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Original Article

# Acute intracranial hypertension management in metastatic brain tumor: A French national survey

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## ABSTRACT

**Background.** – Brain metastases occur in 15–30% of cancer patients and their frequency has increased over time. They can cause intracranial hypertension, even in the absence of hydrocephalus. Emergency surgical management of brain metastasis-related intracranial hypertension is not guided by specific recommendations.

**Objective.** – We aimed to make a French national survey of emergency management of intracranial hypertension without hydrocephalus in the context of cerebral metastasis.

**Methods.** – A national online survey of French neurosurgeons from 16 centers was conducted, consisting of three clinical files, with multiple-choice questions on diagnostic and therapeutic management in different emergency situations.

**Results.** – In young patients without any previously known primary cancer, acute intracranial hypertension due to a seemingly metastatic single brain tumor indicated emergency surgery for all those interviewed; 61% aimed at complete resection; brain MRI was mandatory for 74%. When a primary cancer was known, 74% of respondents were more likely to propose surgery if an oncologist confirmed the possibility of adjuvant treatment; 27% were more likely to operate on an emergency basis when resection was scheduled after multi-disciplinary discussion, prior to acute degradation.

**Conclusion.** – Currently, there is no consensus on the emergency management of intracranial hypertension in metastatic brain tumor patients. In case of previously known primary cancer, a discussion with the oncology team seems necessary, even in emergency. Decision criteria emerge from our literature review, but require analysis in further studies.

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## 1. Introduction

Brain metastases (BM) occur in 15–30% of all cancers [1,2]. They are associated with significant morbidity and have a poor prognosis if untreated [3]. Historically, diagnosis of BM was considered a pre-terminal event, representing the end-stage of an uncontrollable primary disease, and treatment was limited to palliative whole-brain radiotherapy (WBRT) [4]. Incidence of BM has

increased in recent years as a consequence of improved imaging, and of improved survival in primary tumor [5]. Advances in the management of extracranial disease have led to a more aggressive approach in brain metastatic disease, currently validated in a multidisciplinary meeting, with decisions based on results from randomized prospective multicenter studies.

However, neurosurgeons may also be required to manage emergency critical oncological BM cases. BM can cause intracranial hypertension (ICH) even in the absence of hydrocephalus or intratumoral hemorrhage. Hydrocephalus linked to BM and the management of posterior fossa BM compressing the fourth ventricle or brainstem has been a frequently focus of clinical studies. However, medical and surgical management of ICH without hydrocephalus remains poorly defined in emergency situations where multidisciplinary discussion is unfeasible. Emergency surgical management of ICH is not the subject of specific guidelines.

**Abbreviations:** BM, Brain Metastasis; CT, Computed Tomography; GPA, Graded Prognostic Assessment; HTS, Hypertonic Saline; ICH, Intracranial Hypertension; IV, Intravenous; KPS, Karnofsky Performance Status; MRI, Magnetic Resonance Imaging; PS, Performance Status; RPA, Recursive Partitioning Analysis; WBRT, Whole Brain Radiotherapy.

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The goal of the present study was to conduct a French national level survey of emergency management of BM-related ICH without hydrocephalus.

## 2. Methods

A national BM committee was formed with members from two national neurosurgical societies: the Société Française de Neurochirurgie (SFNC) and the Société de Neurochirurgie de Langue Française (SNCLF). The survey questions were developed by consensus by the committee, in the form of three clinical files, with multiple-choice questions about different aspects of diagnostic and therapeutic management in emergency situations. The complete survey is provided in the [Appendix](#).

All neurosurgeons with a valid email address available on the SFNC website were contacted. The survey was administered electronically via the Google Form® website and was open for responses from January to August 2017. Participation was voluntary and unpaid. Responses were collected as a single best answer or as all applicable answers from a drop-down list of options. The online survey tool was able to identify duplicate responses, which were not included in the data analysis. Descriptive statistics were presented in the form of frequencies and percentages.

The survey dealt with the following specific scenarios:

- emergency management of ICH in a patient with a single cystic brain lesion without known primary tumor ([survey questions 1–3](#));
- emergency management of ICH in a patient being treated for melanoma without known metastases, presenting with 3 brain tumors ([survey questions 4–7](#));
- emergency management of ICH in a patient being treated for renal cell carcinoma, with several metastatic cerebral lesions already treated by radiosurgery, one of which had progressed radiologically, with surgical resection decided upon in a multidisciplinary team meeting a few days previously ([survey questions 8–10](#)).

