Karen A. Büsing, MD
Carla Schulte-Sasse
Stephan Flüchter, MD
Tim Süselbeck, MD
Karl K. Haase, MD
Wolfgang Neff, MD
Jochen G. Hirsch, PhD
Martin Borggrefe, MD
Christoph Düber, MD

Published online before print
10.1148/radiol.2351040117
Radiology 2005; 235:177–183

Abbreviation:
DW = diffusion-weighted

[1] From the Departments of Clinical Radiology (K.A.B., C.S.S., W.N., C.D.), Cardiology (S.F., T.S., K.K.H., M.B.), and Neurology (J.G.H.), University Hospital Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1–3, 68167 Mannheim, Germany. Received January 30, 2004; revision requested April 12; revision received May 28; accepted June 28. Supported in part by a junior research grant from the University of Heidelberg. **Address correspondence to** K.A.B. (e-mail: *karen.buesing@rad.ma.uni-heidelberg.de*).

Authors stated no financial relationship to disclose.

Author contributions:
Guarantors of integrity of entire study, K.A.B., W.N., K.K.H., C.D., M.B.; study concepts and design, K.A.B., W.N., K.K.H., C.D.; literature research, K.A.B., C.S.S., S.F., T.S.; clinical studies, K.A.B., C.S.S., S.F.; data acquisition, K.A.B., C.S.S., S.F., J.G.H.; data analysis/interpretation, K.A.B., C.S.S., W.N., S.F., T.S.; statistical analysis, C.S.S., T.S.; manuscript preparation, definition of intellectual content, and editing, K.A.B., W.N., T.S.; manuscript revision/review, W.N., T.S., M.B., K.K.H., J.G.H.; manuscript final version approval, W.N., T.S., M.B., K.K.H., C.D., J.G.H.

Cerebral Infarction: Incidence and Risk Factors after Diagnostic and Interventional Cardiac Catheterization—Prospective Evaluation at Diffusion-weighted MR Imaging[1]

PURPOSE: To prospectively evaluate incidence of clinically silent and clinically apparent embolic cerebral infarction following diagnostic and interventional coronary angiography and associated risk factors.

MATERIALS AND METHODS: Written informed consent was obtained from all patients, and the study was approved by the research ethics committee of University of Heidelberg, Germany. Fifty-two patients, including 37 men (mean age, 66.1 years ± 11.9 [standard deviation]) and 15 women (mean age, 65.3 years ± 10.3), undergoing elective cardiac catheterization were examined 3–26 hours (mean, 15.3 hours ± 6) before and 12–48 hours (mean, 25.9 hours ± 10.4) after cardiac catheterization. Magnetic resonance imaging protocol included isotropic and anisotropic diffusion-weighted single-shot echo-planar sequences. T2-weighted turbo spin-echo and T1-weighted spin-echo sequences also were performed. Apparent diffusion coefficient maps were calculated to exclude false-positive reading results on diffusion-weighted images because of T2 shine-through effect. Images were assessed by two experienced radiologists blinded to clinical data. Cardiac catheterization was performed by 11 experienced cardiologists to exclude operator-related risk. A neurologic examination according to the National Institutes of Health Stroke Scale and Barthel index was performed by a senior cardiologist before acquisition of each image. Sixteen clinical and angiographic variables were analyzed with univariate analysis for ability to predict occurrence of cerebral infarction.

RESULTS: No embolic cerebral lesions could be detected at diffusion-weighted imaging before catheterization. After coronary angiography, seven (15%) of 48 patients demonstrated nine focal cerebral infarcts affecting anterior and posterior circulation. Patients remained asymptomatic. Of all tested variables, only duration of the procedure was identified as an independent predictor of occurrence of cerebral infarction ($P < .05$).

CONCLUSION: In this prospective study, asymptomatic cerebral infarction following cardiac catheterization occurred in 15% of patients in whom duration of the procedure was significantly longer than in those without infarction ($P = .017$).

Cardiac catheterization has been established as the standard for evaluation of coronary artery disease (1). Furthermore, percutaneous coronary interventions have been developed as an alternative to medical and surgical treatment (2). Cardiac catheterization is generally regarded as safe (3–6). It is, however, an invasive diagnostic and therapeutic procedure

involving mechanical stress to the arterial vascular system caused by catheter manipulation and to the aortic valve, if levocardiography (which is evaluation of left ventricular dynamics by means of retrograde catheter passage) is performed. Thus, there has always been concern regarding the risk of cerebral embolism. Retrospective analysis of as many as 20 000 patients revealed that clinically apparent cerebral infarction only occurs in 0.11%–0.38% of these individuals (7–9). Nevertheless, the incidence of asymptomatic cerebral infarctions may be more frequent. For example, after selective cerebral angiography, clinically inapparent infarction has been described in 18.5%–23% of patients (10,11).

The origins of cerebral emboli associated with catheterization seem to be varied. Among those suggested are loosened atherosclerotic plaque caused by catheter manipulation, thrombus formation at the catheter (7,10,11), air embolism (12,13), and—in rare cases—foreign material possibly from the catheter or the guidewire (14). Omran et al (15) showed that retrograde passage of the catheter through the aortic valve for levocardiography in patients with aortic stenosis represents a highly marked risk factor for embolic cerebral lesions. In addition, Segal et al (7) found a slight increase in stroke in a large retrospective analysis of patients who underwent therapeutic cardiac catheterization, such as that for angioplasty and stent implantation.

