

Depression: Is Symptom or Aggravating Factor in Patients with heart failure?

원주의대 김장영

순서

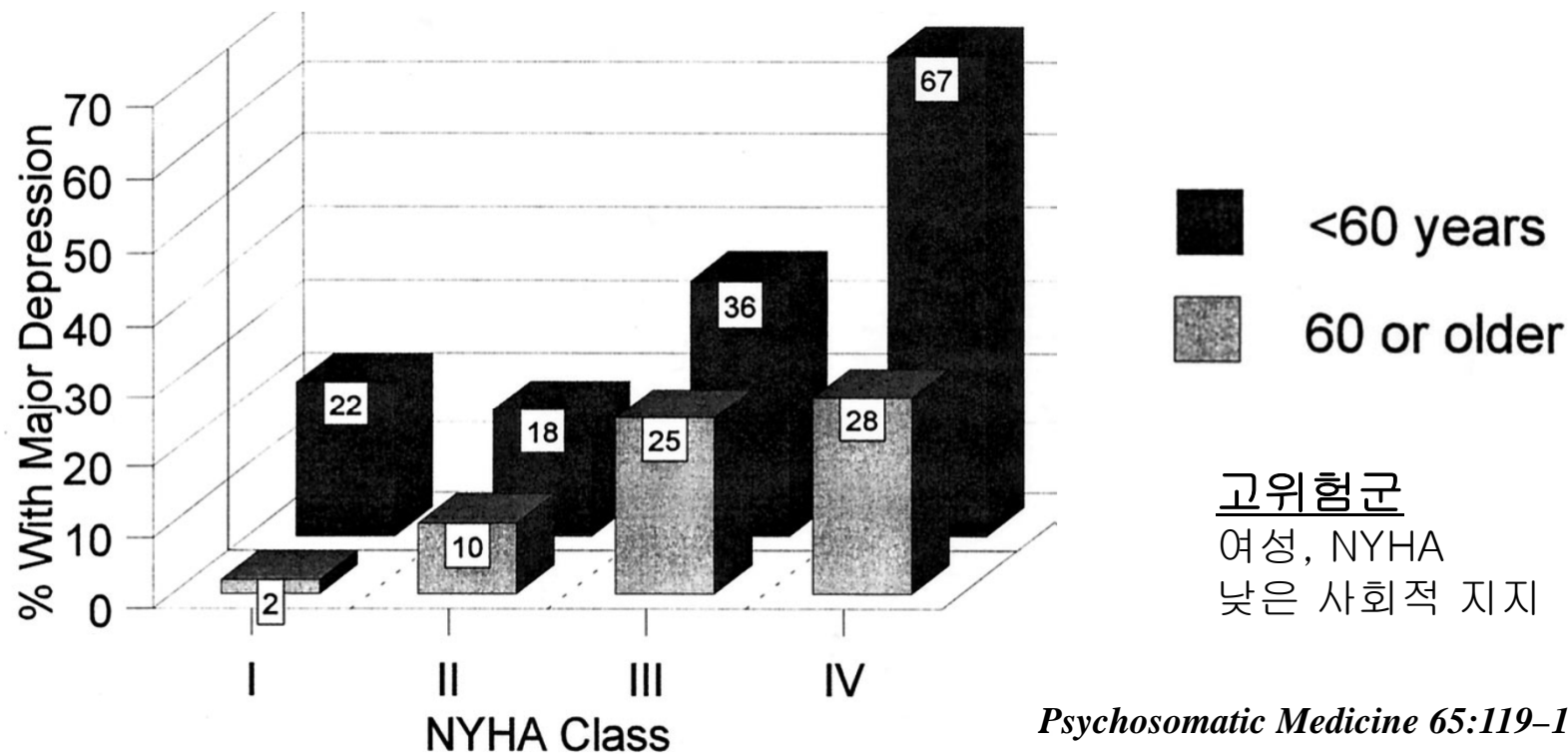
- 심부전에서의 우울증 빈도
- 왜 심부전 환자에서 우울증의 빈도가 높은가?
- 예후
- 치료
- 향후 과제

HF → Depression

Prevalence of major depression in HF

- General population: 4-6 %, Post-MI patients: 15-45%,
- **HF : up to 40% (19-34 % in meta-analysis)**

Am J Psychiatry 2006;163:2141, Ach Intern Med 2001;161;1849

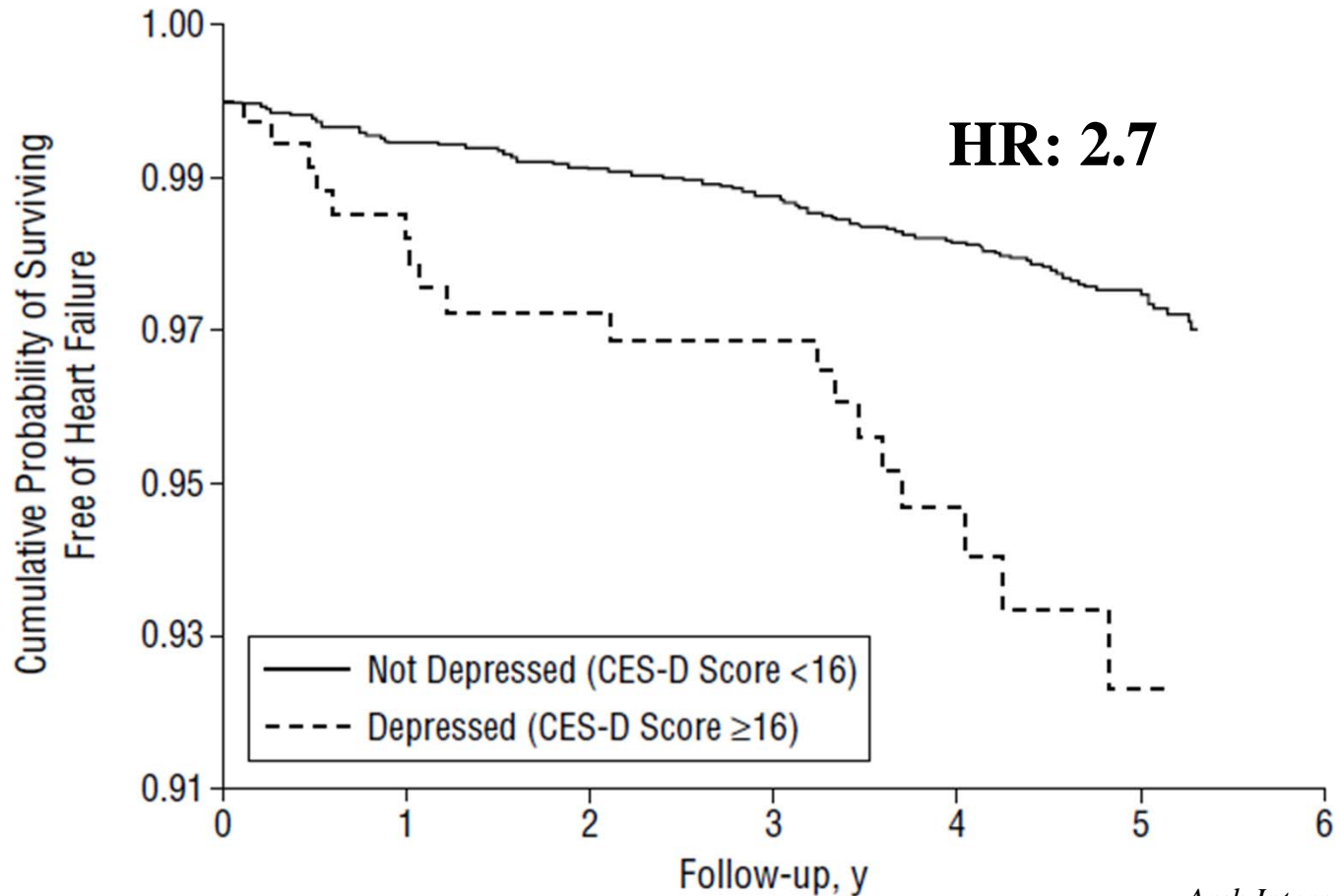


Depression → HF

ORIGINAL INVESTIGATION

Depression and Risk of Heart Failure Among Older Persons With Isolated Systolic Hypertension

