PREVALENCE OF ERECTILE DYSFUNCTION AND ASSOCIATED RISK FACTORS IN PATIENTS WITH RENAL DISEASE UNDER HEMODIALYSIS THERAPY

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ABSTRACT

Objective: Patients with chronic renal failure (CRF) under hemodialysis therapy experience a significant decrease in quality of life, due both to the limitations imposed by the disease as well as the demands of the treatment that they receive. The aim of this study was to determine the prevalence of erectile dysfunction and associated risk factors in patients with renal disease under hemodialysis therapy.

Methods: A cross-sectional study was conducted to determine the prevalence of ED among a community-based hemodialysis (HD) population. The presence and severity of ED were assessed among 134 End stage renal failure patients on hemodialysis therapy using the self-administered International Index of Erectile Function-5 (IIEF-5) questionaire as well as a questionnaire scanning for other risk factors of erectile dysfunction.

Results: The prevalence of any level of ED was 95.5% for all HD subjects. Data were used to examine and test associations between ED and associated medical conditions. Analysis showed that age, hypertension and anti hypertensive medications have a significant association with the presence of ED among HD patients ($p<0.05$).

Conclusions: Erectile dysfunction is extremely prevalent among HD patients. A complete health evaluation of male HD patients should include a discussion about their erectile function in the standard clinical care program of patients with renal disease.

Keywords: Renal Failure, Erectile Dysfunction, IIEF

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LIST OF ABBREVIATIONS

BMI	Body Mass Index
CAD	Coronary Artery Disease
CRF	Chronic Renal Failure
ED	Erectile Dysfunction
ESRD	End Stage Renal Disease
FSH	Follicle-Stimulating Hormone
GFR	Glomerular Filtration Rate
GnRH	Gonadotropin Releasing Hormone
HMG-CoA	Hydroxymethylglutaryl-coenzyme A
NO	Nitric Oxide
NPT	Nocturnal Penile Tumescence
PTH	Parathyroid Hormone
QOL	Quality Of Life
REM	Rapid Eye Movement
R-HuEPO	Recombinant Human Erythropoietin

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GENERAL RISK FACTORS OF ERECTILE DYSFUNCTION

Lifestyle

Well recognized risk factors as aging, coronary artery disease, atherosclerosis, diabetes mellitus, dyslipidemia, high blood pressure, and pelvic surgeries have all been extensively elucidated, however nowadays currently more attention has been paid to the role of lifestyle factors in penile endothelial function and erectile dysfunction (ED). Erectile dysfunction has a significant impact on quality-of-life not only by reducing self-esteem and confidence, but through affecting interpersonal relationships as well, accordingly all aspects of the contributing factors to ED need to be thoroughly evaluated ***(Messina et al., 2007)***. Recently, accumulating evidences from basic science and clinical studies have demonstrated the link between the occurrence of ED and a number of lifestyle factors, as smoking, obesity, alcohol consumption, and lack of physical activity. More importantly, as ED and cardiovascular diseases have epidemiologic and pathophysiologic associations, it is crucial to ascertain these unfavorable lifestyle factors, not only for erectile function but also for a generalized endothelial function assessment ***(Horasanli et al., 2008)***.

Midlife changes may be too late to reverse the effects of smoking, obesity, and alcohol consumption on erectile dysfunction. On contrast, physical activity may reduce the risk of ED even if initiated in midlife ***(Derby et al., 2000)***. The best approach to reduce the burden of ED on the health and well-being of older men may be early adoption of healthy lifestyle. Therefore, elucidating the role of intensive lifestyle modification in improving erectile function and decreasing cardiovascular inflammatory markers of risk one of the most important achievements ***(Bacon et al., 2006)***.

Erectile dysfunction should be considered as a marker of subclinical systemic vascular disease that was shown to precede or even predict subsequent cardiovascular events, highlighting the role of ED in identifying asymptomatic patients who may be at risk of occult coronary artery disease (CAD) ***(Roumeguère et al., 2004)***. Monitoring and early recognition may allow early management of risk factors and conditions associated with endothelial dysfunction, reducing the rate of major cardiovascular events ***(Montorsi et al., 2009)***.

Obesity and physical activity

Nowadays, obesity and dyslipidemia are more prevalent because of increasingly sedentary lifestyles and diets higher in saturated fats ***(Mulhall et al., 2006)***. Obesity was established as an underlying factor in ED after comparing

several erectile capabilities and the findings of penile duplex ultrasonography between 2 groups of patients, the first group was below 120% of the ideal body weight, and the second group was 120% or above ***(Chung et al., 1999).*** Furthermore, one-third of obese men with ED can regain their sexual activity after 2 years of adopting healthy behaviors, mainly regular exercise and reducing body weight ***(Esposito et al., 2005)***. Additionally, cholesterol-lowering interventions and treatment of hyperlipidemia can reasonably be expected to attenuate progression and deterioration of the vascular processes involved in the development of ED ***(Reffelmann and Kloner, 2006)***.

