Complications of Diagnostic Cerebral Angiography: Evaluation of 19 826 Consecutive Patients[1]

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Purpose: To retrospectively evaluate the complications of diagnostic cerebral catheter angiography in 19 826 consecutive patients.

Materials and Methods: This HIPAA-compliant study had institutional review board approval, with waiver of informed consent. Demographic, procedural, and complication data in 19 826 consecutive patients undergoing diagnostic cerebral angiography at one institution from 1981 through 2003 were retrospectively reviewed. Neurologic, systemic, and local complications were recorded on the basis of clinical follow-up results after each angiographic examination. Events that occurred within 24 hours of angiography were considered to be complications of the procedure. Multivariable analysis was employed to identify patient and procedural factors significantly associated with neurologic complications.

Results: Neurologic complications occurred in 522 examinations (2.63%), and 27 of these (0.14%) were strokes with permanent disability. Twelve deaths occurred (0.06%). Access-site hematoma was the most common complication overall (4.2%). Factors independently associated with an increased risk of neurologic complication included the indication of atherosclerotic cerebrovascular disease (odds ratio [OR], 2.494), the indication of subarachnoid hemorrhage (OR, 2.523), and the comorbidity of frequent transient ischemic attack (OR, 1.674). Factors independently associated with a decreased risk of neurologic complication were increasing chronologic year in which the procedure was performed (OR, 0.659 per 5-year interval) and involvement of a trainee in the procedure (OR, 0.710).

Conclusion: In this review, diagnostic catheter cerebral angiography was found to have relatively low complication rates.

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Cerebral angiography has historically been central in the diagnosis, planning of treatment, and treatment of many central nervous system diseases. However, it is an invasive test with potentially severe complications, and the choice of an imaging test in the work-up of central nervous system disease should be accompanied by an accurate assessment of its complication risks.

Estimates of the complication rates of cerebral angiography published in approximately the past 20 years have been based on limited patient numbers (1–5). The largest of these referenced studies was based on 2899 consecutive examinations, and its authors also provide a concise summary of other published literature on cerebral angiography complications (4). A meta-analysis has been performed, combining data from 3517 patients (6). The purpose of our study was to retrospectively evaluate the complications of diagnostic catheter cerebral angiography on the basis of data in 19 826 consecutive patients.

Materials and Methods

Our Health Insurance Portability and Accountability Act–compliant study was approved by the institutional review board. Informed consent was waived by our institutional review board because we included only those patients who had previously provided authorization for use of their medical records for research. We retrospectively evaluated prospectively completed data forms for 23 416 consecutive diagnostic cerebral angiography examinations that were performed in 19 826 patients at our tertiary-quaternary medical center from 1981 through 2003. All patients undergoing diagnostic cerebral angiography in this period were included—both inpatients and outpatients. Interventional or therapeutic procedures, venography, and spinal angiography were not included.

Of these 23 416 examinations, 529 were associated with neurologic complications in 522 patients. For these 522 patients, only their first examination with a neurologic complication was included in the data set. For patients without a neurologic complication, only their first examination was included in the data set. The study data set then consisted of 19 826 examinations in 19 826 patients. These data included the first 1517 procedures, reported in 1984, in our institution (3), and the data sheets and methods of analysis are similar to those described in the previous publication. At our institution, nearly all patients referred for cerebral angiography have been evaluated by staff members of the neurology or neurosurgery services before the procedure.

Angiography Procedure

Information regarding the use of moderate sedation was not included in the data sheets, so exact tabulation of the number of patients receiving moderate sedation was not possible. However, from knowledge of general practice guidelines at our institution, most patients in the study period received moderate sedation, administered either by a radiology nurse or by the anesthesiology service, with intraprocedural cardiovascular monitoring. Cerebral angiography was performed by a staff neuroradiologist or by a resident physician or fellow under the direct supervision of a staff neuroradiologist. The angiographic technique has remained relatively unchanged over time, except that catheters and guidewires have been updated. Commonly used catheters have been 5-F 45° hockey stick–shaped, Simmons curve, vertebral, and pigtail catheters (the latter for aortic arch injections). A continuous catheter flush system with heparinized saline has been employed in our institution since 1990. The replacement of manual subtraction angiography by digital subtraction angiography began at our institution in 1993, and this transition was mostly completed by 1997.

