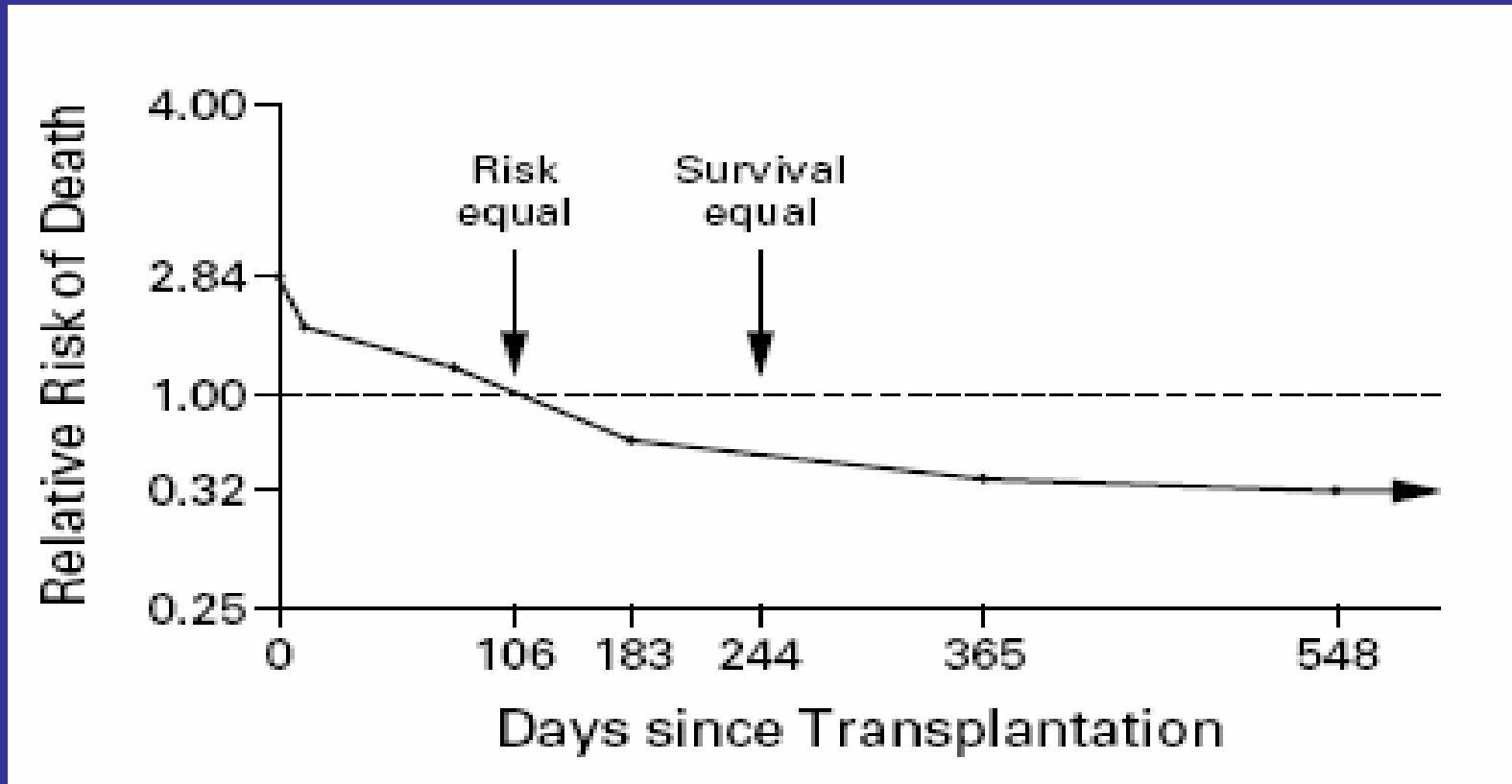


Peritoneal Dialysis: A Good Choice from a Transplant Perspective

Olwyn Johnston MB, MD, MHSc

Education Day
BC Provincial Renal Agency
June 6th 2008

Benefits of Transplant Over Dialysis



Wolfe RA N Eng J Med 1999; 341:1725

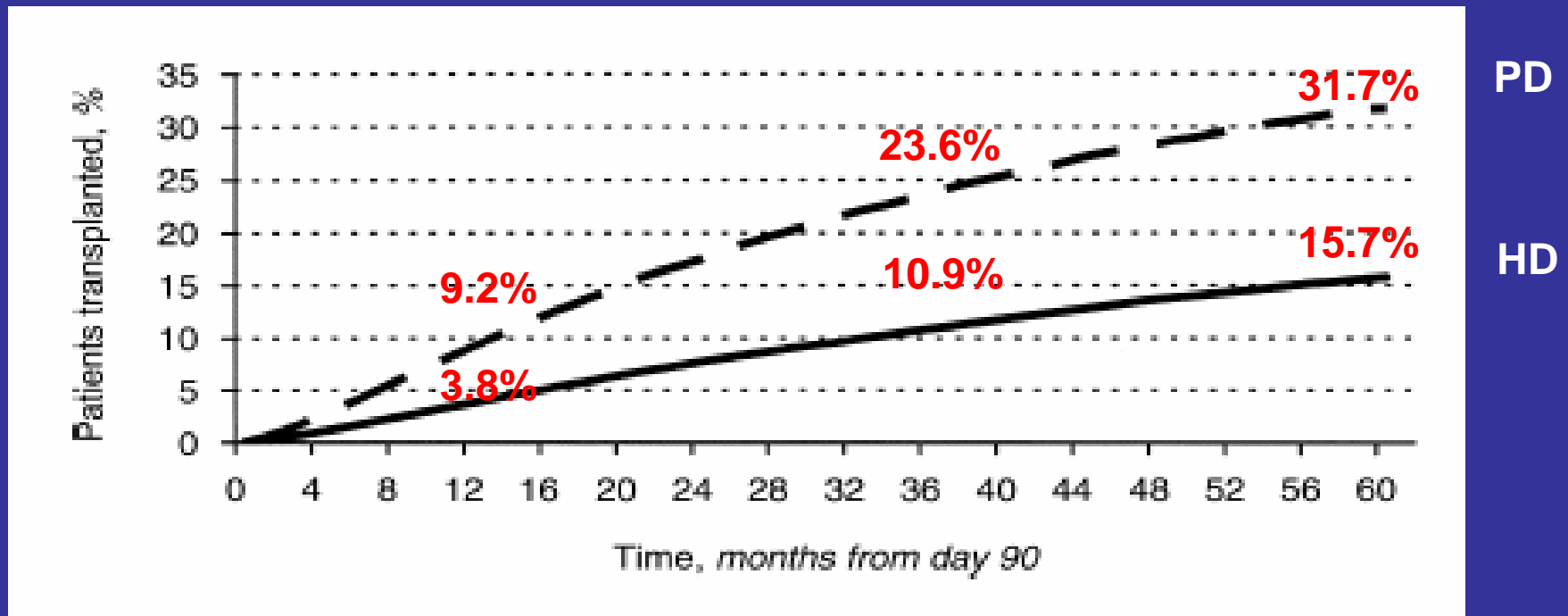
Questions

1. Does the pre-transplant dialysis modality impact post-transplant patient and graft survival?
2. Is a given dialysis strategy associated with particular post-transplant complications?
3. Does the dialysis modality after kidney transplant failure, influence patient survival?

Questions

- 1. Does the pre-transplant dialysis modality impact post-transplant patient and graft survival?**
2. Is a given dialysis strategy associated with particular post-transplant complications?
3. Does the dialysis modality after kidney transplant failure, influence patient survival?

What is the likelihood of receiving a transplant based on initial dialysis modality?



Adjusted likelihood of receiving a transplant was **1.39** (1.35, 1.43) times greater for PD than for HD patients

