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THESE PRESENTEE POUR L'OBTENTION DU DOCTORAT EN MEDECINE
DIPLOME D'ETAT

**Early brain MRI interest in infective endocarditis clinical management:
A prospective study**

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Annexe 1 : revue de la littérature

Brain MRI interest in acute infective endocarditis: A systematic review of the literature.

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Abstract

Nervous system is frequently involved in patients with infective endocarditis (IE).

A systematic review of the literature was realized in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

This study sought to systematically evaluate published evidence of cerebral Magnetic resonance imaging (MRI) contribution in IE. The aim was to identify studies presenting the incidence and the type of MRI brain lesions in IE.

Fifteen relevant studies were isolated using the Medline, Embase and Cochrane databases. Most of them were observational studies with a low number of patients.

MRI studies point out a very high frequency of cerebral lesions around 80% which are mostly clinically occult. The review shows MRI superiority compared to brain computered tomography (CT) scan to diagnose neurologic complications.

Recent developments of sensitive MRI sequences especially allow detection of micro-infarction and micro haemorrhages. However, the clinical significance of these cerebral micro haemorrhages, also call microbleeds (CMBs), remains uncertain.

Because some MRI neurological lesions are a distinctive feature of IE, they can have a broader implication as in diagnose then in therapeutic decisions.

Even if cerebral MRI may offer new perspectives for better IE management, there is not enough scientific proof to provide it in current recommendations: some literature lacunae remain regarding the impact of MRI on treatment dilemmas. CMBs long term prognosis has not been evaluated yet. Further studies must be performed.

To date, brain MRI could be achieved on case by case basis, on clinician appraisal.

Introduction

Despite significant improvements in diagnosis and therapeutic strategies, infectious endocarditis (IE) is still a severe disease. In-hospital mortality rate remains high around 20% (1).

In IE, all lesions have the same anatomic substratum: septic emboli arising from the bacterial vegetation fragmentation (2).

Among systemic complications, the nervous central system is the first involved with a prevalence rate around 30%. Neurologic complications are responsible for a huge part of the morbi-mortality, estimated at 30% (3–5).

Neurological symptoms are delayed, frequent and often infraclinical (3). They can be varied including focal deficit, encephalopathy and seizures. Most often, those symptoms led to perform early brain computerized tomography (CT) scan. Using CT scan, Habib et al documented 62% of cerebral embolism (6) but a part of these imaging lesions are asymptomatic.

It is nowadays acknowledged to perform systematic neuroimaging for all IE patients even those without clinical neurologic symptoms. The significance of asymptomatic lesions is the root cause of this new behaviour. A quick and accurate neurologic assessment seems essential to rapidly decide how to manage the disease. Mainly by the means of cardiac surgery, IE treatment aims to control cardiac involvement, to decrease embolic risk and to master infection widespread. Up to now, some data have showed that Magnetic Resonance Imaging (MRI) is more sensible, more specific than CT scan in this indication. Though, the role of MRI is not accurately definite. The goal of the present review was to summarize current data concerning brain MRI indication in IE management. This review successively

details the prevalence of MRI damages and the characteristics of each type of lesions. Then, the MRI interest in IE diagnoses, in the choice of treatment and in prognosis evaluation are taken up.

Research question and search strategy

We establish a systematic literature review using the PRISMA guidelines to select, analyse and resume the main studies (7).

The Medline, the Cochrane data base and Embase were searched from January 1994 to February 2014.

Using the pub med interface, Mesh term were magnetic resonance imaging, endocarditis, cerebrovascular disorders. Search terms used in the Cochrane library and in Embase were the same then in Pubmed.

We employed the search strategy described in Table 1. Results of searches were stored in an Excel database.

We documented at first 182 references which were stored in the Zotero personal research assistant.

References of full texts were also reviewed in order to identify any else potentially relevant study.

Studies reporting prevalence and types of brain MRI lesions in IE were included.

Because of the shortage of the literature, we selected articles regarding brain MRI and endocarditis with large characteristics but we only retained study having a major criterion with regards to brain MRI interest. For the study selection, decision to retain an article was successively done on the title, the abstract and the complete article. Data were extracted by two reviewers. The discrepancies were resolved after a discussion with a methodologist who also evaluated the validity and the pertinence of the publication. The selection was limited to studies published in English and concerning hospitalized adults patients. Prospective and retrospective studies were included. Articles using CT scan of the brain as a comparator were retained. Studies were excluded if they included less than ten participants or if the endocarditis cases were not diagnosed regarding the international Duke's modified criteria as definite or probable IE.

We achieved a narrative review. Clinical heterogeneity of the studies did not allow to perform summative statistics.

Results

Studies selection and characteristics

By the selection, we set aparted 16 clinical studies that were suitable for inclusion in our review. Among the available full text articles, no response was received from the contacted author in one case. The acquisition of articles is summarized figure 1. Studies characteristics are exposed in table 2. The quality analysis was realized by using the Strobe Statement and the PRISMA checklist. Most of them were transversal studies, cross over studies and retrospective studies. No randomized controlled trials or comparative studies were obtained. The rarity of the disease, the polymorphous features and the numerous prognosis factors may explain the infrequency of IE randomized studies. Most of the time, sample sizes were small and the total number of patients included did not undergo brain MRI. We identified only 5 prospective studies. Most of them have the biggest number of patients and required all our interest.

Separately, due to the rarity of literature concerning infectious aneurysm and brain abscess detection by MRI examination, cases study and reviews on these topics were likewise included. These articles were taken aside and were not included in table 2.

Prevalence of lesions

The use of brain CT scan had previously shown high global rate of cerebral lesions but lower than MRI findings (8).

Including 130 patients, the largest MRI study reported 82% IE cerebral lesions among which 78 % were asymptomatic (9). Radiological data quality was substantial with a use of a standardized protocol

associated to a double blinding analysis by two experimented neuroradiologists. Using Cohen Kappa test, great inter-observer concordance was calculated. All patients underwent promptly MRI with angiography within the 7 days following admission.

Snygg-Martin and Cooper studies reported 65% and 80% brain MRI abnormalities with respectively 35% and 48 % silent lesions as well (10,11). Nonetheless, no diffusion-weighted imaging was performed in the study showing the lower values.

Because all studies excluded patients who underwent emergency surgery before any MRI, the exact incidence remains unknown and the global prevalence could be underdiagnosed.

Most of CT scan undetected lesions and justifying systematic MRI are small hemorrhagic lesions and ischemic strokes (1).

Little infarcts are detected in 53% of cases. MRI identifies cerebral microbleeds (CMBs) with high sensitivity: As a matter of fact, found in 57%, they represent the most frequent cerebral IE damage and they cannot be seen with CT scan examination (7,8).

About CMBs detection, the importance of MRI sequences in study results interpretation have to be bring out (12). Radiological criteria guidelines for CMBs detection and differential diagnoses have not been precisely established (13).Uniformity of neuroimaging protocol and complete assessment using Gradient Echo (GRE) and Diffusion-weighted imaging (DWI) sequences seem necessary to correctly highlight little infarctions and numerous CMB.

Beside, others lesions are less common (parenchymal hemorrhage, subarachnoid hemorrhage, abscess and aneurysm) and have the same prevalence with MRI than with CT scan examinations.

Type of lesions

Ischemic lesions

With CT scan studies, it has previously been demonstrated that ischemic stroke is the main neurological complication of IE. Most of patients show multiple lesions with various patterns (6,13).

Acute and sub-acute ischemic lesions are diagnosed as an hyper intensity signal in FLAIR sequences (for more than 6 hours) and an hyper intensity on DWI sequences. DWI sequences detected very acute and very small ischemic lesions (14). The loss of hyper intensity DWI signal with time is also helpful to differentiate acute and chronic infarction. Infarcts can be as infra then supra tentorials (14). A recent neuroradiologic study showed 40 % of infra tentorial damages (15). The specific severity of a posterior fossa bleeding transformation has to be considered in the therapeutic decision.

Further on, by means of MRI, a neuroimaging embolism spectrum has been hold.

Years ago, Singhal, Barski and Okasaki et al observed the predominance of smaller lesions (14,16,17).

These lesions rather affect cortical and border zone arterial territories (18).

Similarly, Klein, on 109 patients without neurologic symptoms prospectively included, noted the frequency of acute ischemic lesions and of small infarcts widespread in watershed territories (15). In this sample, most patients had multiples bihemispheric lesions lodged in the supratentorial grey-white junction. This corresponds to a prevalent widespread cardiac emboli mechanism. Nevertheless, IE stroke patterns are polymorphic (14): single lesion or territorial infarction suggested a solitary embolus. Multiple emboli mechanism with numerous lesions widely distributed is also possible. Regarding the arterial territories, cortical branch infarction was the most common lesion which usually involved the distal middle cerebral artery tree (14,19).

Valvular vegetation size had correlation with size and number of infarcts (20,21). More still, a recent and large series, found an each millimeter increasing in vegetation length with a 10 % increasing of the toll of ischemic lesions (22).

In several studies, *Staphylococcus aureus* etiology is correlated with emboli (11,23). The structure and function of Staphylococcus cells enables the metastatic diffusion and is association to an higher embolic rate.

Others embolic risk factors are well-known: mitral valve reach, mobile vegetation length >10 mm, systemic embolism (24).

Cerebral microbleeds (CMBs)

On MRI, (T2*- weighted) GRE sequence is planned to see small foci of haemorrhage also called microbleeds. CT scan is not able to detect CMBs.

This hypo intense T2* - weighted MRI round or ovoid signal with a diameter <10 mm can be seen in elderly patients and overall in small-vessel diseases as arteriolosclerosis, chronic hypertension, amyloid angiopathy, multiple cavernoma syndromes and also Alzheimer cases (13,17). They notably have a strong specific IE association. In a case control study about 60 cases, CMBs were more prevalent in IE patients (57%) than in control subject (15%, matched OR: 10) (25). Atherosclerosis factor were similar in the two groups.

CMBs are a pattern of vascular vulnerability and were previously described like a potential indicator of haemorrhagic stroke in IE. This report has been done in a 26 patient's retrospective study with small methodological weight (26). While several analyses found that CMBs might predict future risk of symptomatic intracerebral haemorrhage, some cardiac surgery studies did not found an additional risk of post-surgical bleeding (10). Anticoagulation, when indicated, is still beneficial and is not reconsidered (12,13).

Micro haemorrhages have an upper incidence in IE than in other cerebral diseases and likely a specific distribution (15,25). This specific topography has been revealed in two studies but only one of them was prospective and particularly described IE- CMBs (22,25). CMBs presented at mean a number up to 5, were preferentially distributed in cortical areas for 85% and were mostly large and heterogeneous. They are less frequently localized in subcortical white matter basal ganglia or posterior fossa than in general population. In these studies, no significant relation was found between haemorrhage and CMBs. CMBs were only associated with prosthetic IE and not with prior anticoagulant therapy.

Fundamentally, no relationship between CMBs and ischemic lesions was highlighted. In the light of this major result, it can be cautiously hypothesized that CMBs physiopathology might be not link to an embolic mechanism as for ischemic lesions. CMBs may represent pyogenic vasculitis or sub-acute inflammatory microvascular process (1) and might be due to the severity of infection itself. Hyper intense T2* Halo and T1 enhancement is likewise a specific inflammatory character of CMBs in IE.

Furthermore, among the sparse autopsied brain histopathological data, some pathological correlation studies showed hemosiderin-laden macrophages in CMBs (13). Indeed, inflammatory marker levels are higher in cases of CMBs lesions (12). This fact can also sustain the infection link.

To this day, CMBs etiology is still unclear.

In the view to support the use of these characteristic cranial MRI lesions as an additional diagnostic marker, the underlying pathologic process has to be better known. Predictive factor must also be understood. Although, some other elements have to be confirmed: a study showed a raise in CMBs number after cardiac valve surgery in 19 patients. New CMBs were found in about two thirds of patients but these lesions seem to be different from those found in pre-operative IE (27). They might be due to classical valve micro-fragmentations.

Some genetic factors have also been linked with CMBs especially in amyloid angiopathy disease (12,13). Furthermore, radiological evolution studies have not been performed. The recurrence, the enhancement, the degradation of these subclinical lesions in IE is unknown. In the only study performed on 11 patients who underwent a following brain MRI, the number of CMBs increases over time in comparison with initial MRI examination, suggesting an active process (28).

