Original paper

Early ischemic brain lesions after carotid angioplasty and stenting on diffusion-weighted magnetic resonance imaging study

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Summary

Aim: The aim of the paper is to evaluate the appearance of the new early ischemic lesions in the brain after carotid angioplasty and stenting on diffusion-weighted magnetic resonance imaging, and their relationship with clinical and procedural factors.

Methods: Carotid artery stenting (CAS) procedures performed by a single interventional cardiologist in years November 2006 to January 2013 were evaluated retrospectively. In total, 227 procedures for 211 patients (mean age 69.8 ± 8.5 years) were performed, from which 171 (75.3%) for male and 56 (24.7%) for female patients. Seventy-two (34.1%) patients had symptomatic stenosis of carotid artery. The following protection systems to avoid the distal microembolism were used during the CAS: (1) Filters: FilterWire EZ (Boston Scientific Corporation); Emboshield NAV (Abbott Vascular); SpideRX (EV3); Defender (Medtronic); FiberNet Filter (Invatec-Medtronic); (2) Occlusion MoMa Baloon System (Invatec-Medtronic). Acute ischemic damages of the brain before and after CAS procedure were diagnosed using magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) sequences. Sixty-five (30.8%) patients underwent MRI test. Exact and asymptomatic χ^2 criteria were applied for testing the hypothesis of inter-dependency of the symptoms.

Results: Forty-six (70.8%) patients had new ischemic foci in the brain on MRI DWI after CAS procedures. Among those patients, focal damage of the brain was diagnosed in 36 (78.3%) cases; linear damage of the brain – in 9 (19.6%) patients; ipsilateral damage of the brain – in 37 (80.4%) patients; bilateral damage of the brain – in 16 (34.8%) patients, 38 (82.6%) patients were diagnosed with forebrain damage; 4 (8.7%) patients were diagnosed with damage of brainstem; 5 (10.9%) patients were diagnosed with cerebellum damage. Clinical symptoms of brain damage were diagnosed only for 2 (4.3%) patients. Focal damage of the brain was significantly less frequent only for aortic arch type 1, if compared with aortic arch type 2 and 3: 64.3%, 93.3% and 100.0%, respectively ($p < 0.05$). Focal damage of the brain occurred least in patients (28.6%) with Emboshield NAV protection type, if compared to other types of protection (71.4–100.0%). Linear >10 mm brain damage was less frequent when using FilterWire EZ, Emboshield NAV and SpideRX protection type. Ipsilateral ischemic brain damage also occurred less frequent when using Emboshield NAV protection type; bilateral damage occurred less frequent when using FilterWire EZ, Emboshield NAV and SpideRX protection type. Ischemic forebrain damage was also diagnosed less often in patients for whom protection type FilterWire EZ and Emboshield NAV was applied.

Conclusions: Most frequent findings by MRI after CAS procedures were focal, ipsilateral and forebrain damage (about 80%), but less than 5% patients had clinical symptoms. In the case of aorta arch type 1 focal ischemic damage of the brain was significantly less frequent, then in aortic arch type 2 and 3. The localization and extent of brain damage was associated with the type of protection systems that have been used.

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Introduction

Carotid artery atherosclerotic stenosis is a common cause of cerebral infarction [1]. In case of carotid artery atherosclerotic stenosis, stroke can develop because of atherosclerotic masses or thromboembolism from plaque to the brain, or hypoperfusion of the brain [2]. Carotid artery stenting (CAS) works on both mechanisms by eliminating plaque of the carotid artery, thus also eliminating stenosis. If compared to carotid endarterectomy (CEA), CAS is less traumatic, performed with only local anesthesia, poses no risk of the cranial nerve damage, incurs less problems with the wound, both the procedure and hospitalization period is shorter [3–5]. Researchers have determined that CAS is a safe and effective procedure for those high-risk patients where CEA is difficult to perform considering from technical point of view [4,6,7]. Data from various authors report after-CAS complication rate of 1.5% to 11.3% [8–11]. Data from the SAPPHIRE study yielded complications in 4.4% high-risk patients during the first 30 days after stenting [4]. Results from the CaRESS research are fairly positive, showing after-stenting complications in 2.1% patients only [6]. Further data from later randomized studies indicated complications (stroke, myocardial infarction, or death) in 6.3% to 9.6% patients after stenting [7,12,13].