Effect of Dialysis Modality while on the Wait List for Transplantation

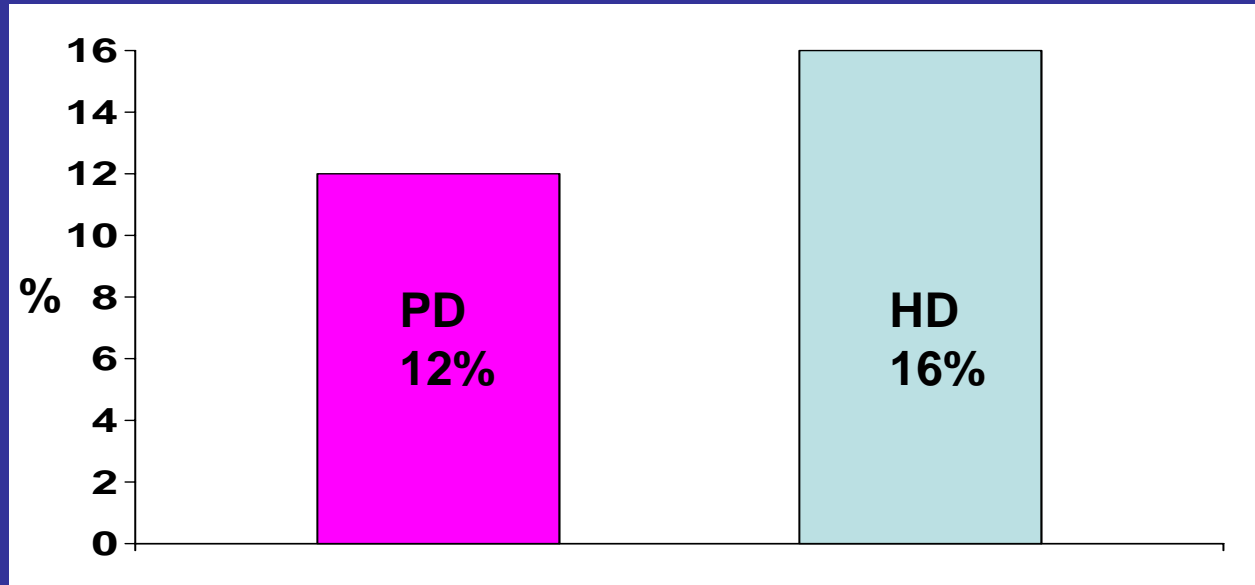
- The choice of initial dialysis modality is associated with equivalent outcomes among patients who have ESRD and are placed on the transplant waiting list before dialysis commencement
- However, patients with BMI >26 kg/m² have increased 2-yr mortality associated with the selection of PD *versus* HD.

Pre-Transplant Dialysis Modality is associated with differences in outcomes after Transplantation

- PD and HD patients have similar overall rates of mortality and all cause graft loss (adjusted)
- In first 3 months after transplantation (but not after 3 months), PD is associated with:
 - ↑ risk for graft failure (RR 1.23; CI 1.09, 1.39)
 - ↑ risk for DCGL (RR 1.33; CI 1.16, 1.53)
 - No difference in mortality (RR 1.03; CI 0.81, 1.30) compared with HD
- (cannot be explained by ↑ rate of infection)

PD is Associated with less Delayed Graft Function than HD

- Delayed graft function (DGF) = requirement for dialysis within the first 7 days of transplantation



- Adjusted OR (PD:HD) for DGF = 0.74 (0.67, 0.81)
(Even adjusted for likelihood of WL)
Snyder JJ Kidney Int 2002; 62:1423-30
- A smaller study showed contrary results
Joseph JT Clin Transplant 2002; 16:18-23

Results of Pre-Transplantation Modality on Outcomes Vary

- Compared with HD, PD, immediately before transplantation predicts a 3% lower risk for graft failure and 6% lower risk for mortality
- PD as the predominant replacement modality, had a protective effect (HR 0.96) for graft survival compared with HD
- Increased number of replacement modalities used during the ESRD course was associated with increased risk of graft failure and mortality

Cheung AK Am J Kidney Dis 2005; 46: 537-549

- In a smaller studies, no difference in post-transplant survival was found between patients treated with PD or HD before transplantation

Helel I Transplant Proc 2007; 39:2547-2549

Joseph JT Clin Transplant 2002; 16:18-23

Questions

1. Does the pre-transplant dialysis modality impact post-transplant patient and graft survival?
- 2. Is a given dialysis strategy associated with particular post-transplant complications?**
3. Does the dialysis modality after kidney transplant failure, influence patient survival?

