ISSN 2220-3230 (online)

World Journal of *Transplantation*

World J Transplant 2022 March 18; 12(3): 27-64

Published by Baishideng Publishing Group Inc

World Journal of Transplantation

Contents

Monthly Volume 12 Number 3 March 18, 2022

REVIEW

MINIREVIEWS

World Journal of Transplantation

Monthly Volume 12 Number 3 March 18, 2022

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Transplantation*, Luca Toti, MD, PhD, Assistant Professor, Lecturer, Transplant Unit, Policlinico Tor Vergata, Rome 00133, Italy. lucatoti@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Transplantation* (*WJT*, *World J Transplant*) is to provide scholars and readers from various fields of transplantation with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJT mainly publishes articles reporting research results obtained in the field of transplantation and covering a wide range of topics including bone transplantation, brain tissue transplantation, corneal transplantation, descemet stripping endothelial keratoplasty, fetal tissue transplantation, heart transplantation, kidney transplantation, liver transplantation, lung transplantation, pancreas transplantation, skin transplantation, *etc*..

INDEXING/ABSTRACTING

The *WJT* is now abstracted and indexed in PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Transplantation

ISSN
ISSN 2220-3230 (online)

LAUNCH DATE
December 24, 2011

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Maurizio Salvadori, Sami Akbulut, Vassilios Papalois, Atul C Mehta

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2220-3230/editorialboard.htm

PUBLICATION DATE
March 18, 2022

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Transplantation

Submit a Manuscript: https://www.f6publishing.com

World J Transplant 2022 March 18; 12(3): 42-54

DOI: 10.5500/wjt.v12.i3.42

ISSN 2220-3230 (online)

MINIREVIEWS

New onset hypertension after transplantation

Mahmoud Nassar, Nso Nso, Sofia Lakhdar, Ravali Kondaveeti, Chandan Buttar, Harangad Bhangoo, Mahmoud Awad, Naveen Siddique Sheikh, Karim M Soliman, Most Sirajum Munira, Farshid Radparvar, Vincent Rizzo, Ahmed Daoud

Specialty type: Medicine, general and internal

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Nemcsik J

Received: June 7, 2021
Peer-review started: June 7, 2021
First decision: July 28, 2021
Revised: August 14, 2021
Accepted: February 19, 2022
Article in press: February 19, 2022
Published online: March 18, 2022

Mahmoud Nassar, Nso Nso, Sofia Lakhdar, Ravali Kondaveeti, Chandan Buttar, Harangad Bhangoo, Vincent Rizzo, Department of Medicine, Icahn School of Medicine at Mount Sinai (NYC Health and Hospitals: Queens), New York, NY 11432, United States

Mahmoud Awad, Department of Medicine, The Memorial Souad Kafafi University Hospital, 6th of October - Giza 0000, Egypt

Naveen Siddique Sheikh, Department of Physiology, CMH Lahore Medical College and Institute of Dentistry, Lahore - Punjab 0000, Pakistan

Karim M Soliman, Department of Medicine, Medical University of South Carolina, Charleston, SC 29425, United States

Most Sirajum Munira, Farshid Radparvar, Division of Cardiology, Department of Medicine, Icahn School of Medicine at Mount Sinai (NYC Health and Hospitals: Queens), New York, NY 11432, United States

Ahmed Daoud, Department of Medicine, Kasr Alainy Medical School, Cairo University, Cairo 11211, Egypt

Corresponding author: Ahmed Daoud, MBChB, MD, MSc, PhD, Lecturer, Staff Physician, Department of Medicine, Kasr Alainy Medical School, Cairo University, Kasr Alainy Street, Cairo 11211, Egypt. ahmed.daoud84@yahoo.com

Abstract

It has been reported that up to 90% of organ transplant recipients have suboptimal blood pressure control. Uncontrolled hypertension is a well-known culprit of cardiovascular and overall morbidity and mortality. In addition, rigorous control of hypertension after organ transplantation is a crucial factor in prolonging graft survival. Nevertheless, hypertension after organ transplantation encompasses a broader range of causes than those identified in non-organ transplant patients. Hence, specific management awareness of those factors is mandated. An in-depth understanding of hypertension after organ transplantation remains a debatable issue that necessitates further clarification. This article provides a comprehensive review of the prevalence, risk factors, etiology, complications, prevention, and management of hypertension after organ transplantation.

Key Words: New onset; Hypertension; Organ; Transplantation; Renal

Core Tip: This article provides a comprehensive review of the prevalence, risk factors, etiology, complications, prevention and management of hypertension after organ transplantation.

Citation: Nassar M, Nso N, Lakhdar S, Kondaveeti R, Buttar C, Bhangoo H, Awad M, Sheikh NS, Soliman KM, Munira MS, Radparvar F, Rizzo V, Daoud A. New onset hypertension after transplantation. *World J Transplant* 2022; 12(3): 42-54
URL: https://www.wjgnet.com/2220-3230/full/v12/i3/42.htm
DOI: https://dx.doi.org/10.5500/wjt.v12.i3.42

INTRODUCTION

The systolic blood pressure of more than 130 mmHg or diastolic blood pressure of above 80 mmHg leads to the development of hypertension requiring medical management *via* antihypertensive medications[1]. The primary and secondary blood pressure elevations potentially increase the risk of various cardiovascular complications. Secondary hypertension develops under the impact of several morbidities and comorbidities. Organ transplantation based on heart, kidney, lung, bone marrow, and liver predisposes 70%-90% of the treated patients to hypertension that potentially impacts their overall survival[2]. The development of posttransplant hypertension also leads to graft-related complications. The systematic prevention and control of organ transplant-related hypertension are paramount to reducing the risk of morbidity/mortality. This review elaborates on the complications, etiology, risk factors, prevalence, incidence, and medical management of hypertension occurring after organ transplantation.

KIDNEY TRANSPLANTATION

Most of renal transplant recipients are already hypertensive before transplant. The prevalence of hypertension in end stage renal disease is around 70%-80%. Hypertension improves in some patients after renal transplantation with the improvement of the renal functions, many patients continue to have renal transplantation related hypertension after transplantation[3].

The renal transplantation-related hypertension prevalence among 47%-82% of children and 50%-80% adults potentially deteriorate their prognostic outcomes. However, the variations in hypertension prevalence between the patient populations potentially deteriorate their medical management and treatment outcomes. More than 27.6% of patients experience hypertension within one year of their organ transplantation. The utilization of immunosuppressants, organ rejection, graft dysfunction, long surgery duration, and advanced donor age are the significant factors that increase the risk of organ transplantation-related hypertension[4]. Other predisposing factors include post-biopsy arteriovenous fistula, post-transplantation glomerulonephritis/renal artery stenosis, and family history of hypertension among organ donors[5].

HEART TRANSPLANTATION

Seventy percent of patients who receive heart transplants experience hypertension and its clinical complications[6]. The elderly hypertensive patients with heart transplant status often experience a marked reduction in estimated glomerular filtration rate and elevation in serum creatinine levels. The findings by United Network for Organ Sharing database indicate hypertension predisposition among heart transplant recipients with age sixty years or above compared to other age groups[7]. The clinical studies reveal a reduction in hypertension incidence among patients who undergo heterotrophic cardiac transplants[8]. The patients who receive an orthotopic heart transplant, however, experience a high risk for hypertension. The obese patients undergoing heart transplantation also remain highly predisposed to hypertensive heart disease. The dependence on steroids, calcineurin inhibitors, and other immunosuppressants further increase the risk of hypertension among heart transplant recipients. Medical literature correlates 70%-90% incidence of hypertension with the use of calcineurin inhibitors among heart transplant patients[9].

LUNG TRANSPLANTATION

A reportable number of patients develop new-onset/episodic hypertension after undergoing lung transplantation. Medical literature confirms the cumulative prevalence of new-onset hypertension among 45% (at one year), 56% (at two years), and 63% (at three years) of lung transplant recipients. These patients frequently develop comorbidities, including diabetes mellitus and hypercholesterolemia [10]. The lung transplant patients who receive cyclosporine treatment or encounter blood pressure elevation (before transplant) also develop hypertension in many clinical scenarios[11].

