002;282: E107-E116. 2. Clin Nutr 2009 Aug;28(4):401-14.

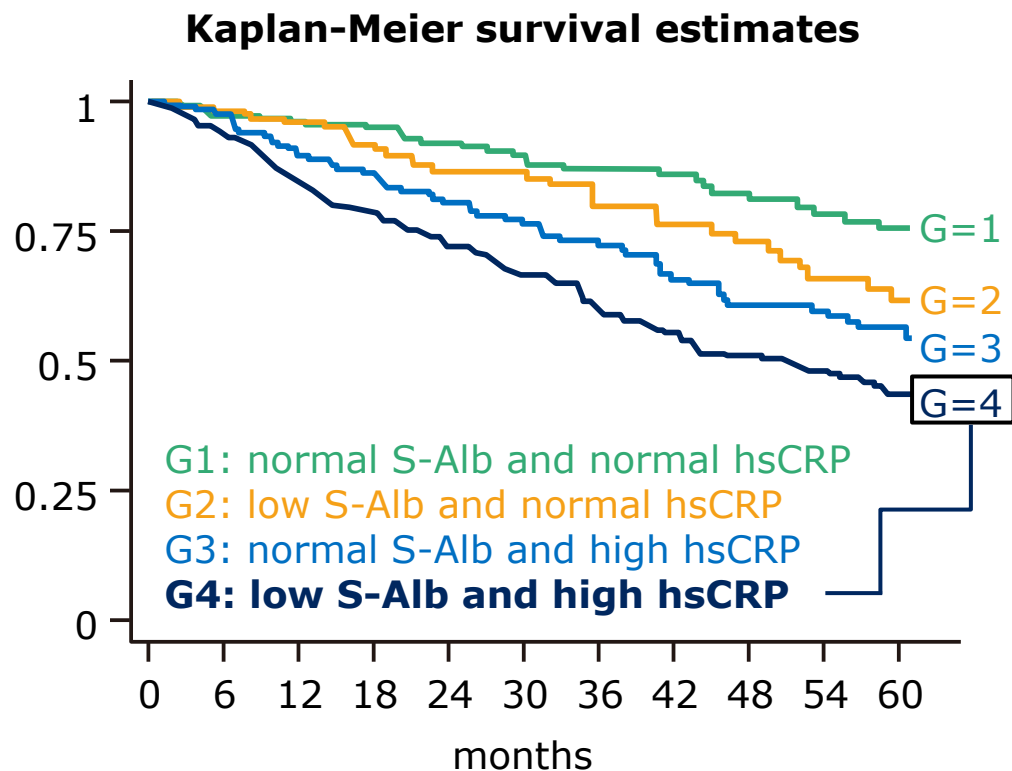
透析病友：發炎指數高



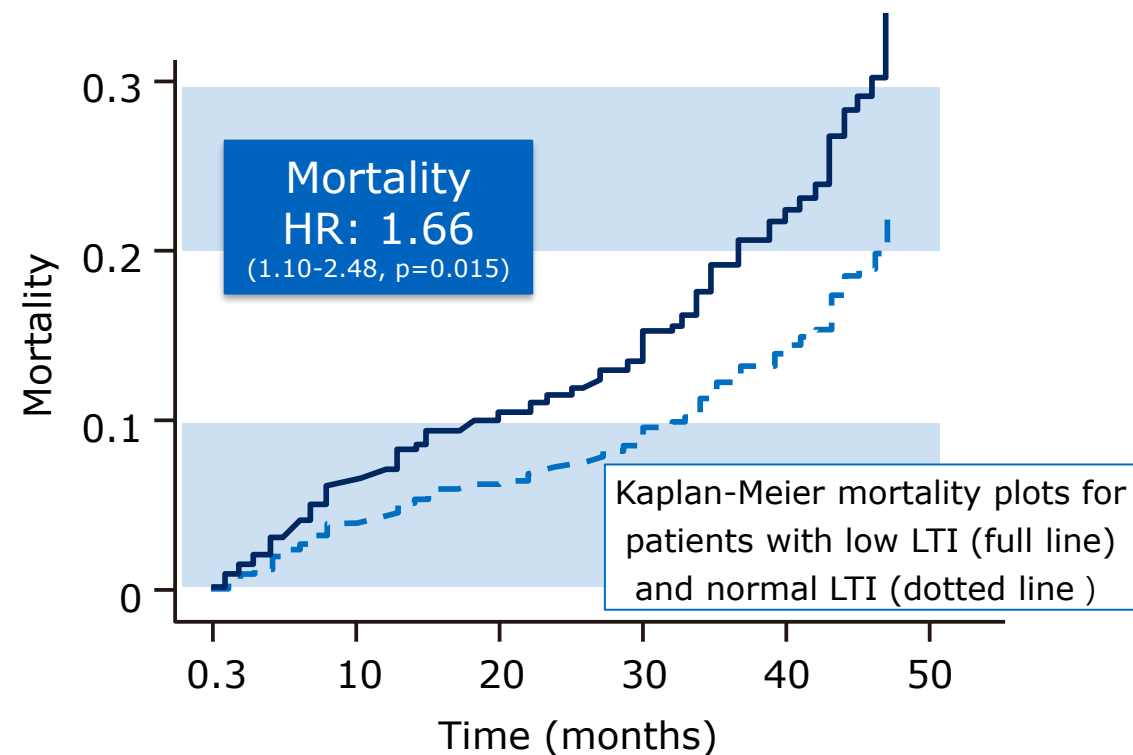
1. Kidney Int Suppl 2002 May;(80):99-102. 2. J Am Soc Nephrol 2002 Jan;13 Suppl 1:S28-36.

營養不良 / 發炎增加死亡風險

- **Mortality risk** was increased in CKD stage 5 patients with **low S-Alb** and **high CRP** (N=822, follow-up 60 mo).



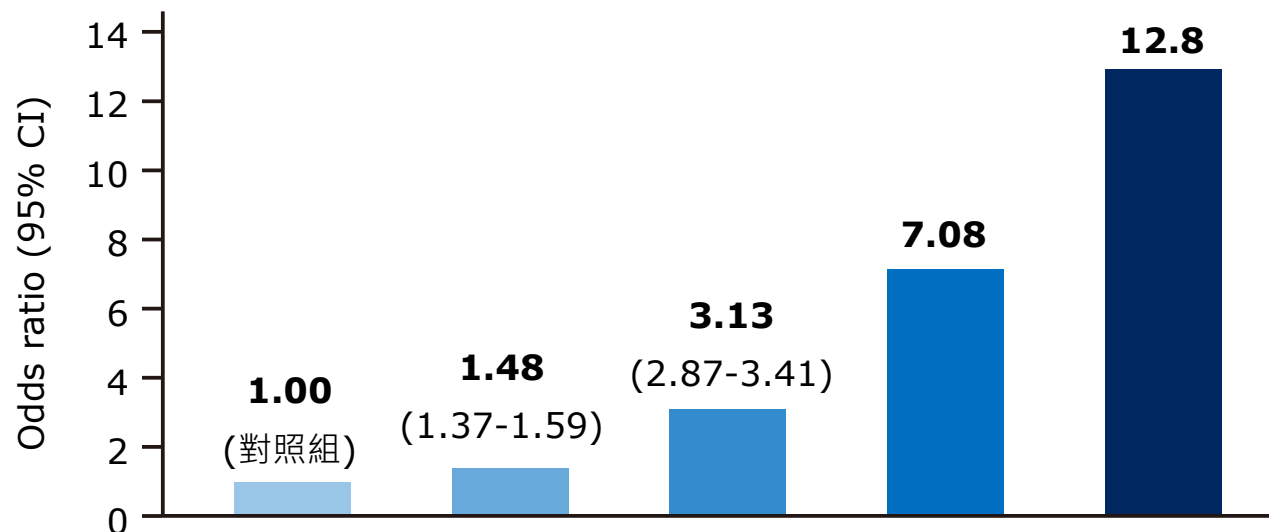
- **Malnourished patients** [lean tissue index (LTI) <10%] had a **1.66-fold higher risk of dying** compared to those with a normal nutrition status.



國人血清白蛋白低於 4 g/dL 比例偏高

血清白蛋白是一項營養指標，若低於 4.0 g/dL 會增加血液透析患者的死亡風險，根據台灣腎病年報，超過 6 成的血液透析患者的血清白蛋白低於 4.0 g/dL

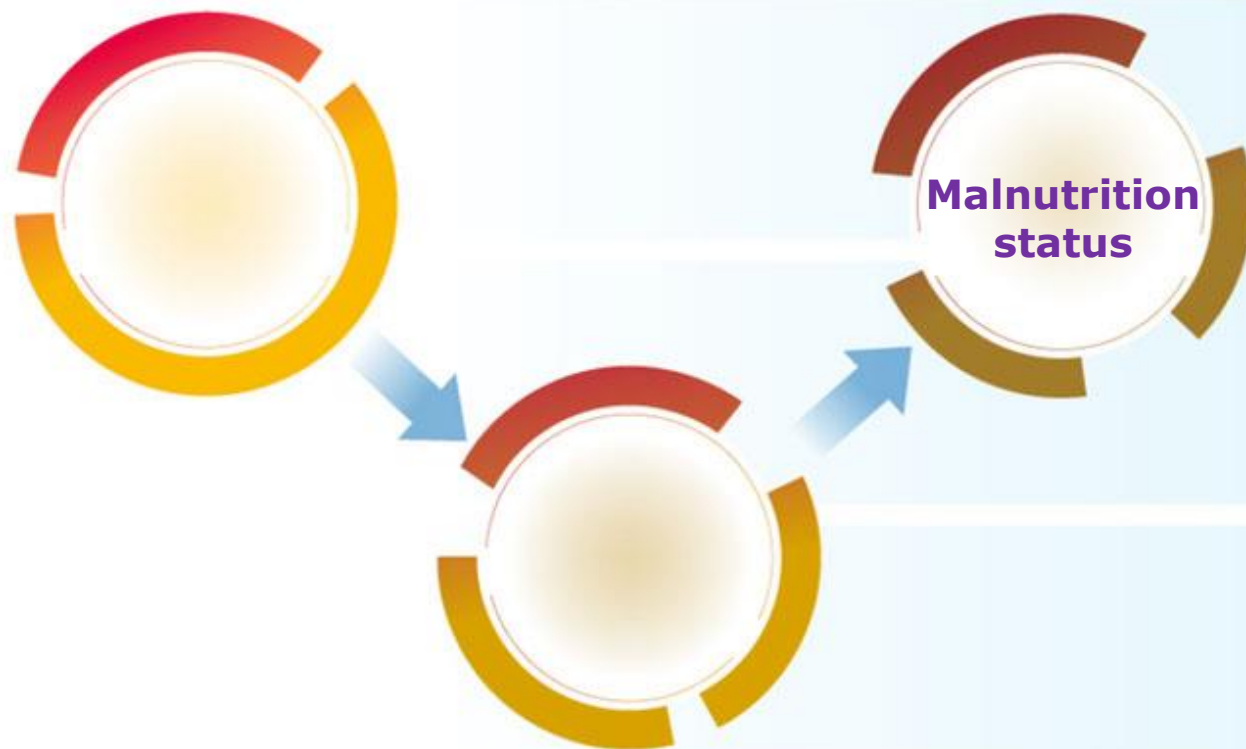
Adjusted risk of death



血清白蛋白濃度	4.0-4.4	3.5-3.9	3.0-3.4	2.5-2.9	<2.5 g/dL
台灣腎病年報	血液透析患者白蛋白分佈告 (%)				
	34.2*	48.0	14.2	3.6	
	腹膜透析患者白蛋白分佈 (%)				
	24.1*	46.2	23.0	6.7	

