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Evaluation of cerebrovascular disease risk with carotid ultrasonography imaging in artificial intelligence framework

Rivan Danuaji, Subandi Subandi, Stefanus Erdana Putra, Muhammad Hafizhan
Neurology Department, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia

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ABSTRACT

Carotid plaque is a biomarker of generalized atherosclerosis, and may predict ischemic stroke. Carotid intima-media thickness (C-IMT) measurement with ultrasonography imaging could capture the condition of carotid plaque. However, manual measurement of C-IMT is observer-dependent, resulting in observer bias and low reproducibility. In this study, we develop artificial intelligence (AI) framework that could automatically measure the C-IMT, and compared it with C-IMT measured by board of expert. This is a retrospective study done in Dr. Moewardi General Hospital, Surakarta, Indonesia. Carotid B-mode ultrasonography images were measured by panel of expert and by AI. After annotation process on Neurabot platform, AI could detect region of interest (ROI), and would do segmentation on the area to measure C-IMT autonomously. Dependent T-test was used to evaluate validity, and Cronbach's alpha was used to find the reliability of C-IMT measured by panel of expert and AI. There was strong correlation (r=0.874; p=0.014) on dependent t-test for C-IMT measured by AI with C-IMT measured by board of expert. The internal consistency reliability coefficients (Cronbach's alpha) were 0.938 and 0.909, for pretest and posttest, respectively. We also analyzed the test-retest reliability by comparing pretest and posttest score with dependent t-test, and we observed strong correlation with r=0.871 (p=0.000). AI developed on Neurabot platform are valid and reliable to measure C-IMT.

Corresponding Author:

Rivan Danuaji
Neurology Department, Faculty of Medicine Universitas Sebelas Maret
Ir Sutami 36A Street, Surakarta, 57126, Indonesia
E-mail: rivan.danuaji@staff.uns.ac.id

1. INTRODUCTION

Stroke is the third leading cause of death and the first leading cause of disability globally. World Health Organization (WHO) estimates that stroke causes 6.7 million deaths annually [1]. In Indonesia, there are 550,000 new stroke cases every year. Almost 70% of stroke cases are classified as ischemic stroke, a type of stroke caused by infarction of artery in the brain, spinal cord, or retina. Early identification of stroke risk factors is substantial in order to reduce morbidity and mortality associated with stroke [2]–[4].

Several conventional risk factors of ischemic stroke have been extensively studied, which include age, gender, hyperlipidemia, hypertension, diabetes mellitus, smoking, alcohol consumption, family history of stroke, and lack of physical activity [5]. One of risk factor of ischemic stroke that have been studied recently is carotid plaque. Carotid plaque, irrespective to their location, increase the risk of anterior circulation infarction [6]. Carotid plaque is also hypothesized as biomarker of generalized atherosclerosis, and may become the source of thrombo-emboli, both may cause ischemic stroke [7]. Study by Gupta *et al*.

was able to combined the assessment of carotid plaque and traditional risk factors to predict stroke incident, further highlight the role of routine carotid assessment on stroke risk evaluation [8].

Risk of stroke is increasing not only on the presence of carotid plaque [9]. Increased carotid intima-media thickness (C-IMT), an early sign of atherosclerosis, also increased the risk of stroke, regardless of carotid plaque presence [10]. B-mode carotid ultrasound is a cheap, noninvasive imaging modality that could capture the condition of the carotid artery lumen by measuring C-IMT and carotid plaque area. However, measurement of C-IMT in daily practice is currently observer-dependent, resulting in observer bias and low reproducibility [11].

Artificial intelligence (AI) has the potential to be applied to various field of study, including in medicine [12]. AI could recognize complex pattern in an image and providing quantitative data, which might be useful for radiological image evaluation [13]. The purpose of this study is to develop artificial intelligence framework that could automatically recognizing the carotid artery, segmenting the wall of the carotid artery, tracing the contours of the intima, media layer and adventitia layer, and measure the C-IMT to reduce the bias previously stated. Then, we compared C-IMT data measured by AI with C-IMT measured by board of expert.

