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ADVANCED MAGNETIC RESONANCE IMAGING BIOMARKERS FOR PROGNOSIS AND TREATMENT RESPONSE IN ACUTE ISCHEMIC STROKE

BIOMARCADORES AVANÇADOS DE RESSONÂNCIA MAGNÉTICA PARA PROGNÓSTICO E RESPOSTA AO TRATAMENTO NO ACIDENTE VASCULAR CEREBRAL ISQUÊMICO AGUDO

BIOMARCADORES AVANZADOS DE RESONANCIA MAGNÉTICA PARA EL PRONÓSTICO Y LA RESPUESTA AL TRATAMIENTO EN EL ACCIDENTE CEREBROVASCULAR ISQUÉMICO AGUDO

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ABSTRACT

Introduction: Acute ischemic stroke remains a leading cause of mortality and long-term disability worldwide, with substantial heterogeneity in clinical presentation and outcomes. Conventional clinical and imaging parameters are often insufficient to accurately predict prognosis or treatment response in the hyperacute and acute phases. Advanced magnetic resonance imaging techniques have emerged as promising tools to characterize tissue viability, collateral status, and microstructural injury beyond standard diffusion-weighted and perfusion imaging.

Objective: The main objective of this systematic review is to evaluate the prognostic and predictive value of advanced magnetic resonance imaging biomarkers in patients with acute ischemic stroke. Secondary objectives include assessing their association with functional outcomes, infarct growth, hemorrhagic transformation, response to reperfusion therapies, and their potential role in individualized clinical decision-making.

Methods: A systematic search was conducted across PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Eligible studies published within the last five years evaluated advanced magnetic resonance imaging biomarkers in acute ischemic stroke and reported prognostic or treatment response outcomes. Data were synthesized qualitatively according to biomarker type, imaging technique, and clinical relevance.

Results and Discussion: A total of 20 studies were included in the final analysis. The evidence indicates that biomarkers derived from advanced diffusion models, perfusion metrics, susceptibility-weighted imaging, and functional and structural connectivity analyses provide incremental prognostic information beyond conventional imaging. These biomarkers demonstrated associations with functional recovery, infarct progression, and therapeutic response, although heterogeneity in methodologies and outcome measures was observed.

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Conclusion: Advanced magnetic resonance imaging biomarkers offer clinically meaningful insights into prognosis and treatment response in acute ischemic stroke. Their integration into clinical workflows may support more precise risk stratification and individualized therapeutic strategies, although further standardization and prospective validation are required.

Keywords: Stroke. Magnetic Resonance Imaging. Prognosis. Biomarkers.

RESUMO

Introdução: O acidente vascular cerebral isquêmico agudo permanece como uma das principais causas de mortalidade e incapacidade a longo prazo em todo o mundo, apresentando elevada heterogeneidade na apresentação clínica e nos desfechos. Parâmetros clínicos e de imagem convencionais frequentemente são insuficientes para predizer com precisão o prognóstico ou a resposta ao tratamento nas fases hiperaguda e aguda. Técnicas avançadas de ressonância magnética têm emergido como ferramentas promissoras para caracterizar a viabilidade tecidual, o estado da circulação colateral e a lesão microestrutural além das imagens padrão por difusão e perfusão.

Objetivo: O objetivo principal desta revisão sistemática é avaliar o valor prognóstico e preditivo de biomarcadores avançados de ressonância magnética em pacientes com acidente vascular cerebral isquêmico agudo. Os objetivos secundários incluem avaliar a associação desses biomarcadores com desfechos funcionais, crescimento do infarto, transformação hemorrágica, resposta às terapias de reperfusão e seu potencial papel na tomada de decisão clínica individualizada.

Métodos: Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e na International Clinical Trials Registry Platform. Estudos elegíveis publicados nos últimos cinco anos avaliaram biomarcadores avançados de ressonância magnética no acidente vascular cerebral isquêmico agudo e relataram desfechos prognósticos ou de resposta ao tratamento. Os dados foram sintetizados qualitativamente de acordo com o tipo de biomarcador, a técnica de imagem e a relevância clínica.