*血清白蛋白濃度 ≥ 4 g/dL 之分佈佔比

Mind the gap: 營養缺口不斷擴大



1 **35-50%** 血液透析患者有厭食
的狀況

2 透析會導致蛋白質分解增加

3 每次透析約有 **8-12** 克的胺基酸
流失

透析病友營養需求量

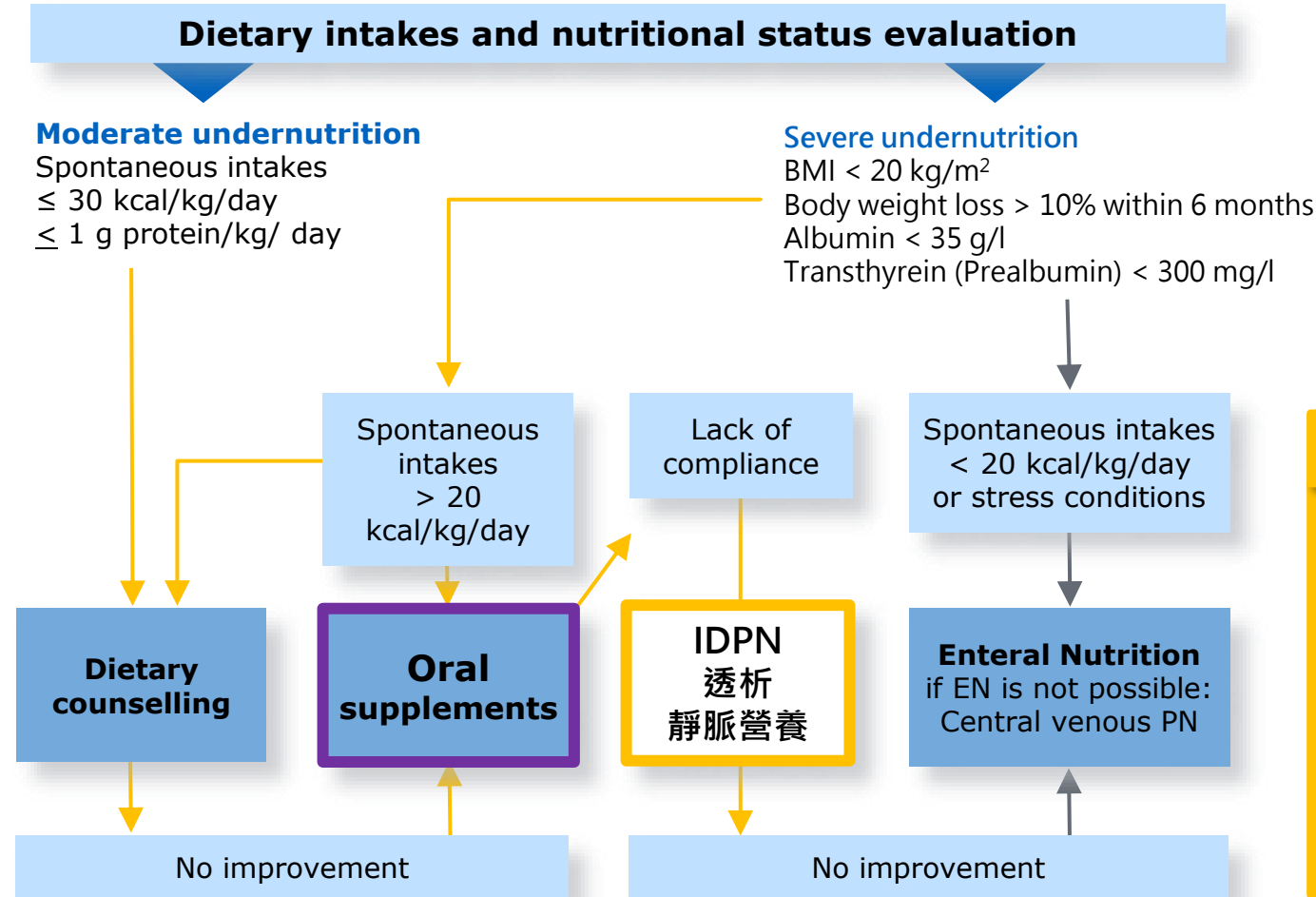
- Recommended minimum protein, energy, and mineral intakes for chronic kidney disease (CKD) and maintenance dialysis patients. A consensus statement by the International Society of Renal Nutrition and Metabolism (ISRNM).

	Nondialysis CKD	Hemodialysis	Peritoneal dialysis
Protein	0.6–0.8 g/kg/day Illness 1.0 g/kg	>1.2 g/kg/day	>1.2 g/kg/day Peritonitis >1.5 g/kg
Energy	30–35 ^a kcal/kg/day	30–35 ^a kcal/kg/day	30–35 ^a kcal/kg/day incl. kcal from dialysate
Sodium	80–100mmol/day	80–100 mmol/day	80–100 mmol/day
Potassium	<1 mmol/kg if elevated	<1 mmol/kg if elevated	Not usually an issue
Phosphorus	800–1000 mg and binders if elevated	800–1000 mg and binders if elevated	800–1000 mg and binders if elevated

Greater than 50% of high biological value protein (complete protein sources containing the full spectrum of essential amino acids) is recommended. ^aBased on physical activity level. In sedentary elderly adults, recommended energy intake is 30 kcal/kg/day. All recommendations are based on ideal body weight. Regular follow-up supports compliance.

ESPEN Guidelines 歐洲臨床營養與代謝學會

Algorithm for nutritional support of HD patients



ESPEN guideline 2021

IDPN shall be applied in malnourished non-critically ill hospitalized patients with chronic kidney disease (CKD) and kidney failure (KF) on hemodialysis, or the same patients if at risk of malnutrition that fail to respond or do not tolerate oral nutritional supplements (ONS) or enteral nutrition (EN).

Grade of recommendation:
A - Strong consensus (91.7% agreement)

1. Clin Nutr 2009 Aug;28(4):401-14. 2. Clin Nutr 2021 Apr;40(4):1644-68.

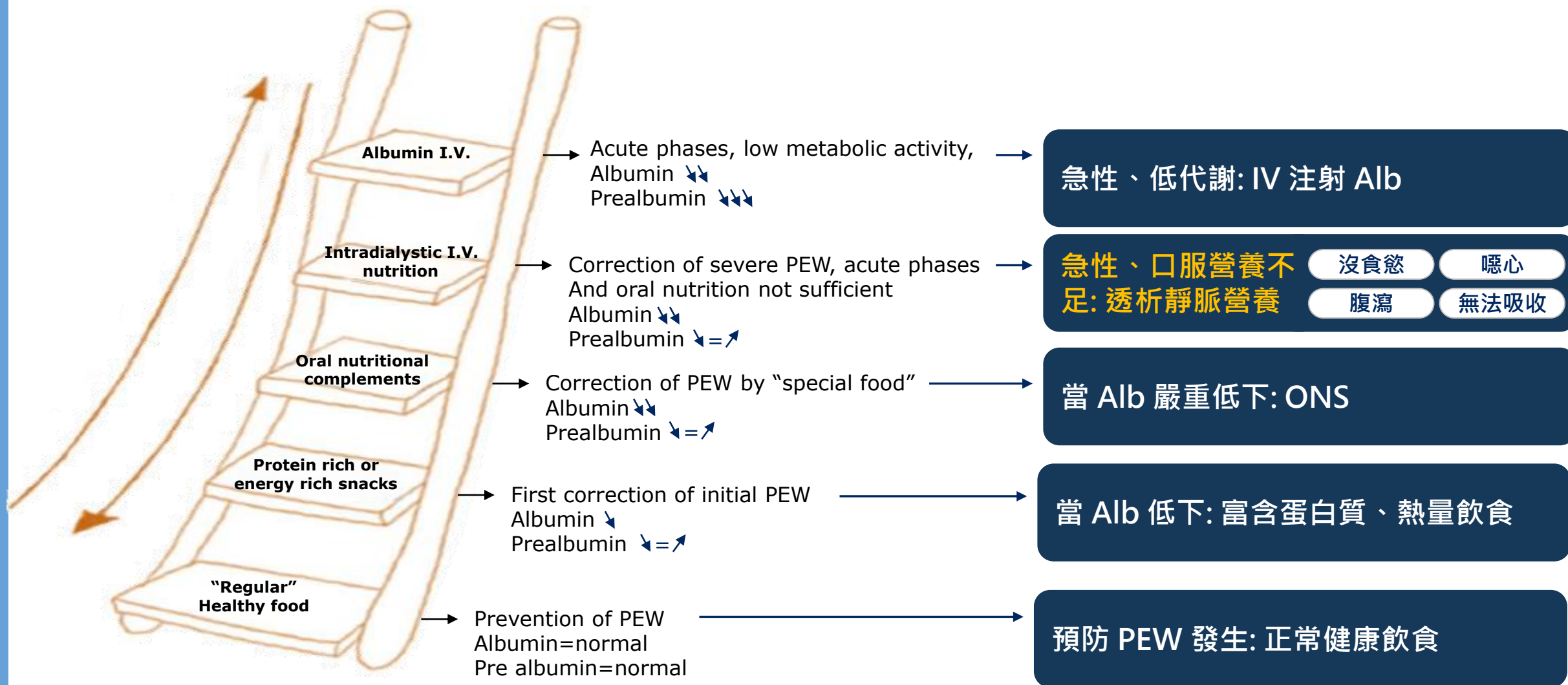
2021 ESPEN guideline: protein requirement

