Mental Health in Geriatric Dialysis Patient: Depression and Cognitive Impairment

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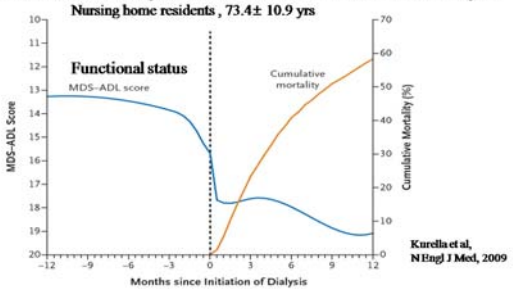
Functional Status of Elderly Pts before and after Initiation of Dialysis

Nursing home residents , 73.4± 10.9 yrs



Among **elderly** Pts, initiation of dialysis is associated with a substantial and sustained decline in **functional status** and very **high mortality**.

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Why?

Patients Characteristics

Age (yr)	73.4 ±10.9
Albumin (g/dl)	2.9 ±0.6
Coexisting condition (%)	
Diabetes	68
Congestive heart failure	66
Coronary artery disease	44
Peripheral vascular disease	37
Cerebrovascular disease	39
Chronic obstructive pulmonary disease	24
Cancer	12
Dementia	22
Depression	35

Geriatric and uremic Pts have several features in common.

1) Malnutrition

2) Cardiovascular disease

3) Mental health problem

Kurella et al, N Engl J Med, 2009

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Mental health problems in Geriatric Dialysis Patient

1. Dementia (Cognitive impairment)
2. Depression

↓↑

Poor economic status, Physical dependency,
Institutionalized , Loss of autonomy,
Late start of dialysis, Interruption of dialysis

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I. Cognitive impairment

Definition:

A new deficit in at least two areas of cognitive functioning
- memory
- executive functioning
- attention or speed of information processing
- perceptual motor abilities
- language

Approximately equivalent to **dementia**

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Cognitive impairment and Dementia

Cognitive impairment ⟸ Symptomatic approach

Normal — Mild — Severe

⬇

Dementia ⟸ Disease entity

- Degenerative (Alzheimer disease)
- **Vascular (multi-infarct) dementia**

1. Quality of life in the elderly
2. Compliance with dialysis schedules
3. Compliance with complex medication regimens
4. Making informed decisions regarding dialysis.

Poor prognosis!

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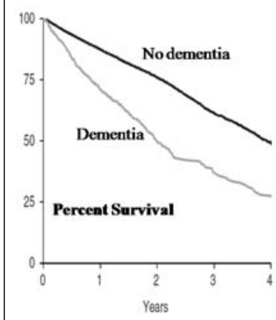
Cognitive impairment (Dementia) as a Predictor of Mortality and Dialysis Withdrawal



RR of death and dialysis withdrawal associated with diagnosed dementia

	Death	Dialysis withdrawal
All DOPPS		
Model 1	1.48 (1.32–1.66)	2.01 (1.57–2.57)
Model 2	1.18 (1.04–1.34)	1.60 (1.22–2.10)

Kurella et al, Nephrol Dial transplant, 2006

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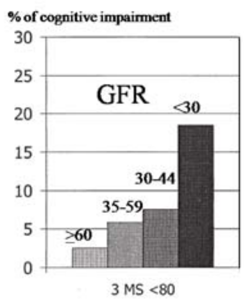
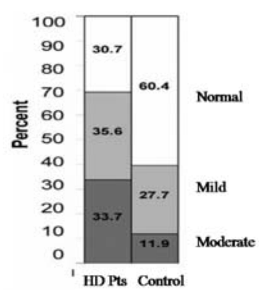
CKD as a Risk Factor for Cognitive Impairment

70% of HD Pts ages>55 yrs have cognitive impairment



Kurella et al, Am J Kidney Dis, 2005



Murray et al, Neurology 2006

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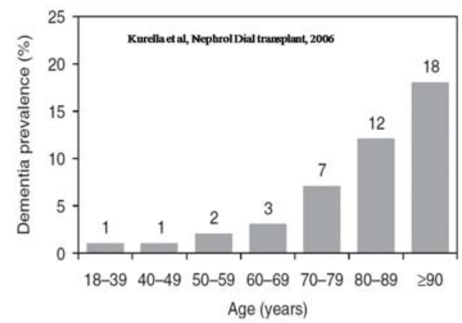
Aging as a Risk Factor for Cognitive Impairment in Dialysis Pts



Increasing prevalence of dementia with aging

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Cognitive Impairment may be **Under-diagnosed** in aged CKD and Dialysis Pts!

(18 versus 70%)

Screening and diagnosis of cognitive impairment

- Neurophysiological tests: EEG, evoked potential

- Neuropsychological examination

: **Mini-Mental state Exam (MMSE)**: most commonly used screening test, lack sensitivity and specificity for mild case

: Comprehensive testing allows for analysis of specific impairments in cognitive function

