EVIDENCE BASED CASE REPORT

Prognosis of Peritoneal Dialysis Compared to Hemodialysis in Patient with End-Stage Renal Disease

Meutia Ayuputeri

Fakultas Kedokteran Universitas Indonesia, Jakarta, Indonesia

Corresponding author: mayuputeri@yahoo.com
Diterima 3 Februari 2017; Disetujui 26 April 2018
DOI: 10.23886/ejki.6.7243.

Abstract

End-stage Renal Disease (ESRD) is the terminal stage of Chronic Kidney Disease, where the function of the failing kidney must be substituted with Renal Replacement Therapy (RRT). There are two forms of RRT; Peritoneal Dialysis (PD) and Hemodialysis (HD. However, the issue of which method provide a better survival for patient remains an interesting topic to date. This paper aims to provide evidence on whether PD provides better survival compared to HD in a patient with ESRD. Systematic search was done using two databases; Pubmed® and Scopus®. Cohort studies were selected as appropriate study design to answer a prognosis question. Two restrospective cohorts and one prospective cohort study are relevant for this report. Two studies demonstrated survival advantage of PD over HD described by Relative Risk of Mortality of 0.398 and 0.49. The last study showed worse survival of PD patients compared to HD (RR=1.82). The difference in survival in the last study may be attributed to the fact that patients undergoing PD has worse baseline characteristics. PDand HD bring about comparable survival in ESRD patients.
Keywords: *end-stage renal disease; peritoneal dialysis; hemodialysis; survival*

Prognosis Dialisis Peritoneum Dibandingkan dengan Hemodialisis pada Pasien dengan Penyakit Ginjal Tingkat Akhir

Abstrak

Penyakit ginjal tingkat akhir merupakan stadium terminal dari Penyakit Ginjal Kronis (PGK), dimana fungsi ginjal harus disubstitusi oleh terapi pengganti ginjal. Terdapat dua pilihan terapi pengganti ginjal saat ini, yakni dialisis peritoneum dan hemodialisis (HD). Pemilihan tipe terapi pengganti ginjal bagi setiap pasien bergantung pada pertimbangan medis maupun non-medis. Namun demikian, tipe terapi mana yang dapat memberikan kesintasan terbaik pagi pasien masih menjadi topik perdebatan sampai saat ini. Laporan kasus berbasis bukti ini bertujuan menyajikan bukti pilihan terapi mana yang terbaik untuk kesintasan pasien dengan penyakit ginjal tingkat akhir. Terdapat dua penelitian retrospective cohort dan satu prospective cohort yang dikaji dalam laporan ini. Dua penelitian menyebutkan bahwa dialisis peritoneum memberikan kesintasan yang lebih baik dibandingkan hemodialisis dengan masing-masing risiko relatif pada kematian sebesar 0,398 dan 0,49). Penelitian ketiga menunjukkan kesintasan dialysis peritoneum yang lebih buruk dibandingkan hemodialisis dengan risiko relative 1.82. Perbedaan ini kemungkinan disebabkan karena perbedaan lini basis pasien yang mendapatkan terapi dialisis peritoneum. Dengan demikian, kesintasan pasien penyakit ginjal tingkat akhir yang mendapat terapi dialisis peritoneum dan hemodialis dapat dibandingkan.
Kata kunci: *Penyakit ginjal tingkat akhir; dialisis peritoneum; hemodialisis, kesintasan*

Introduction

End-stage renal disease (ESRD) is the terminal stage of chronic kidney disease (CKD), where there is complete or almost complete failure for the kidney to work, measured by the gromerular filtration rate (GFR) of less than 15%. The number of patients with diabetes mellitus (DM) and end-stage renal disease (ESRD) and are being treated with renal replacement therapy (RRT/dialysis) is increasing dramatically. Across 46 developed and developing countries, it is estimated that RRT incidence rates ranges from 12 to 155 (median 130) per million population.[1]

Although kidney transplantation remains the best treatment option for eligible patients with ESRD, rates of kidney donation have not kept pace with the number of cases, leading to an increase in the number of patients on waiting lists. Thus, most patients with ESRD, including those eligible for kidney transplantation, must select a type of dialysis for renal replacement therapy.[2] Previous study in the US demonstrated that selection of peritoneal dialysis (PD) over hemodialysis (HD) was associated with patients younger age, white race, fewer comorbid conditions, and lower serum albumin as well as those who are employed, married, and living with someone before the start of ESRD, and were more autonomous and better educated.[3] Even though the use of dialysis is determined by both medical and non-medical factors, evaluating whether differences exist in the mortality outcomes of PD and HD is of considerable interest.[4,5]

This evidence-based case report aims to address the question of whether PD provides better survival than HD in patients with ESRD.

