Base di evidenza relativa al trattamento dietetico dell'IRC in fase sostitutiva - emodialisi

Giorgio Bedogni

Argomenti

- La malnutrizione protido-energetica in emodialisi
- La “reverse epidemiology” in emodialisi

Altri argomenti

- Saranno affrontati in dettaglio da F Pasticci e AL Fantuzzi

Programma

- *La malnutrizione protido-energetica in emodialisi*
- La “reverse epidemiology”

Malnutrizione e dialisi

- La malnutrizione protido-energetica (PEM, protein energy malnutrition) è comune nei pazienti emodializzati (sino al 40%)

- (Solito problema del confronto di stime ottenute con metodi differenti)

  http://www.kidney.org/professionals/kdoqi/guidelines_updates/nut_a02.html

Malnutrizione e dialisi

- I pazienti con PEM hanno una mortalità aumentata

  http://www.kidney.org/professionals/kdoqi/guidelines_updates/nut_a02.html

- (Persiste il problema del confronto di indicatori differenti)

- Sorprendentemente, non sono state effettuate rassegne sistematiche se non per l'albumina e la proteina C-reattiva e soltanto piuttosto recentemente (2010)

Proteine sieriche e mortalità

ELSEVIER

Nutrition 26 (2010) 10–32

NUTRITION

www.nutritionjrnl.com

Review article

Relationship between serum protein and mortality in adults on long-term hemodialysis: Exhaustive review and meta-analysis

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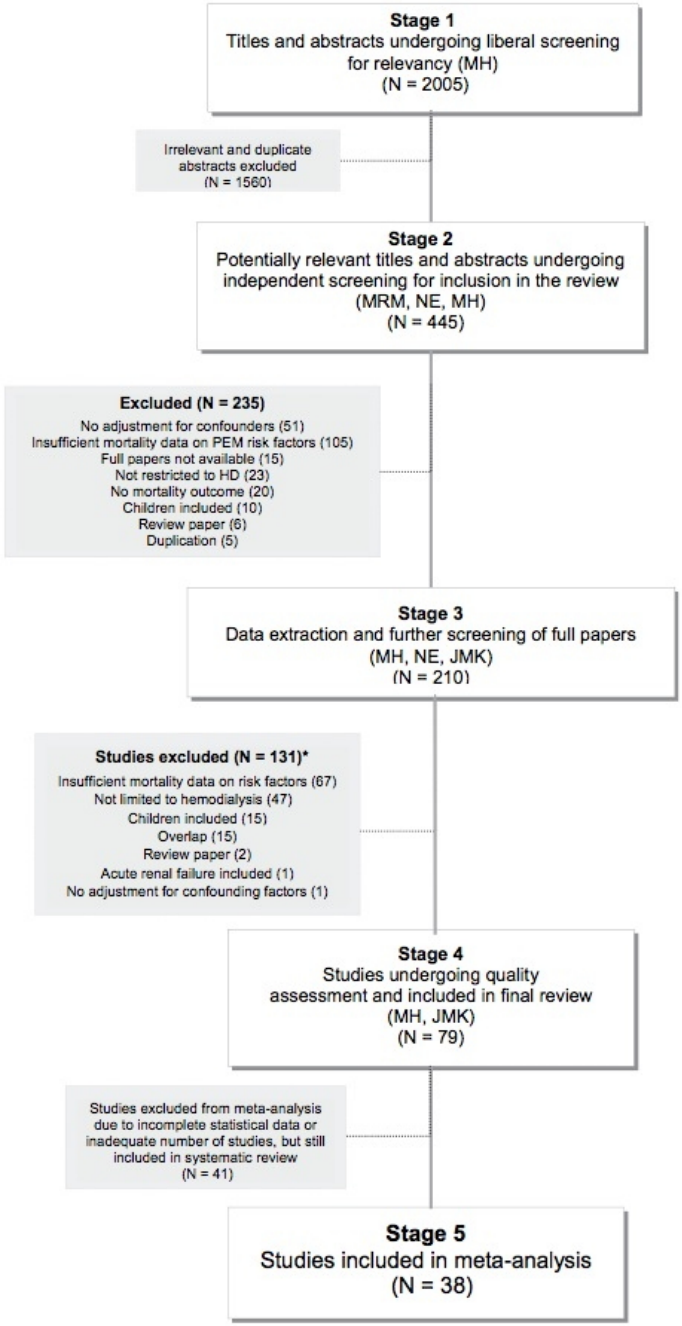
Stage 1
Titles and abstracts undergoing liberal screening for relevancy (MH)
(N = 2005)
Irrelevant and duplicate abstracts excluded
(N = 1560)
Stage 2
Potentially relevant titles and abstracts undergoing independent screening for inclusion in the review
(MRM, NE, MH)
(N = 445)
Excluded (N = 235)
No adjustment for confounders (51)
Insufficient mortality data on PEM risk factors (105)
Full papers not available (15)
Not restricted to HD (23)
No mortality outcome (20)
Children included (10)
Review paper (6)
Duplication (5)
Stage 3
Data extraction and further screening of full papers
(MH, NE, JMK)
(N = 210)
Studies excluded (N = 131)*
Insufficient mortality data on risk factors (67)
Not limited to hemodialysis (47)
Children included (15)
Overlap (15)
Review paper (2)
Acute renal failure included (1)
No adjustment for confounding factors (1)
Stage 4
Studies undergoing quality assessment and included in final review
(MH, JMK)
(N = 79)
Studies excluded from meta-analysis due to incomplete statistical data or inadequate number of studies, but still included in systematic review
(N = 41)
Stage 5
Studies included in meta-analysis
(N = 38)

