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LONG-TERM OUTCOMES AFTER FORMATION OF A LOW-FLOW STA-MCA BYPASS FOR TREATMENT OF SYMPTOMATIC OCCLUSION OF THE INTERNAL CAROTID ARTERY

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Aim. To evaluate short- and long-term effectiveness of low-flow bypass between superficial temporal artery and M4 segment of middle cerebral artery (low-flow STA-MCA bypass) in patients with symptomatic occlusion of the internal carotid artery (ICA).

Materials and methods. Between 2016 and 2019 at the Department of Neurosurgery of the N.V. Sklifosovsky Research Institute of Emergency Medicine, 54 patients who underwent low-flow STA-MCA bypass formation at the side of symptomatic ICA occlusion between 2013 and 2015 were examined. Symptomatic ICA occlusion was more common in men than in women (7:1 ratio). Patient age varied between 48 and 73 years (mean age was 62 years).

During low-flow STA-MCA bypass formation surgery for symptomatic ICA occlusion, intraoperative flowmetry was used in 52 (96 %) patients, in 2 (4 %) patients this diagnostic method was impossible to perform due to technical difficulties. The main examination methods in the long term after cerebral revascularization were evaluation of neurological status dynamics per the National Institute of Health Stroke Scale (NIHSS); modified Rankin scale; Rivermead mobility index; computed tomography angiography of the extra-intracranial arteries; ultrasound (US) examination of the STA-MCA bypass for evaluation of linear and volumetric blood flow velocities; single-photon emission computed tomography. The type and size of trephination were evaluated, and operative time was taken into account.

The patients were divided into 3 groups: group 1 included patients with follow-up period of 1–2 years after cerebral revascularization, group 2–3–4 years, group 3–5–6 years. All results were compared to preoperative, early, and long-term measurements.

Results. In the long-term postoperative period between 1 and 6 years after cerebral revascularization, 54 patients were examined. Computed tomography angiography and US showed functioning STA-MCA bypass in 53 (98 %) patients. According to single-photon emission computed tomography of the brain, regional cerebral blood flow in the long-term postoperative period varied between 28 and 40 mL/100 g/min, median regional cerebral blood flow in the long-term postoperative period was 38 mL/100 g/min. Intraoperative flowmetry was performed in 52 (96 %) patients, median was 15.5 mL/min. US showed that linear blood flow velocity in the STA-MCA bypass varied between 20 and 95 cm/s, median was 49 cm/s. Volumetric blood flow varied between 30 and 85 mL/min with median of 75 mL/min. Resection trephination was performed in 36 (67 %) patients, mean size of trephination hole was 3 cm^3. In the study, operative time was measured: mean value was 212 min; no significant correlation between operative time and trephination size was observed.

Improved neurological status was observed in all study groups. Per the NIHSS, in group 1 (1–2 years) improvement was observed in 59 % of patients, in group 2 (3–4 years) in 48 %, in group 3 (5–6 years) in 47 %. Per the modified Rankin scale, in group 1 improvement was observed in 36.4 % of patients, in group 2 – in 48 %, in group 3 – in 42.9 %. Per the Rivermead mobility index, in group 1 improvement was observed in 63.3 % patients, in group 2 – in 56 %; in group 3 – in 57.1 %. The best outcomes were observed in group 1 (63.3 %).

Conclusion. Instrumental diagnostic methods and evaluation of neurological status showed positive dynamics both in the postoperative period and in long-term period between 1 and 6 years after low-flow STA-MCA bypass formation.

In the long term, repeat abnormalities of cerebral blood flow of ischemic type and repeat transient ischemic attacks were not observed. Correct selection of patients in the preoperative period and comprehensive treatment including drug therapy in the postoperative and long-term periods allow to prevent repeat ischemic cerebrovascular disease and therefore improve patients' quality of life.

Keywords: occlusion of the internal carotid artery, cerebral revascularization, extra-intracranial bypass, low-flow STA-MCA bypass, long-term postoperative period

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BACKGROUND

According to the World Health Organization data, acute ischemic cerebrovascular disease (AICD) is the 2nd leading cause of death. Per 2017 data, incidence of ischemic stroke is approximately 300 cases per 100,000 people per year [1, 2].

Currently, AICD is one of the most severe diseases and is the leading cause of disability not only in elderly people but in people of working age [1, 3]. In many countries, morbidity and mortality due to ischemic stroke have been rising [3]. AICD comprises 70–85 % of all strokes (ratio between ischemic and hemorrhagic strokes is 5:1) [1, 2]. The main risk factors of ischemic cerebrovascular events are elderly age, arterial hypertension, hypercholesterolemia, atherosclerosis of the cerebral and brachiocephalic arteries, heart disease, diabetes mellitus, obesity, and smoking. Currently, treatment of patients with AICD involves conservative and surgical approaches [4, 5].

The most significant causes of AICD are stenosis and occlusion of the brachiocephalic arteries, and occlusion of the internal carotid artery (ICA) is seen in 5–10 % of all abnormalities of the brachiocephalic arteries [6, 7]. Currently, one of surgical methods of prevention of repeat cerebrovascular events in patients with symptomatic ICA occlusion is formation of microsurgical extra-intracranial bypass [3, 5, 6].

During extra-intracranial bypass formation surgery, a low low-flow bypass is usually created between the superficial temporal artery (STA) and the cortical branch of the middle cerebral artery (MCA) (low-flow STA-MCA bypass). This surgery is performed in many neurosurgical centers across the world, but its effectiveness is still under debate, especially in the long-term. Thus, in some studies, the largest of which were EC–IC Bypass Trial (1985) and Carotid Occlusion Surgery Study (2010), effectiveness of surgical treatment for ischemic stroke prevention was not confirmed [7–9]. Regardless of contradictory study results, this surgery is performed all over the world in the absence of another more effective alternative.

Aim. to evaluate short- and long-term effectiveness of low-flow STA-MCA bypass in patients with symptomatic ICA occlusion.

MATERIALS AND METHODS

Between 2016 and 2019, at the Department of Neurosurgery of the N.V. Sklifosovsky Research Institute of Emergency Medicine, 54 (100 %) patients who underwent low-flow STA-MCA bypass formation at the side of symptomatic ICA occlusion between 2013 and 2015 were hospitalized and examined (Fig. 1). Symptomatic ICA occlusion was more common in men than in women (ratio 7:1). Patient age varied between 48 and 73 years, mean age was 62 years.

During statistical analysis, the patients were divided into 3 groups depending on follow-up period: 1st group included patients with follow-up of 1–2 years, 2nd group – 3–4 years, 3rd group – 5–6 years (see Table).

