

Arterial Stiffness in Kidney Transplant Recipients

An Overview of Methodology and Applications

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Introduction: Cardiovascular disease is still a major cause of mortality in kidney transplant patients. This is partially attributed to the nonclassic cardiovascular risk factors including *arterial stiffness*, an established independent predictor of mortality in several patient populations.

Materials and Methods: An extensive search was performed to review the evolution process of the method for arterial stiffness assessment and sphygmology and their applications in chronic kidney disease before and after kidney transplantation.

Results: Despite a marked change in methodology from the ancient medical practice to the current modern medicine, noninvasive assessment of arterial stiffness is still based on pulse analysis. Currently, pulse wave velocity, augmentation index, and pulse wave reflection are preferred indexes for arterial stiffness. Increased arterial stiffness has been reported in diabetes mellitus, hypertension, chronic kidney disease, cardiovascular disease, and elderly, and reduction of arterial stiffness is a key element for efficacy of the treatment and mortality reduction.

Conclusion: Noninvasive assessment of arterial stiffness is suggested as a part of clinical assessment for kidney transplant recipients and donors and facilitates defining high-risk patients for development of cardiovascular disease. A combination of techniques is recommended for this purpose.

Keywords: cardiovascular disease, chronic kidney disease, kidney transplantation, arteries, arterial compliance

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INTRODUCTION

The current evidence shows the mortality rate of transplant patients is 6 and 8 times less than that of dialysis patients with and without diabetes mellitus (DM), respectively.⁽¹⁾ Although this observation can be attributed to a younger age and a lower risk of cardiovascular disease (CVD) in patients who have been selected for transplantation, it may also indicate a reduction in the risk of CVD following transplantation.⁽²⁻⁵⁾ Nevertheless, CVD is still a common cause of posttransplant death.⁽¹⁾ A large database from

a national kidney transplant registry demonstrated that despite improvement in both graft survival and patient survival over the past decade, CVDs still account for a mortality rate of 22% among kidney transplant recipients.⁽¹⁾ However, classic risk factors cannot fully explain the risk of CVD in this population. It is reported that the Framingham cardiovascular risk score significantly underestimates the risk of ischemic heart disease in transplant patients,⁽⁶⁾ and therefore, nonclassic risk factors including C-reactive protein, homocysteine, and kidney function, as well as

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arterial stiffness, may contribute to cardiovascular risk in this population.^(2,7)

Arterial stiffness is now an established independent predictor of mortality and a risk marker for cardiovascular events.⁽⁸⁻¹⁴⁾ Although arterial stiffness is associated with vessel wall sclerosis,⁽¹⁵⁾ it is not solely determined by structural factors within the vessel wall and distending pressure, since there are also functional regulations performed by the autonomic nervous system, vascular smooth muscle, and endothelial derived-nitric oxide. Therefore, arterial stiffness is a summation marker representing many contributing factors on the risk of CVD.

Of paramount importance, arterial stiffness is potentially reversible and is applicable in the patients' follow-up for evaluation of the treatment efficacy.⁽¹⁶⁻¹⁸⁾ Several methods have been used to evaluate arterial stiffness. The noninvasive methods are principally based on pulse transit time and pulse contour analysis⁽¹⁹⁾; new applications of an old science: *sphygmology*.

SPHYGMOLOGY: AN ART FOR ALL SEASONS!

The pulse has been regarded as the basic sign of life across time and culture, and feeling the pulse is a standard part of all the great medical traditions. The significance of the pulse has been recognized for millennia with ancient Egyptian, Chinese, and Ayurvedic traditional medicines appreciating the association of pulse abnormalities with different diseases and heart function. However, the term of *sphygmopalpation* was first used by Paraxagoras (400 BC) and classic sphygmology appearing in scientific texts by Greek physicians, particularly Hippocrates and Herophilus (4th century BC). This was developed by Galen (2nd Century AD), who realized that the pulse was the movement of blood, not air, inside the vessel and wrote extensively on pulse.⁽²⁰⁾ Over centuries, sphygmology was influenced and refined by many nations; Persia (Iran) in particular further developed these sphygmological traditions with the addition of new concepts, theories, and classifications.⁽²¹⁻²³⁾ For instance, Rhazes (Ibn-Zakariya, 865 to 925 AD) described diverse pulse formations in different diseases.⁽²¹⁾

