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Review Article

Glymphatic system dysfunction in cerebral infarction: advances and perspectives based on DTI-derived ALPS measures

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Abstract: The glymphatic pathway plays a crucial role in the clearance of metabolic byproducts and solutes from cerebral tissue. Dysfunction of the glymphatic pathway has been associated with various neurological disorders, including ischemic stroke. Diffusion tensor imaging (DTI) and the derived Analysis aLong the Perivascular Space (ALPS) have emerged as promising tools for evaluating glymphatic pathway function. This review aims to summarize the current evidence on the use of DTI-derived ALPS measures in assessing glymphatic dysfunction in ischemic stroke patients, and to explore their potential implications for diagnosis, prognostication, and treatment monitoring in this patient population.

Keywords: Glymphatic system dysfunction, cerebral infarction, DTI-derived ALPS

Introduction

Cerebral infarction, a leading cause of mortality and morbidity worldwide, presents a significant public health challenge. According to the Global Burden of Disease study, stroke, including ischemic stroke, accounts for approximately 6.55 million deaths annually, ranking as the second leading cause of death globally [1]. Furthermore, the prevalence of stroke survivors is estimated at over 101 million, many of whom experience long-term neurological deficits and reduced quality of life [2]. Despite advancements in acute stroke management, many patients continue to suffer from persistent neurological deficits and cognitive impairment. The mechanisms underlying these enduring deficits are not fully understood, but recent evidence suggests that the glymphatic pathway, a brain-spanning network of perivascular conduits facilitating the removal of metabolic byproducts and solutes, may play a critical role in the pathophysiology of cerebral infarction and its associated complications [3].

The glymphatic system, first described by Nedergaard et al. in 2012, has been increasingly recognized as a crucial component in the clearance of metabolic waste and interstitial fluid in the central nervous system [4]. Its dysfunction has been linked to various neurological disorders, including Alzheimer's disease and traumatic brain injury. However, its role in cerebral infarction has only recently begun to receive attention. Early experimental studies in rodent models demonstrated impaired glymphatic transport following ischemic stroke, providing foundational evidence for its involvement in post-stroke pathology [5]. These findings suggested that ischemia-induced disruptions to perivascular pathways could exacerbate cerebral edema and hinder recovery. Subsequent studies further investigated this connection using advanced imaging techniques, such as diffusion tensor imaging (DTI), which revealed altered perivascular function in stroke patients. The glymphatic pathway has been shown to facilitate the clearance of various substances from the brain, including amyloid-beta (Aβ), tau,

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and other neurotoxic molecules [6]. Impairment of the glymphatic pathway has been implicated in several neurological disorders, including Alzheimer's disease, traumatic brain injury, and stroke [7].

DTI is an advanced magnetic resonance imaging (MRI) technique that enables the assessment of white matter microstructure and brain connectivity [8]. DTI measures the diffusion of water molecules in biological tissues, providing information about the direction and magnitude of diffusion anisotropy [9]. DTI-derived measures, such as fractional anisotropy (FA), mean diffusivity (MD), and radial diffusivity (RD), are widely used to investigate white matter integrity in various neurological disorders [10].

Recently, Along-tract statistics Profiles (ALPS), derived from DTI data, have emerged as a novel approach to assessing glymphatic system function [11]. ALPS measures offer a detailed characterization of water diffusion along white matter tracts, which is believed to reflect the efficiency of glymphatic transport [12]. By quantifying the diffusion properties of water molecules along perivascular spaces, ALPS measures may provide valuable insights into the integrity and function of the glymphatic system [13].

This review aims to summarize the current evidence on the use of DTI-derived ALPS measures to evaluate glymphatic system dysfunction in cerebral infarction patients. The potential implications of glymphatic system dysfunction for the diagnosis, prognosis, and treatment monitoring of cerebral infarction will also be discussed.