Regarding the use of intravenous heparin boluses during angiography, the general clinical practice of angiographers over the study period was mixed. Some routinely administered a heparin bolus during angiography, and others did not. Exact tabulation of the use of intravenous heparin boluses was not possible because this was not recorded in the data sheets. Because the method of arteriotomy hemostasis was not included in the data sheets, exact tabulation of the number of patients who underwent manual groin compression relative to the number who underwent arteriotomy device closure was impossible. The general clinical practice at our institution, however, has been to use manual groin compression at the conclusion of diagnostic cerebral angiography.

Patients were monitored in a recovery area for 30–60 minutes after hemostasis was achieved and then were observed during flat bed rest for a total of 4 hours after hemostasis. Patients who were discharged on the day of the pro-

Advances in Knowledge

- The most common complication of diagnostic cerebral angiography was groin hematoma, which was seen in 4.2% of patients.
- Complications of diagnostic cerebral angiography such as anaphylaxis and death are rare (0.03% and 0.06% of patients, respectively).
- Within 24 hours of diagnostic cerebral angiography, 2.63% of patients experienced a neurologic deficit, although only 0.14% of patients experienced a stroke with permanent disability.

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Abbreviations:
OR = odds ratio
RIND = reversible ischemic neurologic deficit
TIA = transient ischemic attack

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cedure underwent neurologic and peripheral vascular examination performed by staff members of the neuroradiology service at the time of discharge. For inpatients, the examination was performed on the morning after the procedure by staff members of the neuroradiology service and the referring service. Outpatients were telephoned at home by a registered nurse 1 day after the procedure to inquire about any complications.

Data Collection and Complications

Data sheets (Table 1) were begun for all patients at the time of angiography and were completed at the 24-hour evaluation unless there was a neurologic complication; in that instance, clinical follow-up was continued for at least 7 days after the procedure. Over the course of the study, data sheets were completed on weekdays mostly by one registered nurse whose job description included overseeing this database. During her absences, other radiology nurses would complete the data sheets. On weekends, radiology residents completed the sheets for all inpatients who had undergone angiography on the previous day.

Any change in a patient's neurologic status, whether subjective or objective, and whether or not it was thought to be directly related to cerebral angiography, was recorded as a complication of angiography if it occurred within 24 hours of the examination. The medical charts of those patients who died within 24 hours of angiography were individually reviewed.

Statistical Analysis

Descriptive statistics of patient and procedural characteristics and complications were calculated. Univariate and multivariate analyses relating patient and procedural characteristics with complications were performed. Twenty of 19 826 patients had no listed birthdate and were excluded from multivariate models. Neurologic complications, including TIA, reversible ischemic neurologic deficit (RIND), stroke, and death related to a neurologic cause (10 of the 12 instances of death), were grouped as an outcome variable. The predictor variables of age, sex, individual risk factors, indication for the procedure, serum creatinine level, contrast agent type, contrast agent amount, number of catheters used, resident or fellow involvement, and date of procedure were tested for association with the outcome variable of neurologic complication in univariate logistic analysis. Odds ratios (ORs) were estimated, along with their

Table 1

Information on Cerebral Angiography Data Sheets

Category	Information*
Patient data	Patient identification number
	Age
	Sex
Indication (one selected)	Atherosclerotic cerebrovascular disease
	Tumor
	Subarachnoid hemorrhage
	Aneurysm
	Arteriovenous malformation
	Seizure
	Other
Risk factors (yes or no for each)	Diabetes mellitus
	Hypertension
	Stroke
	Frequent TIAs (>1 per day)
	Creatinine level > 1.2 mg/dL (106 μmol/L)
Staff neuroradiologist	Physician name
Angiographic approach	Retrograde femoral
	Direct carotid
	Retrograde brachial
	Axillary
No. of catheters used	1 or >1
Procedure time	No. of minutes
Vessels examined	Right or left carotid artery
	Right or left vertebral artery
	Aortic arch
Contrast medium	Type (one or more selected)
	Volume
Follow-up	Date of follow-up
Local complications	Hematoma (any size)
	Thrombosis
	Infection
	Other (including iatrogenic dissection or perforation)
Systemic or allergic complications	Nausea, vomiting, transient hypotension
	Urticaria, rhinorrhea
	Chest pain, arrhythmia
	Anaphylaxis, circulatory collapse
	Acute renal failure
	Death
Neurologic complications†	Hemiparesis
	Blindness
	Aphasia
	Ataxia
	Other

* TIA = transient ischemic attack.