Haemorrhagic lesions

MRI examination for bleeding diagnosis itself found a limited interest regarding CT scan.

However, several MRI sequences could help to properly diagnose haemorrhages. Haemorrhagic lesions including subarachnoid bleeding are detected on T2* gradient-recalled and FLAIR sequences (22).

Cerebral bleeding may be due haemorrhagic transformation of an ischemic stroke. Equally, suppurred necrotizing focal arteritis can lead to subarachnoid haemorrhage.

Among the different causes of parenchymal haemorrhage a ruptured mycotic aneurysm must be suppressed by a systematic angiography sequence.

Intracranial microbial aneurysm

Microbial aneurysm can be seen with the use of time of flight weighted, angiography and 3-dimensional T1-weighted post contrast (with gadolinium) sequences.

Even if no recent large series were conducted, MRI angiography is as effective as Angio-CT for microbial aneurysm detection. They have both sensibility around 95% for the diagnose of aneurysm with a diameter upper to 5 mm (29).

Until now, conventional angiography remains the best choice to insure a complete and exact diagnose. To our knowledge, only one article demonstrates the same sensitivity for Angio-MRI and for invasive angiography in this indication (27).

This technique allows aneurysm evaluation and treatment too. Coiling may be required as prevention before any cardiac surgery or as curative measure in case of non-aneurysm involution under suitable antibiotic therapy.

Four axes screening is done in order to search multiple brain aneurysms.

Mycotic aneurysm are habitually numerous, bilateral, distal and fusiform, but the angiographic presentations can varied widely (27,30).

The middle artery territory is usually involved, especially the distal tree (15,31). Often vascular occlusion or stenosis can be associated.

In 2 cases studies, infectious aneurysms are described like directly superimposed with CMBs (32,33). For some authors, the sub-acute microvascular process in link with CMBs might be trigger off microbial aneurysm development in distal artery. There is, at present, no strong evidences to severely connected CMBs lesions and mycotic aneurysms.

Brain abscess and meningitis

Abscess is defined as an expansive lesion with central restricted apparent diffusion, hyper intense peripheral oedema on FLAIR sequence and post contrast annular enhancement on T1 gadolinium sequences (34).

There are no obvious advantages of MRI versus CT-scan for macro abscess diagnosis.

Through in IE, numerous micro-abscesses are more frequent than isolated macro abscess and are often infra-centimetrical.

Sometimes a non-specific T2 Flair hyper intense signal of subarachnoid space can be seen. Inconstant adjacent cortical hypo intensity may be associated. These lepto or pachymeningeal contrast enhancement found a more limited implication in IE management and can also be diagnose with CT scan examination.

Discussion

Main results

The present literature review confirmed that MRI is more sensible than CT in brain damages detection. Most of CT scan undetected lesions and justifying systematic MRI are small hemorrhagic lesions and widespread microinfarts. A significant proportion of these brain lesions are clinically occult. Angiography sequences must be done in each case in order to not overlook microbial aneurysms.

MRI timing

Recurrent stroke can be clinically silent and mostly occur during the first week of antibiotherapy (3). It is already acquired that brain imaging has to be performed as early as possible in view to quickly optimize EI management (26). Because neurologic worsening must be considered impend during the acute phase of any IE, clinicians have to foresee neuroimaging screening. Ideally, MRI should be performed in the week after the diagnosis.

MRI timing is obviously under the heel of technical support availability and radiologist approval. Clinical implication of radiologic staff can depose a part of this technical constraint.

Brain MRI: An additional diagnose criteria

IE diagnosis is difficult and frequently delayed with an average time diagnose of 30 days (6). In some insidious presentation, fever can be absent and/ or echocardiography and blood cultures may be falsely negative. Especially on elderly or haemodialysis patients or in case of intracardiac devices, Dukes criteria can be long to acquire. These criteria were initially developed for clinical research studies and have still some clinical practice limitations. This diagnose period, without treatment, is a source of damage progression and sequelae.

With know-how, Infectious Disease Specialists treat patients with major suspicion but without complete Duke's criteria like an IE until proved otherwise. In that way, MRI results might provide additional diagnosis clues. Excluding CMBs, a recent large study suggest that cerebral MRI, performed up to seven days after admission, changed diagnosis classification in 32% of cases (9). Including CMBs, they upgraded the diagnoses in 51% of patients with initially non-definite IE.

More accurately, with Hess study and neuroradiologic precision, the topography of silent lesions (ischemic lesions and CMBs) could become a further diagnosis marker (35). Some other studies are necessary to better know the usefulness of CMBs like an IE feature and to evaluate if they can be consider as a new imaging minor IE criterion.

Brain MRI implication in surgical decision

If cardiac surgery recommendations in circumstances of severe congestive heart failure or persistent severe infection are cleared, embolic arguments for surgery are still more ambiguous (36). It is not always easy to assess the benefit risk ratio of an early surgery. Surgical timing are still often controversial. There is especially a major hesitation for immediate valvular surgery in referring patients with high embolic risk and recent stroke. If cerebral bleeding or major ischemia is a temporary surgical contraindication, cardiac surgery can be safely performed after silent cerebrovascular complications

(23). In cases of embolic risk factors associated with little MRI lesions, there is no benefit for delaying surgery (7). The early removal of the primary infectious household (the vegetation) is, beyond obvious contraindications, the best way to impede neurologic injury.

To date, several surgical studies have shown contradictory results regarding valvular surgery at the acute phase of IE (37–40) but in patients with a high embolic risk, it seems to be a mortality benefit of an early surgery with less risk of new symptomatic events (23,41,42).

In this way, MRI results and neurological complete assessment should lead clinicians to change the surgical strategy with regards to cardiac surgery indication and timing of valve replacement.

A prospective study in 120 IE patients has recently revealed that MRI can impact early surgical management. Excluding CMBs and solely on basis of MRI results, Duval et al, shown 18% of surgical plan modifications (9).

Moreover, brain MRI may be fitted in a complete imaging check-up. Some teams are performing the same day, at an early stage, MRI brain, chest abdomen, and pelvis CT scan and echocardiography for a thoroughly asymptomatic lesions mapping.

Optimal therapeutic strategy may vary in individual patients and this one should be discuss by a multidisciplinary team in each case.

Brain MRI interest in the antibiotic management

Brain MRI findings may also lead to some specific medical cares modifications. A 7% changes was found in the only study aiming for antibiotherapy regimen modifications with the use of systematic brain MRI (43).

If meningitis, abscess, empyema can be seen with CT scan, MRI find specially an interest, on little's lesions diagnose as shown above. In some infectious department, micro ischemia or CMBs are, at present, the trigger of an antibiotic adjustment. Central nervous system infectious must require antimicrobial molecules with high cerebral diffusion. Changes can be an increase in dosage, a switch or a

drogue addition (Rifampicin, Fosfomycin). The obvious continuum between infection and emboli in IE may support the clinicians' decision.

Indeed, IE brain complications can be as much as suppurate, inflammatory or solely ischemic lesions (7). Especially concerning CMBS, etiologic data are not robust and there is no evidence to treat such lesions like micro abscess.

Prognosis evaluation

Cerebral damages, when they are symptomatic, supported a worsening prognosis (5). Only moderate to severe ischemic stroke and brain hemorrhage were significantly associated with a poorer prognosis. Silent lesions are not carrying a significant excess of mortality (23).

In the only MRI study with a 6 month clinical follow-up, Duval showed no link between mortality and type of lesions observed one MRI (9).

Additionally, physiopathology of encephalopathy and neurocognitive sequelae remains unclear.

Snygg-Martins noted an increase in neurochemical markers of brain damages in 6 IE patients with encephalopathy and numerous ischemic lesions (11).

In case of infection, the neurologic whole deterioration may have various causes: excessive microglial activation, impaired cerebral perfusion, blood-brain-barrier dysfunction, altered neurotransmission (36). Neurological disorder may be as well a toxin or an immunological-induced symptom. Immune's complexes and antigen recirculation can also be imputed (44). Neuropathological lesions are through matched to activation of cells of monocyte-microglial lineage throughout the brain (45). Various authors who found relationship between infection and neurologic failure underlined the complex pathogenesis that likelihood involves many host-pathogen interactions (29).

In a similar way, recent reports suggest that septic shock can be associated with acute cerebrovascular imaging lesions and MRI white matter abnormalities (46).

Concerning CMBs implication, association between cognitive impairment, disability and CMBs has been described in non IE patients like Alzheimer cases (27). The exact CMBs implication is not known. In IE, CMBs and small ischemic lesions long term prognosis have never been done. Few longitudinal studies were performed.

MRI: Practical use and limits

Currently, with medical implants evolution, less MRI contraindication remains as new cardiac devices are consistent with MRI achievement.

If MRI examination may still be limited in some instable patients, material improvement makes MRI realisation less restrictive and more safety, even one intubated patients.

Indeed MRI availability is changing from a hospital to another and its access is not always guaranteed. In our view, this constitutes the first use limitation.

Other advantages of this exam have to be underlined: no irradiation and no iodine injection has to be taken into account for IE patients who are often elderly and frail with pre-existent renal failure.

Conversely the innocuousness of Gadolinium is currently contested (47,48).

Furthermore, the impact on cost of this imaging strategy has not yet been evaluated.

Conclusion

Cerebrovascular complications are a serious therapeutic and prognosis issue associated with IE., brain MRI examination studies confirm that the systemic disorder broadly affect the brain and show large patterns of lesions, mainly infraclinical: micro-infarction and microbleeds are among the most frequent damages identified.

This systematic review shows limited prospective data. Large studies are limited too. Despite a use of standard definition of the disease, methodologies are varied and do not allow easy comparability. Few studies have analyzed the aftermath of brain MRI in the course of IE. The influence of CMBs has not

been fully evaluated. Likewise long term prognosis assessment is particularly missing. Further studies are necessary to assess the role of MRI in clinical decision making and the value of microbleeds as potential new imaging clues in infective endocarditis.

To date, there is not high standard of proof and no evidence for a direct positive impact of brain MRI in IE. Even if, some bundles of arguments support a prompt brain MRI using, especially for surgical patients, the literature is nowadays not sufficient.

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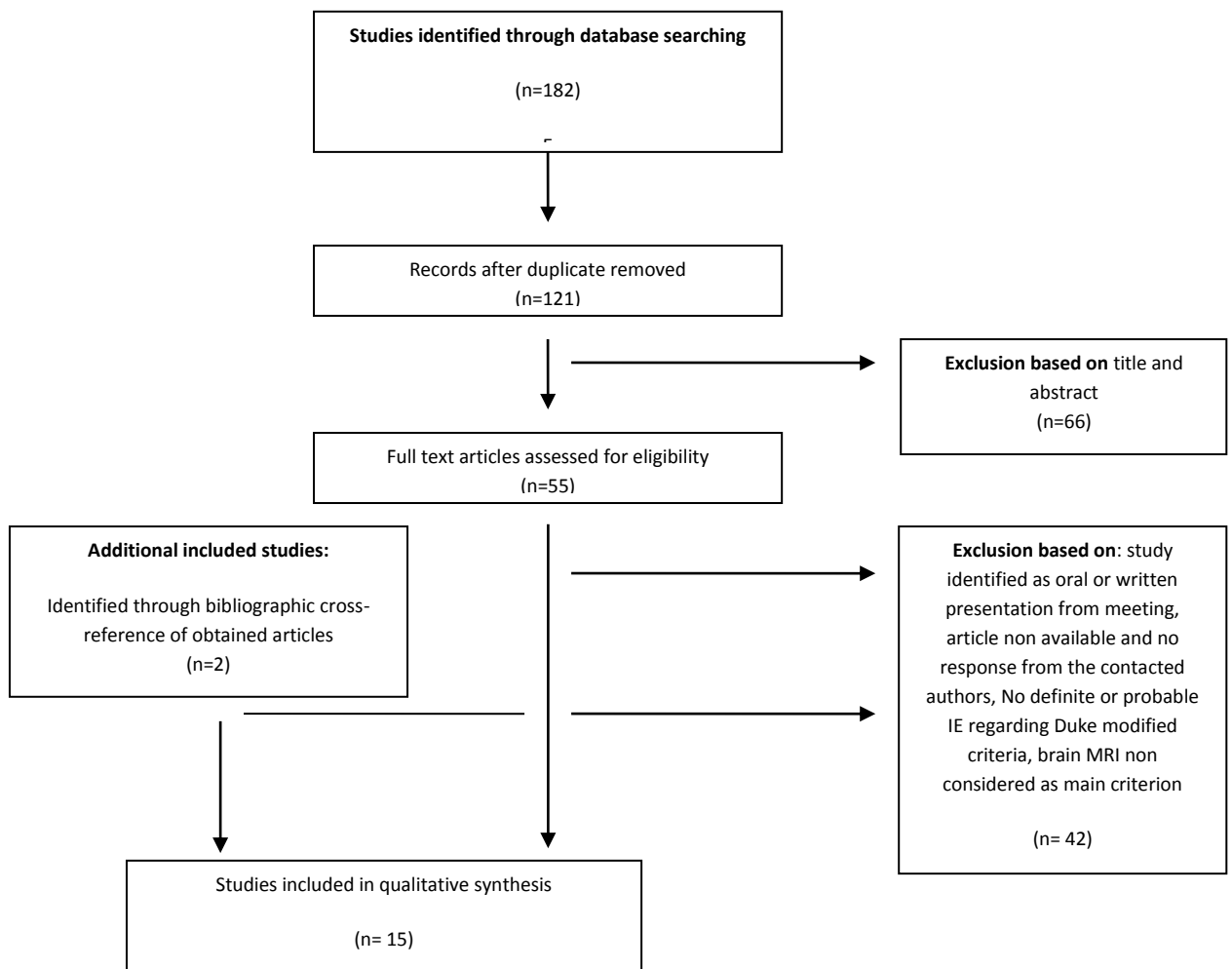
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Figure 1: Flow diagram of study selection