The following emergency management questions were addressed:

- timing ([survey questions 1, 2, 4, 7](#));
- paraclinical management ([survey questions 2, 6, 9](#));
- surgical management ([survey questions 1, 3, 4, 7, 10](#)): surgical approach, resection/puncture for cystic BM ([survey question 3](#)), for multiple BM ([survey questions 8, 9](#));
- multidisciplinary management with oncologist ([survey questions 7, 9](#));
- medical management ([survey questions 1, 8](#)), medical antihypertensive treatment ([survey question 8](#));
- supportive care ([survey questions 5, 8](#)).

## 3. Results

Of the 93 neurosurgeons contacted in 30 neurosurgical centers, 22 (23.7%) from 16 centers responded to the survey. Most respondents were academic neurosurgeons. The age ranges were harmoniously distributed. Demographic characteristics are summarized in [Table 1](#).

### 3.1. Emergency management of ICH in a patient with a single cystic brain lesion without known primary tumor

Emergency management of ICH in a patient with a single cystic brain lesion ([Appendix, clinical case 1](#); [Fig. 1](#))

**Table 1**  
Respondent demographics.

Type of practice (n = 22)	
Government funded	4 (18%)
Academic	18 (82%)
Year of completion of training (n = 22)	
< 1990	6 (27%)
1991–2000	7 (32%)
2001–2010	7 (32%)
2011–2018	2 (9%)
Number of patients with brain metastases seen per year (n = 22)	
1–25	2 (9%)
26–50	14 (64%)
> 50	6 (27%)

KPS: Karnofsky Performans Scale.



**Fig. 1.** Attached file to clinical case 1 of the survey.

#### 3.1.1. Survey question 1 (only one response allowed per participant)

Fifty-seven percent of respondents indicated they would wait to assess the efficacy of medical treatment (osmotherapy, corticosteroids) before discussing emergency surgery ([Fig. 2A](#)).

#### 3.1.2. Survey question 2 (more than one response allowed per participant)

Seventy-four percent of respondents indicated that they would perform brain MRI before deciding whether to operate or not ([Fig. 2B](#)). Twenty-six percent would operate without any further exploration, based on clinical presentation. Only 4% recommended thoraco-abdominopelvic CT-scan before deciding whether to operate or not. None indicated a need for fundus, and none answered that surgery was not indicated in this situation.

#### 3.1.3. Survey question 3 (only one response allowed per participant)

Sixty-one percent of respondents indicated that, if emergency surgery was decided upon, they would recommend maximally complete lesion resection, whereas 39% would perform puncture of the cystic part of the lesion to relieve the ICH and have more time to perform other exploration, such as thoraco-abdominopelvic CT and/or brain MRI, before discussing indications for lesion resection ([Fig. 2C](#)).

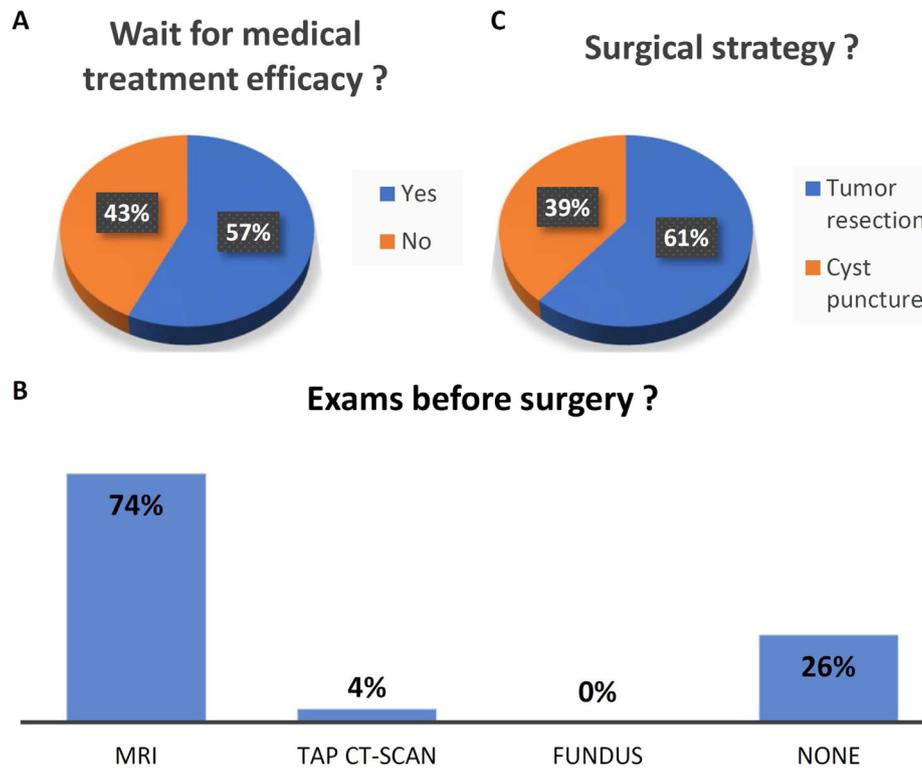


Fig. 2. Responses to clinical case 1.