Obesity is not only linked to ED, but also represents an integral part known of the triad ED, coronary artery disease (CAD), and metabolic syndrome, due to its association with elevated levels of inflammatory marker creating a low grade inflammatory status that may be considered an important pathophysiological linkage between all these disorders ***(Corona et al., 2006)***.

Based on the role of obesity in increasing the risk of ED by 30%, and weight loss combined with physical activity in decreasing ED by 30%, the Princeton consensus emphasized the importance of lifestyle intervention, particularly in men with both ED and CAD ***(Rosen et al., 2006)***.

Smoking

Smoking shows a significant association with ED, a relation which is further strengthened as the number of smoked cigarettes increases ***(Millett et al., 2006)***.Compared with never smokers, former smokers and ever smokers have significantly higher odds of |ED risk. The relationship between smoking and ED was found to be independent to that of smoking and CAD. There is a latent period berween active smoking and symptomatic ED, a pattern noticed in former smokers and current smokers, suggesting that smoking triggers a series of processes finally resulting in ED ***(Chew et al., 2009a)***.

Erectile dysfunction can result from either direct smoking or even passive exposure to cigarettes (second-hand smoking). Smoking is associated with a twofold increase in the risk of ED. The precise cause of ED in men who smoke is not well understood, but appears to involve both long-term structural changes in arteries (atherosclerosis) and functional changes in smooth muscle relaxation including impairment of endothelial-dependent smooth muscle relaxation, increased sympathetic tone, alteration of fibrinogen levels, increased platelet aggregation, and increasing risk of vasospasm of the vascular endothelium ***(Ohl and Quallich, 2004)***.

Smoking was found among the most significant risk factors implicated in the pathogenesis of ED together with the use of recreational drugs, dyslipidemia, hypertension, and obesity. When these significant factors were studied in a multivariate model, the only factors that sustained the statistical significance were smoking and the use of recreational drugs. Additionally, a negative correlation was detected between the smoking index of ED patients and their IIEF-5 score ***(Elbendary et al., 2009***), an association which is further strengthened as the number of cigarettes smoked increases ***(Millett et al., 2006)***.

The role of smoking cessation in reversing ED appear to be confined to younger men with no or few co-existing cardiovascular risk factors with improvement of penile rigidity and tumescence within one month of smoking cessation ***(Montorsi et al., 2009*** and ***Guay et al., 1998)***.

Alcohol

Men with alcohol dependence commonly suffer from alcohol-induced ED and have poor quality of life ***(Ponizovsky, 2008)***, however**,** very limited studies are available concerning the association between alcohol consumption and ED due to the fact that men with very high alcohol intake are unlikely to participate in studies of risk association and reduction, yielding sparse inconclusive data ***(Jackson, 2007)***. Although among the few available studies, a modest negative association

between alcohol consumption and ED and confounding of the association by cardiovascular disease (CVD) and cigarette smoking ***(Chew et al., 2009b)***.

The Metabolic Syndrome (MS)

The metabolic syndrome consists of a cluster of risk factors that increase the risk of cardiovascular disease and type 2 diabetes mellitus ***(Jackson, 2006)***. It is characterized by abdominal obesity, hyperlipidemia, glucose intolerance, hypertension, and insulin resistance. Additionally, it is associated with pro-inflammatory markers and endothelial dysfunction, as well as increased incidence of moderate to severe ED in men over 50 years of age. Furthermore, ED may predict the metabolic syndrome in men with a body mass index (BMI) less than 25 kg/m^2 who otherwise would be considered to be at low cardiovascular risk ***(Jackson, 2007)***.

As the components of the metabolic syndrome increase, so does the presence of organic ED, and the incidence of hypogonadism as well as ***(Corona et al., 2006)***. The strong association between the metabolic syndrome and hypogonadism has led to the speculation that testosterone replacement might be a therapeutic option, however, the evidence primarily supports a lifestyle approach ***(Makhsida et al., 2005)***.

The Mediterranean-style diet rich in whole grain, fruits, vegetables, legumes, walnut and olive oil was found to dramatically improve markers of endothelial function and inflammation in metabolic syndrome patients, in addition to a simultaneous significant decrease in glucose, insulin, low-density lipoprotein (LDL) cholesterol, triglycerides, and blood pressure with an increase in high-density lipoprotein (HDL) cholesterol ***(Esposito et al., 2006)***.

Several studies have shown that lifestyle modification is the first-line treatment for the metabolic syndrome, with focused pharmacological treatment controlling hyperlipidemia, hypertension, and hyperglycemia conferring additional benefit when indicated ***(Sattar et al., 2003)***.

Depression

Depressive disorders range from mild symptoms to major depression with core symptoms of sadness or loss of interest or pleasure in usual activities for a period of at least 2 weeks accompanied by at least five of the following: sleep difficulties, fatigue, low self-esteem, guilt, psychomotor agitation or retardation, and loss of appetite ***(Berg et al., 2009)***.

Not surprisingly depressive symptoms may cause loss of libido and reduced sexual function but, conversely, ED may also lead to depression. Cross-sectional