Recommendation 18 – consensus:
The following protein intakes may be prescribed:

Patient	Illness, treatment	Protein intake (g/kg BW/d)
Hospitalized	CKD & no acute/critical	0.6-0.8
	CKD & KRT & no acute/critical	≥ 1.2
	AKI or AKI on CKD & no acute/critical	0.8-1.0
	AKI or AKI on CKD or CKD & acute/critical & not on KRT	1-1.3 (if tolerated)
Critically ill	AKI or AKI on CKD or CKD on KRT	1.3-1.5
	AKI or AKI on CKD or CKD on CKRT/PIKRT	1.5-1.7

AKI=acute kidney injury; KRT=kidney replacement therapy; CKRT=continuous kidney replacement therapy; PIKRT=prolonged intermittent kidney replacement therapy

階梯式補充營養



靜脈營養的選擇

Amino Acids

Standard AA

Aminoven 5/10/15%

Specific AA

Aminosteril N Hepa 8%

Nephrosteril 7% 

Glutamine AA

Dipeptiven 20%

Paediatric AA

Aminosteril Infant 6%/10%



Lipids

Intralipid 10/20/30%

Lipovenoes MCT 10/20%

SMOFlipid 20%

Supplement

Omegaven 10%



Multi-Chamber Bags

2 CBs

Aminomix Novum

3 CBs

Kabiven & peri

SmofKabiven 493 

SmofKabiven 1477

>> 中心靜脈住院

SmofKabiven 1448

>> 周邊靜脈住院



Additives

Vitamins

Vitalipid Adult

Vitalipid Infant

Soluvit

Phosphate

Glycophos

Trace Elements

Addaven

Peditrace



*IDPN: intra-dialytic parenteral nutrition

Nephrosteril 腎福諾

- Administration: For IV infusion (peripheral or central)

- Volume: 250mL.
- Amino Acid: 7% (60%EAA 40%NEAA)
- Total amino acid: 17.5g
- Nitrogen: 10.8 g/L
- Energy: 1210 KJ/L; 280 Kcal/L
- Osmolarity: 645 mosm/L
- pH: 5.8-6.2
- [Na]: 0

ESPEN guideline: EAA & NEAA are required



Amino acid composition (g/1000 mL)

BCAA % (BCAA/Total AA)	31%
Aromatic amino acids %	8.1%

Essential amino acids 60%	
L-Isoleucine	5.10
L-Leucine	10.3
L-Lysine monoacetate =L-lysine 7.1 g	10.01
L-Methionine	2.80
L-Phenylalanine	3.80
L-Threonine	4.80
L-Tryptophan	1.90
L-Valine	6.20

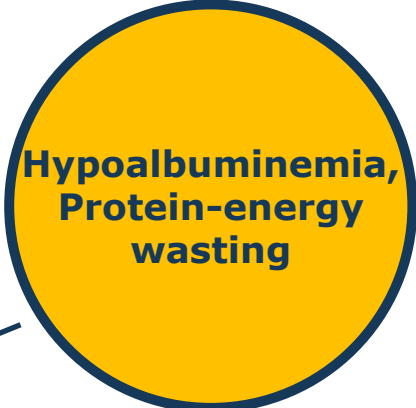
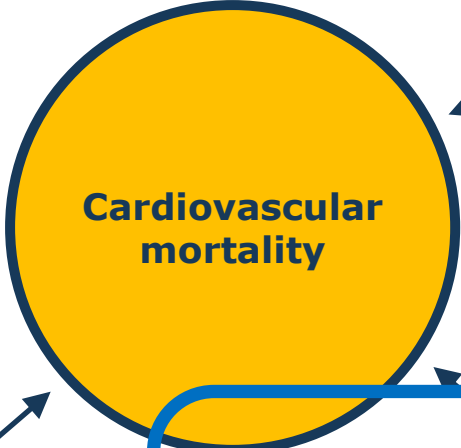
Nonessential amino acids 40%	
L-Arginine	4.90
Acetylcysteine =L-cysteine 0.37 g	0.50
Glycine (Amino acetic Acid)	3.20
L-alanine	6.30
L-Proline	4.30
L-Serine	4.50
L-malic acid	1.50
Glacial acetic acid	1.38
L-Histidine	4.30
L-Aspartic Acid	0
L-Glutamic Acid	0
L-Tyrosine	0

Risk factors account for excess CV mortality in patients with CKD

“Traditional” risk factors

- Physical inactivity
- Smoking
- Aging
- Hypertension
- RAS activation
- Insulin resistance, obesity
- Diabetes
- Volume overload
- Anemia
- Dyslipidemia
- Fibrinogen

- Phosphate
- Calcium
- PTH



- Acidosis
- Altered AA metabolism
- Insulin/GH/IGF resistance
- Anorexia
- Physical inactivity

“Non-Traditional” risk factors

- Oxidative stress
- Inflammation
- Homocysteine
- SAH
- ADMA
- Reduced NO

CKD related risk

● Amino acid homeostasis

The role of the kidney in amino acid and protein metabolism

Amino acid synthesis in the kidney (%)		
Serine	100%	(3–4 g/d)
Cysteine	100%	
Arginine	50%	(~2 g/d)
Tyrosine	50%	(~1 g/d)

% of body disposal	
Glutamine	30%
Proline	60%
Citrulline	100%
SAH	100%
Cysteine-Glycine	90%



- Glomerular filtration, reabsorption, degradation, and resynthesis of amino acid & peptides.

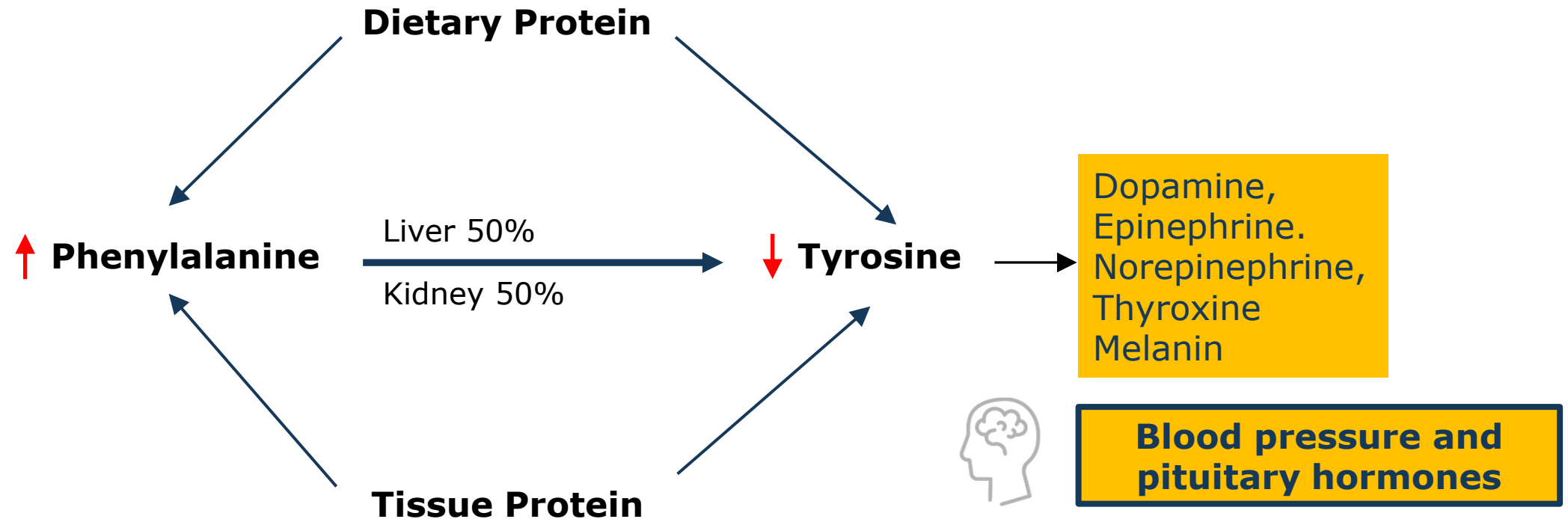
- Gluconeogenesis from amino acids.

- Degradation of peptide hormones (e.g. insulin)

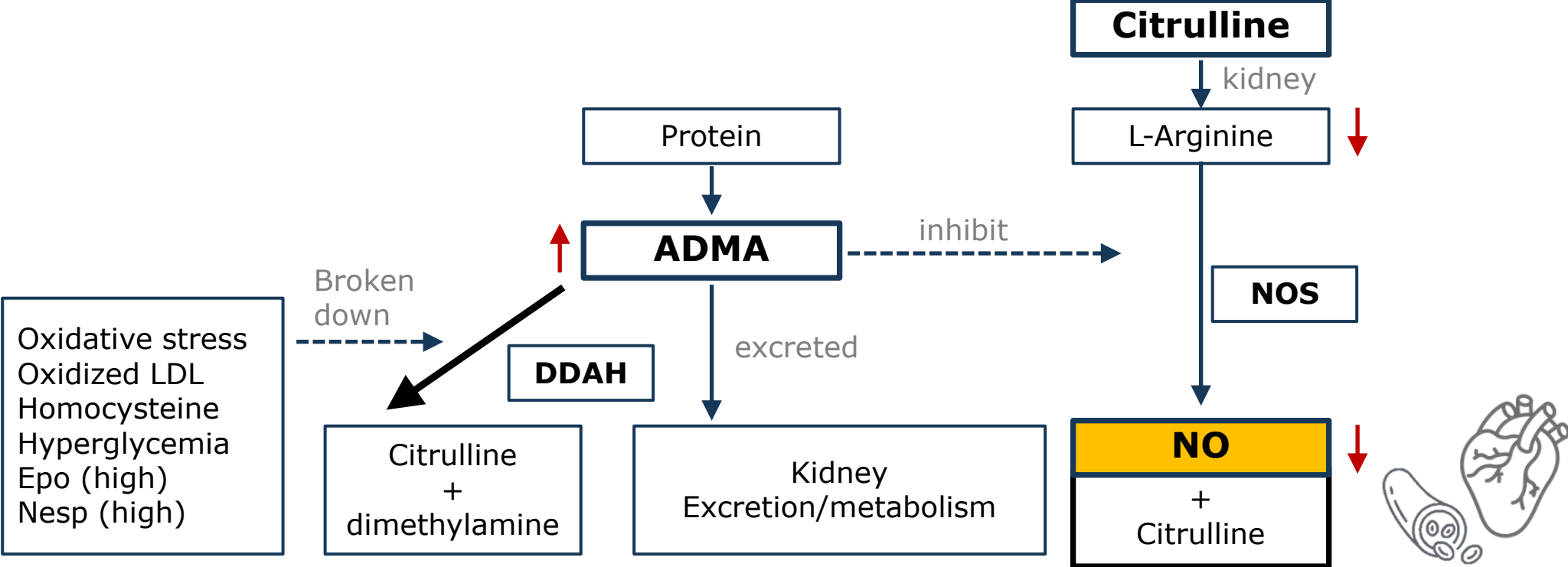
Loss of renal function may therefore be an important contributor to amino acid abnormalities found in CKD

