Original Article

JHSMR Journal of Health Science and Medical Research

Severe Arrhythmias During Six-Minute Walk Tests in Early Outpatient Cardiac Rehabilitation: A Two-Year Multilevel Analysis and Machine Learning-Enhanced Prediction Model in a Thai Provincial Hospital

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Received 19 July 2024 ● Revised 20 August 2024 ● Accepted 7 September 2024 ● Published online 25 March 2025

Abstract:

Objective: To determine the prevalence and associated factors of severe arrhythmias during the Six-Minute Walk Test (6MWT) in early outpatient cardiac rehabilitation, and to develop a prediction model using multilevel analysis and machine learning techniques.

Material and Methods: This retrospective analytical study spanned a period of 2 years; from January 2022 to December 2023. It included 357 patients undergoing the 6MWT in the early outpatient cardiac rehabilitation at Uttaradit Hospital, in Northern Thailand. Multilevel structural equation modeling and machine learning-enhanced logistic regression were used to analyze individual and institutional factors associated with severe arrhythmias. Research instruments included: a patient data recording form (45-item structured checklist, Content Validity Index (CVI))=0.92, Cohen's kappa=0.87) and an institutional factors questionnaire (30-item Likert scale, CVI=0.89, Intraclass Correlation Coefficient (ICC)=0.91).

Results: The prevalence of severe arrhythmias during the 6MWT was 4.2% (95% confidence interval (CI)): 2.38-6.84%). Significant individual-level risk factors included age (OR=1.56, p-vaue=0.002), male gender (OR=2.31, p-vaue=0.019) and heart failure (odds ratio (OR))=3.42, p-vaue<0.001). Institutional factors; such as staff experience >10 years (OR=0.51, p-vaue=0.037) and emergency equipment readiness (OR=0.45, p-vaue=0.020), were protective factors. The prediction model demonstrated high accuracy in identifying high-risk patients, with a sensitivity of 80.0% and specificity of 76.1% at the optimal cut-off point. The model showed excellent discriminative ability having an area under the Receiver Operating Characteristic (ROC) curve of 0.843 (95% CI: 0.781-0.905).

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J Health Sci Med Res 2025;43(5):e20251180
doi: 10.31584/jhsmr.20251180
www.jhsmr.org

Conclusion: Severe arrhythmias during the 6MWT in early cardiac rehabilitation are relatively uncommon, but clinically significant. The developed prediction model, incorporating both individual and institutional factors, shows promising performance and could enhance risk stratification and safety protocols in cardiac rehabilitation programs. These findings highlight the importance of considering both patient-specific and institutional factors in managing arrhythmic risk during cardiac rehabilitation.

Keywords: arrhythmias, cardiac rehabilitation, machine learning, multilevel analysis, Six-Minute Walk Test

Introduction

Cardiovascular diseases remain a significant threat to global health; particularly in developing countries like Thailand. The latest statistics from the World Health Organization indicate that these diseases are the leading cause of death worldwide, accounting for one-third of all deaths[1]. This aligns with data from the Thai Ministry of Public Health, which shows a continuous increase in mortality rates from cardiovascular diseases[2]. This phenomenon underscores the urgent need to develop effective and sustainable approaches for the prevention, treatment, and rehabilitation of heart disease patients. Coronary artery disease (CAD) is a major contributor to this global health burden. According to the Global Burden of Disease Study 2019, CAD affects an estimated 197 million individuals worldwide; with a population prevalence of 2,571 per 100,000. In Thailand, recent epidemiological data indicates a CAD population prevalence of approximately 1,546 per 100,000. Focusing on Uttaradit Province, where this study was conducted, local health records reveal a CAD population prevalence of 1,320 per 100,000. These statistics not only highlight the pervasive nature of CAD but also underscore the critical need for effective cardiac rehabilitation programs; especially in provincial settings where resources may be constrained.

