



Clinical Practice Guideline

for diagnosis, treatment and
rehabilitation of Acute Ischemic Stroke
in population over the age of 18.

Colombian General Social Security System for Health.

Complete guideline (2015) Guide N.54

CLINICAL PRACTICE GUIDELINE FOR DIAGNOSIS, TREATMENT AND REHABILITATION OF ACUTE ISCHEMIC STROKE IN POPULATION OVER THE AGE OF 18.

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This Guideline is part of a group of evidence based Clinical Practice Guidelines that include economic considerations and implementation in the *Sistema General de Seguridad Social en Salud* (SGSSS) context. This Guideline was developed by the Ministerio de Salud y la Protección Social in the context of priority and prevalent topics in the country and through a contract awarded to the Universidad Nacional de Colombia.

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DECLARATION OF EDITORIAL INDEPENDENCE

Funders provided support during the preparation of this document thereby ensuring transferability and applicability of its contents to the context of SGSSS. The scientific research and the development of the recommendations included in this document were conducted independently by the Guidelines Developing Group of the Universidad Nacional de Colombia. The funding institution had no influence on the content of the guidelines. All members of the Guidelines Developing Group and those who participated in both the expert collaboration and external review stated clearly their conflicts of interest.

CONFLICTS OF INTEREST

As a step prior to participation, every party involved in the generation of the recommendations contained in this guideline, revealed their conflicts of interest early in the process. Leaders and participants reported that they had not been involved as researchers in ongoing clinical trials on the subject, that they had not received any grants or benefits by groups interested in the recommendations and that they were not part of professional groups with conflicts of interest. The conception, development and publication of the recommendations had the exclusive financial support of the *Ministerio de Salud y Protección Social* and COLCIENCIAS. Those institutions own the copyrights.

GUIDELINE'S UPDATE

Guideline recommendations must be updated within the next three (3) years or earlier if new evidence that can modify those written here is provided. This process will be developed through the confirmation of an expert panel that will make the required changes.

The panel might develop the following methodology:

1. Select the relevant questions that have to be updated or added.
2. Find new evidence based on primary studies, systematic reviews or other Clinical Practice Guidelines.
3. Assess and analyze new evidence using GRADE methodology.
4. Update or generate new recommendations.
5. Reevaluate the given recommendations and its indicators.
6. Use the UPDATE methodology following GIN (October 2015) initiative.

Glossary : Cerebrovascular división. Asociación Colombiana de Neurología

Terminology suggestions for cerebrovascular disease:

Considerations

This document uses DeCS (Descriptores en Ciencias de la Salud) structure and trilingual vocabulary created by BIREME that serves as unique language for articles indexing of scientific magazines, books, congress annals and technical reports. This language is also used on research of health literature sources. This descriptor was developed based on MeSH- Medical Subject Headings of the U.S. National Library of Medicine (NLM), and it allows the use of common terminology for research in three languages, providing a constant and unique tool for information recovery.

The common terms used in Colombia are compared with the above-mentioned source in order to choose the equivalent international synonyms in Spanish and other languages, without losing their general meaning. Abbreviations are suggested for each term.

Terminology:

Cerebral Attack (CA): This expression was introduced by the Stroke Council of the American Heart Association (currently the American Stroke Association) in the 1990s to be used in a broad sense. This term was equivalent to Heart Attack, and it implied a critical emergent issue requiring immediate care in the closest competent Medical Center.

Transient ischemic attack (TIA): temporary episode, lasting 60 minutes or less, with neurological deficit caused by cerebral, spinal or retinal focal ischemia. This episode does not produce a change in magnetic resonance imaging.

Cerebrovascular attack (CVA): clinical and generic term used during pre-hospital care and emergency services, before categorizing its nature. This term is only used during “hyper-acute” stage and it is not used again once the condition has been established to be an ischemic or hemorrhagic episode. The term is equivalent to *stroke*.

Emergency regulating center (CRUE): Organization responsible for coordinating care and resolution of catastrophic events including medical emergencies occurring in Bogotá, D.C. through the Medical Emergency System.

Cerebrovascular accident Code (CVAC): Recognition method for ischemic stroke as a neurologic emergency. The code aims to generate actions oriented to preserve the cerebral tissue’s integrity through holistic and appropriate care.

Sudden/acute focal neurological deficit (FND): Decrease in brain, spinal cord, muscles or neurologic function that generates a functional anomaly in a specific area of the body.

Diffusion weighted magnetic resonance imaging (DWI): Technique based on the *in vivo* detection of the water molecule's movement, restricted to certain pathologic conditions such as ischemia and tumors.

Functional Tasks Training (RT or Rehabilitation Therapy): Practice of specific motor activities in order to improve functional capacity. It is part of the current approach to rehabilitation of the cerebrovascular attack.

Modified Ranking Scale (MRS): Instrument that measures dependency and functional impact of the cerebrovascular attack.

NIHSS Scale (National Institutes of Health Stroke Scale): Instrument that measures severity and neurologic damage caused by a cerebrovascular accident.

Pharyngeal Electrical Stimulation (PES): Noninvasive technique that aims to improve strength and recover motor control of the deglutition muscles, through electric stimulation.

Neuromuscular Electrical Stimulation (NES): Light stimulation and cutaneous electrical stimulation used to produce muscular contraction. Impulses imitate the action potentials that come from the central nervous system, stimulating muscular contraction.

Transcranial Electric Stimulation (TES): Technique that enables noninvasive and painless electromagnetic stimulation of nervous tissue. It also allows intervention in normal brain activity with possible cognitive effects.

Transcranial direct-current Stimulation (tDCS): Neuro stimulation hat uses low and constant current, delivered to the brain area of interest via small electrodes. It seeks to improve cognitive abilities in a variety of tasks, depending on the stimulated brain areas.

