Android Based Application for Atherosclerosis Early Detection System Using Artificial Neural Networks

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Abstract. Nowadays, Coronary Heart Disease (CHD) is one of the leading health issues in the world. Every year, this disease is the leading cause of death in the world. The number of people who have died from cardiovascular diseases has increased by 17.3 million since 2008. More than three million of these deaths occur before the age of 60. This CHD is primarily caused by atherosclerosis, which is the deposition of fat on the arterial walls. According to the nature of atherosclerosis, which has no symptoms (asymptomatic), the progression varies between individuals, and the presence of several multifactorial factors makes early predictions difficult. Early detection of the causes of CHD is important so that appropriate preventive and treatment measures can be taken to slow down or to treat atherosclerosis.

For this reason, this research aims to develop an Android mobile-based early detection system for atherosclerosis using the Artificial Neural Network (ANN) method which uses primary data from districts hospital medical records in Bali Province – Indonesia for 138 sample subjects.

Based on the results of trials carried out, this system, named ARE (Atherosclerosis Risk Equation), produces a sensitivity value of 95% and a specificity of 93%. These results indicate that ARE can be used as a reference or guideline in the early detection of atherosclerosis in Bali Province, especially as an early effort to prevent the occurrence of coronary heart disease.

Keywords: Coronary heart disease, atherosclerosis, android, ANN, risk equation.

1 Introduction

1.1 Background

Heart disease or cardiovascular and blood vessel disease is one of the main health problems in developed and developing countries. This disease is the number one cause of death in the world every year. Since 2008, it is estimated that 17.3 million deaths were caused by cardiovascular disease. More than 3 million of these deaths occur

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before the age of 60. The incidence of premature death caused by heart disease is around 4% in high-income countries, and 42% occurs in low-income countries. Coronary heart disease and stroke are predicted to continue to increase, reaching 23.3 million deaths in 2030 (Ghani, et al., 2016). The prevalence of atherosclerosis in Indonesia based on a doctor's diagnosis or symptoms of the disease is 1.5%, around 2,650,340 people. (Indonesian Ministry of Health Research and Development Agency, 2013, PERKI, 2017).

Coronary Heart Disease (CHD) is a disease caused by narrowing and blockage of the coronary arteries which supply blood to the heart muscle. The main cause of CHD is atherosclerosis, namely the thickening and hardening of the arterial walls caused by fat accumulation (Sutamti et al., 2015). Atherosclerosis is caused by many risk factors, so atherosclerosis is called a multifactorial disease. Risk factors for atherosclerosis include age, gender, genetics, dyslipidemia, hypertension, obesity, diabetes mellitus, and smoking history (Baber et al., 2015). In connection with its asymptomatic nature, its progressiveness. which varies between individuals, and the causes are multifactorial, it is very difficult to make early predictions of atherosclerosis (Papageorgiou et al., 2017). Early prediction of atherosclerosis can arrest the increasing prevalence of atherosclerosis and is an important step for initiating therapy. Early initiation of therapy with statins has been shown to be effective for primary and secondary prevention of atherosclerotic events in many at-risk individuals (Stone et al., 2014).

Several application systems have been developed to predict atherosclerosis early, such as the Framingham Risk Score (FRS) and other risk estimation systems (Cooney et al., 2010; Pathak et al., 2016). However, the main limitation of any risk estimation system is that the risk algorithm is determined based on epidemiological data, so this system can only be applied to the population from which the data is sourced (Lledo et al., 2016).

For this reason, an early prediction application for the incidence of atherosclerosis was developed using an epidemiological database in several hospitals in the Bali area. This system uses an Artificial Neural Network (ANN) algorithm which was created based on related risk factors that influence hs-CRP levels in dyslipidemia sufferers including determining age, gender, diabetes, smoking, hypertension, total cholesterol, TG, LDL, HDL, and fasting glucose. which is a factor in the occurrence of atherosclerosis (Swastini, 2019). According to previous research (Abimanyu, 2020), smoking habits and hypertension are the most influential in the incidence of atherosclerosis in outpatients aged over 40 years at Sanjiwani Hospital, Bali.

1.2 Problems

How make a prediction system of atherosclerosis in outpatients at community health centers in Bali?

1.3 Objective

The aim of this research is to predict the value and validity of the ARE (Athero sclerosis Risk Equation) system in outpatients at community health centers in Bali.

