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Malnutrition in Acute Stroke: An Article Review

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Abstract

The prevalence of malnutrition after stroke varies widely. It is estimated about one-fifth of patients with acute stroke are malnourished on initial hospital admission, while the prevalence of malnutrition ranges from 6.1 to 62%. Energy requirements increase due to stress caused by stroke, while food intake decreases due to impaired ability to eat, so the body will use its fat and protein stores as fuel to produce glucose. Muscle and fat tissue undergo degradation due to the breakdown of amino acids to form energy. Systemic consequences occur after stroke, peripheral immunodepression in association with overstimulation of the autonomic and neuroendocrine systems. Damage to cerebral tissue can activates the hypothalamus-pituitary-adrenal axis, resulting in increased levels of glucocorticoid hormones, catecholamines, and glucagon, leading to hypermetabolism (increased energy use), hypercatabolism (increased protein breakdown), and persistent hyperglycemia. The prevalence of malnutrition increases with the length of stay and decreased functional improvement during rehabilitation. Malnourished patients with stroke experience a higher stress reaction, which increases the occurrence of peptic ulcers, and infections of the respiratory and urinary tracts, thus extending the length of stay and increasing mortality.

Keywords: Length of stay, malnutrition, mortality, stroke

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I. Introduction

The prevalence of acute stroke malnourished patients varies greatly, which estimated ranges from 6.1 to 62% at the time of admission.[1,2] Differences in time of assessment, type of stroke, history medical conditions, and stroke complications may contribute to the magnitude of this variability. However, many of this variation can also be attributed to differences in nutritional assessment methods.[3,4] Systemic consequences occur after stroke, peripheral immunodepression in association with overstimulation of the autonomic and neuroendocrine systems will contribute increasing length of hospitalization and with decreasing functional improvement during rehabilitation.[2] Malnourished patients with stroke experience a higher stress reaction, which increases the occurrence of peptic ulcers, and infections of the respiratory and urinary tracts, thus extending the length of stay and increasing mortality.[3,4]

II. Epidemiology in Acute Stroke

Based on the American Society for Parenteral & Enteral Nutrition (ASPEN) 2011, in 104 acute stroke patients, the incidence of protein energy deficiency (PEM) occurred in 16.3% of patients upon admission to the hospital, and this figure increased to 26.4% on day 3–7 and 35% on the 14th day of hospitalization.[5] Prevalence data from 7 studies regarding the evaluation of nutritional status in 3 countries on the Asian continent ranged from 22–90% of patients treated with malnutrition, with the highest prevalence in old age.[6] Malnourished conditions stroke patients in several Indonesian hospitals almost have the same prevalence, around 63% of stroke patients

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at Margono Soekardjo Purwokerto Hospital experience malnutrition[4], at Adam Malik Hospital Medan as many as 65.71% of stroke patients with malnutrition[5], 59.5% stroke patients at Ulin Hospital Banjarmasin were malnourished[6], and at Hasan Sadikin Hospital Bandung there were 51.9% of stroke patients with malnutrition.[7] Differences in time and evaluation methods, type of stroke, comorbid conditions and other stroke complications contributed to the heterogeneity of the incidence of malnutrition in patients stroke.[7,8]

III. Metabolism in Stroke Patients

Cerebral ischemia is caused by an interruption of blood flow in the brain, resulting in reduced oxygen and nutrient levels in the area which causes complex and continuous cellular and metabolic pathological conditions. These effects result in tissue damage in the brain, including the death of neuron cells and cerebral infarction.[9] This also occurs in hemorrhagic strokes, the acute process of the emergence of intraparenchymal hematoma lesions causes disruption and changes in tissue position. Secondary process that cause tissue damage also occur due to ischemic processes around the hematoma, the formation of cerebral edema and the toxic effects of the components of the hematoma which cause a decrease in oxidative metabolism around the tissue, with very low oxygen use. This decrease in oxygen use causes damage to mitochondrial function, which initiates the death of neuron cells.[10,11]

