Impacts of Dialysis Replacement Therapies on Insulin Resistance and Assessment of Atherosclerotic Parameters

Diyaliz Replasman Tedavilerinin İnsülin Direnci Üzerine Etkileri ve Aterosklerotik Parametrelerin Değerlendirilmesi

Mehmet KÖROĞLU[1]
Nilgül AKALIN[2]
Selçuk SEZİKLİ[3]
Yıldız OKUTURLAR[3]
Özlem HARMANKAYA[2]

1 Medikal Park Hospital, Department of Internal Medicine, İstanbul, Turkey
2 Bakırköy Dr Sadi Konuk Education and Research Hospital, Department of Nephrology, İstanbul, Turkey
3 Bakırköy Dr Sadi Konuk Education and Research Hospital, Department of Internal Medicine, İstanbul, Turkey

ABSTRACT

OBJECTIVE: We aimed to show the impacts of peritoneal dialysis and hemodialysis replacement therapies on insulin resistance which can provide important contribution to the risk for development of atherosclerosis and cardiovascular disease.

MATERIAL and METHODS: Peritoneal dialysis and hemodialysis patients, who have similar demographic and clinical characteristics, followed-up and treated regularly in the same clinic for at least one year, were included in the study. The patients with hypertension, diabetes, acute – chronic infection and obeses were excluded. Diagnosis of diabetes mellitus and presence of acute-chronic infection in the patients were exclusion criteria.

RESULTS: When peritoneal dialysis and hemodialysis patients which have similar duration of dialysis, age, gender, distribution and adequate dialysis compared with serum homocysteine levels, it is found to be higher in both of patient groups. While serum LDL-cholesterol level was determined to be higher in peritoneal dialysis patient group, no difference was determined between peritoneal dialysis and hemodialysis patient groups regarding presence of insulin resistance.

CONCLUSION: Proper patient selection and administrating appropriate treatment beginning from the first year, we think that dialysis replacement therapies have no superiority to each other regarding the development of morbidity and mortality.

KEY WORDS: Atherosclerosis, Dialysis, Insulin resistance

ÖZ

AMAÇ: Ateroskleroz ve kardiyovasküler hastalık gelişme riskine önemli katkı sağlayabilen insülin direnci üzerinde, periton diyalizi ve hemodiyaliz replasman tedavilerinin etkilerini göstermeyi hedefledik.

GEREÇ ve YÖNTEMLER: Çalışmaya en az bir yıldır aynı klinikte düzenli takip ve tedavi edilen benzer demografik ve klinik özelliklere sahip periton diyalizi ve hemodiyaliz hastaları dahil edildi. Hastalarda; hipertansiyon, obezite, diyabetes mellitus tanısı ve akut- kronik inflamasyon olmama koşulu gözetildi.

BULGULAR: Diyaliz süresi, yaş, cinsiyet dağılımı benzer olan ve diyaliz yeterliliği sağlanmış periton diyalizi ve hemodiyaliz hasta grupları karşılaştırıldığında; her iki hasta grubunda serum homosistein değerleri yüksek bulundu. Periton diyalizi hasta grubunda serum LDL- kolesterol düzeyi yüksek saptanırken; insülin direnci varlığı açısından periton diyalizi ve hemodiyaliz hasta grupları arasında fark saptanmadı.

SONUÇ: Özellikle; tedavinin birinci yılından itibaren uygun hasta seçimi ve uygun tedavi yapılması koşuluyla diyaliz replasman tedavilerinin morbidite ve mortalite gelişimi açısından birbirlerine üstünlükleri olmadığı kanısındayız.

ANAHTAR SÖZCÜKLER: Ateroskleroz, Diyaliz, İnsülin direnci

Received : 04.08.2015
Accepted : 06.10.2015

Correspondence Address:
Mehmet KÖROĞLU
Medikal Park Hastanesi,
İç Hastalıkları Bölümü, İstanbul, Turkey
Phone : + 90 506 692 88 47
E-mail : smkoroglu@hotmail.com

INTRODUCTION

The most important cause of morbidity and mortality in every stage of chronic kidney disease (CKD) and in end-stage renal failure (ESRF) is cardiovascular diseases. Ischemic heart disease and heart failure are the most common cardiovascular diseases seen in chronic kidney patients (1).