GLIAL Fibrillary Acidic Protein (GFAP): One of the fibrous proteins that form intermediate filaments of the intracellular cytoskeleton, particularly in glial cells such as astrocytes and Schwann cells.

Barthel index (BI): Instrument that evaluates disability measuring 10 basic self-care and physical dependency aspects. A regular score is 100 and a lowest score indicates increase of disability. BI>60 corresponds to assisted independency and a BI>40 to severe dependency.

Cerebral Infarction (CI): Clinical syndrome lasting 60 minutes or more. It correlates with imaging and pathologic anatomy, and it has its own time-evolution criteria. It replaces or complements the term Cerebrovascular Stroke.

Active Musculoskeletal Intervention (AMI): Active physical therapy to maintain and recover somatic functions.

LAPSS (Los Angeles Pre-hospital Stroke Scale): Method used to identify potential cerebrovascular attack patients before hospitalization, through evaluation of the medical record, vital signs and current symptoms, in order to rule out other diagnoses.

Hospital Pre-Notification (HPN): Identification of clinical syndromes outside the hospital setting, allowing patient's placement in the nearest appropriate medical facility through prompt notice and advance preparation of the medical personnel to achieve integral care.

Ontario Pre-hospital Stroke Screening Tool (OST): Detection tool for possible cerebrovascular attack, through pre-hospital evaluation of dysarthria, mutism, unilateral weakness and facial asymmetry.

Brain Natriuretic Peptide (BNP) or Natriuretic Peptide Cerebral N-Terminal (NT-PROBNP): 32-aminoacid polypeptide secreted by the ventricles of the heart in response to excessive stretching of heart muscle cells, which produces a decrease of vascular resistance, central venous pressure and increase of natriuresis.

Cerebral Perfusion through Computed Tomography (CPCT): Technique that uses iodine contrast medium. It provides detailed information on brain blood flow that distinguishes non-recoverable infarcted tissues from potentially recoverable shadow areas.

Cerebral Magnetic Resonance (CMR): Cerebral Magnetic Resonance is a non-invasive imaging technology that does not include ionizing radiation. It is based on information about the distribution of certain atoms in the human body. The main element of the equipment is a magnet capable of generating a constant magnetic field of great intensity to provide multi-plane imaging.

Pre-hospital care services (PHC): Operation and coordination system for critical medical issues. It includes all rescue services, medical care and transportation outside the hospital for patients or injured people. It is considered an extension of emergency care treatment.

Constraint- induced movement therapy for undamaged upper limb (CIMT): Therapy for functional restoration of the affected limb through movement restriction of the undamaged upper member and the intensive implementation of exercises and diverse activities of the paretic limb.

Reperfusion therapy (RPT): Intravenous and intra-arterial thrombolysis and mechanic thrombectomy for patients with cerebrovascular stroke to restore cerebral blood flow and improve outcomes.

Computed Tomography (CT): a computer constructed three-dimensional image of a body structure from a series of plane cross-sectional images made along an axis —called also *computed axial tomography, computerized axial tomography, or computerized tomography*

Intracranial hemorrhages are called:

Intracerebral hemorrhage (ICH): This term complements the term acute ischemic stroke once imaging establishes that bleeding in the cerebral tissue is present.

Subarachnoid Hemorrhage (SAH): Term that refers to bleeding in the subarachnoid space.

Transient ischemic attack (TIA): Cerebrovascular event that lasts less than 60 minutes, without changes in resonance imaging.

Acute Neurovascular Syndrome (ANS): This term is similar to the one used in cardiology to refer acute coronary syndrome. It includes all types of symptomatic cerebrovascular disease. It is used while making decisions in the emergency services, similar to the use of myocardium ischemic condition. Despite its rationality, it has been excluded, given its low penetration level among the Colombian medical community.

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CHAPTER 1: PRELIMINARY SECTION

INTRODUCTION:

The development of evidence based Clinical Practice Guideline and its economic considerations is the General Social Security System's strategy to guarantee the provision of high quality health services, without risking coverage, solidarity and equity. It is the Social Security System's responsibility to provide early and efficient medical attention that ensures high standards in order to improve health conditions, medical impact and social results on the cared community.

Clinical Practice Guidelines are one of several tools used by the quality assurance committees that enable health-making decisions based on the best available evidence. They result from scientific research (medicine based evidence) and improvement of practice standards informed by clinical experience. Clinical Practice Guidelines try also to articulate patients' and other health system users' points of view, incorporating their preferences and expectations. The Guidelines consider the circumstances in which care is provided, resource availability, users' perspectives and implementation within the legal framework.

In developing public health policies it is not sufficient to have academically impeccable tools; they must also be easily available for use, flexible and socially accepted. Clinical Practice Guidelines must respond to the most critical system requirements, and they should be monitored to verify their appropriateness and effectiveness.

This Clinical Practice Guideline contains relevant recommendations for diagnosis, treatment and rehabilitation of patients over the age 18 with acute arterial ischemic stroke. According to the task's scope and objectives, this Guideline adapts evidence derived from implemented interventions during the first two weeks of symptom onset.

JUSTIFICATION FOR THE CPG:

Cerebrovascular disease (CVD) includes a heterogeneous group of symptoms and secondary signs resulting from a brain injury (generally focal, transient or permanent) due to alteration of the cerebral blood flow (1). The most frequent cerebrovascular attacks are arterially mediated and comprise: ischemic stroke (CVA), transient ischemic stroke and cerebral hemorrhage (including intra parenchymatous hemorrhage and sub-arachnoid hemorrhage) (2). Venous originated lesions exist in minor proportion, such as cerebral venous thrombosis. (3). The incidence of CVA is higher in the elderly and in people with vascular risk factors. (2). A complex interaction of vascular risk factors, environmental conditions and genetic factors cause vascular damage and atherosclerotic endothelial lesions in most of patients (1). Nevertheless, the CVA also occurs with minor frequency in young adults, resulting from different pathophysiological mechanisms.