2 Literature Review

According to world health statistics, 9.4 million people die from cardio-vascular disease every year and 45% of them die from coronary heart disease. It is estimated that by 2030 this figure will increase to 23.3 million. Coronary Heart Disease (CHD) is the largest contributor to cardiovascular disease. Due to coronary artery stenosis, atherosclerosis or spasm or both, coronary heart disease is a dysfunction of the heart due to insufficient blood supply. Because the cost of the drugs needed to treat coronary heart disease is very expensive, the treatment time is relatively long, as well as other supporting examinations required during the treatment process are also quite expensive. Therefore, early detection of risk factors and various preventive measures to control coronary heart disease are very important (Ghani et al., 2016; Kurniawaty and Yusnita, 2016; Iskandar et al., 2017).

2.1 Pathogenesis of Atherosclerosis Underlying Coronary Heart Disease

Atherosclerosis is chronic inflammation of coronary heart disease. The chronic inflammatory process of atherosclerosis involves a series of cellular and molecular reactions. Atherosclerosis is defined as a fibroproliferative inflammatory response to various forms of endothelial damage (endothelial dysfunction). Endothelial damage caused by various risk factors allows lipid and inflammatory factors to enter the artery wall. Endothelial injury can alter endothelial homeostasis, and increase endothelial permeability, as well as adhesion of white blood cells and platelets to the endothelium. This condition then causes changes in the arterial walls which are characterized by the accumulation of extracellular fat, recruitment and accumulation of white blood cells, formation of foam cells, migration and proliferation of muscle cells, and deposition of extracellular matrix which ultimately causes thickening and stiffness of the arteries. (Figure 1) (Lintong, 2009; George and Jason, 2010).

2.2 Non-Modifiable Risk Factors

Age, CHD is usually clinically asymptomatic until atherosclerotic lesions reach a critical threshold in middle age. CHD is a disease that follows increasing age and all the factors that accompany it. The risk of CHD increases after age 45 in men and after age 55 in women. Women aged 65 years or older have the same risk of cardiovascular disease as men of the same age (Rahman, 2012).

Gender: Men have a greater risk of having a heart attack and it occurs earlier than women. In general, CHD is less common in women, but this difference becomes a little more prominent in the last decades, especially during menopause. This is because the endogenous estrogen hormone is protective in women, but after menopause the incidence of CHD increases rapidly, but not as much as the incidence of CHD in men (Supriyono, 2008).

Genetics, Family history is an independent risk factor for CHD. A positive family history of CHD will increase the possibility of CHD. Certain Mendelian disorders are strongly associated with CHD, for example familial hypercholesterolemia, as well as manifestations of specific single gene disorders that are associated with CHD (Supriyono, 2008).

2.3 Modifiable Risk Factors

Dyslipidemia, is a disorder of lipid metabolism characterized by an increase or decrease in the lipid fraction in plasma. The main lipid fraction abnormalities are increased levels of total cholesterol, triglycerides, LDL cholesterol, and decreased levels of HDL cholesterol. The formation of atherosclerotic plaque begins with irritants, one of which is the increase in plasma lipid levels in dyslipidemia, especially LDL. The role of triglycerides as a risk factor for atherosclerosis is still controversial because increasing triglyceride levels is closely related to the risk of pancreatitis. Hyperlipidemia produces excessive reactive oxygen species (ROS) which can damage the endothelium and can cause atherogenesis (Rahman, 2012; Hur-tubise et al., 2016).

Hypertension, the cause of vascular damage can be a direct result of increased blood pressure in organs or due to indirect effects including the presence of angiotensin II, oxidative stress, and excessive ROS expression. Hypertension can destroy the endothelial layer of vascular smooth muscle cells through changes in pressure and increased oxidative stress. Then this process will trigger a series of processes that trigger the formation of atherosclerotic plaque (Rahman, 2012; Hurtubise et al., 2016).

Obesity, is a condition where excess fat is found in the body. The significant results between obesity and CHD are because obesity can increase blood pressure, lipid levels, glucose resistance and blood clotting (Ghani et al., 2016).

Diabetes Mellitus, Adults who suffer from diabetes mellitus are 2-4 times more likely to develop heart disease than people who do not suffer from diabetes mellitus. People with diabetes tend to experience tissue degeneration and endothelial dysfunction more quickly, resulting in a thickening of the basement membrane of the capillaries and coronary arteries, resulting in narrowing of blood flow to the heart. The existence of glucose resistance causes glucose in the blood to increase so that blood viscosity also increases and the tendency for CHD to occur also increases (Ghani et al., 2016).

