Transplantation;
Who Should Get the Heart First?

Hae-Young Lee
Department of Internal Medicine,
Seoul National University Hospital, Seoul,
Korea.

SNUH 서울대학교병원
SEOUL NATIONAL UNIVERSITY HOSPITAL

Contents

- General selection criteria
- Size matters in transplantation
- Broadened indication
  - Elderly population
  - Hepatitis
  - Renal dysfunction
- Consideration of pulmonary problem

General indication for heart transplantation

- Cardiogenic shock requiring either continuous iv inotropic support or MCS with IABP, ECMO or VAD
- Persistent NYHA class IV congestive HF symptoms refractory to maximal medical therapy (LVEF <20%; peak VO2 <12 mL/kg-1/min-1)
- Intractable or severe anginal symptoms in CAD patients not amenable to percutaneous or surgical revascularization
- Intractable life-threatening arrhythmias unresponsive to medical therapy, catheter ablation, and/or implantation of intracardiac defibrillator

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Definition of recipient status: 응급도 0

- 현행: 중환자실 입원 + 다음 한가지 이상 해당 (8일이내 재등록)
  - (LVAD or RVAD) with ventilator
  - ECMO with ventilator

- 개정안: 다음 한가지 이상 (8일이내 재등록)
  - 체외막형 심폐기(V-A ECMO)* 가동중인 환자
  - 심부전으로 인한 인공호흡 중인 환자
  - **기계적순환보조장치(IABP or VAD)가 필요한 Vtac / Vf**
  - VAD를가진 환자가 심각한 합병증**으로 중환자실 입원
    - 혈전색전증, VAD감염, mechanical failure, 반복적 심실성부정맥
  - **비삽입형 심실조력장치(VAD)**

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Definition of recipient status: 응급도 1

- 현행: 입원 + 한가지 이상 해당 (8일이내 재등록)
  - 인공심장(Artifical heart)
  - (LVAD or RVAD) without ventilator
  - ECMO without ventilator
  - IABP
  - 심부전으로 인한 인공호흡기
  - 연속적으로 4주 이상 정맥내 강심제 투여중

Definition of recipient status: 응급도 1

- 개정안: 입원 + 한가지 이상 해당 (8일이내 재등록)
  - **인공심장(Artifical heart)**
  - (LVAD or RVAD) without ventilator**VAD**
  - ECMO without ventilator → 응급도 0으로 상향
  - **IABP**
  - **심부전으로 인한 인공호흡기 → 응급도 0으로 상향**
  - 연속적으로 4주 이상 정맥내 강심제 투여중
  - 최소 1주 이상 고용량 (Dopa/Dobu > 10μg/kg/min)의 단일 강심제 또는 두가지 이상의 중증도 (Dopa/Dobu > 5μg/kg/min) 이상 강심제
  - 지속성 심실빈맥/심실세동이 자주 반복되거나 심실재세동기(ICD)가 자주 작동하는 경우
    - 항부정맥제 사용이나 부정맥 시술을 시행했던 경우 24시간 이내 ≥ 3회

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Definition of recipient status: 응급도 2

- 현행: 4주 미만 강심제 투여 중 (8일이내 재등록)

- 개정안: 다음 한가지 이상 (1달마다 재등록)
  - 1주 이상 강심제 투여중이나 응급도1이 아닌경우
  - 항부정맥제를 사용중이거나 부정맥 시술을 시행했던 경우로 심실빈맥/심실세동이 나타나거나 ICD가 작동한 경우

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응급도 합산 / 유지

- 대기기간 합산관련 개정
  - 응급도 0, 1, 2인 경우 응급도 하향 조정될 때에는 이전 응급도의 대기기간을 포함

- 응급도 유지기간 개정
  - 응급도가 한번 선정되면 중간에 상태변화가 있어도 유지 기간 동안 유지
    - ECMO로 응급도 0으로 인정받은 사람은 ECMO를 중단하더라도 7일간 응급도 유지

