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FUNCTIONAL INDICATORS OF PERIPHERAL ARTERIAL STIFFNESS IN SOLID ORGAN RECIPIENTS (LITERATURE REVIEW)

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Increased arterial stiffness is an important preclinical indicator of cardiovascular dysfunction, arterial hypertension and target organ injury. This condition increases the risk of long-term adverse events. Solid organ recipients face multiple risk factors for cardiovascular complications due to transplant rejection, lifelong medication use and adaptive features of the transplanted organ. The review presents an analysis of the results of studies on the main functional indicators of peripheral arterial stiffness, as well as the potential effect of immunosuppressive therapy on indicators of vascular stiffness in solid organ recipients.

Keywords: stiffness, arterial stiffness, immunosuppression, recipients.

Increased peripheral arterial stiffness is a biological process associated with increasing age [1, 2], blood pressure [3], inflammation [4, 5] and vascular calcification [6]. Arterial stiffness may also be related to donor age [7], arterial stiffness index in a related kidney donor [8], post-transplant diabetes mellitus [9], cold ischemia time [10], graft function [11], hypomagnesemia [12], and graft rejection [13]. In addition, immunosuppressive therapy may affect arterial stiffness or rigidity [14].

Arterial stiffness or rigidity has become virtually synonymous with pulse wave velocity (PWV), the rate at which pressure waves move down the vessel. Theoretically, this can be demonstrated in such a way that in an elastic tube of homogeneous structure with cross-sectional area A filled with a fluid of density ρ, a perturbation in the system propagates as a wave along this tube at the PWV and is expressed by the Bramwell–Hill equation (Bramwell J.C., Hill A.V., 1922):

$$PWV = \sqrt{\frac{A\partial P}{\rho \partial A}},$$

where ∂A is the change in lumen area in response to a change in pressure ∂P.

$D = \frac{\partial A}{A\partial P}$, where D represents tube extensibility (defined as the relative change in cross-sectional area in response to pressure). Hence, $PWV = \sqrt{\frac{1}{\rho D}}$. Thus, higher vessel stiffness (lower D) results in higher PWV. Despite some limitations, PWV measurement has several advantages for clinical practice. When measured segment by segment (e.g., in the aorta), PWV gives an average value of its stiffness. In clinical practice, PWV is most often calculated using the formula PWV = ΔL/ΔT, where ΔL is the distance between two measurement points and ΔT is the time it takes for arterial pulse to travel from the proximal to the distal measurement point [15]. The aorta is the main elastic vessel in the body, PWV in the aorta or in its segments probably represents the most informative parameter. The most widely used method for measuring aortic PWV is carotid-femoral PWV, the transit time of which is estimated from Doppler signals measured on the carotid and femoral arteries, which are relatively close to the aorta [15].

There are several measurement devices available, including commercially available systems such as Complior [16], Sphygmocor [17], Pulsepen [18] and others, as well as specially designed data acquisition systems (which, for example, have been used in population-based studies by Framingham [19] and Asklepios [20]). Ideally, measurements are performed simultaneously; sequential measurements together with ECG synchronization are the best alternative method. Any ultrasound machine with a vascular probe can also be used, provided the methodology is followed and appropriate software is available. Difficulties arise when estimating the carotid-femoral pathway length: the intra-arterial distance must be estimated from measurements at the body surface, and the pulse wave does not travel strictly straight along a single pathway from the carotid artery to the femoral artery measurement site.

Although there are a number of different ways to determine the distance, which makes it challenging to standardize measurements, PWV is now often calculated

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by multiplying 0.8 by the distance between the common carotid artery and the common femoral artery measurement site [21]. Carotid-femoral PWV is considered the reference standard for clinical trials in Europe and the United States because of the availability of a large database of reference values obtained throughout Europe [22] and studies demonstrating the prognostic significance of this parameter [23–26].

PWV measurements should be evaluated according to patient age. The 2007 European Society of Cardiology Guidelines defined a fixed threshold value of 12 m/s to identify patients at high cardiovascular risk [27]. Later, expert consensus set this value at 10 m/s [21].

Another indicator reflecting arterial stiffness is the augmentation index. The augmentation index is based on pulse wave reflection and is a common measure of arterial stiffness. The augmentation index is defined as the ratio of the augmentation of systolic blood pressure to pulse pressure. To calculate it, it is necessary to determine the point of confluence of the direct and reflected waves (inflection point). According to some observations, this inflection point corresponds to the blood flow velocity peak and several algorithms have been developed for its identification [28–30].

