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Features of blood flow and valve function in the veins of the lower extremities according to duplex scanning data and morphofunctional studies

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Abstract

Aim. To study the mechanisms of venous return and the functioning features of lower extremity venous valves in horizontal and vertical positions.

Methods. The study, conducted from April 2019 to December 2020, included 100 people. The study participants were divided into 2 groups. The first group was represented by 44 patients (88 limbs) with varicose veins, whose venous system was examined by duplex ultrasound scanning during inpatient rehabilitation. The second (control) group consisted of 56 healthy individuals (92 limbs) without visible signs of venous pathology who underwent an outpatient examination of the venous system. The average age of the patients in the two groups was 49.2±2.4 and 51.1±1 years, respectively; women predominated in both groups. The qualitative and quantitative parameters of venous blood flow were studied in the study. Venous valvular insufficiency was assessed by using reflux duration and the Psatakis index. A morphometric study was conducted on 140 limbs of 48 human corpses, from which venous fragments were taken for biomechanical studies of the valves. The clinical characteristics of patients are presented by descriptive statistics, quantitative parameters are reported as the mean value (M) and standard deviation (SD). The differences were tested for significance by using the Student's t-test.

Results. In the study, we introduced the concept of the valve index, the aspect ratio of the ellipse, the shape of which has a venous valve in cross-section. Duplex ultrasound scanning, as well as a morphofunctional examination of the valves, made it possible to establish that the valve index is significantly higher in the presence of signs of varicose veins, which indicates dilation and incipient varicose vein, which leads to valvular insufficiency. The elasticity index defined by us, as the indicator of change in the venous lumen size, measured by the ratio of its diameters, also significantly (p=0.034) differed in the studied groups: the elasticity index in the group of healthy people was 1.37±0.11, in the group of patients with varicose veins — 1.56±0.17. The studied factors allowed us to develop a test that has an important prognostic value for the early diagnosis of varicose veins as well as the implementation of preventive health measures.

Conclusion. The features of venous blood circulation and valve function studied in the study not only have prognostic value for the early diagnosis of varicose veins but are also of practical interest for developing methods of surgical correction of venous valvular insufficiency.

Keywords: duplex scanning, mechanisms of venous return, function of venous valves.

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Background. One of the urgent problems of phlebology is the physiology of lower extremity venous circulation. Several fundamental works by Russian and international researchers provide information on the mechanisms of venous return and valvular function of the lower extremities [1–3]. To date, large scope of information has been accumulated that characterizes the state of venous hemodynamics both under normal and pathological conditions, which is obtained using various invasive techniques, such as phlebomanometry, radiopaque and radionuclide phlebography, plethysmography, etc.

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[4–7]. The advent of modern ultrasound technologies (triplex scanning) has significantly expanded the possibilities of studying the venous system.

However, many controversial and unresolved issues remain in the study of regional venous hemodynamics of the lower extremities. Many questions have been resolved in phlebohemodynamics in clinostasis; however, venous return in orthostasis has been insufficiently studied. The subtle mechanisms of venous valve functions and their behavior in various physiological situations are insufficiently understood [8, 9].

The tonic-elastic property assessment of the venous wall is one of the important problems since damage to the venous wall underlies the formation of valvular insufficiency, venous reflux, and varicose vein (VV) transformation. VV is the most common vascular pathology, thus its prediction and detection in the initial stages represent a very urgent problem [10].

This study aimed to analyze the aspects of venous circulation and valve function in the lower extremities in horizontal and vertical positions using duplex scanning and morphophysiological studies.

Materials and methods. A total of 44 patients (88 extremities) with VV and 56 healthy individuals (92 extremities) without visible signs of venous pathology were included in a retrospective analytical case-control study. These groups of patients were comparable by gender and age (the average age in both groups was 51.1 ± 1.7 and 49.2 ± 2.4 years, respectively; $p = 0.08$). Both groups were predominated by females ($n_1 = 28$, $n_2 = 35$). The lower extremity venous system was studied using ultrasound duplex scanning with color Doppler blood flow mapping. Ultrasound angioscanning was performed on an HDI 5000 apparatus (ATL, USA).