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가산점 제도

- 대기 시간
  - 응급도 0의 경우 0.5점/일 가산되어 최대 8점
  - 응급도 1 이상에서는 매주 0.5점 가산 (최대 8점)
- 혈액형 및 권역별 배분
  - 같은 응급도 내에서는 다음 순서로 배분
    ① 기증자와 같은 권역에 있는 **동일혈액형** 대기자
    ② 기증자와 다른 권역에 있는 동일혈액형 대기자
    ③ 기증자와 **같은 권역**에 있는 호환혈액형 대기자
    ④ 기증자와 다른 권역에 있는 호환혈액형 대기자
  - AB형은 B형과 같이 취급
  - 과거 동일 병원/동일시/동일지역/동일권역/다른 권역을 단순화
- 감염질환유무, 나이차이, 체중차이, 폐크기차이, 원인질환 유형은 삭제
- 본인/친척 기증 전력 항목은 유지

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2015년 혈액형에 따른 심장 이식 환자수

- ABO type에 따른 이식 환자수
  - A 71 (6)
  - B 46 (5)
  - O 42
  - AB 24 (6 B, 5 A)

Initial report of the Korean Heart Transplant Registry:
The first report of Korean Organ Transplant Registry (KOTRY) – Heart transplantation
Korean Circulation Journal. In revision

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연령에 따른 가산점은 대폭 완화됨

종전		개정 후	
만 20세 미만	3점	만 19세 미만	2점
만 20세~55세 미만	2점		
만 55세~65세 미만	1점	만 19세 이상	1점
만 65세 이상	0점	(심장)만 70세 이상 (폐)만 65세 이상	0점

Absolute contra-indication for heart only TPL

- Systemic illness with a life expectancy < 2 y despite HT, including active or recent solid organ or blood malignancy within 5 y
- AIDS with frequent opportunistic infections
- Systemic lupus erythematosus, sarcoid, or amyloidosis that has multisystem involvement and is still active
- Irreversible renal or hepatic dysfunction
- Co-existing lung disease
  - Significant obstructive pulmonary disease (FEV1 <1 L/min)
  - Fixed pulmonary hypertension
  - Pulmonary artery systolic pressure > 60 mm Hg
  - Mean transpulmonary gradient > 15 mm Hg
  - Pulmonary vascular resistance > 6 Wood units

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Current indication of heart size

- Heart size: 30-130% of recipient heart (body weight based)

  undersized donors with
- Weight mismatch > 20% do not result in increased mortality, except in recipients with elevated pulmonary vascular resistances
- When female donors are considered for male recipients, a 10% weight mismatch limit is recommended

Impact of low donor to recipient weight ratios on cardiac transplantation

(J Thorac Cardiovasc Surg 2013;146:1538-43)

Senthil Nathan Jayarajan, MD,[a] Sharven Taghavi, MD,[a] Eugene Komaroff, PhD,[b] and Abeel A. Mangi, MD[c]

- In male donor to male recipient, male donor to female recipient, and female donor to female recipient HT, the use of small heart (donor to recipient body weight ratio 0.6-0.89) did not influence median survival and was not associated with increased mortality.
- In female donor to male recipient HT, WRL was associated with decreased median survival and was associated with increased mortality.

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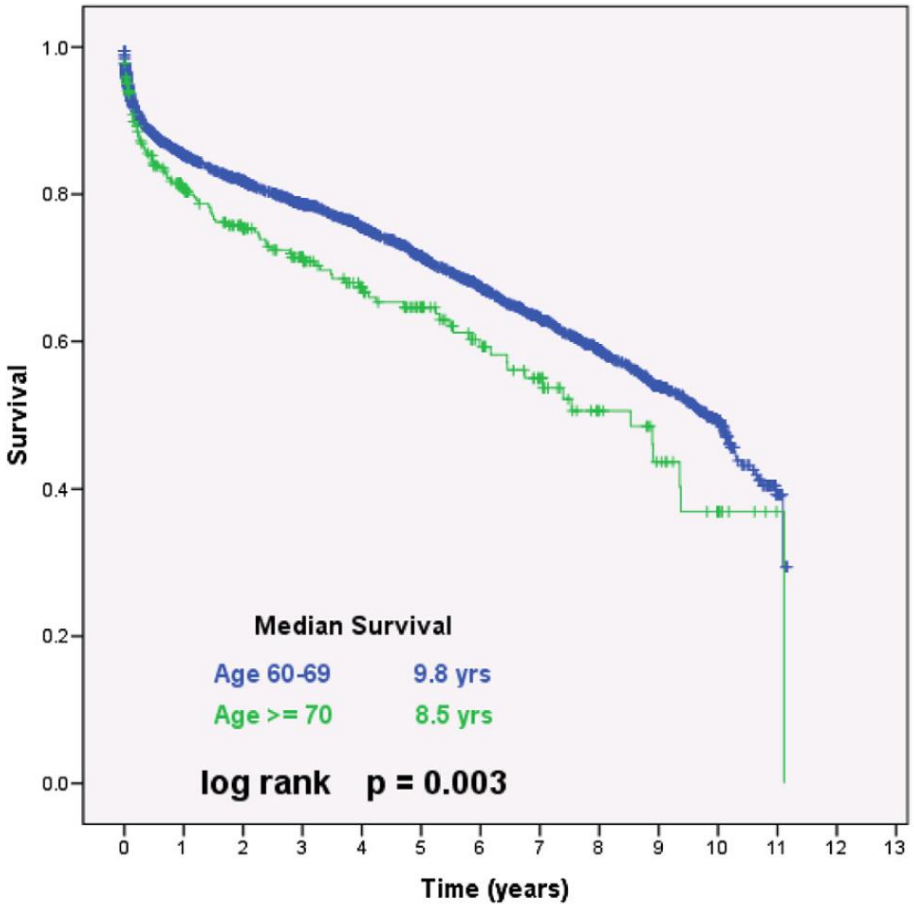
“innocent heart sentenced to life in Cheney?”