Distribution of the patients included in the study depending on the follow-up duration in the long-term postoperative period

Duration of follow-up after surgery, years	*n*	%
1	14	26
2	8	15
3	11	20
4	14	26
5	2	4
6	5	9
Total	*54*	*100*

Instrumental examination methods in the long-term postoperative period included computed tomography (CT) angiography of the extra-intracranial arteries; single-photon emission computed tomography (SPECT) of the brain; ultrasound (US) examination of the low-flow STA-MCA bypass evaluating linear and volumetric blood flow; intraoperative flowmetry; the type and size of trephination, as well as operative time, were also taken into account. All results of examinations were compared to earlier data.

In the long-term postoperative period, neurological status of the patients was evaluated using the modified Rankin scale, National Institutes of Health Stroke Scale (NIHSS), Rivermead mobility index. The results were compared to preoperative, early, and long-term measurements.

RESULTS

After formation of low-flow STA-MCA bypass, in 52 (96 %)patients intraoperative flowmetry was performed. According to our data, intraoperative flowmetry allows

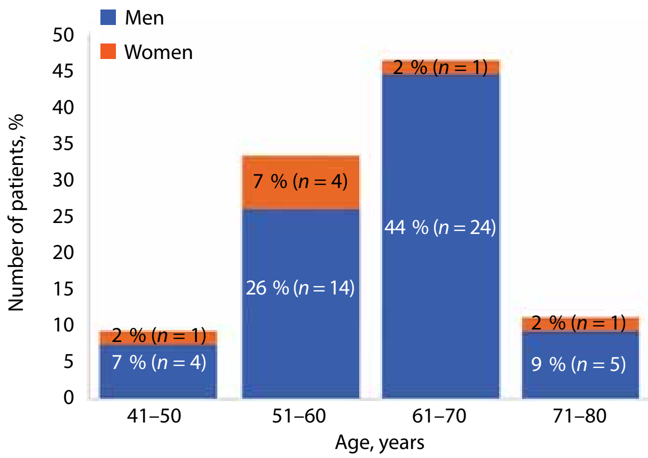

Fig. 1. *Distribution of the patients hospitalized in the long-term postoperative period per sex and age (n = 54)*

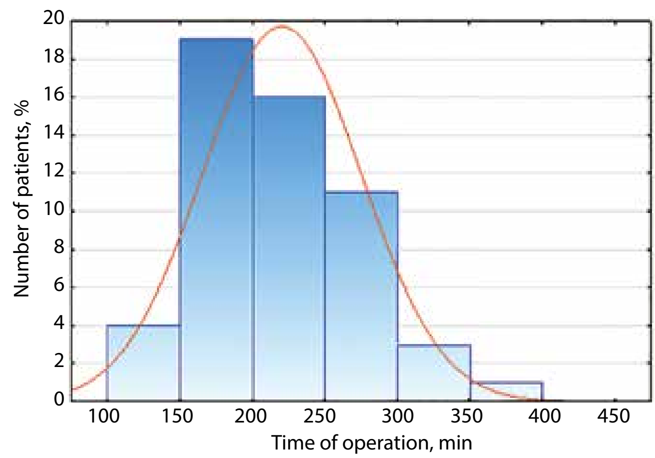

Fig. 3. *Distribution of the patients depending on operative time of low-flow STA-MCA bypass formation*

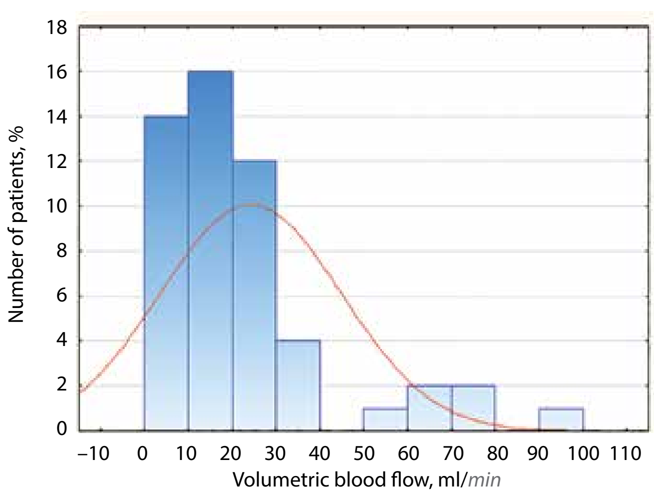

Fig. 2. *Distribution of the patients depending on the characteristics of intraoperative flowmetry (volumetric blood flow) during low-flow STA-MCA bypass formation. Here and on Fig. 3–5, 8–10: low-flow STA-MCA bypass – low-flow bypass between superficial temporal artery and M4 segment of middle cerebral artery*

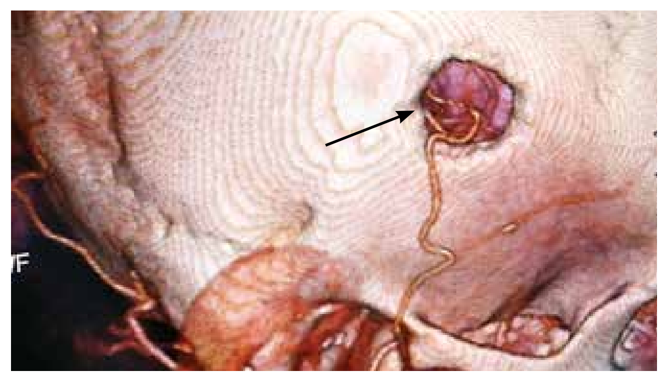

Fig. 4. *Resection trephination of the skull. 3D spiral computed tomography angiography of low-flow STA-MCA bypass on the right: a functioning bypass between the right superficial temporal artery and M4 segment of the middle cerebral artery is visualized (arrow)*

Fig. 5. *Osteoplastic trephination of the skull. 3D spiral computed tomography angiography of low-flow STA-MCA bypass on the left: a functioning bypass between the left superficial temporal artery and M4 segment of the middle cerebral artery is visualized (arrow)*

to predict the thrombosis at the stage of bypass formation and to measure blood flow through the bypass . Volumetric blood flow (VBF) through the bypass varied between 3 and 95 mL/min (Fig. 2). Median flowmetry value was 15.5 mL/min [3, 9].

In the long-term postoperative period, in 1 (2 %) patient thrombosis of the low-flow STA-MCA bypass was diagnosed; intraoperative flowmetry measurement in this patient was 3 mL/min. Based on this, we propose that low intraoperative flowmetry values (<5 mL/min) can indicate high probability of thrombosis of the low-flow STA-MCA bypass in the future.