Both lower limbs were examined in horizontal and vertical positions at rest and using the standardized Valsalva test and standard compression tests. In addition to the qualitative assessment, the quantitative parameters of venous blood flow were also studied, namely the average linear (cm/s) and volumetric (ml/min) blood flow velocity. Venous valve function was assessed by positioning the probe under ultrasound imaging control distal to their usual locations. The valvular incompetence of the femoral vein was assessed by reflux duration (seconds) and its mean linear velocity during the Valsalva maneuver. The Psatakis reflux index was calculated [11] in compression of the saphenous veins with a soft tourniquet distal to the probe to assess the popliteal vein valve incompetence.

Transverse plane scanning was used for a detailed morphological assessment of the venous valves, with the ultrasound probe positioned as close as possible to the commissure area, which measures the size of the valve in patients in the prone position, upright position, and during dynamic tests.

All quantitative indicators were evaluated as the average of three measurements.

Morphometric studies were performed on 140 extremities (84 upper and 56 lower) from 48 corpses of people without visible signs of venous pathology. The frequency of tributaries that enter the sinuses of the deep main venous valves at different levels of the limb was determined. Fragments of veins that contain full-fledged valves were collected, fixed, and stored in a 0.4% glutaric dialdehyde solution for biomechanical studies. These studies were performed using an original unit that creates a pressure of up to 6 atm. The geometric parameters of the venous valves were recorded at physiological laminar antegrade flow and retrograde flow at various values of the applied pressure.

Statistical data processing was performed using the Statistica 6.0 software package (StatSoft Inc., USA). The clinical characteristics of patients were presented by descriptive statistics, and quantitative parameters were presented in mean (M) and standard deviation (SD). Significant differences were determined using the Student's confidence coefficient (*t*). Differences were considered statistically significant at $p < 0.05$.

The study approval was obtained from the local ethical council of the Interregional Clinical and Diagnostic Center (Kazan, Russia) (protocol No. 26 of August 17, 2018).

Results and discussions. Normally, veins during ultrasound examination in B-mode have thin walls, a hypoechoic lumen characteristic of intact vessels, and are completely compressed when compressed by a probe. The examination in a horizontal position revealed an oval shape in the cross-section of the vein, whereas in a vertical position, the vessel diameter increases (by 38% on average), and its lumen in the cross-section becomes rounded.

The examination in color Doppler mode completely stained the lumen of the vein. In a prone position, a laminar antegrade flow is detected. The Doppler pulse-wave mode recorded the antegrade flow with phases that coincide with respiration (decreases with inspiration and increases with expiration). This illustrates the phenomenon of "vis a fronte" (a set of factors that influence the venous blood "pumping" in the prone position). The wave of the Doppler venous spectrum consists of shorter waves that are synchronized with the heart rate, which reflects one of the elements of venous return, the pumping action of the heart (Fig. 1).

Table 1. Indicators of antegrade blood flow in the great veins of the lower extremities in healthy individuals (n = 92).

Indicators	In a prone position			In an upright position
	CFV	GSV	PV	CFV
V_{mean}, cm/s	10.9 ± 1.8	5.0 ± 1.5	6.7 ± 1.7	2.7 ± 0.5
V_{vol}, ml/min	371.4 ± 71.7	69.0 ± 29.4	146.0 ± 37.9	211.3 ± 39.7

Note: V_{mean}: average linear blood flow velocity; V_{vol}: volumetric blood flow velocity; CFV: common femoral vein; GSV: great saphenous vein; PV: popliteal vein.

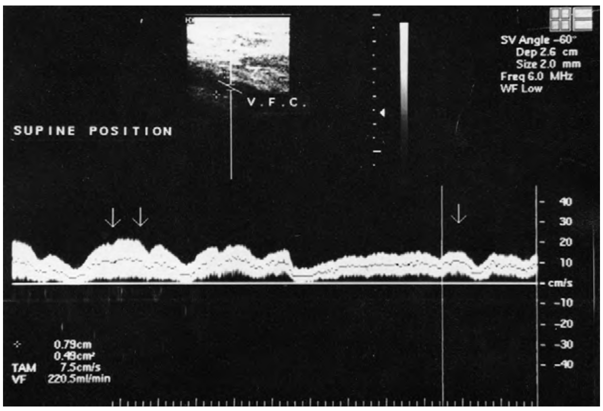

Fig. 1. Blood flow in the femoral vein in spectral Doppler mode in a prone position.

