# REVIEW

# ROLE OF CEREBRAL IMAGING IN THE MINIMALLY INVASIVE TECHNIQUES FOR INTRACEREBRAL HEMATOMA EVACUATION

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**Abstract.** ***Introduction.*** *Intracerebral hemorrhages represent the second most frequent, but the most severe form of stroke, with 1 in 3 patients passing away shortly after its debut. Considering these data, it is necessary to identify efficient ways to evacuate intracerebral hematomas and improve their morbidity and mortality, with brain imaging being truly helpful to neurosurgeons.* ***Objectives****. To identify the role of imaging for the evacuation of spontaneous intracerebral hematomas.* ***Methods****. We performed an extensive literature review, examining the latest published studies and therapeutic protocols. We performed a comprehensive evaluation of the latest imaging and surgical techniques for the diagnosis and treatment of intracerebral hemorrhages.* ***Results****. These studies suggest that surgical intervention and evacuation of the hematoma, based on imaging and clinic, can have an immediate life-saving effect on certain groups of patients, but it does not significantly influence the long-term prognosis and death rate.* ***Conclusions****. Modern imaging techniques help neurosurgeons preoperatively, as they can more accurately estimate the benefits of the surgical intervention, intraoperatively through neuronavigation, and postoperatively, modulating therapeutic management by identifying specific imagistic signs. Surgical interventions, both invasive and especially minimally invasive, have a proven positive effect on the evolution of patients, reducing acute mortality, but with uncertain results regarding improving long-term prognosis.*

**Keywords**: *spontaneous, intracerebral hemorrhage, stroke, hematoma, neurosurgery, radiology.*

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**Abbreviations**
ICH, intracerebral hemorrhage; CT, computed tomography; MRI, magnetic resonance imaging; AHA/ASA, American Heart Association/ American Stroke Association; CTA, CT angiography; HU, Hounsfield units; AVM, arteriovenous malformation; DSA, digital subtraction angiography; SAH, subarachnoid hemorrhage; TNF, tumor necrosis factor;

## INTRODUCTION

Strokes are an important cause of global mortality, responsible for approximately 5.5 million deaths annually [1]. Intracerebral hemorrhages (ICH) represent 10-20% of all cerebrovascular events but account for almost 40% of all deaths, with first-month mortality reaching 40% [2-4]. Despite the technological-related evolution of the treatment of this pathology, there is no conclusive data to prove the increase in survival after an episode of cerebral bleeding [5]. A meta-analysis showed a survival rate of 46% at 1 year and 29% at 5 years [6].

There are primary and secondary cerebral hemorrhages [4]. Atherosclerotic angiopathy and arterial hypertension are the primary causes of hemorrhage, whereas vascular structural abnormalities or anticoagulant therapies are the secondary causes.

## ACUTE IMAGING DIAGNOSIS OF ICH

A quick imaging examination is essential for the diagnosis and management of patients with intracerebral hemorrhage. Rapid examination by computed tomography/ magnetic resonance imaging (CT/MRI) is the first-line recommendation by the American Heart Association and American Stroke Association (AHA/ASA) guidelines [7].

The evolution of hematoma is divided into 5 stages: hyperacute (<12 hours), acute (12-48 hours), early subacute (2-7 days), late subacute (8-30 days), and chronic (>30 days) [8].

Usually, in the hospital, the first-choice imaging examination is a non-enhanced brain CT. This method is affordable, simple, quick, widespread, and has excellent sensitivity for ICH, being able to identify and measure the volume of the hematoma, the presence of cerebral edema and the midline shift (Figure 1), intraventricular extension or the presence of hydrocephalus (Figure 2, Image C) [9]. It is considered the gold standard for the diagnosis of ICH in the emergency room [10]. There are several specific signs by which the hematoma expansion can be detected using non-contrast CT: hypodensities in the area of the hematoma, a swirl sign, a black hole sign, a blend sign, an irregular shape, and heterogeneous densities [11]. These signs have low sensitivity (below 50%) but high specificity (up to 95% in the case of the black hole sign) [11].

Some distinct imagistic patterns can facilitate the differential diagnosis of the underlying pathology that led to ICH. Thus, multiple hemorrhages of different ages suggest amyloid angiopathy; different-aged hemorrhages within the same hematoma suggest hemorrhage induced by anticoagulants; the combination of small ischemic and hemorrhagic lesions suggests vasculitis [8].

According to the AHA/ASA guidelines, contrast or non-contrast brain CT or CT angiography are the next investigations to follow to identify hematoma expansion [7]. These techniques can also help in the identification of the primary cause of an ICH. The spot sign is one of the most reliable signs that prove hematoma expansion and, subsequently, active extravasation of blood, represented by small enhancing areas of about 1-2 mm superimposed in the area of the hematoma, adjacent to vessels, indicating which patients could benefit from (micro)surgical intervention [12-14]. The incidence of this sign is 17-56% [13]. A recent meta-analysis suggests that its presence may reflect a poor prognosis and increased mortality [15].