With respect to coronary angiography, neither the overall incidence of cerebral embolic lesions, including those in clinically inapparent cases, nor the risk of incidence of these lesions after revascularization procedures has been evaluated in a nonselected cohort of patients.

At present, diffusion-weighted (DW) magnetic resonance (MR) imaging is the most sensitive tool for early detection of cerebral infarction (16–19). DW MR imaging provides image contrast based on random translational motion of water molecules, which is substantially altered by acute cerebral ischemia (20). The addition of this method to conventional MR imaging sequences makes it possible to detect very small and hyperacute infarction at almost any anatomic location within the brain hemispheres, the brainstem, and the cerebellum. DW MR imaging has been used to detect structural damage to the brain caused by silent embolism during cerebral and coronary angiography (10,11,15), as well as during surgical and endovascular revascularization procedures in the carotid artery (21–24).

The aim of this study was to prospectively evaluate the incidence of clinically silent and clinically apparent cerebral infarction after diagnostic and interventional coronary angiography and the risk factors associated with the procedures.

MATERIALS AND METHODS

Study Population

From December 2001 to June 2002, 52 patients aged 18 years or older were included in our study. These patients included 37 men (mean age, 66.1 years ± 11.9 [standard deviation]) and 15 women (mean age, 65.3 years ± 10.3). All patients underwent cardiac catheterization for clinical indications such as evaluation of coronary artery disease or valvular dysfunction. Exclusion criteria were contraindications to MR imaging, a history of cerebral ischemia (stroke or transient ischemic attack within the past 3 months), acute coronary syndromes, unstable vital parameters, and pregnancy. Because of limited MR imaging capacity, we were not able to include more than two patients per week. Written informed consent was obtained from all patients, and the study was approved by the research ethics committee of the University of Heidelberg, Heidelberg, Germany.

Study Protocol

A medical history was documented in each patient before further investigations by senior cardiologists (T.S., K.K.H.). These cardiologists assessed cardiovascular risk factors, such as smoking, diabetes, hypertension, hyperlipidemia, and obesity, and preexisting cardiovascular abnormalities, such as arrhythmia, an ejection fraction of less than 35%, aortic valve stenosis, left ventricular aneurysm, and peripheral vascular disease of the second degree or greater. They were also trained to perform the neurologic assessment according to the National Institutes of Health Stroke Scale and the Barthel index before MR imaging. A neurologic complication of catheterization was defined as any increase in the National Institutes of Health Stroke Scale score.

All patients underwent cranial MR imaging with a 1.5-T MR unit (Magnetom Vision; Siemens, Erlangen, Germany) and a circular polarized head coil 3–26 hours (mean, 15.3 hours ± 6) before and 12–48 hours (mean, 25.9 hours ± 10.4) after cardiac catheterization. The imaging protocol included isotropic DW (diffusion weighting in three orthogonal directions and subsequent averaging) and direction-dependent DW (section-selection direction) single-shot echo-planar sequences (repetition time msec/echo time msec, 6000/100; matrix, 128 × 128, interpolated to 256 × 256; section thickness, 5 mm; and *b* values, 0, 500, and 1000 sec/mm^2). Isotropic diffusion weighting overcomes signal changes in diffusion weighting caused by anisotropic diffusion characteristics in white matter fibrous structures. Moreover, apparent diffusion coefficient maps were calculated to exclude false-positive reading results in the DW sequences caused by a T2 shine-through effect. In addition, T2-weighted turbo spin-echo MR imaging (2500/85; matrix, 260 × 512; flip angle, 180°; and section thickness, 5 mm) and T1-weighted spin-echo MR imaging (440/12; matrix, 169 × 256; flip angle, 70°; and section thickness, 5 mm) were performed. There were no adverse events during MR imaging.

Cardiac catheterization was performed by 11 cardiologists (including M.B., K.K.H., and T.S.), each with at least 5 years of experience in cardiac catheterization, with a femoral approach in all patients. The number of cardiologists involved was not restricted. In this way, operator-related risk could be minimized. Standard coronary angiography was performed in all patients with a 5-F catheter (Cordis; Johnson & Johnson, Miami, Fla) by using a guidewire (Scimed; Boston Scientific, New York, NY). A total of 2500 IU of heparin (Heparin-Natrium; Ratiopharm, Ulm, Germany) was given immediately after sheath insertion. As standard procedure, levocardiography was performed in all 52 patients after retrograde passage of a 5-F pigtail catheter. After levocardiography, the catheter was rapidly withdrawn from the left ventricle, with monitoring of the pressure gradient. After diagnostic catheterization, a 6- or 7-F catheter (Cordis; Johnson & Johnson) was used for percutaneous coronary interventions into the aortic root.