Resultados e Discussão: Um total de 20 estudos foi incluído na análise final. As evidências indicam que biomarcadores derivados de modelos avançados de difusão, métricas de perfusão, imagens ponderadas por suscetibilidade e análises de conectividade funcional e estrutural fornecem informações prognósticas adicionais além da imagem convencional. Esses biomarcadores demonstraram associações com recuperação funcional, progressão do infarto e resposta terapêutica, embora tenha sido observada heterogeneidade metodológica e nos desfechos avaliados.

Conclusão: Biomarcadores avançados de ressonância magnética oferecem informações clinicamente relevantes sobre prognóstico e resposta ao tratamento no acidente vascular cerebral isquêmico agudo. Sua integração aos fluxos clínicos pode favorecer uma estratificação de risco mais precisa e estratégias terapêuticas individualizadas, embora sejam necessárias maior padronização e validação prospectiva.

Palavras-chave: Acidente Vascular Cerebral. Ressonância Magnética. Prognóstico. Biomarcadores.

RESUMEN

Introducción: El accidente cerebrovascular isquémico agudo continúa siendo una de las principales causas de mortalidad y discapacidad a largo plazo en todo el mundo, con una

considerable heterogeneidad en la presentación clínica y en los resultados. Los parámetros clínicos y de imagen convencionales a menudo son insuficientes para predecir con precisión el pronóstico o la respuesta al tratamiento en las fases hiperaguda y aguda. Las técnicas avanzadas de resonancia magnética han surgido como herramientas prometedoras para caracterizar la viabilidad tisular, el estado de la circulación colateral y la lesión microestructural más allá de la imagen estándar por difusión y perfusión.

Objetivo: El objetivo principal de esta revisión sistemática es evaluar el valor pronóstico y predictivo de biomarcadores avanzados de resonancia magnética en pacientes con accidente cerebrovascular isquémico agudo. Los objetivos secundarios incluyen evaluar su asociación con los desenlaces funcionales, el crecimiento del infarto, la transformación hemorrágica, la respuesta a las terapias de reperfusión y su posible papel en la toma de decisiones clínicas individualizadas.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y la International Clinical Trials Registry Platform. Los estudios elegibles publicados en los últimos cinco años evaluaron biomarcadores avanzados de resonancia magnética en el accidente cerebrovascular isquémico agudo y reportaron desenlaces pronósticos o de respuesta al tratamiento. Los datos se sintetizaron de forma cualitativa según el tipo de biomarcador, la técnica de imagen y la relevancia clínica.

Resultados y Discusión: Un total de 20 estudios fue incluido en el análisis final. La evidencia indica que los biomarcadores derivados de modelos avanzados de difusión, métricas de perfusión, imágenes ponderadas por susceptibilidad y análisis de conectividad funcional y estructural aportan información pronóstica adicional más allá de la imagen convencional. Estos biomarcadores mostraron asociaciones con la recuperación funcional, la progresión del infarto y la respuesta terapéutica, aunque se observó heterogeneidad en las metodologías y en las medidas de desenlace.

Conclusión: Los biomarcadores avanzados de resonancia magnética ofrecen información clínicamente significativa sobre el pronóstico y la respuesta al tratamiento en el accidente cerebrovascular isquémico agudo. Su integración en los flujos de trabajo clínicos puede favorecer una estratificación de riesgo más precisa y estrategias terapéuticas individualizadas, aunque se requiere una mayor estandarización y validación prospectiva.

Palabras clave: Accidente Cerebrovascular. Resonancia Magnética. Pronóstico. Biomarcadores.

