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Diagnostic Accuracy of Calcified Aortic Knob Found in Chest Radiograph for Detection of Coronary Artery Calcification

Saijai Lertrojanapunya [a*], Chomphunut Vijitsanguan [a], Weeraya Noisiri [a], Jirawan Chayjaroon [a], Narongsak Chaychid [a] and Wasin Laesan [a]

[a] Department of Radiology, Central Chest Institute of Thailand, Bang Kraso, Mueang Nonthaburi, Nonthaburi, 11000, Thailand.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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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 participants who were referred for a CT coronary calcium scoring (CT-CAC). 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.

**Corresponding author: E-mail: plesaijai@yahoo.com;*

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Methodology: This cross-sectional study aims to evaluate the association between calcified aortic knobs on chest radiographs and coronary artery calcification as determined by CT-CAC. The study included 664 patients who underwent CT-CAC between November 1, 2019 and October 31, 2021. We selected participants aged 40 to 75 years without known history of coronary artery disease (CAD) or diabetes (fasting blood sugar levels under 126 mg/dl within past 6 months). A total of 441 eligible patients were included in the final analysis.
Standard chest radiographs within 6 months interval were evaluated and classified into 4 grades, Grade 0 (no visible calcification), Grade 1 (<50% calcification of aortic knob), Grade 2 (>50% calcification of the aortic knob), and Grade 3 (circular calcification of the aortic knob). These findings were then compared with CAC obtained via dual source CT scanner to evaluate the diagnostic accuracy of chest radiographs. Key performance metrics, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), were calculated to determine the effectiveness of aortic knob calcification as a predictor for coronary calcification.
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) correlates strongly with positive CAC (positive predictive value 88.07%). The study's findings of low sensitivity (61.5%) and negative predictive value (46.18%) indicate limitations in using calcified aortic knob on chest radiograph as a standalone screening tool for coronary artery calcification.

Keywords: Coronary artery calcium score (CAC); calcified aortic knob; Chest Radiograph 20 (CXR); Computed Tomography (CT); CT Coronary Artery Calcium score (CT CAC).

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 (Rao et al., 2010). The main cause of coronary arterydisease 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 (D'Agostino et al.,2008). 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 (Greenland et al., 2004).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 (Lloyd-Jones et al., 2019, Grundy et al., 2019). Fat accumulation in the arterial wall is often associated with calcium accumulation; therefore, CAC can help assess the presence of atherosclerosis (Yazdi et al.,2022). 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 (Woo et al., 2016, Ma et al., 2019, Bannas et al., 2013, Yun et al., 2006). and cerebrovascular calcification (Kim et al., 2013). by assessing the calcified aortic knob. It is evident that chest radiographs are widely used and offer substantial value in screening due to their low cost and accessibility. In the previous study by Woo et al., 2016 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 (Bannas et al., 2013, Adaret al., 2015).

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 free of coronary artery disease (CAD). Diabetes was excluded from the study population because it is a significant risk factor for CAD, often leading to higher likelihood of coronary artery calcification. The Framingham heart study has shown that diabetes poses particularly high cardiovascular risk, often surpassing that of hypertension or smoking. Diabetes increases the risk of CAD by two or three times. This elevated risk makes diabetes a significant factor for early and aggressive cardiovascular interventions, often prioritizing management strategies that include statin therapy. The exclusion helps maintain focus on a population with no known CAC risk factor. This could help in utilizing chest radiographs as a guideline for considering statin therapy.

2. MATERIALS AND METHODS

2.1 Study Design and Participants

The study included 664 patients who underwent CT-CAC between November 1, 2019, and October 31, 2021. We selected participants aged 40 to 75 years without known history of coronary artery disease (CAD) or diabetes (fasting blood sugar levels under 126 mg/dl within past 6 months). A total of 441 eligible patients were included in the final analysis. Both chest radiograph and CT coronary calcium score (CAC) assessment were conducted within a six months interval. The study took place from November 1, 2019, to October 31, 2021 at the Central Chest Institute of Thailand. The sample size was calculated based on prior research by Park HE (Park et al.,2012), using Buderer's formula with 95% confidence level and expected sensitivity and specificity of 90%.

