Care of transition period in Korean patients with CKD

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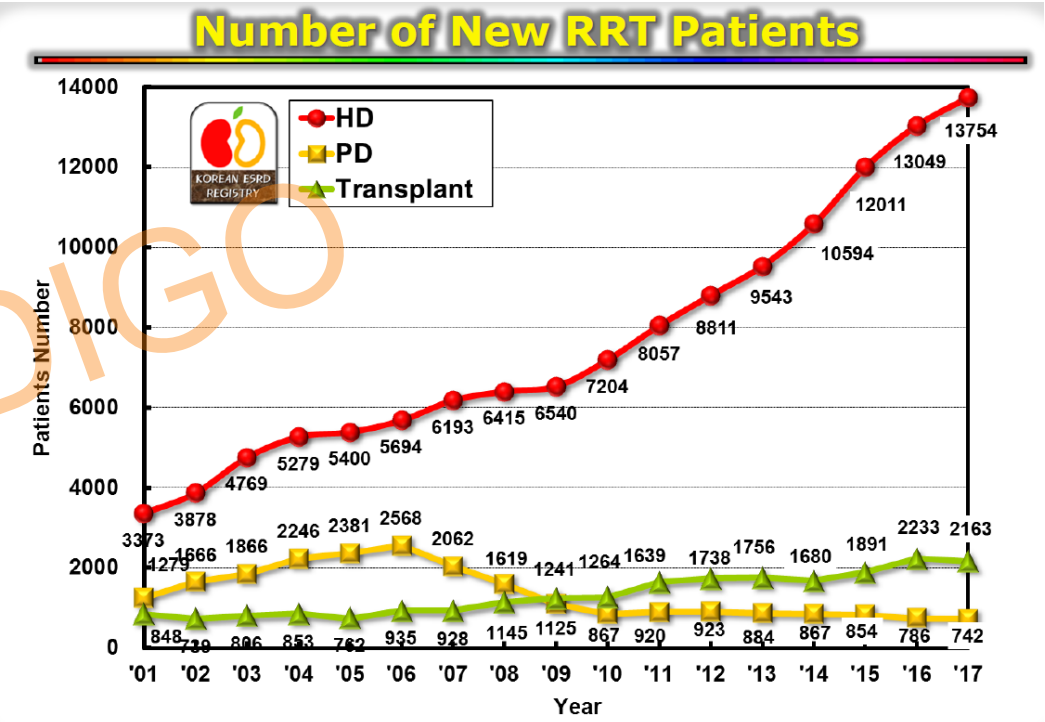
Introduction

- Increasing prevalence of HD patients
  - 400,000 patients on HD (US) and 75,000 (Korea)
  - 100,000 new starts (US) and 14,000 (Korea)



- Start of HD
  - Decrease in health-related quality of life (HRQoL)
  - 7 times increase in mortality

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USRDS and Korean ESRD Registry Data, Annual Meeting of KSN 2018

- **Transition** [tran-**zish**-*uh* n, -**sish**-]

1.movement, passage, or change from one position, state, stage, subject, concept, etc., to another; change:

"the transition from adolescence to adulthood."

- **Start** [stahrt]

1.to begin or set out, as on a journey or activity.

2.to appear or come **suddenly** into action, life, view, etc.; rise or issue suddenly forth.

3.to spring, move, or dart suddenly from a position or place: *The rabbit started from the bush.*

4.to be among the entrants in a race or the initial participants in a game or contest.

5.to give a sudden, involuntary jerk, jump, or twitch, as from a shock of surprise, alarm, or pain:

The sudden clap of thunder caused everyone to start.

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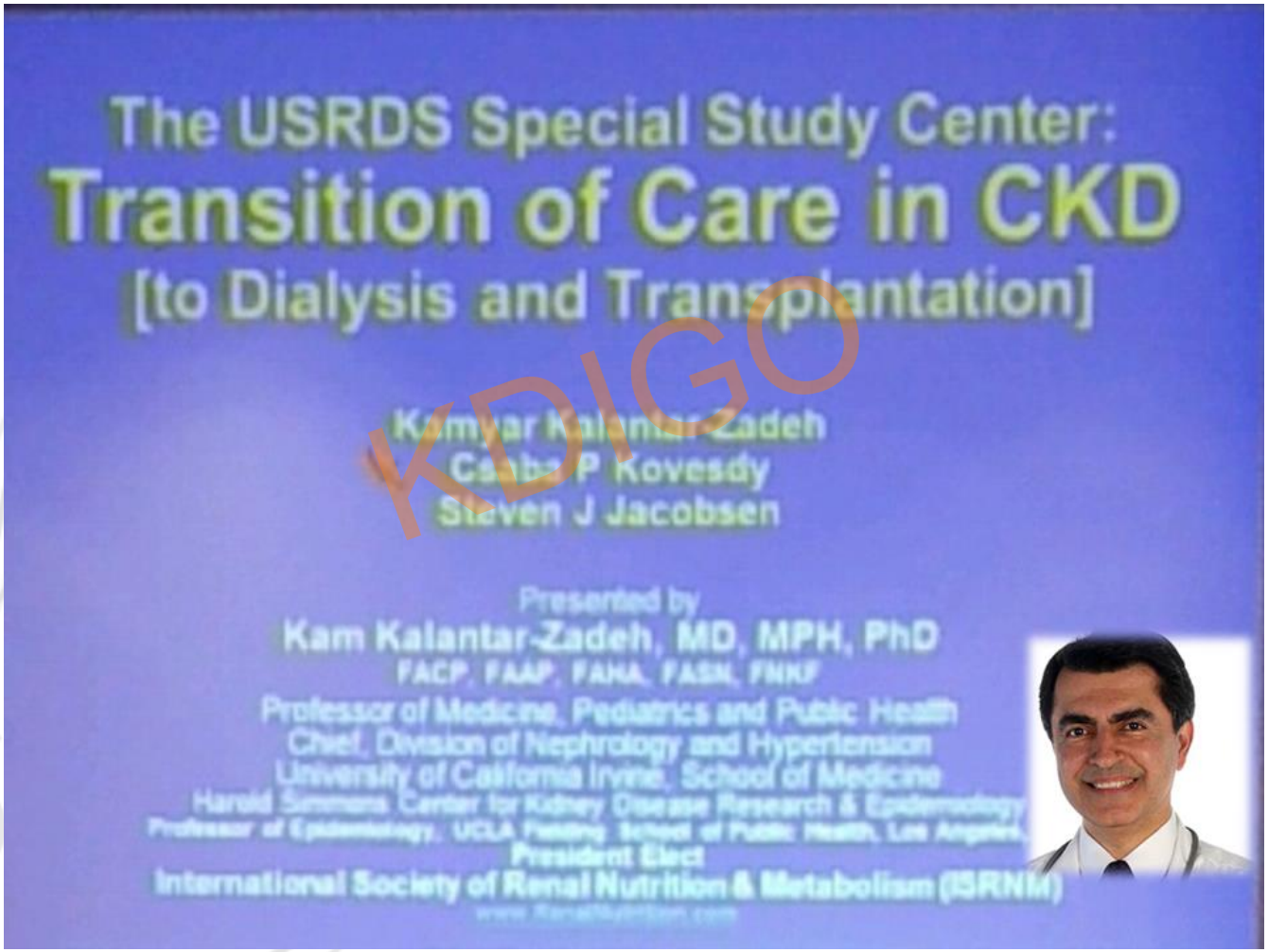
Dictionary.com

Transition of Care in CKD



Transition of Care in CKD

Transition from the pre–ESRD phase to the ESRD phase of CKD

- Defined operationally as before and after initiation of long-term RRT
- focus of a new USRDS Special Study, which published a chapter on "transition of care" in the 2015 USRDS Annual Data Report

- During this transition,
  - patients are at a very vulnerable state
  - rates of adverse events are very high

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Sharief S et al. Am J Kidney Dis. 2017 Jan; 69(1): 8.

Transition of Care in CKD

- The best timing for KRT initiation (early vs. late)
- The optimal KRT type (dialysis vs. transplant)
- In case of dialysis,
  - Best modality (HD vs. PD)
  - In-center vs. Home
  - Frequency (daily vs. thrice-weekly vs. infrequent eg., 2x/week)
  - Vascular access preparation (preemptive AVF, PD catheter placement, no access)

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Optimal transition of care to kidney replacement (dialysis or transplantation) is not known

Challenges of transition from NDD to ESRD

- Higher mortality
- Higher costs
- Best timing?
- Transition of elderly to ESRD
- Transition across race/ethnicity
- Residual renal function
- Best format? Incremental vs. abrupt

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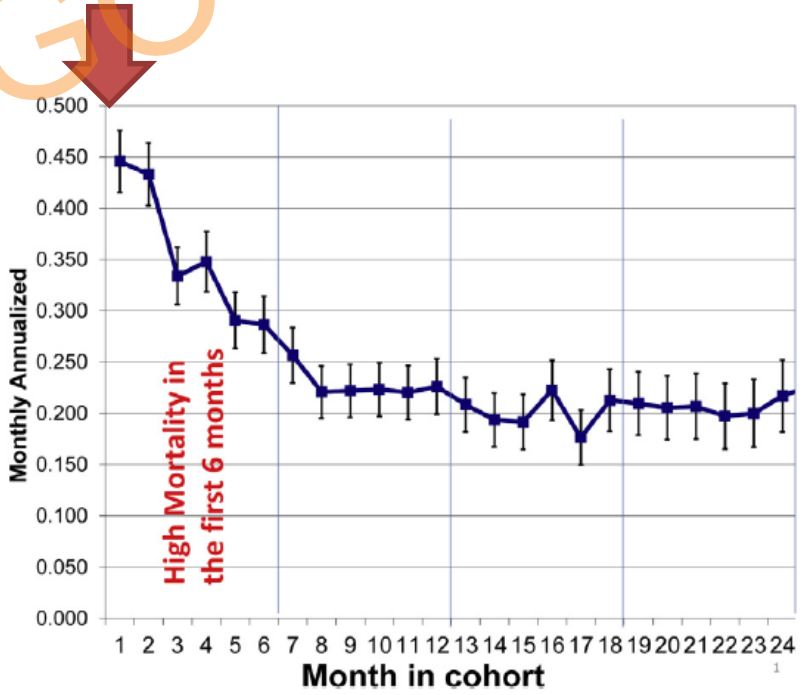
Higher mortality

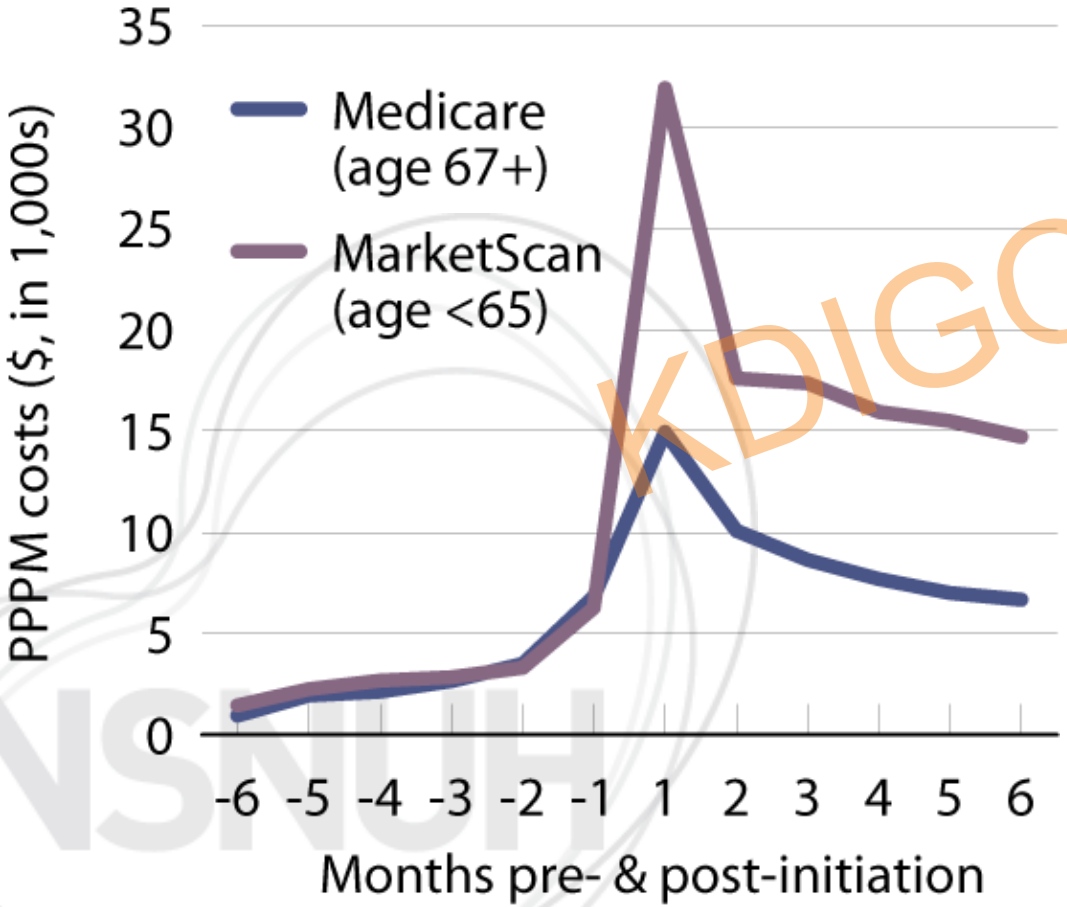
- Highest mortality in the first 6mo of HD > prevalent HD
- The most obvious change
  : abrupt transition from non-dialysis to thrice-weekly HD

- Potential cause of mortality



Lukowsky LR, Kalantar-Zadeh K et al., Am J Nephrol. 2012;35:548

Higher costs - US

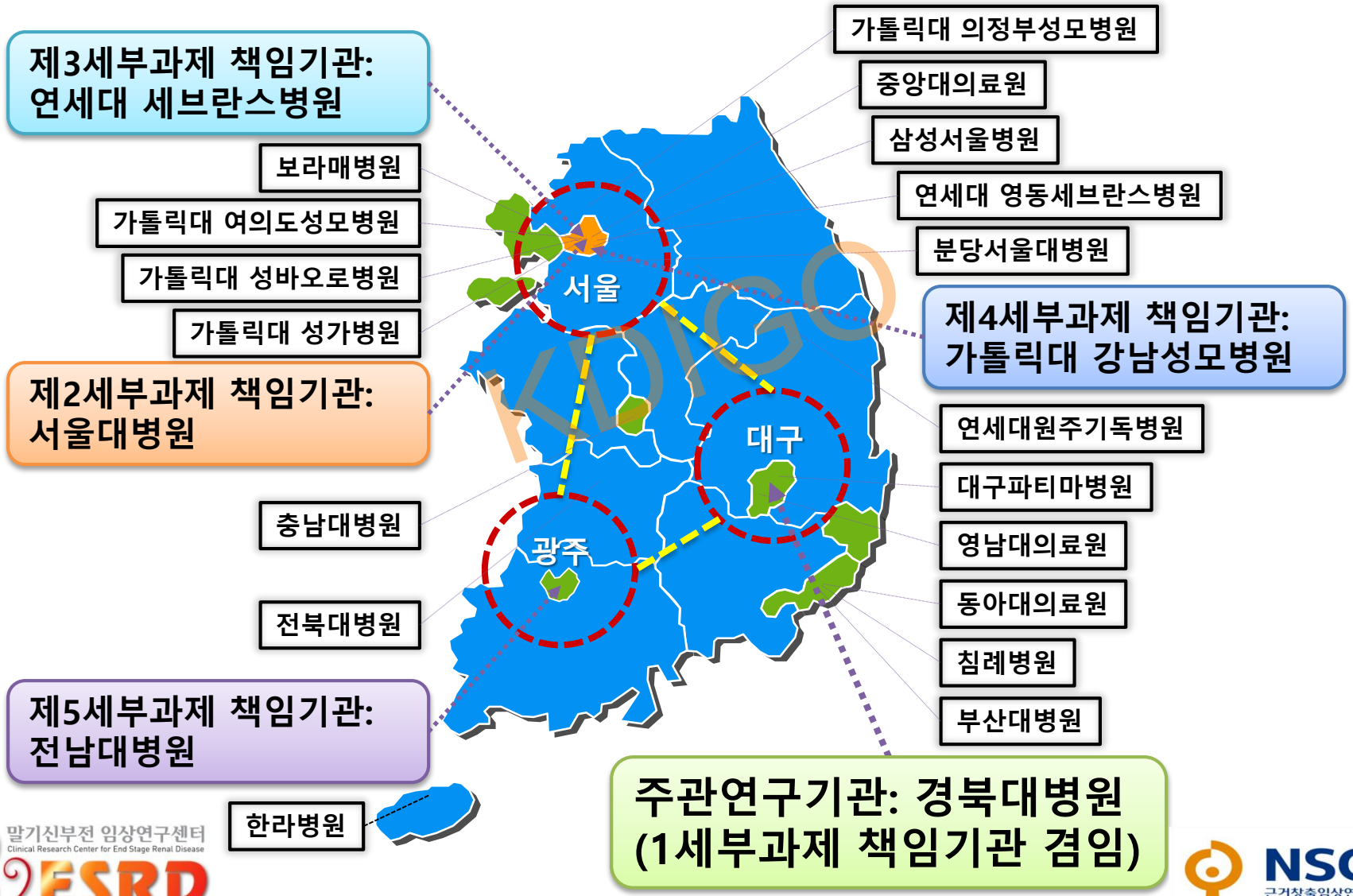


Incident Medicare (age 67+) & MarketScan (age<65) ESRD patients, 2007.