In all, 13 of 48 patients underwent further therapeutic interventions, such as stent implantation and/or balloon dilation, in addition to standard coronary angiography and levocardiography. We administered 5000 IU of heparin as a bolus before the procedure and then another bolus of 2500 IU of heparin during the procedure to maintain an activated clotting time of more than 250 seconds. A standard contrast medium (Ultravist; Schering, Berlin, Germany), 300 mg of iodine per milliliter, was used. For diagnostic angiography, sheaths were removed immediately after the procedure.

TABLE 1
Patient Characteristics with Imaging Results

Characteristic	Postprocedural MR Imaging Result		*P* Value
	Normal (*n* = 41)	New Lesion (*n* = 7)	
Patient risk factor			
Age (y)*	65 ± 11.2	70.9 ± 8.4	.327
Sex			
M	27 (66)	7 (100)	.089
F	14 (34)	0 (0)	. . .†
Previous myocardial infarction	18 (44)	2 (29)	.683
Previous stroke	5 (12)	2 (29)	.267
Cardiovascular risk factor			
Smoking	26 (63)	4 (57)	>.99
Diabetes	5 (12)	1 (14)	>.99
Hypertension	23 (56)	3 (43)	.687
Hyperlipidemia	27 (66)	2 (29)	.097
Obesity (body mass index >25)	28 (68)	3 (43)	.226

Note.—Values are numbers of patients, and numbers in parentheses are percentages unless otherwise indicated.
* Values are the mean ± standard deviation.
† The *P* value was not different from that for male patients (Fisher exact test).

In patients who underwent percutaneous coronary intervention, the sheaths were removed within 4–6 hours after the procedure. After stent implantation, patients received 100 mg of aspirin daily and 300 mg of clopidogrel bisulfate (Iscover; Bristol-Myers Squibb Pharma EEIG, Ickenham, England) as an initial dose, with a daily dose of 75 mg of clopidogrel thereafter for 4 weeks. Both fluoroscopy time and the total duration of the procedure were recorded. No complications were observed during the first 24 hours after cardiac catheterization.

Imaging Assessment

The presence of new focal diffusion abnormalities (areas of hyperintensity) on the postprocedural MR images was regarded as a positive indication of acute cytotoxic edema, most likely caused by a recent embolic infarction. All DW abnormalities were correlated with the findings on the T2- and T1-weighted MR images, as well as on the ADC map. T2-weighted images sometimes showed a corresponding area of hyperintensity, which reflected a beginning vasogenic edema (25). A signal intensity decrease, however, on ADC maps was required to exclude false-positive results caused by a T2 shine-through effect (25). T1-weighted MR images were acquired to reveal other intracranial abnormalities, such as necrosis caused by an old ischemic infarction. For all diffusion abnormalities, the size, vascular distribution, lobe, and area of the brain were determined. All MR images were assessed by two experienced radiologists (W.N., K.A.B., with 10 and 4 years of experience, respectively, in evaluation of cerebral MR images). They were blinded to the neurologic status and were unaware of the cardiac procedure performed. In case of dissent (one lesion in a patient with multiple infarctions), the examination findings were reviewed, and a decision was made with mutual agreement.

Statistical Analysis

For statistical analysis, the patients were classified into two groups, those with negative (normal) and those with positive (new lesion at DW imaging) postprocedural MR imaging results. For categorical variables (cardiovascular risk factors and disease, amount of contrast medium, fluoroscopy time, and duration of cardiac catheterization procedure), the Fisher exact test and the Mann-Whitney *U* test were used to evaluate the differences between the two groups of patients, those with and those without newly developed focal cerebral infarctions. Data analyses were performed by using statistical software (SAS for Windows, release 8.02; SAS Institute, Cary, NC). A difference with $P < .05$ was considered significant.

RESULTS

Final Study Population

In all, 52 patients were included in the study. Cardiac catheterization was performed in 51 patients. One patient was excluded from catheterization because of acute sinusitis revealed at MR imaging. Follow-up MR imaging was performed in 48 patients. The remaining three patients refused to undergo MR imaging after cardiac catheterization, mainly because of aggravated claustrophobia. Therefore, the data in 48 patients (mean age, 65.9 years ± 11; 34 men [mean age, 65.7 years ± 10.5] and 14 women [mean age, 66 years ± 12.3]) could be further analyzed statistically. The difference in mean age with respect to the patient's sex was of no statistical significance ($P > .99$).

Risk Factors

Inherent patient risk factors, such as age, sex, and history of cerebral or myocardial ischemia, and cardiovascular risk factors, such as smoking, diabetes, hypertension, hyperlipidemia, and obesity, did not differ in a statistically significant manner between patients with normal follow-up MR imaging findings and patients with new focal infarctions (Table 1). Furthermore, there was no relevant difference with regard to preexisting cardiovascular abnormalities (ie, arrhythmias, impaired ejection fraction < 35%, aortic valve stenosis, left ventricular aneurysm, or clinical signs of peripheral vascular disease of second degree or greater) (Table 2), nor did the amount of contrast medium administered differ significantly (162.9 mL ± 75.6 vs 220 mL ± 157.2; $P = .895$).