### 3.2. Emergency management of ICH in a patient being treated for melanoma without known metastases, presenting with 3 brain tumors

Emergency management of ICH in a patient being treated for melanoma without known metastases, presenting with 3 brain tumors (Appendix, clinical case 2; Figs. 3–4).

#### 3.2.1. Survey question 4 (only one response allowed per participant)

Sixty-five percent of respondents would consider emergency surgery in this situation (Fig. 4A).

#### 3.2.2. Survey question 5 (only one response allowed per participant)

None of the respondents would consider supportive care management without further exploration (Fig. 4B).

#### 3.2.3. Survey question 6 (more than one response allowed per participant)

Eighty-seven percent of respondents would ask for the opinion of an oncologist before envisaging surgery (Fig. 4C). Seventy-percent would perform brain MRI before deciding whether to operate or not, whereas only 22% would recommend thoraco-abdominopelvic CT. None would ask for a dermatologic examination or fundus in emergency.

#### 3.2.4. Survey question 7 (only one response allowed per participant)

Seventy-four percent of respondents would be encouraged to perform emergency surgery if the oncologist considered prognosis to be rather good and that several therapeutic possibilities remained (Fig. 4D). Twenty-two percent would have performed emergency surgery whatever the oncologic prognosis. Four

percent would not operate on this patient, even in case of previously controlled oncologic disease.

### 3.3. Emergency management of ICH in a patient being treated for renal cell carcinoma, with several metastatic cerebral lesions already treated by radiosurgery, one of which had radiologically progressed, with surgical resection decided upon in a multidisciplinary team meeting a few days previously

Emergency management of ICH in a patient being treated for renal cell carcinoma, with several metastatic cerebral lesions already treated by radiosurgery, one of which had radiologically progressed, with surgical resection decided upon in a multidisciplinary team meeting a few days previously (Appendix, clinical case 3; Figs. 5–6).

#### 3.3.1. Survey question 8 (only one response allowed per participant)

Fifty-four percent of respondents would opt for supportive care only, because of the clinical severity in this context (Fig. 6A). Forty-six percent would perform emergency surgery to remove the lesion for which resection had been suggested before clinical aggravation set in. None would recommend isolated intensive medical management of ICH, without surgery.

#### 3.3.2. Survey question 9 (more than one response allowed per participant)

Thirty-seven percent of respondents declared that the number of cerebral lesions guided their decision (Fig. 6B). Twenty-seven percent were influenced by the decision in favor of surgical resection taken before clinical aggravation set in. Twenty-seven percent took account of the rapidity of clinical aggravation. Only 9% would have preferred to have the opinion of the oncologist so as to get a better idea of overall prognosis.

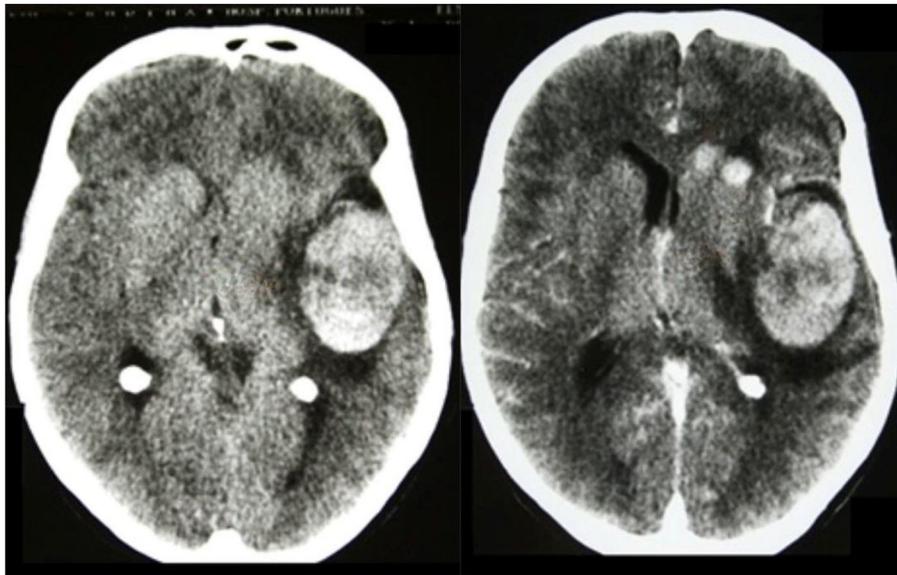


Fig. 3. Attached file to clinical case 2 of the survey.

