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The Role of Micronutrients in Gastrointestinal Function and Protection in Stroke Patients: Literature Review

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Abstract

Stroke is a serious health problem. Micronutrients are nutrients that the body needs in small amounts, such as vitamins and minerals. Neurological deficits due to acute stroke can cause malnutrition during hospital treatment. To determine the role of micronutrients in gastrointestinal function and protection in stroke patients. A systematic-narrative literature review following the PRISMA 2020 guidelines. Data sources included SINTA, Scopus, ClinicalKey, as well as proceedings and dissertations published between 2020 and 2025. Articles were assessed based on methodological quality and relevance to the management of stroke patients in Indonesia. A thematic analysis was conducted to synthesize the latest evidence. Several studies showed that micronutrients such as vitamins A, C, D, E, B9 (folate), B12, zinc, magnesium, and selenium play an important role in maintaining intestinal mucosal integrity, reducing oxidative stress and inflammation, and supporting intestinal microbiota balance in stroke patients. Adequate micronutrient intake helps prevent gastrointestinal complications and accelerates post-stroke motor and cognitive recovery. Micronutrient optimization is important for maintaining gastrointestinal function in stroke patients, supporting recovery, preventing complications, and improving quality of life.

Introduction

Stroke is a serious health problem. Stroke occurs due to abnormalities in the central nervous system, where the blood supply to the brain is disrupted. Stroke is the second leading cause of death and the sixth most common cause of disability (Rahayu, 2023). Data from the World Health Organization (WHO) shows that stroke accounts for 7.9% of all deaths in Indonesia (Familah et al., 2024). Symptoms that lead to a diagnosis of stroke include hemiparesis, sensory disturbances in one side of the body, hemianopia or sudden blindness, diplopia, vertigo, aphasia, dysphagia, dysarthria, ataxia, seizures, or sudden loss of consciousness (Harmawati et al., 2021).

One complication of stroke that can occur is recurrent stroke. Recurrent stroke is a stroke that occurs after the first stroke. It is estimated that approximately 17% of patients with stroke will experience recurrent stroke within 5 years after the first attack. Most recurrent strokes are of a different subtype from the first stroke. The risk factors for recurrent stroke are multifactorial (Fitriyani & Irawan, 2023).

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As one of the most common neurological disorders, stroke remains a leading cause of disability and death worldwide, placing a significant burden on individuals, families, and healthcare systems (H. Guo et al., 2025). Neurological deficits resulting from acute stroke can lead to malnutrition during hospital care. Malnutrition in stroke is associated with poorer clinical outcomes and longer hospital stays, resulting in higher costs (Sari et al., 2020).

Effective stroke prevention and management are crucial to reducing the incidence and long-term impact of stroke. Clinical nutrition interventions have emerged as an important approach in managing key risk factors such as hypertension, diabetes mellitus, and dyslipidemia. Proper nutrition not only reduces the risk of stroke, but also significantly improves clinical outcomes during the post-stroke recovery period (Mauluddy & Sunardi, 2025).

Nutrients in food can be classified into two types: macronutrients and micronutrients. Micronutrients are nutrients that the body needs in small amounts, such as vitamins and minerals (Danial et al., 2024). A deficiency in macronutrients can trigger protein-calorie malnutrition, and when combined with a micronutrient deficiency, it can cause nutritional problems (Aini, 2019). The gastrointestinal system is one of the peripheral organ systems that is disrupted during ischemic stroke. This disruption causes various complications that hinder the post-stroke recovery process (Macom & Brown, 2025).

Siotto and colleagues showed that stroke patients with poor nutritional status and sarcopenia experienced poorer functional recovery compared to patients with good nutritional status, emphasizing the importance of early detection of sarcopenia. In addition, Sato and colleagues found that adequate energy and protein intake during the first week after stroke was associated with higher rates of discharge home and improved activities of daily living (ADL) scores. Irisawa and Mizushima also noted that higher muscle mass and better nutritional status were associated with better motor function recovery in the first four weeks of rehabilitation (Mauluddy & Sunardi, 2025).

Optimal nutrition management can minimize complications such as malnutrition, infection, and inflammation, thereby supporting cognitive and motor recovery and improving patients' quality of life (Mauluddy & Sunardi, 2025). Interventions such as Home Enteral Nutrition (HEN) and Medical Nutrition Therapy (MNT) have been proven effective in improving nutritional status, reducing inflammation, and supporting patients' immune function (Mulyati et al., 2025).