CREST study indicated a clear relationship between age and complications [14]. Patients younger than 60 years of age had 1.7% complication rate, whereas those aged 80 years and more had 12.1% rate. American FDA and Stroke Association Board have concluded that CAS is an alternative method of treatment for high-risk patients. Stenting is not indicated for low-risk patients and patients with minor carotid artery stenosis [15,16]. The amount of CAS procedure risk depends on the patient's general condition, age, concurrent illnesses, angiography and brain CT data [17–19]. Requirements for performing the CAS are the same as for the CEA. New technologies, better experience in stenting and new medicines available have improved and promoted results of stenting procedure in recent years. Modern researchers are still facing multiple CAS-safety-related questions such as reducing the risk of ischemic complications related to this procedure. Other researchers stress the issues in connection with the dependency of ischemic damage on stenting technique and technologies [20]. However, many issues related to early brain ischemic lesions after newer CAS techniques still need further clarification.

The aim of the paper is to evaluate the appearance of the new early ischemic lesions in the brain after device-protected carotid angioplasty and stenting on magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) and their relationship with clinical and procedural factors.

Methods

CAS procedures performed by a single interventional cardiologist in years November 2006 to April 2013 were evaluated retrospectively. Age of patients was from 47 to 93 years; mean average age 69.8 ± 8.5 years. In total, 227 procedures for 211 patients were performed, from which 171 (75.3%) for male and 56 (24.7%) for female patients. 72 (34.1%) patients had symptomatic stenosis of internal and/or common carotid artery. Sixty-five (30.8%) patients underwent MRI DWI investigations.

CAS procedure was performed in accordance with the approved methodology. The main femoral artery was punctured under local anesthesia, an introducer inserted and the common carotid artery reached by specialized catheters. After injection of contrast, stenosis of the internal carotid artery was visualized, protection device was inserted and inflated, and later a stent was introduced and expanded within the stenotic segment of carotid artery.

Acute ischemic abnormalities in the brain after CAS procedure were diagnosed using MRI DWI sequences.

MRI assessments (with DWI applicable in both cases) were performed 24 to 48 hours prior to the CAS procedure and 24 to 72 hours after the procedure. Full body MRI (Avanto, Siemens) with 1.5 Tesla as performed with high-efficiency gradients (speed up to 200 mT/m per ms; diapason up to 40 mT/m) with a dedicated head coil. MRI assessment protocol was applied fully during a single assessment for all the patients. MRI protocol comprised sagittal plane: T1 flash-based gradient echo 3D (three-dimension) sequence (1 mm slices; TE (time to echo): 4.8 ms; TR (time to repeated radio-frequency impulse): 9.5 ms; FA (focal angle of an impulse): 25; matrix 256×256); axial plane: T2 turn-based echo sequence (5 mm slices; TE 89 ms; TR 9000 ms); T2-based inversion sequence (FLAIR) of the dark fluid on the axial plane (5 mm slices; TE 89 ms; TR 9000 ms; TI (time of inversion) 2500 ms). DWI sequence study was performed for all the patients (before and after stenting) on axial and coronary planes in order to improve detection of minor ischemic lesions/focuses and evaluation of their size (5 mm slices; TE 89 ms; TR 3800; matrix 192×192; field of view 250 mm; distance factor 30%; diffusion sensitization b-values of 0, 500 and 1000 s/mm^2). All the MRI gradients were switches to high-power-mode in all the three planes (x, y and z). ADC (diffusion coefficient maps) were formulated and evaluated for all the patients. No contrast medium was used during the MRI procedure.

