

Options for Renal Replacement Therapy: Comparison of Modalities

Joel D. Glickman, M.D.

Director Home Dialysis Programs

Associate Professor Clinical Medicine

University of Pennsylvania School of Medicine

Goals

⇒ Goal

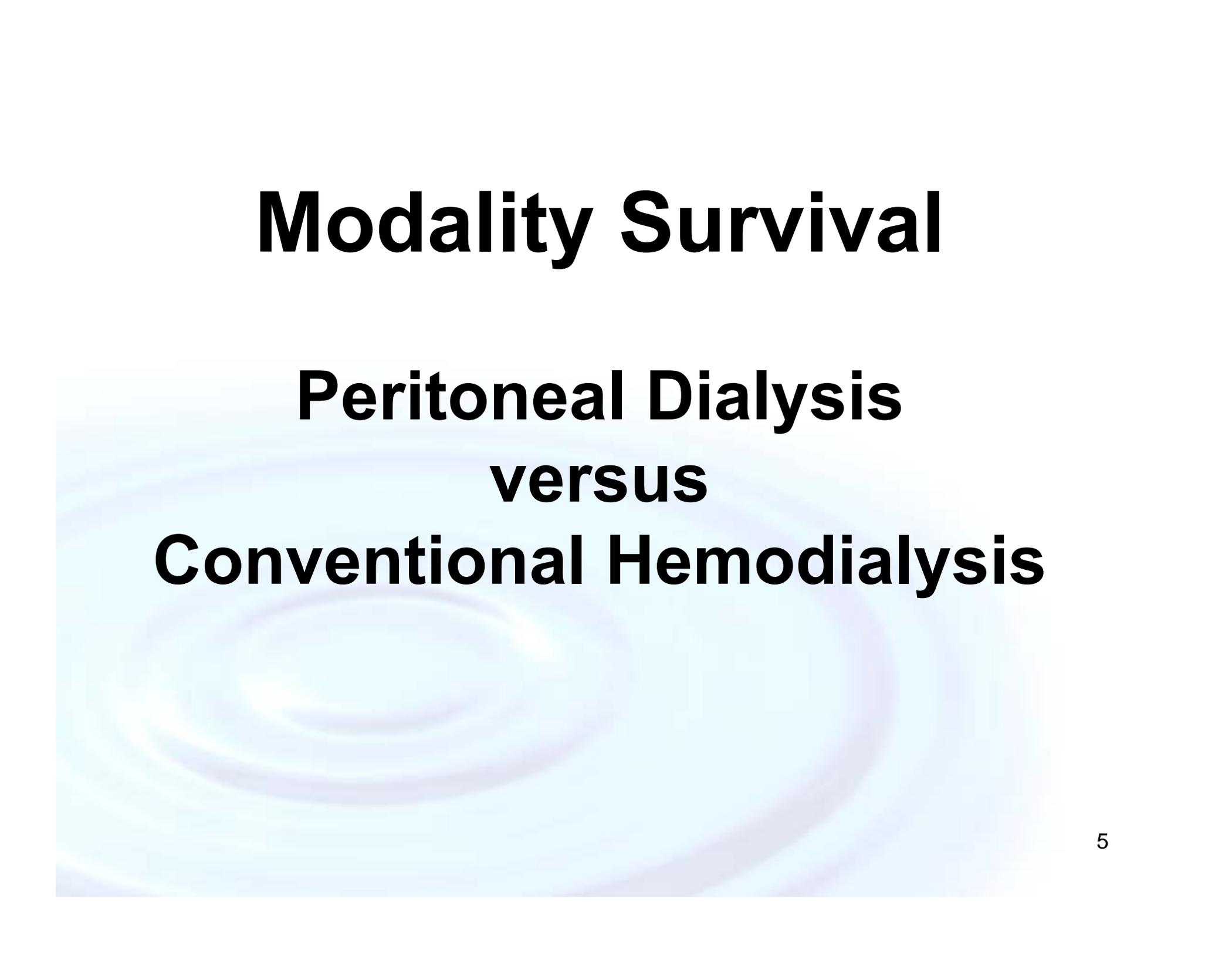
- ⇒ Determine which option for renal replacement therapy (RRT) is ideal or appropriate for an individual patient.
- ⇒ Understand limitations in current literature in determining survival comparison of different options for RRT.
- ⇒ Review pertinent literature comparing options for RRT.
- ⇒ Identify benefits, risks and indications and contraindications of each modality.

Introduction

- Which modality is best?
 - How should we define best?
 - Survival quantity?
 - Survival quality? How do you define or measure quality?
 - Live long or live well?
 - Health policy perspective or individual patient perspective?
- Can we use literature to help make decisions for an individual patient?
 - Ideally, to make an evidence based therapeutic decision regarding a patient the study group in the literature should be representative of that particular patient.
 - Current literature on survival is observational data of a heterogeneous population and does not allow the practitioner to make scientific decisions for an individual patient.

