Brigham and Women's Hospital
Founding Member, Mass General Brigham

Pre-Kidney Transplant Evaluation of Recipients

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DISCLOSURES

Clinical Trials activities :

- Alpine, Phase I/IIa Povetacicept in Primary IgA nephropathy, Membranous nephropathy
- Otsuka, Phase III Sibeprenlimab in Primary IgA nephropathy
- Alexion, atypical HUS global registry
- Natera, The Prospera Kidney Transplant ACTIVE Rejection Assessment registry (ProActive) study
- Novartis, Phase III Iprtacopan in adult atypical hemolytic uremic syndrome (aHUS) patients who are naïve to complement inhibitor therapy

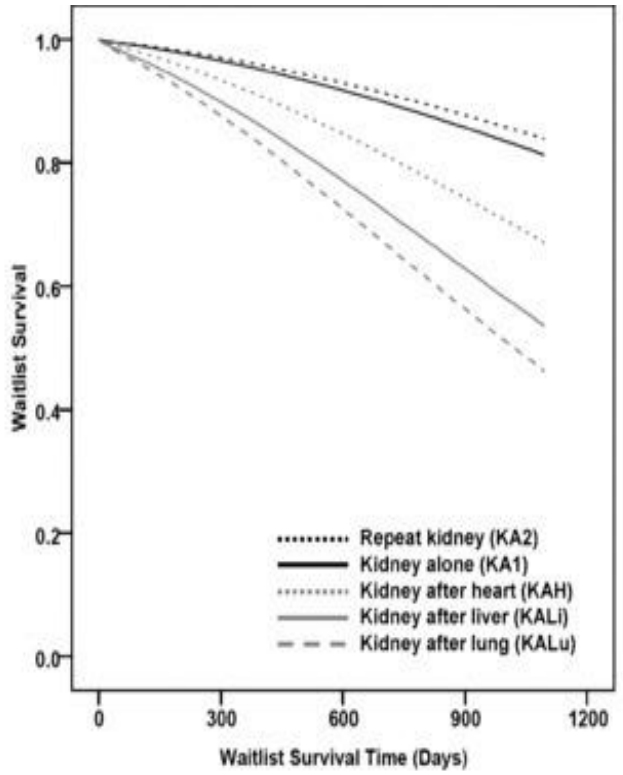
Why get a kidney transplant?

Who should get a kidney transplant?

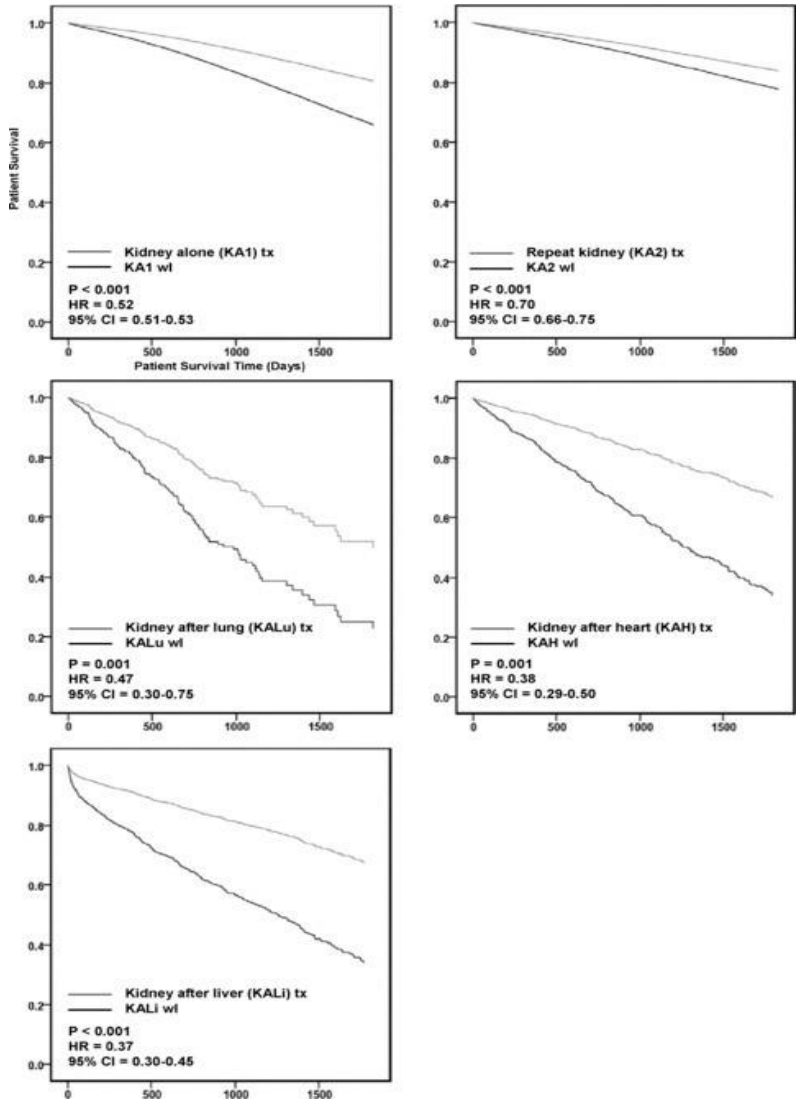
When is the best time for a candidate to get a kidney transplant?