Tyrosine can be therefore considered a “conditionally essential” in CKD

In CKD: Tyr/Phe ratio ↓



Nitric oxide (NO) production is decreased in CKD patients

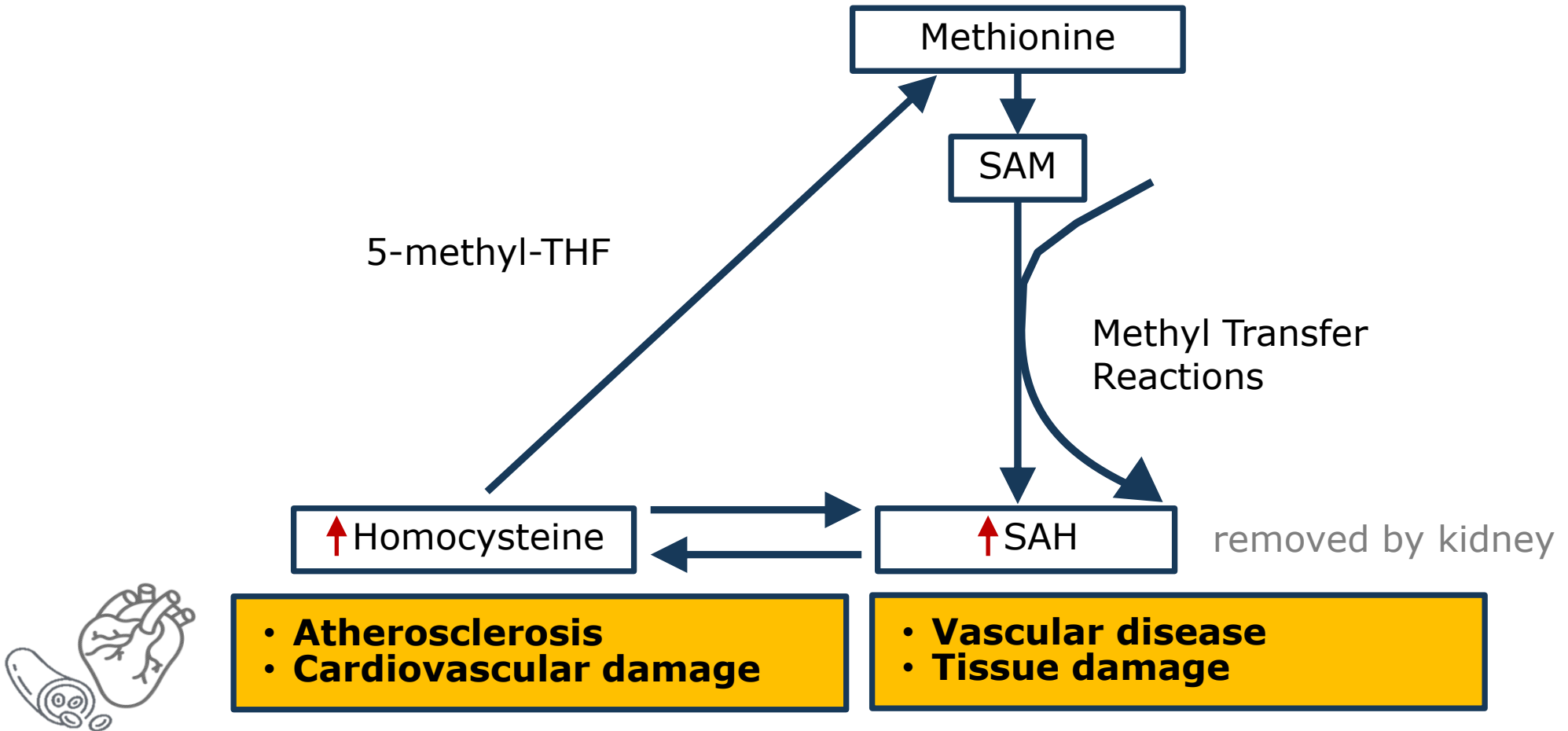


ADMA=asymmetric dimethylarginine;
DDAH=dimethylarginine dimethylaminohydrolase

- Hypertension
- Endothelial cell function
- Atherosclerotic processes

1. Clin Nutr 2010 Aug;29(4):424-33. 2. J Clin Invest 1980;65:1162-73.
3. Curr Opin Nephrol Hypertens 2009;18:68-73.

Kidney plays a unique role in the removal of SAH from the circulation



SAH=S-AdenosylHomocysteine;SAM=S-AdenosylMethionine

1. Clin Nutr 2010 Aug;29(4):424-33. 2. Kidney Int 2009;76:293-6.

Nephrosteril 腎福諾：適應症

適應症

不能攝取適當食物之患者之補助治療劑，蛋白質之消化吸收機能或合成利用障礙，嚴重創傷、火傷、骨折時蛋白質之補給，蛋白質攝取減少之營養失調症。

劑量

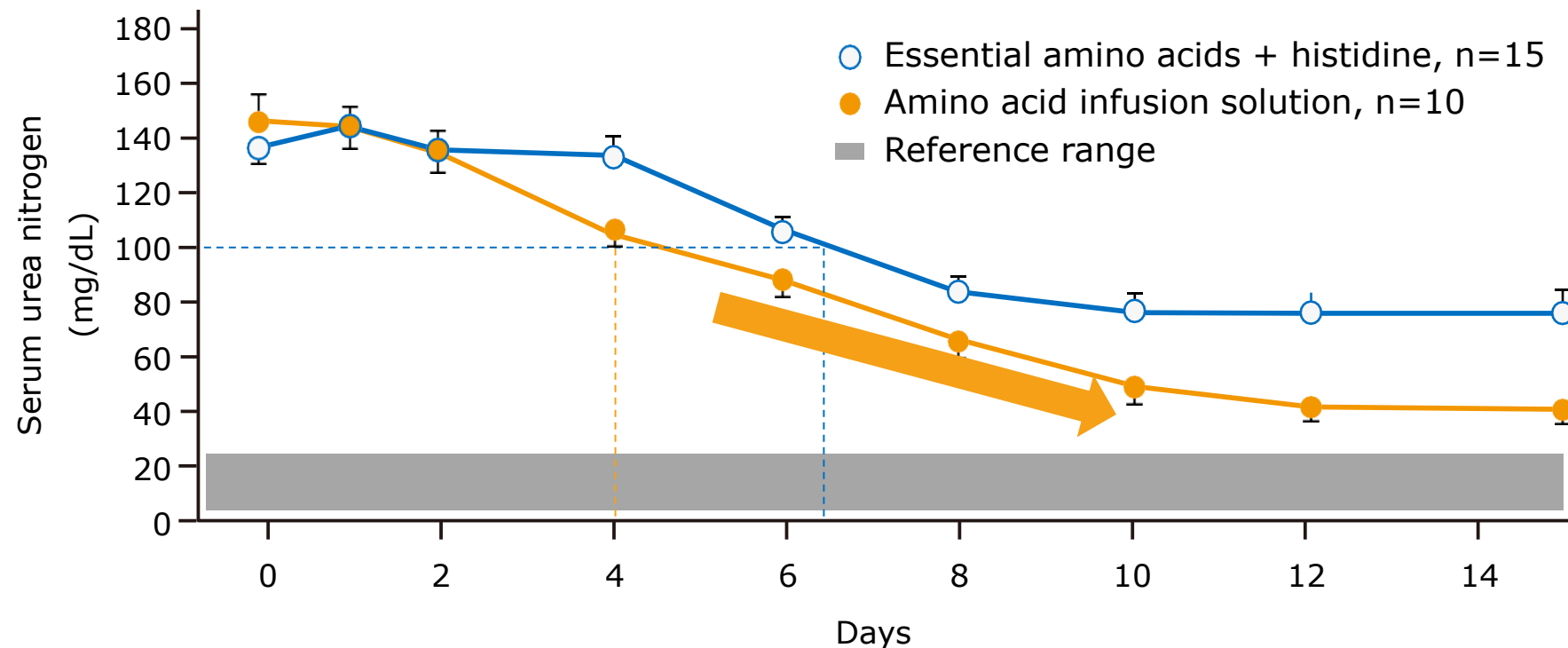
- 對於一般急慢性腎功能不全而未進行血液透析患者，最高劑量每天每公斤體重 0.5公克胺基酸，以 70 公斤體重計算，約等於每天 500 毫升。
- 對於進行血液透析和血液過濾的急慢性腎功能不全患者，最高劑量每天每公斤體重 1 公克胺基酸，以 70 公斤體重計算，約等於每天 1000 毫升。
- 最大劑量：最大劑量每天每天每公斤體重 1.5 公克胺基酸，以 70 公斤體重計算，約等於每天1500 毫升，熱量必須預先或同時以口服或非口服方式供給。