LIVER TRANSPLANTATION

Liver transplantation is the gold standard in a patient with end-stage liver disease. Immunosuppressive therapy is required to reduce rejection after transplantation[12]. Unfortunately, more than half of the liver transplant patients develop hypertension that impacts their prognosis and treatment outcomes six months after surgery. In addition, post-transplant hypertension develops among liver transplant patients based on their calcineurin inhibitor/steroid use, family history of hypertension, obesity, and older age. However, the tacrolimus use, and race of liver transplantation patients do not increase their risk for episodic hypertension[13].

BONE MARROW TRANSPLANTATION

Approximately 2.4% of bone marrow transplant recipients develop pulmonary hypertension that potentially deteriorates their quality of life, life expectancy, and quality-adjusted life-years[14]. The progressive elevation in pulmonary vascular resistance often triggers right ventricular dysfunction and mortality among bone marrow transplant patients. Hemopoietic cell transplantation among adults and children predisposes them to systemic hypertension during the initial two years of their recovery. Sixty-one percent of adults/children experience new-onset hypertension within one month of their hemopoietic cell transplant[15,16].

Etiology

The surgical interventions, immunosuppressive therapy/immune system deterioration, and recipient/donor factors potentially impact the hypertension etiology in patients with organ transplant status.

Donor factors

Hypertension among organ transplant patients also develops under the impact of deceased donor renal graft[17]. Medical literature provides inclusive findings concerning the impact of donor hypertension on the hypertension predisposition of organ transplant patients; however, it independently increases the risk for renal allograft failure[18]. The donor's age often determines the post-transplant hypertension risk of the organ transplant candidates[19]. The kidney transplant patients whose donors exhibit a history of familial hypertension experience ten times greater risk of blood pressure elevation than the patients whose donors do not report a family history of hypertension[12]. The differences between the donors' age and body surface area and their organ recipients also predispose them to episodic hypertension. The nephron underdosing due to reduced recipient/donor body weight ratio potentially triggers chronic inflammation among organ transplant patients, which eventually predisposes them to diabetes mellitus, post-transplant hypertension, and chronic rejection of transplanted organs[20].

Recipient factors

The clinical studies provide inconclusive evidence concerning the impact of behavioral patterns of organ transplant patients on their hypertension predisposition. However, alcohol consumption, smoking, salt intake, and obesity deteriorate the clinical outcomes of organ transplant patients and increase their risk of hypertension compared to the general population. The organ transplant candidates with pretransplant hypertension and obesity experience a high risk of posttransplant hypertension[17-22]. Stable kidney transplant patients with hypovolemia experience a high risk of elevated mean arterial/diastolic/systolic blood pressures[23]. Post-transplant hypertension also develops under the impact of comorbidities (including endocrine tumors and obstructive sleep apnea) and the age of the recipients.

Transplant renal artery stenosis

The development of transplant renal artery stenosis (TRAS) under the impact of renal artery stenosis reduces the vascular supply to the allograft. TRAS triggers hypertension among 1%-5% of renal transplant recipients[24,25]. The initial six months to two years after organ transplant predispose the treated patients to TRAS-related complications[26]. TRAS manifests with transplant dysfunction,

water/salt retention, renal function deterioration, and refractory hypertension. The organ transplant patients eventually experience acute pulmonary edema and hypertensive crisis[26]. TRAS-induced hypoperfusion triggers renin-angiotensin-aldosterone system (RAAS) that potentiates renovascular hypertension in patients with organ transplant status[26]. The potential causes of transplant renal artery stenosis include immune-mediated endothelial deterioration, recipient/donor artery trauma, suturing techniques, donor artery atheroma, and renal artery lesions[27]. TRAS assessment relies on conventional angiography; however, TRAS correction and enhancement of blood pressure/renal perfusion warrants renal vascularization *via* PCTA (percutaneous transluminal coronary angioplasty)[26].

Acute rejection and chronic allograft injury

Hypertensive crisis in organ transplant patients correlates with acute and chronic allograft injury. However, clinical studies provide inconclusive evidence concerning a causal relationship between hypertension and allograft deterioration[22].

Acute rejection

The cases of acute organ rejection warrant diagnostic assessment concerning post-transplant hypertension. The therapeutic management of acute organ rejection often corrects the systolic and diastolic blood pressure elevations in organ transplant patients. These outcomes substantiate the acute organ rejection attribution of hypertension in organ transplant scenarios[22].

Chronic graft injury

The chronic renal allograft injury emanates from recurrent glomerular disease, thrombotic microangiography, tubular atrophy, interstitial fibrosis, and chronic antibody-mediated organ rejection. The focal segmental glomerulosclerosis predominantly associates with hypertension in patients with organ transplant status. The current body of evidence provides inconclusive evidence concerning the cause-and-effect relationship between renal allograft dysfunction and hypertensive crisis among organ transplant patients. However, the findings from a preclinical study advocate the potential of hypertension to cause allograft deterioration in organ transplant scenarios[28].

Immunosuppressive drugs

The toxic effects of immunosuppressive drugs often elevate the risk of hypertension among organ transplant patients.

Steroids

The organ rejection prevention protocol concerning transplantation scenarios relies on the systematic administration of methylprednisolone and prednisone. Corticosteroid maintenance therapy potentially triggers a range of morbidities and comorbidities among patients with organ transplant status. It also increases their risk of hypertension to multiple folds. A plausible mechanism concerning steroid-induced hypertension attributes to volume expansion/sodium retention due to mineralocorticoid receptor overstimulation in organ transplant patients. The exclusion of steroids from the immunosuppressive therapy to mitigate the risk of hypertension could, however, trigger organ rejection and its fatal complications. A recently reported meta-analysis confirmed a 48% incidence of acute organ rejection in patients who did not receive steroids with their immunosuppressive therapies compared to 30% organ rejection incidence among patients who received steroid-controlled immunosuppressive treatments[29].

Calcineurin inhibitors

The multifactorial characteristics of calcineurin inhibitor-induced hypertension are widely debated in the medical literature. The calcineurin inhibitors impact the function of the sodium-potassium pump/sympathetic nervous system and vascular tone that eventually triggers a hypertensive crisis in patients with organ transplants. They further induce nitric oxide metabolism by triggering nicotinamide adenine dinucleotide phosphate oxidase-induced angiotensin-II release in the context of intrarenal renin-angiotensin system activation[30]. Furthermore, renal/systemic vasoconstriction often develops under the impact of cyclosporine therapy[31]. The endothelial receptor type A across preglomerular arteries triggers endothelin production that eventually leads to renal vasoconstriction in organ transplant recipients[29,32]. The clinical studies demonstrated cardioprotective effects of tacrolimus compared to cyclosporin in the setting of organ transplantation[33]. They also reveal the superiority of tacrolimus over cyclosporin in controlling blood pressure elevations among organ transplant patients [21]. Research evidence confirms blood pressure elevation in organ transplant recipients on cyclosporin treatment after increasing their dietary sodium intake. This increase in blood pressure indicates the incidence of sodium-dependent hypertension among patients after their organ transplantation[34]. However, the clinical studies do not provide conclusive evidence related to the sodium retaining effects of calcineurin inhibitors in organ transplant scenarios[35]. However, the medical literature indicates the potential of cyclosporin inhibitors in elevating the activity of sodium-potassium chloride/sodium chloride cotransporters for maximizing sodium reabsorption in organ transplant patients[36]. The clinical studies also emphasize the possibility of replacing calcineurin inhibitors with sirolimus based on

its safety profile and least impact on the 24 h systolic blood pressures of patients with organ transplant status.

PREVENTION MEASURES

Organ transplant-related hypertension prevention warrants the mitigation of risk factors that potentially aggravate systolic and diastolic blood pressures in the treated patients. These risk factors include native kidneys, donor hypertension, smoking, drug use, obstructive sleep apnea, and obesity[37,38]. The findings from various clinical studies recommend lifestyle/behavioral modifications and weight reduction strategies for organ transplant recipients to minimize their risk of postprocedural hypertension. They also advocate the need for evaluating suprarenal masses based on their hypertension attribution[39].