→ Not all patients are suitable candidates for transplantation

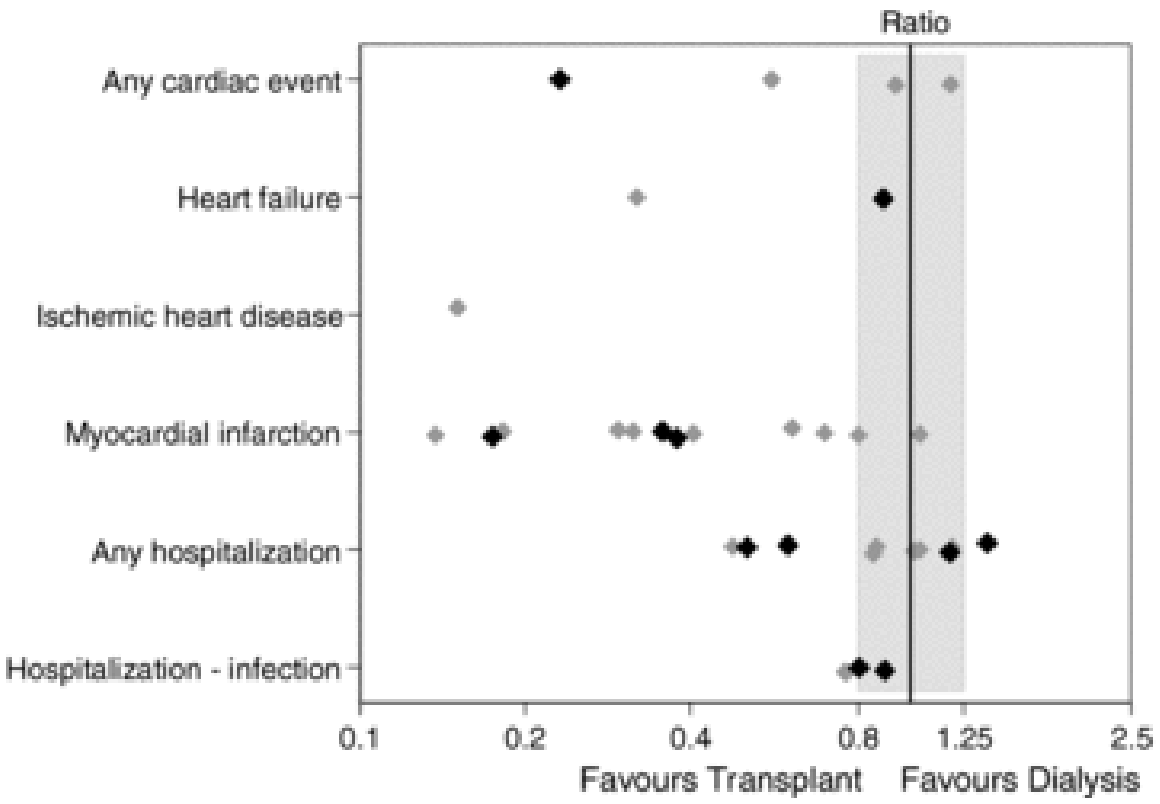
Why get a kidney transplant?

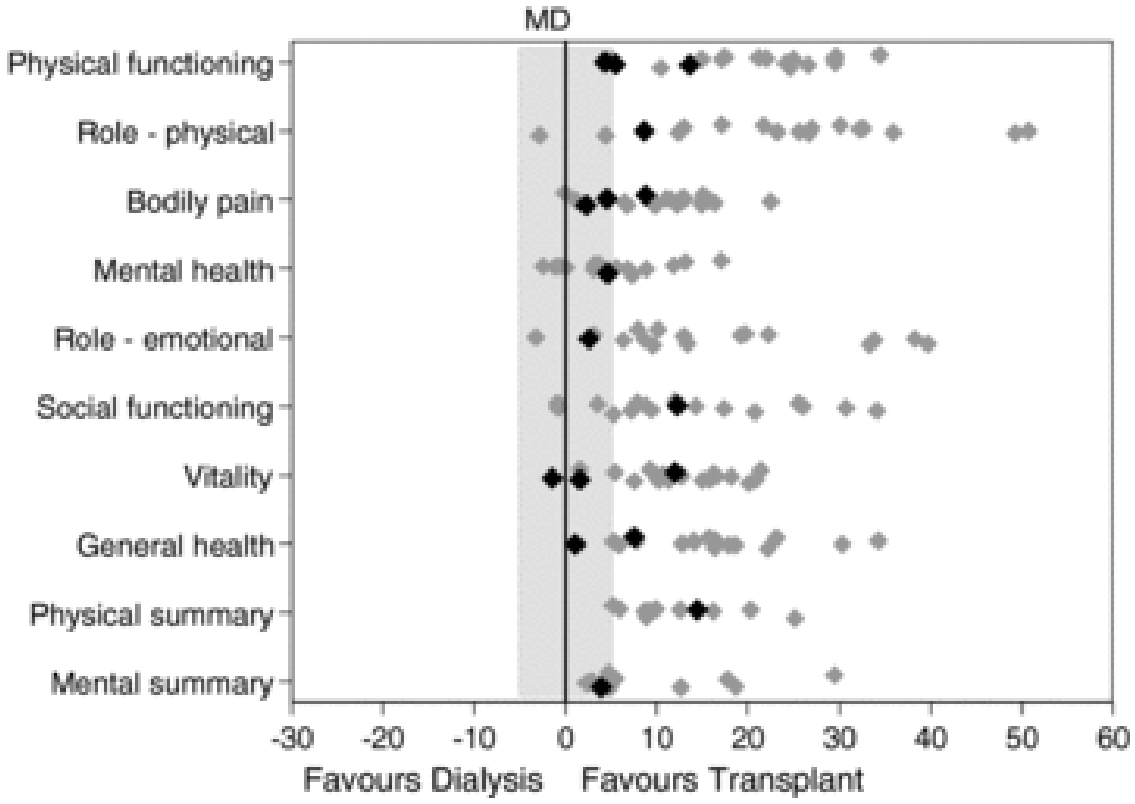


Waitlist Group	Significance	Hazard Ratio	95% Confidence Interval
Kidney alone (KA1)	p < 0.001	reference	
Repeat kidney (KA2)	p < 0.001	0.84	0.81-0.88
Kidney after lung (KALu)	p < 0.001	3.80	3.08-4.69
Kidney after heart (KAH)	p < 0.001	1.92	1.66-2.22
Kidney after liver (KALi)	p < 0.001	2.69	2.46-2.95