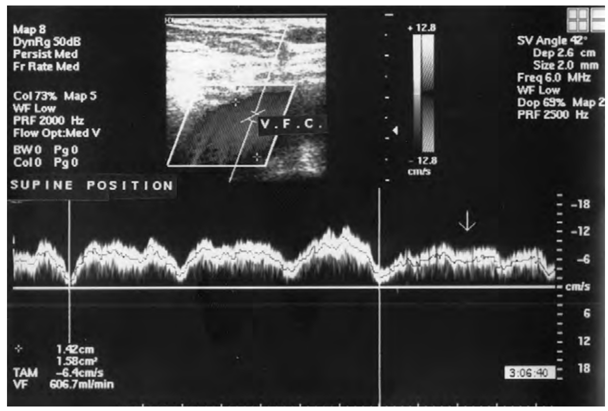

Fig. 2. Blood flow in the femoral vein in spectral Doppler mode during breath-holding on expiration (arrow).

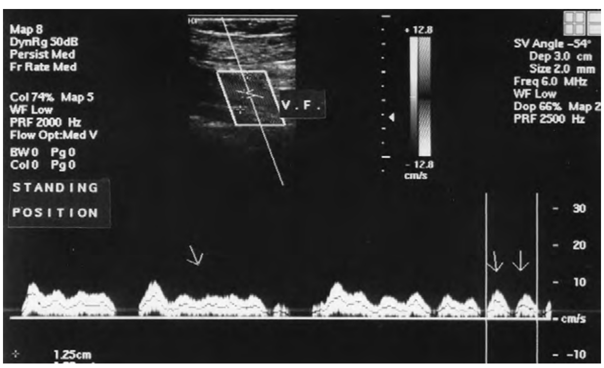

Fig. 3. Blood flow in the femoral vein in spectral Doppler mode in the upright position (two arrows indicate the waves during breath-holding).

Waves that reflect the pumping function of the right atrium and not the transmitting pulsation of the adjacent artery are evidence that this phenomenon is also recorded in patients with adjacent artery occlusion.

The test with a breath-holding on expiration showed the Doppler spectrum of venous blood flow that has less amplitude, without clear waves, and with fluctuations associated with the heart rate. This reflects another component of venous return, namely the “vis a tergo” factor (residual emptying capacity of the heart) (Fig. 2).

Both factors provide a venous return, namely the “pushing” effect is due to the “vis a tergo” factor, whereas the “pumping” effect is due to the “vis a fronte” factor. A sufficient tone of the tissues that surround the vein is naturally important for these factors to completely function [1, 12].

The venous blood flow velocity increases from the peripheral to the central veins. It decreases on average by 75% in a vertical position, whereas the respiratory waves become more pronounced. With a deep breath and breath-holding while inhaling, the venous blood flow rate decreases. Therefore, the patient is asked to hold his breath while exhaling for a correct venous return assessment. In this case, the Doppler spectrum of the venous blood flow becomes a low-amplitude continuous wave with small waves corresponding to the heart rate (Fig. 3).

This type of blood flow indicates that the influence of the “vis a tergo” factor on venous return decreases in an upright position and the “vis a fronte” factor becomes the main factor.

Measurements results of the antegrade venous blood flow of patients in the prone and upright positions are presented in Table 1. The velocity parameters in the ortho-position at the level of the popliteal-tibial segment are low and often cannot be registered; therefore, the parameters obtained in the common femoral vein were used to compare the venous blood flow.

During duplex scanning, the cusps of the venous valve are detected in the venous lumen at different levels of the limb as thin isoechoic linear structures that oscillate during breathing, close when inhaling, and diverge and adjoin the vein walls when exhaling. This helps the blood outflow

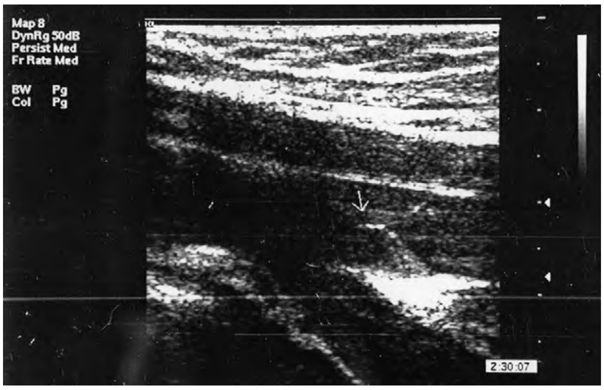

Fig. 4. The competent valve of the femoral vein during the Valsalva maneuver (B-mode, longitudinal projection).