† Neurologic complications were also classified as transient (lasting less than 24 hours after treatment), reversible (lasting more than 24 hours but less than 7 days after treatment), or permanent (lasting more than 7 days after treatment).

Table 2

Patient and Procedure Characteristics

Characteristic	Datum
Year of angiographic examination	
1980–1988	9066 (45.7)
1989–1996	7595 (38.3)
1997–2003	3165 (16.0)
Patient age (y)*	52.9 ± 18.5 (57.0)
Sex	
Male	10 841 (54.7)
Female	8985 (45.3)
Indication	
Atherosclerotic cerebrovascular disease	7619 (38.4)
Tumor	5113 (25.8)
Subarachnoid hemorrhage	2352 (11.9)
Arteriovenous malformation	1545 (7.8)
Seizure	1248 (6.3)
Vasculitis	1231 (6.2)
Aneurysm	663 (3.3)
Dissection and vasospasm	55 (0.3)
Preprocedure comorbidity	
Hypertension	6137 (31.0)†
Elevated serum creatinine level (>1.2 mg/dL [106 μmol/L])	3180 (16.0)†
Frequent TIAs	2127 (10.7)†
Diabetes mellitus	1788 (9.0)‡
Stroke	1168 (5.9)§
Fellow present at procedure	3277 (16.5)
Resident present at procedure	2405 (12.1)
Resident and/or fellow present	5466 (27.6)
Angiographic approach	
Retrograde femoral	19 387 (97.8)
Retrograde brachial	335 (1.7)
Axillary	135 (0.7)
Direct carotid	113 (0.6)
No. of catheters used	
1	13 569 (68.4)
>1	5993 (30.2)
None	261 (13.2)
Not recorded	3 (0.02)
Procedure time (min)	66.6 ± 35.2 (60.0)*
Contrast material type	
Iopamidol (Isovue 4; Bracco Diagnostics, Princeton, NJ)	9444 (47.6)
Iothalamate meglumine (Conray 60; Mallinckrodt Medical, St. Louis, Mo)	8600 (43.4)
Meglumine ioxaglate (Hexabrix; Mallinckrodt Medical)	848 (4.3)
Iohexol (Omnipaque; Nycomed, Princeton, NJ)	635 (3.2)
Diatrizoate meglumine (Hypaque 60; Amersham Health, Princeton, NJ)	634 (3.2)
Diatrizoate meglumine (Renografin 76; Squibb Diagnostics, Princeton, NJ)	76 (0.4)
Iodixanol (Visipaque; GE Healthcare, Princeton, NJ)	4 (0.02)
Maximum volume of primary contrast material (mL)	74.7 ± 38.5 (70)*

Note.—Unless otherwise specified, data are numbers of patients or procedures (of 19 826 procedures in 19 826 patients) with the given characteristic, with percentages in parentheses.

* Data are mean value ± standard deviation, with the median in parentheses.

† Data were missing for one procedure or patient.

‡ Data were missing for two procedures or patients.

§ Data were missing for four procedures or patients.

95% confidence intervals. The indication of tumor was the reference variable used for the indication for angiography. Of these predictor variables, those with a *P* value of less than .10 in univariate logistic analysis were considered as potential predictors in further multivariate logistic regression model building with neurologic complication as the outcome variable.

Statistical tests were two sided, and *P* values less than .05 were considered to indicate a statistically significant difference. All of the statistical analyses were performed by using a commercially available software program (SAS, version 8.0; SAS Institute, Cary, NC).

