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Advances in Prediction for Perihematomal Edema Growth in Intracerebral Hemorrhage

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1 Abstract

Perihematomal edema (PHE) has been represented as an important secondary injury after intracerebral hemorrhage (ICH). The evolution of PHE contributed to mass effect, which could induce the increase of intracranial pressure. The volume of PHE increased rapidly in the early stage of ICH and continued to increase for 7 to 11 days after symptom onset, and the edema extension distance (EED) increased rapidly within 24 hours, accounting for 60% of the peak EED [1-2]. For the timepoint of follow-up CT scans was different, the fastest development stage of PHE could also be 48 or 72 hours after symptom onset [3-4]. If patients with ICH could not benefit from early surgical evacuation of the hematoma, anti-edema treatment may bring better therapeutic effect. Thus, the use of anti-edema treatment may need to be considered for reducing PHE volume during the early phase of PHE development. How to appropriately predict PHE growth is important in patients at the early stage of ICH.

2 Predictions of perihematomal edema growth

Many studies have proved that initial hematoma volume will promote PHE growth. A study included 596 patients showed that baseline hematoma volume seemed to influence PHE growth, and other studies also represented similar results [5-7]. The formation mechanism of PHE is associated with coagulation cascade, erythrocytes lysis and cell toxicity, while lager hematoma induced more severe cellular injury. Furthermore, another experimental study proved that high percentage of surgical hematoma removal will reduce the volume of PHE growth [8]. These conclusions powerfully certify the significant effect of hematoma volume on PHE growth. However, the volume of hematoma could not be the only determinant for promoting PHE. For clinicians, it's still necessary to consider whether patients with relatively small hematoma volume are at risk of edema growth.

Besides hematoma volume, Sprügel et al represented that the morphology of hematoma could also influence the evolution of perihematomal edema, for irregular shape

hematoma had larger relative PHE volume [9]. In this study, researchers found that the surface of hematoma influenced PHE more than volume, providing an explanation that hematoma with irregular shape and relatively small volume had lager relative PHE volume. This study made us realize that volume of hematoma was not the only factor influencing PHE evolution. Thus, we could draw the conclusion that PHE growth really depends on hematoma volume and shape. This conclusion also brings some questions for us. .. Will the effect of hematoma on PHE growth persists for a long term? Whether the shape and density of hematoma only affect PHE growth in the early stage is still unknown. Overall, in the future, more studies are needed to explain the interaction mechanism and identify patients who only need long-term monitoring of PHE growth.

Earlier, the shape and volume of hematoma was listed as factors influencing PHE growth. Interestingly, the hematoma will also be affected by its size and shape. Hematoma growth usually occurs within a few hours after symptom onset, accounting for about 30% patients with ICH, which has been verified as an independent and reliable factor of poor outcomes in patients with ICH [10-12]. For convenience and saving time, signs for predicting early hematoma expansion on admission noncontrast computed tomography (NCCT) scans are really necessary for clinical decision-making. Barras at al have classified the hematoma into to 5 categories according to their shape and density, and other researchers also proposed different NCCT imaging markers for predicting hematoma expansion, including hypodensities, swirl sign, blend sign, black hole sign, island sign, satellite sign and so on [13-14]. Besides presenting the trend of hematoma growth, there signs also reflect density heterogeneity and irregular shape of hematoma. After irregular shape of hematoma was verified to be a factor associated with PHE growth, few study has focused on the effect of hematoma density on the development of PHE. In our study, NCCT imaging markers, which reflect the heterogeneous density of hematoma, were also capable of promoting early PHE development [15]. The result proved that early PHE growth could be predicted by some characteristics of hematoma, which presenting as different NCCT imaging markers, such as blend sign, black hole sign and island sign. In the future, new scale combining clinical characteristics and imaging markers may be proposed and improve the predictive accuracy of PHE growth.

As a secondary injury after intracerebral hemorrhage, many studies have presented that the evolution of perihematomal edema was definitely influenced by hematoma. NCCT imaging markers on initial CT scans could contribute to recognize patients with high risk at hematoma expansion and early perihematomal edema growth. Meanwhile, the relationship between hematoma and edema also provides more possible methods for predicting early edema growth. In recent years, radiomics, machine learning and deep learning are gradually applied for medical regions. For intracerebral hemorrhage, several studies proved that the texture analysis based on NCCT scans, is capable of quantifying the heterogeneity of hematoma, and the performance of discriminating patients at high risk of HE could be improve by including radiomics features in machine learning models with other characteristics [16-17]. Furthermore, several studies also successfully extracted features from perihematomal regions for different prediction [18-19]. In the future, the new technology will be better used for prediction and clinical decision. Though the new radiomics and machine learning methods always showed satisfied performance of prediction, the most important question is still how to improve the prognosis of patients with ICH.

3 Conclusion

In conclusion, the treatment for patients with ICH could not ignore the reaction between hematoma and perihematomal edema. Future prediction models based on artificial intelligence may contribute to saving more time, enhancing the therapeutic effect. The final aim of all means is to provide better outcomes for patients with ICH.

4. Author contribution

All authors have made intellectual contributions to the work.

5. Conflict of interest

The authors declare that they have no conflict of interest.

6. References

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