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Comparison of Safety and Diagnostic Efficacy of Iohexol 240 mgI/mL, Iopamidol 250 mgI/mL, and Iodixanol 270 mgI/mL in Cerebral Angiography: A Prospective, Multicenter Study

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Purpose: This multicenter prospective study aimed to evaluate the quality and diagnostic effectiveness of cerebral angiography images obtained using low-concentration iodinated contrast agents (iohexol 240 mgI/mL, iopamidol 250 mgI/mL, and iodixanol 270 mgI/mL) and to assess the safety thereof. The study addresses the need for safer contrast agent alternatives without compromising the diagnostic quality of identifying cerebrovascular disease.

Materials and Methods: Conducted in 5 medical centers in South Korea, we enrolled patients aged 19 years or older who were referred for diagnostic cerebral angiography under non-emergency conditions, excluding those with specific health conditions and sensitivities. The study design included a prospective, observational approach with a 1-way analysis of variance (ANOVA) for sample size calculation, aiming for a total sample of 231 participants for adequate power. Image quality was evaluated using a 4-level scale by 2 independent, blinded radiologists, and adverse reactions were monitored both immediately and up to 7 days post-procedure. Statistical analysis involved 1-way ANOVA and Kruskal–Wallis tests to assess the image quality and safety profiles of the contrast agents.

Results: Among 266 patients screened, 243 were included in the final analysis. The evaluation revealed no statistically significant differences in image quality among the 3 types of low-concentration contrast agents. Adverse events were observed in 28.8% of patients, with 27.2% experiencing acute reactions, primarily mild reactions, and 3.3% experiencing delayed reactions. The overall safety profile showed no significant changes in vital signs or electrocardiogram readings before and after contrast agent injection.

Conclusion: Using low-concentration iodinated contrast agents for cerebral angiography provides image quality comparable to that of conventional high-concentration agents, with no significant increase in adverse events, suggesting a safer alternative for patients.

Key Words: Cerebral angiography; Contrast media; Iohexol; Iopamidol; Diagnostic imaging; Safety

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INTRODUCTION

Cerebral angiography, the traditional gold standard diagnostic method to identify cerebrovascular diseases, necessitates the use of contrast agents for optimal visualization.[1,2] Within radiological diagnostics and cerebrovascular angiography, a variety of contrast agents, each with unique characteristics, are widely employed, and have undergone rapid evolution and adaptation. Among these agents, iohexol, iopamidol, and iodixanol, iodine-based contrast agents, are extensively utilized in cerebral angiography, contrast-enhanced computed tomography, and various fluoroscopy procedures.[3-5] Furthermore, the safety of these contrast agents has been established through many preceding studies and clinical applications.[6-9]

Historically, high-concentration formulations (iohexol 300 mgI/mL, iopamidol 300 mgI/mL, iodixanol 320 mgI/mL) of iodine contrast agents have been employed in cerebral angiography to achieve high-resolution and well-visualized cerebrovascular angiography images.[6,10] However, subsequent advancements in diagnostic imaging equipment and imaging acquisition techniques have facilitated the acquisition of images of comparable or superior quality to those obtained previously, without necessitating the use of high-concentration contrast agents. Moreover, in many diagnostic radiology procedures, low-concentration contrast agents are preferred over high-concentration agents whenever possible. This preference primarily stems from the perspective that such a practice may offer enhanced safety for patients, considering the potential adverse events associated with high-concentration contrast agents.[11,12] From this perspective, there is an increasing number of cases where cerebral angiography is performed using a low-concentration contrast agent instead of a high-concentration contrast agent in recent clinical settings. However, there is a lack of research confirming the image quality and diagnostic effectiveness of cerebral angiography using low-concentration contrast agents.[13-15] Therefore, in this study, we aim to evaluate the quality and diagnostic effectiveness of images obtained through cerebral angiography performed using representative low-concentration contrast agents (iohexol 240 mgI/mL, iopamidol 250 mgI/mL, and iodixanol 270 mgI/mL) and to assess their safety.

