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Characteristics of Ischemic Stroke Patients Performed by DSA Actions at Chasbullah Abdul Madjid Bekasi Regional General Hospital

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ABSTRACT

Stroke has become the second leading cause of death and the third leading disability globally caused by several factors, such as hypertension, diabetes Mellitus, atrial fibrillation, and cholesterol. DSA (*Digital Subtraction Angiography*) has been the gold standard for diagnosing abnormalities in *cerebrovascular*, such as aneurysms and malformation artery and vena. *Cerebral* DSA is a safe procedure and has the advantage that intervention procedures such as stent insertion or thrombectomy can be performed immediately after angiography. This research is intended to find the characteristic of a stroke patient treated with Digital Subtraction Angiography. The design used in the study is retrospective with a medical record of a stroke ischemic patient who was treated with Digital Subtraction Angiography at RSUD CAM Bekasi from August 2020 - to June 2021. The sampling technique of this study was taken using total sampling techniques; namely, the entire population that the researcher had determined was a research sample. Forty-nine patients are used as the research sample according to the inclusive criteria. As a result, it has been found that the demographic in which Digital Subtraction Angiography has been utilized is 41-59 years old (61.2%), of which 65.3% of them are male patients. Based on their education, most of them come from strata 1, sitting at 61.2%, and their occupation is commercial workers, sitting at 26.5%. Risk factors that come with Digital Subtraction Angiography are hypertension (91.8%) and vertigo symptoms (55.1%). For motoric patients, 12.3% have seen improvements. Meanwhile, according to the *National Institute of Health Stroke Scale*, 46.9% have seen improvements. Digital Subtraction Angiography results show that 53.1% of ischemic stroke patients have improved.

Keywords: *Stroke Ischemic, Digital Subtraction Angiography*

INTRODUCTION

Every year there are an additional 13.7 million new stroke cases globally, and 5.5 million people died each year due to stroke in 2016 [1]. Therefore, stroke is the 2nd leading cause of death globally and the 3rd cause of disability globally [2]. Globally, stroke occurs in 1 in 4 people over 25 years [1]. In Indonesia, stroke prevalence increased 7% in 2013 and increased by 3.9% to 10.9% in 2018 [3]. According to the World Health Organization, stroke is a condition in which clinical signs develop rapidly in focal and global neurologic deficits that can interfere with cerebral function and last more than 24 hours or cause death without any other cause other than vascular. Stroke can occur due to blockage of blood flow to the brain or rupture of arteries to the brain, causing cell/tissue death due to lack of oxygen [4].

The division of stroke is based on anatomic pathology and clinical manifestations, namely ischemic stroke and hemorrhagic stroke. Hemorrhagic strokes occur due to the rupture of blood vessels that cause bleeding in the brain, while ischemic strokes occur due to obstruction, namely blockage or cessation of blood flow to the brain [5]. Based on its incidence, ischemic stroke is a type that often occurs with the incidence of 9.5 million new cases with a mortality rate of 2.7 million every year in the world, while hemorrhagic stroke there are 4.1 million new cases with a mortality rate of 2.8 million each year. in 2016 in the world [1]. Age, sex, race, and genetics are non-modifiable risk factors for stroke, while those that can be modified are hypertension, atrial fibrillation, diabetes, smoking, hyperlipidemia, obesity, diet, and physical activity. There are also new risk factors such as sleep apnea, lipoprotein (a), and antiplatelet medication [6; 7].

Based on the management, the American Stroke Association gives intravenous tissue plasminogen activator (tPA) within 3 hours-4.5 hours after stroke. Public awareness is still low about stroke, making patients often come to the hospital more than the specified time so that patients are not given tissue plasminogen activator (tPA) [8]. DSA (Digital Subtraction Angiography) has become the gold standard for diagnosing cerebrovascular abnormalities such as aneurysms and malformations of arteries and veins and determining the occlusion site in cerebral blood vessels based on the resulting images. DSA itself has been used since 1980 and is a marker of a new era as a diagnostic tool capable of performing endovascular procedures [9]. Cerebral DSA is a safe procedure and has the advantage of performing interventional procedures [10]. Interventional procedures can be performed quickly after angiography, such as thrombectomy and insertion of a stent. To reduce the complications of DSA, anticoagulants such as heparin are usually used. Heparin is an anticoagulant drug and is commonly used as a flushing solution to minimize thrombus formation on the outer surface of the catheter and prevent thromboembolic complications [11].

Based on the above background, the authors are interested in researching the characteristics of ischemic stroke patients treated with DSA at the CAM Bekasi Regional General Hospital. Based on the experience described by the authors, a problem formulation was obtained, namely how the characteristics of ischemic stroke patients who were treated with DSA at the CAM Bekasi Regional General Hospital. With the aim of research to determine the characteristics of ischemic stroke patients who underwent DSA action at the CAM Bekasi Regional General Hospital.