Operative time was analyzed: minimal operative time was 135 min, maximal was 390 min, median was 212 min (Fig. 3). It should be noted that the longest surgeries were performed in 2013. In time, mastering of the equipment and improvement of the surgeons' manual skills allowed to significantly decrease operative time.

During low-flow STA-MCA bypass formation, resection and osteoplastic trephination of the skull were performed (Fig. 4, 5). In 36 (67 %) patients, trephination size was <3 cm in diameter. Minimal trephination size was 1.5 cm, maximal was 5 cm, median was 3 cm.

During the study, no significant correlation between operative time and trephination size was found.

The patients' clinical picture was compared to the relevant measurements in the preoperative, early postoperative, and long-term periods. Notably, none of the operated patients with functioning low-flow STA-MCA bypass (in any of the observation groups) had repeat ischemic events.

Statistically significant dynamics per the NIHSS compared to the early postoperative period were observed in all observation groups (p <0.001). The best neurological status outcomes were observed in the 1st observation group: in 59 % of patients (Fig. 6, *a*). Statistically significant dynamics compared to the preoperative and early postoperative period per the modified Rankin scale were observed in all groups. The best outcomes were found in the 2nd group: in 48 % of patients (p <0.002) (Fig. 6, *b*). Additionally, statistically significant dynamics in the Rivermead mobility index compared to the perioperative, early postoperative period, and long-term periods were

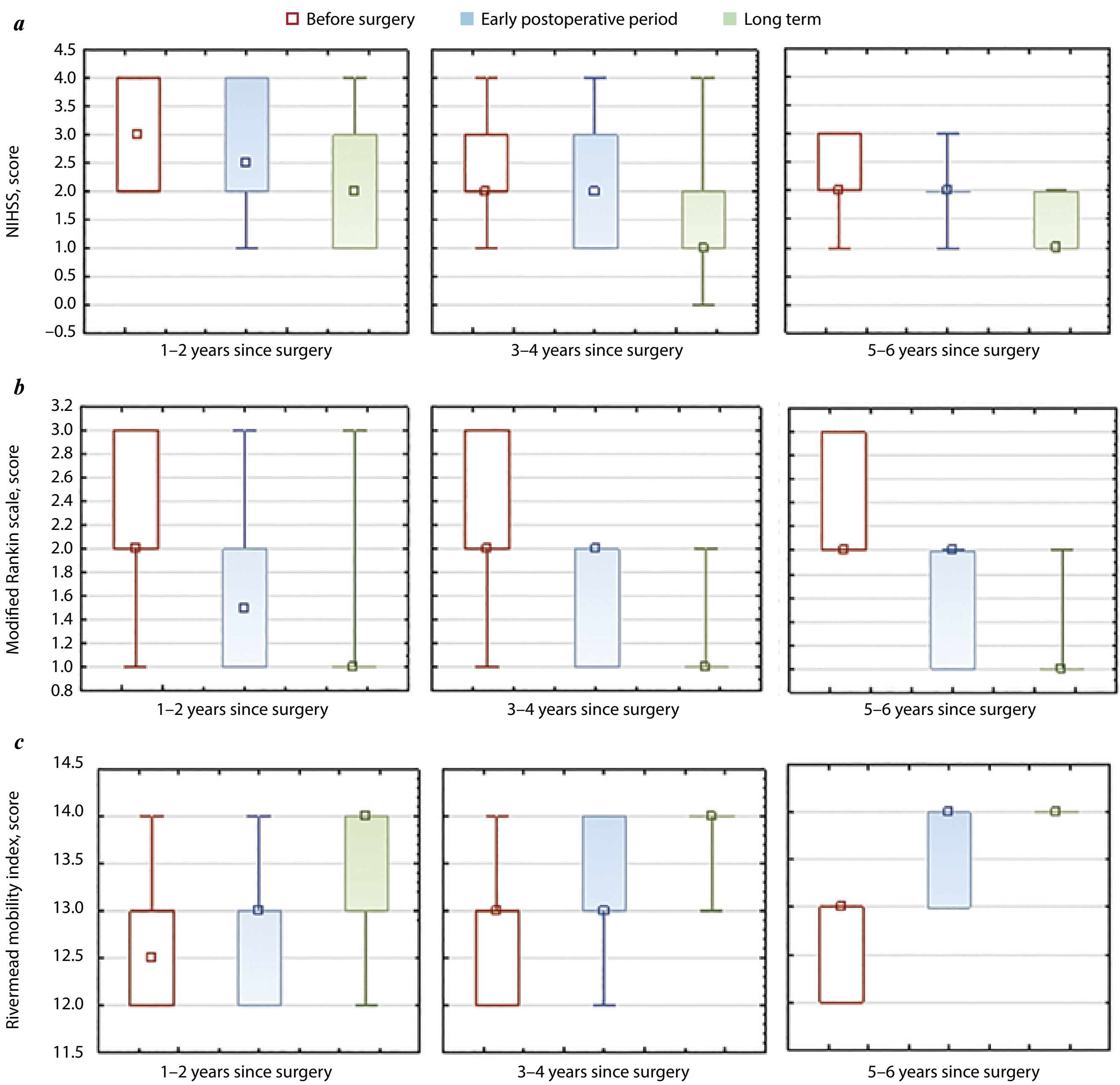

Fig. 6. *Dynamics of the patients' neurological status in different observation groups (1–2 years, 3–4 tears, 5–6 years since surgery): a – National Institute of Health Stroke Scale (NIHSS); b – modified Rankin scale; c – Rivermead mobility index*

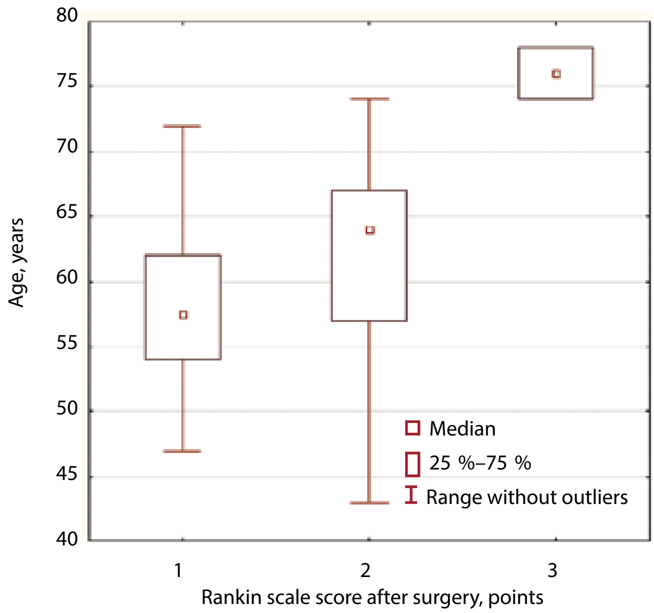

Fig. 7. *Correlation between patient's age and dynamics of neurological status per the modified Rankin scale in the early postoperative period*

observed in all groups (*p* <0.001). The best scores were found in the 1st observation group: in 63.3 % of patients (Fig. 6, *c*).