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Comprehensive test

Primary function assessed	Tests
Orientation: personal, temporal, and spatial	Mini-Mental State Examination (MMSE) Wechsler Memory Scale-Third Edition (WAIS-III) Temporal Orientation Test (TOT) Money Road Map Test (MRMT) Finger Localization Test Left-Right Orientation Test
Intelligence	Estimated Verbal IQ (NAART)
Mental status	Mini-Mental State Examination (MMSE) Mental Status Questionnaire (MSQ) Short-Portable Mental Status Questionnaire (SPMSQ)
Attention and vigilance	Simple Reaction Time (SRT) Choice Reaction Time (CRT) Digit Span tests from the Wechsler Adult Intelligence Scale-III (WAIS III) Digit Span tests from the Wechsler Memory Scale-Third Edition (WMS-III) Attention/Concentration Subtests of the WMS-III Paced Auditory Serial Addition Test (PASAT) Digit Symbol Symbol Search Trail Making Test Cancellation Tests
Verbal skills	Naming Test Boston Naming Test Controlled Oral Word Association Test Sentence Repetition
Memory	Wechsler Memory Scale-Third Edition (WMS-III) Rey Auditory Verbal Learning Test (RAVLT) California Verbal Learning Test (CVLT) Rey-Osterrieth Complex Figure
Depression	Center for Epidemiological Studies Depression Scale Geriatric Depression Scale Beck Depression Inventory

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Pathophysiologic classification of Cognitive Impairment in Dialysis Pts

- Acute decline in cognitive function associated with hemodialysis

- Persistent cognitive impairment (Dementia)

  1) Alzheimer's dementia (14%)

  2) Vascular dementia (86%) Fukunishi et al, Nephron, 2002

  ↓

  Cerebral ischemia associated with vascular disease

  - Clinical stroke: well known major risk for vascular dementia
  - Subclinical Cerebro-Vascular Disease
    Silent Cerebral Infarcts
    White Matter Disease **(leukoaraiosis)**

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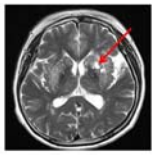
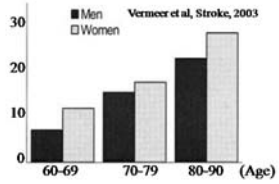
(1) Silent Cerebral Infarct (SCI or silent stroke)

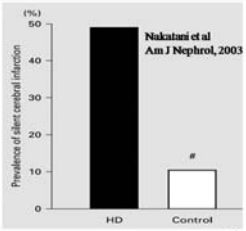


Definition
- Absence of neurological symptom
- Absence of prior stroke and TIA
- Presence of brain parenchymal lesion of vascular origin confirmed by CT or MRI

Higher incidence of SCI in HD patients (50%)

Incidence (%) of SCI: increase with aging





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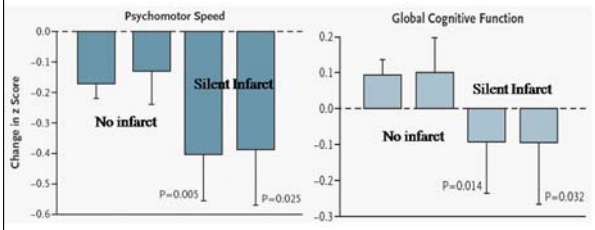
Elderly people with SCI have an increased risk of dementia and a steeper decline in **cognitive function** than control.



Vermeer et al, N Engl J Med, 2003

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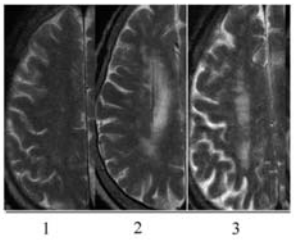
(2) White Matter Disease

represent micro-vascular disease due to chronic hypo-perfusion.

T2 high–signal intensity in Subcortical/Periventricular white matter lesions

48.0 % (CAPD)
versus
17.5 % (Control)



Kim CD et al, Am J Kidney Dis, 2007

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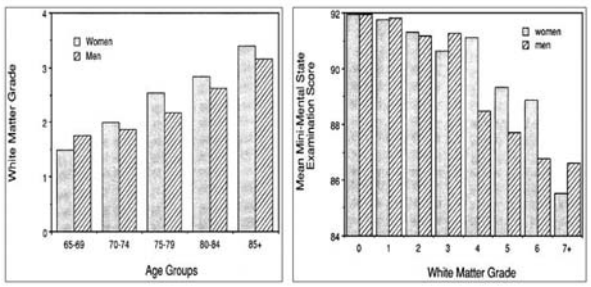
White matter disease and Cognitive Impairment

White matter grade: increased with aging

White matter grade correlated strongly with severity of cognitive impairment



Longstreth et al, stroke 1996

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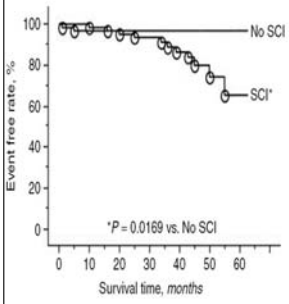
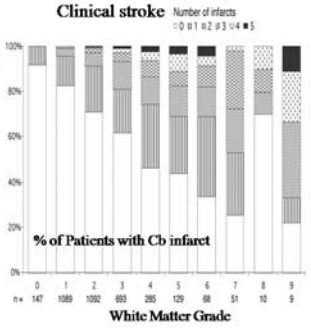
Both SCI and white matter disease predicts clinically evident vascular events in HD patients

Cerebro-Vascular disease



Nagaumma et al, Kidney Int, 2005

Clinical stroke



Kuller, et al. Stroke, 2004

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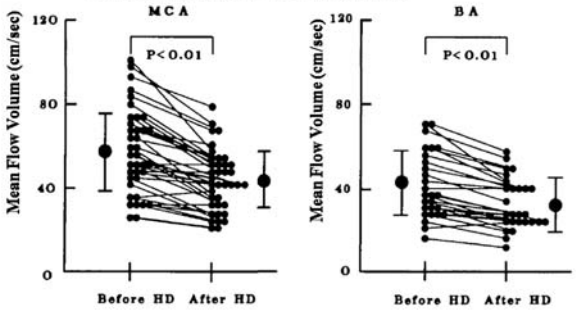
Dialysis Process itself
: risk factor for acute Cognitive Impairment
by inducing recurrent cerebral ischemia