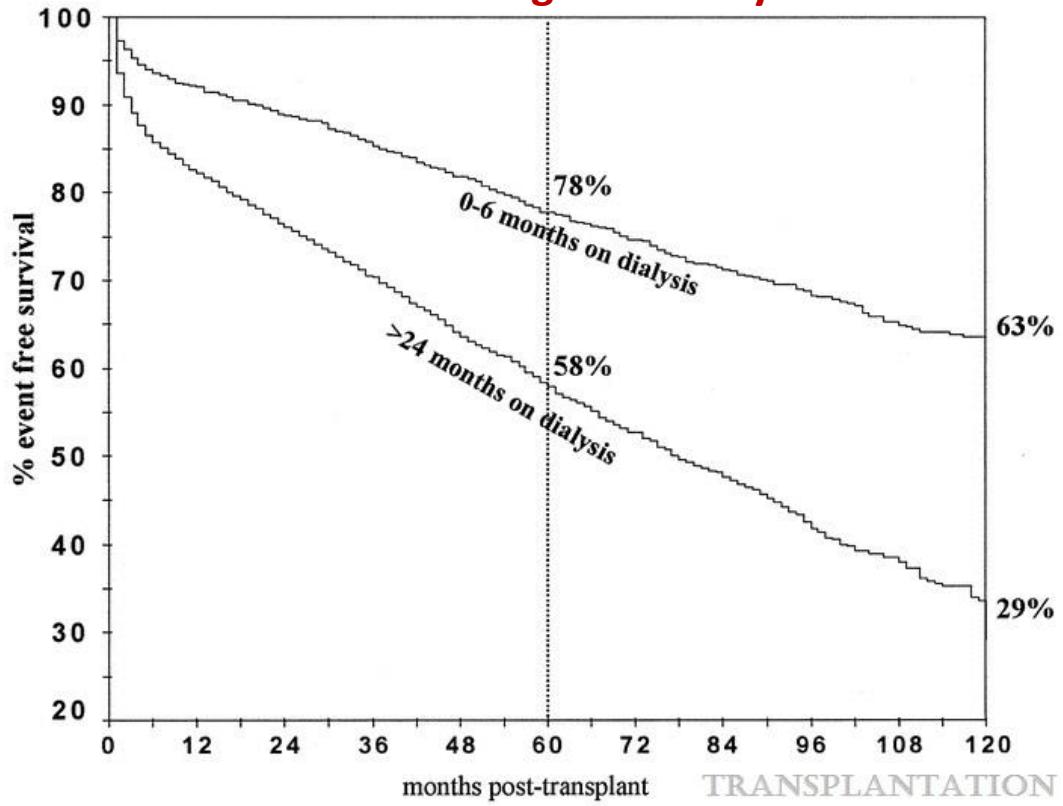
Cassuto JR, et al. Am J Transplant. 2010 Nov;10(11):2502-11.





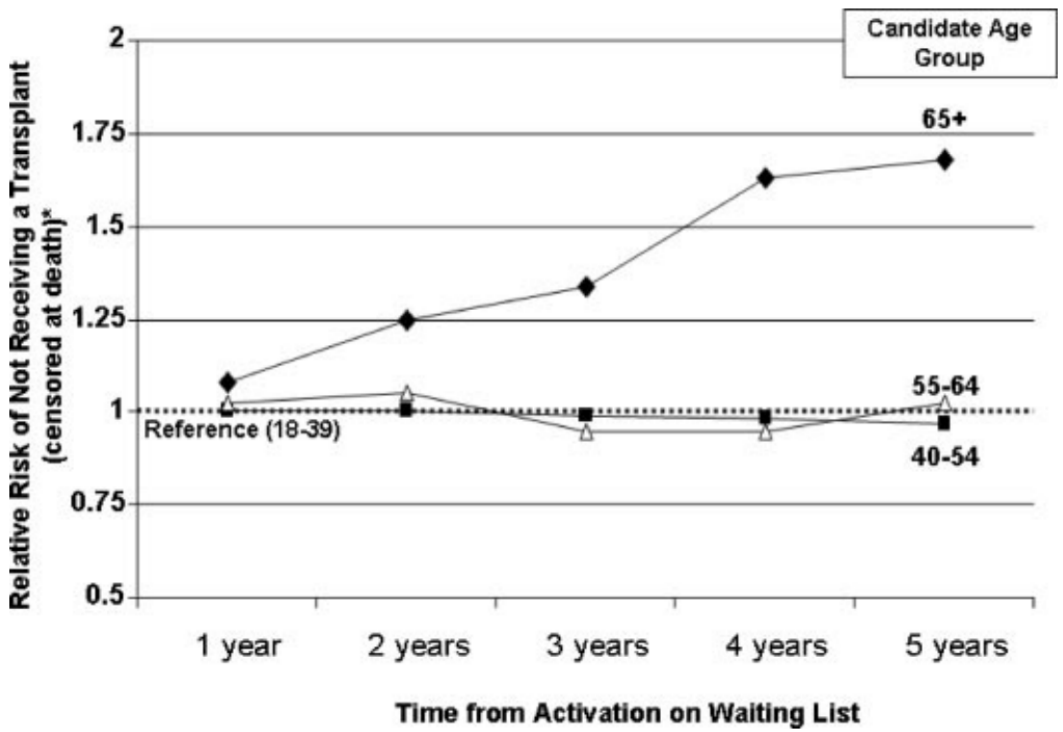
American J Transplantation, Volume: 11, Issue: 10, Pages: 2093-2109