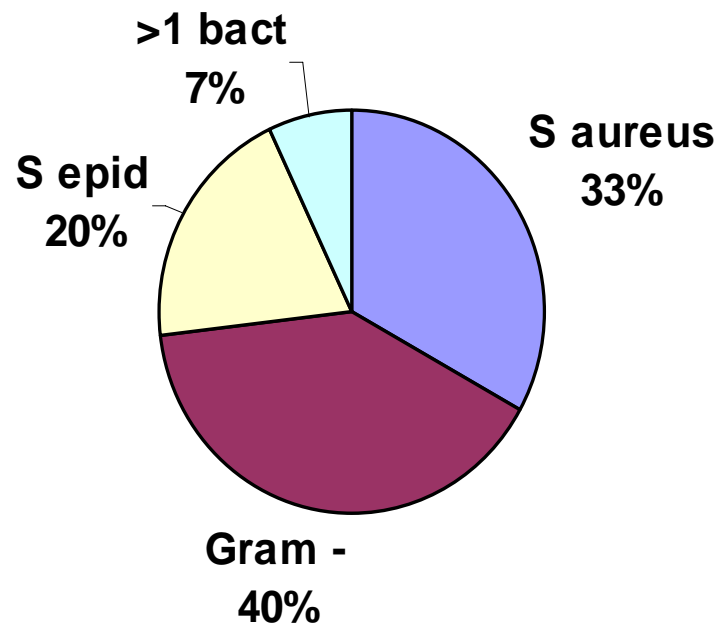
Infection

- Higher rate of infections in PD vs. HD
 - In first 30 days after transplantation
Passalacqua JA Transplantation 1999; 68: 535-540
 - No difference in bacterial infections, but higher rate of sepsis
Binaut R Transplant Proc 1997; 29: 2428
- No difference between rates in PD vs. HD
 - Vanholder R Am J Kidney Dis 1999; 33: 934-940
 - Kang Z Chin Med Sci J 1992; 7: 49-52
 - Helel I Transplant Proc 2007; 39:2547-2549
- Higher rate of infections in HD vs. PD
 - Miemois-Foley J Scand J Infect 2000; 32: 69-73

Peritonitis in PD patients after transplantation

- Incidence 5-40%
- Usually early post transplantation
- Independent risk factors:
 - Pre-transplantation
 - Total number of peritonitis episodes
 - Previous *S aureus* peritonitis
 - Male gender
 - After transplantation
 - Technical surgical problems
 - > 2 AR episodes
 - Permanent graft non-function
 - Urinary leakage

Distribution of micro-organisms in post-transplantation peritonitis



Acute Rejection

- No difference in rate of AR between PD and HD
 - Snyder JJ Kidney Int 2002; 62:1423-30
 - Joseph JT Clin Transplant 2002; 16:18-23
 - Helel I Transplant Proc 2007; 39:2547-2549
- One case control study has shown a reduced incidence of AR in patients treated with PD compared to HD
 - Vanholder R Am J Kidney Dis 1999; 33: 934-940
- Japanese study showed higher rate of AR in PD patients and this was associated with earlier increase and higher number of CD3, CD19 and CD4 lymphocytes after transplantation → higher immune responsiveness
 - Satoh S Int J Urol 2004; 11: 825-830