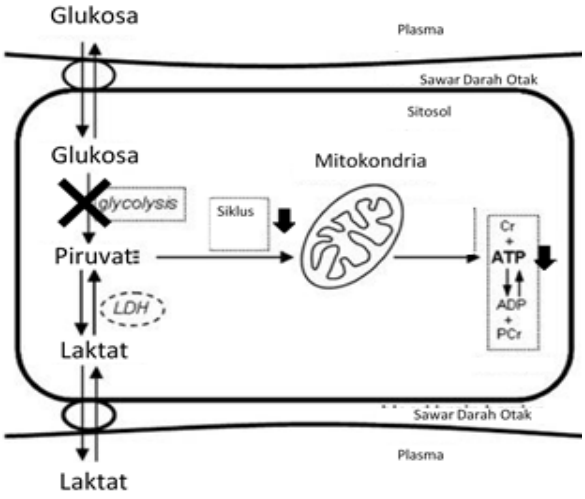

Figure 1. Anaerob Metabolism in Hypoxic Condition.
Note: ATP (Adenosine Triphosphate); ADP (Adenosine Diphosphate); LDH (Lactate Dehidrogenase); Cr (Creatine); PCr (Phospocreatine).[2]

The body's response to a stroke will change over time. After experiencing a stroke, the first phase which lasts for the first 12–24 hours after a stroke is an increase in catecholamine and glucagon levels which increases the breakdown of glycogen (glycogenolysis) and the synthesis of glucose from amino acids such as alanine, serine, glycine, cysteine, methionine and tryptophan (gluconeogenesis) and resulting in a state of hyperglycemia.[12] Glucose metabolism is the most disrupted cycle due to decreased oxygen and nutrients in the area, this is characterized by a change in glycolysis from the aerobic pathway to the anaerobic pathway.[13] The initial process of energy formation is through the process of glycolysis, where glucose is broken down into pyruvic acid molecule. The availability of oxygen will produce energy through aerobic pathways, where pyruvate will enter the tricarboxylic acid cycle or Krebs cycle and electron transport reactions in mitochondria to produce energy in the form of Adenosine Triphosphate (ATP), as much as 34 ATP.

Phosphocreatine in cerebral tissue serves as a short-term energy reserve, reproducing ATP from Adenosine Diphosphate (ADP) in a reaction catalyzed by creatine kinase. Cerebral ischemic conditions with low oxygen levels before decreasing glucose, change metabolism to anaerobic glycolysis in cells, catalyzed pyruvate to lactate by the enzyme lactate dehydrogenase (LDH) which makes the cytosolic environment acidic. This acidity is toxic to cells and the energy produced in anaerobic glycolysis is much less, namely only 2 ATP. The excess proton converts oxygen to hydrogen peroxide and reactive hydroxyl radicals.[13,14] The decreased Krebs cycle is due to the production of oxidative radicals from the predominant anaerobic glycolysis pathway15 as shown in Figure 2.1. Conditions of oxidative stress and the formation of free radicals add to the toxicity conditions in neurons.[10] Low oxygen

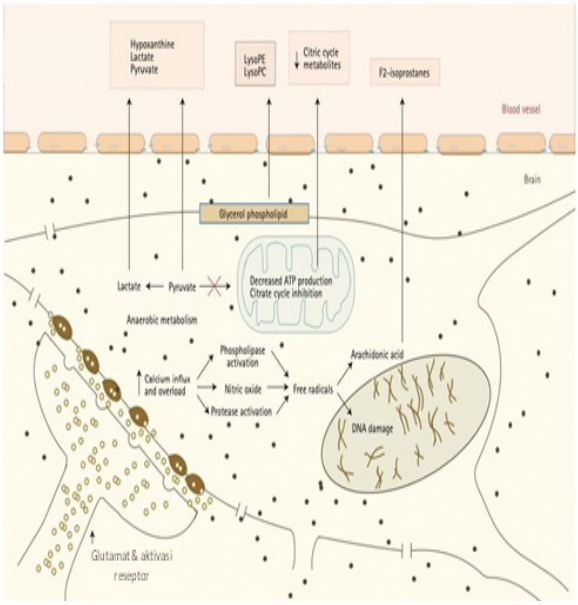

Figure 2. Metabolit in neuron after ischemic condition. Note: BCAA (Branched-chain amino acid); LysoPE (lysophosphatidylethanolamine); LysoPC (lysophosphatidylcholine)[13]

