Tools to Improve Survival in Dialysis: Doing the Most with a Half-Way Technology

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This is to acknowledge that Michael Concepcion, M.D. has disclosed that he does not have any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Concepcion will not be discussing off-label uses in his presentation.

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Biography

Dr. Michael Concepcion is originally for Los Angeles, CA. He received his undergraduate degree from University of California, Los Angeles, and his medical degree from University of Michigan in Ann Arbor. He completed his internal medicine resident at UT Southwestern, and his nephrology fellowship at UT Southwestern. He joined the faculty in July 2014, working primarily at Dallas Veteran's hospital.

Purpose and overview

Nearly all healthcare professionals will encounter patients with end-stage renal disease. This lecture will discuss how to optimally manage these patients in order to increase their survival.

Educational objectives

At the conclusion of this lecture, the listener should be able to:

1. Estimate when a pre-dialysis patient should have vascular access planning
2. Understand the impact of metabolic bone disease on cardiac outcomes
3. Manage the blood pressure of a dialysis patient.
4. Know the differences of cardiac risk factor management between ESRD patients and the general population.
5. Identify the benefits of home hemodialysis.

Message to the reader: The goal of this talk is to review the ways we can maximize survival of the hemodialysis patient. If you need a refresher on how dialysis works, please read the background section. Otherwise, please skip directly to section II.

I. Background

A. How does dialysis work?

Dialysis is an artificial replacement of kidney function. There are two basic ways to do dialysis: Hemodialysis (the primary focus of this talk) during which blood is directly processed in an external filter, and peritoneal dialysis in which the peritoneal membrane is used as the filter. To clarify, in hemodialysis 1) blood is removed from the body, 2) blood is passed through a filter along a semipermeable membrane with dialysate fluid running on the other side picking up the toxins from the blood, and 3) with the cleaned/processed blood then returning to the body. In peritoneal dialysis, 1) dialysate fluid is placed into the abdominal cavity, 2) which interfaces with the blood as the peritoneal membrane is lined with multiple blood vessels, with the dialysate fluid picking up toxins from the blood, and 3) eventually the effluent (the term for dialysate having picked up toxins) is drained out of the belly.

There are 4 basic roles of the kidney: 1) clearance of toxins, 2) clearance of excess electrolytes, like potassium, 3) clearance of acid and 4) clearance of excess volume.
Hemodialysis and peritoneal dialysis accomplishes goals #1-3 similarly using diffusion. For example, in both hemo- and peritoneal dialysis, toxins and excess potassium diffuses from the blood to the dialysis fluid down their natural concentration gradients. A key caveat is that ***neither hemodialysis nor peritoneal dialysis removes acid from the blood (which is what our kidneys physiologically do)***. Instead dialysate fluid contains excess bicarbonate (or bicarbonate equivalent) which is diffused into the blood in both hemo- and peritoneal dialysis – the dialysis patient then expels the acid by exhaling off carbon dioxide.
With regards to clearance of excess volume, ***hemodialysis removes excess fluid from the blood via hydrostatic pressure*** (by mechanically creating a lower hydrostatic pressure in the dialysate space relative to the blood space – this lower pressure is generated by the pre- and post filter dialysis pumps). On the other hand, ***peritoneal dialysis removes excess fluid from the blood via oncotic pressure*** (with the dialysate fluid containing excess glucose which draws water out of the blood and into the peritoneal space).

B. What is the history of hemodialysis?

- 129-216 AD: Galen described that urine is secreted from the blood by the kidneys, and passes to the bladder
- 1700s: It was observed that urinary obstruction (from kidney stones and animal models of ureteral resection) leads to toxicity and death (with post mortem accumulation of urine like fluid in the body.)
- 1800s: "Urea" was isolated from the urine. It was demonstrated the urea accumulated in the blood of patients with kidney disease. *Nonetheless, it was also shown that

injecting urea did not cause toxicity. To the present day we use urea as a marker for toxins, without specific knowledge of all the specific toxins.