Results

Patients and Procedural Characteristics

Mean patient age was 52.9 years, and 54.7% of examinations involved male patients (Table 2). Overall, atherosclerotic cerebrovascular disease was the most common indication, for 38.4% of procedures. Hypertension was the most common comorbidity or risk factor, being present in 31.0% of patients. A trainee (resident and/or fellow) was present at 27.6% of examinations. The vast majority of approaches were retrograde femoral (97.8%). A single catheter was used in the majority of examinations (68.4%). Iopamidol (Isovue 4) and iothalamate meglumine (Conray 60) were the most common contrast medium types used (in 47.6% and 43.4% of procedures, respectively), although iohexol (Omnipaque 300) is what we currently use in nearly all examinations. The mean amount of contrast material used was 74.7 mL.

Complications

The most common complication was groin hematoma (4.2% of examinations); other, more serious groin complications were rare (Table 3). Nausea, vomiting, and/or transient hypotension was the most common systemic complication (1.2%), and anaphylaxis and death were rare (0.03% and 0.06%, respectively). Neurologic events occurred within 24 hours of the procedure in

2.63% of examinations, and they were considered to be complications of angiography for the purposes of this study by virtue of their timing. Of the 12 deaths, 10 were deemed to have a primary neurologic cause, although the majority of these patients had severe preprocedure neurologic morbidity, which was the indication for their angiographic examinations. The majority of neurologic complications were transient or reversible: TIA, 2.09%; RIND, 0.36%. Permanent stroke, without death, was seen after 0.14% of examinations.

Hemiparesis was the most common neurologic complication, and aphasia the second most common, for TIA, RIND, and stroke (Table 4). The indication (Table 5) with the highest rate of neurologic complication was also the most common indication—namely, atherosclerotic cerebrovascular disease (4.0% of examinations in patients with this indication resulted in neurologic complications). Subarachnoid hemorrhage followed as the indication with the second-highest rate of neurologic complications (3.2% of examinations in patients with this indication resulted in neurologic complications). Neurologic complications were more likely to occur in the earlier time periods of the study than in the later time periods: Neurologic complications occurred in 342 of 9066 (3.8%) examinations performed between 1980 and 1988, in 162 of 7595 (2.1%) examinations performed between 1989 and 1996, and in 18 of 3165 (0.57%) examinations performed between 1997 and 2003.

Table 3

Complications of 19 826 Cerebral Angiography Procedures

Complication	No. of Procedures
Local	
Hematoma	828 (4.2)*
Hematoma requiring surgery	5 (0.03)
Thrombosis	9 (0.05)*
Infection	2 (0.01)*
Systemic	
Headaches	105 (0.8)†
Nausea, vomiting, transient hypotension	235 (1.2)‡
Chest pain, arrhythmia	61 (0.3)‡
Urticaria, rhinorrhea	26 (0.1)‡
Death	12 (0.06)‡
Anaphylaxis and/or circulatory collapse	5 (0.03)‡
Acute renal failure	3 (0.02)‡
Neurologic	
TIA	414 (2.09)
Reversible	71 (0.36)
Permanent	27 (0.14)
Death related to neurologic condition	10 (0.05)§
Total	522 (2.63)

Note.—Data in parentheses are percentages.

* Data were missing for two procedures.

† Data were missing for 7037 procedures. The percentage is therefore based on a denominator of 12 789.

‡ Data were missing for four procedures.

§ Data were missing for 10 procedures.

Table 4

Neurologic Complications of 19 826 Cerebral Angiography Procedures

Type of Complication	Transient*	Reversible†	Stroke with Permanent Disability	Stroke with Permanent Disability or Death
Hemiparesis	131 (0.66)	42 (0.21)	18 (0.09)	4 (0.02)
Visual symptoms	34 (0.17)	7 (0.04)	3 (0.02)	1 (0.01)
Aphasia	90 (0.45)	35 (0.18)	14 (0.07)	3 (0.02)
Ataxia	2 (0.01)	2 (0.01)	0	0
Vertebrobasilar insufficiency	3 (0.02)	0	0	1 (0.01)
Decreased consciousness	8 (0.04)	4 (0.02)	2 (0.01)	2 (0.01)
Other	230 (1.16)	28 (0.14)	7 (0.04)	3 (0.02)
Sensory change	9 (0.05)	0	0	0

Note.—Data are numbers of procedures, with percentages in parentheses. Data were missing for 10 procedures (0.05%). Some procedures may have caused more than one complication.

* For example, TIA.

† For example, RIND.