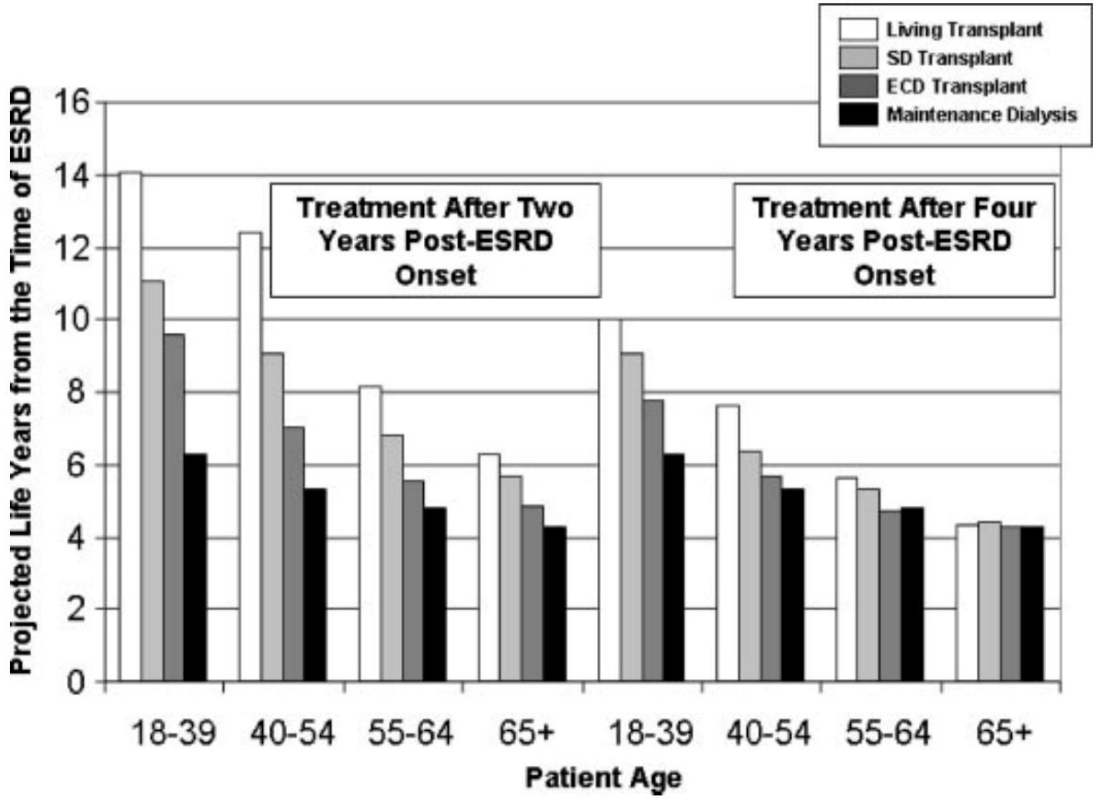
When is the best time for a candidate to get a kidney transplant?



Meier-Kriesche, Herwig-Ulf; Kaplan, Bruce
Transplantation74(10):1377-1381

Unadjusted graft survival in of 2,405 recipients of paired kidneys with short compared to long ESRD time.





Relative risk for not receiving a deceased donor kidney transplant once placed on the waiting list by candidate age (censored for death)

Projected life expectancy after ESRD onset by recipient age and treatment modality for patients with diabetes as the primary cause of ESRD

Jesse DS and Meier-Kriesche HM, CJASN 2006, 1: 532-538

Who should get a kidney transplant?

All patients with chronic kidney disease (CKD) G4-G5 (glomerular filtration rate [GFR] < 30ml/min/1.73 m2) who are expected to reach end-stage kidney disease (ESKD) should be informed of, educated about, and *considered* for kidney transplantation regardless of socioeconomic status, sex, gender identity, or race/ethnicity, except patients with the following conditions

- Multiple myeloma, and light chain deposition disease or heavy chain deposition disease until they receive a potentially curative treatment regimen and are in stable remission;
- Decompensated cirrhosis (consider for combined liver-kidney transplant)
- Severe irreversible obstructive or restrictive lung disease
- Severe uncorrectable and symptomatic cardiac disease that is deemed by a cardiologist to preclude transplantation
- Active malignancy until active treatment and stable remission, except for those with indolent and low-grade cancers

General rules of recipient evaluation

Do no harm to the recipient

Do no harm to the donor

Do no harm to the list

Objectives of recipient evaluation

- Assess various risk factors and comorbid conditions governing an individual's suitability for transplantation

- Identify risk factors that
  - represent absolute conta-indication for Transplantation
  - Requires further work-up
  - Requires specific treatment/management

- Assess patient's suitability based on medical, surgical, social and psychological history. All patients should be considered for transplant regardless of socioeconomic status, sex, age, gender identity, or race/ethnicity.

- Educate the patient about the risk and benefits of transplant

- Discuss donor options, for potential living donor identification

- Plan immunosuppressive management, infectious prophylactic plan and other post transplant management/monitoring

- Use a multidisciplinary team, including at a minimum a transplant physician, transplant surgeon and a health care professional experienced in the psychosocial aspects of transplantation

Contraindication to kidney transplant

Absolute

- Chronic illness with life expectancy< 1 year
- Active infection unless effectively treated
- Decompensated cirrhosis (consider for combined liver-kidney transplant)
- Severe uncorrectable and symptomatic cardiac disease that is deemed by a cardiologist to preclude transplantation
- Active malignancy/active Multiple Myeloma until active treatment and stable remission, except for those with indolent and low-grade cancers

Relative

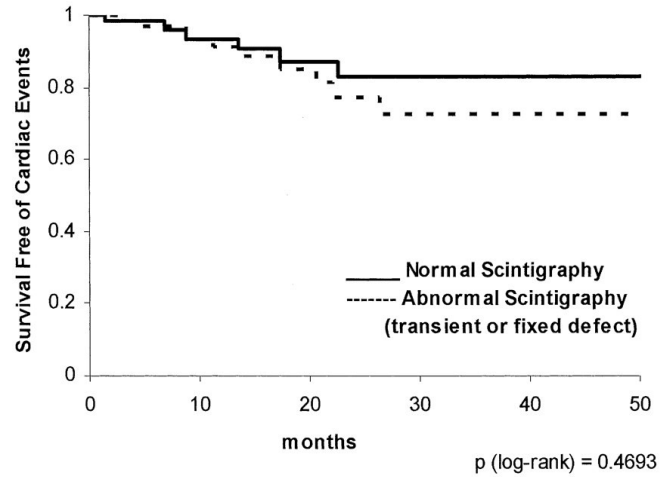
- Class II or class III obesity (BMI ≥ 35kg/m2
- Active glomerulonephritis until in remission
- Frailty with physiologic reserve and the potential for perioperative complications
- Severe peripheral artery disease
- Active substance use util received appropriate treatment and achieved a minimum abstinence period of six months.

