The 20th Budapest Nephrology School
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When to initiate Dialysis?

Is it Really True that the Earlier the Better?

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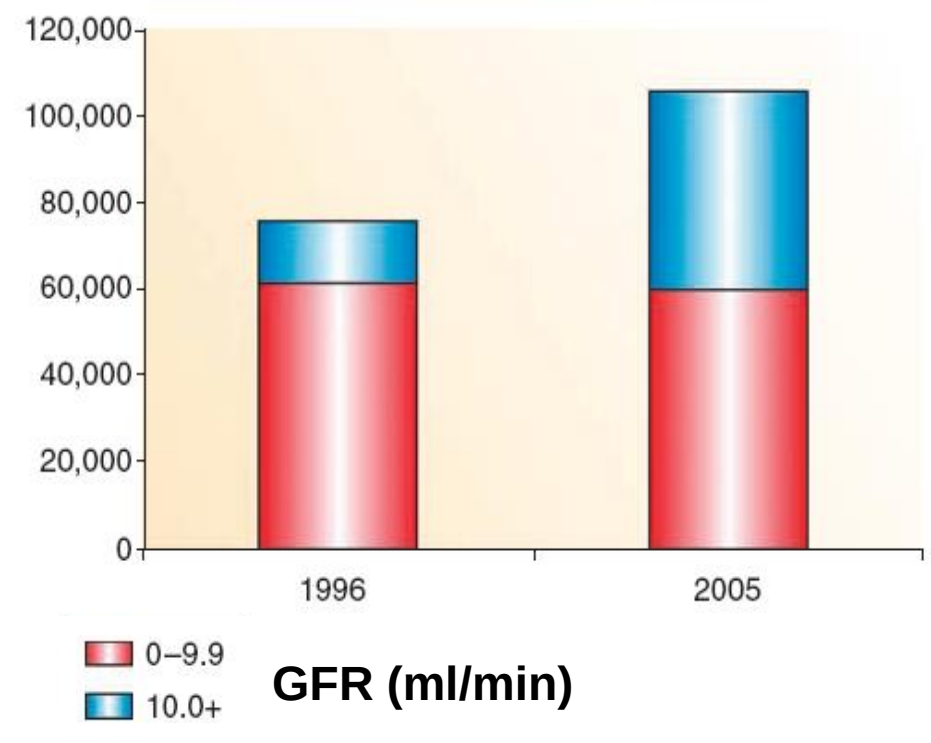
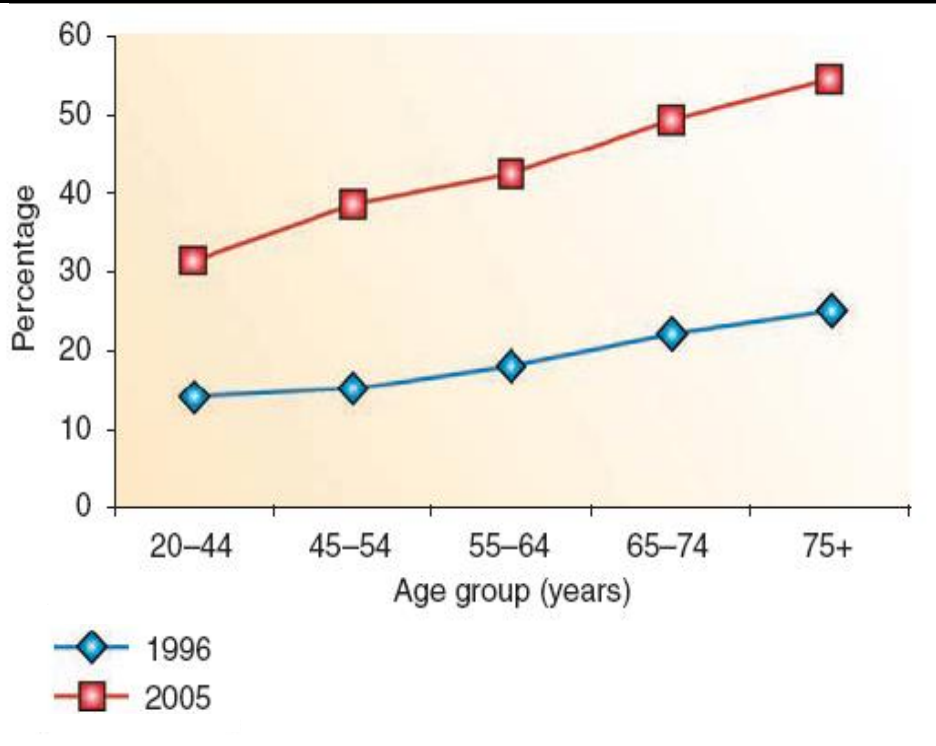
Initiation of dialysis at higher GFRs: is the apparent rising tide of early dialysis harmful or helpful?

