Acta Medica et Biologica
Vol. 43, No. 1, 25-36, 1995

The Usefulness and Limitations of Intravenous Digital Subtraction Angiography Screening in Detecting Unruptured Cerebral Aneurysms and Methods to Improve its Reliability

Satoshi KOBAYASHI

Department of Anatomy, Shinshu University School of Medicine, Matsumoto, Japan

Received December 26 1994; accepted February 6 1995

Summary. **Intravenous digital subtraction angiography (IV DSA) was performed on 3,146 patients in the period between February 1989 and March 1994. They were retrospectively investigated to detect unruptured cerebral aneurysms (An) to determine its incidence and the usefulness of this test to be used for screening purposes. These patients had slight or mild neurological problems but had no history indicative of cerebral Ans. From them, 2,730 (86.8%) IV DSA studies were of excellent image quality. Among these, 161 suggested the presence of unruptured Ans. For these, 142 received cerebral angiography by intra-arterial digital subtraction angiography (IA DSA). Forty-six were confirmed to have Ans (1.9% incidence) and 33 were subjected to surgery. The remaining 96 patients had no An (67.6% false positive). The smallest one detected on IV DSA was 2 mm in size. There were 10 Ans which escaped detection by IV DSA but were confirmed by IA DSA or during surgery (17.4% false negative). All of them were smaller than 3 mm in size. We believe unruptured cerebral Ans over 5 mm in diameter, which pose a greater risk of rupture, can be sufficiently detected by IV DSA. For this procedure, a short catheter with a large caliber was used for pressure injection of the contrast medium via a femoral vein. This method proved to be very adequate in obtaining clear images of IV DSA.**

In the same period, we performed 4,609 IV DSA for various neurological problems including the above cases. In 4,057 of them (88.0%), the pictures were of excellent image quality. In 57 cases (1.2%), there were slight complications. Our study suggests that IV DSA is a useful means of detecting unruptured cerebral Ans for screening purposes.

Correspondence: Satoshi Kobayashi, M.D. Kobayashi Neurosurgical Hospital, 1-5-21 Miwa, Nagano 380, Japan.

INTRODUCTION

Subarachnoid hemorrhage from ruptured cerebral aneurysms (Ans) is a serious disease leading to high rates of mortality (50 to 60%) and morbidity (20 to 30%).[1-7] The catastrophe comes without warning to apparently healthy, unsuspecting people; about half of them die in the following one month period, and the remainder die or suffer major sequelae without definitive treatment.[7-10] Despite this, there has been no ideal screening method for Ans, and the development of a reliable technique has been in great demand.

Lately, magnetic resonance angiography (MRA) has achieved remarkable progress in the diagnosis of cerebrovascular conditions. However, its reliability as a screening test for Ans is questioned by many researchers.[11-14] In our institution we occasionally also use MRA, but feel it is only useful as an adjunctive method.

On the other hand, intravenous digital subtraction angiography (IV DSA) has proved to be a useful means in evaluating the cerebrovascular diseases.[15-21] It is minimally invasive, fairly accurate and a less expensive method for examinig the intracranial vasculature on an outpatient basis. However, there has been a limited number of reports of its usefulness and limitations in detecting unruptured cerebral Ans in recent years.[22,23]

This paper describes our experience of IV DSA to detect unruptured cerebral Ans mainly on an outpatient basis, as well as an evaluation of its reliability as a screening test. A method to improve the quality of the pictures from a technical aspect is provided and complications are reviewed.

PATIENTS AND METHODS

Patients

From February 1989 to March 1994, 4,609 IV DSA studies were performed at our institution in patients with neurological disorders. Among them, 3,146 patients whose history met the following criteria were selected for the present study: 1) A history of slight to mild neurological problems were complained of, including habitual or persistent headache, speech, visual or sensorimotor impairment including transient ischemic attack (TIA), reversible ischemic neurological deficits (RIND), cranial nerve palsy, episodes of unconsciousness or epileptic attack; 2) Patients were suspected of having cerebrovascular disease but their computed tomograms (CTs) were negative for ruptured or unruptured cerebral Ans and they had no history suggestive of ruptured cerebral An; 3) Other organic neurological disorders were excluded; and 4) Patients had no heart diseases including arrhythmias.

The sex and age distribution are shown in Table 1. Eighty-five percent were outpatients.

Equipment and methods

The IV DSA examinations were performed using a DSA imaging system (Toshiba Co., Tokyo, Japan FDP-40 A, image memory 64 M byte, magnetic disk 264.8 M byte, X-ray generator KXO-1250, X-ray tube DXB-1024 CH). It was used routinely with a 0.6 mm focal spot and a 9 inch image intensifier mode. Exposure factors were determined by video peak detector and were generally at 100 mA and 65-75 kVp. The video signal was stored in a 1024 X 1024 X 8 resolution. The serial images were obtained at a rate of 3.25 frames/sec.

Contrast medium was injected into the femoral vein, through a 14 gauge, 6.4 cm long teflon catheter commercially available. This catheter was curved to facilitate its advance into the venous cavity (Fig. 1). After the confirmation that the catheter was properly placed, 45 ml of nonionic contrast medium iohexol (Omnipaque 350; Daiichi Co., Tokyo, Japan) was injected at a rate of 30 ml/sec.

The author's method of femoral vein catheterization was derived from the preliminary studies, which indicated that using a shorter length and larger caliber catheter made it possible to send bolus amount of contrast medium. This is carried as a fast moving mass and migrates into the cerebral arteries at a relatively high concentration. Views were obtained routinely at anteroposterior (AP) and slightly oblique projections: 8° to 10° which made stereoscopic view possible. Lateral or oblique projection might be added in some patients if they had normal renal function. The studies were carried out in the conscious state to obtain the cooperation. Intra-arterial digital subtraction angiography (IA DSA) was done by transfemoral catheterization technique. Omnipaque 300, 4 to 6 ml each time, was injected selectively into three or four vessels.

Table 1. Patients included for screening of unruptured cerebral Ans by IV DSA

Age	Male	Female	Total
20 to 29	92	36	128
30 to 39	136	62	198
40 to 49	292	204	496
50 to 59	409	310	719
60 to 69	404	389	893
70 to 79	339	270	609
80 to 89	37	66	103
Total	1,809	1,337	3,146

Ags were between 22 and 88 years, with the mean being 57 years.