A radiologist evaluated MRI scans from all the patients using a blind/randomized method. All visible anatomic changes were evaluated on the T1, T2 and FLAIR primary test images: atrophy of the brain (a qualitative decrease of brain parenchymal volume; expansion of brain hemisphere curves, expansion of ventricular system and thinning of the curves), leucoaraiosis/leukoencephalopathy (diffuse damage of the white matter due to chronic interstitial edema and disappearance of the myelin), lacunar foci of ischemia (<10 mm diameter lesions in *lenticulostriatum, thalamus* and areas of bridge-perforating arteries), brain infarctions (>10 mm diameter ischemic/gliotic lesions involving cortex, forebrain, main arterial pools and border zone areas).

When evaluating the DWI sequences, new focuses/areas of ischemia (identified by evaluating and comparing pre- and post-stenting images) were described indicating number, size (<10 mm and >10 mm), anatomic localization (forebrain, sub-forebrain, both structures), circulatory pool and laterality (same/opposite hemisphere to the location of the stent; brainstem; cerebellum).

The following distal protection systems against microembolism were used during the CAS procedure: (1) Filters: FilterWire EZ (manufactured by Boston Scientific Corporation); Emboshield NAV (Abbott Vascular), SpideRX (*EV3*), Defender (Medtronic), FiberNet Filter (Invatec-Medtronic), (2) Acclusion MoMa Baloon Protection System (Invatec-Medtronic).

Protection systems were applied for all the patients during CAS to whom MRI DWI was performed. In every third patient FilterWire EZ and MoMa protection system was applied (30.4% and 34.8%, respectively), Emboshield NAV was used for 15.2% of patients, and in every tenth patient (10.9%) Defender protection system was applied; FiberNet and SpideRX systems were applied for 6.5% and 2.2% of patients, respectively.

Statistical analysis

Data was processed with the *Statistical Package for Social Sciences* (*SPSS*) *v.13.0 for Windows*. Descriptive statistics of the quantitative data (symptoms) were calculated. Student t-test was applied for two groups for testing the hypothesis of parity of averages; dispersion ANOVA analysis was applied in presence of more than 2 groups. In case of small ranges, or varied dispersions, nonparametric (range) criteria were applied for group comparison: in case of 2 groups: Mann–Whitney test; in case of more than 2 groups: Kruskal–Wallis test. Exact and asymptomatic χ^2 criteria were applied for testing the hypothesis of inter-dependency of the symptoms.

Results

Sixty-five (30.8%) patients underwent MRI DWI investigations. MRI DWI revealed new ischemic focuses in 46 (70.8%) patients after CAS procedures. Clinical symptoms of brain lesions were diagnosed only for 2 out of 46 (4.3%) patients evaluated by a neurologist.

Among 46 patients diagnosed with new acute ischemic brain lesions during MRI, 54.3% had aortic arch type 1; 32.6% had aortic arch type 2 and 13.1% had aortic arch type 3, respectively. 54.3% subjects had damage of the left carotid artery; 43.5% subjects had damage of the right carotid artery; and 2.2% had damage of both carotid arteries.

MRI DWI showed that 46 (70.8%) patients had new ischemic foci in the brain after CAS procedures, from which focal damage of the brain was diagnosed in 36 (78.3%) CAS cases; linear damage of the brain – in 9 (19.6%) patients; ipsilateral damage of the brain – in 37 (80.4%) patients; bilateral damage of the brain – in 16 (34.8%) patients, 38 (82.6%) patients were diagnosed with forebrain damage; 4 (8.7%) patients – with damage of brainstem; 5 (10.9%) patients – with cerebellum damage (Figure 1).