Modalities

- Main focus
 - **Peritoneal dialysis (PD)**
 - Includes chronic ambulatory peritoneal dialysis (CAPD) and APD (automated peritoneal dialysis). APD includes CCPD (continuous cycler peritoneal dialysis) and NIPD (nightly intermittent peritoneal dialysis).
 - **Conventional hemodialysis (CHD)**
 - Thrice weekly in-center hemodialysis typically of 3-5 hour duration.
- Limited data
 - **Home hemodialysis**
 - Short daily hemodialysis (SDHD) : 5-6 days per week for 2- 3 hours per treatment.
 - Nocturnal hemodialysis (NHD): 5-6 night per week for 6-8 hours per treatment.
 - **In-center nocturnal hemodialysis (ICNHD)**
 - Thrice weekly in-center 6-8 hour treatments.

The background of the slide features a soft, out-of-focus image of concentric ripples on a light blue surface, likely water, creating a calm and clean aesthetic.

Modality Survival

Peritoneal Dialysis versus Conventional Hemodialysis

Randomized Control Trial: PD vs CHD

- Ideal (though not always conclusive) study design.
- Only one RCT was published ¹
 - 38 dialysis units in Netherlands.
 - Of 1232 patients screened 773 patients eligible to participate.
 - Only 38 patients agreed to randomization.
 - Therefore limited data for conclusive results regarding survival.
- Unlikely to ever see a significant RCT comparing survival for PD and in-center HD in the future.

Limitations of survival studies: PD vs CHD

- Population and methodology heterogeneity
 - Co-morbidities
 - Propensity versus regression analysis
 - Incident vs. prevalent patients
 - Prevalent patient studies will favor modalities with high early mortality
 - 90 day exclusion
 - USRDS database study measures mortality after 90 days (favors modality with high early mortality)
 - Cumulative vs. interval survival rates
 - Residual renal function
 - Dialysis vintage
 - Modality switching
 - Extent and quality of pre-dialysis care
 - Socio-economic factors

Limitations of survival studies: PD vs CHD

- **Modality and delivery of care heterogeneity**
 - Center bias
 - Single center or dialysis provider vs multiple centers and providers
 - Center size
 - Larger programs have better outcomes ^{2,3}
 - CAPD vs CCPD or NIPD
 - Technologic advances
 - Studies do not reflect recent use of icodextrin
 - Target Kt/V differences
 - First RCT for target Kt/V for CAPD was published in 2002 ⁴.
 - First RCT for Kt/V in hemodialysis was published in 1985 ⁵.
- **Changes in survival over time**
 - More recent studies demonstrate improvement in PD survivals.

Literature Review: PD vs CHD

- Goal of this section is to present a historical perspective.
- Common misperceptions about comparison survival between PD and CHD are based on some of the studies presented.
- The studies presented were not selected because of their merits, but to point out shortcomings and pitfalls in observational studies comparing survival in PD vs HD.

Literature Review: PD vs CHD

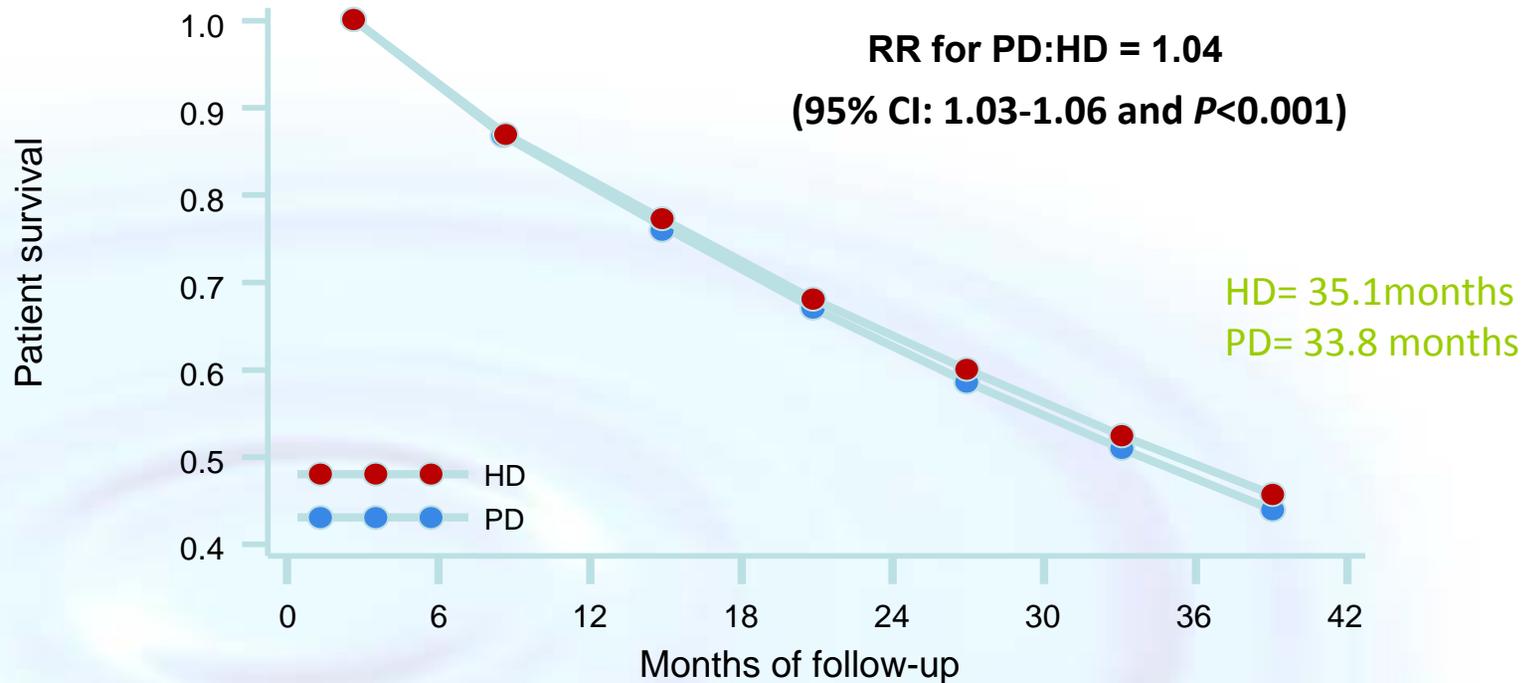
- Bloembergen 1995: studied incident and prevalent patients on therapy 1987-1989 ⁶.
 - PD 19% overall increase risk of death but no difference in patients age <55. Higher risk in diabetics. Did not examine other co-morbid conditions.
 - **Criticism:** *Old data and limited pertinence to today; did not account for dialysis dose.*
- Fenton 1997: studied incident patients from 1990-1994 ⁷.
 - Included some co-morbid conditions as well as primary renal diagnosis.
 - PD patients had a lower mortality first 2 years of therapy but less pronounced in diabetics and patients older than 65.
 - **Criticism:** *Again, old data but again suggests increase risk in diabetics and older patients.*