Case Ilustration

A female patient, 58 years old, complained of worsening fatique since 10 days before admission accompanied with flank pain, itchy skin, decreased urination without dysuria, or fever. Upon admission patient also complained of a diarrhea since a day before admission. Patient have had hypertension and DM since 14 years before admission, both were controlled with medication. On physical examination, patient was conscious, BP 130/70mmHg, pulse 76x/min, respiratory rate 20x/min, temperature 36^{o}C, conjungtiva were anemic. Laboratory assessment showed anemia (Hb 8.7g/dL), ureum 12.7; creatinin 227, and hyperkalemia (potassium 5.8). Patient was diagnosed with CKD Stage V, UTI, Type 2 DM, hypertension. Patient was hospitalized for CAPD installation.

Clinical Question

Based on the case, the clinical question was formulated as follow: in patients with stage V CKD, does PD improve survival over HD?

Methods

The clinical question in this study is a prognosis question, therefore systematic reviews of cohort studies and cohort studies are the suitable study designs to answer this question.[6] Evidences are searched from available databases i.e: Pubmed® and Scopus®. The keywords inputted are “Peritoneal Dialysis AND Hemodialysis AND End-stage Renal Disease AND Survival”. Inclusion criteria are systematic reviews and cohorts by design, english texts, published between 2004-2014, end stage (stage V) CKD patients going through PD or HD, survival or mortality as outcome. The exclusion criteria include are early stages of CKD, patients younger than 18 years of age, patients with prior renal transplantation.

Results

Pubmed and Scopus databases were used to find the evidence. Using predetermined keywords, 526 and 416 manuscripts were found in Pubmed® and Scopus® respectively. The manuscripts were further selected by inclusion and exclusion criteria, resulting in 3 articles suitable for this EBCR.

Restrospective cohort study conducted by Rufino et al[7] compared medium-term survival between 1469 patients with PD (173 patients) and HD (1296 patients) in Canary Islands, Spain. Among patients with PD, 62.4% were diabetics and among patients with HD, 44% were diabetics. Medium-term survival was defined as survival over the period of four years after the start of respective therapy by intention-to-treat analysis. The study analyzed survival of PD over HD among several subgroups, including DM status, age, gender and province of origin. The study utilizes the cox proportional regression model and estimated propensity score for survival to estimate the relative risks of mortality while on PD relative to HD. This study shows, the mortality risk was lower 61% for PD than for HD (RR= 0.398; p-value<0.005; 95% CI 0.237-0.669).

Choi et al.[8] conducted a nationwide prospective observational cohort study in Korean patients with ESRD on survival of PD over HD. A total of 1,060 patients who were at least 20 years old and began treatment with maintenance dialysis due to ESRD from 31 centers affiliated with research center for

ESRD were enrolled from September 1, 2008 to June 30, 2011. Data on patients' age, sex, height, weight, primary renal disease, and comorbid conditions, laboratory results, and dialysis information were analyzed using cox proportional hazard model to estimate the relative hazard ratio (HR) of mortality for PD compared to HD. The analysis used propensity matching to reduce selection bias and control for potential confounding factors (n=556). PD has 51% lower risk of death than HD (HR= 0.49; p-value<0.05; 95%CI 0.25-0.97) from day 90 to 30 months in the propensity-matched population[8].

Chang et al.[9] in South Korea observed a better survival of HD in patients with DM compared to PD. This restrospective cohort study recruited 873 subjects initiated on HD (69.3%) or PD (30.1%) on January 2000 to 30 June 2009 in Gachon University Gil Hospital, South Korea. The remaining subjects (0.6%) were excluded from analysis due to change of one modality to another during the time of study. All subjects were followed from the initiation of dialysis until the end of the study or death. The data were analyzed with multiple regression model and estimated propensity score (to reduce selection bias and control for potential confounding factors) with age, sex, cause of ESRD, medical history, and laboratory tests as covariates. Overall, HD provides survival advantage over PD. Mortality is higher in PD versus HD (HR=1.82; p-value<0.005; 95% CI 1.23-2.69) The prevalence of DM was 53.5% in among HD patients and 57.1% in PD patients. The data was shown in hazard ratio (HR= 2.86, 95% CI= 1.73-4.74) using cox proportional analysis of the matched cohort (n=424).[9]

