Developing an Artificial Intelligence (AI) Model in Predicting the Occurrence of Abdominal Aortic Aneurysm (AAA)

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Contents

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ABSTRAK

Latar belakang: AAA biasanya asimtomatik sehingga komplikasi berlaku seperti pembedahan aorta dan pecah AAA. Pengesanan awal dan pengurusan AAA yang betul mengurangkan kadar kematian keseluruhan akibat pecah. Oleh itu, model AI dicadangkan untuk menangani masalah ini: untuk meramalkan kejadian AAA, juga untuk membantu pakar perubatan untuk pengesanan awal yang membawa kepada pengurusan yang sesuai, dengan itu mengurangkan komplikasi dan kematian.

Objektif: Untuk membangunkan model AI untuk meramal kejadian AAA dan untuk menentukan ketepatan model AI dalam meramalkan kejadian AAA dalam populasi saringan.

Kaedah: Terdapat dua fasa dalam kajian ini: (i) Fasa 1 - data retrospektif yang terdiri daripada faktor risiko AAA diekstrak daripada dua institusi dan digunakan untuk melatih model; (ii) Fasa 2 – data prospektif telah dikumpul dan digunakan untuk mengesahkan model terlatih. Semasa proses latihan, model AI telah dilatih dengan kombinasi ciri yang berbeza. Dua model SVM telah dilatih: (i) normal lwn abnormal (AA kecil dan besar) dan (ii) AA kecil lwn besar, yang ditakrifkan oleh saiz AA. Ketepatan, sensitiviti dan kekhususan telah dilaporkan.

Dapatan: Untuk AA normal vs abnormal, model AI 1 masing-masing mencapai ketepatan 86.1% dan 79.4% dalam Fasa 1 dan 2. Kami mendapati bahawa parameter penting untuk membezakan antara AA normal dan abnormal ialah umur, jantina, hipertensi, tekanan darah sistolik dan diastolik, status dialisis dan tahun hipertensi. Untuk AA kecil vs besar, model AI 2 masing-masing mencapai ketepatan 86.7% dan 60.8% dalam Fasa 1 dan 2. Parameter tambahan untuk membezakan antara AA kecil dan besar termasuk dislipidemia, status merokok, penyakit paru-paru dan penyakit buah pinggang.

Kesimpulan: Kami menunjukkan bahawa model AI mempunyai potensi untuk meramalkan saiz AA dengan ketepatan yang memuaskan hanya menggunakan demografi dan sejarah perubatan pesakit. model-model dibangunkan boleh berguna untuk pakar perubatan yang tidak mempunyai kebolehcapaian kemudahan pengimejan di kawasan daerah untuk meramalkan saiz AA tanpa imej radiografi.

ABSTRACT

Background: AAA is usually asymptomatic until complications occurred such as aorta dissection and ruptured AAA. Early detection and proper management of AAA reduces the overall death rate from rupture. Therefore, an AI model is proposed to tackle this problem: to predict the occurrence of AAA, also to assist physicians for early detection which leads to appropriate management, thereby reducing complication and mortality.

Objective: To develop an AI model to predict occurrence of AAA and to determine the accuracy of AI model in predicting the occurrence of AAA in screening population

Methods: There are two phases in this study: (i) Phase 1 - retrospective data consisting of AAA''s risk factors were extracted from two institutions and was used to train the model; (ii) Phase 2 – prospective data were collected and was used to validate the trained model. During the training process, the AI model was trained with different combinations of the features. Two SVM models were trained: (i) normal vs diseased (small and big AA) and (ii) small vs large AA, which is defined by AA size. Accuracy, sensitivity and specificity were reported.

Results: For normal vs diseased AA, AI model 1 achieved an accuracy of 86.1% and 79.4% in Phase 1 and 2, respectively. We found that important parameters to differentiate between normal and diseased AA were age, gender, hypertension, systolic and diastolic blood pressure, dialysis status and years of hypertension. For small vs large AA, AI model 2 achieved an accuracy of 86.7% and 60.8% in Phase 1 and 2, respectively. Additional parameters to distinguish between small and large AA include dyslipidemia, smoking status, lung disease and kidney diseases.

Conclusions: We showed that the AI model has the potential to predict AA size with satisfactory accuracy using only the patient's demographics and medical history. The models

developed could be useful for physicians who do not have the accessibility of imaging facilities in the district area to predict AA size without radiography images.