While frequency of cardiovascular disease in dialysis patients is 20-fold higher compared to normal population, in consequence of studies performed, it was determined that cardiovascular disease could account for approximately 30,00 % of mortality. Additionally, it has been observed that vascular diseases (peripheral vascular disease etc.) could increase approximately 3-fold in the presence of end-stage renal disease (ESRD) (2, 3).

It has been supported that increased levels of proinflammatory cytokines and reduced levels of anti-inflammatory cytokines in the uremic setting provided contribution to the development of cardiovascular diseases, increased arterial wall thickness, atherosclerosis and endothelial dysfunction which were the most important causes of morbidity and mortality in end-stage renal disease (4).

Studies performed in recent years demonstrated that there was an important association between the levels of cytokine macrophage migration inhibitor factor (MIF) in the circulation and vascular dysfunction. MIF is major regulator of atherogenesis and it has been seen that it has a proinflammatory and proatherogenic function. It has been shown that the functions of endothelium were impaired and there was a positive correlation between endothelial functions and arterial thickness and a negative correlation between endothelial functions and plasma MIF levels in end-stage renal disease. In consequence of these studies, it was accepted that development of atherosclerosis which was considered to be one of the most important risk factors in the development of cardiovascular disease, contributed to increased morbidity and mortality in end-stage renal disease (5, 6).

Higher prevalence rates of chronic kidney disease with higher incidence rate of comorbidity of both chronic kidney disease and cardiovascular diseases caused chronic kidney disease as an important health problem. It was observed that risk for development of cardiovascular disease in every stage of chronic kidney disease as well as risk for development of chronic kidney disease in cardiovascular diseases was increased. It has been shown that glomerular filtration rate was decreased with development of insufficient renal perfusion and followed by peritubular edema with increased volume overload during cardiovascular diseases and especially in heart failure (7). Additionally, presence of atherosclerosis, hypertension, metabolic syndrome, insulin resistance and diabetes mellitus that might cause an increase in risk for development of cardiovascular diseases might also play a role in the development of chronic kidney disease resulted in concentration of the studies on cardiorenal syndromes (5).

In a study, it has been found that increased C-reactive protein which is among the risk factors for atherosclerosis could show risk of cardiovascular disease in every stage of chronic kidney disease (8).

Although current dialysis replacement therapies used in end-stage renal disease have different advantages and disadvantages, it has been accepted that their morbidities and mortalities are not different on condition that administrating appropriate treatment in proper patient (9). Apart from increased risk for insulin resistance and atherosclerosis in dialysis patients,

Presence of diseases like insulin resistance, diabetes mellitus, dyslipidemia, hypertension and metabolic disorders may cause increased morbidity and mortality.

In our study, we also investigated the impacts of dialysis modalities on development of insulin resistance as well as the association between dialysis modalities and some risk factors for atherosclerosis in hemodialysis and peritoneal dialysis patients who have similar demographic characteristics.

MATERIALS and METHODS

This study was approved by the Ethics Committee of Bakirkoy Dr Sadi Konuk Training and Research Hospital and performed with peritoneal dialysis and hemodialysis patients who were followed-up in Nephrology Clinic of Bakirkoy Dr Sadi Konuk Training and Research Hospital. Each patient included in the study was informed about the study and they were included in the study in case of being volunteer. No change, intervention or drug administration was performed in the present treatments of the patients other than their medicines.

30 peritoneal dialysis and 42 hemodialysis patients aged 18-75 years who have similar demographic characteristics and followed-up and treated regularly, administered dialysis therapy for at least one year with adequate dialysis were included in the study. Since a comparison would be conducted regarding presence of insulin resistance and insulin resistance in dialysis groups, the patients were included in the study on condition that presence of similar distribution of female/male genders, arterial blood pressure values of < 140/90 mmHg, absence of obesity (body mass index < 29.90 kg/m^2) and diagnosis of diabetes mellitus. Since the levels of CRP and homocysteine which were among the risk factors for atherosclerosis would be evaluated, the patients with acute inflammatory disease (upper respiratory infection, pneumonia etc.), chronic inflammatory disease (collagen tissue disease, malignancy, diabetic foot etc.), recent myocardial infarction (last six months) or ischemic cerebrovascular disease were excluded from the study. Since it might affect serum homocysteine levels, the requirement of all patients were receiving similar vitamin B12 treatment and having normal serum B12 values have been fulfilled.