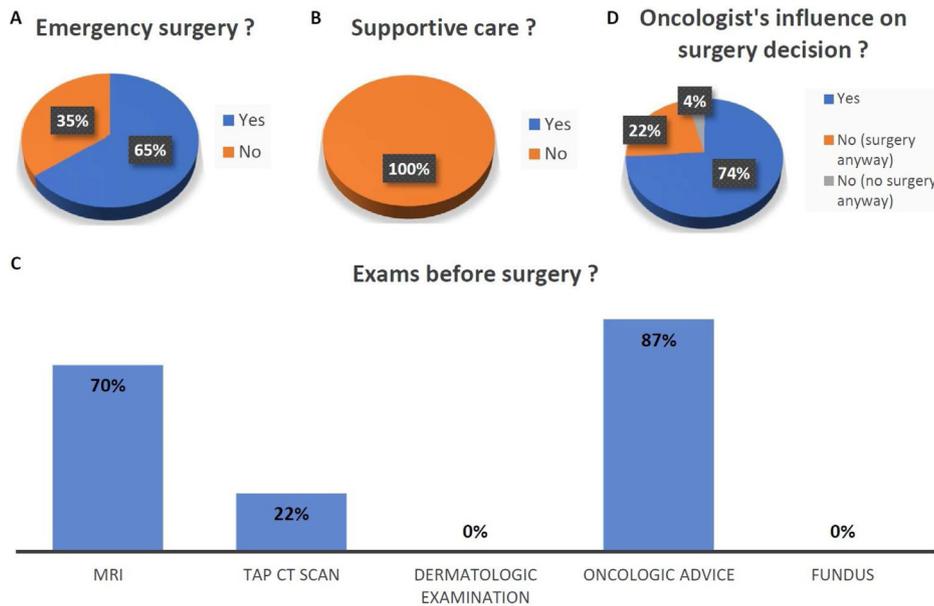


Fig. 4. Responses to clinical case 2.

3.3.3. Survey question 10 (only one response allowed per participant)

All respondents declared that their decision would have been the same if the clinical aggravation had been the consequence of intra-tumoral hemorrhage (Fig. 6C).