In our study population, there were only seven (16.7%) of 48 cases of aortic stenosis, including one in a patient with multifocal cerebral infarctions after cardiac catheterization. Excluding the patients with aortic valve stenosis from our group, however, did not change the results to any relevant extent, since, again, 15% (six of 41) of the patients had positive results.

MR Imaging

DW MR images did not show any abnormalities prior to cardiac catheterization in any of the 48 patients. On the postprocedural MR images, a total of nine new lesions on DW MR images were diagnosed in seven (15%) patients. Of the seven patients, four underwent cardiac catheterization for only diagnostic purposes. Two of the remaining three patients (including the patient with multiple cerebral lesions) underwent angioplasty and stent implantation, and one patient underwent additional angioplasty without stent implantation.

The location of abnormalities was consistent with an embolic pattern of lesions

in the distal vascular territory of small cortical, subcortical, or perforating vessels (Figs 1, 2). All diffusion abnormalities showed a corresponding signal intensity decrease on the ADC maps so that there were no false-positive measurements. In three of seven patients, we observed a corresponding area of hyperintensity on T2-weighted MR images, but no correlating signal change was seen on T1-weighted MR images. Six patients had a single lesion; in five of these patients, the lesion was situated in the territory of the middle cerebral artery, and in one patient, the lesion was in the territory of the posterior inferior cerebellar artery. One patient had multiple lesions; two were found in the territory of the right middle cerebral artery, and one, in the right posterior inferior cerebellar artery territory. There was no significant difference in regard to the location within the two hemispheres (five lesions were in the right hemisphere, compared with four in the left hemisphere; $P > .05$). Each lesion was less than 5 mm in diameter. We did not observe any diffuse alterations of signal intensity at DW MR imaging or in the pattern of watershed ischemia.

TABLE 2
Preexisting Cardiovascular Abnormalities

Abnormality	Postprocedural MR Imaging Result		
	Normal (n = 41)	New Lesion (n = 7)	P Value
Arrhythmia	6 (15)	1 (14)	>.99
Ejection fraction < 35%	3 (7)	1 (14)	.605
Aortic valve stenosis	7 (17)	1 (14)	>.99
Left ventricular aneurysm	2 (5)	1 (14)	.343
Peripheral vascular disease of second degree or greater	3 (7)	2 (29)	.148

Note.—Values are numbers of patients, and numbers in parentheses are percentages.

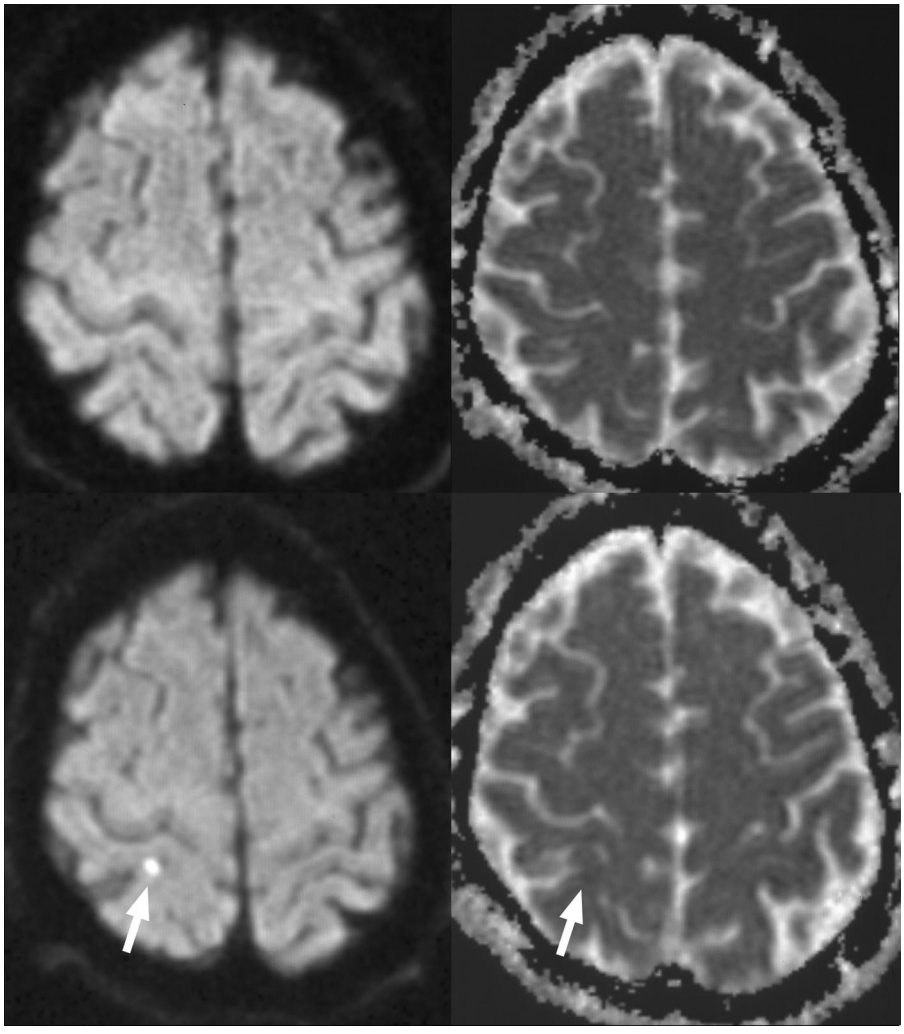

Figure 1. Images obtained in a 63-year-old man after diagnostic catheterization show a focal ischemic lesion (arrow) in the right parietal lobe. Left: Transverse DW MR images (6000/100; matrix, 128 × 128; section thickness, 5 mm; and b value, 1000 sec/mm^2). Right: Transverse apparent diffusion coefficient maps.