levels in cerebral ischemic conditions change metabolism to anaerobic glycolysis, in which much less ATP is produced. This condition results in failure of the calcium and sodium pumps due to limited ATP. Intracellular sodium and calcium levels become excessive while potassium is low, resulting in excessive neuronal depolarization. These conditions activate catabolic enzymes that plays a role in oxidative stress.[19] Oxidative stress in cerebral ischemia is caused by the production of derivatives of oxygen and excessive metabolic dysfunction. Derivatives of oxygen to produce ATP, one of which is Reactive Oxygen Species (ROS), is produced in the mitochondrial respiration chain and superoxide is converted to hydrogen peroxide, as a signal carrier, by the enzyme superoxide dismutase. This over-conversion of hydrogen peroxide makes the environment more acidic, compounded by the conversion of more active molecules, namely hydroxyl radicals. This activation triggers the influx of calcium into cells which mediates cell apoptosis and the formation of F2-isoprostane from the free radical peroxidation process of arachidonic acid. High levels of F2-isoprostane is a marker of oxidative stress.[11,13] The anaerobic pathway also produces molecules other than lactate, namely hypoxanthine and uric acid. This increased level is an indicator that the body is trying to protect itself from the effects of free radicals.[12]

Conditions of oxidative stress trigger an inflammatory response, with activation of glial cells, neutrophils, monocytes, and lymphocytes. Increased proinflammatory cytokines, glutamate neurotransmitters and metabolites associated with inflammation, such as catecholamines, cortisol, glucagon, IL-6, IL-1RA and proteins in peripheral plasma are evidenced of increased inflammation in stroke. This interferes with the metabolism of lysophosphatidylethanolamine (LysoPE) and lysophosphatidylcholine (LysoPC) which are important molecules for phospholipidglycerol metabolism as the backbone of neuronal cell membranes. This inflammation also activates matrix metalloproteinase-9 (MMP-9) which is continuously associated with damage to the blood-brain barrier and toxicity to neuronal cells.[11] Metabolites that plays a role in neuronal damage are shown in Figure 2. The next phase is a period when the body mobilizes nutrients to meet high metabolic needs due to stress.[18] Systemic consequences occur after a stroke, peripheral immunodepression in conjunction with overstimulation of the autonomic and neuroendocrine systems. Damage to cerebral tissue activates the hypothalamic-pituitary-adrenal axis which resulted in increased levels of glucocorticoid hormones, catecholamines and glucagon which will cause hypermetabolism (increased energy consumption), hypercatabolism (increased protein breakdown) and persistent hyperglycemia.[14] Energy requirements increase due to stress caused stroke, while food intake is reduced due to impaired ability to eat, the body will use its fat and protein stores as fuel to produce glucose. Muscle and fat tissue experiences degradation due to the breakdown of amino acids to form energy.[13] The body will enter an adaptation phase where stress hormone levels and glucose levels will decrease and the body's metabolism returns to normal. All of these can happen if nutrient and energy needs are met not only from the body's own stores but also from

food intake, especially oral, enteral nutrition and, if necessary, parenteral nutrition. Malnutrition will occur if adaptation is not achieved.[18]

IV. Malnutrition

Malnutrition is an abnormality in nutritional status where there is an imbalance of energy, protein and other nutrients which causes changes in tissue (shape, size and body composition), physiology, resulting in clinical outcomes.[9,15] This imbalance can be in the form of nutritional deficiencies or excessive nutrition. Metabolic needs that do not match nutritional intake in the long term, cause changes in body composition and function.[8] All forms of malnutrition are associated with various forms of poor health and higher mortality rates.[16] Although the term malnutrition includes excess nutrition, the European Society of Parenteral and Enteral Nutrition (ESPEN) focuses more on nutritional deficiencies as a major problem in hospitals.[14] Nutritional status is a state of balance between the intake of nutrients from food and the need for nutrients needed for body metabolism. Each individual requires different nutritional intake, this depends on age, gender, daily activities and body weight.[17] Nutritional status will change when reserves of energy, protein, water, vitamins or minerals fluctuated, as a result of increased needs, changes in use or changes in intake.[18] Good nutritional status depends on good nutritional intake and it will influence ohysiological condition.[18]