4. Discussion

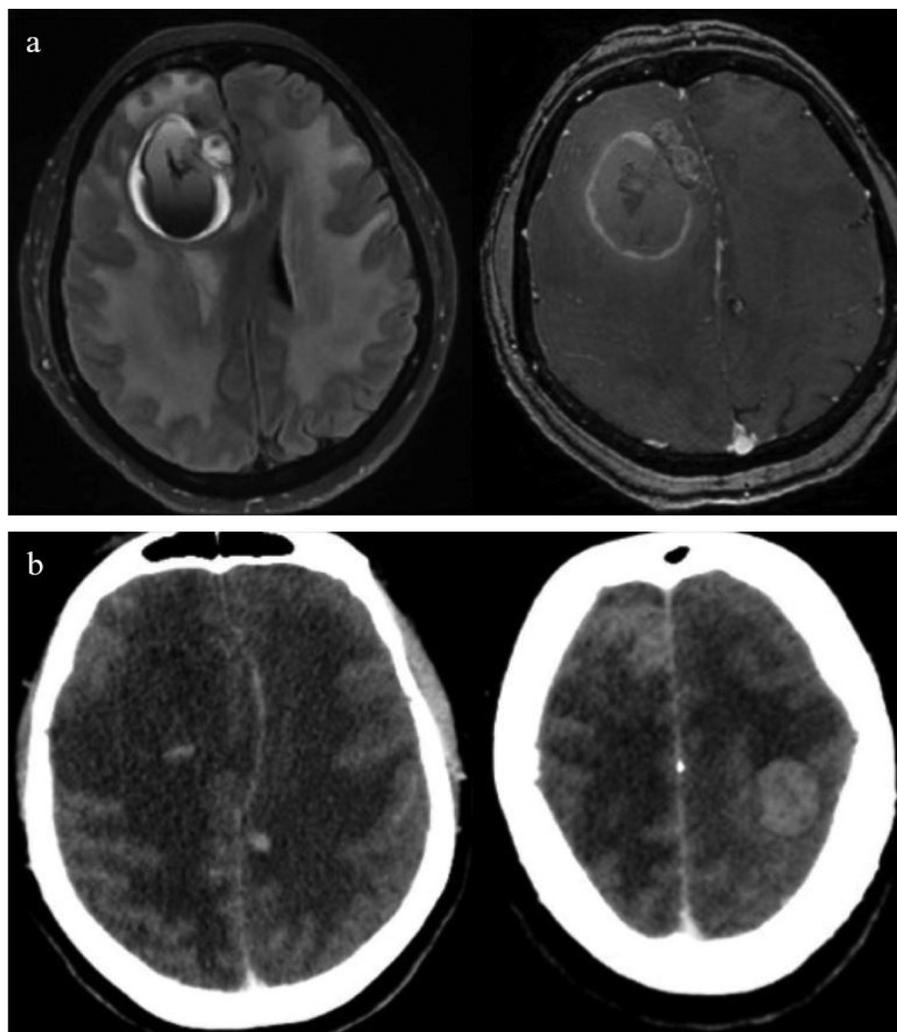
Although the management of some causes of ICH in BM, such as hydrocephalus or posterior fossa lesions [6], is quite consensual, some other situations are more challenging, such as emergency management of raised intracranial pressure due only to tumor volume and surrounding edema [6–8]. The lack of a consensual strategy motivated this French national survey, to address some of the touchiest situations. Responses showed discrepancies and the absence of consensus in the French neurosurgical

community regarding ICH management in case of brain metastasis in the absence of hydrocephalus or intratumoral hemorrhage.

The following discussion will address the state of knowledge underlying current emerging concepts to manage this rare entity, in an educational perspective for neurosurgeons.

4.1. Toward minimal paraclinical management?

Regarding paraclinical assessment before emergency surgery, a large majority of respondents considered brain MRI scan to be essential, whereas almost none felt the need for thoraco-abdominopelvic CT to support their decision. This might be partially due to the poor accessibility to this kind of imaging in emergency, and also to its lack of therapeutic impact in case of uncontrolled ICH, as urgent surgery is needed, whether any primary cancer is found or not. Contrast-enhanced MRI is more sensitive than enhanced CT or unenhanced MRI in detecting brain metastases, particularly within



**Fig. 5.** Attached file to clinical case 3 of the survey: a: last brain MRI-scan available; b: emergency brain CT-scan.

the posterior fossa or multiple punctuate metastases, and can in most cases rule out differential diagnoses [9] such as brain abscess.

There are no pathognomonic radiological features on CT or MRI that distinguish brain metastasis from primary brain tumor Figs. 4–6. When a brain mass is discovered on CT or MRI without history of cancer, it is sometimes difficult to know how far to pursue systemic investigation in emergency cases, to shed light on the prognosis of the potential underlying cancer. Lung cancer being the most common primary tumor giving rise to brain metastasis [10], standard chest X-ray may be associated to head CT-scan, which is fast and accessible [11]. However, further search for a primary tumor is only rarely fruitful without positive features in the patient's history or localizing signs on physical examination to suggest a specific primary tumor [12]. In case of acute ICH due to a seemingly metastatic brain lesion without any known primary, priority goes to dealing with the neurological issue, and detecting other systemic tumoral lesions will not help in making the decision to operate or not. Therefore, in such situations, the only examination we recommend in emergency is brain MRI.

#### 4.2. Medical intensive care management

Management of brain metastasis can be divided into symptomatic therapy and definitive therapy (surgery, radiosurgery, conventional radiotherapy). In emergency, facing acute ICH, apart from non-specific resuscitation management (brain code

resuscitation [13,14]), symptomatic measures to control ICH are usually initiated immediately and are the same for single or multiple metastasis.

##### 4.2.1. Corticosteroids

Corticosteroids have been used for decades to diminish the peritumoral vasogenic edema in BM [15]. Nowadays, dexamethasone is widely chosen worldwide because of its minimal mineralocorticoid effect (although prednisone and methylprednisolone are often used as alternatives in France). Its long half-life allows twice-daily administration. Most patients are successfully managed with starting doses of 4 to 16 mg per day. In the context of severe ICH, patients require higher doses. Up to 75% of patients with BM (without severe ICH) show marked clinical improvement in 24 to 72 hours after beginning dexamethasone [16]. The mechanism of the corticosteroid effect in cerebral edema remains unclear, although it is thought to restore disrupted capillary permeability (partly due to vasoactive substances secreted by tumors resulting in vasogenic edema) [17,18].