Postprocedural Neurologic Assessment

Findings in all postprocedural neurologic assessments were negative; that is, no clinical signs of neurologic diseases or disorders were apparent.

Catheterization Procedures

The statistical analysis of therapeutic cardiac catheterization (13 of 48 patients) versus purely diagnostic angiography (35 of 48 patients) revealed a slight but not statistically significant increased risk for the development of focal cerebral lesions: three (23%) of 13 patients for therapeutic catheterization and four (11%) of 34 patients for diagnostic catheterization (P = .37).

Fluoroscopy Time and Duration of Procedure

In regard to fluoroscopy time, there was no significant difference between patients with normal postprocedural MR imaging findings and those with a newly developed lesion (P = .148). Taking into account that fluoroscopy time for interventional coronary angiography was generally longer than was time for diagnostic angiography (12.4 minutes ± 8.3 vs 5.8 minutes ± 4.5), we further analyzed these two subgroups but were unable to determine any relevant difference (P = .554 [interventional] and P = .534 [diagnostic]; Table 3).

Considering the fact that a cogent correlation between fluoroscopy time and the overall duration of cardiac catheterization cannot be assumed, we also investigated a possible association between the total length of catheterization and the risk of development of cerebral lesions. This analysis revealed a highly significant correlation between the overall

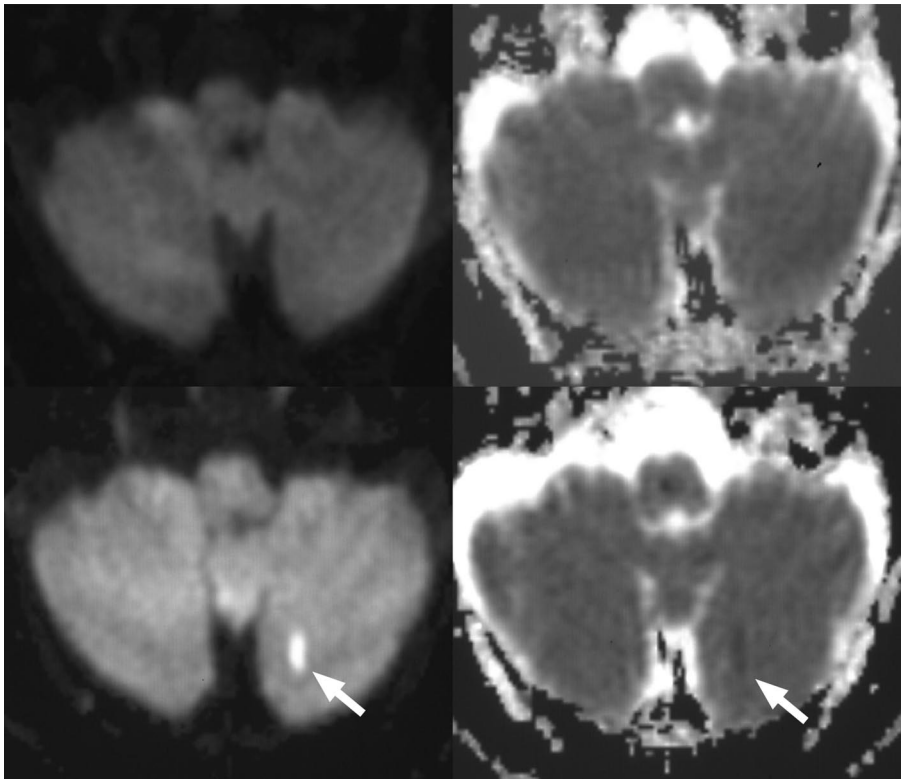

Figure 2. Images obtained in a 69-year-old woman after diagnostic catheterization and stent implantation show a focal ischemic lesion (arrow) in the left cerebellum. Left: Transverse DW MR images (6000/100; matrix, 128 × 128; section thickness, 5 mm; and *b* value, 1000 sec/mm^2). Right: Transverse apparent diffusion coefficient maps.

TABLE 3
Comparison of Total Duration and Fluoroscopy Times in Patients with Normal Results versus Patients with New Lesions at Postprocedural MR Imaging

Duration or Time and Procedures*	Postprocedural MR Imaging Result		*P* Value
	Normal	New Lesion	
All procedures			
Total duration	33.5 ± 18.7 (41)	55.9 ± 22.4 (7)	.017
Fluoroscopy time	7.4 ± 6.2 (41)	10.1 ± 5.9 (7)	.148
Diagnostic procedures			
Total duration	27.7 ± 16.2 (31)	41.5 ± 14.5 (4)	.063
Fluoroscopy time	5.8 ± 4.5 (31)	6.6 ± 4.0 (4)	.534
Interventional procedures			
Total duration	51.6 ± 14.4 (10)	75 ± 15.0 (3)	.045
Fluoroscopy time	12.4 ± 8.3 (10)	14.9 ± 4.6 (3)	.554

Note.—Values are the mean ± standard deviation. Numbers in parentheses are numbers of patients.