Jerome Abramson, PhD; Alan Berger, MD; Harlan M. Krumholz, MD, MPH; Viola Vaccarino, MD, PhD

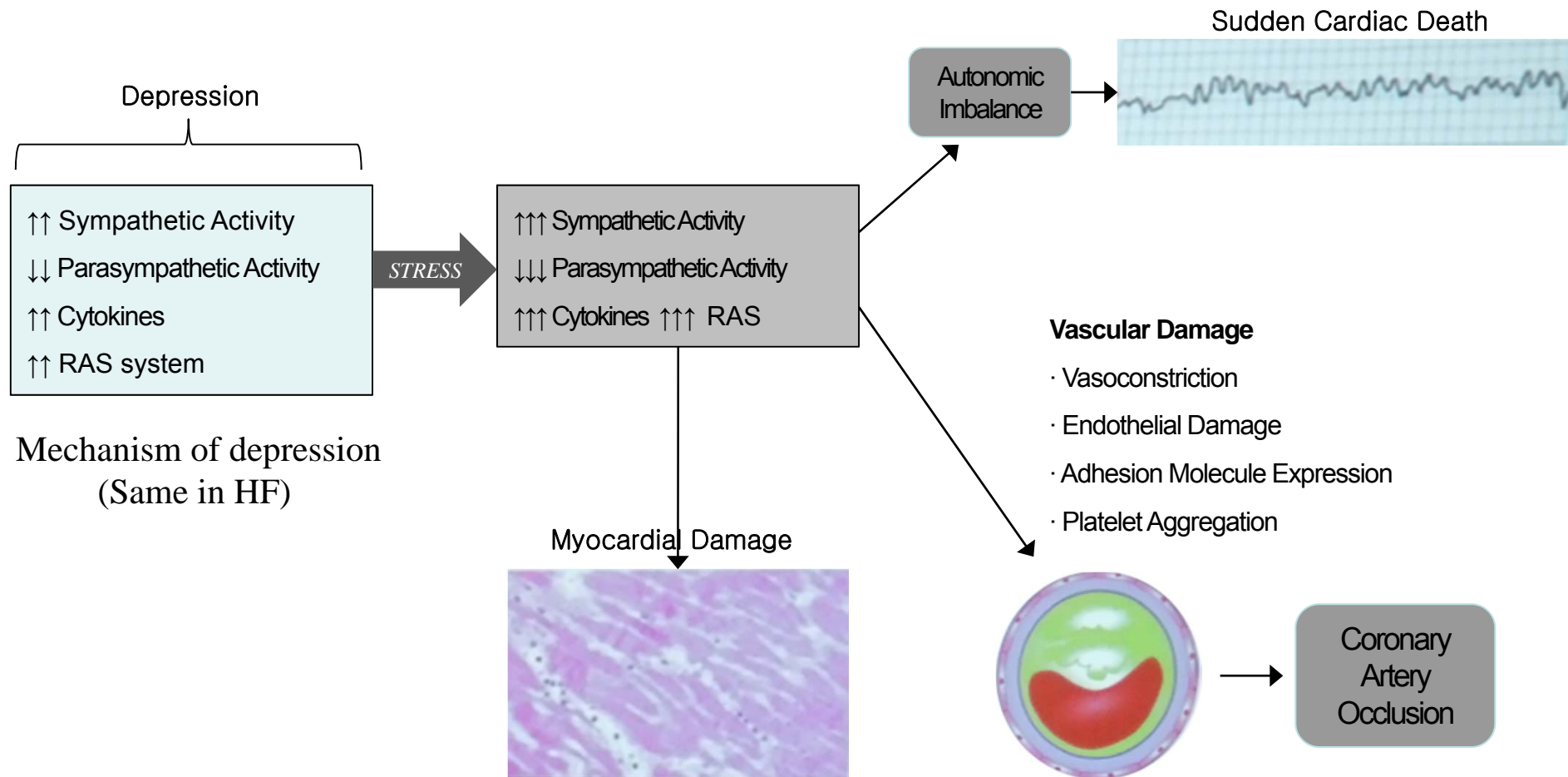


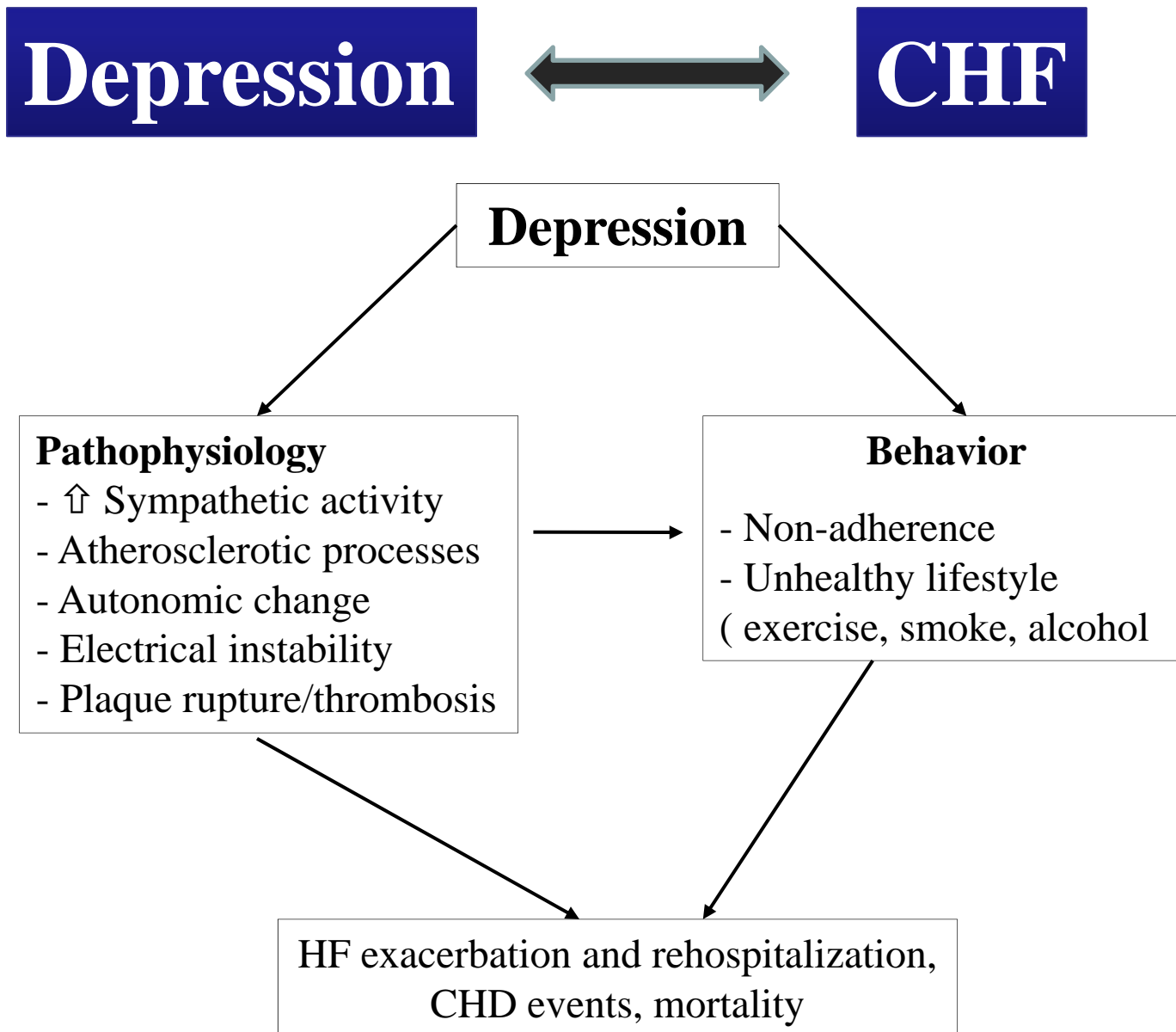
Why high prevalence of depression in HF?
Why predictors of HF in depressed person ?