Of particular interest, 11 features and more than 50 identifiable pulse forms were described by Avicenna (Ibn-Sina, 973 to 1037 AD), the renowned Persian physician. This warranted a separate chapter named *sphygmology* in his 5-volume medical text book, *Canon in Medicine (al-Quanun)*.^(20,24) Perhaps his skill in poetry, music, mathematics, and philosophy impacted his understanding of body music, the pulse and its interpretation. He comprehensively evaluated this subject and recorded the effect of a variety of conditions including environment, food, drink, age, exercise, pregnancy, emotions, and body activity on the pulse and is famous for using the pulse as a lie detector.⁽²⁴⁾ This pulse diagnosis skill gradually advanced until pulse assessment via a piece of string (strapped around the wrist) became a traditional Persian diagnostic method.⁽²²⁾ During this era, many medical texts were written in Arabic, the new official scientific language in the region, which included Greek translations. The visits of Persian and Arab physicians to those parts of Europe which were under Muslim domination, such as Sicily and Spain, and the subsequent translation of these texts into Latin laid the foundations of modern western medicine and stimulated the revolutionary discovery of the circulation by William Harvey (1578 to 1657).^(20,25)

Harvey established the pulse as a manifestation of cardiac ejection and vascular properties and even noted the impact of wave reflection. Years later, Stephen Hales (1677 to 1761) was the first to measure arterial pressure and described peripheral vascular resistance and the vascular cushioning (*Windkessel*) effect. The dynamics, transmission, and reflection of the pulse were further improved by Thomas Young (1773 to 1829) who noted that arterial elasticity is related to the velocity of propagation of the arterial pulse.⁽²⁵⁾ Perhaps, the invention of the kymograph by Carl Ludwig in 1847 was a turning point in the history of modern medicine; since it was adopted years later by Karl Vierordt (1854) for pulse recording.⁽²⁶⁾ The first noninvasive sphygmograph was produced by Ettiene Marey in 1860.^(27,28) Several models were developed and exhibited with one after another becoming popular in the routine clinical practice. Evaluation of cardiac function using sphygmograph records consequently

became a focus in medical research.^(27,29) The first quantitative sphygmograph was invented by Fredrick A Mahomed (1851 to 1884), and the change in systolic and diastolic parts of the pulse contour in essential hypertension was described by him.⁽²⁵⁾ Then, William Osler (1892) in his seminal textbook explained the concepts of atherosclerosis and arteriosclerosis and their relationship with kidney function as well as their sphygmograph manifestations.⁽³⁰⁾

The beginning of the 20th century coincided with the invention of the *sphygmomanometer* following intensive research by Scipione Riva-Rocci and Nicolai Korotkoff.^(25,27) This new device facilitated epidemiologic research including the importance of systolic and diastolic blood pressure (BP). While pulse and BP knowledge was expanding, cardiac catheterization then allowed a comparison of direct waveform records with indirect estimations from peripheral arteries.⁽²⁶⁾ The introduction of the new sphygmomanometry into clinics diminished the importance of the pulse wave for decades.^(25,31) Then in 1960, a new interpretation of pulsatile phenomena was proposed by DA McDonald where the relationship of arterial compliance with forward and backward travelling waves was suggested. Pulse wave analysis was then reintroduced after accurate arterial tonometers were developed.⁽²⁵⁾ More recently, with the development of new computerized equipment, assessment of the pulse pressure wave with a sphygmograph has undergone a renaissance.^(31,32) Besides, the relatively recent realization of the importance of pulse pressure and central arterial pressure rather than brachial systolic or diastolic BP by Michael O'Rourke⁽³³⁾ has encouraged the return to pulse wave measurements as clinical tools.

METHODOLOGICAL ASPECTS

Prior to the assessment of different methods of arterial stiffness evaluation, an important distinction must be made between (1) large conduit arteries, (2) smaller more distal arteries and branch points (reflecting sites), and (3) arterioles (resistance sites). While stiffness of the large arteries leads to an increased pulse propagation velocity and a widening of the pulse pressure, stiffening of the reflecting sites also alters the wave contour and pathologic lesions in arterioles change the mean arterial pressure.⁽³⁴⁾ Also one must distinguish between the term *atherosclerosis* (calcified atheromatosis) and *arteriosclerosis*, although they may occur coincidentally (Table 1). Whereas the former refers to segmental plaques with intimal lesions that may change the pulse pressure and wave contour but not necessarily central pulse wave velocity, the latter represents arterial wall degeneration, predominantly medial, which causes large artery stiffness and consequently alters pulse wave velocity.⁽²⁵⁾ The viscoelastic properties of the large arteries can be described in terms of compliance, distensibility, and stiffness.⁽³⁵⁾

