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CLINICAL STUDY

Cognitive changes associated with cerebral emboli during coronary intervention

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ABSTRACT

OBJECTIVE: To investigate factors influencing the frequency and type of microembolic signals (MES) detected using transcranial Doppler (TCD) in patients undergoing elective coronary intervention, and to correlate MES with silent stroke detected using magnetic resonance imaging (MRI) and cognitive dysfunction.
METHODS: The subset study of a randomized clinical trial was conducted on 70 patients (58 males; mean age 59.9 ± 8.4 years) who underwent bilateral TCD monitoring of middle cerebral arteries (MCAs) during elective coronary interventions. Neurologic examination and brain MRI were performed prior to, and 24 h post-intervention. Cognitive function tests were performed prior to, and on day 30 post-intervention.
RESULTS: The incidence of detected MES was 94.3 %. Eighteen (25.7 %) patients had new clinically asymptomatic ischemic lesions on MRI. The number of solid MES negatively correlated with changes in revised Addenbrooke's Cognitive Examination test (ACE-R) and, the number of solid MES and combinations of solid and gaseous MES negatively correlated with changes in Mini Mental-State Examination (MMSE) conducted on day 30 after the intervention ($p < 0.05$ in all cases).
CONCLUSION: Cardiac catheterization was associated with a high risk of cerebral embolism in our patients. A higher number of solid MES and combinations of solid and gaseous MES was associated with the deterioration in cognitive tests *(Tab. 5, Fig. 3, Ref. 30)*. Text in PDF *www.elis.sk*
KEY WORDS: microembolic signals, transcranial Doppler, coronary intervention, silent cerebral infarction, cognitive changes.

Introduction

Cerebral microembolic signals (MES) occur during specific diagnostic and therapeutic interventions. They are detected during surgical and endovascular carotid interventions (1), heart surgery (2), coronary angioplasty or stenting (3), orthopedic surgery (4), and other invasive procedures (5). However, the association between total MES, stroke and clinically silent cerebral infarctions (SCI) is unclear.

The incidence of symptomatic stroke during coronary catheterizations varies between 0.1 and 0.6 % (6, 7). The incidence of silent SCI is ~22 % (8). Although patients with SCI exhibit no acute neurological symptoms, they may be at high risk of cognitive function impairment and development of dementia in the following months (5). SCI is detected using neuroimaging methods, especially magnetic resonance imaging – diffusion-weighted imaging (MRI-DWI) (5, 9, 10).

Transcranial Doppler (TCD) is a unique method to detect gaseous and solid MES in the intracranial cerebral arteries. According to the definition of the Consensus Committee of the 9th Cerebrovascular Hemodynamics Symposium, MES have the following characteristics: random occurrence during the cardiac cycle, brief duration, high intensity, unidirectional signals, and audible component (11).

Air embolism, thrombus formation inside the catheter or on its surface, and dislocation of aortic atheromas during manipulation and passage of catheters within the aorta are the main sources of embolic material causing ischemic strokes during cardiac catheterization or coronary intervention (8, 12, 13). Macroemboli (> 200 μm) may occlude larger arteries that supply focal vascular territories and produce a clinically apparent stroke. By contrast,

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microemboli can only occlude small arterioles and produce no or only subclinical findings with no apparent physiologic deficits. The reflective properties of the embolic material differ from those of the surrounding red blood cells and produce distinct high-intensity transient signals (HITS) derived from the background-flow velocity pattern. HITS represent both macroemboli and microemboli (14, 15).

Cerebral microemboli generated during the invasive procedure have been hypothesized to be a predictor of cognitive decline. Most studies have focused on the relationship between HITS and cognitive functioning. However, the evidence for the relationship between intraoperative MES and postprocedural cognitive dysfunction is insufficient so far (15, 16, 17).

This study aimed to investigate factors influencing the frequency and type of MES in both middle cerebral arteries (MCAs) as detected using TCD in patients undergoing elective coronary angiography, angioplasty, or stenting, and to correlate these MES with asymptomatic and symptomatic brain ischemic lesions detected using MRI-DWI and changes in cognitive function tests performed on day 30 after the procedure in relation to pretreatment scores.

Materials and methods

Ethical approval and patients consent

The entire study was conducted in accordance with the Declaration of Helsinki of 1964 and its later amendments (including the last in 2013). The study was approved by the Ethics Committee of the Faculty Hospital Nitra, Slovakia on April 29, 2014. All patients provided written informed consent before study enrollment.