## I. Computed tomography (CT)

According to the AHA/ASA guidelines, CT is the gold standard, quick, cheap, and feasible ICH evaluation method for unstable patients [7]. The hematoma density varies depending on the clinical stage of the hemorrhage. Thus, in the hyperacute phase, the densities vary in the range of 30-60 Hounsfield units (HU), while in the acute phase, they tend to increase to values of 100 HU [16]. In the case of abnormal hematocrit values, HU may vary [17].

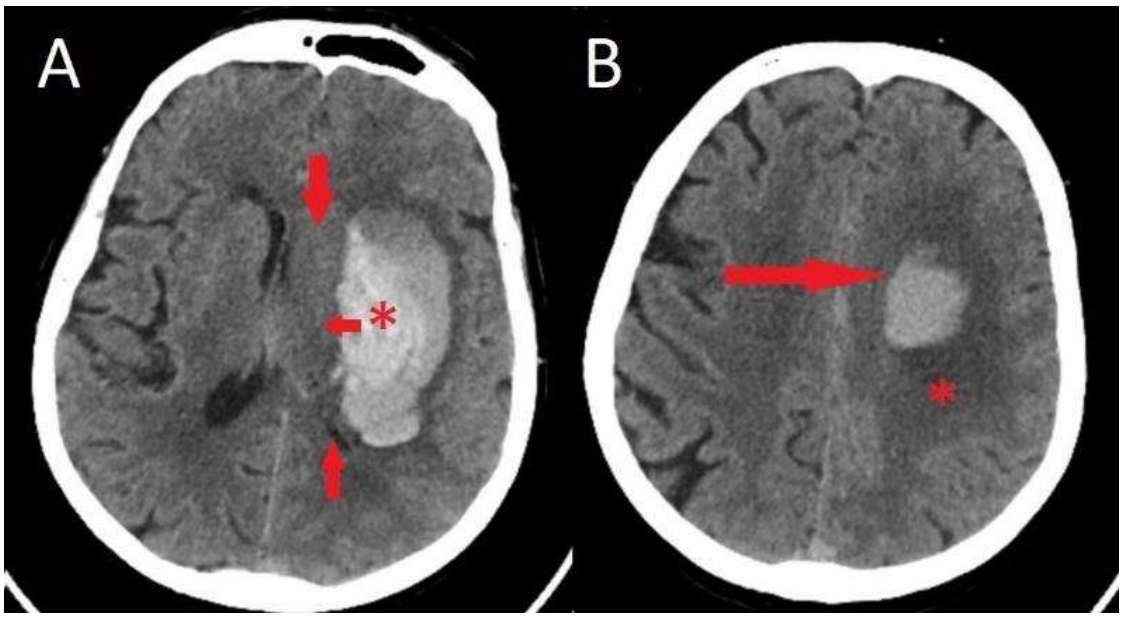


***Figure 1***. *Non–enhanced CT scan of a patient with an acute ICH. A spontaneously hyperdense, heterogeneous lesion with hematic densities, at the level of the left insular cortex and internal capsule (Image A, *) compressing the basal nuclei and lateral ventricle (Image A, arrows), extended subcortically in the frontotemporal region, the left corona radiata and ipsilateral semioval centrum (Image B, arrow), with a mass effect, shifting the midline with about 9 mm. Perilesional edema with a thickness of up to 10 mm surrounds the hematoma (Image B, *)*

In the subacute phase, the lesion will become parenchymatous-isodense, requiring brain MRI for clear differentiation [18]. The hematoma volume can be estimated by using the ABC/2 formula, where A represents the longest axis, B is perpendicular to this axis, and C is the number of slices in which the hematoma is found multiplied by their thickness or the height of the hematoma [19]. Over 60 ml of volume is associated with high mortality [20]. About one-third of the ICH CT-diagnosed patients will show hematoma expansion in the first 3 hours after the symptomatology onset [7].