使用期間

- 急性腎功能不全患者連續使用若干天至最多二週。
- 沒有進行血液透析、血液過濾或腹膜透析治療的慢性腎功能不全患者，可連續使用直到可以口服蛋白質為止。

IV nutrition therapy in renal insufficiency 尿素氮下降

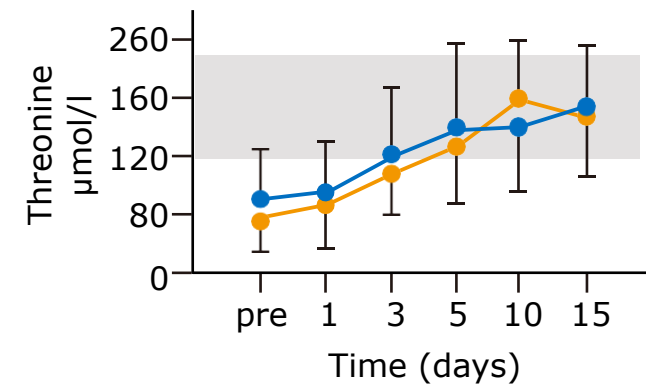
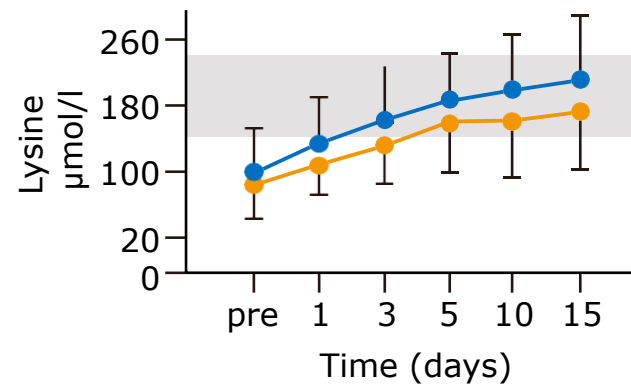
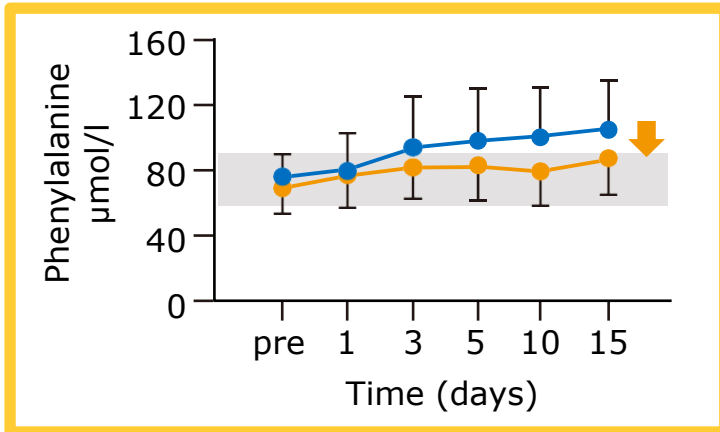
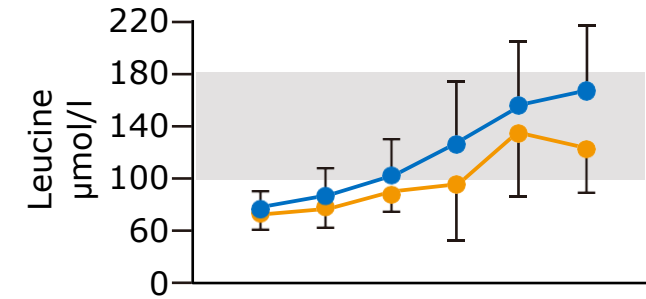
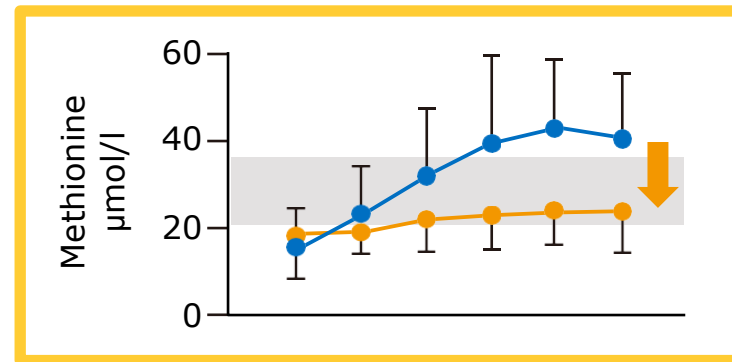
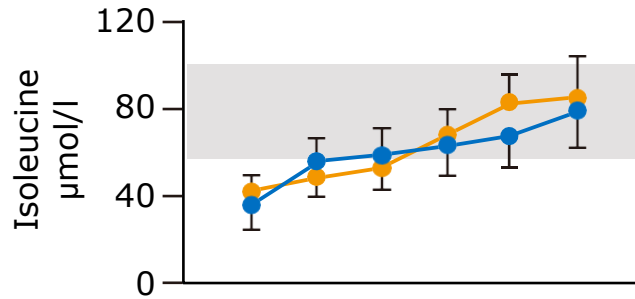
- **Amino acid infusion solution** (0.5g/kg/day) in patients with chronic renal insufficiency (n=10, mean + SD) compared with EAA+His. (n=15)
- More pronounced decrease in **serum urea N**, approaching the normal range



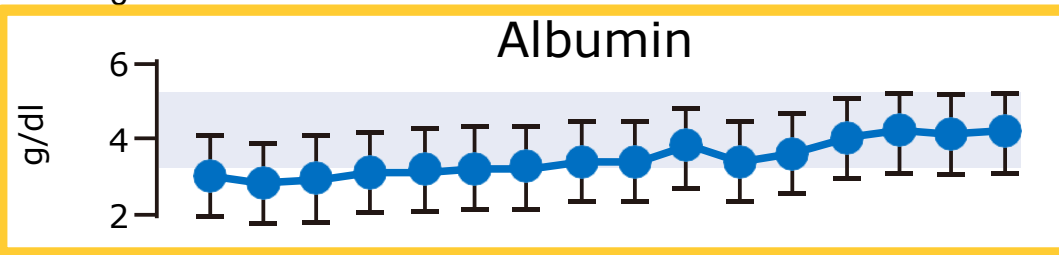
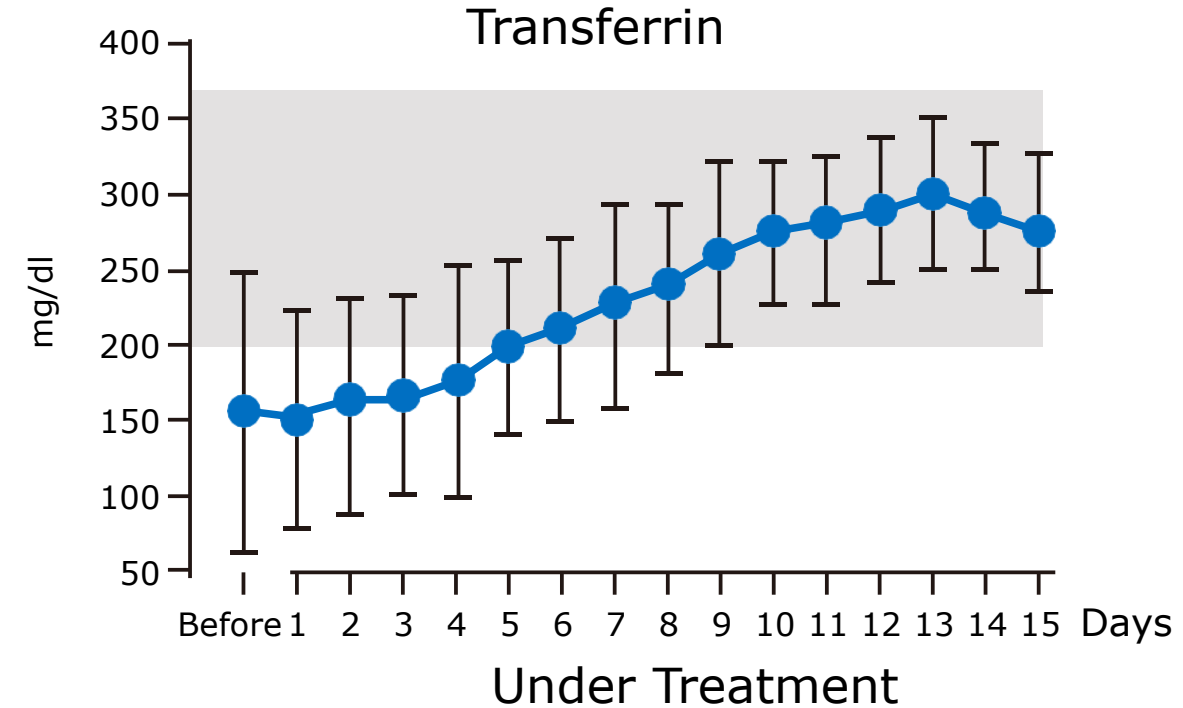
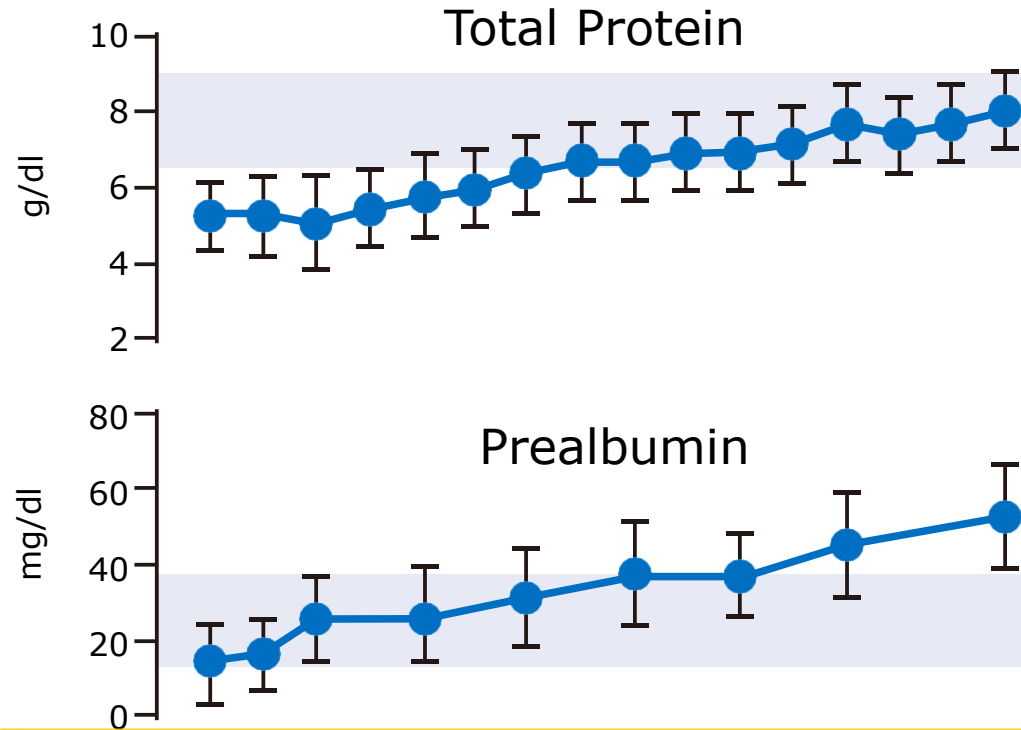
Correct amino acid imbalances 矯正氨基酸不平衡