Literature Review: PD vs CHD - con't

- Vonesh 2004: 398,940 incident Medicare dialysis patients between 1995 and 2000 ⁸.
 - Controlled for age, diabetes and some co-morbidities.
 - Found lower risk of mortality for PD in non-diabetic patients with no co-morbidities of all age groups and diabetic patients with no co-morbidities age <45. HD had lower risk in all diabetic patients older than age 45 regardless of co-morbidities. PD and HD had same risk in non-diabetic patients with co-morbidities of all age groups and diabetics age <45.
 - *This study also includes old data and has usual criticisms of observational studies but suggests that older diabetics have less risk on HD and younger patients have less risk on PD.*

Effect of Sample Size: Clinical vs Statistical Significance⁹

At 3 Years, ≈ 1 Month Difference In Adjusted Median Life Expectancy



*PD/HD Survival Virtually Identical
In Overall Population of 398,940 Patients*

U.S. Medicare patients
(1995–2000)

Literature Review: PD vs CHD - con't

- Jaar 2005: Studied 1041 incident dialysis patients (274 PD) during period 1995-1998. 90% of patients from one dialysis provider ¹⁰.
 - Prospective, non-randomized cohort study.
 - Found same first year survival but increased risk for PD in second year.
 - **Criticism:** *relatively small study, possible center bias because of one provider. 25% of PD patients and 5% of HD patients switched modality.*

Literature Review: PD vs. CHD - con't

- Weinhandl 2010: Retrospective study of 6337 incident patient pairs (propensity matching) who initiated dialysis in 2003 ¹¹.
 - Subgroups analysis of patients by age (>65), diabetes, and CVD.
 - Demonstrated different survival curves if measurement was from initiation of dialysis (day zero) or from 90 day after dialysis initiation.
 - Demonstrated superior survival from dialysis initiation (day zero) in PD patients at 12, 24 months but no difference at 36 and 48 months.
 - Using mortality from day zero, PD survival was similar or better than HD in all subgroups for both year 1 and year 4. Only subgroups of HD patients with better survival were age >65 at year 2 and 3 (but not year 1 and 4) and diabetics at year 3 but not years 1,2 and 4.

PD Outcomes are improving

- Relevance of older observational studies is limited because of improvement in peritoneal dialysis technology and clinical outcomes.

PD Outcomes are improving ¹²

Table 3. Adjusted Hazard Ratios (HRs) for Mortality, Stratified by Cohort Periods, Using Marginal Structural Models With Inverse Probability of Treatment and Censoring Weighting^a

Cohort	HR (95% CI) ^b	<i>P</i> Value
1996-1998	1.07 (1.04-1.11)	<.001
1999-2001	1.08 (1.06-1.11)	<.001
2002-2004	1.03 (0.99-1.06)	.10

Abbreviations: CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis.

^aMedian follow-up time for HD patients with incident ESRD: 1996-1998, 29.1 mo; 1999-2001, 29.5 mo; and 2002-2004, 30.0 mo. Median follow-up time for PD patients with incident ESRD: 1996-1998, 24.9 mo; 1999-2001, 27.0 mo; and 2002-2004, 28.8 mo.

^bOverall relative risk of death between PD and HD over the course of a 5-year follow-up.