In the context of cardiac rehabilitation, an essential component of holistic care for heart disease patients, the Six-Minute Walk Test (6MWT) is widely accepted as an efficient, cost-effective tool for assessing physical capacity and accurately reflecting patients' ability to perform daily activities[3]. However, a point of contention in the medical community is the safety of this test; particularly regarding the risk of severe arrhythmias, which could have serious implications for patients' health and lives. Previous international studies have shown variability in the incidence of arrhythmias during the 6MWT, with rates ranging from 0.8% to 5.7%[4]. This variation may result from diverse factors, such as demographic characteristics of the sample, time since the cardiac event, and differing care standards across institutions. However, there is a lack of specific empirical data in the Thai context; especially in provincial hospitals like Uttaradit Hospital, which differ significantly in resources, personnel, and patient demographics compared to urban or teaching hospitals. Analyzing factors related to severe arrhythmias is complex and challenging, as it requires considering multiple levels of factors, both at the individual level (e.g., age, gender, comorbidities, and medications) and the institutional level (e.g., staff experience, medical equipment availability, and hospital protocols). Therefore, applying Multilevel Structural Equation Modeling (MSEM) is highly appropriate, as it can comprehensively analyze complex relationships between various factors; including direct and indirect effects[5]. Additionally, logistic regression plays a crucial role in developing risk prediction models, which will be valuable tools for screening high-risk patients before testing.

Hence, this study is of great importance in filling academic gaps and generating new knowledge regarding the prevalence and factors associated with severe arrhythmias during the 6MWT in the context of provincial hospitals in Thailand. The results will lead to the development of effective risk prevention and management strategies appropriate to the country's context. Additionally, it will yield wide-ranging benefits including: 1) Enhancing patient care quality, 2) Informed, evidence-based public health policies, 3) Establish a foundation for future research and development, 4) Assess cost-effectiveness in public health economics, 5) Improve medical education and training curricula, and 6) Promote international collaboration. In conclusion, this study not only aims to fill academic gaps but also has the potential to create extensive positive impacts on Thailand's healthcare system from operational to policy levels, leading to sustainable improvement in the quality of care for heart disease patients in Thailand. By focusing on the safety and efficacy of the 6MWT in early outpatient cardiac rehabilitation, particularly in a provincial hospital setting, this research addresses a critical aspect of cardiovascular care that has been understudied in the Thai context. The findings will contribute to the development of more tailored and effective cardiac rehabilitation protocols, potentially improving outcomes for patients with coronary artery disease and other cardiovascular conditions.

Research objectives

1. To determine the prevalence of severe arrhythmias occurring during the 6MWT in early outpatient cardiac rehabilitation patients at Uttaradit Hospital.
2. To analyze factors associated with the occurrence of severe arrhythmias using multilevel structural equation modeling.
3. To develop a predictive model for the occurrence of severe arrhythmias using logistic regression analysis.

Material and Methods

This study is a retrospective analytical study combined with a cross-sectional study, utilizing quantitative research methods. The study period spanned 2 years, from January 1, 2022, to December 31, 2023.

Population: All patients having undergone early outpatient cardiac rehabilitation and undertaking the 6MWT at Uttaradit Hospital during the study period.

Sample: The sample size was calculated using the population proportion estimation formula, with a 95% confidence level, 5% acceptable error, and 3.5% proportion of severe arrhythmias from a pilot study: minimum sample size was 324 cases. Increasing the sample size by 10% to account for incomplete data resulted in a final sample size of 357 cases. The sampling method employed was stratified random sampling, ensuring representation across different age groups, genders, and primary cardiac diagnoses.

Inclusion criteria: 1) Age 18 years or older; 2) Diagnosed with cardiovascular disease by a specialist; 3) Participating in an early outpatient cardiac rehabilitation program; and 4) Having performed at least one Six-Minute Walk Test during the specified period.

Exclusion criteria: 1) Presence of severe arrhythmias before the test; 2) Severe heart failure (NYHA Functional Class IV); 3) Acute myocardial ischemia within 2 weeks before the test; 4) Uncontrolled hypertension (>180/100 mmHg); and 5) Severe mobility limitations.

