Cardiovascular Disease in Post Renal Transplant recipients

Essay submitted for partial fulfillment of Master Degree of Internal Medicine

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Introduction

Cardiovascular diseases (CVD) in transplant recipients accounts for 35%-50 of all causes of mortality in transplant recipients.

Risk factors for CVD are multiple and include; non traditional risk factors unique to patients with chronic kidney disease and transplantation risk factors related to and immunosuppressive medications. transplantation Aggressive treatment of all cardiac risk factors should be performed (David D. Douglas et al., 2008).

Hypertension is prevalent in renal-transplant recipients and is associated with graft loss, congestive heart failure, ischemic heart disease, and death. Anemia, presents in 15 to 25 percent of renal-transplant recipients, is a risk factor for left ventricular enlargement, congestive heart failure and death. Diabetes, smoking, hyperlipidemia, and hyperhomocysteinemia all have adverse cardiac and renal consequences, as they do in patients with chronic renal insufficiency and those receiving dialysis.

In short; aggressive blood-pressure control, early use of angiotensin-converting-enzyme inhibitors, aggressive management of anemia, aggressive lipid control, tight control of diabetes, and lowering of homocysteine levels are likely to have a profound effect on the outcomes of transplantation and should be addressed in clinical trials (Claudio Rigatto, M.D. et al 2002).

Some of the traditional risk factors for cardiac such as hypertension, obesity, left disease and death ventricular hypertrophy (LVH),diabetes, hyperlipidemia,chronic allograft nephropathy, hyperhomocysteinemia are more common in renal transplant recipients. This may be due to persistence of a problem that predated transplantation or may result from renal insufficiency or the use of immunosuppressive medications. Other potential risk factors for heart disease are emerging such as evidence of inflammation (elevated C-reactive protein [CRP] and fibrinogen); cardiac markers (troponins, *B-type natriuretic protein [BNP], and N-terminal pro-BNP)* ; and other factors, such as lipoprotein (a) , elevated (calcium x phosphate) product, and cardiac calcifications (Rachel Becker-Cohen et al., 2006).

Research efforts and resources now are being invested in studying the causes and treatment strategies of CVD in adult transplant recipients(Levey AS et al., 1998).

The aim of work

- 1 To review pre transplant risk factors for cardiovascular diseases and acquired post transplant (specific)risk factors concerning renal transplantation.
- design a protocol, guidelines recommendations to deal with these risk factors before and after renal transplantation.

<u>Acknowledgment</u>

First and above all, all thanks to Allah who granted me the power to accomplish this work.

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Noha El sadaany

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Cardiovascular diseases (CVD) in transplant recipients accounts for 35%-50 of all causes of mortality in transplant recipients. factors for CVD are multiple and include; non traditional risk factors unique to patients with chronic kidney disease and transplantation risk factors related to transplantation and immunosuppressive medications. Aggressive treatment of all cardiac risk factors should be performed. Hypertension is prevalent in renal-transplant recipients and is associated with graft loss, congestive heart failure, ischemic heart disease, and Anemia, presents in 15 to 25 percent of renal-transplant recipients, is a risk factor for left ventricular enlargement, congestive heart failure and death. Diabetes, smoking, hyperlipidemia, and hyperhomocysteinemia all have adverse cardiac and renal consequences, as they do in patients with chronic renal insufficiency and those receiving dialysis. In short; aggressive blood-pressure control, early use of angiotensin-converting-enzyme inhibitors, aggressive management of anemia, aggressive lipid control, tight control of diabetes, and lowering of homocysteine levels are likely to have a profound effect on the outcomes of transplantation and should be addressed in clinical trials. Some of the traditional risk factors for cardiac disease and death hypertension, obesity, left ventricular hypertrophy (LVH), diabetes, hyperlipidemia, chronic allograft nephropathy, and hyperhomocysteinemia are more common in renal transplant recipients. This may be due to persistence of a problem that predated transplantation or may result from renal insufficiency or the use of immunosuppressive medications. Other potential risk factors for heart disease are emerging such as evidence of inflammation (elevated C-reactive protein [CRP] and fibrinogen); cardiac markers (troponins, B-type natriuretic protein [BNP], and Nterminal pro-BNP); and other factors, such as lipoprotein (a), elevated (calcium x phosphate) product, and cardiac calcifications. Research



efforts and resources should be invested in studying the causes and treatment strategies of CVD in adult transplant recipients.

So the aim of work is to review pre transplant risk factors for cardiovascular diseases and acquired post transplant(specific)risk factors concerning renal transplantation and to design a protocol, guidelines and recommendations to deal with these risk factors before and after renal transplantation as modifying these risk factors will reduce cardiovascular events, not only to improve the quality of life but also to offer extended life expectancy compared with dialysis.

List of abbreviations

ACE Angiotensin converting enzyme
ADA American Diabetes Association

ATP II Adult Treatment Panel II
ATP III Adult Treatment Panel III

ALERT Assessment of Lescol in Renal Transplantation trial

AHA American Heart Association
aPL Antiphospholipid antibodies
ARB angiotensin receptor blocker

ARIC study Atherosclerosis risk in communities study
ASCVD Arteriosclerosis cardiovascular disease

BMI Body mass index

CABG Coronary bypass graft surgery
CAD Coronary artery disease

CAN Chronic allograft nephropathy

CBVD Cerebrovascular death
CD Cluster of differentiation
CD30 Cluster of differentiation

CD40L CD40 ligand

CHD Coronary heart disease
CHF Congestive heart failure
CKD Chronic kidney disease
CMV Cytomegalovirus

CMV Cytomegalovirus
CNI calcineurin inhibitors
CRP C-reactive protein
CsA Cyclosporine
CV Cardiovascular