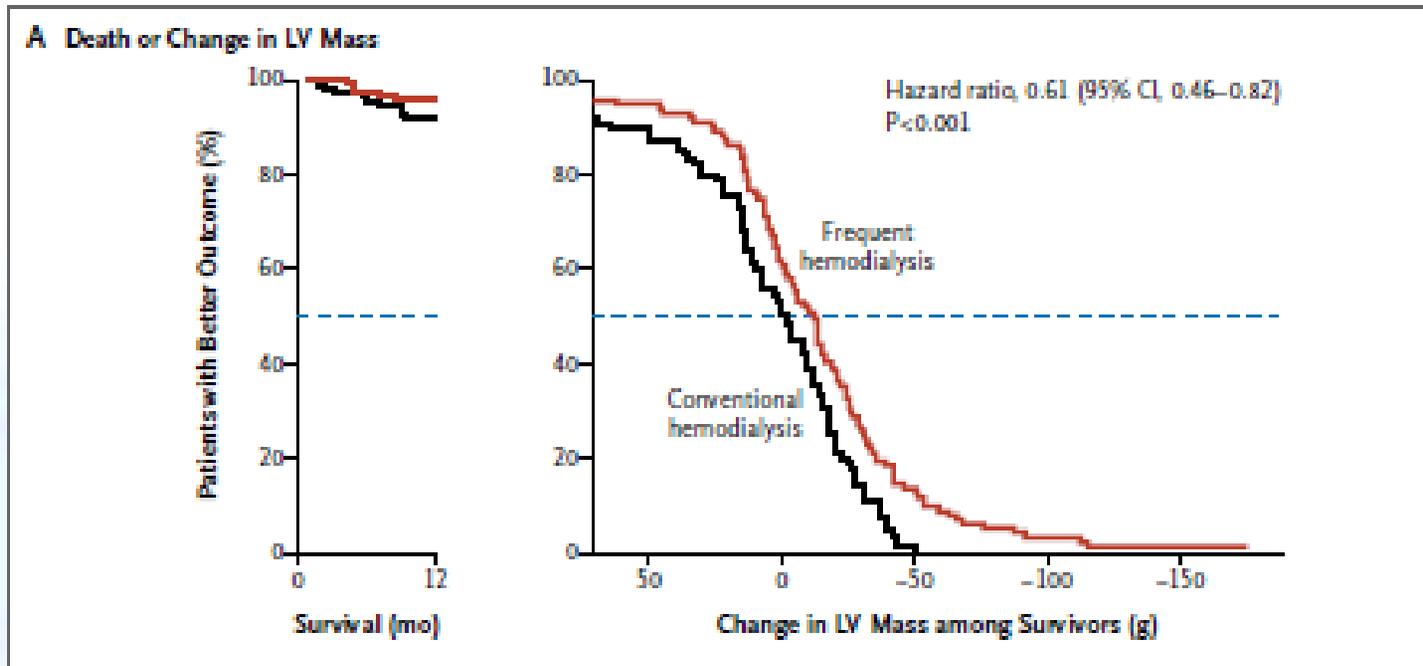
Modality Survival

Short Daily Hemodialysis versus Conventional Hemodialysis

Modality Survival: SDHD vs CHD

- Frequent Hemodialysis Network ¹³
 - Randomized control trial comparing CHD to SDHD (performed in-center)
 - Co-primary outcomes
 - 1-year mortality and, for survivors, change in left ventricular mass (LVM)
 - 1-year mortality and, for survivors, change in RAND SF 36 Physical Health Composite (PHC)