The study showed statistically significant correlation between patient age and neurological status dynamics per the modified Rankin scale in the early postoperative period ($p = 0.003$, R = 0.4) (Fig. 7): the younger the patient, the more favorable clinical effect was achieved.

Therefore, according to the obtained data, it is appropriate to observe patients for 2 years after cerebral revascularization because in cases of functioning anastomosis we did not observe negative neurological dynamics, repeat ischemic events, and ischemic strokes in the long-term.

In the early postoperative period (on day 3–4 after cerebral revascularization), CT angiography was performed in 54 (100 %) patients: anastomosis was functioning in all patients (100 %). In the long-term postoperative period between 1 and 6 years post-surgery, CT angiography showed functioning bypass in 53 (98 %) patients (Fig. 8), in 1 (2 %) patient the thrombosis of low-flow STA-MCA bypass was diagnosed (Fig. 9).

Ultrasound was performed in 54 (100 %) patients in the early postoperative period: bypass was functioning in all

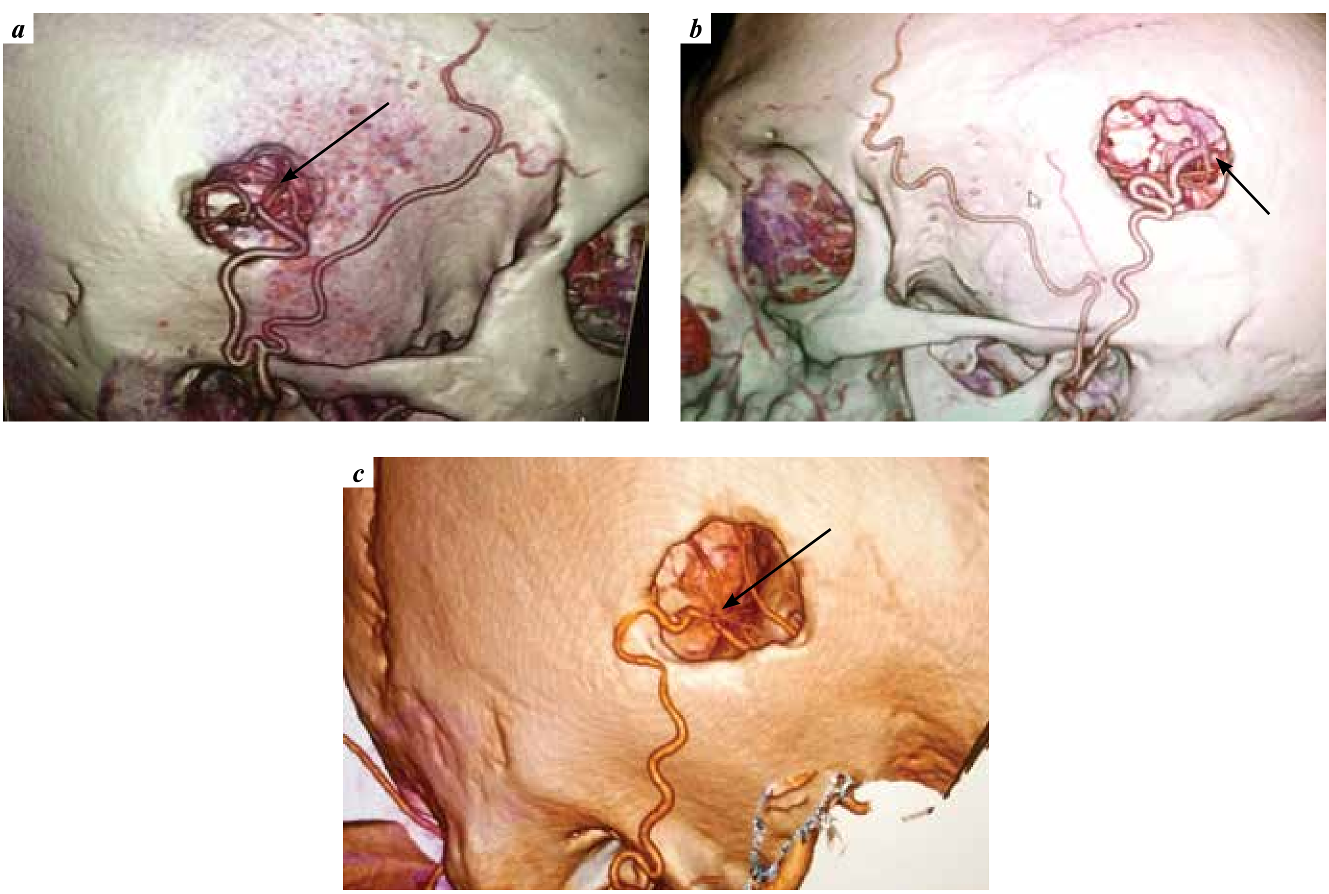

Fig. 8. *3D spiral computed tomography angiography: a – low-flow STA-MCA bypass on the right in patient S. 2 years after surgery: a functioning bypass between the right superficial temporal artery and M4 segment of the middle cerebral artery is visualized (arrow); b – low-flow STA-MCA bypass on the left in patient B. 4 years after surgery: a functioning bypass between the left superficial temporal artery and M4 segment of the middle cerebral artery is visualized (arrow); c – low-flow STA-MCA bypass on the right in patient N. 6 years after surgery: a functioning bypass between the right superficial temporal artery and M4 segment of the middle cerebral artery is visualized (arrow)*