CVD Cardiovascular disease

DASH Dietary Approaches to Stop Hypertension

DIRECT study Diabetes Incidence after REnal Transplantation: Neoral

C₂ ® monitoring versus Tacrolimus

DM Diabetes mellitus

DMMS Dialysis morbidity and mortality study

ECF Extracellular fluid
ECG Electrocardiogram
EPO Erythropiotein

ESA Erythropoiesis- stimulating agents

ESRD End-stage renal disease

FKBP FK Binding-protein Hb Heamoglobin level

HLA Human leucocyte antigen

HMG-CoA 3-hydroxy-3-methylglutaryl coenzyme A

IDL Intermediate density lipoprotein

Ig Immunoglobulin

ICG International consensus guidelines
IVIG Intravenous immunoglobulins

JNC VII Joint National Committee on Prevention, Detection, and

evaluation of High Blood Pressure

K/DOQI Kidney Disease Outcomes Quality Initiative

LDL low density lipoprotein

LVH Left ventricular hypertophy

MACE Major adverse cardiac event

MATRIX Management of Anemia in French Kidney Transplant

Patients

MTHFR Methylenetetrahydrofolate reductase
MPG N-methylpurine- DNA glycosylase

MMF Mycophenolate mofetil

NCEP National Cholesterol Education Program
NCEP III National Cholesterol Education Project Plan III
NODAT New-onset diabetes after transplantation

NRT Nicotine replacement therapy

NKF-DOQI National Kidney Foundation's Disease Outcomes Quality

Initiative

PVD Peripheral vascular disease PTA Post transplantation anemia

PTDM Post transplantation Diabetes mellitus

RCT Randomized controlled trials
RRT Rerenal replacement therapy
RTR Renal transplant recipients

SCr Serum creatinine

sICAM-1 Soluble intracellular adhesion molecule -1

Th2 T helper cell 2

tHcy Total homocysteine

t PA Tissue plasminogen activator USRD U.S. Renal Data System

UNOS United Network for Organ Sharing

VLDL Very-low-density lipoprotein

WW Weight Watchers

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Arabic Summary..... 1





Cardiovascular diseases in chronic kidney disease patients





Cardiovascular diseases in chronic kidney disease patients

Cardiovascular disease (CVD) is the most common cause of death in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD). The clinical epidemiology of CVD in CKD is challenging due to a prior lack of standardized definitions of CKD, inconsistent measures of renal function, and possible alternative effects of 'traditional' CVD risk factors in patients with CKD. These challenges add to the complexity of the role of renal impairment as the cause or the consequence of cardiovascular disease

(K. Kundhal, C.E. Lok et al., 2005).

The Incidence and Prevalence of CVD in CKD (NKF-DOOI CKD Stages 1-4):

•Incidence

Only one prospective study has determined the incidence of CVD in a non-ESRD cohort without CVD at baseline, followed 147 patients for 10 years and found an incidence of CVD events (myocardial infarction, ischemic stroke) of 41% in men and 19% in women (Jungers et al.,1997).

The incidence of myocardial infarction was three times higher in men with CKD than in the general male population in all age groups. The same was true for women until age 65 years, after which the difference became less marked. The mean glomerular filteration rate (GFR) was



31 ml/min at the time of the events. In a prospective cohort of non-ESRD patients that included congestive heart failure (CHF) as part of its CVD outcomes, found, in a patient subset, that 7.4% with no previous CVD developed new cardiac disease (Levin et al., 2001).

is consistent with a population study approximately 16,000 patients atherosclerosis risk in communities study (ARIC study) where the incidence of de novo cardiovascular events was 4.8% (8.3 events/1,000 person-years) if the patient was in stage 2 CKD and 9.3% (16.8/1,000 person years) if in stage 3-4 CKD (Manjunath G et al., 2003).

In a study of 6,223 people in the Framingham study, 18% of men and 20% of women with renal impairment already had CVD. The incidence rate of cardiovascular events (coronary artery disease "CAD", CHF, ischemic stroke) was 21.3/1,000 patient-years for men 25.6/1,000 patient-years for women with stage 3 CKD. This contrasts with 18.5 and 11.0 per 1,000 patient-years in men and women, respectively, with a lower serum creatinine (SCr) (Culleton BF, 1999).

In a Canadian cohort of pre-ESRD patients with known baseline CVD, who were followed for a median of 23 months, 35% developed a new event, worsening CVD, or were hospitalized for cardiac disease (Levin A et al., **2001**).

In the ARIC study, the incidence of recurrent events over a mean duration of 6.2 years was 20.4% (38.1



events/1,000 person years; stage 2 CKD) and 28.4% (60.8/1,000 person years; stage 3-4 CKD)(Manjunath G et al., 2003).

•Prevalence

The Framingham Heart Study found the prevalence of CVD in people with renal impairment (SCr 136-265 µmol/l in men and 120-265 μmol/l in women) to be 64% higher compared with individuals with lower SCr values (Culleton BF et al.,1999).

A population-based study of 1.12 million people found a prevalence in patients with GFR <60 ml/min (CKD stage 3 or less) of 14.9% with CAD, 6.8% cerebrovascular death (CBVD), 5.0% peripheral vascular disease(PVD) 7.1% with CHF (**Go AS et al., 2004**).

In a Canadian multi-center prospective cohort of 313 pre-ESRD patients, the prevalence of all CVD was 38%. The prevalence of left ventricular hypertophy (LVH) has been found to increase with a decline in renal function. Indeed, large population-based studies consistently find a high prevalence of CVD (levin A et al., 2001).

Conversely, in a study of 14,527 people with known CAD (diagnosed myocardial infarction) 33.6% had stage 3 or greater CKD (Navekar NS et al., 2004).