DOI: 10.15825/1995-1191-2023-4-17-21

CHANGES IN COMMON CAROTID ARTERY ELASTICITY IN SOLID ORGAN RECIPIENTS

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Background. Cardiovascular diseases are very common among solid organ recipients. They are associated with worsening transplant outcomes. Arterial vascular wall elasticity is an important prognostic indicator and a risk marker for cardiovascular events. Noninvasive measurement of common carotid artery (CCA) elasticity may be useful in assessing cardiovascular risk in solid organ recipients. **Objective:** To conduct a comparative analysis of indicators of CCA elasticity in solid organ recipients and to study their relationship with factors that potentially have a negative impact on the risk of adverse events. **Materials and methods.** The study included 154 patients aged 10 to 75 years, including heart (n = 77), liver (n = 9), and kidney (n = 35) recipients, as well as 33 patients with end-stage heart failure waitlisted for heart transplantation (HT). In all participants, carotid artery ultrasound was performed, pulse wave velocity was measured, and CCA elasticity was calculated. **Results.** CCA elasticity was found to be strongly inversely correlated with age, body mass index, systolic blood pressure, renal tubular filtration rate, CCA intima media thickness, and aortic pulse wave velocity. In heart recipients, CCA elasticity was significantly lower than in liver and kidney recipients (p = 0,002) and it inversely correlated with the length of time elapsed after transplantation, which is probably associated with cardiac denervation. **Conclusion.** CCA elasticity calculated via noninvasive ultrasound reflects the degree of adverse effects of pathological factors on the main arteries in solid organ recipients.

Keywords: vascular wall elasticity, common carotid artery, heart, kidney, and liver recipients.

INTRODUCTION

Cardiovascular diseases are common in solid organ recipients and are associated with worse transplant outcomes [1]. Cardiovascular risk assessment is clinically important because preventive interventions that are initiated early may reduce the incidence of complications in solid organ recipients. At the same time, inappropriate interventions can be a burden on both the health care system and patients. In this regard, various cardiovascular risk assessment scales are actively used in clinical practice, but their limited accuracy constitutes a significant disadvantage [2]. It is necessary to identify new and more effective ways of assessing cardiovascular risk in solid organ recipients. Assessment of the common carotid artery elasticity is promising among them.

Arterial vascular wall elasticity (AVWE) is an important prognostic indicator and a risk marker for cardiovascular events at the preclinical stage and cardiovascular mortality in the population [3]. Noninvasive measurement of this index on carotid arteries may be a useful method in assessing risk in solid organ recipients.

The AVWE in renal recipients is associated with clinical risk factors and independently predicts mortality, cardiovascular events, and graft dysfunction [4–6]. Data on arterial elasticity in recipients of other solid organs are few and mostly obtained in pediatric recipients.

The **objective** of the study was to comparatively analyze the indicators of CCA elasticity in solid organ recipients and to investigate their association with factors that potentially have a negative impact on the risk of adverse events.

MATERIALS AND METHODS

The examination and treatment of heart, liver and kidney recipients, as well as persons included in the HT waitlist, who are under supervision at Shumakov National Medical Research Center of Transplantology and Artificial Organs, from February 2022 to June 2023, were carried out in accordance with the clinical guidelines of the Russian Transplant Society and protocols adopted at Shumakov National Medical Research Center of Transplantology and Artificial Organs.

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The study included 154 patients aged 10 to 75 years, including 113 males and 41 females. Patient mean age was 47.0 ± 2.2 years.

Among the patients examined were:

– Patients with end-stage heart failure (ESHF) listed for HT (n = 33);
– Heart recipients (n = 77);
– Liver recipients (n = 9);
– Kidney recipients (n = 35).

Inclusion criteria were: 10–75 years of age; a history of heart, liver, or kidney transplantation or the presence of ESHF with inclusion on the HT waiting list.

All patients received mono-, bi-, or triple-drug immunosuppressive therapy after transplantation, including tacrolimus, everolimus, mycophenolic acid drugs, methylprednisolone, cyclosporine, and azathioprine.

Exclusion criteria: over 75 years of age or younger than 10 years.

In addition to routine examinations, carotid artery ultrasound and pulse wave velocity measurement were performed in all participants. The CCA elasticity index was calculated as the ratio of the difference in the cross-sectional area of the CCA in systole and diastole to the systole-diastolic BP difference. The study of functional parameters of the CCA wall was performed using the Vivid S70N ultrasound system with a 9 MHz linear multifrequency transducer by ultrasound scanning method with measurement of the vessel lumen diameter and assessment of hemodynamic parameters using spectral Doppler mode (Fig.).

Statistical analysis followed the International Committee of Medical Journal Editors (ICMJE) recommendations and the Statistical analyses and methods in the Published Literature (SAMPL) guidelines. Statistical significance was determined by the value of 95% confidence interval and number of degrees of freedom. In all cases, $p < 0.05$ was considered statistically significant. WizardPro software was used for mathematical processing.

RESULTS AND DISCUSSION

There were no significant differences in age, sex, and body mass index (BMI) in the presented subgroups of recipients and heart failure patients.