Received heart TPL at the age of 72

Elderly (>70YO) ALSO can derive benefit from TPL, although survival is inferior to that of 60-69 YO

- No difference in the incidence of CVA, length of stay, or pacemaker need between groups
- Less likely to be treated for rejection 1st year
- Age was a multivariate predictor of death (HR, 1.289; 95% CI, 1.039 –1.6; *p* 0.021)
  - Conditional on 1-year survival, recipient age ceases to be a predictive factor for death, suggesting that **advanced age only imparts a higher risk of death during the first year after transplantation**



Data from UNOS. J Heart Lung Transplant 2012;31:679–85

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Multivariate analysis of risk factors for death conditional on 1 year survival

Table 4 Multivariate Predictors of Death

Variable	HR (95% CI)	*p*-value
Age ≥ 70 years	1.289 (1.039–1.6)	0.021
Male recipient	0.81 (0.7–0.936)	0.004
Donor age	1.009 (1.005–1.013)	<0.0005
ABO match vs identical	1.218 (1.055–1.406)	0.007
Diagnosis vs DCM		0.001
Ischemic	1.237 (1.089–1.404)	
Other	0.999 (0.84–1.188)	
Recipient diabetes	1.248 (1.113–1.399)	<0.0005
Ventilator support	1.75 (1.345–2.277)	<0.0005
Bilirubin	1.02 (1.011–1.028)	<0.0005
Creatinine	1.144 (1.088–1.203)	<0.0005
Dialysis	3.245 (1.977–5.325)	<0.0005
Ischemic time	1.064 (1.013–1.116)	0.015

CI, confidence interval; DCM, dilated cardiomyopathy; HR, hazard ratio.

Variable	HR (95% CI)	*p*-value
Donor age	1.006 (1.000–1.012)	0.036
ABO match vs identical	1.283 (1.025–1.606)	0.029
Recipient diabetes	1.441 (1.214–1.711)	<0.0005
Previous malignancy	1.612 (1.197–2.173)	0.002
Treated for rejection 1st year	1.314 (1.121–1.541)	0.001

Early and mid-term (50 months) results in elderly patients (> 60YO) were similar to younger patients

Korean J Thorac Cardiovasc Surg 2013;46:111-116 □ Clinical Research □

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Heart Transplantation in the Elderly Patients: Midterm Results

Sang Yoon Yeom, M.D.[1], Ho Young Hwang, M.D., Ph.D.[1], Se-Jin Oh, M.D.[1], Hyun-Jai Cho, M.D., Ph.D.[2], Hae-Young Lee, M.D., Ph.D.[2], Ki-Bong Kim, M.D., Ph.D.[1]

Background: Heart transplantation in elderly patients has raised concerns because of co-morbidities and limited life expectancy in the era of donor shortage. We examined the outcomes after heart transplantation in elderly patients. ***Materials and Methods:*** From March 1994 to December 2011, 81 patients (male:female=64:17, 49.1±14.0 years) underwent heart transplantation. The outcomes after heart transplantation in the younger patients (<60 years; group Y, n=60) were compared with those in the elderly patients (≥60 years; group O, n=21). The follow-up duration was 51.8±62.7 months. ***Results:*** Early mortality (≤30 days) occurred in 5.0% (3/60) and 4.8% (1/21) of groups Y and O, respectively (p>0.999). There were no differences in overall survival between the two groups (p=0.201). Freedom from rejection was higher in group O than in group Y (p=0.026). Multivariable analysis revealed that age ≥60 years was not a significant risk factor for long-term survival; postoperative renal failure was the only significant risk factor for long-term survival (p=0.011). ***Conclusion:*** Early and mid-term results of heart transplantation in elderly patients were similar to those in younger patients.