Common mind-body?

Mind-heart interactions





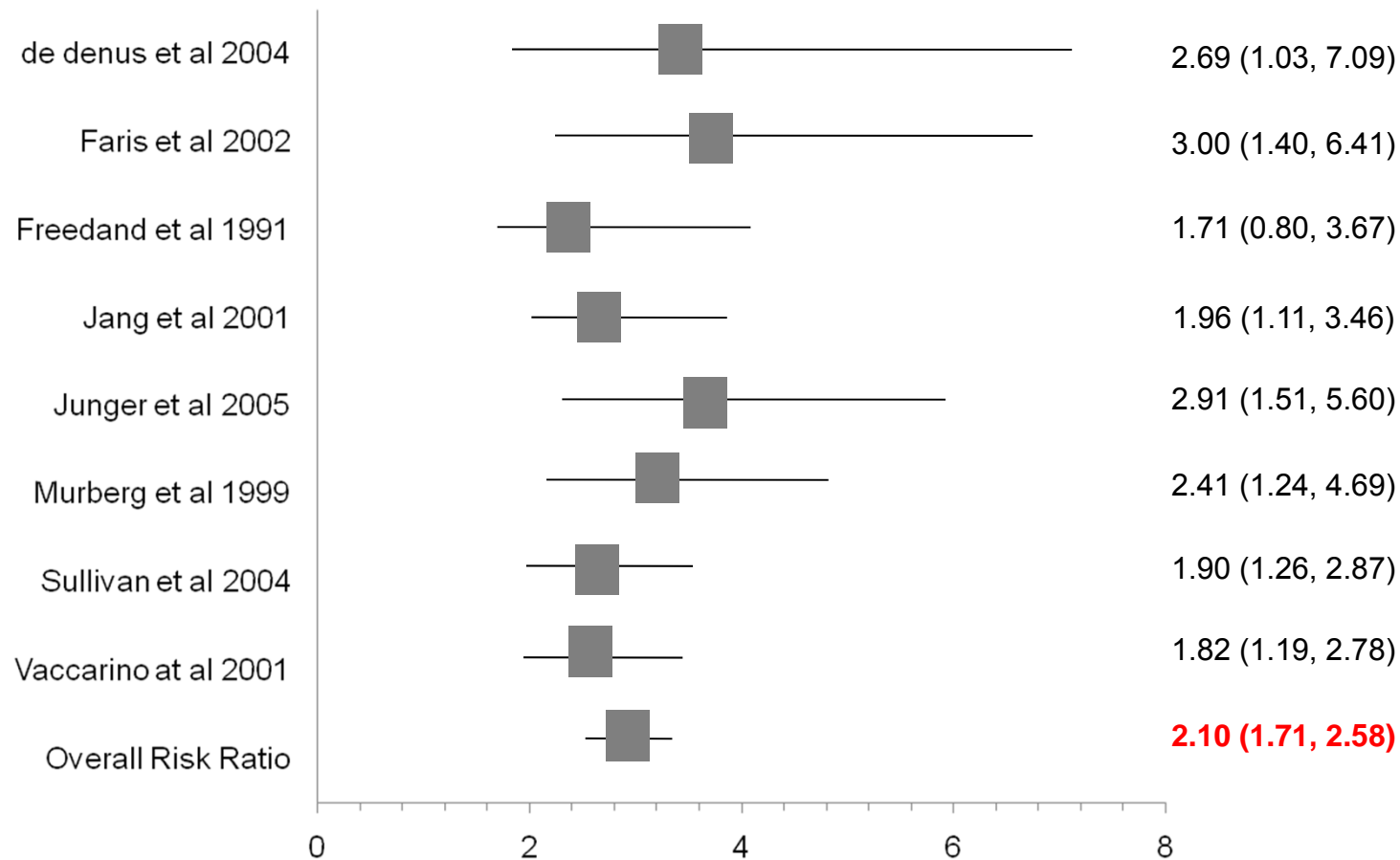
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- 심부전에서의 우울증 빈도
- 왜 심부전 환자에서 우울증의 빈도가 높고 예후에 나쁜 영향을 미치는가?
- 심부전에서 우울증과 예후
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Depression and clinical outcomes

- Depressive symptoms are 1.5 to 3.5 times risk of MI
- Depression increase HF after CAD diagnosis
(adjusted hazard ratio: 1.50) *JACC, 2009;53:1440*
- Depression has higher rate of death and secondary end point in meta-analysis (n=1845, relative risk : 2.1 95% CI, 1.7-2.6) *JACC 2006;48:1527*

Association between depression and clinical events

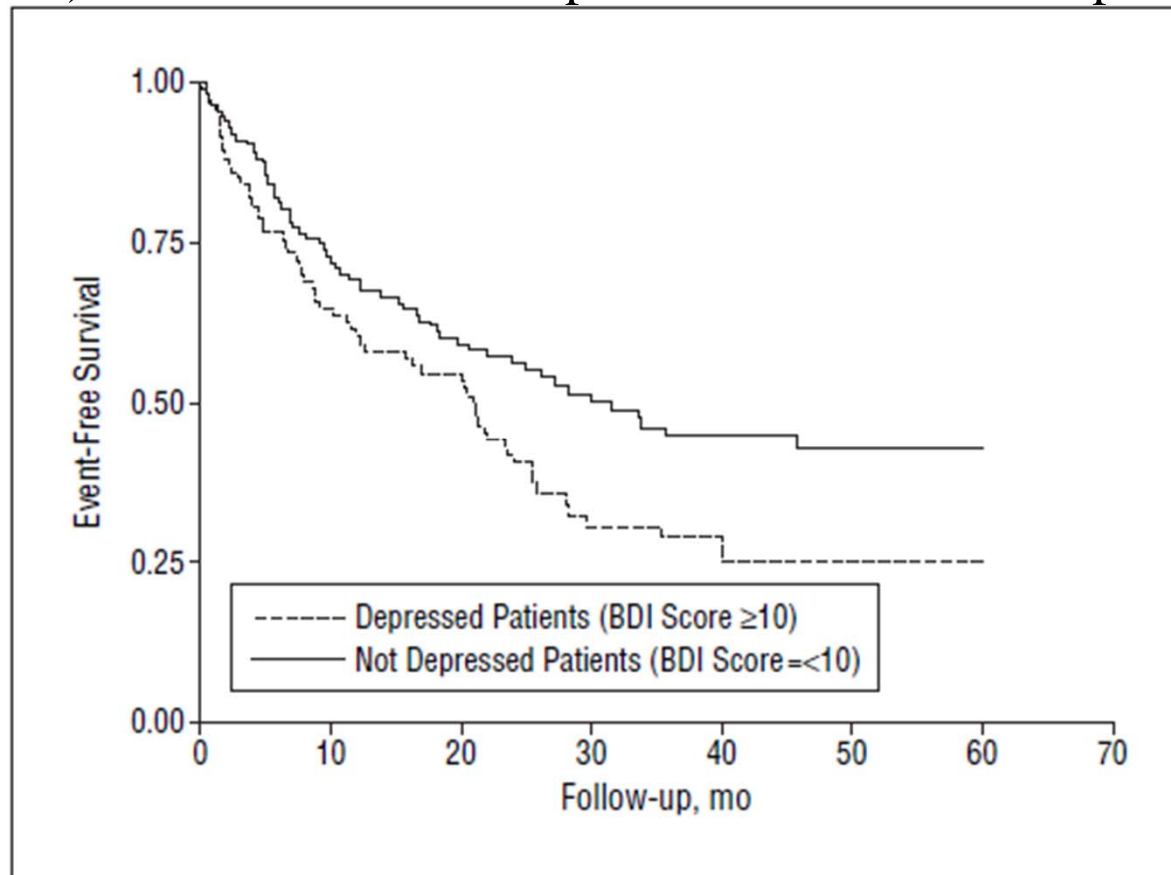


Aggregated risk estimate:

RR 2.1 (95% CI : 1.7-2.6)

Prognosis of HF in depressive patients

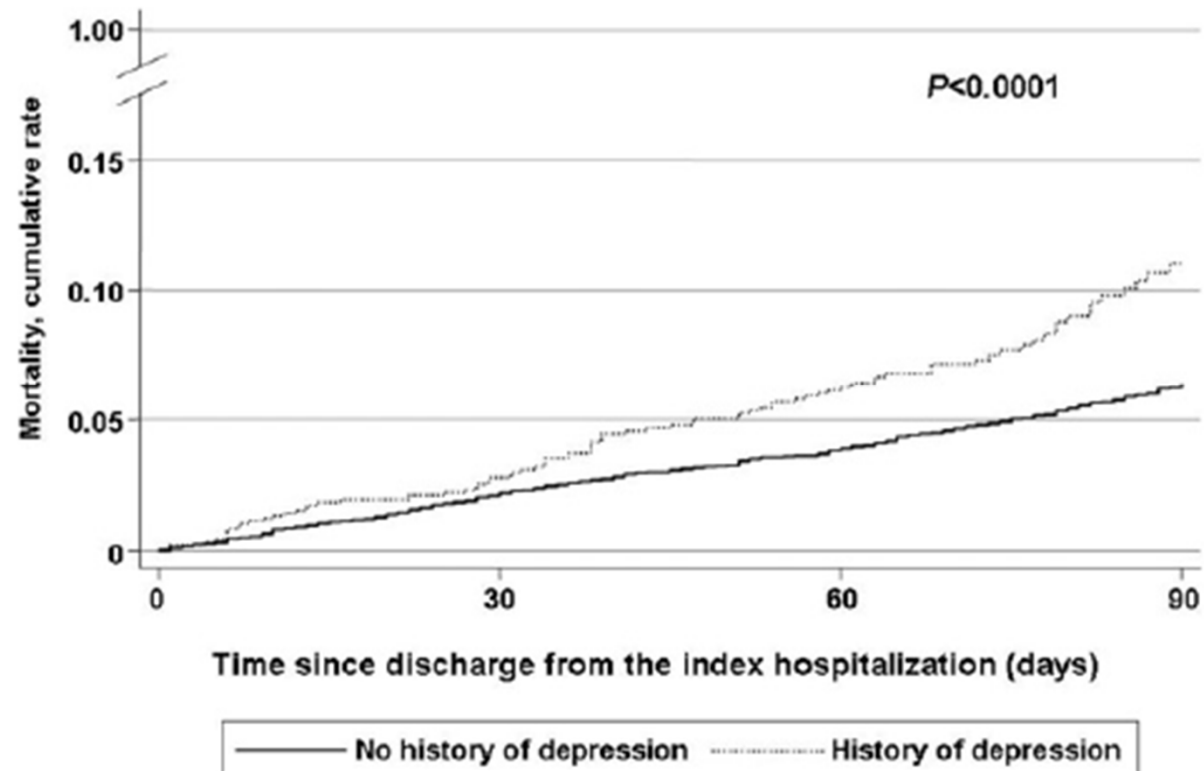
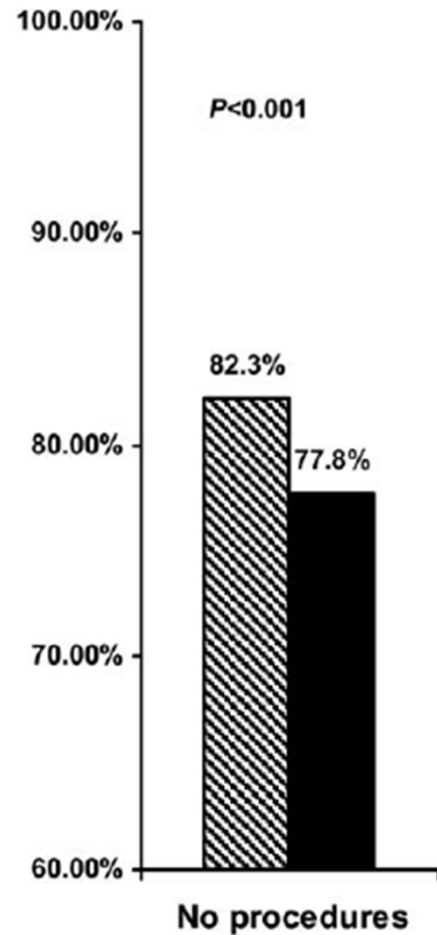
Beck Depression Inventory score (BDI) >10 were associated with a hazard ratio of 1.56 (1.07-2.29) for the combined end point of death or CV hospitalization



Similar hazard ratio: smoking, LV dysfunction and history of MI

Prognosis of HF in depressive patients

Depression history had higher mortality (8.8% vs. 6.4%; $P=0.025$), $n=48,612$, multicenter



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Depression, should be treated?

Treatment of depression

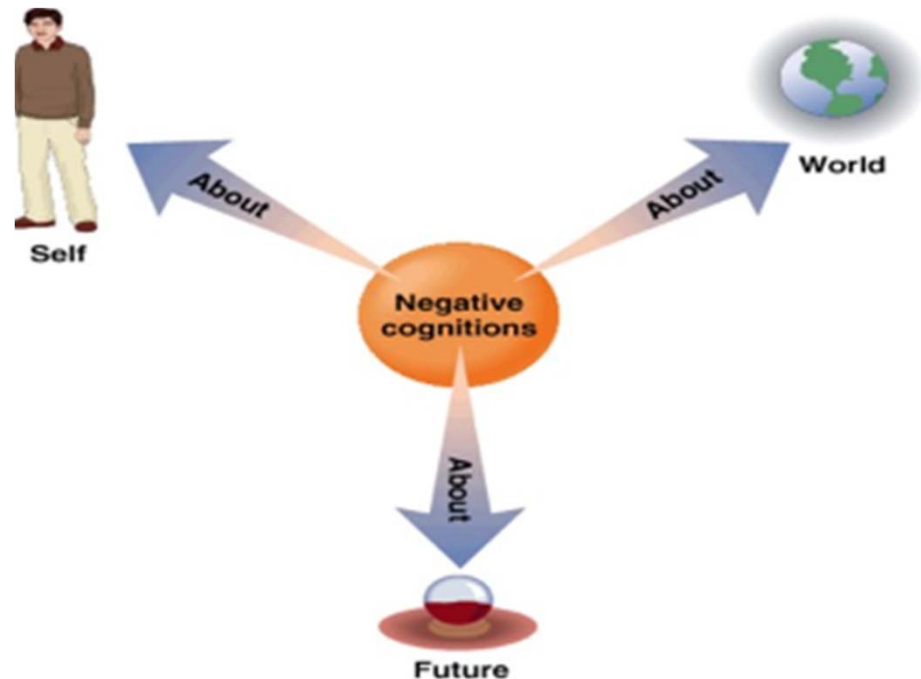
- Cognitive behavior therapy (CBT)
- Aerobic exercise
- Antidepressant Medication
 - selective serotonin **reuptake inhibitor** (SSRI)
 - tricyclic antidepressants (TCA)
 - monoamine oxidase inhibitors (MAOI**s**)
- Electroconvulsive therapy



Treatment of depression

Cognitive behavior therapy (CBT)

- I'm fragile.
- I can't do anything anymore.
- I'm worthless because I can't work.
- I'm a burden on my family.
- My life is over.
- I shouldn't have to deal with this.



Goal is to recognize and changing negative thoughts and maladaptive beliefs.

Outcome study : ?