Although there is growing scientific evidence that micronutrients play an important role in maintaining gastrointestinal function and integrity in stroke patients, in-depth studies on the mechanisms of action and effectiveness of micronutrient interventions in a clinical context are still limited. This situation underscores the need for large-scale, standardized research evaluating the relationship between micronutrient levels and digestive function, inflammatory status, and clinical outcomes in stroke patients, in order to strengthen the scientific basis for the application of more targeted and evidence-based nutritional therapy.

Methods

The steps involved in literature screening include: initial search → deduplication → screening of titles and abstracts → full text review → data extraction. Researchers also assess study quality using tools such as JBI for various designs (case reports, observational studies), AMSTAR 2 for reviews, and AGREE II if guidelines are available.

Inclusion Criteria

Publication type: Original research articles, systematic reviews, meta-analyses, clinical guidelines, case reports with high relevance, or conference proceedings published between 2020 and 2025.

Research population: Patients with ischemic or hemorrhagic stroke, in the acute or subacute phase, without restrictions on gender, age, or comorbidities, who were evaluated for gastrointestinal function or integrity.

Interventions studied: Administration or role of micronutrients (e.g., vitamins A, C, D, E, B-complex, zinc, selenium, magnesium, iron, or copper) in the context of gastrointestinal mucosal protection, intestinal immunity modulation, intestinal barrier function, or prevention of dysbiosis in stroke patients.

Research design: Randomized controlled trials (RCTs), cohort studies, case-control studies, cross-sectional studies, laboratory/clinical experimental studies, as well as systematic reviews or meta-analyses relevant to the topic.

Geographic context: International research with a focus on adaptation in developing countries, including local studies in Indonesia.

Publication language: Articles written in English or Indonesian, with full access to the full text for data review and methodology.

Exclusion Criteria

Publication type: Editorials, opinions, letters to the editor, or preprint articles without peer review.

Population context: Studies that do not involve stroke patients (e.g., healthy populations, patients with primary gastrointestinal diseases, or other neurological diseases such as Parkinson's or Alzheimer's).

Irrelevant interventions: Research focusing on the long-term rehabilitation phase without assessing gastrointestinal function or protection during the acute or subacute phase of stroke.

Methodological quality: Articles with incomplete data, unclear analysis, or insufficient research methods.

Duplication: Duplicate publication of the same research, where only the most complete and recent version will be selected.

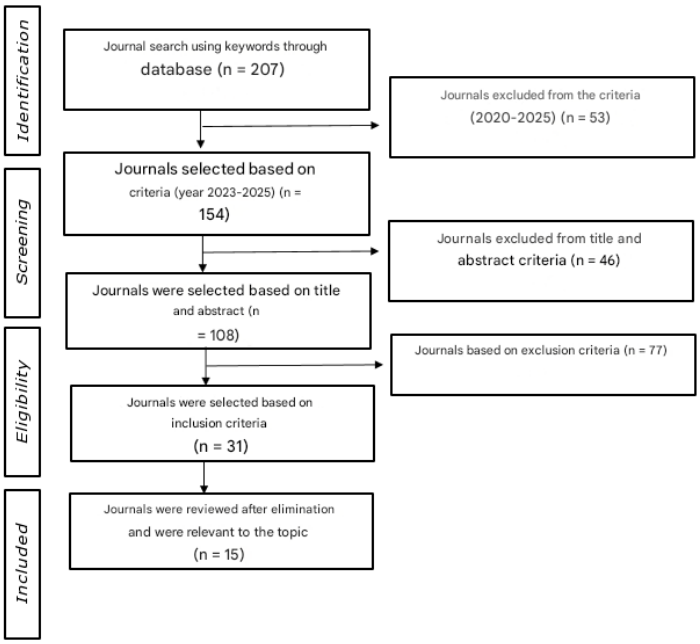

Figure 1. PRISMA 2020 Diagram (Systematic-Narrative Literature Review)

