

UNIVERSITÉ DE NANTES

FACULTÉ DE MÉDECINE

Année: 2021

N° 2021-205

THÈSE

pour le

DIPLOME D'ÉTAT DE DOCTEUR EN MÉDECINE

Radiologie et Imagerie médicale

par

Alexandre PICHERIT

Né le 26 Avril 1992 à Mont-Saint-Aignan (76)

Présentée et soutenue publiquement le 15 Octobre 2021

Neuroradiological imaging paradigm in patients with Infective endocarditis: A National Survey.

Président : Monsieur le Professeur Hubert DESAL

Directeur de thèse : Monsieur le Professeur Romain BOURCIER

Jury : Monsieur le Professeur David BOUTOILLE

Monsieur le Professeur Jean-Christian ROUSSEL

REMERCIEMENTS:

Aux membres du jury,

Le Président du jury, **Monsieur le Professeur Hubert DESAL**, merci de me faire l'honneur de présider mon jury, soyez assuré de mon profond respect.

Mon directeur de thèse, **Monsieur le Professeur Romain BOURCIER**, merci de m'avoir proposé de réaliser ce travail. Ton encadrement d'une grande qualité et ta disponibilité ont été précieux pour l'aboutissement de ce projet.

Monsieur le Professeur Jean-Christian ROUSSEL, merci d'avoir accepté de juger ce travail, je vous témoigne ma gratitude.

Monsieur le Professeur David BOUTOILLE, merci d'avoir accepté de faire partie de mon jury de thèse. Veuillez trouver ici l'expression de mes sincères remerciements.

Aux Professeurs Pascale Schneider et Benoît Veber pour votre soutien fondamental tout au long de mon cursus médical Rouennais.

A mes formateurs en Neuroradiologie à Nantes, Pr Desal, Pr Bourcier, Dr Elisabeth Auffray-Calvier, Dr Alina Lintia-Gaultier, Dr Jesus Aguilar, Dr Benjamin Daumas-Duport, Dr Cédric Lenoble, Dr Pierre-Louis Alexandre, Dr Lili Detraz, merci pour votre enseignement de grande qualité et pour m'avoir transmis la fibre neuroradiologique.

A tous mes formateurs en Radiologie à Nantes, Saint-Nazaire et La Roche/Yon, pour votre professionnalisme et à cette constante bonne ambiance.

Aux Angevins pour leur enseignement Neuroradiologique d'une grande justesse, Dr Labriffe, Dr L'Allinec, Dr Lignon, Dr Tanguy et Dr Girot. Et à la clique de joyeux lurons Isabelle, Antoine et Victor.

A mes parents, pour leur soutien inconditionnel tout au long de mes études et à leur éducation bienveillante.

A ma famille, Barthélémy, Anne-Charlotte, Aymeric, Coralie, Matthieu, Sixtine, Cédric, Mam et Maminouche, pour tous ces moments heureux passés ensemble.

A tous les copains du lycée, Polo, Lixou, Marion, Brib, Vic, Mat, Guigui, Rico, Moreau, Carmiche, VdB, Flo, Marie-Lo, Arnaud, Eugé, Marie, Vico, Biz, Gus, Tib, Agathe.

A mes belles rencontres d'Erasmus, Philou, Léa G, Kimon, Philipp, Nico, Leita, Paula, Marion et tellement d'autres.

Aux merveilles, Schneid' mon Ferguson, Benish mon Choubs d'la casse, Thomish mon Ragnar sensible, Guizz mon Duc de, Benlard apéro mirador.

A la team ski folizz pour ces superbes années passées à Rouen, Agathe, Marco, Emilyy, Philou, Lolo, Guizz, Sarasse, Chachou, Tomish, Schneid, Pabou, Jo et Benish pour la triloc, Ben...

A tous ces moments de vie partagés avec vous en coloc, Kimon, Philipp, Leita, Ben, Schneid, Benoit, Nono, Audrey, Marius, Etienne, Amo, Andy et Jean.

A la team Pyjama-Fraise, pour cette belle cohésion de promo pendant ces 4 années: Toinou j'peux pas j'ai crossfit, Marion notre princesse, Vince maestro de l'hystero, Perraud déglingo, Guigui tisane party.

Aux combats de Coqs sur les parquets de squash nantais, Elliot Coyote, Thibault Bellâtre, Guigui, et peut-être même Flo un jour?

Aux belles rencontres Nantaises: Elise, Coach, Quentin la beauféthie, Adri baroudeur ultrachic, Jet'Rhum, Marie-Em, Audry maman du petit Marcel, Philo et Martin les chtimis, Minou, Amaury quel charisme, Cla, Erwan Calchemise, LP Mme la présidente, Marie la Comtesse.

A tous mes co-internes, Vince, JuChate, Lucie, Tachyy, Jérôme, Antoine, Aymeric, Mymy Massif, Sylvain, Marion, Théo, Pauline, Ravenel Boulot Boulot Boulot, Aude, Irène, Louis, Hernandez, Victor, Antoine et Zoé.

TABLE DES MATIÈRES:

REMERCIEMENTS.....	2
ABBREVIATIONS.....	5
ABSTRACT.....	6
I. INTRODUCTION.....	7
II. METHODS	
A. Population	8
B. Survey.....	9
III. RESULTS	
A. Systematic imaging screening.....	9
B. Modality of initial screening.....	9
C. Initial CT screening.....	10
D. MRI exploration.....	10
E. DSA.....	11
F. Follow-up.....	12
IV. DISCUSSION.....	13
V. SUPPLEMENTARY DATA.....	19
VI. REFERENCES.....	29

ABRÉVIATIONS

IIA: Infective Intracranial Aneurysm

IE: Infective endocarditis

CT: Computed tomography

MRI: Magnetic Resonance Imaging

DSA: Digital subtraction angiography

CMB: Cerebral Microbleed

FLAIR: Fluid Attenuated Inversion Recovery

DWI: Diffusion Weighted Imaging

ADC: Apparent Diffusion Coefficient

T2* GE: T2* weighted Gradient Echo

SWI: Susceptibility Weighted Imaging

CE: Contrast Enhanced

3D TOF-MRA: Three-Dimensional Time-of-Flight Sequence of Magnetic Resonance Angiography

3D T1 GE: 3D T1 weighted Gradient-Echo

3D T1 SE: 3D T1 weighted Spin-Echo

Neuroradiological imaging paradigm in patients with Infective endocarditis: A National Survey.

Abstract

Objectives: The aim of this study was to identify imaging protocols in patients with infective endocarditis through a nationwide survey.

Methods: An electronic evolutionary survey was sent to interventional Neuroradiologists among neuroradiological centers under the aegis of the Société Française de Neuroradiologie.

Among 33 contacted centers, 25 completed the survey (21 university hospitals and 4 peripheric hospitals).

Results: Most of the centers (88%) use systematic imaging screening in IE patients. MRI is the first imaging method used in 66% of cases while CT is used in 44%. When no IIA is detectable in CT-scan screening, 6 (54,54%) use no further investigation, while 9 (81,81%) continue with MRI exploration in case of hemorrhage, ischemia or enhancement. Sulcal hemorrhage in MRI is an indication of complementary DSA in 25 centers (100%). Regarding IIA characterization, 12 centers (48%) use systematic DSA, whereas for 10 centers (40%), DSA is conditioned by hemorrhage or patient status.

Conclusion: We highlighted large variations in Neuroimaging exploration and follow-up of IE patients in real-world practices. Expert guidelines able to standardize practices are warranted to improve the management of this serious and often misdiagnosed pathology.

I. Introduction

Infective endocarditis (IE) is a relatively rare pathology, with an estimated incidence of 3-15/100 000 persons annual cases (1–4). Adherence and microbial proliferation of a cardiac native or prosthetic valve can lead to valvular destruction, systemic embolization and potential heart dysfunction (5).