Several methods have been used to evaluate arterial stiffness. They are principally based on pulse transit time, pulse contour analysis, and direct measurement of arterial geometry.⁽¹⁹⁾ There is still no gold-standard measurement method for arterial stiffness,^(18,31) which cause limits for the of validation studies. However, from the clinical point of view, the central pulse wave velocity (PWV) is now established as a surrogate marker of arterial stiffness and is an independent determinant of mortality,^(34,36) and in the absence of a gold-standard method for measurement of arterial stiffness, central PWV is commonly used in the validation of other devices (Table 2).^(19,37)

Table 1. Contrasting Features of Arteriosclerosis and Atherosclerosis in Human Arteries.⁽²⁵⁾

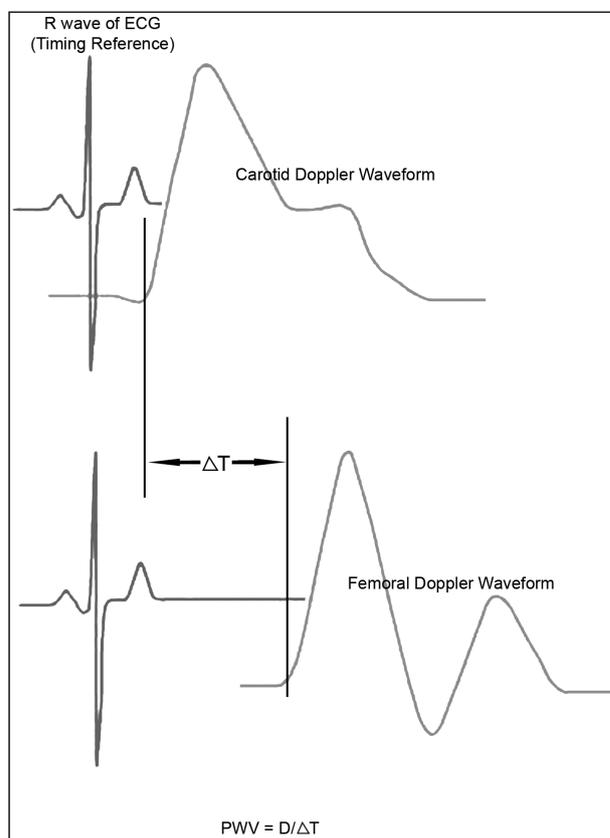
Features	Arteriosclerosis	Atherosclerosis
Anatomic location	Diffuse in elastic arteries	Focal
Vascular location	Media	Intima
Vascular effect	Dilatation	Constriction
Consequence (distal)	Nil*	Ischemia
Consequence (proximal)	Increase left ventricular load	Nil

*Current evidence demonstrates that arteriosclerosis can reduce coronary artery blood flow and accelerate end-organ damage via increased pulse pressure.⁽²⁵⁾

Table 2. Recommended Devices for Assessment of Arterial Stiffness in Clinical Practice*

Device	Type	Blood Pressure Calibration	Measurement Mechanism	Limitations	Approximate Cost, US \$
Complior®	Regional	...	Pulse Transit time delay between arterial sites using foot to foot method for the point determination	Skill dependency Uncertainty in the distance measurement Technical errors in obese patients	11000
SphygmoCor®	Regional for PWV Global for PWA	Required	Pulse transit time delay using electrocardiography as the timing reference for PWV Pressure wave form analysis using applanation tonometry and a generalized transfer function for PWA	Controversies about the validation of a generalized transfer function Confounding factors Dissociation from PWV in particular populations	14000
Pulse Trace System™	Global	...	Volume pressure analysis using a finger plethysmograph	Confounded by skin characteristics Modest correlation with PWV	10000
HD/Pulse Wave™ CR-2000	Regional	Required	Diastolic decay analysis using the Windkessel model	Sensor placement Poor agreement of C1 with PWV and augmentation index Unclear validity in human	36000

*Ellipses indicate not applicable. PWV indicates pulse wave velocity and PWA, pulse wave contour analysis.



The principle for measurement of central PWV. PWV indicates pulse wave velocity; D, the distance between measurement sites; and ΔT , transit time (time delay).