In the patients included in the study, CCA elasticity index ranged from 0.0013 to 0.0137 $m^2 \cdot kPa^{-1}$; on average, this index was 0.0040 ± 0.0001 $m^2 \cdot kPa^{-1}$. In all subgroups, CCA elasticity index was independent of tacrolimus trough levels.

In ESHF patients, CCA elasticity index (ss = 0.007 ± 0.001 $m^2 \cdot kPa^{-1}$) was significantly higher ($p = 0.04$ in both cases) than in liver and kidney recipients (0.005 ± 0.003 and 0.005 ± 0.002 $m^2 \cdot kPa^{-1}$, respectively); in the latter it was significantly higher ($p = 0.02$) than in the subgroup of heart recipients (ss = 0.0040 ± 0.0001 $m^2 \cdot kPa^{-1}$). We did not find similar data for comparison in the available scientific literature.

Statistical analysis revealed that CCA elasticity index inversely correlated with age, BMI, systolic BP levels, glomerular filtration rate (GFR), CCA intima-media thickness index and aortic pulse wave velocity.

Similar data can be found in the work of Cheddani et al. [7]. The authors note that high aortic stiffness is associated with lower GFR, older age, diabetic status (and diabetic nephropathy), smoking and hypertension.

It should be noted that in foreign studies, a measure of blood vessel wall elasticity is usually arterial stiffness [8, 9], which is assessed by the carotid-femoral pulse wave velocity (PWV).

Studies assessing the progression of arterial stiffness over time in patients after transplantation are conflicting [5]. According to published studies, arterial stiffness measured by PWV, is markedly reduced after kidney transplantation [4]. Some studies have shown that this improvement applies primarily to recipients of kidneys from young donors (17–41 years) [11], and was also more pronounced in cases of transplantation from living donors [11]. However, in a 5-year follow-up by Alatič J. et al. [13], which included 48 kidney recipients, PWV did not significantly change during the follow-up period ($p = 0.137$) [12]. No differences in the annual evolution of PWV were also found in the work by Bachelet-Rousseau et al. [13].

Previously, we have shown that the CCA stiffness index does not change significantly over time in heart transplant patients. However, the CCA stiffness index increases during rejection and then decreases during therapy [14]. Thus, the assessment of CCA stiffness index

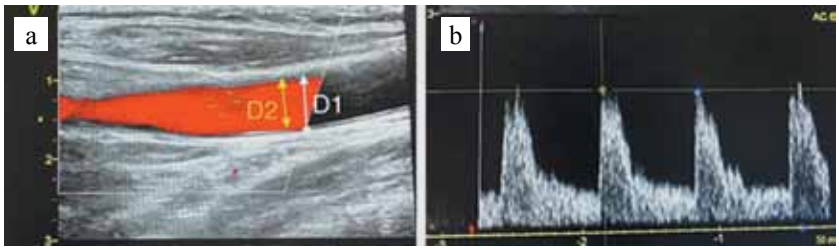

Fig. Technique for investigating CCA conditions. a, measurement of CCA intraluminal diameter; b, measurement of Doppler indicators; Vmax, peak systolic velocity (Vs); D1 and D2, minimum and maximum diameters of the CCA, respectively

can be used to identify heart recipients at high risk of rejection.

In our present study, the CCA elasticity index in cardiac recipients, in contrast to other subgroups, negatively correlated with the length of time elapsed after transplantation. This is probably associated with an additional factor – cardiac denervation. Reduced elasticity of the wall of the main arteries may explain the phenomenon of arterial hypertension that develops in most heart recipients [15] and aggravate injury to target organs (kidneys, brain) against the background of other pathological factors; it suggests the prescription of adjuvant drug therapy for prophylactic purposes.

Arterial stiffness is independently associated with several risk factors (age, blood pressure control, diabetes mellitus, smoking, previous cardiovascular events, total cholesterol, creatinine and triglyceride levels, and GFR) and in liver recipients [16].

In addition, according to Szewc et al. [17], BMI is associated with arterial stiffness in liver recipients. In their study, the PWV level was 7.62 m/s in patients after liver transplantation, whose BMI value was within the normal range, and 8.58 m/s in overweight and obese patients ($p < 0.05$).

Arterial stiffness is also an independent predictor of cardiovascular events and all-cause mortality in cardiac recipients. De Souza-Neto et al. [18] found that arterial hypertension was more than four times more common in patients after heart transplantation with increased arterial stiffness. Major risk factors for arterial stiffness included arterial hypertension, diabetes mellitus, dyslipidemia, and chronic kidney disease.

To date, it is unknown whether therapeutic interventions aimed at increasing arterial wall elasticity will improve outcomes in solid organ recipients.

CONCLUSION

The CCA wall elasticity index, determined by noninvasive ultrasound, reflects the degree of adverse effects of pathological factors on the main arteries; the index is significantly lower in solid organ recipients than in patients on the HT waitlist; it is significantly lower in heart recipients than in liver and kidney recipients and, unlike them, depend on the time elapsed after transplantation.

Studies on the association between CCA elasticity index and other important risk factors for cardiovascular events, as well as assessment of long-term prognostic value allows to answer the question of whether arterial wall elasticity may represent an additional therapeutic target for improving survival among solid organ recipients.

The study had no sponsor support.

The authors declare no conflict of interest.

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The article was submitted to the journal on 10.11.2023