Various populations can be affected, with a mean age of 62,3 years old (SD=15,9), and a male individual predominance (4).

Therapeutic management suffers in many ways from the paucity of randomized studies.

Neurological complications are frequently the first sign of IE. Brain lesions on MRI are very frequent, ranged from hemorrhagic lesions (60%), ischemic stroke in up to 50% of the patients, rarely meningitis (6%) to brain abscess (6%) (6–9). More than half of these lesions are clinically silent (7).

Among all IE neurological complications, infective intracranial aneurysm (IIA) is rather uncommon with an estimated prevalence from 3 to 9% (7,8,10).

This incidence may be underestimated because of the potentially silent forms of IIA and to our knowledge, there is no prospective unbiased cohort of IE with systematic DSA available in the literature.

Studies showed high rates of mortality in patients with IIA (30%) and even higher when ruptured IIA (80%) (11).

Screening for IIA in patients with definite or possible IE is of tremendous importance especially for evaluation of the anticoagulation safety when a surgical valvular replacement is required. Cerebral Computed Tomographic (CT) and Magnetic Resonance Imaging (MRI), are commonly used for initial imaging screening.

However, the gold Standard for IIA screening remains Digital Subtraction Angiography (DSA).

In the absence of official guidelines to date, a high variability of screening methods for IIA and overall, for the IE work-up is expected among centers. Through a nationwide survey, we aimed at recording and analyzing the imaging strategies applied for IE and IIA in French hospitals.

II. Methods:

A. *Population:*

We conducted an observational study in French comprehensive hospitals, using a web-based survey from November 2020 to January 2021.

We first emailed French neuroradiologists through the Société Française de Neuroradiologie (SFNR) mailing list, asking for only one delegate physician for each neuroradiological center. This physician was deemed to report the local and standardized policy in his/her center.

The survey link was sent to each physician: 27 French university hospitals and 6 non university peripheric hospitals.

The non-responders were reminded in December 2020 and in January 2021. We received 25 fulfilled questionnaires from 21 university hospital (Saint-Etienne, Reims, Bordeaux, Tours, APHM, Lariboisière, Pitié-Salpêtrière, Fondation Rothschild, Saint-Anne, Kremlin-Bicêtre, Grenoble, Angers, Nantes, La réunion, Rouen, Limoges, Poitiers, Brest, Rennes, Nancy, Strasbourg) and 4 answers of peripheric hospitals (centre cardiologique du Nord, Valencienne, La rochelle, groupement libéral Tours-Orléans).

B. Survey:

We used a Google Form online survey which was a progressive and evolutionary questionnaire with multiple choice questions (see *supplementary data*). A preliminary survey version was reviewed and tested by expert Neuroradiologists (GB, EAC).

The survey was built with 7 different parts:

1- "Systematic imagery screening" 2- "Modality of initial screening" 3- "*Initial CT-scan screening*" 4- "*MRI exploration*" 5- "*DSA exploration*" 6- "follow-up" 7- "Free comments". The answers were received on google sheets for analysis after closure of the survey and translated into graphics.

III. Results

A. Systematic imaging screening

Among centers that answered the survey, 22 (88%) make a systematic imagery screening in IE patients. In the 3 remaining centers (12%), imagery screening isn't systematic, conditioned by a neurological sign or a surgical project.

B. Modality of initial screening

MRI is the first technique used in 14 centers (56%), whereas CT-scan is used in 11 (44%).

C. Initial CT screening

All 11 centers that use CT-scan as first line technic (100%) have the following protocol regarding the head exploration: non-contrast CT, angiography, and contrast-enhanced acquisition.

Centers pointed out in the free comment part that CT was more accessible in many cases regarding the long duration of MRI sequences in patients potentially unstable.

When the first CT-scan screening is negative for IIA (Fig. 1A), 6 centers (54,54%) use no further investigation, 1 (9,09%) continues with a systematic MRI and 4 (36,36%) have different approaches depending on a potential surgical project.

When sulcal hemorrhage, ischemia or enhancement is detected on CT without IIA observed (Fig. 1B), 9 (81,81%) of the centers continue with MRI exploration, one center (9,09%) chooses systematic DSA, whereas one center (9,09%) uses both direct MRI and DSA.

When IIA is detectable on CT, associated with sulcal hemorrhage, ischemia or enhancement (Fig. 1C), 3 centers (27,27%) continue investigation with MRI, 4 (36,36%) with systematic DSA, 2 (18,18%) with DSA and MRI, whereas 2 centers (18,18%) explore with DSA only if surgical intervention is considered.

D. MRI exploration

About MRI exploration, 16 centers (64%) use indistinctly 1,5T or 3T, whereas 2 centers (8%) use preferably 1,5T and 7 (28%) 3T.

Regarding MRI protocol (Fig. 2), all centers use Diffusion Weighted Imaging (DWI) (100%), 24 (96%) employe Susceptibility Weighted Imaging (SWI) whereas one center (4%) use T2 weighted Gradient Echo (T2*). For vascular exploration, centers mainly answered standard 3D Time-of-flight Magnetic Resonance Angiography (3D

TOF-MRA) in 22 cases (88%), whereas the use of Contrast-enhanced 3D TOF-MRA concerns only 3 centers (12%).

18 centers (72%) use the 3D T2 FLAIR basic sequence, and 7 (28%) use a Contrast-enhanced 3D FLAIR.

About the contrast-enhanced exploration, Contrast-Enhanced 3D T1 weighted Gradient-Echo (CE-3DT1GE) is preferred by 15 centers (60%), comparatively to 10 centers (40%) that use Contrast-Enhanced 3D T1 weighted Spin-Echo (CE-3DT1SE).

Sulcal hemorrhage in MRI without IIA detected is an indication of complementary DSA in 25 (100%) of the centers. Other indications for DSA after MRI are Cerebral Microbleed (CMB) in 6 (24%), cerebral abscess in 5 (20%) and ischemic spots in 3 (12%) (Fig. 3).

E. *DSA exploration*

Regarding the indication of DSA, whatever the first line (CT or IRM) considered, sulcal hemorrhage is an indication of complementary DSA in 24 centers (96%), parenchymal hemorrhage in 18 (72%), whereas ischemic stroke is an indication for DSA in only 3 centers (12%). One center (4%) uses DSA only for intracranial hemorrhage in patients with a surgical valvular project.

In case of IIA detected by non-invasive techniques (Fig. 4A), 12 centers (48%) make a systematic DSA for architectural characterization, whereas 10 (40 %) don't use systematic DSA. In the non-systematic group, 4 centers (16%) use DSA only if intracranial hemorrhage and in 6 (24%) the indication of DSA was discussed depending on patient status.

3 centers (12%) had no local access to DSA.

Regarding the endovascular management of IIA (Fig. 4B), 3 centers perform systematic IIA embolization (12%), 14 centers (56%) treat only IIA associated with intracranial hemorrhage or valvular replacement project.

5 centers (20%) have pluridisciplinary discussion regarding endovascular treatment, 3 centers (12%) are not able to provide endovascular treatment.

F. Follow-up (*fig. 5*)

Regarding IE imaging follow-up, in cases of IIA without neurological complication (Fig. 5A): 3 centers (12%) have no systematic follow-up, when 22 (88%) organize systematic follow-up, with CT for 9 (36%), MRI for 8 (32%), MRI and DSA for 4 (16%), CT and MRI for 1 (4%).

In cases of IIA complicated with intracranial hemorrhage (Fig. 5B), follow-up isn't systematic for 2 centers (8%) and systematic for 23 (92%). It is based on CT for 8 (32%); MRI for 6 (24%), CT+DSA for 3 (12%), MRI+DSA for 3 (12%), DSA only for 2 (8%), MRI+CT for 1 (4%).