The long-term use of calcineurin inhibitors, including tacrolimus and cyclosporine among organ transplant patients, clinically correlates with their hypertensive crises. The clinical studies reveal a reduced impact of tacrolimus (compared to cyclosporine) on the blood pressure levels of organ transplant patients[40]. The organ transplant recipients who receive tacrolimus also exhibit a limited dependence on antihypertensive drugs for managing their blood pressure levels[37]. The clinicians accordingly recommend tacrolimus over cyclosporine for the medical management of organ transplant patients. The medical literature alternatively recommends the selective T-cell co-stimulation blocker (Belatacept) to control T cell proliferation and cytokine production in renal transplant patients for effectively managing their episodic hypertension[41].

The clinical studies further advocate the deleterious impact of corticosteroids on the blood pressure management of organ transplant patients. They provide substantial evidence concerning the dose-dependent relationship between corticosteroid utilization and hypertensive crisis in organ transplant scenarios. The clinicians accordingly recommend minimal dosages of steroids (for example, 5 mg per day dose of prednisone) to achieve long-term immunosuppression in organ transplant patients without increasing their risk for episodic hypertension[42].

The worsening of hypertension in kidney transplant patients clinically correlates with their antibody-mediated and acute cellular organ rejection[43]. The subsequent administration of immunosuppressive therapy (based on thyroglobulin, immunoglobulins, and steroids for reversing organ rejection) further exacerbates the hypertensive crisis[44]. These findings necessitate the development of comprehensive treatment protocols to minimize hypertensive crisis without compromising the outcomes of immunosuppressive therapies in organ transplantation scenarios.

The clinical studies reveal the impact of expanded criteria donor recipient status on worsening cardiovascular complications and hypertensive crises in patients with organ transplant status[45]. Organ transplant patients prevalently develop diabetes, chronic rejection, and hypertension under the impact of reduced donor/recipient body weight ratio[20]. Posttransplant hypertension also triggers under the impact of aortorenal donor atheroma in various clinical scenarios[19]. The medical literature accordingly recommends selecting young and normal-weight donors without a confirmed diagnosis of hypertension or atherosclerosis to minimize the risk of hypertension among organ transplant patients.

A range of genetic factors contributes to the development of hypertensive crises in organ transplant patients. The presence of apolipoprotein L-1 variants in deceased African American donors potentiates early graft dysfunction and eventual blood pressure elevation in the recipients of transplanted organs. The polymorphisms in CYP3A5, ABCC2, and ABC1 transporters further attribute to posttransplant hypertension and poor graft survival in organ transplant scenarios[46,47]. The assessment of these genetic mechanisms and factors is paramount to minimizing the risk of posttransplant hypertension among organ transplant patients.

Post-transplant hypertension also develops under the impact of transplanted renal artery stenosis following kidney transplantation[48]. The clinical studies reveal substantial improvements in blood pressure levels of organ transplant patients after the medical management of their renal artery stenosis [49]. These findings substantiate early diagnosis and therapeutic management of renal artery stenosis to reduce the incidence of posttransplant hypertension and its critical complications.

The therapeutic management of posttransplant hypertension relies on the systematic administration of calcium channel blockers, beta-blockers, and loop diuretics (for volume optimization). The normalization of serum potassium levels and enhancement of kidney function of organ transplant patients further depends on angiotensin receptor blockers and angiotensin-converting enzyme inhibitors[38].

The hypertension risk factors among liver transplant recipients include new-onset hepatic steatosis, alcoholic cirrhosis, and rapamycin use[50]. These findings advocate the need for monitoring organ transplant patients on mTOR inhibitor therapies to reduce their incidence of hypertensive crises.

The patients with allogenic hematopoietic stem cell/bone marrow transplant experience a high risk of hypertension based on several factors including graft *vs* host disease, mycophenolate/calcineurin inhibitor therapies, and lymphoma/Leukemia history[51]. Other hypertension predisposing factors concerning stem cell transplant scenarios include serum creatinine elevation, sinusoidal obstruction syndrome, amphotericin-B therapy, and the young age of the patients in pediatric hematopoietic stem

cell transplant[15]. The clinical studies accordingly advocate consistent monitoring of the bone marrow transplant patients based on their dependence on amphotericin-B, mycophenolate, and calcineurin inhibitors.

DIAGNOSTIC PARAMETERS

The diagnostic assessment of hypertension in organ transplant scenarios relies on 24 h ambulatory/home/office blood pressure monitoring interventions. The office blood pressure assessment warrants the recording of three consecutive blood pressure readings and calculation of their mean value. The home blood pressure monitoring requires averaging two blood pressure readings obtained at home within a tenure of 4 days. The 24 h ambulatory blood pressure assessment relies on averaging various blood pressure readings obtained within a day's duration *via* a digital blood pressure monitor[1]. The 24 h blood pressure evaluation also helps categorize systolic/diastolic blood pressure levels based on their reverse dipping, dipping, and non-dipping patterns.

The clinical studies emphasize marked differences between clinical blood pressure monitoring, home blood pressure assessment, and ambulatory blood pressure monitoring. These studies also advocate the requirement of practicing care and caution while measuring the blood pressure levels of organ transplant patients. The clinical findings prioritize the use of ambulatory blood pressure monitoring for investigating the occurrence of whitecoat/masked/nocturnal hypertension to rule out the risk of cardiovascular complications[52].

The medical literature reveals a substantial increase in night-time systolic blood pressure following kidney transplantation[53]. The 24 h ambulatory blood pressure monitoring effectively tracks nocturnal blood pressure variations in organ transplant patients[54]. This blood pressure evaluation approach is the method of choice for tracking posttransplant hypertension and is recommended over home/office blood pressure monitoring interventions[55].

The diagnostic affirmation of posttransplant hypertension thoroughly relies on the appropriate use of blood pressure recording interventions. The blood pressure monitored at the physician's office may not give an accurate outcome based on the risk of masked/whitecoat hypertension and circadian variation/diurnal rhythm. Masked hypertension could increase the risk of native kidney disease among renal transplant patients[56]. However, clinical studies do not provide conclusive findings determining the impact of masked hypertension on the outcomes of renal transplant patients. These diagnostic intricacies warrant the use of automated electronic devices for blood pressure monitoring to minimize the risk of masked hypertension and the whitecoat effect in organ transplant scenarios[57].

The medical literature advocates optimizing blood pressure cutoff limits to accurately identify the existence or absence of hypertension and initiate antihypertensive therapies for organ transplant patients. The diagnostic parameters for assessing hypertension in posttransplant scenarios rely on the following parameters[4]: Office blood pressure reading of greater than 140/90 mmHg.

An ambulatory blood pressure reading of greater than 135/85 mmHg (awake state) and 120/70 mmHg (sleeping state) The recommendations by KDIGO (Kidney Disease Improving Global Outcomes) advocate the need to administer antihypertensive therapies to kidney transplant patients following their blood pressure elevation above 130/80 mmHg[58].

MAJOR COMPLICATIONS

Approximately 50%-80% of adult organ transplant recipients develop hypertension and its clinical complications. The past medical history of hypertension further increases the incidence of post-transplant hypertension. Additionally, the old age of donors, elevated body mass index, male gender, and African American race include the significant demographic factors attributing to the development of hypertension among organ transplant patients[43].

Types of complications

Medical literature reports a 50% prevalence of hypertensive among patients with organ transplant status[43]. Posttransplant hypertension predominantly triggers graft dysfunction and cardiovascular events in organ transplant patients that eventually lead to their renal failure. The cardiovascular complications related to posttransplant hypertension include coronary artery disease and congestive heart failure. Uncontrolled hypertension in the setting of kidney transplants potentially disrupts cardiorenal outcomes by impacting the overall functions of the heart and renal allograft[21,59].