Table 2. False positive and false negative cases in the diagnosis of unruptured cerebral An by IV DSA

	False positive 96/142=67.6%		False negative 8/46=17.4%		
No. of patients	95/142	1/142	2/13	4/33	2/33
IV DSA	+	+	−	−	−
IA DSA	−	+	+	+	−
Operation	no operation	−	no operation	+	+
Number of Ans	121 false	1 false	3	5	2

+An finding present, − absent

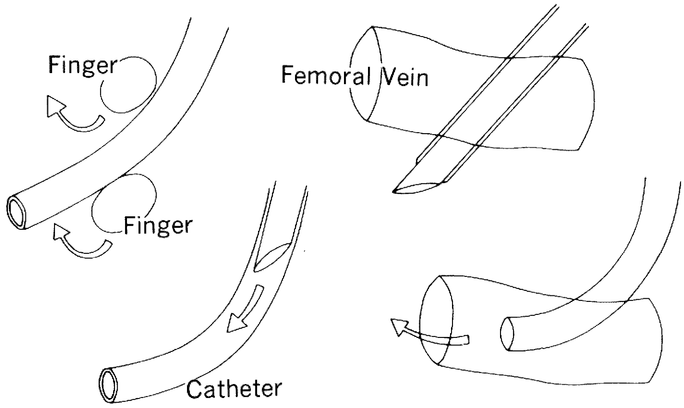


Fig. 1. Insertion method of a 14 gauge 6.4 cm long teflon catheter into the femoral vein.

Data analysis

The quality of the IV DSA pictures was then checked; if they were considered of good quality, the findings were compared to those of IA DSA. The resolution of IV DSA compatible with IA DSA was considered as a golden standard. The number and incidence of Ans was determined on IV and IA DSA. The size of the An was corrected by its enlargement ratio.

The sensitivity, true and false prediction value of Ans in IV DSA were analysed on the basis of the findings of IA DSA as follows;
Sensitivity = Number of pictures with Ans found/All patients with Ans, True predictability = Number of patients with Ans/All patients with Ans on IV DSA, False predictability = Number of patients with false Ans/All patients with Ans on IV DSA (False positive ratio),
The range of the size of Ans was determined to see the resolution limit of IV DSA.

Finally, comparisons of the findings of IV and IA DSA were analysed. Infundibular dilatation, when certain, was not counted as An. Ordinarily it was not the target for surgery.

RESULTS

(1) The quality of IV DSA, and incidence of Ans in IV DSA

In 2,730 of the 3,146 patients (86.8%), IV DSA pictures readily visualized major vessels in good resolution and 2 mm An, if present, could be demonstrated clearly.

In them, Ans including questionable ones were found in 161 patients (5.9%). Of these, 142 patients received IA DSA as described in paragraph (2). Including the series of cases presented here, we have done 4,609 IV DSA studies for various neurological problems during the period from February 1989 to March 1994. From these studies, we obtained very clear pictures in 4,057 cases (88.0%). This is higher than those reported by others, which ranged from 42 to 85%.[16,18,19,22,24-27)]

(2) Comparison between IV DSA and IA DSA

Of 142 patients, the presence of Ans was confirmed in 46 patients (32.4% true predictability). An was absent in the remaining 96 patients (67.6%, false positive). In 46 patients, An was confirmed by IA DSA among estimated population of 2,408 (=2,730×142/161) with clear IV DSA. The chance of diagnosing An in a group of patients who met our selection criteria was 1.9% (46/2,408). Although angiographic criteria was less well defined, other authors reported series suggesting an incidence of about 1 to 5%.[28-33)]

(3) Predictability and false predictability of Ans

If we count the number of Ans instead of patients, the true predictability of Ans by IV DSA was 29.7%. Since 142 patients had 172 questionable Ans in IV DSA and, among them, 46 patients had 51 Ans confirmed by IA DSA.

Out of 121(=172-51) false An in various locations as shown in Table 2, 104 (86%) were due to arterial loops in spite of two different angle views being obtained customarily. The rest were due to artifacts

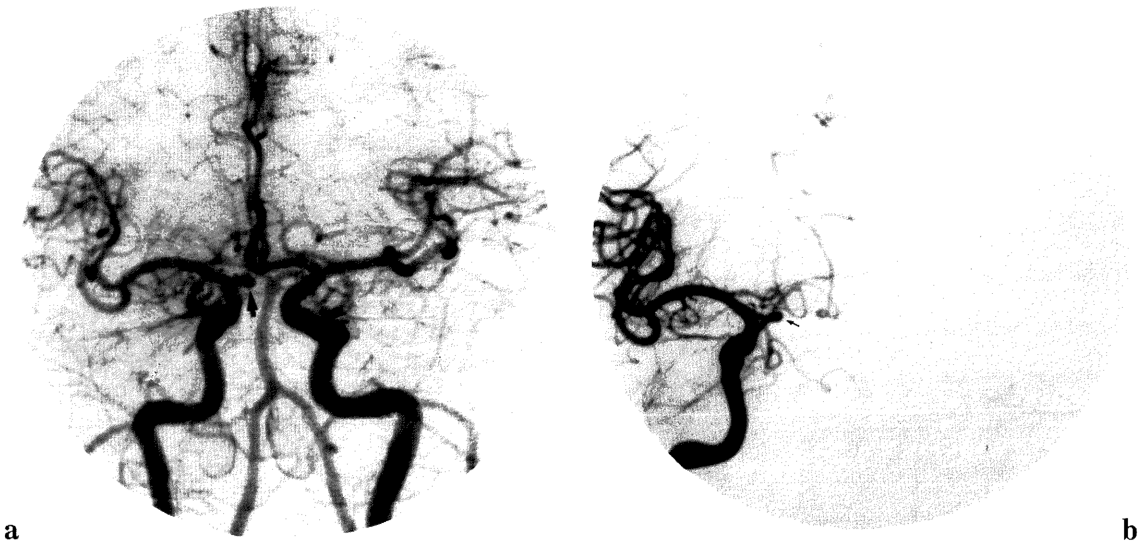


Fig. 2. **a.** IV DSA suggests the presence of an An of the Rt. Internal carotid artery (IC) (*arrow*). **b.** IA DSA reveals a looping vessel (*arrow*), not an An (AP view).