Hata et al, stroke, 1994

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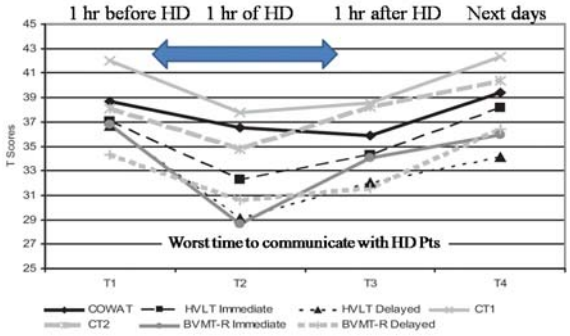
Cognitive Function declined acutely during Hemodialysis.



Murray et al, AmJ Kidney Dis, 2007

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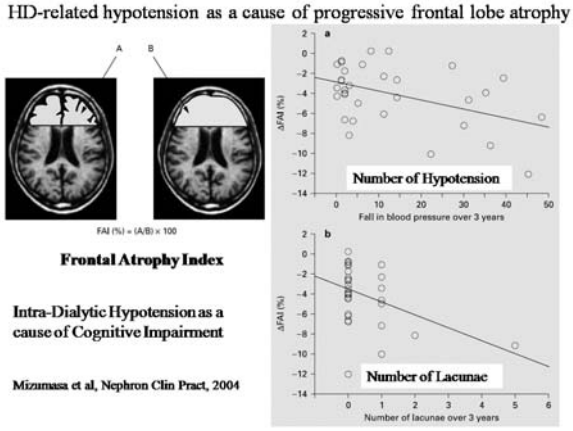
HD-related hypotension as a cause of progressive frontal lobe atrophy



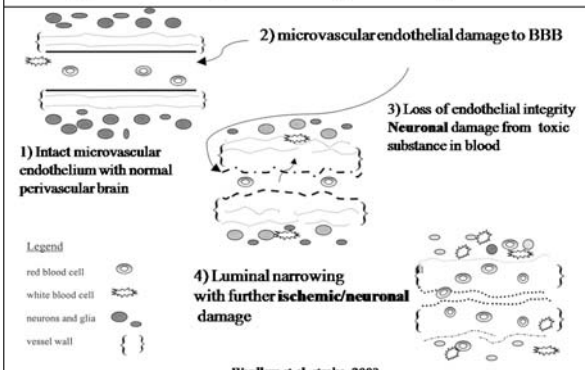
Frontal Atrophy Index

Intra-Dialytic Hypotension as a cause of Cognitive Impairment

Mizumasa et al, Nephron Clin Pract, 2004

Blood brain-barrier (BBB) become permeable (by microvascular damage) and cause damage to surrounding neurons and glial cells

Pathogenesis



Wardlaw et al, stroke 2003

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Cerebral microvascular (ie, BBB) dysfunction, with leakage of plasma components into the vessel wall and surrounding brain tissue lead to ischemia and neuronal damage

Contribute to the development of 3 cerebrovascular conditions:
1) Lacunar stroke (SCI)
2) White matter disease
3) Cognitive impairment (dementia).

Linking mechanism between
ischemic cerebral small-vessel disease and apparently clinically distinct ***cognitive impairment (dementia)***

Wardlaw et al, stroke 2003

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Systemic micro-vascular disease

Renal
Retinal
Cardiovascular

Cerebral

Cognitive Impairment in Dialysis Patients
: An Accelerated Model of Vascular Dementia

A marker of **Systemic Microvascular Disease**

Search for treatable vascular risk factors in geriatric dialysis patients with **cognitive impairments**

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Cognitive Impairment in the Aging Dialysis Populations: an Occult Burden

Early diagnosis/Treatment/Prevention:
Correction of Risk factors for **Systemic Microvascular Disease**

- Traditional CV risk factors; Atherosclerosis/Lipid/BP/DM/Smoking
- Non-traditional (CV) risk factors
  - **Intra-HD hypotension**/Anemia/Homocysteine
  - Hyperparathyroidism/Calcium/Phosphorus/Stiffness
  - Inflammation/Oxidative stress
- Others
  - Poly-pharmacy
  - Psychosocial support/Intellectual stimulation and mental exercise
  - Nocturnal/Home HD
  - Kidney transplantation

Cholinesterase inhibitors (Donepezil, 아리셉트)

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II. Depression

Pts on replacement therapy experiences 3 different phases:

(1) falling in love with dialysis: an improvement in QOL

(2) a progressive disappointment: a period of increased risk,

(3) a slow adaptation to dialysis – with, in the **elderly** patient, an inexorable decline toward ***Depression.***

Levy NB, Adv Ren Replace Ther, 2000

- The most common psychological Cx of ESRD Pts.
- Incidence:10-66%:
  due to different diagnosis criteria/methodology

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Major depression: DSM-IV criteria

(Diagnostic and Statistical Manual of Mental Disorders, 4th Edition)