Cardiovascular complications due to post-transplant hypertension

The recipients of kidney transplants experience a 3%-5% incidence of non-fatal/fatal cardiovascular episodes. They further experience a 50-fold predisposition to cardiorenal complications compared to the general population[60]. Posttransplant mortality often attributes to critical cardiovascular complications

emanating from hypertensive crises. The cardiovascular compromise develops under the impact of posttransplant hypertension and elevates the incidence of morbidity/mortality among the treated patients. The cardiovascular episodes attribute to forty percent of patient deaths in the setting of a kidney transplant[4]. The predominant cardiovascular complications emanating from posttransplant hypertension include stroke, arterial narrowing, coronary artery disease, congestive heart failure, and ischemic heart disease. The kidney transplant scenarios also report a high incidence of diastolic dysfunction, left atrial enlargement and left ventricular hypertrophy. Heart failure with decreased left ventricular ejection fraction potentially increases the mortality risk among organ transplant patients. The clinical studies reveal a strong association between nocturnal hypertension and left ventricular hypertrophy in various organ transplant scenarios[4].

Graft dysfunction due to post-transplant hypertension

The graft dysfunction in posttransplant scenarios predominantly develops under the impact of hypertensive crisis. The deterioration in renal function also correlates with blood pressure elevation in the setting of organ transplants. The renal allograft injury triggered by posttransplant hypertension-induced kidney failure further aggravates episodic hypertension and its potential manifestations[43]. The clinical studies continue to examine the relationship between independent allograft survival and blood pressure levels of organ transplant patients.

The retrospective study by Opelz *et al*[61] (1998) based on 29571 renal transplant recipients revealed the adverse impact of posttransplant hypertension on the renal allograft injury patterns[61]. Another clinical study indicated improvements in cardiovascular mortality and renal allograft function after therapeutic management of systolic blood pressure of patients within 1-3 years of their kidney transplantation[22]. The study outlined positive clinical outcomes in organ transplant recipients with a marked reduction in systolic blood pressure (below 140 mmHg).

A clinical study revealed improvements in renal transplant survival rates among patients with reduced diastolic pressures (ranging between 89-99 mmHg). The study findings advocated the need for monitoring mean arterial/diastolic/systolic blood pressures of the renal transplant patients until one year after transplantation to enhance their allograft survival. The study outcomes further correlated the risk of allograft failure for every 10 mmHg diastolic/systolic blood pressure elevation[61]. The clinical studies also indicate blood pressure reduction is a protective factor for kidney transplant recipients during the initial year of their recovery[4,22]. The evidence-based findings clinically correlate graft failure/chronic allograft nephropathy, renal failure, and cardiovascular compromise with posttransplant hypertension. Organ transplant patients with hypertension accordingly experience a high risk of morbidity and mortality[61].

MEDICAL MANAGEMENT

The treatment guidelines for managing posttransplant hypertension do not differ from the therapeutic protocols adopted for treating hypertension/blood pressure elevation among patients with a high risk for cardiovascular complications (Table 12-3). The clinical studies reveal the impact of diabetes/proteinuria and cardiovascular conditions on the blood pressure elevation in organ transplant patients. The maintenance of systolic/diastolic blood pressure below 140/90 mmHg is highly necessary to reduce the risk of posttransplant hypertensive crisis. The multifactorial origin of posttransplant arterial hypertension in renal transplant cases warrants its systematic monitoring and medical management. Posttransplant hypertension/hypertensive crisis further intensifies under the impact of allograft nephropathy and immunosuppressive therapies. The diagnostic interventions to track and evaluate the causative factors of posttransplant hypertension include assessing 24 h urinary sodium, proteinuria, 24 h urine clearance, renal function tests, and hepatic panel. The candidates for kidney transplantation qualify for renal ultrasound in the context of evaluating their urinary tract blockage and renal artery stenosis.

The pretransplant hypertension of kidney transplant recipients warrant antihypertensive therapy. The clinical studies reveal rare cases (concerning kidney transplantation) that achieve normotensive status in the absence of antihypertensive therapy. These outcomes necessitate pharmacological management of hypertension of kidney transplant patients to reduce the risk of their cardiovascular complications[22]. The non-pharmacological approaches for hypertension management in kidney transplant scenarios rely on lifestyle modification, stress reduction, weight management, smoking cessation, low-salt diet, and exercise management. Clinical studies need to explore the complex interplay between pharmacodynamics and pharmacokinetics of antihypertensive medications to optimize their use in organ transplant scenarios. They also need to investigate drug-drug interactions and their impact on comorbidities and hypertension management of organ transplant patients[62].

The renal transplant scenarios report a high incidence of hypertension emanating from corticosteroid therapy. The novel organ transplantation protocols advocate the exclusion of corticosteroid treatment to minimize the risk of hypertensive crises or episodic hypertension[22]. However, the clinical studies provide inconclusive evidence concerning the discontinuation timings of steroid therapies for renal

Table 1 Management for hypertension following renal transplantation

Blood pressure management	Interventions	Comments
Non-pharmacological management	Dietary sodium restriction; Weight reduction; Exercise; Smoking cessation; Stress reduction	
Pharmacological therapy	Antihypertensive medications: -Diuretics; -Calcium channel blockers; -Beta-blockers; -Renin-angiotensin aldosterone system blockade; -Alpha1 antagonists; -Alpha 2 agonists	Medication choice depends on patient characteristics, adverse effects, tolerability
Invasive interventions	-Transplant renal artery angioplasty +/- stenting; -Continuous positive airway pressure; -Bilateral native nephrectomy; -Native renal denervation	-Transplant renal artery stenosis; -Obstructive sleep apnea; -Failed native kidney; -Sympathetic overactivity
Adjustment of Immunosuppressive Medication	-Steroid withdrawal protocol; -Minimize dose of calcineurin inhibitors; -Replace CsA by using less hypertensive and less nephrotoxic drugs	Other drugs that can be used: -MMF: Mycophenolate mofetil; -Tacrolimus; -Sirolimus

Table 2 Target Blood pressure guideline for kidney transplant recipients

Medical Society/Guideline	Recommended BP target
ACC/AHA[65]	< 130/80 mm Hg
JNC 8 (2014)[66]	Not defined
Kidney disease outcomes quality initiative (KDOQI)[67]	-Goal of 125/75 mm Hg for transplant recipients with proteinuria. -Goal of 130/85 in the absence of proteinuria
Kidney disease: Improving Global outcomes (KDIGO)[68]	< 130/80
European Best Practice Guidelines for Renal Transplantation 2002[19]	Target BP ≤ 125/75 mm Hg in proteinuria patients
Canadian Society of Nephrology[69]	Patients with significant proteinuria; Target Blood pressure is < 130/80 mm Hg
British Renal Association[70]	< 130/80 mm Hg

A reasonable target blood pressure is < 140/90 mmHg for transplant recipients who do not develop proteinuria. (Are you sure about the recommended first line agents?)

transplant patients. The researchers continue to debate regarding the early or late withdrawal of steroid treatments in organ transplant scenarios. Few clinical studies alternatively negate the contention related to the impact of steroid therapies on the hypertensive crisis of organ transplant patients[37].

The medical literature provides some evidence concerning the need for manipulating the currently deployed immunosuppressive therapies to optimize the hypertension management of patients with organ transplant status. This belief reciprocates with the adverse impact of immunosuppressive treatments on posttransplant hypertension. Clinical studies showed that cyclosporine increases the risk of posttransplant hypertension compared to tacrolimus[63]. Furthermore, clinical studies also confirm a marked reduction in systolic/diastolic blood pressures following the dose reduction of cyclosporine or its replacement with tacrolimus in organ transplant scenarios[41]. These findings warrant investigation concerning the hypertension induction effect of cyclosporine in organ transplant patients. The impact of cyclosporine on renal sodium retention probably triggers vasoconstriction of glomerular arterioles leading to posttransplant hypertension[43].

Posttransplant hypertension management primarily relies on first-line therapies based on dihydropyridine calcium channel blockers since they effectively minimize calcineurin-induced vasoconstriction. The beta-blocker therapies further improve the survival rate of organ transplant recipients irrespective of their predisposition to cardiovascular complications[64]. The antihypertensive therapies in organ transplant scenarios must exclude ACE (angiotensin-converting enzyme) inhibitors during the initial 3-6 mo based on the risk of hyperkalemia, anemia, and reduction in glomerular filtration rate[2].

The medical literature provides evidence concerning the development of posttransplant hypertension despite administering antihypertensive therapies. The evidence-based findings elaborate on the necessity for renal arteriography to rule out renal artery stenosis in organ transplant patients. The patients who develop more than 80% renal arterial stenosis qualify for percutaneous transluminal angioplasty. Renal denervation is another viable therapy with the potential to manage refractory hypertension in organ transplant scenarios[4].