Plasma amino acid concentrations under total parenteral nutrition in catabolic patients with CKD (mean \pm SEM)

- EAA + His, n=15
- Amino add infusion solution, n=10



Functional proteins were increased 功能性蛋白指數提升



透析補充胺基酸：減少流失、提升營養狀態

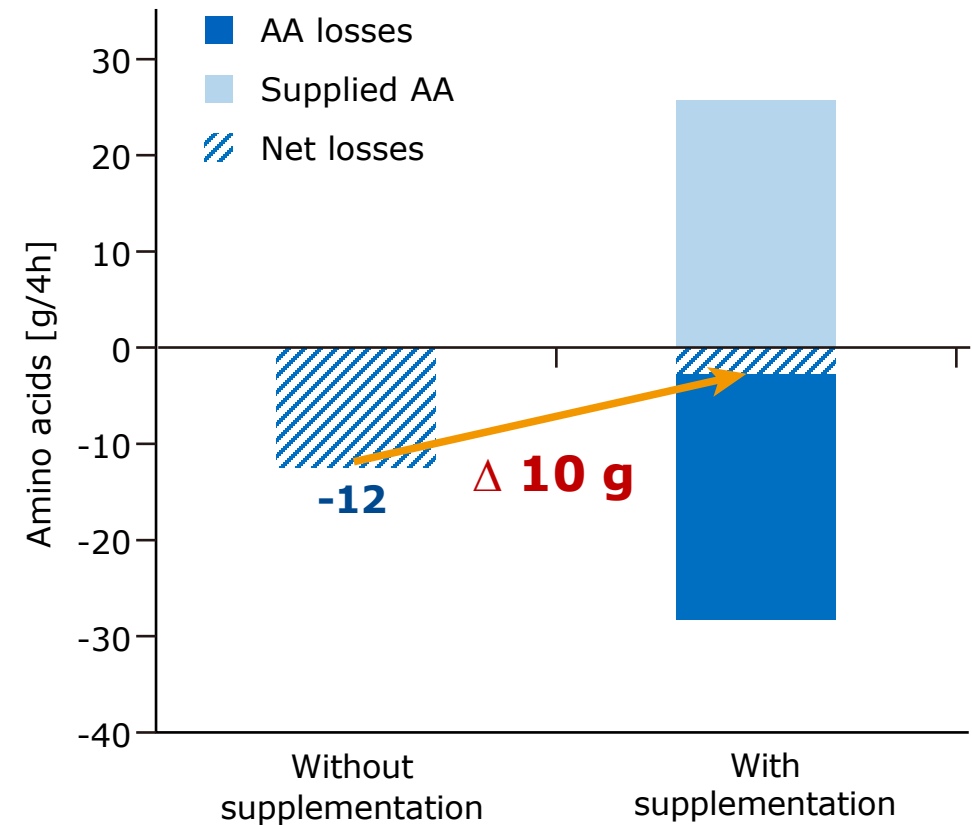
RCT study with & without intradialytic amino acid (AA) supplementation (25.7 g AA) over 4 hours HD

During HD:

- Reduction of net AA losses by 10 g/4h.
- Positive net balance of AAs (10.6 ± 5.6 g for total AAs), preventing a reduction in plasma concentrations.

After 3 months:

- Protein catabolic rate: **1.07** → **1.18** g/kg
- Serum albumin: **36.2** → **42.2** g/L
- Transferrin: **1.78** → **2.01** g/L



Amino acid infusion solution 處方規範

住院

健保藥品給付規定通則（**109.11.25更新**）

四、注射藥品之使用原則：

（三）電解質及營養靜脈補充輸液之使用，應說明理由並有明確需要，以積極治療為目的，始得為之。

#建議加註的理由

1. 蛋白質攝取不足
2. 營養不良：如 Alb 值

健保價：NT 188

透析門診

自費購買

Parenteral nutritions 處方規範

健保藥品給付規定-第三節 代謝及營養劑 (112.4.24更新)

3.1. 靜脈營養輸液 Parenteral nutritions

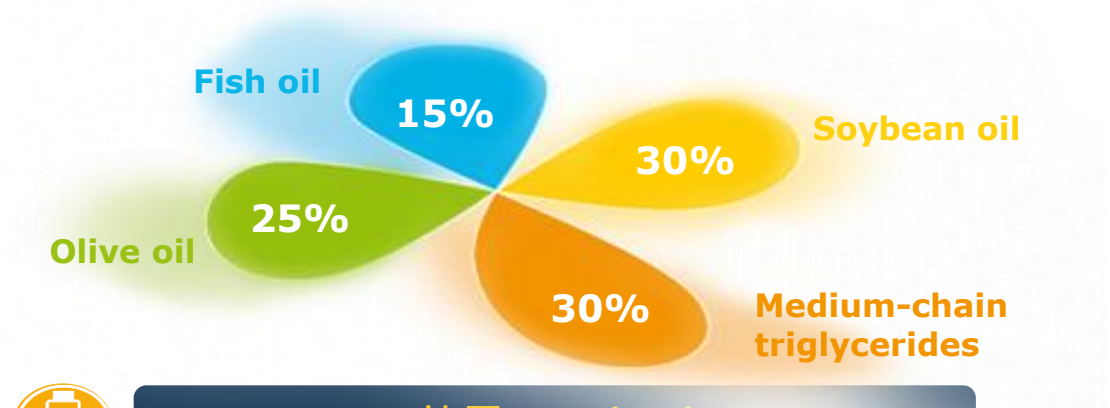
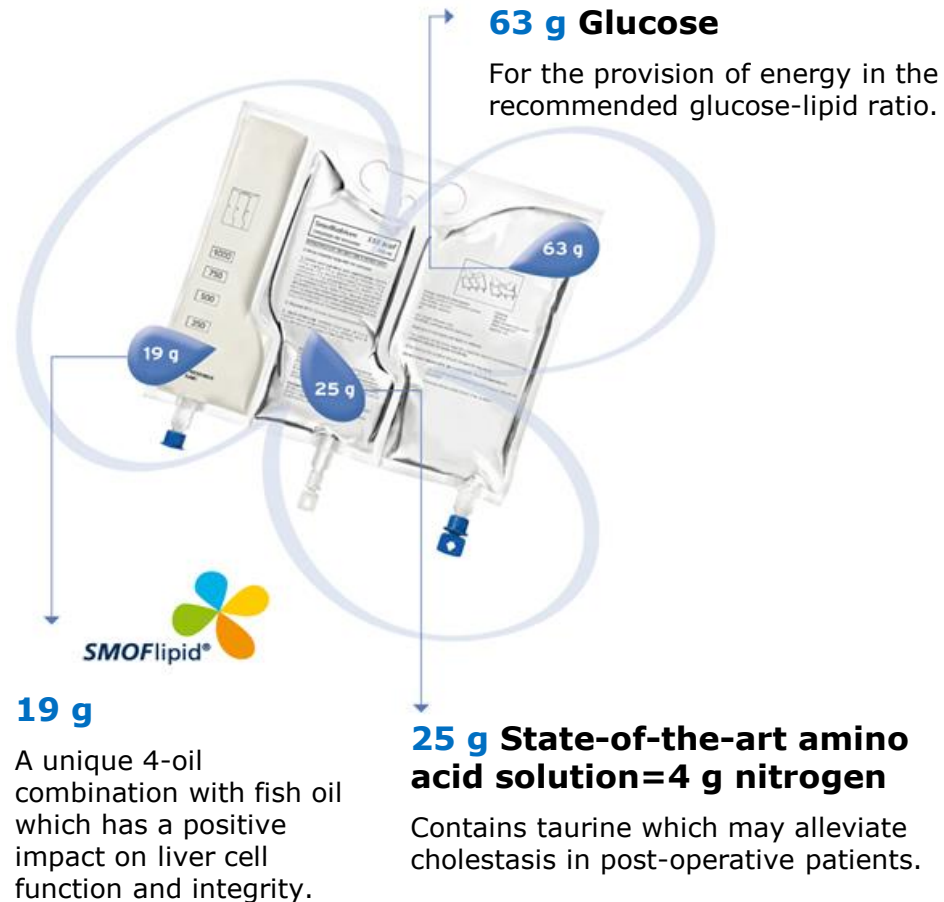
3.1.1. Fat emulsion：或含 Fat emulsion 之靜脈營養輸液(如含 glucose、lipid、amino acid 及 electrolytes 三合一靜脈營養輸液)：(97/11/1、98/7/1、98/12/1)限

1. 嚴重燒傷病人，為靜脈營養補充。
2. 使用全靜脈營養者。
3. 重大手術後五至七天仍不能經腸道進食者，每日不超過一瓶為原則。(98/12/1)

*血液透析患者須自費處方

SmofKabiven 493

儲藏不超過 25°C，不可冷凍未開封保存期限 2年



熱量 550 kcal



接近 4 份肉類蛋白質 (25g 胺基酸)



