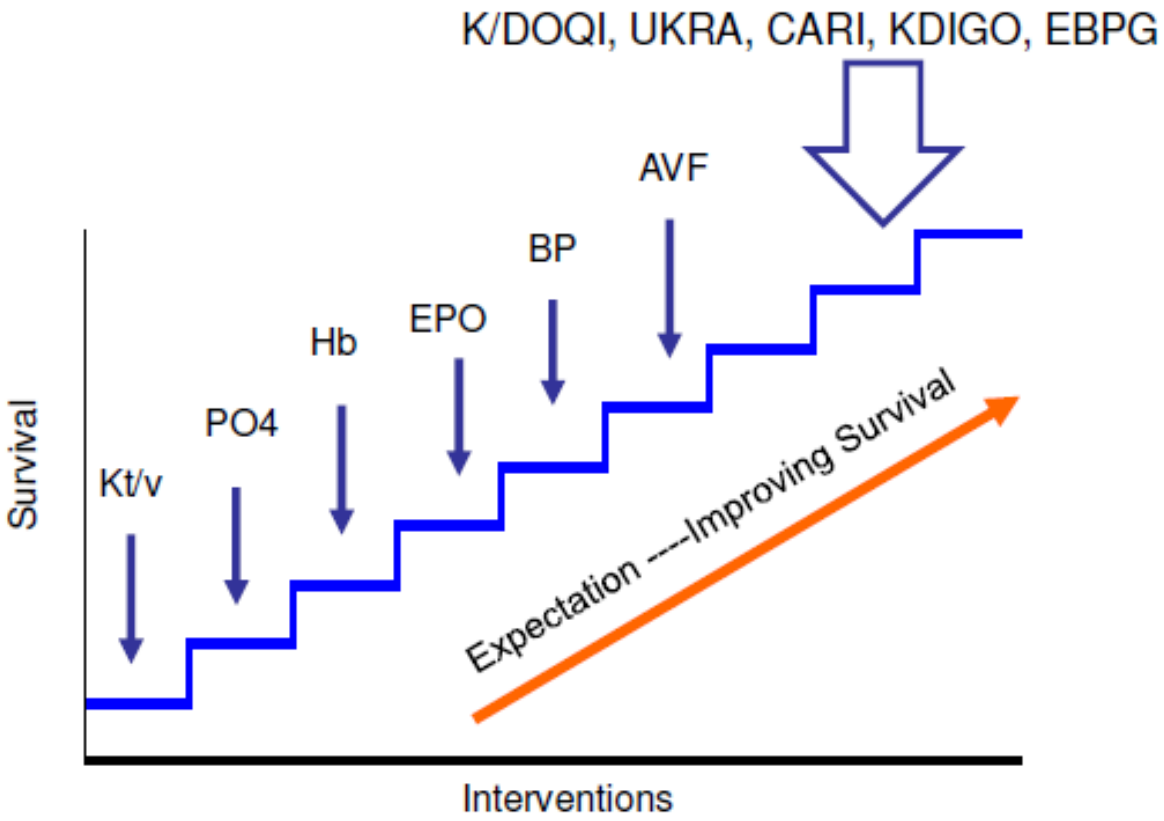
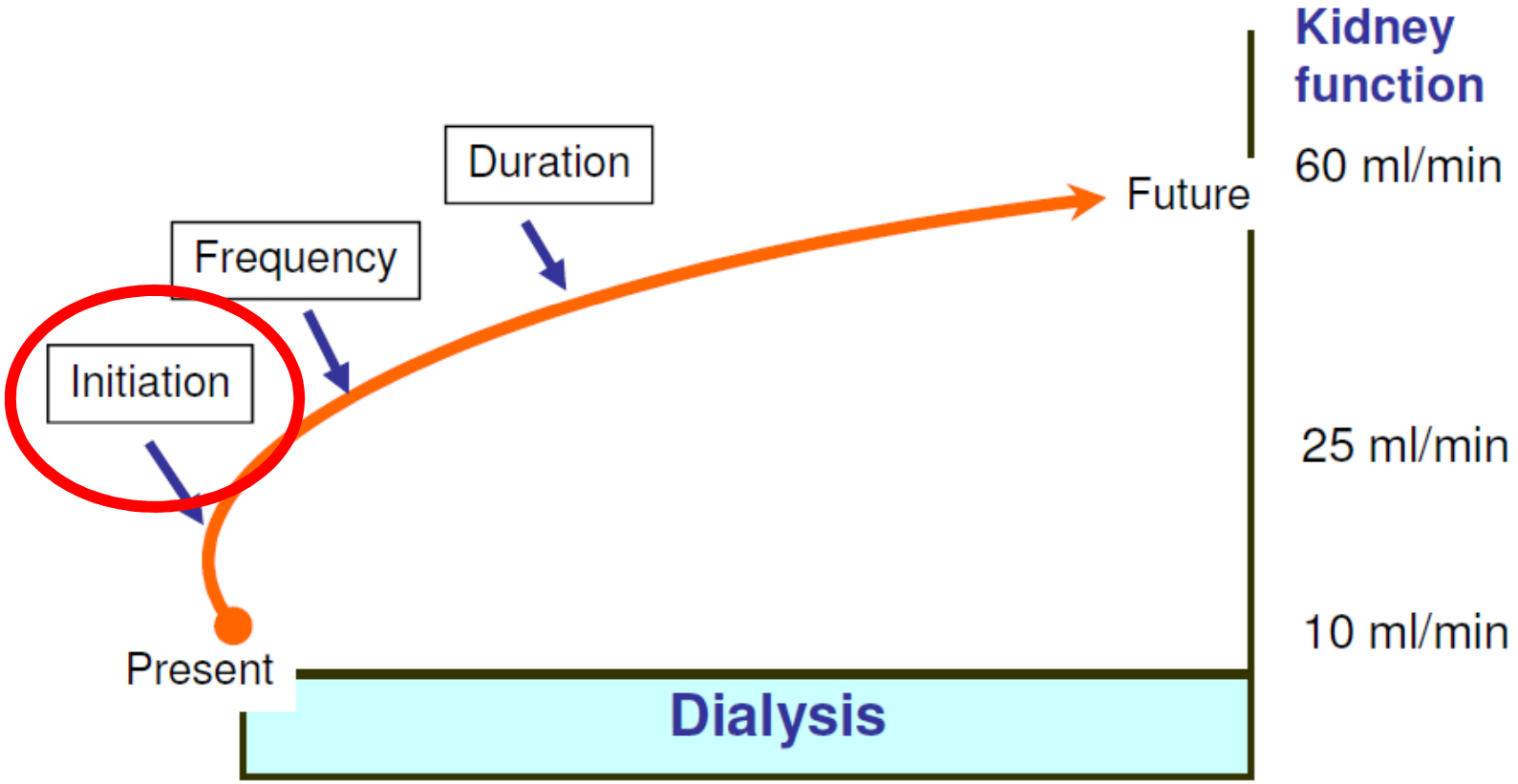
Nowe trendy w leczeniu nerkozastępczym u dzieci

Sylwester Prokurat
Klinika Nefrologii, Transplantacji Nerek i Nadciśnienia Tętniczego
IPCZD Warszawa

OCZEKIWANIA



Potential Dialysis Strategies to Improve Survival



Punktualność –
to podstawa w show-biznesie

a w leczeniu nerkozastępczym?

Nephrol Dial Transplant (2005) 20 [Suppl 9]: ix3–ix7
doi:10.1093/ndt/gfi1116

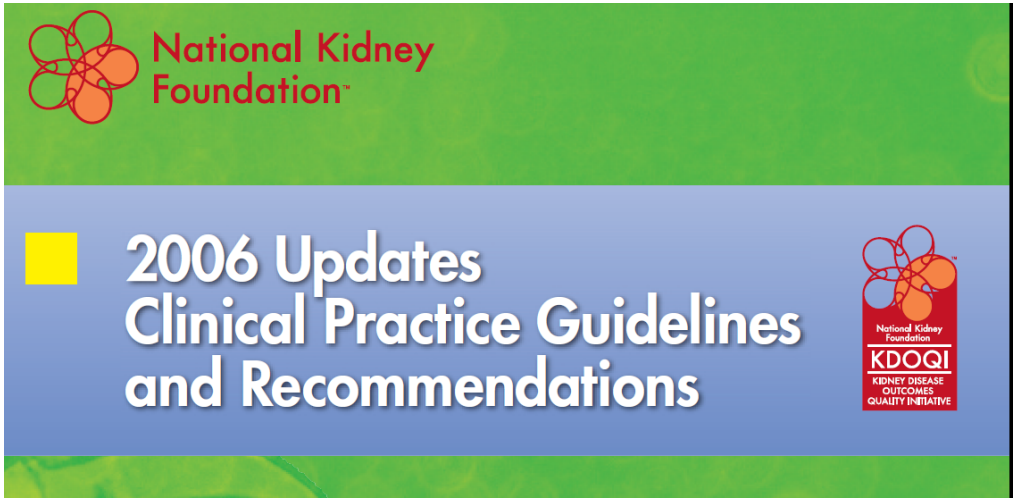
Nephrology
Dialysis
Transplantation

European Best Practice Guidelines

2 The initiation of dialysis

E. Dialysis should be instituted whenever evidence of uraemia is present, or blood pressure and hydration status cannot be controlled, or when a deterioration of the nutritional status is noticed. In any case, dialysis should be started before the GFR is <6 ml/min/1.73 m^2 (creatinine clearance 8 ml/min/1.73 m^2).
(Evidence level C)

For areas in which no pediatric data exist, CPGs and CPRs for adult patients should serve as a minimum standard for pediatric patients.