Supplementary table 2: Characteristics of studies

Study	Period of study	Inclusion criteria	Design study	Number of patients	Mean age	Imaging protocol	Main results	MRI follow up	Neuro cognitive follow up
Morofuji et al 2010 Clinical neurology and neurosurgery Japan (24)	2006-2007	IE diagnosis according the modified Duke criteria	Restrospective monocentric	11	54	T2*- weighted MRI Protocol	72.7% of patients had MRI abnormalities 63.2 % of patients showed CMBs CMBs number increased in 14-28 days in 5 patients with multiples lesions	In the month after initial MRI for 7 patients	no
Aneesth et al 2002 Stroke USA (14)	1993-2000	Definite or possible IE regarding Duke criteria	Retrospective monocentric: comparison of acute and recurrent ischemic stroke in IE and NTBE	35 (27 IE/9 NBTE)	53	DWI- MRI into the 2 week after the onset of neurological symptoms	NBTE patients uniformly had multiple widely distributed , small and large strokes, whereas IE patients exhibit also others patterns like single lesion, territorial lesion, disseminated punctate lesions Disseminated punctate lesions were link with clinical encephalopathy	In the month after initial MRI for 4 IE patients	no

Hess et al 2013 Am J Neuroradiol France (15)	2005-2008	Definite or possible IE according to Duke criteria	Prospective monocentric	109	59	MRI imaging within 7 days after inclusion GRE and DWI sequences Double blinding interpretation	MRI showed abnormalities in 71,5% of patients 37% of ischemic lesions 57% of CMBs 8 patients had acute hemorrhage, 3 had micro-abscesses, 3 had small cortical hemorrhage, 3 had mycotic aneurysm 52,5% of lesions had different ages 62,5% of ischemic lesions were multiple small infarcts disseminated in watershed territories CMBs were preferentially distributed in cortical areas No significant relation was found between ischemia and CMBs	no	no
Klein et al 2009 Stroke France (20)	2005-2008	Definite or possible IE according to Duke criteria	Case control study Retrospective	60 IE matched with 120 control	62	Cerebral MRI within 7 days after admission Standardized protocol GRE and DWI sequences Double blinding interpretation	CMBs were more prevalent in IE patients (57%) than in control subjects (15%; OR 10,06) The OR of IE increased dramatically with CMBs number	no	no

<p>Goulenok et al 2013 Cerebrovascular diseases France (1)</p>	<p>2005-2007</p>	<p>Probable or definite IE according to modified Dukes criteria and clinical neurological damages</p>	<p>Prospective monocentric cohort study</p>	<p>30</p>	<p>58</p>	<p>cerebral MRI within 7 days after admission MRI comparison with non-contrast CT (n=5) and angio-CT (n=26) Imaging review by a blinded neuroradiologist</p>	<p>MRI findings: ischemia (n=25),CMBs (n=17), mycotic aneurysm (n=7), abscess (n=6), subarachnoidal hemorrhage (n=5), vascular occlusion (n=3),hemorrhagic lesion (n=2) In 19/30 cases neurologic symptoms were observed before IE diagnose None of the 16 operated patients underwent a post-operative worsening MRI was more sensitive than CT scan in detecting both symptomatic (100 and 81% respectively) and silencious cerebral lesions (50 and 23% respectively) Therapeutic plans were modified according the MRI results in 27 % of patients including surgical plan in 20 %</p>	<p>no</p>	<p>no</p>
<p>lung et al 2013 Stroke France (18)</p>	<p>2005-2008</p>	<p>Definite or possible IE according Duke criteria</p>	<p>Prospective monocentric cohort study</p>	<p>120</p>	<p>61</p>	<p>Cerebral MRI within 7 days following admission</p>	<p>MRI detect ischemic lesions in 53,3% of patients, CMBs in 60% of patients Ischemic lesions were associated with vegetation length and <i>Staphylococcus aureus</i> CMBs were associated with no prior anticoagulant therapy and prosthetic IE A vegetation length>4 mm identified ischemic lesions with a sensitivity of 74,6% and a specificity of 51,5%</p>		

Cooper et al 2009 Circulation USA (9)	2004-2007	Definite IE according to the modified Duke criteria in whom there was at least one valvular left side heart involvement on echocardiography	Prospective	56	58	Brain MRI as soon as possible and before any surgical intervention Imaging review by a blinded neuroradiologist	80% of acute brain embolization 48% of sub-acute brain embolization Lower risk of mortality at 3 month with cardiac surgery OR 0,1 (0,003-0,6) p=0,008	no	no
Okasaki et al 2013 Cerebrovasc disease Japan (21)	2004-2011	Only definite left-side IE	Retrospective multicentric (6 university hospitals)	85 (47 MRI Imaging)	58	Preoperative operative DWI and fluid attenuated inversion recovery sequences MRI within 14 days after diagnose Imaging reviewed by experimented neurologist in clinical blinding Only few patients underwent T2* GRE sequences No micro hemorrhages investigation	55% of patients had acute ischemic lesions 60% had small lesion 77% had multiple lesions 64% had lesions in multiple vascular territories Plasma CRP level and white blood cell count were associated with ischemic lesions (Respectively OR 2.3 and 2.2) No association were found between post-operative complications and preoperative acute ischemic lesions Only 3 patient underwent post-operative neurologic complications Mean duration of 22 days from MRI to cardiac surgery	no	no
Iung et al 2012 EUR Heart J cardiovasc Imaging France (29)	2005-2008	Definite or possible acute IE according to the Duke modified criteria and "excluded" IE with high clinical suspicion	Prospective monocentric Diagnostic classification and therapeutic plans establishment by 2 experts before and after MRI Comparison of the 2 expertises	58	61	Cerebral and abdominal MRI Standardized protocol Double blinding MRI <7 days of diagnoses GRE and DWI sequences	Based on MRI results and excluding CMBS : 19% therapeutic plans modification and 28% diagnosis classification modification	no	no

Takagi et al 2011 Gen Thorac Cardiovasc Surg Japan (23)	2006- 2010	Active native valve IE with surgical surgical indication	Retrospective monocentric	18	53	Preoperative angio- MRI GRE and DWI sequences	Urgent surgery for 15 patients Among them, 10 (67%) showed IE brain lesions 10 patients had acute or sub-acute brain infarctions 2 had brain infarction with abscess 2 had hemorrhagic brain infarction and did not go on surgery	no	no
Jeon et al 2010 Cerebrovas disease Korea (23)	2005- 2006	No previous cardiac surgery and elective cardiac surgery	Prospective monocentric	45 (19 MRI Imaging)	53	Preoperative and post-operative GRE and DWI MRI Standardized protocol Double blinding Interpretation	26 new post-operative GRE lesions on twelve patients	4 patients	no
Snygg-Martin et al 2008 Clinical Infectious Diseases Sweden (10)	1998- 2001 2002- 2005	High clinical suspicion of left-side IE	Prospective bicentric	60 (49 MRI Imaging)	63,5	brain MRI or CT scan< 10 days of antibiotics Cerebrospinal fluids analyses of inflammatory and neurochemical markers of brain damage No DWI MRI sequences	65% of cerebrovascular complications within 30% were silencious	no	no
Duval et al 2010 Annals of internal medicine France (8)	2005- 2008	Definite or possible acute IE according to the Duke modified criteria and "excluded" IE with high clinical suspicion	Prospective monocentric Cohort study 2 experts jointly established the endocarditis diagnostic classification and therapeutic plans just before and after MRI and then compared them.	130	59	Cerebral MRI within 7 days after admission and before any surgical intervention Double blinding MRI <7 days of diagnoses GRE and DWI sequences	82% of MRI abnormalities. Diagnostic classification of 32% of cases of non-definite IE was upgraded 18% of therapeutic plans modifications including 14% of surgical changes	no	no

Grabowski et al 2011 J Neurol Poland (16)	2002-2008	IE diagnosis according the modified Duke criteria without previous neuro-imaging examination or evident hemorrhagic stroke	Prospective monocentric	65 (52 MRI Imaging)	49	MRI or CT Imaging	On 65 patients: - 13 patients with a clinical neurologic event - 24 patients with silent embolism (46%) - A total of 37 patients with neurologic lesions (56.9%)	no	no
Azuma et al 2009 Jpn J Radiol Japan (18)	2004-2006	IE with clinical neurologic complications	Retrospective monocentric	14	70,4	Cerebral MRI within 9 days following admission Only 4 T1-gadolinium imaging DWI only for 13 patients T2* GRE only for 3 patients	13 patients had cerebral lesions embolization: on 10 patients most often in multiple territory, mainly in cortical and subcortical area for 9 57 % of cases involved the middle cerebral artery and 42,9% of cases concerned the posterior cerebral artery 3 intracranial bleeding 3 abscess 2 cerebritis 4 patients presented CMBs Half patients had more than 2 abnormal MRI findings	no	no

IE: infectious endocarditis; MRI: magnetic resonance imaging; CMBs: cerebral micro bleeds; NTBE: nonbacterial thrombotic Endocarditis; CRP: C reactive Protein; GRE: gradient recalled echo; DWI: diffusion weighted imaging;

Annexe 2 : apport de l'imagerie encéphalique dans la prise en charge des endocardites infectieuses, étude clinique observationnelle

Cerebral imaging in infectious endocarditis: a clinical study

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SUMMARY

Background

Because neurological failure is the most frequent extra-cardiac complication in Infectious Endocarditis (IE), a brain Computed Tomography (CT) scan is usually performed. The benefits of Magnetic Resonance Imagery (MRI) have not been clearly established.

Aims

This study aims to clarify the prevalence and type of cerebral lesions in IE detected using MRI and to compare them with those detected using CT scans.

Methods

In the Grenoble University Hospital, patients diagnosed with definite or probable IE according to Duke's modified criteria were screened from 2010 to 2012. Clinical, echocardiographic, radiologic manifestations were recorded. Brain Angio-CT scan and Angio-MRI were performed as soon as possible after diagnosis.

Results

Of the 62 IE patients who underwent at least one cerebral imaging within 3 weeks of diagnosis: *Streptococcus* (29) was the main microorganisms present followed by *Staphylococcus* (14). Twenty-eight patients underwent cardiac surgery. Eight (13%) died before discharge. Twenty (32%) presented neurological symptoms. A brain CT -scan was performed on 53 (85%) patients and a brain MRI was performed on 43 (69%) underwent brain MRI. CT-scan was pathological in 26 (49%) patients whereas MRI examinations of 32 (74%) patients demonstrated abnormalities. Of the asymptomatic patients, 37 (64%) undergoing MRI showed abnormalities while 12 (46%) presented lesions from a CT examination. The MRI lesions were classified as follows: Ischemia (48%), microbleeds (34%), hemorrhages (16%), abscesses (9%), microbial aneurysms (4%). Of the 37 patients who underwent both MRI and CT examinations, ischemia (48% vs 35%) and microbleeds (34% vs 0%) demonstrated the difference between the two imaging methods.