Smoking, the mechanism that causes increased atherosclerosis is direct endothelial injury due to agents in cigarettes (carbon monoxide and nicotine) which can induce pro-inflammatory cytokines. In addition, the tobacco contained in cigarettes can cause a decrease in oxygen levels carried by the blood and cause the blood to tend to clot easily. Blood clots that form in these arteries can cause CHD as well as stroke and sudden death. Smoking increases the formation of atherosclerotic plaque and promotes coronary thrombosis. Smoking can also reduce the blood's ability to transport oxygen (Ghani et al., 2016)

3 Methodology

3.1 Research Plans

This research is an observational (non-experimental) study with a cross-sectional research design, and subjects were drawn purposively. A cross-sectional research design is a study design that studies the relationship between exposure and disease by observing both simultaneously, namely at the same time (Purnomo and Syamsul, 2017).

This research was conducted as a validation to determine the predictive value of the ARE system and to determine the specificity sensitivity of the results obtained from the ARE system with the results of medical record examination to predict atherosclerosis, so that it can be used as a basis for initiating therapy in community health center patients in Bali. Several stages carried out in this research are as follows.

1. Selection of research population and samples
2. Collecting patient medical record data
3. Calculation of the estimated risk of atherosclerosis using the atherosclerosis potential prediction model system, namely the Atherosclerosis Risk Equation
4. Validate the results of the predictive value of the atherosclerosis potential prediction system using the results of examining health center medical record data.

3.2 Location and Research Timeline

The research locations were carried out at the community health centers in Denpasar, Tabanan and Karangasem. The research was conducted for 4 months from November 2020 to February 2021

3.3 Research Subject

The sampling method used is nonprobability sampling with pur-posive sampling technique (Sugiyono, 2016). In this study, a purposive technique was chosen because only patients who met the inclusion criteria and did not meet the exclusion criteria would be research subjects. The inclusion criteria and exclusion criteria used in this study are as follows.

Inclusion criteria include: (i) Patients aged 30-60 years. (ii) Patients at high risk of atherosclerosis or patients with a diagnosis of dyslipidemia, hypertension and diabetes mellitus, obesity and a history of smoking. (iii) Patients with clear and complete medical record data

Exclusion criteria include: Patients with severe psychological disorders, physical disabilities, cancer, Alzheimer's disease, tuberculosis, immune deficiency syndrome (AIDS), and other infectious diseases.

3.4 Research Scheme

The research flow is explained in detail in the following chart.

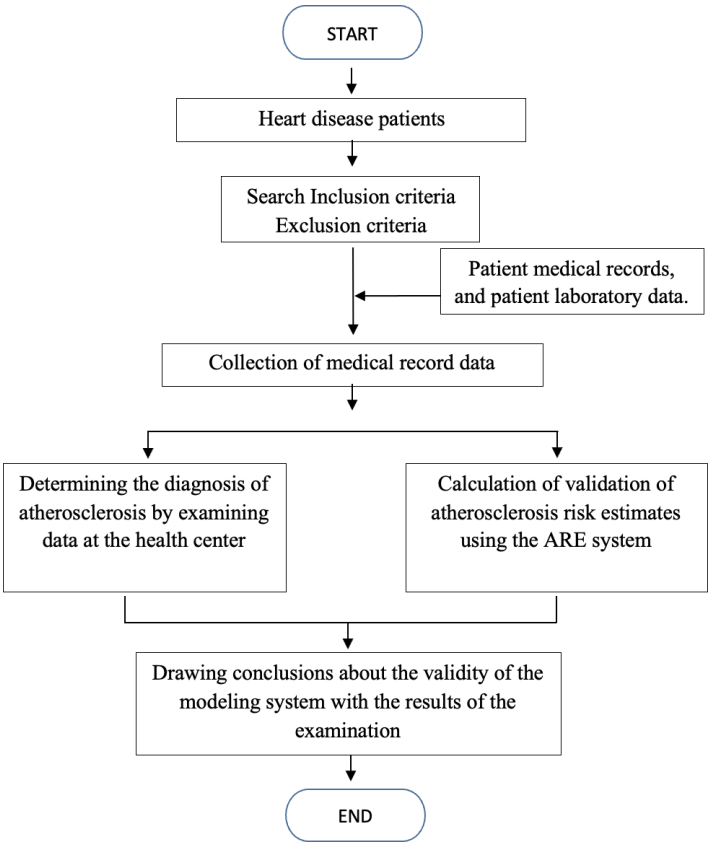

Fig. 1. Research Schematic Chart

3.5 Atherosclerosis Risk Equation (ARE).

The Atherosclerosis Risk Equation system is the latest screening system innovation using an ANN (Artificial Neural Network) system with a backpropagation algorithm that combines a database of variable factors from CHD patients. First, the patient's data is recorded, then continued by recording factors such as: body weight, age, BMI (Body Mass Index), smoker (yes/no), alcoholic, hypertension, and diabetes mellitus. After getting a lot of patient data, it will be entered into Excel format as a database and then used to train the ANN that will be used.

