- 2 Diagnostic accuracy of calcified aortic knob
- 3 found in chest radiograph for detection
- 4 of coronary artery calcification

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## **ABSTRACT**

**Aims:** To validate the diagnostic performance of a calcified aortic knob found in chest radiographs in relation to coronary calcification.

**Study design:** This study is an observational analytical cross-sectional study.

Place and Duration of Study: This study examined the medical history of patients treated at the Central Chest Institute of Thailand, Department of Medical Services, Ministry of Public Health, during the period from November 1, 2019, to October 31, 2021.

**Methodology:** Study was conducted with 441 individuals (236 women) aged 40-75 years, all non-diabetic and without known coronary artery disease. Coronary artery calcium score (CAC) was measured using computed tomography and scored according to the Agatston method. Chest radiographs within 6 months were evaluated and classified into four grades (0-3). The relationship between coronary calcification and a calcified aortic knob was then assessed.

**Results:** Positive CAC (CAC >0) was strongly associated with a calcified aortic knob (grades 1-3), with a high positive predictive value of 88.07%. The diagnostic accuracy, sensitivity, and specificity were 66.9%, 61.5%, and 79.8%, respectively. The negative predictive value was low, at 41.8%.

**Conclusion:** A calcified aortic knob (grades 1-3) is associated with positive CAC in the general population without diabetes and known coronary artery disease. However, the absence of a calcified aortic knob (grade 0) does not rule out coronary calcification.

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**KEYWORD:** Coronary artery calcium score (CAC), Calcified aortic knob, chest radiograph (CXR), computed tomography (CT), CT coronary artery calcium score (CT CAC)

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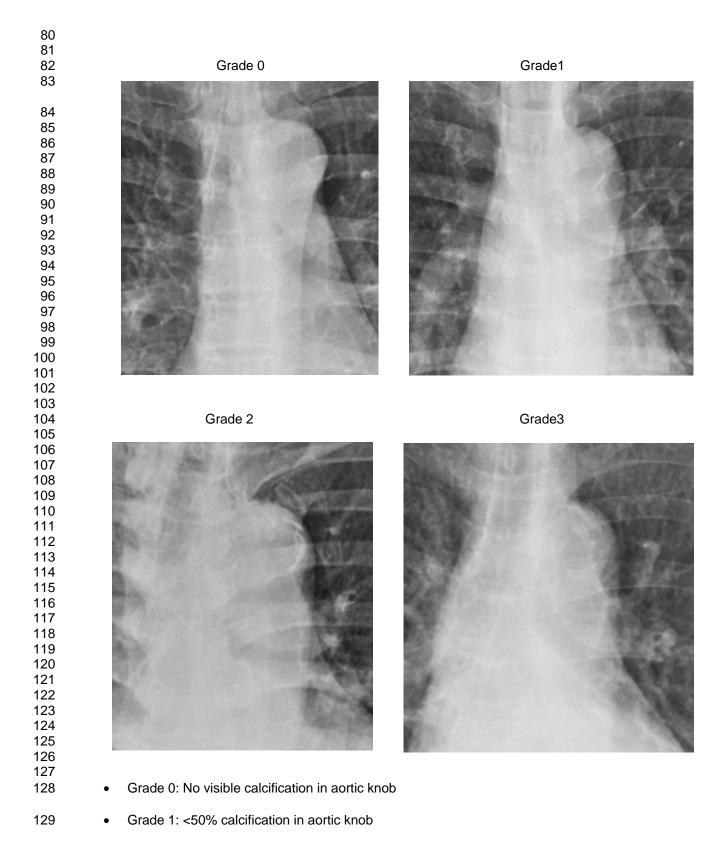
## 1. INTRODUCTION