Body mass indices (BMI) of all patients were calculated by recording their ages, genders, heights and dry weights. For this purpose, the following formula was used: BMI (kg/m^2) = (body weight) / $(height)^2$.

Hemodialysis patients were receiving four-hour dialysis replacement therapy three days in a week. Average daily urine output of hemodialysis patients was calculated to be 100-200 cc/day and Kt/V >1,40 and URR> 70,00 %. Peritoneal dialysis therapies were performing using dialysis solutions including CAPD 2 stay safe peritoneal dialysis solutions of 2000-2500 ml, 1.50% and 2.30 % glucose and 1.25 mmol/L, 1.75 mmol/L calcium with daily 4-6 exchanges by considering clinical and laboratory values of the patients such as volume overload, peritoneal membrane permeability, serum calcium values. The requirement of Kt/V values of all peritoneal dialysis patients were 1.70 and greater has been fulfilled.

Venous blood samples were taken from all of the patients included in the study after 12 hours of fasting and simultaneously and sent to the laboratory in appropriate conditions (without hemolysis etc.) and then measurements were performed at the same devices by the same individuals without waiting. Serum fasting blood glucose, CRP, insulin, homocysteine levels and lipid profiles were evaluated. Insulin resistance, Homeostasis Model Assessment (HOMA) method was used to calculate insulin resistance and the values below 2.50 mmol/l were considered to be normal. Homa-IR = fasting plasma glucose mg/dl x fasting insulin level μU/ml)/405 Serum triglyceride levels were measured by using Abbott ARCHITECTH device and Lipase/ Glycerol Kinase w/o Glycerol Correct method; HDL-cholesterol levels were measured by using Abbott ARCHITECTH device and Non-immunological method, and LDL- cholesterol levels were measured by using Abbott ARCHITECTH device and Immunoturbidimetric Method. Serum urea levels were measured by using Abbott ARCHITECTH device and Urease, Kinetic Method and serum creatinine levels were measured by using Abbott ARCHITECTH device and Alkaline Picrate method.

Serum hemogram levels were evaluated by using Beckman Coulter LH780 device and Coulter Principle. Serum insulin levels were calculated by using Siemens Immulite 2000 device and Enzyme Chemiluminometric Immunoassay method, and serum homocysteine levels were calculated by using Siemens Immulite 1000 device and Competitive Immunoassay method. It was considered that serum homocysteine levels below 10 μmol/l were normal, serum homocysteine levels between 10-30 μmol/l were high and serum homocysteine levels above 30 μmol/l were very high. Serum CRP levels were measured by using Delta Seac analyzer device and nephelometric method and serum CRP levels below 5 mg/dl were considered to be normal.

Statistical Evaluation

In this study, NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program was used for the statistical analysis.

During the evaluation of the data obtained from the study, independent t test was used for the intergroup comparisons of descriptive statistical methods (mean, standard deviation, inter quartile range) as well as comparisons of parameters with normal distribution, Mann Whitney U test was used for the intergroup comparisons of parameters without normal distribution and Chi-Square test was used for the intergroup comparisons of qualitative data. Results were assessed at significance level of $p<0.05$.

RESULTS

Two patient groups receiving hemodialysis and peritoneal dialysis renal replacement therapy for at least one year were included in the study. Forty-two patients were receiving hemodialysis and 30 patients were receiving peritoneal dialysis renal replacement therapy. There was no difference between two patient groups regarding distribution of gender (p= 0.102) (Table I).

Mean age was 49.64 ± 18.51 years in hemodialysis patient group and 45.00 ± 16.21 years in peritoneal dialysis patient group and no statistically significant difference was determined between two patient groups regarding distribution of age (p=0.316) (Table I).

BMI of both patient groups was lower than 29.90 kg/m2 and no difference was found between heights, weights and body

Table I: Comparison of demographic and clinical characteristics of hemodialysis and peritoneal dialysis patients.

	Mean ± SD	Hemodialysis group (n=42)	Peritoneal dialysis group (n=30)	p
Gender (Male/Female)		25/17	12/18	0.102
Age (years)	Mean ± SD	49.64 ± 18.51	45.00 ± 16.21	0.316
BMI (kg/m^2)	Mean ± SD	22.43 ± 2.86	23.53 ± 3.81	0.168
Duration of dialysis (years)	Mean ± SD	3.28 ± 3.01	4.01 ± 2.51	0.076

Oneway Anova *p<0.05

mass indices. Durations of dialysis of both patient groups were found to be similar (p=0.076) (Table I).