- 1830s: Rene Dutrochet discovered osmosis. He placed cells in different solutions, and noted how the cell would change size as water would transfer.
- 1848: Thomas Graham who was a Scottish chemist published his laws of diffusion of gases
- 1855: Fick published his laws of diffusion of dissolved substances
- 1861: Thomas Graham published "Liquid Diffusion Applied to Analysis" during which he describes how solutes diffuse across a semi-permeable membrane. Using starch paper, he coined the terms "crystalloid" which passed through the paper, and colloids which didn't.

  At this point, with knowledge of kidney failure and understanding of diffusion through semipermeable membranes, the stage was set for the initial invention of hemodialysis.

- 1924: First doing animal hemodialysis experiments, the physician George Haas then does the first hemodialysis on a patient in 1924. He used collodion as the material for his semipermeable membrane (not because of bioavailability, but rather it was a material known to allow diffusion while being able to be manufactured into tubes). While he demonstrated a reduction in serum urea, his patients nonetheless passed away (as they had irreversible kidney disease) and Haas abandoned further attempts at dialysis. Part of this may be because dialysis was hard to do – collodion was a material that was damaged easily and did not last long.
- 1930s: Heparin (which was initially discovered in 1916) and cellulose (which was being used for manufacture of sausage casings) was started to be used in experimental dialysis apparatus. With these two advancements in material resources, the stage was set for the establishment of a "sustainable" dialysis.

- 1943: There were three programs that developed dialysis in the 1940s, one of which was from Willem Kolff who did hemodialysis on his first patient in 1943. His Kolff dialyzer consisted of cellulose tubes that wrap around a large barrel, with the tubes dipped in a trough that is filled with dialysate. In 1945, he did dialysis on the first patient who survived (after recovery of acute renal failure)
- June 1950: Korean War started. US soldiers who experienced traumatic injury and were anuric had a mortality rate of 85%. The Kolff-Brigham dialyzer was set up in Pusan, Korea by April 1952. More than 50 patients were dialyzed and mortality fell to 38%. This was one of the 'proofs' that hemodialysis saved lives in the setting of acute renal failure

- March 1960: As frequent venipuncture of native veins eventually lead to loss of dialysis access, irreversible kidney disease was a contraindication to hemodialysis. This all changed in March 1960 when the physician Belding Scribner and engineer Wayne Quinton invented the Scribner-Quinton shunt, the first AV graft. Afterwards, Clyde

Shields, a 39 year old man became the first chronic hemodialysis patient, who received dialysis from 1960 until passing away in 1971 due to a cardiac condition.
*With the birth of chronic dialysis, at the time, Seattle only had three dialysis chairs. In order to decide who would become part of their experimental dialysis program, they created a 7 person committee that consisted of a lawyer, a minister, a banker, a housewife, a state official, a labor leader and a surgeon. They often made their decisions based on the patient's ability to adhere and succeed in treatment, but also on social roles (how many children being left behind, role in the society). It was an unenviable task.

- 1966: James Cimino along with surgeon Keith Appel and resident Michael Brescia invented the AV fistula in the Bronx VA hospital. The AV fistula is superior to AV grafts and is used as the predominant vascular access presently.

- Oct 30, 1972: The Social Security Amendment is signed into law. This extended Medicare coverage to ESRD patients.

Reference for the above timeline:
Alexander, Shana. "Medical miracle and a moral burden of a small committee. They Decide Who Lives, Who Dies" Life, Nov 9, 1962
Cameron, J. Stewart. A History of the treatment of renal failure by dialysis. Oxford University Press, 2002 *this was the primary source.
Rettig, Richard. Special Treatment-The story of Medicare's ESRD Entitlement. NEJM 364:7, Feb 17, 2011

II. Lifetime expectancy and causes of death in dialysis patients

A patient with renal failure has a terminal condition that is otherwise saved by hemodialysis. Although as a "half-way" technology, patients on hemodialysis still have a much shorter lifespan compared to persons of the same age in the general population. For example, a 50 year old man on dialysis has an average life span of 8 years, whereas the average lifespan for a 50 year old in the general population is 27 more years.
As to the reason why dialysis patients die, 47% of deaths are due to cardiovascular reasons (with 29% of deaths due to sudden cardiac death). An additional 8% of deaths is due to infection. [1]

The following sections will deal with how the lifespan of each individual dialysis patient can be extended.