Table 1. Reference Review Results

No	Authors / Source	Year	Article Title	Sample	Location	Main Intervention	Main Conclusion
1	Anggita Citra Resmi & Diana Sunardi	2020	The Role of Nutritional Management in Preventing Stroke and Improving Clinical Outcomes	Literature review and clinical data of adult stroke patients	Indonesia	Evaluation of nutritional management, including macro- and micronutrient balance, for stroke prevention and management	Micronutrient-balanced nutritional management is pivotal for lowering stroke risk, accelerating recovery, and supporting endothelial and gastrointestinal health.
2	Guozhang Dong, Wanqian Xu, Lin Xu	2024	Causal Effect of Macronutrient and Micronutrient Intake on Stroke: A Two-Sample Mendelian Randomization Study	GWAS data from European populations; 15 nutrition GWAS and MEGASTROKE stroke data (~440,000–450,000 participants)	Europe	Mendelian randomization using genetic proxies for macro- and micronutrient intake (vitamins and minerals)	Higher magnesium is causally linked to lower stroke risk (notably cardioembolic); higher vitamin C lowers cardioembolic stroke risk; higher folate lowers small-vessel stroke risk; higher vitamin B6 is associated with higher large-artery stroke risk (interpret cautiously).
3	Maja Czerwińska-Rogowska, Karolina Skonieczna-Żydecka, et al.	2022	Kitchen Diet vs. Industrial Diets Impact on Intestinal Barrier Parameters among	60 stroke patients receiving kitchen or industrial diets	Poland	Comparison of diet types on intestinal barrier integrity markers (zonulin, calprotectin)	Kitchen diets improve intestinal barrier function and reduce inflammation more effectively

No	Authors / Source	Year	Article Title	Sample	Location	Main Intervention	Main Conclusion
			Stroke Patients				than industrial diets.
4	Wang Li, Bo-Min Lv, Yuan Quan, Qiang Zhu, Hong-Yu Zhang	2024	Associations between Serum Mineral Nutrients, Gut Microbiota, and Risk of Neurological, Psychiatric, and Metabolic Diseases: A Comprehensive Mendelian Randomization Study	Multinational human genomic datasets	China (global data analysis)	MR-based assessment of mineral nutrients (e.g., Zn, Se, Mg) and gut microbiota in relation to neurological disease risk	Mineral dysregulation is implicated in gut dysbiosis, which is associated with heightened risk of neurological disorders, including stroke.
5	Kathryn P. Kumar, Liam D. McKay, Connie H.Y. Wong, et al.	2023	Sympathetic-Mediated Intestinal Cell Death Contributes to Gut Barrier Impairment After Stroke	Ischemic stroke mouse model	Australia	Mechanistic evaluation of sympathetic activation and post-stroke intestinal epithelial cell death	Sympathetic activation after stroke drives intestinal epithelial cell death and barrier failure, increasing vulnerability to systemic infection.
6	Xiaolin Tian, Genghong Xia, Mingsi Zhang, et al.	2022	Effect of Enteral Nutrition on the Intestinal Microbiome and Risk of Death in Ischemic Stroke Patients	120 ischemic stroke patients on enteral nutrition	China	Assessment of enteral nutrition effects on gut microbiota and mortality	Early enteral nutrition helps preserve gut microbial diversity and reduces mortality risk in ischemic stroke.

No	Authors / Source	Year	Article Title	Sample	Location	Main Intervention	Main Conclusion
7	Akram Rahimi, Shaimaa A. Qaisar, Jalal Moludi, et al.	2024	Clinical Trial of the Effects of Postbiotic Supplementation on Inflammation, Oxidative Stress, and Clinical Outcomes in Patients with CVA	80 stroke (CVA) patients	Iran	Eight-week postbiotic supplementation	Postbiotics reduce inflammatory and oxidative stress biomarkers, improve gut function, and enhance clinical outcomes in stroke patients.
8	Nick van Wijk, Bettina Studer, Claudia van den Berg, et al.	2022	Evident Lower Blood Levels of Multiple Nutritional Compounds and Highly Prevalent Malnutrition in Sub-acute Stroke Patients with or without Dysphagia	150 sub-acute stroke patients	Netherlands	Measurement of vitamin/mineral levels (vitamin D, B12, folate, Zn, Se)	Multi-micronutrient deficiency and malnutrition are highly prevalent and may contribute to immune dysfunction and delayed recovery.
9	William Roth, Mansour Mohamadzadeh	2022	Vitamin B12 and gut-brain homeostasis in the pathophysiology of ischemic stroke	Literature review	International	Review of vitamin B12 in gut–brain axis homeostasis	Vitamin B12 is integral to gut–brain homeostasis and may modulate pathways relevant to ischemic stroke pathophysiology.
10	Asysyifa Riana, Yuliati Widiastuti, dkk.	2023	Efektifitas Terapi Gizi Medis Terhadap Perbaikan Asupan Makronutrien Pasien	Ischemic stroke patients	Indonesia	Medical nutrition therapy (clinical nutrition intervention)	Medical nutrition therapy effectively improves micronutrient intake, with potential