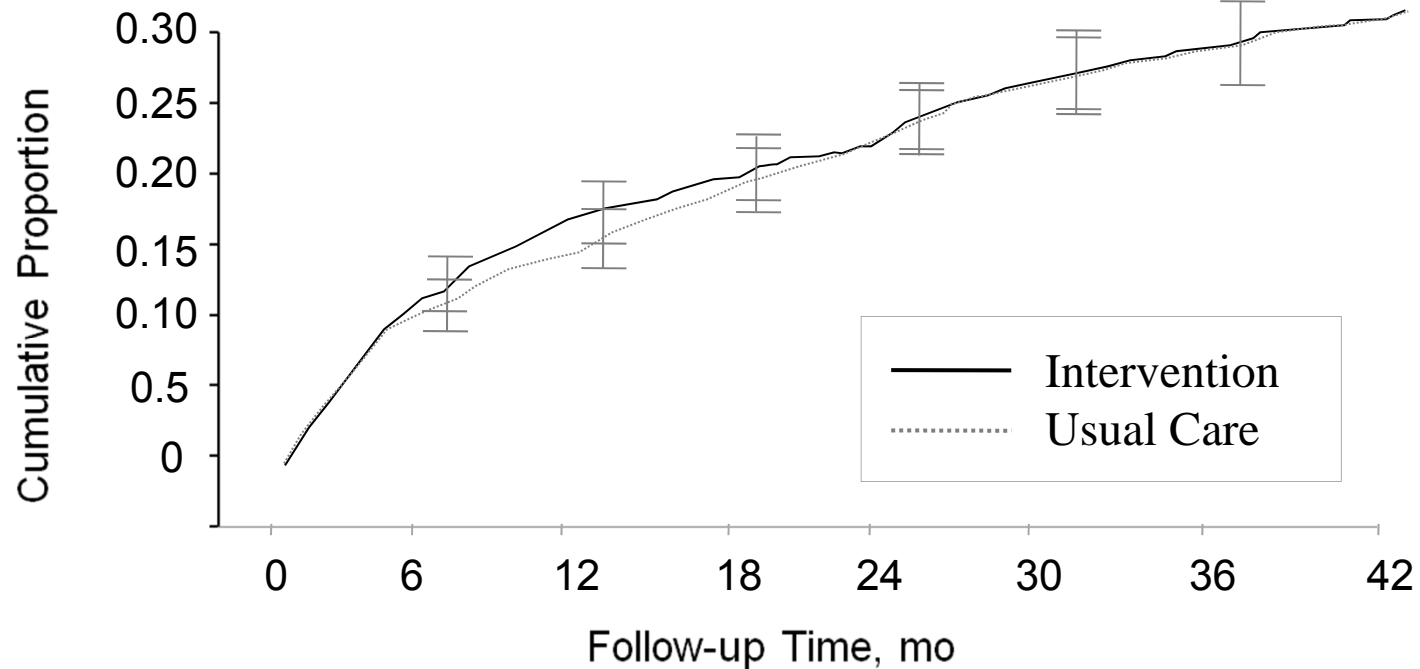
Heart Fail Rev (2009) 14:13–20

ENRICHD Study

- Almost 2500 participants post MI: depressed and/or having low social support
- CBT vs. usual care; seriously depressed patients also could receive sertraline
- Depression improved more in CBT group

ENRICHD (n=2482)

Estimated Probability of Death or Nonfatal Myocardial Infarction



Up to 4-year survival showed no differences in MI recurrence or death; those who received SSRI did better

Aerobic exercise

- Decreased depression
- No evidence of decrease in clinical outcome

(Brosse 2001, review)

- HF patients
- Decreased in depression (22% to 13%)
- Survival benefits only for HF patients with depression who improved exercise capacity

(Milani, 2011)

Depression, should be treated?

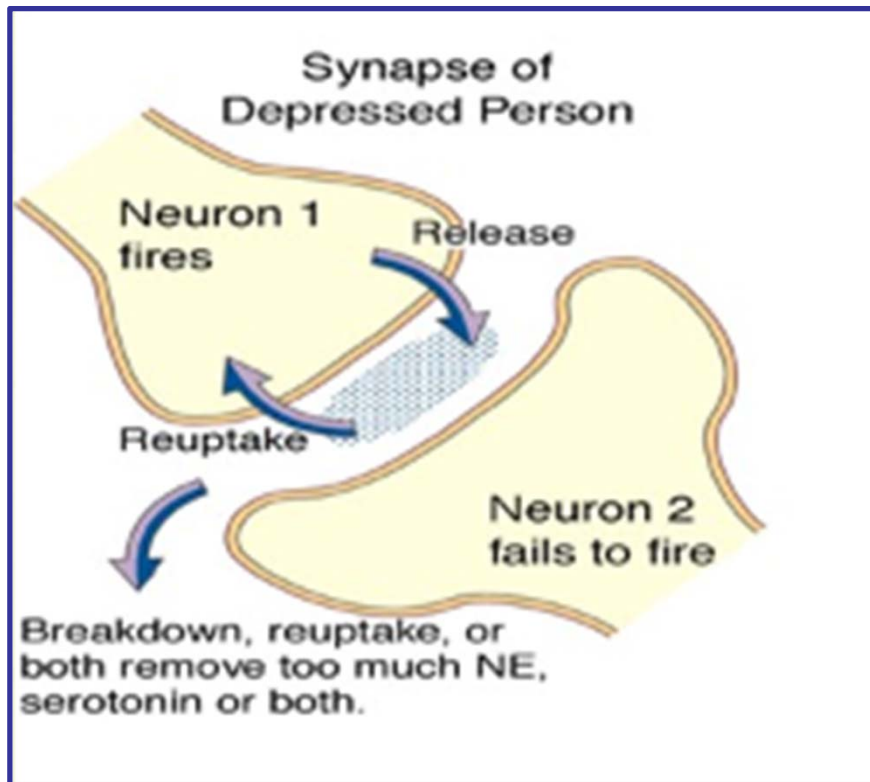
Treatment of depression

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Depression

“ Low levels of norepinephrine and or serotonin ”



- Tricyclic antidepressants (TCA)

- Type Ia antiarrhythmic effects
- increase mortality in HF

- Monoamine oxidase inhibitor (MAOs)