5 > following 9 symptoms for >2 weeks

1. Depressed mood most of the day, particularly in the morning
2. Markedly diminished interest or pleasure in almost all activities
3. Significant weight loss or gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or guilt
8. Impaired concentration, indecisiveness
9. Recurring thoughts of death or suicide

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Major depression: Screening/Diagnosis

1. Beck Depression Inventory (BDI):
   CDI (cognitive subset)
2. Hamilton Depression Rating Scale (HDRS)
3. Zung Self Rating Depression Scale (SDS)

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Beck Depression Inventory (BDI)

- 21 item **self-report** rating inventory
- 4-point Likert scale: 0 - 3 (Total score: 0 - 63)
  10–18, mild to moderate depression
  19–29, moderate to severe depression
  30–63, severe depression
- Well-validated and correlates well with diagnostic criteria.
- 85% of ***western*** dialysis Pts with BDI scores> 11
  : meet the DSM-IV criteria for depression
- Mean BDI of normal ***Korean***:12.7 ± 7.7

***21*: cut-off value for the diagnosis of depression for Korean**

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BDI

1. Sadness
2. Pessimism
3. Sense of failure
4. Dissatisfaction
5. Guilt
6. Expectation of punishment
7. Dislike of self
8. Self Accusation
9. Suicidal ideation
10. Episodes of crying
12. Social withdrawal
13. Indecisiveness
14 Change in body image
15. Retardation
16. Insomnia
17. Fatigability
18. Loss of appetite
19. Loss of Weight
20. Somatic preoccupation
21. Low level of energy

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Cognitive Depression Index (CDI)

Subset of 15 cognitive items from the total 21 BDI items

: Distinguishing somatic symptoms

1. Sadness
2. Pessimism
3. Sense of failure
4. Dissatisfaction
5. Guilt
6. Expectation of punishment
7. Dislike of self
8. Self Accusation
9. Suicidal ideation
10. Episodes of crying
12. Social withdrawal
13. Indecisiveness
14 Change in body image
15. Retardation
16. Insomnia
17. Fatigability
18. Loss of appetite
19. Loss of Weight
20. Somatic preoccupation
21. Low level of energy

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Significant association of depression with mortality in maintenance dialysis

1.Depression, perception of illness and mortality in ESRD patients.
Int J Psychiatry Med, 1991

2.Dialysis Outcomes and Practice Patterns Study (DOPPS). Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe.
Kidney Int, 2002

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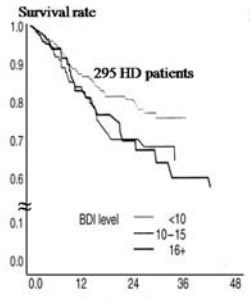
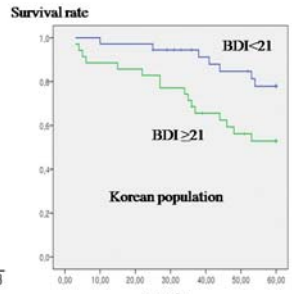
Measurements of depression predict mortality in a longitudinal study of chronic hemodialysis patients



Kimmel et al, Kidney Int 2000



한림대 춘천 성심병원 data

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Significant association of depression with mortality in maintenance dialysis

Why?

1. Disturbance in thinking, problem solving/self efficacy
   : adaptive skill/compliance↓
   : 수동적 자살?? (투석)치료 받기 싫다!
2. Lack of activity and exercise: functional loss
3. **Biological mechanisms: Inflammation/Malnutrition**
4. Cardiovascular disease

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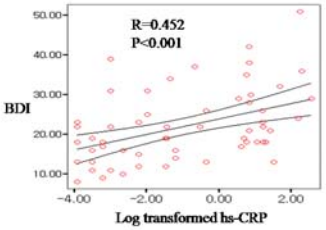
Depression: a inflammatory disorder?

Hyper-secretion of pro-inflammatory cytokines[1,2]
: malfunctioning of noradrenergic/serotonergic neurotransmission in the brain
→ **major symptoms of depression**

1. Adv Exp Med Biol, 1999
2. Scand J Immunol, 1995



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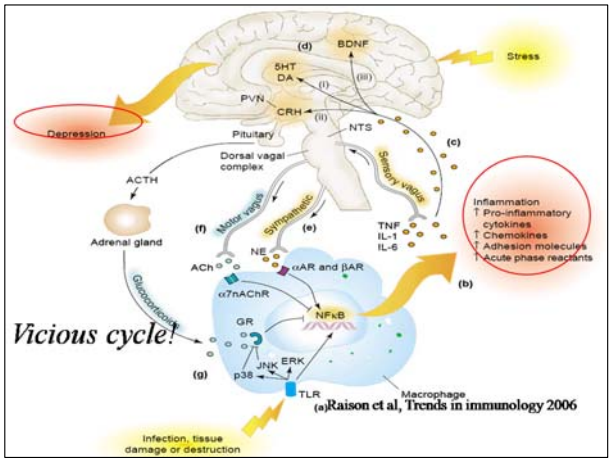

Vicious cycle!

(a)Raison et al, Trends in immunology 2006

Hypothesis

Depression is associated with **Inflammation**

Hyper-inflammatory response in ESRD

poor oral intake

protein catabolism↑

Malnutrition

Mortality↑ in ESRD patients

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Association of Depression with Malnutrition in Chronic Hemodialysis Patients

Koo JR et al, Am J Kidney Dis, 2003

A cross-sectional study to investigate the relation between the **depression** and **nutritional status** in chronic HD Pts.