Characteristic impedance is another arterial stiffness indicator. It relates absolute arterial pressure at a certain location to absolute blood flow velocity at the same location in the absence of reflected waves [31]. Characteristic impedance (Zc) is related to PWV by the formula: Zc = СПВ × ρ. Since blood density is approximately equal to unity, these values are numerically almost identical when expressed in cm/sec or in dyn·s per cm^3 [31]. It is virtually impossible to measure characteristic impedance by non-invasive methods because of the difficulty in excluding reflected wave effects and errors in non-invasive measurement of blood flow velocity and pressure.

OTHER ARTERIAL WALL ELASTIC PROPERTIES

1. Arterial distensibility – the change in relative diameter (or area) with increasing pressure. It is inversely related to the modulus of elasticity.
   $\Delta D/\Delta P \times D$ ($mmHg^{-1}$).
2. Distensibility coefficient – the relative change in vascular cross-sectional area per unit pressure
   $DC = [\Delta A/A]/\Delta P = 2 \times \Delta d/d/\Delta P$.
3. Compliance – the absolute change in diameter (or area) at a given pressure and a given vascular length
   $\Delta D/\Delta P$ (cm/mmHg) or (cm^2/mmHg).
4. Bulk modulus of elasticity – the pressure step required theoretically to increase volume by 100%
   $\Delta P/(\Delta V/V)$ (mm Hg) = $\Delta P/(\Delta D/D)$ (mmHg), without changing length.
5. Elastic modulus – the pressure step required theoretically to stretch the diameter 100% from a resting state at a fixed vascular length
   ($\Delta P \times D/\Delta D$) (mmHg).

PERIPHERAL ARTERIAL STIFFNESS AND IMMUNOSUPPRESSIVE THERAPY

It is known that pathological processes in the vascular wall are triggered by dysregulation of matrix metalloproteinase activity. The effect of immunosuppressive drugs on the activity of matrix metalloproteinases has been reported. Results from a study by Korean authors that examined the effects of cyclosporine on human umbilical vein endothelial cells revealed that the immunosuppressive agent activates most matrix metalloproteinases in endothelial cells, with the exception of MMP-2 [32]. A British study on laboratory animals examined the effect of cyclosporine, tacrolimus and rapamycin on intimal hyperplasia, expression of fibrosis-associated genes and deposition of extracellular matrix proteins. In all groups, there was a significant inhibition of matrix metalloproteinase (MMP)-2, MMP-9, tissue inhibitor of metalloproteinases (TIMP)-1, transforming growth factor (TGF)-beta and collagen III expression ($P < 0.001$) after 14 days, but deposition of extracellular matrix deposits increased [33]. Bianchi et al. investigated how cyclosporine affected the expression of vascular endothelial growth factor (VEGF) and MMP-2 in rat myocardium. In contrast to the control group, cyclosporine-treated laboratory mice showed structural myocardial changes, including fibrosis and degeneration as well as a significant increase in both MMP-2 and VEGF [34].

In a Dutch study including a cohort of 330 kidney transplant patients, PWV was found to be a prognostic factor for cardiovascular events, outcomes and survival, irrespective of patient age. Patients with a PWV of 7.5 m/s or higher had worse survival than patients with a PWV <7.5 m/s [35]. In a 2011 prospective study including 512 renal transplant recipients, PWV, central augmentation pressure, and augmentation index were measured at the time of renal transplantation. The mean follow-up period was 5 years, PWV and augmentation pressure were included in a model based on clinical variables and laboratory data to predict cardiovascular events. The addition of PWV and augmentation pressure data resulted in a 15.9% update and reclassification of cardiovascular events. Moreover, patients with a PWV of 8.1 m/s or higher had worse cardiovascular survival compared to patients with a PWV <8.1 m/s [36].

A study by Norwegian authors including 1,022 renal transplant recipients showed that below a threshold of 12 m/s, each 1 m/s increase in PWV starting at 8 m/s was associated with a 36% increase in mortality risk [37]. The presented study results demonstrate that PWV is a strong predictor of cardiovascular events and death, independent of age and other clinical or laboratory variables. The results also validate the findings of other studies that have been conducted involving different patient populations [38–40].