- 거의 사용 안함

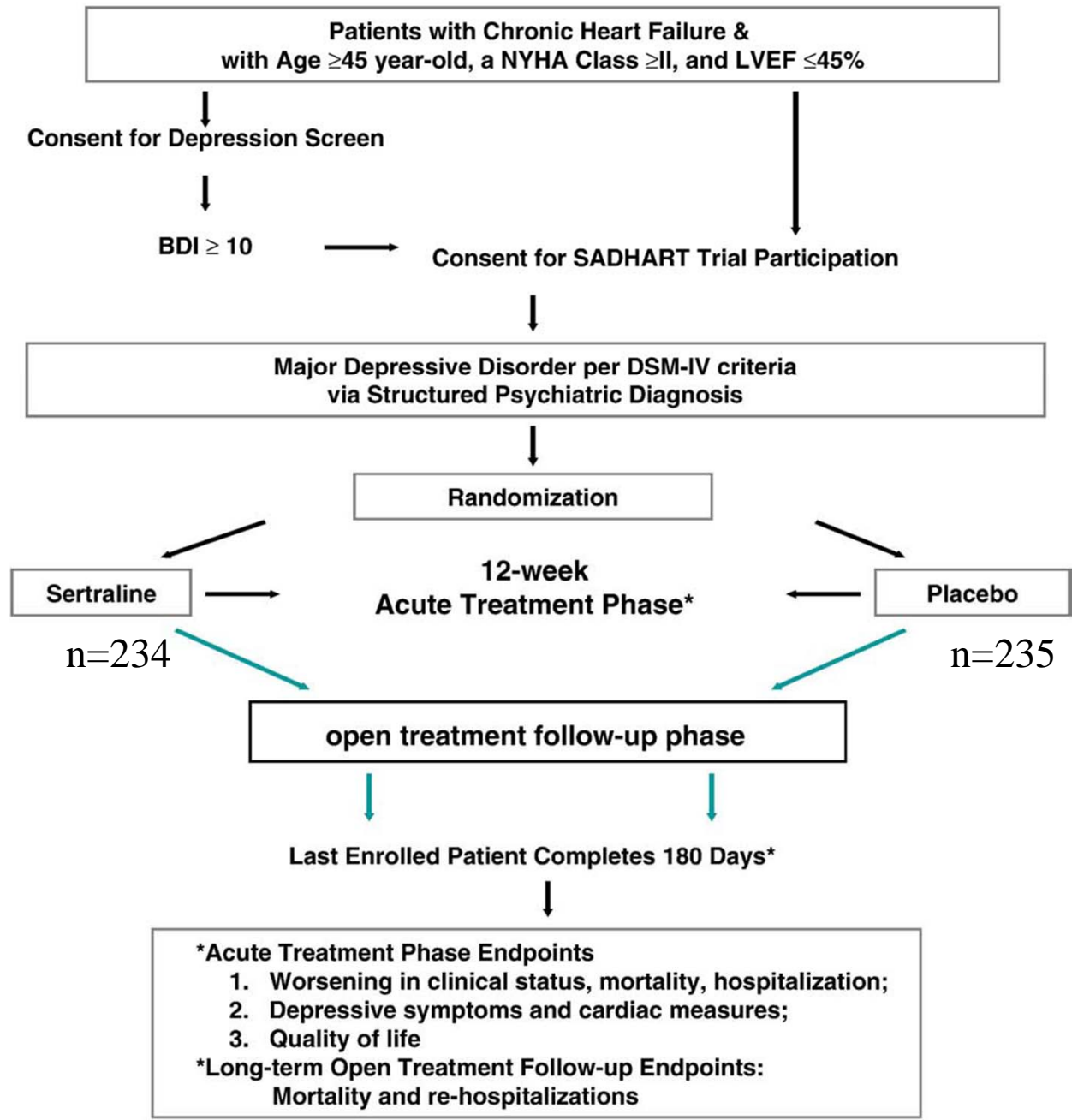
- Selective serotonin antagonist (SSRI)

- Fluoxetine (프로작)
- **Sertraline** (졸로프트)
- Paroxetine (팍실)
- **Citalopram** (씨프람)
- Escitalopram (렉사프로)

Efficacy and safety of antidepressant in HF

<u>Paroxetine</u> CR or placebo for 12 weeks in 28 HF patients (RCT)	Efficacy: changes in BDI score, QoL: changes in MLWHFQ and SF-36	Paroxetine CR significantly improved depression and psychological aspect is of QoL in HF patients
Single dose of <u>imipramine</u> in 15 depressed patients with LVD (open label)	Primary: changes in EF% Secondary: cardiovascular safety	Imipramine does not modify EF% but may be induce severe hypotension (7/15 patients)
<u>Imipramine</u> or bupropione in 10 patients with LVD (RCT, cross-over design)	Cardiovascular safety (EF%, blood pressure)	Imipramine caused severe orthostatic hypotension; bupropione is a safer antidepressant in HF patients
<u>Bupropione</u> (442 ± 47 mg/d) for 3 weeks in 36 depressed HF patients with ventricular arrhythmias and/or conduction delays (open label)	Cardiovascular safety (pulse, blood pressure, 24 h-ECG, EF%)	Bupropion is relatively safe in HF patients. However in 14% of patients bupropion deteriorated arterial hypertension
<u>Fluoxetine</u> (60 mg/d) for 7 weeks in 27 depressed patients with HF, conduction disease and/or ventricular arrhythmias (open label)	Cardiovascular safety (heart rate, 24 h-ECG, EF%, conduction intervals, blood pressure)	Fluoxetine treatment was not associated with the cardiovascular side-effects
<u>Trimipramine</u> (50–200 mg/d) for 28 days in 22 depressed HF patients (NYHA I–III) (open label)	Primary: (efficacy) HAM-D Secondary: cardiovascular safety (24 h-ECG, blood pressure, conduction intervals)	Trimipramine is efficient and relatively safe antidepressant in HF patients. A slight prolongation of QRS was observed.

SSRI is safe and efficient to control the symptom.



SADHART-CHF

HF hospitalization rate
: 8.1% in the sertraline group
: 12.8% in controls (p=0.1)

Depression, should be treated?

- Maybe, yes
 - SSRI and aerobic exercise is effective
 - No treatment options to reduce clinical events so far

순서

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- 심부전에서 우울증이 예후에 미치는 영향
- 치료 및 예후 개선 효과
- **향후 과제**

지침서가 의사들을 움직이게 한다..

AHA Science Advisory

Depression and Coronary Heart Disease

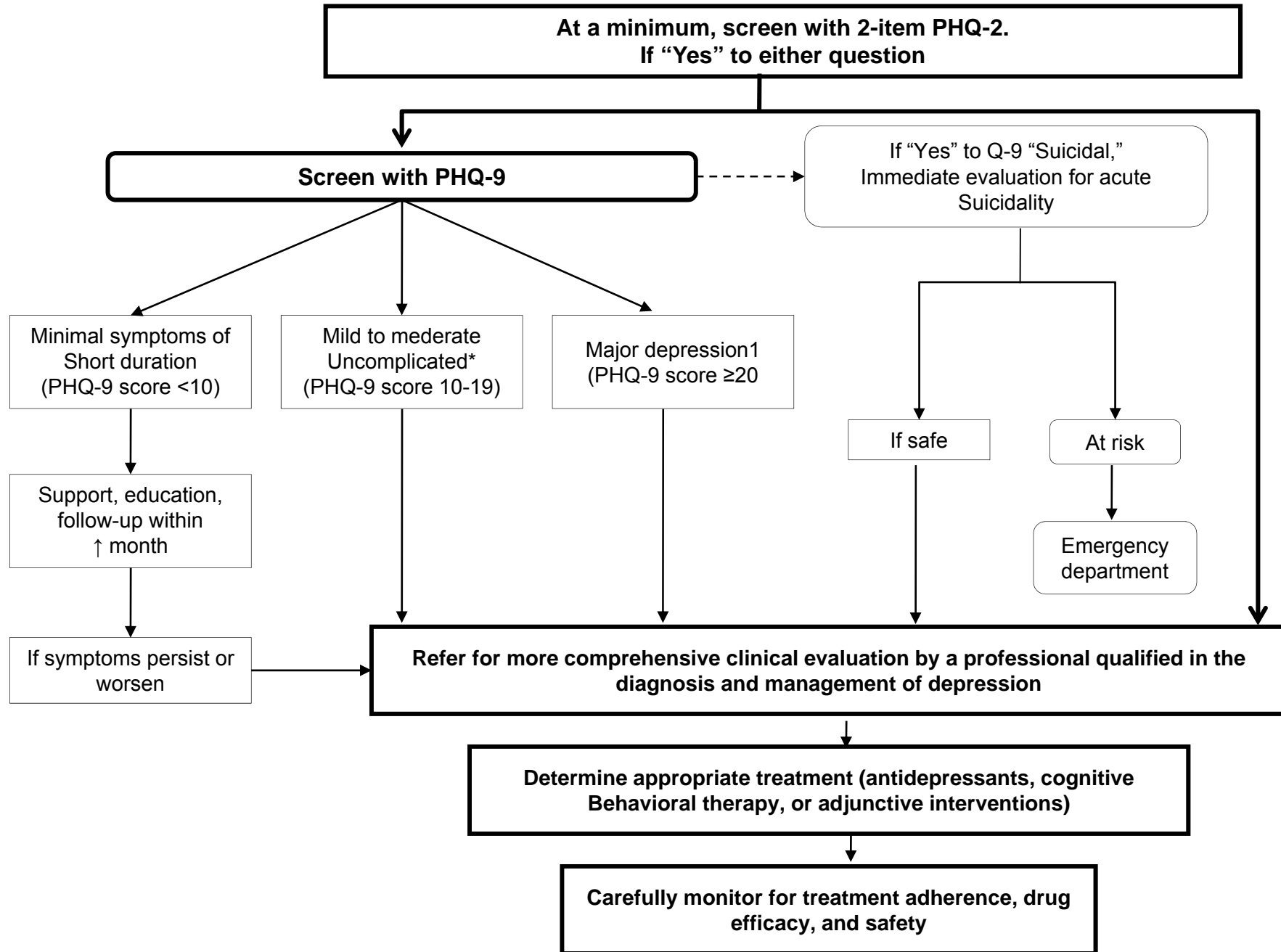
Recommendations for Screening, Referral, and Treatment