1.0 INTRODUCTION

1.1. Introduction & Literature review

Abdominal Aorta Aneurysm (AAA) is most commonly defined as the maximal diameter of the abdominal aorta exceeding 3cm. The prevalence of AAA is 1.3% - 7.2% worldwide [1]. Malaysia is one of the top three countries in Asia with the highest mortality rate (5.2 deaths per 100,000) due to aortic aneurysms and the prevalence of aortic aneurysms was approximately 15,000 [2].

Current AAA treatments include continuous monitoring of risk factors and clinical signs or performing surgery to prevent AA rupture. Early identification of AAA patients offers planned elective repairs, with ten times lower mortality than emergency AAA repair [3]. Past randomized studies also reported that AAA rupture was reduced by 50% when AAA screening was offered [4, 5]. Ultrasound or Computer Tomography (CT) scans are the most commonly used imaging modalities to estimate AA size and thus assess patients' risk of AA rupture. However, most hospitals or health care centers in the district area do not have access to medical imaging equipment. Therefore, physicians have to rely on physical examination and medical history to envisage the risk of AAA rupture, but such a method has low sensitivity (68%) and specificity (75%) [6]. Failure to detect AAA at an early stage and delay in applying early prevention measures may increase the risk of complicated AAA.

Multiple risk factors that are associated with the development of AAA include age [7], gender [8-10], smoking [11, 12], family history of AAA [13] and other medical conditions such as hypertension [14], dyslipidemia [15], coronary arterial disease [16, 17] and chronic obstructive pulmonary disease [18, 19]. Patients with age above 65 were shown to have a higher risk of developing AAA [7, 8] and hence most guidelines suggest performing AAA screening at the age of 65 [20-22]. Moreover, AAA is more prevalent in men [8-10] and

smokers. Smokers were associated with 7.6 times increased prevalence of AAA than a non-smoker and every increased in a year of smoking increased the relative risk of AAA by 4% [12]. Furthermore, patients with a family history of AAA had a two times higher risk of developing AAA [13]. Kobeissi et al. study reported that every 20mmHg and 20mmHg rise in systolic and diastolic blood pressure escalates the risk of AAA development by 14% and 28%, respectively [14].

AAA is complex, and classical statistical approaches may not be able to model the data pattern with high predictive strength. Artificial Intelligence (AI) is a computational approach that can learn non-linear data patterns in large data sets with multiple variables and generate insight to make better decisions and predictions. In the past, AI has been shown to be a promising tool in predicting various diseases, such as heart disease [23, 24], liver diseases [25], and fetus outcomes [26]. Most AI studies related to AAA concentrate on automating the AAA quantitative analysis, such as characterizing arterial morphology, geometry, and fluid flow [27]. A review of AI applications in AAA is available in [28]. However, machine learning studies that focus on predicting AAA risk based on risk factors and patients' demographics are scarce. As such, motivated by the inaccessibility of imaging facilities in the district area, this study aims to develop an AI model to predict AA size using risk factors associated with AAA. Such a model will enable physicians who do not have access to medical imaging equipment to better predict AAA and allow better planning for appropriate clinical management at an early stage.

1.2. Study rationale

It has been a major challenge for physicians to diagnose AAA clinically due to indirect clinical presentation of AAA. Asymptomatic AAA has been detected incidentally by physical examination and radiological images. Patients with AAA may come with pulsatile mass at the epigastric region during physical examination. However,

Howard et all state that the sensitivity and specificity of physical examination to diagnose AAA are low, at 68% and 75% respectively (3). Ultrasound abdomen is a good modality to diagnose AAA due to its high sensitivity (97.7-100%) and specificity (94.1-100%) (4). Most of the district hospitals or health care centers in Kelantan do not have an ultrasound machine. Thus, physicians in district hospitals or health care centers are only able to detect AAA through history taking or physical examination. This is the downside that AAA is frequently misdiagnosed or overdiagnosed.

In this study, an AI model is developed for AAA prediction. It gives a clue to primary center physicians to detect AAA and carry out an appropriate management at its early stage. Besides that, this model can optimize hospital resources by reducing unnecessary ultrasound scanning or tertiary referral. The application of machine learning allows a continuous automated prediction with addition of new data to the system over time.