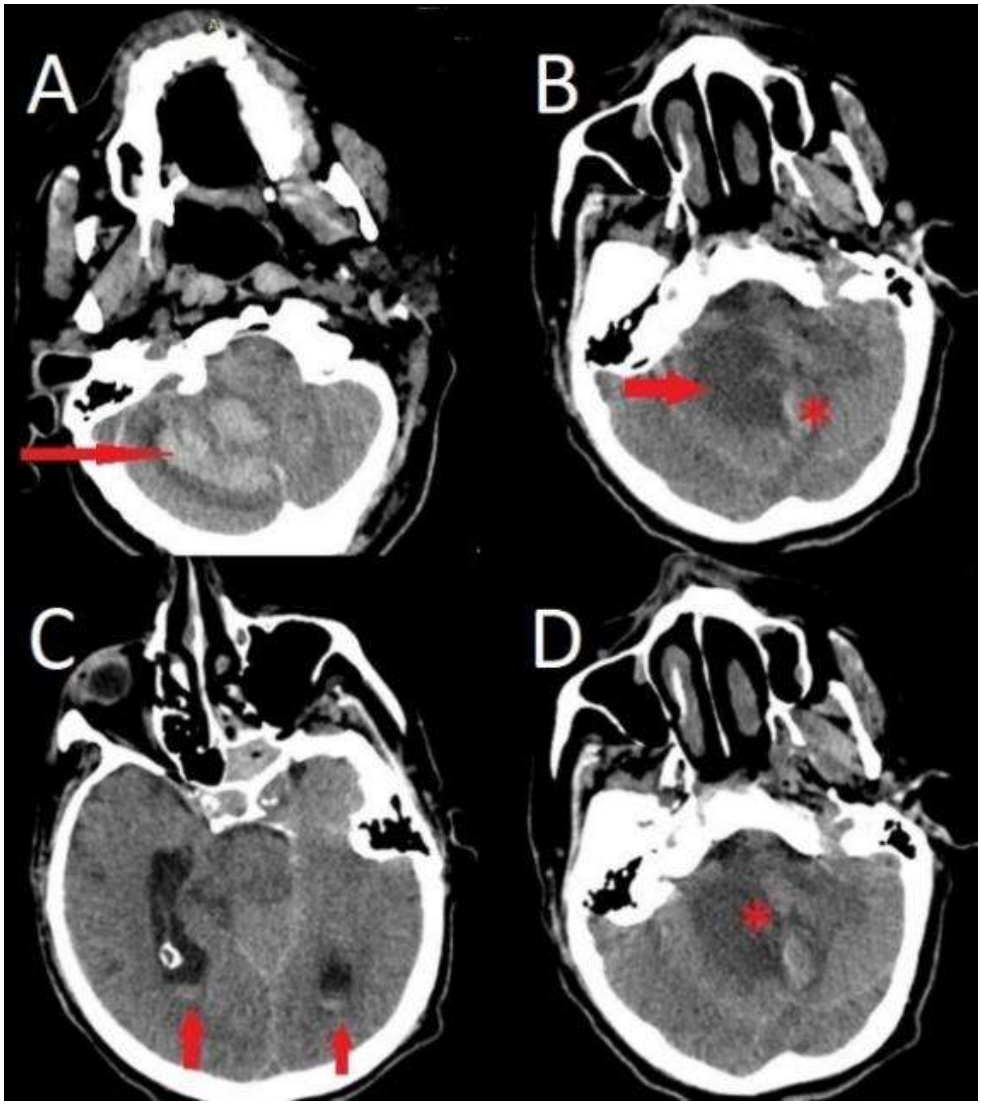


***Figure 2**. Infratentorial hemorrhage with multi-level expansion. Spontaneous hyperdense accumulation, with blood-like densities, in the anterior 2/3 of the right cerebellar hemisphere (image A, arrow) with periventricular extension and at the level of the left cerebellar hemisphere (image B, *), associating neighbouring parenchyma edema (image B, arrow), breaching the lateral ventricles (image C, arrow) and with significant mass effect on the normal parenchyma (midline shift up to 13-14 mm), the 4th ventricle and the medulla oblongata with basal cisterns obstruction (image D, *)*

Several signs that can predict the evolution of a patient with ICH have been described. The black hole sign (Figure 3, B) was defined as a hypoattenuating area encapsulated in the hyperdense hemorrhagic area. Similarly, the blend sign is described as the blending of a well-defined hypodense area within the hematoma area. The latter can be useful on the non-contrast CT examination when CTA is unavailable, demonstrating a high predictive value of neurological damage, similar to that of the spot sign.