* In all entries, procedures are cardiac catheterization procedures.

duration of the catheterization and the development of new ischemic cerebral lesions. For the entire study population, there was a statistically significant difference ($P = .017$). Again, we took into account that the overall duration of catheterization was longer in patients undergoing interventional procedures than in those undergoing diagnostic procedures (51.6 minutes ± 14.4 vs 27.7 minutes ± 16.2), but a separate analysis of these subgroups yielded comparable results ($P = .045$ [interventional] and $P = .063$ [diagnostic]).

Operators

A separate analysis in regard to the 11 cardiologists involved did not reveal any significant operator-related risk for development of cerebral lesions at postprocedural DW imaging ($P > .05$).

DISCUSSION

With DW MR imaging, we analyzed the incidence of cerebral infarction after coronary angiography. In a nonselected group of 48 patients who were undergoing diagnostic and interventional cardiac catheterization, seven (15%) patients developed nine focal ischemic lesions, none of which were clinically apparent. Therefore, the rate of asymptomatic cerebral infarction after cardiac catheterization seems to be about 10-fold higher than it is for clinically apparent cerebral lesions (0.11%–0.38%) (7–9). In fact, in our study population, the rate of cerebral infarction is almost as high as it is in patients who undergo angiography of the brain-supplying arteries (15% vs 18.5%–23%) (10,11). With respect to the fact that there is no catheter manipulation in the carotid arteries during cardiac catheterization, the data strongly indicate that there are important sources of emboli other than loosening of atherosclerotic material from the carotid artery caused by catheter manipulations, as suggested in cases of cerebral angiography (10,11).

Among all clinical and angiographic variables tested within the present study population, however, no potential source of or risk factors for these cerebral emboli could be identified, since endovascular interventions, cardiovascular risk factors, and underlying cardiovascular abnormalities had no significant effect.

Looking at coronary interventions, Segal et al (7) found a slight increase in clinically apparent cerebral ischemia in a retrospective analysis of patients who were undergoing stent implantation and/or angioplasty. With respect to clinically inapparent lesions, we could confirm these findings (11% in diagnostic and 23% in therapeutic cardiac catheterization [$P = .37$]). Still, it must be assumed that different or more important sources of emboli other than coronary interventions are involved. These results, however, would have to be interpreted in consideration of a weaker statistical power that was due to the small sample size, particularly in the interventional subgroup.

Jackson et al (26) found that hypertension, age older than 60 years, peripheral vascular disease, and either nonelective procedures or those involving angioplasty all independently increased the

overall risk of complications from cardiac catheterization. In addition, there was a dose-response relationship between risk and number of risk factors: The risk of a complication was greater than 10% in patients with more than three risk factors. Corresponding to the data from Omran et al (15), our data did not indicate that these risk factors played a marked role with respect to the patient's isolated risk to develop focal ischemic lesions. This finding leads us to the conclusion that the risk factors identified by Jackson et al only seem to affect the overall risk for complications during cardiac catheterization (eg, pericardial effusion and pulmonary embolism) but are not specifically relevant with regard to cerebral embolism.

In this prospective study, only procedural time could be identified as an independent predictor of the occurrence of cerebral infarction ($P < .05$). We took into consideration that interventional coronary catheterization usually takes longer than a diagnostic procedure and that the duration of a procedure may be operator dependent. A separate analysis of these criteria did not reveal any statistically significant difference; thus, the duration itself counts as an independent risk factor. We could not confirm the results from Omran et al (15) and Bendszus et al (11), who independently found a highly significant correlation between fluoroscopy time and cerebral lesions ($P < .01$). The total duration of catheterization, however, represents a suitable parameter with which to measure the overall influence of catheter manipulation. It includes additional periods of time while the catheter, which acts as a potential embolic source because it may lead to thrombus formation or which affects the vessel wall during manipulations, is being placed in the patient's vascular system.

In addition, as assumed by other authors, plaque broken off from the ascending aorta or the aortic arch, blood clots from the tip of the catheter (11,27), and an air embolism must be taken into consideration (12,13). It appears likely that the risk of thrombus formation or of vascular plaque mobilization increases with the duration of the procedure.

Moreover, if levocardiography is performed, the retrograde passage of the catheter through the aortic valve could serve as a source of an embolism (28). In patients with aortic stenosis, Omran et al (15) revealed cerebral ischemic lesions in 22% of 101 patients, including 3% of clinically apparent cases. These data confirm the results of a retrospective study by Bartsch et al (29), who found symptomatic cerebral infarcts after coronary angiography in 0.9% of 457 patients with aortic stenosis. In our study, there were only seven patients with aortic stenosis (seven [15%] of 48), and in one of these seven patients, multifocal cerebral infarctions occurred after cardiac catheterization. Although this sample of patients is too small for a valid statistical analysis, to a certain extent, the results of this analysis support the results of Omran et al (15).