ANN has the ability to learn through a training process in recognizing hidden patterns from datasets. ANN will carry out training using some of the available data from patients affected by coronary heart disease (train data). With this training, the knowledge contained in patient data is absorbed and represented by connection weight

values which are represented in the form of connections between the input layer and the hidden layer as well as connections from the hidden layer to the output layer.

The ANN network structure used is ANN Backpropagation. This ANN consists of 3 layers, 1 input layer (several influencing patient factors), 1 hidden layer, 1 output layer (output in the form of atherosclerosis or not). The back-propagation network algorithm will output errors to change the value of the weights in the backward direction. To get this error, the forward propagation stage must be carried out first. During forward propagation, neurons are activated using the Sigmoid activation function.

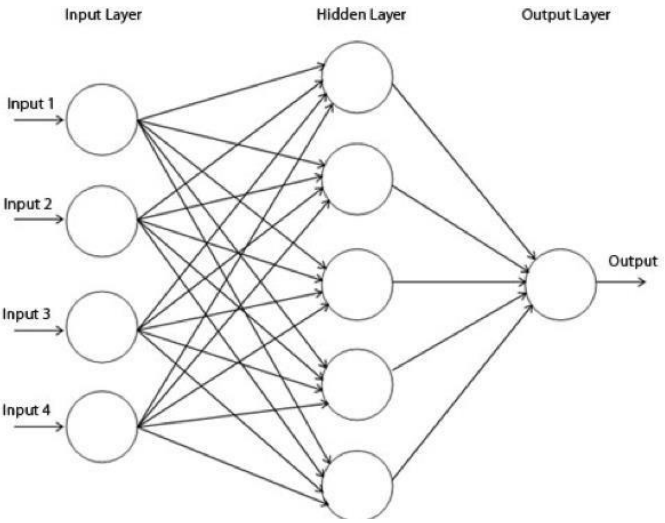

Fig. 2. Arsitektur Artificial Nerural Network

The ANN Backpropagation learning algorithm above contains several things that must be considered. Learning rate (LR) at the time of initiation must be very careful. Choosing the wrong weight will result in no minimum error being found. The LR chosen is an LR that is not too large, usually a random number between —0.5 and 0.5 is chosen. LR will push the input to a neuron to an extreme large or extreme small which the transfer function will saturate. Apart from LR in the ANN algorithm there is also an initial initial weight which is chosen randomly by considering a value that is neither too large nor too small which will be used as a reference for feed forward calculations. At this initial weight training stage it is likely that it will produce suboptimal results. However, with the ability to correct the weights (backward), the weights are slowly corrected in a structured manner based on all training data using the Gradient Descent concept so that in the end the most optimal weights will be obtained with the criteria of achieving a minimum error or achieving a maximum number of epochs.

After going through the train process, the ANN network structure that has been trained will be tested on test data using part of the existing dataset to provide accuracy

results. After the test data has been carried out, the trained ANN model will be converted in the form of a .Tflite (tensor flow lite) extension and will be used in application development on Android devices. The Android application in this case already uses the trained model and is ready to receive input from factors and will determine the classification of whether the patient has atherosclerosis or not.

After going through the train and testing process, the next thing that must be done is the prediction process. This process uses data outside the previous dataset. In this prediction process the system will actually be tested in real life in the field. The success of this prediction will be very significant in assuming the success of the system. If it turns out that the value of the prediction process is low, then improvements need to be made on the training side or also on the amount of data or it could even be that the variables used need to be increased.

3.6 Data Analysis

The predictive value is the magnitude of the possibility using the sensitivity and specificity values as well as the prevalence and the proportion of the population who suffers. The predictive value can be positive, meaning that those with a positive test also suffer from the disease, while the negative predictive value means that those who test negative also do not suffer from the disease. The positive predictive value is greatly influenced by the prevalence of the disease in the community with the provision that the higher the prevalence of the disease in the community, the higher the positive predictive value and the better.