2.0 STUDY PROTOCOL

2.1 Document submitted for ethical approval

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RESEARCH PROPOSAL

Research title: Developing an Artificial Intelligence (AI) Model in Predicting the Occurrence of Abdominal Aortic Aneurysm (AAA)

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Introduction

AAA is an increasingly common problem in Malaysia which has a prevalence of 15299 cases among the total population in Malaysia (1). The major complication of AAA is ruptured which presents as a surgical emergency. The annual mortality rate in Malaysia is 5.2 per 100,000 and this makes Malaysia one of the three countries within Asia with highest mortality rates (1). Study shows that the mortality of elective AAA repair is 5% and it is far better than emergency AAA repair which is 50% (2). Early detection of AAA allows in optimizing clinical management to reduce morbidity and mortality.

Up to now, there is no proper screening programme for AAA in Malaysia. Most of the patients are frequently misdiagnosed as healthy individuals in district hospitals. These patients did not receive proper clinical AAA treatment and result in enlarged aneurysm. Some of them progressed to the stage of near rupture as well. Therefore, an AI model is proposed to tackle this problem: to predict the occurrence of AAA, also to assist physicians for early detection which leads to appropriate management, thereby reducing complication and mortality.

Problem statement & Study rationale

It has been a major challenge for physicians to diagnose AAA clinically due to indirect clinical presentation of AAA. Asymptomatic AAA has been detected incidentally by physical examination and radiological images. Patients with AAA may come with pulsatile mass at the epigastric region during physical examination. However, Howard et all state that the sensitivity and specificity of physical examination to diagnose AAA are low, at 68% and 75% respectively (3). Ultrasound abdomen is a good modality to diagnose AAA due to its high sensitivity (97.7-100%) and specificity (94.1-100%) (4). Most of the district hospitals or health care centres in Kelantan do not have an ultrasound machine. Thus, physicians in district hospitals or health

care centres are only able to detect AAA through history taking or physical examination. This is the downside that AAA is frequently misdiagnosed or overdiagnosed.

In this study, an AI model is developed for AAA prediction. It gives a clue to primary centre physicians to detect AAA and carry out an appropriate management at its early stage. Besides that, this model can optimize hospital resources by reducing unnecessary ultrasound scanning or tertiary referral. The application of machine learning allows a continuous automated prediction with addition of new data to the system over time.

Research Question

What is the accuracy of the AI model to estimate the occurrence of AAA?

Objective

General:

To develop an AI model to predict occurrence of AAA

Specific:

1. To develop an AI model to predict the occurrence of AAA using a retrospective database which divide the sample group into normal (<2.5cm), small size AAA (2.5-5.4cm) and large size AAA (≥5.5cm)
2. To determine the accuracy of AI model in predicting the occurrence of AAA in screening population

Literature review

Abdominal aorta aneurysm (AAA) is defined as dilatation of aorta at least a 50% increase of the normal vessel diameter or diameter of abdominal aorta is ≥ 30mm. AAA is usually asymptomatic until complications occurred such as aorta dissection and ruptured AAA. Early detection and proper management of AAA reduces the overall death rate from rupture (5).

Artificial intelligence (AI) uses a computational approach to learn natural patterns in data that generate insight to make better decisions and predictions. The use of AI has been applied in predicting cardiovascular risk using various data sources such as clinical data (family history), wearable measurements, genomic expression and environmental factors. Detailed reviews of using AI in cardiology can be found in Frank L and Johnson KW et.al studies (6, 7). Different AI models are designed for different applications. In this study, we focus on using the Random Forest (RF) model to predict the occurrence of AAA (normal, small size AAA and large size AAA) using clinical data such as patients' demographics and risk factors of AAA.

RF algorithm is an ensemble (averaging) method that constructs multiple decision trees and identifies the predicted classes (healthy/disease) with the highest votes across the decision trees (Figure 1a) (8). Decision tree is made up of a set of rules that split the datasets into smaller subsets using different rules at every layer. The rules are constructed using the Classification and Regression Tree (CART) algorithm by computing the GINI Impurity (9, 10) from the datasets. The Gini Impurity for each variable (in our case, it will be age, hypertension, etc) will be computed. The variable with the lowest Gini Impurity will be chosen to split the data (10). Then, Gini Impurity is calculated again using the remaining variables and the variable with the lowest Gini Impurity will be chosen again to split the data. This process is repeated until all variables are used or a pure node is reached (Figure 1b).