Predictor Variables

In univariate logistic regression models with neurologic complication (TIA, RIND, stroke, or death related to neurologic cause) as the outcome variable, the majority of the predictor variables were associated with the outcome variable with *P* values of less than .10 and were therefore included in further multivariate analysis. The most significant predictor variables (Table 6) positively associated with neurologic complications were the imaging indications of subarachnoid hemorrhage (OR, 2.523), atherosclerotic cerebrovascular disease (OR, 2.494), arteriovenous malformation (OR, 2.072), and "other" (OR, 1.935). The comorbidity of frequent TIAs was also significantly and positively associated with neurologic complications (OR, 1.674). Advancing patient age was also significantly associated with higher rates of neurologic complications, but the effect size for this variable was quite small (OR, 1.011).

Two variables were associated with

significantly decreased risk of neurologic outcome: involvement of a resident and/or fellow in the case (OR, 0.710) and increasing year of procedure (OR, 0.659 for 5-year intervals). Although associated with the outcome variable of neurologic complication with *P* values less than .10 in univariate analysis, the predictor variables of hypertension, elevated creatinine level, contrast agent volume, and particular type of contrast agents lost any significant association when covariance was controlled for in multivariable analysis.

Discussion

Our retrospective review of prospectively collected data for diagnostic cerebral angiography procedures in 19 826 consecutive patients reveals relatively low complication rates. A groin hematoma occurred in 4.2% of examinations and was the most common complication. Neurologic complications occurred within 24 hours of angiography in 2.63% of examinations, but the substantial majority of these complications were transient or reversible. Stroke with permanent disability occurred in 0.14% of examinations, and death occurred in 0.06% of examinations.

Patients being imaged for the indications of subarachnoid hemorrhage and atherosclerotic cerebrovascular disease were 2.5 times more likely than patients with the reference indication of tumor to have a neurologic complication within 24 hours. Patients with a history of frequent TIAs were 67% more likely than those without such history to have a neurologic complication. However, the participation of a trainee in an angiographic examination appears to have been protective, with neurologic complications 29% less likely to occur. The rate of neurologic complications decreased significantly with time over the 24-year duration of this study; a neurologic complication was 34% less likely to occur with each 5-year progression in time. Neurologic complications occurred in 3.8% of examinations during the first one-third of the study and in 0.57% of examinations during the last one-third.

Our discovered rate of neurologic complications associated with cerebral angiography, 2.63%, is similar to that found by other researchers, who have reported rates of 0.9%–4% (1–5,7–10). Our discovered rate of stroke with permanent disability or death in approximately 0.2% of cerebral angiographic examinations is slightly lower than that of other researchers, who have reported rates of 0.3%–1.3% (1–5,7–10). This could be reflective of differences in clinical follow-up between the current study and previously reported studies or of differences in patient populations or clinical practice. Our findings of an increased rate of neurologic complications in patients known to have or suspected of having atherosclerotic cerebrovascular disease and in patients with a history of frequent TIAs is consistent with the findings of other authors (1,3,4,6).

Neurologic complications have significantly decreased in more recent years, which could potentially represent an improvement in equipment, angiographer skill, or both. Patient selection variables have certainly changed with time (eg, angiography for diagnostic tumor evaluation is now substantially less common than previously), but the decreased rate of neurologic complications over time persisted even when the major patient selection criteria were controlled for in multivariate analysis. Heparinized saline catheter flush systems entered standard use in approximately 1990 and could be protective against neurologic complications. The shift from manual subtraction angiography to digital subtraction angiography began in 1993 at our institution and was mostly complete by approximately 1997, and associated decreases in injection volumes and rates could potentially be related to decreased neurologic complication rates.

We realize there were potential limitations of our study. Its data accuracy depended very strongly on the reliability of our clinical follow-up. There were

Table 5

Neurologic Complications of 19 826 Cerebral Angiography Procedures according to Indication

Indication	No. of Procedures without Complication	Transient*	Reversible†	Stroke with Permanent Disability	Leading to Death	Total‡
Atherosclerotic cerebrovascular disease	7308	240	43	19	4	306/7614 (4.0)
Tumor	5043	57	7	5	0	69/5112 (1.3)
Subarachnoid hemorrhage	2277	64	6	1	4	75/2352 (3.2)
Arteriovenous malformation	1515	21	6	1	0	28/1543 (1.8)
Seizure	1238	8	1	1	0	10/1248 (0.8)
Vasculitis	1205	19	6	0	1	26/1231 (2.1)
Aneurysm	653	5	2	0	1	8/661 (1.2)
Dissection	43	0	0	0	0	0
Vasospasm	48	0	0	0	0	0

Note.—Data were missing for 13 procedures (0.07%).