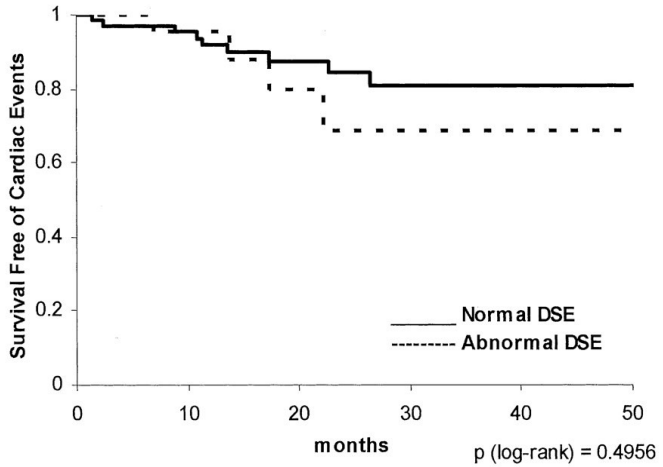
Medical evaluation: by systems

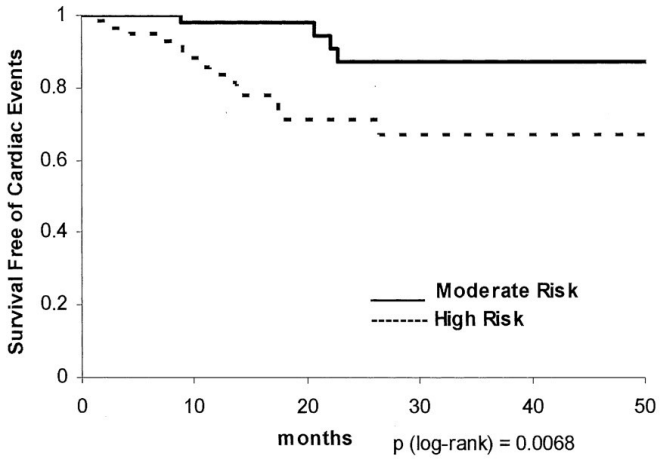
- Cardio-vascular
- Nephrology
- Infection
- Cancer
- Hematology
- Pulmonary
- Gastro-enterology
- Urology
- psychiatric

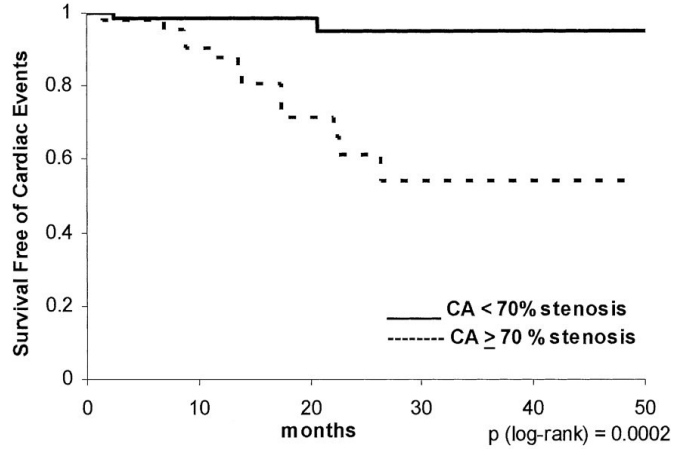
Cardio-vascular

- Cardiology assessment and management of patients with active cardiac disease (eg, angina, arrhythmia, heart failure, symptomatic valvular heart disease)
- Non invasive CAD screening for patients with high risk for coronary artery disease (CAD) (eg, diabetes, previous CAD, dialysis for at least two years) >>ECHO, stress test
- Cardiology assessment for patients with estimated pulmonary systolic pressure greater than 45mm Hg by echocardiographic, and those with risk factors for pulmonary hypertension (eg, portal hypertension, connective tissue disease, congenital heart disease, chronic obstructive pulmonary disease)
- Patients with severe heart failure (NYHA III/IV) who are otherwise suitable for kidney transplantation should be assessed by a cardiologist and considered for combined/ simultaneous heart and kidney transplantation
- Evaluate all candidates for presence and severity of peripheral arterial disease (PAD) with history and physical examination and non-invasive vascular testing as indicated