Stiffness of the large arteries increases the systolic blood pressure and decreases the diastolic blood pressure, and therefore, creates a wide pulse pressure (PP). Pulse pressure is determined by ventricular ejection and the aortic cushioning function; hence, it is the simplest achievable marker of arterial stiffness in clinical practice.⁽³⁸⁾ Furthermore, PP amplification from the central to the peripheral arteries may represent the ventricular function.⁽³⁹⁾ However, there are several factors that affect PP and it could not be applied as a single surrogate of arterial stiffness. Pulse wave velocity is usually assessed by the delay in the upstroke pulse between the feet of two corresponding waves in proximal and distal sensors (foot-to-foot method) divided by the distance traversed ($D/\Delta T$; Figure). Despite the general acceptance of the method itself and several reports of its validity and reliability,^(40,41) the distance measurement between the arterial points is still debated. While many studies use surface distance between the adjacent skin

on the measurement site (according to the manufacturer's instructions),⁽⁴²⁾ the real distance may be overestimated or underestimated due to branching and tortuous arterial segments and individual diversity in the vascular pathway and adjacent structures. Also, a large abdomen or breast can artificially increase the distance measured between the probes. Furthermore, since the pulse travels between the aorta (not the carotid) and femoral artery, it is suggested that the distance between the sternal notch and the carotid probe must be subtracted from the carotid-femoral length.⁽⁴³⁾ Although a different PWV result is expected with adjusted distance measurements, they must be strongly correlated and should not affect epidemiologic studies on arterial stiffness. Nevertheless, the method of the distance measurement is of great concern when studies are compared or pooled. In terms of interpretation, PWV represents segmental arterial compliance (carotid-femoral or carotid-radial) and probably does not reflect the compliance of the vasculature as a whole.⁽³⁷⁾

The other method for evaluation of arterial stiffness is pulse wave contour analysis (PWA) using applanation tonometry. Although the tonometer can be applied on any artery that lies on a rigid structure, such as bone, carotid tonometry is difficult, especially in persons with thick necks, and it is commonly accompanied by artifacts. This method is also uncomfortable and carries the risk of carotid plaque dislodgement. Consequently, radial artery tonometry is preferred because it is easier to master and the variability is far less than other sites.⁽³³⁾

Each pulse *pressure waveform* contains two major parts. The systolic part (the incident wave) is mainly determined by left ventricular ejection and the impedance of ejection.⁽³¹⁾ Approximately, 80% of this forward wave is reflected backward from the periphery (the reflected wave)^(25,33) and accounts for the dicrotic wave in the diastolic part of the pulse contour. The impact of the reflected wave on the pulse contour depends on its amplitude and timing; amplitude is affected by the speed of energy transfer and luminal mismatch, and the timing itself is associated with the arterial stiffness (the stiffer the wall, the faster the

wave return), aortic length, and the site of reflection.^(25,38) While the arrival of the reflected wave facilitates coronary blood flow during diastole in normal circumstances, with stiff arteries, the reflected wave returns faster with augmentation of the systolic pressure wave. This increases ventricular load on the one hand and diminishes coronary blood flow on the other.

The amount of augmentation is commonly expressed as the augmentation index (AI) which is the ratio of augmentation pressure to pulse pressure. Since heart rate has a great impact on the waveform timing and augmentation, computer software adjusts the AI value for heart rate according to a built-in normogram. Apart from the augmentation pressure, PWA provides additional information including ejection duration, the timing of the incident and the reflected waves, subendocardial viability ratio, and more importantly, an estimation of the central arterial BP. The latter is calculated according to a mathematical transfer function that has been a subject of long-term debate regarding the validity of both transfer function and AI.^(33,44) This issue was recently reviewed in detail by our group.⁽⁴⁵⁾ But in general, the method is valid and reliable and is Food-and-Drug-Administration approved for clinical practice. It is noteworthy, however, that the interpretation of the results in diabetic patients, the elderly, and those with chronic kidney disease (CKD) needs adequate expertise.

Recent studies suggest that augmentation index (AI) might be a more significant marker of arterial stiffness in younger individuals whereas aortic PWV is likely to be a better measure in older individuals.⁽⁴⁶⁾ Therefore, a combination of the methods including PWV, AI, and central BP has been suggested for a full assessment of the arterial system.^(16,36) Nevertheless, method selection depends on the purpose of the measurement as well as the target population and funding. Yet, the bottom line and the simplest might be the use of ambulatory PP.