LITERATURE REVIEW

Ischemic stroke is a heterogeneous multifactorial disorder recognized by neurological signs directly related to the location of the brain that is damaged where the pathological process takes place with a sudden onset [12]. According to the AHA/ASA, ischemic stroke is defined as neurological dysfunction caused by focal cerebral, spinal, and retinal infarction19 and represents 71% of stroke cases globally [6]. According to the World Stroke Organization, in 2016, the global incidence of ischemic stroke was 9.5 million new cases, 60% of new cases occurred under 70 years of age, and 7% of new cases occurred under 44 years of age [1]. In terms of gender, more men suffered from ischemic stroke, namely 52%, as many as 5 million new cases, and women with ischemic stroke as many as 48%, namely 4.5 million patients. Every year 2.7 million people die from ischemic stroke. In men, 49% of deaths from ischemic stroke, and 51% in women. The prevalence of hemorrhagic stroke is more than 15 million people affected by a hemorrhagic stroke, with 4.1 million people suffering from a hemorrhagic stroke in 2016. Hemorrhagic stroke is influenced mainly by people under 70 years of age, as many as 60% of new cases, and

10% under 44 years old. The incidence of hemorrhagic stroke is more significant than in women, with 53% in men and 47% in women. Most deaths from stroke are due to hemorrhagic stroke, which is 51%.

Ischemic stroke can occur due to a circulatory disorder of the brain, which is usually caused by thromboembolism, resulting in cell necrosis due to a lack of oxygen and energy in the nerve cells, which disrupts the transmembrane ion gradient and homeostasis so that it will cause damage to the blood-brain barrier. There is also a response: excitotoxicity, oxidative and nitrate stress, inflammatory response, and apoptosis [13]. The pathological process causes severe damage to neurons, glial and endothelial cells.

A decrease in oxygen levels in the brain is caused by blockage resulting in ischemia, failure of oxidative phosphorylation, and ATP synthesis, making ATP consumed within 2 minutes [9]. Reduction of ATP synthesis results in the transmembrane ion gradient loss, which prevents the Na+/K+, ATPase, and Ca2+-ATPase pump from functioning correctly, causing sodium to accumulate in the cell and release potassium in the extracellular membrane was, leading to the opening of L-type Ca2+ voltage gate channels and pumps. Na/Ca2+ makes calcium unable to get out, so calcium builds up in the intracellular membrane, which causes high Ca2+ levels resulting in cell depolarization and triggering the release of glutamate. It causes excessive cell excitation, resulting in the release of harmful substances such as ROS (Reactive Oxygen Species) and the activation of signaling proteins such as proteases, phospholipases, endonucleases, and DNases which are a group of calcium-dependent degrading enzymes [14; 15]. When phospholipases disrupt the cellular membrane, many harmful chemicals enter the cell, causing the release of apoptotic signals from the mitochondria and triggering the caspase cascade that causes cell death. The accumulation of sodium in the cells also increases the intracellular pressure, making H2O follow a higher gradient so that it enters the cell and causes cytotoxic edema [14].

When ischemia occurs, the activation of -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) and N-methyl-D-aspartate (NMDA), which are glutamate receptors, causes the membrane to depolarize so that there is an increase in intracellular calcium causing excitotoxicity. Expression of the sodium-calcium exchange gene NCX influenced by cerebral ischemia may ameliorate the consequences of ischemic brain damage, but decreased expression in the NMDAR-mediated NCX gene results in calcium overload. When excitotoxicity occurs, there is also an increase in mitochondrial calcium concentration, which produces ROS and will induce neuronal cell death [16].

NMDAR has subunits that are divided into NR1, NR2, and NR3. The NR2 subunits have different diverse structures and have other signaling functions. In stroke, NR2AR and NR2BR are subunits required for glutamate mediation and are associated with neuronal cell death and neuronal cell survival. Under normal conditions, NMDAR (NR2A dominant) synaptic transmission stimulates neuronal survival (NSC) signaling, but under pathological conditions, an increase in extracellular glutamate concentration causes excitatory and excessive NMDAR (NR2B dominant) synaptic activation [16]. Activation of NR2B causes an increase in calcium, promotes ADAPK (active death-associated protein kinase), and binds to NR2B [17]. It leads to activation of the cell death complex signaling (NDC), thereby suppressing the synaptic neuronal survival complex activity. In addition, the excitotoxicity of the cell death complex also involves death signaling proteins such as calpains. Increased calpains cause calcium influx through NMDAR, resulting in neuronal cell damage.

Mitochondria have an essential role in cellular energy homeostasis. When ischemia occurs, where the energy balance

is disturbed, there is a reduction in ATP synthesis and ROS increase, leading to disruption of membrane channels essential for normal function. The damage caused by ROS to proteins, fats, and DNA is very high. Fat peroxidation disrupts neuronal homeostasis and induces apoptosis by involving the production of a toxic aldehyde called 4-hydroxynonenal, which binds to membrane molecules, thereby interfering with their normal function. The occurrence of a rapid calcium influx and the circumstance of excitotoxicity leads to calcium accumulation in the mitochondria, which causes dysfunction resulting in the opening of the mitochondrial permeability transition pore (MPTP) and triggers the death pathway through caspase-dependent (Cytochrome C) and caspase-independent (AIF) processes. Factors leading to apoptosis and brain cell death [18].