FHN SDHD Study

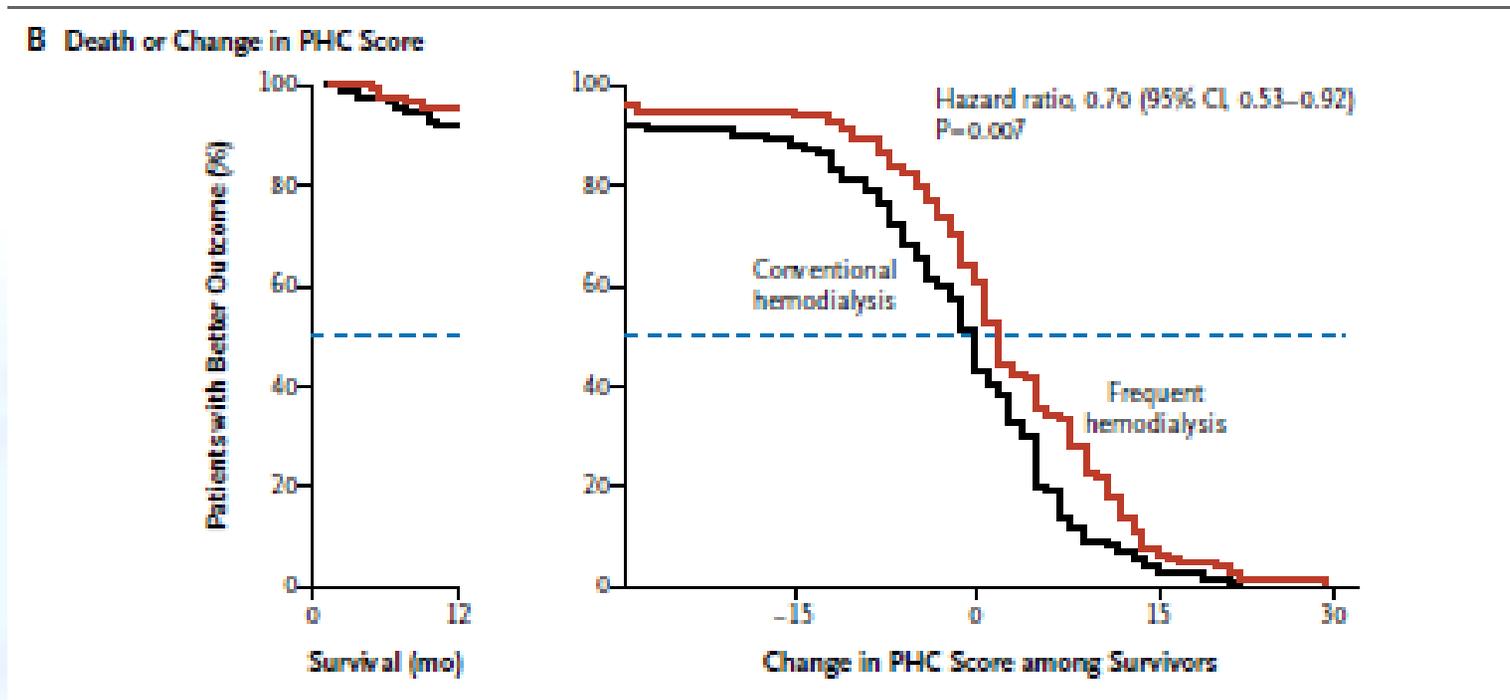


Co-primary endpoint:

1-year mortality and, for survivors, change in LVM

RESULTS: Statistical significant improvement

FHN SDHD Study



Co-primary endpoint:

1-year mortality and, for survivors, change in PHC

RESULTS: Statistical significant improvement

Overview:

Advantages, disadvantages and other factors contributing to patient modality selection

- Conventional Hemodialysis
- Peritoneal Dialysis
- Home (more frequent) Hemodialysis
- In-center Nocturnal Hemodialysis

In-center hemodialysis

- Accounts for 92% of US dialysis patients.
- Patient and patient family do not need to participate in delivery dialysis.
 - Though some dialysis units have “self-care” options where patients cannulate themselves, monitor vital signs and administer saline as needed.
 - Good for patients who are not independent and lack support system.
- Allows for better monitoring of adherence with treatments and administration of parenteral medications (erythropoietin and vitamin D analogues).

In-center dialysis

- Outcomes
 - High mortality rate.
 - Infections are frequently bacteremia and lead to increase mortality ¹⁴.
- Quality of Life
 - Inflexible schedule.
 - Most patients have hypertension requiring medications.
 - Hypertension fluctuates during inter-dialytic period ¹⁵ .
 - Travel to dialysis and planning a vacation is difficult.
 - Inability to work.
 - Post dialysis fatigue.
 - Decreased cognitive function/sense of well-being.

PD: Advantages

- Patients more satisfied with overall care compared with HD¹⁶.
- Flexible schedule
 - Especially attractive for patients who work or have children at home
- Ease of travel
- Partner not required
- Body image
 - Catheter concealed under clothing
 - No permanent disfiguring of arm seen in hemodialysis access
- “Needless and bloodless”
 - Lower risk bacteremia
- Steady-state treatment
 - Better hemodynamic stability.

PD: Advantages, con't

- Opportunity to control BP with minimal if any blood pressure medications if diet and prescription appropriately adjusted ¹⁷.
 - Requires staff attention to dialysis prescription
- Better preservation of residual renal function¹⁸.
- Less “lead time” for access placement.
 - Can place PD catheter within 2 weeks of starting PD
 - CHD requires months to develop mature AVF. 80% of CHD patients start HD with a central venous dialysis catheter
- Lower cost than HD.

Special Populations that may benefit from PD

- No or difficult venous access
 - Central vein occlusion
 - “Steal syndrome”
- High risk and morbidity of bacteremia
 - Recurrent bacteremia and endocarditis
 - Endovascular device: e.g. mechanical valve
- Patients who cannot tolerate HD because of cardiomyopathy, ischemic heart disease or extensive peripheral vascular disease
 - Allows for more gentle and continuous fluid removal
- Prolonged ATN
- Bridge to transplant

PD: Challenges

- Peritonitis
 - Rates are improving
- Catheter insertion and mechanical complications
 - Hernias and catheter malfunction
 - Requires committed surgeon
- Metabolic complications
 - Protein losses
 - Hyperglycemia
 - Hypertriglyceridemia
 - Weight gain
 - **Icodextrin** can mitigate hyperglycemia, hypertriglyceridemia and weight gain