USRDS 2010 ADR

CRC-ESRD cohort (Comprehensive Prospective Study of Clinical Research Center for End Stage Renal Disease in Korea**), 2008.7-**

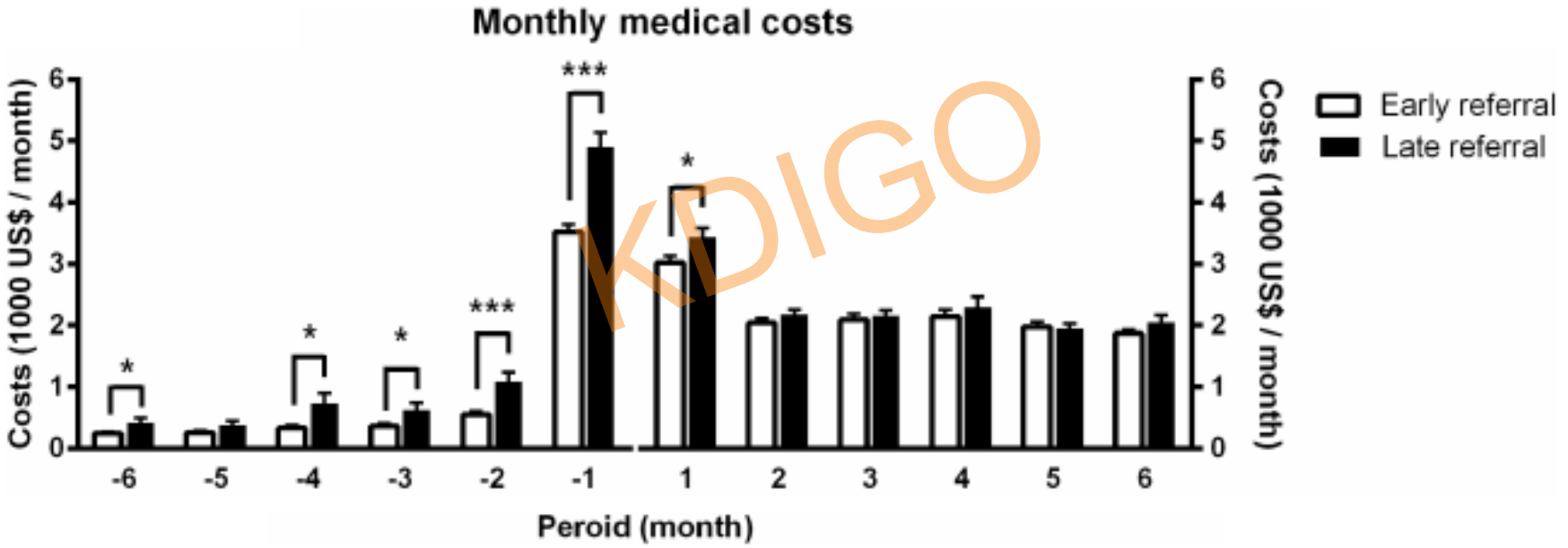
Nationwide web-based multi-center joint network prospective cohort in the Korea



말기신부전 임상연구센터
Clinical Research Center for End Stage Renal Disease
CRC ESRD

NSCR
근거창출임상연구국가사업단
National Strategic Coordinating Center for Clinical Research

Higher costs - Korea



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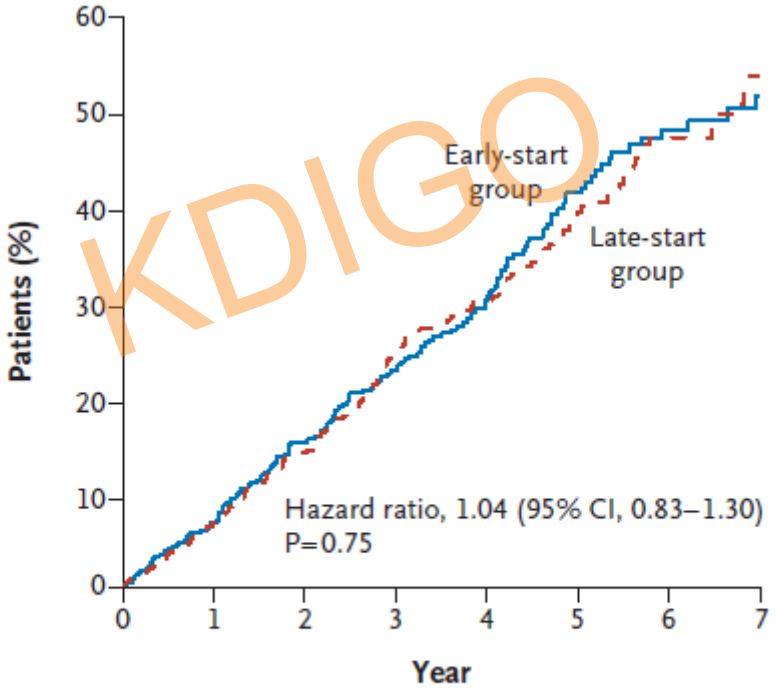
Lee J, Lee JP et al., PLoS One 2014

Best timing?

- The IDEAL study did NOT show any superiority of EARLY transition to dialysis



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No. at Risk

Early start	404	358	305	249	177	99	59	32
Late start	424	385	333	254	187	115	60	32

Cooper et al., NEJM 2010, IDEAL study

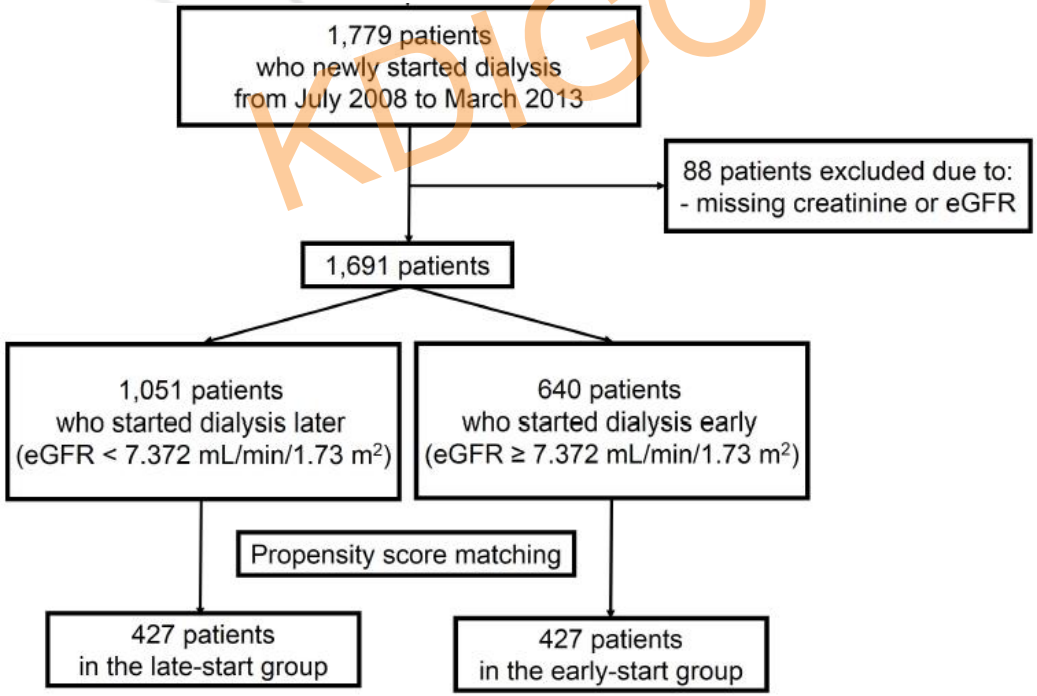
Best timing in Korea

OPEN ACCESS Freely available online

PLOS | ONE

Effect of Dialysis Initiation Timing on Clinical Outcomes: A Propensity-Matched Analysis of a Prospective Cohort Study in Korea

Jeonghwan Lee[1,2], Jung Nam An[3], Jin Ho Hwang[4], Yong-Lim Kim[2,5], Shin-Wook Kang[2,6], Chul Woo Yang[2,7], Nam-Ho Kim[2,8], Yun Kyu Oh[2,3], Chun Soo Lim[2,3], Yon Su Kim[2,9], Jung Pyo Lee[2,3]*



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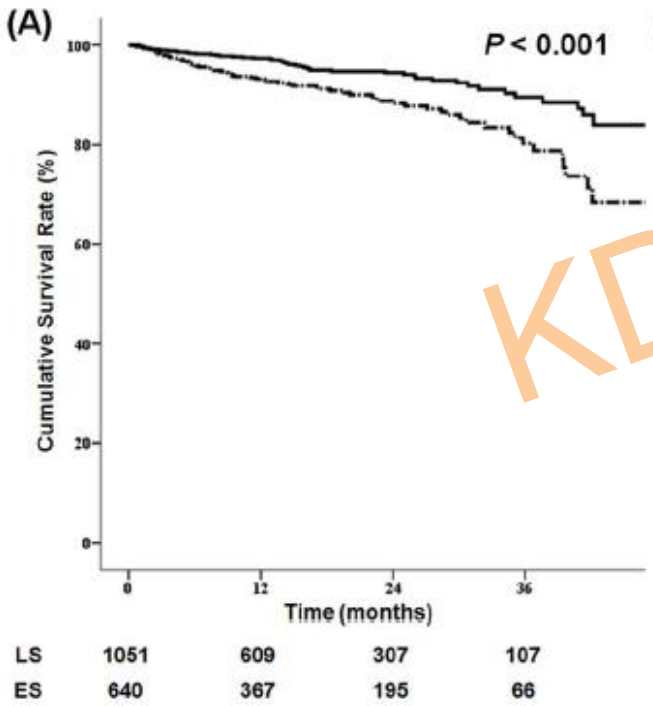
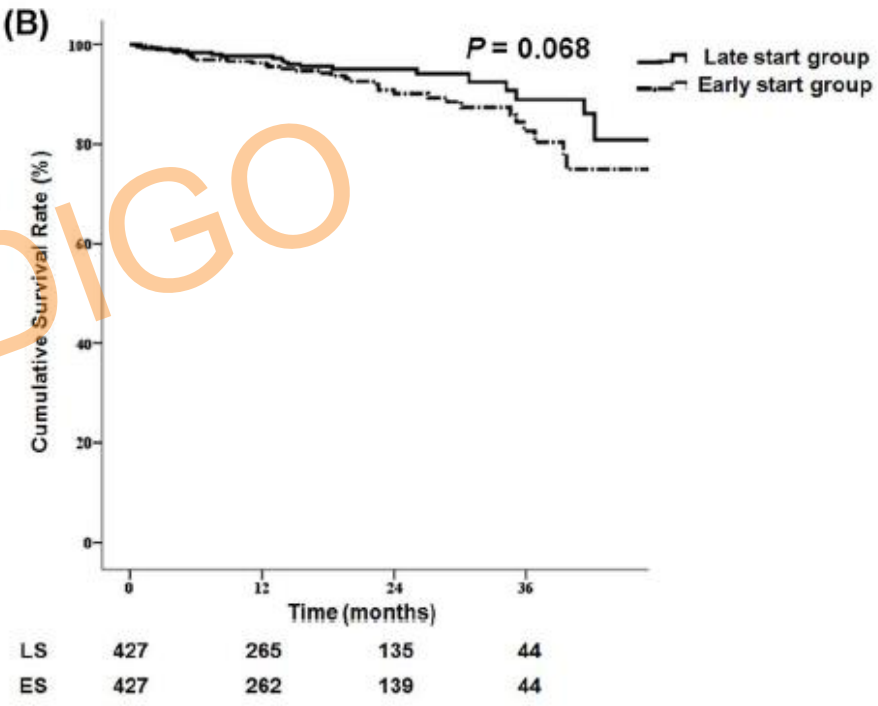
Lee J , Lee JP et al, PLoS One, Aug 2014

Best timing in Korea

Before PSM



After PSM



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Lee J , Lee JP et al, PLoS One, Aug 2014

Transition of elderly to ESRD

- The number of elder grew from 29.6 million in 1990 to 36.8 million in 2008, representing a 20% growth in US.

- In 1990, 2000 and 2010, 39%, 43%, and 44% of all prevalent dialysis patients, and 4%, 10%, and 20% of all kidney transplant recipients were older than 65 years, respectively, in US.

- It is not clear whether the poor outcomes of KRT justify these expensive therapies in the elderly esp. if mortality remains essentially unchanged.

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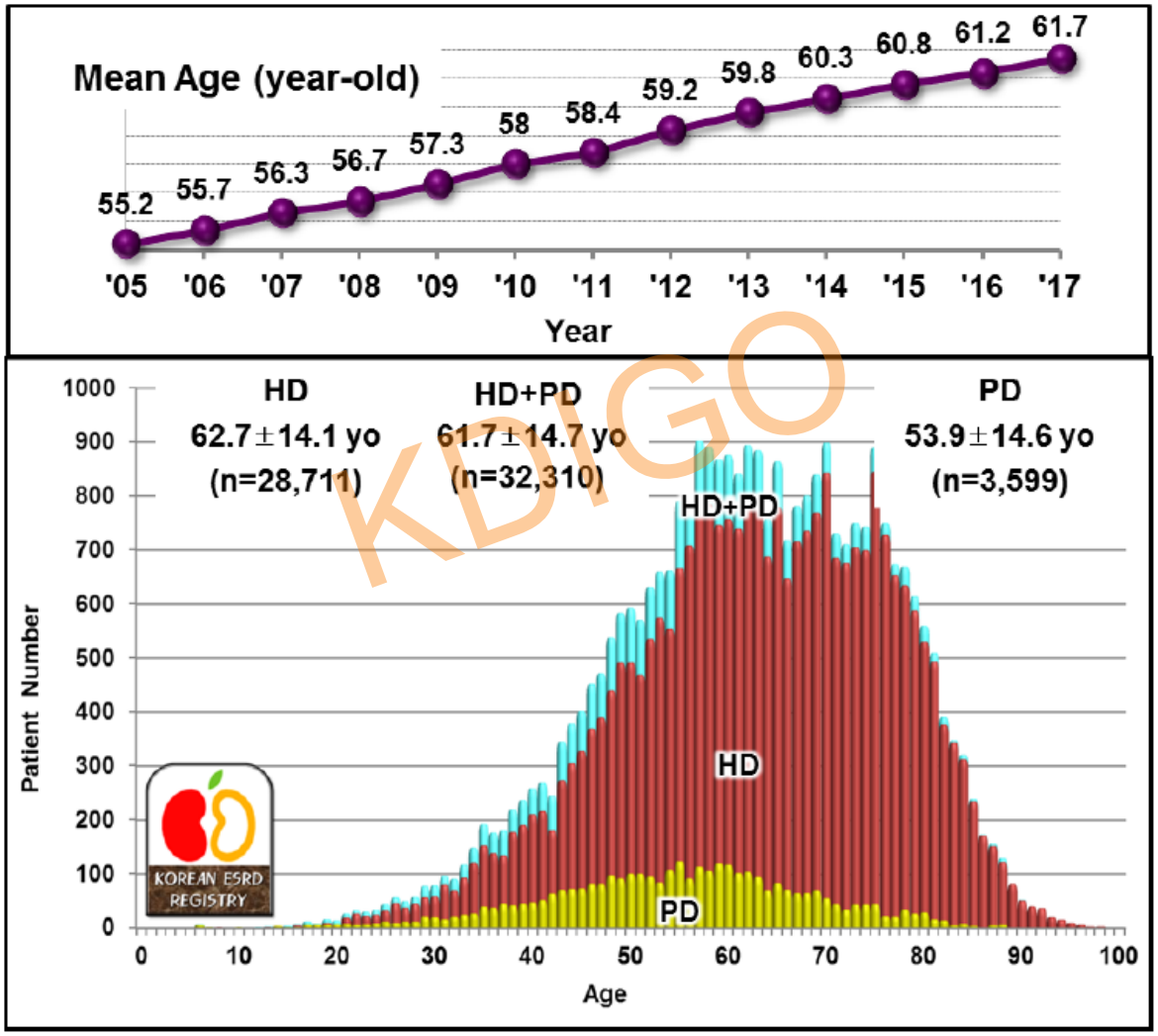
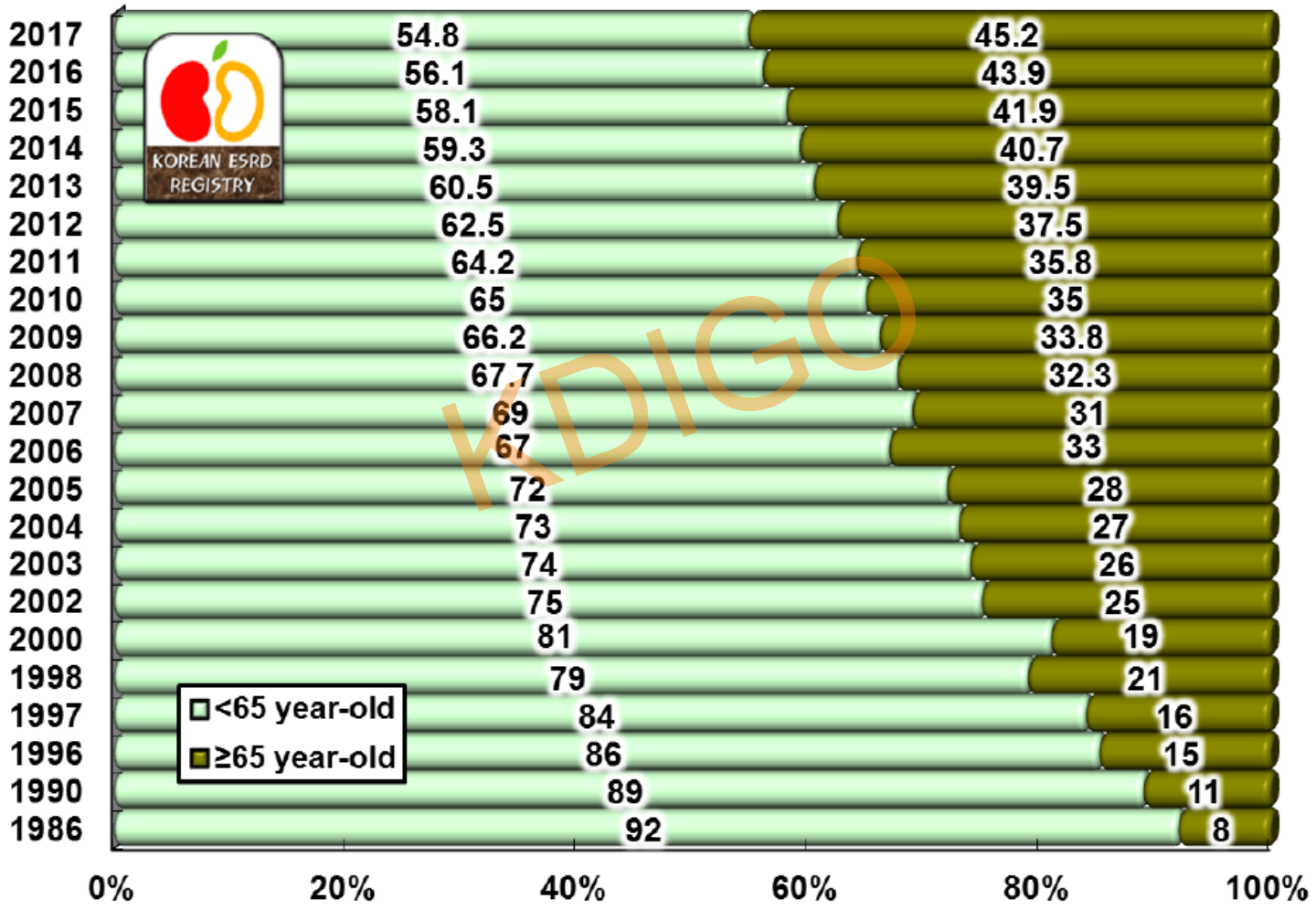
Age Distribution of Dialysis Patients