Glymphatic system

The glymphatic system (GS) is a crucial pathway for clearing metabolic waste and maintaining interstitial fluid balance in the brain. Cerebrospinal fluid (CSF) flows into the brain through the perivascular space of arterial vessels, mixes with interstitial fluid (ISF), and is subsequently drained via the perivascular space of venous vessels into the meningeal lymphatic system. This process, mediated by aquaporin-4 (AQP4) channels located at the end feet of astrocytes, facilitates the exchange and circulation of CSF and ISF [14, 15]. The glymphatic system consists primarily of arteries, perivascular spaces, and astrocytic end feet expressing AQP4, forming a highly efficient "cleaning system" for the brain.

The glymphatic system clears metabolic waste products, including neurotoxic substances like β-amyloid, thereby maintaining the brain's internal environment and supporting neuronal function [16]. This system plays a pivotal role in brain health, influencing development, aging, and the response to injury and disease. Disruptions in glymphatic function have been implicated in various neurological disorders, including Alzheimer's disease, traumatic brain injury, and ischemic stroke [17]. Recent studies suggest that ischemic stroke impairs glymphatic transport by disrupting AQP4 polarization and altering perivascular flow, leading to the accumulation of neurotoxic metabolites and exacerbating brain damage [18].

Dysfunction of the glymphatic system in cerebral infarction is primarily attributed to disruptions in its structural and functional components, particularly AQP4 polarization and perivascular flow. Ischemic stroke induces significant oxidative stress, inflammation, and vascular damage, all of which compromise the efficiency of perivascular fluid exchange [19, 20]. One key mechanism is the loss of AQP4 polarization on the astrocytic end feet, which impairs the bidirectional movement of CSF and ISF. This disruption leads to the accumulation of neurotoxic substances, such as β-amyloid and lactate, exacerbating neuronal injury and brain edema [21, 22]. Additionally, ischemic conditions alter the morphology and function of astrocytes and the extracellular matrix, further hindering the fluid dynamics within the perivascular space. Pro-inflammatory cytokines released during ischemia, such as TNF-α and IL-1β, contribute to changes in vascular permeability and the breakdown of the blood-brain barrier, intensifying glymphatic dysfunction [23]. Moreover, impaired arterial pulsatility, which drives glymphatic circulation, reduces the convective flow of CSF, further compromising waste clearance [24]. These mechanisms not only exacerbate secondary injury after stroke but also create a pathological feedback loop, wherein the accumulation of toxic metabolites perpetuates inflammation and neuronal damage. Understanding these processes is critical for identifying novel therapeutic targets aimed at restoring

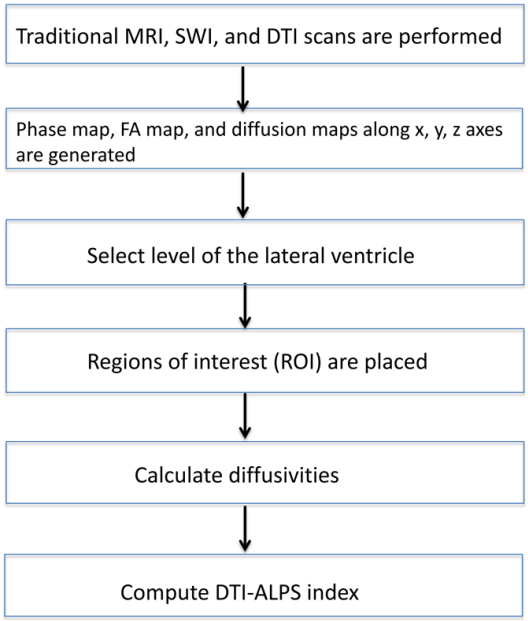

Figure 1. DTI-ALPS index calculation process. Diffusion tensor imaging of the perivascular space technology (DTI-ALPS).

glymphatic function to improve outcomes in stroke patients.