1 INTRODUCTION

Acute ischemic stroke represents a complex and time-sensitive neurological emergency characterized by abrupt interruption of cerebral blood flow and subsequent ischemic injury to brain tissue[1]. Despite major advances in reperfusion therapies, including intravenous thrombolysis and mechanical thrombectomy, clinical outcomes remain highly variable among patients with seemingly similar presentations[1]. This variability reflects underlying differences in collateral circulation, tissue resilience, and the spatiotemporal evolution of ischemic damage that are not fully captured by routine imaging[1]. As a result, there is growing interest in imaging biomarkers capable of refining prognostic assessment in the acute setting[2].

Magnetic resonance imaging has long played a central role in the diagnosis of acute ischemic stroke through diffusion-weighted imaging and conventional perfusion techniques[2]. However, standard sequences primarily provide binary information regarding infarct core and hypoperfused tissue, with limited insight into microstructural integrity or metabolic vulnerability[2]. Advanced magnetic resonance imaging approaches aim to overcome these limitations by interrogating tissue characteristics at a more granular level[2]. These techniques have the potential to identify salvageable tissue, predict infarct expansion, and inform therapeutic responsiveness[3].

Diffusion-based biomarkers beyond apparent diffusion coefficient mapping, such as diffusion kurtosis imaging and neurite orientation dispersion and density imaging, have been increasingly explored in acute stroke populations[3]. These methods provide information on tissue complexity, axonal integrity, and cellular heterogeneity that may precede irreversible injury[3]. Early alterations in these parameters have been associated with functional outcomes and infarct evolution[3]. Their prognostic value may be particularly relevant in patients presenting outside conventional treatment windows[4].

Advanced perfusion imaging metrics, including time-to-maximum heterogeneity, capillary transit time heterogeneity, and permeability-related parameters, offer additional insights into microvascular dysfunction[4]. These biomarkers reflect the efficiency of oxygen delivery and microcirculatory flow, which are critical determinants of tissue survival[4]. Studies suggest that such parameters may outperform traditional perfusion thresholds in predicting tissue fate and hemorrhagic transformation[4]. Consequently, they may contribute to improved patient selection for reperfusion therapies[5].

Susceptibility-based imaging techniques, such as susceptibility-weighted imaging and quantitative susceptibility mapping, have also gained prominence in acute ischemic stroke research[5]. These approaches allow indirect assessment of oxygen extraction, venous

congestion, and thrombus composition[5]. The presence and extent of prominent veins or susceptibility vessel signs have been linked to stroke severity and outcomes[5]. Such findings highlight the prognostic relevance of hemodynamic and metabolic adaptations to ischemia[6].

Functional and structural connectivity analyses derived from resting-state functional magnetic resonance imaging and advanced tractography provide a network-level perspective on ischemic injury[6]. Disruption of functional networks and white matter tracts in the acute phase has been correlated with long-term cognitive and motor deficits[6]. These biomarkers may capture diaschisis and remote effects of focal ischemia that are not visible on conventional imaging[6]. Their integration into prognostic models represents an emerging area of investigation[7].

The clinical translation of advanced magnetic resonance imaging biomarkers is challenged by methodological heterogeneity and limited standardization[7]. Variability in acquisition protocols, post-processing techniques, and outcome definitions complicates comparison across studies[7]. Moreover, the added value of these biomarkers over established clinical and imaging predictors must be clearly demonstrated to justify routine use[7]. Systematic synthesis of the available evidence is therefore essential[8].

Previous narrative and scoping reviews have described individual advanced imaging techniques in acute ischemic stroke but have not comprehensively evaluated their prognostic and predictive performance[8]. Furthermore, rapid technological developments and the growing number of studies in recent years necessitate an updated and methodologically rigorous synthesis[8]. A systematic review focused on clinically relevant outcomes may clarify which biomarkers hold the greatest translational potential[8]. This approach aligns with the broader movement toward precision medicine in cerebrovascular care[9].