No	Authors / Source	Year	Article Title	Sample	Location	Main Intervention	Main Conclusion
			Stroke Iskemik				benefits for overall nutritional status in ischemic stroke patients.
11	Helene M. Flatby, Anuradha Ravi, Jan K. Damås et al.	2023	Circulating levels of micronutrients and risk of infections: a Mendelian randomization study	Genetic analyses of >300,000 individuals (GWAS)	Multinational (Europe; UK Biobank & FinnGen)	Genetic instruments for micronutrient levels (vitamins A, C, D, E; zinc, copper, selenium) vs infection risk	Higher micronutrient levels—particularly zinc and copper—are causally associated with reduced infection risk, including gastrointestinal infections, supporting protective roles in immunity and mucosal barrier integrity.
12	Na Guo, Ying Zhu, Dandan Tian, et al.	2022	Role of diet in stroke incidence: an umbrella review of meta-analyses of prospective observational studies	>40 prospective meta-analyses (millions of participants)	Global	Synthesis of dietary patterns and nutrient intake associated with stroke incidence	Higher intake of micronutrients (e.g., vitamins C, E, folate, magnesium, potassium) and fruit/vegetable-rich diets are linked to lower stroke risk, whereas high sodium intake is linked to higher risk.
13	Ping Chen, Alberto Melo Soares,	2023	Association of vitamin A and zinc status with	293 children aged 2–9 years in a	Northeastern Brazil (Fortaleza)	Serum retinol and plasma zinc assessed against intestinal	Vitamin A and zinc deficiencies are associated

No	Authors / Source	Year	Article Title	Sample	Location	Main Intervention	Main Conclusion
	Aldo A. M. Lima, et al.		altered intestinal permeability : analyses of cohort data from northeastern Brazil	longitudinal cohort		permeability markers (lactulose/mannitol ratio)	with increased intestinal permeability (“leaky gut”), underscoring micronutrient contributions to mucosal barrier integrity.
14	Elizabeth A. Del Rio, Mary Carmen Valenzano, Katherine M. DiGuilio, et al.	2025	Orally Administered Zinc Gluconate Induces Tight Junctional Remodeling and Reduces Passive Transmucosal Permeability Across Human Intestine in a Patient-Based Study	20 healthy volunteers undergoing intestinal endoscopy	United States	Oral zinc gluconate (26 mg twice daily for 14 days) vs placebo; tight junction protein expression and plasma D-lactate	Zinc supplementation significantly strengthens the intestinal barrier by enhancing tight junction proteins (e.g., claudin, tricellulin) and reducing mucosal permeability.
15	Xinrong Chen, Yanjie Hu, Xingzhu Yuan, et al.	2022	Effect of early enteral nutrition combined with probiotics in patients with stroke: a meta-analysis of randomized controlled trials	26 RCTs (2,216 acute stroke patients)	China (multi-center hospitals)	Early enteral nutrition + probiotics vs enteral nutrition alone; outcomes: GI complications, barrier markers (DAO, D-lactate), infections, nutritional status	Early enteral nutrition plus probiotics improves gut barrier function and microbiota profiles, enhances nutritional status, and reduces infectious complications after stroke.

Result and Discussion

Abstracts from 15 recent publications (2020–2025) indicate that nutritional management plays a central role in stroke prevention and treatment, particularly through the regulation of

macronutrient and micronutrient intake and the modulation of gut microbiota. Recent empirical evidence confirms that nutritional balance not only affects vascular risk, but also neurological recovery, immune function, and gastrointestinal integrity after stroke.

Stroke is a global health problem that is now the second leading cause of death and the third most common cause of disability worldwide (Pluta et al., 2021). The Primary Prevention Guidelines for Stroke published by the American Heart Association/American Stroke Association state that vitamin B complex (folic acid, vitamin B12, and vitamin B6) may be considered for the prevention of ischemic stroke in patients with homocysteinemia (Brodska et al., 2023; Zhang et al., 2024). Identifying modifiable risk factors for stroke is crucial for implementing effective prevention strategies (Jiang et al., 2025).

Research by Guozhang Dong et al. (2024) using a Mendelian randomization approach shows that magnesium, folate, vitamin B6, and vitamin C intake has a protective effect against stroke risk (Dong et al., 2024). Vitamin intake, especially vitamin B6, folic acid, and vitamin B12, plays an important role in maintaining brain health (Nurfitriani & Soviana, 2025). These results reinforce the study by Anggita Citra Resmi & Diana Sunardi (2020), which shows that balanced nutritional management can reduce the incidence of stroke and improve clinical outcomes for patients in Indonesia. The combination of essential nutrients and control of metabolic risk factors is the main strategy in primary prevention (Mauluddy & Sunardi, 2025).