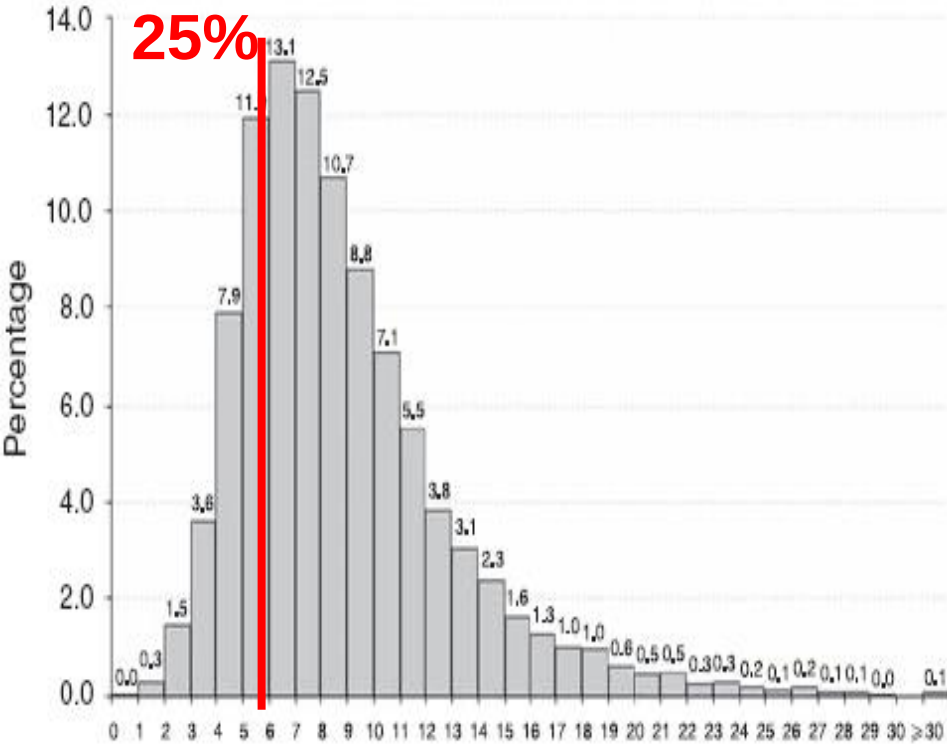
Patients starting dialysis at higher GFRs