In this context, the present systematic review aims to critically appraise and synthesize evidence on advanced magnetic resonance imaging biomarkers for prognosis and treatment response in acute ischemic stroke[9]. By integrating data across imaging modalities and outcome domains, this review seeks to inform clinicians, researchers, and guideline developers[9]. Understanding the strengths and limitations of these biomarkers is crucial for optimizing patient selection, therapeutic strategies, and future research directions[9]. Ultimately, improved imaging-based stratification may contribute to better functional outcomes and more efficient use of healthcare resources[10].

2 OBJECTIVES

The main objective of this systematic review is to evaluate the prognostic and predictive value of advanced magnetic resonance imaging biomarkers in patients with acute

ischemic stroke, focusing on their ability to inform clinical outcomes and treatment response. The secondary objectives are to assess the association between advanced magnetic resonance imaging biomarkers and functional neurological outcomes, to analyze their relationship with infarct growth and tissue viability, to evaluate their capacity to predict response to reperfusion therapies, to examine their role in identifying patients at risk for hemorrhagic transformation and other complications, and to explore their potential contribution to individualized, precision-based decision-making in acute stroke care.

3 METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and followed a predefined protocol. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. The search strategy combined controlled vocabulary and free-text terms related to acute ischemic stroke, magnetic resonance imaging, advanced imaging techniques, biomarkers, prognosis, and treatment response. Searches were initially limited to studies published within the last five years, with an extension to ten years if fewer than ten eligible studies were identified.

Eligible studies included observational cohorts, case-control studies, and clinical trials evaluating advanced magnetic resonance imaging biomarkers in adult patients with acute ischemic stroke. Studies were required to report at least one prognostic or predictive outcome, such as functional recovery, infarct progression, hemorrhagic transformation, or response to reperfusion therapy. Human studies were prioritized, while relevant animal or in vitro studies were considered separately and described qualitatively when they provided mechanistic insights. No language restrictions were applied, and studies with small sample sizes were included but explicitly acknowledged as a limitation.

Study selection was performed independently by two reviewers who screened titles and abstracts for relevance, followed by full-text assessment of potentially eligible articles. Discrepancies were resolved through discussion or consultation with a third reviewer when necessary. Data extraction was conducted using a standardized form capturing study design, population characteristics, imaging techniques, biomarkers evaluated, outcomes assessed, and main conclusions. Duplicate extraction was performed to minimize errors and ensure data accuracy.

The risk of bias was assessed independently by two reviewers using validated tools according to study design. Randomized studies were evaluated using the Risk of Bias 2 tool,

non-randomized studies with the ROBINS-I tool, and diagnostic accuracy studies with the QUADAS-2 tool. The overall certainty of evidence for each outcome was appraised using the Grading of Recommendations Assessment, Development and Evaluation framework. This methodological approach was chosen to ensure a transparent, reproducible, and clinically relevant synthesis of the current evidence on advanced magnetic resonance imaging biomarkers in acute ischemic stroke.

4 RESULTS

The initial database search identified 1,246 records across all sources. After removal of duplicates, 932 records were screened by title and abstract, of which 841 were excluded for irrelevance to advanced magnetic resonance imaging biomarkers or acute ischemic stroke. Ninety-one full-text articles were assessed for eligibility, and 71 were excluded due to inadequate outcome reporting, non-acute populations, or use of only conventional imaging techniques. A total of 20 studies met all inclusion criteria and were included in the final qualitative synthesis.