Albumina e mortalità

Table 3
Subgroup analysis for serum albumin (HR with 95% CI)

Groups (no. of studies)	HR	95% CI		Difference between subgroups (*P*)
		Lower limit	Upper limit	
All studies combined ($n = 33$)	0.7355	0.6775	0.7984	—
All-cause mortality ($n = 25$)	0.7038	0.6367	0.7781	0.0014
Cardiovascular mortality ($n = 8$)	0.8726	0.7909	0.9628	
All-cause mortality only ($n = 25$)*				
Prospective ($n = 16$)	0.7803	0.7141	0.8526	0.0748
Retrospective ($n = 9$)	0.6759	0.5680	0.8044	
Lower-quality study ($n = 12$)	0.6553	0.5330	0.8057	0.0678
Higher-quality study ($n = 11$)	0.7774	0.7123	0.8485	
Adjusted for inflammation ($n = 10$)	0.7790	0.6886	0.8811	0.0406
Not adjusted for inflammation ($n = 13$)	0.6595	0.5729	0.7593	
Duration 0–3 y ($n = 14$)	0.6403	0.5418	0.7566	0.0116
Duration >3 y ($n = 11$)	0.8070	0.7233	0.9005	
Patients ≤60 y ($n = 12$)	0.6013	0.5019	0.7204	0.0012
Patients >60 y ($n = 11$)	0.8328	0.7468	0.9287	
Sample size ≤225 ($n = 13$)	0.8102	0.7206	0.8909	0.0236
Sample size >225 ($n = 12$)	0.6702	0.5821	0.7716	
Not adjusted for Kt/V ($n = 17$)	0.6767	0.5895	0.7769	0.0027
Adjusted for Kt/V ($n = 4$)	0.8651	0.7798	0.9597	
Not adjusted for comorbidity ($n = 3$)	0.4721	0.2440	0.9134	0.1144
Adjusted for comorbidity ($n = 18$)	0.7120	0.6367	0.7960	

CI, confidence interval; HR, hazard ratio; Kt/V, adequacy of dialysis
* Excluding studies reporting on cardiovascular mortality and studies with incomplete data on subgroup categories.

Proteina C-reattiva e mortalità

- Pooled results for C-reactive protein showed a weak but significant direct relation with all-cause mortality (HR 1.0322, 95% CI 1.0151–1.0496), but there was not a significant relation between C-reactive protein and cardiovascular mortality (HR 1.0172, 95% CI 0.9726-1.0639).