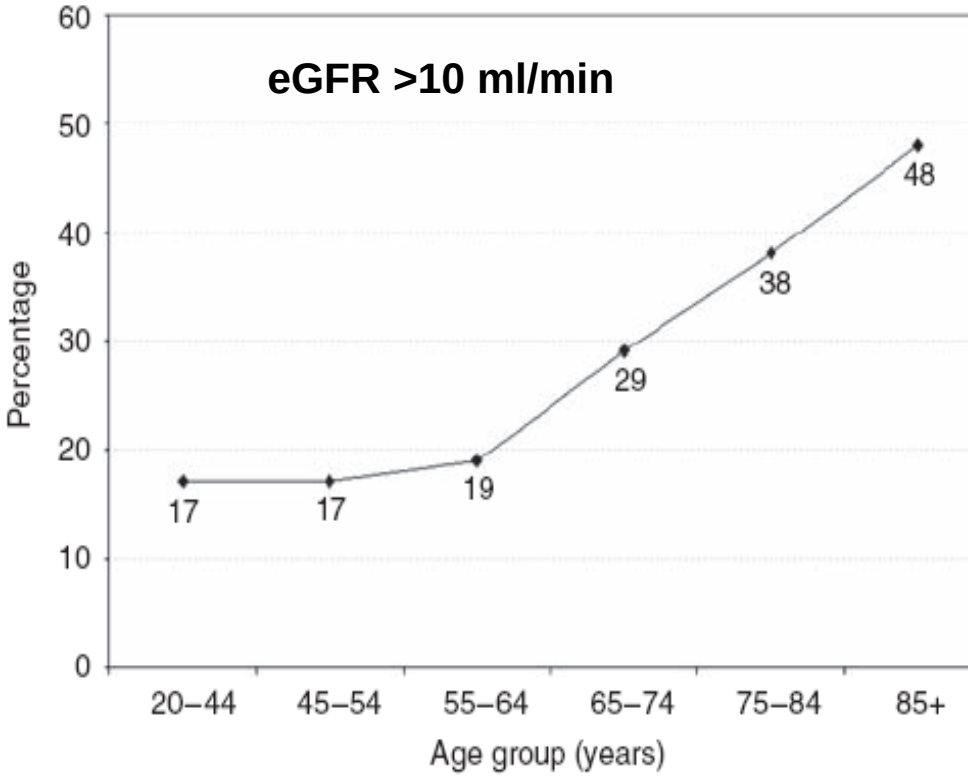




Rosansky SJ, et al. Kidney Int 2009; 76: 257-261

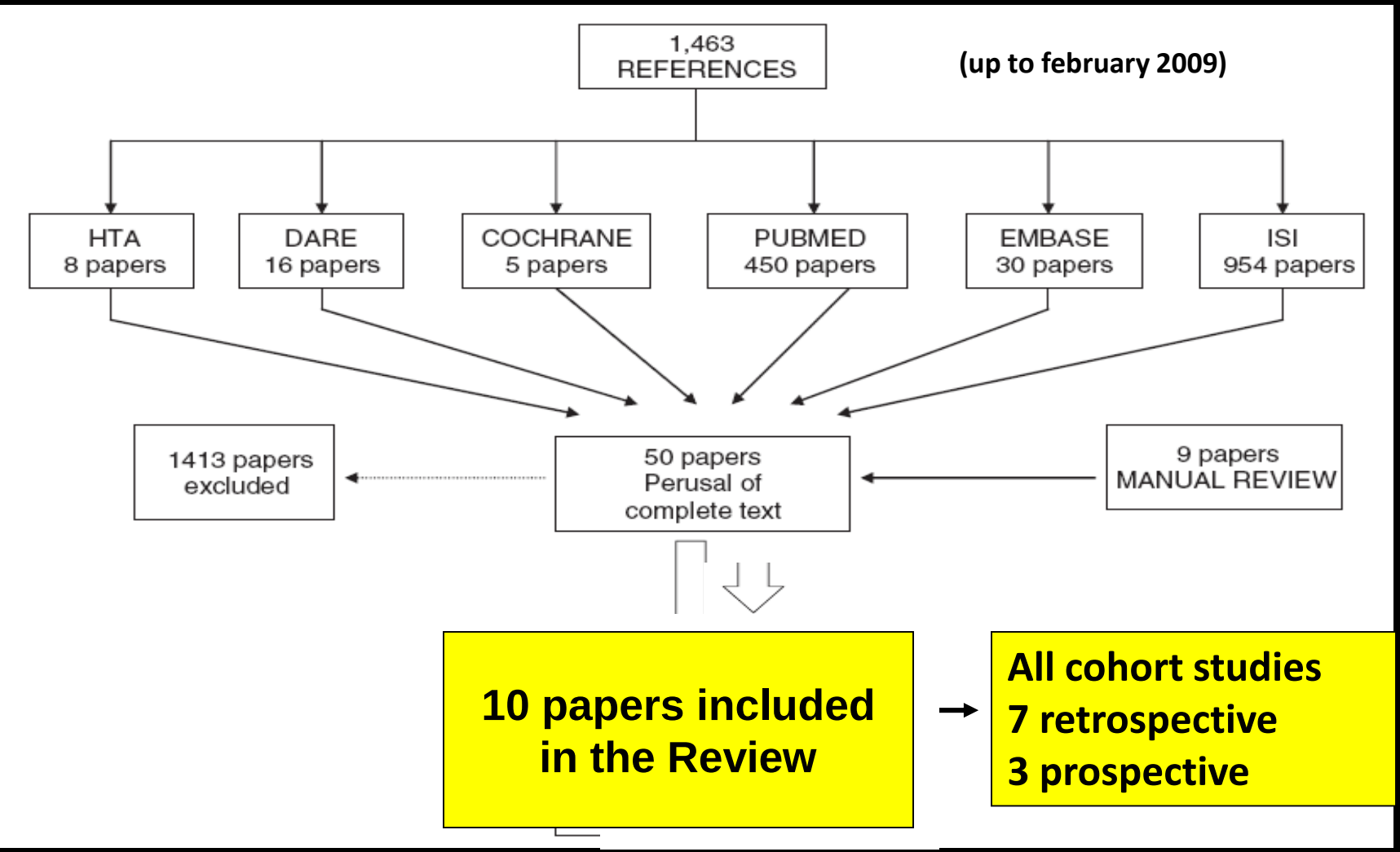
Age and comorbidity may explain the paradoxical association of an early dialysis start with poor survival





Lassalle M, et al. Kidney Int 2010; 77: 700-707

Influence of early dialysis among patients with advanced chronic renal disease: results of a systematic review



Cantero-Munoz P et al. Nephrol Dial Transplant 2010; 25: 2214-2221

Influence of early dialysis among patients with advanced chronic renal disease: results of a systematic review

Time of treatment initiation and dialysis modality

- Studies of patients on HD (Kazmi, Wilson), reported a higher mortality with early treatment
- Studies of patients on PD indicated better survival with early initiation in one case (Tang) and “contradictory” results in the other (Shiao)
- Mixed HD/PD studies in one case (Beddhu) indicated a 1.4-fold rise in the risk of death for every increase of 5 mL/min in eGFR at initiation of treatment, and in the other (Korevaar) a small beneficial effect of early initiation

Cantero-Munoz P et al. Nephrol Dial Transplant 2010; 25: 2214-2221

Influence of early dialysis among patients with advanced chronic renal disease: results of a systematic review

- The main limitation of these studies is the presence of lead-time bias: an erroneous survival benefit is

The main limitation is the presence of lead-time bias

that is, earlier initiation of dialysis prolongs time on dialysis but does not change patient survival