Malnutrition is a serious problem in post-stroke patients. It is important to note that malnutrition worsens during hospitalization and is related to somatic and psychological factors, as well as a lack of knowledge among those accompanying patients.(Cichon et al., 2021) Nutritional management during hospitalization is tailored to meet the nutritional and functional needs of patients, including nutritional screening, nutritional assessment, and the provision of high-energy, high-protein foods (Mangalik et al., 2023).

The role of micronutrients in gut and brain health has also received considerable attention. A study by Wang Li et al. (2024) confirmed the relationship between mineral imbalances (Zn, Se, Mg) and gut microbiota dysbiosis, which contributes to the pathogenesis of neurological diseases, including stroke (Li et al., 2024). In line with this, Roth & Mohamadzadeh (2022) emphasize the importance of vitamin B12 in maintaining gut–brain axis homeostasis, which, if disrupted, can exacerbate systemic inflammation and ischemic neuronal damage (Roth & Mohamadzadeh, 2021).

Research by Maja Czerwińska-Rogowska et al. (2022) shows that a natural diet (kitchen diet) improves intestinal barrier integrity by reducing inflammatory markers such as zonulin and calprotectin, compared to an industrial diet (Czerwińska-Rogowska et al., 2022). These findings are supported by Xiaolin Tian et al. (2022), who reported that early enteral nutrition maintains gut microbiota diversity and reduces mortality in ischemic stroke patients. This evidence reinforces the view that early nutritional intervention has a protective effect against infectious complications and accelerates neurological recovery (Tian et al., 2022).

In the context of nutritional status, two studies by van Wijk et al. (2021, 2022) revealed that the majority of subacute stroke patients experience multiple micronutrient deficiencies (vitamins D, B12, folate, Zn, Se) that impact immune dysfunction and slow recovery (Van Wijk et al., 2023). There are several problems arising from stroke, one of which is a disorder of the digestive system. Changes in gastrointestinal function include slowed peristalsis and changes in secretion (Purhadi & Wuryaningdyah, 2024). Research by Asysyifa Riana et al. (2024) in Indonesia found that individualized medical nutrition therapy was effective in increasing micronutrient intake and improving nutritional status in ischemic stroke patients (Riana et al., 2024).

Interventional approaches are also beginning to focus on postbiotic supplementation to suppress post-stroke inflammation. Rahimi et al. (2024) showed that eight weeks of postbiotic

administration reduced inflammatory and oxidative stress biomarkers, while improving intestinal function and clinical scores in patients with cerebrovascular accident (CVA). These findings confirm that manipulating the microbiota, whether through enteral nutrition or bioactive supplements, has long-term therapeutic potential (Rahimi et al., 2024). Although some dietary supplements have functions that enhance stamina and the immune system, improper use can have negative effects on users because supplements are not like drugs and are not intended to cure diseases (Diyah et al., 2024).

Meanwhile, research by Kumar et al. (2023) adds a new dimension by finding that post-stroke activation of the sympathetic nervous system can trigger intestinal epithelial cell death and barrier function impairment, thereby increasing the risk of systemic infection. Therefore, maintaining intestinal physiological stability through nutrition and oxidative stress control is an important strategy in post-stroke care (Kumar et al., 2025).

A study by Flatby et al. (2023) using a Mendelian randomization approach showed that higher levels of micronutrients, such as zinc, copper, and vitamins, are causally associated with a lower risk of infection, including gastrointestinal infections (Flatby et al., 2023). A review by Guo et al. (2022) showed that a diet rich in fruits, vegetables, vitamins (C, E, B9), and minerals (magnesium, potassium) is correlated with a reduced risk of stroke. Conversely, high consumption of sodium and saturated fat increases the risk (N. Guo et al., 2022). A classic study by Chen et al. (2003) in Brazil provides strong evidence of the relationship between vitamin A and zinc deficiency and increased intestinal permeability in children (P. Chen et al., 2003).

A human experimental study by Del Rio et al. (2025) reinforces the evidence that oral zinc gluconate supplementation can improve tight junction structure and reduce intestinal mucosal permeability (Del Rio et al., 2025). A meta-analysis by Chen et al. (2021) provides strong clinical evidence in stroke patients that early enteral nutrition combined with probiotics improves intestinal barrier function, reduces mucosal damage biomarkers (DAO, D-lactate), and reduces the incidence of infection and gastrointestinal complications (Chen et al., 2022).