Patients and inclusion criteria

This subset study included patients who had been enrolled in the SONOREDUCE trial (18) and had undergone coronary diagnostic angiography or angioplasty/stenting of coronary artery with periprocedural TCD monitoring of both MCAs. Patients were indicated for elective coronary angioplasty, stenting, or diagnostic coronary angiography. Their age was in the range of 35–90 years; their temporal bone window was sufficient for TCD examination with detectable blood flow in both MCAs, while the modified Rankin (mRS) scale before the procedure was 0–2 points.

The SONOREDUCE randomized clinical trial was registered at www.clinicaltrials.gov (NCT02351050) before the enrollment of patients.

Monitoring of embolic signals

The TCD was fixed in the required position using a headset. Bilateral TCD monitoring of the MCAs was performed using a diagnostic TCD system (EMS-9PB, Delica, Shenzen, China) with 2-MHz diagnostic transcranial Doppler probes and multirange embolus detection software (DTCD8100TM). The parameters were set at depth of 55 mm, power of 150 mW/cm^2, sample volume of 10 mm, sweeping speed of 6 s, and fast Fourier transform of 256 points. A threshold detection of 7 dB with a duration of 20–200 ms was used for HITS detection. All HITS (solid MES, gaseous MES, and artifacts) were automatically saved on a computer hard disk and analyzed by two experienced observers blinded to the study by agreement. Observers were stroke neurologists trained and certificated in neurosonology. TCD monitoring was performed in all patients from the beginning of catheterization to the access of site closure, and maximal recording time was set to 240 min.

Coronary artery angiography, angioplasty, and stenting

Cardiac catheterizations were performed in the catheterization laboratory by interventional cardiologists using a standard Seldinger technique. Femoral or radial artery was used as the access site. Unfractionated heparin (100 IU/kg) was administered intravenously at the beginning of the coronary angioplasty or stenting; the dose for diagnostic angiography from the transradial approach was 3,000–5,000 IU. Patients were treated with dual antiplatelet therapy before intervention (combination of aspirin, clopidogrel, prasugrel, or ticagrelor).

Magnetic resonance imaging

In this subset study, we used MRI data from the SONOREDUCE trial (18). All MRI examinations were performed using the 1.5 Tesla Avanto system (Siemens, Erlangen, Germany). Three sequences were used, namely transverse T2-weighted spin-echo (1), fluid-attenuated inversion recovery and DWI with an apparent diffusion coefficient (ADC) parametric map (3). Parameters have been described in greater detail in the SONOREDUCE trial (18). MRI was performed prior to, and 24 h post-intervention. New ischemic brain lesions were defined as "hyperintense regions" detected on post-intervention MRI while not being present on pre-treatment images.

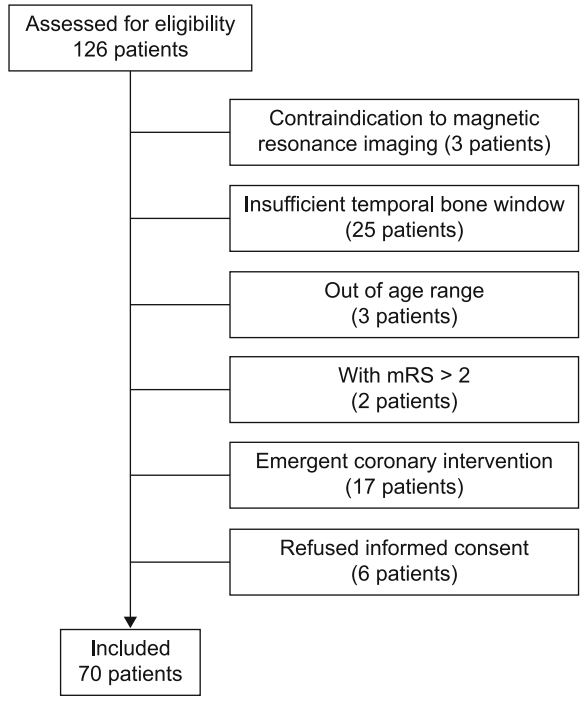

Fig. 1. Flow chart diagram of the study.

Tab. 1. Baseline characteristics. Quantitative values are expressed as median ± standard deviation (range). Qualitative data are expressed as absolute (relative) frequencies. Statistical comparison was made using the Mann-Whitney U-test and Fisher's exact test. Significantly different values are indicated in bold.