Relationship between the ischemic focuses (MRI DWI) after CAS procedure (%) and the type of the aortic arch is presented in Table 1. Focal damage of the brain was significantly less fre-

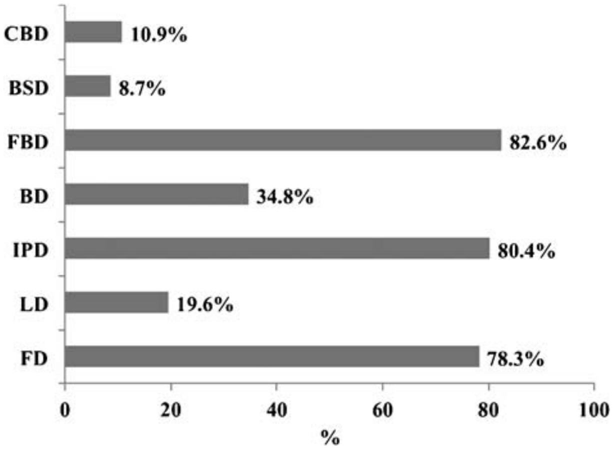

Figure 1. The rate (%) of brain ischemic focuses on MRI DWI for patients who underwent CAS procedure. BD – bilateral damage; BSD – brainstem damage; CBD – cerebellum damage; FBD – forebrain damage; FD – focal damage; LD – linear (>10 mm) damage; IPD – ipsilateral damage.

Table 1.
Dependency between the ischemic focuses (MRI DWI) after CAS procedure (%) and the type of the aortic arch

Damage	Symptoms	Type of the aortic arch			Significance
		1	2	3	
Focal	None	36.0	6.7	0.0	$\chi2 = 6.658$
	Present	64.0	93.3	100.0	$lls = 2$
					$p = 0.036$
>10 mm linear damage	None	88.8	66.7	83.3	$\chi2 = 2.748$
	Present	12.0	33.3	16.7	$lls = 2$
					$p = 0.253$
Ipsilateral	None	32.0	6.7	0.0	$\chi2 = 5.502$
	Present	68.0	93.3	100.0	$lls = 2$
					$p = 0.064$
Bilateral	None	72.0	53.3	66.7	$\chi2 = 1.446$
	Present	28.0	46.7	33.3	$lls = 2$
					$p = 0.485$
Forebrain	None	24.0	13.3	0.0	$\chi2 = 2.195$
	Present	76.0	86.7	100.0	$lls = 2$
					$p = 0.334$
Brainstem	None	92.0	86.7	100.0	$\chi2 = 0.993$
	Present	8.0	13.3	0.0	$lls = 2$
					$p = 0.609$
Cerebellum	None	96.0	80.0	83.3	$\chi2 = 2.717$
	Present	4.0	20.0	16.7	$lls = 2$
					$p = 0.257$

quent only for aortic arch type 1, if compared with aortic arch type 2 and 3: 64.3%, 93.3%, and 100.0%, respectively ($p < 0.05$). No significant differences of other findings of brain damage depending on the type of aortic arch were revealed.

Dependency between the new ischemic focuses (MRI DWI) after CAS procedure (%) and the side of CAS damage is presented in Table 2. Analysis of the data showed no significant dependency between the side of CAS damage and the acute ischemic findings in the brain on MRI DWI investigation.

Dependency between the ischemic focuses (MRI DWI) after CAS procedure (%) and the type of the protection type is presented in Table 3. Analysis of the data revealed that the focal damage of the brain occurred least in those patients (28.6%) with Emboshield NAV protection type, if compared to other types of protection (71.4–100.0%). Linear >10 mm brain damage was less frequent when using FilterWire EZ, Emboshield NAV and SpideRX protection type. Ipsilateral brain damage occurred less when using Emboshield NAV protection type; bilateral damage occurred less when using FilterWire EZ, Emboshield NAV and SpideRX protection type. Damage of the forebrain during MRT DWI was diagnosed less often for patients with applied FilterWire EZ and Emboshield NAV protection types, if compared to other types of protection: 64.3%, 57.1% and 100.0%, respectively ($p < 0.05$). No significant impact of the type of protection on the frequency of damage of the cerebellum was observed.