2. RESEARCH METHOD

2.1. Patients and study design

This was a retrospective study done in Dr. Moewardi General Hospital, Surakarta, Indonesia. All patients in neurology clinic between January 2018 and June 2021 that had carotid B-mode ultrasonography were enrolled in this study. In this study, we classified patients into stroke and non-stroke patient, based on criteria from American Heart Association/American Stroke Association (AHA/ASA) 2018. Data of stroke conventional risk factor, i.e., age, sex, body mass index, smoking and alcohol consumption, also history of hypertension, diabetes, and dyslipidemia were collected from medical record. Patients with missing data and aged <25 years were excluded from this study. To find the validity and reliability of AI, we compared C-IMT from B-mode ultrasonography images that were measured by AI with C-IMT that were measured by our panel of expert.

2.2. C-IMT measurement

Ultrasonography of carotid artery were performed by experienced neurologist blinded from patient clinical data. In this study, we measured whole carotid tree, instead of only several segment of common carotid artery to find best location that represent atherosclerosis [14]. Whole carotid tree, consisted of right common carotid artery, bifurcation, and internal carotid artery were first identified, and the thickest segment were selected to be measured. We also select thicker side of either near wall or far wall to be analyzed in this study. Area where C-IMT was measured than captured to be analyzed by AI.

Images from ultrasonography study [14] then uploaded to Neurabot site (https://neurabot.ai/). Annotation then done the in Neurabot platform by panel of expert. In this process, panel of expert are marking the tunica intima and tunica media, and AI would learn specific marking of each layer, Annotation could be considered of transfer of knowledge process to artificial intelligence platform. Trained AI then tried to detect region of interest (ROI), and if it matched to area identified by panel of expert, AI will do segmentation on the area to measure C-IMT autonomously. To obtain segmentation value, AI will calculate automatically using binary cross (1). Furthermore, AI would scan through the segmented area and measure pixels of the thickest area as C-IMT, and convert it to millimeter using (2) and (3). Algorithm of measurement of C-IMT using AI could be observed on Figure 1.

$$BCE(x) = -\frac{1}{N}\sum_{i=1}^{N} y_i \, log(h(x_i;\theta)) + (1 - y_i)log(1 - h(x_i;\theta)) \quad (1)$$

$$C - IMT\ Result = \frac{Greatest\ pixel\ of\ Y\text{-}axis\ on\ segmented\ area}{Converted\ value\ from\ pixel\ to\ millimeter} \quad (2)$$

$$Converted\ value\ from\ pixel\ to\ millimeter = \frac{Images\ height\ on\ pixel}{Images\ height\ on\ millimeter} \quad (3)$$

2.3. Data analysis

Data obtained was analyzed with Kolmogorov Smirnov test to determined data distribution, with p>0.05 considered normal distribution. Dependent T-test was used to evaluate validity of C-IMT measured by panel of expert and AI. Furthermore, Cronbach's alpha was used to find the reliability of C-IMT measured by panel of expert and AI. A p-value of <0.05 is considered statistically significant.

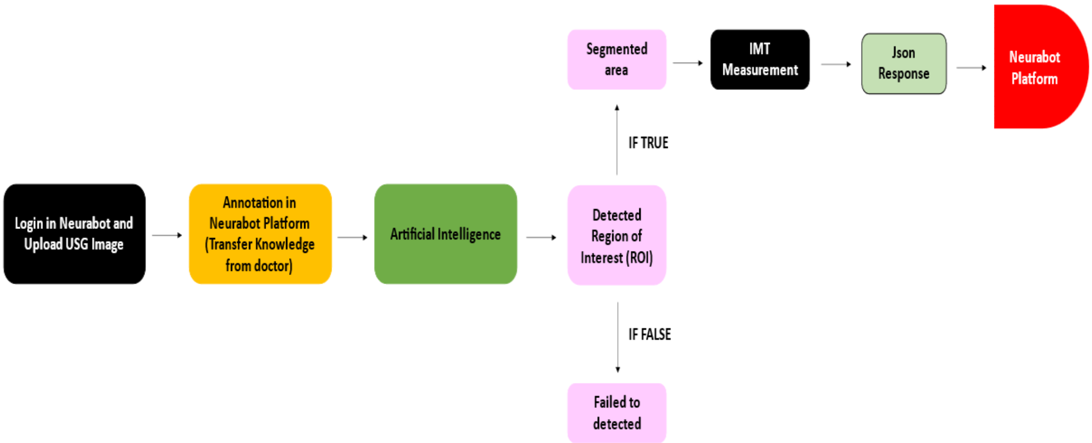

Figure 1. Algorithm of C-IMT measurement using AI

3. RESULTS

Sixty-four B-mode ultrasonography images were collected from neurology clinic registry, and four patients were excluded regarding missing data. A total of 60 patients C-IMT data were included in this study. we evaluated B-mode ultrasonography of 32 (53.3%) stroke and 28 non-stroke patients. Thirty-eight patients (63.3%) were male, and 31 (51.6%) were aged 45 to 55 years old. Patients' demographic characteristic on this study is presented on Table 1.