III. Vascular access planning

The best access for hemodialysis is an arteriovenous fistula. A fistula is created by attaching a vein to an artery. The arterial pressure then causes the vein to expand, and the consequent

'fistula' can then be used for dialysis. In the United States, it takes approximately 2-4 months before the vein can expand and the fistula is ready for use.[2] Meanwhile, approximately 39.7% of fistulas never mature (i.e. this is described a 'primary failure'). Of the ones do that mature and are initially usable, a fistula lasts for a median 5.2 years.[3]

After an AV fistula, the next best option for hemodialysis access is an AV graft. An AV graft is created by attaching an artery and vein using a synthetic material – with the synthetic material itself being used as the dialysis access point. As an AV graft does not need to mature, in the United States, they can usually be used within 2 weeks, [2] with newer graft materials allowing use within 24 hours. While it's initial failure rate of 18% is much better compared to an AV fistula, an AV graft only lasts for a median 2 years. [3]

The least desirable access type for hemodialysis is a tunneled dialysis catheter – with increased risk of infection being the reason. These are placed in the semi-emergent setting when a patient needs hemodialysis but does not have an AV fistula or graft ready. A tunneled dialysis catheter is created by inserting the catheter tip in a internal jugular central vein (very similar to how an ICU resident would place a central line) followed by burial of the dialysis catheter hub under the skin in the chest (unlike a typical ICU central line which remains hanging out of the neck). Whereas a "non tunneled" dialysis catheter can remain in place for approximately 2 weeks before the infection rate starts to exponentially increase, a tunneled dialysis catheter can remain indefinitely. Nonetheless, it has been demonstrated that a tunneled dialysis catheter has a 46% infection rate at 6 months.[4]

One risk factor that leads to the inability to place an AV fistula is a history of peripherally inserted central lines. These lines are initially placed in the peripheral vein but advanced through the central veins and eventually end with the tip resting in the superior vena cave. Throughout its course, it can damage the vascular endothelium. PICC lines have been associated with central vein (axillary, subclavian, and brachiocephalic) stenosis at a rate of 7%.[5] Furthermore, patients who receive a PICC line are at a 20% lower chance of getting a functional AV fistula compared to dialysis patients who have never had a PICC line.[6]

Timing is the other risk factor that precludes initiating dialysis via an AV fistula. Given that it takes approximately 1 month for the patient to undergo pre-surgical evaluation, and furthermore that it takes approximately 2-4 months before a surgically placed fistula becomes mature, the recommendation is a dialysis fistula should be placed at least 6 months before the dialysis date. Cohort observational studies have shown that a fistula placed 4 months before dialysis initiation is associated with a much lower chance of developing sepsis due to a tunneled dialysis catheter, than a fistula placed at the start of dialysis.[7] While there is a clear benefit to early placement of a fistula, there is also a danger in placing a fistula *excessively* early – a fistula that is placed years before a patient needs dialysis may end up clot before it is ever used. The difficult part is knowing exactly when a patient will need dialysis.

The difficulty in guessing a patient's ESRD date is that chronic kidney disease progression is often not steady and may be punctuated by episodes of acute renal failure. The Kidney Failure

Risk equation[8] was developed from a cohort of chronic kidney disease patients with GFR less than 30ml/min – it predicts the risk of progression using current GFR, sex, geographic location and proteinuria. A different author using a separate population cohort also confirmed its accuracy in predicting end-stage renal disease.[9] A surgical referral is indicated when the 1 year risk of end-stage renal disease is approximately 20%.

Given the timing issues with an AV fistula, another option is placement of a peritoneal dialysis catheter to instead pursue peritoneal dialysis. A peritoneal dialysis catheter can be used within 24 hours to 2 weeks of surgical placement,[10] making timing less difficult than a fistula. Furthermore, peritoneal dialysis has a 70% chance of still being viable at 5 years. Survival with peritoneal dialysis is actually slightly improved compared to AV fistula/graft hemodialysis in the first 2 years , with comparable survival afterwards.[11] This early improved survival maybe because peritoneal dialysis preserves residual kidney function better, with outcomes then similar to hemodialysis when residual kidney function is eventually lost.