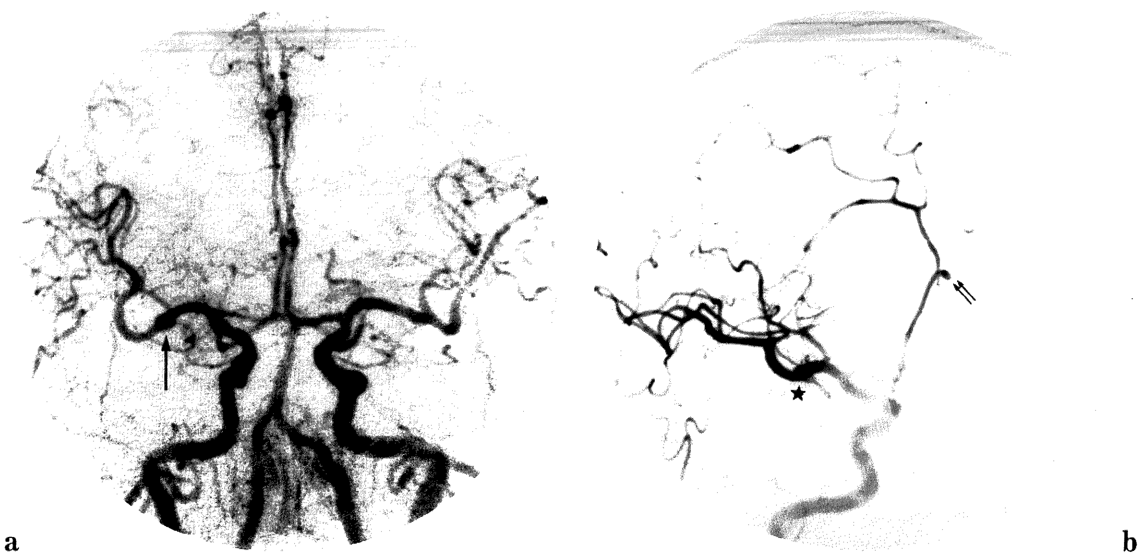


Fig. 3. **a.** IV DSA suggests Rt. middle cerebral artery (MC) An (*arrow*). **b.** IA DSA reveals Rt distal anterior cerebral artery (AC) An (*arrows*), and no MC An (★).

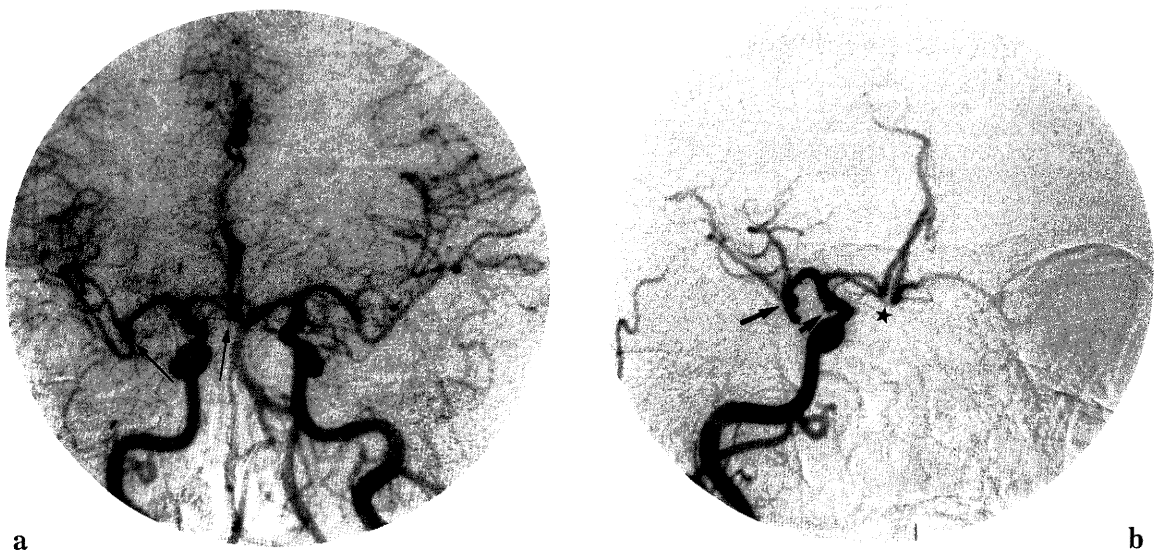


Fig. 4. **a.** On IV DSA, Rt. MC An (*arrow*) and anterior communicating artery (Acom) An (*arrow*) are suspected. **b.** IA DSA proves the presence of Rt. MC An (*arrow*) and a small Rt. IC junctional dilatation (*arrow*) and the absence of Acom An (★).