Oxidative stress and nitrates occur when the production of free radicals such as nitrogen species or reactive oxygen species (ROS/RNS) is formed due to a lack of capacity of the antioxidant system. After an ischemic stroke occurs, the lack of energy causes lactic acid to accumulate and causes acidosis in the neuron cells. Acidosis has a pro-oxidant effect by increasing the concentration of H+ and increasing the rate of conversion of superoxide (O-2) to hydrogen peroxide (H2O2) and hydroperoxyl radicals (HO2). The brain is vulnerable to free radical attack due to the highly oxygenated environment of the neurons, coupled with low levels of peroxidable lipids and endogenous antioxidants [19].

In ischemic stroke, several ROS-producing enzymatic systems are activated, including NADPH oxidase (NOX), mitochondrial depolarization, xanthine oxidase (XO), and nitric oxide synthase (NOS). Cyclo-oxygenase (COX). NADPH oxidase produces most of the superoxide anion [20]. RNS enhances ROS signaling in cells. NO (Nitric Oxide) has three sources, namely endothelial NOS (eNOS), which helps maintain cerebral blood flow, but if it binds to O2- it produces nitrosative stress, NOS neurons (nNOS/NOS1), and NOS induction (iNOS/NOS2) which can lead to excessive NO production from different stimuli in glial cells. NO (Nitric Oxide) is highly reactive, and superoxide can combine to form a highly toxic anion, namely peroxynitrite. Free radicals trigger the PI3-kinase/Akt pathway and rearrange NF-KB's transcription factors [6].

Cerebral ischemia reduces blood supply to the penumbra region and triggers a complex cascade. The immune response that occurs when an injury occurs first is the innate body system such as macrophages, neutrophils, dendritic cells, NK cells that are released from intracellular compartments or produced by the action of lytic enzymes released from dead cells on matrix proteins which are usually called danger-associated molecular pattern molecules (DAMPs). DAMPs activate microglia, astrocytes, macrophages, and endothelial cells through pattern recognition receptors (PRPs) such as the Toll-like Receptor (TLR) [21].

Microglia activation and release of pro-inflammatory cytokines such as TNF-, IL-1β, and IL-6 and the release of chemokines CCL2 and CCL3 for neutrophil recruitment and CCL2 and CC chemokine receptor 2 (CCR2) receptors, are responsible for macrophage recruitment [30]. In addition, in early stroke, fractalkines are released from ischemic-affected neurons to recruit NK cells to the ischemic zone. NK cells make ischemic neuron cells release the main cytokine, TNF, increasing glutamate release and producing hyperactivity and excitotoxicity. Other cytokines are also released, such as IFN-γ and GM-CSF, which will activate microglia, macrophages, and astrocytes, which release inflammatory mediators such as IL-6, IL-1β, and NO [22].

Ischemia also activates macrophages present in the perivascular space and releases pro-inflammatory cytokines, chemokines, ROS, and NO. ROS causes the expression of pro-inflammatory genes such as nuclear factor kappa B (NFkB), interferon regulatory factor 1 (IRF1),

hypoxia-inducible factor 1 (HIF1), and STAT3, which will increase the expression of cytokines and adhesion molecules. Cellular adhesion molecules such as ICAM-1, P-selectin, and E-selectin are expressed in inflammatory brain endothelial cells. The function of adhesion molecules is for the migration of neutrophils [19].

Matrix metalloproteinases (MMPs) are a family of proteolytic enzymes responsible for the breakdown of the extracellular matrix that can degrade all of its components. MMP expression is increased in the brain in response to injury. After the injury, MMP expression is shown in several cells, such as astrocytes, microglia, and endothelial cells. Experimental studies have shown that MMPs such as MMP-9 and MMP-2 are responsible for disrupting the blood-brain barrier and leading to hemorrhagic transformation after ischemic stroke. MMP-9 is associated with neuronal cell inflammation [19; 22].

The adaptive immune system takes a long time. CD4+ and T helper cells activate and direct other immune cells such as CD8+ and cytotoxic T cells that can directly induce cell death. Regulatory T cells (Tregs) exert their neuroprotective function by secreting inhibitory cytokines, such as TGF, IL-10, and IL-35 [22]. Intrinsic stimuli for apoptosis are activated by mitochondrial signaling pathways, while extrinsic incentives trigger cell surface death such as TNF-, Fas (CD95/APO1), and TRAIL (TNF-related apoptosis-inducing ligand) receptors [19]. During ischemia, the activation of NMDARs causes the accumulation of Ca2+ in the intracellular, which causes cleavage of the Bcl-2 interacting domain (BID) to truncated Bid (tBid). The mitochondrial surface (tBid) interacts with pro-apoptotic proteins such as Bad-Bax and opens mitochondrial transition pores (MTP). MTP opening promotes the release of mitochondrial cytochrome c (Cytc) and apoptosis-inducing factor (AIF). In the presence of ATP/dATP, Cytc binds to Apaf-1 (apoptotic protease activating factor 1) and procaspase 9 to form apoptosome. Apoptosomes will activate caspase nine, which results in the activation of caspase 3. Caspase 3 results in the nuclear DNA repair enzyme cleavage, resulting in damage and cell death [23].