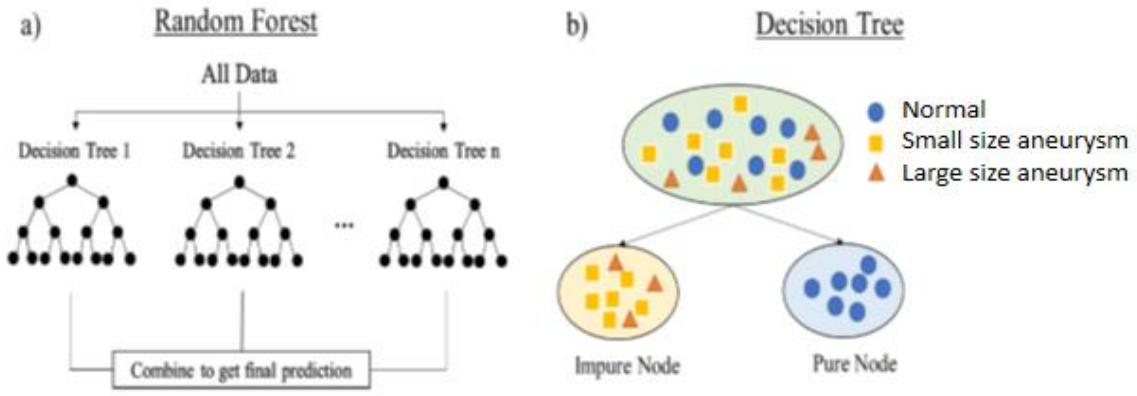


Figure 1 (a) Random Forest Model Architecture. (b) Decision Trees.

From the literature search, there are many risk factors such as age, gender, hypertension, dyslipidemia, coronary arterial disease (CAD), smoking and family history of AAA associated with AAA. We believed that the AI model is able to predict the size of abdominal aorta by using these risk factors as input variables and thus able to help the physician especially those working in district hospitals without ultrasound machines to manage the patient.

The median age group of AAA was 69 years old with 87.9% being 60 years old and above in Hospital Kuala Lumpur (HKL), vascular center in West Malaysia (11). The median age group of AAA was 70 years old with a significant incidence rate raise for the patient more than 70 years old in Sarawak (12). NICE guidelines recommended age ≥ 66 years old with certain risk factors should be subject to screening AAA (13). Society vascular surgery recommended age from 65 to 75 years of age with a history of smoking or healthy patients older than 75 years old should screen for AAA (14). Study reported that progressive increase in abdominal aorta diameter occurs with advancing age (43). Using the Random Forest model, it can determine the age that best differentiate between healthy and the patient with risk of developing AAA.

From the literature review, gender does play a role in determining AAA risk. In HKL, Zainal et al. showed male predominance (84.7%) has AAA (11). Ming Kon Yii reported the incidence

of AAA as male to female ratio of 3.5:1 in Sarawak (12). Ana. M et al. reported that both the Caucasian group (72%) and the Asian group (50%) are male predominant to develop AAA (15). The reason is unclear.

Hypertension is one of the risk factors for AAA. Hypertension increases the risk of developing AAA by 66% (16). The study also reported that 14% increase risk of AAA for every 20mmHg rise in systolic blood pressure and 28% increase risk of AAA for every 10mmHg rise in diastolic blood pressure (16). Cornuz J et al. also stated that patients with hypertension have a higher risk of AAA in a population-based study (17). Hypertension may cause shifts in elastin and collagen fibres content within vessel walls and smooth muscle cells and this leads to an increased risk of AAA.

Elevated lipoprotein concentration has a correlation with AAA risk in a prospective population-based cohort study (18). Besides that, there is a significant association between LDL and small aneurysm (19). High cholesterol level that deposited in the intimal layer of vessels damages the vascular endothelium and causes inflammation that results in vessel degeneration. Thus, increases the risk of occurrence of AAA.

Smoking is one of the most common risk factors of AAA. Current smokers are associated with 7.6 times increase in the prevalence of AAA than a non-smoker and each year of smoking increased the relative risk of AAA by 4% (20). Besides that, Teun's study showed that the amount of cigarette smoked had not reached the statistically significant after adjustment was made for the duration of smoking (20). Juraj M et al. study showed that smoking is an independent risk factor for AAA (21).

A meta-analysis concludes that CAD is a strong predictor of AAA occurrence (22). Patients with CAD are 2.4 times increased the risk of AAA compared to those patients without CAD (23).

Patients with family history of AAA have the double risk to develop AAA especially first-degree relatives (24). There is a 4.33-fold increased risk of AAA in the individual with family history of AAA (25).