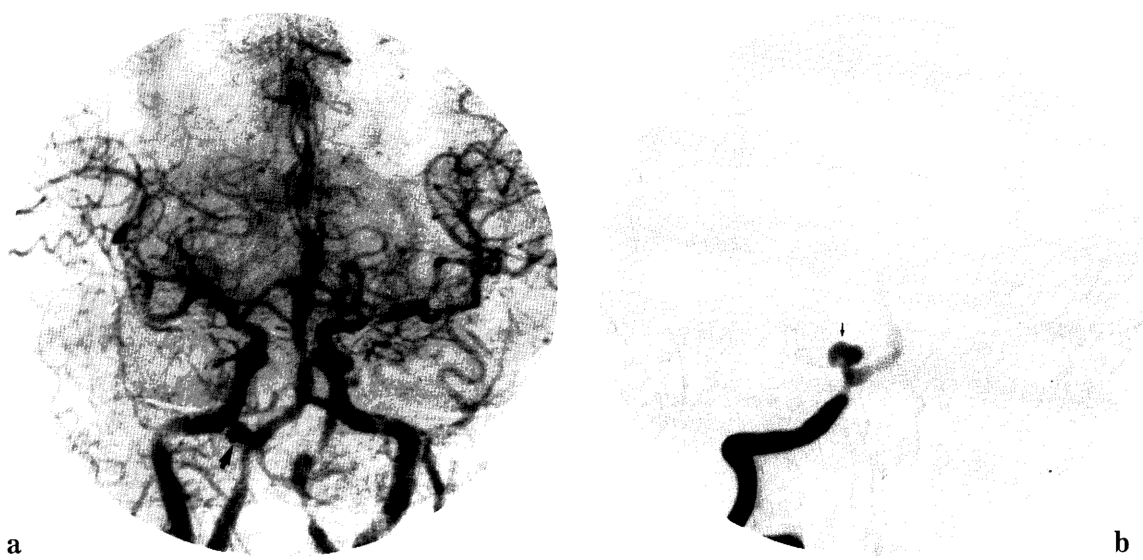
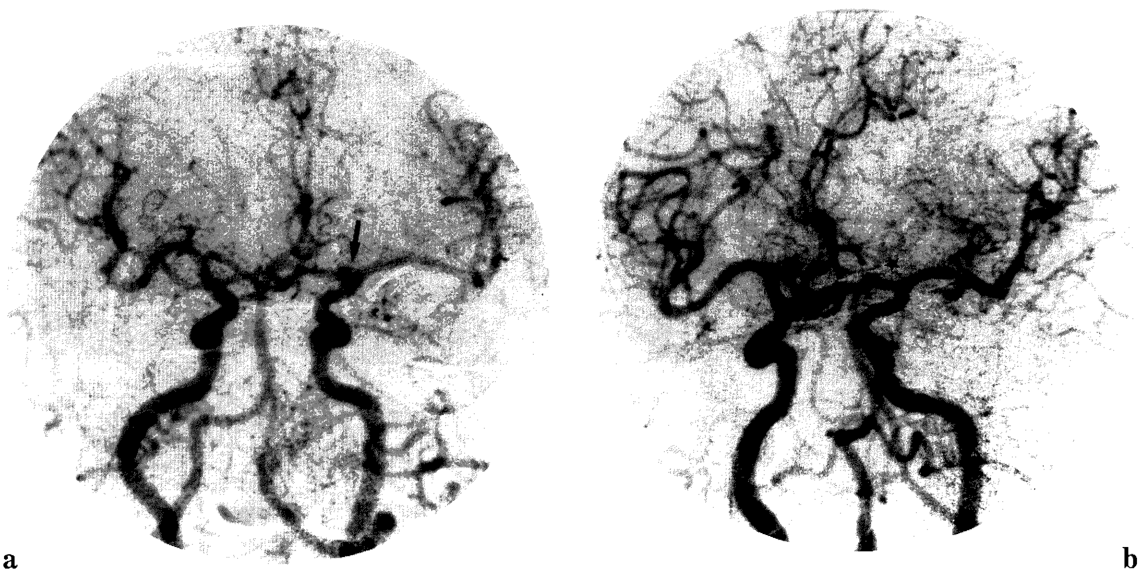


Fig. 5. **a.** IV DSA suggests Rt. vertebral artery (VA) An (*arrow*). **b.** Vertebral IA DSA strongly indicated a diagnosis of An, but surgery revealed a complicated loop of a dilated artery (*arrow*).

a b

Fig. 6. **a.** IV DSA suggests an An at the top of the basilar artery (BA) (*arrow*). **b.** Vertebral IA DSA gives no conclusion as to diagnosis (*arrow*).



a b

Fig. 7. **a.** IV DSA suggests an An (*arrow*) in the proximal Lt. A 1 segment. **b.** IV DSA, oblique view. This was an artifact and there was no An (★).