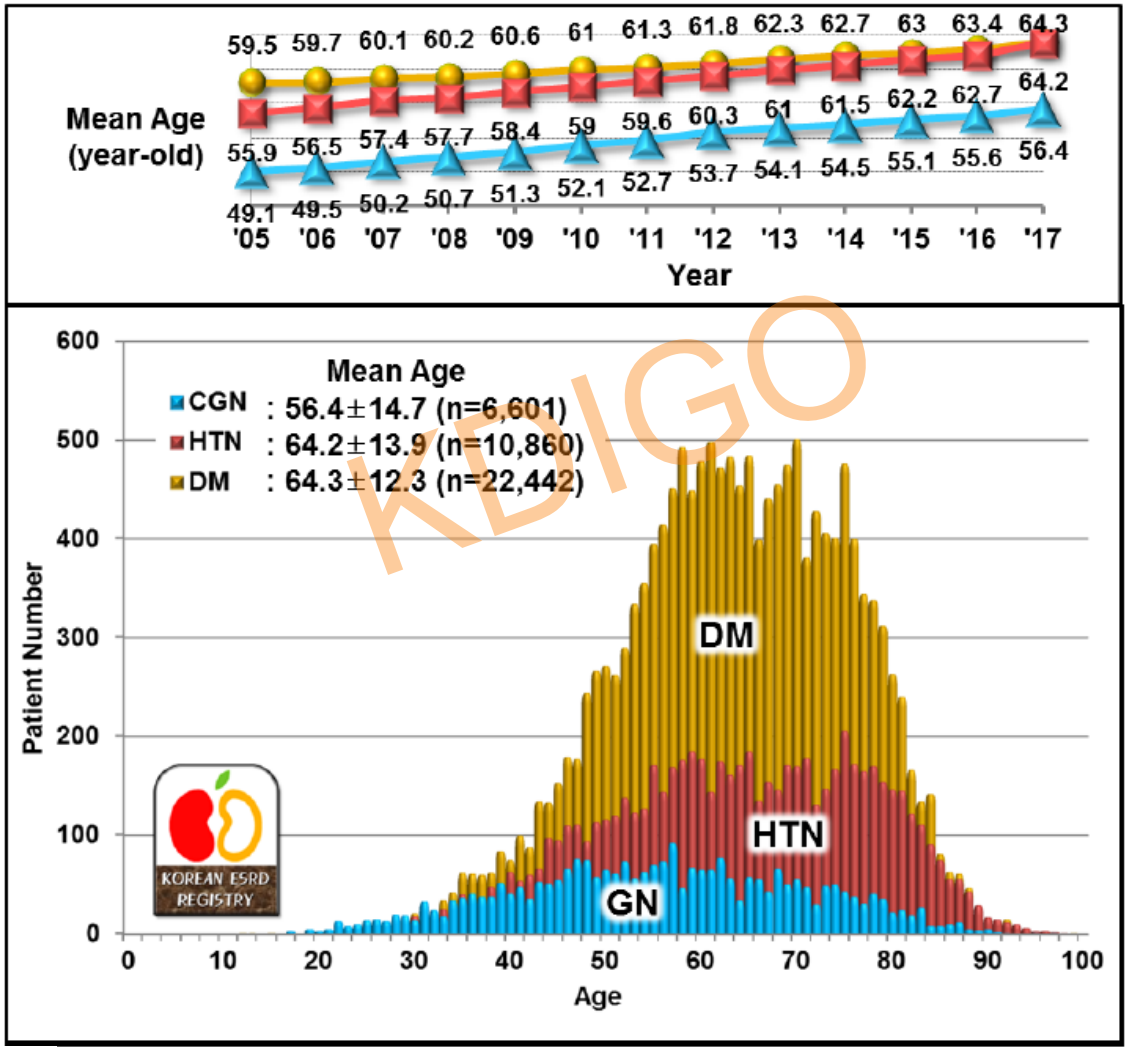
Korean ESRD Registry Data, Annual Meeting of KSN 2018

Percent of Elderly Dialysis Patients



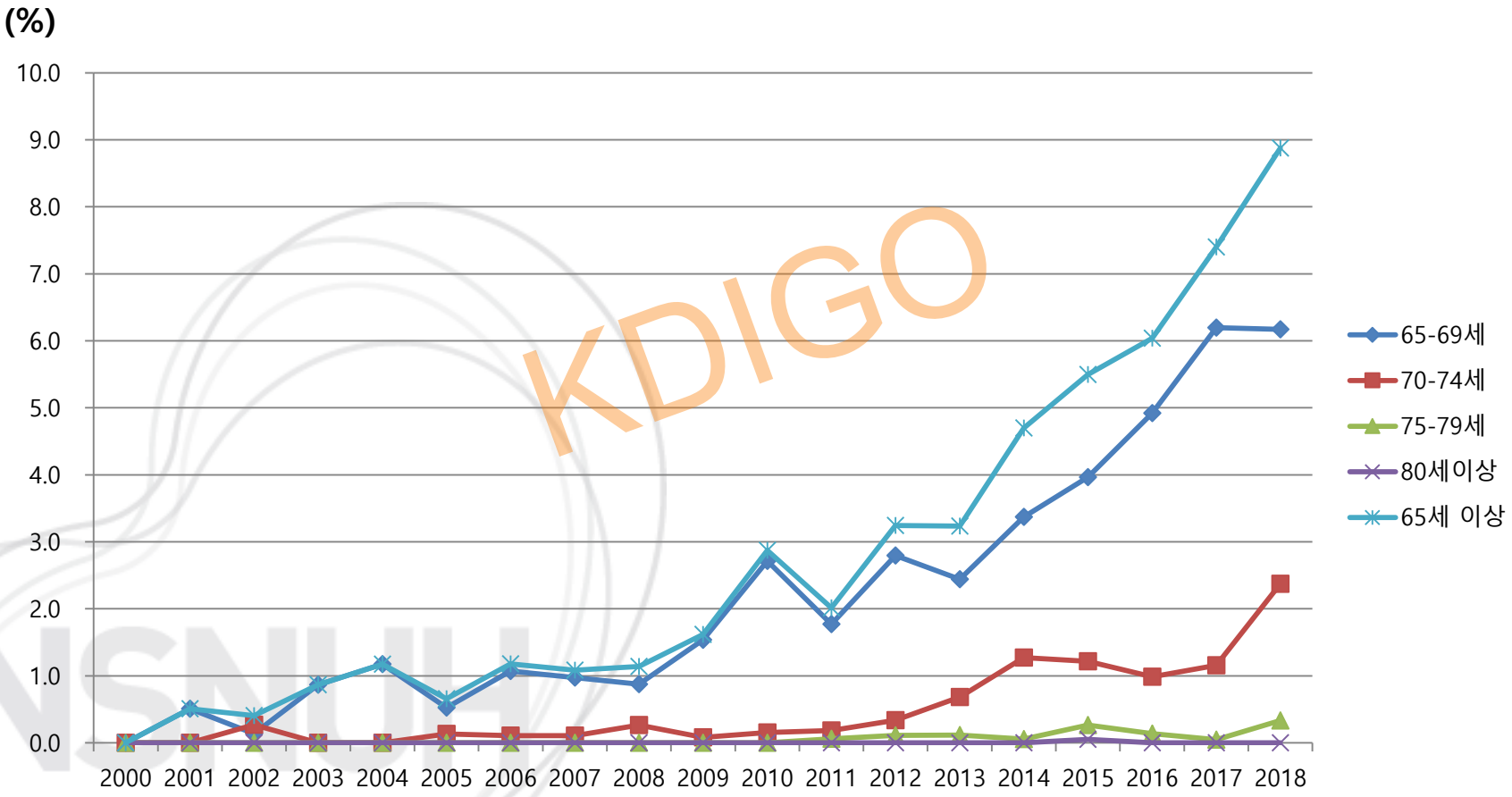
Korean ESRD Registry Data, Annual Meeting of KSN 2018

Age Distribution according to ESRD Causes



Korean ESRD Registry Data, Annual Meeting of KSN 2018

Percent of Elderly Kidney Transplant Patients



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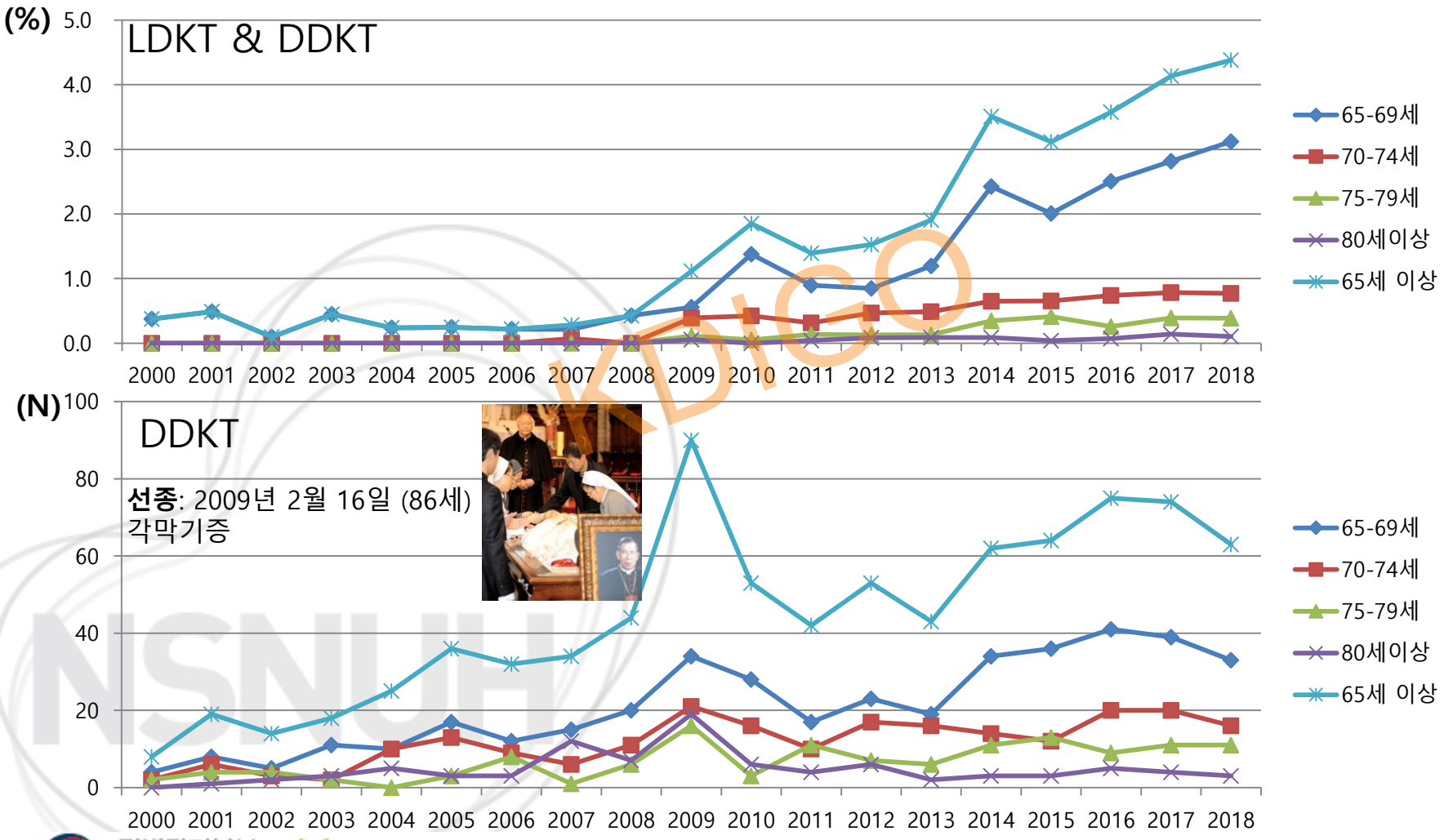
KONOS (Korean Network of Organ Sharing) Data

Percent of Elderly Kidney Transplant Donor



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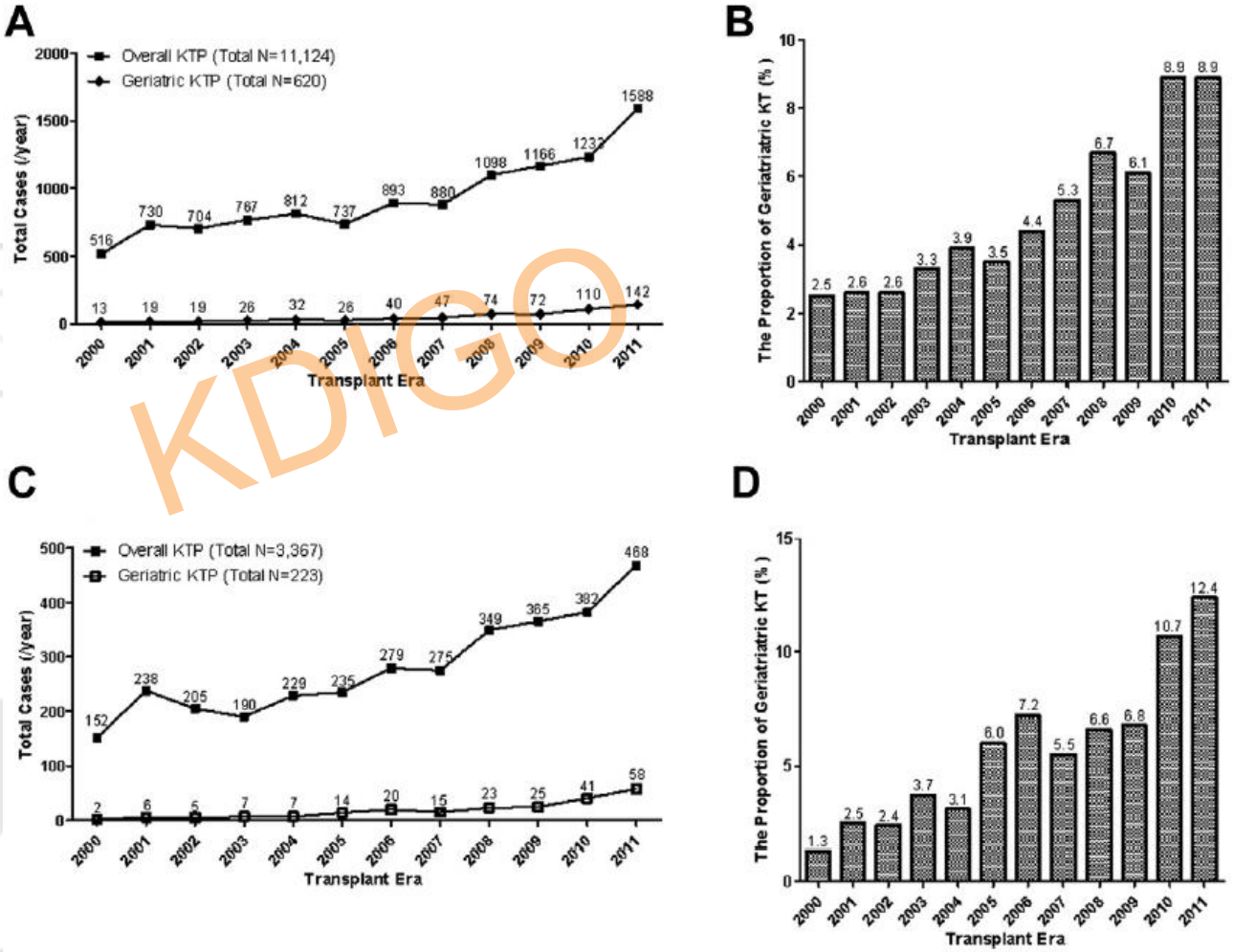
Transition of elderly to ESRD: 1. KT

KONOS database

Multicenter cohort



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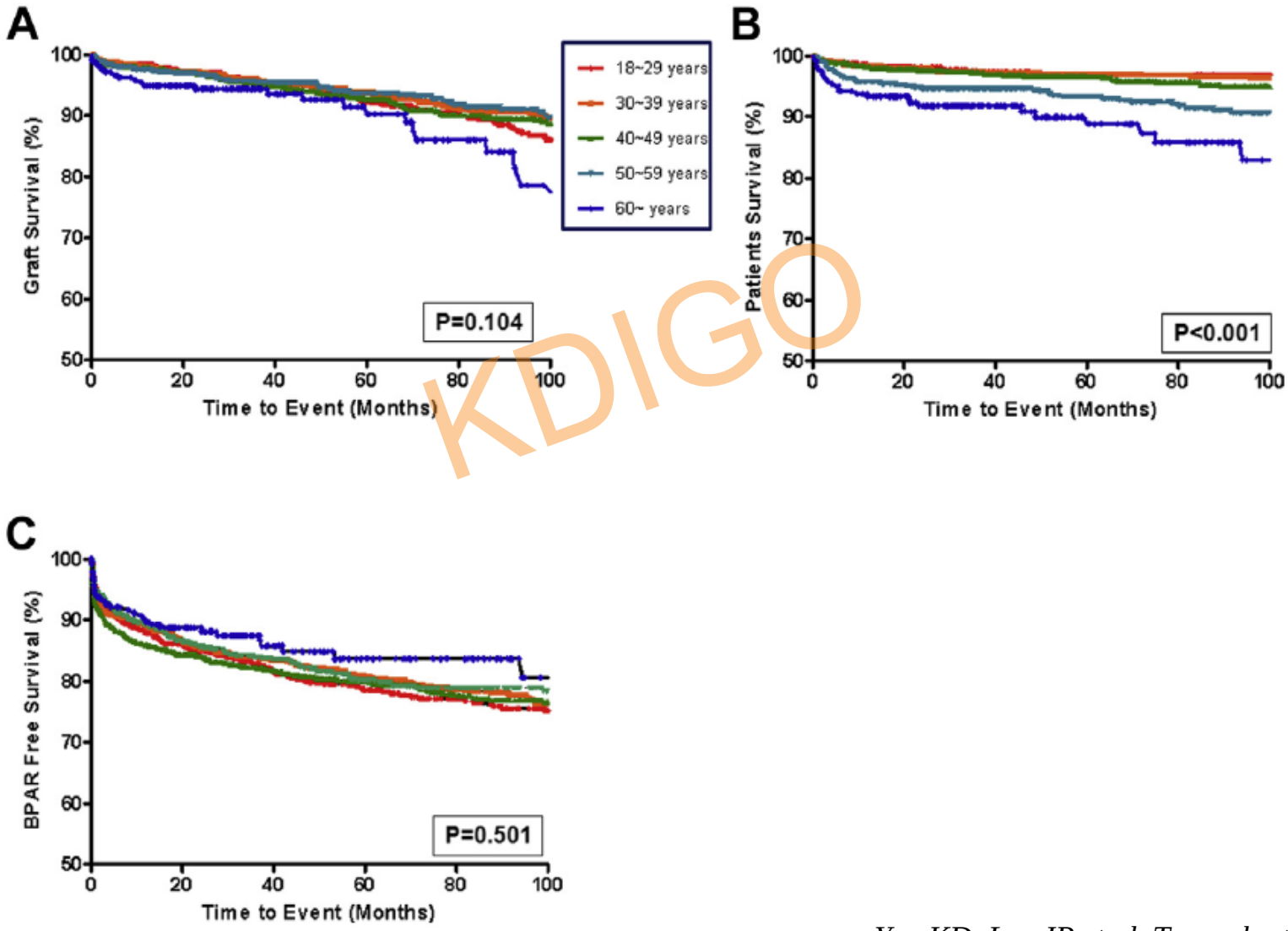
Yoo KD, Lee JP et al, Transplant Proc, 2015

Transition of elderly to ESRD: 1. KT



KDIGO

Yoo KD, Lee JP et al, Transplant Proc, 2015

DDKT Donor (M/79)-> Recipient (F/71)

마음을 나누다 두근 두근

김복임 환자 / 장기이식센터 신장이식팀

신장질환 환자에게 희망을 전해요.

보라매병원 장기이식센터 신장이식팀이 70대 고령자의 양측 신장 동시 이식에 성공했다. 고난도 수술을 성공리에 마치고 건강을 회복한 김복임 환자는 보라매병원 의료진에게 감사의 말을 전했다. 그리고 신장질환으로 고통을 겪는 고령의 환자들에게 용기와 희망의 메시지를 전했다.

글 이성주 / 사진 고안순

22

<KBS뉴스, 신장내과 이정표 교수 '고령자 신장이식'>
2. 19.

<외과, 고령자 양측 동시 신장이식>

연합뉴스

"수혜자 70세·기증자 79세…신장 2개 동시이식 성공"

서울대 보라매병원 신장이식팀·"고령자들에 새로운 희망"

(서울=연합뉴스) 김잔디 기자 = 70세 이상 고령자들끼리 신장을 주고받는 수술이 국내에서 성공적으로 이뤄졌다. 더욱이 이번 수술은 뇌사자의 신장 두 개를 한꺼번에 이식하는 것이어서 통상의 수술보다 위험도가 더 컸다는 평가다.

mini interview

믿음에 보답하고자 최선을 다하겠습니다.