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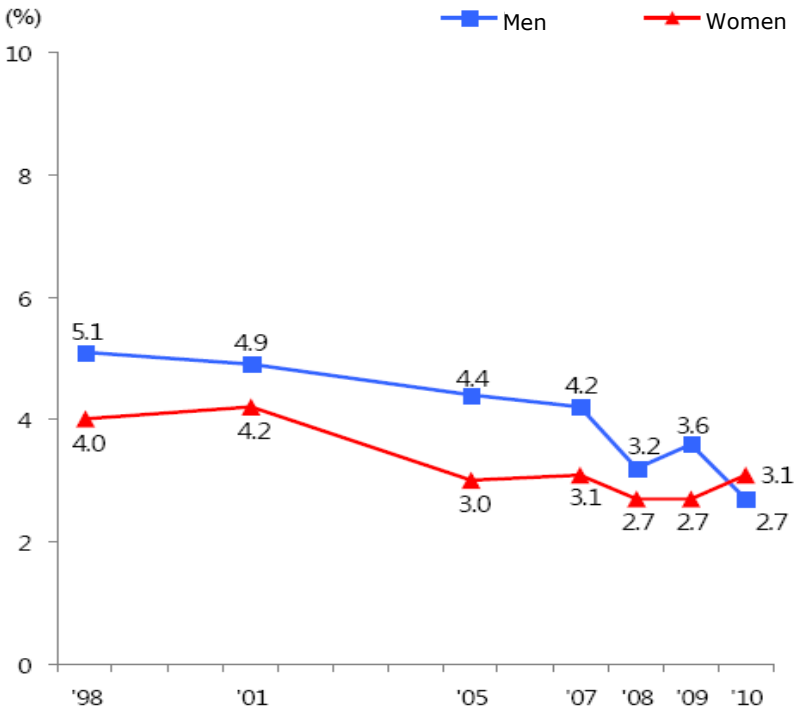
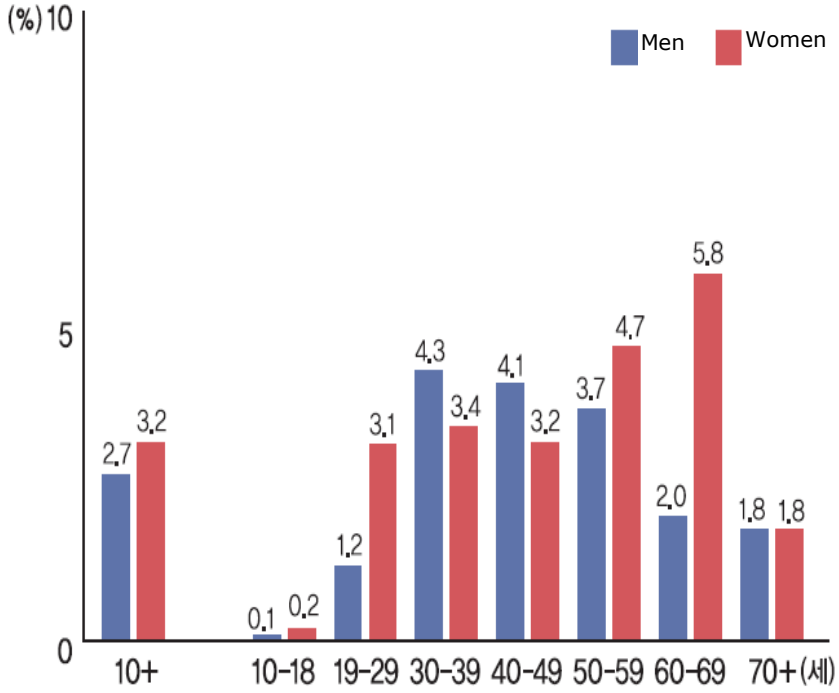
HBV infection is endemic in Korea