2.2 Diagnostic Comparison

Standard posterior-anterior chest radiographs were evaluated for the presence of calcified aortic knob, grade on a scale of 0 to 3 based on criteria established in a prior study by Woo JS (Fig. 1). Two experience radiologists, each with over ten years of practice, independently graded the radiographs while being blinded to the CAC results to prevent bias. The analysis compared chest radiographs grades, focusing on cases graded as 0 (no visible calcification of the aortic

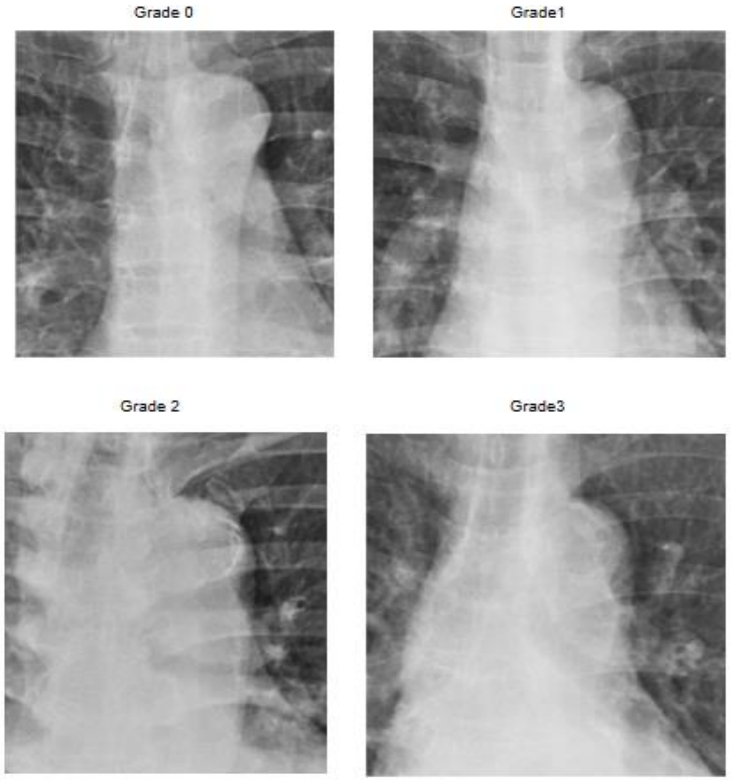

Fig. 1. Assessment of aortic arch calcification from chest radiograph (Woo et al., 2016)
Grade 0: No visible calcification in aortic knob; Grade 1: <50% calcification in aortic knob; Grade 2: >50% calcification in aortic knob; Grade 3: circumferential calcification in aortic knob

knob) against those graded 1-3 (indicating varying degrees of calcification). This was cross-referenced with CAC scores obtained from CT dual-source SOMATOM Definition Flash scanner and qualified following the Agatston method. The focus was on cases with CAC score of 0 (no coronary calcification) versus those with a score greater than 0 (indicating coronary calcification). Statistical methods employed included calculations for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) to evaluated the diagnostic accuracy ofradiographs in predicting the presence of CAC.

2.3 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

3.1 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

Table 3. Diagnosis test accuracy 163

	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

Table 4. Result statistic of the predicting model

Results Statistic	Value	95% CI
Sensitivity	61.54%	55.89% to 66.96%
Specificity	79.84%	71.88% to 86.39%
Positive Likelihood Ratio	3.05	2.14 to 4.35
Negative Likelihood Ratio	0.48	0.41 to 0.57
Disease prevalence (*)	70.75%	66.26% to 74.96%
Positive Predictive Value (*)	88.07%	83.82% to 91.32%
Negative Predictive Value (*)	46.19%	42.12% to 50.31%
Accuracy (*)	66.89%	62.29% to 71.27%