The extrinsic pathway is initiated through ligand receptors that can induce independent caspase activation. One of the ligand receptors such as TRAIL, FASL, and TNF binds to the TNF receptor, Fas (Faso), TRAIL, which causes the activation of caspase eight and caspase ten which will activate caspase three, which can result in mitochondrial membrane permeabilization, chromatin condensation, DNA fragmentation which leads to death. cell [19]. In hypertension, there is an increase in systemic pressure in the microvasculature, which causes premature aging. The impaired release of EDRF (endothelium-derived relaxing factors), decreased levels of NO synthesis and increased ROS production causes vasoconstriction and increased systemic vascular resistance. Oxidative stress and endothelial dysfunction are associated with inflammation. Changes in endothelial cells can lead to Atherosclerosis, which can lead to inflammation and thrombosis if released. In hypertension, Ang II triggers TF expression in monocytes, endothelial cells, and vascular smooth muscle cells through the Ang II type 1 receptor. Acellular lipids are high in fat, and cytokines, such as TNF, stimulate their expression at the endothelial level-, interleukin-1β, CD40 ligand, and by biogenic amines, such as serotonin, histamine, and mediators such as thrombin, oxidized LDL, or by mediators of vascular endothelial growth factor, such as TNF, CD40 ligand, histamine, thrombin, endotoxin, platelet-derived growth factor-BB (PDGF-BB) and LDL aggregate [24].

Standard arterial walls have a trilaminar structure. The outermost layer, the adventitia, contains nerve endings, mast cells, and the vasa vasorum, the micro blood vessels that nourish the outer layer of the media. The tunica media comprises smooth

muscle cells and a well-organized extracellular matrix composed of elastin, collagen, and other macromolecules. Atherosclerotic plaques form in the deepest layer, the tunica intima. In the early stages of low-density lipoprotein (LDL) particles accumulating in the intima, monocytes circulating in the blood vessels can bind to adhesion molecules expressed by endothelial cells.

Chemokines can trigger the migration of bound monocytes to the arterial wall. Monocytes can turn into macrophages in the intima that bind to oxidized LDL and form foam cells, and smooth muscle cells can migrate into the intima in response to the accumulation of leukocytes. Smooth muscle cell recruitment produces extracellular matrix molecules (interstitial collagen, elastin, proteoglycans, and glycosaminoglycans) that contribute to intima layer thickening. However, T cell mediators such as IFN-γ can impair the ability of smooth muscle cells to synthesize interstitial collagen, which will affect the ability to repair and maintain the fibrous covering of the necrotic nucleus. Activated macrophages produce enzymes from the class of matrix metalloproteinases (MMPs), which degrade interstitial collagen, resulting in thinning and structural weakening of the fibrous cover, making it easy to rupture. Smooth muscle cells and macrophages undergo apoptosis. Debris from dead cells Smooth muscle cells and macrophages undergo apoptosis, and debris from dead cells collects and forms a necrotic, lipid-rich atheroma core. Impaired efferocytosis, i.e., clearance of dead cells, can contribute to the formation of necrotic nuclei [25].

Rupture of the fibrous cover within the atherosclerotic plaque allows clotting components to access the core of the plaque. Pro-coagulant substances such as tissue factors can trigger thrombosis, leading to occlusion of blood vessels and acute ischemic events. Thrombus is a source of transforming growth factor-β (TGFβ) and platelet-derived growth factor, which is elaborated by the activation of platelets, which can stimulate smooth muscle cell migration and production of extracellular matrix, leading to increased volume and disruption of the arterial lumen. White thrombi have characteristics that are rich in platelets. It occurs because there is superficial erosion, whereas red thrombi are characterized by being rich in fibrin and trapped erythrocytes. It is associated with plaque rupture [26].

The left atrial appendage (LAA) originates from the atrial thrombus. Atrial fibrillation induces blood stasis, hypercoagulability, and platelet activation. Atrial tissue increases cytosolic calcium by activating calcium-dependent proteases and phosphatases, leading to the destruction of contractile filaments, impaired mitochondrial function, and atrial myocyte hypertrophy. In addition, there is an increase in ROS that causes the synthesis of prothrombotic tissue factors in the left endocardial endothelium, such as plasminogen activator inhibitor (PAI)-1, von Willebrand factor (vWF), and adhesion molecules (ICAM, VCAM, selectin). Angiotensin-II affects left atrial endothelium adhesion, which may increase the incidence of atrial thrombi [27].