MATERIALS AND METHODS

Study Patients and Design

This prospective observational study was conducted using established practice protocols at 5 medical centers in South Korea and was approved by the institutional review boards of all 5 centers. All procedures involving human participants were performed according to the ethical standards specified by the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments or equivalent ethical standards. All participants provided written informed consent before enrollment.

We included patients aged 19 years or older who were referred for diagnostic cerebral angiography in non-emergency situations, provided they were conscious, capable of comprehending the study purpose, and consented to participation. We excluded individuals under 19 years of age; pregnant or breastfeeding female; individuals with known hypersensitivity to contrast medium; those unable to articulate their symptoms due to academic background or physical condition; patients requiring general anesthesia; individuals who had received intravascular contrast agent injections within 48 hours prior to the test; those scheduled for examinations involving contrast agents within 7 days of the test; individuals scheduled for surgery within 7 days of the examination; and patients with severe thyroid disease, clear renal or hepatic dysfunction, abnormal electrolyte balance, known hemorrhagic disease, or known clear electrocardiogram (EKG) abnormalities.

The expected number of study participants was calculated as follows. In a 1-way analysis of variance (ANOVA) study, sample sizes of 77 were obtained from each of the 3 groups whose means were to be compared. The total sample of 231 participants achieved 80% power to detect differences between the means versus the alternative of equal means using an F-test, with a significance level of 0.05. The variation in the means is represented by their standard deviation, which was 0.11. The standard deviation for each group was assumed to be 0.55. Considering a 10% dropout rate, each group required 86 participants, for a total of 258 participants. Based on these findings, we prospectively enrolled a total of 266 patients who underwent cerebral angiography between October 2020 and January 2022 (Fig. 1).

The primary endpoint of the study was to compare and evaluate the image quality of cerebral angiography using iohexol 240 mgI/mL, iopamidol 250 mgI/mL, and iodixanol

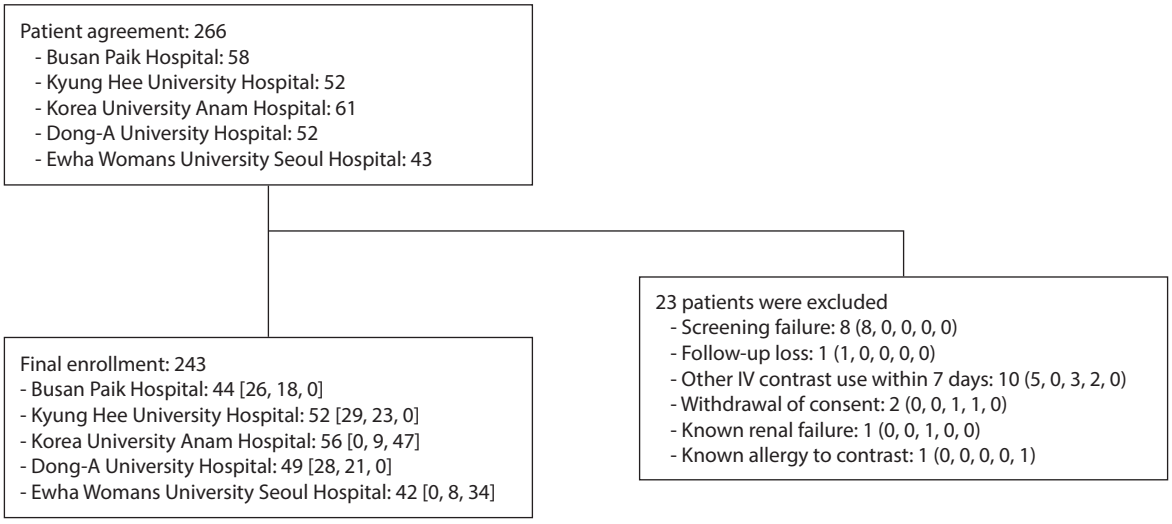

Fig. 1. Flow chart of enrollment of study patients. Numbers in parentheses represent: Busan Paik Hospital, Kyung Hee University Hospital, Korea University Anam Hospital, Dong-A University Hospital, and Ewha Womans University Seoul Hospital. Numbers in square brackets represent: iodixanol, iohexol, and iopamidol.