Table 3 Studies regarding the management of posttransplant hypertension

	Study type	Title	Ref.	Intervention	Outcome	Conclusion
1	Four cross-sectional Retrospective analysis	Treatment of Hypertension in Renal Transplant Recipients in Four Independent Cross-Sectional Analysis	Kuxmiuk-Glembin *et al*[64], 2018	-Beta-blockers 80%); -Calcium channel blockers (53%); -Diuretics (37%); -Alpha-blockers (35%); -Angiotensin-converting enzyme inhibitors (ACEi) (32%); -ARB (7%)	Blood pressure controlled using BB (43.9 controlled, 56.1 not controlled P = 0.007); -Number of antihypertensive agents: 2.43 +/- 1.3 (controlled BP); 1.88 +/- 1.5 (Uncontrolled BP) P < 0.001. -ACEI &/ARB: Yes: 57.1 (controlled, 42.9 (Uncontrolled); No ACEI/ARB: 48 (Controlled), 52 (uncontrolled) P = 0.08	The commonly used monotherapy agents:-BB followed by CCB. -Use of ACEI, diuretics, and alpha-blockers was about the same. -ARB therapy was least utilized. -Significant increase was observed in the mean number of antihypertensive drugs per patient in subsequent years
2	Randomized controlled trials systemic review	Antihypertensive treatment for kidney transplant recipients	Cross *et al* [71], 2009	60 studies involving 3802 recipients. -29 studies (2262 participants) compared calcium channel blocker to placebo/no treatment. -10 studies (445 participants) compared ACEi to placebo/no treatment. -7 studies (405 participants) compared CCB to ACEi	-CCB compared to placebo/no treatment reduced graft loss (RR 0.75, 95%CI: 0.57-0.99) and improved glomerular filtration rate (GFR), (MD, 4.45 mL/min, 95%CI: 2.22-6.68). -ACEi versus placebo/no treatment were inconclusive for GFR (MD -8.07 mL/min, 95%CI: -18.57-2.43) and variable for graft loss, precluding meta-analysis. -Direct comparison with CCB, ACEi decreased GFR (MD -11.48 mL/min, 95%CI: -5.75 to -7.21), proteinuria (MD -0.28 g/24 h, 95%CI: -0.47 to -0.10), hyperkalaemia (RR 3.74, 95%CI: 1.89-7.43)	CCB may be used as first-line agents for hypertensive kidney transplant recipients. ACEi have few detrimental effects in kidney transplant recipients
3	Double-blind, randomized, placebo-controlled trial.	Angiotensin II blockade in kidney transplant recipients.	Ibrahim *et al*[72], 2013	-The effect of losartan compared to placebo and initiated within three months of transplantation	Doubling of renal cortical volume – Measure of interstitial fibrosis/tubular atrophy	-Use of losartan tended to be protective, with an odds ratio (OR) of 0.39 (95%CI: 0.13–1.15, P = 0.08). -Losartan had no significant effect on time to a composite of ESRD, death, or doubling of creatinine level. The mean time to doubling of serum creatinine was longer in the losartan group, compared with placebo (1065 versus 450 d [hazard ratio (HR) 7.28, 95%CI: 2.22–32.78])
4	Prospective Controlled Trial	Converting-enzyme inhibitor versus calcium antagonist in cyclosporine-treated renal transplants	Mourad *et al*[73], 1993	-6 mo after transplantation, patients were randomly allocated to treatment by the angiotensin-converting enzyme inhibitor lisinopril (ACEI, alone or associated with frusemide; n = 14), or the calcium antagonist, nifedipine (CA, alone or associated with atenolol; n = 11)	-Before initiation of antihypertensive therapy, the two groups had similar mean arterial pressures and GFRs. -Both ACEI and CA treatments were associated with no change in renal function, a similar change in mean arterial pressure (ACEI -18 +/- 3; CA -13 +/- 5 mm Hg), and identical trough blood levels cyclosporine	In cyclosporine-treated transplant recipients, satisfactory control of hypertension was obtained by ACEIs based on their potential to minimize arterial pressures
5	Prospective Randomized Trial	Randomized trial of steroid withdrawal in kidney recipients treated with mycophenolate mofetil and cyclosporine	Pellitier *et al*[74], 2006	-121 patients were randomized either to discontinue or remain on steroids (60 patients per group)	There were no significant differences in patient and graft survival rates at 1 year or at last follow-up (approximate 3.7y). -Incidence of acute and chronic rejection as well as graft function were the same within 1 yr	Steroid withdrawal in low-risk kidney transplant recipients is safe and ameliorates many of the unwanted side effects of steroid use
6	Retrospective study	Lack of long-term benefits of steroid withdrawal in renal transplant recipients	Sivaram *et al*[75], 2001	-Retrospective review identified 58 patients administered cyclosporine, azathioprine, and prednisone who underwent complete steroid withdrawal	-Post-steroid withdrawal follow up: 7.6 +/- 1.9 years; -9 patients restarted therapy; 3 patients lost their graft (2 of which are those who restarted prednisone therapy). -2 died with functioning grafts	When prednisone dosage was tapered from 10 mg/d to 10 mg every other day, clinically significant improvements were seen in weight, systolic and diastolic blood pressures, glycosylated hemoglobin levels, and diabetes-related outcomes

CONCLUSION

Posttransplant hypertension increases the risk of graft-related complications in patients with a known history of (pretransplant) hypertension. Steroids, cyclosporine, calcineurin inhibitors, and other immunosuppressive drugs further increase the predisposition of organ transplant patients to hypertension. Hemopoietic cell transplantation predominantly adds to the 2-year risk of systemic hypertension in children and adults. The donor factors for episodic hypertension attributes to the donors' age and body surface area. The recipient factors, however, include hypovolemia and pre-existing comorbidities. TRAS-induced hypoperfusion triggers RAAS that potentiates renovascular hypertension in organ transplant patients. Posttransplant hypertension is a significant cause of cardiovascular complications and graft dysfunction. The 24 h blood pressure monitoring is, therefore, necessary to effectively manage hypertensive crises in organ transplant recipients. The evaluation also helps categorize systolic/diastolic blood pressure levels based on their reverse dipping, dipping, and non-dipping patterns.

FOOTNOTES

Author contributions: All authors contributed equally in writing, editing, and reviewing the manuscript of the article.

Conflict-of-interest statement: The authors declare that there is no conflict of interest.

Country/Territory of origin: United States

ORCID number: Mahmoud Nassar 0000-0002-5401-9562; Nso Nso 0000-0002-0340-169X; Sofia Lakhdar 0000-0001-5320-2990; Ravali Kondaveeti 0000-0003-2335-5296; Chandan Buttar 0000-0003-4777-5439; Harangad Bhangoo 0000-0001-8893-3005; Mahmoud Awad 0000-0002-9243-3449; Naveen Siddique Sheikh 0000-0002-8549-2029; Karim M Soliman 0000-0002-0960-2644; Most Sirajum Munira 0000-0002-4691-1550; Farshid Radparvar 0000-0001-9631-9208; Vincent Rizzo 0000-0002-5530-447X; Ahmed Daoud 0000-0001-6311-3887.