A Science Advisory From the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research

Endorsed by the American Psychiatric Association

Judith H. Lichtman, PhD, MPH, Co-Chair; J. Thomas Bigger, Jr, MD;
James A. Blumenthal, PhD, ABPP; Nancy Frasure-Smith, PhD; Peter G. Kaufmann, PhD;
François Lespérance, MD; Daniel B. Mark, MD, MPH; David S. Sheps, MD, MSPH;
C. Barr Taylor, MD; Erika Sivarajan Froelicher, RN, MA, MPH, PhD, Co-Chair

Abstract—Depression is commonly present in patients with coronary heart disease (CHD) and is independently associated with increased cardiovascular morbidity and mortality. Screening tests for depressive symptoms should be applied to identify patients who may require further assessment and treatment. This multispecialty consensus document reviews the evidence linking depression with CHD and provides recommendations for healthcare providers for the assessment, referral, and treatment of depression. (*Circulation*. 2008;118:1768-1775.)



우울 스크린 방법은 간단 : 5-10분

- No standardization
- Common screening tool in Korea
 - Zung Self-rating scale (SDS)
 - 20개 문항을 1-4점
 - 50점 이상 cut-off value (정확도 80%)
 - Beck Depression Inventory (BDI)
 - 전 세계적으로 가장 널리 사용
 - 국내에서도 타당도가 인정
 - 21개 문항을 각 항목당 0-3점으로 평가
 - 16점을 Cut-off value (국내)
 - 외국의 연구에서는 10점을 cut-off value

Zung의 자가평가 우울 척도(Zung Self-Rating Depression Scale)

항목	아니다	가끔 그렇다	자주 그렇다	항상 그렇다
나는 매사에 의욕이 없고 우울하거나 슬플 때가 있다.	1	2	3	4
나는 하루 중 기분이 가장 좋은 때는 아침이다.	4	3	2	1
나는 갑자기 얼마동안 울음을 터뜨리거나 울고 싶을 때가 있다.	1	2	3	4
나는 밤에 잠을 설칠 때가 있다.	1	2	3	4
나는 전과 같이 밥맛이 있다(식욕이 좋다).	4	3	2	1
나는 매력적인 여성(남성)을 보거나, 앉아서 얘기하는 것이 좋다	4	3	2	1
나는 요즈음 체중이 줄었다.	1	2	3	4
나는 변비 때문에 고생한다.	1	2	3	4
나는 요즈음 가슴이 두근거린다.	1	2	3	4
나는 별 이유 없이 잘 피로하다.	1	2	3	4
내 머리는 한결 같이 맑다.	4	3	2	1
나는 전처럼 어려움 없이 일을 해낸다.	4	3	2	1
나는 안절부절해서 진정할 수가 없다.	1	2	3	4
나의 장래는 희망적이라고 생각한다.	4	3	2	1
나는 전보다도 더 안절부절한다.	1	2	3	4
나는 결단력이 있다고 생각한다.	4	3	2	1
나는 사회에 유용하고 필요한 사람이라고 생각한다.	4	3	2	1
내 인생은 즐겁다.	4	3	2	1
내가 죽어야 다른 사람들 특히 가족들이 편할 것 같다.	1	2	3	4
나는 전과 다름없이 일하는 것은 즐겁다.	4	3	2	1

Summary

- 심부전에서 우울증은 40%에 이르는 높은 유병률을 보이며, 주요한 예후 인자이다.
- 서로 연관성이 많은 것은 생물학적 요인 및 사회심리학적 요인에 기초한다
- 치료는 유산소운동과, SSRI가 유효하나, 예후 호전의 증거는 없다.
- 심부전에서 우울증의 예후를 개선할 수 있다는 표준화된 생활치료 (명상, 요가, 등) 에 대한 RCT가 필요
- 한국에서도 임상의 들에게 심부전 치료지침에 우울 스크린 및 정신과에 대한 의뢰할 수 있는 기준이 필요

Q; Depression: Is Symptom or Aggravating Factor in Patients with HF?

A: Depression or depressed mood is an associated symptom of heart failure and independent predictor of worse outcome in patients with HF.

감사합니다

표 7-1. 주요우울삽화의 DSM-IV 진단기준 (요약)

A. 다음 증상 중 5가지 이상이 최소 2주일 간 거의 매일 지속되어야 하며 과거 기능의 변화를 반영해야 한다; 최소한 한 가지 증상은, (1) 우울한 기분 또는 (2) 흥미나 쾌락의 상실이어야 한다.

(1) 하루의 대부분 동안 우울한 기분(소아 및 청소년에서는 과민성 *irritability*)