270 mgI/mL. The secondary endpoint involved evaluating adverse reactions associated with contrast agents following cerebral angiography using these contrast agents.

Protocol of Cerebral Angiography

The angio equipment used in the research at each institution included the Artis zee PURE (Siemens Healthineers), Azurion (Philips Healthcare), Innova IGS 630 (GE Health-care), Artis Q pure (Siemens Healthineers), and AXIOM Artis dBA (Siemens Healthineers). The Artis zee PURE and Artis Q pure systems were operated at 73 kV, the Azurion and Innova IGS 630 at 75 kV, and the AXIOM Artis dBA at 77 kV during imaging.

Each institution conducted cerebral angiography using 2 of the 3 currently available contrast agents, following a prescribed order outlined in the contrast media sequence table. Existing medical procedures do not have standards for contrast media use, prompting the use of a flowchart for convenience. There is no standardized dosage for the contrast agents, and the amount administered may vary according to the researcher's discretion and the patient's condition. At each hospital, all procedures, including contrast agent dilution, adhered to the protocols established.

The studies entailed a standard 4-vessel examination covering the bilateral internal carotid artery and bilateral vertebral artery anteroposterior and lateral angiograms. An automatic pressure injector was employed in all studies, and hand injection procedures were explicitly documented if they were utilized. Contrast administration relied on a stock solution, whereas parameters such as field of view, injector settings, angles, and radiation doses adhered to routine hospital protocols.

Evaluation of Overall Image Quality

Two independent radiologists, who were blinded to the study participant information, evaluated the image quality. The raters were completely unaware of any details that could influence image assessment, including the participant's medical history and other imaging findings, such as physical examinations and final diagnosis results. In addition, they were unaware of each other's evaluation outcomes. Image quality was assessed using a 4-level scale as follows: excellent (4 points), excellent visualization of both large and small vessels; good (3 points), excellent visualization of large vessels with minimal compromise in small vessel visualization; fair (2 points), adequate visualization of large vessels but compromised visualization of small vessels; and poor (1 point), non-diagnostic or compromised visualization of both large and small vessels. In this image evaluation, the criteria for small vessels were evaluated based on whether the lenticulostriate artery is clearly visible in the anterior circulation and whether the thalamoperforating artery is clearly visible in the posterior circulation. The image evaluation was conducted based solely on conventional angiography images.

Patient Observations and Safety

Physical measurements, creatinine confirmation, indication

confirmation, and participant registration were performed within 48 hours before the procedure. Premedication and procedure information were checked on the day of the procedure and immediately before the procedure. Blood pressure, pulse rate, EKG, and acute adverse events were evaluated using open-ended questions immediately before the procedure, before contrast injection during cerebral angiography, immediately after contrast injection during cerebral angiography, and 1 hour after the first contrast injection. The measurement time was changed according to the patient's condition; however, the measurements were performed as soon as possible.

Clinically significant abnormal results immediately before contrast medium injection were recorded in the history and clinically significant abnormal results after contrast medium injection were recorded as acute adverse events. On the 7th day after cerebral angiography, delayed adverse events were confirmed through open-ended questions *via* phone or during an outpatient visit.

The severity of adverse events was classified as mild, moderate, and severe according to the American College of Radiology manual on contrast media, and each was further classified into allergic-like and physiological reactions.[16] Mild allergic-like reactions are characterized by limited urticaria, pruritus, cutaneous edema, "itchy/scratchy" throat, nasal congestion, and sneezing/conjunctivitis/rhinorrhea. Mild physiological reactions include limited nausea/vomiting, transient flushing/warmth/chills, and light headache/dizziness/anxiety/altered tastes. Allergic-like responses progressing to moderate reactions comprise diffuse urticaria/pruritus, diffuse erythema with stable vital signs, facial edema without dyspnea, throat tightness or hoarseness without dyspnea, and wheezing/bronchospasm with mild or no hypoxia. Conversely, moderate physiological reactions include protracted nausea and vomiting, hypertensive urgency, isolated chest pain, and vasovagal reactions that respond to treatment. Severe reactions, including allergic-like and physiological reactions, include diffuse edema or facial edema with dyspnea, diffuse erythema with hypotension, laryngeal edema with stridor and/or hypoxia, wheezing/bronchospasm with significant hypoxia, anaphylactic shock (hypotension+tachycardia), vasovagal reactions resistant to treatment, arrhythmia, convulsions, seizures, and hypertensive emergencies.