S-Editor: Wu YXJ
L-Editor: A
P-Editor: Wu YXJ

REFERENCES

1 **Whelton PK**, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018; **71**: e13-e115 [PMID: 29133356 DOI: 10.1161/HYP.0000000000000065]

2 **Zbroch E**, Małyszko J, Myśliwiec M, Przybyłowski P, Durlik M. Hypertension in solid organ transplant recipients. *Ann Transplant* 2012; **17**: 100-107 [PMID: 22466914 DOI: 10.12659/AOT.882641]

3 **Bucharles SGE**, Wallbach KKS, Moraes TP, Pecoits-Filho R. Hypertension in patients on dialysis: diagnosis, mechanisms, and management. *J Bras Nefrol* 2019; **41**: 400-411 [PMID: 30421784 DOI: 10.1590/2175-8239-jbn-2018-0155]

4 **Severova-Andreevska G**, Danilovska I, Sikole A, Popov Z, Ivanovski N. Hypertension after Kidney Transplantation: Clinical Significance and Therapeutical Aspects. *Open Access Maced J Med Sci* 2019; **7**: 1241-1245 [PMID: 31049114 DOI: 10.3889/oamjms.2019.264]

5 **Sanchez OA**, Ferrara LK, Rein S, Berglund D, Matas AJ, Ibrahim HN. Hypertension after kidney donation: Incidence, predictors, and correlates. *Am J Transplant* 2018; **18**: 2534-2543 [PMID: 29498216 DOI: 10.1111/ajt.14713]

6 **Przybylowski P**, Malyszko J, Malyszko JS, Kobus G, Sadowski J, Mysliwiec M. Blood pressure control in orthotopic heart transplant and kidney allograft recipients is far from satisfactory. *Transplant Proc* 2010; **42**: 4263-4266 [PMID: 21168679 DOI: 10.1016/j.transproceed.2010.09.025]

7 **Weiss ES**, Nwakanma LU, Patel ND, Yuh DD. Outcomes in patients older than 60 years of age undergoing orthotopic heart transplantation: an analysis of the UNOS database. *J Heart Lung Transplant* 2008; **27**: 184-191 [PMID: 18267225 DOI: 10.1016/j.healun.2007.11.566]

8 **Taegtmeyer AB**, Crook AM, Barton PJ, Banner NR. Reduced incidence of hypertension after heterotopic cardiac

transplantation compared with orthotopic cardiac transplantation: evidence that excision of the native heart contributes to post-transplant hypertension. *J Am Coll Cardiol* 2004; **44**: 1254-1260 [PMID: 15364328 DOI: 10.1016/S0735-1097(04)01240-9]

9 **Ponticelli C**, Cucchiari D, Graziani G. Hypertension in kidney transplant recipients. *Transpl Int* 2011; **24**: 523-533 [PMID: 21382101 DOI: 10.1111/j.1432-2277.2011.01242.x]

10 **Savioli G**, Surbone S, Giovi I, Salinaro F, Preti P, Meloni F, Oggionni T, Perlini S. Early development of metabolic syndrome in patients subjected to lung transplantation. *Clin Transplant* 2013; **27**: E237-E243 [PMID: 23414418 DOI: 10.1111/ctr.12098]

11 **Silverborn M**, Jeppsson A, Mårtensson G, Nilsson F. New-onset cardiovascular risk factors in lung transplant recipients. *J Heart Lung Transplant* 2005; **24**: 1536-1543 [PMID: 16210127 DOI: 10.1016/j.healun.2005.01.004]

12 **Alfishawy M**, Nso N, Nassar M, Ariyaratnam J, Bhuiyan S, Siddiqui RS, Li M, Chung H, Al Balakosy A, Alqassieh A, Fülöp T, Rizzo V, Daoud A, Soliman KM. Liver transplantation during global COVID-19 pandemic. *World J Clin Cases* 2021; **9**: 6608-6623 [PMID: 34447809 DOI: 10.12998/wjcc.v9.i23.6608]

13 **Krämer BK**, Montagnino G, Del Castillo D, Margreiter R, Sperschneider H, Olbricht CJ, Krüger B, Ortuño J, Köhler H, Kunzendorf U, Stummvoll HK, Tabernero JM, Mühlbacher F, Rivero M, Arias M; European Tacrolimus vs Cyclosporin Microemulsion Renal Transplantation Study Group. Efficacy and safety of tacrolimus compared with cyclosporin A microemulsion in renal transplantation: 2 year follow-up results. *Nephrol Dial Transplant* 2005; **20**: 968-973 [PMID: 15741208 DOI: 10.1093/ndt/gfh739]

14 **Jodele S**, Hirsch R, Laskin B, Davies S, Witte D, Chima R. Pulmonary arterial hypertension in pediatric patients with hematopoietic stem cell transplant-associated thrombotic microangiopathy. *Biol Blood Marrow Transplant* 2013; **19**: 202-207 [PMID: 22960385 DOI: 10.1016/j.bbmt.2012.08.022]

15 **Kwon DH**, Jung S, Lee EJ, Lee JY, Moon S, Lee JW, Chung NG, Cho B, Kim HK. Incidence and risk factors for early-onset hypertension after allogeneic hematopoietic stem cell transplantation in children. *Korean Circ J* 2013; **43**: 804-810 [PMID: 24385991 DOI: 10.4070/kcj.2013.43.12.804]

16 **Majhail NS**, Challa TR, Mulrooney DA, Baker KS, Burns LJ. Hypertension and diabetes mellitus in adult and pediatric survivors of allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant* 2009; **15**: 1100-1107 [PMID: 19660723 DOI: 10.1016/j.bbmt.2009.05.010]

17 **Stabouli S**, Printza N, Dotis J, Gkogka C, Kollios K, Kotsis V, Papachristou F. Long-Term Changes in Blood Pressure After Pediatric Kidney Transplantation. *Am J Hypertens* 2016; **29**: 860-865 [PMID: 26657420 DOI: 10.1093/ajh/hpv192]

18 **Altheaby A**, Al Dalbhi S, Alghamdi Y, Almigbal TH, Alotaibi KN, Batais MA, Alodhayani A, Alkhushail A, Alhantoushi M, Alsaad SM. Effect of donor hypertension on renal transplant recipients' blood pressure, allograft outcomes and survival: a systematic review and meta-analysis. *Am J Cardiovasc Dis* 2019; **9**: 49-58 [PMID: 31516763]

19 **Ducloux D**, Motte G, Kribs M, Abdelfatah AB, Bresson-Vautrin C, Rebibou JM, Chalopin JM. Hypertension in renal transplantation: donor and recipient risk factors. *Clin Nephrol* 2002; **57**: 409-413 [PMID: 12078942 DOI: 10.5414/CNP57409]

20 **el-Agroudy AE**, Hassan NA, Bakr MA, Foda MA, Shokeir AA, Shehab el-Dein AB. Effect of donor/recipient body weight mismatch on patient and graft outcome in living-donor kidney transplantation. *Am J Nephrol* 2003; **23**: 294-299 [PMID: 12902614 DOI: 10.1159/000072819]

21 **Artz MA**, Boots JM, Ligtenberg G, Roodnat JI, Christiaans MH, Vos PF, Moons P, Borm G, Hilbrands LB. Conversion from cyclosporine to tacrolimus improves quality-of-life indices, renal graft function and cardiovascular risk profile. *Am J Transplant* 2004; **4**: 937-945 [PMID: 15147428 DOI: 10.1111/j.1600-6143.2004.00427.x]

22 **Tantisattamo E**, Molnar MZ, Ho BT, Reddy UG, Dafoe DC, Ichii H, Ferrey AJ, Hanna RM, Kalantar-Zadeh K, Amin A. Approach and Management of Hypertension After Kidney Transplantation. *Front Med (Lausanne)* 2020; **7**: 229 [PMID: 32613001 DOI: 10.3389/fmed.2020.00229]

23 **Chan W**, Bosch JA, Jones D, McTernan PG, Inston N, Moore S, Kaur O, Phillips AC, Borrows R. Hypervolemia and blood pressure in prevalent kidney transplant recipients. *Transplantation* 2014; **98**: 320-327 [PMID: 24770615 DOI: 10.1097/TP.0000000000000066]

24 **Agüera Fernández LG**, Zudaire JJ, Isa WA, Sánchez de la Muela PL, Rosell D, de Castro F, Robles JE, Errasti P, Berian JM. [Vascular complications in 237 recipients of renal transplant from cadaver]. *Actas Urol Esp* 1992; **16**: 292-295 [PMID: 1636451]

25 **Srivastava A**, Kumar J, Sharma S, Abhishek, Ansari MS, Kapoor R. Vascular complication in live related renal transplant: An experience of 1945 cases. *Indian J Urol* 2013; **29**: 42-47 [PMID: 23671364 DOI: 10.4103/0970-1591.109983]

26 **Chen W**, Kayler LK, Zand MS, Muttana R, Chernyak V, DeBoccardo GO. Transplant renal artery stenosis: clinical manifestations, diagnosis and therapy. *Clin Kidney J* 2015; **8**: 71-78 [PMID: 25713713 DOI: 10.1093/ckj/sfu132]