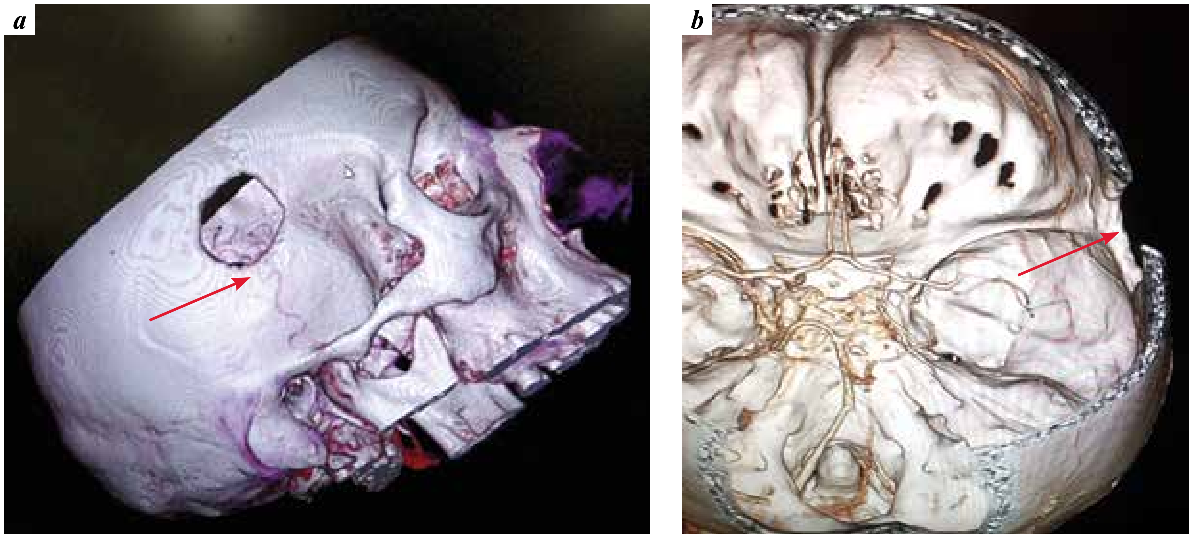

Рис. 9. *3D spiral computed tomography angiography of patient T.: a – functioning low-flow STA-MCA bypass in the early postoperative period; b – nonfunctioning low-flow STA-MCA bypass on the right 4 years after surgery: thrombosis of the left superficial temporal artery is visualized (arrow)*

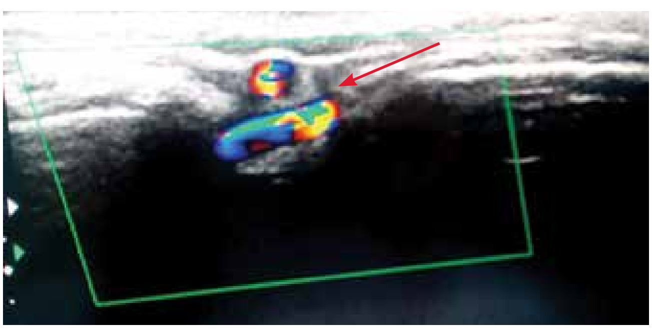

Fig. 10. *Ultrasound in the long-term postoperative period: functioning low-flow STA-MCA bypass (arrow)*

patients. In the long-term, microsurgical bypass was functioning in 53 (98 %) patients (Fig. 10).

In the early postoperative period (on day 3–4 after low-flow STA-MCA bypass formation), linear blood flow varied between 25 and 96 cm/s (median 59 cm/s), in the long-term postoperative period it varied between 20 and 95 cm/s (median 49 cm/s) (Fig. 11, *a*).

VBF in the early postoperative period (on day 3–4) per US of the bypass varied between 25 and 75 mL/min (median 60 mL/min), in the long-term postoperative period it varied between 30 and 85 mL/min (median 75 mL/min) (Fig. 11, *b*).

Therefore, according to the obtained data, in the long-term postoperative period linear blood flow through the bypass decreases while VBF increases. From our point of view, when the bypass works properly it develops with time and increases in diameter.

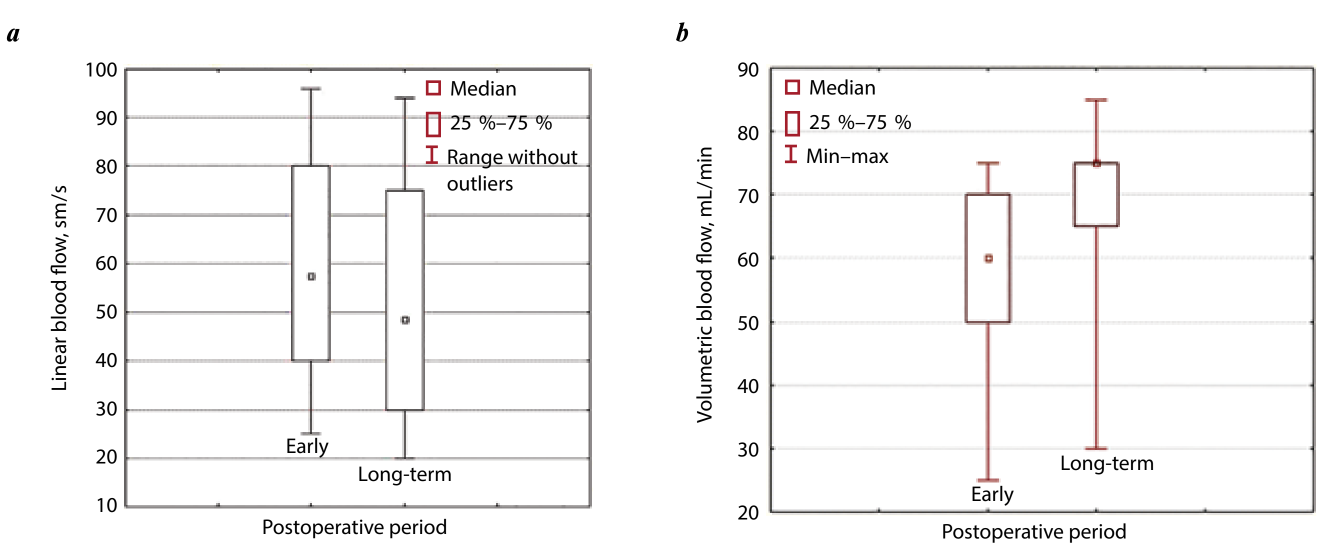

Fig. 11. *Linear blood flow (a) and volumetric blood flow (b) per ultrasound measurement after low-flow STA-MCA bypass formation in the early and long-term postoperative periods*