Risk factors associated to the development of CVA can be classified as modifiable and non-modifiable:

1. **Modifiable risk factors:** hypertension, diabetes, tobacco addiction, abnormal obesity, high ingestion of red meat, high fat diet, high salt consumption, sedentary lifestyle, frequent alcohol consumption, psychosocial stress, depression and dyslipidemia (4).
2. **Non-modifiable risk factors:** age, gender and genetic factors (5).

BACKGROUND:

Cerebral ischemia represents 80% of acute cerebrovascular attacks (CVA) worldwide, hence, the main cause of the CVA (2). Cerebral ischemia occurs when the brain's oxygen supply diminishes or is interrupted. Nervous tissue is especially vulnerable to the decrease of oxygen supply due to its high metabolic rate and poor energy reserves. Neuronal metabolism depends almost entirely on glucose. Neurons do not have the capacity to store glycogen. Once blood flow stops the specific characteristics of neuronal metabolism result in rapid and irreversible damage after approximately 5 minutes. Acute processes in cerebrovascular ischemic disease occur in rapid succession. In general, the tissue damage is completely established and delimited within the first 48 to 72 hours. After approximately 14 days, the nervous tissue has evolved to a chronic stage in which reorganization and cerebral plasticity occur. (6).

Once the cerebral stroke has occurred, the nervous tissue starts a slow recovery process. There is no tissue regeneration after a cerebral stroke but scar formation process is started by the microglia (7). Functional recovery is mainly due to reactivation of the nervous tissue that enters into a "hibernation" state because of the ischemia, but does not suffer a permanent lesion. Likewise, the appearance of new connections through the synaptic plasticity process facilitates the functional recovery observed in the majority of patients. (8)

The most frequent cause of the cerebral stroke is arterial vessel occlusion. This obstruction may develop anywhere in the arterial tree that supplies the brain. Arterial occlusion has two main causes: *in situ* thrombosis and arterial embolism (7). Thrombosis *in situ* is the most frequent cause of arterial occlusion. It occurs when a thrombus is formed in a layer of an atherosclerotic lesion. Arterial embolism occurs when a thrombus, formed in the heart or a large arterial vessel, is carried through the bloodstream to a distal cerebral artery.

For purposes of study and treatment, ischemic CVA causes have been grouped according to the diversity of pathophysiological mechanisms. There are several etiological classification systems for the CVA, the most commonly used is TOAST (*Trial of Org 10172 in Acute Stroke Treatment*). The TOAST system divides cerebral strokes in five groups depending on their origin (9). The first group consists of strokes caused by emboli originating in heart. The most common causes of these emboli are atrial fibrillation and valvular heart disease. The second group comprises ischemic CVA from emboli originating in the large intracranial vessels or from carotid disease. The third group includes lacunar diseases. The size of lacunar strokes is smaller than 15 mm in its acute phase and generally occurs due to an occlusion of an arteriole. This process is known as lipohyalinosis. The fourth group consists of rare, infrequent miscellaneous causes (non-atherosclerotic vascular diseases, coagulation or hematologic disorders). Finally, the fifth group comprises cerebral strokes with undetermined causes. They constitute a third of ischemic CVA cases.

MAGNITUDE OF THE PROBLEM:

CVA is the second cause of death after ischemic heart disease and the third cause of Disability Adjusted Life Years (DALY) worldwide (10). CVA is directly associated with 6.2 million deaths a year, 10% of the world mortality rate. Data supplied by the Global Burden of Disease's report (GBD) reveals a significant increase of DALY related to CVA during the last 20 years.

The increase of CVA is due to important regional and socio-economical differences. In countries where income per capita is high, the improvement in primary prevention has been associated with a progressive decrease of CVA's impact. On the contrary, in developing countries the proportion of patients with cardiovascular diseases is increasing. It is estimated that the percentage of non-communicable diseases (cardiovascular diseases, chronic pulmonary disease, among others) in developing countries will represent 57% of total global diseases in 2020 (11).

In Colombia, the incidence of CVA has not shown any significant change during the last 20 years (97.43 cases/ 100.000 citizens/ year in 1990 versus 97.39 cases/100.000 citizens /year in 2010). According to this report, mortality rates associated with CVA have been reduced to 24.1% during the same period of time (12). However, the incidence estimates of CVA for Colombia are derived from indirect sources. The only direct evidence comes from the study of a demographic cohort of 13.588 individuals from Sabaneta, Antioquia that were followed during one year (13). The occurrence of CVA from 1992 to 1993, adjusted by gender and age was 0.89/1.000 citizens.

The prevalence of CVA in Colombia has been evaluated by multiple regional studies, which have been published over the last 30 years. Most of these studies have followed the World Health Organization's (WHO) recommendations for epidemiology studies of neurological diseases. In general, the prevalence estimates of CVA adjusted by age and gender have fluctuated between 1.4 and 1.9 per 1.000 citizens (14).

CVA also generates important costs to the Health Systems. Multiple studies have assessed the direct expenses (medical care) of patients with CVA. Demaerschakly *et al* identified 28 studies that evaluated the direct costs of patients with ischemic cerebrovascular disease in the United States (15). Updating these values to 2008, average costs related to hospitalization per patient have fluctuated between \$8.000 and \$23.000 USD, with intra-hospital stay between 4.6 to 12.4 days.