Average LDL levels of peritoneal dialysis patient group was found to be statistically significantly higher than the average LDL levels of hemodialysis patient group (p=0.003) (Table II). No statistically significant difference was observed between average HDL levels of hemodialysis patient group and peritoneal dialysis patient group (p=0.322) (Table II).

No statistically significant difference was observed between average triglyceride levels of hemodialysis patient group and peritoneal dialysis patient group (p=0.298) (Table II).

No statistically significant difference was determined between average serum albumin concentrations of both patient groups (p=0.444) (Table II).

No statistically significant difference was observed between CRP and homocysteine values of hemodialysis patient group and peritoneal dialysis patient group (p=0.408, p=0.054; respectively) (Table II).

No statistically significant difference was observed between insulin values and HOMA-IR values of hemodialysis patient group and peritoneal dialysis patient group (p=0.796, p=0.819; respectively) (Table III).

DISCUSSION

In chronic kidney disease, disturbances of mineral metabolism, anemia, fluid overload, uremic toxicity, oxidative stress and inflammation developing with falling of glomerular filtration rate below 60 ml/min have been implicated among important causes of increased risk of cardiovascular morbidity and mortality (10).

Dyslipidemia, insulin resistance, infection, hypertension, metabolic syndrome are also important causes of morbidity and mortality other than unmodified risk factors such as age, gender and genetic in dialysis patients not differently from chronic kidney disease patients. It has been shown in the studies that insulin resistance might develop beginning from the early stages of chronic kidney disease and glucose metabolism might be impaired. In consequence of studies performed, it has been demonstrated that anemia, dyslipidemia, uremia, malnutrition, vitamin D deficiency, metabolic acidosis, increase in plasma free fatty acids and proinflammatory cytokines might cause an increase in risk for development of insulin resistance in every stages of chronic kidney disease (11).

In our study, we also aimed to evaluate the risk for development of insulin resistance and risk factors providing contribution to the development of insulin resistance in different

Table II: Comparison of biochemical parameters of hemodialysis and peritoneal dialysis patients.

	Mean ± SD	**Hemodialysis group**	**Peritoneal dialysis group**	**p**
Urea (mg/dl)	Mean± SD	145.50 ± 51.51	116.03 ± 44.02	0.013
Creatinine (mg/dl)	Mean± SD	7.90 ± 2.86	9.00 ± 2.85	0.112
Hemoglobin (mg/dl)	Mean± SD	10.37 ± 1.55	10.62 ± 1.31	0.468
Albumin (mg/dl)	Mean± SD	3.64 ± 0.53	3.55 ± 0.38	0.444
HDL-cholesterol (mg/dl)	Mean± SD	35.98 ± 10.72	38.40 ± 9.32	0.322
Triglyceride (mg/dl)	Mean± SD	164.81 ± 99.17	143.00 ± 66.37	0.298
LDL-cholesterol (mg/dl)	Mean± SD	95.14 ± 39.66	123.00 ± 36.25	0.003
C-reactive protein (mg/dl)	Mean± SD	1.04 ± 0.91	1.18 ± 1.60	0.408
Homocysteine (μM/l)	Mean± SD	21.64 ± 12.35	27.31 ± 11.69	0.054

Oneway Test, Student-t Test *p<0.05

Table III: Comparison of insulin resistances of hemodialysis and peritoneal dialysis patients.

	Mean ± SD	**Hemodialysis patient group (n=42)**	**Peritoneal dialysis patient group (n=30)**	**p**
Insulin (mmol/l)	Mean ± SD	7.36 ± 7.51	8.35±8.86	0.796
HOMA-IR (mmol/l)	Mean ± SD	1.66 ± 1.62	1.94±2.19	0.819

Oneway Test, Student-t Test *p<0.05

dialysis modalities. When we compared peritoneal dialysis patient group and hemodialysis patient group who had similar demographic characteristics and duration of dialysis regarding some metabolic parameters and risk factors for atherosclerosis, it was seen that there was no difference between both dialysis groups regarding presence of insulin resistance and risk factors for atherosclerosis but serum LDL-cholesterol level was elevated in peritoneal dialysis patient group.