신장이식팀 이정표 교수

지난 3년간 저희 보라매병원을 믿고 와주셔서 감사했습니다. 김복임 환자분께서 앞으로 신장이식 후 면역억제제를 복용하며 사는 과정은 투석과 비교될 정도는 아니겠지만 어려운 일일 것입니다. 지금까지 희망을 잃지 않고 노력해주셔서 감사합니다. 그 믿음에 보답하기 위해 보라매병원 신장이식팀은 앞으로도 최선을 다하겠습니다.

고위험 환자의 이식을 위해서 수술을 진행하는 외과 외에도 저희 신장내과, 혈압 작치료 시 반드시 필요한 혈장교환술과 많은 면역학적 검사를 실행한 진단검사의학과, 조직검사와 신장초음파를 진행한 영상의학과, 조직검사 결과를 빠르게 판독해주신 병리과 교수진, 이식환자의 철저히 관리해준 병동 간호사 및 감염내과 그리고 보라매병원 장기이식을 관리해준 코디네이터 등 다양하고 많은 직종의 전문가들이 환자분의 건강을 위해 함께 노력했습니다. 보라매병원은 언제나 안성콩팥병 환자분과 신장이식 환자들을 위해 앞으로도 변함없이 노력하겠습니다.

for Most 보라매병원은 서울대학교병원 교수진이 진료합니다!

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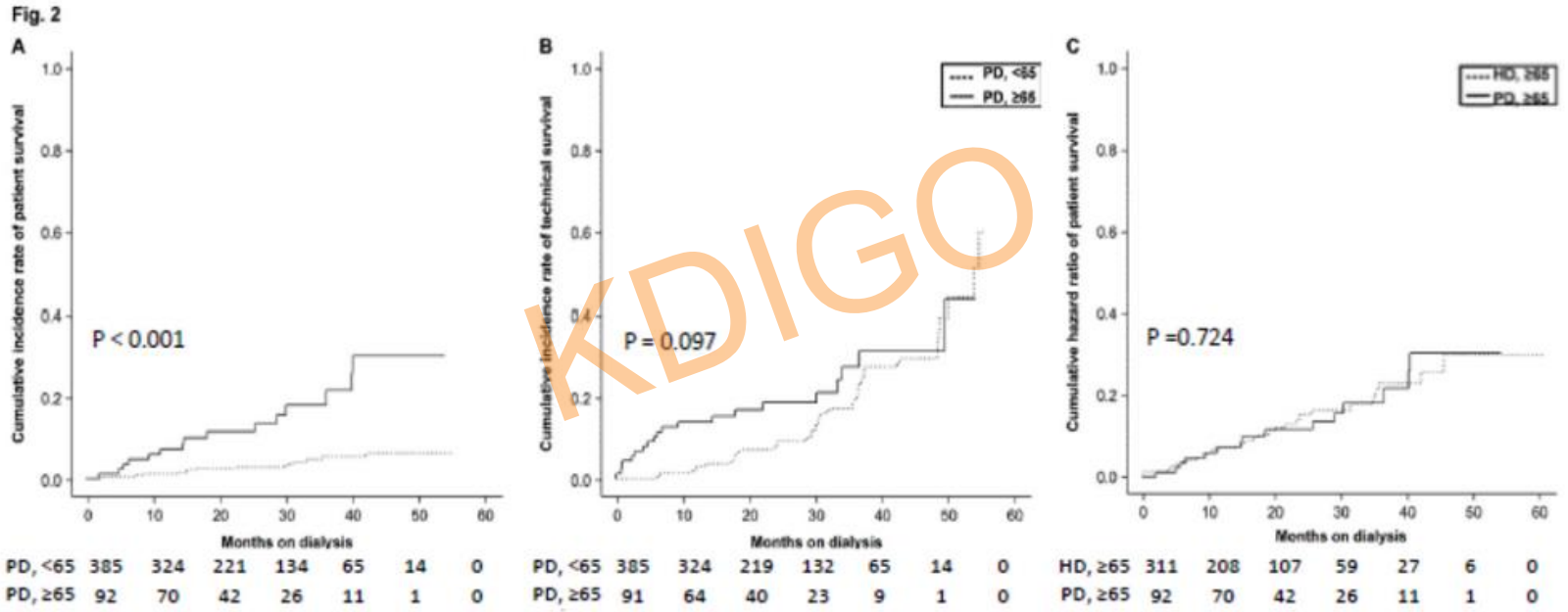
Transition of elderly to ESRD: 2. HD vs PD



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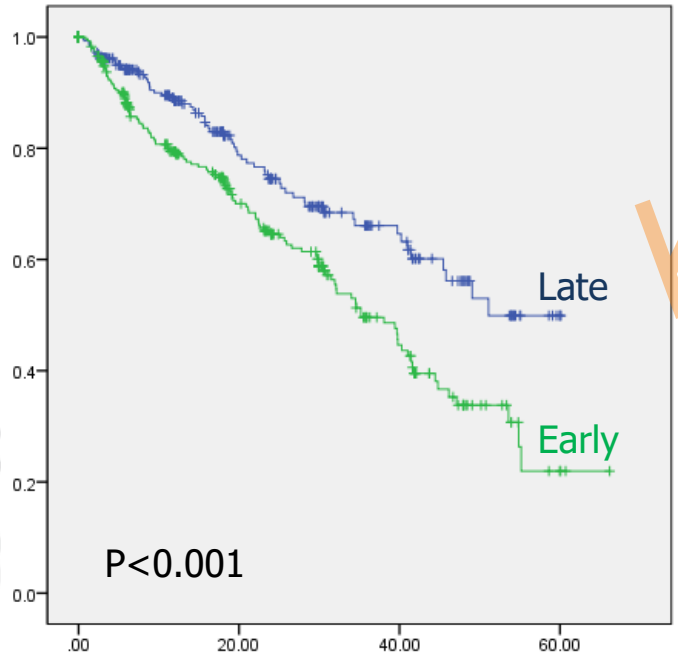
Competing risk analysis

Kim H , Lee JP et al, PLoS One 2015

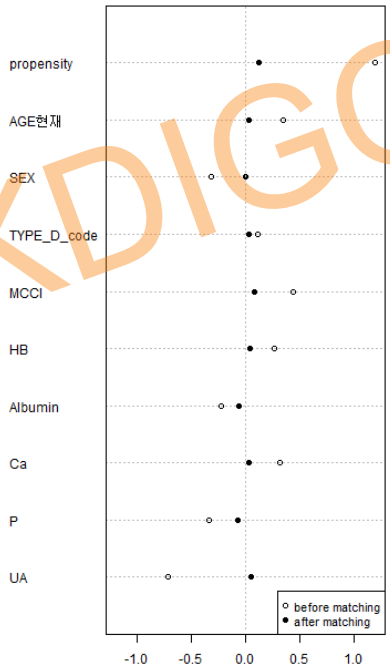
Transition of elderly to ESRD: 3. Dialysis initiation

- Definition of "early" dialysis: eGFR ≥ median (8.845 ml/min/1.74m^2)

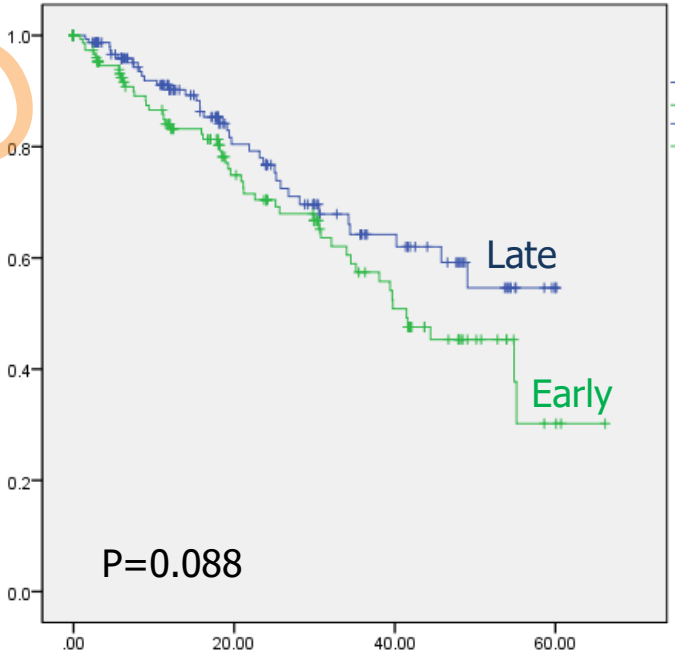
Before PSM



PSM



After PSM



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Park JY , Lee JP et al, PLoS One 2017

Lack of Appropriate Care/Late Referral

- More rapid progression
- Worse health status at time of initiation
- Higher mortality after starting RRT
- Decreased access to transplant

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Interventions to Improve CKD Outcomes

- Formal CKD education extends time to starting dialysis.

Devins et al. AJKD. 2003

- Directed CKD care increases initial fistula utilization.

Lee, W. et al. Nephrol. Dial. Transplant. 2006

- Multidisciplinary care improves survival.

Hemmerlgarn et al. JASN 2007

- CKD clinics decreased hospitalizations post initiation.

Goldstein et al. AJKD. 2004.

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General Nephrology - Time Referral to the Nephrologist

Guideline Organization	Recommendation (Evidence Level)	Comments
CARI-Australia **2003**	Patients with **Ccr <30 ml/min/1.73m^2.** Earlier referral should be considered in patients who are hypertensive or who have significant proteinuria (>1g/24hours). (Level B)	Reasons for timely referral - high risk progressive deterioration renal function - specialist management of renal failure - adequate preparation for dialysis
CSN-Canada **1999**	Refer patients with **Ccr <30ml/min** to a nephrologist for opinion regarding management of renal failure (Opinion)	
EBPG-Europe **November 2002**	A. Referral should be considered when GFR<60ml/min and is **mandatory when GFR<30ml/min** B. If GFR is not available, referral should be when on 2 consecutive measurements Scr > 150μmol/L (1.7 mg/dL) in men and 120μmol/l (1.35 mg/dL) in women. (Opinion)	
KDOQI-US **February 2004**	In general, patients with **GFR <30 mL/min/1.73 m^2** should be referred (stage 4). (Opinion)	Consultation and/or co-management with a kidney disease care team is **advisable during Stage 3 (30-59ml/min)**, and **referral to a nephrologist in Stage 4 (15-29ml/min)** recommended. Kidney function may need to be monitored four times per year or more.
UK-Guidelines **August 2002**	Patients with progressive RF should be referred early with Scr 150-200μmol/l (1.7-2.25 mg/dL) to enable dialysis to be started in a planned fashion. (Good Practice)	

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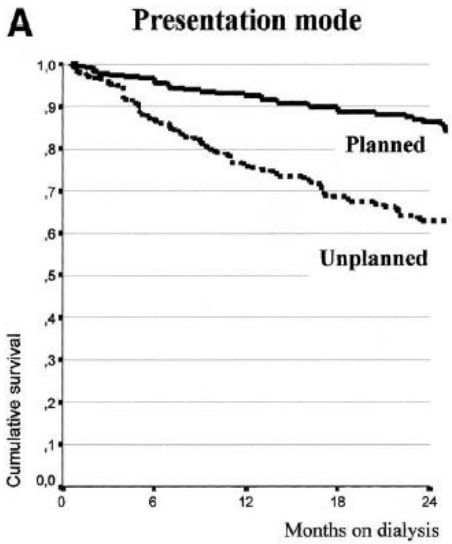
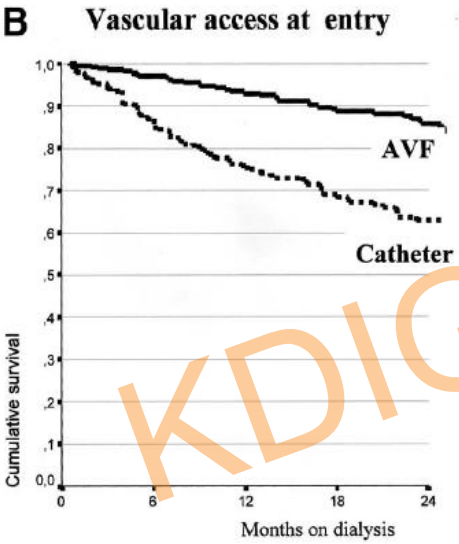
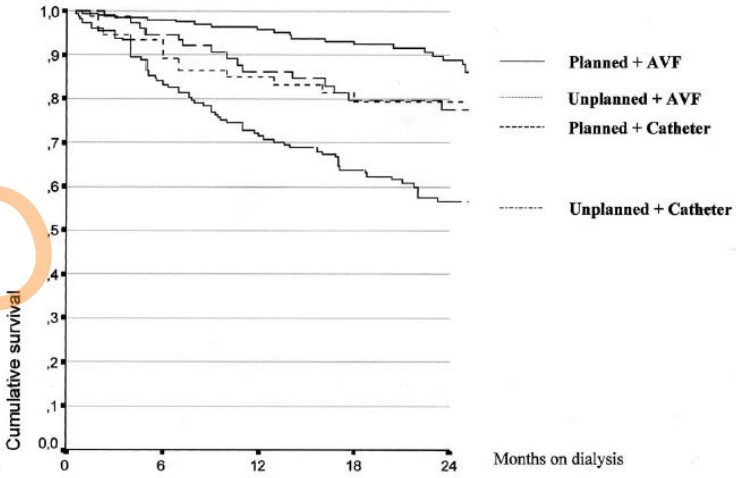


Planned	281	211	133
Unplanned	257	169	106



AVF	284	213	142
Catheter	254	167	97



Planned + AVF	206	156	102
Planned + Catheter	75	55	31
Unplanned + AVF	78	57	40
Unplanned + Catheter	179	112	66

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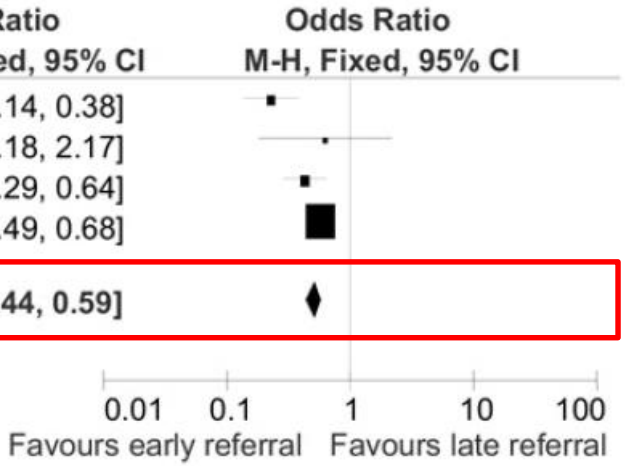
Am J Kidney Dis. 2004 Jun;43(6):999-1007

A All cause mortality at 3 months

Study	Early referral Events	Total	Late referral Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Jungers 2006a	24	971	42	420	11.5%	0.23 [0.14, 0.38]
Schmidt 1998	8	180	4	58	1.2%	0.63 [0.18, 2.17]
Stoves 2001a	48	793	61	467	14.5%	0.43 [0.29, 0.64]
Winkelmayer 2003	465	1975	363	1039	72.9%	0.57 [0.49, 0.68]
Total (95% CI)		**3919**		**1984**	**100.0%**	**0.51 [0.44, 0.59]**
Total events	545		470			

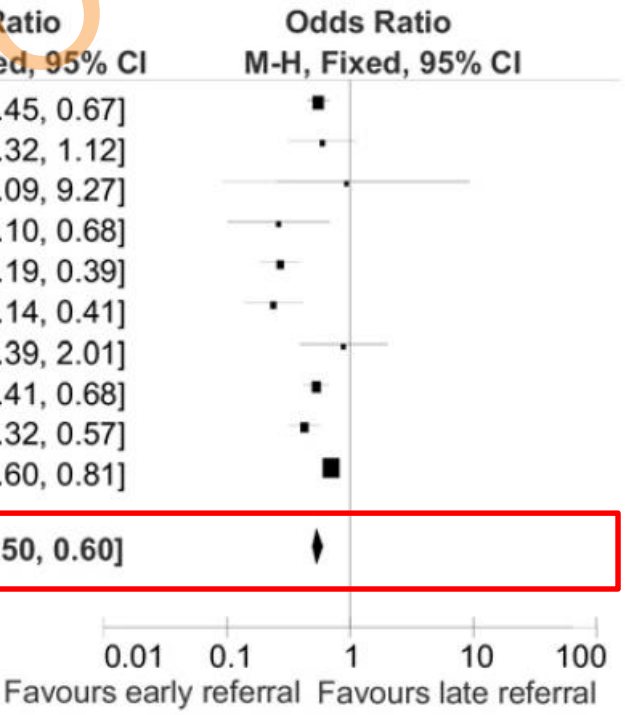
Heterogeneity: Chi² = 12.14, df = 3 (P = 0.007); I² = 75%
Test for overall effect: Z = 9.06 (P < 0.00001)



B All cause mortality at 12 months

Study	Early referral Events	Total	Late referral Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Cass 2002	292	3102	181	1141	20.9%	0.55 [0.45, 0.67]
Ellis 1998	37	134	25	64	2.1%	0.60 [0.32, 1.12]
Gallego 2003	3	106	1	33	0.1%	0.93 [0.09, 9.27]
Hoffmann 2006	14	110	10	28	1.2%	0.26 [0.10, 0.68]
Jungers 2006a	55	971	76	420	8.7%	0.27 [0.19, 0.39]
Lorenzo 2004	19	281	60	257	5.1%	0.24 [0.14, 0.41]
Roubicek 2000	17	177	10	93	1.0%	0.88 [0.39, 2.01]
Stack 2003	157	1442	134	717	13.9%	0.53 [0.41, 0.68]
Stoves 2001a	103	793	121	467	11.6%	0.43 [0.32, 0.57]
Winkelmayer 2003	876	1975	553	1039	35.2%	0.70 [0.60, 0.81]
Total (95% CI)		**9091**		**4259**	**100.0%**	**0.55 [0.50, 0.60]**
Total events	1573		1171			

Heterogeneity: Chi² = 39.68, df = 9 (P < 0.00001); I² = 77%
Test for overall effect: Z = 12.59 (P < 0.00001)



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Neil A et al. *Am J Med.* 2011 Nov;124(11):1073-80

Early referral vs. Late referral

	n. Of study	OR or mean difference (95% Confidence Interval)	*P value*
PD	14	2.1 (1.9-2.3)	*<.00001*
Temporary Access	11	0.18 (0.16-0.20)	*<.00001*
AVF	7	3.0 (2.5-3.5)	*<.00001*
Erythropoietin	7	3.9 (3.2-4.9)	*<.00001*
Hemoglobin (11.1g/L)	12	11.1(10.3-12)	*<.00001*

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Neil A et al. *Am J Med.* 2011 Nov;124(11):1073-80

OPEN ACCESS Freely available online

PLOS ONE

Early Referral to a Nephrologist Improved Patient Survival: Prospective Cohort Study for End-Stage Renal Disease in Korea

Do Hyoung Kim[1,9], Myounghee Kim[2,9], Ho Kim[3,9], Yong-Lim Kim[4,9], Shin-Wook Kang[5,9], Chul Woo Yang[6,9], Nam-Ho Kim[7,9], Yon Su Kim[1,9], Jung Pyo Lee[8,9]*

1 Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, **2** Department of Dental Hygiene, College of Health Science, Eulji University, Seongnam, Korea, **3** Department of Epidemiology and Biostatistics, School of Public Health, Seoul National University, Seoul, Korea, **4** Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea, **5** Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, **6** Department of Internal Medicine, The Catholic University of Korea College of Medicine, Seoul, Korea, **7** Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea, **8** Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul, Korea, **9** Clinical Research Center for End Stage Renal Disease in Korea, Daegu, Korea