Take home points for Vascular Access:
-Dialysis mortality from infection can be decreased by avoiding tunneled dialysis catheters.
- This can be achieved by avoiding PICC lines in patients with chronic kidney disease and by referring to vascular surgery at an appropriate time (using the Kidney Failure Risk Equation as a predictive tool).
-Peritoneal dialysis is an alternative with a more forgiving surgical timing (can be used 1 day after surgery) and is equal in efficacy compared to hemodialysis via an AV fistula/graft.

IV. Metabolic bone disease

A. Pathophysiology

Due to decreased renal clearance, phosphorus rises in the setting of kidney disease. The compensatory response is that osteocytes increase their secretion of fibroblast growth factor-23 (FGF23), which increases renal excretion of phosphorus. Meanwhile, the rising phosphorus along with the rising FGF levels and decreased renal mass causes a decreased activity of 1-alpha hydroxylase (which normally converts vitamin D to its final, active 1-25 form). Low levels of vitamin D 1-25 leads to decreased calcium absorption. The combination of low calcium and low vitamin D 1-25 then leads to rising levels of parathyroid hormone (PTH), which causes increased turnover of the bone in an attempt to restore normal serum calcium levels while concurrently increasing renal excretion of phosphorus. Despite these attempts to keep serum phosphorus and calcium levels normal, eventually as the patient approaches ESRD, the phosphorus and PTH continue to rise. If over-stimulation of PTH secretion continues, there can be a transition from secondary to tertiary hyperparathyroidism, in which phosphorus, PTH and Ca are elevated.

B. Clinical outcomes

Patients with metabolic bone disease have an increased lifetime fracture risk. The high PTH causes increased bone turnover, leading to an abnormal bone architecture (osteitis fibrosa cystic) which predisposes to fractures. This can be countered by giving activated vitamin D 1-

25, or cinacalcet. Both therapies can lower PTH, with interval improvement in markers of bone turnover. Meanwhile, over-suppressing PTH can lead to adynamic bone disease, which is also associated with increased fractures.[12]

The other outcome of CKD-metabolic bone disease is increased vascular calcification. While the mechanism of vascular calcification is complex, the three basic components are transformation of vascular smooth muscle cells to osteoblast like cells (with the transformation induced by high phosphorus, uremia, increased cytokines and other factors), increased serum levels of phosphorus and calcium, and decreased levels of inhibitor of calcification (the predominant one being fetuin-A). The transformed smooth cells then lay down extracellular matrix incorporated with the elevated phosphorus and calcium from the serum into the blood vessls.[13]

Clinical support for this model comes from observational studies that show a high phosphorus and an interval rise in serum calcium is associated with increased mortality.[14] Furthermore, observational studies have also shown that a high phosphorus and a high calcium is associated with coronary artery calcification,[15] and that coronary artery calcification is associated with increased mortality.[16]

Treatment consists of using a low phosphorus diet, but with concurrent care to avoid hypoalbuminemia (as hypoalbuminemia is also associated with increased mortality in end-stage renal disease[17]). If diet alone is not effective, the next step is adding on a phosphorus-binder, which is a medication taken with food that lowers the serum phosphorus by 'binding' the phosphorus and preventing absorption. There is a preference towards using non-calcium based binders, as they lead to less coronary artery calcification[18] and with a single meta-analysis demonstrating improved mortality of sevelamer compared to calcium based binders.[19]

Take home points for CKD associated metabolic bone disease:
-Metabolic bone disease is driven by high serum phosphorus which leads to a maladaptive response of an elevated PTH with excessive bone turnover. Meanwhile, medically over-suppressing PTH can also lead to an adynamic bone disease.
-Metabolic bone disease increases fracture risk; it also causes coronary artery calcification.
-Treatment involves decreasing serum phosphorus with a low phosphorus diet (while making sure not to cause malnutrition) and using phosphorus binders.