V. Factors that Influence Malnutrition in Stroke Patients

Old age, degree of severe stroke, hemorrhagic stroke, lack of family support and care, previous mobility limitations or previous stroke with sequelae and impaired swallowing are at high risk for malnutrition in stroke patients.[11] Ninety percent of stroke patients are over 65 years of age, may increase the likelihood of additional nutritional problems.[19] At the time of hospital admission, the presence of chronic diseases, polypharmacy, feeding difficulties, and functional disabilities are associated with an increased risk of malnutrition, especially in elderly patients.[8] The main effects on the gastrointestinal tract after stroke are impaired oral, pharyngeal, and esophageal function, which will manifest as dysphagia. Dysphagia can improve by itself after a few days of stroke onset but there are some patients who even persist for a longer period of time.[12] The appearance of dysphagia is a major risk factor for malnutrition in stroke patients. In the acute phase, dysphagia appears in 30–50% of patients and increases the risk of aspiration pneumonia and malnutrition by twelve times. Patients without dysphagia can still fall into a state of malnutrition when nutritional intake is inadequate, especially protein.[12] Feeding tube have been used in dysphagia in stroke patients were strong predictors of malnutrition upon admission to hospital.[19,20] Malnutrition will worsen as a result dysphagia if nutritional intake is substantially reduced from daily and weekly requirements.[20]

Female gender is said to be a risk factor for malnutrition in stroke patients.[12] In general, the prevalence of malnutrition in women is higher than in men. This can be caused by socioeconomic, cultural, demographic and dietary characteristics factors. Differences in thinking patterns, appearance demands and psychological conditions in women are also factors that play a role in the fall in malnutrition.[11] These psychological conditions can also influence the emergence of depression, especially post-stroke depression.[12] Post-stroke depression can reduce appetite and affect daily life activities recovery. Stroke patients are often given antidepressants and xerostomia prevention drugs, the effect of this treatment must be monitored so that eating difficulties do not occur.[20] Several studies say that depression is a major determinant of malnutrition due to low food intake where poor appetite and chewing disorders are experienced by patients.[13] Disorders of cognition, visual, language and speech are all results in impaired communication, especially regarding food choices and feelings of hunger and satiety which lead to the possibility of malnutrition. Fatigue when eating can be a factor in stopping eating early in stroke patients.[12,20]

In healthy older adults, muscle protein synthesis can reduce by 30% and reduce leg muscle mass by

6% resulting in a decrease in muscle strength by 16% after 10 days of bed rest. Patients with stroke also often experience fatigue which resulted in eating disorder. Patients can stop eating before they are full, because the patient needs to rest or even fall asleep. If the patient eats and drinks too little it can worsen fatigue and result in malnutrition.[18] Malnutrition at the start of treatment is the basis for worsening nutritional status and increases the likelihood of developing pneumonia, infection and gastrointestinal bleeding. All of these conditions increase nutritional needs in stroke patients, but the correlation between pneumonia and other infections and malnutrition is not sufficiently proven due to data instability.[12] Gastrointestinal bleeding is one of the complications of stroke which is still a serious problem because it can interfere with nutritional intake so that it is at risk for malnutrition, increasing morbidity and mortality.

The incidence of gastrointestinal bleeding in hemorrhagic stroke is around 26.7%, while infarct stroke is lower, namely 0.1–8%.[19] The mechanism of gastrointestinal bleeding in hemorrhagic stroke and infarction is different. The space pressure effect due to a hematoma in a bleeding stroke will suppress the pituitary gland so that it secretes adrenocorticotropic hormone (ACTH) which will stimulate the adrenal cortex to produce cortisol. Cortisol will stimulate the release of stomach acid and pepsin which causes ulcers and gastrointestinal bleeding. Meanwhile, stroke infarction is mainly caused by a neuroinflammatory process, namely an increase in inflammatory mediator cells due to brain ischemia. This neuroinflammatory process stimulates vagal hyperactivity in the brainstem which resulted in increased stomach acid.[19,20] Other important factors when assessing the risk of malnutrition in stroke patients is the level of decreased consciousness, mobility, paresis of the face and arms and also oral hygiene.[12] The type and severity of stroke are the main risk factors for malnutrition, especially in subarachnoid hemorrhage strokes which produce a condition of hypercatabolism in the body, However, on the contrary, stroke location, dominant paresis of the arm, socioeconomic status, and education were not significantly associated with malnutrition.[20] Vitamin B, vitamin D, antioxidants (vitamins A, C, and E), and zinc often decrease in patients with acute stroke at the time of hospital admission and decrease further during treatment.[2] These deficiencies contribute to changes in blood vessels in the brain and increase the risk recurrent stroke and cognitive impairment in old age.[18]