Increased concentrations of inflammatory markers such as CRP (C-reactive protein) and IL-6 can mediate inflammatory signals that affect the prothrombotic state. Coagulation factors, such as thrombin, factor X, and factor II exert significant cellular effects induced by binding clotting factors to proteinase-activated receptors (PAR). Activation of clotting factor X (FXa), factor V (FVa), phospholipids, and calcium ions from a prothrombinase complex will activate prothrombin (FII) to thrombin (FIIa). FXa may also act as a mediator of inflammatory signaling through PAR1 and PAR2 activation. The synergistic action of FXa and atrial tachyarrhythmias results in a response that causes an increase in inflammatory molecules and oxidative stress that is inflammatory and prothrombotic in the atrial endocardium [28].

RESEARCH METHOD

The type of research used by the researcher is a descriptive content analysis study that aims to determine the characteristics of ischemic stroke patients who underwent DSA action at the CAM Bekasi Regional General Hospital. It is based on past medical records to see the situation objectively and is expected to be able to use as input for performing DSA in ischemic stroke patients. The location of data collection in this research was carried out at CAM Bekasi Hospital. The study's processing, assembly, and implementation time was carried out from April 2021 to January 2022. The population of this study was all ischemic stroke patients who underwent DSA action at CAM Bekasi Hospital from August 2020 to June 2021. The samples taken in this study were ischemic stroke patients from August 2020 to June 2021. The sampling technique of this study was taken using the Total Sampling technique; namely, the entire population that the researcher has determined is the research sample. The research instrument used is secondary data: the medical record of ischemic stroke patients for August 2020 - June 2021 at the CAM Bekasi Regional General Hospital. Research data processing is done through data editing, tabulation, and analysis. The identity of Ischemic Stroke patients at the CAM Bekasi Regional General Hospital from August 2020 to June 2021 is kept confidential and is not included in the study results.

RESULT AND DISCUSSION

This study was obtained from data on ischemic stroke patients carried out by DSA from August 2020 to June 2021 at the CAM Bekasi Regional General Hospital, with 49 patients included in the inclusion criteria. The data of 49 patients obtained data on age, gender, symptoms, onset, education, occupation, risk factors, motor, NIHSS, and post DSA. These data are the variables used in this study.

Table 1. Age Distribution of Ischemic Stroke Patients Performed DSA

Age	Frequency	%
19-24 Years	2	4,1%
25-40 Years	7	14,3%
41-59 Years	30	61,2%
60 Years	10	20,4%
Total	**49**	**100%**

Based on the table above, it was found that the most ischemic stroke patients who underwent DSA were in the age range of 41-59 years, with a frequency of 30 of 49 patients (61.2%), while the age range of 25-40 years had a frequency of 7 patients (14, 3%), and 60 had a frequency of 10 patients (20.4%), and the smallest was in the age range of 19-24 years with a frequency of 2 patients (4.1%). In the age range, 41-59 years has the highest frequency. With the improvement of the country's economic status as a developing country, the purchasing power of the people increases. Increased financial status makes lifestyle changes, such as eating fast food, buying sugary drinks, lack of physical activity caused by advanced technology, and controlling risk factors such as hypertension, diabetes, and dyslipidemia which are still very lacking. Based on HOPE Asia, hypertension in Indonesia is 34.1%; diabetes mellitus as much as 10.9%; dyslipidemia as much as 35.9%; 33.5% physical inactivity, and 29.3% smoking, all of which are which can increase the incidence of ischemic stroke [29].

Table 2. Gender Distribution of Ischemic Stroke Patients Performed by DSA

Gender	Frequency	%
Man	32	65,3%
Woman	17	34,7%
Total	**49**	**100%**

Men are the largest population of ischemic stroke patients who underwent DSA with 32 out of 49 patients (65.3%), compared to women with a frequency of 17 out of 49 patients and 34.7%. It is also found in the World Stroke Organization data, which states that men are more likely to suffer from an ischemic stroke than women. It is related to lifestyle, where men have the habit of smoking and drinking

alcohol, increasing the incidence of hypertension and increasing the risk of ischemic stroke [30].

Table 3. Education Distribution of Ischemic Stroke Patients Performed by DSA

Education	Frequency	%
Bachelor	30	61,2%
Senior High School	17	34,7%
Junior High School	2	4,1%
Total	**49**	**100%**

Bachelor with a frequency of 30 out of 49 patients (61.2%), then Senior High School with a frequency of 17 out of 49 patients (34.7%), and the last one was junior high school, with 2 of 49 patients (4.1%). From the results, it can be seen that S1 is the most frequent. It is related to socioeconomic status. According to Wang et al., high socioeconomic status has the possibility of low physical activity, and the level of stress received from social life and work can affect it. Stress can increase the risk of ischemic stroke by affecting blood pressure, cerebral endothelium, and coagulation. People who have the habit of relieving the anxiety they receive from stress by eating can lead to overeating, which tend to consume high-calorie foods frequently [31].