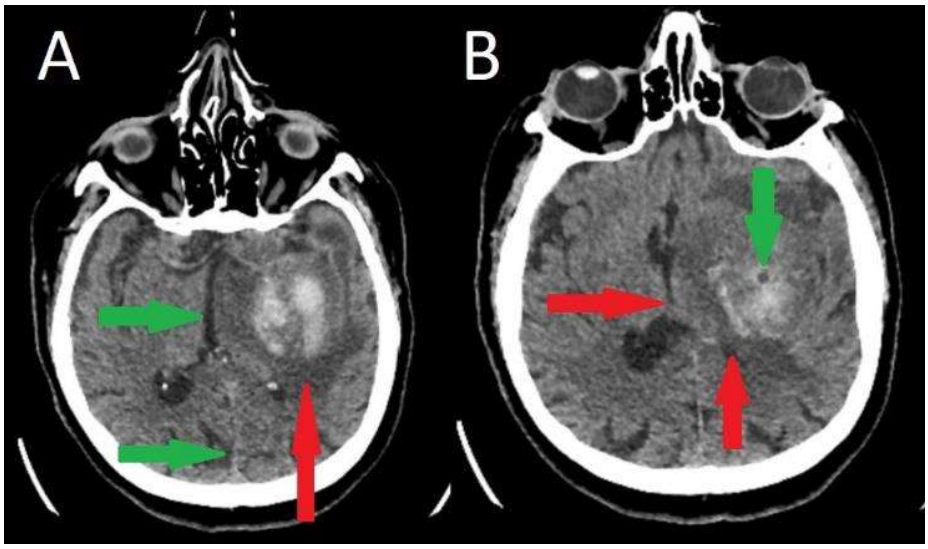


***Figure 3**. Heterogeneous intraparenchymal hematoma located in the left hemisphere, with significant perilesional edema (Images A and B, red arrow), midline shift (Image A, green arrows), involvement of the ipsilateral thalamus and compression of the lateral and third ventricle (Image B, red arrows). Black hole signature (Image B, green arrow).*

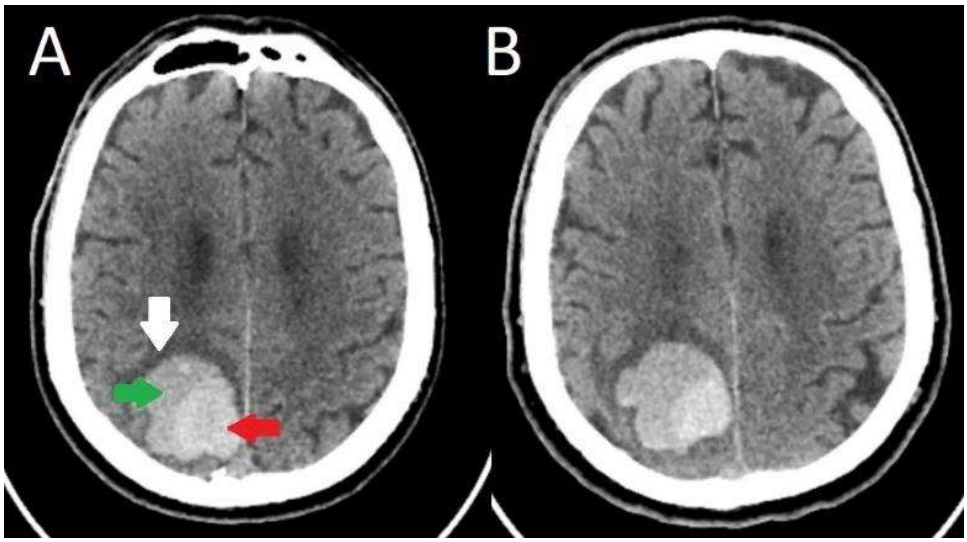


***Figure 4**. Right parietal-temporal intraparenchymal hematoma in the acute-subacute stage with heterogeneous appearance, suggesting blood products in different stages of evolution (blend sign - Image A, green and red arrows), associating perilesional edema (Image A, white arrow) but without deviation of the median line. Image B shows a stationary aspect 4 days after the onset of symptoms.*

Among these techniques' disadvantages are the difficulty of highlighting hemorrhage in a patient with < 10g/dl of Hgb, the posterior fossa evaluation being difficult due to artifacts, or the omission of thin blood collections due to partial volume artifacts.

The most common sites of intraparenchymal hemorrhage are capsular (40%) (Figure 5), lobar (30%), thalamic (10%), cerebellar (10%), pontine (7%), and intraventricular (3%) (Figure 5) [12].

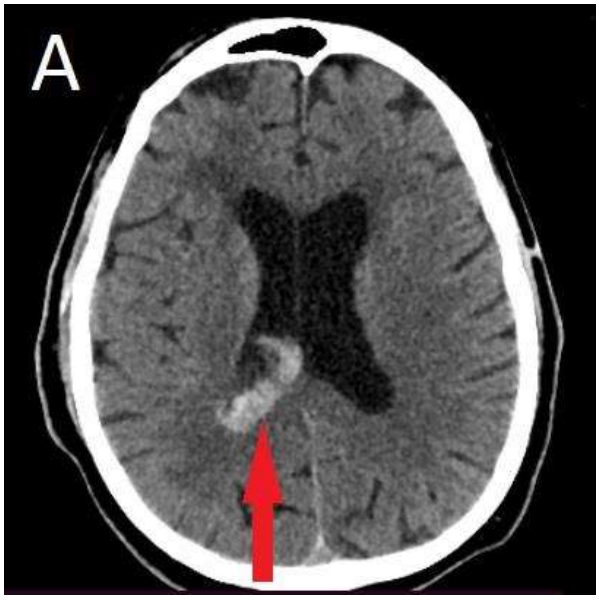


***Figure 5***. *Intraventricular hemorrhage. Spontaneous hyperdense image at the level of the body and atrium of the right lateral ventricle with a thickness of up to 6 mm, without obstructive hydrocephalus.*