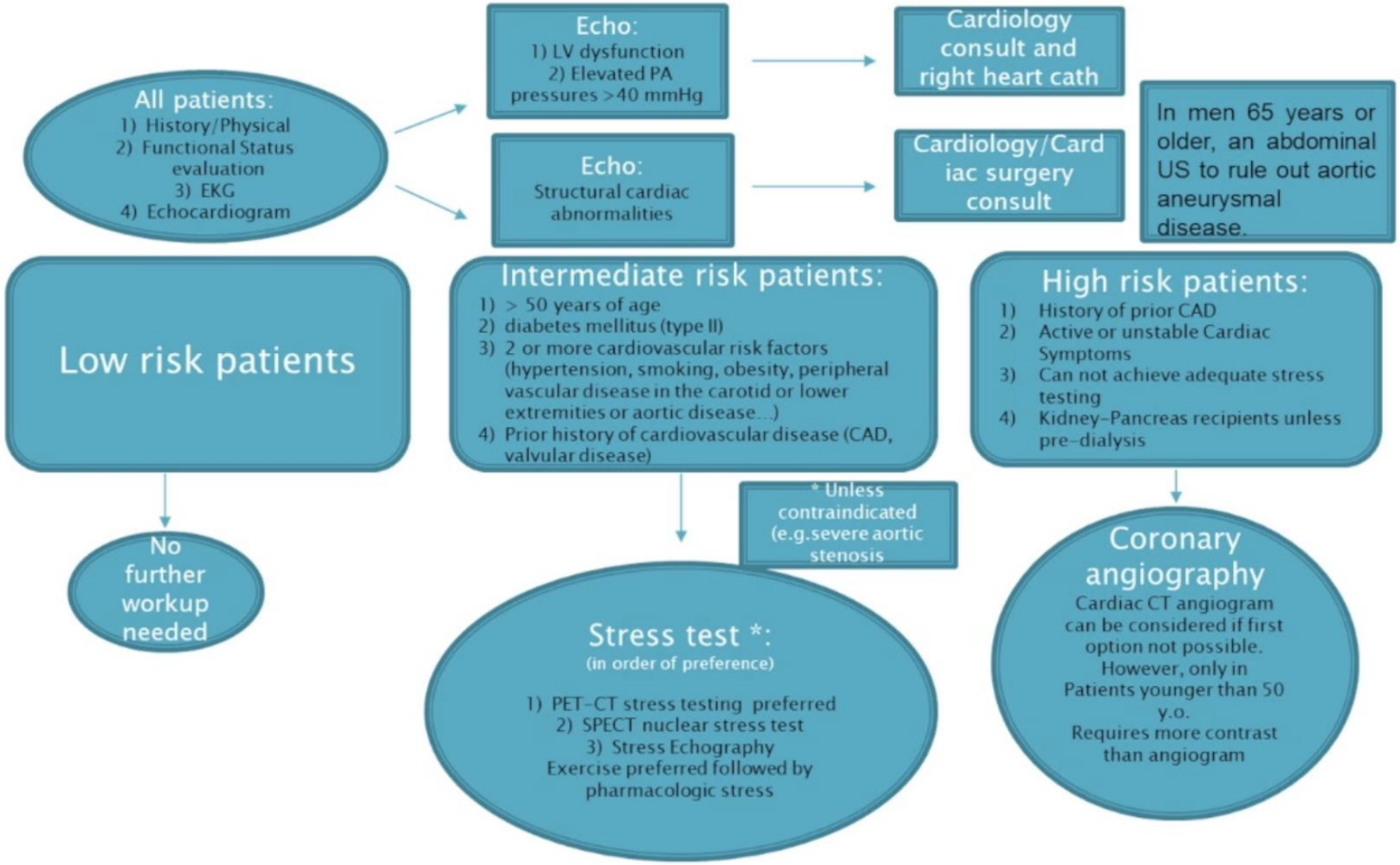






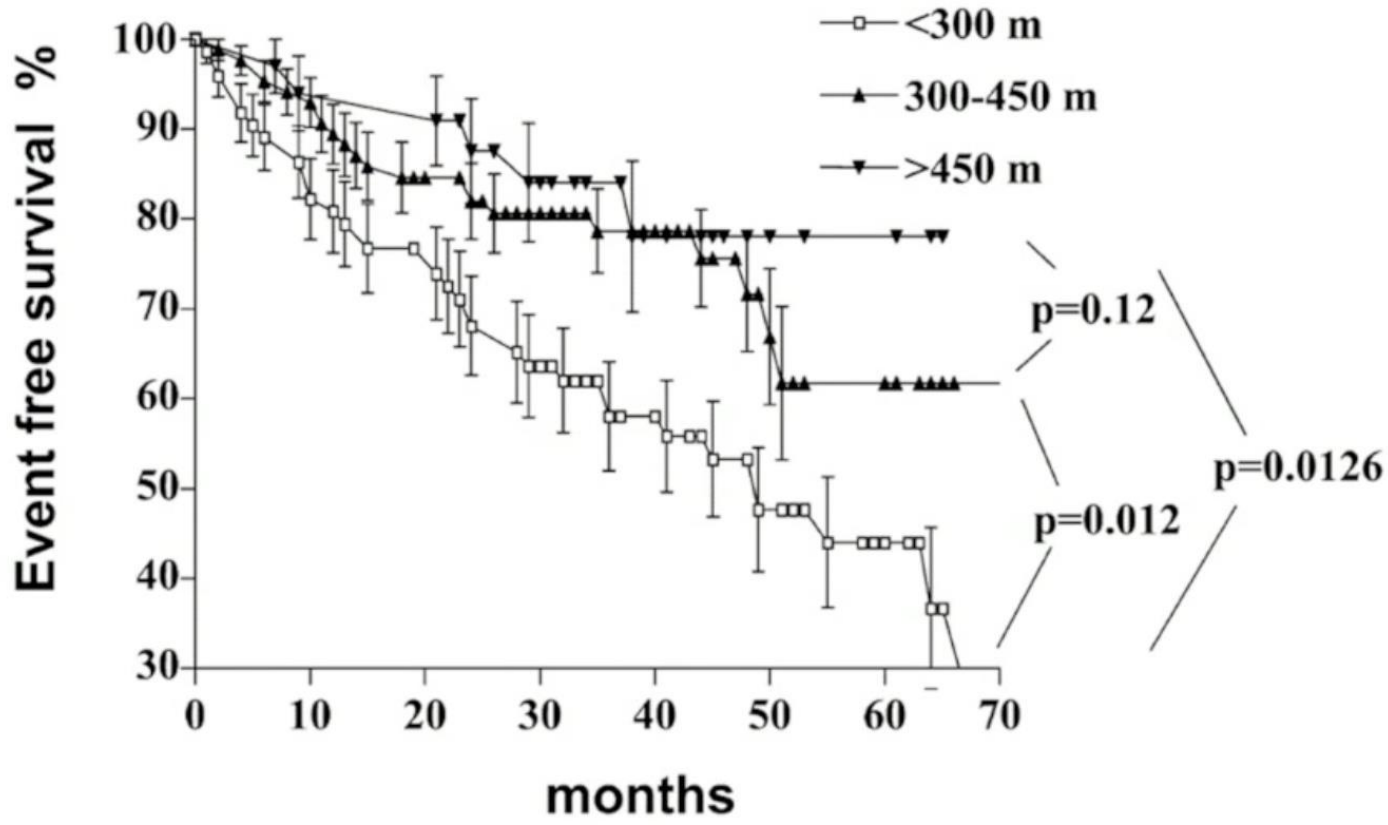


Jose Jayme G. De Lima. Hypertension., Volume: 42, Issue: 3, Pages: 263-268,



Cardiac Evaluation at the Brigham

The 6 minute walk test



Gensini et al, Eur J HF 2003

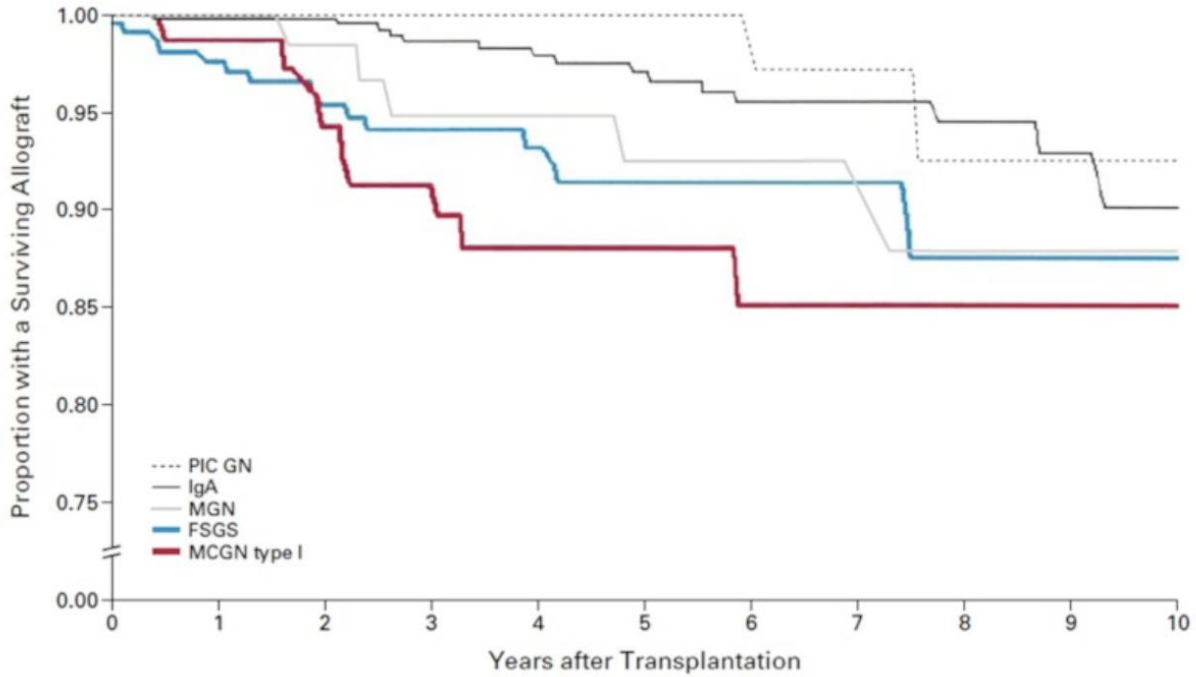
Nephrology

- Cause to ESKD
- Genetic testing when etiology of ESKD unclear
- Evaluate risk of recurrence
- Defer transplant until primary disease is quiescent: Lupus nephritis, anti-phospholipid syndrome and ANCA associated vasculitis
- Monoclonal Immunoglobulin deposition Disease (MIDD) after curative treatment regimen and are in stable remission

Risk of recurrence

FSGS: 20-30%
IgA: 20-60%
MN: 10-30%
MPGN: Type 1: 20-30%
Type 2: 50-100%
HUS/TTP (non-infectious): 60%
SLE: 2-10%
ANCA: 17%
Anti-GBM disease: 15%

Recurrent disease



No. at Risk											
PIC GN	102	90	74	62	56	48	36	26	16	5	2
IgA	532	462	398	312	253	217	153	119	87	47	15
MGN	81	70	60	49	44	40	31	20	15	9	5
FSGS	221	189	156	124	103	91	65	54	36	19	5
MCGN type I	88	75	64	57	48	40	28	25	16	12	4

Briganti et al. N Engl J Med. 2002 Jul 11;347(2):103-9.

Infections

- ✓ Treat active infections
- ✓ Screen for latent TB at the time of candidate evaluation and start treatment prior to or immediately following kidney transplantation
- ✓ Screen for HIV HBV and HCV, and treat
- ✓ Screen for CMV EBV HSV VZV
- ✓ Screen and eventually treat for strongyloids and Syphilis
- ✓ Complete inactivated vaccines ideally prior to kidney transplant (Efficacy of vaccination usually decreases)
- ✓ Complete live attenuated vaccination prior to kidney transplant

Cancer

- Routine cancer screening, as per local guidelines for the general population
  - chest imaging prior to transplantation in all candidates