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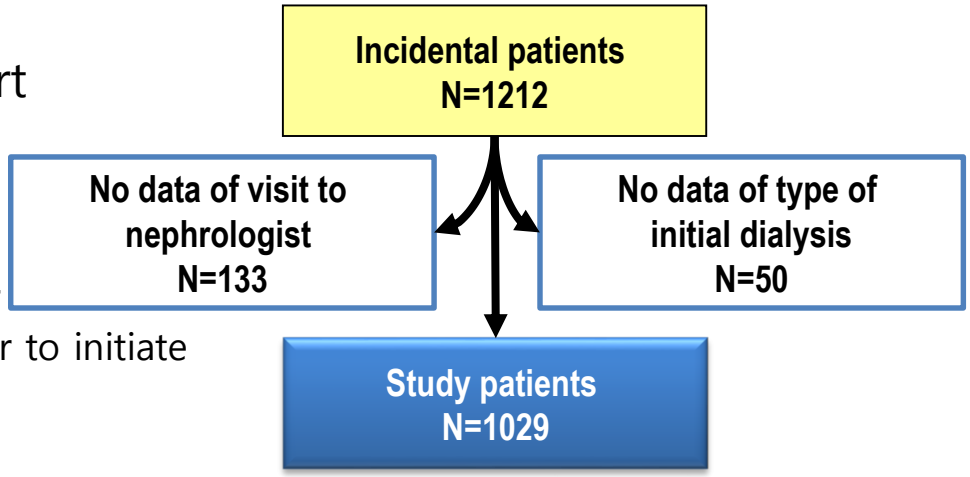
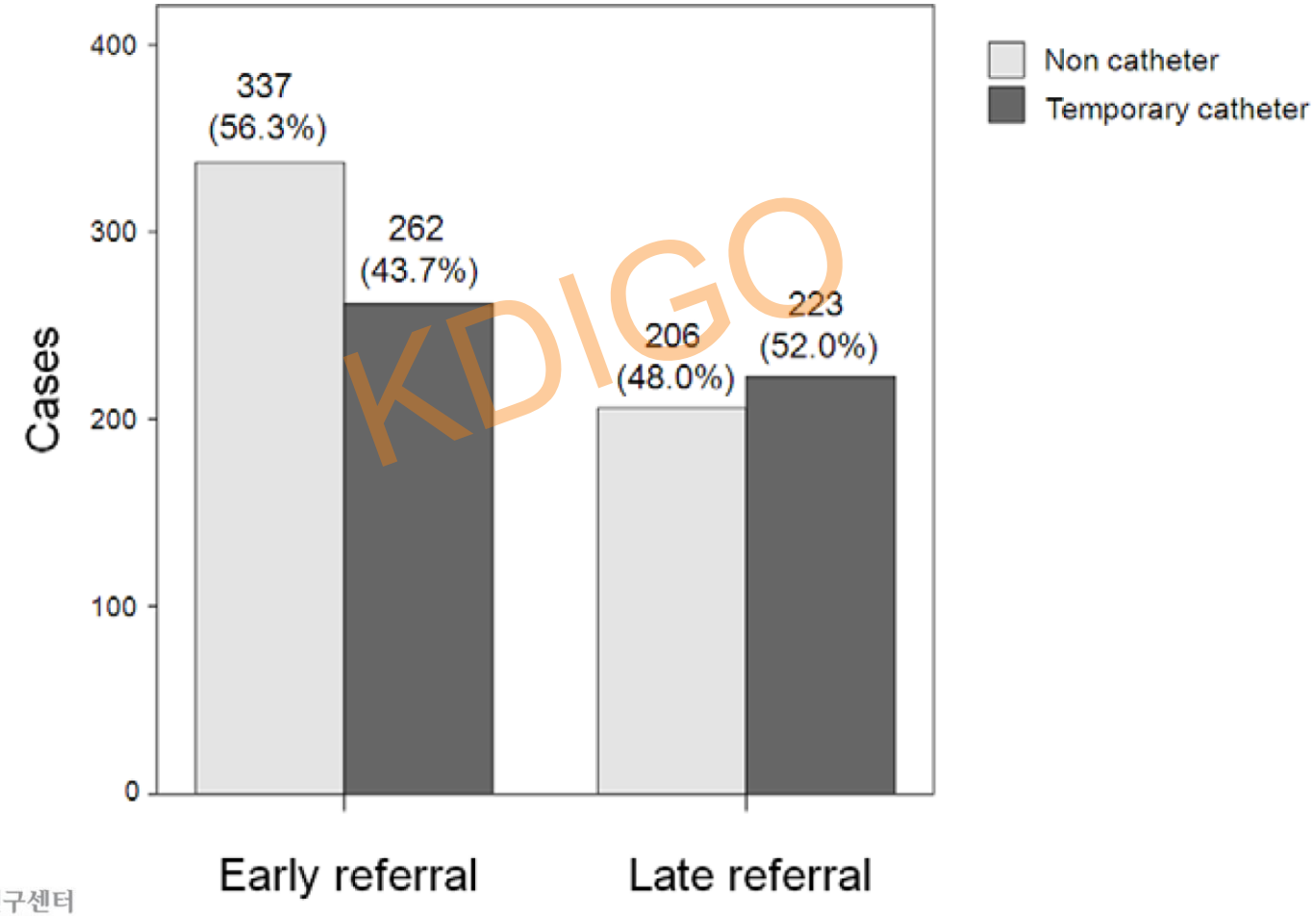
- 2008.7~2011.10 CRC-ESRD cohort
  - Incidental patients
  - 33 hospitals (N=1029)
- Definition of "Early Referral"
  - Time from Referral to Dialysis>1 year
  - Number of Visit to Nephrologist prior to initiate Dialysis ≥ 2 times, and
  - Education for Dialysis (from nurse or nephrologist) prior to initiate dialysis



Kim DH, Lee JP et al., PLoS One 2012

Timely referral to a nephrologist reduces dialysis initiation via temporary catheter



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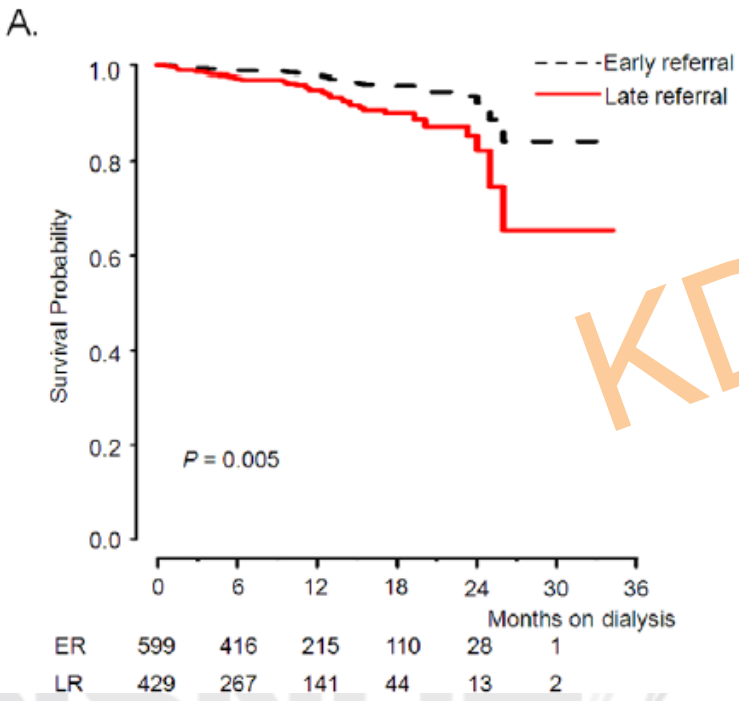
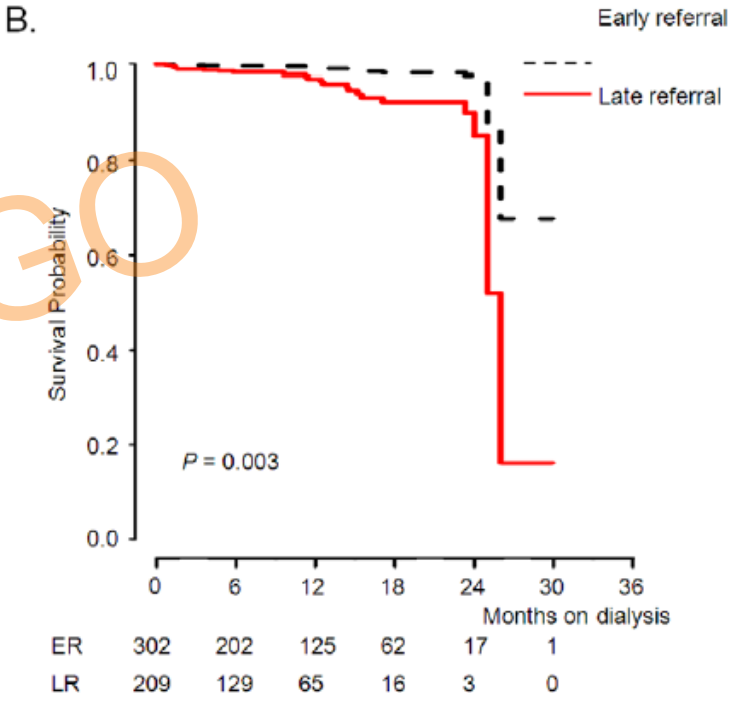
Kim DH, Lee JP et al., PLoS One 2012

Timely referral to a nephrologist at least 1 year before dialysis initiation reduces mortality.

Total patients



DM ESRD patients



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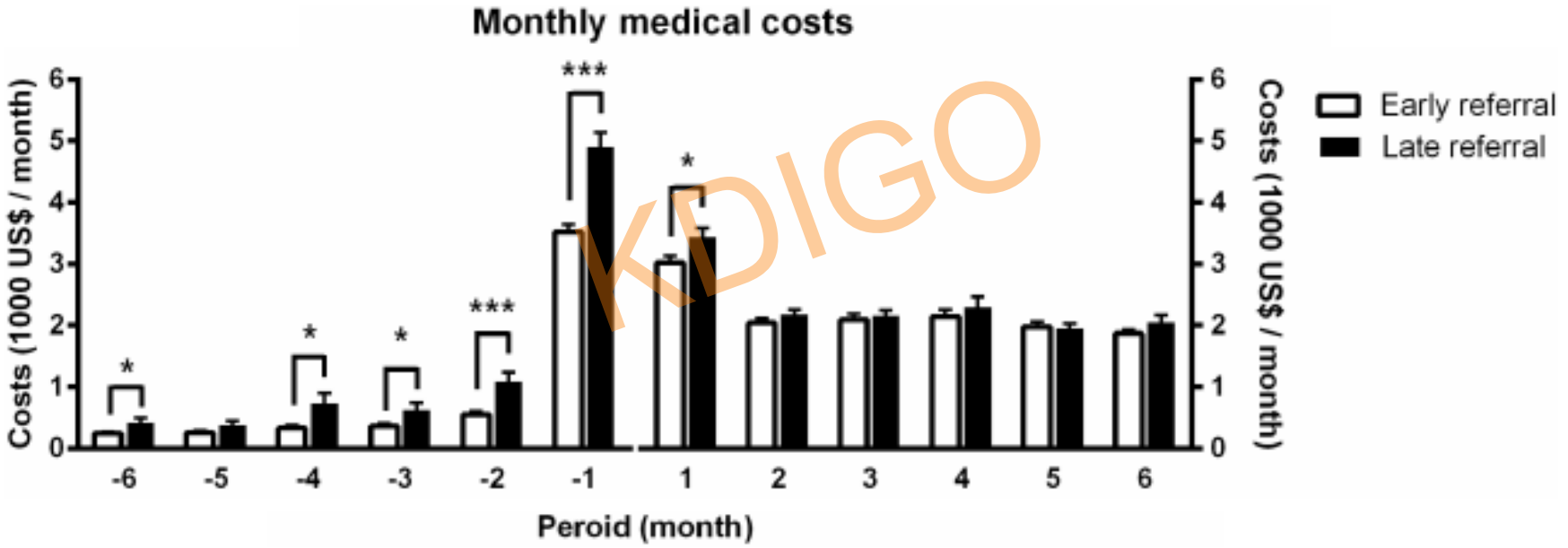
adjusted for age, gender, modified CCI, BMI, eGFR, serum hemoglobin, calcium, iPTH, uric acid, triglycerides, total cholesterol, and HDL cholesterol.

Kim DH, Lee JP et al., PLoS One 2012

Timely referral to a nephrologist reduces medical cost during transition period.



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Lee J, Lee JP et al., PLoS One 2014

Table 2. Medical costs during the first year before and after dialysis therapy.

	Periods	Costs (USD)		
		Early referral	Late referral	P Value
After dialysis initiation (month)	0~1	3029±2219	3438±2821	0.025
	1~2	2044±1679	2181±1515	0.223
	2~3	2091±2087	2162±1669	0.597
	3~4	2148±2317	2301±3079	0.456
	4~5	1975±1623	1953±1258	0.844
	5~6	1871±1148	2046±2086	0.215
	0~12	18947±11864	19104±11501	0.845
Before dialysis initiation (month)	−1~0	3529±2696	4896±4629	<0.001
	−2~−1	555±1297	1092±2624	<0.001
	−3~−2	367±922	635±1779	0.015
	−4~−3	333±1003	725±3092	0.032
	−5~−4	259±705	382±1180	0.108
	−6~−5	247±520	417±1352	0.042
	−6~0	4926±3811	7162±6762	<0.001
	−12~0	6206±5873	8610±7820	<0.001

Costs are expressed as the mean ± standard deviation values.

Table 3. Multivariate analysis for the medical costs during the first month after dialysis initiation.

	Univariate model		Multivariate model	
Variables	Parameter estimates	P Value	Parameter estimates	P Value
Type of referral (early referral)	−409.1±174.3	0.019	−428.5±172.3	0.013

Table 4. Multivariate analysis for medical costs during the 1 year before dialysis initiation.

	Univariate model		Multivariate model	
Variables	Parameter estimates	P Value	Parameter estimates	P Value
Type of referral (early referral)	−2404.1±447.4	<0.001	−2534.0±436.2	<0.001

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Table 2. Group comparisons of KDQOL-36 and BDI scores (early *vs.* late referral).

	Total Mean (SD)	Early referral Mean (SD)	Late referral Mean (SD)	p Value*
At 3 months after dialysis				
KDQOL-36				
PCS	40.4 (9.4)	40.3 (9.3)	40.4 (9.6)	0.810
MCS	40.5 (10.0)	40.8 (10.1)	40.0 (9.9)	0.349
Symptom/problem list	80.0 (15.8)	80.3 (15.9)	79.4 (15.6)	0.491
Effect of disease	69.6 (18.8)	69.7 (18.5)	69.5 (19.1)	0.892
Burden of disease	33.7 (22.6)	33.8 (22.6)	33.6 (22.6)	0.916
BDI	15.4 (10.6)	15.5 (11.0)	15.2 (10.0)	0.714
At 1 year after dialysis				
KDQOL-36				
PCS	42.3 (9.3)	42.2 (9.1)	42.5 (9.7)	0.799
MCS	41.5 (9.0)	41.9 (8.8)	40.8 (9.4)	0.316
Symptom/problem list	82.3 (13.9)	82.0 (13.6)	83.0 (14.5)	0.548
Effect of disease	72.6 (17.9)	72.0 (17.3)	73.7 (18.9)	0.438
Burden of disease	35.3 (24.0)	36.1 (23.8)	33.8 (24.4)	0.424
BDI	14.6 (10.0)	14.2 (9.8)	15.3 (10.5)	0.358

Table 3. Group comparisons of KDQOL-36 and BDI scores (planned *vs.* unplanned dialysis patients).

	Total Mean (SD)	Planned Mean (SD)	Unplanned Mean (SD)	p Value*	p Value†
At 3 months after dialysis					
KDQOL-36					
PCS	40.4 (9.4)	41.2 (9.5)	39.5 (9.3)	0.027	0.103
MCS	40.5 (10.0)	41.2 (9.9)	39.7 (10.1)	0.060	0.014
Symptom/problem list	80.0 (15.8)	81.6 (15.0)	78.1 (16.4)	0.006	0.006
Effect of disease	69.6 (18.8)	71.5 (17.3)	67.4 (20.1)	0.005	0.032
Burden of disease	33.7 (22.6)	35.8 (22.6)	31.3 (22.3)	0.012	0.273
BDI	15.4 (10.6)	15.0 (10.1)	15.8 (11.2)	0.317	0.047
At 1 year after dialysis					
KDQOL-36					
PCS	42.3 (9.3)	43.2 (9.3)	41.0 (9.2)	0.058	0.004
MCS	41.5 (9.0)	42.1 (9.0)	40.5 (8.9)	0.142	0.157
Symptom/problem list	82.3 (13.9)	84.2 (12.8)	79.8 (15.2)	0.016	0.008
Effect of disease	72.6 (17.9)	74.2 (16.8)	70.11 (19.3)	0.065	0.384
Burden of disease	35.3 (24.0)	37.1 (23.6)	32.5 (24.4)	0.115	0.535
BDI	14.6 (10.1)	13.4 (9.4)	16.3 (10.8)	0.015	0.038

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Park JI, Lee JP et al., PLoS One 2015

Challenges of transition from NDD to ESRD

- Higher mortality
- Higher costs
- Best timing?
- Transition of elderly to ESRD
- Transition across race/ethnicity
- Residual renal function
- Best format? Incremental vs. abrupt

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Residual kidney function

- Benefits of RKF
  - ↑clearance of middle molecule & uremic toxin
  - Maintenance of liquid balance
  - Improve BP control & LVH↓
  - Endocrine: Ca, P, VitD
  - Malnutrition↓ & inflammation↓
  - Survival↑ & QoL↑

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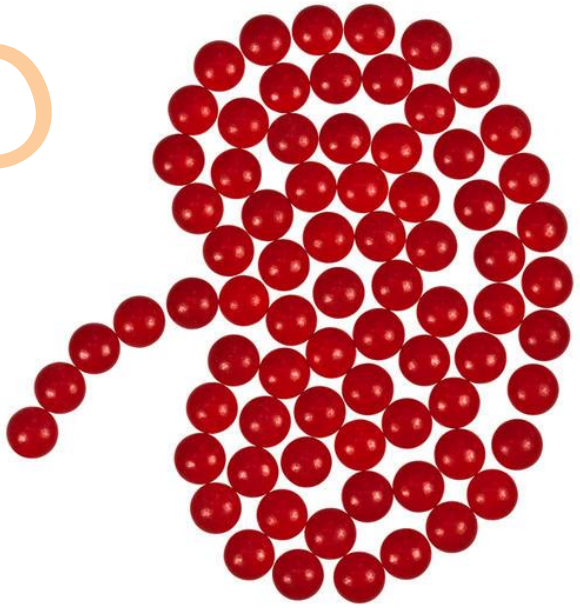

- Therapeutic options
  - Avoidance of nephrotoxic drug
  - RAAS blockade
  - BP control?
  - Avoidance of hypovolemia
  - Peritonitis in PD↓

Residual kidney function

- Progressive loss of RKF is associated with increased mortality
- Higher RKF in HD patients
  - Better HRQoL
  - Decrease in proinflammatory mediators
  - Better survival

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- Loss of RKF : faster in HD than PD
  - HD may cause episodic ischemic damage to kidneys
  - Intense HD may remove stimulus for hyperfunctioning of remaining nephrons ("intact nephron hypothesis" of Bricker et al.)
  - Incremental dialysis used successfully in the initiation of PD.