HBsAg (+) rate was 2.7% in men, 3.1% in women.
Age range is narrowed 30 to50, the prevalence is 5%

Korean National health and nutrition examination survey , 2010

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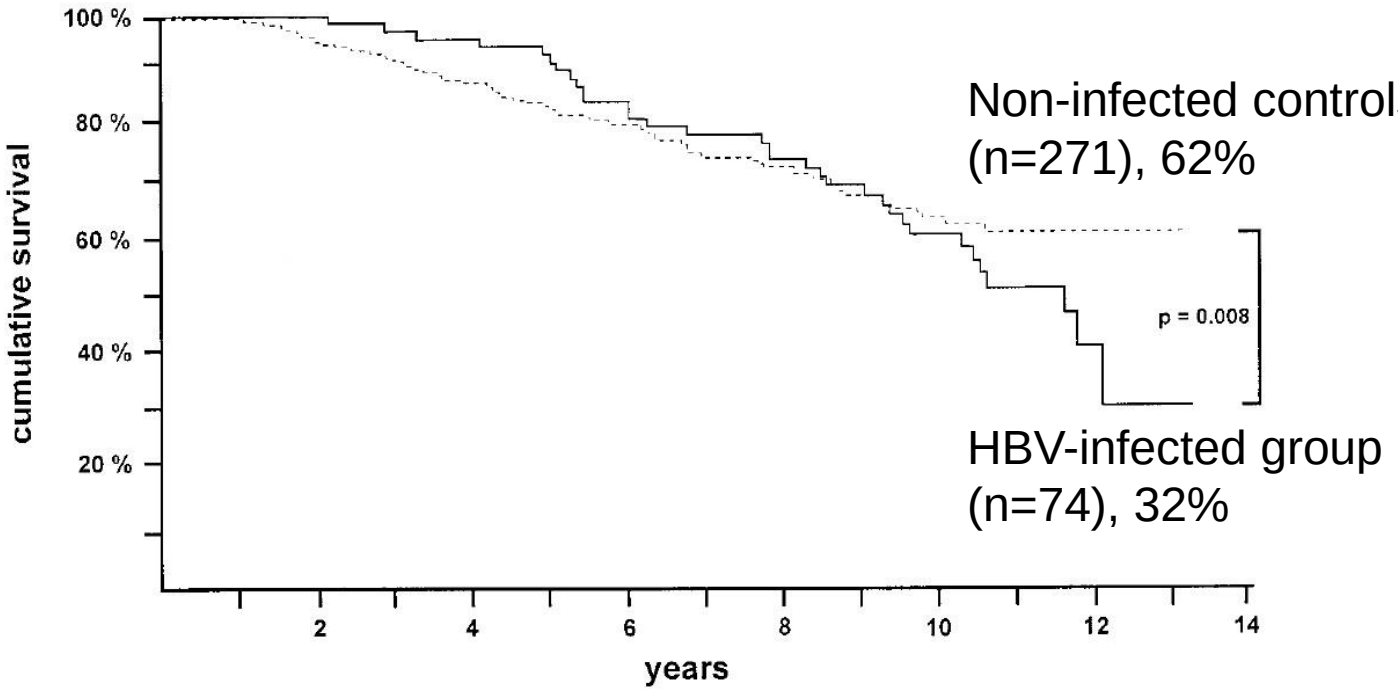
Long-term outcome of HBV in heart transplantation



Cumulative survival was significantly reduced after more than 10 years.
6/74 HBsAg-positive patients died caused by liver failure.

HBV-infection: de novo infection(n=69),
HBsAg-positive before TPL(n=3),
HBsAg-negative but anti-HBc positive before TPL (n=2)

Wedemeyer H, et al. Transplantation. 1998 Nov 27;66(10):1347-53.

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HBV (+) recipients have perioperative results and long-term survival rates comparable to HBV (–) recipients.