1. **Beck Depression Inventory (BDI)/CDI questionnaire**
2. DSM-IV criteria: for the patients with BDI > 18

Nutritional markers

1. Modified subjective global assessment (SGA)
2. Anthropometric measurements
   BMI, triceps skinfold thickness (TSF)
   mid-arm muscle circumference

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Results

- **Mean BDI score:** 22.7±11.4: moderate/severe depression
  - 35 (56.5%) pts: BDI score > 21
  - 34 pts met DSM-IV criteria for major depression
- **Prevalence of depression: 54.8 % (34/62)**
- **BDI score > 21:** good screening tool for depression

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Correlations between the Severity of Depression and Nutritional Parameters

Nutritional parameters	BDI score		CDI score	
	r value	p value	r value	p value
Serum albumin	-0.47	<0.001	-0.37	<0.005
nPCR	-0.32	<0.05	-0.30	<0.05
Subjective global assessment	-0.47	<0.01	-0.42	<0.05
Triceps skinfold thickness	-0.40	<0.05	-0.41	<0.05
Midarm muscle circumference	-0.57	<0.01	-0.50	<0.01
Body mass index	-0.28	<0.05	-0.28	<0.05

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Multivariate Analysis: Effects of Different Variables on Nutritional Parameters

	Nutritional Parameters (regression coefficients)											
	Albumin		nPCR		SGA		TSF		MAMC		BMI	
Variables (risk factors)	BDI	CDI	BDI	CDI	BDI	CDI	BDI	CDI	BDI	CDI	BDI	CDI
Severity of depression	−0.640*	−0.368	−0.570*	−0.518*	−0.592*	−0.533*	−0.660*	−0.677*	−0.550*	−0.509*	−0.640*	−0.453*
Kt/V_{urea}	−0.053	0.059	−0.241	−0.200	0.425	0.425*	0.478*	0.509*	0.012	0.033	−0.190	−0.147
Age	−0.449*	−0.607*	−0.016	−0.088	−0.252	−0.332	−0.023	−0.110	0.187	0.098	0.144	−0.086
Sex (women)	0.045	0.294	−0.230	−0.268	0.078	0.049	0.015	−0.020	−0.096	−0.095	−0.375	−0.220
Diabetes mellitus (yes)	−0.374	−0.511*	0.235	0.215	−0.013	−0.105	0.216	0.144	−0.314	−0.373	−0.231	0.099
Hematocrit	0.148	0.251	−0.531*	−0.492*	−0.225	−0.148	−0.100	−0.060	−0.308	−0.209	−0.571*	−0.298
Plasma bicarbonate	−0.078	−0.092	−0.043	−0.071	−0.008	−0.034	0.021	−0.028	−0.166	−0.193	0.089	0.002
Hemodialysis duration	−0.021	0.083	0.225	0.272	−0.167	−0.110	−0.466*	−0.412	0.070	0.108	−0.516*	−0.303

*P<0.05

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Differences in the Nutritional Parameters and Other Clinical Variables between Patients With Depression and Without Depression by DSM-IV criteria

Variables	With Depression (n = 34)	Without Depression (n = 28)
Severity of depression		
BDI score	30.7 ± 7.9*	13.0 ± 6.4
CDI score	24.1 ± 6.1*	10.1 ± 5.4
Nutritional parameters		
Triceps skinfold thickness (mm)	8.2 ± 2.8*	12.2 ± 4.6
Midarm muscle circumference (cm)	20.7 ± 2.1*	22.7 ± 1.4
Body mass index (kg/m^2)	20.1 ± 2.5	21.5 ± 3.4
SGA	4.03 ± 1.24*	5.26 ± 1.70
Serum albumin (g/dL)	3.73 ± 0.20*	4.15 ± 0.41
Serum urea nitrogen (mg/dL)	68.7 ± 15.8	75.4 ± 16.0
Normalized protein catabolic rate (g/kg/d)	1.04 ± 0.24*	1.19 ± 0.20
Other clinical variables		
Age (y)	52.5 ± 11.2*	44.4 ± 9.3
Men (%)	52.9	60.7
Hemodialysis duration (mon)	53.8 ± 35.3	49.2 ± 29.6
Diabetes mellitus (%)	41.2*	14.3
Kt/V_{urea}	1.26 ± 0.26	1.28 ± 0.22

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Conclusion

- Depression is closely related with nutritional status.
- Depression could be an independent risk factor for malnutrition in chronic HD patients.

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Depression and Inflammation

1. Hyper-secretion of pro-inflammatory cytokines[1,2]:
   malfunctioning of noradrenergic/serotonergic neurotransmission in the brain
   → **major symptoms of depression**

2. Anti-depressants (SSRI):
   ↓pro-inflammatory cytokines from activated macrophages
   ↑endogenous cytokine antagonists (IL-1 RA and IL-10)[3,4]

1. Adv Exp Med Biol, 1999
2. Scand J Immunol, 1995
3. Prog Neuropsychopharmacol Biol Psychiatry, 2001
4. Immunopharmacol, 1996

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The Effects of Antidepressant Treatment on Serum Cytokines and Nutritional Status in Hemodialysis Patients

Sang-Kyu Lee, Ja-Ryong Koo, Bong-Ki Son, et al
J Korean Med Sci, 2004

A longitudinal study to investigate the effects of **anti-depressant** treatment (Fluoxetine 20mg/day for 8 weeks) on the level of serum cytokines in chronic HD patients