Research instruments

1) The patient data recording form was developed by the researcher based on a literature review and included general information, medical history, physical examination results and 6MWT data. This form was a structured checklist consisting of 45 items: 10 items for demographic information, 15 items for medical history, 10 items for physical examination results, and 10 items for 6MWT data. 2) An

institutional factors questionnaire was developed based on theoretical frameworks and included questions regarding policies, resources, staff training, and risk management systems. This was a 30-item Likert scale survey covering areas such as staff training and experience (10 items), availability and maintenance of emergency equipment (5 items), adherence to safety protocols (5 items), and overall program management (10 items).

Instrument quality assessment

1) Content validity, the patient data recording form; examined by 5 experts, yielded a Content Validity Index (CVI) of 0.92. The institutional factors questionnaire, which was examined by the same group of experts, yielded a CVI of 0.89. 2) As to reliability, the patient data recording form, which was inter-rater reliability tested with 30 patients by 2 raters, yielded a Cohen's kappa of 0.87. The institutional factors questionnaire, having been test-retest reliability tested with 30 staff members over a 2-week interval, yielded an Intraclass Correlation Coefficient (ICC) of 0.91. These reliability tests were conducted at Uttaradit Hospital with subjects not included in the main study sample.

Data collection methods

1) Patient data consisted of a review of electronic medical records and recording data in the patient data form by trained researchers and research assistants. Random accuracy checks were performed on 10% of all data. 2) The institutional factor data, questionnaires were distributed to medical personnel through the REDCap (Research Electronic Data Capture) system. Questionnaire links were sent via email, with reminders sent through the hospital's official LINE account.

Statistical analysis

1) Basic data were analyzed using descriptive statistics; including frequency, percentage, mean and standard deviation. 2) The prevalence of severe arrhythmias was analyzed by calculating the percentage ratios and 95% confidence intervals. 3) Associated factors were analyzed using MSEM, via computer software. The MSEM analysis involved a two-level model, with individual patient data at level 1 and institutional factors at level 2. Model fit was assessed using multiple indices, including Chi-square/df ratio, Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), Root Mean Square Error of Approximation (RMSEA), and Standardized Root Mean Square Residual (SRMR). 4) A predictive model was developed using Multivariate Logistic Regression analysis, via computer software. The dataset was split into training (70%) and testing (30%) sets. Feature selection was performed using recursive feature elimination with cross-validation. The model's performance was evaluated using the area under the Receiver Operating Characteristic (ROC) curve, sensitivity, specificity, and the Hosmer-Lemeshow goodness-of-fit test. All data analyses used a statistical significance level of 0.05.

Results

Table 1 shows the general characteristics of the sample and results of the 6-minute walk test. Out of 357 patients, the majority were male (61.1%), having a mean age of 62.7 years and a mean body mass index (BMI) of 26.4 kg/m^2. The most common cardiovascular diagnosis was coronary artery disease (52.9%). Frequent comorbidities included: hypertension (68.6%) and hyperlipidemia (55.5%). The mean walking distance was 348.6 meters. Severe arrhythmias were observed in 4.2% of all patients.

Among 357 patients, 15 cases of severe arrhythmias were observed; representing a prevalence of 4.20% (95% confidence interval (CI)): 2.38-6.84). The most common type was Ventricular Tachycardia, with a prevalence of 1.96% (95% CI: 0.79-4.00); followed by Atrial Fibrillation with Rapid Ventricular Response at 1.40% (95% CI: 0.46-3.24). While the overall prevalence of severe arrhythmias is

not high, it is clinically significant; especially for Ventricular Tachycardia, which can be life-threatening. The wide 95% confidence intervals suggest variability in the population and indicate that further studies with larger sample sizes may be needed for more precise estimates. Although Complete Heart Block had the lowest prevalence, it requires attention as it can lead to cardiac arrest if not treated promptly. This data is crucial for planning patient care and monitoring during 6-minute walk tests as well as for preparing medical teams and necessary emergency equipment.

