

FAILED TRANSPLANT NEPHRECTOMY

PROS and CONS



IMPORTANCE OF THE ISSUE

- ❖ About 20% of Renal Transplant waiting list has previously failed allograft

J. Perle, et al. *Semin Dial* 21(3):239-244

- ❖ Patients on dialysis and wait listed but not yet retransplanted have high mortality rate (10 year survival <40%)

B. Kaplan, et al *AJT* 2:930-932



MANAGEMENT OF THE FAILED RENAL TRANSPLANT

- ❖ Discontinue or reduce Immunosuppression
 - Quick vs. slow taper ?
- ❖ Return to Dialytic Renal Replacement
- ❖ PD vs Hemo
- ❖ Nephrectomy by protocol or for cause



REASONS FOR NEPHRECTOMY

- ❖ Protocol Decision
- ❖ Necrotic Tissue
- ❖ Symptomatic Chronic or Acute Rejection
- ❖ Make Room for Subsequent Transplant
- ❖ Avoid the Residual Inflammatory State
- ❖ Improved Patient Outcomes after Failed Allograft



REASONS FOR NO NEPHRECTOMY

- ❖ Protocol Decision
- ❖ Avoiding another surgery with potential morbidity and mortality
- ❖ Tenuous Clinical Condition of Patient with Failed Graft
 - Recent Major Anti-Rejection Treatment
 - Age
 - Comorbid Disorders at time of Graft Failure
- ❖ Worse Outcomes for Graft Survival after Primary Nephrectomy
- ❖ Increased sensitization after Graft Removal



PRO

THEORETICAL REASONS FOR TRANSPLANT NEPHRECTOMY

1. The presence of foreign HLA antigens will lead to inflammation with higher mortality and morbidity
2. HLA antigens will make subsequent transplants immunologically more likely to reject
3. Adjuvant Effect
4. Epitope Spreading



Lets explore 3 Issues:

1. Is There an Inflammatory state of retained failed grafts?
2. Are There Outcomes Penalties to Retransplant with retained grafts- surgical, sensitization, survival
3. Are there penalties to dialysis patients with retained grafts



IS THERE
INFLAMMATION WITH
RETAINED FAILED
RENAL ALLOGRAFTS?



Presence of a failed kidney transplant in patients who are on hemodialysis is associated with chronic inflammatory state and erythropoietin resistance

Lopes-Gomes JM et al JASN15: 2494, 2004



METHODS

3 Groups studied:

Group A1 failed transplant patients on HD with fever and other constitutional symptoms

Group A2 failed transplant patients on HD without constitutional symptoms

Group B incident, non transplanted HD patients



INFLAMMATORY MARKERS

	A1	A2	B
Hg	9.8 ± 1.8	11.6 ± 1.5	12.7 ± 1.4
Alb	3.1 ± 0.7	3.4 ± 0.4	3.8 ± 0.4
CRP	6.6 ± 5.2	3.1 ± 4.2	1.3 ± 1.9
	p<0.05		NS



CONCLUSIONS FROM DATA

1. Group A1 had higher inflammatory markers and more EPO resistance than A2 or B
2. Group A2 and B had no statistically significant inflammatory markers
3. Most of Groups A were still on steroids with none of Groups B which alters data and conclusions.



Are there penalties to retransplant outcomes with retained failed renal allografts?



CON

**FAILED ALLOGRAFT NEPHRECTOMY
ASSOCIATED WITH NO IMPROVEMENT
OR ACTUALLY WORSE REGRAFT
OUTCOMES**



CON

**No Improvement or detriment
in
Regraft Outcomes**

1.Sumrani et al *Transplantation* 53:52,1992

2.Douzdjian et al *Clin Transpl* 10:203,1996



RISK FACTORS AFFECTING SECOND RENAL TRANSPLANT OUTCOME, with SPECIAL REFERENCE to PRIMARY ALLOGRAFT NEPHRECTOMY

Abouljoud MS, Deierhoi MH, Hudson SL, Diethelm AG.
Transplantation 1995 Jul 27;60(2):138-44



CON

- 1. 192 patients at UAB received 2nd graft over 13 years period**
- 2. All comers: Graft survival statistically worse after Primary Nephrectomy**
- 3. Examined cohort where primary graft survived at least 6 months before failure – primary nephrectomy still led to statistically worse regraft survival.**



Impact of a failed allograft nephrectomy on initial function and graft survival after kidney retransplantation