Depending on the results and the bleeding patterns, further imaging tests may be necessary: repeating the CT scan to identify hematoma expansion, midline shift, or cerebral edema; CT angiography (CTA) or digital subtraction angiography (DSA) for subarachnoid hemorrhage (SAH) or arterio-venous malformation (AVM) related to hemorrhage. Unenhanced brain MRI for suspected hemorrhagic transformation (HT) of an ischemic stroke; contrast-enhanced brain MRI when suspicioning an underlying tumor or an infectious process; CT venogram in case of suspected venous thrombosis [21].

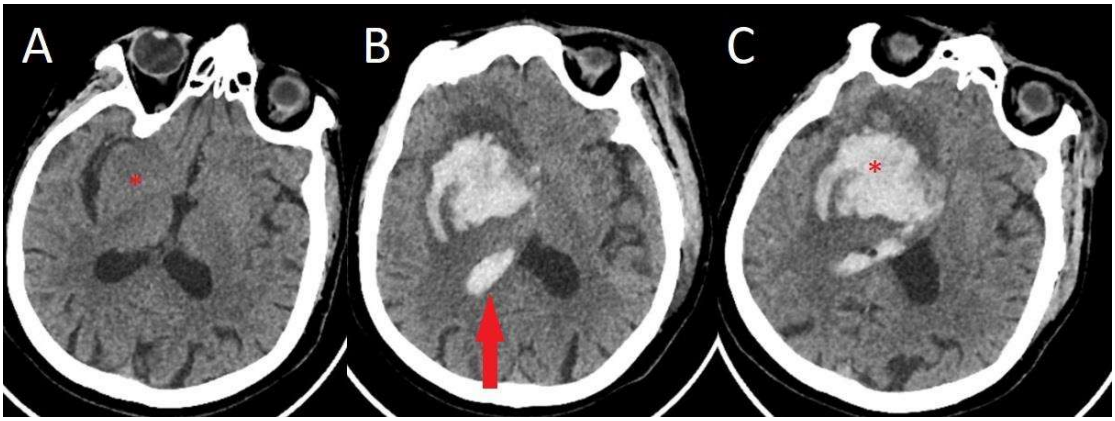


***Figure 6***. *Reassessment 24 and 48 hours after the onset of an ischemic stroke. Image A. Ischemic stroke at the level of the basal ganglia and internal capsule on the right side (*); Image B. The worsening of the symptoms led to a second CT examination, 24 hours after the onset of the symptoms, which revealed the significant dimensional hemorrhagic transformation associated with a midline shift contralaterally by 12 mm and ventricular effusion at the level of the occipital horn of the left ventricle (arrow). Image C. The evolution of the hematoma 48 hours after the onset of ischemic symptoms shows minimal dimensional evolution of the hematoma.*

**II. Magnetic resonance imaging (MRI)**

Even though the CT exam is considered the gold standard, the HEME study demonstrated that MRI can even exceed the sensitivity of CT in certain cases, such as highlighting chronic bleeding or microhemorrhages through magnetic susceptibility sequences [22,23]. Also, MRI is essential to perform a differential diagnosis between the two most common causes of intracerebral hemorrhage: amyloid angiopathy and hypertensive vasculopathy [24]