2.8g 魚油:含 ω -3 調節免疫、發炎

橄欖油 (單元不飽和) 降低多元不飽和含量

黃豆油提供必需脂肪酸

中鏈脂肪酸 (MCT) 快速提供能量

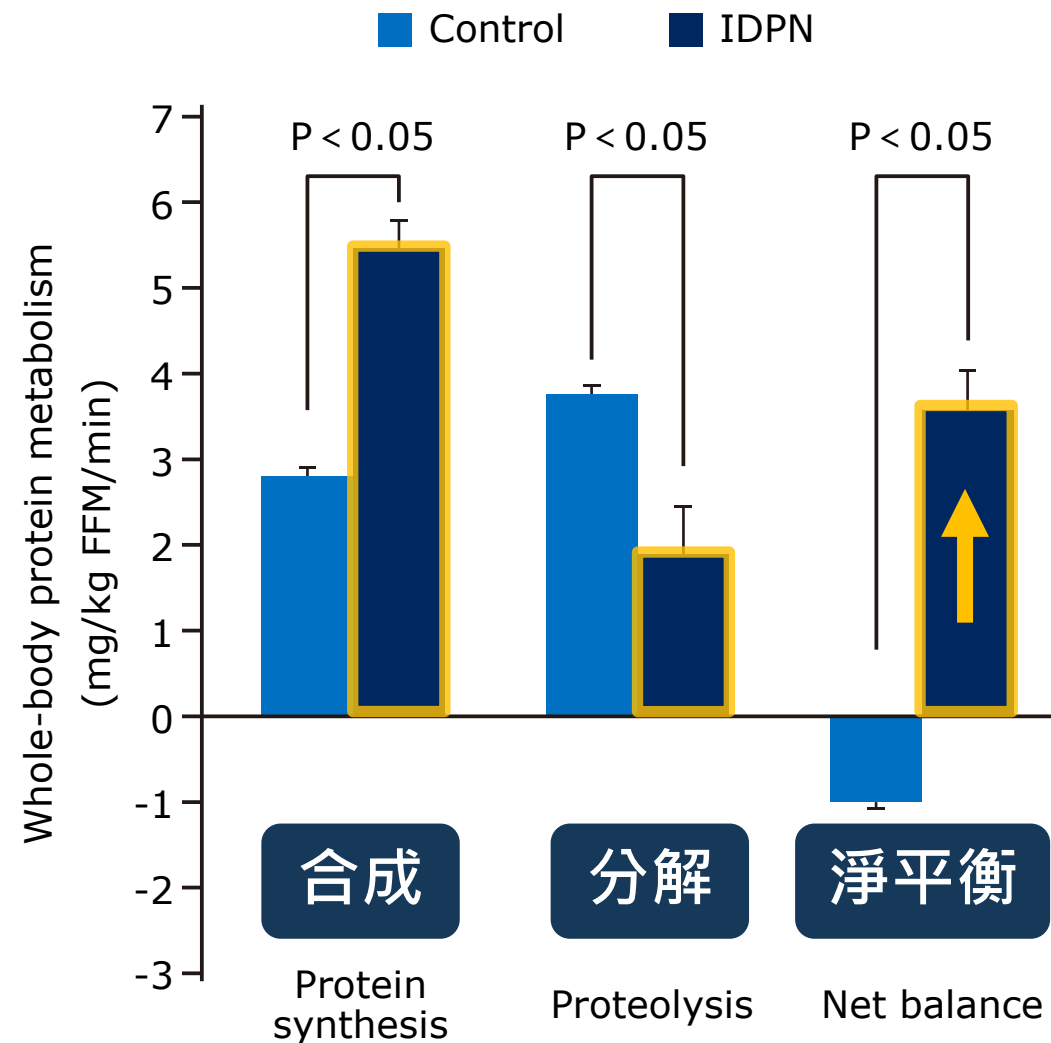
適應症：靜脈營養輸注，適用於無法由口腔進食或經腸道獲取足夠營養，或禁止由口腔及腸道進食之成年患者及 2 歲以上兒童

Using an electrolytes-free formula in case of severe hyperkalemia (>6 mmol/L) and hyperphosphatemia (>5.5 mg/dL) might be optimal for HD patients.

透析過程補充 IDPN 提高淨平衡

- Randomized crossed over study (n=7)
- IDPN treatment: 300 ml 15% AAs+150 ml 50% dextrose+150 ml 20% lipids

Baseline biochemistries	Control	IDPN
Serum albumin (g/dL)	4.24 ± 0.3	4.09 ± 0.3
Serum prealbumin (mg/dL)	43.7 ± 8.0	40.7 ± 7.0
Serum transferrin (mg/dL)	189 ± 37	195 ± 28
Serum cholesterol (mg/dL)	187 ± 27	165 ± 20
Total CO ₂ (mg/dL)	22.3 ± 1.9	23.1 ± 2.1
CRP (mg/dL)	0.74 ± 0.4	0.81 ± 0.7
Hematocrit (%)	38.7 ± 2.2	38.1 ± 3.1
N-PCR (g/kg/day)	0.97 ± 0.14	1.00 ± 0.17

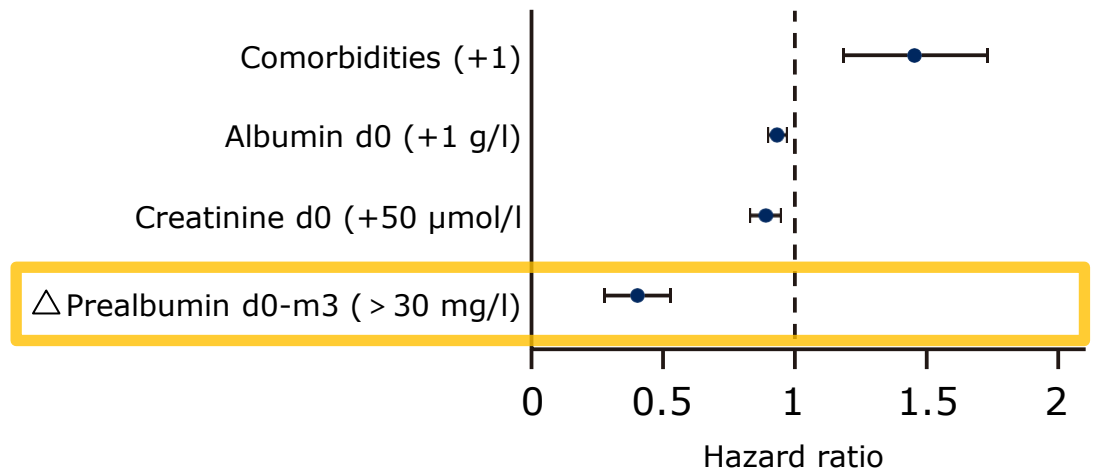


Nutritional improvement decrease mortality

營養改善時死亡率會減少

Prospective, randomized trial in which 186 malnourished HD patients.
Oral nutritional supplements with or without 1 year of IDPN.

Parameter (baseline)	Control (n=93)	IDPN (n=93)
Age (yr; mean ± SD)	67.2 ± 10.8	68.8 ± 9.9
Gender ratio (M/F)	0.90	0.94
Diabetes [n (%)]	19 (20)	26 (27)
nPNA (g/kg per d; mean ± SD)	1.09 ± 0.40	1.10 ± 0.33
Hemoglobin (g/dL; mean ± SD)	10.6 ± 1.3	10.7 ± 1.3
BMI (mean ± SD)	22.4 ± 3.7	23.1 ± 4.7
Serum albumin (g/L; mean ± SD)	31.5 ± 3.7	31.6 ± 4.4
Serum prealbumin (mg/L; mean ± SD)	239 ± 55	240 ± 49
Serum C-reactive protein [mg/l, median (min to max)]	11 (0.5 to 168)	10 (0.5 to 197)
Predialysis creatinine (µmol/L; mean ± SD)	652 ± 178	642 ± 177
Plasma cholesterol (mmol/L; mean ± SD)	4.47 ± 1.15	4.54 ± 1.25
Plasma triglycerides (mmol/L; mean ± SD)	1.49 ± 0.64	1.56 ± 0.87
Serum ALAT (UI/L; mean ± SD)	18.5 ± 10.6	18.6 ± 10.4
Serum GGT (UI/L; mean ± SD)	50.4 ± 46.5	61.2 ± 118.0

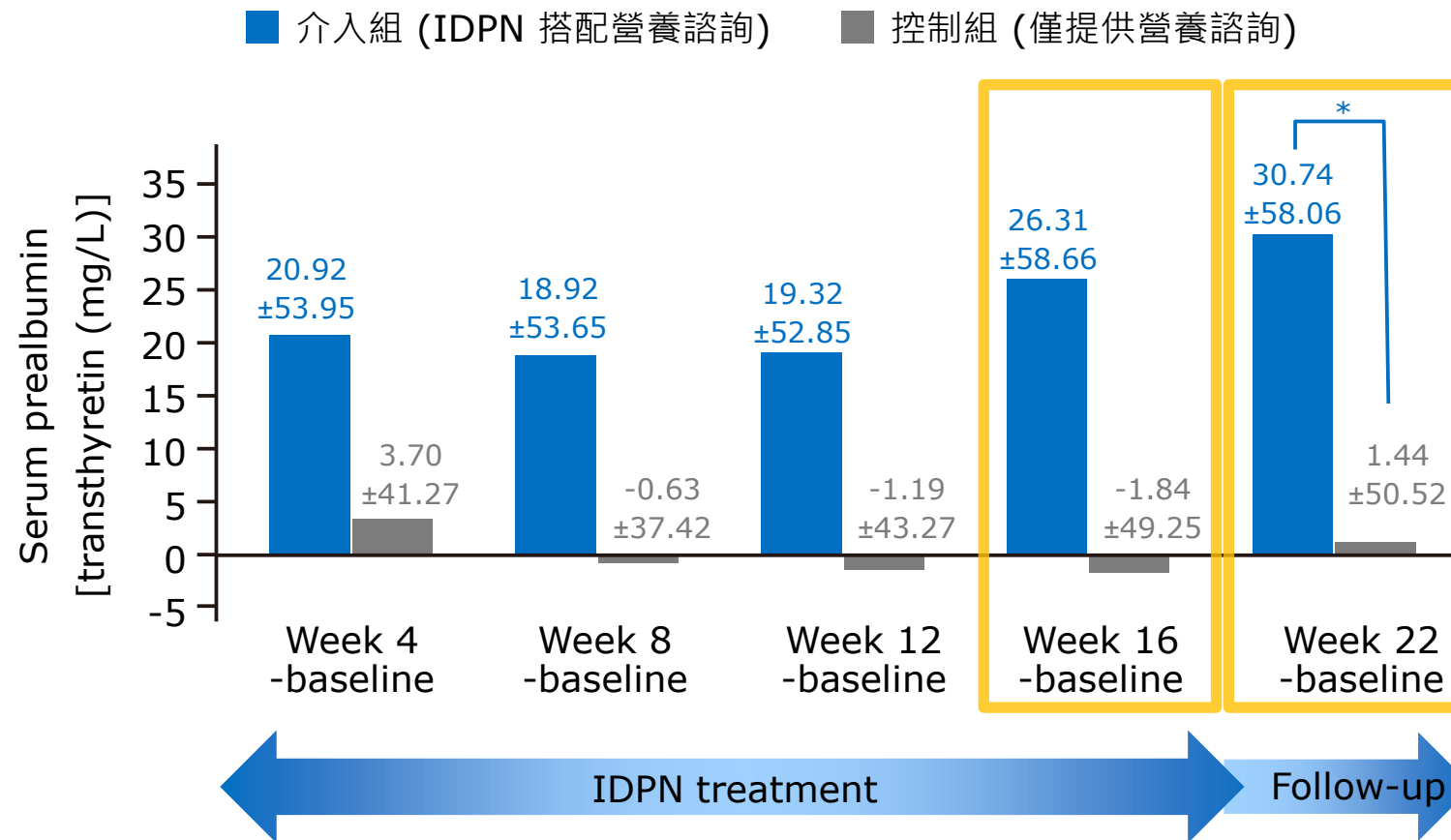


- 口服營養額外再補充 IDPN 沒有額外效果
- 整體而言，三個月內 Prealbumin 能提升 30 mg/L 的族群，能下降 54% 兩年死亡率、住院、改善生活品質 (Karnofsky score)

^a NO significant difference was found between the two groups. ALAT=alaine amino transferase; BMI=body mass index; IDPN=intradialytic parenteral nutrition; GGT=γ-glutamyl transferase; nPNA, normalized protein nitrogen appearance.