##### 4.2.2. Osmotherapy

For acute ICH, hyperosmolar therapy, with either mannitol or hypertonic saline (HTS), has shown equivalent efficacy in lowering intracranial pressure [19]. Mannitol is administered as a 0.5–1 g/kg intravenous (IV) bolus through a peripheral intravenous line and may be repeated every 4–6 hours if serum osmolality is monitored

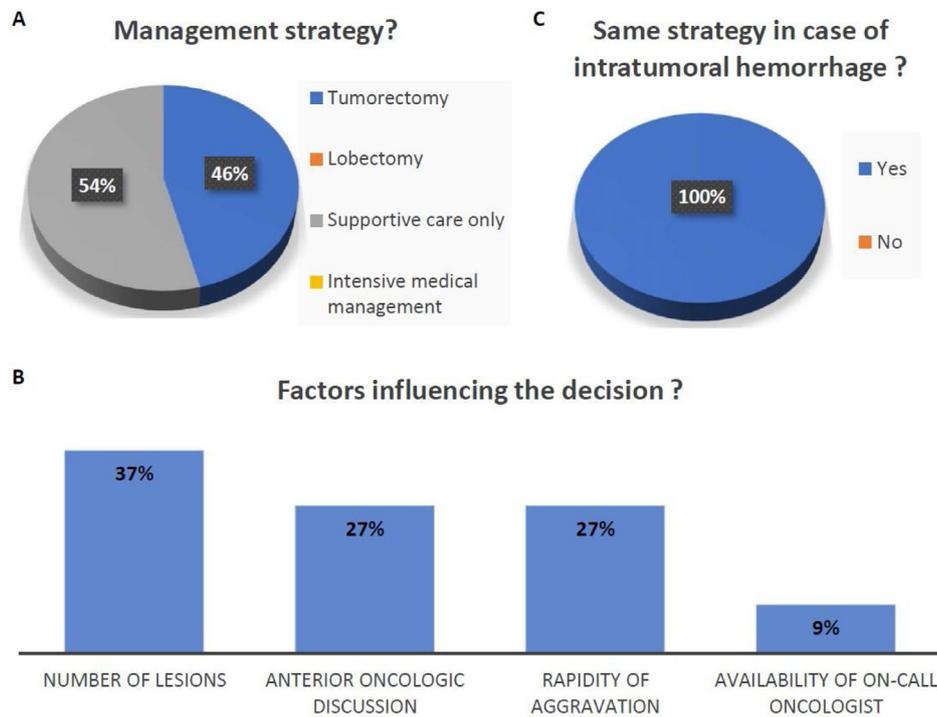


Fig. 6. Responses to clinical case 3.

[20], HTS is available in concentrations from 2% to 23.4% and can be administered as a bolus alone or associated to mannitol. HTS boli (concentration, 7.5%) should be administered via a central venous catheter; for lower concentrations, peripheral lines may be used, but the infusion should be to a large vessel, and the IV site should be carefully monitored for infiltration. NaCl 23.4% administered by boli can reduce intracranial pressure and reverse transtentorial herniation [14].

4.3. What timing for surgery?

Evidence is lacking about the timing of surgery in BM with severe ICH. To our knowledge, there are no studies of the recommended interval between diagnosis and treatment in ICH secondary to brain metastasis. As expected, the French neurosurgical congress advises young surgeons that the more severe the neurological status, the more promptly surgery should be performed.

4.4. Emergency surgical armamentarium for brain metastasis: Technical nuances

4.4.1. Surgical resection

The oncological evidence in favor of resecting BM is well known for single metastases, strongly supported by 2 randomized clinical trials [21,22] and a 2005 Cochrane review [23]. However, surgery for multiple brain metastasis remains controversial, as no prospective randomized clinical trial has yet compared resection of single versus multiple brain metastasis, and patients with multiple brain metastasis are considered poor candidates for resection owing to their shorter expected survival [24]. Thus, questions arise about oncological status assessment and the role of multidisciplinary decision-making in the management of severe ICH in BM (see section 4.5 The role of the oncologist below). Nevertheless, advances in surgical techniques and intraoperative tools and technologies, resulting in more aggressive and safer resection, have facilitated surgery for multiple brain metastasis. In the present survey, most respondents were in favor of maximally complete resection, even

Table 2 Recursive-partitioning analysis (RPA) (Gaspar et al., 1997).