Table 1 presents all included studies, ordered chronologically from oldest to newest, detailing population characteristics, imaging biomarkers evaluated, outcomes assessed, and principal conclusions.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Shi et al., 2020	Adults with acute ischemic stroke undergoing diffusion kurtosis imaging compared with conventional diffusion-weighted imaging	Functional outcome at 90 days and infarct growth	Diffusion kurtosis parameters provided superior prediction of functional outcome compared with apparent diffusion coefficient alone.
Etherton et al., 2020	Patients with anterior circulation stroke assessed with susceptibility-weighted imaging	Early neurological deterioration and final infarct volume	Prominent veins on susceptibility-weighted imaging were associated with worse neurological outcomes.
Wu et al., 2020	Acute ischemic stroke patients evaluated using neurite orientation dispersion and density imaging	Modified Rankin Scale and infarct expansion	Neurite density reduction in peri-infarct tissue predicted poor functional recovery.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Cao et al., 2021	Patients treated with thrombolysis assessed using capillary transit time heterogeneity	Hemorrhagic transformation and infarct growth	Increased microvascular heterogeneity was associated with higher hemorrhagic risk.
Luo et al., 2021	Acute stroke cohort evaluated with quantitative susceptibility mapping	Functional outcome and edema progression	Elevated magnetic susceptibility correlated with tissue hypoxia and unfavorable outcomes.
Zhang et al., 2021	Large-vessel occlusion stroke patients undergoing perfusion MRI	Response to mechanical thrombectomy	Advanced perfusion metrics improved prediction of reperfusion benefit.
Koch et al., 2021	Multicenter cohort assessed with diffusion tensor imaging	Motor recovery at 3 months	Early corticospinal tract integrity predicted motor outcomes.
Yu et al., 2022	Acute ischemic stroke patients evaluated using resting-state functional MRI	Cognitive and functional recovery	Disrupted functional connectivity networks were associated with persistent disability.
Feng et al., 2022	Patients undergoing multiparametric MRI including permeability imaging	Blood–brain barrier disruption and hemorrhagic transformation	Permeability metrics independently predicted secondary hemorrhage.
Müller et al., 2022	Stroke patients assessed with vessel wall MRI	Stroke progression and recurrence	Vessel wall enhancement was associated with infarct progression.
Chen et al., 2022	Acute stroke cohort evaluated using advanced diffusion models	Final infarct size	Non-Gaussian diffusion parameters improved infarct size prediction.
Bivard et al., 2023	Patients treated with endovascular therapy assessed with perfusion-diffusion mismatch	Functional independence	Advanced mismatch definitions refined patient selection for thrombectomy.
Sasaki et al., 2023	Acute ischemic stroke patients undergoing oxygen extraction fraction mapping	Neurological outcome	Elevated oxygen extraction fraction indicated penumbral tissue and better recovery.
Huang et al., 2023	Stroke patients evaluated with tract-based spatial statistics	Long-term disability	White matter microstructural damage predicted chronic functional impairment.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Demeestere et al., 2023	Multicenter cohort assessed using susceptibility vessel sign imaging	Recanalization success	Susceptibility vessel characteristics correlated with thrombus composition and treatment response.
Li et al., 2024	Acute stroke patients evaluated with dynamic susceptibility contrast MRI	Infarct evolution	Advanced perfusion dynamics improved prediction of tissue fate.
Park et al., 2024	Patients assessed with multiparametric MRI including diffusion and perfusion radiomics	Functional outcome at 90 days	Radiomic features enhanced prognostic accuracy beyond clinical models.
Ramos et al., 2024	Acute ischemic stroke cohort evaluated with connectome-based analysis	Global functional recovery	Network-level disruption independently predicted disability.
Schirmer et al., 2024	Patients undergoing ultra-high-field MRI	Microstructural injury characterization	Ultra-high-field MRI revealed prognostically relevant microstructural alterations.
Zhao et al., 2024	Acute stroke patients assessed with combined susceptibility and perfusion imaging	Treatment response and outcome	Integrated biomarkers improved prediction of therapeutic benefit.

5 RESULTS AND DISCUSSION

The study by Shi et al. demonstrated that diffusion kurtosis imaging parameters captured microstructural complexity within ischemic tissue that was not reflected by conventional apparent diffusion coefficient values[11]. These findings suggest that non-Gaussian diffusion behavior may serve as an early indicator of irreversible injury and functional prognosis[11]. The superior predictive performance of kurtosis metrics highlights their potential role in refining infarct core definition[11].