Diffusion tensor imaging of the perivascular space technology (DTI-ALPS)

To advance the study of glymphatic function, researchers have developed innovative imaging methods such as DTI-ALPS, which enable in vivo measurement of glymphatic activity. Diffusion tensor imaging (DTI) is an advanced imaging technique that quantifies the diffusion of water molecules in living tissues. This method allows for the analysis of the diffusion direction and speed of water molecules in various tissues without the use of contrast agents [25-28].

The DTI-ALPS index is used to assess glymphatic system (GS) activity. The calculation of this index involves the use of traditional MRI sequences, susceptibility-weighted imaging (SWI), and DTI to generate phase maps, color-coded fractional anisotropy (FA) maps, and diffusion maps along the x, y, and z axes. The calculation process includes several key steps: (1) selecting the level of the lateral ventricle body, (2) defining regions of interest (ROIs) in projection fibers and association fibers, and (3) measuring diffusivity along the x, y, and z directions. Projection fibers (e.g., corona radiata) extend along the cranio-caudal direction (z-axis), association fibers (e.g., superior longitudinal fasciculus) project in the anterior-posterior direction (y-axis), and subcortical fibers are arranged along the x-axis. Since the perivascular space (PVS) is perpendicular to the projection and association fibers, diffusivity along the PVS is influenced by differences in diffusivity along the x-axis (Dxproj, Dxasso) and diffusivity perpendicular to the x-axis (Dyproj, Dzasso). The formula for the DTI-ALPS index is:

DTI-ALPS index = average value (Dxproj, Dxasso)/average value (Dyproj, Dzasso).

This index is positively correlated with GS activity [29, 30]. While the standard calculation process provides valuable insights, several improvements have been developed to address specific limitations and enhance the utility of the DTI-ALPS index. Below, we describe and analyze these improvements. The DTI-ALPS index calculation process flowchart is shown in **Figure 1**.

Several advancements have been proposed to enhance the calculation of the DTI-ALPS index, addressing its limitations and improving its applicability in diverse scenarios. One major improvement involves the incorporation of advanced imaging sequences, such as high-resolution diffusion-weighted imaging (DWI) and multi-shell DTI techniques. These methods significantly enhance spatial and angular resolution, allowing for a more detailed capture of microstructural features within the perivascular space (PVS). This improvement is particularly advantageous for detecting smaller PVS structures and subtle variations in GS activity. However, these techniques come with the drawback of requiring extended scan times and specialized imaging equipment, which may not be accessible in routine clinical settings. As such, they are primarily suitable for research applications or specialized clinical settings.

Another approach is the use of dynamic diffusion imaging, which involves acquiring diffusion data over multiple time points. This method enables real-time assessment of GS functionality by capturing dynamic changes in water diffusion. It is particularly useful for studying physiological processes such as sleep-wake cycles or responses to interventions. Despite its ben-

efits, this method increases patient burden due to prolonged scanning sessions and introduces challenges in motion correction and data analysis. Consequently, dynamic imaging is better suited for research focused on physiological changes or treatment effects, rather than for routine clinical use. Improved region of interest (ROI) placement strategies represent another important advancement. These methods utilize automated or semi-automated algorithms, often supported by machine learning, to reduce operator-dependent variability. Automated ROI placement enhances reproducibility and consistency across studies, particularly in large-scale clinical trials or longitudinal research. However, these algorithms may struggle with individual anatomical variability, requiring manual adjustments in some cases. Nevertheless, these strategies are invaluable for ensuring standardization in data acquisition and analysis.

Finally, the adoption of advanced computational models, particularly machine learning, has shown promise in analyzing complex diffusion data. These models can identify subtle, nonlinear patterns in diffusion anisotropy, improving the sensitivity and specificity of the DTI-ALPS index. Moreover, they can predict clinical outcomes based on imaging features. Despite their potential, these models require large training datasets and significant computational resources, limiting their use in routine clinical practice. They are best suited for advanced research settings or facilities equipped with high-performance computing infrastructure.