The volume of published information on indirect costs is less abundant. The evidence confirms that indirect costs constitute the greatest portion of the economic costs of cerebrovascular disease. Taylor *et al* calculated the indirect cost and the aggregate cost of the cerebrovascular disease in the United States in 1990 (16). The indirect cost was 23.6 billion dollars, mainly associated with loss of income due to premature mortality and earnings loss in survivors. The aggregated costs were estimated to be 40.6 billion dollars, which were associated with early care (first two years after symptoms onset), long term ambulatory care and chronic care centers.

In Colombia, information about direct and indirect costs related to CVA is limited. In a cost-effectiveness study of recombinant tissue plasminogen for treatment of ischemic CVA carried out by Muñoz *et al*, the direct and indirect costs for CVA patients and conventional care were

determined (17). In order to establish direct costs, the authors reviewed the clinical records of patients with ischemic CVA treated in four hospitals in Bogotá using rates from Seguros Sociales during the year 2004. The indirect costs were calculated by the average income decrease during Quality-Adjusted Life Years (QUALY) due to ischemic CVA, taking into account the information provided by the Departamento Administrativo Nacional de Estadística (DANE) and current minimum monthly wage for the year 2008 (\$461.500 cop). In 2008 the direct costs were \$696.300 COP and indirect were \$9.889.593 COP, with a total cost of \$10.585.893 COP per patient. Given the population's estimates of DANE and the adjusted incidence by identified age in previous studies, the total costs of ischemic CVA in Colombia would be approximately \$450.000.000.000 COP annually.

In summary, CVA is a heterogeneous disease from the medical and pathophysiological point of view, with an increasing incidence associated with great social and economic expenses worldwide. Developing countries are more vulnerable to CVA. Lowering morbidity-mortality rate of CVA could be associated with an important social impact for Colombia (18).

SCOPE:

The target of this CPG is the population over the age of 18 that presents focal neurological deficits of sudden onset and rapid progression, clinically compatible with an acute arterial ischemic stroke. Likewise, this CPG includes aspects related to diagnosis, treatment and rehabilitation during the first 15 days of symptoms onset.

This CPG does not cover primary prevention. However, consideration of Clinical Practice Guidelines for chronic arterial hypertension, acute coronary syndrome and diabetes mellitus is recommended. Their scope and objectives include prevention of vascular diseases, which include ischemic cerebrovascular disease. This guideline will remit the reader to the final recommendations included in the guidelines mentioned above.

GENERAL OBJECTIVE:

This CPG offers recommendations for diagnosis, treatment and rehabilitation of patients over the age of 18 with acute arterial ischemic stroke, with the purpose of improving prognosis and health outcomes. Best available evidence was used to accomplish these recommendations; they were prioritized according to the level of evidence and strength of recommendation.

SPECIFIC OBJECTIVES:

- To develop recommendations with the best quality standards for care of patients with acute arterial ischemic stroke.
- To provide directions for diagnosis, treatment and rehabilitation of patients with acute arterial ischemic stroke according to the different complexity levels.
- To contribute to rational use of resources in the different complexity levels of patients with acute arterial ischemic stroke.

- To diminish unjustified variability in diagnoses, treatment and rehabilitation phases of patients with acute arterial ischemic stroke.

GUIDELINE'S USERS:

POPULATION:

CONSIDERED GROUPS:

This CPG gives recommendations for patients' care over the age of 18 with focal neurological deficit with sudden onset and rapid progression, clinically compatible with acute arterial ischemic stroke. It also includes related issues for diagnosis, treatment and rehabilitation during the first 15 days of symptoms onset.

GROUPS THAT ARE NOT TAKEN INTO ACCOUNT:

This CPG does not provide recommendations for:

- A. Patients with arterial ischemic stroke, with NO acute phase (after 15 days of symptoms onset)
- B. Patients with hemorrhagic ischemic stroke (including subarachnoid hemorrhage or post-trauma hemorrhage) caused by hemorrhage(vessel spasm).
- C. Patients with secondary ischemic stroke, traumatic brain injury (TBI), autoimmune disease, neoplastic disease or infectious disease.
- D. Patients with complications resulting from the care of vascular arterial ischemic stroke.
- E. Patients with acute arterial ischemic stroke during gestation and lactation period.

HEALTH CARE DELIVERY SETTINGS

This CPG is addressed to pre-hospital care teams, emergency staff, primary care professionals, clinical specialist in diverse levels of responsibility for the health care of patients with acute ischemic stroke and other participants.

CARE LEVELS:

This CGP issues recommendations in all care levels:

1. **Pre-hospital care:** provides to pre-hospital care teams necessary information to *suspect* that a patient is suffering an acute arterial ischemic stroke. Indications for initial treatment and timely transfer to a hospital care center are given.
2. **Low level of complexity:** offers the necessary information to general practitioners and other health professionals in order to provide adequate, timely and standardized *diagnosis* for the acute arterial ischemic stroke with indications for treatment and early referral to a higher complexity center.

3. **High level of complexity:** guidelines are given for appropriate diagnosis and efficient treatment of the disease, with indications for adequate selection of patients that require an intravenous or intra-arterial thrombolysis. Additionally, recommendations for early rehabilitation are given.

CENTRAL CLINICAL ASPECTS:

CLINICAL ASPECTS COVERED WITHIN THE GUIDELINE:

This Clinical Practice Guideline refers to diagnosis, treatment and rehabilitation of acute arterial ischemic stroke episodes in the population over the age of 18. This Clinical Practice Guideline addresses the following clinical aspects:

- Diagnosis
- Treatment
- Rehabilitation

GUIDELINE'S AUDIT SUPPORT:

This Clinical Practice Guideline incorporates revision criteria and evaluation indicators.

SOCIALIZATION OF RELEVANT QUESTIONS:

Questions were selected, prioritized and classified according to different clinical management stages of patients with acute ischemic stroke over the age of 18, based on the Guideline's scopes and objectives. Such questions resulted from the consensus between thematic and methodology experts. They defined a management algorithm.