Discussion

CAS is currently an acceptable and approved alternative method of treatment for high-risk patients. New technologies, better experience in stenting and new medicines available have significantly improved the results of stenting procedures in recent years. MRI DWI neuroimaging was used most often for the evaluation the early cerebral complications of CAS procedures and control thereof; this test allows quite precise diagnosis of the acute ischemic brain abnormalities [21]. Researchers applying MRI DWI test report 17.3% to 73.0% frequency rate of the silent asymptomatic embolic brain damage [22–27]. Individual researchers indicated significantly less

Table 2.
Relationship between the ischemic focuses (MRI DWI) after CAS procedure (%) and the side of CAS damage

Damage	Symptoms	Side of carotid artery damage			Significance
		Left side	Right side	Both sides	
Focal	None	20.0	20.0	100.0	$\chi2 = 3.680$
	Present	80.0	80.0	0.0	*lls* = 2
					$p = 0.159$
>10 mm linear damage	None	72.0	90.0	100.0	$\chi2 = 2.536$
	Present	28.0	10.0	0.0	*lls* = 2
					$p = 0.281$
Ipsilateral	None	16.0	20.0	100.0	$\chi2 = 4.315$
	Present	84.0	80.0	0.0	*lls* = 2
					$p = 0.116$
Bilateral	None	60.0	70.0	100.0	$\chi2 = 1.035$
	Present	40.0	30.0	0.0	*lls* = 2
					$p = 0.596$
Forebrain	None	16.0	15.0	100.0	$\chi2 = 4.863$
	Present	84.0	85.0	0.0	*lls* = 2
					$p = 0.088$
Brainstem	None	92.0	90.0	100.0	$\chi2 = 0.153$
	Present	8.0	10.0	0.0	*lls* = 2
					$p = 0.926$
Cerebellum	None	88.0	90.0	100.0	$\chi2 = 0.171$
	Present	12.0	10.0	0.0	*lls* = 2
					$p = 0.918$

frequent acute brain lesions diagnosed by MRI DWI after CAS procedure [28]. MRI DWI data of our study showed focal brain damage in 78.3% cases; linear brain damage in 19.6% patients; ipsilateral brain damage in 80.4% patients; bilateral brain damage in 34.8%; forebrain damage in 82.6% patients; brainstem damage was diagnosed in 8.7% patents; 10.9% of patients were diagnosed with cerebellum damage.

Analysis of the data revealed no significant connection between the side of CAS and the laterality of ischemic brain lesions on MRI DWI test. Other authors present similar data after the evaluation of CAS complications with MRI test [8, 29–32].

Type of the aortic arch has a great significance for the more frequent development of CAS complications also. Our research data shows that focal damage of the brain was significantly rarer for only aortic arch type 1, if compared with aortic arch type 2 and 3: 64.3%, 93.3% and 100.0%, respectively. No significant differences of other findings of brain damage depending on the type of aortic arch were revealed. Aortic arch type 3 is less favourable for CAS procedures, leading to increased risk of microembolism; therefore specific systems of protection must be applied and the duration of the procedure itself is also increased. Moreover, it is less favorable for older patients. Other authors present similar data after evaluation of the impact of specific types of the aortic arch on elder patients [33,34].

Correct selection of the type of the protection system during CAS seems of great importance for the successful performance of the procedure and for reduction of cerebral ischemic complications. Damage of the brain must be avoided during CAS procedure. Analysis of the MRI DWI data revealed that the focal damage of the brain occurred less in those patients (28.6%) with Emboshield NAV protection type if compared to other types of protection (71.4–100.0%). Linear >10 mm brain damage was less frequent when using FilterWire EZ, Emboshield NAV and SpideRX protection type. Ipsilateral brain damage occurred less when using Emboshield NAV protection type; bi-lateral damage occurred less when using FilterWire EZ, Emboshield NAV and SpideRX protection type. Damage of the forebrain during MRI DWI was diagnosed less often for patients with applied FilterWire EZ and Emboshield NAV protection types, if compared to other types of protection:

Table 3.
Dependency between the ischemic focuses (MRI DWI) after CAS procedure (%) and the type of protection