Validation has two components, namely sensitivity and specificity, while the terms for these two components are:

a. **True positive**, which refers to the number of cases that actually suffer from the disease with positive test results.
b. **False positive**, which shows the number of cases that are not actually sick but the test shows positive results.
c. **True negative**, indicates the number of cases that are not sick with negative test results.
d. **False negative**, which refers to the large number of cases that actually suffer from the disease but the test results are negative.
   Examples of terms from these two components if entered into the data calculation table are as follows:

		DISEASE		AMOUNT
		POSITIVE (F/T)	NEGATIVE (F/T)	
CHECK UP RESULT	POSITIVE	A	B	A+B
	NEGATIVE	C	D	C+D
AMOUNT		A+C	B+D	A+B+C+D

Table 1. Confusion Metrics

From table 1 above, the values in question can be calculated, namely:

e. Sensitivitas : $\frac{A}{A+C}$ x 100 %
f. Spesifisitas : $\frac{B}{B+D}$ x 100 %
g. True positive : A
h. False positive : B
i. True negative : D
j. False negative : C
k. Positive predictive value : $\frac{True\ positive}{True\ positive+false\ positive}$ x 100 %
l. Negative predictive value : $\frac{True\ negative}{True\ negative+false\ negative}$ x 100 %

A good screening tool (test) has a higher level of validity, the better it is. The value of these two parameters is of course determined by the value of the medical record data that has been diagnosed. (Lapau, 2017)

4 Result and Discussion

4.1 Basic Characteristics of Research Subjects

Characteristics of the research subjects included demographic data such as age, gender, body mass index (BMI), smoking, alcohol consumption, diabetes mellitus, hypertension, and dyslipidemia in Bali (Table 2). The subject's age category was partly in the 30 to 40 year age range with a total of 17.39%, in the 40 to 50 year age range with a total of 42.02%, in the 50 to 60 year old range with a total of 40.57%. Mostly men were the research subjects, amounting to 52.17% and women amounting to 47.82%. The normal BMI in this study was 40.87%, while the obesity group was 59.42%. Smoking history data showed that 34.78% of patients had a history of smoking and 65.21% of 138 patients had no history of smoking. The history of alcohol consumption shows that the majority of patients are in the group who do not consume alcohol, namely 20.28% and those who do not consume it are 79.71. Subject characteristics based on diabetes mellitus data with a total of 47.10% and those with no history of diabetes amounting to 52.89%, and hypertension with a total of 55.07% for those with a history of hypertension and those without a history of hypertension amounting to 44.92% , data on a history of dyslipidemia was 46.37% and those without a history of dyslipidemia were 53.62%. Data on those diagnosed with cardiovascular disease in this study was 48.55% and those who were not diagnosed with cardiovascular disease were 51.44%. Table 2 tells about characteristics of research data in the Bali region.

4.2 Application

The application was built using the Python programming language, using the TensorFlow Lite library, and created using Android Studio. The results are as follows:

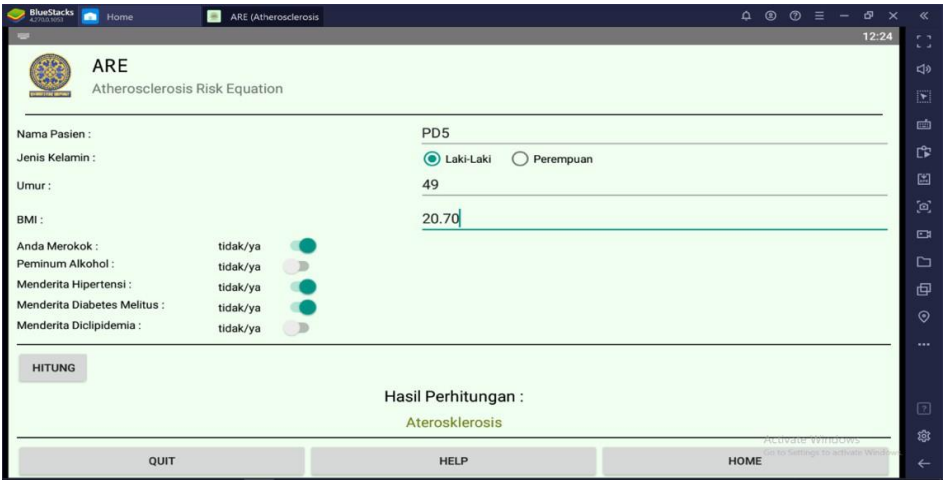

Fig. 3. Output results that have the potential for atherosclerosis

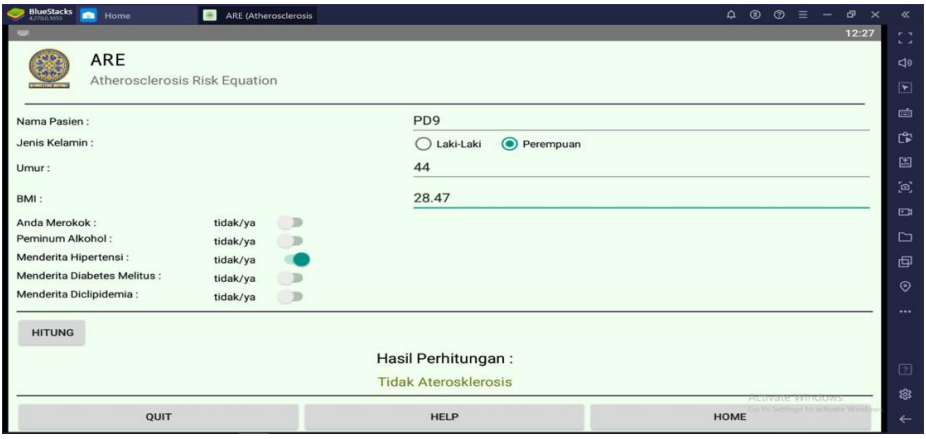

Fig. 4. Output results that do not have the potential for atherosclerosis

Based on the results obtained, it can be interpreted that the system's ability to determine the risk of atherosclerosis is quite good, because the closer it is to 100%, the stronger the diagnostic system's ability to predict disease in a population (Gordis, 2014). Judging from the results which are quite good with a sensitivity value of 95% and specificity of 93%, this instrument system has great potential in the future to help the early detection system for atherosclerosis in Indonesia because an instrument system only applies to the population that is the data source because the risk estimation

algorithm is based on data. epidemiological origin of the system was created (Bansal et al., 2015). Therefore, it is necessary to add a database of the ARE system from all districts or provinces in Indonesia to strengthen its ability to determine the risk of atherosclerosis through population risk factors in Indonesia.

Basic Characteristics of Research Subjects	Frequency (n=138)	Percentage (%)
Age		
30-40	24	17,39
41-50	58	42,02
51-60	56	40,57
Gender		
Male (M)	72	52,17
Female (F)	66	47,82
IMT		
Normal (IMT < 25)	56	40,57
Obesitas (IMT ≥ 25)	82	59,42
Smoking		
Yes	48	34,78
No	90	65,21
Drink Alcohol		
Yes	28	20,28
Not	110	79,71
Diabetes Melitus		
Yes	65	47,10
No	73	52,89
Hipertensi		
Yes	76	55,07
No	62	44,92
Dislipidemia		
Yes	64	46,37
No	74	53,62
Diagnosis CAD		
Yes	67	48,55
No	71	51,44

Table 2. Basic Characteristics of Research Subjects

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		DISEASE		AMOUNT
		POSITIVE (F/T)	NEGATIVE (F/T)	
CHECK UP RESULT	POSITIVE	57 (A)	5 (B)	A+B = 62
	NEGATIVE	3 (C)	73 (D)	C+D = 76
AMOUNT		A+C = 60	B+D =78	A+B+C+D = 138

Table 3. Data Calculation

Apart from that, the output capability of ARE, which is currently only able to classify whether a person is suffering from atherosclerosis or not, should be expanded

to include the stage of atherosclerosis. Along with the stage of atherosclerosis, treatment suggestions that are appropriate to the stage experienced by a person can also be added as a feature so that ARE's early predictions can function appropriately to provide treatment suggestions before atherosclerosis reaches a severe stage so that a person's level of pain in atherosclerosis can be minimized.

As explained in the previous subchapter, the ANN architecture is very dependent on the training data owned by the system, so changes in the ARE output will certainly result in data changes and changes to the ANN architectural model. However, supported by a good dataset, and ANN's ability to make adjustments to the data, the author believes that the weight changes between input layer-hidden layer, and hidden layer-output layer will remain in the optimal position so as to produce a capable system, having high sensitivity and specificity.

5 Conclusions and Recommendation

5.1 Conclusions

The results of the system validation value based on the test results showed that the sensitivity of the ARE test was 95%, which means that the ability of the ARE test to get positive results among 138 patients at risk of developing atherosclerosis was 95% while the rest were negative (false negative) and the specificity of the ARE test was 95%. 93%, which means the ability of the ARE test to get negative results among 138 patients who were not at risk of atherosclerosis was 93% while the rest were positive (false positive). This means that the ARE application is able to represent the ability of a doctor or expert to carry out predictive analysis of whether a person has the potential for atherosclerosis or not.