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Results

	Baseline	8 Weeks
Severity of depression		
BDI	14.7±1.4	
HAMD	13.54±0.99	10.07±1.22*
Cytokines		
IL-1β (pg/mL)	18.87±2.1	10.52±1.18*
IL-2 (pg/mL)	0.57±0.04	0.72±0.12
IL-6 (pg/mL)	7.26±2.51	10.58±2.37*
TNF-α (pg/mL)	80.67±11.4	65.37±5.97
CRP (mg/mL)	2.19±0.5	2.34±0.6

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Antidepressant in ESRD

- decrease IL-1β
- increase IL-6

IL-6: both pro/anti-inflammatory cytokine
highly pleiotropic cytokine, functioning as a mediator to control secretion of other cytokines
- Gene expression is strongly controlled by cortisol

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1. Depression is an independent risk factor for malnutrition in chronic HD patients.
2. Antidepressant treatment affect immunological functions and cytokine networks in chronic HD pts.

3. What's the effects of anti-depression treatment on nutritional status?

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Treatment of depression in ESRD Pts

1. The impact of ESRD on the Sx and the Pts response to antidepressant.
2. The pharmacokinetics and safety of antidepressant?
3. Psychosocial supports are associated with reduced mortality in chronic HD patients[1].
4. Only small percentage of depressed ESRD patients (16%) were being treated for depression[2].

1. Psychosocial factors, behavioral compliance and survival in urban HD patients. Kidney Int, 1998
2. The prevalence and treatment of depression among patients starting dialysis. Am J Kidney Dis 2003.

48

Identification and treatment of depression in a cohort of patients maintained on CAPD.

Wuerth et al, Am J Kidney Dis 2001

- 45% of the eligible depressed patients agreed to further assessment with possible treatment.
- 11 of 20 patients completed 12 weeks of anti-depressant therapy.

Depression is treatable with anti-depressant medication in a small but significant percentage of ESRD patients on CAPD.

- Patient's needs and acceptance for medication/psychiatric referral
- **Nephrologist's comfort** with prescribing antidepressants.

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Anti-depressant medication

TCA and selective serotonin reuptake inhibitor (SSRI)

All antidepressants
1. are effective in 75 % of patients.
2. require 4-6 weeks for full effect.
3. are protein bound, hepatically metabolized, and not removed significantly by dialysis.

: No dose adjustment except paroxetine and venlafaxine

- SSRI: ease of administration (once-daily), absence of active metabolites, less side effect (cardiotoxicity < TCA).

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Treatment of Depression and Effect of Anti-depression Treatment on Nutritional Status in Chronic Hemodialysis Patients

Ja-Ryong Koo, Sang-Kyu Lee, Bong-Ki Son, et al

Am J Med Sci 2005

1. To examine the feasibility of treating depressed HD Pts.
2. To evaluate the effect of anti-depression treatment on nutritional status in chronic HD Pts.

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Methods

34 chronic HD patient: BDI>18, meet DSM IV criteria

Anti-depression treatment for 8 weeks

1. SSRI: paroxetine 10mg/day
2. Supportive psychotherapy

- Patients contact every HD session (compliance/side effect)
- Psychotherapy/psychological counseling q 2 wks.

- HDRS and Zung SDS, pre and after treatments

- Kt/V, nPCR, albumin
- Nutritional marker: multi-frequency BIA (Inbody 2.0, Biospace)

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Results-1

- **All** pts successfully completed 8 weeks course of Tx
- Paroxetine: No evidence of major adverse events
  4 Pts (8.3 %): mild CNS symptoms (drowsiness, dizziness)

1. **Combined psychosocial support and nursing staff's effort to increase compliance.**
2. **Cultural/racial differences in patient's response to medical recommendation.**
3. **Rural area *versus* Urban area**

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Results-2

Changes in Nutritional Status in the Treatment and Control groups

	Treatment Group (n = 34)		Control Group (n = 28)	
	Baseline	8 Weeks	Baseline	8 Weeks
Severity of depression				
HDRS	16.6 ± 7.0	15.1 ± 6.6[a]	Not measured	Not measured
SDS	59.2 ± 10.9	56.0 ± 12.6	Not measured	Not measured
Nutritional parameters				
Serum albumin (g/L)	37.3 ± 2.0[b]	38.7 ± 3.2[a]	41.5 ± 4.1	41.6 ± 4.3
BUN (mmol/L)	24.3 ± 5.6	30.2 ± 7.9[a]	26.9 ± 5.7	28.5 ± 6.6
nPCR (g/kg/day)	1.04 ± 0.24[b]	1.17 ± 0.29[a]	1.19 ± 0.20	1.18 ± 0.22
Bioimpedance analysis				
Intracellular fluid volume (L)	19.7 ± 3.6	20.1 ± 3.6[a]	21.0 ± 4.2	21.1 ± 4.4
Extracellular fluid volume (L)	10.0 ± 1.8[b]	9.6 ± 1.6[a]	11.2 ± 2.4	11.3 ± 2.4
Lean body mass (kg)	42.9 ± 7.5	42.9 ± 7.3	45.4 ± 8.8	45.3 ± 9.2
Fat mass (kg)	8.9 ± 4.2	9.1 ± 4.1	9.6 ± 3.9	9.6 ± 4.0

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Conclusion

Anti-depressant medication with supportive psychotherapy

1) can successfully treat depression.
2) improve nutritional status.

in most of chronic HD patients with depression.