Results from early studies on the effects of calcineurin inhibitors on large artery function were conflicting. In a prospective study, Zoungas et al. compared PWV before and after renal transplantation in 36 patients [41]. Twelve months after transplantation, PWV improved in all patients regardless of the use of cyclosporine or tacrolimus, although the decrease in augmentation index was greater in patients receiving tacrolimus (8.0 ± 16.5% *vs.* 27.4 ± 18.2%; P = 0.01). In a small study by Covic et al., it was demonstrated that cyclosporine dramatically reduced the augmentation index [42]. However, the study lacked a control group, and the decrease in augmentation index after cyclosporine administration was linked to shorter reflected wave time, which may lead to increased PWV in the long term.

In the same period, a parallel study (including 250 stable renal transplant recipients) showed that cyclosporine increased augmentation index and blood pressure to a significantly greater extent than tacrolimus [43]. In 2007, Strozecki et al. compared PWV in 76 patients receiving cyclosporine and 76 patients taking tacrolimus [44]. The two study groups were matched for key clinical characteristics (age, blood pressure, duration of hemodialysis, diabetes mellitus). Higher PWV were found in the cyclosporine group compared to the tacrolimus group (9.33 ± 2.10 versus 8.54 ± 1.35, respectively; P < 0.01). In another study by the same authors using stepwise multiple regression analysis, it was observed that age, male sex, mean arterial pressure, cyclosporine (compared with tacrolimus), and fasting glucose levels were independently linked to higher PWV [45].

The effect of cyclosporine on arterial stiffness is probably due to increased vascular tone or impaired vasodilatory properties of nitric oxide. Given that cyclosporine administration is associated with higher PWV, switching to tacrolimus may reduce arterial stiffness. This hypothesis was tested in a small study where stable kidney recipients who had been taking cyclosporine for more than 10 years were converted to tacrolimus. PWV and ambulatory daily blood pressure monitoring (ABPM) were measured at baseline and 3 months after conversion, and no differences were found in either blood pressure or PWV, probably due to the short time interval after drug change [46]. All the studies cited suggest a possible negative effect of calcineurin inhibitors, especially cyclosporine, on PWV. In a randomized clinical trial, 17 of 27 patients were switched from cyclosporine to everolimus 6 months after kidney transplantation. PWV remained stable in the everolimus group (9.50 ± 1.92 *vs.* 9.13 ± 1.62 m/s, ΔPWV –0.37 ± 1.14 m/s), whereas it was elevated in the cyclosporine group (9.93 ± 1.94 *vs.* 10.8 ± 2.24 m/s, ΔPWV +0.89 ± 1.47 m/s) [47].

In a study by Gungor et al., no benefit in PWV or augmentation index (Aix) was found in patients treated with mTOR inhibitors (at least 6 months – either sirolimus or everolimus) compared with treatment with calcineurin inhibitors (cyclosporine or tacrolimus) [48]. In linear regression analysis, only classical risk factors (age, blood pressure, cholesterol level, and proteinuria) were found to be predictors of arterial stiffness. In a more recent randomized clinical trial, the effects of switching late from calcineurin inhibitors (tacrolimus) to mTOR inhibitors (everolimus) were examined. The findings demonstrated that left ventricular hypertrophy decreased in both groups. As secondary outcomes, changes in blood pressure (ABPM) and PWV were measured both before and after switching. The tacrolimus group (25 patients) and the everolimus group (31 patients) had median post-transplant durations of 1.7 and 1.3 years, respectively. Despite the fact that most patients receiving everolimus had dipper status, blood pressure in both groups was very well-controlled 24 months after randomization; 30% of those receiving tacrolimus were non-dippers, compared to 22% receiving everolimus. PWV at baseline, at 12 and at 24 months were within the normal range, with no significant differences between the two groups [49].

Another study evaluated PWV and blood pressure (ABPM) [50]. PWV was measured in 277, 223 and 184 patients after 12 and 24 months. Patients who switched to everolimus had a slight decrease in PWV (month 12: 0.24 m/s; month 24: 0.03 m/s), whereas patients taking cyclosporine showed a progressive increase in PWV (month 12: 0.11 m/s; month 24: 0.16 m/s); baseline values were within normal limits (mean 7.8 m/s for the everolimus group and 7.6 m/s for the cyclosporine group). Follow-up at 24 months confirmed the prognostic value of PWV, as the incidence of cardiovascular events in the entire cohort was low (2.8% in the everolimus group and 4.8% in the cyclosporine group). Since even small changes (0.4–0.5 m/s) usually occur over a long period of time, the follow-up period (at 24 months) was probably insufficient to detect any significant changes in PWV [51, 52]. Since patients with initially high PWV tend to have a more rapid increase in PWV [53], it is possible that switching to mTOR inhibitors may be beneficial in this patient cohort.