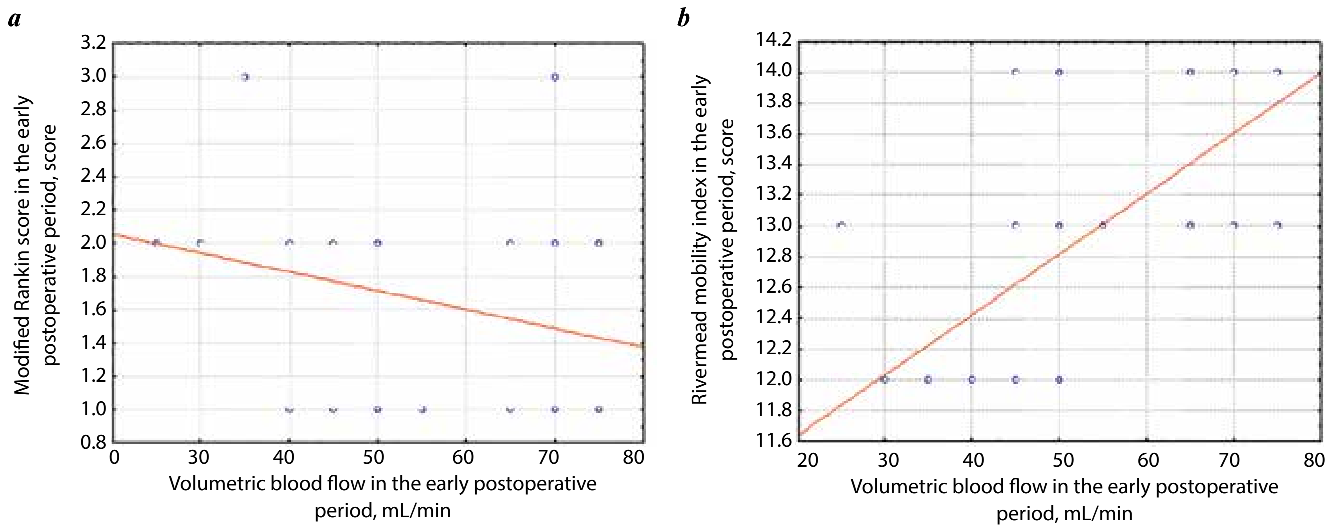

Fig. 12. *Detected correlations between neurological status evaluation and volumetric blood flow per ultrasound measurement in the early postoperative period: a – between the modified Rankin scale score and volumetric blood flow (Rs = 0.27; p <0.04); b – between Rivermead mobility index and volumetric blood flow (Rs = 0.66; p <0.001)*

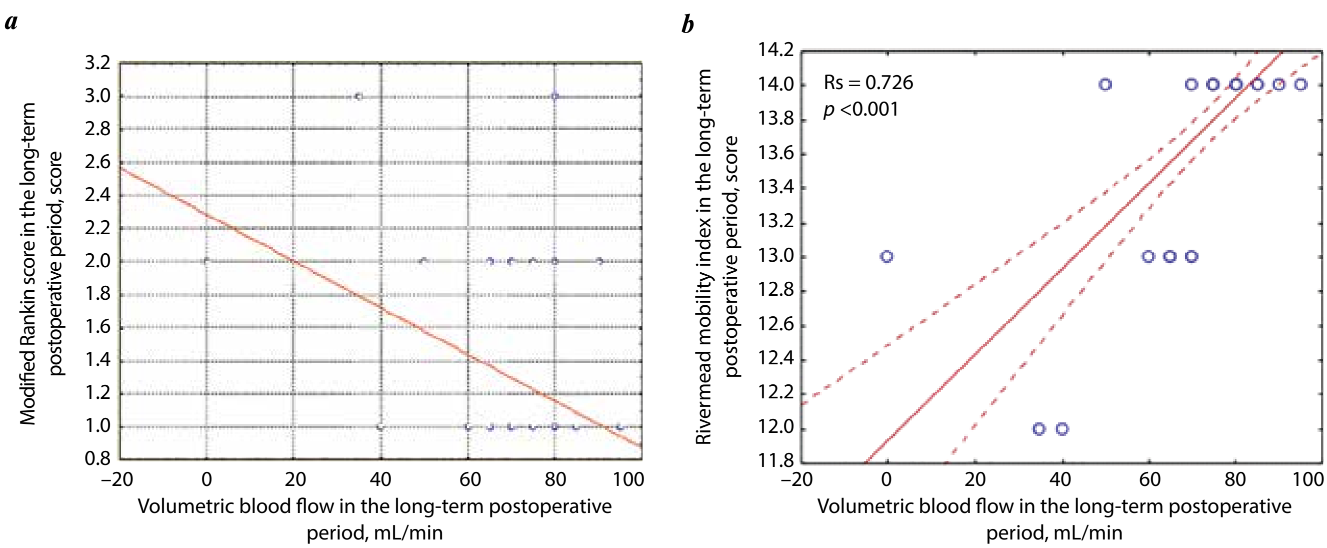

Fig. 13. *Detected correlations between neurological status evaluation and volumetric blood flow per ultrasound measurement in the long-term postoperative period: a – between the modified Rankin scale score and volumetric blood flow (Rs =0.59, p <0.003); b – between Rivermead mobility index and volumetric blood flow (Rs = 0.726; p <0.001)*

Additionally, we found statistically significant positive correlations between the modified Rankin scale score, Rivermead mobility index and VBF per US in the early postoperative period (Fig. 12). Notably, higher VBF in the early postoperative period correlated with better neurological outcome. Statistically significant correlations between the Rivermead mobility index, modified Rankin scale score and VBF in the long-term postoperative period were also observed (Fig. 13).

Higher volumetric blood flow velocity through the bypass was accompanied by better clinical picture in the operated patients.

All patients ($n = 54$, 100 %) at first hospitalization underwent SPECT of the brain with acetazolamide challenge to evaluate cerebrovascular reserve in the postoperative period. In all patients, insufficiency of cerebrovascular reserve (perfusion increase <10 %) was observed. Statistically significant decrease in regional cerebral blood flow (rCBF) per SPECT in the long-term compared to the postoperative values was found in all observation groups ($p < 0.001$) (Fig. 14).

The lowest rCBF values were observed in the 2nd group (3–4 years). We propose that rCBF decrease per SPECT in the long-term postoperative period is caused by development of collateral circulation and uniform blood flow distribution in the brain after low-flow STA-MCA bypass formation. Although we observed decreased rCBF (to 35 mL/100 g/min) compared to the early postoperative period (to 38 mL/100 g/min), it still was higher than preoperative blood flow (to 23 mL/100 g/min) (Fig. 15).