C. Schleicher et al Transplant International
24:284,2011



Methods

Schleicher et al

1. Retrospective analysis of Eurotransplant data 2000-2008
2. Comparison of retransplant after failed nephrectomy (n=121) with retransplant with retained failed graft
3. Outcome measures
 - Sensitization rate (PRA)
 - Primary nonfunction rate
 - Graft survival



RESULTS

Schleicher et al 2011

	<u>Nephrectomy n=121</u>	<u>none n=45</u>	
PRA			
>30	19	1	p<0.02
>70	6	0	
PNF	18(15%)	2(4%)	p<0.05
Gft survival	82 mos	99 mos	p<0.03



CONCLUSIONS

Schleicher et al 2011

Failed transplant nephrectomy prior to retransplant leads to more sensitization and worse graft outcomes



MORTALITY AFTER FAILED GRAFT NEPHRECTOMY

- ❖ Rates of Mortality Range from Low 1.5% to High of 37%

JASN 2010 vol. 21(2):374-380

- ❖ Older the Study the Higher the Rate
- ❖ Hard to Interpret: No data about mortality of Transplant Nephrectomy performed without cause.



Surgical complications of failed graft nephrectomy in the modern transplant era

Mazzucchi et al J Urol
170:734.2003

1. Increased blood loss
2. Increased peri operative complications
3. Increased infections



CON

THEORY NOT MET WITH ACTUAL DATA

1. Asymptomatic HD patients with Retained Grafts did not have statistically increased inflammatory markers over non transplanted dialysis patients
2. Although retrospective review of UNOS shows a decreased retransplant rate of retained failed grafts (Ayus JC, JASN 21:374-380,2010) graft survival after retransplant with or without retained failed transplant has never been shown to be better
3. Preformed anti HLA antibody titers actually rise after failed transplant nephrectomy.
Khakhar et al, "The Impact of Allograft Nephrectomy on Percent Panel Reactive Antibody and Clinical Outcome" *Transplantation Proceedings* 35.2 (2003): 862-863.
2003 Sumrani 1992



ACTUAL FATE OF FAILED RENAL ALLOGRAFT

1. Lopez – Gomez, et al (2004) 67% of patients returned to HD after failed allograft had transplant nephrectomy for clinical symptoms
2. Vanderbilt Experience (2010) 58% of failed allografts removed for clinical cause.



VANDERBILT EXPERIENCE

1. Data from 1/88 – 12/01
2. 952 transplants were performed , followed 8.3 yr (18mos – 14 yr)
3. 200 or 21 % failed in that period
4. 58% of the failed grafts removed for cause
5. All patients returned to dialysis had CNI and cytotoxic agents stopped by 4 weeks of return and were free of steroids by 2 months



115 Transplant Nephrectomies

(Chuang et al 2010)

At Failure	42
≤ 1 mo	65 (additional 23)
≤ 1 yr	87 (76%)
≤ 3 yr	115 (100%)
≥ 3 yr	None



Early Removal

Late Removal

Symptoms

Pain and Fever

Pain, fever, failure to thrive, GI

Histology

Necrosis 100%

IFTA 76%

Acute Rejection 44%

Both 34%



Indications for Removal

1. Known technical failure or vascular catastrophe (56%)
2. 21% graft pain alone with rejection
3. 12% fever alone with rejection
4. 8% both with rejection
5. 7% other (hematuria, HBP, mental status changes)



Are there penalties to be paid by
the dialysis patient with a retained
failed renal allograft ?