In many studies comparing the superiorities of dialysis modalities each other, success rates of risk factors (glucose metabolism disorder, dyslipidemia, anemia, bone-mineral metabolism etc.) were compared at the end of dialysis therapies. While different results were obtained, it was observed that survival, morbidity and mortality were not changed in the long-term. The idea of obtaining different outcomes in these studies might be resulting from characteristics of patient groups (genetic, ethnicity, age, gender), conditions of patients for initiation of therapy (emergency or elective conditions in followed-up patients) and selection of appropriate treatment was accepted (10,12).

It has been demonstrated that metabolic disorders could be seen more commonly in peritoneal dialysis patients with the use of glucose-containing dialysis solutions as dialysis solution. However, in consequence of cardiovascular risk, morbidity and mortality studies performed in peritoneal dialysis patients, the followings were observed to be among the most important causes of morbidity and mortality: hypoalbuminemia, hyperhomocysteinemia, reduced peritoneal membrane permeability, infection and fluid overload (13,14).

In the studies investigating the impact of hemodialysis and peritoneal dialysis replacement therapies on anemia and metabolic disorders, while it was determined that development of insulin resistance in both dialysis therapies was similar, it was seen that dialysis replacement therapies did not affect the development of anemia and response of erythropoietin treatment to anemia therapy (15,16). In this study, increased frequency of metabolic syndrome in dialysis patients with effective anemia control supported the importance of the relationship of anemia to the nutritional status.

In different studies, the impact of dialysis modalities on dyslipidemia was investigated and in general while elevated serum triglyceride levels were found to be dominant in dialysis patients with a rate of 82.00 %, it was determined that HDL-cholesterol was reduced with a rate of 51.00 % and LDL-cholesterol was elevated with a rate of 40.00 %. In dialysis patients, while it was observed that risk for dyslipidemia was increased, it was supported that the effects of dialysis modalities on development of dyslipidemia were similar (10).

Also in our study, when we compared peritoneal dialysis and hemodialysis patient groups ,who do not have hypertension, diabetes mellitus and obesity, with similar durations of dialysis and demographic characteristics, we found that the serum levels of CRP, homocysteine that were considered to be among risk factors for atherosclerosis and presence of insulin resistance were similar but serum homocysteine levels were increased in both dialysis groups. We did not determine the presence of insulin resistance in dialysis patients of our study. We think that this condition will be associated with durations of dialysis and dialysis adequacies of the patients apart from metabolic controls and regular treatments of them. Determination of higher levels of serum LDL-cholesterol in peritoneal dialysis patient group can be associated with content of peritoneal dialysis solutions. Especially in recent years, observation of metabolic syndrome and obesity in peritoneal dialysis patients suggested that peritoneal dialysis solutions should be improved and it was accepted that glucose content of peritoneal dialysis solutions could contribute to the development of insulin resistance, metabolic syndrome and increase in plasma free fatty acids (12). In general, change of lipid profile in peritoneal dialysis patient population, advanced glycation end products and increased insulin resistance supported this view.

Similar to many studies, we also showed in our study that dialysis modalities did not cause different impact on development of insulin resistance and although it was tried to provide control in terms of metabolic syndrome, risk factors for atherosclerosis could increase in dialysis patients. Today, the most efficient factors about superiorities of dialysis therapies each other are timing of treatment initiation and selection of treatment. However, we think that improvement of uremic environment and metabolic disorders can affect the result. Performing continuous dialysis with peritoneal dialysis therapy may provide favorable contribution to the uremic environment. Therefore, improvement of peritoneal dialysis solutions and selection of peritoneal dialysis in proper patients can provide contribution to reducing morbidity and mortality.

CONCLUSION

Today, many factors such as increased life expectancy, increased frequencies of obesity, hypertension and diabetes mellitus have caused chronic kidney disease became an important health problem. Thus, we think that the treatment success of end-stage renal disease is important other than detection of chronic kidney disease in the early stage and prevention of disease progression. Improvement of dialysis modalities will provide a significant contribution to morbidity and mortality. Also improvement of dialysis solutions will be an important target on this subject.

