time interval from symptom onset to CT angiography, estimation of ICH size that is strongly confounded by hematoma expansion, and the quantification of perihematoma edema size, which is markedly dynamic during the first 14 days after the ICH. Conversely, imaging may be used to guide therapeutic decisions in the absence of a reliable neurologic history, provided that imaging characteristics can be correlated well enough with changes of the underlying pathophysiology over time. In order to control for bias arising from timing of imaging studies, clinical data acquisition has to be thorough and CT time in relation to preceding and subsequent events has to be documented and accounted for in the analysis. In our study, a dedicated investigator gathered all available data including history information for each patient. The onset time was documented after discussion with the treating attending and fellow taking all information into account. Future studies investigating dIVH should ideally prospectively also include only patients with a reliable history regarding bleed onset.

The strengths of our study include a relatively large sample size and a prospective mode of data collection. Furthermore, all CT scans were evaluated in an interdisciplinary meeting. Limitations might arise from a less rigid imaging protocol in comparison to the previous study. Our imaging protocol did not include routine follow-up CTs before 12 hours after admission, since awake and cooperative patients can be sufficiently evaluated by neurologic examination alone. Importantly, because all patients received an admission and follow-up CT scan, we do not believe we underestimated the incidence of IVH after hospital admission. Though a longer latency to follow-up CT after admission may prolong the time to dIVH detection, it would most likely not prevent dIVH detection.

It is conceivable that ICH patients with IVH may be subdivided into 2 clinically meaningful groups: one that develops IVH simultaneously with the ICH, and one in which IVH occurs after the ICH as a consequence of hematoma expansion. Our findings of CT timing–dependent detection of IVH illustrate the latter pathomechanism. However, the significantly smaller IVH volumes in the dIVH group compared to the IVH group indicate that possibly another mechanism of dIVH, e.g., rebleeding in coagulopathic patients during the hospital course, might account for some dIVH cases, possibly leading to smaller IVH volumes than in patients who develop IVH initially.

Our findings challenge recent observations associating dIVH with acute mortality. Moreover, they suggest that the timing of obtaining the admission CT scan is the main driver for categorizing IVH into early vs delayed. Future studies should test these hypotheses in larger patient samples in order to account for the overall relatively low incidence of dIVH. The CT timing aspect of intraventricular expansion in ICH should ideally be studied in an ICH cohort with a short onset to CT time (e.g., ≤2 hours).

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References


Comment: Intraventricular hemorrhage—It’s the blood that matters, not the timing

Intracerebral hemorrhage (ICH) is a highly morbid form of stroke. Recent research has sought to identify pathologic processes that continue to evolve after patients present for medical care, with the hope that those delayed injuries may be effectively detected and intervened upon to improve outcomes. Our group recently reported an observation that delayed intraventricular hemorrhage (dIVH) developed in 21% of ICH subjects with no intraventricular hemorrhage (IVH) present on initial imaging. IVH has been characterized as an independent contributor to poor outcomes, and recognizing that delayed development of IVH was fairly common, along with the more widely recognized phenomenon of parenchymal hematoma growth, advanced it as another potential candidate for hematoma treatments. Moreover, dIVH showed approximately the same effect size in contributing to death within 2 weeks and poor outcomes at 3 months as IVH on initial imaging, suggesting that IVH posed similar morbid consequences regardless of when it occurred.

The present work by Witsch and colleagues provides additional insight into this phenomenon. A substantial number of patients in their cohort had dIVH (15%), and they similarly found that the discovery of dIVH was related to the scan timing, reinforcing the concept that intraventricular extension is a phenomenon that evolves for several hours after hemorrhage ictus. The effect of dIVH on outcomes did not reach statistical significance in their multivariate model, perhaps due to a lower observed incidence and a regression technique that dichotomized outcomes did not reach statistical significance in their multivariate model, perhaps due to a lower observed incidence and a regression technique that dichotomized the modified Rankin Scale (mRS) rather than using an ordinal regression shift analysis. Ordinal statistical approaches to analyzing the mRS have become favored over dichotomization because they increase statistical power by using information from every stratum of the scale, and can identify clinical and significant effects not identified by simple binary regression. That 20%–30% of patients with dIVH in these studies required ventriculostomy placement itself is notable and important. Their and our outcome analyses should not be interpreted as attempts to demonstrate or refute that dIVH is physiologically novel and distinct from initial IVH, but rather to confirm that they are similar and similarly morbid. What is remarkable from the data of Witsch et al. is how the effect estimates from the regression models confirm the similar morbidity of initial and delayed IVH: odds ratio of 2.70 and 2.87, respectively, for poor outcome (mRS 4–6 vs 0–3).

These findings are physiologically intuitive: Why would IVH affect outcomes differently when it occurs a few hours earlier, or when discovered in a patient who arrives at the hospital a few hours earlier? The key message for practicing clinicians is that important pathologic processes continue to evolve while patients are under our observation and care. The challenge ahead lies in elucidating the most effective methods for preventing, detecting, and treating these evolving and harmful processes.

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Author Contributions

Jens Witsch drafted, revised, and gave final approval for the manuscript and conducted the statistical analysis. Eliza Bruce provided suggestions.