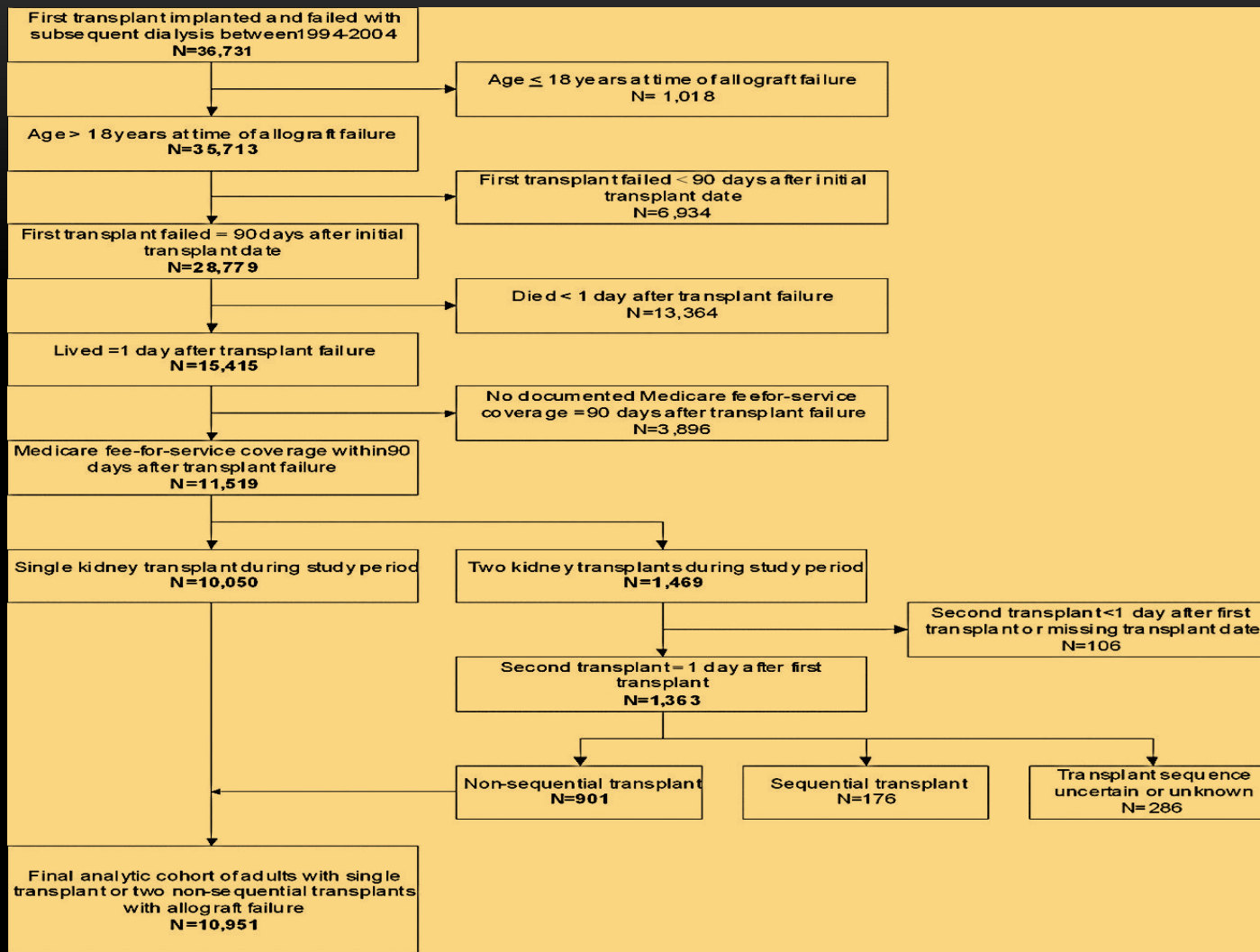
Transplant Nephrectomy Improves Survival following a Failed Renal Allograft.

Ayus et al

J Am Soc Nephrol 21:374-380,2011



Assembly of analysis cohort of 10,951 patients who returned to maintenance dialysis after a failed kidney transplant between 1994 and 2004 in the USRDS is shown.