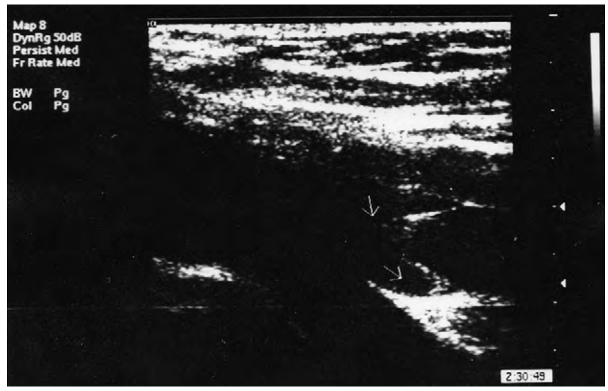

Fig. 5. Echogram (B-mode, longitudinal projection) of the femoral vein valve in an upright position (the arrow below indicates a higher echogenicity of blood in the “niche” of the valvular sinus).

from the valvular sinuses. The valve cusps collapse when performing the functional tests (proximal muscle compression and Valsalva test), which can be seen with ultrasound, both directly and due to the greater echogenicity of the blood above the valves due to its temporary stasis (Fig. 4).

The venous diameter expands in the sinus area of the valves. The venous blood flow velocity that is recorded in the spectral Doppler mode increases with expiration or with the cessation of muscle compression. Normally, during these dynamic tests, hemodynamically insignificant short reflux flow can be recorded, which is due to a small delay in the valve closure time [13]. The time and linear velocity of the reflux flow averaged at 0.34 ± 0.11 s (no more than 0.5 s) and 1.22 ± 0.3 cm/s (no more than 1.5 cm/s), respectively. The reflux index did not normally exceed 0.4.

In the upright position and with quiet breathing examination, the main venous valves are slightly opened and the cusps are at an angle of 30–40° to the venous wall. The valve cusps oscillate in the venous lumen with an amplitude of approximately 5–15°. In the “niches” of the valvular sinuses, the blood looks more echogenic, which is due, in our opinion, to its compaction and the formation of strand coins of erythrocytes, as well as the turbulent blood flow in these areas (Fig. 5).

The same phenomenon can be seen in the sinuses of thickened and pathologically altered valves, not only in the vertical but also in the horizontal position, which indicates that the zone of the valvular sinuses is more thrombogenic.

Venous valve closure in the standing position occurs only with deep breathing or physical exertion associated with the abdominal muscle tensions. With the tension of the muscles of the leg and thigh that imitate walking, the valve cusps are constantly open, whereas the linear and volumetric velocities of the venous blood flow significantly increase.

The morphological study results revealed that one to three small tributaries are often drained into the valvular sinuses area. In the valves of the brachial veins, tributaries were identified in 78.2% of cases. A single valveless tributary with a diameter of 2–3 mm, entering the projection of the valvular sinus at different levels, was more common. In the area of the permanent valve of the femoral vein, which is located under the orifice of the deep vein of the thigh, one or two similar tributaries were detected in 28.3% of the extremities. A high frequency of sinus tributaries was noted in the popliteal vein valves, with two tributaries (which orifice were located in both sinuses) revealed in 56.4% of cases, a single tributary in 47.8% of cases, and three tributaries in 1.8% of cases. They are distinctively characterized by the presence of mono-cusp near-orifice valves (Fig. 6).