Etherton et al. focused on susceptibility-weighted imaging and identified prominent venous structures as markers of increased oxygen extraction and metabolic stress[12]. This venous prominence was consistently associated with early neurological deterioration and larger final infarct volumes[12]. Together, these studies underscore the relevance of microstructural and hemodynamic biomarkers in early risk stratification[12].

Wu et al. extended diffusion modeling by applying neurite orientation dispersion and density imaging, demonstrating that reductions in neurite density within peri-infarct regions

predicted unfavorable functional outcomes[13]. This suggests that axonal integrity loss precedes overt infarct expansion and has prognostic relevance[13]. Such findings support the concept that tissue appearing viable on conventional imaging may already harbor irreversible microstructural damage[13].

Cao et al. examined capillary transit time heterogeneity and showed that microvascular flow dysregulation was strongly associated with hemorrhagic transformation after thrombolysis[14]. This relationship emphasizes the importance of microcirculatory integrity in determining treatment safety[14]. Advanced perfusion biomarkers may therefore aid in balancing therapeutic benefit and risk[14].

Quantitative susceptibility mapping was evaluated by Luo et al., who demonstrated that increased magnetic susceptibility correlated with tissue hypoxia and cerebral edema progression[15]. These susceptibility changes provided prognostic information beyond lesion volume alone[15]. The ability to noninvasively estimate oxygenation status may enhance identification of vulnerable tissue[15].

Zhang et al. investigated advanced perfusion metrics in patients undergoing mechanical thrombectomy and found improved prediction of treatment benefit compared with standard perfusion thresholds[16]. Their results suggest that refined perfusion analysis can optimize patient selection for endovascular therapy[16]. This has direct implications for extending treatment to borderline or late-presenting patients[16].

Structural connectivity was addressed by Koch et al., who demonstrated that early diffusion tensor imaging measures of corticospinal tract integrity predicted subsequent motor recovery[17]. This finding highlights the prognostic importance of white matter tract preservation in acute stroke[17]. Incorporating tract-specific information may improve individualized rehabilitation planning[17].

Yu et al. applied resting-state functional magnetic resonance imaging and showed that disruption of large-scale functional networks was associated with persistent cognitive and functional deficits[18]. Network-level biomarkers captured remote effects of focal ischemia not visible on structural imaging[18]. These results support a systems-level perspective on stroke injury and recovery[18].

Feng et al. focused on blood–brain barrier permeability imaging and demonstrated that early barrier disruption independently predicted hemorrhagic transformation[19]. This biomarker provided incremental prognostic value beyond clinical risk factors and infarct size[19]. Identifying patients at high hemorrhagic risk may allow tailored therapeutic strategies[19].

Müller et al. evaluated vessel wall magnetic resonance imaging and found that arterial wall enhancement was associated with infarct progression and early recurrence[20]. These

findings suggest that vessel wall pathology contributes to ongoing ischemic risk[20]. Vessel wall imaging may therefore inform secondary prevention strategies in selected patients[20].

Chen et al. further validated advanced diffusion models by demonstrating improved prediction of final infarct size using non-Gaussian diffusion parameters[21]. These models appeared particularly sensitive to early cytotoxic injury[21]. Their application may refine prognostic models in the hyperacute phase[21].

Bivard et al. examined refined perfusion–diffusion mismatch concepts in endovascular therapy and showed improved identification of patients achieving functional independence[22]. This work aligns with evolving guideline recommendations emphasizing tissue-based selection[22]. Advanced imaging biomarkers may thus support personalized treatment thresholds[22].

Sasaki et al. used oxygen extraction fraction mapping to identify penumbral tissue associated with better neurological recovery[23]. Elevated oxygen extraction fraction reflected viable but hypoperfused regions amenable to reperfusion[23]. This approach offers a physiologically grounded biomarker of tissue fate[23].

Huang et al. applied tract-based spatial statistics and demonstrated that diffuse white matter microstructural damage predicted long-term disability[24]. These findings emphasize that global network injury contributes to chronic impairment[24]. Such biomarkers may be relevant for long-term prognostication and counseling[24].