GUIDELINE 8. PEDIATRIC HEMODIALYSIS PRESCRIPTION AND ADEQUACY

8.1 Initiation of HD:

8.1.1 Dialysis initiation considerations for the pediatric patient should follow the adult patient guideline of a GFR less than 15 mL/min/1.73 m^2. (A)

8.1.2 For pediatric patients, GFR can be estimated by using either a timed urine collection or the Schwartz formula. (A)

8.1.3 Dialysis therapy initiation should be considered at higher estimated GFRs when the patient's clinical course is complicated by the presence of the signs and symptoms listed in Table 11, CPR 1 for adult patients, as well as malnutrition or growth failure for pediatric patients. Before dialysis is undertaken, these conditions should be shown to be refractory to medication and/or dietary management. (A)

Clinical practice recommendations for the care of infants with stage 5 chronic kidney disease (CKD5)

Aleksandra M. Zurowska · Michel Fischbach · Alan R. Watson · Alberto Edefonti · Constantinos J. Stefanidis · on behalf of the European Paediatric Dialysis Working Group

Pediatr Nephrol Published online: 09 October 2012

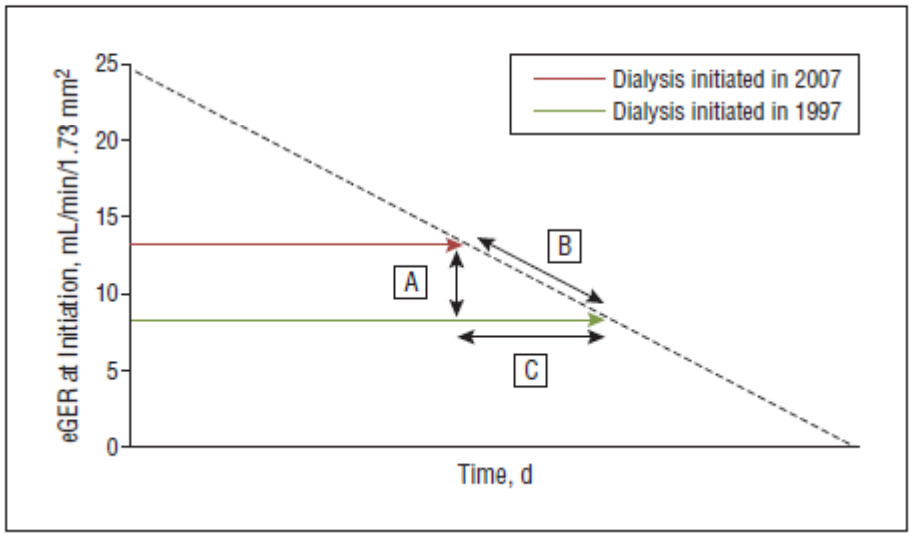
Recommendation 3: The timing of initiating RRT in infants with CKD5 needs to be individualised with a major determinant being maintenance of adequate growth, nutrition and development (1B).

LESS IS MORE

Trends in Timing of Initiation of Chronic Dialysis in the United States

Ann M. O'Hare, MD, MA; Andy I. Choi, MD, MS†; W. John Boscardin, PhD; Walter L. Clinton, PhD; Ilan Zawadzki, MD; Paul L. Hebert, PhD; Manjula Kurella Tamura, MD, MPH; Leslie Taylor, PhD; Eric B. Larson, MD, MPH

Arch Intern Med. 2011;171(18):1663-1669



CURRENT OPINION

Timing of initiation of dialysis: time for a new direction?

Curr Opin Nephrol Hypertens 2012, 21:329–333
DOI:10.1097/MNH.0b013e328351c244

Graham Abra and Manjula Kurella Tamura

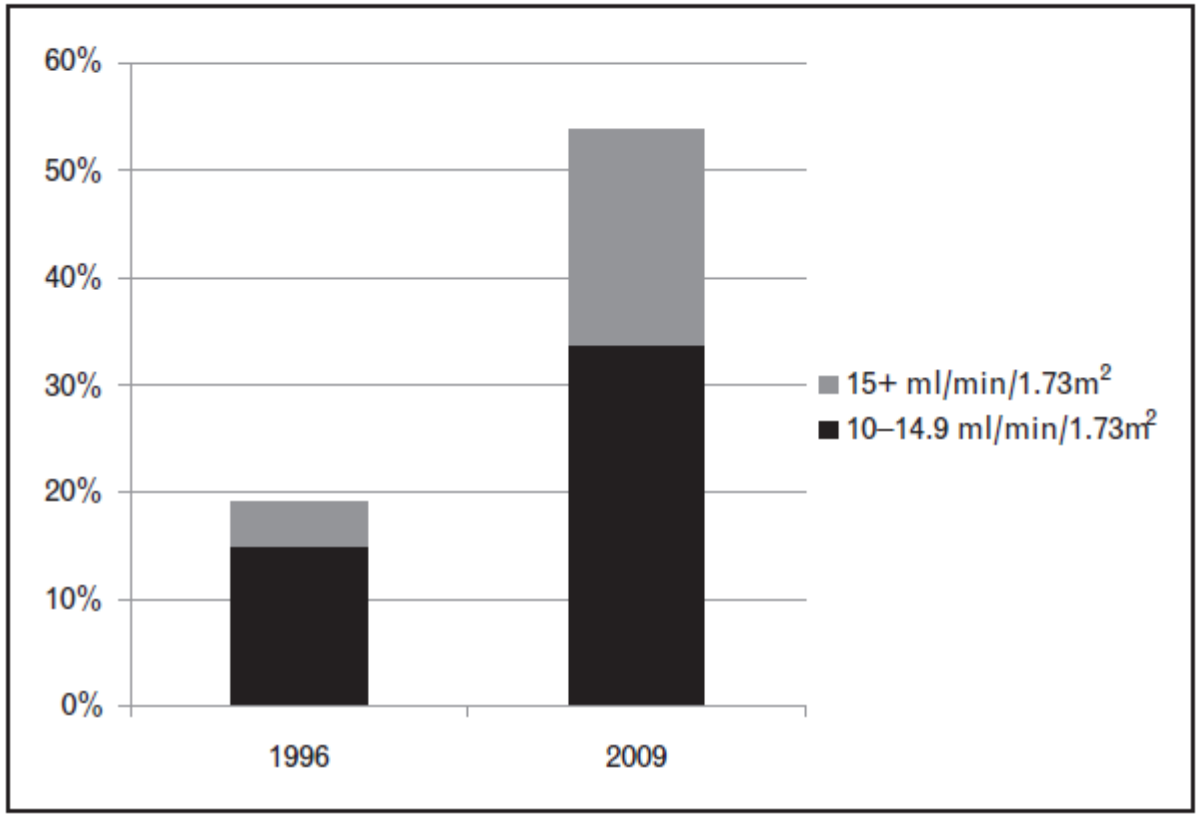
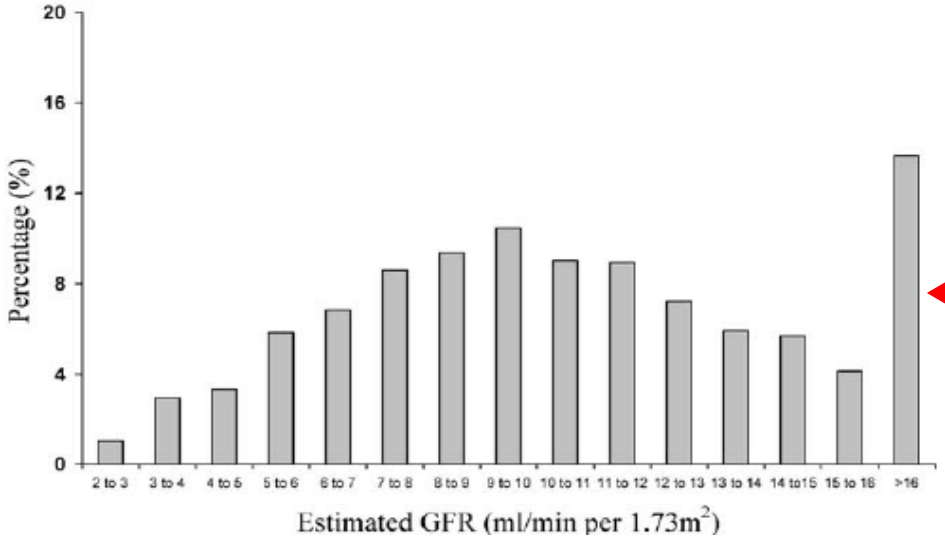


FIGURE 1. Percentage of incident ESRD patients initiating dialysis with an estimated glomerular filtration rate at or above 10 ml/min/1.73m^2. ESRD, end-stage renal disease.

Mouin G. Seikaly · Nina Salhab · Richard Browne

Patterns and time of initiation of dialysis in US children

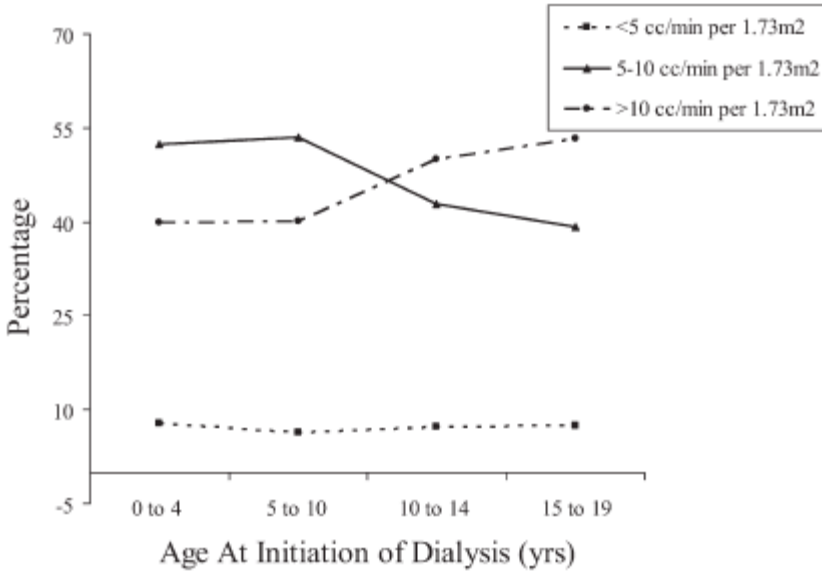
Pediatr Nephrol (2005) 20:982–988
DOI 10.1007/s00467-004-1803-7