The physiological expediency of equipping the venous valves with tributaries based on the following considerations was explained. Studies have shown convincingly that the area of the valvular sinuses is the most thrombogenic. The blood flow from the tributaries to the valvular sinuses, along with retrograde blood flow, which causes the closure of the valve cusps, prevents thrombogenesis due to the washing out of the blood corpuscles from the sinuses. The location of the orifices of the tributaries in the projection of the valvular sinus and the direction of the stream of the incoming blood (especially if the tributary is muscular) can change the position of the valve cusps, which is rational for their closure. Leading phlebologists provide similar data on the functional significance of the tributaries of the valvular sinuses [5, 14, 15]. The possible role of valveless tributaries in damping of supravalvular hypertension when exposed to retrograde blood flow is not excluded.

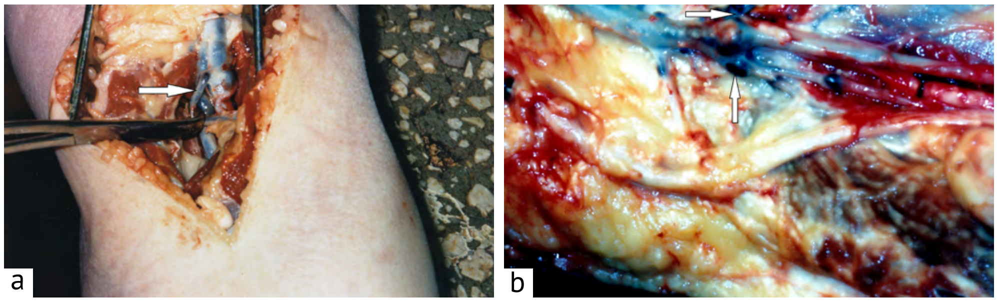

Fig. 6. Sinus branches (indicated by arrows) of the popliteal venous valves: a — single branch; b — two branches located in the valvular sinuses.

In our opinion, these mechanisms contribute to a certain extent to the normal venous valve function. The constant location of the tributaries in the popliteal venous valves, which carry a high hemodynamic load, also indicates their functional significance. The obtained information served as an idea for the development of a new method for restoring the valvular function of deep veins by free transplantation of a venous valve with the formation of a microanastomosis of its sinus tributary with a comitant vein of the recipient area [16].

The valvular geometric parameter determination established an elliptical shape both in a horizontal and vertical position in cross-section. The diameters of the ellipse corresponding to its major and minor axes are defined by us as D_{max} and D_{min} (Fig. 7). The D_{max}/D_{min} ratio is called the valve index.

With physiological antegrade and retrograde blood flow at pressures from 0 to 40 mm Hg, the cross-section of the bicuspid valve has an elliptical shape, which is characterized by the valve index. It is constant for all competent valves and amounts to 1.21 ± 0.12. With increased retrograde pressure, the valve stretching along D_{min} is almost absent, but its diameter along the long axis D_{max} increases, which can lead to commissure divergence and valve insufficiency. This testifies the importance of the cushioning function of the venous wall in the valvular sinus areas as one of the mechanisms that level the intensity of the retrograde flow and thereby prevent damage to the valve cusps.

The extensibility of the venous valve walls is within 0–120 mm Hg, that is, within the limits of possible physiological pressures. The valves are practically inextensible at high pressures.

The study of competent valves that are intraoperatively collected from patients with VV revealed a significantly higher valve index, which indicates dilatation, and the onset of varicose transformation, which results in valvular insufficiency. With the development of incompetent valves under study, their extravasal correction was performed with A.N. Vedensky frame spirals and spiral cone-shaped correctors Gran made by MIT (Russia), and valve correction was simulated along the major and minor axes. The valve narrowing, according to D_{min}, led to a valve insufficiency aggravation, whereas the correction according to D_{max} eliminated it.

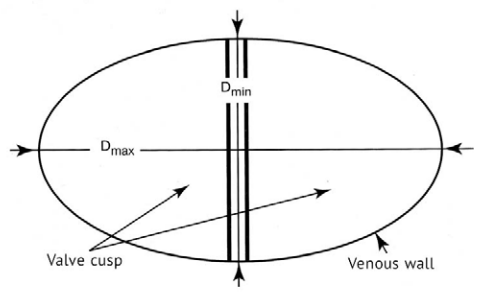

Fig. 7. Diagram of the cross-section of the vein in the valvular area.