Statement of Informed Consent and Statement of Human Right

All participants gave their written informed consent prior to participation in the study. The work information was received to as a directly. Volunteer participants were included to the study.

Current treatment of patients has not been changed, additional medical treatment and interventional procedures are not implemented. This article does not contain any studies with human by the any of the authors. All sources of revenu paid directly to our instituation. No money was not received to all participiant in this study. No money was tken from all participiant in the study.

This study was approved by the Ethics Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital and conducted in accordance with the principles of the Declaration of Helsinki. This study was not supported from any third party and the work was received any financial support.

REFERENCES

1. Shani S, Sarnak MJ: Cardiovascular disease and CKD: Core Curriculum 2010. Am J Kidney Dis 2010;56:399-417
2. Centers for Disease Control and Prevention: National Chronic Kidney Disease Fact Sheet: General Information and National Estimates on Chronic Kidney Disease in the United States. 2010. Atlanta GA: U.S. Department of Health and Human Services. CDC, 2010
3. Jovanović DB: Cardiovascular morbidity and mortality risk factors in peritoneal dialysis patients. Srp Arh Celok Lek 2008;136:313-318
4. Penko M, Hojs Fabjan T, Bevc S, Kanič V, Hojs R: A prospective study about impact of renal dysfunction and morbidity and mortality on cardiovascular events after ischemic stroke. Cardiol J 2014;21:163-169
5. Rosner MH, Ronco C, Okusa MD: The role of inflammation in the cardio-renal syndrome: A focus on cytokines and inflammatory mediators. Semin Nephrol 2012;32:70-78
6. Rammos C1, Hendgen-Cotta UB, Sobierajski J, Adamczyk S, Hetzel GR, Kleophas W, Dellanna F, Kelm M, Rassaf T: Macrophage migration inhibitory factor is associated with vascular dysfunction in patients with end-stage renaldisease. Int J Cardiol 2013;168:5249-5256
7. Ronco C, Cicoira M, McCullough PA: Cardiorenal syndrome type 1 pathophysiological crosstalk leading to combined heart and kidney dysfunction in the setting of acutely decompensated heart failure. J Am Coll Cardiol 2012;60:1031-1042
8. Udeanu M, Guizzardi G, Di Pasquale G, Marchetti A, Romani F, Dalmastri V, Capelli I, Stalteri L, Cianciolo G, Rucci P, La Manna G: Relationship between coronary artery disease and C-reactive protein levels in NSTEMI patients with renal dysfunction: A retrospective study. BMC Nephrology 2014;15:152
9. Lee CC, Sun CY, Wu MS: Long-term modality-related mortality analysis in incident dialysis patients. Perit Dial Int 2009;29:182-190
10. Fortes PC, Versari PH, Stinghen AE, Pecoits-Filho R: Controlling inflammation in peritoneal dialysis: The role of pd-related factors as potential intervention targets. Perit Dial Int 2007;27:S76-81
11. Fortes PC, de Moraes TP, Mendes JG, Stinghen AE, Ribeiro SC, Pecoits-Filho R: Insulin resistance and glucose homeostasis in peritoneal dialysis. Perit Dial Int 2009;29:S145-148
12. García-López E, Carrero JJ, Suliman ME, Lindholm B, Stenvinkel P: Risk factors for cardiovascular disease in patients undergoing peritoneal dialysis. Perit Dial Int 2007;27:S205-209
13. Balafa O, Krediet RT: Peritoneal dialysis and cardiovascular disease. Minerva Urol Nefrol 2012;64:153-162
14. Vogt BP, Souza PL, Minicucci MF, Martin LC, Barretti P, Caramori JT: Metabolic syndrome criteria as predictors of insulin resistance, inflammation and mortality in chronic hemodialysis patients. Metab Syndr Relat Disord 2014;12:443-449
15. Satirapoj B, Supasyndh O, Phantana-Angkul P, Ruangkanchanasetr P, Nata N, Chaiprasert A, Kanjanakul I, Choovichian P: Insulin resistance in dialysis versus non dialysis end stage renal disease patients without diabetes. J Med Assoc Thai 2011;94:S87-93
16. Uyar ME, Tutal E, Bal Z, Sezer S: Dialysis patients with the metabolic syndrome need less recombinant human erythropoietin for similar hemoglobin levels. Transplant Proc 2013;45:3481-3484