Conclusion

Through the early diagnosis of cerebral damage, even in asymptomatic cases. MRI may have a role in the management of neurological lesions in IE, influence any surgical decision and assist in prognosis assessment. Further clinical studies regarding the role of cerebral MRI in IE are necessary.

Keywords

Infectious endocarditis; magnetic resonance imaging; brain ischemia; cardiac surgical procedures; cerebral microbleeds.

ORIGINAL ARTICLE

BACKGROUND

Infective endocarditis remains a serious disease carrying a considerable risk of morbi-mortality (49,50). Despite improvements in therapy, mortality remains high (around 20%) [2]. With regard to extracardiac complications, cerebral lesions are frequent, appear early and have a poor prognosis (51). They are many and varied, often infra-clinical (1,20). Since embolic risk remains high during the first week of antibiotherapy, neuroimaging diagnosis needs to be performed quickly (52).

Diagnosis management benefits from the extensive use of computerized tomography to detect systemic embolic complications. Nevertheless, Magnetic Resonance Imaging of the brain has been shown to be more sensitive than angio-CT, particularly in the detection of cerebral microbleeds and acute small ischemia (25,26,53). These CMBs, only detectable by using T2* sequences, have previously been associated with sub-acute microvascular process (28). Some studies are in favor of using systematic brain MRI as early as possible to detect such asymptomatic lesions (9,34). Nowadays, this examination is not systematically recommended by guidelines. Indeed, it seems that it could change the medico-surgical strategy [11] .

We conducted a study to determine the incidence and the type of cerebral IE lesions detected by MRI and to compare them with those detected by CT. We particularly wanted to analyze the frequency of CMBs.

METHODS

Study design

An observational retrospective study of patients hospitalized with IE was performed in the Grenoble University Hospital, France.

Population

In 2010, IE local guidelines were applied in cardiology and infectiology units. These guidelines included a recommendation to perform brain imaging as soon as possible.

Positive blood cultures were screened every day with the assistance of the bacteriologic department. For all patients with suspected IE (compatible pathogens, sustained bacteremia), the clinician who cared for the patient was alerted and a set of examinations was collected for diagnosis assessment. Clinicians were encouraged to perform brain imaging systematically, including MRI.

The study included all adult patients with definite or probable IE diagnosis according to Duke's modified criteria between April 2010 and December 2012. Only patients who underwent CT scan and/or MRI of the brain within 3 weeks of diagnosis were included. Minor patients and patients who underwent early surgery before cerebral imaging were excluded.

Data collection

Data were collected from medical records by an infectious disease specialist using a standard form.

Patients' characteristics included age, sex, IE predisposing factors.

The clinical data included fever, neurological signs, immunologic and vascular phenomena.

We collected positive blood cultures or serologic evidence of infection by a compatible microorganism, circulating immune complexes, urine electrophoresis, transthoracic and/or transesophageal echocardiography and performed a CT body scan to check for evidence of septic embolism such as renal or splenic infarcts.

We documented all data for cardiac surgery, in-hospital mortality within 6 months and recovery.

Brain imaging

Imaging examinations were performed using a standardized protocol: Angio-CT scan during the first week after diagnosis and angio-MRI as soon as possible.

CT scan was performed following 2 usual IE protocols as referred below:

A CT scan before and after an iodine contrast injection (used for the TAP scanner, usually 120 cc) or a CT scan before contrast, angioscan C1 at vertex with 80 cc iodine contrast visualizing carotid tracking (cervical level), and CT scan after iodine contrast.

The MRI procedure was standardized as following: *Axial diffusion, axial FLAIR, axial T2 EG (*), axial or sagittal T1, axial or sagittal T1 3D with gadolinium injection, intracranial MRI angiography and MRI in time of fly with gadolinium.*

MRI and CT scan interpretations were made by experienced neuroradiologists.

Imaging criteria for defining the different lesions are detailed below.

Ischemic lesions were detected as a hyperintensity signal in FLAIR (for more than 6 hours), a hyperintensity signal on diffusion b1000 sequences (for about 1 month) and a diffusion restriction (for less than about 10 days).

Microbleed was defined as a round hypo intense T2*-weighted MRI signal with a diameter of < 10 mm.

FLAIR and T2* were used to diagnose parenchymal and subarachnoidal hemorrhages.

Mycotic aneurysms were identified by using time of flight angiography sequences and 3-dimensional T1-weighted sequences with gadolinium.

An abscess was defined as an expansive lesion with central restricted apparent diffusion, hyperintense peripheral edema on FLAIR sequences and post-contrast annular enhancement in T1 gadolinium sequences.

Outcomes

The primary outcome was the prevalence of brain lesions detected by MRI. There were five types of lesions: ischemic lesions, parenchymal hemorrhagic lesions, CMBs, mycotic aneurysm, abscess.

Statistical analysis

Data are presented as a proportion or as the mean and standard deviation. Categorical variables were compared using Fisher's exact test. The Student's t-test was used for continuous variables. All statistical analyses were performed using Stata software. The level of 0.05 was used for statistical significance.

RESULTS

Study sample and patients' characteristics

During the study period, 91 patients met Duke's criteria and 62 of them underwent at least 1 cerebral imaging examination and were included in the study (Table 1).

IE was confirmed for 51 patients and probable for 11. Eleven cases of IE developed on cardiac prosthesis and 1 on a cardiac device. Fever above 38°C occurred in 40 patients (64%).

Streptococcus was the most common microorganism (n=29, 46%) followed by *Staphylococcus* (n=29, 22%) and *Enterococcus* (n=6, 9%). Some germs were less frequent such as Pneumococci for 3 patients, *Candida* for 3 and *Coxiella* for one. Blood cultures were negative in 3 cases.

Eleven transthoracic and 51 transesophageal echocardiographies were performed. In 10 cases, echocardiography did not discover abnormalities. Valve regurgitation was reported in 52 patients (83%). Nineteen (30%) had severe regurgitation. Concerning the type of lesions: trigon abscesses were diagnosed in 10 (16%) and valvular perforation in 5 (8%) patients. Vegetation was shown in 36 (58%) patients with an 11 mm mean length. It was mobile in 11 of these patients. The vegetation was on the mitral valve in 19 (30%) patients. Fifteen (24%) patients had aortic involvement. Tricuspid vegetation was detected in one patient and both aortic and mitral IE were diagnosed in one patient.

Twenty-eight (45%) patients underwent valve surgery. Surgery was performed on native valve for 23 patients and on prosthetic valve for 5. Eight patients with neurologic symptoms underwent surgery.

Neurological damages and Medical imaging

Twenty (32%) patients presented neurologic clinical abnormalities. Half of the patients with *Staphylococcus* IE had neurological symptoms.

During the study period, 53 (85%) patients underwent an angio-CT and 43 (69%) an angio-MRI. Thirty-seven patients (59%) underwent CT scan and MRI. The median time taken to perform the MRI was 7 days. The median time between CT scan and MRI was 6 days.

An MRI was not performed on 19 (32%) patients because 3 died, 2 underwent urgent cardiac surgery and 3 had an incompatible pacemaker. Two patients were clinically unstable, hospitalized in the intensive care unit and neuroimaging was not feasible. For one patient, the imaging was refused by the neuroradiologists and for another patient, clinicians turned down the examination for ethical reasons (palliative treatment). Because of a technical issue, one patient did not have the examination. The reason is unknown for the other 5 patients.

The CT scan was abnormal in 26 patients (48% of the patients who underwent CT scan). Twelve asymptomatic patients had at least one lesion detected by CT scan (Table 2).

MRI was abnormal for 32 patients, i.e. 74% of the patients who underwent MRI (Figures 1 and 2) and showed acute ischemic lesions in 48% patients (21), CMBs in 34% (Table 2) (15).

Both imaging methods were abnormal in 19 cases (54%) and normal for 8 (23%). The total incidence of cerebral lesions was 77%. Of the 37 patients who underwent MRI and CT scans, ischemia (48% vs 35%) and microbleeds (34% vs 0%) demonstrated the difference between the imaging methods (Table 3). Of the 20 patients with no neurologic symptoms, 12 had lesions detected by CT scan (46.1%) whereas 27 presented lesions with MRI (62.8%).

The risk of imaging embolism was 15% for *Staphylococcus*, 32% for *Streptococcus* and 83% for *Enterococcus* (p=0.048).

In one case of *Streptococcus constellatus*, IE appears as a jugular thrombosis with a subdural empyema.

All intracranial infectious aneurysms were situated near the middle cerebral artery bifurcation and were equally detected by CT scan and MRI. The diagnosis of aneurysm was not confirmed by cerebral angiography.

Seventeen (60%) surgical patients underwent an MRI, of whom 15 (88%) had at least one lesion. Of the surgical patients 34% showed CMBs. There were no significant differences between surgical and non-surgical patients for the repartition of lesions.

Mortality

Eight patients died (13%) before hospital discharge. Of those patients who underwent surgery, five (17%) died. Three patients with neurologic symptoms died. No significant association was found between death and MRI lesions (50% versus 50% $p=0.53$) or between vegetation length and death (6.0 mm versus 8.6 mm $p=0.76$).

DISCUSSION

Our results are consistent with previous data showing that cerebrovascular complications in IE are common [9,18,19] . The total prevalence of cerebral lesions was 77%. The most frequently detected lesions were the same as those described in previous studies: ischemia was present in two-thirds of patients [7]. However, in our sample, CMBs were less frequent than in other studies where they were diagnosed in 50% of cases [20,21] . The lack of susceptibility-weighted MR sequences in our protocol may explain this difference. In our study, MRI detected subclinical lesions in 62% of cases. Previous studies found a rate of around 50% [7,18] .

In comparison with CT scans, MRI is more useful especially for ischemic lesions and CMBs diagnosis.

CMBs and ischemia were not associated with any type of other neurologic lesions.

Microbial aneurysms were mainly on the sylvian artery, which is concordant with a recent review [16, 17]. We noted similar sensitivity in CT and MRI for aneurysm detection, but no extensive study was conducted to analyze the advantages of MRI angiography in IE. We also found a slightly higher rate of abscess and aneurysms in comparison with previous data [22,23] . In older studies, imaging screening was not systematically used and as a result historical prevalence may have been underestimated.

Finally, we discovered a high prevalence of cerebral lesions detected by MRI in IE. MRI results can, therefore, assist in the management of IE. Recently, a prospective trial showed that MRI findings could change diagnosis, therapeutic and surgical plans in 28% of cases [12]. If urgent surgery is necessary when a poor hemodynamic tolerance appears, embolic indications for surgery remain controversial. Optimal surgical timing is often difficult to establish although several studies have shown that surgery is possible in patients with asymptomatic brain lesions and a low risk of neurological deterioration [8,15,16,24]. A reduction in embolic risk and mortality was achieved with early surgery in patients with high embolic risk [20,21]. For those patients, surgery has to be performed without delay [3]. IE needs rapid diagnosis and accurate risk stratification of embolism to decide the best therapeutic strategy [11,25]. Surgical timing should be discussed by a multidisciplinary team in each case. Moreover, the advantages of MRI with non-iodine injection have to be considered in frail patients.

Some data showed a specific IE-CMBs topography, mainly situated in cortical areas. These non-pathognomonic IE lesions have a specific endocarditis pattern and may represent an additional imaging marker [20].

Our bacteriological results are in accordance with present IE epidemiology: in the last 50 years, changes in epidemiology have occurred due to an increasing rate of health care associated endocarditis, particularly in elderly patients [3–5]. *Staphylococcus* incidence has increased and this microorganism is responsible for the majority of severe cases [7]. The *Enterococcus* IE rates have also increased. The rate of acute Streptococci IE remains stable even though antibiotic prophylaxis has been reduced for dental procedures (57).