Taking into account the results obtained in morphofunctional studies of the valves, the shape of the valvular sinuses was studied using duplex scanning. In transverse scanning in the orthostatic position, the great venous valves have an elliptical shape. Valve index of competent valves varied within 1.11 and 1.14. During the Valsalva test, the large diameter of the ellipse mainly increases with an increase in the valve index to 1.19–1.23. The obtained data indicate the prognostic significance of this index for diagnostics of the development of venous valve insufficiency.

This information has a certain value in the development of an extravasal corrector to eliminate venous valve incompetence. In our opinion, it should have an elliptical section with the ratio of the major and minor axes within 1.2. To a certain extent, these requirements are met by the cone-shaped correctors "Gran" (MIT, Moscow).

The role of venous tone in the venous return implementation and postural reaction prevention during the transition to the orthostatic state is well known [1, 4]. Within the generally accepted theory of VV, one of the main trigger factors for valve incompetence development and venous reflux formation is a decreased venous wall elasticity. Therefore, the importance of assessing the venous tone

Table 2. Indicators of the elasticity index in healthy individuals and patients with varicose veins.

Examined groups	Elasticity index	p
1. Healthy individuals (n = 36)	1.37 ± 0.11	—
2. Patients with varicose veins with competent deep vein valves (n = 42)	1.56 ± 0.17	$p_{2–1}$ = 0.034
3. Patients with varicose veins with valve incompetence of the femoral vein (n = 32)	1.74 ± 0.15	$p_{3–1}$ = 0.027 $p_{3–2}$ = 0.150

state, which has a certain prognostic value with the risk of developing VV, is beyond doubt.

A test has been developed based on the idea of assessing the tone of the common femoral vein, in which a decrease becomes a “trigger” factor in the development of descending VV, to assess the tonic-elastic properties of the lower extremities deep veins [17–19]. Thus, the common femoral venous diameter under the inguinal fold was determined in the prone position of the subject and free orthostatic state. The change in the venous diameter when these two positions are changed reflects the state of the venous wall more clearly than the change in diameters during the Valsalva maneuver. First, it is a relatively standardized study that is independent of the patient; secondly, when changing to an upright position under the influence of hydrostatic pressure and baroreceptor irritation to a greater extent than when performing the Valsalva maneuver, the sympathetic nerve plexus of the venous wall is activated, which is responsible for the regulation of the venous tone, that is, this test is more correct for assessing the true state of the venous tone than the Valsalva maneuver.

The degree of change in the venous lumen that is measured by the ratio of its diameters in the listed positions was defined as the elasticity index. Table 2 presents its indicators in healthy individuals and patients with VV.

Table 2 indicates that the elasticity index in patients with VV significantly differs (p = 0.034) from that in healthy individuals. Its value increases in patients with ectasia and femoral vein valve incompetence. In 3 (12.5%) patients in the control group and 4 (9%) patients with VV, the contralateral limb study without visible superficial VV manifestations revealed a significantly increased elasticity index (up to 1.8–2), which was regarded as a prognostically unfavorable sign with VV development and progression.

The proposed test is technically simple, standardized, and can be recommended for the early diagnostics and prognosis of VV. It can be recommended for screening in the population (especially in risk groups), which is of certain importance for therapeutic and prophylactic measures (prescription of venotonics and preventive medical garments) implementation.

Thus, the information obtained from the studies on venous circulation characteristics and valvular function has a certain informative value and is also of practical interest from the standpoint of expanding the possibilities of diagnosing the pathology of the venous system and developing methods for surgical correction for venous valve insufficiency. Additionally, the authors, for the first time, determined the factors of venous return, as well as the processes of valvular function in the orthostatic position for non-invasive technologies of ultrasound duplex scanning.

The studied factors enabled the authors to develop a test that has an important prognostic value for the early diagnostics of VV and the implementation of preventive treatment and prophylactic measures. Practical application of the obtained data includes the ability to design a mathematical model of the valve, which will develop optimal correctors of venous valves to eliminate their incompetence.

CONCLUSIONS

The aspects of venous circulation and valvular function studied in the course of the study, not only have prognostic value for early diagnostics of VV but are also of practical interest from the standpoint of developing methods for surgical correction of venous valve insufficiency.

Author contributions. I.M.I. was the work supervisor, collected the material, and analyzed the data; V.V.E. and S.Yu.A. collected the material and conducted the research; E.G.G. collected and analyzed the results.

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