Table 1. Patients demographic

Subject characteristics	Total (Percentage)
Stroke	32 (53.33%)
Non-stroke	28 (46.67%)
Age (years)	
- 25-35	3 (5%)
- 35-45	9 (15%)
- 45-55	31 (51.67%)
- >55	17 (28.33%)
Gender	
- Male	38 (63.33%)
- Female	22 (36.67%)
Body mass index (kg/m^2)	
- <18.5	4 (6.67%)
- 18.5-24.9	37 (61.67%)
- 25-29.9	13 (21.67%)
- ≥30	6 (10%)
Smoking	
- Yes	36 (60%)
- No	24 (40%)
Alcohol consumption	
- Yes	4 (6.67%)
- No	56 (93.33%)
Hypertension	
- Yes	42 (70%)
- No	18 (30%)
Diabetes mellitus	
- Yes	39 (65%)
- No	21 (35%)
Dyslipidemia	
- Yes	38 (63.33%)
- No	22 (36.67%)

Kolmogorov-Smirnov test on both C-IMT measured by board of expert and AI found all data were normally distributed. We discovered p=0.115 and p=0.063 (p>0.05) for IMT measured by board of expert and AI, respectively. To analyzed AI validity, we compare C-IMT measured by AI with C-IMT measured by board of expert with dependent T-test, and we found strong correlation (r=0.874; p=0.014).

The internal consistency reliability coefficients (Cronbach's alpha) were 0.938 and 0.909, for pretest and posttest, respectively. We also analyzed the test-retest reliability by comparing pretest and posttest score with dependent t-test. We observed strong correlation with r=0.871 (p=0.000).

4. DISCUSSION

Atherosclerosis on carotid artery contributes fundamentally on incidence of ischemic stroke [15]. Identification of carotid plaque with radiologic modality is important to prevent stroke in patient with multiple risk factors [16]. Digital subtraction angiography (DSA) is considered the gold standard to identify and classify the severity of carotid plaque [17]. However, DSA is an invasive and high-cost imaging modality with risk of complication and radiation exposure, making its role in routine imaging workup is rather limited [18]. Magnetic resonance imaging, could also be used for stratifying stroke risk. A meta-analysis study by Gupta *et al*. showed that intraplaque hemorrhage, lipid-rich necrotic core, and thinning/rupture of fibrous cap observed in magnetic resonance imaging (MRI) study of carotid plaque is correlated with incidence of ischemic stroke and transient ischemic attack (TIA). Although MRI is safe and could provide detailed images of soft tissues, its limited availability and high cost make it not widely used to assess carotid plaque [8]. Ultrasonography, on another hand, has lower cost and relatively safer since it does not use ionizing radiation to produce images, thus it becomes first choice for carotid plaque screening [19]. Scanning of carotid artery using ultrasonography should be done circumferentially from anterior to posterior angle on common carotid artery, bulbs, and internal carotid artery [20]. Plaque that could be seen should be assessed for its location, thickness, and echo-density. C-IMT is also an important to be measured as it reflects the burden of atherosclerosis and is an independent risk factor of cerebrovascular accident [21], [22]. However, ultrasonography has its own limitation. Ultrasonography produce a relatively lower quality image and it is dependent on operator's skill and experience to assess abnormalities [21].

Utilization of AI is growing rapidly in the field of medicine [23]. AI and machine learning were optimized to detect several abnormalities on radiological images, i.e., tuberculous pleural effusion, breast cancer, and diabetic retinopathy [24]–[26]. AI could recognize complex pattern, and using its algorithm, interpret radiologic images. Its ability to provide quantitative, rather than qualitative data, and makes AI more valuable. Huge amounts of images could be assessed rapidly by AI, which potentially could help radiologist to prioritized images suspected with abnormality. In this study, we use convolutional neural network (CNN) algorithm, a learning base algorithm that could extract information from data, self-process and self-thought its own system, and could produce desired outcome. However, further evaluation is needed to ensure AI ability to measure specific characteristic. In this study, we developed algorithm to measure C-IMT thickness automatically by recognizing marking of tunica intima and tunica media [27], [28]. Several studies also use similar principal to measure tissue thickness. A study by Gupta *et al.* also use marking to measure myometrial layer thickness for detection of uterine cancer [29]. After recognize the marker of each layer, our AI scan through the layer to find thickest part and measure pixels of C-IMT. Thickness data in pixels then converted to millimeter to be compared with measurement done by panel of expert.