Malnutrizione e infiammazione

- Protein-energy malnutrition (PEM) and inflammation are common and usually concurrent in maintenance dialysis patients. Many factors that appear to lead to these 2 conditions overlap, as do assessment tools and such criteria for detecting them as hypoalbuminemia.

  Kalantar-Zadeh K. Am J Kidney Dis. 2003;42:864.

Malnutrizione e infiammazione

- PEM in dialysis patients has been suggested to be secondary to inflammation; however, the evidence is not conclusive, and an equicausal status or even opposite causal direction is possible. Hence, malnutrition-inflammation complex syndrome (MICS) is an appropriate term.

  Kalantar-Zadeh K. Am J Kidney Dis. 2003;42:864.

Malnutrizione e infiammazione

- Because MICS leads to a low body mass index, hypocholesterolemia, hypocreatininemia, and hypohomocysteinemia, a “reverse epidemiology” of cardiovascular risks can occur in dialysis patients.

  Kalantar-Zadeh K. Am J Kidney Dis. 2003;42:864.

Cause di PEM

- Anorexia*
  - Uraemic toxicity
  - Impaired gastric emptying
  - Inflammation with/without co-morbid conditions*
- Emotional and/or psychological disorders
- Dietary restrictions
  - Prescribed restrictions: low-potassium, low-phosphorous regimens
  - Social constraints: poverty, inadequate dietary support
  - Physical incapacity: inability to acquire or prepare food to eat
- Nutrient losses during dialysis
  - Loss through haemodialysis membrane into dialysate
  - Adherence to haemodialysis membrane or tubing
  - Loss into peritoneal dialysate
- Hypercatabolism caused by co-morbid illness
  - Cardiovascular disease*
  - Diabetic complications
  - Infection and/or sepsis*
  - Other co-morbid conditions*
- Hypercatabolism associated with dialysis treatment
  - Negative protein balance
  - Negative energy balance
- Endocrine disorders of uraemia
  - Resistance to insulin
  - Resistance to growth hormone and/or insulin-growth factor-1
  - Increased serum level of/or sensitivity to glucagon
  - Hyperparathyroidism
- Other endocrine disorders
  - Acidaemia with metabolic acidosis

*may be associated with inflammation

Pasticci F et al. Journal of Renal Care 2012;38:50.

Valutazione dello stato protido-energetico

Category	Measure	Minimum Frequency of Measurement
I. Measurements that should be performed routinely in all patients	Predialysis or stabilized serum albumin	Monthly
	% of usual postdialysis body weight, body mass index[a] and interdialytic weight gain[a]	Monthly
	% of standard (NHANES II) body weight	Every 4 months
	Subjective global assessment	Every 6 months
	Dietary interview and/or diary	Every 6 months
	nPNA (nPCR)	Monthly
II. Measures that can be useful to confirm or extend the data obtained from the measures in Category I	Predialysis or stabilized serum prealbumin (transthyretin)	As needed
	Skinfold thickness	As needed
	Midarm muscle area, circumference, or diameter	As needed
	Dual energy x-ray absorptiometry	As needed
III. Clinically useful measures, which, if low, might suggest the need for a more rigorous examination of protein-energy nutritional status	Predialysis or stabilized serum	
	—Creatinine	As needed
	—Urea nitrogen	As needed
	—Cholesterol	As needed
	Creatinine index	

http://www.kidney.org/professionals/kdoqi/guidelines_updates/nut_a02.html

Introito proteico raccomandato

- “Surprisingly few studies have assessed the dietary protein requirements for these patients. Moreover, there is not a single randomized controlled trial in which patients undergoing MHD were randomly assigned to different levels of DPI and the effect on morbidity and mortality was examined”

Kopple JD et al. Nutritional management of renal disease.
Lippincott Williams & Wilkins; 2004, p. 440.