CONCLUSION

Stiffness or rigidity of the elastic and muscular-elastic arterial wall is a known independent predictor of adverse cardiovascular events [54–56]. Clinical practice has widely adopted noninvasive methods for examining systemic and local stiffness based on the measurement of PWV, augmentation index and other indicators [57, 58]. Published reports on mechanisms of regulation and the effect of immunosuppressive medications on vascular wall stiffness markers suggest that reducing arterial stiffness may be a therapeutic target for improving the quality of life in solid organ recipients [59–62].

The authors declare no conflict of interest.

REFERENCES

1. *Mitchell GF, Parise H, Benjamin EJ, Larson MG, Keyes MJ, Vita JA et al.* Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. *Hypertension.* 2004; 43 (6): 1239–1245.
2. *Giudici A, Li Y, Yasmin, Cleary S, Connolly K, McEniery C et al.* Time-course of the human thoracic aorta ageing process assessed using uniaxial mechanical testing and constitutive modelling. *J Mech Behav Biomed Mater*. 2022; 134: 105339.
3. *Belhadjer Z, Ladouceur M, Soulat G, Legendre A, Gencer U, Dietenbeck T et al.* Increased aortic pressures and pulsatile afterload components promote concentric left ventricular remodeling in adults with transposition of the great arteries and arterial switch operation. *Int J Cardiol*. 2024; 15 (405): 131969.
4. *Mahmud A, Feely J.* Arterial stiffness is related to systemic inflammation in essential hypertension. *Hypertension.* 2005; 46 (5): 1118–1122.
5. *Elçioğlu BC, Baydar O, Helvacı F, Karataş C, Aslan G, Kılıç A et al.* Evaluation of pulmonary arterial stiffness and comparison with right ventricular functions in patients with cirrhosis preparing for liver transplantation. *J Clin Ultrasound*. 2022; 50 (6): 749–755.
6. *Alcici-Moreira AM, Vitarelli MO, Velloso TA, Carvalho-Ribeiro IA, Dario DM, Polese JC et al.* Aortic pulse wave analysis and functional capacity of heart transplantation candidates: a pilot study. *Sci Rep*. 2024; 14 (1): 10504.
7. *Delahousse M, Chaignon M, Mesnard L, Boutouyrie P, Safar ME, Lebret T et al.* Aortic stiffness of kidney transplant recipients correlates with donor age. *J Am Soc Nephrol.* 2008; 19 (4): 798–805.
8. *Bahous SA, Khairallah M, Al Danaf J, Halaby R, Korjian S, Daaboul Y et al.* Renal function decline in recipients and donors of kidney grafts: role of aortic stiffness. *Am J Nephrol.* 2015; 41 (1): 57–65.
9. *Birdwell KA, Jaffe G, Bian A, Wu P, Ikizler TA.* Assessment of arterial stiffness using pulse wave velocity in tacrolimus users the first year post kidney transplantation: a prospective cohort study. *BMC Nephrol.* 2015; 16: 93.
10. *Strózecki P, Adamowicz A, Kozłowski M, Włodarczyk Z, Manitius J.* Long graft cold ischemia time is associated with increased arterial stiffness in renal transplant recipients. *Transplant Proc.* 2009; 41 (9): 3580–3584.
11. *Salib M, Girerd N, Simon A, Kearney-Schwartz A, Duarte K, Leroy C et al.* Levels of Procollagen Type I C-Terminal Pro-Peptide and Galectin-3, Arterial Stiffness Measured By Pulse Wave Velocity, and Cardiovascular Morbidity and Mortality in 44 Patients 2 Years After Kidney Transplantation. *Ann Transplant*. 2023; 28: e938137.