Table 1 General characteristics of the sample and results of the Six-Minute Walk Test (N=357)

Variable	Number (%) or Mean±S.D.
Gender	
Male	218 (61.1)
Female	139 (38.9)
Age (years)	62.7±11.3
Body mass index (kg/m^2)	26.4±4.2
Cardiovascular diagnosis	
Coronary artery disease	189 (52.9)
Heart failure	98 (27.5)
Valvular heart disease	45 (12.6)
Others	25 (7.0)
Comorbidities	
Hypertension	245 (68.6)
Diabetes	128 (35.9)
Hyperlipidemia	198 (55.5)
Distance walked (meters)	348.6±87.2
Heart rate (beats/min)	
Before test	72.4±11.6
Immediately after test	98.7±18.3
Blood pressure (mmHg)	
Before test	128.5/78.3±15.7/9.4
Immediately after test	142.3/82.6±18.2/10.8
Severe arrhythmias	15 (4.2)

S.D.=standard deviation

The MSEM analysis reveals that both individual and institutional factors are significantly associated with the occurrence of severe arrhythmias. At the individual level, increased age (β=0.032, p-value<0.001) and male gender (β=0.185, p-value=0.010) are positively associated with the occurrence of arrhythmias. Patients with coronary artery disease (β=0.228, p-value=0.007) and heart failure (β=0.301, p-value=0.001) have higher risks. Increased BMI (β=0.041, p-value=0.023) and hypertension (β=0.156, p-value=0.048) also increase the risk. Additionally, greater walking distance is negatively associated with the occurrence of arrhythmias (β=-0.003, p-value=0.003). At the institutional level, staff experience of more than 10 years (β=-0.245, p-value=0.017) and specialized training (β=-0.318, p-value=0.004) are negatively associated with the occurrence of severe arrhythmias. Emergency equipment readiness (β=-0.276, p-value=0.005) and good protocol awareness (β=-0.202, p-value=0.023) help reduce the risk of severe arrhythmias.

Model fit indices:

Chi-square/df=2.34 (p-value=0.078)

Comparative Fit Index (CFI)=0.953

Tucker-Lewis Index (TLI)=0.941

RMSEA=0.062 (90% CI: 0.043-0.081)

SRMR=0.038

These indices indicate that the model has a good fit (CFI and TLI >0.90, RMSEA <0.08, SRMR <0.05).

Summary: The MSEM analysis shows that both individual and institutional factors affect the occurrence of severe arrhythmias during the 6-minute walk test. This information can be used to develop guidelines for screening high-risk patients and improve preventive measures at the institutional level.

This structural equation model visually represents the complex interplay between individual-level factors and institutional-level factors in predicting the occurrence of severe arrhythmias during the 6MWT. Solid lines indicate direct effects, while dashed lines represent indirect effects. The thickness of each line corresponds to the strength of the association. Key findings illustrated in this model

include: 1) The strong, direct effect of heart failure (β =0.301, p-value=0.001) on arrhythmia occurrence. 2) The protective effect of increased walking distance (β=-0.003, p-value=0.003) at the individual level. 3) The significant impact of staff experience >10 years (β=-0.245, p-value =0.017) in reducing arrhythmia risk at the institutional level. 4) The indirect effect of age on arrhythmia occurrence, mediated through reduced walking distance. This model provides a comprehensive view of the multifaceted nature of arrhythmia risk during cardiac rehabilitation, incorporating both patient-specific and institutional factors.

As shown in Table 2, the prevalence of severe arrhythmias during the 6MWT was 4.20% (95% CI: 2.38-6.84%), with Ventricular Tachycardia being the most common type (1.96%, 95% CI: 0.79-4.00%), followed by Atrial Fibrillation with Rapid Ventricular Response (1.40%, 95% CI: 0.46-3.24%).

Table 3 presents the results of our MSEM analysis, which revealed that both individual and institutional factors were significantly associated with the occurrence of severe arrhythmias. At the individual level, increased age (β=0.032, p-value<0.001) and male gender (β=0.185, p-value=0.010) were positively associated with arrhythmia risk.