Cardiovascular diseases are currently a major public health issue in Thailand. Coronary artery disease leading to myocardial ischemia is one of the leading causes of death, ranking fourth in men and third in women [1]. The main cause of coronary artery disease is the accumulation of fat and thickening of the arterial wall, which is considered a form of atherosclerosis, leading to narrowing of the coronary arteries. This results in insufficient blood supply to the heart muscle, causing symptoms such as chest pain or easy fatigue. If the accumulated fat ruptures, it can lead to sudden coronary artery blockage, causing acute myocardial infarction, complications, or sudden death. The risk of coronary artery disease is assessed using the Framingham Risk Score, which categorizes patients into low, medium, and high risk, considering factors such as gender, age, comorbidities like diabetes, hypertension, hyperlipidemia, smoking, and family history [2]. Currently, CT coronary artery calcium score (CT CAC) is recommended as a screening method for patients at risk of coronary artery disease to help guide treatment with statin therapy [3]. Studies in asymptomatic patients with intermediate risk of coronary artery disease have found that positive CAC is one of the factors used to consider statin therapy for primary prevention to prevent plaque rupture [4, 5]. Fat accumulation in the arterial wall is often associated with calcium accumulation; therefore, CAC can help assess the presence of atherosclerosis [6]. Although CT CAC is useful for determining treatment, it is expensive and less accessible. Studies have found that chest radiograph may help predict coronary calcification [7-10] and cerebrovascular calcification [11] by assessing the calcified aortic knob. It is evident that chest radiographs are widely used and offer substantial value in In the previous study by Woo et al [7], screening due to their low cost and accessibility. the grading of calcified aortic knob on chest radiographs was divided into four levels: Grade 0 (no visible calcification), Grade 1 (small spots of calcification or a single thin area of calcification), Grade 2 (one or more areas of thick calcification), and Grade 3 (circular calcification of the aortic knob). If calcification is visible at grade 2 or higher, there is a correlation with the CT CAC showing coronary artery calcification [9, 12]. This study aims to determine the correlation between calcified aortic knob detected on chest radiographs and coronary artery calcification detected on CT CAC in individuals without diabetes and who have not been diagnosed with coronary artery disease. This could help in utilizing chest radiographs as a guideline for considering statin therapy.

#### 2. MATERIAL AND METHODS

The study was conducted by reviewing medical records of patients and collecting data from chest radiographs and CT Coronary Calcium Score of the individuals aged 40-75 years, without a history of coronary artery disease or diabetes, and fasting blood sugar levels not exceeding 126 mg/dl within six months. The chest radiograph and CT Coronary Calcium Score were performed within six months of each other. The study period spanned from November 1, 2019, to October 31, 2021 at Central Chest Institute of Thailand and involved a total of 441 participants, calculated based on related research by Park HE [13]. The sample size was calculated using Buderer's formula with 95% confidence level with expected sensitivity and specificity of 90%. Quality chest radiographs were selected for grading the calcified aortic knob into four grades according to prior study from Woo JS (7, figure 1), evaluated by two radiologists with over ten years of experience. The radiologists were blinded to the result of CAC. The correlation between chest radiographs and CT Coronary Calcium Score were determined.

Figure 1: Assessment of aortic arch calcification from chest radiograph [7]



- Grade 2: >50% calcification in aortic knob
  - Grade 3: circumferential calcification in aortic knob

## **Data Analysis**

Data was conducted using IBM SPSS version 22. Descriptive statistics are reported as percentages for categorical variables and as means with standard deviations for continuous variables if they follow a normal distribution. Inferential analysis of categorical data was performed using McNemar's test. Statistical significance was set a p-value of less than 0.05 The diagnostic performance metrics of the chest radiographs, including sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

## 3. RESULTS AND DISCUSSION

#### **RESULTS**

The study included 441 individuals with 236 females (53.5%) and 205 males (46.5%).

From the analysis, general characteristics of the sample were summarized by comparing those with and without a calcified aortic knob on chest radiographs. There were slightly more females than males (table 1), and the mean age was 66.02 years for those with a calcified aortic knob and 57.82 years for those without (table 2).

Table 1: The population between males and females in both groups

Variable	Male	Female
Total = 441	205	236
CXR grade 0	106	117
CXR grade 1-3	99	119

Table 2: The age groups of the population with and without calcified aortic knob

Group	N	Mean age	Standard deviation	95% confidence interval
CXR grade 0	223	57.82	9.09	56.62 /59.02
CXR grade 1- 3	218	66.02	6.66	65.13/ 66.91

Table3: Table for diagnosis test accuracy

	CAC >0	CAC = 0	Total
CXR- calcified aortic knob (grade 1-3)	192	120	312
CXR- no calcified aortic knob (grade 0)	26	103	129
Total	218	223	441

Figure2: The diagnostic performance of the predicting model

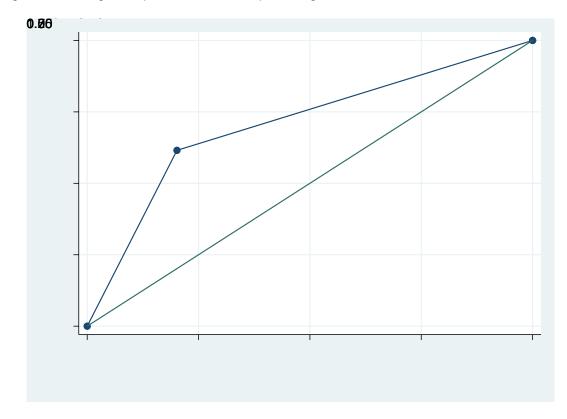


Table4: Result statistic of the predicting model

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195	Sensitivity	61.54%	55.89% to 66.96%
196	Specificity	79.84%	71.88% to 86.39%
197	Positive Likelihood Ratio	3.05	2.14 to 4.35
198	Negative Likelihood Ratio	0.48	0.41 to 0.57
199	Disease prevalence (*)	70.75%	66.26% to 74.96%
200	Positive Predictive Value (*)	88.07%	83.82% to 91.32%
201	Negative Predictive Value (*)	46.19%	42.12% to 50.31%
202	Accuracy (*)	66.89%	62.29% to 71.27%

203 (\*) These values are dependent on disease prevalence.