5.2 Recomendation

Based on the research results, suggestions that can be given regarding this research are the need to carry out similar research in other regions of Indonesia as an addition to the database of risk factors for cardiovascular disease in Indonesia. Another suggestion that can be given is that research can still be expanded by developing risk estimation results into atherosclerosis stage classes and providing treatment solutions that are appropriate to that stage.

6 Bibliography

Abimanyu, M.D. 2020, ‘Faktor Risiko Terjadinya Aterosklerosis pada Pasen Rawat Jalan di Rumah Sakit Umum Sanjiwani Karangasem, Skripsi, Program Studi Farmasi, Fakultas Ilmu Pengetahuan Alam’, Universitas Udayana.

Aboyans, V., Criqui., M. H., Abraham, P., Allison, M. A., Creager, M. A., Diehm, C., et al. 2012. Measurement and Interpretation of the Ankle-Brachial Index: A Scientific Statement from the American Heart Association. Circulation, 126:2890-2909.

Amalia, Carine. 2018. Penilaian Uji Validitas Instrumen Skrining Hipertensi. Jurnal Berkala Epidemiologi. Surabaya. Vol. 6 No. 2 95-102

Baber, U., Mehran, R., Sartori, S., Schoos, M. M., Sillesen, H., Muntendam P., et al. 2015, Prevalence, Impact, and Predictive Value of Detecting Subclinical Coronary and Carotid Atherosclerosis in Asymptomatic Adults, Journal of The American College of Cardiology, 65:1065-1074.

Badan Penelitian dan Pengembangan Kementerian Kesehatan RI. 2013, 'Riset Kesehatan Dasar 2013' diakses pada 10 Oktober 2020, <http://www.depkes.go.id/article/view/15021800003/situasi-kesehatan-jantung.html>.

Boston Scientific. 2014. Angioplasty and Stent Education Guide. Marlborough: Boston Scientific Corporation.

Coll, B., Betriu, A., Alonso, M., Lourdes, M. B., Maria, C., Amoedo, L., et al. 2010, Cardiovascular Risk Factors Underestimate Atherosclerotic Burden in Chronic Kidney Disease: Usefulness of Non-Invasive Tests in Cardiovascular Assessment, Nephrol Dial Transplant, 25:3017–3025.

Cooney, M. T., Dudina, A., D'Agostino, R., and Graham, I. M. 2010, Cardiovascular Risk-Estimation Systems in Primary Prevention: Do They Differ? DoThey Make a Difference? Can We See the Future?, Circulation, 122:300-310.

Dinkes Bali. 2019, Profil Kesehatan Provinsi Bali 2019, Denpasar: Dinas Kesehatan Provinsi Bali.

George, S. J. dan Johnson, J. 2010, Atherosclerosis: Molecular and Cellular Mechanisms, Willey-VCH Verlag GmbH and KgaA, Weinheim.

Ghani, L., Susilawati, M. D. dan Novriani, H. 2016, Faktor Risiko Dominan Penyakit Jantung Koroner di Indonesia, Buletin Penelitian Kesehatan, 44:153-164.

Gordis, Leon. 2014. Epidemiology 5th Ed. Philadelphia Canada, PA: Elsevier Saunders

Greenland, P., Alpert, J. S., Beller, G. A., Benjamin, E. J., Budoff, M. J., Fayad, Z. A., et al. 2010, 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults, Journal of the American College of Cardiology, 56:e50-e103.

Harvey, David., (2000), Modern Analytical Chemistry. New York: McGraw-Hill Comp.

Hurtubise, J., McLellan, K., Durr, K., Onasanya, O., Nwabuko, D., and Ndisang, J. F. 2016, The Different Facets of Dyslipidemia and Hypertension in Atherosclerosis, Current Atherosclerosis Reports, 18:1-12.

Iskandar, Hadi, A., dan Alfridsyah. 2017, Faktor Risiko Terjadinya Penyakit Jantung Koroner pada Pasien Rumah Sakit Umum Meuraxa Banda Aceh, Aceh Nutrition Journal, 2: 32-42.

Kumar V., Abbas A. K., and Aster J. C. 2018, Robbins Basic Pathology, Tenth Edition, Pennsylvania: Elsevier, Philadelphia.

Kurniawaty, E. dan Yusnita, A. R. 2016, Pengaruh Konsumsi Bluberi (Vaccinium cyanococcus) terhadap Penurunan Oksidasi LDL sebagai Pengobatan untuk Penyakit Jantung Koroner, Majority, 5:6-10.

