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Review article

Hematoma volume as the major determinant of outcomes after intracerebral hemorrhage

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ABSTRACT

Intracerebral hemorrhage (ICH) is a leading cause of morbidity and mortality, greatly linked to hematoma volume. Understanding the characteristics and size of hematoma is integral to evaluating severity and prognosis after ICH. Examination of the literature suggests that markers for hematoma size vary, but the key range between 20–30 mL is most widely used as the cut-off for classification of hematoma volume. The role of hematoma volume in episodes of hematoma expansion and re-bleeding further impact outcomes, with increased growth associated with larger hematoma volume. Additionally, many commonly used predictors of ICH outcomes are directly related to hematoma volume, implicating it as an important variable when determining outcomes. In conclusion, hematoma volume is likely the most significant determinant of outcomes in intracerebral hemorrhage.

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1. Introduction

Intracerebral hemorrhage (ICH) contributes to 10–15% of all strokes, and accounts for significant associated morbidity and mortality [1]. ICH has a 30 day mortality rate of 35–52%, varying with location of the hemorrhage [2–6]. It carries significant mortality, and for those who survive, considerable morbidity. Despite advancement of diagnostic tools, ICH remains the most deadly form of stroke, magnified by the difficulty to quantify severity and understand superior outcome measures for prognosis and management [2,3,7–9].

The injury caused by ICH occurs in two phases, the first of which occurs mechanically with initial hemorrhage into cerebral architecture compressing and displacing tissue, the second of which occurs non-mechanically as a result of hematoma enlargement or perihematomal edema [10–15]. Therefore, understanding the mechanism of injury caused by hematoma volume, the role of hematoma volume in injury, and the interaction of its volume with other prognostic factors in ICH can lead to further developments in prognosis and management. It is the purpose of this review to identify the role of hematoma volume in ICH as a predictor of outcomes, explore predictors of hematoma volume,

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and examine the interplay of hematoma volume with other known prognostic factors in ICH.

2. Impact of hematoma volume in ICH

Hematoma volume, size, and diameter on admission has often been shown to significantly correlate with short term mortality [4,16–20]. Several studies have also demonstrated that hematoma volume is a good predictor of long term mortality, beyond the acute period. ICH volume is widely suggested as the most important predictor of outcomes in ICH. Survival at 3 months and 3 years showed statistically significant correlation with smaller hematoma volume [21]. Additionally, hematoma volume, of less than 30 mL, correlates with functional recovery at 90 days [17]. More positive outcomes, such as recovery or moderate disability, are inversely correlated with hematoma volume [22]. Hemorrhage size was also found to correlate with the National Institute of Health Stroke Scale (NIHSS) at admission, proving a significant predictor of ICH severity [23].

While no clear criteria have determined the standard cutoff for hematoma volume associated with more favorable outcomes, many studies have identified ranges of hematoma volumes correlating to prognosis. Studies found that a large ICH volume, of over 25 mL has been associated with predicting poor outcomes at discharge and at the 30 day mark [24,25]. Another study demonstrated that a hematoma volume of less than 30 mL was associated with favorable functional outcomes and was an independent predictor of in-hospital mortality [26]. Table 1 identifies the major studies that have identified ICH cutoffs for hematoma volumes and associated outcomes.

As described in Table 1, the most commonly used cutoffs for hematoma volume, in terms of prognosis, ranges from 20 mL to 30 mL, with volumes higher than that carrying significant association with mortality and morbidity. Table 1 also demonstrates the intricate nuances of association with outcomes in the unclear range between 20 and 30 mL of volume. Of note, Table 1 was constructed without the use of a meta-analysis, so as to not lose subtle differences in findings, as reported by each study, upon pooling of data. While a meta-analysis for 30-day mortality to test the effect of a cutoff of 30 mL would produce an analysis of whether there is significant heterogeneity in published results on this question, this statistical analysis was not performed as all included studies specified results of hematoma volume in varying ranges.