DIAGNOSIS:

1. Which are the most effective strategies to suspect the presence of an arterial ischemic stroke during pre-hospital care?
2. Which are the diagnostic studies that confirm the presence of an acute ischemic stroke in population over the age of 18?
3. Which are the most effective scales to classify the severity of the arterial ischemic stroke in population over the age of 18?

TREATMENT

4. How effective and safe are the care units for cerebrovascular attack to treat patients with acute ischemic stroke?
5. Which are the most effective and safe interventions, different from arterial recanalization, for the initial treatment of a patient with acute ischemic stroke?

6. How *secure and effective is the arterial recanalization strategy* for treatment of patients with acute arterial ischemic stroke?
7. Which are *the most effective and safest interventions* for neuro protection of a patient with acute ischemic stroke?

REHABILITATION:

8. Which are *the most effective and secure interventions for rehabilitation* of a patient with acute arterial ischemic stroke during the first 15 days after symptoms onset?

ECONOMIC QUESTIONS:

9. What is the difference between *cost- effectiveness of stroke care units* (CVA units) versus cost- effectiveness of general ward care for patients with acute ischemic stroke?
10. What is the cost-effectiveness of combined reperfusion therapy through endovenous thrombolysis and arterial recanalization of acute ischemic stroke of less than 4.5 hours of evolution compared to endovenous thrombolysis with unique rtpa in patients with confirmed proximal occlusion?

LEVELS OF EVIDENCE AND GRADES OF RECOMMENDATION:

GRADE System (Grading for Recommendations, Assessment, Development and Evaluation) was used to determine levels of evidence and recommendation’s strength in the current Guideline.

LEVELS OF EVIDENCE

Qualification	Judgment	Characteristics
A	High ⊕⊕⊕⊕	It is highly unlikely that new studies will change the estimated result’s confidence level.
B	Moderate ⊕⊕⊕○	It is probable that new studies will have an important impact on the estimated result’s confidence level and that these may modify the result.
C	Low ⊕⊕○○	It is very probable that new studies will have an important impact on the estimated result’s confidence level and that these may modify the result.
D	Very Low ⊕○○○	Any estimated result is very uncertain.

GRADES OF RECOMMENDATION:

Strength of the recommendation

STRENGTH OF RECOMMENDATION	MEANING
Strong in Favor	The desirable consequences clearly exceed the undesirable consequences. DEFINITELY TO DO IT.
Weak in Favor	The desirable consequences probably exceed the undesirable consequences. PROBABLY TO DO IT.
Weak Against	The undesirable consequences probably exceed the desirable consequences. PROBABLY NOT TO DO IT.
Strong Against	The undesirable consequences clearly exceed the desirable consequences. DEFINITELY NOT TO DO IT.
Key Implementation considerations/ key considerations	Recommended practice, based on clinical experience, of the Guideline’s Development Group.

Which are the most effective strategies to suspect the presence of an arterial ischemic stroke during pre-hospital care?

1.	The use of pre-hospital care LAPSS scale (Los Angeles Pre-hospital Stroke Scale) in patients that present a sudden focal neurologic deficit or rapid onset is recommended in order to suspect the presence of an acute arterial ischemic stroke.
Strength	Strong in Favor
Quality	Very Low Evidence ⊕○○○
2.	The use of the tool OPSS (Ontario Pre-hospital Stroke Screening Tool) is recommended in clinical scenarios where the use of glucometry to apply the pre-hospital care LAPSS scale is not possible.
Strength	Strong in Favor
Quality	Very Low Evidence ⊕○○○
3.	The use of mass media campaigns to raise public awareness on the importance of appropriate identification and immediate treatment of patients with ischemic cerebrovascular stroke is recommended. These campaigns must also highlight the importance of activating the emergency transportation services.
Strength	Strong in Favor
Quality	Very Low Evidence ⊕○○○

Key point practice	Communication campaigns and strategies should: <ol style="list-style-type: none"> 1. Be implemented continuously. 2. Be multimodal or personalized according to the characteristics of the target population.
4.	It is recommended that all patients with clinical suspicion of cerebrovascular stroke, within the first 6 hours of symptoms onset, should be immediately transported by the emergency services with priority level 1 or high in order to increase the possibility of receiving arterial reperfusion therapy.
Strength	Strong in Favor
Quality	Low Evidence ⊕⊕○○
5.	It is recommended that all patients with clinical suspicion of an ischemic cerebrovascular stroke, within the first 7 to 24 hours of symptoms onset, should be transported as priority by the emergency medical services to receive appropriate medical care.
Strength	Strong in Favor
Quality	Very Low Evidence ⊕○○○
6.	It is recommended that all patients with clinical suspicion of ischemic cerebrovascular stroke should be immediately and directly transported to the closest medical facility with capacity to provide arterial recanalization therapy.
Strength	Strong in Favor
Quality	Very Low Evidence ⊕○○○
7.	It is recommended that pre-hospital care centers and regulation centers notify immediately the transfer of patients with clinical suspicion of ischemic cerebrovascular stroke, in order to reduce time lapse of treatment's initiation.
Strength	Strong in Favor
Quality	Very Low Evidence ⊕○○○
Key point practice	ER personnel should collect information about time of symptoms onset, severity, comorbidities and medication the patient is taking.
8.	It is recommended that the emergency care services design and establish a protocol that allows rapid treatment and apply it appropriately to patients with acute ischemic stroke.
Strength	Strong in Favor
Quality	Very Low Evidence ⊕○○○
Key point practice	Once the protocol is activated in any of the care levels, all members of the health care team involved must be notified in order to accomplish autonomously and expeditiously the assigned task.
Key point practice	The CVA code must be activated through pre-hospital notification carried out by the emergency care services.
Key point practice	Facilities should have a pre-defined set of medical orders that allow rapid diagnosis and treatment of patients with evidence of CVA. These orders should be rapidly available and should be immediately executed, once the CVA code is active.