The positive predictive value was high as 88.07% (95% CI: 83.82%-91.32%), indicating the probability that a patient would have coronary artery calcification if a calcified aortic knob was detected. The negative predictive value was low 46.18% (95% CI: 42.12%-50.31%), indicating the probability of not having coronary calcification if a calcified aortic knob was not detected. The diagnostic accuracy was 66.89% (95% CI: 62.29%-71.27%).

#### Discussion

Coronary Artery Calcification (CAC) is recommended as a screening method for patients at risk of coronary artery disease to help guide treatment with statin therapy [3]. Although CT Coronary Calcium Score is an accurate assessment method and useful for determining treatment, it is relatively expensive and less accessible. Chest radiographs are widely used and offer substantial value in screening due to their low cost and accessibility. Previous studies have found that chest radiograph may help predict coronary calcification [7-10] by assessing the calcified aortic knob.

The grading of calcified aortic knob on chest radiographs was divided into four levels: Grade 0 (no visible calcification), Grade 1 (small spots of calcification or a single thin area of calcification), Grade 2 (one or more areas of thick calcification), and Grade 3 (circular calcification of the aortic knob).

The previous studies conducted by Adar et al [12]. and Kalsch et al [14]. provide substantial evidence that aortic calcification, detectable through imaging such as chest radiographs or CT scans, is significantly associated with coronary artery calcification (CAC). Specifically, Adar et al.'s study found a strong correlation between aortic calcification (graded 2 or higher) and high coronary calcium scores (above 400), with high specificity (98%) and diagnostic accuracy (95%).

Similarly, Kalsch et al.'s study demonstrated that individuals with aortic calcification were at increased risk of developing CAC over a five-year follow-up period, further establishing the predictive value of aortic calcification for coronary artery disease (CAD).

The study by Bannas et al. [9] supports the role of chest radiography in detecting severe aortic arch calcification (AAC) as a strong predictor of coronary artery calcification.(CAC) given the high correlation between severe AAC and CAC.

Our study supports findings from prior studies, such as those by Adar et al. and Kalsch et al. that demonstrated a significant relationship between aortic calcification and coronary artery calcification. Specifically, our study indicates that the detection of calcified aortic knobs via chest radiographs can be a useful predictor for coronary artery calcification with a positive predictive value of 88.07%. This is consistent with the findings from Adar et al., which showed a strong correlation between aortic calcification and CAC. Given the high cost and limited accessibility of CT coronary calcium scoring, using chest radiographs to screen for aortic calcification provides a cost-effective and accessible alternative for initial screening. The high specificity (79.8%) in our study suggests that aortic knob calcification detected on chest radiographs can help identify patients who may benefit from more definitive testing with CT calcium scoring. This has implications for clinical decision-making, particularly in resource-limited settings where CT scans are not widely available.

# Conclusion

In conclusion, using chest radiographs to detect calcified aortic knobs may be useful in predicting coronary artery calcification, especially in cases where a calcified aortic knob is detected, as there is a high probability of concurrent coronary artery calcification. However, in cases where no aortic calcification is detected on chest radiographs, it does not correlate with the presence or absence of coronary calcification.

### Limitations

Although the specificity and positive predictive value are high, the sensitivity was found to be relatively low at 61.5%. This indicates that a significant proportion of patients with coronary calcification may not be identified solely through chest radiographs. Therefore, the absence of aortic calcification does not rule out coronary artery disease. The negative predictive value (46.18%) also suggests that the absence of calcified aortic knobs is not a reliable indicator of the absence of CAC, which highlights the need for additional risk factor assessments in patients without visible aortic calcification.

#### Potential Areas for Future Research

Future studies should focus on larger, prospective cohorts to validate the utility of chest radiographs in predicting CAC and coronary artery disease (CAD). Long-term follow-up studies could help determine whether the progression of aortic calcification, as seen on serial chest radiographs, corresponds to the development of coronary artery disease. Additional research could explore whether incorporating other risk factors, such as age, gender, and comorbidities, alongside chest radiographic findings could enhance the predictive value of CAC detection.

#### CONSENT

287 It is not applicable.

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## ETHICAL APPROVAL

This study has received ethical approval from the Thoracic Disease Institute, Department of Medical Services, reference number COA 001/2565.

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