(*) These values are dependent on disease prevalence

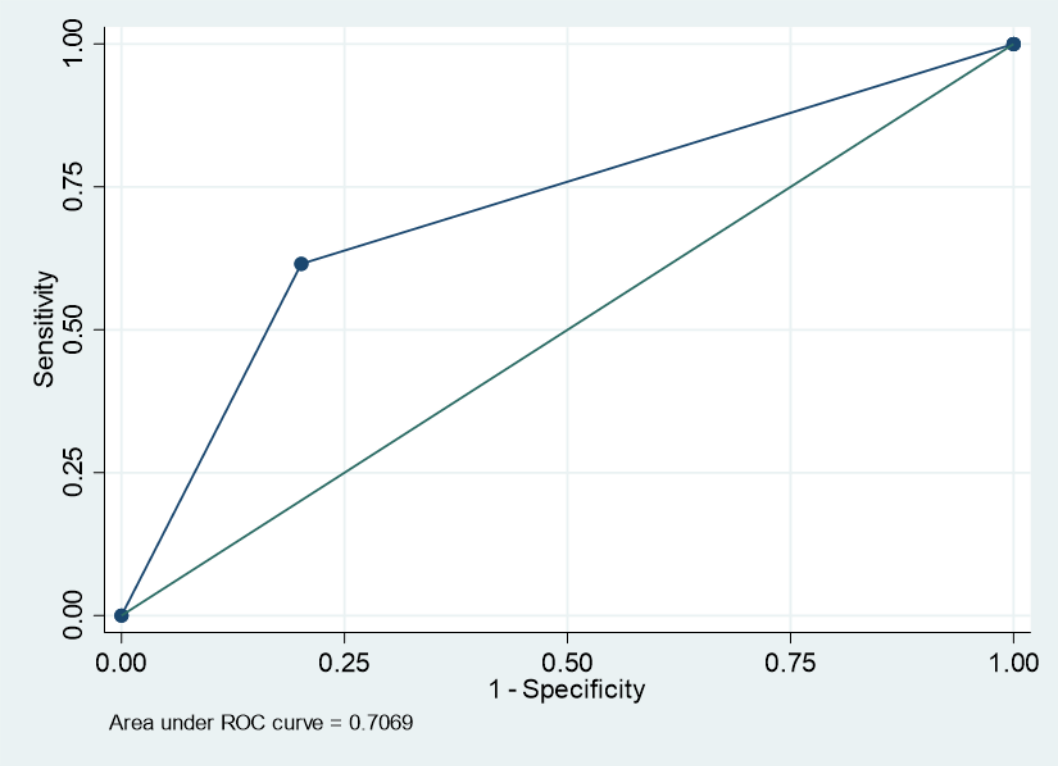

Fig. 2. The diagnostic performance of the predicting model

The study reported a sensitivity of 61.54% (95%CI: 55.89 to 66.96%) and specificity of 79.84% (95%CI: 71.88% to 86.39%). While the specificity is reasonably strong, the low sensitivity raises concerns about the potential for undetected CAC in participants. This suggests that a significant proportion of cases with CAC may be missed when relying solely on this imaging method.

The positive predictive value (PPV) of the study was notably high as 88.07 % (95% CI: 83.82%-91.32%). This indicates a strong likelihood that a participant with a calcified aortic knob would have coronary artery calcification.

Conversely, the negative predictive value (NPV) was low 46.18% (95% CI: 42.12%- 50.31%). This suggests that absence of calcified aortic knob does not reliable excluded coronary calcification.

3.2 Discussion

Coronary artery calcium score (CAC) is increasingly recommended as a screening method for patients at risk of coronary artery disease to help guide treatment decisions, particularly for statin therapy (Greenland et al., 2004).

Although CAC is an accurate assessment method and useful for determining treatment, its relatively high cost and limited accessibility can be barrier to widespread implementation. In contrast, chest radiographs are widely used and offer substantial value in screening due to their low cost and broad accessibility.

Previous studies have found that chest radiograph may help predict coronary calcification by assessing the calcified aortic knob. The grading system for calcified aortic knob on chest radiographs was divided into four levels: Grade 0 (no visible calcification) Grade 1 (small spots of calcification or <50% calcification of aortic knob), Grade 2 (>50% of calcified aortic knob), and Grade 3 (circular calcification of the aortic knob).