The second place of Staphylococci may be due to the mild severity of the condition of our patients. We excluded patients with more severe conditions, ruling out those who underwent surgery before MRI. This could also explain the low mortality and constitute a selection bias. This may also explain why we had fewer surgical rate than in other studies.

Some limitations must be taken into account:

First, because the most severe patients (surgical patients and intensive care patients) did not undergo an MRI examination, we can assume that the rate of damage detected by MRI may have been underestimated.

Second, as the sample size is small, we cannot confirm recent data showing an association between vegetation length and ischemic lesions [26]. Large, highly mobile vegetations (> 10 mm) are the cause of recurrent emboli despite appropriate treatment. Therefore, there is an advantage in early cardiac surgery in the case of oscillating large vegetation even without cardiac failure [27].

Third, because of the period of 6 days between the CT scan and the MRI, a true comparison may be uncertain.

It could be interesting to make a neurological assessment in the long run by studying the CMBs-cognitive dysfunction relationship. Several studies have proved an association between CMBs and several broad neurological impairments (cognitive impairment, depression, gait instability) (4,12,13).

These case studies were also conducted to obtain a better understanding of the benefits of an early MRI examination. This examination could be used in a larger study to assess the role of MRI in a clinical algorithm of IE management.

CONCLUSIONS

MRI appears to be more sensitive than CT in detecting subclinical cerebrovascular complications particularly for ischemia and microbleeds.

MRI of the brain is useful for an early complete embolic assessment and a risk stratification strategy, hence helping physicians in complex decision-making [24]. Further studies are necessary to assess the consequences of MRI findings in diagnosis and decision-making and to understand the underlying process of IE-CMBs. It might also be appropriate to carry out a prognostic study to clarify IE-CMBs and the cognitive impairment link.

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Table 1: Characteristics of patients

Characteristics	Patients, (n=62)	
Mean age, mean, [SD]	63.5	[15.5]
Mean age among surgical patients, mean, [SD]	59	[13.1]
Men, n	42	
Women, n	20	
Patients who underwent surgery, n (%)	28	(45)
Duke' s criteria		
Definite IE, n	51	
Probable IE, n	11	
Fever above 38°C, n (%)	40	(64)
Neurologic signs, n (%)	20	(32)
Microorganism, n (%)		
<i>Streptococcus</i>	29	(46)
<i>Staphylococcus aureus</i>	14	(22)
<i>Enterococcus</i>	6	(9)
<i>Pneumococcus</i>	3	(4.8)
<i>Candida</i>	2	(3)
<i>Coxiella burnetti</i>	1	
Other microorganisms	4	(6.2)
No microorganism identified	3	(4.8)
Native IE, n (%)	49	(81)
Prosthetic valve IE	11	(18)
Cardiac device IE	1	
Echocardiography data		
Regurgitation, n (%)	52	(83)
Vegetation, n (%)	36	(58)
Aortic, n	15	
Mitral, n	19	
Aortic and mitral, n	1	
Tricuspid, n	1	
Mean vegetation length, mm, mean,[SD]	11.1	[4.9]
Vegetation mobility, n (%)	11	(17.7)
Cardiac abscess, n (%)	10	(16)
Perforation, n (%)	5	(8)
Total deaths, n (%)	8	(12.9)
Without cardiac surgery	3	(8)
With cardiac surgery	5	(8)

Table 2: Imaging brain lesion distribution

Lesions Characteristics	Patients n=62		Clinical neurologic failure n=20		Death n=8	
		(%)		(%)		(%)
CT Angiography	53	(85.4)				
Ischemic lesions	16	(29.6)	9	(56.2)	4	(25)
Hemorrhagic lesions	7	(12.9)	4	(57.1)	2	(28.6)
Aneurysms	5	(9.2)	3	(60)	1	(20)
Abscesses	4	(7.4)	1	(25)	0	
MR Angiography	43	(69.3)				
Ischemic lesions	21	(48.8)	11	(52.4)	3	(14.3)
Microbleeds	15	(34.8)	5	(3.3)	1	(6.7)
Hemorrhagic lesions	7	(16.2)	4	(57.9)	2	(28.6)
Aneurysms	2	(4.6)	2	(100)	1	(50)
Abscesses	4	(9.3)	3	(75)	0	

Table 3: Brain lesion distribution in the 37 patients who underwent both types of imaging examinations

	CT angiography		MRA	
	n=37	(%)	n=37	(%)
Ischemic lesions	13	(35.1)	18	(48.6)
Hemorrhagic lesions	5	(13.3)	7	(18.9)
Microbleeds	0		12	(32.4)
Aneurysms	2	(5.4)	2	(5.4)
Abscesses	2	(5.4)	3	(8.1)

Figure 1: *Staphylococcus* endocarditis with impaired consciousness. Small acute spread infarction. Lesions were hyperintense on DWI (A, C) and were also visible on FLAIR sequences (B). Ischemia were supra and infra tentorial (B, C). Microbleeds occurred in the same area (D)

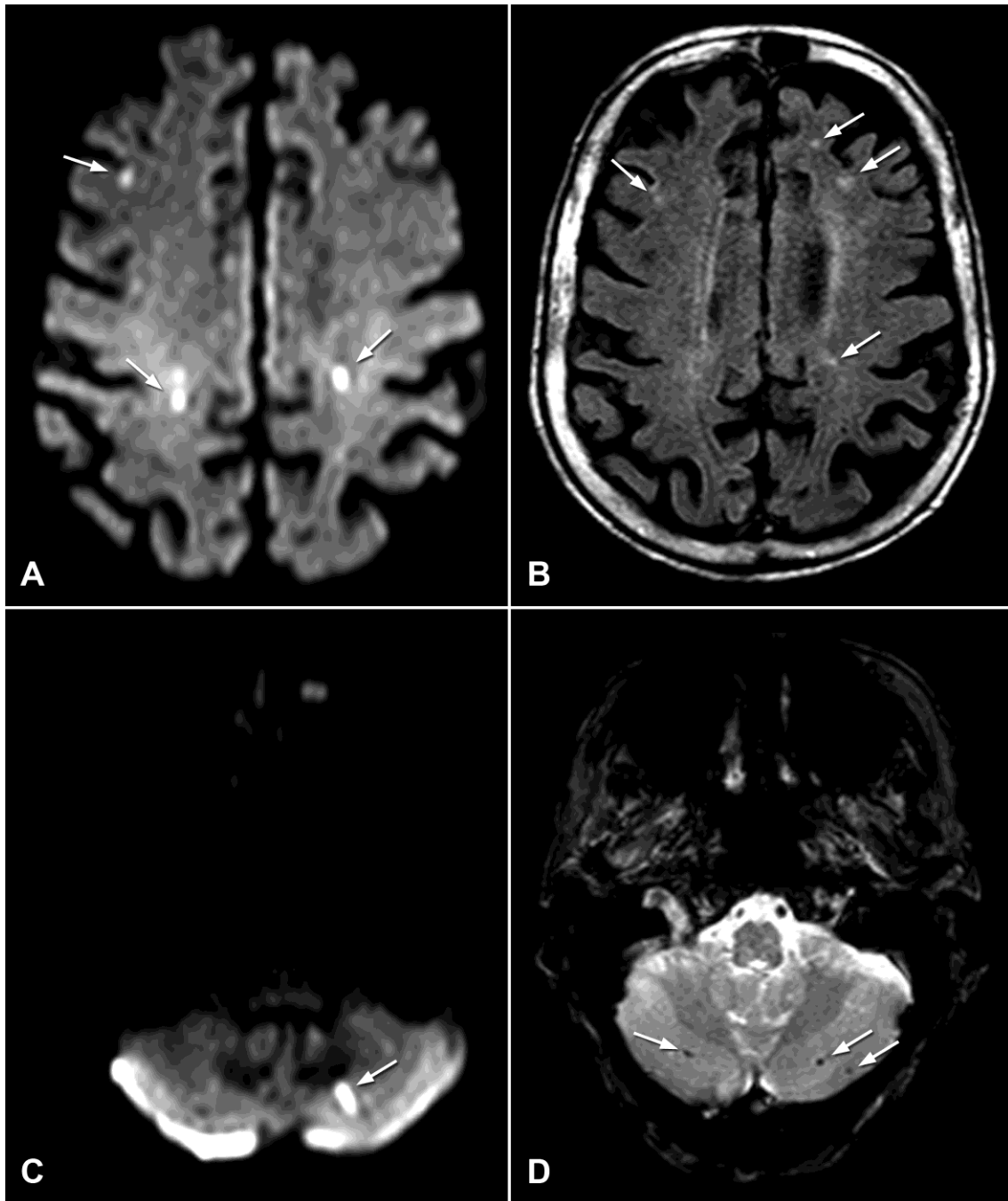
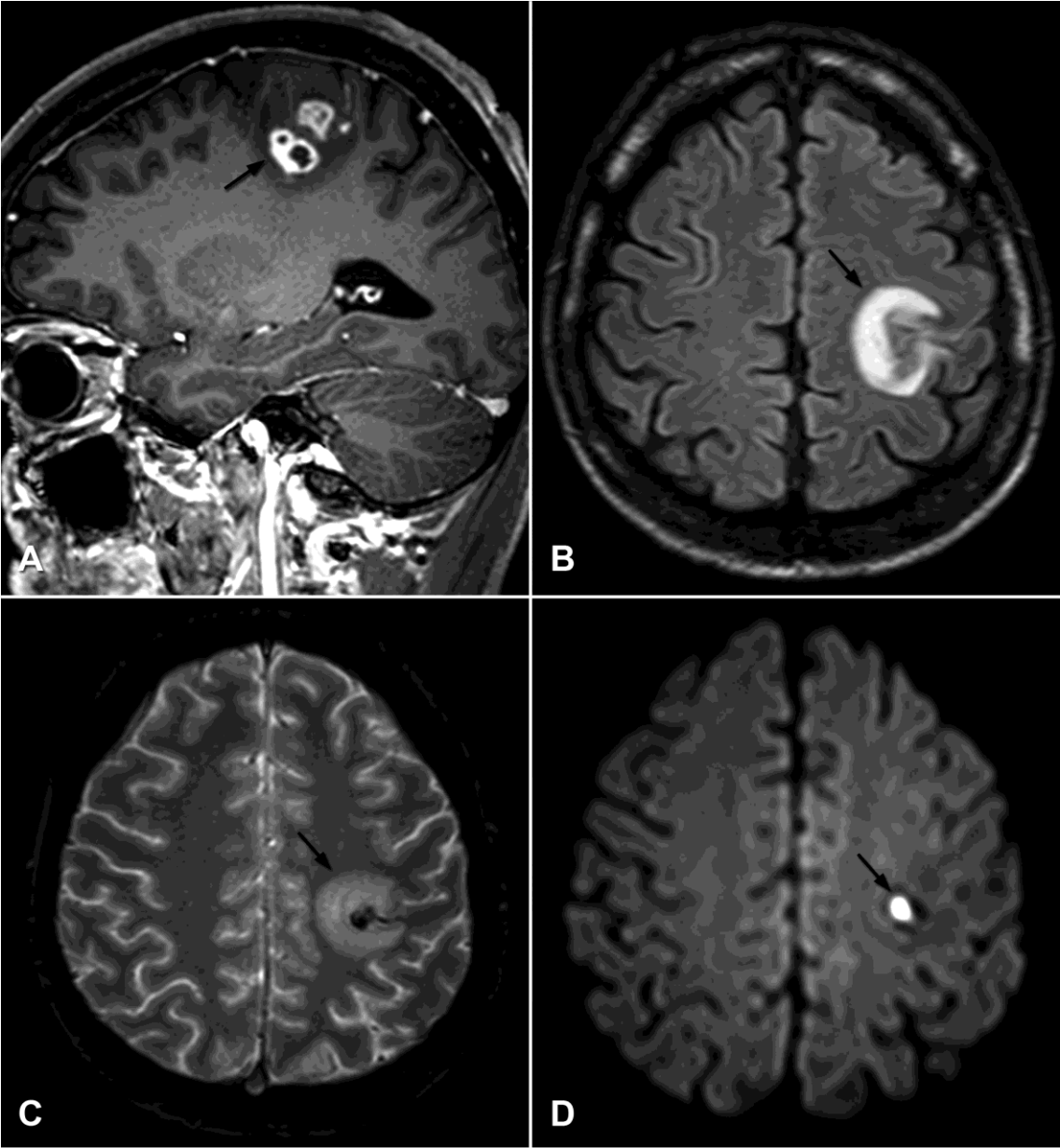


Figure 2: patient with a weakness in his right arm and recent intermittent fever. Adjoining cortico-subcortical abscesses (A) with a surrounding edema on FLAIR sequences. (B).The center appears hyper intense on DWI (D). T2* sequences show slight associated bleeding (C). The results suggest a pyogenic abscess.