Introito proteico raccomandato

	Haemodialysis	Peritoneal dialysis
DOQI	1.2 g/kg IBW/day	1.2–1.3 g/kg IBW/day
	≥50% HBV	≥50% HBV
ESPEN	1.2 g/kg IBW/day	1.2–1.5 g/kg IBW/day
	≥50% HBV	≥50% HBV
		Greater intake if peritonitis
EBPG	At least 1.1 g/kg IBW/day	
	Balanced intake of high quality animal protein and vegetable protein source	
EDTNA/ERCA	1.1–1.2 g/kg IBW/day	1.0–1.2 g/kg IBW/day
		1.5 g/kg IBW/day if peritonitis
	≥50% HBV	≥50% HBV

Table 3: Suggested protein intake for the dialysis patient.
DOQI = Disease Outcomes Quality Initiative; ESPEN = European Society for Parenteral and Enteral Nutrition; EBPG = European Best Practice Guidelines; EDTNA/ERCA = European Dialysis and Transplant Nurses Association/European Renal Care Association; IBW = ideal body weight; HBV = high biological value. Adapted from: NKF 2000 (DOQI); Toigo *et al*. (2000) (ESPEN); EDTNA/ERCA 2002; Fouque *et al*. (2007) (EPBG).

Pasticci F et al. Journal of Renal Care 2012;38:50.

Malnutrizione e infiammazione

- Because MICS leads to a low body mass index, hypocholesterolemia, hypocreatininemia, and hypohomocysteinemia, a “reverse epidemiology” of cardiovascular risks can occur in dialysis patients.

  Kalantar-Zadeh K. Am J Kidney Dis. 2003;42:864.

Programma

- La malnutrizione protido-energetica in emodialisi
- *La “reverse epidemiology”*

“Reverse epidemiology”

CARDIOVASCULAR AND SURVIVAL PARADOXES IN DIALYSIS PATIENTS

What Is So Bad about Reverse Epidemiology Anyway?

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2007 pp. 593–601
DOI: 10.1111/j.1525-139X.2007.00360.x

“Reverse epidemiology”

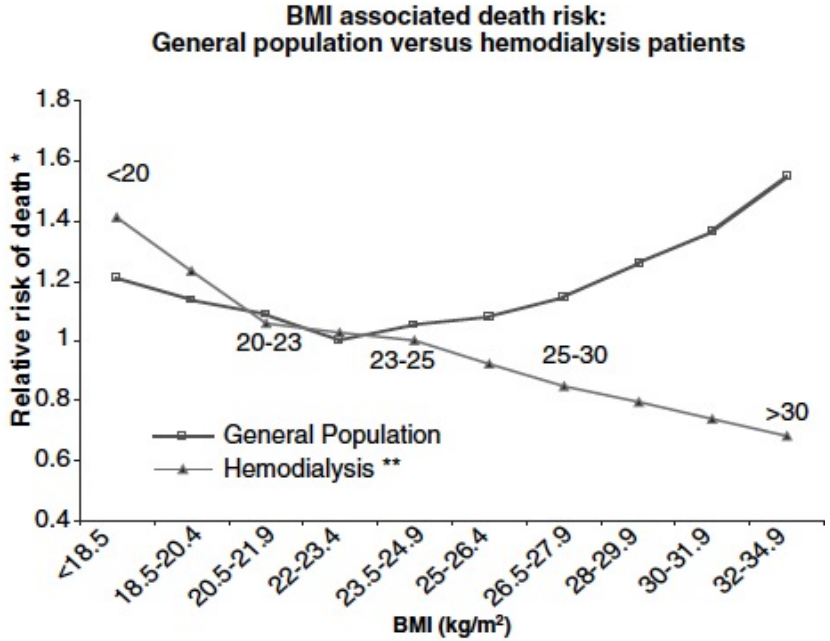

FIG. 1. Crossing curves of the Obesity Paradox: Dialysis patients vs. the general population. Comparison between the impacts of body mass index (BMI) on all cause mortality in the general population (■) versus in maintenance hemodialysis population (▲). The general population data are adopted from Calle et al., NEJM 1999, 341:1097–1105 (combined men and women, healthy, nonsmoker) (108). The hemodialysis data are adopted from Leavey et al., Neph Dialysis Transplant 2001, 16:2386–94 (combined US and Europe data) (109). *Note that each population has a different follow-up period: 14 years for the general population vs. 4 years for hemodialysis patients. **BMI stratifications are different in two populations: X-axis is based on the original graph of the general population, and the original hemodialysis BMI subgroup ranges are printed additionally along the hemodialysis curve. [adapted, with permission, from Kalantar-Zadeh et al. (15)].