3. Hematoma expansion, re-bleed, and growth

Often hematoma volume changes with expansion, re-bleeding, and growth of the ICH. Expansion occurs in approximately 70% of ICH patients, contributing to worse outcomes [30]. Growth is defined as an increase in hematoma volume by 33%, occurs early, primarily in the first 3 h, and is associated with worsening neurological status [31]. Believed to occur hours after symptom onset and initial hemorrhage, expansion occurs with an increase in intracranial pressure, violating the integrity of surrounding tissue, including the blood–brain barrier, and compromising venous outflow, thereby inducing the release of thromboplastin from surrounding tissue, contributing to coagulopathy in the offended area [32]. The exact timeframe and mechanism of hematoma expansion are not yet fully understood [33]. Additional, existing evidence supports the hypothesis that it occurs secondary to bleeding from adjacent ruptured vessels to initial bleeding site, and less commonly due to re-bleeding [33]. Re-bleeding has been seen in up to 24% of patients after a mean follow-up of 84.1 months after the first hemorrhage, and carried the highest risk within the first year after hemorrhage [34].

Hematoma expansion is associated with larger ICH volumes, greater than 25 mL [35], and is less likely in hematomas smaller than 10 mL [36,37]. Conflicting evidence in the literature exists regarding the impact of limiting hematoma expansion in mortality and outcome prediction. However, it has been suggested that targeting hematoma expansion provides inlets for interventional therapies and is the main mechanism of their utility [33]. Several studies have not shown a significant correlation between hemorrhage growth and 30 day mortality or functional

Table 1
Hematoma volume and outcomes.

Study	Year	Design	Hematoma volume	Outcomes	Additional findings
Broderick J, et al. [4]	1993	Retrospective Cohort	>60 cm^3 30–60 cm^3 <30 cm^3	Mortality was 93% for deep and 71% for lobar hemorrhage. Mortality was 64% for deep and 60% for lobar hemorrhage. All patients with a pontine hemorrhage > 5 cm^3 or a cerebellar hemorrhage > 30 cm^3 had died at 30 days. Mortality was 23% for deep and 7% for lobar hemorrhages.	When combined with GCS scores of ≤8 and ≥9, hematoma volume was a highly sensitive (97%) and specific (97%) predictor of 30 day mortality.
Inagawa T, et al. [27]	2003	Prospective Cohort	>20 mL 6–20 mL <5 mL	Volume of the hematoma was the most important predictor of prognosis and significantly associated with 30-day mortality ($p = 0.003$).	Presenting GCS and location of hematoma, along with volume, significantly impact long-term outcomes.
Kim KH, et al. [17]	2009	Retrospective Cohort	>60 mL 30–59 mL <30 mL	Hematoma volume of >60 mL correlated with higher 30-day mortality. Unclear association of hematoma volume 30–59 mL with outcome. Hematoma volume of <30 mL correlated with higher functional recovery at 90-days.	Age, limb weakness, and hematoma volume most powerfully predict functional recovery.
Hallevi H, et al. [28]	2009	Retrospective Cohort	>30 mL >25 mL	ROC analysis yielded a cutoff of 30 mL ICH volume for mortality. ROC analysis yielded a cutoff of 25 mL ICH volume for poor outcome.	Total volume (ICH + IVH) ROC analysis yielded a cutoff of 40 mL for poor outcome, and 60 mL for mortality.
Jaffe J, et al. [21]	2008	Prospective Cohort	30 cm^3> >25 cm^3	Significantly lower mortality and better functional outcomes were achieved at 30 days. Significant predictor of mortality.	Worse outcomes and morbidity were seen with older age, larger ICH, and lower GCS. Patients with a GCS score of <8 and an ICH volume of >40 cm^3 had a significant higher mortality rate than patients with GCS score 9–15 and a volume of <20 cm^3 with an odds ratio of 95.3 and a p-value = 0.004.
Oh JW, et al. [30]	2012	Retrospective Cohort	>31 mL	A hematoma volume of <31 mL had a significant correlation with age < 65 and prognosis; a volume of >31 mL has no significant correlation with age and prognosis.	Predictors of a good prognosis included age 65>, good initial mental status, hematoma volume of 31 mL>, and a midline shift <4.5 mm.