27 **Lacombe M**. Arterial stenosis complicating renal allotransplantation in man: a study of 38 cases. *Ann Surg* 1975; **181**: 283-288 [PMID: 1093485 DOI: 10.1097/00000658-197503000-00007]

28 **Ganji MR**, Harririan A. Chronic allograft dysfunction: major contributing factors. *Iran J Kidney Dis* 2012; **6**: 88-93 [PMID: 22388603]

29 **Cavarape A**, Endlich K, Feletto F, Parekh N, Bartoli E, Steinhausen M. Contribution of endothelin receptors in renal microvessels in acute cyclosporine-mediated vasoconstriction in rats. *Kidney Int* 1998; **53**: 963-969 [PMID: 9551405 DOI: 10.1111/j.1523-1755.1998.00852.x]

30 **Griendling KK**, Sorescu D, Ushio-Fukai M. NAD(P)H oxidase: role in cardiovascular biology and disease. *Circ Res* 2000; **86**: 494-501 [PMID: 10720409 DOI: 10.1161/01.RES.86.5.494]

31 **Kaye D**, Thompson J, Jennings G, Esler M. Cyclosporine therapy after cardiac transplantation causes hypertension and renal vasoconstriction without sympathetic activation. *Circulation* 1993; **88**: 1101-1109 [PMID: 8394783 DOI: 10.1161/01.CIR.88.3.1101]

32 **Lanese DM**, Conger JD. Effects of endothelin receptor antagonist on cyclosporine-induced vasoconstriction in isolated rat renal arterioles. *J Clin Invest* 1993; **91**: 2144-2149 [PMID: 8486781 DOI: 10.1172/JCI116440]

33 **Golbaekdal K**, Nielsen CB, Pedersen EB. The acute effects of FK-506 on renal haemodynamics, water and sodium

excretion and plasma levels of angiotensin II, aldosterone, atrial natriuretic peptide and vasopressin in pigs. *J Pharm Pharmacol* 1996; **48**: 1174-1179 [PMID: 8961168 DOI: 10.1111/j.2042-7158.1996.tb03916.x]

34 **Curtis JJ**, Luke RG, Jones P, Diethelm AG. Hypertension in cyclosporine-treated renal transplant recipients is sodium dependent. *Am J Med* 1988; **85**: 134-138 [PMID: 3041828 DOI: 10.1016/S0002-9343(88)80331-0]

35 **Damiano S**, Scanni R, Ciarcia R, Florio S, Capasso G. Regulation of sodium transporters in the kidney during cyclosporine treatment. *J Nephrol* 2010; **23** Suppl 16: S191-S198 [PMID: 21170880]

36 **Hoorn EJ**, Walsh SB, McCormick JA, Zietse R, Unwin RJ, Ellison DH. Pathogenesis of calcineurin inhibitor-induced hypertension. *J Nephrol* 2012; **25**: 269-275 [PMID: 22573529 DOI: 10.5301/jn.5000174]

37 **Aparicio LS**, Alfie J, Barochiner J, Cuffaro PE, Rada M, Morales M, Galarza C, Waisman GD. Hypertension: the neglected complication of transplantation. *International Scholarly Research Notices* 2013 [DOI: 10.5402/2013/165937]

38 **Aziz F**, Clark D, Garg N, Mandelbrot D, Djamali A. Hypertension guidelines: How do they apply to kidney transplant recipients. *Transplant Rev (Orlando)* 2018; **32**: 225-233 [PMID: 30293557 DOI: 10.1016/j.trre.2018.06.002]

39 **Luke RG**. Pathophysiology and treatment of posttransplant hypertension. *J Am Soc Nephrol* 1991; **2**: S37-S44 [PMID: 1932642 DOI: 10.1681/ASN.V22s37]

40 **Taylor DO**, Barr ML, Radovancevic B, Renlund DG, Mentzer RM Jr, Smart FW, Tolman DE, Frazier OH, Young JB, VanVeldhuisen P. A randomized, multicenter comparison of tacrolimus and cyclosporine immunosuppressive regimens in cardiac transplantation: decreased hyperlipidemia and hypertension with tacrolimus. *J Heart Lung Transplant* 1999; **18**: 336-345 [PMID: 10226898 DOI: 10.1016/S1053-2498(98)00060-6]

41 **Rossi AP**, Vella JP. Hypertension, living kidney donors, and transplantation: where are we today? *Adv Chronic Kidney Dis* 2015; **22**: 154-164 [PMID: 25704353 DOI: 10.1053/j.ackd.2015.01.002]

42 **Masson P**, Henderson L, Chapman JR, Craig JC, Webster AC. Belatacept for kidney transplant recipients. *Cochrane Database Syst Rev* 2014; CD010699 [PMID: 25416857 DOI: 10.1002/14651858.CD010699.pub2]

43 **Weir MR**, Burgess ED, Cooper JE, Fenves AZ, Goldsmith D, McKay D, Mehrotra A, Mitsnefes MM, Sica DA, Taler SJ. Assessment and management of hypertension in transplant patients. *J Am Soc Nephrol* 2015; **26**: 1248-1260 [PMID: 25653099 DOI: 10.1681/ASN.2014080834]

44 **Orbach H**, Katz U, Sherer Y, Shoenfeld Y. Intravenous immunoglobulin: adverse effects and safe administration. *Clin Rev Allergy Immunol* 2005; **29**: 173-184 [PMID: 16391392 DOI: 10.1385/CRIAI:29:3:173]

45 **Blanca L**, Jiménez T, Cabello M, Sola E, Gutierrez C, Burgos D, Lopez V, Hernandez D. Cardiovascular risk in recipients with kidney transplants from expanded criteria donors. *Transplant Proc* 2012; **44**: 2579-2581 [PMID: 23146460 DOI: 10.1016/j.transproceed.2012.09.086]

46 **Joy MS**, Hogan SL, Thompson BD, Finn WF, Nickeleit V. Cytochrome P450 3A5 expression in the kidneys of patients with calcineurin inhibitor nephrotoxicity. *Nephrol Dial Transplant* 2007; **22**: 1963-1968 [PMID: 17395652 DOI: 10.1093/ndt/gfm133]

47 **Grisk O**, Steinbach AC, Ciecholewski S, Schlüter T, Klöting I, Schmidt H, Dazert E, Schaeffeler E, Steil L, Gauer S, Jedlitschky G, Schwab M, Geisslinger G, Hauser IA, Völker U, Kroemer HK, Rettig R. Multidrug resistance-related protein 2 genotype of the donor affects kidney graft function. *Pharmacogenet Genomics* 2009; **19**: 276-288 [PMID: 19214140 DOI: 10.1097/FPC.0b013e328328d4e9]

48 **Beecroft JR**, Rajan DK, Clark TW, Robinette M, Stavropoulos SW. Transplant renal artery stenosis: outcome after percutaneous intervention. *J Vasc Interv Radiol* 2004; **15**: 1407-1413 [PMID: 15590798 DOI: 10.1097/01.RVI.0000141338.62574.F4]

49 **Valle JA**, McCoy LA, Maddox TM, Rumsfeld JS, Ho PM, Casserly IP, Nallamothu BK, Roe MT, Tsai TT, Messenger JC. Longitudinal Risk of Adverse Events in Patients With Acute Kidney Injury After Percutaneous Coronary Intervention: Insights From the National Cardiovascular Data Registry. *Circ Cardiovasc Interv* 2017; **10** [PMID: 28404621 DOI: 10.1161/CIRCINTERVENTIONS.116.004439]

50 **Di Stefano C**, Vanni E, Mirabella S, Younes R, Boano V, Mosso E, Nada E, Milazzo V, Maule S, Romagnoli R, Salizzoni M, Veglio F, Milan A. Risk factors for arterial hypertension after liver transplantation. *J Am Soc Hypertens* 2018; **12**: 220-229 [PMID: 29366595 DOI: 10.1016/j.jash.2018.01.002]