Damage	Symptom	Type of protection						Significance
		FilterWire EZ Boston	MoMa	Emboshield NAV	Defender	FiberNet	SpideRX	
Focal	None	28.6	6.3	71.4	0.0	0.0	0.0	$\chi 2 = 15.299$
	Present	71.4	93.8	28.6	100.0	100.0	100.0	*lls* = 5
								$p = 0.009$
>10 mm linear damage	None	100.0	75.0	100.0	40.0	33.3	100.0	$\chi 2 = 15.075$
	Present	0.0	25.0	0.0	60.0	66.7	0.0	*lls* = 5
								$p = 0.01$
Ipsilateral	None	28.6	6.3	57.1	0.0	0.0	0.0	$\chi 2 = 10.994$
	Present	71.4	93.8	42.9	100.0	100.0	100.0	*lls* = 5
								$p = 0.05$
Bilateral	None	85.7	50.0	100.0	20.0	33.3	100.0	$\chi 2 = 14.344$
	Present	14.3	50.0	0.0	80.0	66.7	0.0	*lls* = 5
								$p = 0.014$
Forebrain	None	35.7	0.0	42.9	0.0	0.0	0.0	$\chi 2 = 11.695$
	Present	64.3	100.0	57.1	100.0	100.0	100.0	*lls* = 5
								$p = 0.039$
Brainstem	None	92.9	93.8	85.7	100.0	66.7	100.0	$\chi 2 = 3.304$
	Present	7.1	6.3	14.3	0.0	33.3	0.0	*lls* = 5
								$p = 0.653$
Cerebellum	None	100.0	75.0	100.0	80.0	100.0	100.0	$\chi 2 = 6.777$
	Present	0.0	25.0	0.0	20.0	0.0	0.0	*lls* = 5
								$p = 0.238$

64.3%, 57.1% and 100.0%, respectively. No significant impact of the type of protection on the frequency of damage of the cerebellum was observed. Data from our research corresponds to the data received by l other researchers evaluating the application of protection systems during CAS procedure by MRI DWI testing [35,36]. Other researchers also present similar data [25,37–39].

Likelihood of brain damage after CAS procedure depends on various factors, as data from various researchers indicate. Some investigators have shown the connections of early post procedural brain ischemic abnormalities with male gender [32,40], others – with older age [41], yet others – with concomitant illnesses such as ischemic cardiac disease or diabetes [42], with certain peculiarities of anatomy and physiology of the body and the type of the aortic arch [33,34], and also with such risk factors as overweight/obesity, dyslipidemia and smoking [39,43]. Results of our study confirm other researchers' findings that the type of the aortic arch and application of certain systems of protection during the CAS procedure may determine worse early results after the CAS procedure and a more frequent worse outcome [44]. Differences from the results obtained by other studies may also be due to rather small amount of CAS cases and short follow-up term of such cases. The strong side of the present study is the fact that all the CAS procedures were performed by the same researcher, using standard intervention procedures and tools manufactured by the same manufacturers.

Conclusions

1. Most frequent findings by MRI after CAS procedures were focal, ipsilateral and forebrain damage (about 80%), but less than 5% patients had clinical symptoms. In the case of aortic arch type 1 focal ischemic damage of the brain was significantly less frequent, then in aortic arch type 2 and 3. No significant interrelation between other findings of brain damage and the type of an aortic arch were found. No significant connection between the side of CAS damage and the laterality and location of brain damage was observed.
2. The localization and extent of brain damage was associated with the type of protection systems that have been used. Analysis of the

MRI testing data revealed that the focal damage of the brain occurred less in those patients (28.6%) with Emboshield NAV protection type. MRI DWI test data shows that linear > 10 mm brain damage was less frequent when using FilterWire EZ, Emboshield NAV and SpideRX protection type.

3. Ipsilateral ischemic brain damage also occurred less when using Emboshield NAV protection type; bilateral damage occurred less when using FilterWire EZ, Emboshield NAV and SpideRX protection type. Ischemic forebrain damage revealed by MRI DWI test was also diagnosed less often in patients, for whom protection type FilterWire EZ and Emboshield NAV was applied.

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