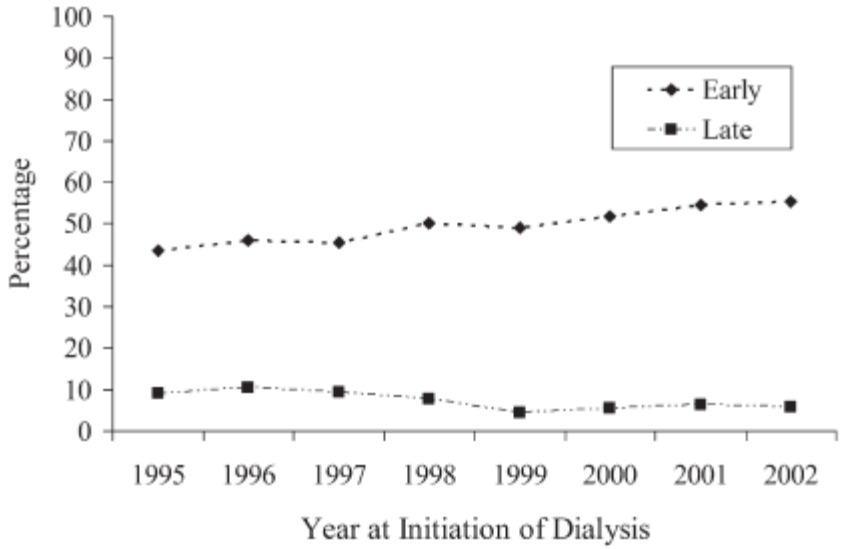


> 16ml/min/1.73m2 (13%)

50% z ponad 4000 dzieci rozpoczęło RRT >10ml/min/1.73

985





Determinants of eGFR at start of renal replacement therapy in paediatric patients

Karlijn J. van Stralen[1], E. Jane Tizard[2], Kitty J. Jager[1], Franz Schaefer[3], Karel Vondrak[4], Jaap W. Groothoff[5], Ludmila Podracká[6], Christer Holmberg[7], Augustina Jankauskiené[8], M. A. Lewis[9], Rita van Damme-Lombaerts[10], Conceição Mota[11], Patrick Niaudet[12], Gregor Novljan[13], Amira Peco-Antic[14], Emilija Sahpazova[15], Ülle Toots[16] and Enrico Verrina[17]

Nephrol Dial Transplant (2010) 25: 3325–3332

ESPN/ERA-EDTA

Table 2. Number of patients treated according to the guidelines

	Median eGFR *N* = 938 *N* (%)
European guidelines	
<10 mL/min/1.73 m^2	467 (49.8)
10–15 mL/min/1.73 m^2	282 (30.1)
>15 mL/min/1.73 m^2	189 (20.2)[a]
KDOQI guidelines	
<8 mL/min/1.73 m^2	313 (33.4)
8–14 mL/min/1.73 m^2	398 (42.4)
>14 mL/min/1.73 m^2	227 (24.2)[a]

8% Pree-emptive

Śr eGFR 10.4ml/min/1.73m2
(4.0-26,9ml/min/1.73m2)

Determinants of eGFR at start of renal replacement therapy in paediatric patients

Nephrol Dial Transplant (2010) 25: 3325–3332

Table 3. Median eGFR at the start of RRT

	Median eGFR (95% CI) $N = 938$	Median $eGFR_{adj}$ (95% CI) $N = 938$[b]	Median $eGFR_{adj}$ (95% CI) $N = 912$[b,c]
All	10.4 (10.0–10.8)	10.4 (10.0–10.8)	9.7 (9.4–10.0)
Age			
0–1	9.4 (8.5–10.5)	8.3 (7.3–9.3)*	6.2 (5.7–6.9)*
2–5	9.3 (8.0–10.7)	8.9 (7.9–10.1)	8.9 (8.1–9.8)
6–12[a]	9.3 (8.3–10.6)	9.7	9.3
13–17	12.8 (11.3–14.5)*	13.5 (12.3–14.8)*	12.8 (11.9–13.8)*
Gender			
Males[a]	10.6 (10.0–11.2)	10.7	10.0
Females	10.1 (9.3–11.0)	9.9 (9.2–10.8)	9.1 (8.6–9.7)*
Treatment modality at start of RRT			
Haemodialysis	10.3 (9.5–11.3)	10.1 (9.2–11.1)	9.4 (8.7–10.1)
Peritoneal dialysis[a]	10.0 (9.5–10.6)	10.1	9.4
Transplantation	13.8 (11.7–16.1)*	13.5 (11.6–15.7)*	12.8 (11.4–14.5)*
Primary renal disease			
Glomerulonephritis	10.6 (9.5–11.6)	10.5 (9.2–11.9)	9.8 (8.9–10.8)
Pyelonephritis	10.1 (8.8–11.6)	9.4 (8.3–10.7)	9.4 (8.5–10.4)
Cystic kidney	9.3 (7.9–10.8)	9.3 (8.1–10.8)	9.2 (8.3–10.3)
Hereditary nephropathy	20.5 (17.2–24.6)*	24.7 (20.8–29.2)*	11.3 (9.7–13.1)*
Hypoplasia or dysplasia[a]	9.5 (8.3–10.9)	9.6	9.7
HUS	11.2 (8.5–14.6)	11.9 (9.2–15.3)	12.1 (10.0–14.7)*
Miscellaneous	10.2 (8.7–11.5)	9.8 (8.6–11.2)	9.5 (8.6–10.5)
Unknown	8.9 (7.4–10.6)	8.5 (7.2–10.1)	8.4 (7.4–9.5)*
Region			
Nordic countries[a]	11.4 (10.7–12.2)	11.1	9.6
Western countries	9.8 (8.9–10.9)	9.9 (8.9–11.0)*	9.5 (8.8–10.3)
Eastern countries	11.0 (8.4–14.5)	11.6 (9.0–14.9)	11.6 (9.6–14.1)*
Southern countries	9.2 (8.3–10.2)*	9.6 (8.7–10.6)*	9.6 (8.9–10.4)

3.4ml/min/1.73

Repercussions of early versus late initiation of dialysis

Nefrologia 2011;31(4):392-6

L.M. Ortega, A. Nayer

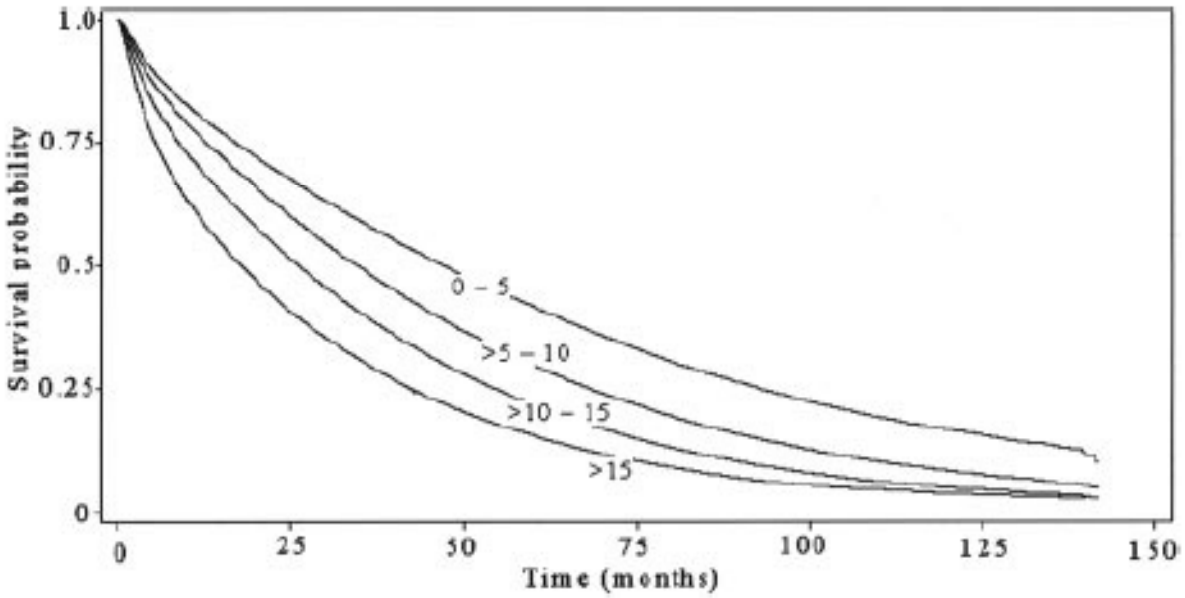
Table 1. Survival outcomes in early versus late initiation of dialysis

Autor year	Study design	No. Patients typr	Dialysis ml/min	eGFR	Renal function at initiation/mortality	Limitations
Fink et al 1999	Retrospective Observational cohort HCFA	5,398	HD/PD	Serum Creatinine	↓Creatinine ↓survival each Scr 1 mg/dl ↑ / 4% ↓ risk of death RR=0.96;P=0,01	HCFA 2728 Inaccurate reporting confounders
Korevaar et al 2001	Prospective	253	HD/PD	E-7.1(2.4) L-4.9(1.7)	↑ mortality late start Adjusted HR 1.66(95%cCI)	Lead-time bias Retrospective Small # patients
Traynor et al 2002	Prospective Glasgow Registry	235	HD/PD	E-10.4 (eCrCl) L- 6.7 Median 8.3	Every ↑ 1 ml/min CrCl 10% ↑ HR P=0.02 Lower eCrCl survive longer	Selection bias Lack of data in initiation Lead time bias
Beddhu et al 2003	Prospective Registry USRDS DMMS II study	2,920	HD/PD	E-5.6 L-10.9	each ↑ 5 ml/min GFR/MDRD ↑ HR 1.14,P=0.002 entire cohort ↑ GFR subgroup; ↑ HR 1.27 for each 5 ml/min ↑ GFR, P< 0.001	Unmeasured confoumders Lead-time/survival bias Lack of data in initiation
Kazmi et al 2005	Retrospective CMS	302,287	HD	< 5 5-7,5 7.6-10 > 10	GFR > 10 42% ↑ risk death	Unmeasured GFR Incomplete comorbidity data Lead time/survival bias
Wright et al 2010	Retrospective USRDS	212,741 (896,546 Incident)	HD/PD	<5 > 5-10 >10-15 >15	GFR< 5 ml/min ↓,HR 0.88 GFR >10-15 ↑ RR,HR 1.15 GFR>15 HR 1.44,P=0.001	Selection bias Retrospective-no causation Lead-time bias Residual confounding
Rosansky et al 2010	Retrospective CMS	81,176	HD	<5, 5-9.9 10-14.9, >15	Unadjusted 1, year mortality 6.8% GFR<5 ,HR 1.27,(5-9.9) 20.1% GFR>15, HR 2.18	No reported comorbidities Unobserved covariates Unmeasured comorbidities
Clark et al 2010	Retrospective Canadian registry	25,910	HD	Mean GFR E-15.5 L-7.1	Mean GFR 7.1 Unadjusted HR 1.48, 95% CI	Observational bias AKI capture patients Lack of data in initiation