Excluding the patients with aortic valve stenosis from our group did not change the results to any relevant extent (again, results in 15% of the patients were positive); thus, these data support the relevance of additional potential embolic sources mentioned previously.

Omran et al (15) also analyzed a control group ($n = 32$) of patients without aortic valve stenosis who were undergoing coronary angiography and levocardiography. In many ways, this cohort appears comparable to the group of patients in this study. In contrast to our results, however, their analysis revealed that none of the controls demonstrated new lesions at DW MR imaging after cardiac catheterization. A closer analysis did not reveal any decisive differences between the two groups in terms of demographic data, patient treatment (especially during catheterization), or data analysis. All our catheterization procedures were carried out at a high-volume center, where more than 2500 diagnostic and 750 interventional procedures are performed per year, so a lack of qualification can be largely excluded. Differences in the interpretation of the MR images seem to be very unlikely, too, since DW MR imaging has been an established routine sequence for diagnosis of infarcted brain tissue for some years now, and all images were evaluated by experienced radiologists.

Therefore, these data confirm that cardiac catheterization can be considered a safe procedure with respect to severe or life-threatening complications but that it bears a surprisingly high risk for silent focal cerebral infarction, even in patients without degenerative aortic valve stenosis. Thus, other embolic sources appear to have an important influence, too.

In our sample, all lesions were either located in noneloquent brain areas or were too small to be clinically apparent. When lesions affect more areas of the brain, such as the motor cortex, that are susceptible to structural damage, however, they could produce severe clinical sequelae. Clinically manifest neurologic deficits after angiography represent, therefore, only a part of the total risk of structural brain damage, and the overall risk of structural brain damage has been grossly underestimated. So far, the long-term effect of such lesions has not been investigated, but there are indications that they may lead to impaired cognitive function (27,30–32).

Our findings in a nonselected cohort of patients imply that the safety of coronary catheterization still needs to be improved and that patients may benefit from a reduction of the overall duration of the procedure. DW MR imaging can be used to monitor the effects of this and other procedural changes.

With respect to the evaluation of cerebral embolic infarction after cardiac catheterization, the number of patients is sufficient to give a first impression of a potentially underestimated problem. In particular, the evaluation of potential risk factors requires a much larger cohort of patients in order to reach a decisive difference in statistical power. Therefore, the statistical basis of the present results is weak. To carry out such a large study is hardly feasible and practical in a single department; however, the present underlying data could now potentially serve as a baseline for a multicenter study.

Previous investigators demonstrated that the diagnostic value of levocardiography is in general no greater than that of transthoracic and transesophageal echocardiography (33–36). Furthermore, particularly in patients with aortic valve stenosis, the time for retrograde passage of the valve can be as long as 30 minutes or longer and may well present a highly significant risk for further ischemic cerebral lesions (15). Therefore, a possible method for reducing the length of the procedure would be to exclude levocardiography from routine cardiac catheterization. DW MR imaging can be used to monitor the effects of this and other procedural changes.

References

1. Kopp AF. Angio-CT: heart and coronary arteries. Eur J Radiol 2003; 45(suppl 1): S32–S36.
2. SoS Investigators. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. Lancet 2002; 360:965–970.
3. Heuser RR. Outpatient coronary angiography: indications, safety, and complication rates. Herz 1998; 23:21–26.
4. Sabri N. Complications of cardiac cathe-