Adverse reactions to contrast agents were categorized as acute (within 1 hour of injection) or delayed (occurring 1 hour to 7 days post-injection). Delayed adverse events include allergic-like and cutaneous reactions (e.g., urticaria, persistent rash, angioedema, maculopapular rash, Stevens–Johnson syndrome, toxic epidermal necrolysis, and cutaneous vasculitis), as well as physiological reactions (e.g., nausea, vomiting, fever, drowsiness, headache, severe hypotension, cardiopulmonary arrest, iodine-related sialadenopathy, and acute polyarthropathy).

In the event of adverse reactions, patients underwent observation or received treatment, such as hydration, analgesics, hypotensive agents, antiemetics, antihistamines, and/or corticosteroids, based on symptom severity and hospital protocols. Safety assessments entailed vigilant monitoring of abnormal findings in blood pressure, pulse, and EKG results, as well as acute and delayed adverse reactions.

Statistical Analysis

Our statistical analysis was conducted using SAS (version 9.4; SAS Institute Inc.), and a 2-sided test with $P<0.05$ was considered significant. A 1-way ANOVA was used to compare the average grading scores among the 3 groups, with pairwise comparisons performed if a significant difference was observed. Significance levels for pairwise comparisons were interpreted using Bonferroni correction. If the data did not follow a normal distribution, the Kruskal–Wallis test, a nonparametric statistical analysis, was utilized.

Our statistical analysis had 2 primary objectives. First, we determined whether there was a statistically significant difference in the image quality based on the type of contrast agent used. First, we checked whether there was a statistically significant difference in image quality depending on the type of contrast agent used. Normality tests were conducted for each of the 2 independent image evaluators' results. The Kruskal–Wallis test was employed because neither result satisfied the normality assumption. Second, a statistical analysis was conducted to evaluate the safety profile of the contrast agent. This investigation involved examining the type and frequency of acute and delayed adverse reactions, categorized by the type of contrast agent used and the institution where the study was conducted.

RESULTS

Characteristics of Study Participants

Among 266 patients from 5 hospitals who were screened for participation in the study, 23 were excluded for the following

reasons: dropout during the screening process (8), follow-up loss (1), use of intravenous contrast medium within 7 days for reasons other than this test (10), withdrawal of consent to study participation after passing the screening (2), known renal failure (1), and known allergy to contrast (1). Accordingly, 243 patients were included in the study and underwent statistical analysis (Fig. 1). The mean age of the enrolled patients was 59.8±11.85 years. The patient demographic characteris-

Table 1. Demographic characteristics of patients who underwent cerebral angiography

Patients	All (n=243)	Iodixanol (n=79)	Iohexol (n=83)	Iopamidol (n=81)	P-value
Females	154 (63.4)	25 (31.6)	34 (41.0)	30 (37.0)	0.467
Mean age (y)	59.80±11.85	58.41±10.52	60.31±11.36	61.42±12.61	0.254
History					
Hypertension	110 (45.3)	32 (40.5)	33 (39.8)	45 (55.6)	0.074
Diabetes mellitus	8 (3.3)	2 (2.5)	2 (2.4)	4 (4.9)	0.668
Coronary heart disease	4 (1.6)	2 (2.5)	0 (0)	2 (2.5)	0.399
Asthma/allergies	11 (4.5)	4 (5.1)	6 (7.2)	1 (1.2)	0.168
Thyroid dysfunction	4 (1.6)	2 (2.5)	1 (1.2)	1 (1.2)	0.696
CNS disorder	4 (1.6)	0 (0)	3 (3.6)	1 (1.2)	0.328
Renal insufficiency	1 (0.4)	0 (0)	0 (0)	1 (1.2)	0.658

Values are presented as number (%) or mean±standard deviation.
CNS, central nervous system.