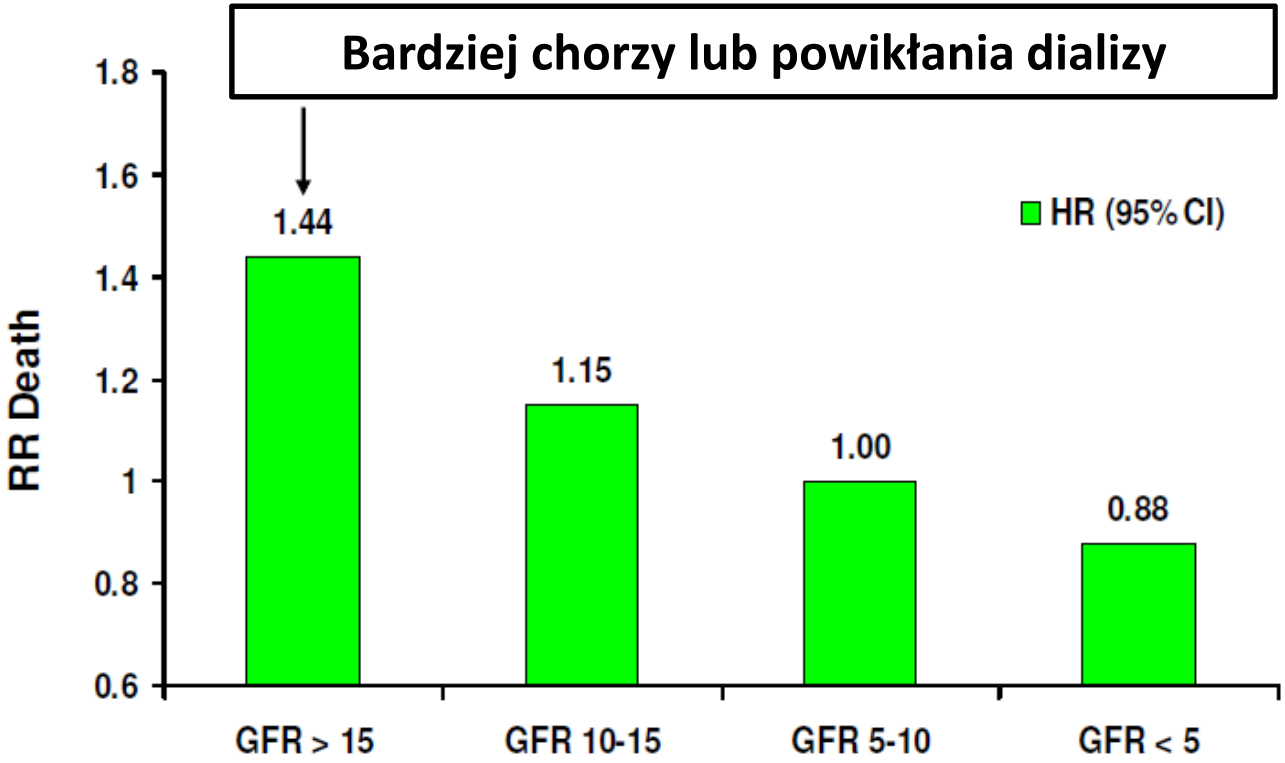
Timing of Dialysis Initiation and Survival in ESRD

Seth Wright,* Dalia Klausner,† Bradley Baird,‡ Mark E. Williams,§ Theodore Steinman,§ Hongying Tang,‖ Regina Ragasa,‖ and Alexander S. Goldfarb-Rumyantzev§‖

Clin J Am Soc Nephrol 5: 1828–1835, 2010. doi: 10.2215/CJN.06230909



Czas rozpoczęcia dializ i śmiertelność

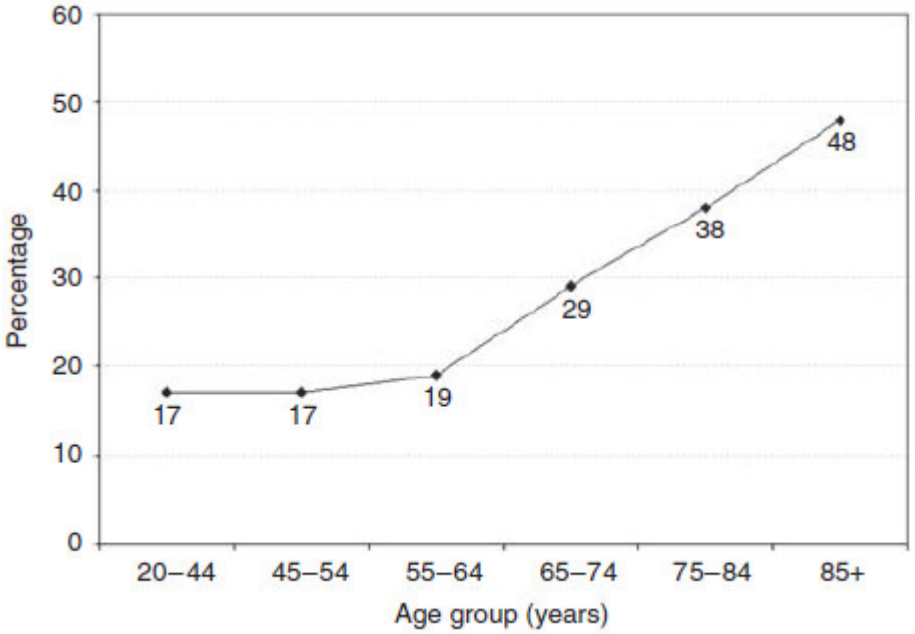


Wright S et al. CJASN 2010

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

Kidney International (2010) 77, 700–707

Mathilde Lassalle[1], Michel Labeeuw[2], Luc Frimat[3], Emmanuel Villar[2], Véronique Joyeux[4], Cécile Couchoud[1] and Bénédicte Stengel[5,6] on behalf of the REIN Registry