12. *Van Laecke S, Maréchal C, Verbeke F, Peeters P, van Biesen W, Devuyst O et al.* The relation between hypomagnesaemia and vascular stiffness in renal transplant recipients. *Nephrol Dial Transplant*. 2011; 26 (7): 2362–2369.
13. *Shevchenko AO, Tyunyaeva IYu, Nasyrova AA, Mozheiko NP, Gautier SV.* Dynamics Of Irig In Treatment Of Heart Transplant Rejections. *Russian Journal of Transplantology and Artificial Organs*. 2015; 17 (3): 8–13. [In Russ, English abstract]. doi: 10.15825/1995-1191-2015-3-8-13.
14. *Martínez-Castelao A, Sarrias X, Bestard O, Gil-Vernet S, Serón D, Cruzado JM et al.* Arterial elasticity measurement in renal transplant patients under anticalcineurin immunosuppression. *Transplant Proc.* 2005; 37 (9): 3788–3790.
15. *Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D et al.* European Network for Non-invasive Investigation of Large Arteries. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J.* 2006; 27 (21): 2588–2605.
16. *O'Brien E, Stergiou G, Palatini P, Asmar R, Ioannidis JP, Kollias A et al.* Validation protocols for blood pressure measuring devices: the impact of the European Society of Hypertension International Protocol and the development of a Universal Standard. *Blood Press Monit.* 2019; 24 (4): 163–166.
17. *Giudici A, Wilkinson IB, Khir AW.* Review of the Techniques Used for Investigating the Role Elastin and Collagen Play in Arterial Wall Mechanics. *IEEE Rev Biomed Eng.* 2021; 14: 256–269.
18. *Salvi P, Lio G, Labat C, Ricci E, Pannier B, Benetos A.* Validation of a new non-invasive portable tonometer for determining arterial pressure wave and pulse wave velocity: the PulsePen device. *J Hypertens.* 2004; 22 (12): 2285–2293.
19. *Mitchell GF, Hwang SJ, Vasan RS, Larson MG, Pencina MJ, Hamburg NM et al.* Arterial stiffness and cardiovascular events: the Framingham Heart Study. *Circulation*. 2010; 121 (4): 505–511.
20. *Segers P, Rietzschel ER, De Buyzere ML, Vermeersch SJ, De Bacquer D, Van Bortel LM et al.* Asklepios investigators. Noninvasive (input) impedance, pulse wave velocity, and wave reflection in healthy middle-aged men and women. *Hypertension*. 2007; 49 (6): 1248–1255.
21. *Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank JK, De Backer T et al.* European Society of Hypertension Working Group on Vascular Structure and Function; European Network for Noninvasive Investigation of Large Arteries. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. *J Hypertens*. 2012; 30 (3): 445–448.
22. *Elosua R, Toloba A, Arnold R, De Groot E, Martí-Lluch R, Degano IR et al.* Carotid artery stiffness and risk of vascular events and mortality: the REGICOR study. *Rev Esp Cardiol (Engl Ed).* 2024; 77 (4): 314–323.
23. *Park HW, Ozcan I, Toya T, Ahmad A, Kanaji Y, Kushwaha SS et al.* Invasive aortic pulse pressure is linked to cardiac allograft vasculopathy after heart transplantation. *Int J Cardiol*. 2023; 370: 167–174.
24. *Cameron K, El Hassan M, Sabbagh R, Freed DH, Nobes DS.* Experimental investigation into the effect of compliance of a mock aorta on cardiac performance. *PLoS One*. 2020; 15 (10): e0239604.