From the literature review, most of the studies reported the relationship between the risk factors and the occurrence or expansion rate of the AAA. However, there was no literature on the risk factor correlate with the size of AAA.

Six countries are implementing AAA screening programmes (39). All screening programmes use a single ultrasound scan to determine the aortic diameter (39). Computed tomography angiography is the "gold standard" to detect AAA but this expose patient to radiation. Ultrasound is highly sensitive (97.5%) and specific (98.9%) in detecting AAA (40). Screening AAA by using ultrasound is a suitable test that has high accuracy, cost effective and not hazardous to screened population which is fit to the principle of screening adopted by the World Health Organization (WHO) (41).

Few scoring systems that predict mortality in ruptured AAA patients such as scoring systems such as Glasgow Aneurysm score, Edinburgh Ruptured Aneurysm score, Vancouver Scoring System and Hardman Index (26-29). AI is widely used in patients with AAA to improve radiological imaging, to predict the risk of AAA rupture, to determine the prognosis of patients with AAA and more (30). However, there is no model yet to predict the occurrence of AAA which can guide us on early management of AAA.

Classic statistical methods have been used to evaluate warning signs and determine risk criteria for abdominal aortic aneurysm rupture. However, the complexity of the clinical profiles and the overlapping levels of factors makes the structure of clinical data complex, and only limited variables included in the statistical models. Furthermore, statistical models are shown to have low predictive power as the purpose of statistical models is to infer the relationship between

independent variables and outcome (31). The purpose of the AI model, on the other hand, is to have high predictive power and studies showed that promising AL model in predicting various diseases such as cardiovascular disease (31, 32).

The objective of this study is to find out the relevant risk factors of AAA to develop an AI model to predict the occurrence of AAA.

Conceptual framework

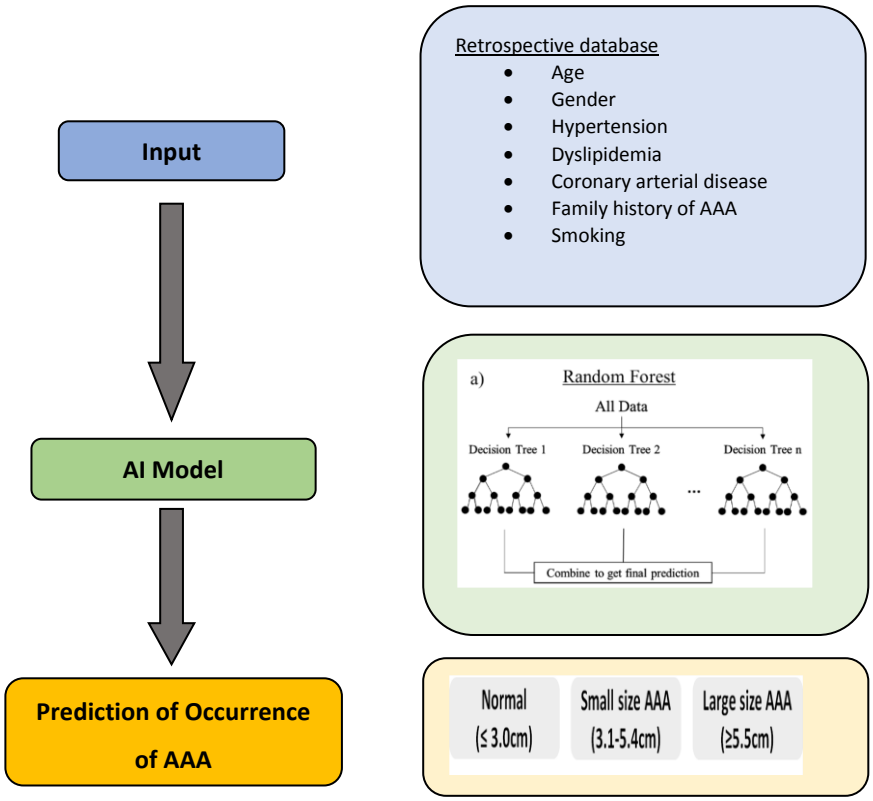


Figure A: Demographics, risk factors of AAA and size of abdominal aorta of patient based on retrospective database use to train the AI model. AI model predicts the occurrence of AAA.

Research design

This study consists of 2 phases.

In phase 1, retrospective data will be used to develop an AI model to predict the occurrence of AAA.