PD: Challenges

- No days off
 - Patient and family burnout
 - If significant residual renal function, can decrease prescription and possibly provide days off
- Body image
- Technique failure
 - Better in larger programs
- Supply space
 - Smaller living spaces may not have room for supplies and might require more frequent home deliveries

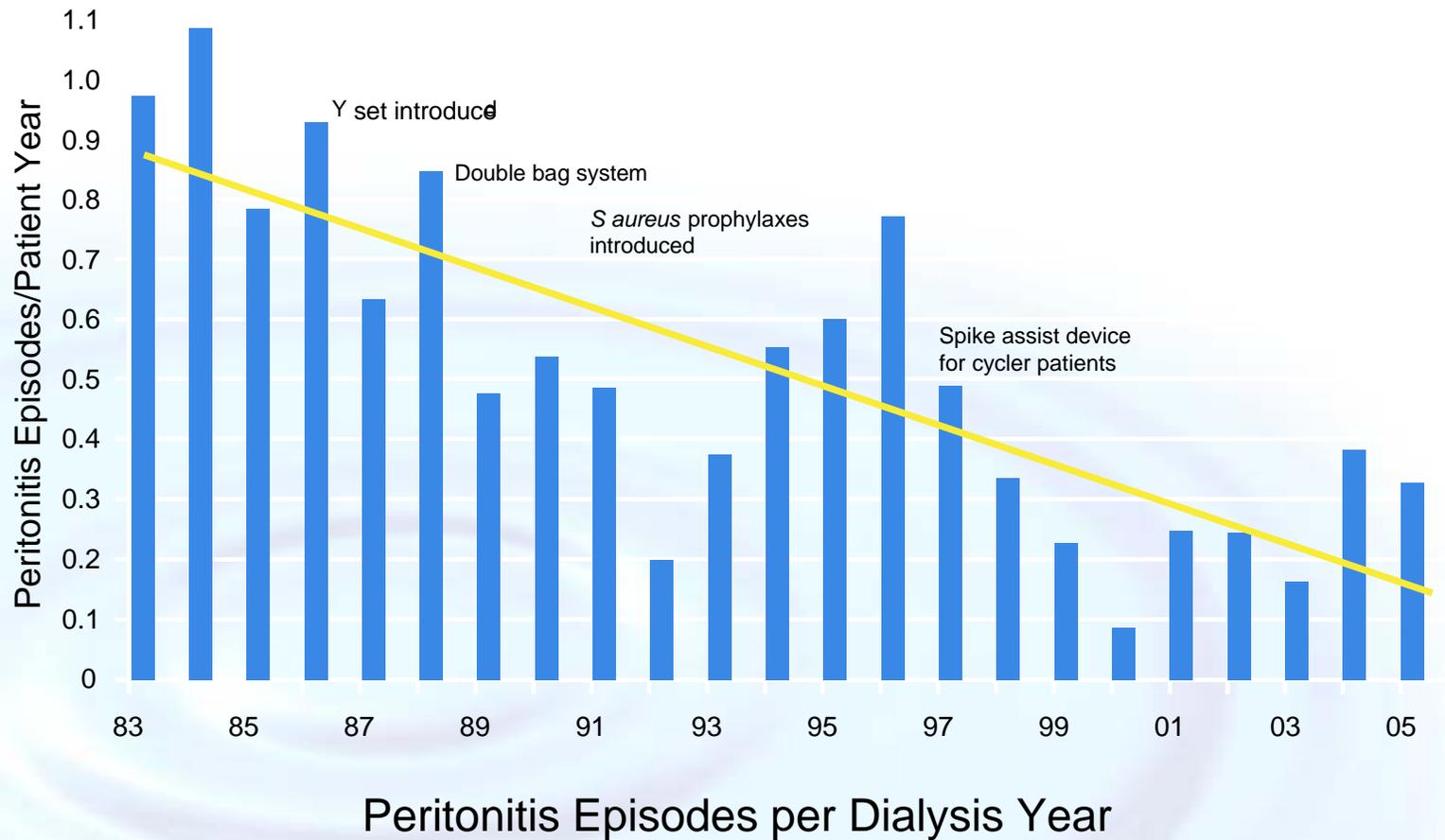
PD: Contraindications

- Absolute
 - Large mesenteric resections
 - Cutaneous feeding tubes
 - Known peritoneal defects or pleural communications
 - Severe chronic obstructive disorders
- Relative
 - Ostomies, urostomies
 - Multiple adhesions
 - Large abdominal hernias
 - ?Obesity (more than 125 kg)