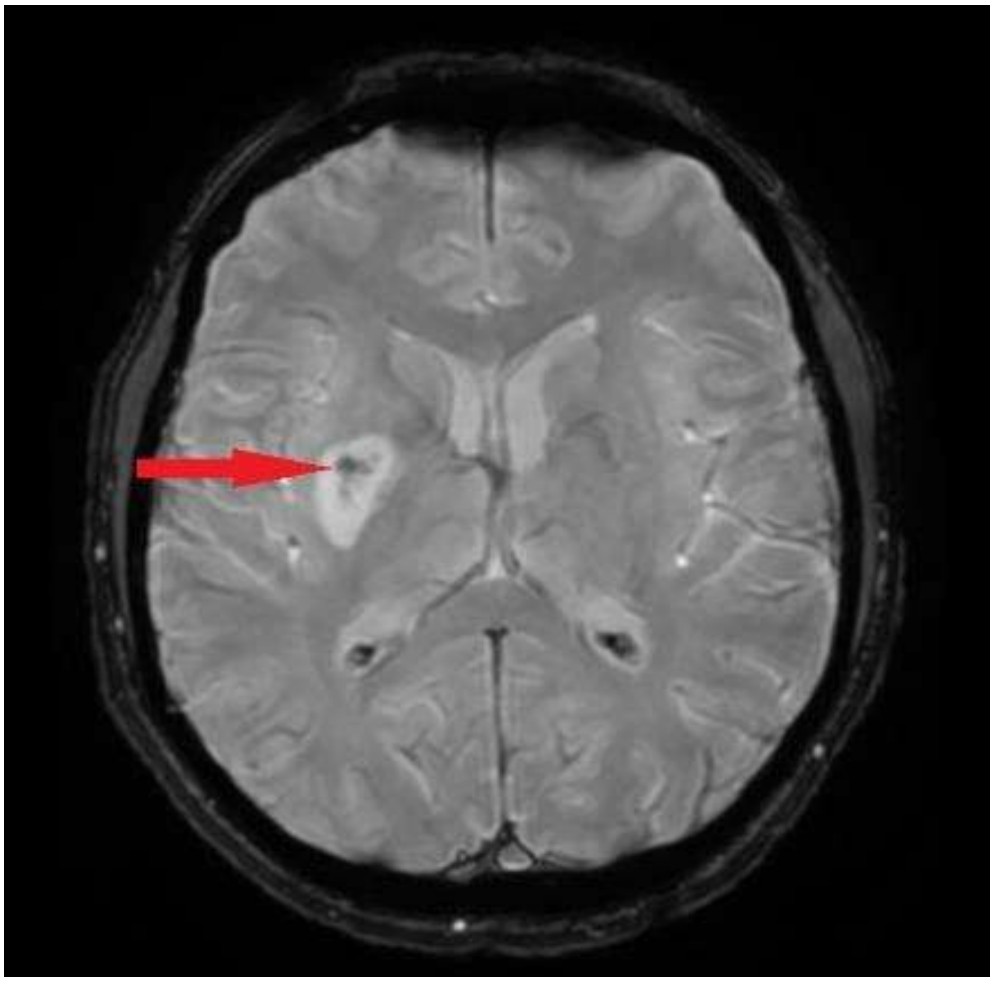

***Figure** 7. Evidence of magnetic susceptibility changes on the SWI sequence (arrow) with a suggestive appearance for the hemorrhagic transformation of a deep ischemic stroke, in the capsule-lenticular region.*

In the hyperacute phase, the hematoma is isointense on the T1-weighted sequence, and hyperintense on the T2-weighted and FLAIR sequences. In the acute phase, the lesion is isointense on the T1-weighted sequence and markedly hypointense on the T2-weighted and FLAIR sequences. In the subacute phase, the lesion shows hyperintensities on T1-weighted, T2-weighted, and FLAIR sequences, and in the chronic phase, the T2-weighted hyperintense center is surrounded by a hypointense ring, the images being in the mirror with the FLAIR sequence (hypointense centre, hyperintense ring) [25]. On magnetic susceptibility sequences, in all phases, the lesion is hypointense or markedly hypointense.