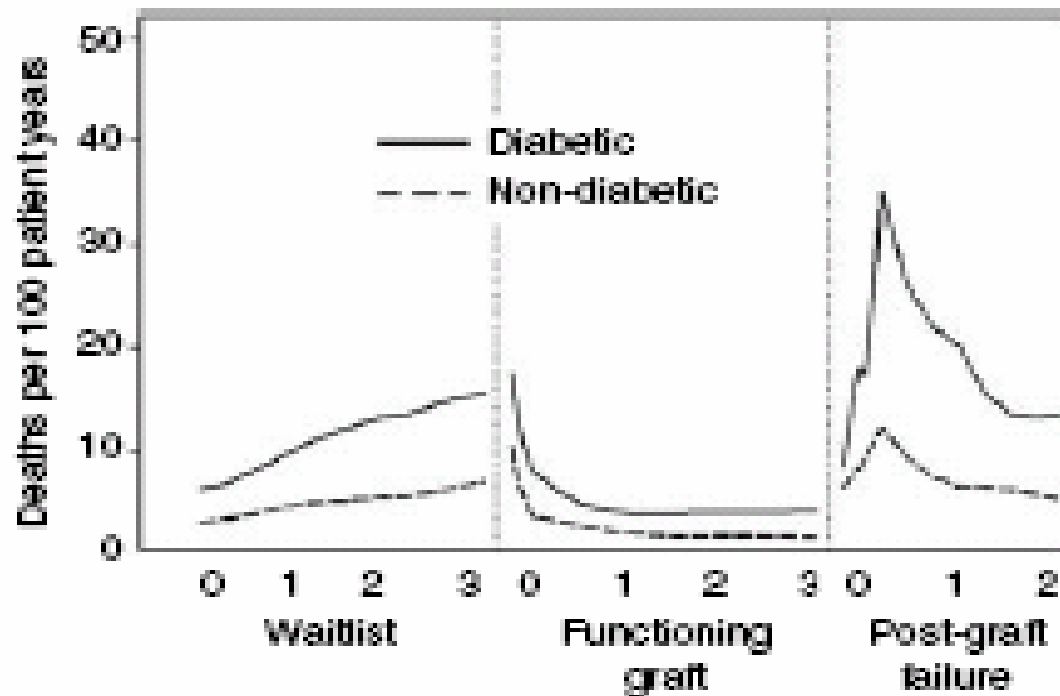
Graft Thrombosis

- For patients whose graft failed immediately or after discharge, graft thrombosis was more common in PD vs. HD patients (p=0.02)
Snyder JJ *Kidney Int* 2002; 62:1423-30
- Other studies show similar results
Ojo AO *Kidney Int* 1999; 55: 1952-1960
Vats AN *Transplantation* 2000; 69: 1414-1419
Palomar R *Transplant Proc* 2007; 39: 2128-2130
- Only one study with no difference in rate of graft thrombosis in PD vs. HD patients
Perez Fontan M *Peritoneal Dial Int* 1998; 18: 311-316