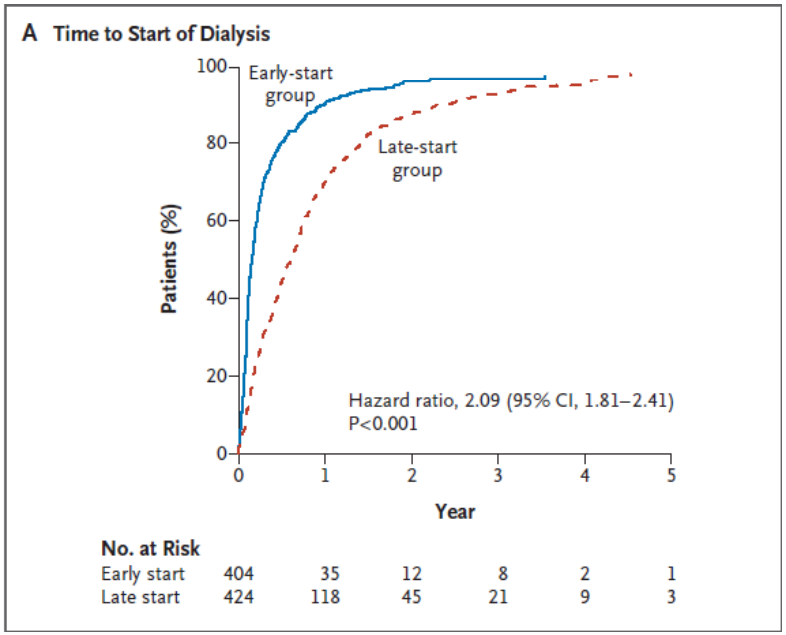


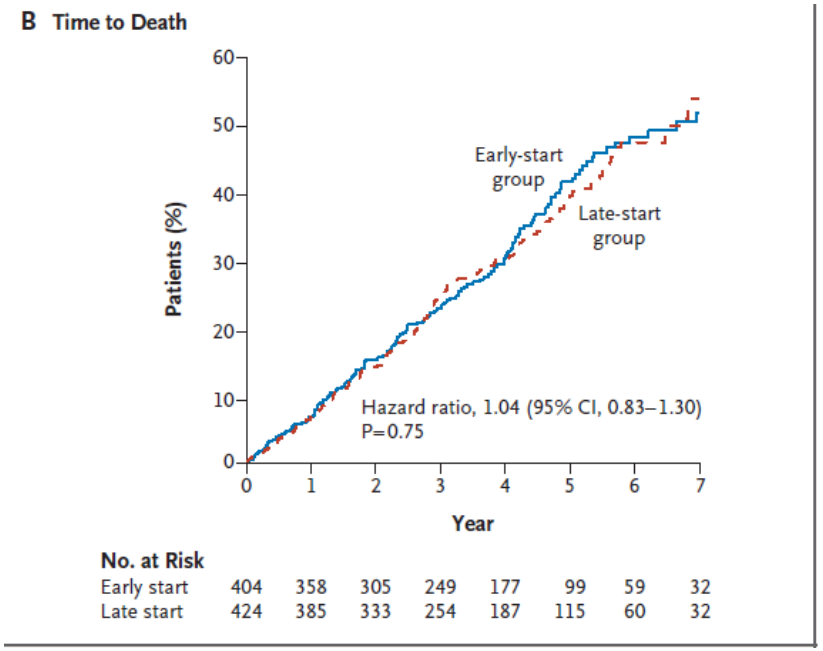
The NEW ENGLAND JOURNAL of MEDICINE

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*





Badanie IDEAL 32 ośrodki z Australii i Nowej Zelandii – 828 chorych

Wczesne rozpoczęcie = GFR 10-14ml/min/1.73m2

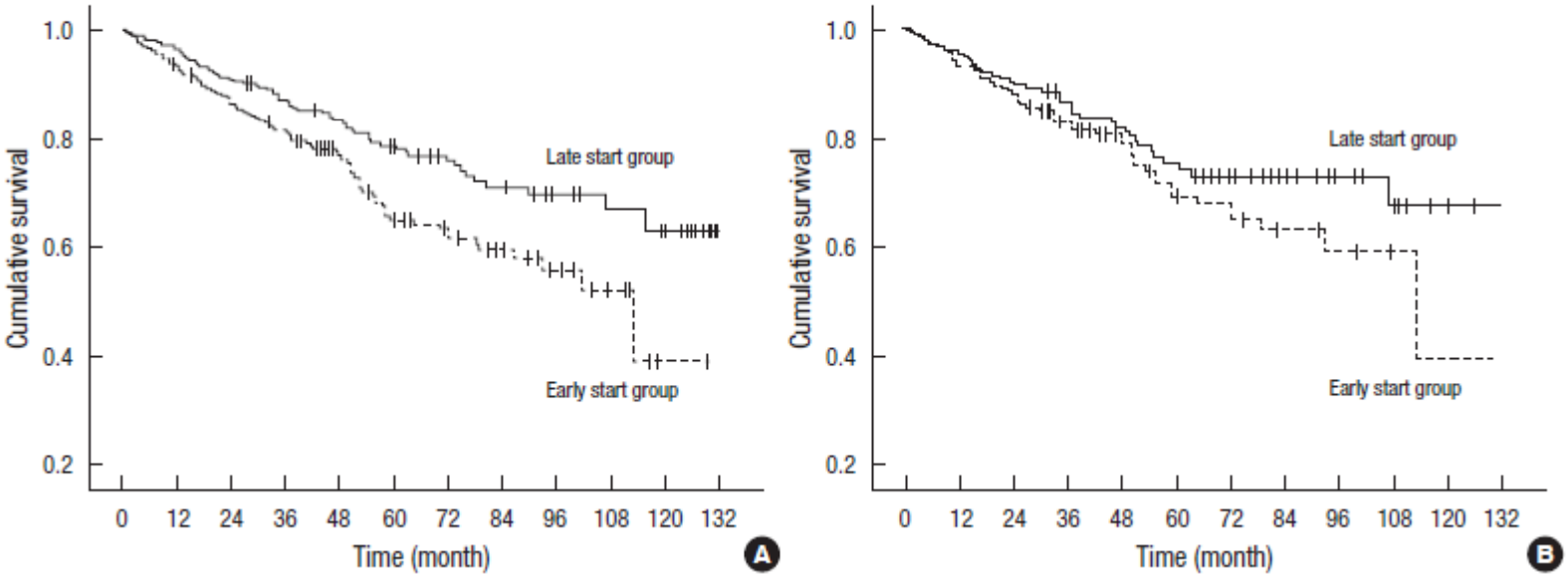
ORIGINAL ARTICLE
Nephrology

JKMS

http://dx.doi.org/10.3346/jkms.2012.27.10.1177 • J Korean Med Sci 2012; 27: 1177-1181

Early Start of Dialysis Has No Survival Benefit in End-Stage Renal Disease Patients

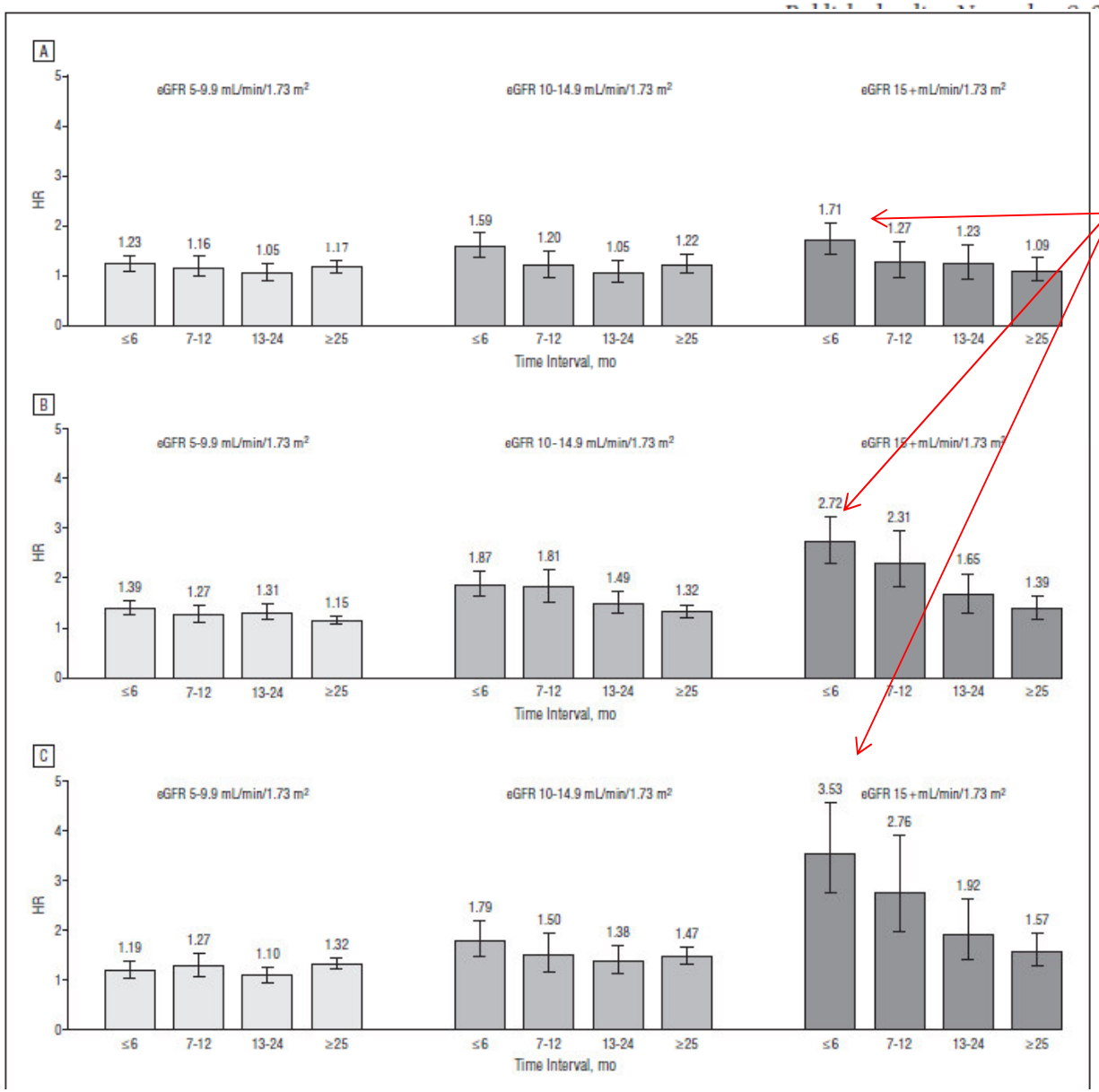
Jae Hyun Chang[1]*, Min Young Rim[1]*, Jiyoon Sung[1], Kwang-Pil Ko[2], Dong Ki Kim[3], Ji Yong Jung[1], Hyun Hee Lee[1], Wookyung Chung[1], and Sejoong Kim[4]



Early Start of Hemodialysis May Be Harmful

Steven J. Rosansky, MD; Paul Eggers, PhD; Kirby Jackson, BA; Richard Glassock, MD; William F. Clark, MD

Arch Intern Med. 2011;171(5):396-403.

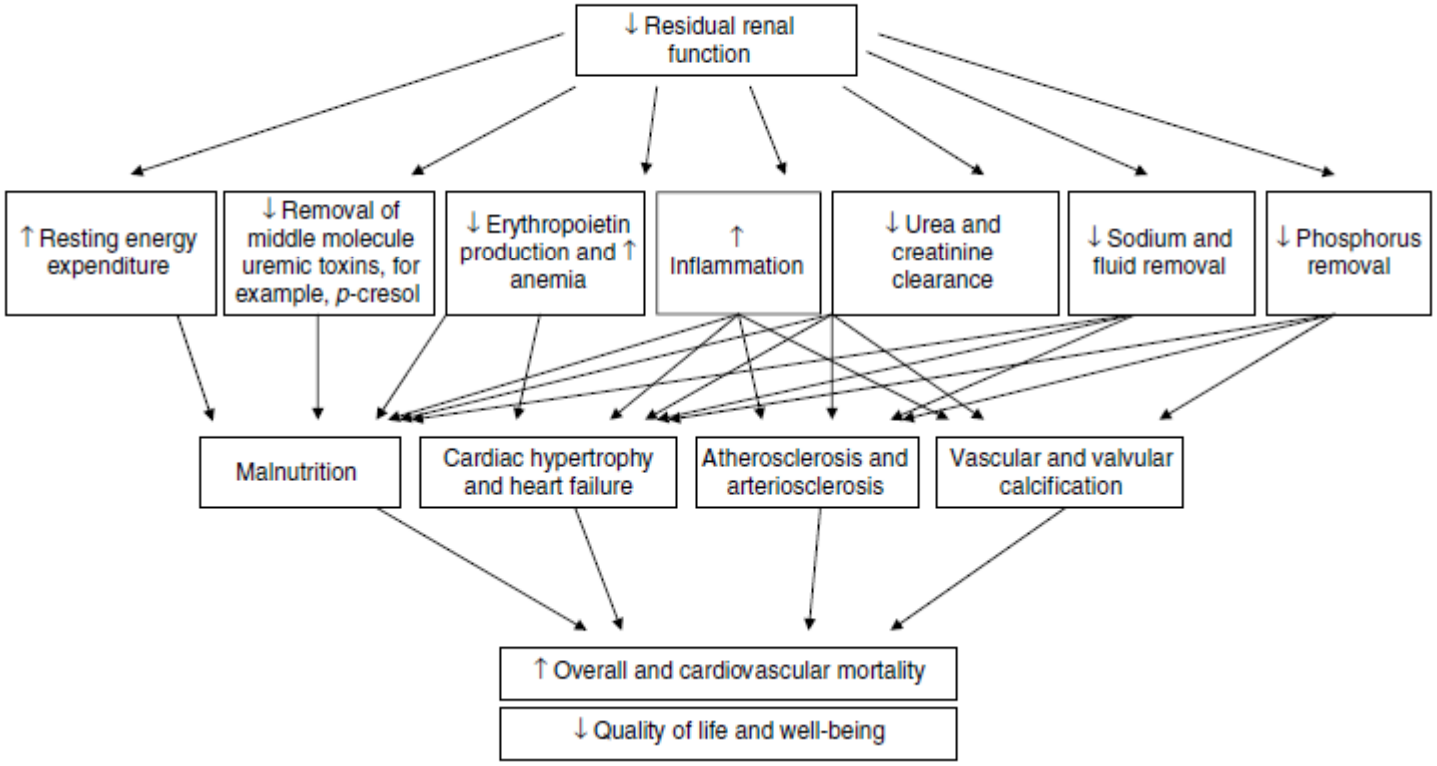


Albuminy

The importance of residual renal function in dialysis patients

Kidney International (2006) **69**, 1726–1732

AY-M Wang[1] and K-N Lai[1]