Table 2. Image quality evaluation results of evaluator 1 and 2

	Image quality	Type of contrast agent			P-value
		Iodixanol	Iohexol	Iopamidol	
Evaluator 1	3	3 (3.8)	5 (6.0)	6 (7.4)	
	4	76 (96.2)	78 (94.0)	75 (92.6)	
	Total	79 (100)	83 (100)	81 (100)	0.6151
Evaluator 2	3	2 (2.5)	3 (3.6)	0 (0)	
	4	77 (97.5)	80 (96.4)	81 (100)	
	Total	79 (100)	83 (100)	81 (100)	0.2495

Values are presented as number (%).

Table 3. Changes in blood pressure and pulse before and after administration of contrast agent according to the type of contrast agent

Type of contrast	Vital signs	Before injection	After injection	P-value
Iodixanol (n=79)	sBP	142.3±15.0	139.6±14.8	0.026
	dBP	81.3±9.9	79.7±9.8	0.067
	Pulse	75.5±15.8	75.7±17.3	0.847
Iohexol (n=83)	sBP	136.8±17.4	134.7±18.3	0.072
	dBP	80.3±12.0	79.2±14.0	0.233
	Pulse	73.4±14.2	73.4±13.5	0.945
Iopamidol (n=81)	sBP	138.5±22.8	137.6±20.9	0.419
	dBP	75.2±12.6	74.2±12.1	0.238
	Pulse	70.9±14.0	72.5±13.9	0.023

Values are presented as mean±standard deviation.
sBP, systolic blood pressure; dBP, diastolic blood pressure.

tics are shown in Table 1. There was no statistically significant difference in the mean age, sex, and past medical history of patients included in each group by contrast agent type (Table 1).

Overall Image Quality

Both independent image evaluators obtained a score of 3 or 4 for all imaging tests, regardless of the contrast agent used. As the normality test result of both image evaluators was P<0.05, normality was not satisfied. Therefore, the image evaluation scores between the 3 contrast agent groups were compared using the Kruskal–Wallis test, a nonparametric statistical analysis. For each imaging evaluator, the P-value was >0.05, indicating that there was no statistically significant difference in the imaging evaluation scores between the 3 contrast agents (Table 2). In cases where both evaluators assessed the score as 4, this occurred in 224 out of a total of 243 cases (92%). Among these, the frequencies of iodixanol, iohexol, and iopamidol were respectively found to be 74, 75, and 75.

Safety Assessment

Blood pressure, pulse, and electrocardiogram

The mean, standard deviation, and median values of the systolic and diastolic blood pressure and pulse before and after the injection of each contrast agent were recorded (Table 3). The statistical analysis results of the changes in systolic and diastolic blood pressure, and pulse before and after the injection of each contrast agent were also described in Table 3. Additionally, no changes in EKGs were observed in any patient except for 5 patients who showed clinically meaningless EKG abnormalities before the procedure.

Adverse Events

A total of 103 adverse were observed in 70 patients (28.8%, 70/243) (Table 4).

Acute adverse events

In total, 95 acute adverse events occurred in 66 patients (27.2%). Among these events, 88 cases (85.4%, 88/103) were mild, and 7 cases (6.8%, 7/103) were moderate. No severe acute adverse events were reported. Among the patients who experienced acute adverse events, 47 (71.2%, 47/66) experienced a single event, while 19 (28.8%, 19/66) experienced multiple adverse events.

Acute adverse events were categorized as allergic-like (6 events in 5 patients) or physiological (89 events in 64 patients). Among these mild adverse events, transient flushing/warmth/chills were the most common (n=54, 61.4%), followed by headache, dizziness, anxiety, and altered taste (n=25, 28.4%). In the case of moderate adverse events, each of the 7 types of adverse events appeared differently. According to the type of contrast agent used, the frequency of acute adverse events was as follows: for mild cases, there

Table 4. Incidence of adverse events in patients who underwent cerebral angiography according to onset time and severity