2. Which are the diagnostic studies that confirm the presence of an acute ischemic stroke in population over the age of 18?

9.	It is recommended that all patients with acute focal neurological deficit that suggests CVA should be tested with glucometry and electrolyte (Na, K, Ca, Cl) in order to exclude the presence of other clinical conditions that may be confused with CVA
	Strong in favor
	Very Low Evidence ⊕○○○
10.	Clinical prediction models are not recommended to classify the type of cerebrovascular attack (ischemic or hemorrhage) of a patient with acute focal neurological deficit that suggests CVA.
Strength	Strong against
Quality	Very Low evidence ⊕○○○
11.	An electrocardiogram for patients with suspicion of acute CVA is suggested, in order to detect pathology of cardiovascular origin.
Strength	Weak in favor
Quality	Very Low Evidence ⊕○○○
12.	A priority brain imaging (TC or DWI) on patients with suspicion of acute ischemic stroke is recommended to determine the type of event and its localization.
Strength	Strong in favor
Quality	Very Low Evidence ⊕○○○
Key point practice	Type of imaging used will depend on technical availability, patient's comorbidities and time available.
13.	DWI magnetic resonance as first alternative for diagnosis of patients with focal neurological deficit with minor or transitory symptoms is suggested. In case of no DWI magnetic resonance availability, an immediate CT is suggested.
Strength	Weak in favor
Quality	Very Low Evidence ⊕○○○
14.	Performing a DWI on all patients with focal neurological deficit, with minor or transient symptoms is recommended in the emergency services that cannot provide an MRI or a cranial CT to confirm diagnosis and exclude other diagnosis alternatives.
Strength	Strong in favor
Quality	Very Low Evidence ⊕○○○
15.	CAT test on patients with clinical suspicion of an ischemic stroke between 4.5 and 6 hours is suggested. It should include a perfusion study to identify potentially viable tissue with arterial reperfusion therapy.
Strength	Weak in favor
Quality	Very Low Evidence ⊕○○○
Key point practice	Perfusion imaging and on time interventions are recommended for treatment of patients with acute ischemic stroke.

16.	In order to assess the early recurrence risk, the use of transcranial Doppler on patients suffering an acute ischemic stroke is suggested.
Strength	Weak in favor
Quality	Very Low Evidence ⊕○○○
Key point practice	Transcranial Doppler and on time interventions recommended for treatment of patients with acute ischemic stroke should be accomplished.
17.	Serum markers for diagnosis of patients with acute ischemic stroke are not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
18.	Measurement of serum levels of BNP or NT-proBN to establish the prognosis of a patient with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
19.	Troponin measurement on patients with acute ischemic stroke is suggested to identify patients with greater death risk associated with acute cerebrovascular stroke.
Strength	Weak in favor
Quality	Very Low Evidence ⊕○○○

3. Which are the most effective scales to classify the severity of the arterial ischemic stroke in population over the age of 18?

20.	The application of the NIHSS scale (National Institutes of Health Stroke Scale) to determine the severity of the acute arterial ischemic stroke is recommended.
Strength	Strong in favor
Quality	Very Low Evidence ⊕○○○
Key point practice	All health professionals involved in care of patients with CVA should receive training in the appropriate application of the NIHSS scale.

4. How effective and safe are the care units for cerebrovascular accident to treat patients with acute ischemic stroke?

21.	It is recommended that patients with acute ischemic stroke be treated in specialized care units in order to decrease mortality rates, sequelae and the necessity of institutional care.
Strength	Strong in favor
Quality	Moderate Evidence ⊕⊕⊕○

5. Which are the ***most effective and safe interventions, different from arterial recanalization,*** for the initial treatment of a patient with acute ischemic stroke?

22.	A non-invasive Continuous Intensive Monitoring on patients with acute ischemic stroke is recommended to decrease mortality levels and disability.
Strength	Strong in favor
Quality	Very Low Evidence ⊕○○○
23.	Deliberate modification of arterial pressure on patients with acute ischemic stroke is not suggested.
Strength	Weak Against
Quality	Very Low Evidence ⊕○○○
Key Point Practice	In CVA patients that are not candidates for arterial reperfusion with arterial pressure equal or over 220/120mmHg, arterial pressure should diminish 15% within the first 24 hours of symptoms onset
Key Point Practice	CVA patients,candidates to reperfusion therapy should maintain their arterial pressure lower than 185/110 mmHg. Likewise, patients that have had reperfusion therapy should have their arterial pressure lower than 180/105 mmHg within the first 24 hours.
24.	Therapeutic hypothermia as part of the treatment for patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
Key Point Practice	In CVA patients with temperature levels over 38 C degrees beginning antipyretic treatment with pharmacologic and non-pharmacologic actions is recommended.
25.	Strict glucose control (72 to 135 mg/dl) for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
Key Point Practice	It is reasonable that patients with acute ischemic stroke have glucose levels between 140 and 180 mg/dl.
Key Point Practice	Close monitoring of glucose levels on patients with acute ischemic stroke should be made to prevent hypoglycemia. In case of hypoglycemia it should be properly treated.
26.	The use of external counterpulsation as part of the treatment for patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
27.	The use of telemedicine is recommended in geographic areas where there is no specialized personnel, aiming adequate decision taking on treatment on patients with acute ischemic stroke.
Strength	Strong in favor
Quality	Very Low Evidence ⊕○○○