- **No conclusions can be drawn as to the optimal time for initiating RRT as these studies are contradictory and include methodological shortcomings**

from prospective studies

Cantero-Munoz P et al. Nephrol Dial Transplant 2010; 25: 2214-2221

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 12, 2010 VOL. 363 NO. 7

A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis

Bruce A. Cooper, M.B., B.S., Ph.D., Pauline Branley, B.Med., Ph.D., Liliana Bulfone, B.Pharm., M.B.A., John F. Collins, M.B., Ch.B., Jonathan C. Craig, M.B., Ch.B., Ph.D., Margaret B. Fraenkel, B.M., B.S., Ph.D., Anthony Harris, M.A., M.Sc., David W. Johnson, M.B., B.S., Ph.D., Joan Kesselhut, Jing Jing Li, B.Pharm., B.Com., Grant Luxton, M.B., B.S., Andrew Pilmore, B.Sc., David J. Tiller, M.B., B.S., David C. Harris, M.B., B.S., M.D., and Carol A. Pollock, M.B., B.S., Ph.D., for the IDEAL Study*

Multicenter, randomized, controlled trial

- **To examine whether the timing of the initiation of maintenance dialysis influenced survival among patients with chronic kidney disease.**
- **Primary outcome: death from any cause.**

Study Course

July 2000 – Nov. 2008

GFR 10-15 ml/min

2928 pts were screened

32 Centers in Australia and New Zealand

mean 60.4 years
542 M, 286 F

828 underwent randomization

(355 diabetes)

Early-Start Group

Late-Start Group

GFR 10-14 ml/min/1.73 m²	Cockroft-Gault	GFR 5-7 ml/min/1.73 m²
n.		n.
404	randomized	424
10	deaths before dialysis start	22
383	started dialysis	386
1.8 months	median time to dialysis initiation	7.4 months
(95% CI, 1.60 to 2.23)		(95% CI, 6.23 to 8.27)

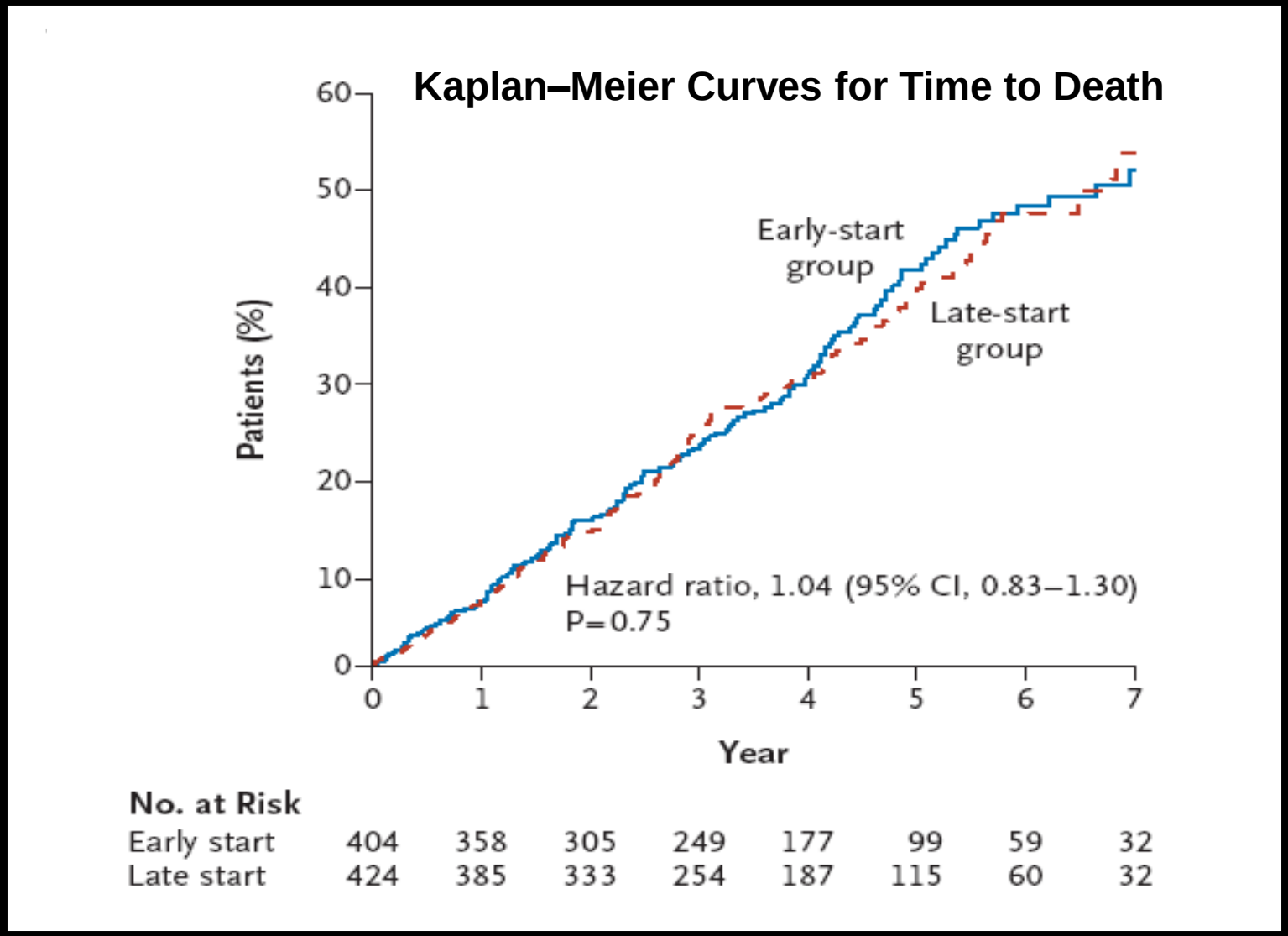
Cooper BA et al. N Engl J Med 2010;363:609-19