→ **Incremental HD?**

AJKD
Perspective

Twice-Weekly and Incremental Hemodialysis Treatment for Initiation of Kidney Replacement Therapy

Kamyar Kalantar-Zadeh, MD, MPH, PhD,[1,2] Mark Unruh, MD,[3] Philip G. Zager, MD,[3] Csaba P. Kovesdy, MD,[4] Joanne M. Bargman, MD,[5] Jing Chen, MD,[6] Suresh Sankarasubbaiyan, MD,[7] Gaurang Shah, MD,[2] Thomas Golper, MD,[8] Richard A. Sherman, MD,[9] and David S. Goldfarb, MD[10]

Kalantar-Zadeh K et al., Am J Kidney Dis. 2014 Aug;64(2):181-6.

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Seminars in Dialysis

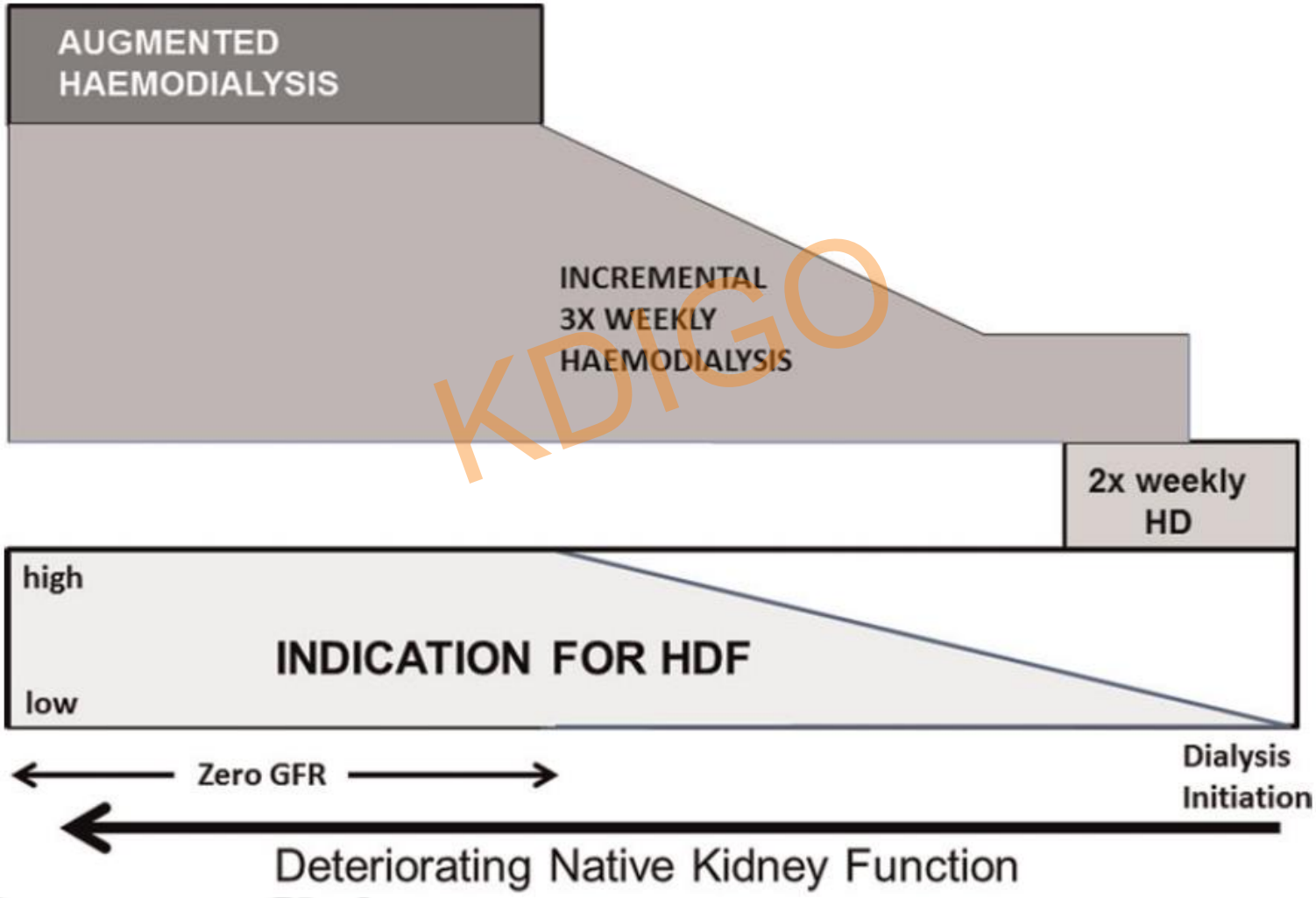
TRANSITION TO DIALYSIS: CONTROVERSIES IN ITS TIMING AND MODALITY

Infrequent Dialysis: A New Paradigm for Hemodialysis Initiation

Connie M. Rhee,* Mark Unruh,† Jing Chen,‡ Csaba P. Kovesdy,§¶ Phillip Zager,†** and Kamyar Kalantar-Zadeh*

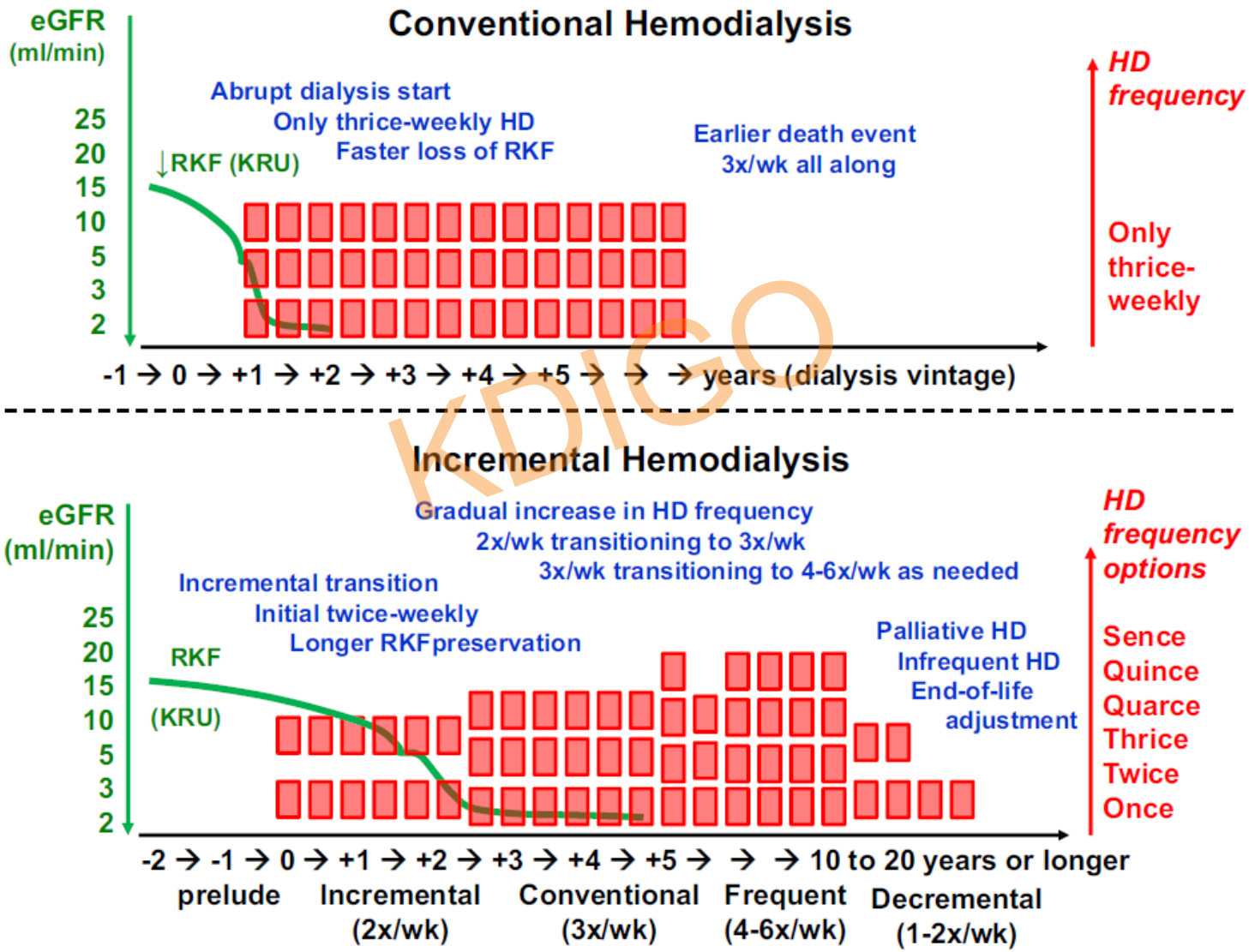
Rhee CM et al., Semin Dial. 2013 Nov-Dec;26(6):720-7

Incremental Dialysis



Wong J et al., Nephrol Dial Transplant. 2015 Oct;30(10):1639-48.

TWICE-WEEKLY HEMODIALYSIS



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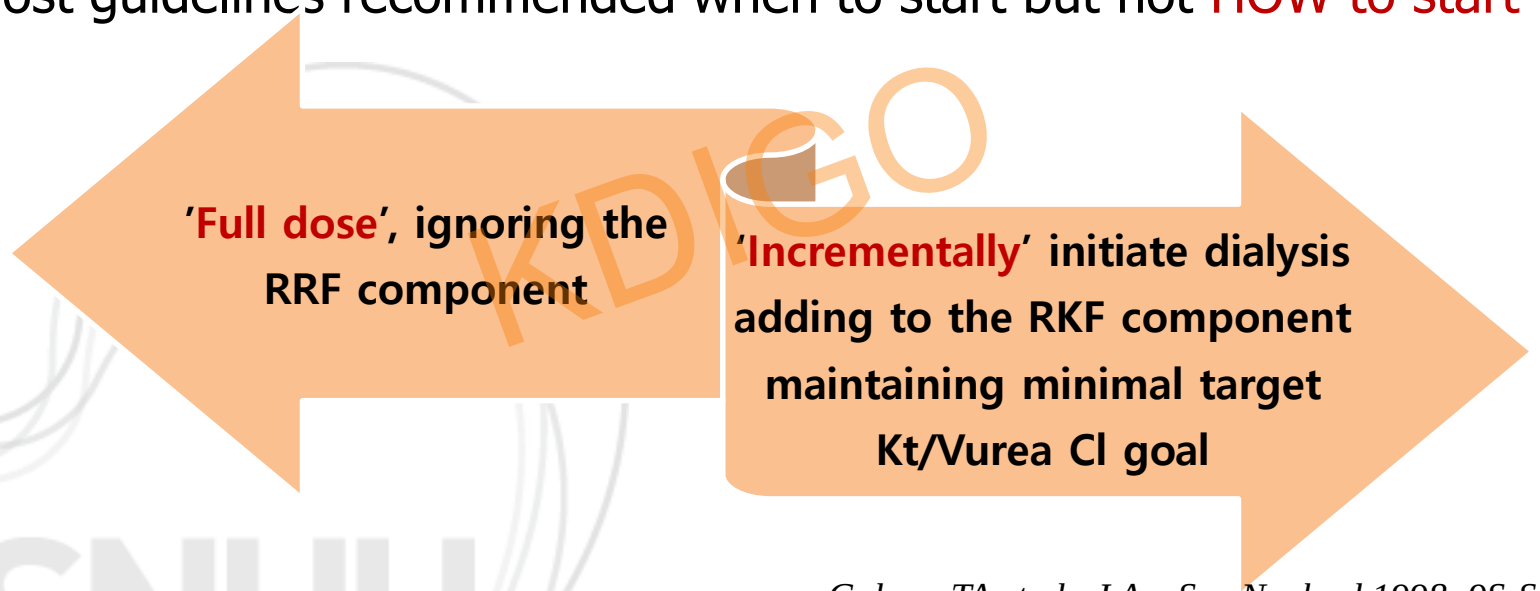
Semin Nephrol. 2018 Jul;38(4):325

Best format? Incremental vs. abrupt

- Dialysis Frequency
  : daily vs. thrice-weekly vs. infrequent eg., 2x/week
- Most guidelines recommended when to start but not HOW to start



Golper TA et al., J Am Soc Nephrol 1998; 9S:S107-S111

- Potentially benefitial for preserving RKF, protecting vascular access
- May improve HRQOL, nutritional status, patient survival
- Reduce costs

MANY patients want Infrequent Hemodialysis

Patients want infrequent HD

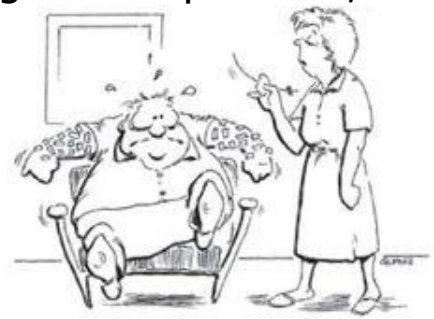
- Inconvenience of travelling 3 times a week
- Skepticism about their need for more frequent dialysis (or dialysis at all)
- Involvement with infirm family members and children requiring time & attention
- Postdialysis fatigue

Elderly or debilitated with cancer and other comorbidities

- HRQoL or life expectancy unlikely to benefit from more frequent dialysis
- End-of life concerns and palliative considerations, including less frequent HD, are more important

Fragile or otherwise tenuous dialysis vascular accesses

- benefit from infrequent puncture and smaller needles



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Kalantar-Zadeh K et al., Am J Kidney Dis. 2014 Aug;64(2):181-6.

Best format? Incremental vs. abrupt

Common practice in Western countries to prescribe same dialysis dose and frequency when starting HD in patients with significant RKF and anuric patients

→ Why not physiologically lower dialysis doses for patients with higher RKF?

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Beliefs that:

(1) It will be difficult to make patients adhere to the inevitable increase in dialysis time and/or frequency;

(2) RKF declines rapidly and generally is not monitored, and the overlooked loss of RKF will result in inadequate HD

(3) more frequent HD than is required can only benefit patients

Kalantar-Zadeh K et al., Am J Kidney Dis. 2014 Aug;64(2):181-6.

Best format? Incremental vs. abrupt

However,

- Twice-weekly HD is commonly practiced in many regions of the world and under circumstances with financial constraints and scarce resources.
- Even in US, patients may choose twice-weekly HD for convenience and better QoL or end-of-life constellation.

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Kalantar-Zadeh K et al., Am J Kidney Dis. 2014 Aug;64(2):181-6.

Why Incremental and Twice-weekly HD

Incremental HD including twice-weekly HD on transition to kidney replacement therapy

: may lead to an important **paradigm shift** in current nephrology practice

- Alternative to the abrupt transition to the usual thrice-weekly HD treatments
  → Novel approach to timing the initiation of maintenance dialysis therapy
- May better preserve RKF and inflammation.
- May improve patient-centered outcomes, including HRQoL, satisfaction, end-of-life concerns, while significantly containing costs and resources.

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Twice-Weekly HD and Outcomes

Guidelines advocating incremental or infrequent HD on first transition to RRT

1997 KDOQI (Kidney Disease Outcomes Quality Initiative) PD Adequacy Work Group report (AJKD, 1998)

K/DOQI clinical practice guidelines for hemodialysis adequacy. Am J Kidney Dis. 1998.

European Best Practice Guidelines Expert Group on Hemodialysis

Nephrol Dial Transplant. 2002;17(suppl 7):S16-S31.

Suggested using incremental HD to maintain RKF

Best format? Incremental vs. abrupt

- Thailand, prospective cohort study
- 2 times/week (n=504) vs. 3 times/week (n=169)
- Similar survival and hospitalization

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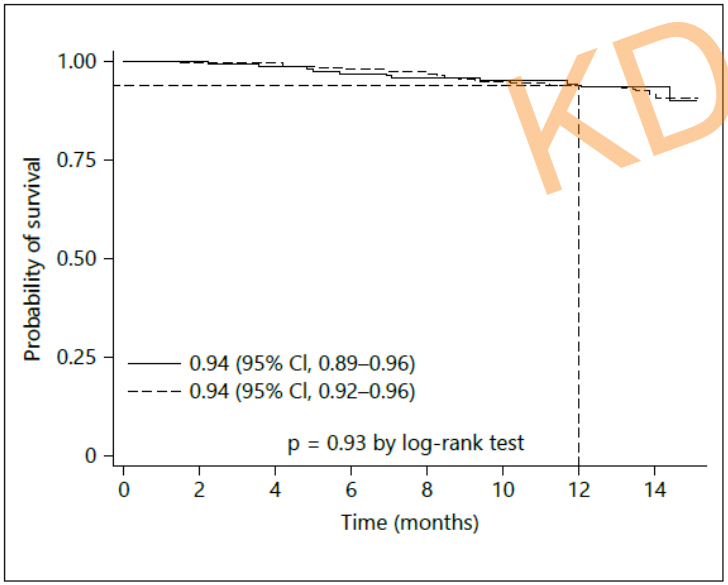

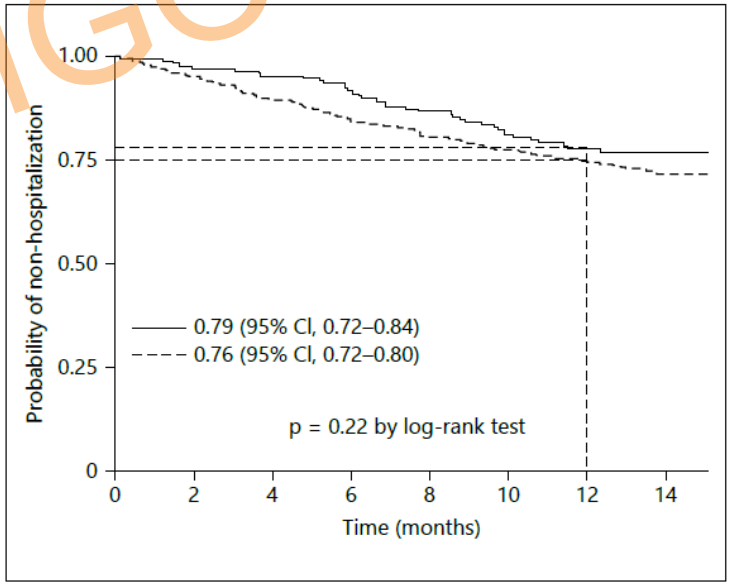

Blood Purif 2014;38:253–262

Best format? Incremental vs. abrupt

- China cohort study
- 2 times/week (n=30) vs. 3 times/week (n=55)
- 2 times/week
  : better RKF preservation

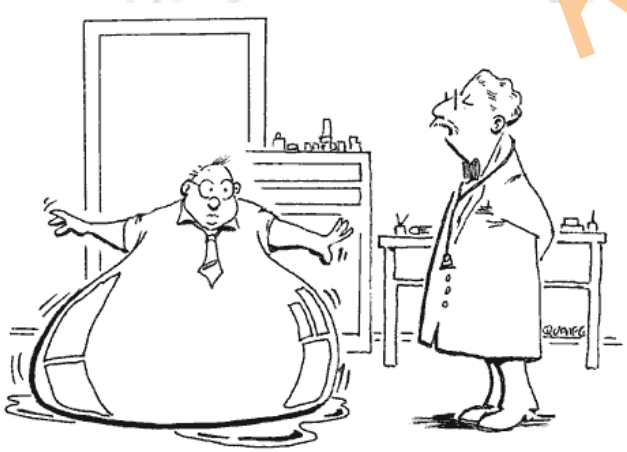

Table 3. RKF-related factors of 85 MHD patients currently in the main cohort

	Group A 2/week HD (n = 30)	Group B 3/week HD (n = 55)	p
Patients with RKF, % (n)	40 (12)	18 (10)	0.03
Residual GFR[a], ml/min/1.73 m^2	1.82±1.97	0.35±0.29	0.03
Urine output, ml/day	579.17±602.06	390.00±284.6	0.67
Patients with RKF loss[b], % (n)	60 (18)	82 (45)	0.03
≤1 years on HD	10 (3)	40 (22)	0.02
1–3 years on HD	37 (11)	25 (14)	0.28
>3 years on HD	13 (4)	16 (9)	0.96
Average time for RKF loss, month	33.8±32.3	20.7±18.5	0.05

Values indicate means ± SDs or percentage (number). RKF = Residual kidney function; URR = urea reduction ratio.