When C-IMT thickness measured by board of expert and by AI were compared, we observed strong correlation with r=0.874 (p=0.014). This finding indicates that AI we developed is reliable to measure C-IMT. This finding is similar to other studies evaluating C-IMT with AI using different approach. Biswas *et al.* also use AI to measure atherosclerotic wall thickness and plaque burden on carotid ultrasound using two-stage AI model. From the images taken, they segregated common carotid artery from other arteries, and then segmented the far wall region. This study also does further evaluation of total plaque area to evaluate risk for cardiovascular and stroke risk [30]. To evaluate the internal consistency reliability coefficients, we with Cronbach's alpha analysis and found coefficient of 0.938 and 0.909, on pretest and posttest respectively. Strong correlation between pretest and posttest was also found with r=0.871 (p=0.000). This finding indicates that our platform could produce a reliable result and could be further developed to be utilized in daily practice.

In this study, we create an algorithm to automatically measure C-IMT. This might be useful to both patient and clinicians since it is a safe, non-invasive, cheap, and repeatable method of assessment. Although showing big potential to measure C-IMT precisely, further study with bigger number of samples is needed to ensure its validity and reliability. In algorithm we developed, we did not proceed images which ROI was failed to be detected. Analysis of factors contributed to detection failure is needed to enhanced its capability. There are several approaches of AI to measure C-IMT with variable validity and reliability, thus a meta-analysis and systematic review are needed to standardized protocol and guideline for AI utilization on C-IMT evaluation. When our algorithm can be easily replicated and achieve the same or similar results in the future as this original study, it gives greater validity to the findings and those results can be generalized to the larger population. Pattern recognition on AI also could also be expanded to evaluate other characteristic of plaque, for instance, neovascularization, intraplaque hemorrhage, and plaque volume. AI also could be used to stratified risk of stroke or cardiovascular event by incorporating risk factors data (i.e., hypertension, diabetes, dyslipidemia, and body mass index (BMI) to statistical analysis.

5. CONCLUSION

AI could detect ROI and would do segmentation on the area to measure C-IMT autonomously. Our AI could automatically recognize the carotid artery, segment the wall of the carotid artery, trace the contours of the intima, media layer and adventitia layer, and measure the C-IMT. AI developed on Neurabot platform are valid and reliable to measure C-IMT, that potentially could reduce bias and provide faster images interpretation. Further study with bigger number of samples is still needed to ensure the validity and reliability of our algorithm.

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BIOGRAPHIES OF AUTHORS

Rivan Danuaji is a lecturer of Medical Faculty, Universitas Sebelas Maret, Surakarta. He is a medical doctor and neurovascular consultant in Dr. Moewardi General Hospital, Surakarta. He is interested in research about neurorestoration and neuroengineering, neuroimaging, and pain management. He can be contacted at email: rivan.danuaji@staff.uns.ac.id.

Subandi is a lecturer of Medical Faculty, Universitas Sebelas Maret, Surakarta. He is a medical doctor and neuro-intervention consultant in Dr. Moewardi General Hospital, Surakarta. He is interested in research about neurovascular, neurotrauma, and neurointerventional management. He can be contacted at email: dr_subandineuro@staff.uns.ac.id.

Stefanus Erdana Putra is a student of neurology residency program of Medical Faculty, Universitas Sebelas Maret, Surakarta. He is interested in reseach on neurological disease. His major interests in research are about epidemiology, neurocommunity, and neuroimmunology. He can be contacted at email: stefanuserdanaputra@student.uns.ac.id.

Muhammad Hafizhan is a student of neurology residency program of Medical Faculty, Universitas Sebelas Maret, Surakarta. He is interested in reseach on neurological disease. His major interests in research are about neurocommunity, neurorestoration, and neurovascular. He can be contacted at email: hafizhanmuhammad@student.uns.ac.id.