51 **Chalela CM**, Uribe JC, Luna-Gonzalez M, Peña AM, Jimenez SI, Salazar LA, Rosales M, Ardila-Baez M, Espinosa K, Baez J, Reyes DL, Rey JJ, Serrano S, Sandoval-Sus J, Sossa CL. Prevalence and Associated Factors for Arterial Hypertension in Adults Following Hematopoietic Stem Cell Transplantation. *Blood* 2019; 5689 [DOI: 10.1182/blood-2019-129321]

52 **O'Brien E**, Parati G, Stergiou G. Ambulatory blood pressure measurement: what is the international consensus? *Hypertension* 2013; **62**: 988-994 [PMID: 24060895 DOI: 10.1161/HYPERTENSIONAHA.113.02148]

53 **Lee MH**, Ko KM, Ahn SW, Bae MN, Choi BS, Park CW, Kim YS, Yang CW, Chung BH. The impact of kidney transplantation on 24-hour ambulatory blood pressure in end-stage renal disease patients. *J Am Soc Hypertens* 2015; **9**: 427-434 [PMID: 26051924 DOI: 10.1016/j.jash.2015.04.001]

54 **Taler SJ**, Textor SC, Canzanello VJ, Wilson DJ, Wiesner RH, Krom RA. Loss of nocturnal blood pressure fall after liver transplantation during immunosuppressive therapy. *Am J Hypertens* 1995; **8**: 598-605 [PMID: 7544983 DOI: 10.1016/0895-7061(95)00077-3]

55 **Ramesh Prasad GV**. Ambulatory blood pressure monitoring in solid organ transplantation. *Clin Transplant* 2012; **26**: 185-191 [PMID: 22220828 DOI: 10.1111/j.1399-0012.2011.01569.x]

56 **Borrelli S**, Provenzano M, Gagliardi I, Michael A, Liberti ME, De Nicola L, Conte G, Garofalo C, Andreucci M. Sodium Intake and Chronic Kidney Disease. *Int J Mol Sci* 2020; **21** [PMID: 32635265 DOI: 10.3390/ijms21134744]

57 **Parati G**, Stergiou GS, Asmar R, Bilo G, de Leeuw P, Imai Y, Kario K, Lurbe E, Manolis A, Mengden T, O'Brien E, Ohkubo T, Padfield P, Palatini P, Pickering TG, Redon J, Revera M, Ruilope LM, Shennan A, Staessen JA, Tisler A, Waeber B, Zanchetti A, Mancia G; ESH Working Group on Blood Pressure Monitoring. European Society of Hypertension practice guidelines for home blood pressure monitoring. *J Hum Hypertens* 2010; **24**: 779-785 [PMID: 20520631 DOI: 10.1038/jhh.2010.54]

58 **Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group**. KDIGO clinical practice guideline

for the care of kidney transplant recipients. *Am J Transplant* 2009; **9** Suppl 3: S1-155 [PMID: 19845597 DOI: 10.1111/j.1600-6143.2009.02834.x]

59 **Totzeck M**, Schuler M, Stuschke M, Heusch G, Rassaf T. Cardio-oncology - strategies for management of cancer-therapy related cardiovascular disease. *Int J Cardiol* 2019; **280**: 163-175 [PMID: 30661849 DOI: 10.1016/j.ijcard.2019.01.038]

60 **Jardine AG**, Gaston RS, Fellstrom BC, Holdaas H. Prevention of cardiovascular disease in adult recipients of kidney transplants. *Lancet* 2011; **378**: 1419-1427 [PMID: 22000138 DOI: 10.1016/S0140-6736(11)61334-2]

61 **Opelz G**, Wujciak T, Ritz E. Association of chronic kidney graft failure with recipient blood pressure. Collaborative Transplant Study. *Kidney Int* 1998; **53**: 217-222 [PMID: 9453022 DOI: 10.1046/j.1523-1755.1998.00744.x]

62 **Gill JS**. Cardiovascular disease in transplant recipients: current and future treatment strategies. *Clin J Am Soc Nephrol* 2008; **3** Suppl 2: S29-S37 [PMID: 18309001 DOI: 10.2215/CJN.02690707]

63 **Algarem N**, Sholkamy A, Alshazly M, Daoud A. New-onset diabetes and hypertension as complications of liver transplantation. *Transplant Proc* 2014; **46**: 870-872 [PMID: 24767368 DOI: 10.1016/j.transproceed.2013.12.007]

64 **Kuźmiuk-Glembin I**, Adrych D, Tylicki L, Heleniak Z, Garnier H, Wiśniewski J, Rutkowski P, Rutkowski B, Dębska-Ślizień A. Treatment of Hypertension in Renal Transplant Recipients in Four Independent Cross-Sectional Analyses. *Kidney Blood Press Res* 2018; **43**: 45-54 [PMID: 29402869 DOI: 10.1159/000486905]

65 **Unger T**, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, Wainford RD, Williams B, Schutte AE. 2020 International Society of Hypertension global hypertension practice guidelines. *J Hypertens* 2020; **38**: 982-1004 [PMID: 32371787 DOI: 10.1097/HJH.0000000000002453]

66 **Armstrong C**; Joint National Committee. JNC8 guidelines for the management of hypertension in adults. *Am Fam Physician* 2014; **90**: 503-504 [PMID: 25369633]

67 **Wald R**, Tentori F, Tighiouart H, Zager PG, Miskulin DC. Impact of the Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for Bone Metabolism and Disease in a large dialysis network. *Am J Kidney Dis* 2007; **49**: 257-266 [PMID: 17261428 DOI: 10.1053/j.ajkd.2006.11.027]

68 **Becker GJ**, Wheeler DC, De Zeeuw D, Fujita T, Furth SL, Holdaas H, Mendis S, Oparil S, Perkovic V, Rodrigues CIS. Kidney disease: Improving global outcomes (KDIGO) blood pressure work group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney International Supplements. 2012: 337

69 **Ruzicka M**, Quinn RR, McFarlane P, Hemmelgarn B, Ramesh Prasad GV, Feber J, Nesrallah G, MacKinnon M, Tangri N, McCormick B, Tobe S, Blydt-Hansen TD, Hiremath S. Canadian Society of Nephrology commentary on the 2012 KDIGO clinical practice guideline for the management of blood pressure in CKD. *Am J Kidney Dis* 2014; **63**: 869-887 [PMID: 24725980 DOI: 10.1053/j.ajkd.2014.03.003]

70 **Andrews PA**, Burnapp L. British Transplantation Society / Renal Association UK Guidelines for Living Donor Kidney Transplantation 2018: Summary of Updated Guidance. *Transplantation* 2018; **102**: e307 [PMID: 29688993 DOI: 10.1097/TP.0000000000002253]

71 **Cross NB**, Webster AC, Masson P, O'Connell PJ, Craig JC. Antihypertensive treatment for kidney transplant recipients. *Cochrane Database Syst Rev* 2009; CD003598 [PMID: 19588343 DOI: 10.1002/14651858.CD003598.pub2]

72 **Ibrahim HN**, Jackson S, Connaire J, Matas A, Ney A, Najafian B, West A, Lentsch N, Ericksen J, Bodner J, Kasiske B, Mauer M. Angiotensin II blockade in kidney transplant recipients. *J Am Soc Nephrol* 2013; **24**: 320-327 [PMID: 23308016 DOI: 10.1681/ASN.2012080777]

73 **Mourad G**, Ribstein J, Mimran A. Converting-enzyme inhibitor *vs* calcium antagonist in cyclosporine-treated renal transplants. *Kidney Int* 1993; **43**: 419-425 [PMID: 8382753 DOI: 10.1038/ki.1993.61]

74 **Pelletier RP**, Akin B, Ferguson RM. Prospective, randomized trial of steroid withdrawal in kidney recipients treated with mycophenolate mofetil and cyclosporine. *Clin Transplant* 2006; **20**: 10-18 [PMID: 16556147 DOI: 10.1111/j.1399-0012.2005.00430.x]

75 **Sivaraman P**, Nussbaumer G, Landsberg D. Lack of long-term benefits of steroid withdrawal in renal transplant recipients. *Am J Kidney Dis* 2001; **37**: 1162-1169 [PMID: 11382684 DOI: 10.1016/S0272-6386(01)99001-8]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com