While each improvement addresses specific limitations of the standard DTI-ALPS calculation, their applicability depends on the clinical or research context. High-resolution imaging is optimal for precise anatomical studies, while dynamic diffusion imaging excels at assessing functional changes. Automated ROI placement and machine learning offer scalability and reproducibility but require significant computational infrastructure. A balanced approach that combines these techniques may provide a comprehensive solution for future studies.

Progress of the DTI-ALPS

The calculation of the ALPS index requires the manual placement of ROI, a process that is both time-consuming and resource-intensive. To address this issue, researchers have developed automated techniques for calculating the ALPS index. By registering the color-coded FA map to a template space and using the “vecreg” function in FSL software to reorient tensors and vectors, a reoriented diffusivity map is generated. This approach eliminates the influence of head position and imaging plane variations [33-36]. Combined with semi-automatic or fully automatic ROI placement methods, this technique enhances the accuracy and repeatability of the ALPS index.

Some studies have further refined the DTI-ALPS method. For example, the traditional process involving the placement of two ROIs for projection and association fibers in the unilateral hemisphere has been expanded to include four ROIs for corresponding fibers in both cerebral hemispheres. The average value of the bilateral ALPS index is then calculated [37-40]. This modification requires only DTI scanning and the pre-placement of ROIs according to a standard brain template. Studies have demonstrated a strong correlation between this improved ALPS index and the glymphatic system clearance rate, which is typically measured using intrathecal gadolinium contrast injection. This method offers a more convenient and stable approach for further research into the glymphatic system [41].

Taoka et al. [42] simplified the DTI-ALPS method, using DWI to retrospectively generate apparent diffusion coefficient (ADC) maps along the x, y, and z axes. These ADC maps are then used to create a composite color image for ROI placement, and the ADC values within the ROI replace the diffusivity values in the original calculation formula, resulting in the DWI-ALPS index. Earlier studies [43-47] have identified a significant correlation between the ALPS index derived from a gradient field applied in three directions (DWI) and the DTI-ALPS index, which uses a gradient field in twelve directions. Compared to DTI, DWI has a shorter imaging time and is more practical for routine clinical use. If the DWI-ALPS method is validated, it could allow for regular evaluation of glymphatic system function alongside daily clinical imaging [48, 49]. However, the application of the DWI-ALPS method remains limited, and further research is needed to verify its accuracy and clinical applicability.

DTI-ALPS has emerged as a cutting-edge technique that has attracted significant attention in the scientific community. Over recent years, extensive studies have been conducted to explore and enhance this method [50]. Researchers have been focusing not only on understanding its theoretical foundations but also on improving its accuracy and reliability [51]. These efforts have led to a deeper insight into how DTI-ALPS functions and its potential applications across a range of disciplines. Through continuous experimentation and innovation, new techniques and algorithms have been developed to optimize the DTI-ALPS process [52], resulting in improved performance and better outcomes. Collaborative efforts among different research groups have further accelerated progress, with teams exchanging insights and experiences to refine the methodology. The research is not limited to technical improvements but also includes validating the method's effectiveness in real-world applications. As a result, the DTI-ALPS method is evolving rapidly, opening up new possibilities in fields like medical imaging, neuroscience, and materials science, while offering exciting opportunities for both scientific exploration and practical application.

Application of DTI-ALPS technology in evaluating GS function in cerebral infarction

DTI-derived ALPS measures are increasingly used to assess GS dysfunction in cerebral infarction patients. A clinical study by Zhang et al. [53] investigated GS dysfunction in patients with acute ischemic stroke. By analyzing DTI scans from 50 stroke patients and 50 age-matched controls, the study found that the mean DTI-ALPS index in stroke patients was significantly lower (0.78 ± 0.12) compared to that in controls (1.02 ± 0.09, $P < 0.001$). This reduction was attributed to impaired clearance of interstitial fluid and metabolic waste, and core functions of the glymphatic system, establishing a clear link between GS dysfunction and cerebral infarction.