V. Blood pressure

Similar to non-dialysis patients, high blood pressure (as measured in between dialysis sessions) is associated with increased risk of cardiovascular events.[20] While a specific blood pressure target is not known, meta-analysis of randomized controlled trials of blood pressure treatment vs. control therapy in dialysis patients has shown that treating blood pressure improves the rate of cardiovascular events (with the baseline blood pressure being in the 135-155 systolic, and the treatment arms dropping the blood pressure by 4.5 points on average). [21] Hypertension in

dialysis patients is driven by fluid overload, as a randomized controlled trial has shown that decreasing the dry weight by 1kg can lead to a significant improvement in blood pressure. [22]

On the other hand, excessive blood pressure control may also be harmful. Intradialytic hypotension, defined as the systolic blood pressure dropping less than 90 mmHg at any time during dialysis, has been associated with worse outcomes.[23] In the same vein as intradialytic hypotension, doing excessive ultrafiltration (i.e. more than 13ml/kg/hour, for example removing 1300ml/hour in a 100kg man) has also been associated with worse outcomes.[24]

Nonetheless (and not surprisingly) it has also been shown that chronic fluid overload as measured by bioimpedance spectroscopy is also a negative prognostic indicator.[25] Thus, the philosophy of blood pressure control in hemodialysis is to keep the patients normotensive and euvolemic, while avoiding excessive ultrafiltration. A key part to this strategy is limiting fluid gains in between dialysis sessions.

Take home points for blood pressure control in dialysis patients:
-Treatment of high blood pressure improves cardiovascular outcomes.
-Hidden fluid overload is a driver of hypertension.
-While the long term goal is to maintain euvolemia, fluid removal has to be done in a safe way in which intradialytic hypotension is avoided.

VI. Role of cardio-preventative therapies

While dialysis patients have a high risk of death from cardiovascular disease, the majority of cardiovascular death is due to sudden cardiac death (rather than plaque thrombosis leading to myocardial infarction). This brings up the question of the role of traditional cardio-preventative therapies.

A. Hyperlipidemia

While statins have been shown to be highly effective in primary and secondary prevention of coronary artery disease in the non-dialysis population, its benefit in end-stage renal disease is less certain. The SHARP trial randomized 9270 patients with chronic kidney disease (3023 on dialysis and 6247 not on dialysis) to simvastatin 20mg with ezetimibe 10mg VS. placebo. While there were less cardiovascular events in the treatment group as a whole, the treatment benefit was less in the subgroup of patients that were already on dialysis.[26] The 4D trial which randomized 1255 dialysis patients with diabetes (of which 30% of patients had coronary artery disease) did not show a benefit with atorvastatin 20mg vs placebo.[27] Finally, the AURORA trial which randomized 2776 dialysis patients (of which 40% had cardiovascular disease) did not show a benefit of rosuvastatin 10mg vs. placebo.[28] As such, we typically do not initiate statins in dialysis patients, but nonetheless will still continue the medication if patients are already taking it.

B. Aspirin

In non-dialysis patients with high risk factors or with known cardiovascular disease, aspirin has a benefit in preventing myocardial infarction. The question is whether it confers this same benefit to patients on hemodialysis. In dialysis patients, a meta-analysis comparing aspirin to placebo has shown that aspirin reduces the risk of myocardial infarction (with relative risk 0.82 with confidence interval 0.47- 1.42 based on 6 studies with 2929 participants), does not alter the risk of stroke, and does not affect all cause mortality (with relative risk relative risk 0.82 with confidence interval 0.63 to 1.06 based on 13 studies with 4363 participants). Meanwhile, aspirin may increase the risk of major bleeding (with overall relative risk of all CKD patients at 1.35, although a subgroup analysis of only dialysis patients with relative risk of 0.93 with confidence interval 0.55 to 1.57 based on 13 studies).[29] As such, aspirin may be given in dialysis patients with careful consideration of the risks of bleeding.

C. Revascularization for stable coronary artery disease

In non-dialysis patients, the general consensus is that revascularization via stenting for stable coronary artery disease does not have a survival benefit until there is involvement of a large portion of the myocardium via left main or three vessel disease, in which case revascularization (possibly via bypass) is indicated. Given that CKD and dialysis patients are underrepresented in these cardiology studies, it is unknown where the 'revascularization threshold' for dialysis patients lies.