  - Mammogram annually starting at age 40 for women
  - Pap test startfor women >21 y
  - PSA 50 for men >50 y
  - Annual liver US and alpha feto protein for patients with Hx of cirrhosis
  - colonoscopy starting at age 45, in patients with inflammatory bowel disease
  - Low dose CT Chest annually for men and women with ≥20 pack-year cigarette smoking history starting at age 50
  - Patients with increased risk for RCC, including ≥ 3 years dialysis, family history of renal cancer, acquired cystic dis- ease or analgesic nephropathy, should be screeded with renal US

Recommended waiting times between cancer remission and kidney transplantation[91]

Breast	Early	At least 2 years
	Advanced	At least 5 years
Colorectal	Dukes A/B	At least 2 years
	Duke C	2-5 years
	Duke D	At least 5 years
Bladder	Invasive	At least 2 years
Kidney	Incidentaloma (< 3 cm)	No waiting time
	Early	At least 2 years
	Large and invasive	At least 5 years
Uterine	Localized	At least 2 years
	Invasive	At least 5 years
Cervical	Localized	At least 2 years
	Invasive	At least 5 years
Lung	Localized	2-5 years
Testicular	Localized	At least 2 years
	Invasive	2-5 years
Melanoma	Localized	At least 5 years
	Invasive	Contraindicated
Prostate	Gleason ≤6	No waiting time
	Gleason 7	At least 2 years
	Gleason 8-10	At least 5 years
Thyroid	Papillary/Follicular/ Medullary	
	Stage 1	No waiting time
	Stage 2	At least 2 years
	Stage 3	At least 5 years
	Stage 4	Contraindicated
	Anaplastic	Contraindicated
Hodgkin Lymphoma	Localized	At least 2 years
	Regional	3-5 years
	Distant	At least 5 years
Non-Hodgkin Lymphoma	Localized	At least 2 years
	Regional	3-5 years
	Distant	At least 5 years
Post-transplant lymphoproliferative disease	Nodal	At least 2 years
	Extranodal and cerebral	At least 5 years