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The impact of hepatitis B on heart transplantation: 19 years of national experience in Korea

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Hyo-Sun Shin
BCD 1,2 Hyun-Jai Cho
AB 3 Eun-Seok Jeon
AB 4 Jae-Joong Kim
B 2,5 Ho Young Hwang
B 2,5 Ki-Bong Kim
B 1,2 Byung-Hee Oh
ABCDEFG 1,2 Hae-Young Lee

1 Division of Cardiology, Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea
2 Seoul National University Hospital Transplantation Center, Seoul, South Korea
3 Department of Cardiology, Samsung Medical Center, Seoul, South Korea
4 Division of Cardiology, Department of Internal Medicine, Asan Medical Center, College of Medicine, University of Ulsan, Seoul, South Korea
5 Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul, South Korea

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HBV (+) recipients have perioperative results and long-term survival rates comparable to HBV (–) recipients.

- HBV (+) recipients have perioperative results and long-term survival rates comparable to HBV (–) recipients.
- However, **absence or cessation of antiviral prophylaxis indiscriminately brought reactivation of HBV**, which rapidly progressed to hepatic failure and death.
- Nineteen years of national experience strongly suggests that **long-term antiviral prophylaxis is necessary for HBV (+) recipient.**

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Preoperative and postoperative prophylaxis

- Perioperative prophylaxis
  - Donor 가 HBsAg (+) 인 경우
    - HBIg를 이용한 passive immunization: HBIG 20,000 IU (원내: IV-Hepabig 10 vials 임)
    - 이식 전 48시간 이내에 투여 (D-code).
  - Donor 가 HCV Ab (+) 인 경우 HCV RNA titer 0 + Liver 가 정상임이 확인되지 않으면 심장 이식 시행 불가
- Post-operative long term treatment
  - Prophylactic antiviral therapy is required with the initiation of immunosuppressive therapy
  - Entecavir or tenofovir as first choice in case of high levels of HBV DNA or when long-term treatment periods are expected.

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Combined heart-kidneyTPL could reduce postoperative mortality in end-stage HF with renal dysfunction.

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Original Paper

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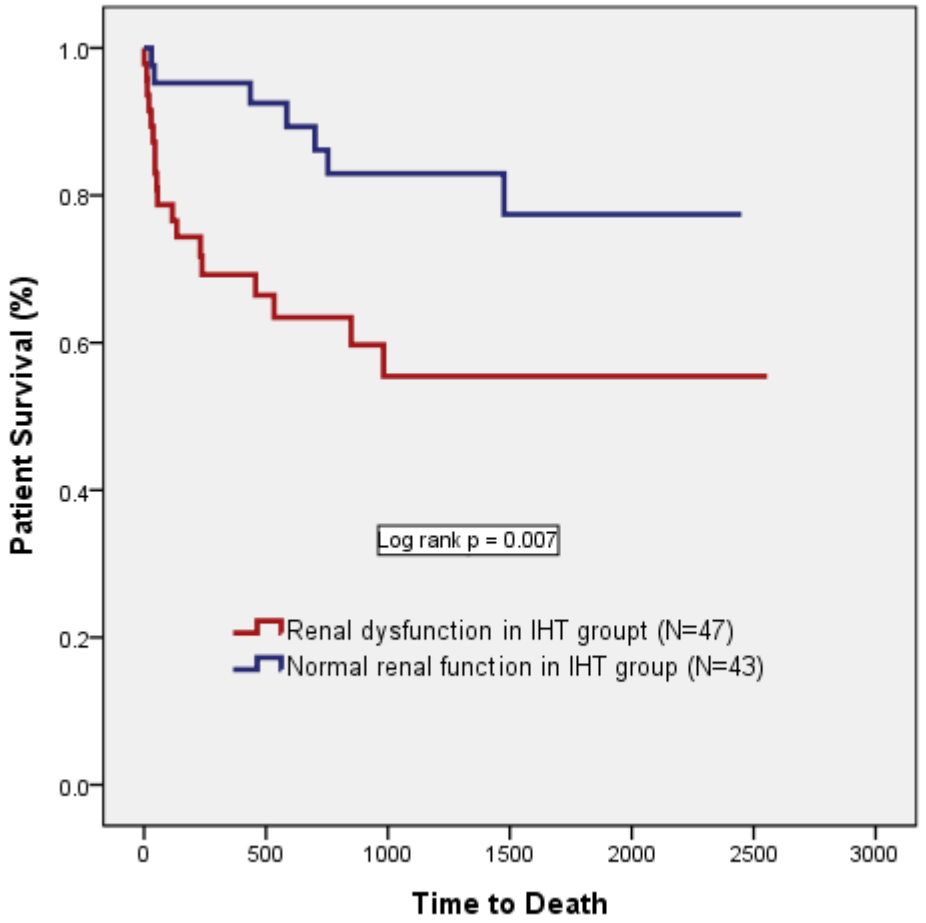
Impact of perioperative renal dysfunction in heart transplantation: Combined heart and kidney transplantation could help to reduce postoperative mortality