Common PD misconceptions

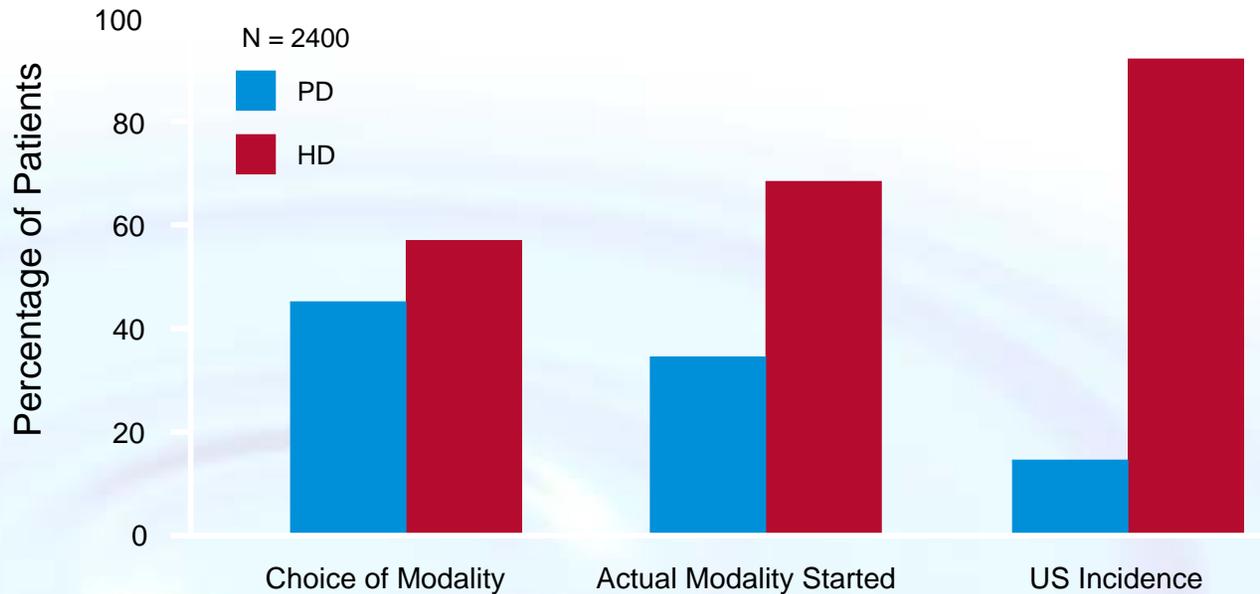
- “Survival is worse”
 - Addressed in beginning of talk.
- “Can’t achieve adequate solute clearance”
 - 2000 KDOQI recommended Kt/V of 2.0 but based on subsequent RCT the target was set at 1.7. It is fairly easy to achieve this goal in most patients.
- “Infection rate too high”
 - Peritonitis rates are decreasing- see next slide. Furthermore risk of bacteremia is lower on PD than HD and bacteremia is associated with significant morbidity and cardiovascular death.
- “Patients don’t want PD”
 - Just not true – see next slide

Infection Rates Reduced In PD As Innovations and Protocols Are Introduced ¹⁹



The More Patients Know, The More They Choose PD

After Pre-ESRD Education, 45% Chose PD
and 33% Actually Started PD ²⁰



The National Pre-ESRD Education Initiative Survey

Summary: Modality Comparison

Patient Preferences

CHD	PD
Dependent –patients are taken care of	Independent: patients are empowered for self-care
Rigid Schedule – difficult to travel	Flexible schedule – easier to travel
Venous access – needle sticks	Peritoneal Access – “bloodless”
Access Complications	Access Complications
Bacteremia	Peritonitis
Steal	Fluid leak
Central vein occlusion	Hernia
Home Consideration :None	Home Consideration: Storage space
Post-dialysis fatigue: average recovery 8 hours	No post dialysis recovery or fatigue

Home Hemodialysis Options

- Short Daily (SDHD)
 - 5-6 days per week
 - 2-3 hours per treatment depending on body size and equipment used
 - Equipment options
 - Traditional dialysis equipment: requires plumbing and electrical modification to the home. Equipment not portable.
 - NxStage- Low dialysate volume/high efficiency with portable dialysis machine. Patients can travel.

Home Hemodialysis Options

- Nocturnal (NHD)
 - Typically 5 days per week for 6-8 hours depending on patient's sleep habits.
- Hybrid (SDHD and NHD)
 - Knowledgeable patients can alternate between short daily and nocturnal hemodialysis depending on schedule. Allows for more flexibility. Few patients or physicians utilize this strategy.
- Conventional
 - For patients who prefer comfort of home dialysis but not committed to performing more frequent dialysis. Does not provide benefits of more frequent hemodialysis but can serve as a “bridge” to home NHD or SDHD.

Home (more frequent) HD: Advantages

- Outcomes
 - Improved Survival
 - Observation suggests improved survival compared with in-center HD ²⁵.
 - Observational data suggests equivalent survival to renal transplant ²⁶.
 - Quality of life ^{21,22}
 - Average recovery time after dialysis treatment is 30-60 minutes compared with 420-480 minutes for in-center HD.
 - Patients feel better and have less intra-dialytic symptoms.
 - Maybe less hospitalizations ²⁴
 - Ability to travel

Home HD: Advantages, con't

- Better phosphorous control
 - Nocturnal hemodialysis patients maintain normal serum phosphorous levels on no or less phosphate binders²³.
 - SDHD patients do not have impressive improvement.
- Cardiovascular
 - Less BP medications – most patients on none²³.
 - Regression LVH
- Sleep apnea²⁷.
 - Patients sleep better with less episodes of hypopnea and apnea

HHD: Patient Selection

Inclusion and Exclusion Criteria

- Home environment: requires reasonably sanitary conditions with appropriate water supply and electricity. Similar to PD, patients require sufficient space for storage.
- Patient and/or partner's abilities: Most patients require a partner though many patients do dialysis alone. They require basic skills including ability to read basic instructions, visual acuity, ability to hear alarms and basic manual dexterity.
- Patients need a cooperative attitude and must adhere to all procedures.
- Patient and/or partner need to be able to make appropriate decisions or follow instructions. They should not have significant psychiatric disease, chronically use of sedating medications, have a history of ongoing illicit drug use, have significant neurologic disease or dementia.