VI. Malnutrition as a Poor Prognostic Factor in Stroke Patients

Many evidences have been found that malnutrition is associated with a poor prognosis in patients with ischemic and hemorrhagic strokes.[12,20] Lack of protein energy (PEM) at the time of admission affects the mechanism of ischemic brain injury and impairs recovery. PEM can cause changes in gene expression related to plasticity associated with recovery mechanisms after extensive ischemia.[7] Lack of protein energy can also cause changes in proteins related to hippocampal plasticity, indicating that PEM can cause abnormalities in the structure, function, and plasticity of hippocampal fibers.[17] After extensive ischemia, KEP intensifies the expression of trkB and GAP-43 proteins in the hippocampus, which exhibits increased stress response and hyperexcitability in hippocampal circuits.[17,20] Malnourished patients with stroke experience a higher stress reaction, which increases the occurrence of peptic ulcers, infections of the respiratory tract and urinary tract, thus extending the length of stay and increasing mortality.[11,20] In a recent large-scale epidemiological study of 21,884 stroke patients who were treated , the mortality rate after 5 years was higher in the underweight group.[17] Among 2,194 post-stroke patients who were given the Feed Or Ordinary Diet (FOOD) trial, patients with poor nutrition were more likely to experience pneumonia, infection, and gastrointestinal bleeding. Malnourished patients also had a higher mortality rate over a median follow-up period of 196 days.[12]

Low serum protein and albumin values are markers of malnutrition, which are associated with impaired functional body status, poor prognosis, and high mortality.[12] However, the role of serum protein and albumin as markers of malnutrition

is still controversial in stroke patients, because as a critical disease, it can increase the occurrence of inflammation, thereby increasing energy expenditure and increasing muscle catabolism resulting in decreased levels of circulating protein. Therefore, a low protein value in stroke patients is a doubt between malnutrition or inflammation.[10] However, in patients with acute stroke, a low serum albumin concentration can predict mortality during hospitalization and the need for treatment.[12] In young patients with an ischemic stroke, serum prealbumin (transthyretin, PA) is also an independent predictor of clinical course.

Serum values of vitamins A, E, and C often fall in patients with acute stroke at the time of admission and decrease further during hospitalization.2 These decreased values indicate malnutrition or are the result of increased oxidative stress during acute stroke.[15] Low vitamin values associated with more extensive cerebral infarction, functional decline, and a higher mortality rate.[2] Dehydration can exacerbate the ischemic process by increasing the hematocrit and blood viscosity and lowering blood pressure. Dehydration increases the risk of recurrent stroke and stroke patients with high plasma osmolality values at the time of hospital admission have a survival rate of less than 3 months.[15] Comorbid lung infections increase nutritional needs which have increased with inflammation in stroke, this is not accompanied by increased intake due to neurological deficits, especially swallowing disorders/dysphagia, so that nutritional needs are not met.[13] Stroke patients are reported to experience swallowing disorders by 30 - 50%.[14] This neurological deficit interferes with nutritional intake and increases the risk of aspiration, which can cause comorbid lung infections which also pose a risk of falling into undernutrition status. This research is in line with Amalia's research conducted in Bandung which showed a high prevalence of comorbid lung infections in stroke patients with malnutrition status,[16] however the correlation between lung infections and malnutrition is not yet sufficiently proven due to data instability.[13] Malnutrition status at the start of treatment is the basis for worsening nutritional status and increases the possibility of complications in stroke patients. Disruption of the recovery process due to insufficient nutrition can increase the morbidity and mortality of stroke patients, this will worsen existing malnutrition.[8]

VII. Conclusion

Systemic consequences occur after a stroke, peripheral immunodepression in conjunction with overstimulation of the autonomic and neuroendocrine systems. Energy requirements increase due to stress caused stroke, while food intake is reduced due to impaired ability to eat, the body will use its fat and protein stores as fuel to produce glucose. Malnutrition will occur if adaptation is not achieved. Malnourished patients with stroke experience a higher stress reaction, which increases the occurrence of peptic ulcers, infections of the respiratory tract and urinary tract, thus extending the length of stay and increasing mortality, if not fulfilled properly the nutritional needs.

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