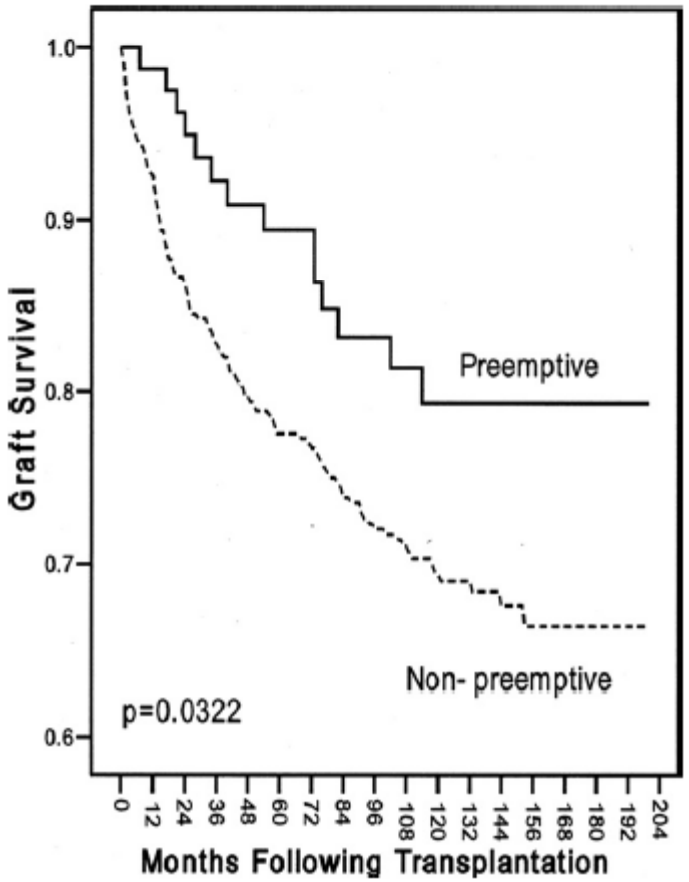


Wczesne rozpoczęcie zwłaszcza HD doprowadza do szybkiej utraty diurezy resztkowej

Pre-emptive kidney transplantation – Just do it!!

Pediatr Transplantation 2010: 14: 561–564

Jaki jest optymalny czas?



Preemptive transplantation and the transplant first initiative

Connie L. Davis

Current Opinion in Nephrology and Hypertension 2010, 19:592–597

Przeżycie graftu od dawcy zmarłego (a), żywego (b) preemtive lub w zależności od długości czasu dializ

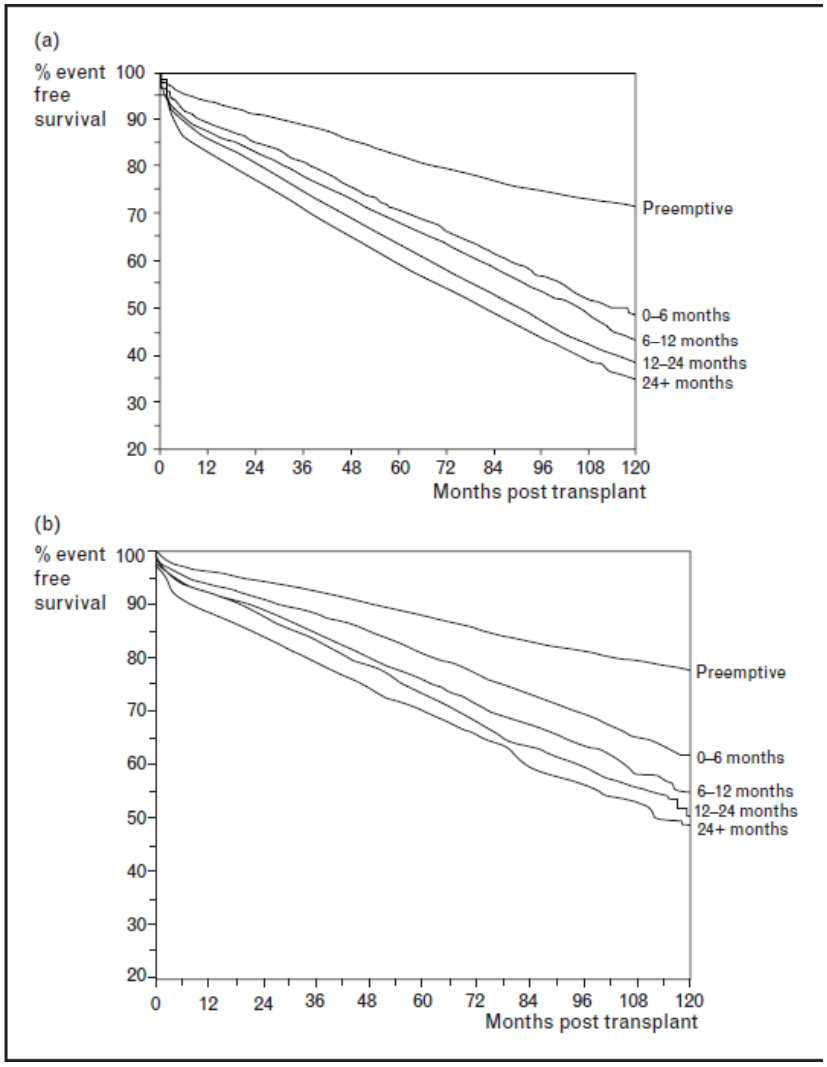
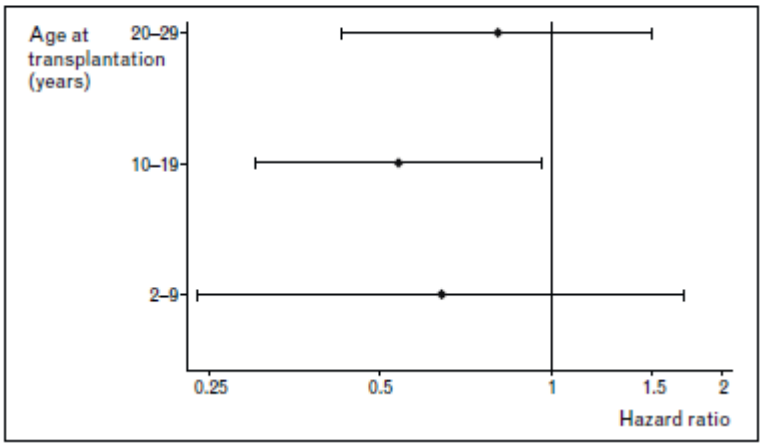


Figure 2 The impact (hazard ratio) of recipient age on graft failure according to timing of the transplant, preemptive compared to six to 24 months after starting dialysis



Reviews/Editorial comments

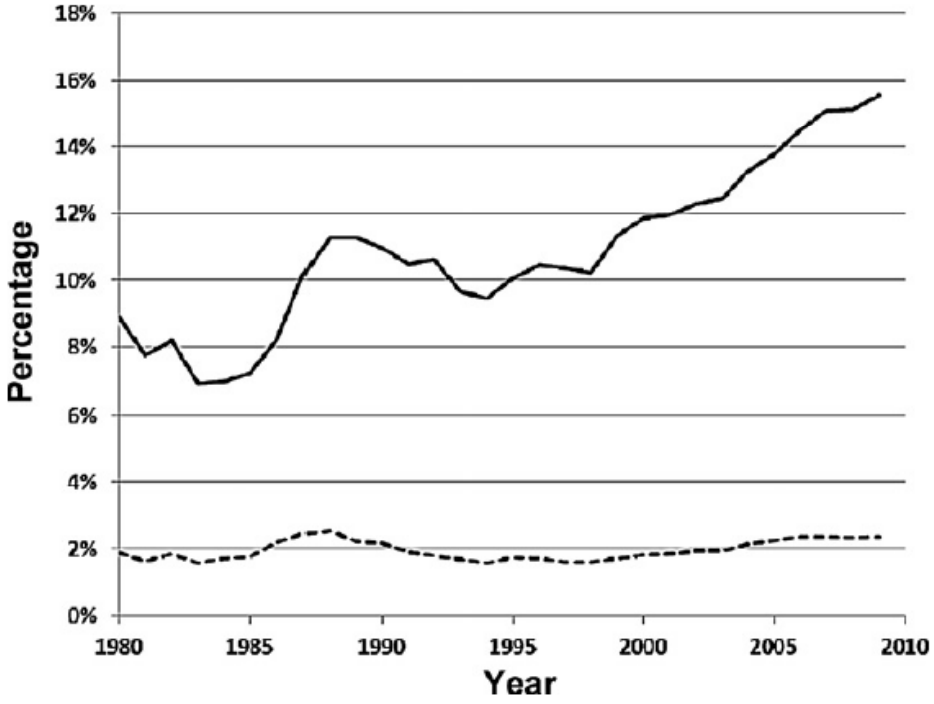
Preemptive kidney transplantation: Has it come of age?

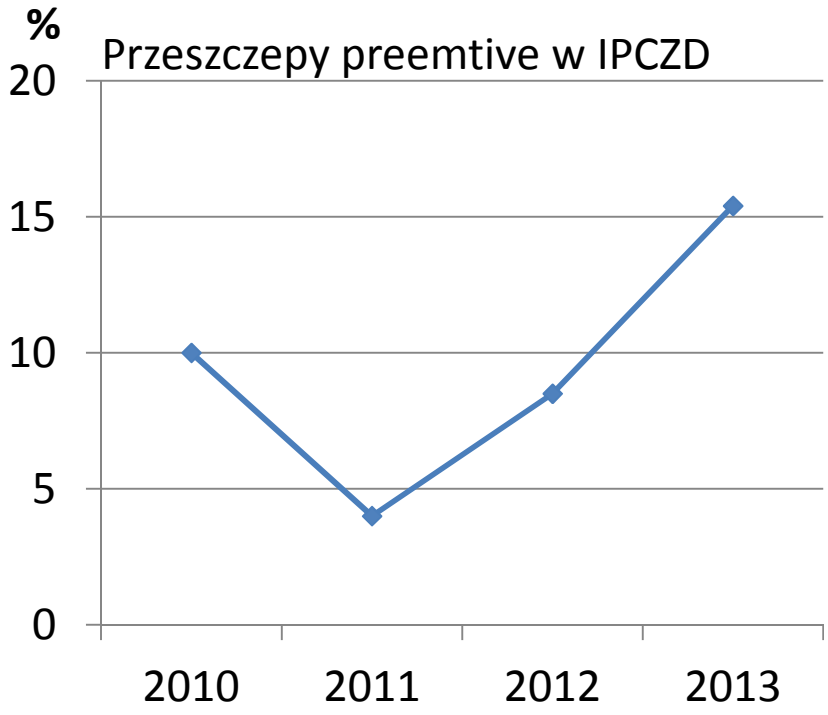
Transplantation rénale préemptive : est-il temps ?