In cases of CMB or sulcal hemorrhage in noninvasive techniques (Fig. 5C), 5 centers (20%) suggest no follow-up, when follow-up is systematic for 20 centers (80%), within 3 days of diagnostic for 5 (20%), from 3 to 7 days for 8 (32%), from 1 to 3 weeks for 6 (24%) and after 3 weeks for 1 (4%).

In cases of IIA detected by invasive or noninvasive techniques (Fig. 5D), systematic follow-up is suggested for 23 (92%) of the centers, within a week for 7 (28%), from 1 to 3 weeks for 10 (40%), 3 to 6 weeks for 2 (8%), and superior to 6 weeks for 4 (16%).

IV. Discussion

IE is a rare pathology and IIA exploration is a relatively uncommon situation for neuroradiologists (1,6,8). Various mechanisms can damage cerebral parenchyma or vascular wall. Septic emboli from an infected valve can occlude a cerebral vessel causing septic infarction. It is supposed that IIA formation begins with an adventice destruction due to septic emboli of the vasa-vasorum. Arteritis then extends medially destroying internal elastic lamina, causing focal vessel weakness (12). IIA can form anywhere in the cerebrovascular system but with a predilection for terminal branches of the middle cerebral artery (70%) (13). In the absence of specific guidelines for IE work-up, we brought here an overview of the discrepancies regarding Neuroradiological imaging protocols in patients with IE in neuroradiological centers.

In our survey, most centers (88%) use systematic noninvasive imaging. First noninvasive technique used is MRI (66%) compared to CT (44%). No center uses DSA in the first instance. High sensitivity of cross-sectional neuroimaging modalities has been reported in the detection of non-infective aneurysm, with sensitivity over 95% for both CT and MRI, with no significant difference between the two techniques

(14,15). However, the usual distal location and small size of IIA may induce a loss of sensitivity of noninvasive techniques (12,13,16).

Only few studies analyzed cross sectional imaging performance for IIA detection. In a meta-analysis, *Wang et al.* (17) showed a sensitivity of 70% and a specificity of 90% of pooled MR and CT. Nevertheless, a recent study showed high detection rates (Sensitivity=98%) for small non infective aneurysms (<3mm), using MRI black blood vessel imaging technique (18). However, all available studies that focused on IIA suffer from significant methodological biases, hence the need for prospective studies with systematic MRI and DSA.

Furthermore, MRI is more sensitive to detect parenchymal symptomatic or asymptomatic lesions that can have an impact on therapies (12,19).

However, interesting observations from the free comments part of the survey points that in many cases, MRI exploration may be complicated considering the incompatibility of neurological/hemodynamical status of IE patients and the long duration of MRI sequences.

Regarding CT-scan screening, even if there is no clear recommended protocol for IE exploration, all 11 centers (100%) used a non-contrast, an angiographic, and a contrast-enhanced acquisition to maximize IIA detection.

Regarding MRI hemorrhage complication screening, most centers use SWI sequence (96%). Cerebral Microbleed (CMB) is a frequent pattern in IE patients, and a common hypothesis is that they reflect microvasculitis. *Okazaki et al.* (20), showed that CMB had a predictive value for impending intracranial hemorrhage in IE patients. Two specific studies showed the superiority of SWI versus T2* in CMB detection, at 1,5T

and 3T (21,22). In our study, the detection of CMB is an indication for further DSA exploration in 6 centers (24%).

Regarding parenchymal and vascular MRI exploration, we found that contrast enhanced 3D TOF-MRA and contrast-enhanced 3D FLAIR were a minority.

To our knowledge, no study focused on the diagnostic performances of contrast-enhanced MRA or FLAIR in the setting of IE and IIA. Post gadolinium 3D T1 sequence was systematic in all centers, however, we highlighted large variability in the types of sequence with 3DT1-GE in 60% of centers versus 3DT1-SE in 40%.

Spin-Echo and gradient-Echo enhanced T1 sequences have different neuroimaging applications. For instance, recent studies showed higher sensitivity of Black-blood SE sequence for leptomeningeal enhancement (23) and vascular wall diseases exploration (24). On the contrary, studies showed higher sensitivity of Gradient-Echo sequence for multiple sclerosis lesion detection (25,26).

It would be interesting to realize further examinations of each technique sensitivity for IIA detection.

It's interesting to note that, in all centers that have responded to our survey, there is no indication of preoperative DSA in the absence of noninvasive technique abnormalities. On the other hand, a sulcal hemorrhage was a systematic indication of complementary DSA (100% and conditioned by further surgical project in only one center (4%)).

Recent MRI studies analyzed the interesting association of Sulcal SWI lesion with contrast enhancement to screen IIA with a good sensitivity (6,27,28).

One of them showed a 90% sensitivity of contrast enhancement with microbleed, a 80% sensitivity of microbleed>5mm or sulcal SWI lesion, and a 100% sensitivity of any MRI hemorrhage, suggesting low interest of DSA in absence of MRI hemorrhage(28) but validation in unbiased prospective studies with systematic MRI and DSA is needed.

Whether there is a need for systematic DSA in case of definite IE is a matter of debate. In our study we found that the two main indications of complementary DSA were sulcal hemorrhage (100%) and cerebral microbleed (24%). Comparably, Migdady et al.(6), showed that in their study, patterns frequently associated with IIA were sulcal SWI lesions with or without enhancement, and cerebral microbleeds.

The management of IIA largely depends on the center habits, from conservative treatment with antibiotic therapy to systematic endovascular treatment. In our survey, 3 centers (12%) perform systematic endovascular treatment whereas the majority use endovascular treatment only in case of cerebral hemorrhage or replacement valvular project (56%).

Surgical valvular replacement is required in 25 to 50% of the cases during acute IE infection (29). Even with precise preoperative neuroimaging modalities, it is difficult to assess intracranial hemorrhage (IH) risks per or postoperative. However, *Kume et al.*(30), found no significant postoperative risk of IH in IE patients with preoperative IH. On the contrary, in the same study, the presence of preoperative IIA was an independent risk factor of postoperative intracranial hemorrhage.

The postponement of surgical valve replacement because of neurological complications remains controversial. In the case of IIA, preventive endovascular treatment might reduce the risk of postoperative hemorrhage, allowing early surgical replacement. Validation in dedicated studies is also needed.

The natural history of IIA is difficult to assess due to its low prevalence.

The follow up of IE patients showed that, even treated with antibiotic therapy, IIA either regressed, stabilized, enlarged or ruptured (31,32). Considering these asserts, and knowing the high morbid-mortality of IIA (11), a close follow-up is warranted. In our survey, follow-up of IIA was systematic for 88% of the centers with a large variation between the techniques used, from CT, MRI, DSA or combined follow-up.

Timelines of follow-up also showed wide variations between centers, with a majority of 3 to 7 days for cerebral bleeding and 1 to 3 weeks for IIA follow-up.

Historically, repeated angiographic controls were recommended for IIA follow-up (33).

With the development of non-invasive imaging techniques, CT and MRI quickly showed their interest in the follow-up (32).

Two studies monitored IIA evolution by systematic DSA (31,34), but to our knowledge no recent study focused on IIA monitoring with non-invasive techniques since Ahmadi et al (32).

Our study has limitations, due to its descriptive, self-reported design.

Only 50% of French university centers took part in the study.

Declaration of the respondents can not be controlled, and a single physician per center was designated to answer the online questionnaire, still this potential bias is limited by the use of protocols in most centers.

Conclusion

This neuroimaging survey showed wide differences in the neuroradiological management of IE patients. Hence, further high-quality research in this field is essential for the development of future expert guidelines.