terization, coronary angiography, and coronary interventions. J Invasive Cardiol 1994; 6:300–305.
5. de Bono D. Complications of diagnostic cardiac catheterisation: results from 34,041 patients in the United Kingdom confidential enquiry into cardiac catheter complications—the Joint Audit Committee of the British Cardiac Society and Royal College of Physicians of London. Br Heart J 1993; 70:297–300.
6. Bernardes L, Ramos JM, Quininha J, Figueiredo L, Goncalves JM, Rato JA. The complications associated with the performance of heart catheterizations (diagnostic and therapeutic): the results in the Hemodynamics Laboratory of Hospital de Santa Marta. Rev Port Cardiol 1993; 12: 851–856, 805. [Portuguese]
7. Segal AZ, Abernethy WB, Palacios IF, Be-Lue R, Rordorf G. Stroke as a complication of cardiac catheterization: risk factors and clinical features. Neurology 2001; 56:975–977.
8. Fuchs S, Stabile E, Kinnaird TD, et al. Stroke complicating percutaneous coronary interventions: incidence, predictors, and prognostic implications. Circulation 2002; 106:86–91.
9. Leker RR, Pollak A, Abramsky O, Ben-Hur T. Abundance of left hemispheric embolic strokes complicating coronary angiography and PTCA. J Neurol Neurosurg Psychiatry 1999; 66:116–117.
10. Hahnel S, Bender J, Jansen O, et al. Clinically silent cerebral embolisms after cerebral catheter angiography. Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 2001; 173:300–305. [German]
11. Bendszus M, Koltzenburg M, Burger R, Warmuth-Metz M, Hofmann E, Solymosi L. Silent embolism in diagnostic cerebral angiography and neurointerventional procedures: a prospective study. Lancet 1999; 354:1594–1597.
12. Wijman CA, Kase CS, Jacobs AK, Whitehead RE. Cerebral air embolism as a cause of stroke during cardiac catheterization. Neurology 1998; 51:318–319.
13. Stygall J, Kong R, Walker JM, Hardman SM, Harrison MJ, Newman SP. Cerebral microembolism detected by transcranial Doppler during cardiac procedures. Stroke 2000; 31:2508–2510.
14. Jassal DS, Fast MD, McGinn G. Multifocal brain MRI hypointensities secondary to cardiac catheterization. Neurology 2000; 54:2023–2024.
15. Omran H, Schmidt H, Hackenbroch M, et al. Silent and apparent cerebral embolism after retrograde catheterisation of the aortic valve in valvular stenosis: a prospective, randomised study. Lancet 2003; 361: 1241–1246.
16. Fiebach J, Jansen O, Schellinger P, et al. Comparison of CT with diffusion-weighted MRI in patients with hyperacute stroke. Neuroradiology 2001; 43:628–632.
17. Fiebach J, Schellinger P, Jansen O, et al. CT and diffusion-weighted MR imaging (DWI) in randomized order: DWI results in higher accuracy and lower interrater variability in the diagnosis of hyperacute ischemic stroke. Stroke 2002; 33:2206–2210.
18. Beauchamp NJ Jr, Barker PB, Wang PY, van Zijl PC. Imaging of acute cerebral ischemia. Radiology 1999; 212:307–324.
19. Burdette JH, Ricci PE, Petitti N, Elster AD. Cerebral infarction: time course of signal intensity changes on diffusion-weighted MR images. AJR Am J Roentgenol 1998; 171:791–795.
20. Fiebach JB, Schellinger PD, Sartor K, Heiland S, Warach S, Hacke W. Stroke MRI. Darmstadt, Germany: Steinkopff-Verlag, 2003.
21. Jaeger HJ, Mathias KD, Drescher R, et al. Diffusion-weighted MR imaging after angioplasty or angioplasty plus stenting of arteries supplying the brain. AJNR Am J Neuroradiol 2001; 22:1251–1259.
22. Tomczak R, Wunderlich A, Liewald F, Stuber G, Gorich J. Diffusion-weighted MRI: detection of cerebral ischemia before and after carotid thromboendarterectomy. J Comput Assist Tomogr 2001; 25:247–250.
23. Lovblad KO, Pluschke W, Remonda L, et al. Diffusion-weighted MRI for monitoring neurovascular interventions. Neuroradiology 2000; 42:134–138.
24. Wityk RJ, Goldsborough MA, Hillis A, et al. Diffusion- and perfusion-weighted brain magnetic resonance imaging in patients with neurologic complications after cardiac surgery. Arch Neurol 2001; 58: 571–576.
25. Fiebach JB, Schellinger PD. Modern magnetic resonance techniques with stroke. Nervenarzt 2002; 73:104–117. [German]
26. Jackson JL, Meyer GS, Pettit T. Complications from cardiac catheterization: analysis of a military database. Mil Med 2000; 165:298–301.
27. Moody DM, Bell MA, Challa VR, Johnston WE, Prough DS. Brain microemboli during cardiac surgery or aortography. Ann Neurol 1990; 28:477–486.
28. Kapila A, Hart R. Calcific cerebral emboli and aortic stenosis: detection of computed tomography. Stroke 1986; 17:619–621.
29. Bartsch B, Haase KK, Voelker W, Schobel WA, Karsch KR. Risk of invasive diagnosis with retrograde catheterization of the left ventricle in patients with acquired aortic valve stenosis. Z Kardiol 1999; 88:255–260. [German]
30. Fukutake T, Akada K, Ito S, Okuda T, Ueki Y. Severe personality changes after unilateral left paramedian thalamic infarct. Eur Neurol 2002; 47:156–160.
31. Desmond DW. Cognition and white matter lesions. Cerebrovasc Dis 2002; 13(suppl 2):53–57.
32. Van Zandvoort MJ, De Haan EH, Kappelle LJ. Chronic cognitive disturbances after a single supratentorial lacunar infarct. Neuropsychiatry Neuropsychol Behav Neurol 2001; 14:98–102.
33. Yeager M, Yock PG, Popp RL. Comparison of Doppler-derived pressure gradient to that determined at cardiac catheterization in adults with aortic valve stenosis: implications for management. Am J Cardiol 1986; 57:644–648.
34. Otto CM. Doppler echocardiographic evaluation of aortic and mitral stenoses. Echocardiography 1999; 16:675–676.
35. Hoffmann R, Flachskampf FA, Hanrath P. Planimetry of orifice area in aortic stenosis using multiplane transesophageal echocardiography. J Am Coll Cardiol 1993; 22:529–534.
36. Tardif JC, Rodrigues AG, Hardy JF, et al. Simultaneous determination of aortic valve area by the Gorlin formula and by transesophageal echocardiography under different transvalvular flow conditions: evidence that anatomic aortic valve area does not change with variations in flow in aortic stenosis. J Am Coll Cardiol 1997; 29:1296–1302.