Joo Myung Lee[1ABCDEF], Seung-Ah Lee[1AB], Hyun-Jai Cho[1ABCDEF], Han-Mo Yang[1ABC], Hae-Young Lee[1ABC], Ho Young Hwang[2AB], Ki-Bong Kim[2AB], Sang-Il Min[3AB], Jongwon Ha[3AB], Jae Seok Yang[4AB], Curie Ahn[4AB], Young-Bae Park[1AB], Byung-Hee Oh[1AB]

[1] Department of Internal Medicine and Cardiovascular Center, Seoul National University Hospital, Seoul, Korea
[2] Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul, Korea
[3] Department of Surgery, Seoul National University Hospital, Seoul, Korea
[4] Department of Internal Medicine and Transplantation Center, Seoul National University Hospital, Seoul, Korea

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Renal dysfunction significantly impairs patients' survival



	1M	3M	6M	1Y	5Y
Normal renal function	42 (95%)	40 (95%)	39 (95%)	37 (95%)	
Renal dysfunction	42 (79%)	37(77%)	32 (74%)	25 (69%)	2 (55%)

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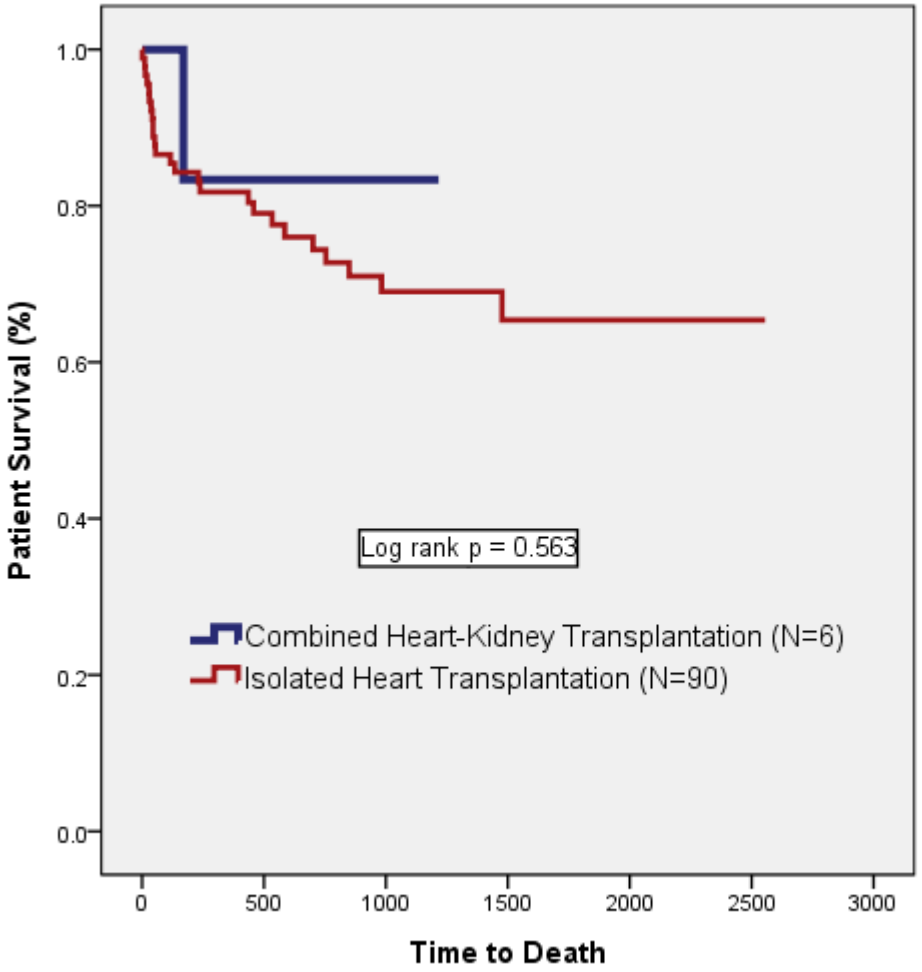
Combined heart-kidneyTPL could reduce postoperative mortality in end-stage HF with renal dysfunction