* For example, TIA.

† For example, RIND.

‡ Data in parentheses are percentages.

very few missing data points, which may relate to the presence of a single, highly reliable nurse overseeing clinical follow-up data collection for the majority of the time period of the study. The collection of clinical follow-up data on weekdays was performed by or directly overseen by this nurse, but on weekends was dependent on residents performing rounds on inpatients and was therefore less person specific. Clinical follow-up on weekends may have been performed by individuals less experienced in evaluating medical records or in examining patients.

Another potential limitation of our data collection was that patients were evaluated clinically at 24 hours, and data sheets were completed at that time for patients who did not have new neurologic deficits. Therefore, we could potentially have missed neurologic complications occurring more than 24 hours after angiography that have been reported to occur (2). Also, our estimation of the rate of contrast material–induced nephropathy, which may manifest more than 24 hours after angiography, may thus be falsely low.

A limitation of our data collection with converse effects on results would be that adverse clinical outcomes were considered to be complications of cerebral angiography solely on the basis of the timing of their occurrence. Patients with a history of frequent TIAs, for example, had relatively more neurologic events in the first 24 hours after cerebral angiography than did patients without this history, but it is conceivable that at least some of these neurologic events would have occurred in these patients whether or not they underwent angiography. Another example of the bias created by the underlying disease is that, at chart review of the 10 neurologically related patient deaths, at least half of these patients were noted to have had severe morbidity before angiography that indeed was the indication for the angiography and that may have caused the patient's death within the same time frame, with or without angiography.

We did not record the use of intravenous heparin boluses in our database, which would have been an interesting variable to study with regard to neurologic complications (11). Also in this study we did not collect diffusion-weighted magnetic resonance imaging data, which in other studies have shown subclinical ischemic injuries in 9% or less of examinations to as many as 26% of examinations (12–15). We allow that subtle neurologic deficits could have been missed in the patients' clinical follow-up.

In conclusion, results of our retrospective study of prospectively gathered data in 19 826 consecutive patients show a relatively low rate of complications of diagnostic cerebral angiography.

Table 6

ORs of Predictor Variables in Multivariable Models with Outcome Variable of Neurologic Complication

Predictor Variable	OR	95% Confidence Interval	*P* Value
Patient age	1.011	1.004, 1.017	.001
Hypertension	0.982	0.808, 1.193	.852
Frequent TIAs	1.674	1.320, 2.125	<.001
Creatinine level > 1.2 mg/dL (106 μmol/L)	1.138	0.915, 1.417	.246
Use of iohexol (Omnipaque)	1.0*	. . .	. . .
Use of diatrizoate meglumine (Hypaque 60)	0.730	0.345, 1.541	.409
Use of diatrizoate meglumine (Renografin 76)	0.732	0.316, 1.694	.466
Use of iothalamate meglumine (Conray 60)	0.800	0.420, 1.526	.499
Use of meglumine ioxaglate (Hexabrix)	1.236	0.654, 2.334	.514
Use of iopamidol (Isovue 4)	0.804	0.443, 1.458	.472
Contrast material volume	1.002	0.999, 1.004	.158
Tumor	1.0*	. . .	. . .
Atherosclerotic cerebrovascular disease	2.494	1.869, 3.328	<.001
Subarachnoid hemorrhage	2.523	1.793, 3.550	<.001
Arteriovenous malformation	2.072	1.312, 3.273	<.002
Seizure	0.965	0.490, 1.902	.918
Other indication	1.935	1.266, 2.958	.002
Presence of resident or fellow at procedure	0.710	0.512, 0.985	.040
Year of procedure†	0.659	0.559, 0.776	<.001

* Reference condition.

† Five years equals one incremental unit.

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