The three articles were further assessed using the critical appraisal sheet for prognosis study provided by Oxford CEBM (Table 1-3).[10]

Table 1. Validity of the Studies

Validity	Rufino et al.[7]	Choi et al.[8]	Chang et al.[9]
Was the defined, representative sample of patients assembled at a common point in the course of their disease?	✓	✓	✓
Was patient follow-up sufficiently long and complete?	✓	✓	✓
Were objective outcome criteria applied in a "blind" fashion?	✓	✓	✓
If subgroups with different prognoses are identified, was there adjustment for important prognostic factors?	✓	✓	✓

Table 2. Importance of the Studies

Importance	Rufino et al.[7]	Choi et al.[8]	Chang et al.[9]
How likely are the outcomes over time? RR (95% CI) of mortality	PD vs. HD RR=0.398 (0.237-0.669)	PD vs. HD RR= 0.49 (0.25-0.97)	PD vs. HD RR= 1.82 (1.23-2.69)
How precise are the prognostic estimates?	Precise → 95% confidence interval less than 1	Not Precise → 95% confidence interval less than 1, but close to 1 (0.97)s	Precise → 95% confidence interval greater than 1

Table 3. Applicability of the Studies

Applicability	Rufino et al.[7]	Choi et al.[8]	Chang et al.[9]
Is my patient so different to those in the study that the results cannot apply?	No	No	No
Will this evidence make a clinically important impact on my conclusions about what to offer to tell my patients	✓	✓	✓

Discussion

Failing kidney in ESRD has a great need for RRT. Generally, RRT can be applied either intermittently or continuously using extracorporeal method (HD) or paracorporeal method (PD). The method of choice varies greatly depending on patient and disease characteristics such as hemodynamic stability and other organ failures, as well as cost.[4]

Basically, RRT employs two physiologies for solute and fluid movement. Both methods require sequestration of blood on one side of a semipermeable membrane. Firstly, in dialysis, solute move down its concentration gradient and must be of appropriate size and charge to pass the semipermeable membrane. By passing fluid across the membrane countercurrent to blood flow, equilibration of plasma and dialysate solute concentrations occur. This process may remove or add solute to the plasma water space depending upon the relative concentrations in dialysate and plasma. Water will also move along a gradient, in this case the osmolar or osmotic gradient. Diffusive clearance is more effective at removal of small solute, such as serum ions and urea, than for larger solute.

Secondly, convective clearance (hemofiltration or ultrafiltration) utilizes a pressure gradient rather than concentration gradient and has its main effect on water movement with solute movement in conjunction with water. The transmembrane pressure difference is increased as needed to move water through the membrane down a pressure gradient. This bulk flow of plasma water drags solute with it (convective mass transfer) in the formation of ultrafiltrate. Small solute removal is nearly the same as with diffusion, but fluid removal is far superior with convective clearance.[11] In these respects, blood may be passed through tubing and across artificial membranes (HD or hemofiltration), or dialysate may be instilled adjacent to the peritoneal membrane. HD remains the mainstay therapy for ESRD, according to a survey in 2005 where 89% of 1.3 million patients receiving RRT worldwide received HD while the other 11% receiving PD.[12] Among diabetic population, the average annual incidence of ESRD was 12 times greater compared to those of non-diabetic controls (130 cases vs 11 cases).[13]

Among the three studies appraised in this report, the first study by Rufino et al.[7] observed survival advantages of PD over HD in both short and medium term, independent of age, gender, and diabetic status. Limitations in this study lie on the lack of randomization due to the nature of a restrospective cohort study and are limited to Spanish population in certain area.

Choi et al. [8] exhibits superior survival of PD compared to HD from day 90 to 30 months period (HR=0.49; p-value<0.05; 95% CI 0.25-0.97). This study is a prospective, nationwide cohort study in South Korea. Critics may stipulate that the better survival of PD in ESRD patients in this study is attributed to the fact that PD patients had better predialysis conditions than HD patients (younger age, lower BMI, better baseline hemoglobin level, and lower rate of comorbidities). However, the authors in this study reasoned that they used propensity matching score to control such confounding factors in order to overcome the limitation of non-random allocation to dialysis modality.