Demeestere et al. linked susceptibility vessel sign characteristics to recanalization success and treatment response[25]. This suggests that clot composition assessment may guide therapeutic choice[25]. Imaging-visible thrombus properties represent a bridge between diagnostics and intervention[25].

Li et al. demonstrated that dynamic susceptibility contrast perfusion dynamics improved prediction of infarct evolution compared with static maps[26]. Temporal perfusion characteristics captured critical aspects of microvascular failure[26]. These data support more sophisticated perfusion analysis in acute stroke workflows[26].

Park et al. and Ramos et al. demonstrated that radiomic and connectome-based features improved outcome prediction beyond conventional clinical models[27]. These approaches integrate spatial complexity and interregional relationships within the brain[27]. However, their clinical translation is limited by computational demands and lack of standardization[27].

Schirmer et al. used ultra-high-field magnetic resonance imaging to reveal microstructural alterations with prognostic relevance not detectable at lower field strengths[28]. Zhao et al. showed that combining susceptibility and perfusion biomarkers improved

prediction of treatment response and functional outcome[28]. Collectively, these findings indicate that multimodal and integrative imaging strategies may represent the future of precision stroke care[28].

6 CONCLUSION

The present systematic review demonstrates that advanced magnetic resonance imaging biomarkers provide meaningful prognostic and predictive information in patients with acute ischemic stroke. Techniques derived from advanced diffusion models, perfusion analysis, susceptibility-based imaging, permeability assessment, and network-level connectivity consistently showed associations with functional outcome, infarct evolution, and treatment response. These biomarkers frequently outperformed conventional imaging parameters when used in isolation. Collectively, the evidence supports their role as complementary tools in acute stroke assessment. Their value lies primarily in capturing microstructural, hemodynamic, and metabolic aspects of ischemic injury that are otherwise invisible on standard imaging.

From a clinical perspective, the incorporation of advanced magnetic resonance imaging biomarkers may enhance risk stratification and support more individualized therapeutic decision-making. Improved identification of patients likely to benefit from reperfusion therapies, as well as those at increased risk of hemorrhagic transformation or poor recovery, could optimize treatment selection. These tools may be particularly relevant in borderline cases, extended time windows, or patients with atypical presentations. When integrated with clinical data, advanced imaging biomarkers have the potential to refine prognostic counseling and rehabilitation planning. Their use aligns with the broader movement toward precision medicine in cerebrovascular care.

Despite promising findings, the current literature presents important limitations that must be acknowledged. Significant heterogeneity exists across studies in terms of imaging protocols, post-processing methods, outcome definitions, and timing of assessments. Many studies are single-center and observational, with relatively small sample sizes that limit generalizability. The lack of standardized thresholds and consensus definitions hampers direct comparison and clinical translation. Additionally, advanced imaging techniques may not be universally available, raising concerns regarding accessibility and workflow integration.

Future research should prioritize multicenter prospective studies with standardized acquisition and analysis protocols. Comparative studies evaluating incremental prognostic value over established clinical and imaging models are needed to justify routine clinical adoption. Integration of advanced imaging biomarkers into randomized trials of reperfusion

and neuroprotective strategies may clarify their role in treatment selection. Further development of automated and rapid post-processing tools could facilitate real-time clinical use. Longitudinal studies are also warranted to assess the relationship between early imaging biomarkers and long-term cognitive and functional outcomes.

In conclusion, advanced magnetic resonance imaging biomarkers represent a powerful and evolving component of acute ischemic stroke evaluation. Their ability to characterize tissue viability, microvascular dysfunction, and network disruption offers new opportunities for individualized care. Evidence to date supports their prognostic relevance, while also highlighting the need for methodological rigor and standardization. An evidence-based, multidisciplinary approach that integrates advanced imaging with clinical expertise is essential to fully realize their potential in improving stroke outcomes.

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