[a] Estimated as the arithmetic mean of creatinine and urea clearance in MHD patients with urine.

[b] Defined as urine volume <200 ml/day.

Am J Nephrol 2014;40:140–150

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www.lightersideofdialysis.com

Best format? Incremental vs. abrupt

- China DOPPS data
- 2 times/week (n=304) vs. 3 times/week (n=982)
- Similar quality of life scores

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Table 4. China DOPPS: Laboratory values and quality of life in patients dialyzing two times versus three times per week

	Mean (SD)		Difference (β): 2× (versus 3×)	
Outcome measures	2× per week(n = 304)	3× per week(n = 982)	Unadjusted[a] β (95% CI)	Adjusted[b] β (95% CI)
Urea reduction ratio, %	69.1 (11.4)	67.4 (10.0)	+2.02 (0.39,3.66)*	+0.29 (−1.45,2.02)
Standardized Kt/V[c]	1.45 (0.19)	2.11 (0.26)	−0.67 (−0.72, −0.62)*	−0.73 (−0.77, −0.69)*
Intradialytic weight loss, %	4.1 (2.5)	4.1 (1.8)	−0.02 (−0.28,0.25)	+0.25 (−0.03,0.52)
nPCR, g urea nitrogen/kg/day	0.68 (0.24)	0.83 (0.32)	−0.13 (−0.17, −0.09)*	−0.16 (−0.20, −0.11)*
Serum calcium$_{Alb}$, mg/dL[d]	8.7 (1.1)	9.1 (1.0)	−0.35 (−0.49, −0.21)*	−0.26 (−0.42, −0.10)*
Serum albumin, g/dL	4.0 (0.5)	3.9 (0.5)	+0.06 (−0.01,0.12)	+0.03 (−0.03,0.10)
Serum PTH, pg/mL	398 (425)	376 (408)	+20.6 (−44.2,85.4)	+65.3 (−5.3,135.9)
Serum phosphorus, mg/dL	6.3 (2.3)	6.0 (2.1)	+0.22 (−0.07,0.51)	+0.25 (−0.08,0.57)
Hemoglobin, g/dL	10.2 (2.2)	10.6 (2.0)	−0.31 (−0.57, −0.04)*	−0.23 (−0.53,0.07)
QoL: SF-12 physical component summary	36.7 (9.5)	36.1 (9.1)	+0.78 (−0.57,2.14)	−0.61 (−2.03,0.82)
QoL: SF-12 mental component summary	43.4 (9.0)	43.8 (9.5)	−0.24 (−1.61,1.14)	−1.13 (−2.72,0.45)

Nephrol Dial Transplant (2014) 29: 1770–1777

Nephrol Dial Transplant (2017) 32: 355–363
doi: 10.1093/ndt/gfw332
Advance Access publication 28 September 2016

Comparison of outcomes between the incremental and thrice-weekly initiation of hemodialysis: a propensity-matched study of a prospective cohort in Korea

Ji In Park[1,2], Jung Tak Park[2,3], Yong-Lim Kim[2,4], Shin-Wook Kang[2,3], Chul Woo Yang[2,5], Nam-Ho Kim[2,6], Yun Kyu Oh[2,7], Chun Soo Lim[2,7], Yon Su Kim[2,8] and Jung Pyo Lee[2,7] on behalf of the CRC for ESRD Investigators

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NSNUH

Park JI , Lee JP et al, Nephrol Dial Transplant 2017

Methods

- CRC-ESRD dataset
  - Nationwide, multi-center, web-based, prospective cohort
  - Patients initiated hemodialysis from Aug 2008 to Aug 2014
  - Approved by principal investigators of CRC-ESRD group

- Patient classification
  - Abrupt initiation group : 3 times per week
  - Incremental initiation group: 1-2 times per week

- Propensity score matching
  - Abrupt- and incremental initiation groups in 2:1 ratio

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Park JI , Lee JP et al, Nephrol Dial Transplant 2017

Methods

- Outcome

  Patient survival

  KDQOL-SF ver 1.3 and Beck's depression inventory (BDI)

  Data at baseline and 12mo after HD including

    Comorbidities and laboratory data

    Subjective Global Assessment (SGA)

    24hr urine output

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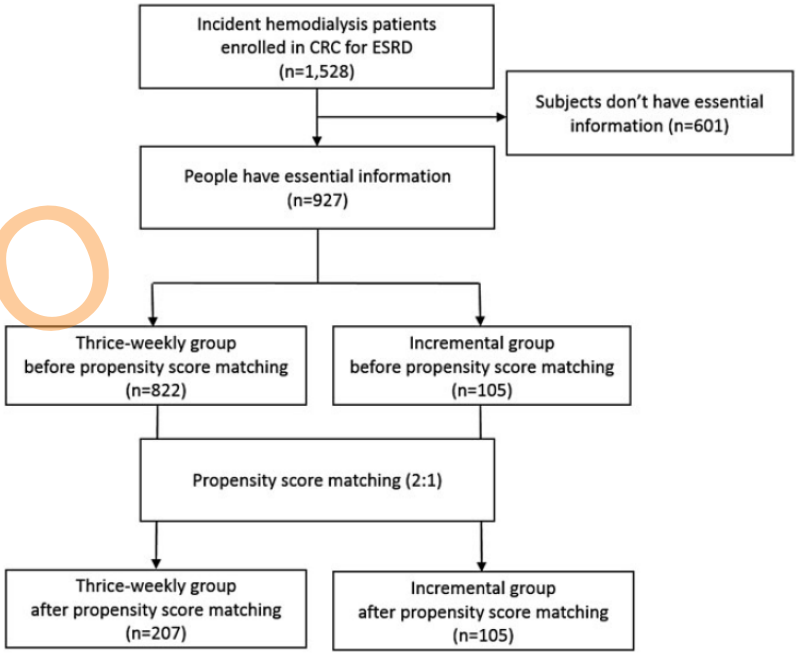
Park JI , Lee JP et al, Nephrol Dial Transplant 2017

Baseline characteristics

Table 1. Patient characteristics before and after PSM

	Before PSM			
	Thrice-weekly group ($n = 822$)	Incremental group ($n = 105$)	P-value	Standardized difference
Age (years)	57.3 ± 14.4	60.2 ± 13.3	0.051	0.217
Sex (male)	512 (62.3)	61 (58.1)	0.405	0.085
Primary renal disease			<0.001	0.397
Diabetes	497 (60.5)	45 (42.8)		
Hypertension	110 (13.4)	13 (12.4)		
Glomerulonephritis	121 (14.7)	19 (18.1)		
Other	83 (10.1)	27 (25.7)		
Unknown	11 (1.3)	1 (1.0)		
Systolic BP (mmHg)	144.7 ± 23.7	140.4 ± 19.3	0.044	
Diastolic BP (mmHg)	78.15 ± 14.2	75.5 ± 13.5	0.075	
BMI (kg/m^2)	23.2 ± 3.6	22.8 ± 3.1	0.228	
mCCI	5.4 ± 2.4	5.6 ± 2.2	0.449	
SGA			0.067	
A	494 (63.9)	74 (75.5)		
B	275 (35.6)	24 (24.5)		
C	4 (0.5)	0 (0.0)		
Hemoglobin (g/dL)	8.7 ± 1.6	8.7 ± 1.5	0.705	
Phosphorus (mg/dL)	5.6 ± 2.0	5.0 ± 1.9	0.003	
Uric acid (mg/dL)	8.2 ± 2.6	7.6 ± 2.6	0.036	
Albumin (g/dL)	3.3 ± 0.6	3.5 ± 0.6	0.002	0.322
BUN (mg/dL)	83.6 ± 38.9	69.4 ± 32.3	<0.001	−0.440
Creatinine (mg/dL)	8.7 ± 4.4	8.1 ± 5.8	0.148	
eGFR (mL/min/1.73 m^2)	7.3 ± 6.5	7.5 ± 3.4	0.691	
Cholesterol (mg/dL)	156.5 ± 49.1	156.5 ± 49.1	0.215	
24-h urine volume			0.004	0.329
<500 mL	330 (40.1)	27 (25.7)		
≥500 mL	492 (59.9)	78 (74.3)		
Single-pool Kt/V	1.3 ± 0.4	1.4 ± 0.3	0.386	
Weekly Kt/V	4.0 ± 1.1	2.7 ± 0.6	<0.001	
Urea reduction rate (%)	66.1 ± 9.7	68.3 ± 8.0	0.116	
UF/session (kg)	1.4 ± 1.2	4.2 ± 3.5	0.022	
Weekly UF (kg)	4.2 ± 3.5	1.8 ± 1.8	<0.001	
Weekly fluid ingestion (L)	5.6 ± 5.2	6.5 ± 4.5	0.092	

The data are presented as mean ± SD or as a n (%).
PSM, propensity score matching; BP, blood pressure; BMI, body mass index; mCCI, modified Charlson co
tration rate.



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Baseline characteristics

Table 1. Patient characteristics before and after PSM

	Before PSM				After PSM			
	Thrice-weekly group ($n = 822$)	Incremental group ($n = 105$)	P-value	Standardized difference	Thrice-weekly group ($n = 207$)	Incremental group ($n = 105$)	P-value	Standardized difference
Age (years)	57.3 ± 14.4	60.2 ± 13.3	0.051	0.217	61.7 ± 13.4	60.2 ± 13.3	0.350	−0.124
Sex (male)	512 (62.3)	61 (58.1)	0.405	0.085	124 (59.9)	61 (58.1)	0.759	0.029
Primary renal disease			<0.001	0.397			0.293	0.052
Diabetes	497 (60.5)	45 (42.8)			90 (43.5)	45 (42.9)		
Hypertension	110 (13.4)	13 (12.4)			35 (16.9)	13(12.4)		
Glomerulonephritis	121 (14.7)	19 (18.1)			39 (18.8)	19 (18.1)		
Other	83 (10.1)	27 (25.7)			36 (17.4)	27 (25.7)		
Unknown	11 (1.3)	1 (1.0)			7 (3.4)	1 (1.0)		
Systolic BP (mmHg)	144.7 ± 23.7	140.4 ± 19.3	0.044		145.0 ± 24.1	140.4 ± 19.3	0.080	
Diastolic BP (mmHg)	78.15 ± 14.2	75.5 ± 13.5	0.075		77.8 ± 13.4	75.5 ± 13.5	0.165	
BMI (kg/m^2)	23.2 ± 3.6	22.8 ± 3.1	0.228		23.3 ± 3.4	22.8 ± 3.1	0.184	
mCCI	5.4 ± 2.4	5.6 ± 2.2	0.449		5.5 ± 2.3	5.6 ± 2.2	0.793	
SGA			0.067				0.069	
A	494 (63.9)	74 (75.5)			121 (62.4)	74 (75.5)		
B	275 (35.6)	24 (24.5)			72 (37.1)	24 (24.5)		
C	4 (0.5)	0 (0.0)			1 (0.5)	0 (0.0)		
Hemoglobin (g/dL)	8.7 ± 1.6	8.7 ± 1.5	0.705		9.0 ± 1.6	8.7 ± 1.5	0.214	
Phosphorus (mg/dL)	5.6 ± 2.0	5.0 ± 1.9	0.003		5.1 ± 1.6	5.0 ± 1.9	0.705	
Uric acid (mg/dL)	8.2 ± 2.6	7.6 ± 2.6	0.036		7.9 ± 2.7	7.6 ± 2.6	0.399	
Albumin (g/dL)	3.3 ± 0.6	3.5 ± 0.6	0.002	0.322	3.5 ± 0.6	3.5 ± 0.6	0.986	0.006
BUN (mg/dL)	83.6 ± 38.9	69.4 ± 32.3	<0.001	−0.440	72.4 ± 33.4	69.4 ± 32.3	0.438	−0.093
Creatinine (mg/dL)	8.7 ± 4.4	8.1 ± 5.8	0.148		7.5 ± 2.8	8.1 ± 5.8	0.376	
eGFR (mL/min/1.73 m^2)	7.3 ± 6.5	7.5 ± 3.4	0.691		8.2 ± 9.1	7.5 ± 3.4	0.465	
Cholesterol (mg/dL)	156.5 ± 49.1	156.5 ± 49.1	0.215		158.5 ± 47.6	156.5 ± 49.1	0.151	
24-h urine volume			0.004	0.329			0.622	−0.065
<500 mL	330 (40.1)	27 (25.7)			48 (23.2)	27 (25.7)		
≥500 mL	492 (59.9)	78 (74.3)			159 (76.8)	78 (74.3)		
Single-pool Kt/V	1.3 ± 0.4	1.4 ± 0.3	0.386		1.4 ± 0.3	1.4 ± 0.3	0.683	
Weekly Kt/V	4.0 ± 1.1	2.7 ± 0.6	<0.001		4.0 ± 1.0	2.7 ± 0.6	<0.001	
Urea reduction rate (%)	66.1 ± 9.7	68.3 ± 8.0	0.116		67.5 ± 10.1	68.3 ± 8.0	0.652	
UF/session (kg)	1.4 ± 1.2	4.2 ± 3.5	0.022		1.2 ± 1.0	1.1 ± 1.0	0.501	
Weekly UF (kg)	4.2 ± 3.5	1.8 ± 1.8	<0.001		3.6 ± 3.0	1.8 ± 1.8	<0.001	
Weekly fluid ingestion (L)	5.6 ± 5.2	6.5 ± 4.5	0.092		6.8 ± 4.4	6.5 ± 4.5	0.601	

The data are presented as mean ± SD or as a n (%).

PSM, propensity score matching; BP, blood pressure; BMI, body mass index; mCCI, modified Charlson comorbidity index; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate.

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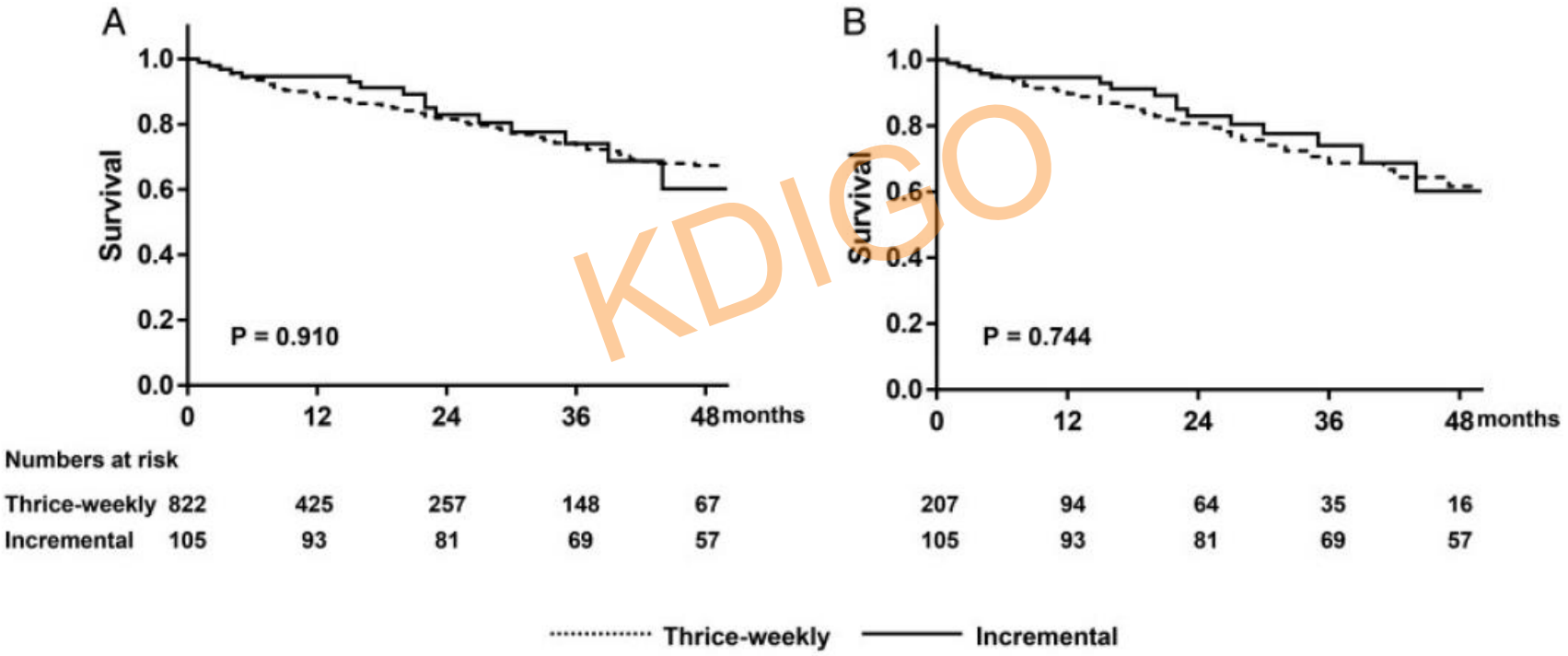
Patient survival

Before matching

After matching



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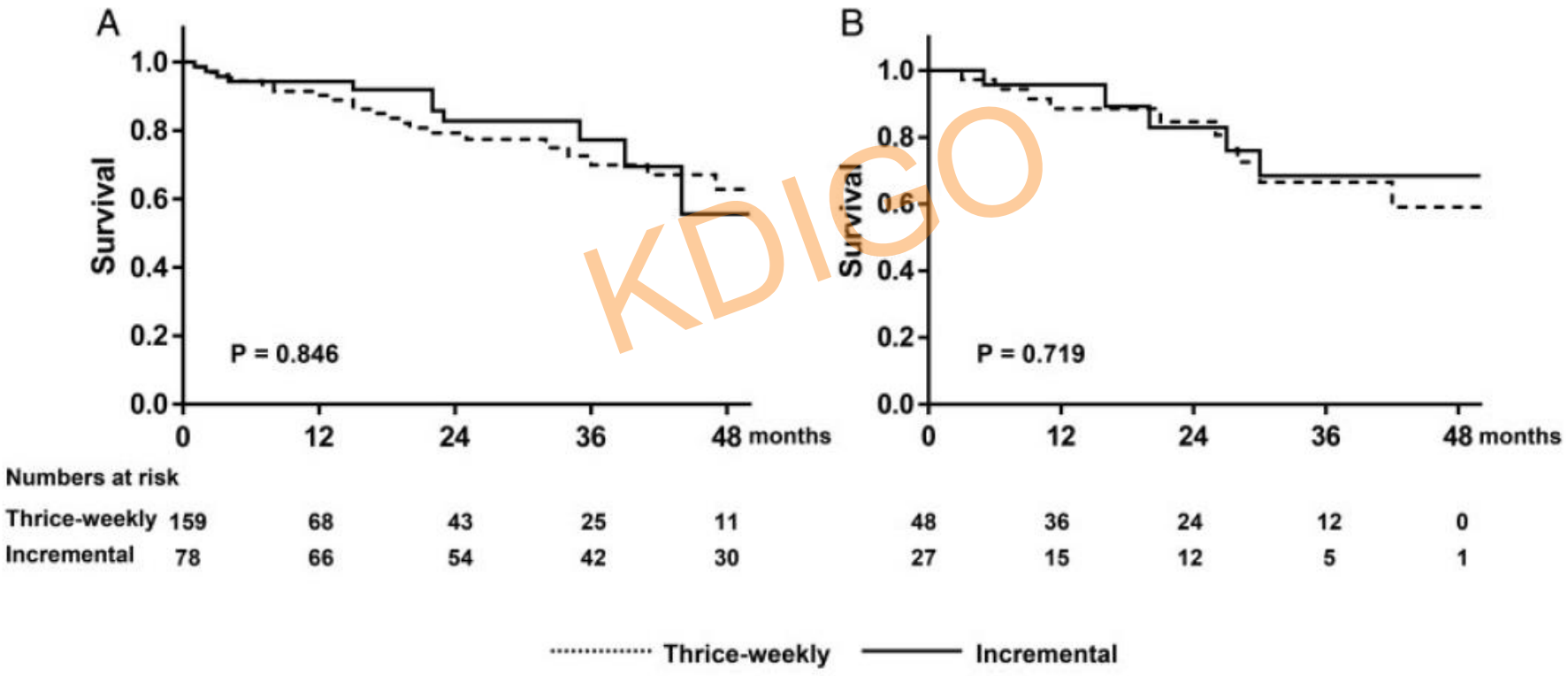
Patient survival