Variable	All	No of MES	Solid MES	Solid and gaseous MES
	(n = 70)	(n = 4)	(n = 66)	(n = 48)
Age (years)[a]	60±9.2 (36-81)	54.5±9.8 (47–68)	60.5±9.2 (36–81)	59.5±8.6 (36–81)
Male[b]	58 (82.9)	4 (100)	54 (81.8)	39 (81.3)
Arterial hypertension[b]	60 (85.7)	3 (75)	57 (86.4)	42 (87.5)
Ischemic heart disease[b]	69 (98.6)	4 (100)	65 (98.5)	48 (100)
Atrial fibrillation[b]	5 (7.1)	1 (25)	4 (6.1)	1 (2.1)
History of MI[b]	48 (68.6)	2 (50)	46 (70.0)	34 (70.8)
Diabetes mellitus[b]	27 (38.6)	0 (0)	27 (40.9)	21 (43.8)
Hyperlipidemia[b]	48 (68.6)	1 (25)	47 (71.2)	31 (64.6)
Stroke or TIA[b]	8 (11.4)	0 (0)	8 (12.1)	4 (8.3)
History of PE[b]	4 (5.7)	1 (25.0)	3 (4.5)	1 (2.1)
Cancer[b]	6 (8.6)	1 (25)	5 (7.6)	3 (6.3)
History of coronary PCI or CABG[b]	51 (72.9)	1 (25)	50 (75.8)	38 (79.2)
Right ICA stenosis ≥50 %/occlusion[b]	8 (11.4)	0 (0)	8 (12.1)	7 (14.6)
Left ICA stenosis ≥50 %/occlusion[b]	11 (15.7)	0 (0)	11 (16.7)	8 (16.7)
BMI [a]	29.7±4.1 (19.1–39.7)	29.4±1.4 (29.1–32.0)	29.8±4.2 (19.1–39.7)	29.9±3.7 (19.1–39.7)
Smoking[b]	9 (12.9)	1 (25)	8 (12.1)	5 (10.4)
Alcohol use[b]	2 (2.9)	1 (25)	1 (1.5)	0 (0)

BMI – body mass index; CABG – coronary artery bypass graft; ICA – internal carotid artery; MES – microembolic signals; MI – myocardial infarction; PCI – percutaneous coronary intervention; PE – pulmonary embolization; TIA – transient ischemic attack. [a]Mann-Whitney U-test; [b]Fisher's exact test

Clinical examinations and observed parameters

Patient age, sex, comorbidities (arterial hypertension, ischemic heart disease, atrial fibrillation, myocardial infarction, diabetes mellitus, hyperlipidemia, stroke, TIA, history of pulmonary embolization, cancer, coronary intervention), current medications, smoking status, alcohol use, internal carotid artery stenosis ≥ 50 %, and type of intervention were documented. Physical and neurologic examinations, vital signs measurements, and the assessment of neurological deficit (using the National Institutes of Health Stroke Scale, NIHSS) and self-sufficiency (using the mRS) were performed prior to, and 24 h and 30 days after intervention. Cognitive functions were tested prior to, and on day 30 post-procedure by means of the ACE-R, MMSE, clock-drawing test (CDT), and verbal fluency test (VFT) extracted from ACE-R.

Statistical analyses

The correlation between ordinal variables was calculated using Spearman's correlation coefficient. Negative values of cor-