Annexe 3 : cahier de recueil des données. Etude neuro-EI

Cahier de recueil

Critère d'inclusion:

Patient présentant une endocardite infectieuse du cœur gauche ou du cœur droit, certaine ou probable, selon les critères de Duke's modifiés et pouvant bénéficier d'une IRM encéphalique dans les **7 jours** suivant le diagnostic.

Critères d'exclusion :

- Patient mineur
- Indication chirurgicale en extrême urgence (< 24h)
- Contre-indication à l'IRM (cf. annexe 1 en fin de livret)
- EI prise en charge initialement ailleurs et ayant déjà bénéficié de plus de 7 jours de traitement antibiotique bien conduit

DIAGNOSTIC POSITIF

Critères de la Duke University (modifiés par Li)

CRITERES MAJEURS

Hémocultures positives

1- présence dans 2 hémocultures différentes de micro-organismes communément rencontrés dans l'EI

- *Strepto. viridans* (y compris les streptocoques déficients), *Strepto. bovis*, micro-organismes du groupe HACEK O
- *Staphylococcus aureus* ou entérocoques (en l'absence de foyer primaire) O

2- hémocultures positives de façon persistante pour des micro-organismes susceptibles d'engendrer une EI

- sur 2 échantillons prélevés à plus de 12 heures d'intervalle O
- ou sur 3, ou la majorité des 4 (ou plus) échantillons prélevés à plus d'une heure d'intervalle entre le premier et le dernier O

3- hémoculture positive à *Coxiella burnetii*

ou anticorps IgG phase I > 1/800 O

Évidence d'une atteinte de l'endocarde

Échocardiogramme montrant des signes d'EI

ETO indispensable si prothèse valvulaire, EI classée comme au moins "possible", ou EI compliquée [abcès paravalvulaire]

ETT en première intention chez les autres patients

- masse intracardiaque animée de mouvements oscillants, implantée sur une valve (ou sur ses structures de soutien, ou sur un matériel intracardiaque) ou située dans le courant d'un jet de régurgitation — cela en l'absence d'autre diagnostic anatomique — O
- abcès O
- déhiscence partielle, nouvellement apparue, d'une prothèse valvulaire O

Régurgitation valvulaire nouvellement apparue (l'augmentation ou la modification d'un souffle préexistant n'est pas suffisante) O

CRITERES MINEURS

Prédisposition : atteinte cardiaque prédisposante ∞, ou toxicomanie intraveineuse O

Fièvre ≥ 38° O

Phénomènes vasculaires : embolie artérielle majeure, infarctus pulmonaires septiques, anévrisme mycotique, hémorragie intracrânienne, hémorragies conjonctivales, lésions de Janeway O

Phénomènes immunologiques : glomérulonéphrite, nodosités d'Osler, taches de Roth, facteur rhumatoïde O

Évidence microbiologique

- hémoculture(s) positive(s) ne réunissant pas les critères majeurs ci-dessus (et à l'exclusion des cas où une seule culture est positive pour des staphylocoques coagulase négative ou pour des micro-organismes qui ne causent pas d'EI) O
- ou évidence sérologique d'une infection en évolution due à un micro-organisme pouvant causer une EI O

∞ Prothèse valvulaire, atcd EI, cardiomyopathie congénitale

EI certaine	EI possible	EI exclue
<p>Critères anatomopathologiques</p> <ul style="list-style-type: none"> • micro-organismes : découverts à la culture, ou à l'examen histologique, d'une végétation in situ ou embolisée ou dans un abcès intracardiaque ○ • ou lésions anatomiques : présence d'une végétation ou d'un abcès intracardiaque, avec confirmation histologique d'une EI en évolution ○ <p>○</p> <p>Critères cliniques</p> <ul style="list-style-type: none"> • 2 critères majeurs ○ • ou 1 critère majeur et 3 critères mineurs ○ • ou 5 critères mineurs ○ 	<p>1 critère majeur et 1 critère mineur ○</p> <p>ou</p> <p>3 critères mineurs ○</p>	<ul style="list-style-type: none"> • Certitude acquise que les manifestations sont liées à une autre cause ○ • Disparition des manifestations au terme de 4 jours ou moins de traitement antibiotique ○ • Absence à l'examen anatomique (autopsique ou chirurgical) de lésions d'EI après 4 jours ou moins de traitement antibiotique ○ <p>○</p>

Endocardite CERTAINE ou POSSIBLE

présentant au moins un critère majeur

(Bactériémie soutenue ou atteinte ETT / ETO) :

oui

non

Jour du diagnostic : /__ / __ / __ /

Validation expert : (infectiologue, cardiologue, réanimateur, chirurgien cardiaque)

.....

COORDONNEES PATIENTS

Page à détacher dès l'inclusion du patient et à adresser au

Dr Patricia Pavese

Unité mobile d'infectiologie

Hôpital A .Michallon

Chartreuse 3eme étage unité F

CHU de Grenoble

CS1021738043 GRENOBLE Cedex 09

Tel (+33) 476765291

Fax (+33) 476765838

NOM: / _____ /

Prénom: / _____ /

Date De Naissance : / ____ / ____ / ____

Numéro de téléphone :

Numéro d'inclusion : correspondant au rang d'inclusion et au numéro du centre

/ _ _ / _ _ _ /

Seul ce numéro devra être reporté sur toutes les feuilles du cahier de recueil.

DONNEES DEMOGRAPHIQUES

Sexe: Masculin Féminin

Nationalité patient :

Coordonnées Médecin Traitant :

Coordonnées Patient :

_Dr

Adresse :

Adresse :

- Le patient a-t-il des facteurs de risque connus d'endocardite ?

oui non

Si oui,

- Valve prothétique mécanique Mitrale Aortique Tricuspide
- Bio prothèse Mitrale Aortique Tricuspide
- Pace maker
- Antécédents d'endocardite infectieuse
- Cardiomyopathie congénitale
- Valvulopathies
- Cardiomyopathie hypertrophiques obstructive
- Toxicomanie par voie IV

- A-t-il une maladie chronique nécessitant une prise en charge hospitalière régulière (HDJ ou de semaine ou HC) au moins 3 fois/an ?

oui non

Si oui,

- /_/ Maladie respiratoire
- /_/ Maladie cardiaque
- /_/ HTA
- /_/ Maladie hépatique ou digestive
- /_/ Maladie neurologique
- /_/ Maladie hématologique
- /_/ Maladie Rénale
- /_/ Diabète
- /_/ Immunodépression, précisez : _____
- /_/ Maladie rhumatologique chronique (anti Tnf α , anti CD20...)
- /_/ Autre pathologie, précisez : _____

- Reçoit-il un traitement régulier par :
 - /_/ Hémodialyse ou dialyse péritonéale
 - /_/ Chimiothérapie ambulatoire
 - /_/ Soins à domicile, nécessitant au moins une visite de soignant hebdomadaire (Ide, AS, Kinésithérapeute)
 - /_/ Anticoagulants
 - /_/ Antiagrégants plaquettaire
 - /_/ Antibiotiques

- Le patient est-il tabagique actif ?

oui non

- Présence d'une autre pathologie chronique

oui non

Si oui, préciser :

En cas de pathologie chronique, indiquer si celle-ci est :

- /_/ Non-fatale ou potentiellement fatale dans un délai de > 5 ans
- /_/ Probablement fatale dans un délai de 1 à 5 ans
- /_/ Probablement fatale dans un délai de <1 an

DONNEES A L 'ADMISSION

• Date d'admission à l'hôpital (j/m/a): _____

• Service d'admission :

Infectiologie

Réanimation /Soins intensifs

Chirurgie cardiaque

Cardiologie

Autre, précisez :

• Mode d'entrée du patient (provenance) :

Domicile Venant d'une Institution (si domicile habituel) Autres structure hospitalière

COMORBIDITES

Index de Charlson

Insuffisance cardiaque

Insuffisance rénale modérée à sévère

Infarctus myocardique

Démence

Vasculopathie périphérique

Tumeur solide

Maladie cerebrovasculaire

Hémiplégie

BPCO

SIDA

Hépatopathie modérée

Hépatopathie modérée à sévère

Ulcère

Connectivite

Diabète

Diabète avec complications

Leucémie

Tumeur solide métastatique

Lymphome

DONNEES CLINIQUES

(J0 = Admission ou jour de réalisation de la 1° hémoculture positive)

Présentation Clinique :

- Présentation principale à l'admission

(Coder les éventuels diagnostic(s) principal (ux) autres que la bactériémie, présents à l'admission ou dans les 24 premières heures de l'admission, tels que notés par ex. au SAU)

Cardiovasculaire

(OAP, hypotension, oligurie, trouble du rythme ou de conduction)

Rénal

Fièvre prolongée

Respiratoire

Hématologique

Neurologique

Gastro intestinal

Autres (préciser):

- Examen neurologique normal :

oui non

Si non,

Epilepsie

coma

confusion

Syndrome méningé

Focalisation, précisez :

- Si signes neurologiques, précisez le jour du diagnostic : (j/m/a): _____

- Date de début du syndrome infectieux (fièvre ou frissons ou syndrome inflammatoire)

- date (Jours/mois/année): _____

Syndrome septique à J0 :

- Absence de SRIS (0-1 critère)
- SRIS (≥ 2 critères SIRS)
- Sepsis
- Sepsis Sévère
- Choc septique
- Transfert en réanimation/USC dans les 1^{er} 24h suivant le diagnostic d'endocardite et défaillances d'organes :
 - Neurologique (GCS <14 , confusion, agitation, ..) Avec Coma
 - Hémodynamique avec drogues vasopressives ou inotropes
 - Respiratoire avec ventilation invasive ou non invasive
 - Rénale avec nécessité d'épuration extra rénale
 - Surveillance continue sans défaillance d'organe avérée

Evaluation des défaillances d'organes le jour (1° 24h) de la 1° hémoculture positive

<i>Score SOFA</i>	0	1	2	3	4
Respiratoire PaO ₂ / FIO ₂	> 400	≤ 400	≤ 300	≤ 200 avec Vent. Art.	≤ 100 avec Vent. Art.
Coagulation Plaquettes	> 150 10 ³ /mm ³	≤ 150 10 ³ /mm ³	≤ 100 10 ³ /mm ³	≤ 50 10 ³ /mm ³	≤ 20 10 ³ /mm ³
Hépatique Bilirubine	< 20 μmol/L	20 – 32 μmol/L	33 – 101 μmol/L	102 – 204 μmol/L	> 204 μmol/L
Cardiovasculaire Hypotension	absence	MAP < 70 mmHg	Dopa ≤ 5 Ou Dobutrex	Dopa > 5 Ou Epi ≤ 0,1 Ou Norepi ≤ 0,1	Dopa > 15 Ou Epi > 0,1 Ou Norepi > 0,1
Système Nerveux Central GCS	15	13 - 14	10 - 12	6 - 9	< 6
Rénal Créatinine Ou Diurèse	< 110 μmol/L	110 - 170	171 - 299	300 – 440 ou < 500 ml/jour	> 440 ou < 200 ml/jour
Total =					