It is noteworthy that much of the available data about these techniques has been collected in a controlled environment and in steady-state conditions at a standard time and medication,

and smoking and caffeine withheld for a defined period before testing. Also, the impact of diurnal variation, fasting state, and exercise prior to testing, appear to cause a significant variability in measurement results.⁽¹⁸⁾ Specific attention must be paid to the accuracy of the BP measurement for a proper calibration. Furthermore, since the operator expertise may markedly affect the result, standardized training and qualification are required. It is also necessary to improve the accuracy of distance measurements with PWV analysis. With respect to the utility of the results, the reliability of changes in arterial stiffness as a guide of therapeutic efficacy is yet to be confirmed,⁽³⁴⁾ and reference values must be developed and validated.

ASSOCIATED FACTORS WITH ARTERIAL STIFFNESS

Arterial stiffness is influenced by a large number of modulators including physiologic, pathologic, psychologic, and pharmacologic factors. Increased arterial stiffness has been proposed as a normal vascular aging process^(46,47) and mainly affects central and more elastic proximal arteries.⁽⁴⁸⁻⁵⁰⁾ Therefore, we have constructed an age-specific reference interval for PWV which facilitates its clinical application (Table 3).⁽⁵¹⁾ The result of PWA is also compared with the normal values of the patients' age.

Women have a greater PP and AI, but a lower PWV than men; the latter is partially attributed to the greater sympathetic activity in men.⁽⁵²⁾ Also, increased cardiovascular events associated with shorter stature may be partially due to increased PWV and earlier return of the pulse wave reflection in the arterial tree^(53,54); however,

this cannot explain the lower PWV and the risk of CVD in women. Central obesity and increased BMI have also been demonstrated to be associated with impaired arterial compliance.⁽⁵⁵⁾ Moreover, several studies reported racial difference in the arterial compliance, demonstrating stiffer and more pressure-sensitive arteries in black and Afro-Caribbean populations, an ethnic diversity that is mainly expressed in peripheral arteries.⁽⁵⁶⁻⁵⁸⁾

Blood pressure is frequently reported as the main determinant of arterial stiffness.^(31,50) Therefore, the original causes of increased arterial pressure may increase arterial stiffness as well. On the other hand, PWV can be BP-independent in various conditions such as the response to BP lowering medications^(33,59) and exercise training.⁽⁶⁰⁾ Determining the effect of heart rate on arterial compliance is difficult; since an increased heart rate increases PP and decreases AI, and reports on its effect on PWV are conflicting.⁽⁶¹⁾ Since BP, heart rate, vasoactive hormones, and blood volume all have diurnal variations, such a fluctuation is also expected for arterial compliance as was shown by Bodlaj and colleagues for AI and subendocardial viability.⁽⁶²⁾

Of technical and epidemiologic importance, smoking, alcohol consumption, and caffeine can increase arterial stiffness indexes and the effect may persist for 3 hours.^(50,63-67) These factors are not only important clinically, but also must be considered from a technical point of view during the measurement of arterial stiffness.

Finally, many drugs including antihypertensive drugs such as nitrates,⁽²⁵⁾ beta-blockers,⁽³¹⁾ calcium-channel blockers,⁽⁶⁸⁾ angiotensin-converting

Table 3. Age-specific Reference Index of Pulse Wave Velocity⁽⁵¹⁾

Age, y	Pulse Wave Velocity							
	2.5th	5th	10th	50th	75th	90th	95th	97.5th
20	5.93	6.31	6.76	8.36	9.28	10.27	10.94	11.58
30	5.72	6.15	6.66	8.45	9.47	10.58	11.33	12.05
40	5.59	6.07	6.63	8.63	9.75	11.02	11.86	12.66
50	5.57	6.10	6.71	8.90	10.14	11.51	12.43	13.30
60	5.70	6.27	6.94	9.33	10.68	12.17	13.18	14.13
70	6.01	6.63	7.36	9.96	11.38	13.06	14.15	15.19
80	6.48	7.15	7.93	10.72	12.27	14.04	15.21	16.32
90	7.15	7.87	8.70	11.68	13.39	15.23	16.48	17.67

enzyme inhibitors, and angiotensin receptor blockers have substantial impact on arterial stiffness, acutely and chronically.⁽⁶⁹⁻⁷¹⁾ These facts should be carefully considered in the interpretation of the results.