Results

	Early-Start	Late-Start	
eGFR (ml/min/1.73 m^2) (Cockroft-Gault)	12.0 (18.6%<10)	9.8 (75.9%>7)	P< 0.001
MDRD (post-hoc)	9.0	7.2	P < 0.001
started HD/PD	n. 383	n. 386	
completed follow-up	134	166	
years of f-up (median, CI)	3.64 (0.03-9.15)	3.57 (0.02-8.78)	
DEATHS	152 (37.6%)	155 (36.6%)	P < 0.75

Cooper BA et al. N Engl J Med 2010;363:609-19

Primary Outcome



Cooper BA et al. N Engl J Med 2010;363:609-19

A randomized, controlled trial of early versus late initiation of dialysis

Conclusions of the Authors

- Early initiation of dialysis, which has enormous implications in terms of cost and organization, had no s… h f… r complications of dialysis)

Early initiation of dialysis had no significant effect on clinical outcomes

- Dialysis should not be started on the basis of an … l … e … e traditional clinical indicators for HD initiation are present

Dialysis should not be started on the basis of GFR alone

Cooper BA et al. N Engl J Med 2010;363:609-19

A randomized, controlled trial of early versus late initiation of dialysis

Acknowledged Study Limitations

- **Use of eGFR based on the Cockcroft–Gault equation.**

  MDRD equations were not widely used when the trial was designed and had not been validated in patients with low levels of renal function.

- **Lack of the use of a uniform method of creatinine assessment. Pitfalls related to creatinine level variability with sex, race, mass, etc.** Likely to have been mitigated by patients stratification according to the study center.

- **Mean eGFR difference of only 2.2 ml/min between the two groups.**

  … its effect was an important difference of 6 months between groups in the start time for HD, reflecting the importance of close clinical follow-up in these patients.

Cooper BA et al. N Engl J Med 2010;363:609-19

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

The initiation of Renal-Replacement Therapy — Just-in-time delivery

Lameire N and Van Biesen W

- Do the results of the IDEAL trial imply that the initiation of dialysis can be delayed until an estimated GFR of 5 to 7 ml/min x 1.73 m^2 is r[illegible] **Clinical symptoms and patient follow up are of greater importance than eGFR** [illegible] patient follow-up are of greater importance in decision making than eGFR.
- A mean difference between the groups of 2.2 ml/min x 1.73 m^2 in [illegible] **Starting RRT on the basis of predefined eGFR does not improve the outcome** [illegible] and that starting RRT on the basis of a predefined eGFR does not improve the outcome.