In phase 2, the AI model will be tested using the prospective data.

Study area

Hospital Raja Perempuan Zainab II (HRPZ II)

Hospital Universiti Sains Malaysia

Study population

Reference population

Phase 1

-Patients who underwent ultrasound abdomen or computed tomography angiography (CTA).

Phase 2

- Patient who are scheduled for computed tomography that captured the abdominal aorta and give consent to participate in this study will be recruited to screen for AAA.

Target population

Phase 1

-Patients who underwent ultrasound abdomen or CTA with the information of abdominal aorta size documented in HRPZ II and HUSM.

Phase 2

- Patient who are scheduled for computed tomography that captured the abdominal aorta and give consent to participate in this study will be recruited to screen for AAA.

Source population/sampling pool

Phase 1

-Patients who underwent ultrasound abdomen or CTA in HRPZ II and HUSM will be identified from the "Sistem Pengurusan Pesakit SPP", "Synapse" and "Universal Viewer Zero Footprint Client" system. These systems are centralized, prospectively maintain database that allows sharing of medical records, radiology images and reports among the hospital staffs in HRPZ II and HUSM.

-Patients information such as hypertension, dyslipidemia, CAD, family history of AAA, smoking history are traced from patient medical record or electronic medical records in HRPZ II and HUSM.

Phase 2

Patient who are scheduled for computed tomography that captured the abdominal aorta and give consent to participate in this study will be recruited to screen for AAA.

Sampling frame
Phase 1

-Patients who underwent ultrasound abdomen or CTA with the indication of to rule out AAA in HRPZ II from Jan 2017 to Dec 2020.

Phase 2

1. 200 patients who are scheduled for computed tomography that captured the abdominal aorta and give consent to participate in this study will be recruited to screen for AAA.

2. Patient who are diagnosed to have AAA in HRPZ II during 2021 will be recruited in this study.

Subject criteria
Phase 1
Inclusion criteria

1. Patient age more than 18 years old
2. All the patients who underwent ultrasound abdomen or CTA in HRPZ II and HUSM with the information of abdominal aorta size documented from Jan 2017 to Dec 2020.

Exclusion criteria

1. Patient with incomplete data

Phase 2
Inclusion criteria

1. Patient age more than 18 years old
2. Patient scheduled for ultrasound abdomen in HUSM

Exclusion criteria

1. Patient not consented for the study

Sample size estimation

There will be no sample size estimation in this study because statistical model is not used in this study and we will be using AI model. AI study mostly uses convenient sampling, taking samples within a period time (33, 34).

In this study, k-fold cross validation algorithm is used and study showed that it provides optimistically biased performance estimates. Completely separating testing and training data is enough to obtain unbiased performance estimates regardless of sample size. Some studies showed that high prediction accuracy in small sample sizes with a median of 88 (42).

In phase 1, all the patients who underwent ultrasound abdomen or CTA in HRPZ II and HUSM with the information of abdominal aorta size documented from Jan 2017 to Dec 2020 will be recruited.

In phase 2, we are recruiting all patients scheduled for ultrasound abdomen in HUSM from 1st July to 31st August 2021 and give consent to participate in this study will be recruited to screen for AAA by ultrasound. Sample size estimated for phase 2 is 100 patients.

Sampling method and subject recruitment

Phase 1

- Patients who underwent ultrasound abdomen or CTA in HRPZ II and HUSM will be identified from the "SPP", "Synapse" and "Universal Viewer Zero Footprint Client" system. These systems are centralized, prospectively maintained databases that allow sharing of medical records, radiology images and reports among the hospital staff in HRPZ II and HUSM.
-Patients information such as hypertension, dyslipidemia, CAD, family history of AAA, smoking history are traced from patient medical records or electronic medical records in HRPZ II and HUSM.

Phase 2

-Patients who scheduled for ultrasound abdomen in HUSM and give consent to participate in this study will be recruited to screen for AAA by ultrasound.

-Ultrasound abdomen will be done by registra radiology medical officer.

Research tool

We used Random Forest (RF) models in predicting AAA risk. In brief, RF algorithms constructed multiple decision trees and identified the predicted classes (normal, small size AAA and large size AAA) with the highest votes across the decision trees.

Analysis of RF will be performed using the Scikit-learn package available in Python language.

Operational definition

Artificial Intelligence (AI) Model

-defined as the simulation of human intelligence in machines that are programmed to think like humans and mimic their actions. The term may also be applied to any machine that exhibits traits associated with a human mind such as learning and problem-solving (35).