Table 2 Prevalence of severe arrhythmias during the Six-Minute Walk Test

Type of arrhythmia	Number of cases	Prevalence (%)	95% CI
All severe arrhythmias	15	4.20	2.38-6.84
Ventricular tachycardia	7	1.96	0.79-4.00
Atrial fibrillation with rapid ventricular response	5	1.40	0.46-3.24
Supraventricular tachycardia	2	0.56	0.07-2.01
Complete heart block	1	0.28	0.01-1.55

CI=confidence interval

Table 3 Results of Multilevel Structural Equation Modeling (MSEM) analysis of factors associated with severe arrhythmias

Variable	Coefficient (β)	SE	p-value	95% CI
Individual level				
Age	0.032	0.009	<0.001	0.014-0.050
Gender (male)	0.185	0.072	0.010	0.044-0.326
Body Mass Index	0.041	0.018	0.023	0.006 -0.076
Coronary artery disease	0.228	0.084	0.007	0.063-0.393
Heart failure	0.301	0.092	0.001	0.121-0.481
Hypertension	0.156	0.079	0.048	0.001-0.311
Diabetes	0.132	0.075	0.079	-0.015-0.279
Distance walked	-0.003	0.001	0.003	-0.005--0.001
Institutional level				
Staff experience (>10 years)	-0.245	0.103	0.017	-0.447--0.043
Specialized training	-0.318	0.112	0.004	-0.538--0.098
Emergency equipment readiness	-0.276	0.098	0.005	-0.468--0.084
Protocol awareness	-0.202	0.089	0.023	-0.376--0.028

SE=standard error, CI=confidence interval

The multivariate logistic regression analysis (Table 4) identified several factors significantly increasing the risk of severe arrhythmias, including age (OR=1.56, p-value=0.002), male gender (OR=2.31, p-value=0.019), and heart failure (OR=3.42, p-value<0.001). Conversely, factors such as staff experience >10 years (OR=0.51, p-value=0.037) and emergency equipment readiness (OR=0.45, p-value=0.020) were protective.

Figure 1 illustrates the structural equation model representing the complex interplay between individual-level and institutional-level factors in predicting the occurrence of severe arrhythmias during the 6MWT. The model demonstrates the direct effects of heart failure and the protective effect of increased walking distance at the individual level, as well as the significant impact of staff experience in reducing arrhythmia risk at the institutional level.

The multivariate logistic regression analysis shows:

1. Factors significantly increasing risk:

-Age increase per 10 years (OR=1.56, p-value =0.002)

-Male gender (OR=2.31, p-value=0.019)

-BMI ≥30 kg/m^2 (OR=1.89, p-value=0.040)

-Coronary artery disease (OR=2.75, p-value= 0.005)

-Heart failure (OR=3.42, p-value<0.001)

-Hypertension (OR=1.98, p-value=0.038)

2. Factors significantly decreasing risk:

-Distance walked increase per 50 meters (OR =0.78, p-value=0.009)

-Staff experience >10 years (OR=0.51, p-value =0.037)

-Specialized training (OR=0.39, p-value=0.010)

-Emergency equipment readiness (OR=0.45, p-value=0.020)

Model evaluation:

Hosmer-Lemeshow Goodness of Fit Test: χ^2= 6.82, df=8, p-value=0.556

Area under the ROC Curve (AUC): 0.843 (95% CI: 0.781-0.905)

Nagelkerke R^2=0.372

Table 4 Results of multivariate logistic regression analysis of factors associated with severe arrhythmias