The evidence collected indicates the involvement of impaired nutritional status in patients in the post-stroke recovery process and unsatisfactory rehabilitation outcomes (Ciancarelli et al., 2024).

Overall, these findings indicate that timely, balanced, and personalized nutritional interventions can improve clinical conditions, reduce mortality, and accelerate recovery in stroke patients. The integration of nutritional therapy with monitoring of gut biomarkers and micronutrient status needs to be adapted into national clinical guidelines, particularly in Indonesia, to accommodate resource limitations and variations in local dietary patterns. This evidence-based approach opens opportunities for the development of precision nutritional therapy in modern neurological rehabilitation.

Conclusion

Based on a review of the latest literature from 2020–2025, micronutrients play an important role in maintaining physiological function and protecting the gastrointestinal tract in stroke patients. Cerebral perfusion disorders and post-stroke inflammatory responses often affect the digestive system, including decreased intestinal motility, absorption disorders, and increased mucosal permeability. In this context, micronutrients such as vitamins A, C, D, E, B9 (folate), B12, zinc, selenium, and magnesium play an essential role in supporting intestinal epithelial regeneration, suppressing oxidative stress, reducing inflammation, and maintaining intestinal microbiota balance.

Current literature shows that micronutrient adequacy is closely related to gastrointestinal mucosal resilience, reduced risk of gastrointestinal infections, and improved nutrient

absorption efficiency in stroke patients, especially those with dysphagia or enteral nutrition. A nutritional approach that pays attention to micronutrient levels has been shown to contribute to improved mucosal immune function, digestive system stability, and overall metabolic recovery.

Overall, recent research confirms that optimizing micronutrient status is an integral aspect of stroke patient rehabilitation, not only to support neurological function, but also to protect gastrointestinal integrity and prevent gastrointestinal complications. Integrating micronutrient assessment and management into stroke patient nutritional therapy is a strategic step in improving prognosis, recovery effectiveness, and quality of life in both the acute and chronic phases of post-stroke.

Suggestion

Recommendations for Clinical Implementation

Develop a protocol for assessing micronutrient status in stroke patients in hospitals, including routine testing of levels of essential vitamins and minerals such as vitamin D, B9, B12, zinc, magnesium, and selenium.

Integrating evidence-based micronutrient supplementation into standard nutritional therapy for stroke patients, both in the acute phase and during rehabilitation, to support gastrointestinal function and metabolic recovery.

Developing national clinical guidelines on micronutrient management in stroke patients, compiled through multidisciplinary collaboration between neurologists, nutritionists, gastroenterologists, and clinical pharmacologists.

Improving education and training for healthcare professionals on the importance of micronutrients in maintaining gut health and preventing gastrointestinal complications in stroke patients.

Encourage further research on optimal doses, effective combinations, and the mechanisms of action of micronutrients on intestinal mucosal function and their effect on clinical outcomes in stroke patients.

Utilizing digital technology and electronic medical record systems to continuously monitor patients' nutritional status, enabling rapid and precise adjustments to nutritional interventions.

Improving coordination between stroke care units and clinical nutrition teams to ensure that nutritional strategies are implemented comprehensively and consistently throughout all stages of patient care.

Recommendations for Further Research

Conducting a multicenter study with a randomized controlled trial (RCT) design to evaluate the effectiveness of micronutrient supplementation (vitamins D, B9, B12, zinc, magnesium) on gastrointestinal function and clinical recovery in stroke patients.

Examine the relationship between micronutrient levels and biomarkers of intestinal mucosal integrity, such as zonulin, LPS, and proinflammatory cytokines, to gain a deeper understanding of the protective mechanisms of the gastrointestinal tract.

Conducting a longitudinal study to assess changes in micronutrient status and its relationship with the occurrence of gastrointestinal complications during the acute phase to post-stroke rehabilitation.

Develop personalized nutrition-based intervention studies, considering patients' nutritional status, stroke type, and metabolic conditions, to determine the optimal combination and dosage of micronutrients.

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Conduct qualitative research on the perceptions of healthcare workers and patients regarding the importance of micronutrients in stroke management, in order to improve compliance and the effectiveness of nutritional therapy implementation.

Establishing a national stroke patient nutrition registry that contains data on micronutrient levels, nutritional status, and clinical outcomes, as a basis for nutritional intervention policies and further nutritional research in Indonesia.

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