Urine volume≥500mL/day

Urine volume<500mL/day



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HRQOL and BDI at 12month

Table 3. HRQOL and BDI scores at 12 months after dialysis

Variables	Before PSM			After PSM		
	Thrice-weekly group ($n = 221$)	Incremental group ($n = 31$)	P-value	Thrice-weekly group ($n = 51$)	Incremental group ($n = 31$)	P-value
HRQOL measure						
SF-36						
PCS	42.4 ± 9.1	43.4 ± 10.2	0.577	41.9 ± 9.4	43.4 ± 10.2	0.481
MCS	40.9 ± 8.9	42.5 ± 9.9	0.365	40.6 ± 8.6	42.5 ± 9.9	0.364
Physical functioning	67.7 ± 25.0	69.4 ± 24.9	0.735	63.9 ± 27.6	69.4 ± 24.9	0.374
Role-physical	60.9 ± 35.2	65.3 ± 38.0	0.516	63.0 ± 32.9	65.3 ± 38.0	0.770
Bodily pain	68.3 ± 22.5	72.7 ± 23.4	0.312	68.2 ± 23.9	72.7 ± 23.4	0.406
General health	46.2 ± 21.6	47.4 ± 21.9	0.771	49.1 ± 22.5	47.4 ± 21.9	0.739
Mental health	50.8 ± 17.4	53.8 ± 20.0	0.375	49.6 ± 16.9	53.8 ± 20.0	0.316
Role-emotional	59.4 ± 42.6	68.8 ± 41.2	0.250	56.9 ± 45.8	68.8 ± 41.2	0.227
Social functioning	59.7 ± 32.4	66.5 ± 32.3	0.281	56.9 ± 33.4	66.5 ± 32.3	0.206
Vitality	51.0 ± 15.9	56.6 ± 20.1	0.145	49.8 ± 16.5	56.6 ± 20.1	0.098
Kidney disease targeted						
Symptoms/problems	80.5 ± 16.5	81.5 ± 14.3	0.745	81.0 ± 17.0	81.5 ± 14.3	0.875
Effects of kidney disease	68.1 ± 18.5	69.7 ± 20.5	0.652	70.0 ± 16.9	69.7 ± 20.5	0.946
Burden of kidney disease	30.5 ± 22.1	33.8 ± 25.0	0.438	30.8 ± 20.8	33.8 ± 25.0	0.554
Work status	40.0 ± 24.2	45.7 ± 26.9	0.231	39.5 ± 24.9	45.7 ± 26.9	0.296
Cognitive functioning	65.2 ± 17.9	72.3 ± 19.9	0.043	65.6 ± 18.4	72.3 ± 19.9	0.129
Quality of social interaction	65.2 ± 20.6	69.7 ± 22.9	0.263	67.6 ± 20.2	69.7 ± 22.9	0.676
Sexual function	68.1 ± 32.1	75.0 ± 22.4	0.611	65.0 ± 28.0	75.0 ± 22.4	0.447
Sleep	62.0 ± 23.3	63.7 ± 21.4	0.697	59.9 ± 20.4	63.7 ± 21.4	0.424
Social support	68.8 ± 19.8	74.3 ± 20.7	0.149	71.3 ± 18.4	74.3 ± 20.7	0.497
Dialysis staff encouragement	75.1 ± 18.7	77.8 ± 14.8	0.437	74.5 ± 17.8	77.8 ± 14.8	0.388
Overall health	34.4 ± 47.6	38.7 ± 49.5	0.638	39.2 ± 49.3	38.7 ± 49.5	0.964
Patient satisfaction	54.1 ± 19.4	60.6 ± 20.0	0.082	55.9 ± 18.0	60.6 ± 20.0	0.269
BDI	16.6 ± 10.7	15.1 ± 10.1	0.478	17.0 ± 11.2	15.1 ± 10.1	0.449

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Other clinical outcomes at 12 months

Table 4. Clinical outcomes at 12 months after dialysis before and after PSM

Variables	Before PSM			After PSM		
	Thrice-weekly group ($n = 436$)	Incremental group ($n = 57$)	P-value	Thrice-weekly group ($n = 108$)	Incremental group ($n = 57$)	P-value
Hemoglobin (g/dL)	10.7 ± 1.3	10.9 ± 1.1	0.291	10.9 ± 1.3	10.9 ± 1.1	0.936
Phosphorus (mg/dL)	4.6 ± 1.4	4.7 ± 1.5	0.622	4.5 ± 1.2	4.7 ± 1.5	0.312
Uric acid (mg/dL)	6.8 ± 1.8	7.5 ± 2.2	0.011	6.6 ± 1.7	7.5 ± 2.2	0.013
Albumin (g/dL)	3.9 ± 0.5	4.0 ± 0.4	0.520	3.9 ± 0.5	4.0 ± 0.4	0.471
BUN (mg/dL)	56.5 ± 19.0	65.2 ± 23.5	0.002	52.5 ± 17.7	65.2 ± 23.5	0.001
Creatinine (mg/dL)	8.8 ± 3.3	9.8 ± 4.0	0.056	8.3 ± 2.7	9.8 ± 4.0	0.017
Cholesterol (mg/dL)	151.3 ± 39.4	150.1 ± 36.7	0.822	153.0 ± 39.1	150.1 ± 36.7	0.653
24-h urine volume	409.4 ± 498.7	531.1 ± 522.1	0.167	416.4 ± 412.7	531.1 ± 522.1	0.228
24-h urine volume			0.107			0.416
<500 mL	144 (33.0)	22 (38.6)		33 (30.6)	22 (38.6)	
≥500 mL	85 (19.5)	16 (28.1)		28 (25.9)	16 (28.1)	
Unknown	207 (47.5)	19 (33.3)		47 (43.5)	19 (33.3)	
SGA			0.134			0.717
A	311 (87.6)	41 (95.3)		78 (91.8)	41 (95.3)	
B	44 (12.4)	2 (4.7)		7 (8.2)	2 (4.7)	
C	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	

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Park JI , Lee JP et al, Nephrol Dial Transplant 2017

Summary

Incremental hemodialysis in Korea

- Approximately 11.3%
- Old patients having more severe cormobidities
- Relatively lower BUN/Cr, lesser 'E imbalance

Outcomes: Abrupt vs. Incremental

- HRQOL, BDI at 3mo, 12mo
- Patient survival
- Nutritional parameters at 12mo
- 24hr urine output (limited data)

All comparable

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Transition to thrice-weekly HD

→ when urine output declines

→ interdialytic weight gain increases over time

→ hypertension becomes more difficult to control

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- However, many patients may continue twice-weekly HD for extended periods and with acceptable outcomes.
- Potential issue
  - Increased mortality on Mondays and Tuesdays → May reflect higher interdialytic weight gains and fluid gains & hyperK
- With twice-weekly HD regimen, patients would be subjected to 3- and 4-day intervals

  → Propose threshold of 2.5 L of fluid gain, potassium eligibility cutoffs

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Proposed Criteria for Twice-Weekly HD

1. Good RRF with urine output > 0.5 L/d
2. Limited fluid retention b/w 2 consecutive HD treatments with fluid gain < 2.5 kg (or <5% of ideal dry weight) without HD for 3-4 d
3. Limited or readily manageable cardiovascular or pulmonary symptoms without clinically significant fluid overload
4. Suitable body size relative to RKF; patients with larger body size may be suitable for 2x/wk HD if not hypercatabolic
5. HyperK (K>5.5 mEq/L) is infrequent or readily manageable
6. HyperP (P>5.5 mg/dL) is infrequent or readily manageable
7. Good nutritional status without florid hypercatabolic state
8. Lack of profound anemia (Hb > 8 g/dL) and appropriate responsiveness to anemia therapy
9. Infrequent hospitalization and easily manageable comorbid conditions
10. Satisfactory health-related quality of life

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Kalantar-Zadeh K et al., Am J Kidney Dis. 2014 Aug;64(2):181-6.

Implementation Strategies

1. In order to initiate and maintain 2X/wk HD, the patient should meet the first criterion (urine output >0.5 L/d) plus most (5 of 9) of the other criteria

2. Examine these criteria every month in all 2X/wk HD patients & compare outcome between 2X/wk and 3X/wk HD to ensure outcome non-inferiority for continuation of 2X/wk HD

3. Consider transition from 2X/wk to 3X/wk HD regimen if patient's urine output decreases (<0.5 L/d) or patient's nutritional status or general health condition shows a deteriorating trend over time

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Kalantar-Zadeh K et al., Am J Kidney Dis. 2014 Aug;64(2):181-6.

Table 1: Types of incremental dialysis protocols.

Note that in all protocols, residual kidney function needs to be monitored judiciously

Type of Incremental Dialysis Protocol	Assumption	Suitability
Hemodialysis (HD)		
Type A: Less frequent HD (less than thrice-weekly)*	Maintaining at least 3 to 4 hours of HD treatment time per session	May be more suitable for in-center HD patients
pe B: Shorter HD treatment e (less than 3 hours)	Maintaining at least thrice-weekly HD frequency	Suitable for both in-center and home HD
e C: Any combination of the above protocols	n/a	Suitable for home and in-center HD.
Peritoneal Dialysis (PD)		
Type D: Shorter total PD dwell time or fluid volume per day	Maintaining daily (7 days a week) PD	Home dialysis
Type E: Less than 7 days a week of PD therapy*	Maintaining standard dwell time and volume	Home dialysis
Type F: Any combination of the above PD protocols	n/a	Home dialysis
Type G: Any combination of PD with sporadic HD sessions	n/a	Combination of home and in-center dialysis

Gedney & Kalantar-Zadeh. *Seminars in Nephrology* July 2018

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Incremental (twice-weekly) HD may be a superior way to transition from CKD to ESRD to preserve RKF longer, to achieve better quality of life and to save costs and resources.

-Kalantar-Zadeh K., 2018, KSN-

Incremental initiation of hemodialysis: a cohort in Korea

Jung Pyo Lee, MD, PhD

Associate Professor
Seoul National University College of Medicine
SNU-SMG Boramae Medical Center

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	Individualized **Incremental Hemodialysis** Study • 122 participants • January 1, 2018 • December 2020 • Survival (24 mo)	• **Hemodialysis** Complication • ESRD • Renal Failure	• Procedure: Individualized Incremental hemodialysis • Procedure: Conventional thrice weekly hemodialysis	• Mansoura University Mansourah, Alexandria, Egypt • kidney and Urology Center Alexandria, Egypt
2	☐	Recruiting	**Incremental Haemodialysis** in Incident Patients • 152 participants • March 14, 2018 • July 2021 • Survival (24 mo)	• Renal Disease, End-Stage	• Procedure: Incremental haemodialysis • Procedure: Conventional haemodialysis	• FundeSalud. Junta de Extremadura Mérida, Badajoz, Spain • Hospital Virgen del Puerto Plasencia, Cáceres, Spain • Hospital San Pedro de Alcántara Cáceres, Spain
3	☐	Recruiting	**Incremental Hemodialysis** as a Starting Way of Renal Replacement Therapy • 7 participants • April 4, 2017 • December 30, 2020 • RRF (12mo)	• Chronic Renal Failure	• Procedure: Incremental hemodialysis • Procedure: Conventional hemodialysis	• Hospital Ramón y Cajal Madrid, Spain
4	☐	Recruiting	Does **Incremental** Initiation of **Haemodialysis** Preserve Native Kidney Function? • 50 participants • January 8, 2018 • March 2, 2019 • RRF (12 mo)	• Kidney Failure • Dialysis	• Procedure: Standard Haemodialysis • Procedure: Incremental dialysis	• East and North Hertfordshire NHS Trust (incorporating Mount Vernon Cancer Centre) Stevenage, United Kingdom

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Deira *et al. BMC Nephrology* (2019) 20:8
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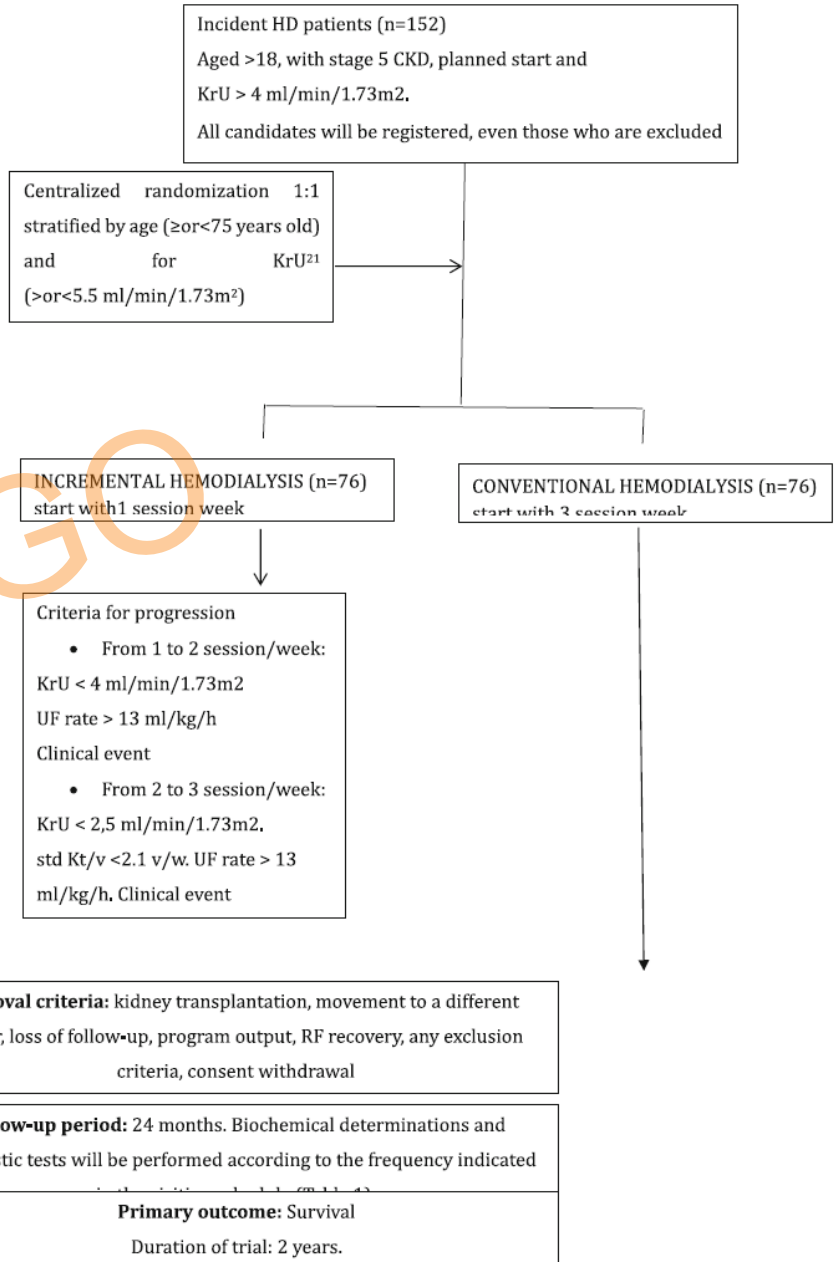
BMC Nephrology

STUDY PROTOCOL Open Access

IHDIP: a controlled randomized trial to assess the security and effectiveness of the incremental hemodialysis in incident patients

Javier Deira[1*], Miguel A. Suárez[2], Francisca López[3], Emilio García-Cabrera[4], Antonio Gascón[5], Eduardo Torregrosa[6], Giannina E. García[7], Jorge Huertas[8], Jose C. de la Flor[9], Suleya Puello[10], Jonathan Gómez-Raja[11], Jesús Grande[12], José L. Lerma[13], Carlos Corradino[14], Carlos Musso[14], Manuel Ramos[15], Jesús Martín[16], Carlo Basile[17] and Francesco G. Casino[17,18]



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ClinicalTrials.gov Identifier: NCT03239808

Recruitment Status : Recruiting
First Posted : August 4, 2017
Last Update Posted : April 13, 2018

Incremental Haemodialysis in Incident Patients (IHDIP)

Study Design

Go to

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	152 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Intervention Model Description:	This is a prospective, multicenter, randomized clinical trial. It has two strata: for age (≥or< 75 years old) and for KrU21 (≥or< 5,5 ml/min/1.73m2). It is controlled through usual clinical practice. Intervention consists in reducing the frequency or number of sessions per week with which patients start the HD treatment. The experimental group will start with one session/week, then the number of weekly sessions will be increased to two and later to three as per criteria for progression.
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Assessment of the Incremental Haemodialysis Security and Effectiveness in Incident Patients
Actual Study Start Date :	March 14, 2018
Estimated Primary Completion Date :	July 2019
Estimated Study Completion Date :	July 2021

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Arms and Interventions

Go to

Arm	Intervention/treatment
Experimental: Experimental group 76 patients who start RRT with the incremental HD regimen.	Procedure: Incremental haemodialysis It consists in reducing the frequency or number of sessions per week with which patients start the HD treatment. The experimental group will start with one session/week, then the number of weekly sessions will be increased to two and later to three as per criteria for progression
Active Comparator: Control group 76 patients who start RRT with the conventional HD (3 sessions per week)	Procedure: Conventional haemodialysis It is controlled through usual clinical practice, based on starting the HD treatment with three sessions per week (control group).

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Summary

- The pre-ESRD and ESRD phases of CKD are along the continuum of the same disease process.

- Improved understanding of the natural history of the pre-ESRD to ESRD transition may potentially help physicians identify opportunities to apply targeted interventions at the most opportune time points along the disease progression trajectory to reduce morbidity and mortality.

- Timely referral to a nephrologist provides identification and correction of reversible causes of CKD, and preparation of dialysis. Timely referral at least 1 year before dialysis initiation is important to reduce mortality and medical cost during the transition.

- Incremental HD in incident patients can be performed safely, and probably is associated with preserved RKF & a similar mortality rate to convention initiation of HD.

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