A very small randomized controlled trial of 26 diabetic, dialysis patients that underwent cardiac catheterization for transplant evaluation, and found to have an average of 1.5 stenotic lesions, were treated with revascularization vs. best medical management. In this small trial, there were less cardiovascular events and death in the group that was revascularized.[30]

Overall as this was a small study, the answer is still unknown. Two randomized controlled trials that may help answer this question are the Canadian-Australian Randomised Trial of Screening Kidney Transplant Candidates for Coronary Artery Disease (CARSK study) which will randomize patients already on the transplant wait list to surveillance non-invasive cardiac screening vs. no screening; and the ISCHEMIA-CKD trial that will randomize CKD patients (GFR <30 or on dialysis) with moderate ischemia on non-invasive cardiac stress test to cardiac catheterization vs. conservative medical therapy.

D. ICD for primary prevention and secondary prevention

Sudden cardiac death is when someone loses responsiveness due to an arrhythmic event; it accounts for 29% of all dialysis patient deaths. Risk factors for sudden cardiac death in hemodialysis patients include altered blood flow in the setting of coronary artery calcification, left ventricular hypertrophy (due to decreased hypertension/volume overload, decreased vascular compliance from calcification, anemia) and fluid and electrolyte shifts. The importance of the contribution of fluid and electrolyte shifts can be seen in relation to the day when dialysis patients are most likely to die. Dialysis patients have the highest risk of death in the first dialysis session of the week, after two consecutive without dialysis, after which potassium and fluid has accumulated the most.[31] Furthermore, a study of 66 patients

implanted with a cardiac loop recorder demonstrates that ventricular arrhythmias are most common during the first dialysis of week, while bradycardic episodes are common in the 12 hours before each dialysis session.[32]
Given that dialysis patients have a predilection for sudden cardiac death and arrhythmias, the question is whether ICDs would improve survival in primary prevention. A study of 75 dialysis patients with ejection fraction <35% equipped with a wearable cardioverter defibrillator who experienced a sudden cardiac death had a 30 day survival rate of 50.7% - this is improved compared to the non-ICD post cardiac arrest survival rate of 25%.[33] Meanwhile, an observational matched cohort study of 172 dialysis patients with ejection fraction <35% treated with ICD vs. no ICD showed no mortality benefit to ICD placement.[34] The only prospective randomized controlled trial is the ICD2 trial, which treated 188 dialysis patients with ejection fraction >35% to ICD placement vs control. Despite 14% of the ICD patients receiving an appropriate shock, the rate of sudden cardiac death and survival in both groups were the same.[35] This raises the question of whether a sicker group (i.e. baseline ejection less than 35%) would have benefited from an ICD.
Meanwhile, observational studies in secondary prevention may suggest a benefit. In a cohort study of dialysis patients who survived a sudden cardiac arrest, long term survival of patients who subsequently received an ICD was better than patients who did not receive an ICD.[43]

Take home points for cardio-preventative therapies in ESRD:
-The cardiovascular benefit of statins in dialysis patients is limited.
-Aspirin may prevent myocardial infarction but at the risk of increased bleeding.
-The role of revascularization for stable coronary artery disease is currently unknown.
-ICDs as primary prevention in dialysis patients with EF >35% is not beneficial. It is still unknown whether it is beneficial for primary prevention for dialysis patients with ejection fraction <35%.
-ICDs for secondary prevention may be beneficial.

VII. Future of hemodialysis

Given that hyperphosphatemia, hypertension, fluid overload, and rapid fluid and electrolyte shifts contribute to the increased mortality of dialysis patients, it can be reasoned that a therapy which treats all of these conditions simultaneously will improve survival. One such treatment is more frequent hemodialysis.

As a background, since the 1990s, the minimum standard of hemodialysis is three sessions a week, with each session removing 65% of the initial blood urea nitrogen. The HEMO study[36] (published in 2002) was a randomized controlled trial of 1846 dialysis patients treated with either the standard hemodialysis prescription vs. a more intensive prescription. In the more intensive treatment arm, patients were still dialyzed three times a week, but the amount of BUN removed was increased to 75%. With a five year follow up, there was no difference in mortality. Although, it raised the question of whether giving more intensive dialysis by

increasing the frequency (rather than just increasing how much BUN is removed) will improve survival.