Table 4. Occupational Distribution of Ischemic Stroke Patients Performed by DSA

Work	Frequency	%
Housewife	11	22,4%
Government employees	3	6,1%
General employees	13	26,5%
Student	1	2%
Trader	8	16,3%
Self-employed	7	14,3%
Doesn't work	6	12,2%
Total	**49**	**100%**

Private employees are the most common occupations for ischemic stroke patients treated by DSA with a frequency of 13 out of 49 patients with 26.5%. It is associated with acute stress hormones and the occurrence of vascular disorders. When stress occurs, activation of the sympathetic-adrenal-medullary (SAM) axis will increase catecholamines, norepinephrine, and epinephrine, increasing the response of the endothelium and platelets to increase the occurrence of disorders of the blood vessels percentage 22.4%. It is related to the use of oral contraceptives, which can lead to hypercoagulability, in addition, and causes decreased estrogen levels, which can lead to increased blood pressure and metabolic syndrome, which increases the risk of ischemic stroke [30]. Traders became the subsequent most occupation with a frequency of 8 out of 49 patients with a percentage of 16.3%. It is related to stress risk factors. Stress can increase cerebrovascular disease by increasing sympathetic activity,58 then self-employed with 7 of 49 patients with a percentage of 14.3%. Based on Wang et al., people with high socioeconomic status have a great desire to shop and consume high-calorie foods and meat in excess, increasing the risk for obesity and cardiovascular disease and increasing the risk of ischemic stroke [31]. Patients who are no longer working also have a frequency of 6 out of 49 patients with a percentage of 12.2%. From the data on patients who do not work, it is found that most of them are retired, civil servants. Based on Kim et al., sleep deprivation due to changes in sleep schedules, loneliness, and lack of exercise in retirees are risk factors for ischemic stroke [32]. Civil servants have a frequency of 3 out of 49 patients with 6.1%. It is related to a sedentary lifestyle, which has low physical activity. Insufficient physical activity can increase the risk of ischemic stroke. Based on Balla et al., the work environment has undergone significant changes in technology, which makes people less physically active, which can lead to obesity, increasing the risk of ischemic stroke [33]. In a study conducted by Loprinzi et al., it was stated that when there was an increase in physical activity every 60 minutes/day, there was a 28% reduction in cases leading to stroke death [34]. Finally, students are 1 out of 49 patients with a frequency of 2%.

Table 5. Distribution of Hypertension Risk Factors in Ischemic Stroke Patients Performed DSA

Hypertension	Frequency	%
Yes	45	91,8%
No	4	8,2%
Total	**49**	**100%**

Hypertension is the most common symptom experienced by ischemic stroke patients undergoing DSA, with a frequency of 45 out of 49 patients with 91.8%. It is related to increased blood pressure due to impaired EDRF release, decreased NO, and increased ROS that can cause vasoconstriction and impaired endothelial function. It can lead to the formation of Atherosclerosis which, if there is a rupture of an atherosclerotic plaque, can trigger an inflammatory process and the occurrence of thrombosis so that it can trigger an ischemic stroke [24].

Table 6. Distribution of Cholesterol Risk Factors in Ischemic Stroke Patients Performed by DSA

Cholesterol	Frequency	%
Yes	26	53,1%
No	23	46,9%
Total	**49**	**100%**

In cholesterol ischemic stroke patients who underwent DSA, the frequency was 26 out of 49 patients who experienced it, 53.1%. Cholesterol is usually divided into LDL and HDL. An increase in LDL can lead to ischemic stroke. It is related to LDL that accumulates in the intima, which causes circulating monocytes to bind to the arterial walls, which can turn into macrophages which will attach to oxidized LDL and form foam cells. After that, smooth muscle cells migrate into the intima, producing the extracellular matrix that causes the thickening of the intima layer. Activated macrophages produce enzymes that can degrade interstitial collagen, resulting in thinning and structural weakening of the fibrous cover, making it easy to break. If it fails, thrombosis can occur, which causes occlusion of blood vessels and triggers an ischemic process.

Table 7. Distribution of Risk Factors for Diabetes Mellitus in Ischemic Stroke Patients Performed by DSA

Diabetes Mellitus	Frequency	%
Yes	16	32,7%
No	33	67,3%
Total	49	**100%**

In patients with diabetes mellitus, the frequency was 16 of 49 patients with diabetes mellitus with a percentage of 32.7%. The occurrence of diabetes mellitus is associated with increased circulating platelets through the induction of inflammatory pathways that lead to increased production of thrombopoietin, fibrinogen, plasminogen activator inhibitor-1 (PAI-1), tissue factor (TF), and factor VII (FVII), as well as decreased levels of anticoagulants as thrombomodulin and protein C, are increased which triggers thrombin formation which will trigger thrombus formation [35].