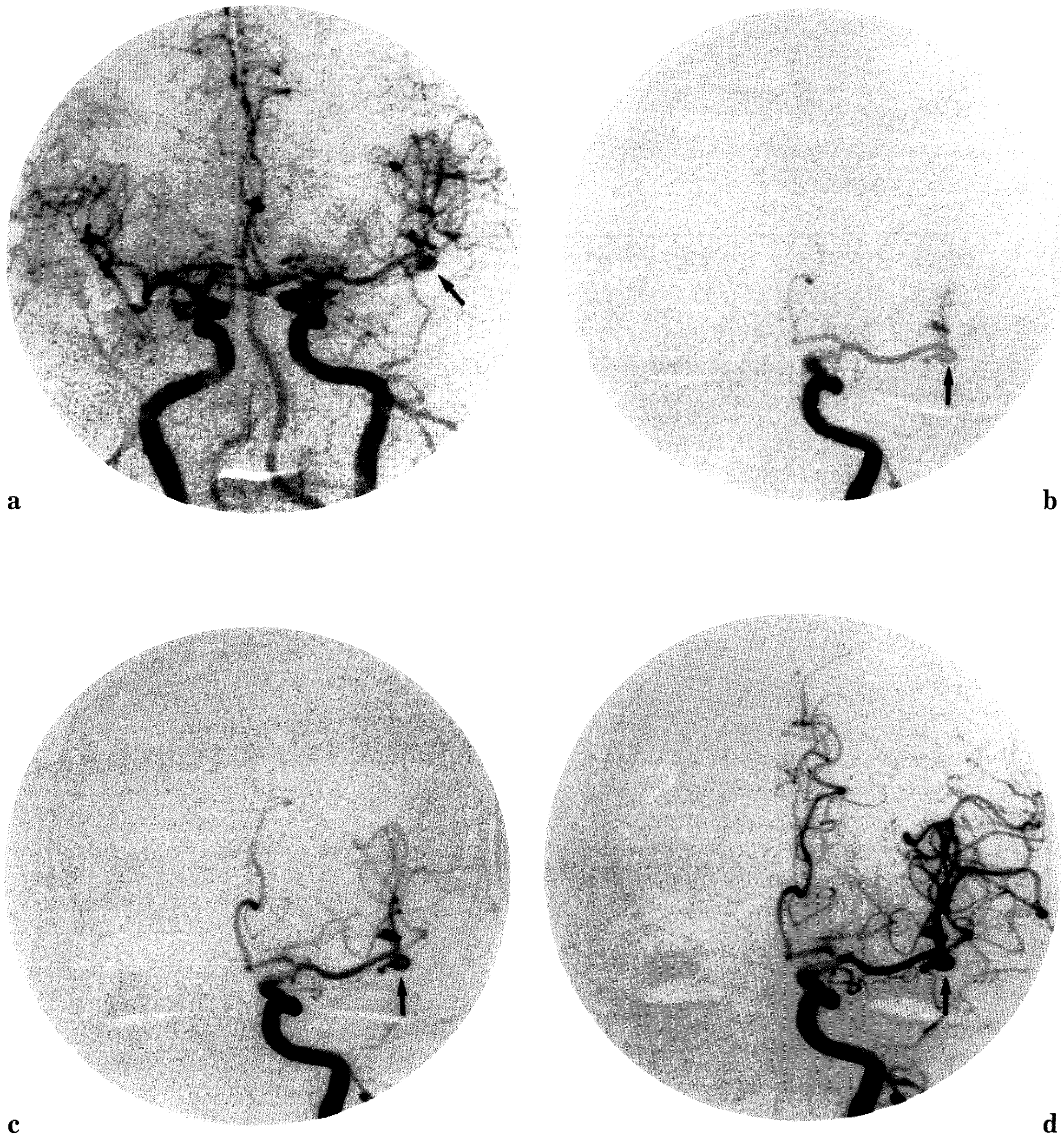


Fig. 8. **a.** On IV DSA an An was suspected in Lt. MC bifurcation (*arrow*). **b, c, d.** The IA DSA pictures could be mistaken for an arterial loop, because of the intraluminal laminar flow, although it was an An (*arrow*).

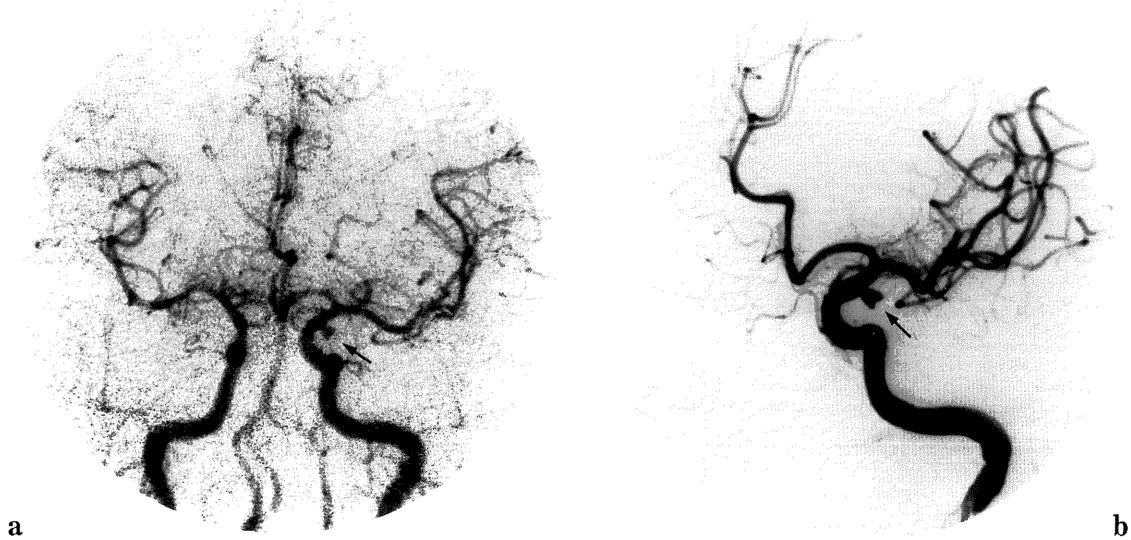


Fig. 9. **a.** IV DSA shows an An of the Lt. IC (*arrow*). **b.** IA DSA oblique view (*arrow*). This 5 mm An was arrowhead-shaped because of an indentation created by its impinging upon an oculomotor nerve.

or due to overlapping with other vessels. There was one An-looking structure which was diagnosed as An by IV DSA and IA DSA but at surgery proved to be a complicated loop of a dilated artery. False predictability (False positive ratio) was 67.6%.

Among false negative cases, there were three Ans in 13 cases which were not shown on IV DSA but seen on the IA DSA. They were not surgical candidates. In the surgical group of 33 patients, there were five Ans which were not shown on the IV DSA but apparent on IA DSA. Two small Ans of 2 mm in diameter each not recognized on either IV DSA or IA DSA were incidentally found during clipping procedure for other known Ans. All 10 false negative Ans by IV DSA were 3 mm or less in size. False negative ratio was 17.4%. The causes of false positive and false negative diagnosis were patients' motion, arterial loop, overlapping with other structure and artifacts. The representative cases are shown in Fig. 2 through 9.

(4) Ranges of size of Ans

All 51 Ans of the 46 patients confirmed by IA DSA were larger than 2 mm. The diameter of the smallest An recognized by IV DSA in this study was 2 mm at the proximal portion of the right anterior cerebral artery (Fig. 10). As mentioned above, all 10 Ans that escaping detection by IV DSA were 3 mm or smaller in size.

Table 3. Complications in IV DSA studies for 4,609 cases

Nausea	10
General discomfort	4
Chest discomfort	2
Heat sensation in the face or body	11
Chills	2
Skin eruption	6
Slight hypotension	1
Slight dyspnea	1
Local hematoma	20
Total	57(1.2%)

(5) Complications

We encountered 57 (1.2%) minor complications in 4,609 IV DSA studies, but none of them was serious (Table 3). Thirty-seven of them seemed to be due to a hypersensitive reaction to the contrast medium. However, none of them needed intensive treatment. Oxygen inhalation and the administration of steroids were given in 16 cases after which symptoms soon disappeared. There were 19 cases of slight local hematoma at the site of puncture but resolved spontaneously. In one case, a hematoma was evacuated and lacerated small arterial branch had to be ligated.