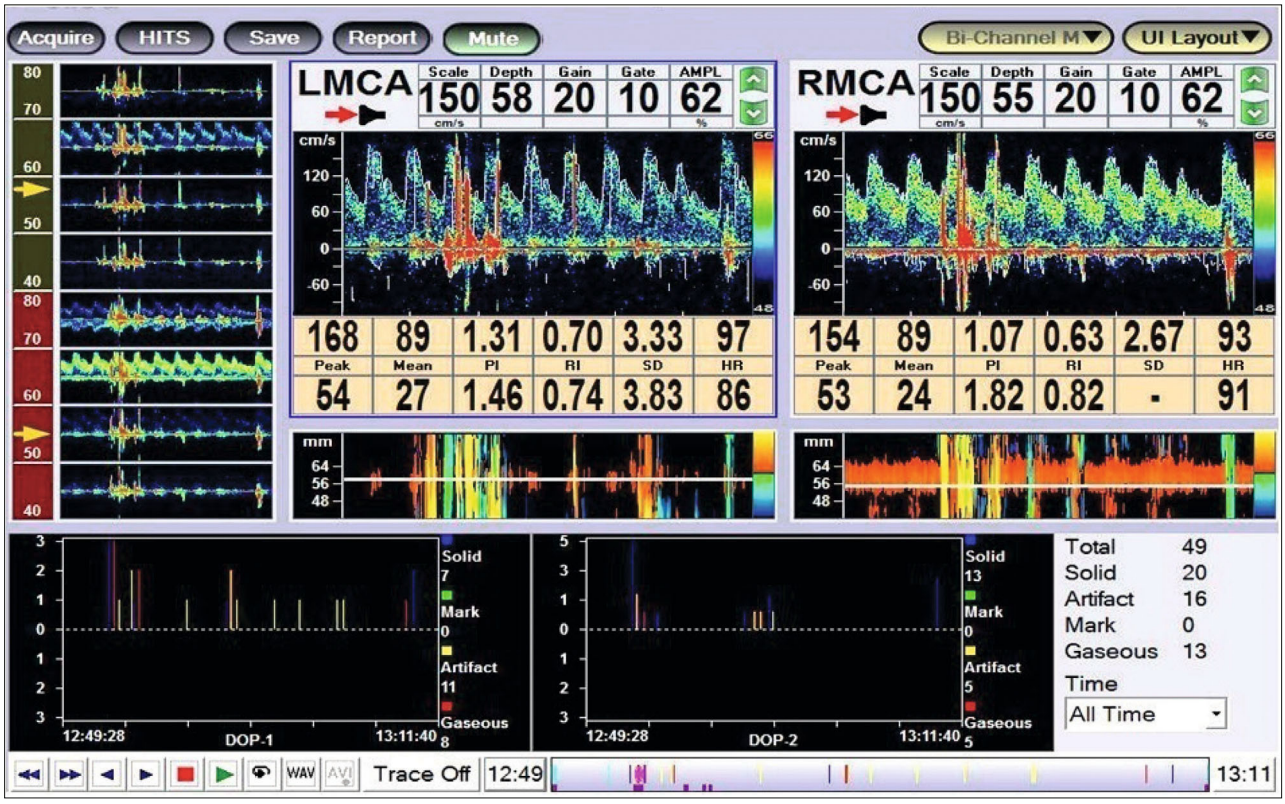

Fig. 2. Flow in middle cerebral arteries and microembolic signals´ detection using transcranial Doppler monitoring.

Tab. 2. Procedural characteristics. Quantitative values are expressed as median ± standard deviation (range). Qualitative data are expressed as absolute (relative) frequencies. Statistical comparison was made using the Mann-Whitney U-test and Fisher's exact test. Significantly different values are indicated in bold.

Variable		All	Number of MES	Number of solid MES	Number of solid and gaseous MES
		(n = 70)	(n = 4)	(n = 66)	(n = 48)
Time to procedure from onset of symptoms (days)		99.5±72.2 (3–365)	14.0±42.8 (3–95)	110.5±71.3 (3–365)	102.0±50.6 (9–270)
Therapy before coronary intervention[b]	No antiplatelets/ anticoagulants	4 (5.7)	0 (0)	4 (6.1)	3 (6.3)
	Antiplatelet monotherapy	8 (11.4)	0 (0)	8 (12.1)	5 (10.4)
	Dual antiplatelet therapy	52 (74.3)	3 (75)	49 (74.2)	39 (81.3)
	Triple therapy	6 (8.6)	1 (25)	5 (7.6)	1 (2.1)
	Statin use	62 (88.6)	4 (100)	58 (87.9)	45 (93.8)
	Use of fibrates/other hypolipidemic drugs	5 (7.1)	0 (0)	5 (7.6)	3 (6.3)
Therapy during coronary intervention[b]	No therapy	2 (2.9)	0 (0)	2 (3.0)	1 (2.1)
	Heparin	60 (85.7)	4 (100)	56 (84.8)	40 (83.3)
	Heparin + 1 antiplatelet	4 (5.7)	0 (0)	4 (6.1)	4 (8.3)
	Heparin + 2 antiplatelets	4 (5.7)	0 (0)	4 (6.1)	3 (6.3)
Number of treated coronary vessels[a]	0	10 (14.3)	3 (75)	7 (10.6)	4 (8.3)
	1	43 (61.4)	1 (25)	42 (63.6)	35 (72.9)
	2	16 (22.9)	0 (0)	16 (24.2)	9 (18.8)
	3	1(1.4)	0 (0)	1 (1.5)	0 (0)
Number of implanted stents[a]	0	15 (21.4)	3 (75)	12 (18.2)	8 (16.7)
	1	24 (34.3)	0 (0)	24 (36.4)	19 (39.6)
	2	24 (34.3)	1 (25)	23 (34.8)	16 (33.3)
	3	6 (8.6)	0 (0)	6 (9.1)	4 (8.3)
	4	1 (1.4)	0 (0)	1 (1.5)	1 (2.1)
Contrast volume (ml)[a]		100.0±51.9 (2–270)	50.0±50.0 (50–150)	100.0±51.7 (2–270)	100.0±52.9 (2–270)
Arterial puncture[b]	Right radial artery	54 (77.1)	4 (100)	50 (75.8)	36 (75.0)
	Right femoral artery	15 (21.4)	0 (0)	15 (22.7)	11 (22.9)
	Left femoral artery	1 (1.4)	0 (0)	1 (1.5)	1 (2.1)