- Prostate cancer: If calculated 5-year disease free survival for surgically treated disease ≥ 90%, no minimal waiting period required. At he end of the wait, patient must have a low and stable PSA and get clearance from Urology

- Oncology Clearnce and no waiting time for candidates with history of indolent and low-grade cancers such as prostate cancer (Gleason score ≤ 6), superficial non- melanoma skin cancer, renal tumors (≤ 3cm in maximum diameter), carcinoma in situ (ductal carcinoma in situ, cervical, others); thyroid cancer (follicular/ papillary < 2cm of low grade histology)

- Low risk breast cancer: women with low-risk disease such as DCIS and stage 1 breast cancer should be considered as transplant candidates after completion of standard treatment. Endocrine treatment should not affect the timing of transplant

Hematology

- Screening for thrombophilia in candidates who have experienced venous thromboembolic events
- Evaluate patients with significant cytopenias
- Avoid transplanting patients with leukemia or lymphoma until they have received curative therapy, achieved remission and remained cancer free for a period to be determined in consultation with a hematologist/oncologist and the transplant program

Pulmonary

- CT for current or former heavy tobacco users (≥ 30 pack-years) as per local guidelines, and chest radiograph for other candidates
- pulmonary function testing in candidates with impaired functional capacity, heavy tobacco use, or known pulmonary disease
- patients with severe irreversible obstructive or restrictive lung disease maybe excluded from kidney transplantation

Gastro-enterology

- Same screening as the general population
- Screen for Colon cancer
- Assess for severe GI symptoms (diarrhea, cramping..) for Mycophenolate side effect
- Diabetic patients with gastroparesis symptoms (risk for poor meds intake and efficacy)
- Treatment of HepC and Immunization for HepB

Psychological and Psychiatric assessment

Refer candidates with:

- a diagnosable psychiatric or psychological condition
- substance use disorder
- Hx of nonadherence

Transplant for special population

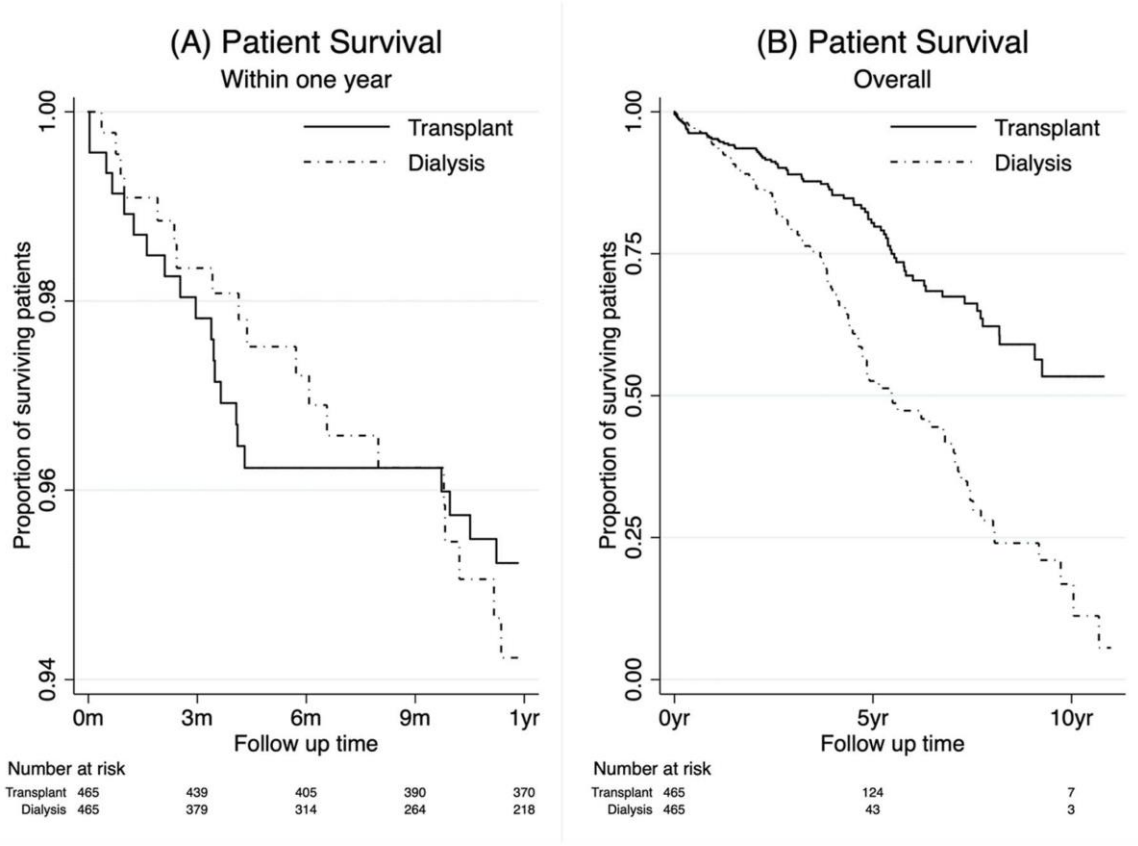
❖ HIV is no longer an absolute contraindication

Infection needs to be controlled
Short-term transplant outcome comparable to general transplant population
Drug-drug interaction

❖ Elderly patients

No limit for age
Evaluate functional status
Assess risk for overimmunosuppression
Extended criteria deceased donor

Elderly recipients incurred an increased risk of death in the first 9 months after transplantation but experienced progressively superior survival rates thereafter.



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Immunological assessment

- All sensitizing events (eg, blood product transfusion, including platelets, pregnancy or miscarriage, previous SOT)
- Perform HLA antibody testing at transplant evaluation, at regular intervals prior to transplantation and after a sensitizing event or a clinical event that can impact PRA

TAKE HOME MESSAGES

- ✓ Clear survival benefit in kidney transplantation compared to remaining on dialysis/waiting list

- ✓ Clear survival benefit in preemptive transplantation

- ✓ Evaluate the recipient for risk factors That:
  - Represent absolute contraindication for transplantation
  - Warrant treatment
  - Require special testing and other specialty expertise before proceeding to transplantation

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5. Gensini et al, Eur J HF 2003

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