Variable	Adjusted OR	95% CI	p-value
Age (per 10-year increase)	1.56	1.18-2.07	0.002
Gender (male vs female)	2.31	1.15-4.64	0.019
BMI (≥30 vs <30 kg/m^2)	1.89	1.03-3.47	0.040
Coronary artery disease (yes vs no)	2.75	1.36-5.55	0.005
Heart failure (yes vs no)	3.42	1.67-7.01	<0.001
Hypertension (yes vs no)	1.98	1.04-3.77	0.038
Distance walked (per 50m increase)	0.78	0.65-0.94	0.009
Staff experience (>10 years vs ≤10 years)	0.51	0.27-0.96	0.037
Specialized training (yes vs no)	0.39	0.19-0.80	0.010
Emergency equipment readiness (ready vs not ready)	0.45	0.23-0.88	0.020

OR=odds ratio, CI=confidence interval

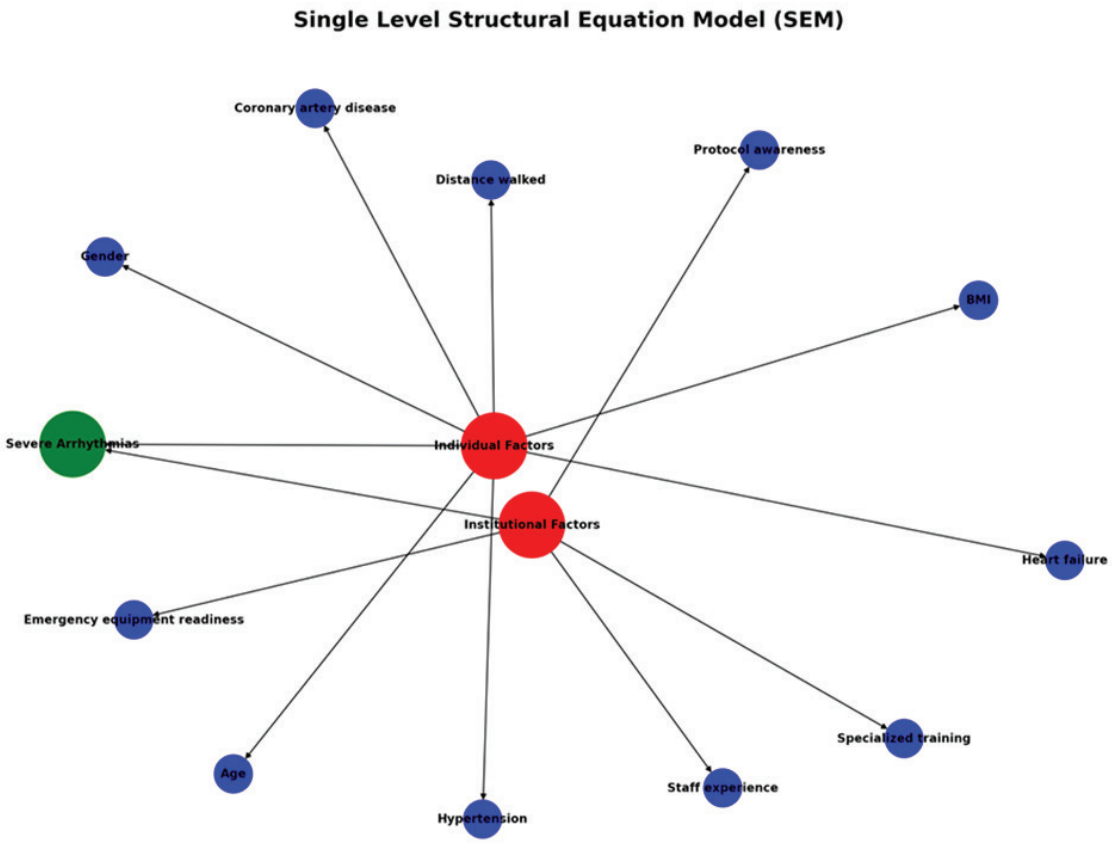

Figure 1 Structural equation model of factors associated with severe arrhythmias during Six-Minute Walk Tests in early outpatient cardiac rehabilitation

Prediction equation for the probability of severe arrhythmias:

log(odds)=-5.623+0.445(Age/10)+0.837(Male)+0.637(BMI≥30)+1.011(CAD)+1.230(HF)+0.683(HT)-0.248(Distance/50)-0.673(Experience>10y)-0.942(Training)-0.799(EquipReady)

Wherein:

-Variables are 0 or 1: 0=no/false, 1=yes/true

-Age: unit is 10 years

-Distance: unit is 50 meters

Probability=1/(1+e^-log(odds))

Summary: This model can predict the occurrence of severe arrhythmias fairly well (AUC=0.843). Age, gender, BMI, comorbidities and physical capacity affect the risk, while institutional factors, such as staff experience and preparedness, help reduce the risk. This information can be used to develop screening guidelines and monitoring protocols for high-risk patients.