TCD – transcranial Doppler. [a]Mann-Whitney U-test; [b]Fisher's exact test

relation coefficients indicate a negative correlation, and positive values of correlation coefficients indicate a positive correlation. Correlation coefficients were calculated by correlating the count of solid MES only with changes in ACE-R, MMSE, VFT and CDT. Correlations with the count of solid and gaseous MES were calculated in the same way. The changes were calculated as a difference between the first and second measurements. The normality of data distribution was checked using the Shapiro-Wilk test. For the statistical analysis of MES, nonparametric methods were used. The comparisons of two independent selections were performed with the Mann-Whitney U-test while the Kruskal-Wallis test was used to compare additional independent selections. *Post hoc* tests of multiple comparisons with the Bonferroni correction were subsequently performed. The analyzed variables were included in univariate and multiple logistic regression analyses. All tests were performed at an alpha level of significance of 0.05. The data were analyzed with SPSS v23.0 software (IBM, Armonk, NY, USA).

Tab. 3. Correlation between numbers of detected microembolic signals and selected quantitative or ordinary covariate variables. A statistical correlation was made using Spearman's correlation coefficient. Significant p values are indicated in bold.

Variable	Any solid MES		Solid and gaseous MES	
	Correlation coefficient (r)	p	Correlation coefficient (r)	p
Age	0.153	0.221	0.231	0.115
BMI	–0.101	0.418	–0.125	0.399
Number of treated vessels	0.073	0.558	0.062	0.675
Number of implanted stents	0.050	0.692	–0.003	0.984
Time to intervention (days)	–0.018	0.893	0.126	0.416
Dose of contrast agent (ml)	**0.272**	**0.030**	0.236	0.114
Right ICA stenosis ≥ 50 %	0.012	0.929	–0.021	0.896
Vertebrobasilar territory stenosis ≥ 50 %	0.007	0.957	–0.025	0.875

BMI – body mass index; ICA – internal carotid artery; MES – microembolic signals

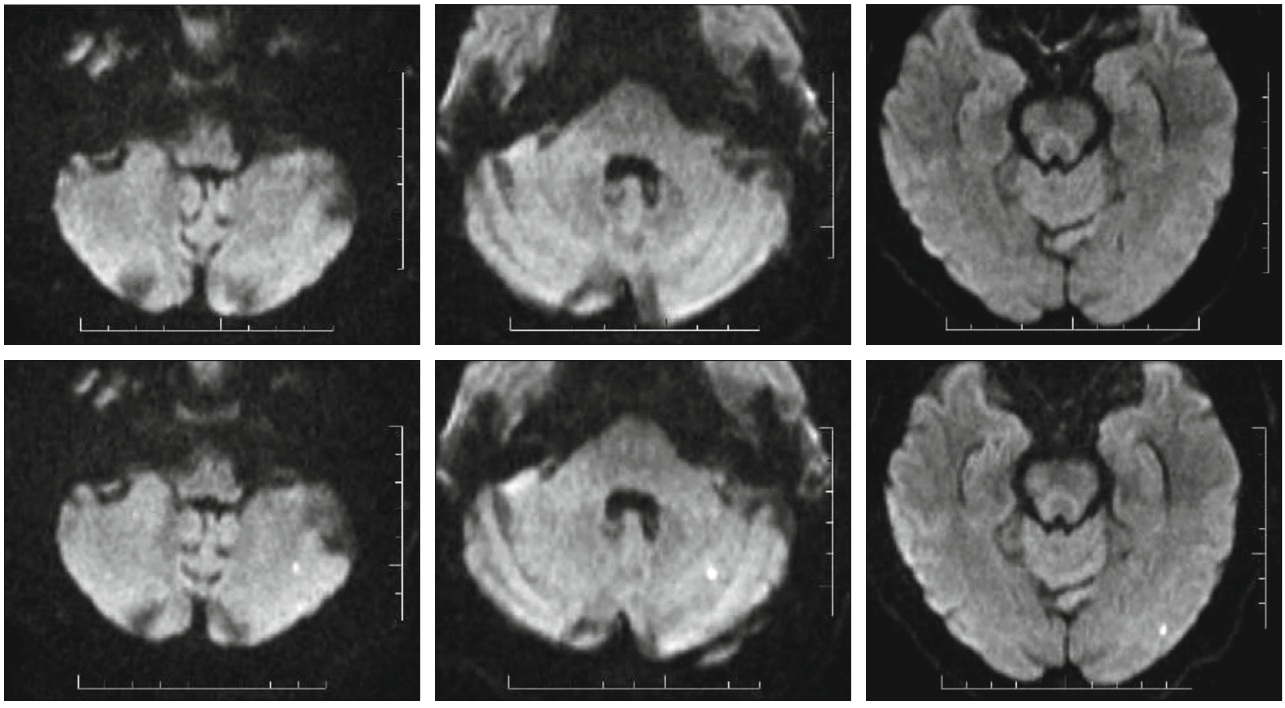

Fig. 3. Magnetic resonance imaging – diffusion-weighted images. Normal initial finding (top row) and brain infarctions of the left cerebellar hemisphere and left occipital lobe (bottom row