28.	The use of antiplatelet therapy as part of the treatment of patients with acute ischemic stroke is recommended to decrease mortality risk and disability.
Strength	Strong in favor
Quality	Moderate Evidence ⊕⊕⊕○
Key Point Practice	Acetylsalicylic acid is the chosen platelet anti-aggregant. Start 300 mg dose orally within the first 24 to 48 hours and then continue with 100mg doses daily.
Key Point Practice	Acetylsalicylic acid should not be used as a replacement for thrombolytic therapy.
Key Point Practice	Anti-aggregant treatment should not be administered within the first 24 hours after thrombolytic therapy performed.
29.	The use of dual anti-aggregation as part of treatment for patients with acute ischemic stroke is not suggested.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○
30.	The glycoprotein IIA/IIB inhibitor for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
31.	Immediate anticoagulation as part of treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Moderate Evidence ⊕⊕○○
32.	Immediate anticoagulation as replacement of anti-aggregant for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Moderate Evidence ⊕⊕⊕○
33.	The use of agents against fibrinogen as part of treatment for patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
34.	The use of statins as part of treatment for patients with acute ischemic stroke is recommended to decrease major vascular events incidence in the long term.
Strength	Strong in favor
Quality	Very Low Evidence ⊕○○○
35.	Steroids use for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
36.	The use of glycerol for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○

37.	The use of prostacyclin for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
38.	The use of theophylline or aminophylline for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
39.	Nitric oxide for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
40.	The use of amphetamines for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
41.	The use of hemo-dilution for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
42.	Hyperbaric oxygen for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○
43.	The use of GinkoBiloba for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
44.	Acupuncture for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Very Low Evidence ⊕○○○

6. How secure and effective is the arterial recanalization strategy for treatment of patients with acute arterial ischemic stroke?

45.	Administration of thrombolytic therapy for treatment of patients with acute ischemic stroke is recommended in order to obtain a good functional outcome and decrease dependency.
Strength	Strong in favor
Quality	Low evidence ⊕⊕○○
Key Point Practice	Administration of thrombolytic therapy should be started within the first hour of the patient's arrival to the hospital.

Key Point Practice	Patients and their families should be informed about the risks and benefits of thrombolytic therapy. The patient or his/her closest relative should fill in the informed consent and it must be added to his/her medical record.
46.	The use of recombinant tissue plasminogen activator as thrombolytic agent for treatment of patients with acute ischemic stroke is recommended in order to obtain a good functional outcome and decrease dependency.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
47.	The use of recombinant tissue plasminogen activator in doses of 0.9 mg/kg for treatment of patients with acute ischemic stroke is recommended in order to obtain a good functional outcome and decrease dependency.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
48.	Intravenous thrombolysis as preferred treatment for administration of thrombolytic therapy on patients with acute ischemic stroke is recommended in order to obtain a good functional outcome and decrease dependency.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
49.	Administration of tissue plasminogen activator during the first 3 hours after symptoms onset is recommended as part of treatment for patients with acute ischemic stroke of all ages, in order to obtain a good functional outcome and decrease dependency.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
50.	Administration of tissue plasminogen activator between the first 3 to 4.5 hours after symptoms onset is recommended as part of treatment for patients with acute ischemic stroke under the age of 80, in order to obtain a good functional outcome and decrease dependency.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
51.	Administration of tissue plasminogen activator between the first 3 to 4.5 hours after symptoms onset is suggested as part of treatment for patients with acute ischemic stroke over the age of 80, in order to obtain a good functional outcome and decrease dependency.
Strength	Weak in favor
Quality	Low Evidence ⊕⊕○○
52.	Intravenous administration of tissue plasminogen activator to patients with acute ischemic stroke is not recommended after the first 4.5 hours of symptoms onset.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
53.	Administration of tissue plasminogen activator to patients with acute ischemic stroke with NIHSS score between 4 and 25 is recommended in

	order to decrease dependency and good functional outcome.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
54.	Administration of intra-arterial reperfusion therapy to patients with acute ischemic stroke that have an inadequate response to intravenous thrombolysis or have an absolute contraindication to intravenous thrombolysis, is suggested in order to decrease dependency and functional outcome, if they are in the previously established narrow time window.
Strength	Weak in favor
Quality	Low Evidence ⊕⊕○○
55.	Intra-arterial thrombolysis as part of treatment for patients with acute ischemic stroke that have relative contraindications for administration of intravenous thrombolysis (recent intracranial or intraspinal surgery, recent major extracranial surgery or without susceptible pressure location, recent ischemic CVA in a different vascular territory) is suggested, while they are still in the previously defined narrow time window, in order to decrease dependency and functional outcome.
Strength	Weak in favor
Quality	Low Evidence ⊕⊕○○
56.	Administration of isolated endovascular thrombolysis for treatment of patients with acute ischemic stroke is not suggested.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○
57.	Combined therapy is suggested to improve functional independence for patients with acute ischemic stroke with proximal obstruction (first or second portion of the middle cerebral artery, anterior or posterior cerebral artery) and evidence of potentially recoverable tissue, without recanalization after intravenous thrombolysis.
Strength	Weak in favor
Quality	Low Evidence ⊕⊕○○
58.	The use of assessed thrombolysis by ultrasound for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○

7. Which are the most effective and safest interventions for neuroprotection of a patient with acute ischemic stroke?

59.	The use of GABA receptor agonist is not recommended for treatment of patients with acute ischemic stroke.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○

60.	The use of colony stimulating factors for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
61.	Tirilazard for treatment of patients with ischemic cerebrovascular stroke is not recommended.
Strength	Strong against
Quality	Moderate Evidence ⊕⊕⊕○
62.	Calcium antagonists for treatment of patients with acute ischemic stroke are not suggested.
Strength	Weak against
Quality	Very Low Evidence ⊕○○○
63.	Excitatory amino acids antagonists for treatment of patients with acute ischemic stroke are not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
64.	The use of mannitol for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
65.	Piracetam for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
66.	Methyl xantines for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
67.	The use of Glanglosides for treatment of patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
68.	Citicoline for treatment of patients with acute ischemic stroke is not recommended.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○

8. Which are the most effective and secure interventions for rehabilitation of a patient with acute arterial ischemic stroke during the first 15 days after symptoms onset?