Our study's sensitivity and specificity values are similar to those found in Adar et al.,2015 which have sensitivity, specificity of 68 % and 98 %, respectively, suggesting of comparable diagnostic capability in detecting CAC using chest radiographs for initial screening, although radiographs are less sensitive than CT in smaller calcification. Our study's lower diagnostic accuracy possible due to differences in grading criteria. While Adar et al. focused on higher

grades of aortic calcification (grade 2 or above) to predict high coronary calcium scores, our study utilized a different approach. We compared cases with no calcification (grade 0) to those with varying degrees of calcification (grades 1-3) on chest radiographs to determine the presence or absence of coronary artery calcification. This methodological difference allowed us to explore the diagnostic potential of even minimal aortic calcification in predicting CAC, aiming to assess the broader applicability of chest radiography in initial screenings

Our study's higher sensitivity compared to Bannas et al.,2013 means it may better identify cases with coronary artery calcification using chest radiographs However, the lower NPV indicates a weaker ability to rule out CAC when calcification is absent on radiograph. Although the PPV is comparable, the lower NPV suggests that despite catching more cases, our method is less reliable at excluding CAC when no calcification is visible. This could be due to variations in imaging protocols, grading thresholds, or patient demographics.

Comparing our study to Kalsch et al.,2014 Our study shows lower sensitivity and specificity. The difference could stem from the imaging techniques. While Kalsch et al focusing on the predictive value of aortic calcification in assessing long-term coronary risk. They found that aortic calcification was significantly associated with an increased risk of developing CAC. In contrast, our study is cross-sectional, aiming to assess the immediate association between calcified aortic knobs on chest radiographs and the presence of CAC identified through CT calcium scoring. Rather than tracking progression, we evaluated diagnostic metrics like sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) to determine the effectiveness of chest radiographs as a screening tool for CAC. By comparing cases with different degrees of aortic calcification (grades 0-3) against CAC presence or absence, we provide insights into the potential role of chest radiographs in immediate risk assessment, especially in settings where CT is less accessible.

Our study supports findings from prior studies 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%. 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 widelyavailable.

4. 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.

5. 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. Low sensitivity and NPV have significant implication in clinical settings, especially in the context of screening for CAC which highlights the need for additional risk factor assessments in patients without visible aortic calcification. The potential reasons could be from the limitation of chest radiograph which have lower sensitivity in detecting early or less extensive calcification, as their resolution may not capture smaller deposits of calcium that could indicate early stage CAC.

6. BENEFICIAL AND LIMITED SCENARIOS

In healthcare settings with limited access to advanced imaging technologies, chest radiographs are a practical tool for initial CAC screening due to their low cost and wide availability. Patients in rural of low resource areas, where access to CT scans is limited, may

still benefit for chest radiographs as a preliminary step to identify those a higher risk who need further investigation. For patients with multiple risk factors for CAD, the presence of calcified aortic knob on chest radiograph can indicate a higher likelihood of CAC. This can prompt clinicians to prioritize these patient for further testing or initiating statin therapy. Fow the individuals at lower cardiovascular risk, the limited sensitivity of chest radiograph makes them less reliable for CAC screening. In these cases, a non-calcified aortic knob does not reliably rule of the presence of CAC, and the test low NPV may lead to a false sense of security.

7. 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.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc have been used during writing or editing of this manuscript. Below are the details of the AI tools used, along with prompts and specific input provided.

Generative AI Tool: Chat GPT
Model and Version: GPT-4
Source: Open AI

Details of AI Usage are given below:

1. Purpose: Writing assistance, language refinement, and idea generation.
2. Prompts Provided
- Initial drafts: Input prompts such as “Provide an overview of the topics” and “summarize findings on research area.
- Editing: Prompts to refine language, rephrase sentences.
The authors reviewed and adapted all AI-generated content to ensure accuracy and appropriateness for the manuscript. All findings, interpretations, and conclusions remain the responsibility of the authors.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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