V. Supplementary data

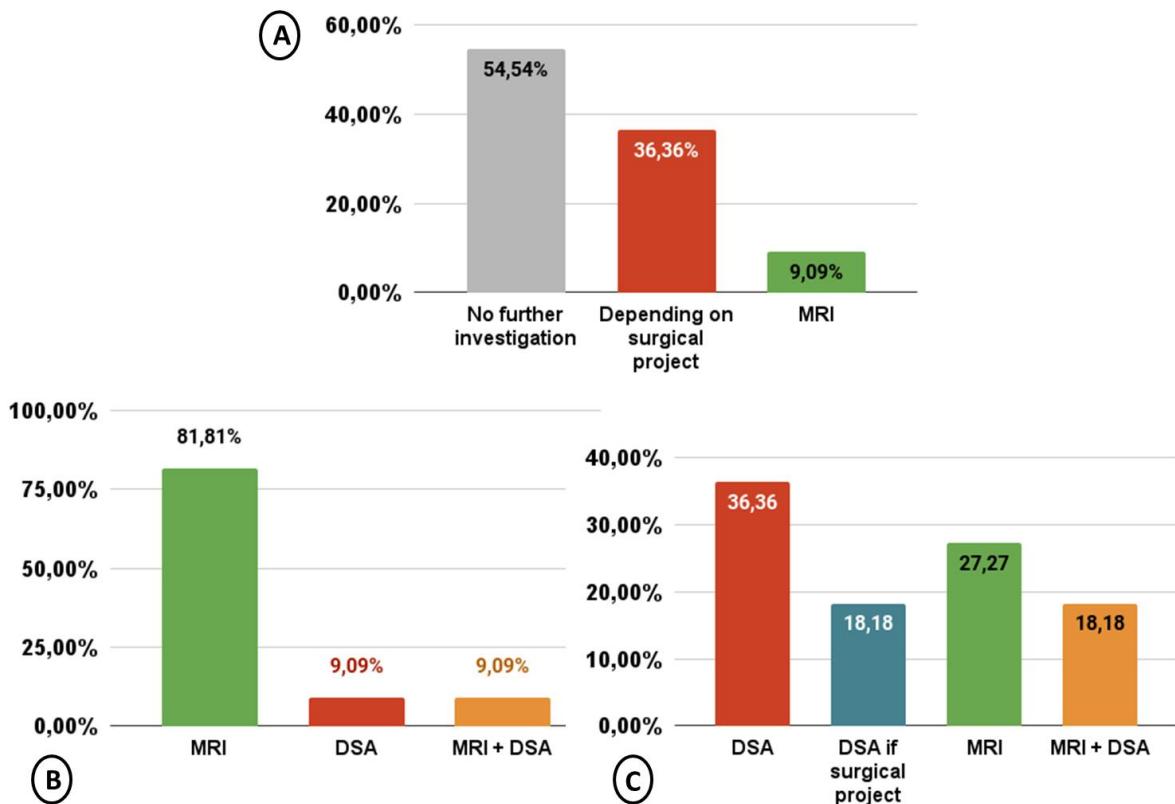


Fig 1. Additional work-up according to the CT findings. **A** No IIA detectable in CT-scan. **B** Sulcal hemorrhage, ischemia or enhancement, without IIA detectable. **C** Sulcal hemorrhage, ischemia or enhancement, with IIA detected.

MRI: magnetic resonance imaging; DSA=Digital Subtraction Angiography

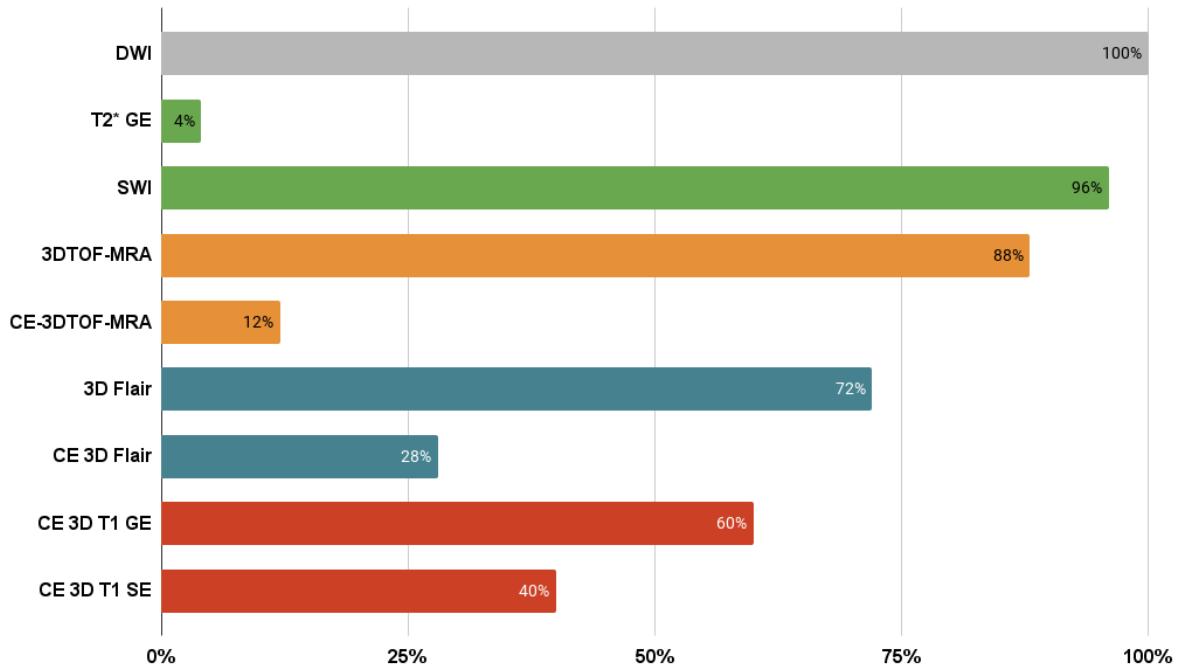


Figure 2. MRI sequences performed in the general work up of IE.

DWI=Diffusion weighted imaging; T2* GE= T2* weighted Gradient Echo; SWI=Susceptibility weighted imaging; CE=Contrast enhanced; 3D TOF-MRA=Three-Dimensional Time-of-Flight Sequence of Magnetic Resonance Angiography; Flair= Fluid attenuated inversion recovery; 3D T1 GE= 3D T1 weighted Gradient-Echo; 3D T1 SE=3D T1 weighted Spin-Echo.

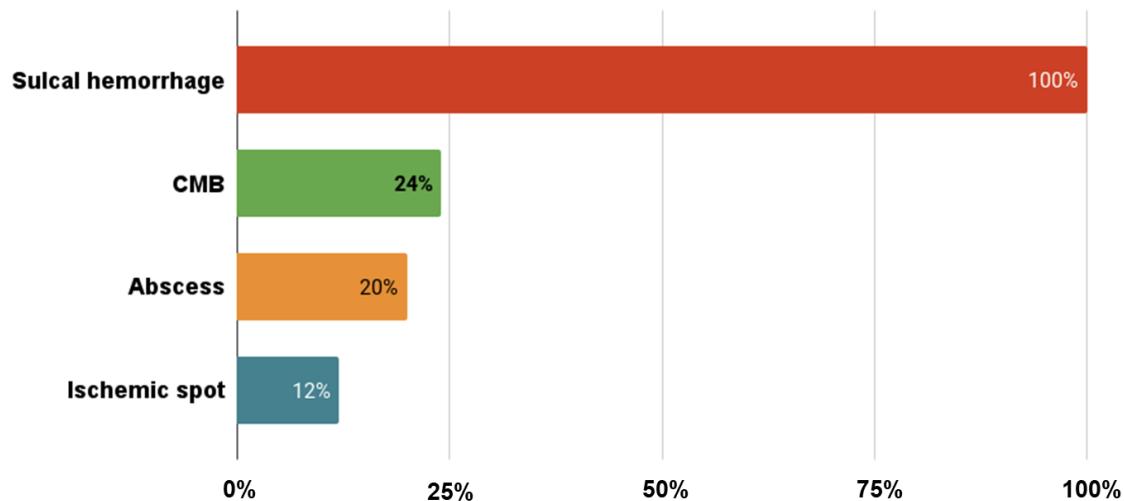


Figure 3. Indication for complementary DSA confronting MRI findings.