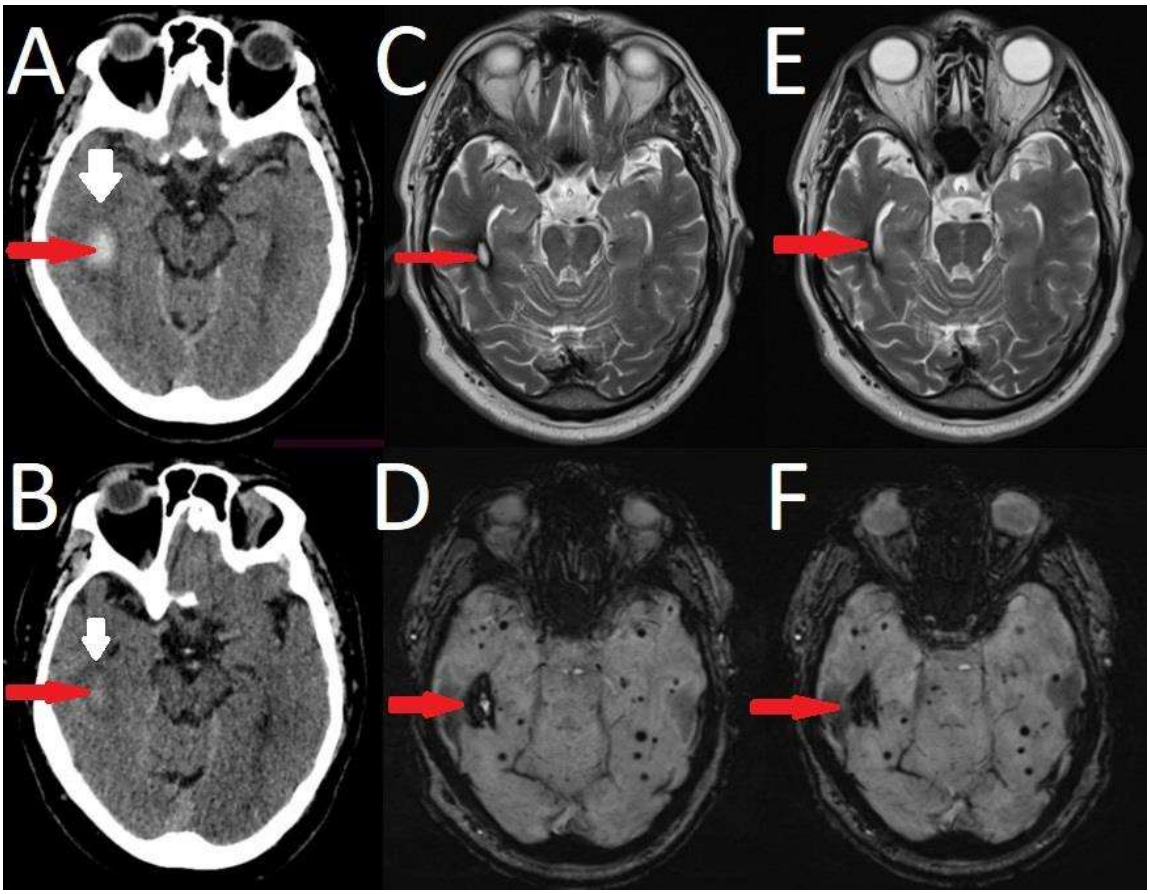


***Figure 8***. *Image A. Acute right temporal ICH (red arrow) with peripheral edema (white arrow); Image B. Partial resolution of the hematoma and peripheral edema at 7 days; Images C and D. MRI exam 2 months after the onset of symptoms. The T2-weighted sequence (image C, red arrow) shows a partially resolved hematoma while the susceptibility-weighted sequence (image D, red arrow) shows a globulous deposit of hemosiderin. Images E and F. Another MRI exam 3 months after the onset of symptoms. T2-weighted sequence (image E, red arrow) shows complete resorption of the hematoma, while the SWI sequence (image F, red arrow) has minimal changes. Besides the right temporal hematoma, the patient had lots of SWI-hypointense lesions with lobar and non-lobar distribution (Images D and F)*

**III. CT angiography (CTA)**

CT angiography is the most frequently used imaging method for cerebrovascular evaluation, having a high sensitivity and specificity for the detection of vascular anomalies [7,26]. Besides these, CTA can select patients at risk by identifying extravasation of the contrast in the volume of the hematoma, known as the spot sign [27].

On the other hand, the use of CTA is limited by its elements: radiation and contrast. The contrast agent can lead to acute renal injury in patients with renal comorbidities, while radiation limits the number of possible exposures.

Two clinical scores, the Intracerebral Hemorrhage (ICH) score and the Bleeding assesment Practical (BAT) score (Tables 1 and 2), are used to more accurately predict the possibility of hematoma expansion, with two others being optional, namely BRAIN and a score described by Browers *et al.* [28,29,32].

**Table 1.** Bleeding assesment Practical (BAT) score.

| Variable | Points |
|---|---|
| **Blend sign** | |
| Present | 1 |
| Absent | 0 |
| **Hipodensities** | |
| Present | 2 |
| Absent | 0 |
| **Time from onset to CT scan** | |
| <2,5h | 2 |
| >2,5h | 0 |

A BAT score >3 is correlated with hematoma expansion

| Variable | Points |
|---|---|
| **GCS score** | |
| 3-4 | 2 |
| 5-12 | 1 |
| 13-15 | 0 |
| **ICH volume, cubic cm** | |
| >30 | 1 |
| <30 | 0 |
| **IVH** | |
| Yes | 1 |
| No | 0 |
| **Infratentorial origin of ICH** | |
| Yes | 1 |
| No | 0 |
| **Age** | |
| >80 | 1 |
| <80 | 0 |

An ICH score of 0 has a minimum risk of mortality. A score of 6 means an over 95% risk of mortality.

**Table 2.** Intracerebral Hemorrhage (ICH) score.

**IV. Neuronavigation**

Neuronavigation is an indispensable system in neurosurgery [33]. The technological advances of the last decades are expressed most strongly in the field of imaging, and actions unthinkable a few decades ago can usually be achieved today thanks to these implemented technological innovations. The improvement of the quality of preoperative imaging, combined with the integration of imaging techniques in mini-devices, has allowed, in the last 30 years, the migration of some imagistic equipment into the operating room and its use even during surgical interventions, thus becoming an irreplaceable aid for neurosurgeons. The evacuation of intraparenchymal hematomas is one of the branches of neurosurgery that has benefited the most from these innovations, allowing a minimally invasive approach. Current neuronavigation systems allow a precision of a few millimeters [34,35]. Using classic neuronavigation systems, imaging scans could be displayed in real-time, 2D, on screens directly in the operating room. In recent years, however, the focus has been on the implementation and use of intuitive 3D augmented reality systems, involving the intuitive superposition of virtual images over the real-world images obtained by cameras. Some of these even allow the projection of relevant data, such as target lesions or operator planning, directly in the operator's visual field, without being distracted by other elements (such as other display systems) [36-38]. These systems identify and adapt the projected data, in real-time and depending on the operator's progress.