Results

Seventy patients indicated for elective coronary intervention were enrolled in the study after signing the informed consent (58 males; mean age of 59.9 ± 8.4 years) (Fig. 1). Baseline characteristics are presented in Table 1, and procedural characteristics and medical conditions are shown in Table 2.

MES were not detected during coronary intervention in 4 (5.7 %) out of 70 patients. In the remaining 66 patients (94.3 %), any solid MES (both solid MES only (n = 18) and combination of solid and gaseous MES (n = 48)) were detected with a median of 16 (min–max: 1–164). Solid emboli entered the right MCA in 59 patients (84.3 %) with a median of 5 and the left MCA in 56 patients (80.0 %) with a median of 7. Out of 66 patients detected as having any solid MES, the combination of solid and gaseous microemboli was present in 48 patients (68.6 %) with a median of 10 (Fig. 2). As for the combination of solid and gaseous MES, their median was 10. The presence of atrial fibrillation (n = 5) was associated with a significantly lower frequency of the combination of solid and gaseous MES counts ($p < 0.05$) (Tab. 1). In patients with no detected MES, the coronary catheterization was performed sooner, and all these patients underwent diagnostic angiography (Tab. 2). The volume of the administered contrast agent was associated with a significantly higher frequency of solid MES during the procedure in both MCA territories (Tab. 3).

All four patients with no detected MES had no ischemic lesions on control MRI-DWI. Conversely, a new ischemic lesion was detected in 18 (27.3 %) out of 66 patients with detected MES ($p < 0.01$) (Fig. 3). In 13 (72.2 %) of these 18 patients, a new ischemic lesion was localized in the MCA territory. All lesions were clinically asymptomatic. The distribution of new brain infractions and MES counts are shown in Table 4.

No significant correlation was found between the type and frequency of MES or between the count of new ischemic lesions and their volume ($p > 0.05$ in all cases) (Supplementary Table S1). No stroke, TIA, myocardial infarction, death, or intracranial bleeding were recorded during 30 days after the procedure.

Tab. 4. Distribution of new brain infarctions and microembolic signals count. Values are expressed as number or median (min–max). Statistical comparison was made using the Kruskal-Wallis test.

Variable	Number of patients	Number of any solid MES	p	Number of solid and gaseous MES	p
New ischemic lesion location			0.669		0.689
Right hemisphere	6	20.5 (3–103)		22.5 (6–146)	
Left hemisphere	5	5.0 (4–16)		16.0 (4–35)	
Both hemispheres	2	15.0 (9–21)		24.0 (15–33)	
Infratentorial region	1	12.0 (12–12)		55.0 (55–55)	
Supratentorial + infratentorial region	4	19.5 (4–46)		26.0 (4–46)	

MES – microembolic signals

Tab. 5. Correlation between the number of detected microembolic signals and 30-day cognitive function tests results. The statistical correlation was made using Spearman's correlation coefficient. Significant P values are indicated in bold.

Variable	Any solid MES (n=66)		Solid and gaseous MES (n=48)	
	Correlation coefficient (r)	p	Correlation coefficient (r)	p
Changes in ACE-R from baseline	–0.326	0.024	–0.277	0.056
Changes in MMSE from baseline	–0.338	0.020	–0.324	0.026
Changes in VFT from baseline	–0.136	0.353	–0.154	0.291
Changes in CDT from baseline	0.021	0.888	–0.211	0.155

ACE-R – revised Addenbrooke's Cognitive Examination; CDT – clock drawing test; MMSE – Mini Mental-State Examination; VFT – verbal fluency test

Supplementary Table S1. Correlation between the number of detected microembolic signals and number and volume of brain infarctions. Statistical correlation was made using the Spearman's correlation coefficient. There are no statistically significant correlations.