CMB=cerebral microbleed.

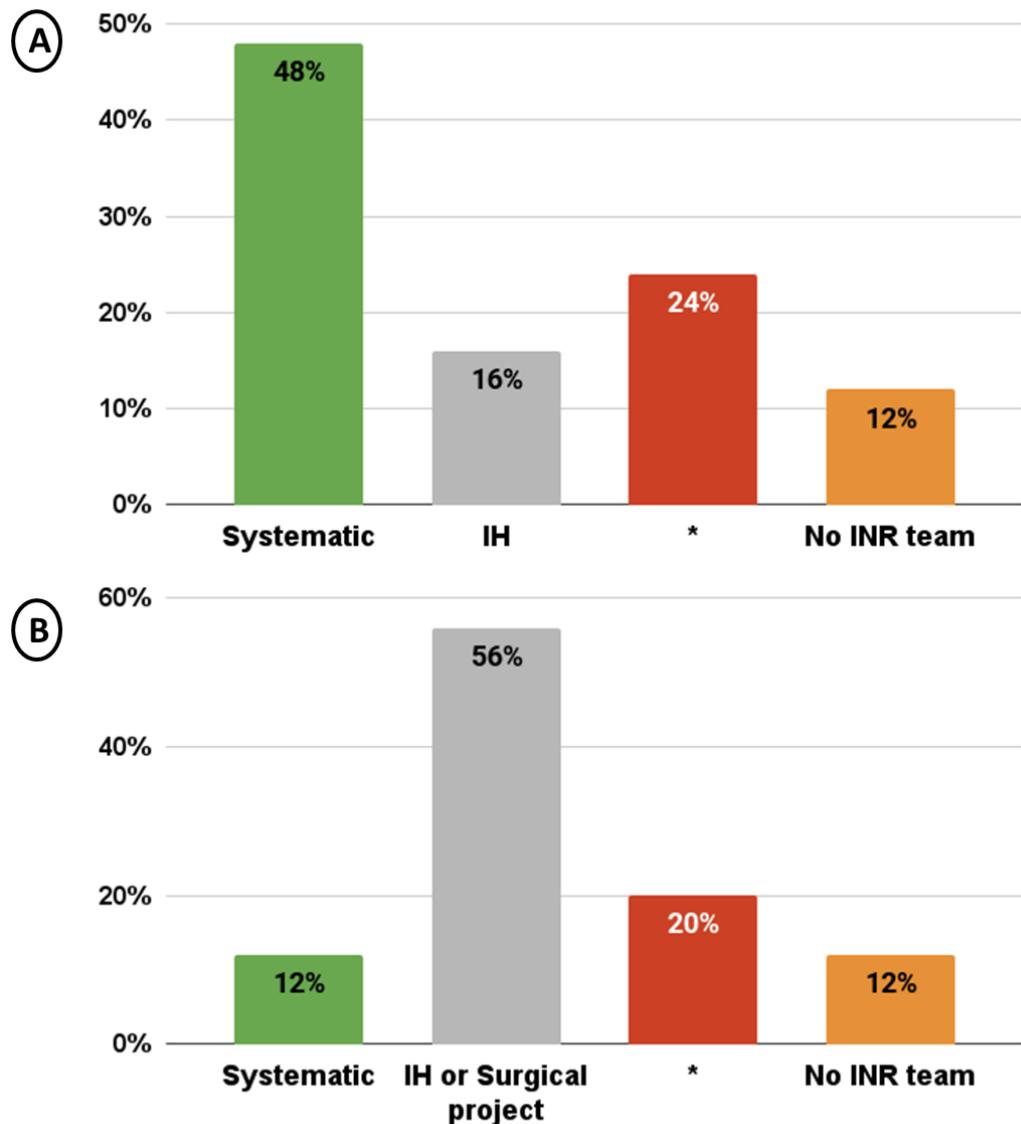


Figure 4. Angiographic management of Infective intracranial aneurysm.

A. Indication of DSA exploration; **B** Indication of endovascular treatment.

*: Depending on patient status.

DSA=Digital Subtraction Angiography. IH=Intracranial hemorrhage.

No INR team: centers that don't have an interventional neuroradiological crew.

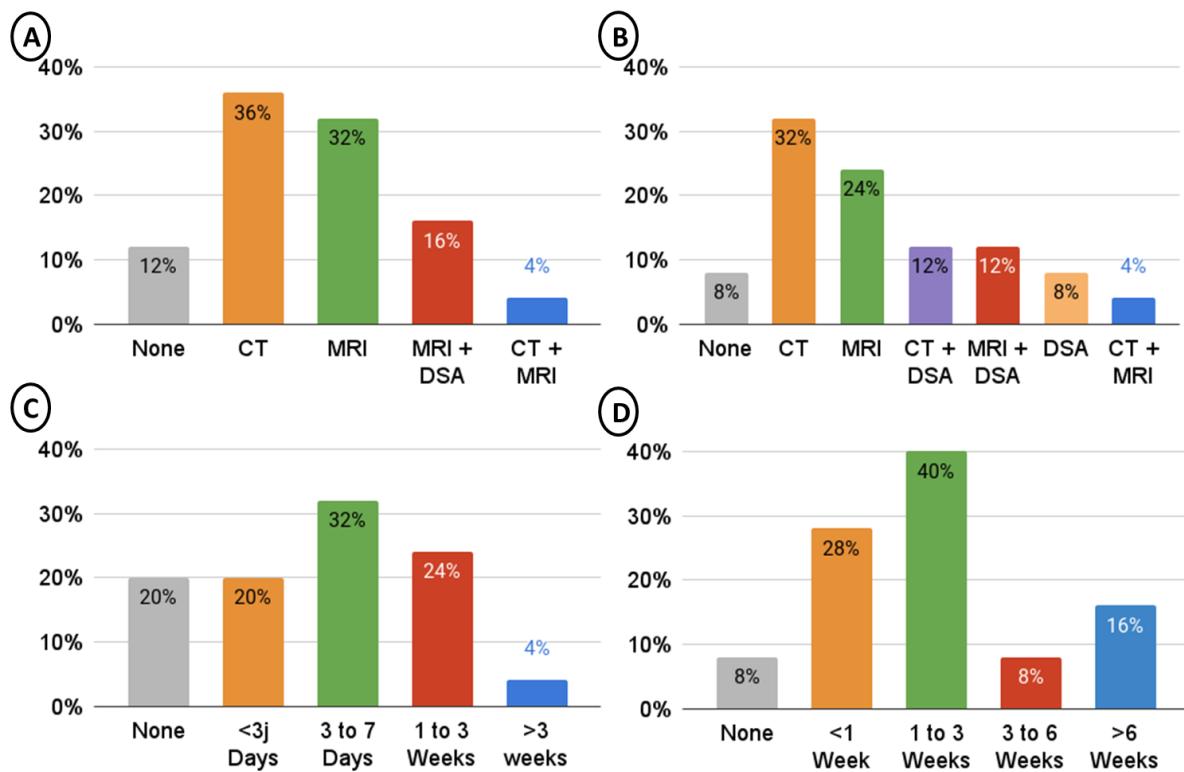


Figure 5. Neuroradiological imaging follow-up of IE patients.

A Follow-up of IIA without neurological complication. **B** Follow-up of IIA with intracranial hemorrhage complication. **C** Follow-up of microbleed or sulcal hemorrhage. **D** Follow-up of IIA.