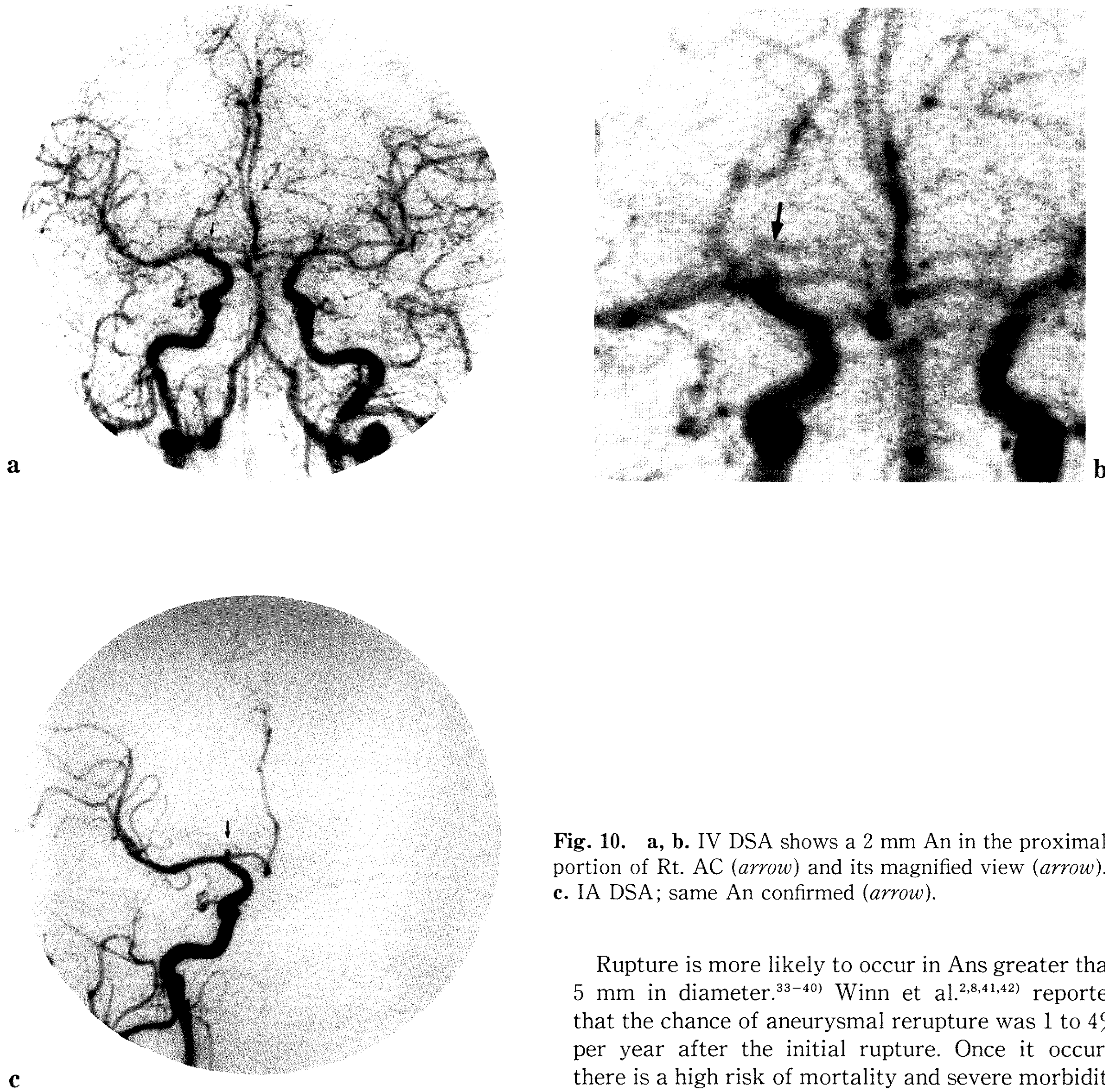


Fig. 10. a, b. IV DSA shows a 2 mm An in the proximal portion of Rt. AC (*arrow*) and its magnified view (*arrow*). c. IA DSA; same An confirmed (*arrow*).

DISCUSSION

The surgical treatment of unruptured cerebral An remains controversial since its natural history is not well known. However, in order to determine whether or not screening examination and consequent prophylactic surgery is needed, it is necessary to clarify the incidence and natural history of cerebral Ans in the general population.

Rupture is more likely to occur in Ans greater than 5 mm in diameter.[33-40] Winn et al.[2,8,41,42] reported that the chance of aneurysmal rerupture was 1 to 4% per year after the initial rupture. Once it occurs, there is a high risk of mortality and severe morbidity in survivors.[1-7] The value of screening depends on how individual neurosurgical teams manage the patients with unruptured Ans. Thomas et al. elaborated their opinion, taking the most recent literature into consideration, that a reasonable surgical candidate who has a life expectancy of at least 3 years should have surgery.[33]

The author advocates the surgical treatment for unruptured Ans because of its low operative mortality and morbidity.[1,7,37,43,44] However, the surgical indication of unruptured cerebral Ans should be carefully decided upon, depending on the individual situation.

For IV DSA to be used for screening unruptured

Ans, there are several important points. The most basic is to obtain a high quality picture. As described, the author's method of pressure injection of larger amount of contrast medium into the comparatively thick and the near centrally situated femoral vein serves the purpose. Many investigators practice the peripheral injection technique for IV DSA study.[18-20,22-26,45,46] Other authors used a central catheterization technique.[16,27,46-48] We believe, however, that if the contrast medium injection is made into a small peripheral vein or through a long thin catheter into a central vein, the resistance in pressure injection is great and flow rate becomes restricted, then the bolus effect would ordinarily be diminished. Complications such as vein rupture could occur in these circumstances. Our method has overcome these shortcomings. Then needless to say, the cooperation of the patients to remain still during picture taking through their cooperation is essential. Motion during each injection caused misregistered subtraction artifacts between the mass image and the contrast containing image, which was the cause of most of uninterpretable IV DSA images. For uncooperative patients, we occasionally used venous anesthesia with thiopental sodium. Patients with heart trouble, especially atrial fibrillation, are usually very unfavorable subjects for IV DSA because the contrast medium becomes diluted due to slow systemic circulation.

The arterial loop is actually the main problem in screening the Ans. This usually projects a heavier shadow on the film and arouses the examiner's attention. However, if not solved by another view, one has to resort to the next step of IA DSA. Middle cerebral artery (MC) bifurcation area was the most susceptible place for this type of misinterpretation. Also, vertebral artery (VA) and basilar artery (BA) were unfavourable areas since occasionally the imaging contrast is poorer and superimposition occurs with anterior circulation.