Variable	Solid MES		Solid and gaseous MES	
	Correlation coefficient (r)	p	Correlation coefficient (r)	p
Volume of brain lesions prior to intervention (ml)	0.202	0.094	0.118	0.332
Volume of brain lesions after intervention (ml)	0.172	0.155	0.143	0.237
Number of new brain lesions	0.043	0.725	0.050	0.681
Volume of new brain lesions (ml)	0.040	0.740	0.041	0.736
Number of new brain ischemic lesion in MCA territory	–0.058	0.634	–0.133	0.274
Volume of new brain ischemic lesion in MCA territory(ml)	–0.056	0.645	–0.132	0.277
Volume of new brain ischemic lesion in the right MCA territory(ml)	–0.004	0.975	–0.064	0.599
Volume of new brain ischemic lesion in the left MCA territory(ml)	–0.104	0.390	–0.149	0.218
Number of new brain ischemic lesion in other territory	0.071	0.561	0.098	0.421
Volume of new brain ischemic lesion in other territory(ml)	0.065	0.594	0.078	0.521

MCA – middle cerebral artery; MES – microembolic signals.

The count of solid MES correlated negatively with changes in ACE-R and, the counts of solid MES and combinations of solid and gaseous MES correlated significantly negatively with changes in MMSE performed on day 30 after the intervention ($p < 0.05$ in all cases), i.e., a higher count of MES was associated with deterioration in these cognitive tests. No significant correlations were found between MES and results of other cognitive tests ($p > 0.05$ in all cases) (Tab. 5, Supplementary Table S2).

Discussion

The present study showed that cardiac catheterization was associated with a high risk of cerebral embolism and the number of MES correlated negatively with changes in cognitive function tests conducted on day 30 after the procedure.

The total number of solid, and gaseous MES varies in published studies (19, 20, 21). Fischer reported 95 + 45 MES in 52 patients during left heart catheterization. MES were detected in 67.5 % of patients (19). During coronary interventions only, rotablation was followed by a massive increase in MES. All MES were clinically silent. In another trial, a median number of 754 cerebral MES was detected, of which 92.1 % were gaseous and 7.9 % were solid (20). New cerebral lesions were observed in 15.2 % of patients who underwent transradial catheterization, but in none of those

Supplementary Table S2. Baseline and 30th-day cognitive function tests results.

Variables	All (n = 70)	No MES (n = 4)	Any solid MES (n = 66)	Solid and gaseous MES (n = 48)
ACE-R 1 (baseline visit); mean, median (IQR); points	85.0, 88.0 (81.0–94.0)	84.5, 86.0 (78.5–90.5)	85.0, 88.0 (81.0–95.0)	87.1, 88.5 (84.0–95.0)
ACE-R 2 (30 days); mean, median (IQR); points	87.2, 90.0 (82.0–94.0)	89.0, 88.0 (87.0–92.0)	87.1, 90.0 (82.0–95.0)	88.1, 91.0 (84.0–95.0)
MMSE 1 (baseline visit); mean, median (IQR); points	28.4, 28.0 (27.0–29.0)	27.3, 27.5 (26.5–28.0)	28.5, 28.0 (27.0–29.0)	27.8, 28.0 (27.0–29.0)
MMSE 2 (30 days); mean, median (IQR); points	28.4, 29.0 (27.0–30.0)	28.7, 29.0 (28.0–29.0)	28.4, 29.0 (27.0–30.0)	28.6, 29.0 (27.0–30.0)
CDT 1 (baseline visit); mean, median (IQR); points	2.8, 3.0 (3.0–3.0)	2.8, 3.0 (2.5–3.0)	2.8, 3.0 (3.0–3.0)	2.9, 3.0 (3.0–3.0)
CDT 2 (30 days); mean, median (IQR); points	2.5, 3.0 (2.0–3.0)	2.7, 3.0 (2.0–3.0)	2.5, 3.0 (2.0–3.0)	2.4, 3.0 (2.0–3.0)
VFT 1 (baseline visit); mean, median (IQR); points	9.8, 10.0 (8.0–12.0)	9.0, 9.5 (7.0–11.0)	9.8, 10.0 (8.0–12.0)	10.3, 10.0 (8.0–13.0)
VFT 2 (30 days); mean, median (IQR); points	9.1, 9.0 (7.0–12.0)	7.0, 8.0 (4.0–9.0)	9.3, 10.0 (7.0–12.0)	9.2, 9.0 (6.0–12.0)

ACE-R – revised Addenbrooke's Cognitive Examination; CDT – clock drawing test; MMSE – Mini Mental-State Examination; VFT – verbal fluency test.