New Eng J Med 2010; 363 (7): 678-680

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

The initiation of Renal-Replacement Therapy — Just-in-time delivery

Lameire N and Van Biesen W

- T… or a… 6 m…

For asymptomatic patients, RRT can be delayed by an average of 6 months

- An important prerequisite for a “wait and see” policy is careful c… ly a… g p… at permits the immediate initiation of dialysis if the patient becomes symptomatic

An important prerequisite for a “wait and see” policy is careful clinical follow up

- … on … he cornerstones of such a strategy

Early referral, patient-education program and planning before dialysis are the cornerstones

New Eng J Med 2010; 363 (7): 678-680

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CORRESPONDENCE

The patients were relatively healthy

No clear criteria for diagnosis of “uremia”

The Authors have not provided data on urinary output

The IDEAL study is not representative of CKD patients in US and UK

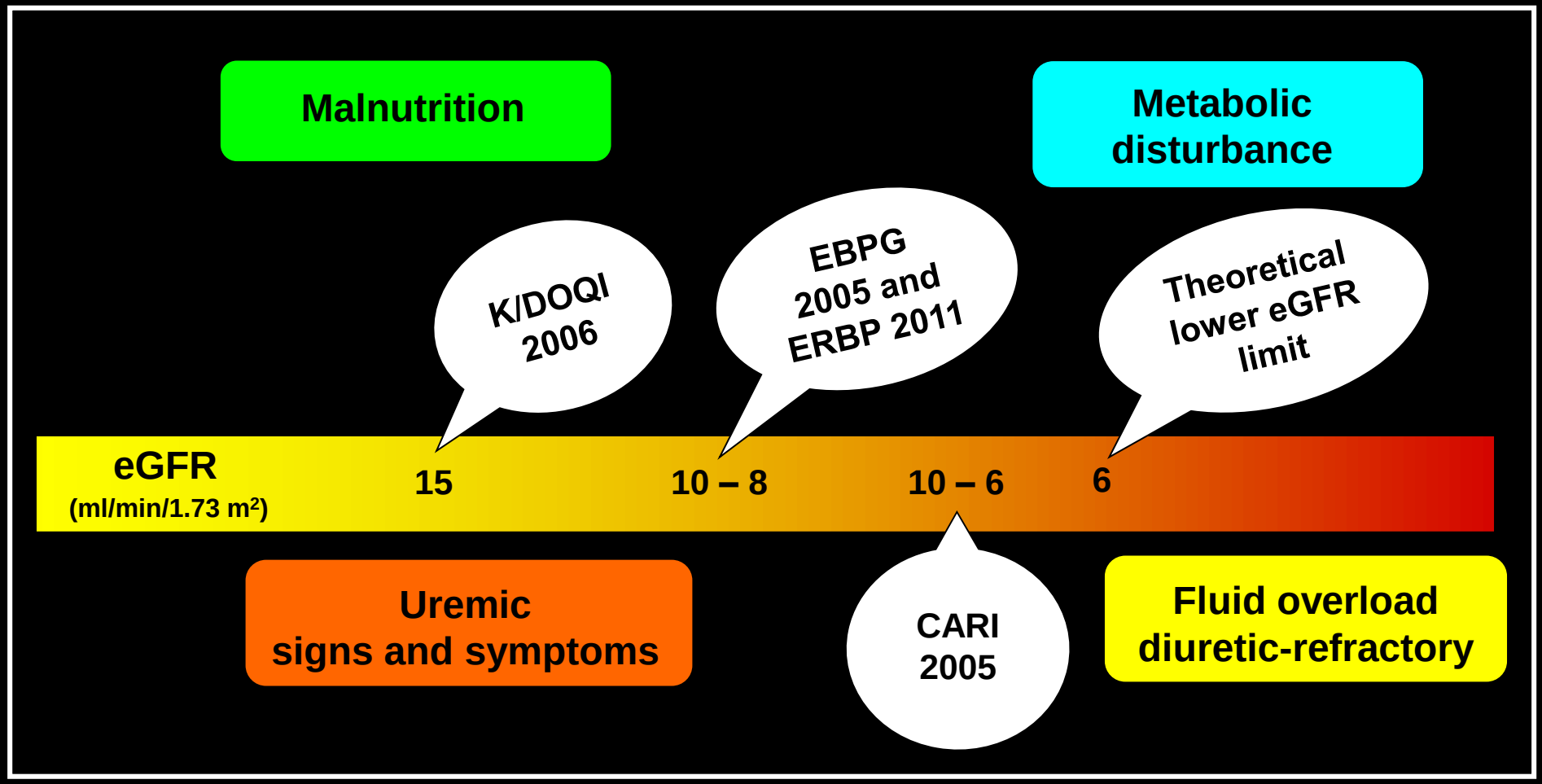
N Engl J Med 2010; 363 (24):2368-2370

Lessons learnt from the IDEAL study

- No benefit from “early-dialysis”
- Conservative therapy is possible also till GFR <10 ml/min (corresponding to 6 months dialysis delay)
- Importance of close clinical follow up in non-dialysis CKD stage 5 patients
- Pay more attention to patient symptoms than to eGFR
- Importance of nutritional status assessment
- Data from 24 hour urine collection (urea, sodium) are mandatory
- It is possible to safely reduce economic burden due to earlier dialysis

Locatelli F et al. Contrib Nephrol 2011

Dialysis beginning according to international guidelines and clinical data



Locatelli F et al. Contrib Nephrol 2011

Lessons from recent trials in hemodialysis

The IDEAL study: what can we learn?

- Even if with some limitations, the IDEAL study represents a very important trial. Its main message is the lack of a fixed GFR value at which to start dialysis in asymptomatic patients, suggesting to give more relevance to close patient monitoring (uremic signs and symptoms, fluid overload, malnutrition, etc.)