CT=Computed tomography; MRI: magnetic resonance imaging; DSA=Digital Subtraction Angiography.

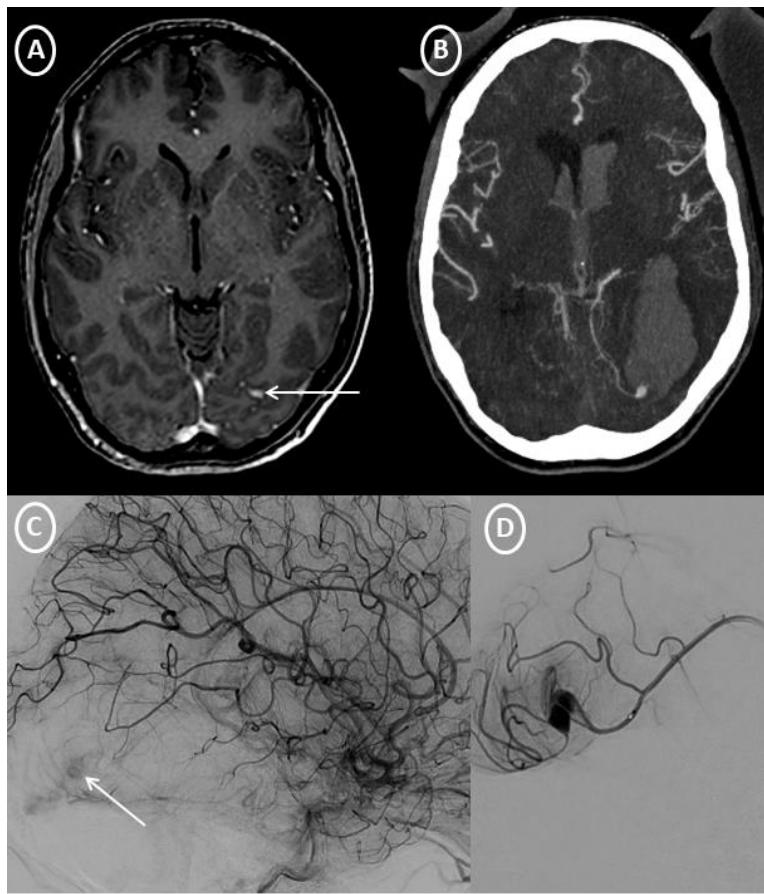


Figure 6. A 23 yo male, IE was diagnosed without abnormality detected on the first CT-scan realised one day after admission. **a** MRI CE-3DT1-EG sequence 10 days after admission for persistent headache, showed left occipital sulcal enhancement. **b** CT-scan 14 days after admission, reveals parenchymal and ventricular hemorrhage associated with saccular occipital IIA. **c, d** DSA showed saccular IIA of a distal occipital branch of the left postérior cerebral artery.

IE infective endocarditis, MRI magnetic resonance imaging, CE-3DT1-EG Contrast enhanced 3D T1 gradient-echo, IIA intracranial infective aneurysm, DSA digital subtraction angiography.

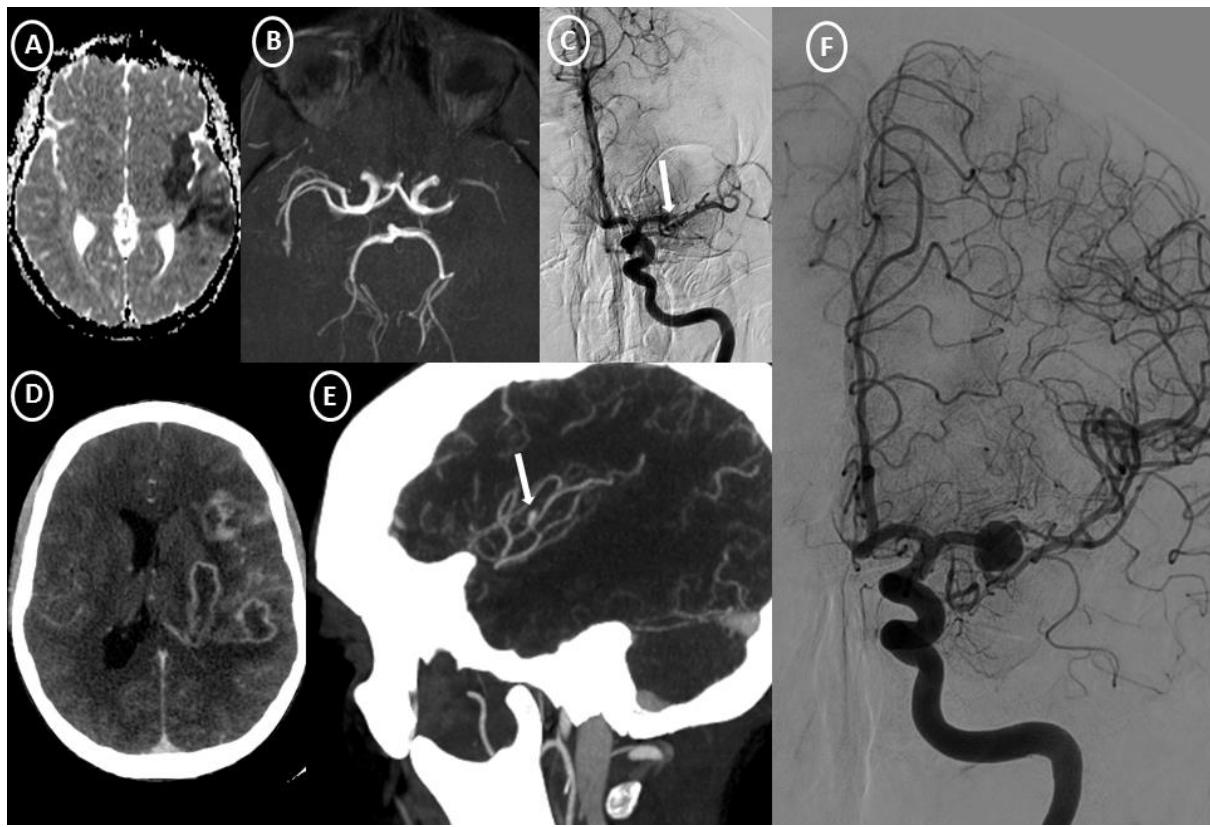


Figure 7. A 37 yo male with sudden aphasia and right hemiplegia. Infective mitral endocarditis was diagnosed in early cardiologic work-up (*Enterococcus faecalis* and MSSA). **a,b,c** ADC and 3D TOF reveals recent left temporo-insular ischemic stroke with occlusion of MCA (M2 segment), treated by mechanical thrombectomy. **d,e** Follow-up showed parenchymal abcession and a left MCA distal IIA, 10 days after admission. **f** Later follow-up showed regression of abscess and distal IIA under antibiotic treatment, with progressive enlargement of a left MCA bifurcation IIA.

MSSA *Methicillin-susceptible Staphylococcus aureus*; ADC Apparent Diffusion Coefficient; 3D TOF 3D time-of-flight, MCA middle cerebral artery, IIA infective intracranial hemorrhage.

Survey:

I-Systematic imaging screening?

1-Systematic imaging in patients with definite or possible infective endocarditis?

- A. Yes
- B. No

2-Indication of radiological exploration in the group non-systematic imaging:

- A. Surgical project.
- B. Neurological sign.

II-Modality of initial screening.

3-Initial first screening method:

- A. Cerebral Computed Tomography (CT).
- B. Magnetic Resonance Imaging (MRI).

III- CT-scan screening.

4- CT protocol:

- A. Non contrast head CT.
- B. Head computed-tomographic angiogram (CTA).
- C. Contrast-enhanced acquisition.

5-No Infective Intracranial Aneurysm (IIA) detectable in CT:

- A. No further investigation.
- B. Complementary exam depending on a potential surgical project.
- C. Complementary MRI.
- D. Complementary Digital subtraction Angiography (DSA).