A detailed case study by Xie et al. [54] examined a 65-year-old male with a left middle cerebral artery infarction. DTI-ALPS analysis showed regional alterations in the ALPS index, with a significantly lower value (0.68) in the infarcted hemisphere compared to the contralateral hemisphere (1.05). This case highlighted the ability of DTI-ALPS to detect regional glymphatic dysfunction caused by localized tissue damage in stroke patients.

Further supporting these findings, a longitudinal study by Liu et al. [55] explored changes in the ALPS index after reperfusion therapy in 40 acute ischemic stroke patients. The study measured the ALPS index at baseline (pre-therapy) and three months after thrombectomy. Patients with favorable clinical outcomes showed significant improvements in their ALPS index, from 0.74 ± 0.10 at baseline to 0.89 ± 0.08 ($P < 0.01$). In contrast, patients with poor clinical outcomes showed no significant changes, demonstrating its potential to monitor glymphatic recovery and predict therapeutic effectiveness.

Moreover, the ALPS index has been linked to clinical outcomes in cerebral infarction patients. Wang et al. conducted a cohort study involving 100 patients and found that those with lower ALPS values were more likely to experience severe disability, as measured by the modified Rankin Scale (mRS). Specifically, patients with an ALPS index below 0.80 had a significantly higher risk of severe disability ($mRS \geq 3$) compared to those with an ALPS index above 0.90 (odds ratio: 2.8, $P = 0.002$). This underscores the prognostic value of the DTI-ALPS index in assessing functional outcomes in stroke patients [56].

Together, these studies demonstrate that DTI-derived ALPS measures effective detect glymphatic system dysfunction in cerebral infarction patients. The DTI-ALPS index is sensitive to regional and global glymphatic alterations, provides insights into recovery following reperfusion therapy, and serves as a predictor of clinical outcomes. As such, it is a valuable biomarker for evaluating glymphatic system function in both research and clinical settings.

In cerebral infarction patients, the increased free water (FW) values and decreased fractional anisotropy (FA) values in the white matter regions indicate impaired glymphatic clearance and associated white matter degeneration. These areas are crucial for CSF-ISF exchange and solute clearance, and their dysfunction may contribute to the progression of stroke-related pathology. A study [57] also reported associations between ALPS measures (FW, FA),

arterial stiffness, blood pressure, and white matter hyperintensity burden, suggesting potential mediation effects among these factors. The correlation between glymphatic pathway impairment, as indicated by altered ALPS measures (ALPS-index), and the extent of neurocognitive decline, evaluated by the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA), underscores the clinical significance of assessing glymphatic function in cerebral infarction patients. Impaired glymphatic clearance may contribute to the accumulation of neurotoxic substances, such as amyloid-beta (Aβ) and tau, leading to neuronal damage and cognitive decline. Therefore, DTI-derived ALPS measures may serve as valuable biomarkers for predicting cognitive impairment and monitoring disease progression in cerebral infarction patients [58-60].

The precise mechanisms underlying glymphatic dysfunction in cerebral infarction remain unclear but are likely multifactorial. One proposed mechanism involves the deposition of Aβ and tau proteins in the perivascular spaces, which may obstruct glymphatic flow and impair CSF-ISF exchange [61-63]. Additionally, the depletion of AQP4 water channels on astrocytic endfeet, which are vital for glymphatic transport, has been observed in Alzheimer's disease and may contribute to dysfunction in glymphatic clearance pathways [20]. Additionally, vascular abnormalities, including arterial stiffness and blood-brain barrier (BBB) disruption, may also alter the driving forces for glymphatic flow, further impeding the clearance of metabolic waste products [64, 65].