Overlapping with other vessels is also a common factor in misinterpreting images. However, this can be recognized since it also casts a heavier shadow. This kind of observation is generally more common with IV DSA than IA DSA since the concentration of the contrast media is thinner and the contrast effect of overlapping structure will be accentuated.

Artifacts in IV DSA are another problem but usually additional projections from different angles will solve this .

The smallest An found in our series was 2 mm in diameter. The author believes An of this size will be found by our method with high probability. Also, 2 mm was the smallest limit of aneurysmal size in our IA DSA series. We believe important roles of the IV DSA as a screening method should be basically to choose questionable cases from a large group.

As one becomes more meticulous in interpreting IV DSA pictures, the false positive cases will increase and accordingly the chance of missing true Ans decreases, since a detailed study will follow these cases. Therefore, we are not concerned about a high ratio of false positive. In this series. chance of finding An by IV DSA was 32.4%. This figure is lower than that reported by other authors.[22,23]

In spite of number of the above mentioned limitations of IV DSA for the screening of Ans, we believe its considerably high reliability and feasibility outweighs these shortcomings. Such screening tests, which can be casually and repeatedly conductible for follow-up study would be in great demand. This is especially so in view of the common knowledge of newly developing An, rapidly growing An, familial An and rather high incidence of multiple Ans.

This study indicates that 2 mm An could be seen and all 10 false negative Ans were 3 mm or less in diameter. Accordingly, the author assumes that the Ans with a diameter of about 4 mm or larger can be detected by means of IV DSA with good accuracy. Therefore, it would seem reasonable that most asymptomatic unruptured Ans large enough to pose a considerable risk for their rupture, i.e. 5 mm in diameter, can be identified on IV DSA.

This study indicates that IV DSA performed by the author's method is a useful means of detecting unruptured cerebral Ans for screening purposes.

A summary of the beginning part of this study was presented by the author at the 49th Annual Meeting of The Japan Neurosurgical Society on October 25, 1990 in Tokyo.

Acknowledgements. The author would like to thank Proffessor Yoshifusa Shimizu for his useful advice, Dr. Akira Horiuchi, all the staff doctors and X-ray technicians of Kobayashi Neurosurgical Hospital for their performance and assitance in procedure. Mrs. Kyoko Horiuchi for her help in the preparation of this paper.

REFERENCES

1) Drake CG: Management of cerebral aneurysm. *Stroke* **12:** 273-283, 1981.
2) Winn HR, Almaani WS, Berga SL, Jane JA, Richardson AE: The long-term outcome in patients with multiple aneurysms. *J Neurosurg* **59:** 642-651, 1983.
3) Maurice-Williams RS: Ruptured intracranial aneurysms: has the incidence of early rebleeding been over-estimated? *J Neurol Neurosurg Psychiatr* **45:** 774-779, 1982.

4) Pakarinen S: Incidence, aetiology, and prognosis of primary subarachnoid hemorrhage. A study based on 589 cases diagnosed in a defined urban population during a defined period. *Acta Neurol Scand* **43** (Suppl. 29): 1-128, 1967.
5) Rosenørn J, Eskesen V, Schmidt K, Espersen JO, Haase J, Harmsen A, Hein O, Knudsen U, Midholm S, Marcussen E, Rasmussen P, Rønde F, Voldby B, Hansen L: Clinical features and outcome in 1076 patients with ruptured intracranial saccular aneurysms: a prospective consecutive study. *Br J Neurosurg* **1:** 33-46, 1987.
6) Sundt TM Jr., Kobayashi S, Fode NC, Whisnant JP: Results and complications of surgical management of 809 intracranial aneurysms in 722 cases. *J Neurosurg* **56:** 753-765, 1982.
7) Jane JA, Winn HR, Richardson AE: The natural history of intracranial aneurysms: rebleeding rates during the acute and long term period and implication for surgical management. *Clin Neurosurg* **24:** 176-184, 1977.
8) Heiskanen O: Risk of bleeding from unruptured aneurysms in cases with multiple intracranial aneurysms. *J Neurosurg* **55:** 524-526, 1981.
9) Moyes PD: Surgical treatment of multiple aneurysms and incidentally-discovered unruptured aneurysms. *J Neurosurg* **35:** 291-295, 1971.
10) Weir B: Intracranial aneurysms and subarachnoid hemorrhage: an overview. In: Wilkins RH, Rengachary SS (eds) Neurosurgery, Vol 2. McGraw-Hill, New York 1985, p 1308-1329.
11) Futatsuya R, Seto H, Kamei T, Nakashima A, Kakishita M, Kurikoto M, Endo S: Clinical utility of three-dimensional time-of-flight magnetic resonance angiography for the evaluation of intracranial aneurysms. *Clin-Imaging* **18(2):** 101-6, 1994.
12) Masaryk TJ, Ross JS: MR angiography: clinical applications. In: Atras SW (ed) Magnetic resonance imaging of the brain and spine. Raven Press, New York 1991, p 1079-1098.
13) Miki H, Hamamoto K: MR Angiography. *Nichidoku-Iho* **37** (Heft 4): 31-41, 1993.
14) Ross JS, Masaryk TJ, Modic MT, Ruggieri PM, Haacke EM, Selman WR: Intracranial aneurysms: evaluation by MR angiography. *AJNR* **11:** 449-455, 1990.
15) Borgstein RL, Brown MM, Warerston J Butler P, Thakkar CH, Wylle IG, Swash M: Digital subtraction angiography (DSA) of the extra cranial vessels: a direct comparison between intravenous and intraarterial DSA. *Clin Radiol* **44(6):** 402-5, 1991.
16) DeFilipp GJ, Pinto RS, Lin JP, Kricheft II: Intravenous digital subtraction angiography in the investigation of intracranial disease. *Radiology* **148:** 129-136, 1983.
17) Foley WD, Smith DF, Milde MW, Lawson TL, Towne JB, Bandyk DF: Intravenous DSA examination of patients with suspected cerebral ischemia. *Radiology* **151:** 651-659, 1984.
18) Forbes GS, Earnest F 1V, Kispert DB, Folger WN, Sundt TW Jr: Digital angiograhy. Introducing digital techniques to clinical cerebral angiography practice. *Mayo Clin Proc* **57:** 683-693, 1982.
19) Modic MT, Weinstein MA, Chilote WA, Pavlicek W, Duchesneau PM, Furlan AJ, Little JR: Digital subtraction angiography of the intracranial vascular system: comparative study in 55 patients. *AJR* **138:** 299-306, 1982.
20) Wood GW, Lukin RR, Tomsick TA, Chambers AA: Digital subtraction angiography with intravenous injection: assessment of 1,000 carotid befurcations. *AJR* **140:** 855-859, 1983.
21) Zimmerman RD, Leeds NE, Goldman MJ: Digital subtraction angiography in the evaluation in patients with cerebrovascular disease. In: Fein JM, Flamm ES (eds) Cerebrovascular Surgery, Vol 2. Springer-Verlag, New York 1985, p 343-358.
22) Fukaya H, Saeki N, Sunami K, Hoshi S, Komiya H: Intravenous DSA as a screening method for cerebral aneurysm *Rinsho Hoshasen* **35(9):** 1005-10, 1990.
23) Samejima H, Iwabuchi S, Aoki K, Mizokami T, Sato T, Kasai K, Tsuzuki T, Yoshii N: Study of screening test for cerebral aneurysms. *Surg Cerebr Str* **15:** 8-12, 1987.
24) Edward F. Crocker, Jr., Roger HT, John CB: The role of intravenous digital subtraction angiography in the evaluation of extracranial carotid artery disease. Can the decision for carotid artery surgery be made solely on the basis of its findings? *Vascular Surg* Vol. 4, No. 2, 157-163, 1986.
25) Doris I, Hochhauser L, Vaughn WC, Stolberg HO, Romero MA: Intravenous digital subtraction angiography by peripheral injection. *J Cana Asso Radiol* **38:** 7-10, 1987.
26) Huber G, Piepgras U: Update and trends in venous (VDSA) and arterial (ADSA) digital subtraction angiography in neuroradiology In: Advances and Technical Standards in Neurosurgery. Vol. 11, Springer-Verlag, Wien-New York 1984, p 37-57.
27) Michael G, Hoffman Antoinette S, Gomes S, Osher P: Limitations in the interpretation of intravenous carotid digital subtraction angiography. *AJR* **142:** 261-264, 1984.
28) Atkinson JLD, Sundt TM Jr., Houser OW, Whisnant JP: angiographic frequency of anterior circulation intracranial aneuysms. *J Neurosurg* **70:** 551-555, 1989.
29) Hassler O: Morphological studies on the large cerebral arteries, with reference to aetiology of subarachnoid hemorrhage. *Acta Psychiat Scand* (Suppl.) **154:** 1-145, 1961.
30) McCormick WF: Problems and pathogenesis of intracranial arterial aneurysms, In: Moossy J, Janeway R (eds) Seventh conference cerebral vascular diseases, Grune & Stratton, New York 1971, p 219-231.
31) Stehbens WE: Aneurysms and anatomical variation of cerebral arteries. *Arch Pathol* **75:** 45-64, 1963.