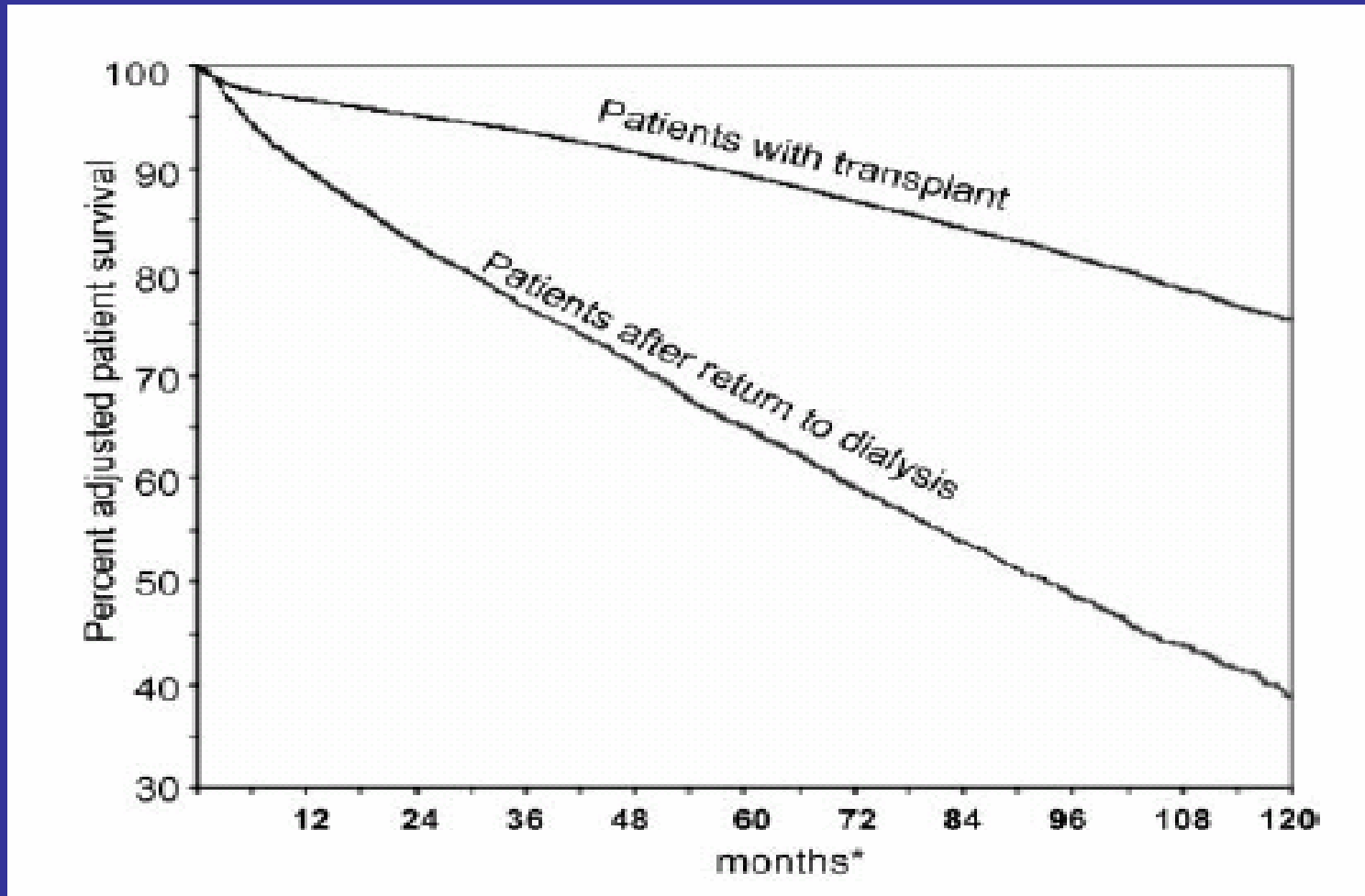
Questions

1. Does the pre-transplant dialysis modality impact post-transplant patient and graft survival?
2. Is a given dialysis strategy associated with particular post-transplant complications?
3. **Does the dialysis modality after kidney transplant failure, influence patient survival?**

Patients returning to dialysis after graft failure are at increased risk of death compared with patients with functioning grafts



Annual Adjusted Mortality Increases 3-fold Higher After Graft Loss versus Before Graft Loss



Failed Kidney Transplant Patients constitute a Unique Group with Specific Risk Factors

- Longer duration of ESRD
Sasal J Peritoneal Dial Int 2001; 21: 405-410
- Concomitant immunosuppression
Sasal J Peritoneal Dial Int 2001; 21: 405-410
- Possibly more rapid loss of residual renal function
Davies SJ Peritoneal Dial Int 2001; 21:S280-S284
- Start dialysis at levels of hematocrit, serum albumin, and GFR that may be suboptimal
Gill JS Kidney Int 2002; 61: 2193-2200

Characteristics of Failed Graft Patients Commencing PD versus Patients with Failed Native Grafts

- Failed graft patients starting PD are more likely to be:
 - Younger
 - Caucasian
 - Lower BMI
 - Poorer initial renal functioncompared to patients starting PD who were never transplanted

PD after Graft Failure has Outcomes Comparable to PD after Failed Native Kidneys

Patients starting PD after graft failure

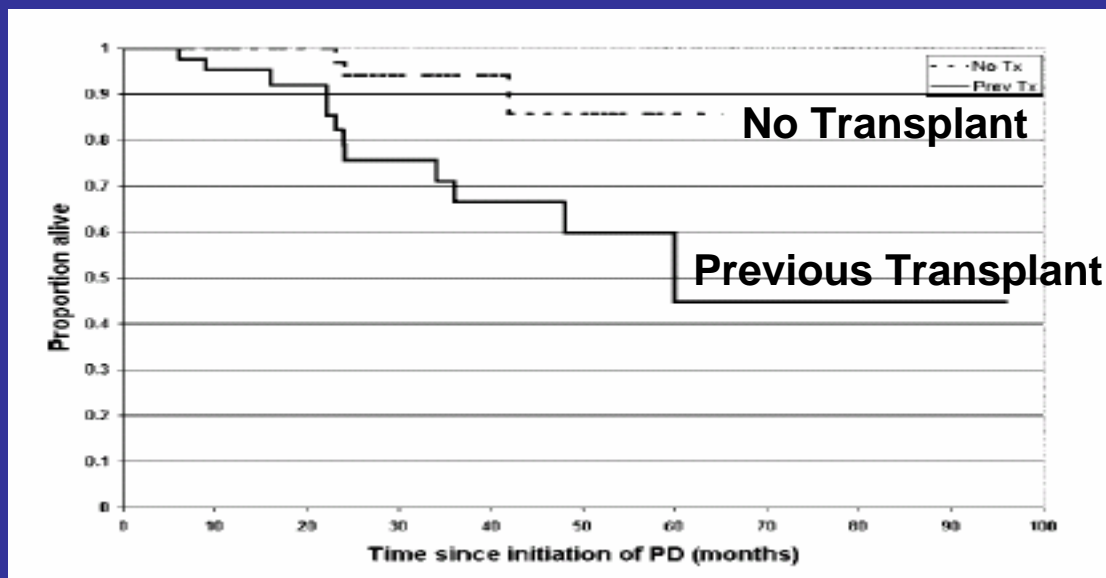
vs.