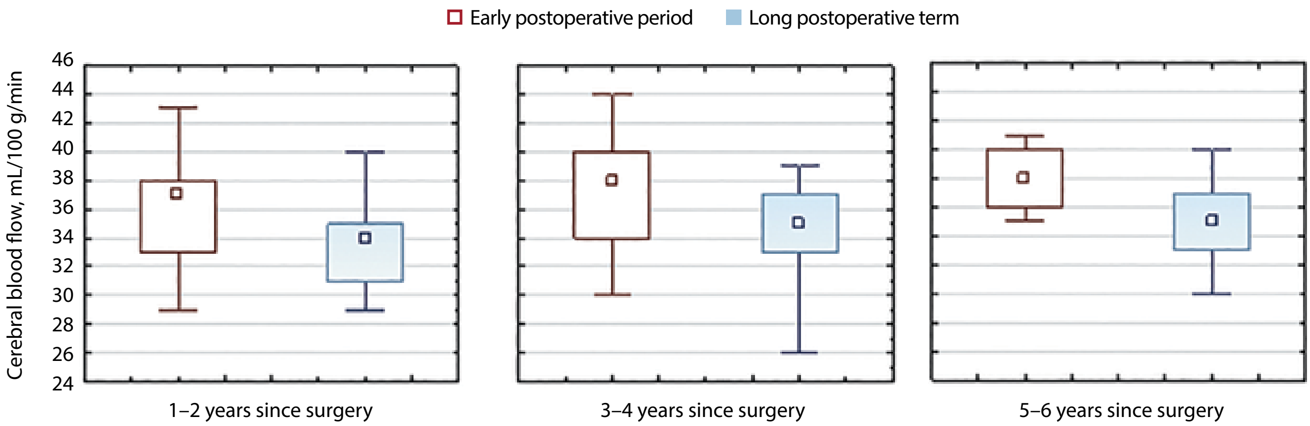

Fig. 14. *Distribution of regional cerebral blood flow per SPECT in the early and long-term postoperative period in different observation groups. Here and in Fig. 15–17: SPECT – single-photon emission computed tomography*

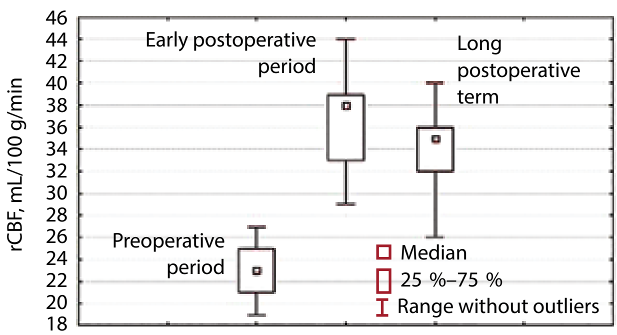

Fig. 15. *Dynamics of regional cerebral blood flow (rCBF) per SPECT of the brain in the preoperative, early postoperative, and long-term periods*

Absence of repeat cerebrovascular events in all observation groups indicates sufficient rCBF.

The study showed statistically significant correlations between rCBF per SPECT, VBF per US, and Rivermead mobility index in the early postoperative period (Fig. 16). Therefore, we propose that higher VBF in the early postoperative period is accompanied by higher rCBF and better clinical outcomes.

In the long-term postoperative period, we also observed significant statistical correlations between rCBF, VBF per US, modified Rankin scale score, and Rivermead mobility index (Fig. 17).

Analysis of the obtained results showed direct link between VBF, rCBF and clinical outcomes in the operated patients in the long-term postoperative period.

DISCUSSION

We have analyzed the results of low-flow STA-MCA bypass formation in 54 patients with symptomatic ICA occlusion within 6 years after surgery. Earlier international studies including studies on cerebral revascularization (including the first randomized EC-IC Bypass Trial performed by Dr. Henry Barnett [3, 5, 10–13]) did not show positive results of ischemic stroke treatment using cerebral revascularization. The aim of the above-mentioned trial was determination of the effectiveness of low-flow STA-MCA bypass formation as a method for decreasing the risk of AICD and post-stroke mortality. In the operated patient group,

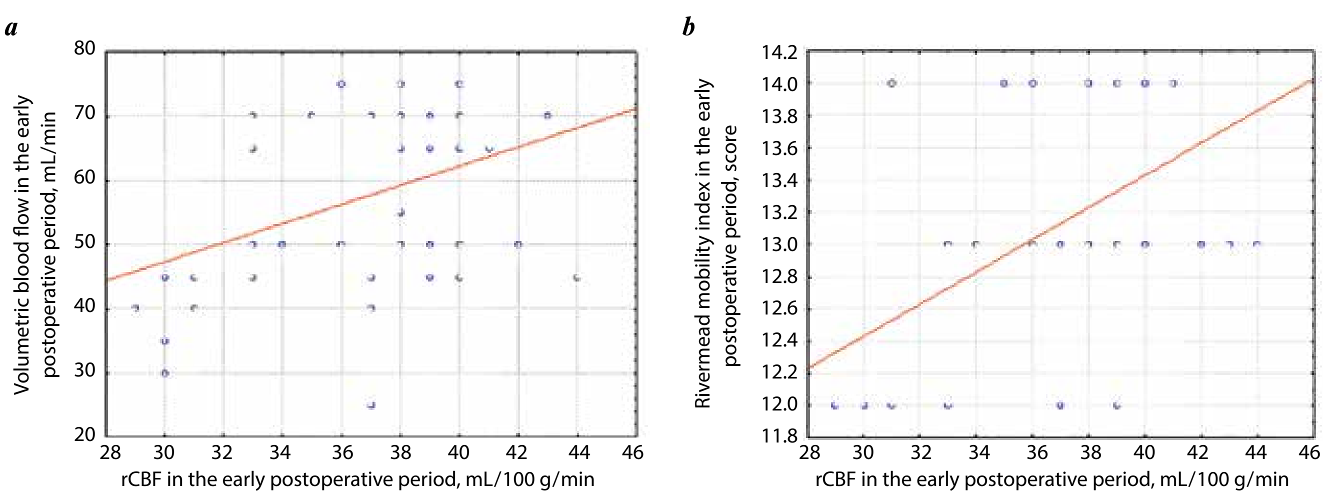

Fig. 16. *Detected correlations between the analyzed characteristics in the early postoperative period: a – between regional cerebral blood flow (rCBF) per SPECT of the brain and volumetric blood flow per ultrasound (Rs = 0.31; p <0.02); b – between rCBF per SPECT of the brain and Rivermead mobility index (Rs = 0.42; p <0.001)*