32) Stornelli SA, French JD: Subarachnoid hemorrhage—factors in prognosis and management. *J Neurosurg* **21:** 769-780, 1964.
33) Thomas MW, John G, Joseph MZ, Robert F: Spetzler Management of unruptured intracranial aneurysms *BNI QUARTERLY* Vol 8, No. 1, 2-7, 1992.
34) Crompton MR: Mechanism of growth and rupture in cerebral berry aneurysms. *Br Med J* **1:** 1138-1142, 1966.
35) Ferguson GG, Peerless SJ, Drake CG: Natural history of intracranial aneurysm. *New Engl J Med* **305:** 99, 1981,
36) Freytag E: Fatal rupture of intracranial aneurysms. *Arch Pathol* **81:** 418-424, 1966.
37) Jomin M, Lesoin F, Lozes G, Fawaz A, Villette L: Surgical prognosis of unruptured intracranial arterial aneurysms. Report of 50 cases. *Acta Neurochir (Wien)* **84:** 85-88, 1987.
38) Locksley HB: Report on the cooperative study of intracranial aneurysms and subarachnoid hemorrhage (Section V). Part II. Natural history of subarachnoid hemorrhage, intracranial aneurysms and arteriovenous malformations. *J Neurosurg* **25:** 321-368, 1966.
39) Ojemann RG: Management of the unruptured intracranial aneurysm. *New Engl J Med* **304:** 725-726, 1981.
40) Wiebers DO, Whisnant JP, Sundt TM Jr., O'Fallon WM: The significance of unruptured intracranial saccular aneurysms. *J Neurosurg* **66:** 23-29, 1987.
41) Wiebers DO, Whisnant JP, O'Fallon WM: The natural history of unruptured intracranial aneurysms. *New Engl Med* **304:** 696-698, 1981.
42) Winn HR, Richardson AE, O'Brien W: Long-term prognosis in untreated cerebral aneurysms: II. late morbidity and mortality. *Ann Neurol* **4:** 418-426, 1978.
43) Mizoi K, Suzuki J, Yoshimoto T: Surgical treatment of multiple aneurysms: Review of experience with 372 cases. *Acta Neurochir (Wien)* **96:** 8-14, 1989.
44) Salazar JL: Surgical treatment of asymptomatic and incidental intracranial aneurysms. *J Neurosurg* **53:** 20-21, 1980.
45) P. Butler, M. R. C. P., F. R. C. R., C. E. L. Freer., M. R. C. P., F. R. C. R., A. N. Jha, F. R. C. S. R. H. Lye, M. Sc., F. R. C. S: Intravenous digital subtraction angiography in intracranial aneurysms. *Br J Radiol* 60, 323-326, 1987.
46) Enzmann DR, Brody WR, Riederer S, Keyes G, Collins W, Pele N: Intracranial intravenous digital subtraction angiography. *Neuroradiol* **23:** 241-251, 1982.
47) Raymond FC, Janice RL Smith, Joachim FS, Theron WO, M Paul Capp: Intracranial applications of digital intravenous subtraction angiography. 1 *Radiology* **144:** 529-534, 1982.
48) Hasuo K, Tamura S, Kudo S, Uchino A, Carlos R, Matsushima T, Kurokawa T, Kitamura K: Moya moya disease: Use of digital subtraction angiography in its diagnosis. *Radiology* 1985, p 157-111.