VARIABLES	26	13	12	11	9	7	6	5	4	3	2	0	1	2	3	4	6	7	8	9	10	12	15	16	17	18	
Age en années												<40						40-59				60-69	70-74	75-79		≥80	
F.C. en bpm				<40							40-69	70-119				120-59											
P.A. systolique en mm Hg		<70						70-99				100-199		≥ 200													
Température en °C												<39°			≥ 39°												
PaO2/FiO2 si VM ou CPAP en mmHg				<100	100-199		≥200																				
Diurèse en l/24h				<0.50				0.50-0.999				≥ 1.000															
Urée en mmol/l (ou g/l)												<10.0 (<0.60)					10.0-29.9 (0.60-1.79)									≥30.0 (≥1.80)	
Leucocytes 10 ³ /mm ³			<1.0									1.0-19.9			≥ 20.0												
Kaliémie en mmol/l										<3.0		3.0-4.9			≥ 5.0												
Natrémie en mmol/l								<125				125-144	≥145														
HCO3 ⁻ en mEq/l						<15			15-19			≥ 20															
Bilirubine si ictère en µmol/l (mg/l)												<68.4 (<40.0)				68.4-102.5 (40.0-59.9)					≥ 102.6 (≥ 60.0)						
Score de Glasgow *** en points	<6	6-8			9-10			11-13				14-15															
Maladies chroniques																					Cancer méta.	Mal. hém.				SIDA	
Type d'admission											Chir. prog.						Méd.		Chir. urg.								
Sommes des points																											

Score IGS II

Cocher la valeur la plus anormale pendant les 24 premières heures

Syndrome septique à H72 :

- Absence de SRIS (0-1 critère)
- Sepsis (≥ 2 critères SIRS)
- Sepsis Sévère
- Choc septique
- Transfert en réanimation/USC dans les 1^{er} 24h suivant le diagnostic d'endocardite et défaillances d'organes :
 - Neurologique (GCS <14 , confusion, agitation, ..) Avec Coma
 - Hémodynamique avec drogues vasopressives ou inotropes
 - Respiratoire avec ventilation invasive ou non invasive
 - Rénale avec nécessité d'épuration extra rénale
 - Surveillance continue sans défaillance d'organe avérée

EUROSCORE à H72 : _____

- Age Précisez : -----
- Sexe féminin OUI
- Créatinémie > 200 µmol/l OUI
- FEVG <30% 30- 50% >50%
- BPCO OUI
- Chirurgie de l'aorte thoracique OUI
- Artériopathie périphérique OUI
- Troubles neurologiques OUI
- Endocardite active OUI
- Etat préopératoire critique OUI
- Angor instable OUI
- Infarctus myocardique (<90j) OUI
- PAPS>60 mm hg OUI
- Chirurgie cardiaque antérieure OUI
- Réparation septale post infarctus OUI
- Chirurgie cardiaque associée ou non aux coronaires OUI

Définitions-BPCO: utilisation au long cours de bronchodilatateurs ou de stéroïdes.

Artériopathie périphérique: un ou plus des éléments suivants: claudication des membres inférieurs, occlusion ou sténose carotidienne > 50%, ATCD ou intervention programmée sur l'aorte abdominale, les membres inférieurs ou les carotides.

Troubles neurologiques: trouble affectant la déambulation ou les actes de la vie courante.

Chirurgie cardiaque antérieure: toute intervention ayant nécessité une ouverture péricardique.

Endocardite: patient sous antibiotiques pour endocardite lors de la chirurgie.

Etat préopératoire critique : au moins un des événements suivants : tachycardie ventriculaire, fibrillation ventriculaire, "mort subite" récupérée, massage cardiaque préopératoire, ventilation mécanique préopératoire, agents vasopresseurs , ballon de contrepulsion, Insuffisance rénale aigue (anurie ou oligurie < 10 mL/h).

Angor instable: angor de repos requérant des dérivés nitrés jusqu'à l'arrivée au bloc opératoire.

Urgence: patient programmé avant le début du prochain jour opératoire.

Chirurgie de l'aorte thoracique: aorte ascendante, crosse aortique ou aorte descendant

Evaluation des défaillances d'organes à 72h :

Score SOFA	0	1	2	3	4
Respiratoire PaO ₂ / FIO ₂	> 400	≤ 400	≤ 300	≤ 200 avec Vent. Art.	≤ 100 avec Vent. Art.
Coagulation Plaquettes	> 150 10 ³ /mm ³	≤ 150 10 ³ /mm ³	≤ 100 10 ³ /mm ³	≤ 50 10 ³ /mm ³	≤ 20 10 ³ /mm ³
Hépatique Bilirubine	< 20 μmol/L	20 – 32 μmol/L	33 – 101 μmol/L	102 – 204 μmol/L	> 204 μmol/L
Cardiovasculaire Hypotension	absence	MAP < 70 mmHg	Dopa ≤ 5 Ou Dobutrex	Dopa > 5 Ou Epi ≤ 0,1 Ou Norepi ≤ 0,1	Dopa > 15 Ou Epi > 0,1 Ou Norepi > 0,1
Système nerveux central GCS	15	13 - 14	10 - 12	6 - 9	< 6
Rénal Créatinine Ou Diurèse	< 110 μmol/L	110 - 170	171 - 299	300 – 440 ou < 500 ml/jour	> 440 ou < 200 ml/jour
Total =					

Ref : Vincent JL et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction / failure. *Intensive Care Med.* 1996;22:707-710

DONNEES MICROBIOLOGIQUES

En cas de bactériémie :

- Micro -organisme isolé :

Infection mono microbienne :

Espèce 1: _____

Infection poly microbienne

Espèce 2: _____

Espèce 3: _____

- Date du prélèvement de la première hémoculture positive
- date (Jour / mois / année): _____
- Date de la première hémoculture négative (même espèce, même phénotype)
pour le même épisode
- date (Jour / mois / année) _____
- Nombre de flacons d'hémocultures prélevés dans les 48 premières heures
après la première hémoculture positive |_|_|
- Nombre de flacons positifs dans les 48 premières heures après la première
hémoculture positive |_|_|
- Nombre de flacons d'hémocultures positifs au total sur le nombre de flacon
prélevés_ |_|_| / |_|_|
- CRP :mg/L (chiffre le plus haut si différents prélèvements)

En l'absence de bactériémie :

- Sérologies positives : oui non

Si oui,

Legionnelle Bartonella Coxiella Autres, précisez :.....

- PCR sur valve : oui non

Si oui, précisez le microorganisme : _____

Faire une copie des antibiogrammes effectués

Et les joindre au cahier de recueil.

Porte d'entrée :

Présumée **Inconnue**

Confirmée (Identification du même germe dans un site et/ou démonstration clinique/imagerie/intervention sur un foyer infectieux)

- Dentaire
- ORL
- Infection respiratoire basse
- Infection intra-abdominale
 - Péritonite, Abscès, cholécystite, pancréatite, ... Fibroscopie digestive
- Infection génito urinaire
 - Pyélonéphrite ou Prostatite Chirurgie urologique
- Infection de la peau et des parties molles. Précisez :
- Infection endo-vasculaire
 - Thrombophlébite suppurée Bactériémie sur KT
 - Autre (artérite infectieuse..)
- Méningite, abcès cérébral
- Infection ostéo-articulaire
- Médiastinite
- Infection du site opératoire
- Infection Primitive** (ie, Bactériémie « primaire » sans porte d'entrée ou foyer source identifié)
- Autres :

Endocardite liées aux soins : oui non

Précision concernant le foyer primaire si nécessaire :

.....
.....
.....

TRAITEMENTS ADMINISTRES

- **Traitements antibiotiques reçus** (après réalisation de la première hémoculture)

Date de début du traitement (Jour / mois / année) : / ___ / ___ / ___ /

Poids du patient (en kg) : / ___ / ___ / ___ / kg

*Pour dose, rythme et voie d'administration mettre **1** si adapté, **0** si inadapté*

Molécule (DCI)	Dose unitaire	Rythme/ jour	Voie	Durée (jours)

- **Traitement complémentaire du foyer infectieux :**

Non Nécessaire, mais non réalisable Oui, chirurgie cardiaque :

Si oui, Remplacement valvulaire mécanique biologique

Oui, autres (exemple : ponction aspiration d'un abcès intracrânien) :

Date et nature du geste : / ___ / ___ / ___ /

.....

DONNEES ECHOGRAPHIQUES

Echographie n°1 DATE :

ETT

ETO

- Fuite valvulaire : oui non

Si oui, degré : minime moyen sévère

- Types de valves atteintes : mitrale aortique tricuspide

- Végétations : oui non

Si oui, -taille : mm

-Localisation :

-Mobilité : oui non

- Absès : oui non

Si oui, localisation :

- Perforations valvulaires : oui non

- Insuffisance cardiaque échographique : oui non

Si oui, Type : Systolique Diastolique

Echographie n°2 (si réalisée) DATE :

ETT

ETO

- Fuite valvulaire : oui non

Si oui, degré : minime moyen sévère

- Types de valves atteintes : mitrale aortique tricuspide

- Végétations : oui non

Si oui, -taille :

-Localisation :

-Mobilité : oui non

- Abscès : oui non

Si oui, localisation :.....

- Perforations valvulaires : oui non

- Insuffisance cardiaque échographique : oui non

Si oui, type : Systolique Diastolique

Echographie n°3 (si réalisée) DATE :

ETT

ETO

- Fuite valvulaire : oui non

Si oui, degré : minime moyen sévère

- Types de valves atteintes : mitrale aortique tricuspide

- Végétations : oui non

Si oui, -taille :.....

-Localisation :

-Mobilité : oui non

- Abscès : oui non

Si oui, localisation :.....

- Perforations valvulaires : oui non

- Insuffisance cardiaque échographique : oui non

Si oui, Type : Systolique Diastolique

Echographie n°4 (si réalisée) DATE :

ETT

ETO

- Fuite valvulaire : oui non

Si oui, degré : minime moyen sévère

- Types de valves atteintes : mitrale aortique tricuspide

- Végétations : oui non

Si oui, -taille :

-Localisation :

-Mobilité : oui non

- Abscès : oui non

Si oui, localisation :

- Perforations valvulaires : oui non

- Insuffisance cardiaque échographique : oui non

Si oui, Type: Systolique Diastolique

DONNEES RADIOLOGIQUES

Pour chaque lésion, merci de préciser le nombre (:...)

SCANNER TAP ET PRE CRANE AVANT J3

ANGIOIRM AVANT J5

Pour chaque examen, faire une copie des comptes rendus d'imagerie

Et les joindre au cahier de recueil.

Angio-IRM cérébrale

DATE :

AVANT

J 7

Attention, contrôle à S6 si anormale

Anomalies IRM : oui non

Si oui,

Ischémie :

Lésion ischémique étendue:.....

Petite lésion ischémique:.....

Hémorragies :

Microhémorragies (microbleeds):.....

Hémorragie sous arachnoïdienne:.....

Lésion hémorragique intra parenchymateuse:.....

Anévrisme mycotique:..... Si oui, artériographie de contrôle ? oui non

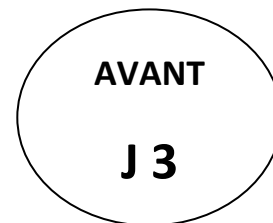
Abscesses:.....

Autres (exemple : thrombophlébite, processus expansif) : Précisez

.....

➤ Si patient inclus mais n'ayant pas eu l'IRM, pourquoi ?

Scanner thoraco-abdomino-pelvien injecté et Scanner cérébral non injecté:



DATE :

- Lésions emboliques : oui non

Si oui,

Localisation et nombre :

- Abscès systémiques : oui non

Si oui,

Localisation et nombre :

- Autre, précisez :

.....
.....

En dehors des cas de contre-indications à l'injection de produit de contraste (allergie, défaillance rénale), le scanner TAP doit être injecté.

**Joindre également le CR de scanner cérébral si cet
examen a été effectué.**

<h2>CONTROLE IRM A S6</h2>

Si IRM initiale anormale uniquement

Pour chaque examen, faire une copie des comptes rendus d'imageries

Et les joindre au cahier de recueil.