METHODS

1. Interrogation of USRDS Database 1/94-12/04
2. Had to be on Medicare
3. Final sample N = 10,951

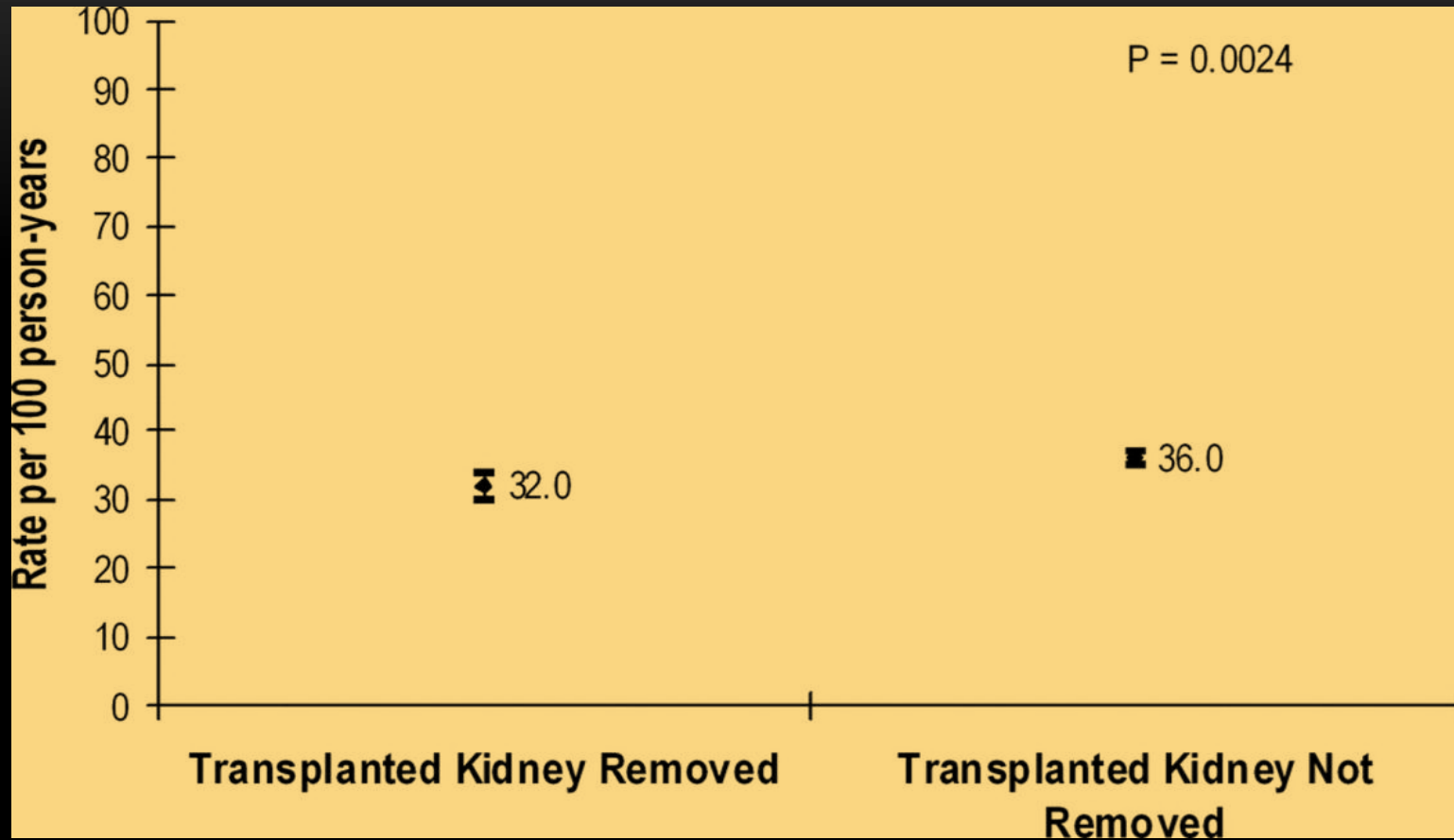


PATIENT CHARACTERISTICS

1. 3451 OF 10,951 failed patients had nephrectomy
2. Those without Nephrectomy were:
 - Younger
 - African American
 - More likely to have had an MI, CAD, CHF, Diabetes, Cancer
3. Thus the basic mortality risk was different for the two cohorts , arguably worse for the No Nephrectomy group
4. No information provided as to:
 - Residual immunosuppression
 - Rejection History



PRO



Ayus J C et al. JASN 2010;21:374-380



INTERPRETATION OF MORTALITY

Actual data has small difference

- 36 v. 32 deaths per 100 patients – years statistically significant because of large numbers
- The No Nephrectomy cohort are different, have more comorbid disorders
- The authors cannot know in this retrospective analysis **WHY** patients were left on dialysis without nephrectomy - ? Sicker ? frail



Pro/Con Failed Transplant Nephrectomy Discussion Cries Out for Evidence to make Informed Judgements

- Ayus data of retrospective data is hypothesis forming at best
- Needs a randomized prospective study of patients equal in all respects except Nephrectomy



WHAT TO DO?

1. Firstly, for more than ½ of failed allograft patients the question is moot – they will get a nephrectomy early and for cause
2. Immunosuppression needs to be tapered off on risk/benefit analysis, especially if Ayus is correct that nephrectomy on balance is a positive management step



WHAT TO DO?

None of the extant data are compelling Pro/Con to suspend Good Clinical Judgment for each patient as an individual.

- Do No Harm if Patients are Asymptomatic, off immunosuppressives, on dialysis:
 - Group A2 of Ayus not inflamed
 - No Nephrectomy mortality or morbidity
 - Avoids Sensitization



WHAT TO DO?

➤ Low threshold to remove failed grafts for:

- Ischemic Necrosis
- Fever
- Pain
- GI Upset
- Persistent Hematuria
- Failure to Thrive