	Patients	Adverse events
Total adverse events	70 (28.8)	103 (100)
Acute adverse events	66 (27.2)	95 (92.2)
Mild	62 (25.5)	88 (85.4)
Allergic-like	2	
Nasal congestion		1
Limited ulticaria/pruitis		1
Limited "itchy"/"scratchy" throat		1
Physiologic	60	
Sneezing/conjunctivitis/ rhinorrhea		1
Cutaneous edema		1
Headache/dizziness/anxiety/ altered taste		25
Limited nausea/vomiting limited		4
Transient flushing/warmth/chills		54
Moderate	6 (2.5)	7 (6.8)
Allergic-like	3	
Wheezing/bronchospasm, mild or no hypoxia		2
Throat tightness or hoarseness without dyspnea		1
Physiologic	4	
Isolated chest pain		2
Vasovagal reaction		1
Protracted nausea/vomiting		1
Severe		
Allergic-like	0	0
Physiologic	0	0
Delayed adverse events	8 (3.3)	8 (7.8)
Allergic-like and cutaneous	6	6
Physiologic	2	2

Values are presented as number (%) or number only.

were 40 cases of iodixanol, 32 cases of iohexol, and 16 cases of iopamidol; for moderate cases, there were 3 cases of iodixanol and 4 cases of iohexol. Overall, no significant changes were observed in the vital signs (blood pressure and pulse) and EKG readings before, during, and after contrast agent injection.

Delayed adverse events

Eight delayed adverse events occurred in 8 patients (3.3%). Allergic-like and cutaneous events were present in 6 patients (pruritus in 1, urticaria and/or persistent rash and/or angioedema in 5), and physiological events in 2 patients (nausea, vomiting, fever, drowsiness, and headache). According to the type of contrast agent used, the frequency of acute adverse events was as follows: 5 cases with iodixanol and 3 cases with iohexol use. No delayed adverse events were associated with iopamidol use.

DISCUSSION

We compared and evaluated the image quality of cerebral angiography using the well-known and relatively widely used low-concentration iodinated contrast agents iohexol 240 mgI/mL, iopamidol 250 mgI/mL, and iodixanol 270 mgI/mL. Furthermore, we analyzed adverse events related to the contrast agent after cerebral angiography using these agents. Our evaluation revealed no statistically significant differences in image quality among the 3 types of low-concentration contrast agents. Adverse events were observed in 28.8% of patients, with 27.2% experiencing acute reactions, primarily mild reactions, and 3.3% experiencing delayed reactions. The overall safety profile showed no significant changes in vital signs or EKG readings before and after the contrast agent injection. This study is the first multicenter prospective study to examine the image quality of cerebral angiography using different types of low-iodination contrast agents.

Cerebral angiography using contrast agents is the gold standard for diagnosing cerebrovascular diseases. It has been continuously performed from ancient times to the present.[1,2] Various types of contrast agents have been used for cerebral angiography from the past to the present, and their advantages and disadvantages have been evaluated through many studies.[17-20] Consequently, the types of contrast agents used in cerebral angiography have continuously changed.

We aimed to investigate whether there is a change in the frequency of known side effects related to the contrast agents used in cerebral angiography when relatively low-concentration contrast agents are used without affecting the quality of images in diagnosis. Our results confirmed that the images were of sufficient quality for interpretation, consistent with previous studies that used low-concentration contrast agents for examinations, and indicated that when performing cerebral angiography using low-concentration contrast agents, the image and diagnostic quality are satisfactory, similar to those using conventional contrast agents.[21-25]

Regarding side effects, our frequency of acute side effects was relatively high compared to previous studies.[21-23,26] However, this is thought to be due to warmth and altered taste side effects, which may have been included due to discomfort rather than as side effects in previous studies.[10,27] Excluding these results, we show a frequency of acute side effects of 3.3%, which is similar to that in previous studies and lower than that in the study by Heo et al.[14] We observed delayed side effects in 8 (3.3%) patients, which was lower than in previous studies.[14,28] Similar to previous studies, the most common side effects in delayed reactions were allergic skin reactions and nonspecific headaches.[14,28,29] This is consistent with previous studies reporting allergic skin reactions as the most common delayed side effects associated with iodinated contrast agents.