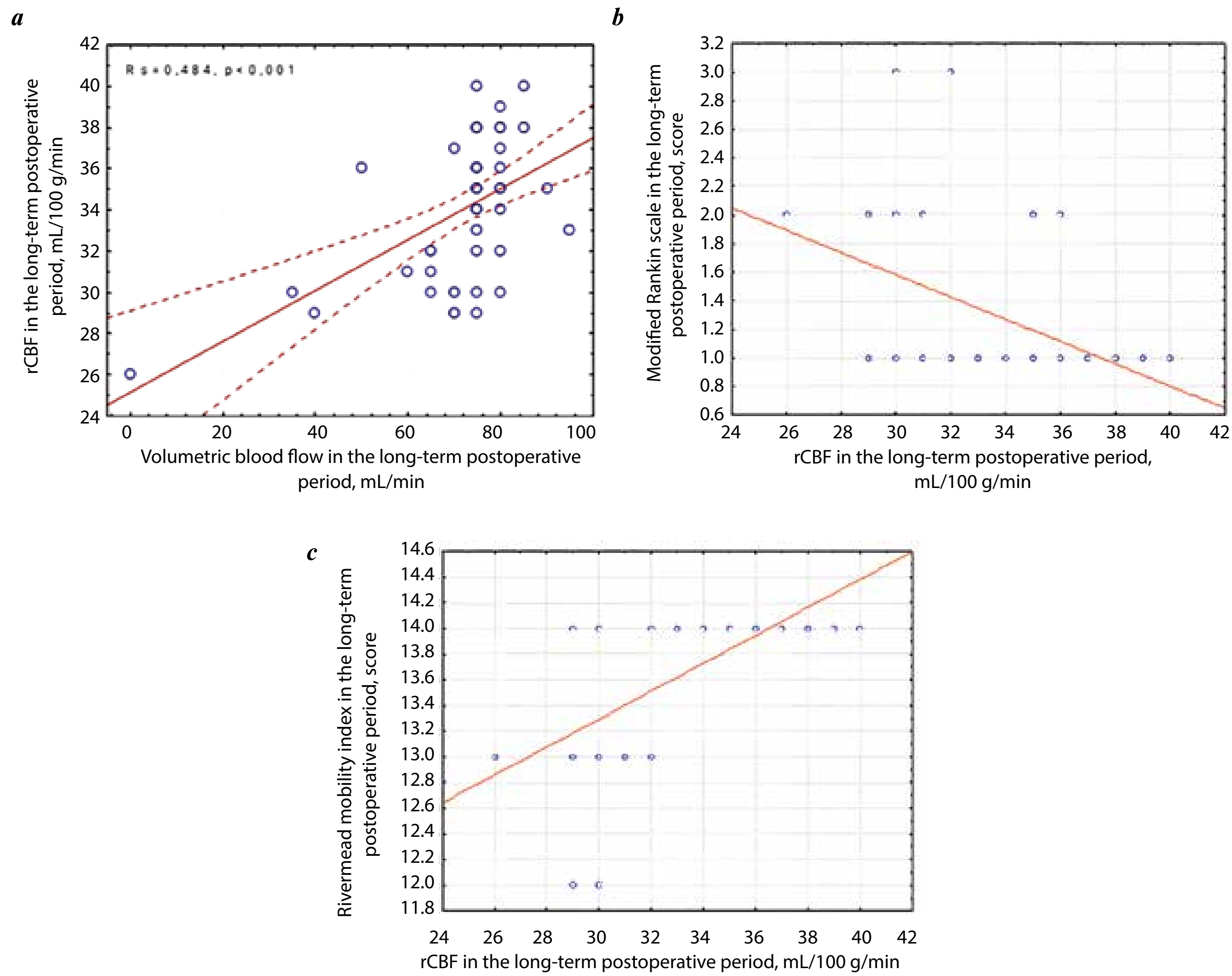

Fig. 17. *Detected correlations between the analyzed characteristics in the long-term postoperative period: a – between regional cerebral blood flow (rCBF) in bypass per SPECT of the brain and volumetric blood flow by microsurgical anastomosis per ultrasound (Rs = 0.484; p <0.001); b – between rCBF per SPECT of the brain and modified Rankin scale score (Rs = 0.466; p <0.001); c – between rCBF per SPECT of the brain and Rivermead mobility index (Rs = 0.65; p <0.001)*

repeat strokes were more frequent and developed earlier than in the group of patients receiving only conservative treatment. The researchers concluded that low-flow STA-MCA bypass is not an effective method of cerebral ischemia prevention in patients with symptomatic ICA occlusion [10–15]. However, it is important to note that in this trial patients in more severe condition (per neurological status) were selected for surgical treatment. Not all patients underwent instrumental diagnosis of the cerebral vessels for ICA occlusion confirmation and measurement of perfusion of the brain in the preoperative period and after cerebral revascularization.

Development of such modern diagnostic methods as computed tomography, magnetic resonance (MR) imaging, MR angiography, CT angiography, CT and MR perfusion of the brain, positron emission tomography and SPECT, allowed to identify patients with higher risk of repeat ischemic stroke. In our study, all patients underwent CT angiography of the brain and perfusion evaluation using SPECT before cerebral revascularization and in the preoperative, early and long-term postoperative periods after low-flow STA-MCA bypass formation.

In our study, CT angiography showed functioning bypass in the long-term postoperative period in 53 (98 %) patients. Dynamic study of low-flow STA-MCA bypass functional characteristics showed that linear blood flow of a functioning bypass decreases with time (on average from 59 to 48.5 cm/s), while VBF increases (on average from 60 to 75 mL/min). Low-flow STA-MCA bypass formation is associated with improved rCBF (on average from 23 to 35 mL/100 g/min) which directly depends on VBF through the bypass. Improved brain perfusion in the postoperative period is accompanied by better clinical outcomes.

In the Japanese EC-IC Bypass Trial [3, 5, 16] based on brain perfusion study using SPECT, positive results of revascularization of the brain in patients with symptomatic

ICA occlusion were also demonstrated. Repeat ischemic cerebrovascular events were observed in only 5 % of patients with low-flow STA-MCA bypass and in 14 % of patients of the control group (conservative treatment).

The American Carotid Occlusion Surgery Study (COSS) (2002–2010) did not confirm robust positive effect after low-flow STA-MCA bypass formation in comparison with patient group receiving conservative treatment [3, 5, 16, 17]. The number of repeat ischemic strokes in 2 years was 21 % in the operated group and 22.7 % in the non-operated group. However, the researchers noted good perfusion restoration at the bypass side in all operated patients.

During low-flow STA-MCA bypass formation bypass is possible through a mini-access without the loss of time or surgical quality. To predict the results of bypass functioning, intraoperative use of flowmetry is advisable.

In our study, no repeat cerebrovascular events were observed in the postoperative and long-term periods in patients with functioning bypass. In the long-term after cerebral revascularization, improved neurological status per the NIHSS was observed in 59 % of patients in the 1st group (1–2 years); per Rivermead mobility index in 63.3 % patients in the 1st group (1–2 years); per the modified Rankin scale in 48 % of patients of the 2nd group (3–4 years).

CONCLUSION

Taking into account the results of our study, we propose that low-flow STA-MCA bypass is an effective method of AICD prevention and improves neurological status of patients with symptomatic ICA occlusion. Therefore, we can recommend this surgery for improving patients» quality of life in the long-term after the disease.

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