ARTERIAL STIFFNESS BEFORE KIDNEY TRANSPLANTATION

Several reports have associated arterial stiffness with a broad range of diseases. Consequently, measurement of arterial stiffness in kidney transplant candidates with hypertension, DM, and CKD is of great importance in respect of its potential utility in the early diagnosis, prevention, and treatment of these chronic diseases.

It is generally accepted that hypertension increases stiffness of the large arterial wall via hypertrophy and changes in the extracellular matrix, mainly due to increased collagen.⁽⁷²⁾ Current evidence also shows that the treatment of hypertension must include arterial stiffness reduction, as another facet of the cardiovascular health, to be effective in reducing mortality.^(33,73,74) Several studies have indicated an increased arterial stiffness in CKD, particularly in end-stage renal disease (ESRD).^(19,35,75-77) While these patients usually have other atherogenic cardiovascular risk factors, structural changes in the intima, media, and adventitia as well as endothelial dysfunction causes the elevated arterial stiffness.⁽⁷⁸⁾ While hemodialysis improves arterial compliance both in short-term and long-term, dialysis membrane bioincompatibility may play a role in maintaining increased arterial stiffness during dialysis.⁽⁷⁹⁾ Mourad and coworkers demonstrated that patients with stiffer arteries had lower BP response to dialysis and thereby are at a higher risk,⁽⁸⁰⁾ and Covic and colleagues reported that a lack of reduction in AI after dialysis is associated with left ventricular dysfunction.⁽⁸¹⁾

A variety of techniques have demonstrated that arterial compliance is reduced in DM and is associated with its complications.^(60,82-85) It is also related to glucose control,⁽⁸²⁾ autonomic dysfunction,⁽⁸⁶⁾ and kidney function.⁽⁸⁷⁾ In addition, reduced arterial compliance precedes microalbuminuria⁽⁸⁸⁾ or even DM itself.^(89,90) Consequently, assessment of arterial stiffness

may even facilitate the early diagnosis of DM complications.

Prognostic Value of Arterial Stiffness Indexes

The risk of cardiovascular events is directly and independently associated with PP.^(13,91-94) It is also associated with end-organ damage and cardiovascular events (except for stroke) in hypertension.^(13,95,96) An elevated PP also indicated a high risk of death or dialysis in patients with primary stages of CKD⁽⁹⁷⁾ and predicted CVD and total mortality better than systolic or diastolic BP in patients on hemodialysis.⁽⁹⁸⁾ However, among patients with ESRD, central rather than peripheral PP predicted mortality.⁽⁸⁾ Even in mild to moderate renal insufficiency, PP and arterial stiffness are linked to plasma creatinine levels and microalbuminuria,⁽¹³⁾ and they are associated with left ventricular hypertrophy and possibly cardiomyopathy.⁽⁹⁹⁾

Arterial stiffness as measured by PWV has been recognized as a strong and independent predictor of mortality in patients with hypertension,⁽¹²⁾ DM,⁽¹¹⁾ ESRD,^(75,100) and the elderly.^(101,102) Of great importance, Guerin and colleagues demonstrated a decrease in mortality when aortic distensibility was improved by medication as defined by a reduced PWV.⁽⁷⁴⁾ Nakano and colleagues found greater prevalence of CVD, ischemic heart disease, and cerebrovascular disease with a 1 m/s PWV increment in cross-sectional analysis. Cerebrovascular disease was also associated with a PWV greater than 10 m/s in the follow-up period of their study.⁽¹⁰³⁾

Augmentation index has been shown to be predictive of coronary artery disease severity in hypertensive patients⁽¹⁰⁴⁾ and future cardiovascular and all-cause mortality in ESRD.⁽¹⁰⁰⁾ This index also correlated with a cardiovascular risk score in symptomatic and asymptomatic patients with CVD.⁽¹⁰⁵⁾ However, there was a marked overlap between the risk levels, and AI failed to stratify individuals in relation to risk. Nevertheless, this does not indicate a low prognostic value of AI, rather it shows that AI outperforms classical risk factors.⁽¹⁴⁾

Other arterial stiffness indexes such as stiffness index, ambulatory arterial stiffness index, and stroke volume/PP ratio have also been demonstrated to be associated with adverse outcomes.⁽¹⁰⁶⁻¹¹⁰⁾ However, further discussion of the indexes is beyond this review.