Abdominal aorta aneurysm

-defined as dilatation of aorta at least a 50% increase of the normal vessel diameter or diameter of abdominal aorta is $\geq$ 30mm.

Classification of abdominal aortic aneurysm (36)

Classification	Diameter of abdominal aorta
Normal	1.5-3.0cm
Small	3.1-5.4cm
Large	≥5.5cm

Dyslipidemia

-Defined as patient who received treatment for high cholesterol.

Coronary arterial disease (CAD)

- Defined as patient who received medical or surgical treatment for CAD disease.

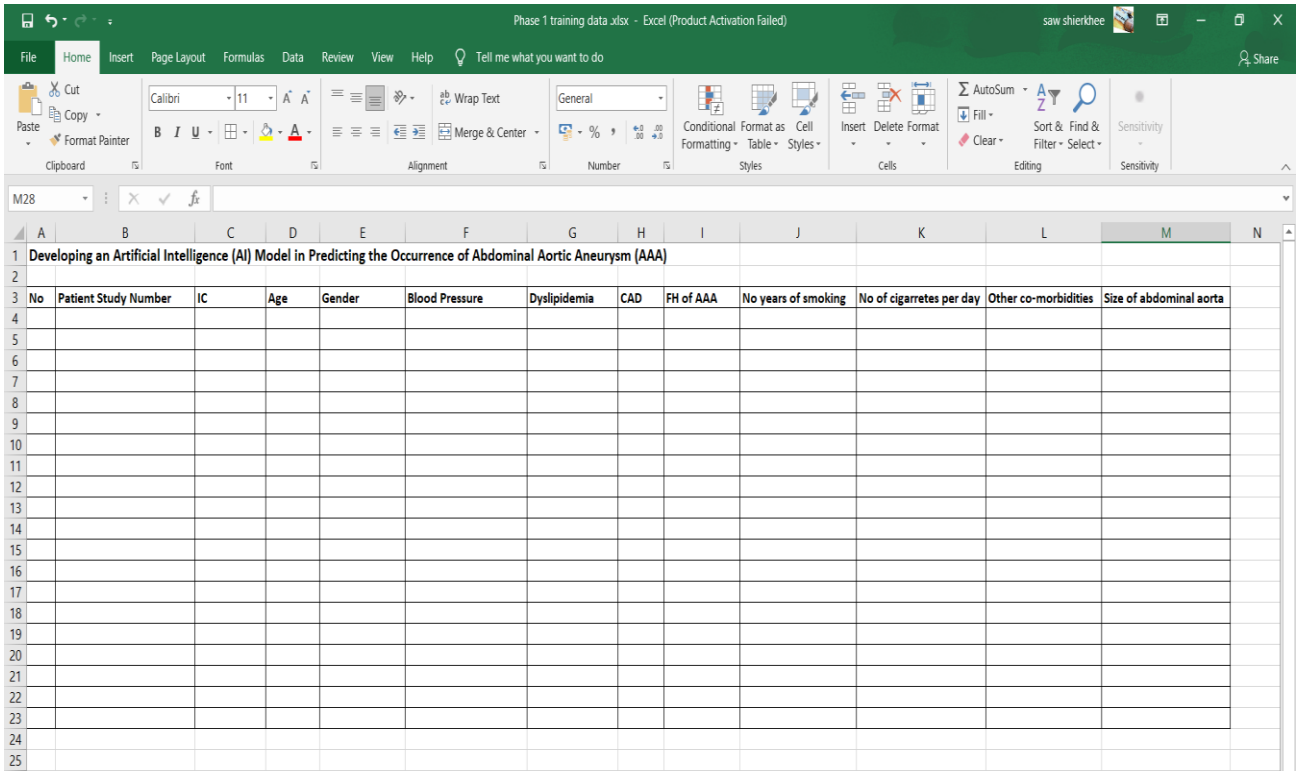
Smoking history

-This included the number of years of smoking and number of cigarettes smoked per day.

Data collection method

Phase 1

-Data will be recorded in the data collection excel sheet



Phase 1 training data .xlsx - Excel (Product Activation Failed)

No	Patient Study Number	IC	Age	Gender	Blood Pressure	Dyslipidemia	CAD	FH of AAA	No years of smoking	No of cigarretes per day	Other co-morbidities	Size of abdominal aorta

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Phase 2