Lapau, Buchari. (2017). Prinsip dan Metode Epidemiologi. Edisi I. Jakarta: Kencana.

Lintong, P. M. 2009, Perkembangan Konsep Patogenesis Aterosklerosis, Jurnal Biomedik, 1: 12-22.

Lledo, A. G., Mur, J. L. M., Mir, V. P., Aparicio, S. N., Barrio, A. S., Sanz, C. A., et al. 2016, Relationship Among Risk Score Systems and Coronary Atherosclerosis Determined by Multislice Computed Tomography, Clinical Cardiology, 39:603-607.

Mukherjee D. 2009. Peripheral Arterial Disease: Considerations in Risks, Diagnosis and Treatment, J Nafl Med Assoc., 101:999-1008.

Muntaha. 2018. Gambaran Risiko Penyakit Jantung Koroner Pada Penyandang Diabetes Melitus Di Puskesmas Purwosari. Skripsi thesis. Universitas Muhammadiyah Surakarta.

Papageorgiou, N., Briasoulis, A., Androulakis, E., and Tousoulis, D. 2017, Imaging Subclinical Atherosclerosis: Where Do We Stand?, Current Cardiology Reviews, 13:47-55.

PERKI. 2017, Panduan Tata Laksana Dislipidemia 2017, Perhimpunan Dokter Spesialis Kardiovaskular Indonesia, Jakarta.

Rahman, A. 2012, Faktor-Faktor Risiko Mayor Aterosklerosis pada Berbagai Penyakit Aterosklerosis di RSUP Dr. Kariadi Semarang, Penelitian Karya Tulis Ilmiah, Fakultas Kedokteran, UNDIP Semarang.

Riccioni, G., and V. Sblendorio. 2012. Atherosclerosis: from biology to pharmacological treatment. Journal of Geriatric Cardiology. 9: 305-317.

Stone, N. J., Robinson, J. G., Lichtenstein, A. H., Merz, C. N. B., Blum, C. B., Eckel, R. H., et al. 2014, 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, Journal of the American College of Cardiology, 63:2889–2934.

Sugiyono. 2016, Metode Penelitian Kuantitatif, Kualitatif, dan R&D. Alfabeta, Bandung.

Supriyono, M. 2008, 'Faktor-Faktor Risiko yang Berpengaruh terhadap Kejadian Penyakit Jantung Koroner pada Kelompok Usia <45 Tahun (Studi Kasus di RSUP Dr. Kariadi dan RS Telogorejo Semarang)', Tesis, Magister Epidemiologi, Program Pasca Sarjana, Universitas Diponegoro, Semarang.

Sutamti, Purwanto A.P., dan Tjahjati, M. I. 2015, Oxidized-Low Density Lipoprotein dan Derajat Stenosis Penyakit Jantung Koroner, Indonesian Journal of Clinical Pathology and Medical Laboratory, 21: 266–272.

Sujarweni, V. W. 2015, Statistik untuk Kesehatan, Gava Medika, Yogyakarta.

Swastini, D. A., Wiryanthini, I. A. D., Ariastuti, N. L. P., & Muliantara, A. (2019). Atherosclerosis Prediction with High Sensitivity C-Reactive Protein (hs-CRP) and Related Risk Factor in Patient with Dyslipidemia. Open Access Macedonian Journal of Medical Sciences, 7(22), 3887.

Tjay, T. H. dan Rahardja K. 2015. Obat-Obat Penting: Khasiat, Penggunaann, dan Efek-efek Sampingnya. Edisi Ketujuh. Jakarta: PT Gramedia.

Walsworth M. K., Bie R., Figoni A., O'connell J. 2017, Peripheral Artery Disease: What the Orthopedic Physical Therapist Need to Know, J Orthopedic Physical., 4:1-26.

Wolk, M. J., Bailey, S. R., Doherty, J. U., Douglas, P. S., Hendel, R. C., Kramer, C. M., et al. 2014, ACCF/ AHA/ ASE/ ASNC/ HFSA/ HRS/ SCAI/ SCCT/ SCMR/ STS 2013 Multimodality Appropriate Use Criteria for the Detection and Risk Assessment of Stable Ischemic Heart Disease, Journal of the American College of Cardiology, 63:380-406.

Xu, D, Li, J., Zou, L., Xu, Y., Hu, D., Pagoto, S.L., and Ma, Y. 2010, Sensitivity and Specificity of The Ankle–Brachial Index to Diagnose Peripheral Artery Disease: A Structured Review, Vascular Medicine, 15:361-369.