with transfemoral catheterization (p = 0.567). These lesions were significantly associated with a higher number of solid MES (p = 0.016) and longer fluoroscopy time (p = 0.039). An Australian study analyzed 51 patients during coronary angiography. In all patients, MES were detected in MCA with a count range of 22–904 per patient (median 194; IQR 100–290). Median counts of gaseous and solid MES were 155 (IQR 82.5–254.5) and 23 (IQR 15.5– 0), respectively (23). Overall, 84 % of MES were classified as gaseous and ranged from 74 to 100 % of MES per patient. The frequency of solid emboli and rate of new brain ischemic lesions on control MRI recorded in our study were higher than those in previously published studies (19, 20, 21). MES were detected in 94 % of patients during coronary intervention with a median number of 16. The distribution between the right and left MCAs did not show significant differences. No MES were detected in 5.7 % of patients. The possible reasons for these discrepancies could be explained by differences in TCD devices and software, Doppler settings, definitions of HITS, modes of HITS calculation (manual and/or automated), and number of cerebral arteries insonated (19, 20, 21, 22, 23, 24, 25, 26). Other reasons could lie in the risk profile of the patient and therapy before and during the procedure.

No significant differences in the prevalence of MES were detected using different approaches in our study. However, all four patients with no MES detected underwent coronary intervention via the radial approach. Jurga et al. did not find correlations between the cerebral microemboli, vascular access site, and cognitive functions using the MoCa test (22). By contrast, in the study performed by Lund et al., new brain ischemic lesions were observed in 15.2 % of patients using the radial approach and in none when using the femoral approach (20).

The association between the number of MES and brain infarctions is unclear. Brain ischemic lesions were significantly associated with a higher number of solid microemboli in a Norwegian study (20), but no such significant association between new brain infarctions detected by MRI and number of procedural solid microemboli was demonstrated in several other studies (21, 22). New brain ischemic lesions were detected in 25.7 % of patients in the present study. All these lesions were clinically asymptomatic. A higher frequency of MRI-detected new brain infarctions was reported after coronary intervention in patients with acute coronary syndrome. Murai et al. reported new SCI in 35 % of these patients (26).

The volume of administered contrast agents was associated with a higher frequency of solid MES in the present study. Fischer et al. reported 67.5 % of total MES counts during injection of contrast media or saline solution; 30 % during movements of wire and catheter, and 2 % during catheter manipulation. All MES were clinically silent (19).

The history of atrial fibrillation was associated with lower frequency of the combination of solid and gaseous MES, but we consider that this finding should be interpreted with caution. Very few patients with atrial fibrillation (n = 5) were enrolled in our study. All of them used anticoagulation therapy. Published studies reported that the prevalence of microemboli is higher in patients with symptomatic atrial fibrillation (29 %) than in those with asymptomatic atrial fibrillation (10 %). Similarly, the prevalence of microemboli was higher in cases with valvular atrial fibrillation as compared to non-valvular atrial fibrillation, which corresponds to a higher risk for thromboembolic events (27).

In our study, the presence of MES was significantly associated with cognitive dysfunction conducted on day 30 after cardiac catheterization. The number of solid MES negatively correlated with changes in the ACE-R test while the number of solid and combined solid and gaseous MES negatively correlated with changes in MMSE. Martin et al. did not demonstrate a causal link between intraoperative HITS, while the postoperative cognitive decline in their systematic literature review focused on three invasive procedures (cardiac surgery, carotid endarterectomy, orthopedic surgery) (15). The possible causes could be explained by the different number of MES in invasive procedures, heterogeneous methods used to analyze HITS, and by the fact that the studies differ as to the batteries of cognitive tests and testing batteries and time at which they were delivered. The impact of the intraprocedural MES counts on the occurrence of new MRI-DWI lesions, neuropsychological capability, or overt neurologic deficits after pulmonary vein isolation was not demonstrated in a German multicentric study (28).

Spontaneous cerebral emboli were significantly more frequent in patients with Alzheimer's disease and in those with vascular dementia as compared with sex- and age-matched controls in a British study (29). The authors concluded that MES might be a potentially preventable or treatable cause of dementia. On the contrary, Scott et al. did not demonstrate an association of cognitive dysfunction with the microemboli load (30).

Several limitations of our study should be acknowledged. Firstly, the small size of our patient cohort did not allow for relevant conclusions regarding particular subgroups of patients (e.g., patients with atrial fibrillation). Secondly, a serial follow-up comparisons of MRI fluid-attenuated inversion recovery and DWI images were not performed to compare the progression or persistence of ischemic lesions. Thirdly, the neuropsychological test battery should be more complex and repeatedly performed; this is the aim of our future study.

In conclusion, in our patients, cardiac catheterization was associated with a high risk of cerebral embolism with a 94.3 % incidence of detected MES and 25.7 % incidence of SCI. We also confirmed a significant correlation between the number of detected MES and worsening of the results in cognitive function tests conducted on day 30 after coronary catheterization.

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