Patients starting PD after failed native kidneys

- Comparable patient mortality
(HR 1.09; CI 0.81, 1.45)
- Comparable death-censored technique failure
(HR 0.91; CI 0.75, 1.10)
- Comparable peritonitis-free survival
(HR 0.92; CI 0.72, 1.16)

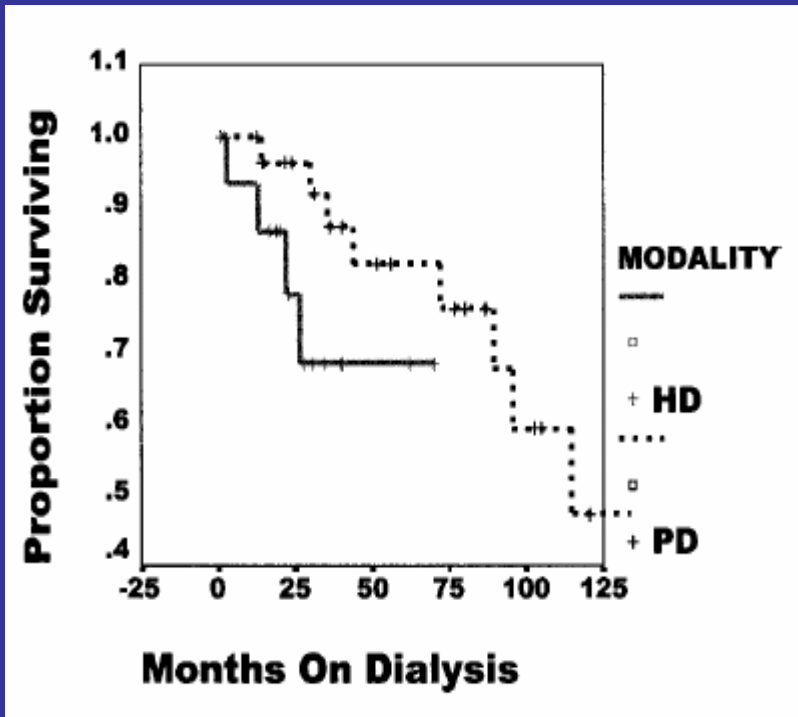
Late graft failure (>2 months) is a poor prognostic factor for PD initiation

- Outcomes compared between patients starting PD after a failed graft vs. patients starting PD with failed native kidneys
- Increased complications with late graft loss patients starting PD e.g. time to 1st peritonitis, subsequent peritonitis, catheter change or transfer to HD, occurred at much faster rate

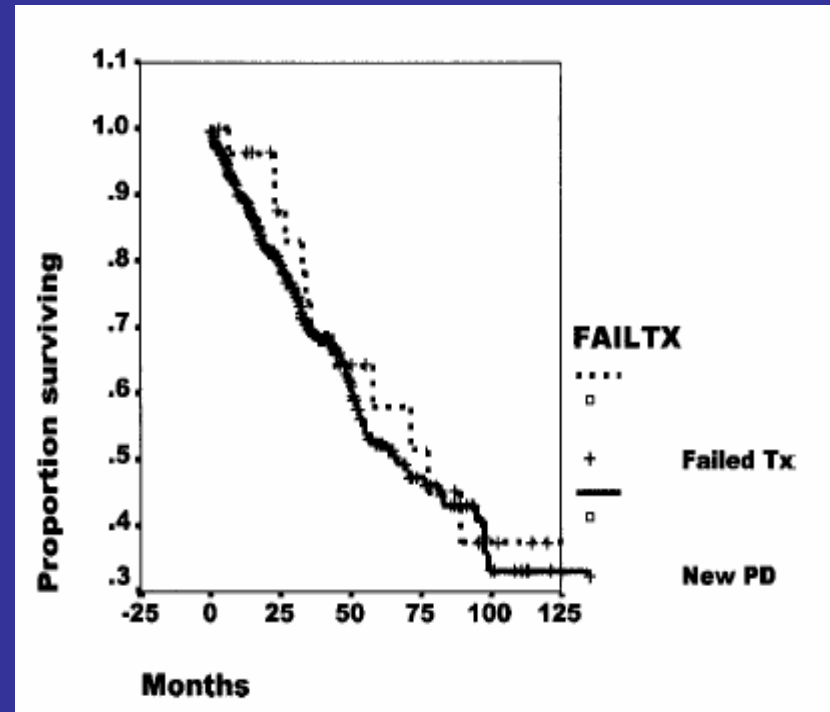


- Significantly increased risk of death ($p < 0.01$)