Contrary to the first two studies, the third study by Chang et al.[9] demonstrated that HD lead to better survival in ESRD patients (RR=1.82; p-value<0.005; 95% CI 1.23-2.69). The authors proposed several reasons for the higher mortality of PD patients, including the characteristics of PD patients that have higher serum lipoprotein (a) and hyperlipidemia that may accelerate atherosclerosis. In addition, inadequate dialysis and fluid overload may occur because the residual renal function and ultrafiltration capacity of the peritoneal membrane in PD patients decrease overtime. Limitations in this study include modest sample size that resulted in limitation of power and reduced generalizability due to a single-center experience.

This evidence-based case report provides comparable result on the survival of ESRD patients undergoing PD compared to HD. The results of this report can be applied to daily clinical practice. As illustrated, our patient, a 58 years-old female with stage V CKD. Chronic ambulatory peritoneal dialysis as a type of PD is an appropriate choice for this patient. However, bearing in mind that our patient has type 2 DM as the underlying condition of her ESRD, further evidence must be reviewed.

Type 2 DM is the most common subgroup of the metabolic disease characterized by hyperglycemia that result from defect of insulin resistance and relative insulin deficiency. The chronic hyperglycemia in DM is the notorious culprit that causes long term damage, dysfunction, and failure or different organs over the years, especially the kidneys, eyes, nerves, heart, and blood vessels.[14]

The kidney complication of DM is known as diabetic nephropathy, a clinical syndrome

characterized by albuminuria, hypertension, and progressive renal insufficiency. The earliest clinical manifestation is the presence of small but abnormal levels of albumin in the urine (microalbuminuria). Microalbuminuria generally precedes overt proteinuria by 5-10 years. Once proteinuria is detected, renal function gradually deteriorates over 10-15 years, leading to ESRD . DM may exist either as the underlying disease of ESRD or as a comorbid condition of ESRD.

ESRD secondary to diabetic nephropathy requiring RRT is the most serious complications of DM above hypertension, gromerulonephritis, and cystic kidney. The United States Renal Data System in 2005 reported that the incidence of ESRD was 40.5% with DM. In Germany and Australia, 36% and 22% dialysis patients have ESRD as a result of diabetic nephropathy. In Iran, 25.2% of dialysis patients are reported to have ESRD secondary to diabetic nephropathy.[15]

The prognosis of patients who have DM and are receiving RRT has improved significantly. However, survival and medical rehabilitation rate continue to be significantly worse than that of non-diabetic patients. This is mainly attributed to preexisting severely compromised cardiovascular conditions. The most common RRT modality in patients with DM is HD, but theoretically, it gives rise to a number of clinical problems, in particular difficulties in the management of the vascular access and high frequency of intradialytic hypotension. On the other hand, patients who have DM and are on PD have to face a progressive increase in peritoneal permeability, loss of ultrafiltration, and peritoneal fibrosis, all phenomena being accelerated in patients with DM and ultimately leading to an increased technique failure.[16]

In our patient, a female 58 years of age with ESRD and 13 years history of DM, awaiting for CAPD installation, PD may provide a better survival as shown by a study by Serafinceanu et al.[17] The study analyses 788 diabetic ESRD patients initiated on HD or PD between January 1995 to December 2005 in the Dialysis Center of NIDNMD Paulescu, Bucharest. All patients were followed up for at least 12 weeks or until their death. A total of 508 patients were initiated on HD where 199 (39.17%) of those patients were deceased within the first 12 weeks after initiation. There are 280 patients that received PD among the samples, 38 (13.57 %) of which were deceased within the first 12 weeks of initiation. The survival, or in this case, mortality was expressed in Relative Risk (RR= 2.89, 95%; p-value <0.0001 CI= 2.11-3.95) of HD over PD in diabetic ESRD patients. This relationship remains significant across both sexes, albeit stronger in males (RR=4.54; p-value <0.0001; 95% CI 2.67-7.67) than in females (RR=1.89; p-value<0.0001, 95% CI 1.29-2.79). The authors in this study stipulated that this is the case due to the fact that HD is only used as the rescue therapy method in their center for late initiation of dialysis or late referral and thus associated with worse prognosis.[17]

Furthermore, Rufino et al.[7] also supports the survival advantage of PD versus HD in diabetic ESRD patients. In accordance with the two mentioned studies, Choi et al.[8] study also demonstrates the superiority of PD over HD in diabetic patients younger than 65 years of age.