Screening of Arterial Stiffness

The above evidence suggest that a proper risk assessment of the potential kidney transplant patients could be targeted by implementation of arterial stiffness assessment, which accompanies several advantages when compared to the current evaluation program. Moreover, application of this approach to evaluate potential kidney donors reveals incipient hemodynamic disorders and facilitates selection of the best candidates, and thereby, reduces the donor complications.

ARTERIAL STIFFNESS AFTER KIDNEY TRANSPLANTATION

Arterial stiffness is an established cardiovascular risk marker and an independent predictor of cardiovascular events and mortality in various groups of patients including kidney transplant patients.^(7,10-12,101,111) Several studies have also demonstrated a substantial cardiovascular risk reduction after kidney transplantation when compared to patients on hemodialysis.^(2,3) While this observed difference could be due to selection bias (younger age in transplant recipients compared to patients on hemodialysis), a large study including 46 164 patients who were placed on a waiting list for kidney transplantation (virtually a homogenous population) revealed a long-term mortality reduction of 48% to 82% among patients who underwent transplant surgery.⁽⁴⁾ This is in parallel to researches reporting improved posttransplant arterial function. For instance, Kocak and colleagues reviewed 30 patients during hemodialysis and after transplantation and demonstrated an improvement in endothelial function after transplantation.⁽¹¹²⁾ In addition Zoungas and colleagues evaluated systemic arterial compliance and AI in 36 patients before and after transplantation and found a significant decrease in serum lipids and homocysteine,

systolic and diastolic BP, and heart rate as well as AI and peripheral and central PWV following transplantation.⁽¹¹³⁾ Our findings in a follow-up study also demonstrated that the improvement in arterial function after kidney transplantation is continuous during the posttransplant period. However, research is required to see if this benefit continues to occur over the life of the kidney transplant as well as its cause. This is mainly attributed to the resolution of systolic and diastolic ventricular dysfunction and regression of left ventricular hypertrophy after successful kidney transplantation.⁽¹¹⁴⁾

Since the CVD is still the leading cause of mortality in the kidney transplant patients, following up the patients identifies those at risk of CVD after kidney transplantation. It is likely that the role of arterial stiffness in left ventricular systolic pressure, left ventricular hypertrophy, and ventricular oxygen and blood demand explains the higher cardiovascular morbidity in kidney transplant recipients with decreased arterial distensibility.⁽⁷⁾

Several comorbidities may have influence on the cardiovascular function in transplant patients, of which DM is one of the most important determinants. Although patients with DM are not traditionally preferred candidates for kidney transplants, the number of the procedures on diabetic patients is increasing.⁽¹⁾ Cardiac function in transplant candidates with DM is carefully evaluated prior to transplantation and left ventricular systolic and diastolic function improves shortly after a successful kidney transplant.^(5,114,115) Consequently, recent reports did not demonstrate a considerable difference for the outcome of kidney transplantation in patients with and without DM.⁽¹¹⁶⁾

Although hypertension is a common problem in ESRD, it is less frequent among kidney transplant patients due to their posttransplant medication which in many cases includes calcium channel blockers.⁽¹¹³⁾ However, it is noteworthy that reduction of the peripheral BP is not sufficient to reduce the cardiovascular risk, and central BP (which could be estimated accurately by PWA) must be reduced in order to reduce the risk.⁽⁷⁴⁾

Some posttransplant drugs cause vascular damage and increase cardiovascular risk in the kidney recipients. While some reports claim a lack of difference in arterial stiffness between patients with and without cyclosporine administration,⁽⁷⁾ other reports indicate conversion from cyclosporine to tacrolimus improves cardiovascular risk profile.⁽¹¹⁷⁾ Parallel to this report, we recently found in our analysis advantages of mycophenolate mofetil for arterial distensibility when compared to the other immunosuppressant drugs. The benefit of mycophenolate mofetil on the graft and patient survival compared to azathioprine has been reported elsewhere.⁽¹¹⁸⁾

CONCLUSION

Arterial stiffness is an independent marker and predictor of cardiovascular risk and mortality in diverse groups of individuals including kidney transplant patients. While assessment of arterial stiffness in pretransplant CKD is beneficial, implementing this approach into the follow-up program of the patients after transplantation may enhance the value of cardiovascular risk assessment and prevent CVD mortality and morbidity in this group of patients. Furthermore, assessment of arterial stiffness appears to be a reliable and important step in the screening of the potential kidney donors and prevent complications after donation.

CONFLICT OF INTEREST

None declared.

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