IDPN increased prealbumin and sustained response thereafter 改善 prealbumin 且有延續效果

Change in serum prealbumin over time



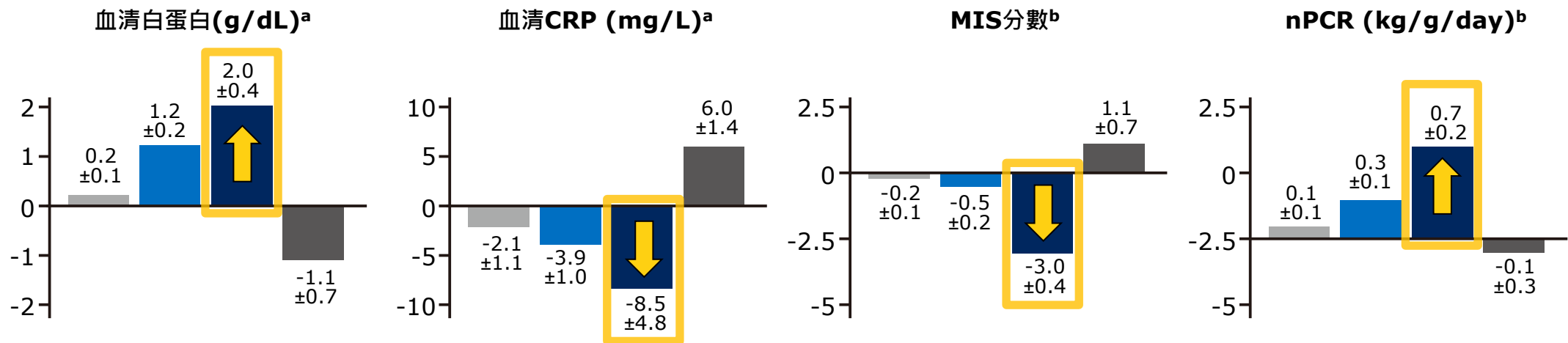
- 第四週 41.0% IDPN 組達顯著 prealbumin 提升 (> 15%)，控制組 20.5%
- 停止 IDPN 後，仍可維持提升 prealbumin 的反應持續 6 週
- 中等營養不良族群 (SGA score B) 有更佳 Prealbumin 療效

ONS + IDPN is associated with improved nutritional status and decreased inflammation 改善營養與發炎

Observational study: 56 malnourished patients on MHD for 12 months. ice

Subject characteristics	Group 1 (n=14) (only ONS)	Group 2 (n=14) (only IDPN)	Group 3 (n=10) (ONS+IDPN)	Group 4 (n=18) (control)	P value
Age (mean ± SD) (years)	61.7 ± 4.5	66.4 ± 1.3	65.8 ± 2.3	67.9 ± 2.7	0.956
Albumin (mean ± SD) (g/dL)	2.3 ± 0.2	2.2 ± 0.3	2.2 ± 0.8	2.7 ± 0.3	0.686
CRP (mean ± SD) (mg/L)	10.7 ± 1.7	9.7 ± 2.2	10.3 ± 0.3	9.9 ± 2.0	0.911
nPCR (g/kg/day)	0.7 ± 0.1	0.7 ± 0.8	0.8 ± 0.2	0.7 ± 0.8	0.540

■ 口服營養品 ■ IDPN ■ IDPN 搭配口服營養品 ■ 僅提供營養諮詢



^aIDPN組及IDPN搭配口服營養品組與他組相比達顯著差異 (p < 0.05); ^b僅有IDPN搭配口服營養品組與他組相比達顯著差異(p < 0.05)

IDPN improve albumin and nutritional status

改善 albumin 與營養狀態

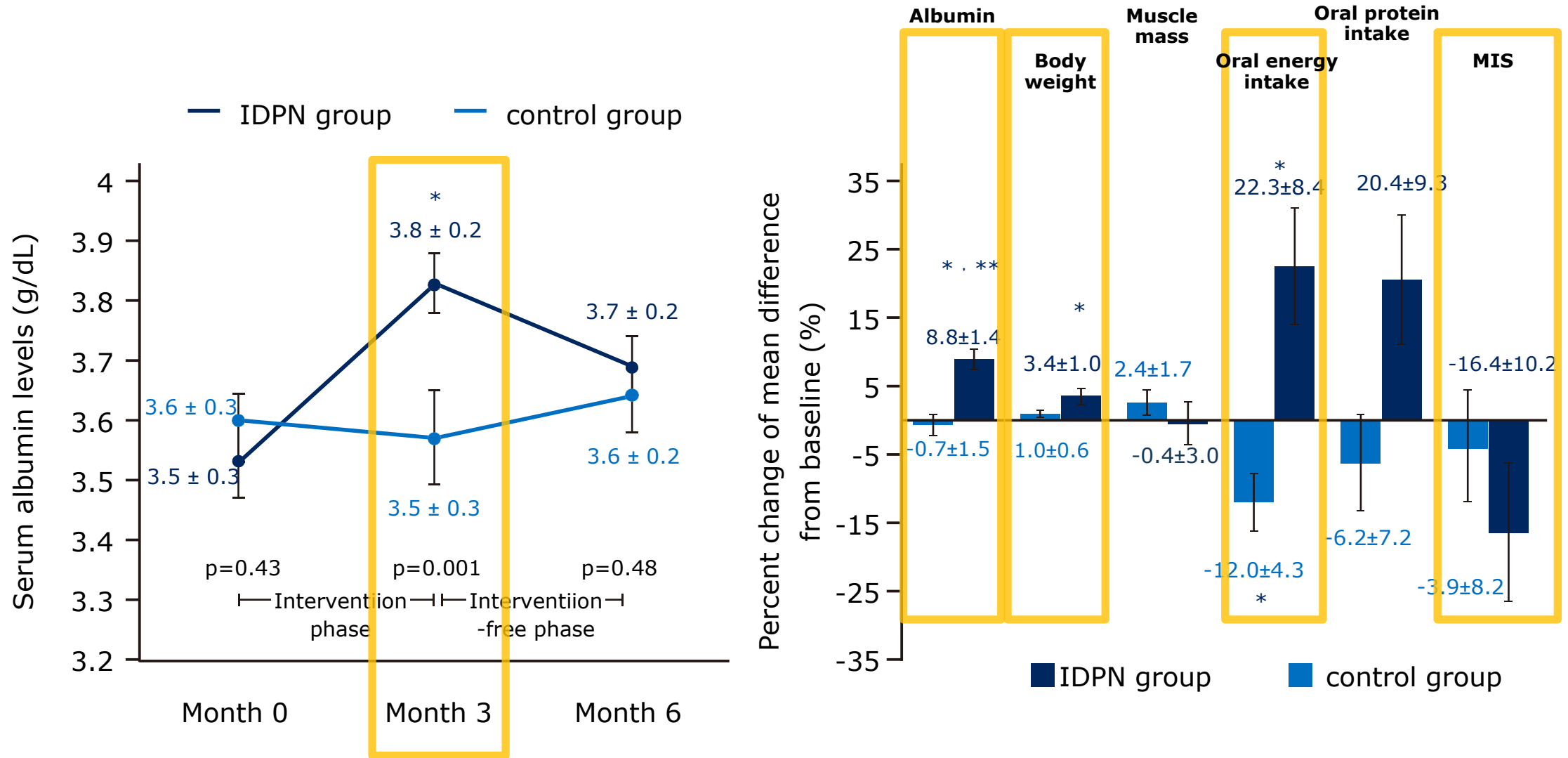
RCT trial, n=38 patient. 3 months intervention and 3 months follow-up.

- **IDPN group** (n=20): SMOF Kabiven during HD
- **Control group** (n=18): intensive dietary counselling once weekly

Parameters (baseline)	Total (n=38)	Control (n=20)	IDPN (n=18)	p value
Age, years	67.6 ± 10.8	64.4 ± 11.6	71.1 ± 8.9	0.05
SGA in category B, %	40.5	31.6	50.0	0.25
MIS, scores	8.2 ± 3.2	7.7 ± 2.8	8.7 ± 3.8	0.39
Normalized PCR, g/kg/day	1.1 ± 0.3	1.1 ± 0.4	1.1 ± 0.3	0.52
3-day dietary record				
Energy, kcal/kg/day	21.3 ± 7.8	23.2 ± 7.8	20.0 ± 7.5	0.13
Protein, g/kg/day	0.9 ± 0.3	0.9 ± 0.3	0.8 ± 0.3	0.12
Serum albumin, g/dL	3.5 ± 0.3	3.6 ± 0.3	3.5 ± 0.3	0.43
Serum prealbumin, mg/dL	27.9 ± 6.8	27.6 ± 7.9	28.2 ± 5.6	0.79

IDPN improve albumin and nutritional status

改善 albumin 與營養狀態





透析靜脈營養 (IDPN)



*以60公斤為例，大約4小時可以輸注完畢

Thank you for your attention