## V. TREATMENT

The results of conservative treatment of a cerebral hemorrhage are well defined [39]. ICH care can be improved by treating the patient in a neurological intensive care unit, but a better prognosis has not been demonstrated [40].

Two therapeutic approaches are taken into account: the conservative one and the surgical one. We will approach the surgical one.

The role of early surgery in ICH is controversial. There have been several studies conducted over the years to quantify the effectiveness of this therapeutic method. The best known are the STICH study, from 2005, and its continuation, STICH II, from 2013. These two studies have not demonstrated the expected surgical benefits in the case of intracerebral hemorrhages [41,42].

There are lots of minimally invasive surgical techniques that can be applied to patients with intracerebral hemorrhages, but regardless of whether we are talking about minimally invasive surgery, thrombolytic techniques, or non-thrombolytic techniques, the results are still equivocal when we refer to prognosis improvement [43]. The MISTIE study, designed to examine the applicability of minimally invasive surgery and its impact on the reduction of side effects after craniotomy, is one of the most important of its kind. The MISTIE III study, published in 2019, included 499 patients with intracerebral hemorrhages with a volume greater than 30 ml, treated minimally invasively in 78 centers around the world [44]. A good prognosis was obtained in patients with a reduction of the hematoma volume by >53% or a decrease in its volume below 30 ml.

The most common minimally invasive techniques for cerebral hematomas are stereotactic aspiration with thrombolysis [44,45], endoscopic evacuation of cerebral hematomas [46], craniopuncture (the most used technique in China) [47,48], evacuation through endoport [49, 50] or evacuation through the surgiscope [51].

## DISCUSSION

Intraparenchymal hemorrhage is, most of the time, a multifactorial result of multiple untreated chronic pathologies; therefore, the discovery of a standard treatment is not feasible, with each patient having to be treated differently.

The poor prognosis is due to the primary injury and, mainly, to the physiopathological responses of the body that materialize through the secondary injury. The inflammatory response from secondary injury is mainly due to interleukins and TNF-α [52].

Arterial hypertension is a comorbidity that is frequently associated with deep hemorrhages, but less so with intralobular hemorrhages, the latter being associated with amyloid angiopathy, according to the Boston criteria [53-55].

Despite the initial hypothesis, which suggests that surgical intervention for the evacuation of intraparenchymal hematomas will decrease the degree of morbidity and mortality, the reality is different. Multiple large studies have obtained equivocal results, with some authors questioning the benefits of the intervention compared to conservative, medical management. It has been demonstrated that surgery in the hyperacute phase is associated with recurrent bleeding, and the prognosis can be affected by several factors such as the surgical technique or the location and size of the hematoma [56]. In the opinion of some authors, endoscopic and minimally invasive interventions have comparable efficiency when their goal is to evacuate the hematoma and decompress the brain, considering that the interventional injury is much lower than the injury caused by hematic degradation [57]. Despite some large cascade studies, the results remained ambiguous, largely due to the heterogeneity of the patient groups [42,58]. However, the STICH II study concludes that the clinical benefits of minimally invasive surgery are minimal but relevant [42]. In another series of studies, comparing minimally invasive surgical interventions with conventional ones,

aspiration with thrombolysis determined the dimensional reduction of the hematoma in up to 70% of cases, with a hematoma size of less than 15 ml correlating with an improvement in the mortality rate at 1 year [44,59].

At this moment, it is difficult to recommend surgical intervention for the evacuation of intraparenchymal hematomas, even with all the data obtained from the multitude of existing studies [57].

## CONCLUSIONS

Pre- and intraoperative imaging play a crucial role in the diagnosis and neurosurgical treatment of spontaneous intracerebral hemorrhages. Despite contradictory data in the literature, there is a tendency to recommend minimally invasive interventions for the treatment of hemorrhagic events, with their benefits in improving long-term mortality slightly outweighing the risks of the intervention itself. Next, collaboration within the multidisciplinary team is essential, as the patient should be evaluated and balanced quickly in the emergency and intensive care departments, so that the therapeutic management is then established by a team made up of a neurologist, neurosurgeon, and radiologist, this being, of course, individualized for each patient depending on the clinical condition and the paraclinical data obtained.

**Author contributions:**

*R.I.D conceived the original draft preparation. G.S.T and C.A.S. were responsible for the conception and design of the review. R.I.D. and G.S.T. were responsible for the data acquisition. C.A.S. was responsible for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review. All authors contributed equally to the present work, and have read and agreed with the final version of the manuscript.*

**Compliance with Ethics Requirements:**

*The authors declare no conflict of interest regarding this article.*

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