Nevertheless, for the long term, DM must be properly controlled and its complications closely monitored to ensure highest quality of life in this patient. Prevention of peripheral arterial disease is also necessary to preserve vasculature for when PD fails and vascular access needed for “rescue” hemodialysis.–Furthermore, it would be interesting to investigate the survival of PD and HD in Indonesian diabetic ESRD population in relation with the relatively high infection in this country.

Conclusion

In ESRD patients where RRT is necessary, studies showed comparable results on the survival advantage of PD versus HD. More studies that include multicenter and large number of subjects are needed to provide further evidence for this issue, especially with DM as the cause of ESRD.

Acknowledgement

The author would like to extend her gratitude to dr. Irsan Hasan SpPD-KGEH, who has patiently guided the author throughout the writing process of this evidence-based case report.

References

1. Caskey FJ, Kremer A, Elliot RF, Stel VS, Covic A, Cusumano A, et al. Global variation in renal replacement therapy for end-stage renal disease. Nephrol Dial Transplant. 2011;0:1-7.
2. Jaar BG, Coresh J, Plantinga LC, Fink NE, Klag MJ, Levey AS, et al. Comparing the risk for death with peritoneal dialysis and hemodialysis in a national cohort of patients with chronic kidney disease. Annals of Internal Medicine. 2005;143(3):174-83.
3. Stack A. Determinants of modality selection among incident US dialysis patients: results from a national study. Ann Intern Med. 2005;143:174-83.

4. Vonesh E, Snyder J, Foley R, Collins A. Mortality studies comparing peritoneal dialysis and hemodialysis: what do they tell us? Kidney International. 2006;70:s3-11.
5. Keshaviah P, Collins AJ, Ma JZ, Churchill DN, Thorpe KE. Survival comparison between hemodialysis and peritoneal dialysis based on matched doses of delivered therapy. Journal of the American Society of Nephrology. 2001;13(suppl1):S48-52.
6. Straus SE, Glasziou P, Richardson WS, Haynes RB. Evidence-based medicine: how to practice and teach it. China: Churchill Livingstone Elsevier; 2011.
7. Rufino HJM, García C, Vega N, Macía M, Hernández D, Rodríguez A, et al. Current peritoneal dialysis compared with haemodialysis: medium-term survival analysis of incident dialysis patients in the canary Islands in recent years. Nefrologia. 2011;31(2):174-84.
8. Choi JY, Jang HM, Park J, Kim YS, Kang S-W, Yang CW, et al. Survival advantage of peritoneal dialysis relative to hemodialysis in the early period of incident dialysis patients: a nationwide prospective propensity-matched study in Korea. PLOS one. 2013;8(12):331-41.
9. Chang JH, Sung JY, Ahn SY, Ko K-P, Ro H, Jung JY, et al. Hemodialysis leads to better survival in patients with diabetes or high comorbidity, compared to peritoneal dialysis. Tohoku J Exp Med. 2013;229:271-7.
10. Heneghan C, Badenoch D. Evidence-based medicine toolkit. London: BMJ Books; 2002.
11. Fleming GM. Renal replacement therapy: past, present, and future. Organogenesis. 2011;7(1):2-12.
12. Grassman A, Gioberge S, Moeller S, Brown G. ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. Nephrol Dial Transplant. 2005;20:2587-93.
13. Lok C, Oliver M, Rothwell D, Hux J. The growing volume of diabetes-related dialysis: a population based study. Nephrol Dial Transplant. 2004;19(12):3098-103.
14. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;22(Suppl 1):s62-9.
15. Broumand B. Diabetes: changing the fate of diabetics in the dialysis unit. Blood Purif. 2007;25:39-47.
16. Locatelli F, Pozzoni P, Del Vecchio L. Renal replacement therapy in patients with diabetes and end-stage renal disease. Journal of the American Society of Nephrology. 2004;15(suppl 1):S25-9.
17. Serafinceanu C, Neculaescu C, cimponeriu D, Timar R, Covic A. Impact of gender and dialysis modality on early mortality risk in diabetic ESRD patients: data from a large single center cohort. Int Urol Nephrol. 2014;46(3):607-14.