In-center nocturnal hemodialysis

- Slow, 7-8 hr treatment during the night allows for more gentle fluid removal
- More overall dialysis treatment time
- Especially beneficial for large patients with inadequate clearance, patients with chronic volume expansion or hyperphosphatemia.
- Allows patients to have days free and is an good alternative option for patients who want to work or have other daytime obligations.
- Improved patient outcomes
 - Possibly lower mortality and hospitalization compared with in-center HD ²⁸.
 - Improved blood pressure control with less blood pressure medication ²⁹.
 - Improvement in nutritional status ²⁹.

Question #1

- A 58 year old female with stage 4 CKD secondary to autosomal dominant polycystic kidney disease is approaching the need for renal replacement therapy. She does not have a potential kidney donor and has been on the transplant waiting list for about 2 years. She was told by the transplant team that it might be another 2-3 years before she receives a deceased donor kidney. She has a history of mitral valve replacement secondary to severe mitral valve prolapse with regurgitation. She works full time and has teenage children at home who are on several high school varsity teams. She wants to know what are the advantages and disadvantages of the different dialysis modalities specifically as they pertain to her. She also wants to know if ADPKD is a contraindication for PD.
- Please discuss specific benefits and risks of each modality.

Answer #1

- Most striking in her history is the presence of a mitral valve replacement. For certain we would like to decrease her risk of bacteremia and potential endocarditis. The risk of bacteremia is less with PD than HD. Therefore PD might be better than all the hemodialysis options.
- She has residual renal function (RRF) and presence of RRF predicts outcome in both PD and HD. She still has a significant wait before her kidney transplant and we would like to keep her as well as possible until then. PD preserves RRF and would likely be maintained to some degree until he receives a kidney transplant.
- She would like to continue work and PD gives her the flexibility to continue to work and to attend his kid's games!
- Finally, recent literature reports no difference in survival, technique failure or peritonitis in PD patients with ADPKD compared to non-diabetic matched controls³⁰.

Question #2

- A 39 year old male with ESRD secondary to focal glomerulosclerosis (FGS) is currently on hemodialysis and is doing very poorly. His blood pressure is high despite 3 medications and his treatments are characterized by severe intra-dialytic hypotension. He feels “washed out” after dialysis. He had two failed kidney transplants, one due to recurrent FGS and was told he is not a candidate for a kidney transplant. He was on PD for 5 years before his renal transplants and no longer has RRF. His work performance is failing and he fears he will be fired. More importantly he cannot spend enough quality time with his 5 and 7 year old sons. He has an excellent AVF.
- He wants to know what his options are.

Answer #2

- He needs a modality that will give him flexibility so he can continue work and play with his children. But he also needs a modality that will give him the energy to work and keep his blood pressure under control.
- PD could address these issues but he no longer has residual renal function, and was on PD for 5 years and therefore we don't know how well his peritoneum will perform. More importantly, in this young man with children, who will never get a kidney transplant, he doesn't want to measure survival in years but rather in decades.
- Therefore his best option is home more frequent hemodialysis; either SDHD or nocturnal HD. Both these therapies will improve BP control on minimal medications and will decrease post dialysis fatigue. His schedule will be more flexible and he should be able to continue working.

Question #3

- A 62 year old male has been on hemodialysis for 4 years and has no interest in PD. He weighs 298 pounds and loves to eat. He is still in pretty good shape and exercises regularly. His typical weight gains between treatments are 4-5 kilograms. His blood pressure is always high and he typically has 1+ edema. His phosphorous levels are typically around 8 mg/dL and are never normal even if he takes all his phosphate binders. He is on 5 hour treatments 3 days per week and his urea Kt/V measurements are only 1.1-1.2. He lives alone in a small apartment. He doesn't work but likes to babysit for his grandchildren during the day.
- What recommendations can you make for better dialysis therapy and why?

Answer #3

- He has reached the limit of what conventional can provide and is still inadequately dialyzed. He needs more dialysis that can be provided with either more frequent treatments, longer treatments or both. Ideally he should receive nocturnal HD 5 days per week but his home situation may not allow it. Therefore the best solution for him is in-center nocturnal HD three times per week. Eight hour treatments will be able to remove fluid and will improve phosphorous control. He will definitely achieve target Kt/V in an 8 hour treatment. And since he will dialyze (and sleep) at night he has the added benefit of free time during the day to play with his grandchildren.

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