“Reverse epidemiology”

- Most recently there have even been emerging longitudinal studies showing that gaining body weight and total fat are associated with improved survival overtime.

- These apparently counterintuitive observations have been collectively referred to as “reverse epidemiology”, “risk factor paradox” such as “obesity paradox”, and “altered risk factor pattern”.

“Reverse epidemiology”

- As over two-thirds of dialysis patients are already dead within 5 years of commencing dialysis treatment, the long-term effects of conventional risk factors on future mortality is essentially irrelevant.

“Reverse epidemiology”

- What we consider ‘‘reverse’’ epidemiology, i.e., the stronger impact of undernutrition and short-term death, may indeed be the ‘‘natural’’ epidemiology of mankind.

“Reverse epidemiology”

TABLE 2. Possible pathophysiologic mechanisms leading to survival advantages of obesity in dialysis patients

Pathophysiologic mechanisms of Obesity Paradox
Time differential of competitive risk factors: overnutrition vs. undernutrition (71)
Dominant role of wasting in chronic disease states (77)
Irrelevancy of risk factors of long-term mortality (68)
Selected genotype resulting from survival selection over the CKD progression (107)
Role of the visceral compartment as the source of uremic toxin (55)
Containment/storage of uremic toxins in fat tissue (24)
Salutary anti-inflammatory cytokines related to fat, including adiponectins (113)
Tumor necrosis factor alpha receptors (47)
Endotoxin-lipoprotein hypothesis (49)
Stability of hemodynamic status in obese patients (45)
Neurohormonal alterations in obesity (46)
Alteration of conventional risk factors in uremic milieu
Protecting role of fat storage during hardship episodes in the history of mankind (69)

“Reverse epidemiology”

- As physicians and scientists with professional integrity committed to the ‘‘cause-no-harm’’ motto, we should feel uneasy by the readiness with which the Liu et al. dismiss the paradoxical associations as mere confounding without biological plausibility and replace them with the more speculative concept that cholesterol should be lowered in all dialysis patients no matter what.

Statine, colesterolo ed emodialisi

HMG CoA reductase inhibitors (statins) for dialysis patients

Sankar D Navaneethan[1,*], Sagar U Nigwekar[2], Vlado Perkovic[3], David W Johnson[4], Jonathan C Craig[5], Giovanni FM Strippoli[6]

Editorial Group: Cochrane Renal Group

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Assessed as up-to-date: 20 JUL 2008

DOI: 10.1002/14651858.CD004289.pub4

Statine, colesterolo ed emodialisi

- Compared with placebo, statin use was associated with a significantly lower end of treatment average total cholesterol (14 studies, 1823 patients; MD -42.61 mg/dL, 95% CI -53.38 to -31.84), LDL cholesterol (13 studies, 1801 patients; MD -43.06 mg/dL, 95% CI -53.78 to -32.35) and triglycerides (14 studies, 1823 patients: MD -24.01 mg/dL, 95% CI -47.29 to -0.72).

Statine, mortalità ed emodialisi

- Compared to placebo, statins did not decrease all-cause mortality (10 studies, 1884 patients; RR 0.95, 95% CI 0.86 to 1.06) or cardiovascular mortality (9 studies, 1839 patients: RR 0.96, 95% CI 0.65 to 1.40).

- There was a lower incidence of nonfatal cardiovascular events with statins compared to placebo in haemodialysis patients (1 study, 1255 patients; RR 0.86, 95% CI 0.74 to 0.99).

Grazie