	Class I	Class II	Class III
KPS	≥ 70	≥ 70	< 70
Age (years)	< 65	> 65	
Primary	Controlled	Not controlled	
Extracranial metastases	No	Yes	
Median survival (months)	7.1	4.2	2.3

in emergency, in case of a single cerebral lesion without known primary.

4.4.2. Tumoral cyst puncture

Most metastatic brain tumors are solid, but cystic transformation can occur, due to inflammation, tumor degeneration or hemorrhage, creating a larger overall volume even though the number of tumor cells is relatively small [25]. Although cyst aspiration followed by gamma-knife radiotherapy is feasible and safe in non-emergency cases [26], it is not as effective as surgical resection followed by radiosurgery, which remains the standard of care. However, for some patients who could not expect longer survival after intracranial metastasis, stereotactic aspiration to reduce cyst volume can be an alternative treatment option.

4.4.3. Ommaya reservoir placement

Some studies have shown a significant rate of local cystic reaccumulation after cystic brain aspiration [27]. For patients with BM, reducing the number of invasive procedures could be important, because these patients have a relatively poor chance of systemic disease control or long-term survival; thus some authors suggest fitting an Ommaya reservoir to reduce the rate of repeat procedures [25].

**Table 3**  
Graded Prognostic Assessment (GPA) worksheet to estimate survival from brain metastases (BM) by diagnosis (Sperduto et al., 2012).

Non-small-cell and small-cell lung cancer		GPA scoring criteria				
Prognostic factor		0	0.5	1.0		
Age (years)		>60	50–60	<50		
KPS		<70	70–80	90–100		
ECM		Present	–	Absent		
N° of BM		>3	2–3	1		
Median survival (months) by GPA: 0–1.0=3.0; 1.5–2.0=5.5; 2.5–3.0=9.4; 3.5–4.0=14.8						
Melanoma		GPA scoring criteria				
Prognostic factor		0	1.0	2.0		
KPS		<70	70–80	90–100		
N° of BM		>3	2–3	1		
Median survival (months) by GPA: 0–1.0=3.4; 1.5–2.0=4.7; 2.5–3.0=8.8; 3.5–4.0=13.2						
Breast cancer		GPA scoring criteria				
Prognostic factor		0	0.5	1.0	1.5	2.0
KPS		≤50	60	70–80	90–100	N/A
Subtype		Basal	N/A	LumA	HER2	LumB
Age (years)		≥60	<60	N/A	N/A	N/A
Median survival (months) by GPA: 0–1.0=3.4; 1.5–2.0=7.7; 2.5–3.0=15.1; 3.5–4.0=25.3						
Renal cell carcinoma		GPA scoring criteria				
Prognostic factor		0	1.0	2.0		
KPS		<70	70–80	90–100		
N° of BM		>3	2–3	1		
Median survival (months) by GPA: 0–1.0=3.3; 1.5–2.0=7.3; 2.5–3.0=11.3; 3.5–4.0=14.8						
Gastrointestinal cancers		GPA scoring criteria				
Prognostic factor		0	1	2	3	4
KPS		<70	70	80	90	100
Median survival (months) by GPA: 0–1.0=3.1; 2.0=4.4; 3.0=6.9; 4.0=13.5						

Basal: triple negative; LumA: ER/PR positive, HER2 negative; LumB: triple positive; HER2: ER/PR negative, HER2 positive; ECM: extracranial metastases; ER: estrogen receptor; HER2: human epidermal growth factor receptor 2; KPS: Karnofsky performance scale; LumA: luminal A; LumB: luminal B; PR: progesterone receptor.

#### 4.5. The role of the oncologist: Toward multidisciplinary decision-making in emergency situations

Identifying preoperative oncological prognosis factors may guide decision-making for emergency ICH management in BM. The primary cancer may (metachronous metastasis) or may not (synchronous metastasis) be known at the time of diagnosis, resulting in different situations [28]. The number of lesions also appears to be a deciding factor, although cut-off is not consensual [6]. In an oligometastatic patient with known primary, most respondents would perform emergency surgery, even without information on oncologic status, but still consider the oncologist's opinion desirable.