Table 8. Distribution of Atrial Fibrillation Risk Factors in Ischemic Stroke Patients Performed by DSA

Atrial Fibrillation	Frequency	%
Yes	12	24,5%
No	37	75,5%
Total	49	**100%**

Atrial fibrillation is one of the risk factors for stroke, with a frequency of 12 out of 49 patients who experience it 24.5%. It is related to the formation of atrial thrombus. Atrial fibrillation induces blood stasis, hypercoagulability, and platelet activation. Coagulation factors, such as thrombin, factor X, and factor II exert significant cellular effects caused by binding clotting factors to proteinase-activated receptors (PAR). Activation of clotting factor X (FXa), factor V (FVa), phospholipids, and calcium ions from a prothrombinase complex will activate prothrombin (FII) to thrombin (FIIa). FXa may also act as a mediator of inflammatory signaling through PAR1 and PAR2 activation. The synergistic action of FXa and atrial tachyarrhythmias results in a response that causes an increase in inflammatory molecules and oxidative stress that is inflammatory and prothrombotic in the atrial endocardium. It is also influenced by Angiotensin II, which impacts atrial endothelium adhesion so that it can increase the incidence of thrombus formation in the atria [27; 28].

Table 9. Distribution of Onset of Ischemic Stroke Patients Performed by DSA

Onset	Frequency	%
Acute phase	2	4,1%
Early subacute phase	7	14,3%
Late subacute phase	26	53,1%
Chronic phase	14	28,6%
Total	49	**100%**

The late subacute phase had the largest population, namely 26 of 49 patients with a percentage of 53.1%, which means that ischemic stroke patients who underwent DSA had an onset of more than 1-6 months. Furthermore, the chronic phase has a population of 14 out of 49 patients with a percentage of 28.6%, meaning ischemic stroke patients undergoing DSA have onset starting from 7 months and more. The early subacute phase had 7 of 49 patients with a percentage of 14.3%, which means that ischemic stroke patients who underwent DSA had an onset ranging from 1-to 4 weeks. The acute phase was the smallest, with a population of 2 of 29 patients with a percentage of 4.1%, meaning ischemic stroke patients undergoing DSA have an onset ranging from 1-7 days. From the results obtained that the late subacute phase is the largest population. It is related to the lack of knowledge about stroke symptoms and the robust community paradigm toward alternative medicine.

Table 10. Distribution of Symptoms in Ischemic Stroke Patients Performed by DSA

Symptom	Frequency Yes	%	Frequency No	%	Total
Vertigo	27	55,1%	22	44,9%	100%
Cranial Nerve Deficit	22	44,9%	27	55,1%	100%
Hemihypesthesia	12	25,5%	37	75,5%	100%
paresthesia	7	14,3%	42	85,7%	100%
Cephalgia	6	12,2%	43	87,8%	100%
Aphasia	4	8,2%	45	91,8%	100%

Based on the table above, the most vertigo symptoms experienced by ischemic stroke patients undergoing DSA were 27 of 49 patients and 55.1%. Then cranial nerve deficits became one of the symptoms of ischemic stroke patients undergoing DSA, namely with a total as many as 22 of 49 patients experienced it and had a percentage of 44.9%, hemihypestensi with a total of 12 of 49 patients experienced it and had a percentage of 25.5%. With 7 out of 49 patients, Paraesthesia experienced it and had 14.3%. Cephalgia is one of the symptoms experienced by ischemic stroke patients undergoing DSA, with 6 out of 49 patients experiencing it and having a percentage of 12.2%. The last is aphasia, with a frequency of 4 out of 49 patients with a percentage of 8.2%.

Table 11. Motor Distribution of Ischemic Stroke Patients Before DSA

Right Motor	Frequency	%
Muscles don't contract	1	2%
The joint movement against gravity, cannot resist resistance	1	2%
Joint movement, against gravity and light resistance	19	38,8%
Joint movement, against gravity and full resistance	28	57,1%
Total	**49**	**100%**

In the table above, it can be seen that there are 1 in 49 patients with a percentage of 2% who have non-contracting muscles, which means that based on the Manual Muscle Testing Scale (MMTS) has a score of 0 and also 1 in 49 patients experience joint movement against gravity but cannot resist resistance, which means it has a score of 3. For a score of 4, there are 19 of 49 patients, 38.8%, which means they experience joint movement against gravity and can resist light resistance. On a score of 5, there were 28 of 49 patients with a percentage of 57.1%, which means the patient experiences joint movement against gravity and can fight complete resistance.

Table 12. Motor Distribution of Ischemic Stroke Patients After DSA

Right Motor	Frequency	%
Muscles don't contract	1	2%
The joint movement against gravity cannot resist resistance	1	2%
The joint movement against gravity and light resistance	13	26,5%
The joint movement against gravity and complete resistance	34	69,4%
Total	49	**100%**

In the table above, it can be seen that there are 1 in 49 patients (2%) who have non-contracting muscles, so they have a score of 0. Also, 1 in 49 patients experience joint movement against gravity but cannot fight resistance, which means they have a score of 3, and for a score of 3, 4 found in 13 of 49 patients with a percentage of 26.5%, which means that they experience joint movement against gravity and can resist light resistance and it can be seen that after the DSA there was a decrease in the frequency of motor scores four from 19 to 13 people (12.3%). On a score of 5, there are 34 of 49 patients with a percentage of 69.4%, which means the patient experiences joint movement against gravity and can fight complete resistance. It shows that six patients experienced motor improvement after DSA, and it can be seen from the patients' frequency, which increased from 28 to 34 out of 49 patients, and there was an increase in the percentage of 12.3%.