69.	Early feeding (during the first week) as part of treatment of patients with acute ischemic stroke is recommended in order to maintain adequate caloric intake.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
70.	The use of conventional nasogastric tube for feeding patients with acute ischemic stroke that cannot be fed orally is recommended in order to maintain adequate caloric intake.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
71.	The use of percutaneous endoscopic gastrostomy, as an alternative to guarantee food delivery in the long term is suggested on patients that can neither eat orally nor have a nasogastric tube nor experience deglutition recovery during the acute phase of the disease (e.g. patients decompressive craniotomy, ischemia in basilar territory).
Strength	Weak in favor
Quality	Low Evidence ⊕⊕○○
72.	Nutritional supplement as part of treatment for patients with acute ischemic stroke is recommended in order to decrease frequency of pressure ulcers and improve caloric and protein intake.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
Key point practice	Patients with acute ischemic stroke diagnosed with dysphagia (deglutition disorder) should be evaluated by nutrition professional.
73.	Behavioral interventions as part of deglutition therapy in patients with acute ischemic stroke are recommended to decrease the proportion of patients with dysphagia.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
74.	Acupuncture for treatment of deglutition alterations on patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
75.	Pharmacologic interventions for treatment of deglutition alterations on patients with acute ischemic stroke are not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
76.	Electric neuromuscular stimulation for treatment of deglutition alterations on patients with acute ischemic stroke is not recommended.

Strength	Strong against
Quality	Low Evidence ⊕⊕○○
77.	Electric pharyngeal stimulation for treatment of deglutition alterations on patients with acute ischemic stroke is not recommended.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
78.	Physical stimulation (thermic or tactile) as part of deglutition therapy on patients with acute ischemic stroke is recommended.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
79.	Transcranial stimulation with direct electrical stimulation for treatment of deglutition symptoms on patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
80.	The use of magnetic transcranial stimulation for treatment of deglutition symptoms on patients with acute ischemic stroke is not recommended.
Strength	Strong against
Quality	Low Evidence ⊕⊕○○
81.	Physical rehabilitation on patients with acute ischemic stroke is recommended to improve functional independency, mobility, balance and walking speed.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
Key point practice	Specialist from different fields such as rehabilitation medicine, neurology, physical rehabilitation, occupational rehabilitation, language rehabilitation, nursery, psychology, and social work specialists should conform a multidisciplinary team to improve the results.
Key point practice	Early assessment on phono-audiology or speech therapy during the acute phase of the ischemic stroke should be done to detect the presence of communications disorders such as aphasia, apraxia or dysarthria.
Key point practice	Patients, their family and/or caregivers should be involved in the rehabilitation process to improve the results.
Key point practice	It is a key practice point to include a neurophysiologic assessment during evaluation of patients with acute ischemic stroke in order to have an early detection of cognitive and perceptual alterations.
82.	Early start of physical rehabilitation (within the first 72 hours) on patients with acute ischemic stroke is recommended to improve functionality recovery.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
83.	Early start of physical rehabilitation at home for treatment of patients with acute ischemic stroke is recommended to decrease mortality rates, dependency and hospital stay.
Strength	Strong in favor

Quality	Moderate evidence ⊕⊕⊕○
Key practice point	Evaluation of visual deficit on patients with acute ischemic stroke before hospital discharge should be done.
84.	Physical therapy as active component for muscles and bones in treatment of patients with acute ischemic stroke is suggested to improve daily activities and motor recovery.
Strength	Weak in favor
Quality	Low Evidence ⊕⊕○○
85.	Training in functional tasks as part of physical rehabilitation on patients with acute ischemic stroke is not suggested.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○
86.	Neurophysiologic interventions as part of physical therapy for patients with acute ischemic stroke are not suggested.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○
87.	Training in repetitive tasks as part of physical therapy for patients with acute ischemic stroke is not suggested.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○
88.	Transcranial stimulation with direct electrical stimulation as part of physical rehabilitation for treatment of patients with acute ischemic stroke is not suggested.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○
89.	Early mobilization (waking to the bathroom, sitting somewhere else different than the bed, standing up or walking within the first 48 hours) on patients with acute ischemic stroke is suggested to reduce complications derived from immobilization.
Strength	Weak in favor
Quality	Low Evidence ⊕⊕○○
90.	Constrain induced movement therapy for paretic upper limb during treatment of patients with acute ischemic stroke is recommended to improve limb's function.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○
91.	The regular use of support device to prevent or treat subluxation of the shoulder on patients with acute ischemic stroke is not suggested.
Strength	Weak against
Quality	Low Evidence ⊕⊕○○
92.	Oral care interventions (use of toothbrush, mouthwash and team's training for promotion and oral hygiene care) on patients with acute ischemic stroke are recommended to decrease pneumonia risk.
Strength	Strong in favor
Quality	Low Evidence ⊕⊕○○

In order to make this CPG effective the Development Guideline's Group (DGG) created a document with plans and specific strategies to disseminate and implement the Guide, which may be consulted in the annex of the current document. Additional materials were also made: summary document (short Guideline), educational tools (Guidelines for patients) and clinical support tools(flow charts). Additional material can be accessed online through the webpage of this agency (Ministerio de salud y Protección Social, Colombia).

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Clinical Practice Guideline
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age of 18.



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