25. *Petrova M, Li Y, Gholipour A, Kiat H, McLachlan CS.* The influence of aortic stiffness on carotid stiffness: computational simulations using a human aorta carotid model. *R Soc Open Sci.* 2024; 11 (3): 230264.
26. *Laugesen E, Olesen KKW, Peters CD, Buus NH, Maeng M, Botker HE, Poulsen PL.* Estimated pulse wave velocity is associated with all-cause mortality during 8.5 years follow-up in patients undergoing elective coronary angiography. *J Am Heart Assoc*. 2022; 11 (10): e025173.
27. *Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G et al.* Management of Arterial Hypertension of the European Society of Hypertension; European Society of Cardiology. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2007; 25 (6): 1105–1187.
28. *Sharkey EJ, Di Maria C, Klinge A, Murray A, Zheng D, O'Sullivan J, Allen J.* Innovative multi-site photoplethysmography measurement and analysis demonstrating increased arterial stiffness in paediatric heart transplant recipients. *Physiol Meas*. 2018; 39 (7): 074007.
29. *Spronck B, Terentes-Printzios D, Avolio AP, Boutouyrie P, Guala A, Jerončić A et al.* 2024 Recommendations for Validation of Noninvasive Arterial Pulse Wave Velocity Measurement Devices. *Hypertension*. 2024; 81 (1): 183–192.
30. *Katsuda SI, Hazama A.* Estimation of Central Systolic Blood Pressure from Peripheral Pressure Waves using a Novel Second Systolic Pressure-Based Method in Normal and Heritable Hypercholesterolemic Rabbits. *J Atheroscler Thromb*. 2023; 30 (9): 1132–1141.
31. *Nichols WW, O'Rourke MF, Hartley C.* McDonald's blood flow in arteries: theoretic, experimental, and clinical principles. 7-th ed. London: Arnold; New York: Oxford University Press, 2022: 320–384.
32. *Ha E, Mun KC.* Effects of cyclosporine on metalloproteinase in endothelial cells. *Transplant Proc*. 2012; 44 (4): 991–992.
33. *Waller JR, Brook NR, Bicknell GR, Nicholson ML.* Differential effects of modern immunosuppressive agents on the development of intimal hyperplasia. *Transpl Int*. 2004; 17 (1): 9–14.
34. *Bianchi R, Rodella L, Rezzani R.* Cyclosporine A upregulates expression of matrix metalloproteinase 2 and vascular endothelial growth factor in rat heart. *Int Immunopharmacol.* 2003; 3 (3): 427–433.
35. *Mitchell IA, McKay H, Van Leuvan C, Berry R, McCutcheon C, Avard B et al.* A prospective controlled trial of the effect of a multi-faceted intervention on early recognition and intervention in deteriorating hospital patients. *Resuscitation*. 2010; 81 (6): 658–666.
36. *Verbeke F, Van Biesen W, Honkanen E, Wikström B, Jensen PB, Krzesinski JM et al.* CORD Study Investigators. Prognostic value of aortic stiffness and calcification for cardiovascular events and mortality in dialysis patients: outcome of the calcification outcome in renal disease (CORD) study. *Clin J Am Soc Nephrol*. 2011; 6 (1): 153–159.
37. *Dahle DO, Eide IA, Åsberg A, Leivestad T, Holdaas H, Jenssen TG et al.* Aortic Stiffness in a Mortality Risk Calculator for Kidney Transplant Recipients. *Transplantation*. 2015; 99 (8): 1730–1737.
38. *Heleniak Z, Illersperger S, Dębska-Ślizień A, Budde K, Halleck F.* Kidney graft function and arterial stiffness in renal transplant recipients. *Acta Biochim Pol*. 2021; 68 (2): 331–339.
39. *Olczyk P, Małyszczak A, Gołębiowski T, Letachowicz K, Szymczak A, Mazanowska O et al.* Arterial Stiffness Assessed by Oscillometric Method in Kidney Transplant, Predialysis, and Dialysis Patients. *Transplant Proc*. 2020; 52 (8): 2337–2340.
40. *Coppola JA, Gupta D, Lopez-Colon D, DeGroff C, Vyas HV.* Elevated Aortic Stiffness after Pediatric Heart Transplantation. *Pediatr Cardiol*. 2023; 10.1007/s00246-023-03245-3.
41. *Zoungas S, Kerr PG, Chadban S, Muske C, Ristevski S, Atkins RC et al.* Arterial function after successful renal transplantation. *Kidney Int*. 2004; 65 (5): 1882–1889.
42. *Covic A, Gusbeth-Tatomir P, Goldsmith DJ.* Arterial stiffness in renal patients: an update. *Am J Kidney Dis*. 2005; 45 (6): 965–977.
43. *Ferro CJ, Savage T, Pinder SJ, Tomson CR.* Central aortic pressure augmentation in stable renal transplant recipients. *Kidney Int*. 2002; 62 (1): 166–171.
44. *Strózecki P, Adamowicz A, Włodarczyk Z, Manitius J.* The influence of calcineurin inhibitors on pulse wave velocity in renal transplant recipients. *Ren Fail*. 2007; 29 (6): 679–684.
45. *Strózecki P, Adamowicz A, Włodarczyk Z, Manitius J.* Factors associated with increased arterial stiffness in renal transplant recipients. *Med Sci Monit*. 2010; 16 (6): CR301-6.
46. *Gelens MA, Christiaans MH, v Hooff JP.* Do blood pressure and arterial wall properties change after conversion from cyclosporine to tacrolimus? *Transplant Proc*. 2005; 37 (4): 1900–1901.
47. *Seckinger J, Sommerer C, Hinkel UP, Hoffmann O, Zeier M, Schwenger V.* Switch of immunosuppression from cyclosporine A to everolimus: impact on pulse wave velocity in stable de-novo renal allograft recipients. *J Hypertens*. 2008; 26 (11): 2213–2219.
48. *Gungor O, Kircelli F, Carrero JJ, Hur E, Demirci MS, Asci G, Toz H.* The effect of immunosuppressive treatment on arterial stiffness and matrix Gla protein levels in renal transplant recipients. *Clin Nephrol.* 2011; 75 (6): 491–496.
49. *Cruzado JM, Pascual J, Sánchez-Fructuoso A, Serón D, Díaz JM, Rengel M et al.* Controlled randomized study comparing the cardiovascular profile of everolimus with tacrolimus in renal transplantation. *Transpl Int*. 2016; 29 (12): 1317–1328.
50. *Holdaas H, de Fijter JW, Cruzado JM, Massari P, Nashan B, Kanellis J et al.* Cardiovascular Parameters to 2 years After Kidney Transplantation Following Early Switch to Everolimus Without Calcineurin Inhibitor Therapy: An Analysis of the Randomized ELEVATE Study. *Transplantation*. 2017; 101 (10): 2612–2620.