PD is a good option for patients with failing grafts



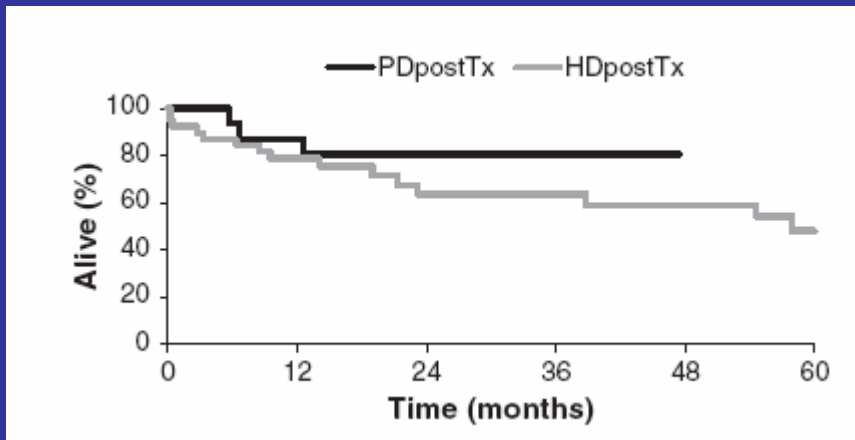
Overall survival in failed graft patients commencing PD vs. HD was similar $p=0.11$



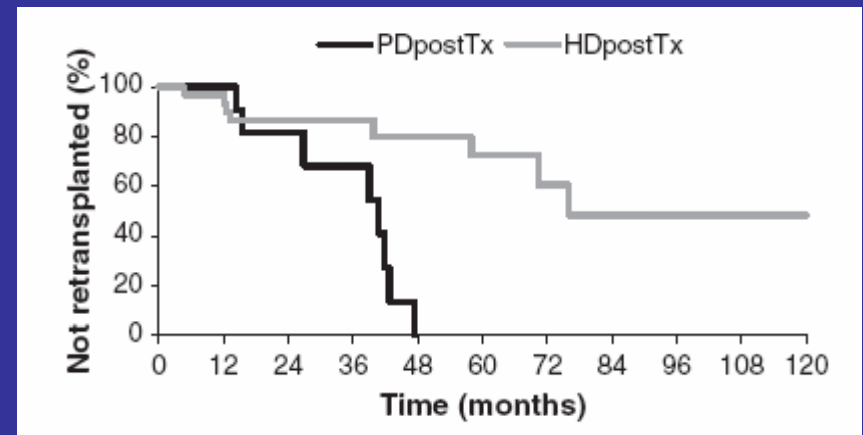
Technique survival in failed graft patients starting PD vs. new patients starting PD was similar $p=0.57$

Outcome starting PD after graft failure is at least as good as starting HD

- Comparison of patients starting PD after graft failure vs. patients starting HD after graft failure



Patient survival was similar
in both groups
P=0.24



Retransplantation rate was similar
In both groups (diff after 27 months)
P=0.14

Summary

1. Effect of dialysis modality prior to transplantation on outcomes post transplantation

- PD patients are approximately 50% more likely to undergo transplantation than HD patients even after adjustment for differences in patient characteristics (element of selection bias)
- Increased risk of graft loss for PD patients occurs early (≤ 3 months after transplantation)
- This is despite the apparent beneficial effects of a lower incidence of DGF in PD patients

Summary

2. Effect of modality on adverse effects post transplantation

- Conflicting results regarding infection rates
- Peritonitis rate can be high early post transplantation with *S aureus* and gram negative bacteria being the predominant organisms
- No difference in the rates of AR between PD and HD
- Reduced risk of DGF with PD compared with HD
- Increased risk of graft thrombosis with PD compared with HD

Summary

3. Effect of dialysis modality after graft failure

- Outcomes for PD patients after graft failure are comparable to PD patients after native kidney failure (patient, technique and peritonitis-free survival)
- Late graft failure (>2 months) is a poor prognostic factor for PD initiation
- Patient and technique survival are similar in failed graft patients commencing PD vs. HD
- Re-transplantation rates are similar in failed graft patients commencing PD vs. HD but a difference may start after 27 months (PD with a greater rate)

Conclusion

- **PD is a good option for ESRD patients *prior to transplantation.***

Important to be aware of certain factors: increased graft thrombosis risk and peritonitis risk with catheter in situ.

- **PD is also a good option for renal replacement *after graft failure.***

Attention must be given to prevent the accrual of cardiovascular risk e.g. the use of immunosuppression (to slow the decline in residual renal function) vs. discontinuation of immunosuppression with transplant nephrectomy (to prevent infection)

- Large prospective studies are required to directly examine the effect of PD vs. HD prior to transplantation, on outcomes after transplantation and also to compare the outcomes of PD with HD after transplant failure.