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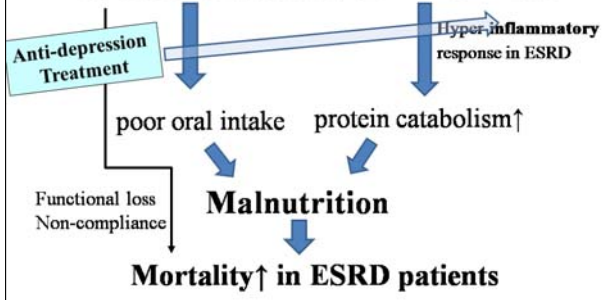
Hypothesis

Depression is associated with **Inflammation**



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Significant association of depression with mortality in maintenance dialysis

Why?

1. Disturbance in thinking, problem solving/self efficacy
   : adaptive skill/compliance↓
   : 수동적 자살?? (투석)치료 받기 싫다!
2. Lack of activity and exercise: functional loss
3. Biological mechanisms: Inflammation/Malnutrition
4. **Cardiovascular disease**

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Vascular disease as a risk factor of **late life** (>65) Depression

Factor[1]	Unadjusted model	Adjusted	
		Model 1[2]	Model 2[3]
Stroke	3.68*** (1.99 to 6.79)	4.38*** (2.30 to 8.34)	2.56* (1.26 to 5.22)
Heart disease	2.32*** (1.48 to 3.64)	2.22** (1.40 to 3.52)	1.43 (0.83 to 2.43)
Hypertension	1.48 (0.98 to 2.27)	1.45 (0.94 to 2.24)	1.25 (0.79 to 1.96)
Diabetes	1.67 (0.94 to 2.99)	1.72 (0.95 to 3.09)	1.41 (0.75 to 2.64)
HDL	−4.83** (−7.82 to −1.84)	−4.82** (−7.85 to −1.78)	−4.30** (−7.45 to −1.14)
LDL	9.05* (2.1 to 15.9)	5.76 (−0.96 to 12.5)	4.68 (−2.31 to 11.7)

Korean Population, Kim et al, Brit J Psych, 2004

Concept of Vascular or Post-stroke Depression

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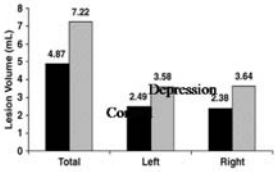
White matter disease and **SCI** are associated with **elderly Depression**

White matter lesion volume



Taylor et al, Psychiatry Research, 2005

Silent Cerebral Infarct

TABLE 1. Silent Cerebral Infarction in Presenile Major Depression

	n (M/F)	Age, y	No. With SCI (%)
JP group	31 (12/19)	56.7±3.6	7/31 (22.6)
PP group	70 (25/45)	58.2±3.6	36/70 (51.4)*

TABLE 2. Silent Cerebral Infarction in Senile Major Depression

	n (M/F)	Age, y	No. With SCI (%)
PS group	41 (11/30)	67.6±2.4	27/41 (65.9)
SS group	63 (22/41)	72.8±5.3*	59/63 (93.7)†