	1M	3M	6M	1Y	5Y
CHKT	6 (100%)	6 (100%)	5 (83%)	4 (83%)	
IHT	84 (87%)	77(85%)	71 (84%)	92 (82%)	9 (65%)

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Combined heart-kidneyTPL could reduce postoperative mortality in end-stage HF with renal dysfunction

- The main criteria of CHKT included
  - baseline estimated eGFR for 3 months < 40 ml/min/1.73 m2,
  - preoperative eGFR less than 40 ml/min/1.73 m2 despite hemodynamic optimization with intravenous inotropes and vasodilators measured on at least 3 occasions, or mechanical circulatory support.
  - 말기 신부전 환자 중 심장 수축 기능이 35% 이하로 떨어져 있으며 3-4 개월 이상 최상의 심부전 치료로도 심장 기능의 회복이 없는 환자

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- **Consideration of pulmonary problem**

Pulmonary artery hypertension

- Heart transplantion contraindicated
  - transpulmonary gradient > 15 mmHg
  - fixed pulmonary vascular resistance >5 Wood units
- Re-evaluate after vasodilator treatment
  - selective pulmonary vasodilators (sildenafil), LVAD등을 이용하여 pulmonary pressures를 감소
  - pulmonary vascular resistance 상승된 환자에서 4-8주간 milrinone ± pulmonary vasodilators (including sildenafil) 등을 사용하여 PVR을 낮추고 reevaluation

Consideration of heart-lung co-transplantation

- WHO functional class III or IV
- Mean right atrial pressure >10 mmHg
- Mean pulmonary arterial pressure >50 mmHg
- Cardiac index <2.5 L/min per m2
- Failure to improve functionally despite medical Tx
- Rapidly progressive disease

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심폐동시 이식 응급도 완화

- **55세 미만 심폐동시대기자의 경우 심장이 매칭이 되면 폐 응급도 0이 없는 경우 심폐를 같이 이식**
- **폐이식 응급도 0**
  - **입원한 환자로 다음 한가지 이상 해당(8일이내 재등록)**
    - **호흡부전증으로 인공호흡기를 부착중**
    - **체외막형 심폐기를 가동중**
- **폐이식 응급도 1**
  - 2개월마다 재등록하며 검사시점과 상관없이 인정
  - (개정) 산소 투여 없이 측정한 PaO2〈 55mmHg
  - (개정) 평균폐동맥혈압 〉65mmHg, 또는 평균우심방혈압 〉15mmHg
  - (현행유지) Cardiac index 〈 2L/min/m2 인 경우
  - (신설) 동맥혈검사상 PCO2≧80mmHg인 경우
  - (신설) 입원환자중 high flow nasal cannula 30L FiO2≧0.6로 2주 이상 유지중인 경우(유지중에만 인정)

Economical/Emotional stress: Need for familial support

- Considerable number of patients died due to self discontinuation of immunosuppressive agents… "Suicide in fact"
- Economic burden during/after heart transplantation (본인 부담)
  - 이식 수술 입원비: 20,000,000 – 28,000,000원
  - 외래 관리비 (약제비 포함) : 140,000 – 170,000원/월
  - 조직 검사 입원비: 약 500,000원 x 연간 2회
- Familial relationship must be considered seriously before transplantation
- Further social support required to reduce economical burden

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요약 및 결론

- 개정 예정인 심장 응급도의 개요
  - 심실조력장치, 인공심폐기 등 세부항목 개정
  - 부정맥 항목 신설
- 가산점 항목 개정
  - 대기기간 가산점을 대폭 상향조정
  - 나이 및 임상적 판단의 부분은 가산점 완화/삭제
  - 혈액형, 권역에 따른 우선배분 원칙 적용
- 심폐 동시이식 제도 개선
  - 심폐 응급도 유지기간 개정
  - 심폐 대기기간 합산관련 개정
- 심폐동시대기자 대상 완화

Thank you for your attention.

고용량 또는 중등도 강심제

	고용량	중등도
Dopamine	10	5
Dobutamine	10	5
Milronone	0.75	0.5
Epinephrine	0.1	0.05
Norepinephrine	0.1	0.05
Isoproterenol	0.05	0.03

μg/kg/min

SNUH