Pour chaque groupe de lésions précisez l'évolution :

	Régression	Stabilité	Aggravation
•	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
•	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
•	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
•	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
•	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
•	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Si nouvelles lésions, précisez le type, le nombre, la localisation :

- : _____
- : _____
- : _____
- : _____

M3 : EVALUATION CLINIQUE

Evaluation des défaillances d'organes à M3 :

<i>Score SOFA</i>	0	1	2	3	4
Respiratoire PaO ₂ / FIO ₂	> 400	≤ 400	≤ 300	≤ 200 avec Vent. Art.	≤ 100 avec Vent. Art.
Coagulation Plaquettes	> 150 10 ³ /mm ³	≤ 150 10 ³ /mm ³	≤ 100 10 ³ /mm ³	≤ 50 10 ³ /mm ³	≤ 20 10 ³ /mm ³
Hépatique Bilirubine	< 20 μmol/L	20 – 32 μmol/L	33 – 101 μmol/L	102 – 204 μmol/L	> 204 μmol/L
Cardiovasculaire Hypotension	absence	MAP < 70 mmHg	Dopa ≤ 5 Ou Dobutrex (qq soit la dose)	Dopa > 5 Ou Epin ≤ 0,1 Ou Norepi ≤ 0,1	Dopa > 15 Ou Epin > 0,1 Ou Norepi > 0,1
Système Nerveux Central GCS	15	13 - 14	10 - 12	6 - 9	< 6
Rénal Créatinine Ou Diurèse	< 110 μmol/L	110 - 170	171 - 299	300 – 440 ou < 500 ml/jour	> 440 ou < 200 ml/jour
Total =					

- **Durée d'hospitalisation cumulée :**jours

- **Avez-vous pris une décision de limitation des soins ?**

oui non Si oui, date (Jour/mois/année) : /__/__/__

- **Complications neurologiques fatales ou non à 3 mois**

oui non

Si oui , précisez :

- **Récurrence de la maladie :**

oui non

- **Guérison** (négativation des hémocultures et absence de rechute après l'arrêt de l'antibiothérapie)

oui non

- **Statut à M3:**

Vivant

DCD Date du décès (Jour/mois/année) /__/__/__

- **Statut à la sortie de l'hôpital :**

Vivant

DCD Date du décès (Jour/mois/année) /__/__/__

Si décédé. Précisez la cause du décès :

- **Si vivant, devenir du patient à la sortie :**

- Retour à domicile
- Transfert autre hôpital de court séjour
- Transfert en secteur SSR-SLD
- Transfert en EHPAD ou maison de retraite
- Transfert en HAD

STATUT A UN AN

- **Durée d'hospitalisation cumulée :**jours

- **Avez-vous pris une décision de limitation des soins ?**

oui non si oui date (Jour/mois/année) : /__/__/__

- **Complications neurologiques fatales ou non a un an :**

oui non

Si oui , précisez :

- **Récurrence de la maladie :**

oui non

- **Chirurgie cardiaque, reprise chirurgicale dans l'année :**

oui non

Si oui, précisez :

- **Guérison** (négativation des hémocultures et absence de rechute après l'arrêt de l'antibiothérapie)

oui non

- **Statut à un an :**

Vivant

DCD Date du décès (Jour/mois/année) /__/__/__

Si décédé. Précisez la cause du décès :

• **Statut à la sortie de l'hôpital :**

Vivant

DCD Date du décès (Jour/mois/année) / ___/___/___/

EVENEMENTS INDESIRABLES

Précisez si effets indésirables liés à l'IRM :

.....

.....

.....

Annexe 4 :

Fiche data expertises. Etude neuro-EI

Numéro de dossier : /...../....

Date :

DIAGNOSTIC FINAL :

DUKES : Endocardite Certaine Probable Exclue

CLINIQUEMENT : Endocardite Certaine Probable Exclue

CHIRURGIE CARDIAQUE :

Oui Non Indication théorique Cardiologie interventionnelle

Si oui :

-Type de prothèse : Bioprothèse Prothèse mécanique

-Délais : Urgent Semi urgent Différée

ANTIBIOTHERAPIE

Molécule(s) :

Dose(s) :

Durée :

ANTICOAGULATION CURATIVE :

Oui Non

Annexe 5 :

Contre-indication à l'IRM

Contre-indications absolues

- Certains dispositifs médicaux implantables actifs : stimulateurs cardiaques (Pace maker) et défibrillateurs cardiaques implantables
- Des patients porteurs de certains de ces dispositifs de fabrication récente ont pu bénéficier d'une exploration IRM au prix du suivi d'une procédure extrêmement précise et contraignante pour le personnel et pour le patient : neuro-stimulateurs et implants cochléaires
- Certains systèmes d'injections automatisées implantés : pompe à insuline
- Clips vasculaire ferromagnétiques intracérébraux
- Certains systèmes de régulation de la température corporelle
- Corps étrangers métalliques, en particulier, intraoculaires ou situés à proximité de zone à risque (système nerveux et vasculaire)

Contre-indications relatives

- Grossesse avant M3 (principe de précaution)
- Implants métalliques divers
- Claustrophobie
- En post interventionnel, si implants légèrement ferromagnétiques (stents, coils, filtres), il est préférable d'attendre 6 à 8 semaines
- Eclats métalliques
- Dispositifs transdermiques (patch) : risque de brûlures
- Tatouages en zone étudiée

Annexe 6 :

Indications chirurgicales

Recommandations européennes de 2009 préconisant la chirurgie en cas d'EI sur valve native :

- **EN EXTREME URGENCE (dans les 24 heures)**

En cas d'EI aortique ou mitrale avec régurgitation aigue sévère, obstruction valvulaire ou fistule dans une cavité cardiaque ou dans le péricarde entraînant un œdème pulmonaire réfractaire ou un choc cardiogénique ; en cas d'IA sévère avec insuffisance cardiaque même temporaire ou simplement radiologique.

- **EN URGENCE (dans les premiers jours)**

-En cas d'infection locale non contrôlée, de fièvre persistante et d' hémocultures positives après 7 – 10 jours , d'infection causée par un champignon ou un microorganisme multi résistant .

-En cas d'EI aortique ou mitrale avec végétations > 10 mm après 1 ou des embolies malgré des antibiotiques appropriés, d'EI aortique ou mitrale avec végétations > 10 mm et présence de facteurs prédictifs d'évolution compliquée ; en cas de grosses végétations isolées (> 15 mm)

-En cas d'apparition ou d'aggravation d'un trouble conducteur AV lors d'une EI aortique.

- **SANS URGENCE (après 1 ou 2 semaines d'antibiotiques)**

En cas d'EI aortique ou mitrale avec régurgitation sévère et sans insuffisance cardiaque

Annexe 7 :

Lettre d'information et consentement éclairé

**LETTRE D'INFORMATION DESTINEE AUX PATIENTS POUR PARTICIPATION A UNE
RECHERCHE BIOMEDICALE**

**Intérêt de l'IRM encéphalique précoce dans la prise en charge des endocardites
infectieuses**

Madame, Monsieur, Nous vous proposons de participer à une étude de recherche clinique. Cette lettre d'information vous détaille en quoi consiste cette étude.

Vous pourrez prendre le temps pour lire et comprendre ces informations, pour réfléchir à votre participation, et pour demander au médecin responsable de l'étude de vous expliquer ce que vous n'aurez pas compris.

BUT DE L'ETUDE

Le diagnostic d'endocardite infectieuse vient d'être porté pour vous. Les complications neurologiques de l'endocardite ne sont pas rares et peuvent parfois être grave. L'IRM permet de dépister précocement des lésions qui ne s'expriment pas cliniquement et qui pourraient éventuellement évoluer vers des complications plus graves. Nous souhaitons analyser ces anomalies précoces pour améliorer la prise en charge des patients souffrant d'endocardite.

BENEFICE(S) ATTENDUS

La connaissance de ces anomalies précoces permettrait d'organiser une surveillance neurologique plus précise et une meilleure adaptation du traitement de l'endocardite.

DEROULEMENT DE L'ETUDE

Votre EI sera prise en charge selon les recommandations habituelles. L'étude consiste en la réalisation d'une IRM cérébrale au cours des 7 premiers jours de votre prise en charge. Un enquêteur recueillera par ailleurs les renseignements les plus importants concernant votre infection, les traitements qui seront réalisés. Il vous recontactera à votre sortie de l'hôpital ; mais aussi 3 mois et 1 an après le début des signes pour faire le point sur votre état clinique.

Si l'IRM cérébrale retrouve des anomalies, nous contrôlerons leur disparition à la fin du traitement antibiotique, soit autour de la sixième semaine.

RISQUES POTENTIELS

L'examen n'est pas douloureux, mais il est souvent un peu long et le bruit peut être désagréable. Il ne comporte pas de risque particulier en dehors des contre-indications connues que nous aurons pris le soin de rechercher avant de vous inclure dans l'étude.

FRAIS MEDICAUX

Conformément à la loi, tous les frais liés à l'étude seront pris en charge par le CHU de Grenoble.

LEGISLATION – CONFIDENTIALITE

Conformément aux articles L. 1121-1 et suivants du Code de la Santé Publique, le Comité de Protection des Personnes Rhône-Alpes a étudié ce projet de recherche et a émis un avis favorable à sa réalisation le xx/xx/xxxx.

Un contrat d'assurance « 135751 » a été souscrit par le promoteur de l'essai, « CHU de Grenoble » auprès de la compagnie : « Société Hospitalière d'Assurances Mutuelles SHAM-18, rue Edouard Rochet - 69 372 LYON cedex08 » pour couvrir les risques liés à cette recherche.

Toute information vous concernant recueillie pendant cet essai sera traitée de façon confidentielle. Seuls les responsables de l'étude et éventuellement les autorités de Santé pourront avoir accès à ces données. A l'exception de ces personnes ; qui traiteront les informations dans le plus strict respect du secret médical ; votre anonymat sera préservé. La publication des résultats de l'étude ne comportera aucun résultat individuel.

Les données enregistrées à l'occasion de cette étude feront l'objet d'un traitement informatisé. S'agissant de données nominatives, vous bénéficiez à tout moment, du droit d'accès , de rectification et d'opposition des données vous concernant auprès des responsables de l'étude et , en ce qui concerne les informations de nature médicale, ce droit est exercé par l'intermédiaire du Docteur Pavese Patricia conformément à la loi 78-17 du 06 janvier 1978 relative à l'Informatique, aux Fichiers et aux Libertés, modifiée par la loi n°94-548 du 1er juillet 1994, relative au traitement des données nominatives ayant pour fin la recherche dans le domaine de la santé. Le projet a reçu un avis favorable de la CNIL en date du

Conformément à l'article L 1122-1 du Code de la Santé Publique (loi de Mars 2002 relative aux droits des malades les résultats globaux de l'étude pourront vous être communiqués si vous le souhaitez.

Si vous avez des questions pendant votre participation à cette étude, vous pourrez contacter le médecin responsable de l'étude, le Dr Patricia Pavese, tél : 04 76 76 52 91.

Vous êtes libre d'accepter ou de refuser de participer à cette étude. Cela n'influencera pas la qualité des soins qui vous seront prodigués.

Nous vous remercions d'avoir pris le temps de lire cette lettre d'information. Si vous êtes d'accord pour participer à cette recherche, nous vous invitons à signer le formulaire de consentement ci-joint.

FORMULAIRE DE CONSENTEMENT POUR LA PARTICIPATION A UNE RECHERCHE BIOMEDICALE

Titre de la recherche : Intérêt de l'IRM encéphalique précoce dans la prise en charge des endocardites infectieuses

Je soussigné(e) (*Nom et prénom du patient*), accepte de participer à l'étude **Intérêt de l'IRM encéphalique précoce dans la prise en charge des endocardites infectieuses**

Les objectifs et modalités de l'étude m'ont été clairement expliqués par le Dr..... (*Nom et prénom du médecin*).

J'ai lu et compris la fiche d'information qui m'a été remise.

J'accepte que les documents de mon dossier médical qui se rapportent à l'étude puissent être accessibles aux responsables de l'étude et éventuellement aux autorités de santé. A l'exception de ces personnes, qui traiteront les informations dans le plus strict respect du secret médical, mon anonymat sera préservé. J'accepte que les données nominatives me concernant recueillies à l'occasion de cette étude puissent faire l'objet d'un traitement automatisé par les organisateurs de la recherche. Je pourrai exercer mon droit d'accès et de rectification auprès du Dr Patricia Pavese.

J'ai bien compris que ma participation à l'étude est volontaire. Je suis libre d'accepter ou de refuser de participer, et je suis libre d'arrêter à tout moment ma participation en cours d'étude. Cela n'influencera pas la qualité des soins qui me seront prodigués.

Mon consentement ne décharge pas les organisateurs de cette étude de leurs responsabilités. Je conserve tous mes droits garantis par la loi.

Après en avoir discuté et avoir obtenu la réponse à toutes mes questions, j'accepte librement et volontairement de participer à la recherche qui m'est proposée.

Fait à.....

le

Nom et signature de l'investigateur

Signature du patient