- This approach has been proven to be safe for the patients and effective in temporary delaying the need for dialysis

Locatelli F et al. Contrib Nephrol 2011

ERBP

European Renal Best Practice

When to start dialysis: Updated guidance following publication of the Initiating Dialysis Early and Late (IDEAL) study

James Tattersall, Friedo Dekker, Olof Heimbürger, Kitty Jager, Norbert Lameire, Elizabeth Lindley, Wim Van Biesen, Raymond Vanholder, Carmine Zoccali on behalf of the ERBP Advisory board.

Updated guidance

The 2002 guidance is not significantly changed. The evidence levels are increased by the studies published since 2002. The caution against using creatinine and CC to guide dialysis start is strengthened. A caution that eGFR calculated by the MDRD method is not useful in determining need for dialysis has been added. The emphasis on using GFR of 6 ml/min/1.73m^2 as an absolute lower limit to starting dialysis is made more vague. Support for establishing advanced CKD clinics has been added.

Nephrol Dial Transplant 2011,

KDIGO Controversies Conference

Novel techniques and innovation in blood purification:
How can we improve clinical outcomes in hemodialysis?

14-15 October, 2011
Paris, France

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Lessons from recent trials in hemodialysis

- Randomised controlled studies in dialysis are welcomed
- The HEMO, MPO, Italian Convective Study and the Contrast,the Turkish and Catalonian studies, comparing hemodialysis, hemodiafiltration and hemofiltration trials gave important information on how to improve the management of dialysis patients
- The IDEAL and the FHN Daily Trial are well designed randomized controlled trials aimed at improving the everyday quality of dialysis treatment

Locatelli F et al. Contrib Nephrol 2011