The findings from this evaluation offer several important clinical implications for the management of cerebral infarction patients. First, DTI-derived ALPS measures may serve as a valuable diagnostic aid for the early detection of glymphatic pathway impairment, helping to identify patients at higher risk of neurocognitive decline and long-term functional deficits [66-68]. Second, monitoring changes in ALPS measures over time may provide insights into the recovery of glymphatic function, potentially guiding the development of targeted interventions to promote glymphatic clearance [69-72]. Finally, therapeutic strategies aimed at enhancing glymphatic function, such as promoting sleep [73], reducing inflammation [27-30], and modulating AQP4 expression [74-77], may represent novel therapeutic approaches for improving outcomes in cerebral infarction patients.

To address these limitations and fully realize the potential of glymphatic-targeted interventions, future research should focus on the following key areas. First, the validation of findings from this review in larger, more diverse cohorts of cerebral infarction patients is essential. Studies should aim to improve study designs and expand inclusion criteria to encompass various stroke subtypes, severities, and demographic characteristics, ensuring the generalizability of results [78-80]. Longitudinal studies with extended follow-up durations are critical to investigating the temporal progression of glymphatic pathway impairment. These studies should correlate changes in the DTI-ALPS index over time with long-term neurocognitive outcomes (e.g., memory and executive function) and functional recovery (e.g., modified Rankin Scale scores). A clear timeline for follow-ups, such as evaluations at 3, 6, and 12 months post-stroke, would provide robust data on the evolution of glymphatic dysfunction [81, 82].

The DTI-ALPS method also requires specific improvements. One key area is enhancing the resolution and accuracy of DTI imaging protocols to better capture the perivascular space (PVS) and associated diffusion dynamics [83]. This could include the use of high-resolution diffusion-weighted imaging (DWI) and advanced motion-correction algorithms to minimize artifacts. Additionally, incorporating machine learning-based approaches for automated region of interest (ROI) placement and ALPS index calculation would help reduce variability and improve reproducibility [84]. These advancements should be tested in controlled environments before being implemented in multicenter trials. Furthermore, the establishment of standardized DTI acquisition protocols and ALPS analysis methods is pivotal for ensuring the reproducibility and comparability of findings across studies. Researchers should reference existing guidelines, such as those from the Quantitative Imaging Biomarkers Alliance (QIBA) and the European Society of Radiology (ESR), to define key parameters, including diffusion gradient directions, voxel size, b-values,

and scanning duration [85]. Standardizing ROI placement criteria, particularly in projection and association fibers, is necessary to reduce inter-observer variability. A consensus document or guideline outlining these parameters would promote broader adoption and consistency across research groups.

Another critical direction is the identification of optimal ALPS index cut-off values for detecting glymphatic system dysfunction. This requires establishing normative data based on healthy controls stratified by age, sex, and other relevant factors. Comparative studies involving cerebral infarction patients and matched controls can help define thresholds that distinguish between normal and impaired glymphatic function. Receiver operating characteristic (ROC) curve analyses should be used to determine the sensitivity and specificity of these cut-off values for clinical application [86].

Finally, the exploration of novel therapeutic strategies targeting the glymphatic system could improve outcomes for cerebral infarction patients. Specific interventions, such as enhancing sleep quality through behavioral therapies or pharmacological agents, should be systematically evaluated for their effects on glymphatic function and neurocognitive recovery. Anti-inflammatory treatments aimed at reducing glymphatic pathway impairment and AQP4 modulators designed to regulate water transport in the PVS represent promising avenues for future investigation. Preclinical studies followed by randomized controlled trials would be the ideal approach for evaluating these therapeutic options, with the DTI-ALPS index serving as both a biomarker and a measure of therapeutic efficacy.

This review provides evidence supporting the use of DTI-derived ALPS measures in assessing glymphatic pathway impairment in cerebral infarction individuals [87, 88]. The insights indicate that glymphatic pathway impairment is widespread in cerebral infarction and is correlated with the degree of neurological deficits and neurocognitive decline. DTI-derived ALPS measures could serve as valuable biomarkers for predicting the risk of cognitive decline and long-term functional outcomes in these patients [89, 90]. However, further research is needed to validate these findings in larger cohorts, establish standardized ALPS measures and cut-off values, and explore the therapeutic potential of targeting the glymphatic system in cerebral infarction.