The Frequent Hemodialysis Network Trial[37] randomized 145 dialysis patients to conventional hemodialysis vs. in center 6 days per week hemodialysis. The conventional dialysis group received dialysis 3x/week at 3.5 hours each session, while the frequent hemodialysis group received dialysis 5-6x/week at 2.5 hours each session. After a follow up of 1 year, there were significant improvements in blood pressure, left ventricular hypertension and serum phosphorus levels in the frequent dialysis group – these are all impactful surrogate outcomes which are strongly tied with long term mortality. Nonetheless, there was no difference in survival in the 1 year mark.

The Frequent Hemodialysis Network Nocturnal Trial[38] randomized 87 patients to conventional hemodialysis vs. at home nocturnal hemodialysis (with patients receiving dialysis 5x/week with each session lasting 6.3 hours). After 1 year of follow up, there were significant improvements in blood pressure and serum phosphorus levels, but no difference in survival.

The limiting factor in both of these randomized controlled trials is the small patient number and limited follow up of only 1 year. It raises the question of whether the improvements in left ventricular hypertrophy, blood pressure and phosphorus levels would translate to increased survival had the studies been done with larger numbers and longer follow up. Meanwhile, observational studies have shown that more frequent hemodialysis is associated with a longer life. In a cohort study of 338 intensive hemodialysis patients (that received dialysis 5 nights a week for 7.4 hours each session) compared to a matched 1388 patients on conventional HD followed for 4 years, the hazard ratio for death was 0.55 (confidence interval 0.34-0.87) in the intensive hemodialysis group.[39]

From an economic standpoint, the theoretic benefit of more frequent hemodialysis does *not* come at a higher monetary cost. Compared to conventional hemodialysis, while cost of supplies and biomedical engineering support increases with more frequent at home hemodialysis, it also comes with savings from decreased rate of hospitalization (as patients who get more frequent HD require less hospital admissions) and less labor cost (as patients perform home hemodialysis on their own without direct nurse cannulation or machine operation). In total, there is actually a cost savings.[40]

A potential future technology is a portable hemodialysis machine – this would provide the benefit of continuous toxin and fluid removal while decreasing the work load on the patient. The technology of a portable dialysis machine, called the “wearable artificial kidney” does currently exist. Just like stationary hemodialysis, the wearable artificial kidney still relies on a dialysis filter through which the patient’s blood runs countercurrent with dialysis fluid across a semipermeable membrane. The unique feature is that the effluent (i.e. dialysate waste) is passed through a series of adsorption cartridges that essentially remove the toxins and excess electrolytes from the effluent, thereby generating refreshed dialysate that can be used to continuously filter the patient’s blood. In a pilot study of 10 renal failure patients that used this

device for 24 hours, the clearance rate of electrolytes and urea was similar to conventional hemodialsyis.[41] A negative feature is that blood access was obtained through a tunneled dialysis catheter, which as stated earlier is associated with increased infection risk. Therefore, if this was ever to become a standard therapy, a better way of accessing the blood will need to be found.

Ultimately, the best renal replacement is not an artificial kidney, but an actual kidney itself – i.e. renal transplantation. Compared to patients who remain on the renal transplant list, recipients of a kidney transplant start accruing a survival benefit as early as 106 days after the renal transplantation,[42] which ultimately leads to a longer life. Expected remaining life years for a 20 year old who receives a kidney transplant is 43.7 years – this is a vast improvement compared to the life expectancy of 18.5 years on hemodialysis.[1]

VIII. Conclusion

While hemodialysis saves kidney failure patients from an immediate death, it also does not give patients a full life. Yet, despite its limitations, over the years survival on hemodialysis has actually improved. Since 2001, the net reduction in mortally has decreased by 28%. This is thought to be from improvements in metabolic bone disease management, nutrition optimization, and blood pressure and volume management, as discussed above. Furthermore, these improvements in survival have occurred despite frequent home hemodialysis (which has the potential for increased survival) still being a rarely used modality. With potential changes in Medicare reimbursement to give a greater financial incentive to pursue home dialysis, the goal is to continue to make incremental improvements in dialysis survival to create a bridge to renal transplantation.

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