The motor cortex regulates motor function in our body in the brain. In stroke patients who experience motor impairment, it is caused by reduced neuronal impulses in the motor cortex. Anatomically, there are two essential components in the motor cortex, namely the primary motor cortex (M1) and secondary motor cortex, which are divided into Posterior Parietal Cortex (PPC), Premotor Cortex, and Supplementary Motor Area (SMA). Neural impulses are triggered by M1, which controls the final execution of the motor system, after which the PPC functions to convert visual information into motor commands and, the Premotor Cortex as planning and coordinates movements and actions, the last SMA functions as planning for complex activities. Muscle contraction can occur when there is stimulation of neuronal impulses from the primary motor cortex, after which it passes through the corticospinal and peripheral motor neurons to send signals for contraction and movement to occur. When there is a lesion in the M1 area, due to the ischemic process, it can cause necrosis which will cause damage to the motor pathway and will cause a reduction in the ability to move muscles, so that muscle weakness occurs, and it is difficult to contract.

Table 13. Distribution of NIHSS Before Ischemic Stroke Patients Performed DSA

NIHSS Before	Frequency	%
Have no symptoms of a stroke	14	28,6%
Mild stroke	32	65,3%
Medium stroke	3	6,1%
Total	49	**100%**

NIHSS is done before and after the DSA action. From the table above, it can be seen that those who do not have stroke symptoms based on the NIHSS, namely 14 of 49 people (28.6%), have an NIHSS score of 0. In mild stroke, 32 out of 49 patients (65.3%) had a total NIHSS score of 1-4, then 3 out of 49 patients had a mild stroke (6.1%) and had a total NIHSS score ranging from 5-15.

Table 14. Distribution of NIHSS After Ischemic Stroke Patients Performed DSA

NIHSS After	Frequency	%
Have no symptoms of a stroke	37	75,5%
Mild stroke	9	18,4%
Medium stroke	3	6,1%
Total	49	**100%**

NIHSS is done before and after the DSA action. From the table above, it can be seen that those who do not have stroke symptoms based on the NIHSS, which are 37 out of 49 people (75.5%), have an NIHSS score of 0. It shows an improvement after the DSA with an increase of 23 people who do not have stroke symptoms, with a percentage increase of 46.9%. In mild stroke, the total NIHSS score ranged from 1 to 4, obtained nine patients from 49 patients with a percentage of 18.4%, which means that it has a decrease in the frequency of 23 people (46.9%). Of 49 patients (6.1%) and had a total NIHSS score ranging from 5 to 15.

Table 15. Distribution of Post DSA Results in Ischemic Stroke Patients Performed by DSA

Post DSA	Frequency	%
Yes	26	53,1%
No	23	46,9%
Total	49	**100%**

In the table above, it can be seen that there were changes in symptoms, motor and

NIHSS scores improvement experienced after DSA in as many as 26 of 49 patients (53.1%). It is related to the type of thrombus. There are usually two types of thrombi in stroke, namely rich in fibrin and rich in red blood cells. Thrombus permeability can increase the rate of dissolution of thrombolytic drugs, and permeability increases the contact surface area of the medicine with the thrombus, facilitating the fibrin network's dissolution. When a thrombus forms, there is a clot shrinkage in the resolution phase of the thrombus, leading to a redistribution of platelets and fibrin to the periphery of the clot and red blood cells inward. Red blood cells are compressed into polyhedrocytes. The permeability of polyhedrocytes is so low that it can have significant implications for the penetration and effectiveness of heparin compounds [36].

CONCLUSION

Based on the objectives and results of this study, it can be concluded that: a) The most age group of ischemic stroke patients undergoing DSA is 41-59 years old; b) Men are the largest population of ischemic stroke patients undergoing DSA; c) The most education of ischemic stroke patients who received DSA was strata 1; d) Private employees are the occupations with the most ischemic stroke patients being treated by DSA; e) Hypertension is the most common risk factor for ischemic stroke patients undergoing DSA; f) The most common symptom experienced by ischemic stroke patients undergoing DSA is vertigo; g) Onset of ischemic stroke patients undergoing DSA, most of which are in the late subacute phase; h) In ischemic stroke patients who underwent DSA, it was found that there were motor changes, with the result that there were 6 patients who experienced motor changes for the better; i) In the NIHSS scores after and before DSA, it was found that there was an improvement in 23 people after DSA; and j) In ischemic stroke patients who underwent DSA, 26 of 49 patients experienced changes. Thus, it is hoped that further research can be carried out with more samples, and this research can be used as a reference for further research.

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