Some factors have been identified as prognostically favorable in BM: a high performance status (PS), single brain metastasis, absence of systemic metastases, controlled primary tumor, and younger age (<60–65 years) [29]. Gaspar [30] used the RTOG (Radiation Therapy Oncology Group) databases for a recursive-partitioning analysis (RPA) of 1,200 BM patients (Table 2). On univariate analysis, Karnofsky Performance Status (KPS) was the most important prognostic factor and became the first node in a prognostic tree. In case of KPS ≥ 70, primary tumor status was the second most important prognostic factor, age the third and systemic metastasis the fourth. RPA classes thus provide significant prognostic information that can be used to select a minority of patients for intensive surgery.

These results led some authors to propose that surgical management of secondary brain lesions could be proposed except in

case of ≥ 4 brain metastases, RPA class III or patients not eligible for adjuvant radiotherapy [31].

In 2008, Sperduto et al. [32] proposed a Graded Prognostic Assessment (GPA) index to easily assess life expectancy for BM patients. It was later refined with diagnosis-specific prognostic indices [33] for patients with BM from breast carcinoma, small-cell and non-small-cell lung carcinoma, gastrointestinal cancer, melanoma, and renal cell carcinoma (Table 3). Although nothing can replace the oncologist's opinion, this tool may be an easy way to get an idea of the global prognosis of patients with BM, thus guiding the decision to operate in emergency in case of ICH if no oncologic referent is available.

Sometimes in patients with a known BM, a multidisciplinary team meeting may have recommended surgical resection of the brain lesion, as in the third clinical case in our survey. In the event of acute neurological deterioration prior to scheduled surgery, the medico-legal aspect may certainly be considered before “going against” a previous decision taken during a multidisciplinary meeting, but it must be borne in mind that the decision was made for a patient in a given clinical condition, and that rapid clinical aggravation can make the decision obsolete.

#### 4.6. Management suggestions

The results of the survey were presented during the annual course of the French Neurosurgery Society (SFN) in 2017 at Issy-Les-Moulineaux, France. Discussing these results, the French Neurosurgical College of academic neurosurgeons emphasized the

importance of the following advice regarding the management of ICH in BM:

- recognizing the clinical entity of ICH without hydrocephalus in BM;
- performing at least an MRI scan to rule out differential diagnoses, hydrocephalus and intratumoral hemorrhage, and at most a chest X-Ray when no primary cancer is known;
- integrating oncologic prognostic factors, preferably in an emergency multidisciplinary team meeting or using validated tools (RPA classification or GPA index) to estimate overall survival;
- analyzing the mechanism of ICH: local phenomena, predictive of good surgical response, versus diffuse phenomena such as diffuse edema, suggestive of poor response;
- discussing all surgical options: resection if possible, tumoral cyst puncture, or Ommaya reservoir placement;
- keeping in mind the role of non-surgical treatments.

#### 4.7. Limitations

The main issue concerning this study concerns the response rate of 23.7%: out of 93 neurosurgeons contacted, only 22 answered our questionnaire. The representativeness of a questionnaire survey is entirely dependent upon the response rate, which is notoriously poor among medical practitioners [34]. Following Cottrel's [35] analysis, the present low response rate might have been due to time pressure in the neurosurgical community, despite our effort to keep the length of the questionnaire short. Despite these limitations, questionnaire surveys are a valuable research method, enabling large sample sizes to be contacted to gather data efficiently and relatively cheaply, using a consistent stimulus, at a single time-point [34,35].

Another concern is that most respondents were academic surgeons, which is not representative of the neurosurgical community as a whole. Nevertheless, our study is, to our knowledge, the first to specifically address the issue of the management of ICH in BM without hydrocephalus and intratumoral hemorrhage. The Discussion is intended as an educational reference for neurosurgeons in the management of BM. The aim was not to dictate surgical management, but rather to open the debate in the neurosurgical community about the tenets underlying surgical decision-making in emergency cases.

## 5. Conclusion

Acute ICH linked to BM without hydrocephalus is a more and more frequent clinical situation, with divergences in management because of the lack of specific guidelines. There is no current consensus on emergency management, and we argue that this condition must be considered as a distinct entity. We advocate minimal paraclinical assessment by MRI, and multidisciplinary discussion with an oncology team, even in emergency, to assess oncological prognosis before deciding whether to operate or not. When no oncologist is available, certain tools, such as the RPA or the GPA, are an easy way for the neurosurgeon to assess overall prognosis. Management of acute ICH without hydrocephalus should be studied on prospective controlled clinical trials to better assist neurosurgeons in emergency cases.

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## Disclosure of interest

The authors declare that they have no competing interest.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.neuchi.2019.07.003>.

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