The glymphatic system represents a promising frontier in understanding and managing cerebral infarction and its associated complications. By facilitating the clearance of neurotoxic substances and maintaining cerebral homeostasis, the glymphatic pathway plays a critical role in preserving neuronal health and cognitive function [91-93]. The development of imaging techniques, such as DTI-derived ALPS measures, that allow for the non-invasive assessment of glymphatic function opens new opportunities for the early detection, monitoring, and treatment of glymphatic system dysfunction in cerebral infarction patients [94-96].

As the field of glymphatic inquiry progresses, it is imperative to integrate insights from basic science with clinical observations to cultivate a comprehensive understanding of the glymphatic pathway's role in cerebral infarction. While this knowledge holds significant promise for creating novel diagnostic tools, prognostic markers, and therapeutic strategies, several challenges must be addressed to successfully implement glymphatic-targeted treatments.

One key challenge is the complexity of the glymphatic system, which is influenced by numerous factors, including sleep, vascular health, and inflammation. Our current understanding of this pathway, particularly in the context of cerebral infarction, remains incomplete. This knowledge gap complicates the identification of precise therapeutic targets. For example, while AQP4 channels play a vital role in water transport within the glymphatic system, variability in AQP4 expression across individuals and disease states presents a significant obstacle in designing effective treatments. To address this, preclinical studies should focus on characterizing AQP4 expression patterns in stroke models and exploring the dose-dependent effects of AQP4 modulators on glymphatic function and neuroprotection.

Another challenge lies in the development of pharmacological therapies aimed at modulating the glymphatic system. The blood-brain barrier presents a major obstacle for delivering drugs that can effectively target glymphatic dysfunction. Drug candidates must exhibit high

BBB permeability while minimizing systemic side effects. Innovative drug delivery systems, such as nanoparticle-based carriers or intranasal delivery routes, may offer potential solutions by enhancing brain-specific targeting of therapeutic agents. However, these approaches require rigorous testing in preclinical models to confirm their safety and efficacy before progressing to clinical trials.

Designing clinical trials for glymphatic-targeted therapies also presents unique challenges. One significant issue is the lack of standardized biomarkers to assess glymphatic function and treatment response. While the DTI-ALPS index shows promise as a non-invasive biomarker, its reliability and sensitivity need validation in larger, multicenter cohorts. Additionally, identifying clinically meaningful cut-off values for the ALPS index would facilitate patient stratification based on the severity of glymphatic dysfunction. Furthermore, selecting appropriate clinical endpoints is crucial. Traditional stroke outcomes, such as the mRS or National Institutes of Health Stroke Scale (NIHSS), may not fully capture the effects of glymphatic-targeted interventions. Instead, trials should incorporate endpoints related to neurocognitive recovery, sleep quality, and long-term functional independence, all of which are closely linked to glymphatic function. Longitudinal imaging studies using advanced DTI protocols should also be included as secondary endpoints to track glymphatic recovery over time.

Lastly, the interplay between sleep and glymphatic function calls for a multidisciplinary approach in clinical trials. Given the role of sleep in promoting glymphatic clearance, it is essential to explore combined pharmacological and behavioral strategies, such as cognitive behavioral therapy for insomnia (CBT-I), to improve sleep quality. Integrating these approaches may maximize the therapeutic potential of glymphatic-targeted treatments.

Conclusion

This review highlights the potential of DTI-derived ALPS measures in evaluating glymphatic system dysfunction in cerebral infarction patients. It also underscores the need for further research to advance our understanding of the glymphatic system in cerebrovascular disorders. Incorporating glymphatic imaging into the clinical management of cerebral infarction may represent a significant advancement, offering new opportunities for personalized and targeted therapeutic approaches for this challenging condition.

Disclosure of conflict of interest

None.

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