6-Sulcal hemorrhage, ischemia or enhancement, without IIA detectable:

- A. complementary MRI.
- B. Direct DSA.
- C. MRI+DSA
- D. DSA only if surgical project.

7-Sulcal hemorrhage, ischemia or enhancement, with IIA detection.

- A. Complementary MRI.
- B. DSA.
- C. MRI+DSA
- D. DSA only if surgical project.

IV. MRI

8-Technic modality.

- A. 1,5 Tesla (T).
- B. 3 Tesla (T).
- C. Indistinctly.

9-Protocol.

- A. Diffusion Weighted Imaging.
- B. T2* weighted gradient echo.
- C. Susceptibility Weighted Imaging.
- D. 3D TOF Magnetic Resonance Angiography.
- E. Contrast-enhanced 3D TOF Magnetic Resonance Angiography.
- F. 3D FLAIR.
- G. Contrast-enhanced 3D FLAIR.
- H. Contrast enhanced 3D T1 weighted Gradient-Echo.
- I. Contrast enhanced 3D T1 weighted Spin-Echo.

10-Free comment for eventual other center protocol.

11-Indication for complementary DSA confronting MRI findings:

- A. Sulcal hemorrhage.
- B. Cerebral microbleed.
- C. Abscess
- D. Ischemic stroke.

V. DSA

12- Indication of DSA, all imagery screening methods combined:

- A. Sulcal hemorrhage.
- B. Parenchymal hemorrhage.
- C. Recent ischemia.
- D. Intracranial hemorrhage and surgical project.
- E. Surgical project without abnormality in non invasive technique imaging.

13-IIA detected in non imaging techniques:

- A. No systematic DSA.
- B. DSA only if intracranial hemorrhage in CT or MRI.
- C. Systematic DSA without endovascular treatment in the first place.
- D. Endovascular treatment only if cerebral hemorrhage in non invasive techniques.
- E. Endovascular treatment if cerebral hemorrhage or surgical project.
- F. Systematic endovascular treatment.
- G. No local access to the DSA.

14-In case of IIA detected only in DSA.

- A. Architectural characterization without endovascular treatment in the first place.
- B. Endovascular treatment only if cerebral hemorrhage.

- C. Endovascular treatment if cerebral hemorrhage or surgical project.
- D. Systematic endovascular treatment.
- E. No local access to the DSA.

VI. Follow-up

15- Imaging follow-up of IIA without cerebral complication.

- A. No follow-up.
- B. CT-scan.
- C. MRI.
- D. DSA.

16-Imaging follow-up of IIA with cerebral hemorrhage complication.

- A. No follow-up.
- B. CT-scan.
- C. MRI.
- F. DSA.

17- Timing of follow-up for sulcal hemorrhage or cerebral microbleed.

- A. No follow-up.
- B. < 3 days.
- C. 3 to 7 days.
- D. 1 to 3 weeks.
- E. > 3 weeks.

18- Timing of follow-up of IIA:

- A. No follow-up.
- B. < 1 week.
- C. 1 to 3 weeks.
- D. 3 to 6 weeks.
- E. > 6 weeks.

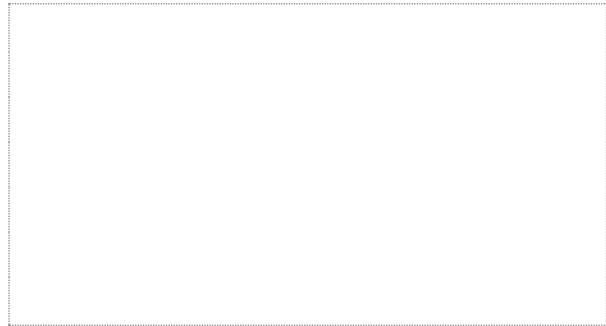
19-Free comment for specific center habits.

VI. References

1. Cahill TJ, Prendergast BD. Infective endocarditis. *The Lancet*. févr 2016;387(10021):882-93.
2. Pant S, Patel NJ, Deshmukh A, Golwala H, Patel N, Badheka A, et al. Trends in Infective Endocarditis Incidence, Microbiology, and Valve Replacement in the United States From 2000 to 2011. *J Am Coll Cardiol*. mai 2015;65(19):2070-6.
3. Duval X, Delahaye F, Alla F, Tattevin P, Obadia J-F, Le Moing V, et al. Temporal Trends in Infective Endocarditis in the Context of Prophylaxis Guideline Modifications. *J Am Coll Cardiol*. mai 2012;59(22):1968-76.
4. Selton-Suty C, Célard M, Le Moing V, Doco-Lecompte T, Chirouze C, Iung B, et al. Preeminence of *Staphylococcus aureus* in Infective Endocarditis: A 1-Year Population-Based Survey. *Clin Infect Dis*. 1 mai 2012;54(9):1230-9.
5. Hubers SA, DeSimone DC, Gersh BJ, Anavekar NS. Infective Endocarditis: A Contemporary Review. *Mayo Clin Proc*. mai 2020;95(5):982-97.
6. Migdady I, Rice CJ, Hassett C, Zhang LQ, Wisco D, Uchino K, et al. MRI Presentation of Infectious Intracranial Aneurysms in Infective Endocarditis. *Neurocrit Care*. juin 2019;30(3):658-65.
7. Duval X. Effect of Early Cerebral Magnetic Resonance Imaging on Clinical Decisions in Infective Endocarditis: A Prospective Study. *Ann Intern Med*. 20 avr 2010;152(8):497.
8. Hess A, Klein I, Iung B, Lavallée P, Illic-Habensus E, Dornic Q, et al. Brain MRI Findings in Neurologically Asymptomatic Patients with Infective Endocarditis. *Am J Neuroradiol*. août 2013;34(8):1579-84.
9. Sotero FD, Rosário M, Fonseca AC, Ferro JM. Neurological Complications of Infective Endocarditis. *Curr Neurol Neurosci Rep*. mai 2019;19(5):23.
10. Hui FK, Bain M, Obuchowski NA, Gordon S, Spiotta AM, Moskowitz S, et al. Mycotic aneurysm detection rates with cerebral angiography in patients with infective endocarditis. *J NeuroInterventional Surg*. juin 2015;7(6):449-52.
11. Ducruet AF, Hickman ZL, Zacharia BE, Narula R, Grobelny BT, Gorski J, et al. Intracranial infectious aneurysms: a comprehensive review. *Neurosurg Rev*. janv 2010;33(1):37.
12. Kannoth S, Thomas SV. Intracranial Microbial Aneurysm (Infectious Aneurysm): Current Options for Diagnosis and Management. *Neurocrit Care*. août 2009;11(1):120-9.
13. Ferro JM, Fonseca AC. Infective endocarditis. In: *Handbook of Clinical Neurology* [Internet]. Elsevier; 2014 [cité 25 juill 2021]. p. 75-91. Disponible sur: <https://linkinghub.elsevier.com/retrieve/pii/B9780702040863000072>
14. Sailer AMH, Wagemans BAJM, Nelemans PJ, de Graaf R, van Zwam WH. Diagnosing Intracranial Aneurysms With MR Angiography: Systematic Review and Meta-Analysis. *Stroke*. janv 2014;45(1):119-26.
15. Wang H, Li W, He H, Luo L, Chen C, Guo Y. 320-Detector row CT angiography for detection and evaluation of intracranial aneurysms: Comparison with conventional digital subtraction angiography. *Clin Radiol*. janv 2013;68(1):e15-20.
16. Schwab KE, Gailloud P, Wyse G, Tamargo RJ. LIMITATIONS OF MAGNETIC RESONANCE IMAGING AND MAGNETIC RESONANCE ANGIOGRAPHY IN THE DIAGNOSIS OF INTRACRANIAL ANEURYSMS. *Neurosurgery*. 1 juill 2008;63(1):29-35.
17. Wang TKM, Griffin B, Cremer P, Shrestha N, Gordon S, Pettersson G, et al. Diagnostic Utility of CT and MRI for Mycotic Aneurysms: A Meta-Analysis. *Am J Roentgenol*. nov 2020;215(5):1257-66.
18. Songsaeng D, Sakarunchai I, Mongkolnaowarat S, Harmontree S, Pornpunyawut P, Suwanbundit A, et al. Detection and Measurement of Intracranial Aneurysm Compared between Magnetic Resonance Intracranial Black Blood Vessel Imaging and Gold Standard Cerebral Digital Subtraction Angiography. *J Neurosci Rural Pract*. oct 2020;11(04):545-51.