Yihung Huang *, Millie Samaniego

Division of Nephrology, University of Michigan, Michigan, USA

Néphrologie & Thérapeutique 8 (2012) 428–432

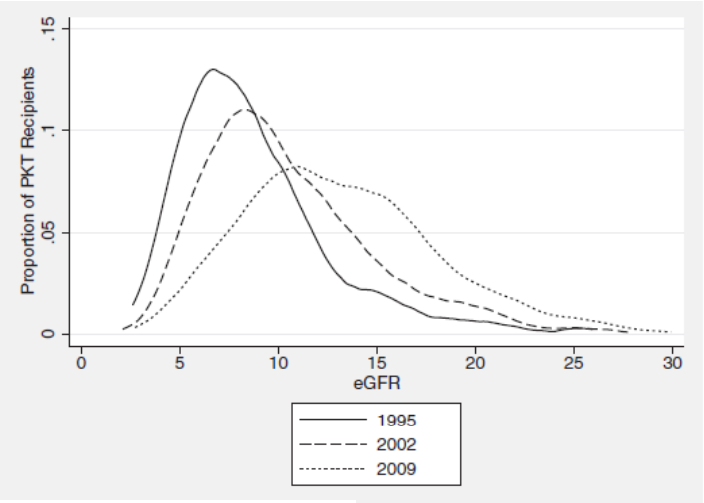


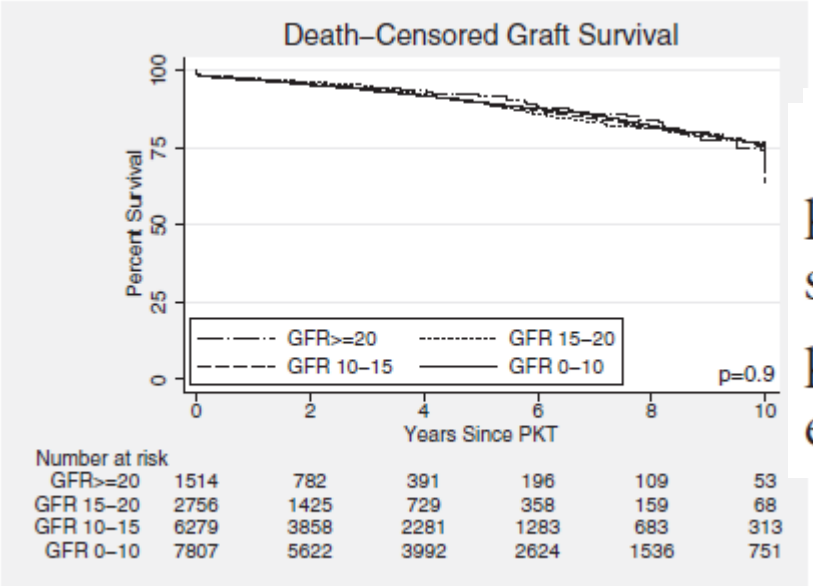


Trends in the Timing of Pre-emptive Kidney Transplantation

Morgan E. Grams,*† Allan B. Massie,†‡ Josef Coresh,*† and Dorry L. Segev†‡

J Am Soc Nephrol **22:** 1615–1620, 2011



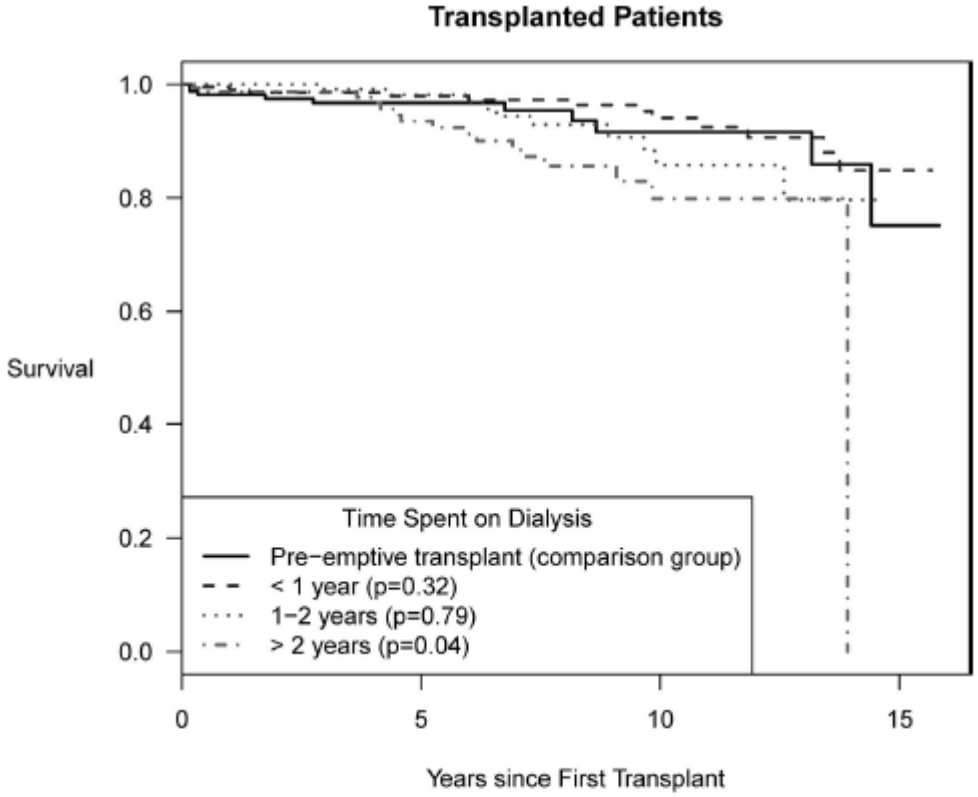


Until better data are available, providers and transplant programs should strive to individualize transplant timing decisions to avoid PKT too early in the course of CKD.

Survival in Pediatric Dialysis and Transplant Patients

Susan M. Samuel,†† Marcello A. Tonelli,‡ Bethany J. Foster,§‖ R. Todd Alexander,‡ Alberto Nettel-Aguirre,*†
Andrea Soo,* Brenda R. Hemmelgarn,* and the Pediatric Renal Outcomes Canada Group*

Clin J Am Soc Nephrol 6: 1094–1099, May, 2011

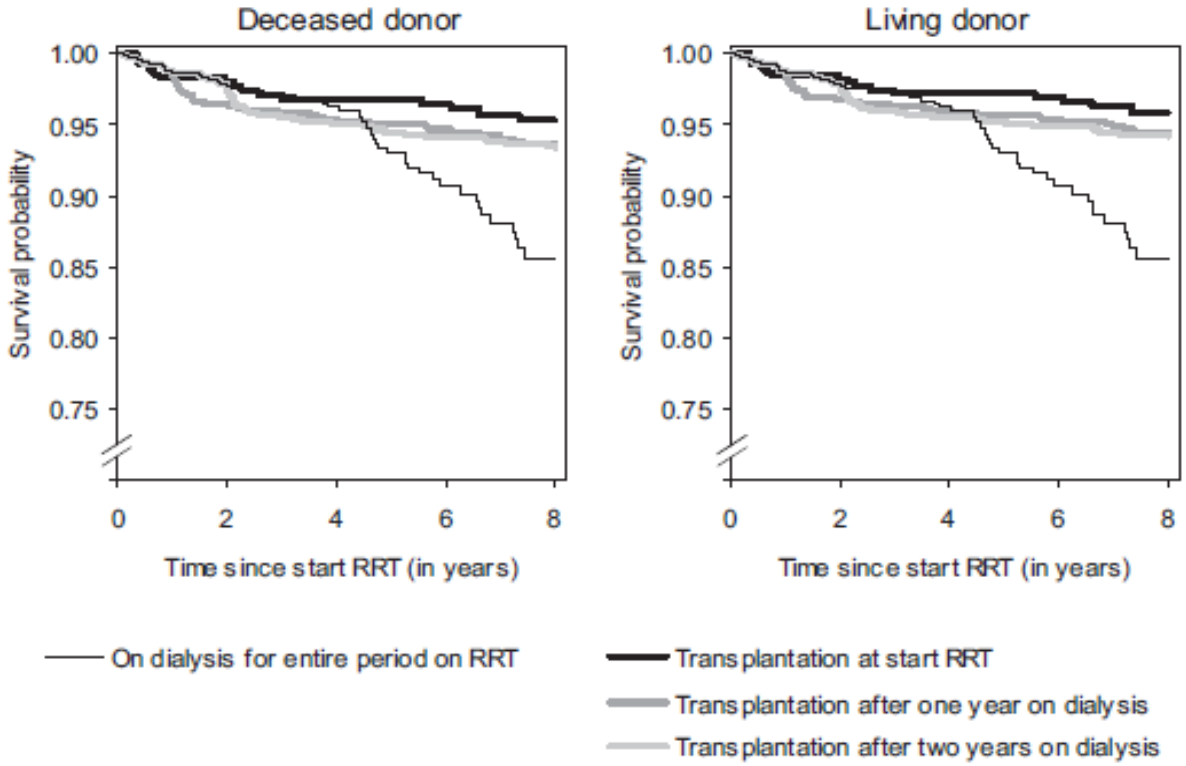


Time Spent on Dialysis			
Pre−emptive Transplant	100	31	5
< 1 year	153	76	11
1−2 years	94	34	–
> 2 years	86	23	–

The effect of timing of the first kidney transplantation on survival in children initiating renal replacement therapy