(2) 거의 모든 활동에서 흥미나 쾌감이 현저히 저하

(3) 현저한 체중 감소 또는 증가, 또는 식욕의 감소 또는 증가

(4) 불면 또는 수면과다

(5) 정신운동성 초조 또는 지체

(6) 피로 또는 에너지 상실

(7) 무가치감 또는 과도하거나 부적절한 죄책감

(8) 사고능력 또는 집중력의 저하 또는 우유부단

(9) 반복적인 죽음에 대한 관념, 자살 사고 또는 자살기도 또는 자살기도에 관한 구체적인 계획

B. 증상이 혼재성 삽화의 기준을 충족시키지 않음

C. 증상이 사회적, 직업적, 또는 다른 중요한 기능 영역에서 임상적으로 심각한 고통이나 장애를 일으킨다.

D. 증상이 물질이나 다른 신체질환에 의한 것이 아님

E. 증상이 사별에 의해 더 잘 설명되지 않는다.

Patient Health Questionnaire-9 (PHQ-9)* Depression : cut-off value > 10

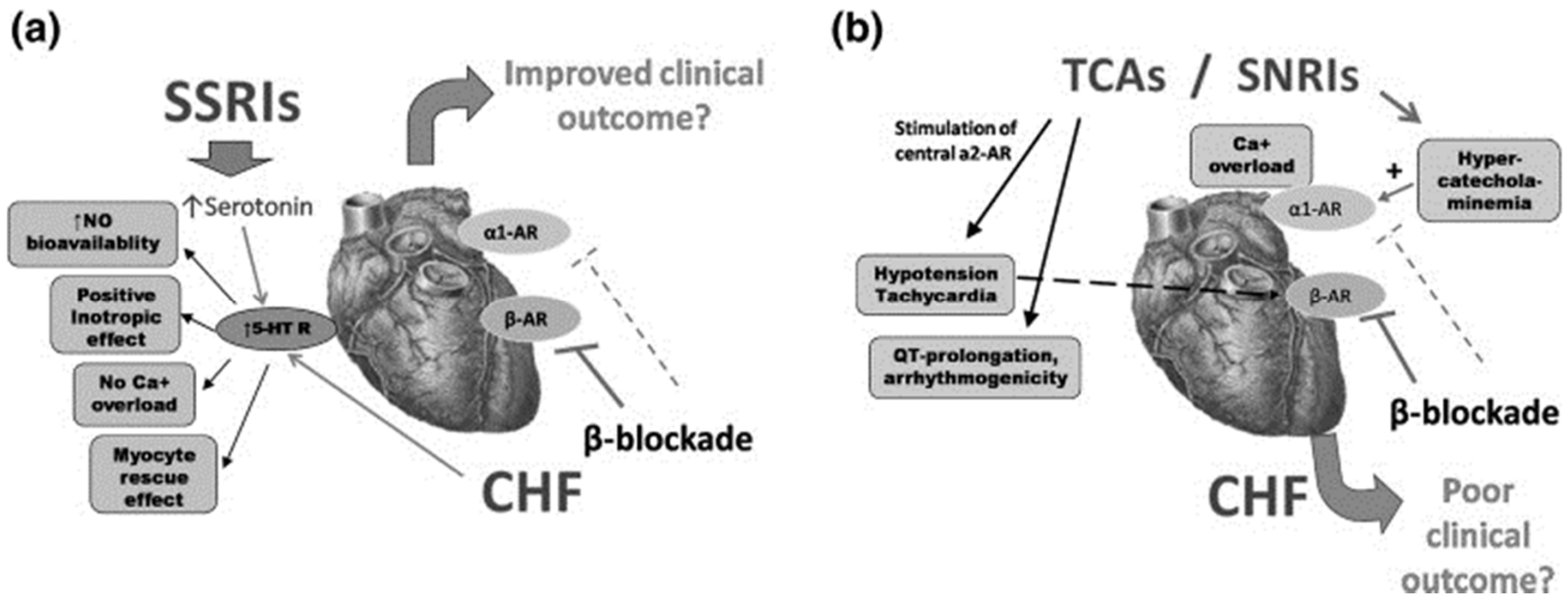
- (1) Little interest or pleasure in doing things.
- (2) Feeling down, depressed, or hopeless.
- (3) Trouble falling asleep, staying asleep, or sleeping too much.
- (4) Feeling tired or having little energy.
- (5) Poor appetite or overeating.
- (6) Feeling bad about yourself, feeling that you are a failure.
- (7) Trouble concentrating on things such as reading or watching TV.
- (8) Moving or speaking so slowly that other people could have noticed.
- (9) Thinking that you would be better off dead or that you want to hurt yourself

*Questions are scored: not at all 0; several days 1; more than half the days 2; and nearly every day 3.
Add together the item scores to get a total score for depression severity.

Antidepressant and HF outcome

(proposed mechanism and interaction with beta blocker)

SSRI is safer than TCA or SNRI



TCA: tricyclic antidepressant, SSRI: selective serotonin reuptake inhibitor
SNRI: serotonin norepinephrine reuptake inhibitors

Treatment of depression

Cognitive behavior therapy (CBT)

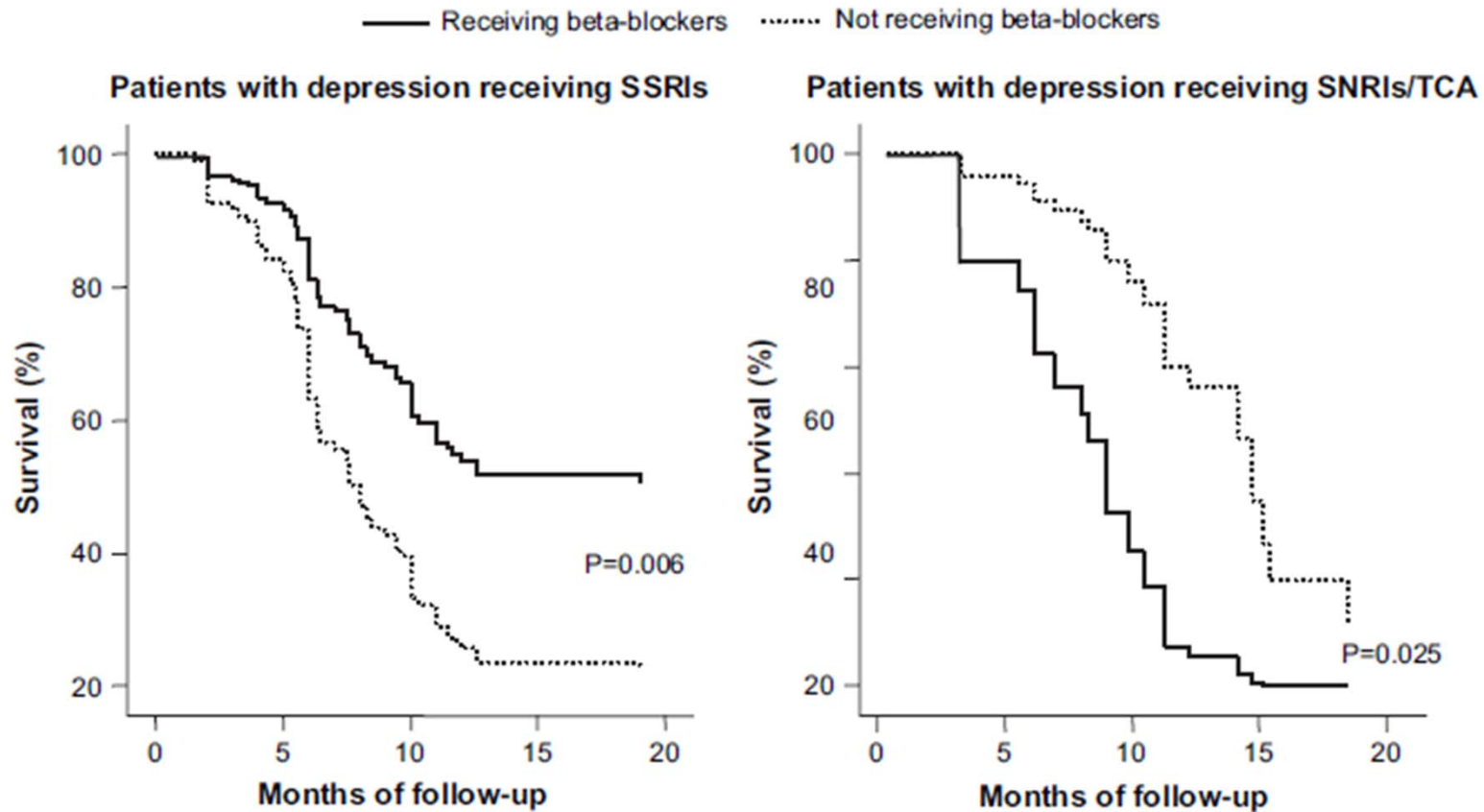
Goal is to recognize and changing negative thoughts and maladaptive beliefs.

Strategy	Intervention
Behavioral activation	(1) <i>activities of daily living</i> (i.e., bathing, grooming, making meals), (2) <i>daily excursions outside of the home</i> (i.e., taking short walks out of the home or going to the store), (3) <i>pleasurable activities</i> (i.e., reading, meditating, doing crossword puzzles), and (4) <i>social stimulation</i> (i.e., attending church or temple, sharing a meal with friends/family members)
Increasing independence	Taking over their daily grooming activities, managing the scheduling of their medical appointments, and shopping and cooking for themselves
Positive health behaviors	Increasing regular exercise and improving dietary intake
Cognitive restructuring	Noticing and challenging automatic thoughts surrounding CHF and depression
Redefining life roles	Challenging old ways of defining the value and worth of your life and attempting to find new activities and roles to take pride in and to define yourself
Coping skills training	Using new coping skills including playful problem solving, positive reappraisal, and seeking social support from family and friends
Family engagement	Incorporating family members into all aspects of cognitive behavioral treatment plan for depression

Outcome study : ?

Heart Fail Rev (2009) 14:13–20

Antidepressant and HF outcome (interaction with beta blocker)



Why high prevalence in HF?

(Biologic and psychosocial factors)

- Underlying biological mechanism of depression (Same in HF)
 - Increased RAA axis
 - Increased hypothalamus-hypophysis axis
 - Increased catecholamine level
 - Low grade systemic inflammation
 - Increased serotonin levels
- Psychological factors
 - Reduced ability for exercise and self-service
 - Poor psychological and social support