Fujikawa et al, Stroke, 1993

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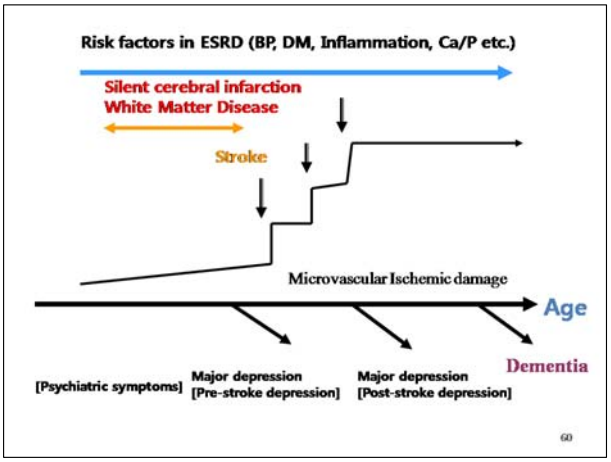
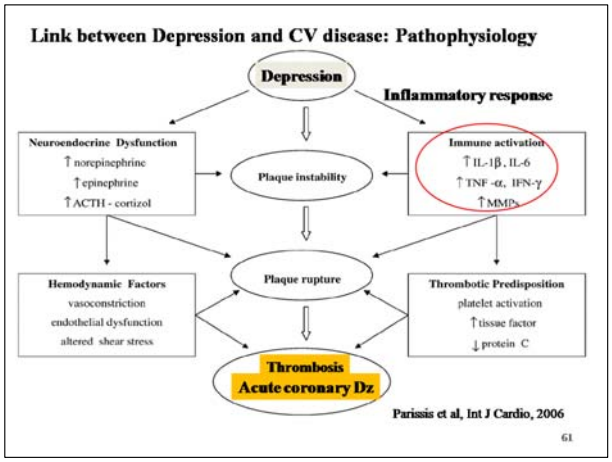
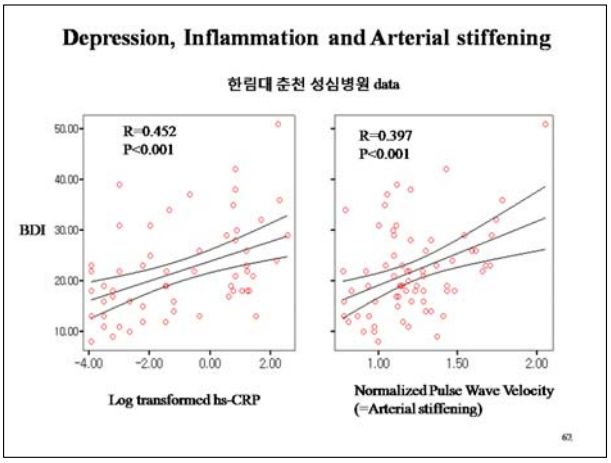
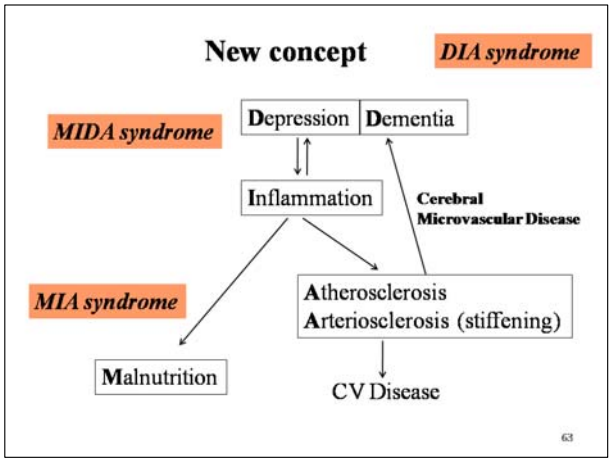
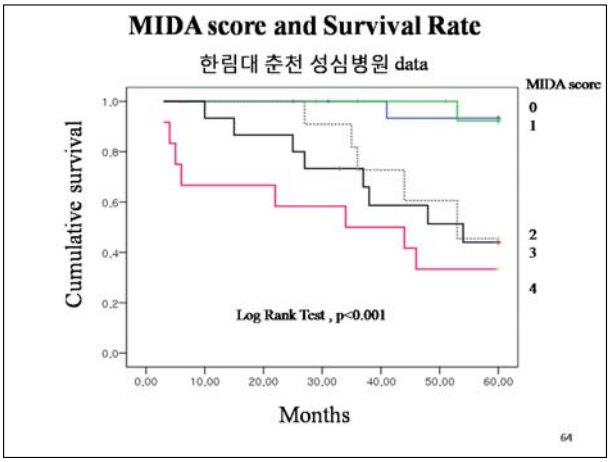
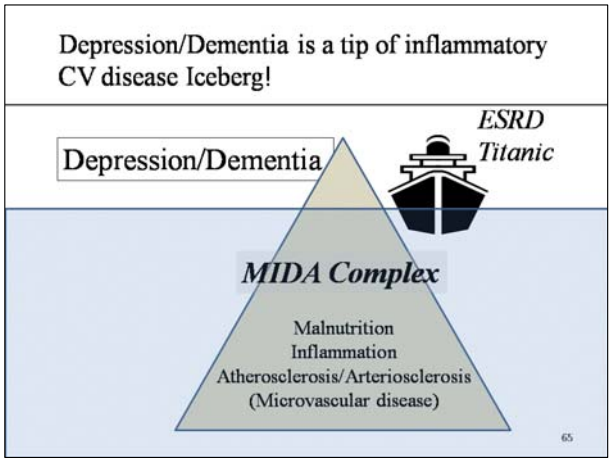

Risk factors in ESRD (BP, DM, Inflammation, Ca/P etc.)
Silent cerebral infarction
White Matter Disease
Stroke
Microvascular Ischemic damage
Age
Dementia
[Psychiatric symptoms]
Major depression
[Pre-stroke depression]
Major depression
[Post-stroke depression]
60


Link between Depression and CV disease: Pathophysiology
Depression
Inflammatory response
Neuroendocrine Dysfunction
↑ norepinephrine
↑ epinephrine
↑ ACTH - cortizol
Plaque instability
Immune activation
↑ IL-1β, IL-6
↑ TNF -α, IFN-γ
↑ MMPs
Plaque rupture
Hemodynamic Factors
vasoconstriction
endothelial dysfunction
altered shear stress
Thrombotic Predisposition
platelet activation
↑ tissue factor
↓ protein C
Thrombosis
Acute coronary Dz
Parissis et al, Int J Cardio, 2006
61


Depression, Inflammation and Arterial stiffening
한림대 춘천 성심병원 data
R=0.452
P<0.001
R=0.397
P<0.001
BDI
Log transformed hs-CRP
Normalized Pulse Wave Velocity
(=Arterial stiffening)
62


New concept
DIA syndrome
MIDA syndrome
Depression
Dementia
Inflammation
Cerebral
Microvascular Disease
MIA syndrome
Atherosclerosis
Arteriosclerosis (stiffening)
Malnutrition
CV Disease
63


MIDA score and Survival Rate
한림대 춘천 성심병원 data
MIDA score
0
1
2
3
4
Cumulative survival
Log Rank Test , p<0.001
Months
64


Depression/Dementia is a tip of inflammatory
CV disease Iceberg!
ESRD
Titanic
Depression/Dementia
MIDA Complex
Malnutrition
Inflammation
Atherosclerosis/Arteriosclerosis
(Microvascular disease)
65

Take Home Messages

In elderly dialysis patients

- Depression and Dementia (=Cognitive impairment), (D & D) are common but **hidden** burden.
- D & D are associated with significant **functional loss** and very **high mortality**.
- D & D are systemic **microvascular/inflammatory** disorders.
- D & D may be a component of **MIDA** complex (Tip of iceberg)
- **Early** detection (white matter disease/SCI)/treatment and prevention of D & D are urgently required.

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