Anneke Kramer[1], Vianda S. Stel[1], Ronald B. Geskus[2], E. Jane Tizard[3], Enrico Verrina[4], Franz Schaefer[5], James G. Heaf[6], Reinhard Kramar[7], Leah Krischock[8], Torbjørn Leivestad[9], Runólfur Pálsson[10,11], Pietro Ravani[12,13] and Kitty J. Jager[1]

Nephrol Dial Transplant (2012) 27: 1256–1264



Autorzy po włączeniu ponad 2000 dzieci leczonych RRT uwzględnili zgony w czasie prowadzenia dializoterapii przed Tx, wykazali nieznaczną przewagę 8 letniego przeżycia chorych preemptive Tx nad tymi, którzy otrzymali Tx po krótkim okresie dializoterapii

Comparison of parameters of chronic kidney disease following paediatric preemptive versus non-preemptive renal transplantation

Pediatr Transplantation 2010: 14: 583–588

Rajiv Sinha and Stephen D. Marks

Variables	PRT (39)	NPRT (90)	p Value (95th CI)
CKD Stage 2 (T)	13 (33%)	30 (33%)	–
CKD Stage 3 (T)	25 (64%)	45 (50%)	0.2 (−5 to 30.7%)
CKD Stage 4 (T)	1 (3%)	14 (16%)	0.03 (0.8 to 22%)
Hypertension	12 (31%)	48 (53%)	0.02 (4 to 38.3%)
Median height SDS (range)	1.11 (4.28–1.71)	1.33 (6.55–1.26)	0.4 (0.28–0.77%)
Short stature	9 (23%)	28 (31%)	0.4 (−22.6 to 9.5%)
Hypocalcaemia	2 (5%)	3 (3%)	0.6 (−0.6 to 5%)
Hyperphosphataemia	4 (10%)	15 (17%)	0.3 (−17 to 8.3%)
PTH, pmol/L (range)	3.8 (0.6–19.7)	4.6 (0.3–36.9)	0.32 (−1.7 to 0.5%)
Hyperparathyroidism	29 (74%)	55 (61%)	0.14 (−4.8 to 28.4%)
Albumin, g/dL (range)	43.3 (38.3–47.7)	42.6 (20–49.7)	0.23 (−0.64 to 1.4%)
Hypoalbuminaemia (%)	5 (13%)	15 (17%)	0.6 (−13.7 to 8.7%)
Urinary albumin creatinine ratio, mg/mmoL (range)	3.6 (0.6–97)	4.1 (0–1023)	0.34 (−2.1 to 1.1%)
Micro- or macroalbuminuria	20 (51%)	54 (60%)	0.3 (−20.7 to 3.3%)
Bicarbonate, mmoL/L	23 (19.3–27)	22 (15.3–31)	0.3 (16 to 50.5%)
Acidosis	10 (26%)	42 (47%)	0.02 (3 to 36.1%
Anaemia	25 (64%)	62 (69%)	0.5 (−22.7 to 12%)
Medications			
Sodium bicarbonate	12 (31%)	35 (39%)	0.4 (−24 to 10%)
Anti hypertensive agents	12 (31%)	46 (51%)	0.03 (1.7 to 36.2%)
Iron	11 (28%)	46 (51%)	0.02 (4.3 to 38%)
Erythropoietin	1 (3%)	18 (20%)	0.01 (4.7 to 27%)
Phosphate binders	1 (3%)	8 (9%)	0.2 (−14.3 to 5%)
1-alfacalcidol	22 (56%)	67 (74%)	0.04 (0.7 to 35.4%)

Although the information from this study may strengthen the argument for PRT, we still need clearer evidence-based guidelines for its exact timing.

What have 20 years of data from the North American Pediatric Renal Transplant Cooperative Study taught us about growth following renal transplantation in infants, children, and adolescents with end-stage renal disease?

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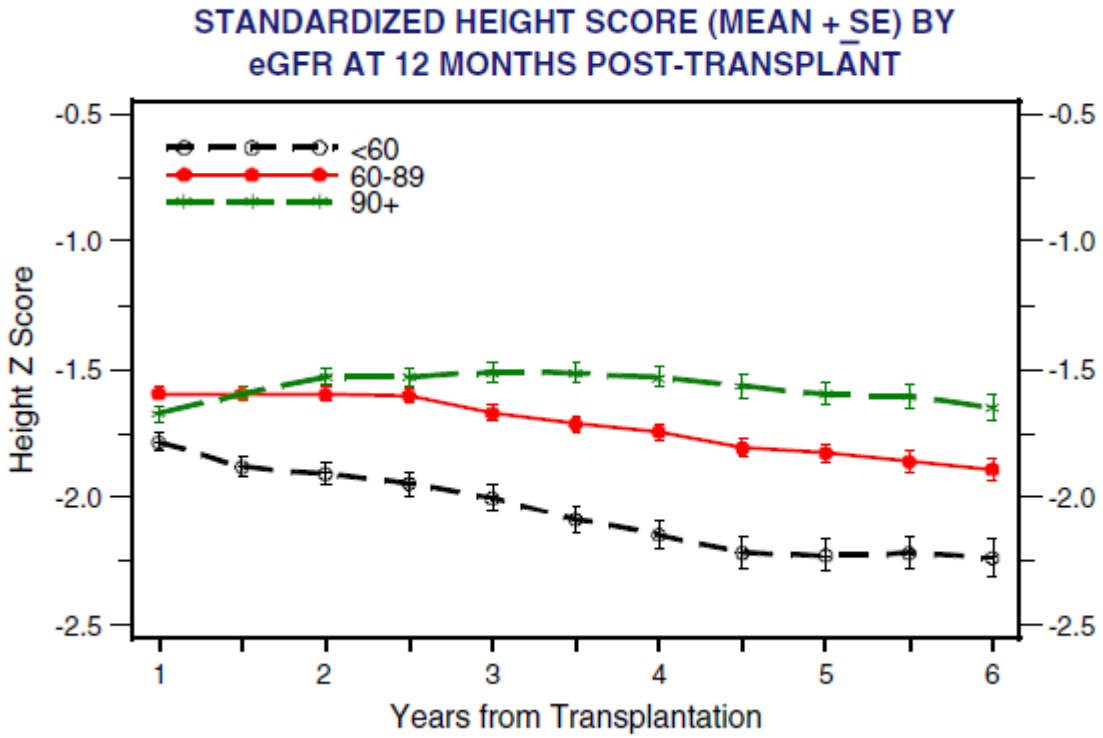
Richard N. Fine · Karen Martz · Donald Stablein



Earlier Is Not Necessarily Better in Preemptive Kidney Transplantation

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Wiley Periodicals Inc.

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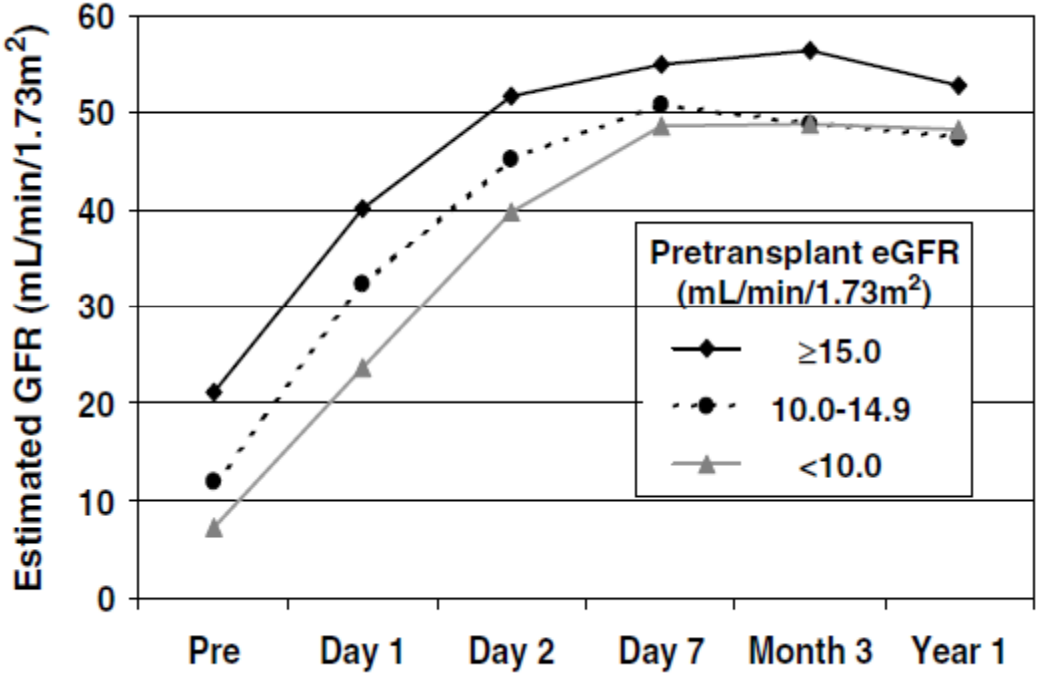
A. J. Matas[d] and B. L. Kasiske[a,b,*]



This analysis suggests that earlier transplantation and better pretransplant function does not necessarily result in better graft survival.

Podsumowanie

- W ostatniej dekadzie odnotowuje się tendencję do wczesneśniejszego rozpoczynania leczenia nerkozastępczego (dializy i pre-emtive) zarówno u dorosłych jak i u dzieci
- U osób dorosłych nie wykazano korzystnego wpływu na przeżycie i jakość życia pacjentów, którzy rozpoczynali RRT przy wyższym eGFR z wyjątkiem tych ze schorzeniami współistniejącymi i cechami mocznicy
- Dokładny czas rozpoczęcia RRT zwłaszcza u dzieci powinien być oceniany indywidualnie biorąc pod uwagę wiek i wagę, wielkość diurezy resztkowej, „możliwości dializacyjne”. Istnieje tendencja do opóźnionego startu RRT w tym preemptive Tx u niemowląt
- Proponowanie przeszczepów wyprzedzających pozostaje nadal jednym z najlepszych sposobów leczenia nerkozastępczego u dzieci przed ukończeniem wzrastania.
- Dotychczasowe zalecenia dotyczące optymalnego czasu rozpoczęcia leczenia nerkozastępczego powinny być zrewidowane uwzględniając ponadto inne (bardziej dopasowane do niewydolności nerek) pomiary filtracji kłębuszkowej
- Idealny czas rozpoczęcia leczenia nerkozastępczego aktualnie nie jest ostatecznie sprecyzowany