51. *McEniery CM, Yasmin, Hall IR, Qasem A, Wilkinson IB, Cockcroft JR; ACCT Investigators.* Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo-Cardiff Collaborative Trial (ACCT). *J Am Coll Cardiol*. 2005; 46 (9): 1753–1760.
52. *AlGhatrif M, Morrell CH, Becker LC, Chantler PD, Najjar SS, Ferrucci L et al.* Longitudinal uncoupling of the heart and arteries with aging in a community-dwelling population. *Geroscience*. 2021; 43 (2): 551–561.
53. *Cohen JB, Mitchell GF, Gill D, Burgess S, Rahman M, Hanff TC et al.* Arterial Stiffness and Diabetes Risk in Framingham Heart Study and UK Biobank. *Circ Res*. 2022; 131 (6): 545–554.
54. *Boutouyrie P, Chowienczyk P, Humphrey JD, Mitchell GF.* Arterial Stiffness and Cardiovascular Risk in Hypertension. *Circ Res*. 2021; 128 (7): 864–886.
55. *Xuereb RA, Magri CJ, Xuereb RG.* Arterial Stiffness and its Impact on Cardiovascular Health. *Curr Cardiol Rep*. 2023; 25 (10): 1337–1349.
56. *Regnault V, Lacolley P, Laurent S.* Arterial Stiffness: From Basic Primers to Integrative Physiology. *Annu Rev Physiol*. 2024; 86: 99–121.
57. *Banegas JR, Townsend RR.* Arterial stiffness and reference values. *Rev Esp Cardiol (Engl Ed)*. 2020; 73 (1): 11–13.
58. *Oliveira AC, Cunha PMGM, Vitorino PVO, Souza ALL, Deus GD, Feitosa A et al.* Vascular Aging and Arterial Stiffness. *Arq Bras Cardiol*. 2022; 119 (4): 604–615.
59. *Alidadi M, Montecucco F, Jamialahmadi T, Al-Rasadi K, Johnston TP, Sahebkar A.* Beneficial Effect of Statin Therapy on Arterial Stiffness. *Biomed Res Int*. 2021; 2021: 5548310.
60. *Maruhashi T, Higashi Y.* Is carotid arterial stiffness a therapeutic target of statin therapy? *Hypertens Res*. 2023; 46 (3): 768–770.
61. *Heleniak Z, Illersperger S, Brakemeier S, Bach P, Dębska-Ślizień A, Budde K, Halleck F.* The renin-angiotensin-aldosterone system blockade and arterial stiffness in renal transplant recipients – a cross-sectional prospective observational clinical study. *Acta Biochim Pol*. 2020; 67 (4): 613–622.
62. *Lees JS, Mangion K, Rutherford E, Witham MD, Woodward R, Roditi G et al.* Vitamin K for kidney transplant organ recipients: investigating vessel stiffness (ViKTORIES): study rationale and protocol of a randomised controlled trial. *Open Heart*. 2020; 7 (2): e001070.

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