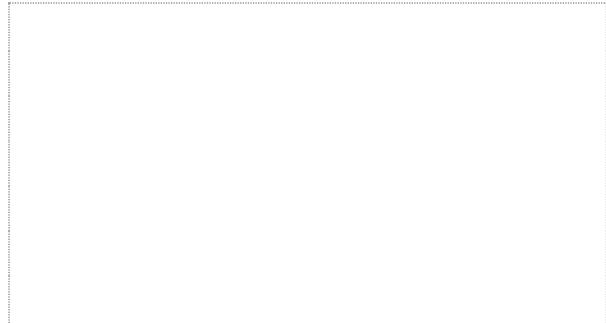
19. Goulenok T, Klein I, Mazighi M, Messika-Zeitoun D, Alexandra JF, Mourvillier B, et al. Infective Endocarditis with Symptomatic Cerebral Complications: Contribution of Cerebral Magnetic Resonance Imaging. *Cerebrovasc Dis.* 2013;35(4):327-36.
20. Okazaki S, Sakaguchi M, Hyun B, Nagano K, Tagaya M, Sakata Y, et al. Cerebral Microbleeds Predict Impending Intracranial Hemorrhage in Infective Endocarditis. *Cerebrovasc Dis.* 2011;32(5):483-8.
21. Shams S, Martola J, Cavallin L, Granberg T, Shams M, Aspelin P, et al. SWI or T2*: Which MRI Sequence to Use in the Detection of Cerebral Microbleeds? The Karolinska Imaging Dementia Study. *Am J Neuroradiol.* juin 2015;36(6):1089-95.
22. Goos JDC, van der Flier WM, Knol DL, Pouwels PJW, Scheltens P, Barkhof F, et al. Clinical Relevance of Improved Microbleed Detection by Susceptibility-Weighted Magnetic Resonance Imaging. *Stroke.* juill 2011;42(7):1894-900.
23. Oh J, Choi SH, Lee E, Shin DJ, Jo SW, Yoo R-E, et al. Application of 3D Fast Spin-Echo T1 Black-Blood Imaging in the Diagnosis and Prognostic Prediction of Patients with Leptomeningeal Carcinomatosis. *Am J Neuroradiol.* 12 juill 2018;ajnr;ajnr.A5721v1.
24. Edjlali M, Qiao Y, Boulouis G, Menjot N, Saba L, Wasserman BA, et al. Vessel wall MR imaging for the detection of intracranial inflammatory vasculopathies. *Cardiovasc Diagn Ther.* août 2020;10(4):1108-19.
25. Aymerich FX, Auger C, Alcaide-Leon P, Pareto D, Huerga E, Corral JF, et al. Comparison between gadolinium-enhanced 2D T1-weighted gradient-echo and spin-echo sequences in the detection of active multiple sclerosis lesions on 3.0T MRI. *Eur Radiol.* avr 2017;27(4):1361-8.
26. Crombé A, Saranathan M, Ruet A, Durieux M, de Roquetaeil E, Ouallet JC, et al. MS Lesions Are Better Detected with 3D T1 Gradient-Echo Than with 2D T1 Spin-Echo Gadolinium-Enhanced Imaging at 3T. *Am J Neuroradiol.* mars 2015;36(3):501-7.
27. Cho S-M, Rice C, Marquardt RJ, Zhang LQ, Khouri J, Thatikunta P, et al. Magnetic Resonance Imaging Susceptibility-Weighted Imaging Lesion and Contrast Enhancement May Represent Infectious Intracranial Aneurysm in Infective Endocarditis. *Cerebrovasc Dis.* 2017;44(3-4):210-6.
28. Cho S-M, Marquardt RJ, Rice CJ, Buletko AB, Zhang LQ, Khouri J, et al. Cerebral microbleeds predict infectious intracranial aneurysm in infective endocarditis. *Eur J Neurol.* juill 2018;25(7):970-5.
29. Prendergast BD, Tornos P. Surgery for Infective Endocarditis: Who and When? *Circulation.* 9 mars 2010;121(9):1141-52.
30. Kume Y, Fujita T, Fukushima S, Shimahara Y, Matsumoto Y, Yamashita K, et al. Intracranial mycotic aneurysm is associated with cerebral bleeding post-valve surgery for infective endocarditis†. *Interact Cardiovasc Thorac Surg.* 1 nov 2018;27(5):635-41.
31. Rice CJ, Cho S-M, Marquardt RJ, Zhang LQ, Khouri J, Hardman J, et al. Clinical course of infectious intracranial aneurysm undergoing antibiotic treatment. *J Neurol Sci.* août 2019;403:50-5.
32. Ahmadi J, Tung H, Giannotta SL, Destian S. Monitoring of Infectious Intracranial Aneurysms by Sequential Computed Tomographic/Magnetic Resonance Imaging Studies. *Neurosurgery.* 1 janv 1993;32(1):45-52.
33. Cantu RC, LeMay M, Wilkinson HA. The Importance of Repeated Angiography in the Treatment of Mycotic-Embolic Intracranial Aneurysms. *J Neurosurg.* août 1966;25(2):189-93.
34. Corr P, Wright M, Handler LC. Endocarditis-related cerebral aneurysms: radiologic changes with treatment. *AJNR Am J Neuroradiol.* avr 1995;16(4):745-8.

Vu, le Président du Jury,



Professeur Hubert DESAL

Vu, le Directeur de Thèse,



Professeur Romain BOURCIER

Vu, le Doyen de la Faculté,



Professeur Pascale JOLLIET

Titre de thèse: Neuroradiological imaging paradigm in patients with Infective endocarditis: A National Survey.

RÉSUMÉ

Objectives: The aim of this study was to identify imaging protocols in patients with infective endocarditis (IE) through a nationwide survey.

Methods: An electronic evolutionary survey was sent to interventional Neuroradiologists among neuroradiological centers under the aegis of the Société Française de Neuroradiologie.

Among 33 contacted centers, 25 completed the survey (21 university hospitals and 4 peripheric hospitals).

Results: Most of the centers (88%) use systematic imaging screening in IE patients. Magnetic Resonance Imaging (MRI) is the first imaging method used in 66% of cases while computed tomography (CT) is used in 44%. When no Infective Intracranial Aneurysm (IIA) is detectable in CT-scan screening, 6 (54,54%) use no further investigation, while 9 (81,81%) continue with MRI exploration in case of hemorrhage, ischemia or enhancement. Sulcal hemorrhage in MRI is an indication of complementary Digital subtraction angiogram (DSA) in 25 centers (100%). Regarding IIA characterization, 12 centers (48%) use systematic DSA, whereas for 10 centers (40%), DSA is conditioned by hemorrhage or patient status.

Conclusion: We highlighted large variations in Neuroimaging exploration and follow-up of IE patients in real-world practices. Expert guidelines able to standardize practices are warranted to improve the management of this serious and often misdiagnosed pathology.

MOTS-CLÉS

Infective endocarditis, infective intracranial aneurysm, CT-scan, MRI, DSA.