We assessed the agreement between 2 evaluators regarding the analysis of image quality. Since image quality was essentially evaluated only in categories 3 and 4, we calculated the Kappa statistic (95% confidence interval) to determine the agreement between these 2 categories. However, the result was Kappa=−0.131, which is very low. The reason for the low Kappa statistic in this data is believed to be due to the distribution being skewed towards 1 side, where both evaluators assessed the image quality as 4 in 224 out of 243 cases, which equals a very high proportion of 0.92. The Kappa statistic is a measure that adjusts for the probability of chance agreement (statistically) between evaluators and is commonly used in inter-rater reliability analyses. However, in cases like this data, where the proportion of agreement within a single category is very high, the Kappa value can unexpectedly appear small. This issue has been addressed in published papers.[30] In such cases, we think it might be more effective to describe or show the proportion of agreement in the text or a table rather than presenting the Kappa value,

as this can more effectively represent the level of agreement between the evaluators.

In the results regarding changes in blood pressure and pulse rate before and after contrast agent injection, statistically significant decreases in systolic blood pressure were observed with iodixanol (P=0.011), and statistically significant increases in pulse rate were observed with iopamidol (P=0.005). While these changes could potentially have real significance, considering the fact that previous studies did not show any remarkable hemodynamic changes with the aforementioned contrast agents, the actual changes in mean values in this study were not substantial, and only 1 numerical value differed for each of the 2 contrast agents among the 3 variables measured, it is deemed that there is not significant clinical significance.[6] Furthermore, it is considered difficult to exclude the possibility of changes due to other factors that may affect blood pressure or pulse rate, apart from contrast agent injection.

This study had several limitations. First, despite being a prospective study, standardization of cerebral angiography methods and contrast agent injection procedures was not achieved across each center where the actual procedures were conducted. Therefore, we could not control the injection rate of the contrast agent or determine whether the contrast agent was diluted uniformly. However, according to previous studies, the injection rate of the contrast agent is not significantly associated with the frequency of acute side effects,[31] so it is thought that this limitation will not greatly affect the study results. Furthermore, it was deemed that the impact of trying to administer the contrast agent at the same speed or dosage for all patients would not be significant since it is practically impossible. Additionally, procedures related to cerebral angiography were carried out through routine processes in most centers, which were considered standardized procedures commonly practiced. They, thus, were judged not to have a significant impact on the results of the study. Nevertheless, it is deemed beneficial to conduct further research by proceeding with standardized procedural protocols and contrast agent injection procedures to investigate whether these variables have an impact. Second, each center had predetermined types of available contrast agents. Therefore, all centers could not use all 3 different types of contrast agents. Consequently, the frequency of adverse effects according to the type of contrast agent has not been studied under completely controlled conditions, and consideration of these limitations is necessary when interpreting the results. Third, it is believed that the number of cases included in this study may be sufficient to demonstrate differences in image quality. However, it is difficult to determine whether it is sufficient to conclude safety conclusively. Therefore, to alleviate these concerns, larger prospective studies are deemed necessary.

CONCLUSION

This multicenter prospective study confirmed that, when performing cerebral angiography using low-concentration contrast agents, there was no significant difference in image quality compared with studies using conventional contrast agents widely used for diagnosis, and there was no significant difference in the reported occurrence rate of side effects. These results indicate that performing cerebral angiography using low-concentration contrast agents is relatively safe without significant changes in image quality.

Fund

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Ethics Statement

This paper does not include any images or information that may identify the person.

This study was approved by the Institutional Review Board at Inje University Busan Paik Hospital (IRB No. 20-0055), Dong-A University Hospital (IRB No. DAUHIRB-20-095), Korea University Anam Hospital (IRB No. K2020-0827), Kyung Hee University Hospital (IRB No. KHUH 2020-09-039) and Ewha Womans University Seoul Hospital (IRB No. SEUMC 2020-05-006).

Conflicts of Interest

The authors have no conflicts to disclose.

Author Contributions

Concept and design: HWJ, MK, BK, EJK, and SML. Analysis and interpretation: JB, YJH, and SY. Data collection: HWJ, JB, MK, BK, EJK, SML, BL, YJH, and SY. Writing the article: JB. Critical revision of the article: HWJ. Final approval of the article: JB. Statistical analysis: JB. Obtained funding: HWJ. Overall responsibility: HWJ.

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