Discussion

This study provides crucial insights into the prevalence and risk factors associated with severe arrhythmias during the 6MWT in early outpatient cardiac rehabilitation at a provincial hospital in Thailand. The findings

have significant implications for clinical practice, patient safety, and healthcare policies on a global scale; particularly in the context of developing countries.

The prevalence of severe arrhythmias during the 6MWT in our study (4.20%) aligns with the range reported in recent international literature (0.8% to 5.7%)[1]. However, our study uniquely contributes to the understanding of this phenomenon in the context of a developing country's healthcare system. This is particularly relevant as the global burden of cardiovascular diseases continues to shift towards low- and middle-income countries[2]. Our findings, based on data from Uttaradit Province with a CAD population prevalence of 1,320 per 100,000, provide valuable insights into cardiac rehabilitation safety in areas with limited resources. The specific challenges faced by healthcare systems in these countries; such as resource limitations and diverse patient populations, make our findings especially valuable for global health initiatives. Furthermore, our study addresses the gap in knowledge regarding the safety of the 6MWT in resource-limited settings. As highlighted by Pesah et al.[19], there is a significant disparity in cardiac rehabilitation availability and implementation between high-income and low- to middle-income countries[3]. Our findings provide valuable data that can inform the adaptation of cardiac rehabilitation protocols in diverse healthcare settings.

Our findings regarding individual risk factors not only align with recent studies but also offer new perspectives. The strong association between heart failure and severe arrhythmias during the 6MWT (OR=3.42, p-value<0.001) underscores the need for heightened vigilance in this patient subgroup. This aligns with the work of Cahalin et al.[7], who emphasized the prognostic value of 6MWT in heart failure patients[4]. However, our study extends this concept by quantifying the arrhythmic risk, which has implications for test protocol modifications and monitoring strategies. The increased risk associated with coronary artery disease (OR=2.75, p-value=0.005) adds to the growing body of evidence linking coronary pathology with arrhythmic events. This finding supports the need for careful risk stratification in patients with known coronary disease before undertaking functional tests; as suggested by Chaudhry et al.[8] in their recent review of exercise testing in coronary artery disease[5]. The impact of hypertension (OR=1.98, p-value =0.038) on arrhythmic risk during the 6MWT is a notable finding that warrants further investigation. It suggests that optimal blood pressure control might be crucial in reducing arrhythmic events during functional testing. This aligns with the recent work by Williams et al.[9] on the importance of blood pressure management in cardiovascular risk reduction[6]. Our findings contribute to the growing evidence supporting intensive blood pressure management in high-risk cardiovascular patients: as demonstrated in the SPRINT trial follow-up by Bress et al.[18].

The negative association between walking distance and arrhythmia risk (OR=0.78 per 50m increase, p-value= 0.009) is a novel finding that warrants further investigation. It suggests that improved functional capacity may have a protective effect against arrhythmias, supporting the broader benefits of cardiac rehabilitation programs. This finding contributes to the growing body of evidence on the multifaceted benefits of exercise in cardiovascular health: as highlighted in the recent review by Ambrosetti et al.[10] Moreover, this inverse relationship between functional capacity and arrhythmic risk provides a strong rationale for early initiation and consistent participation in cardiac rehabilitation programs. It suggests that improvements in exercise capacity not only enhance quality of life but may also directly contribute to reducing the risk of serious cardiac events. This finding aligns with the recent work of Ozemek et al.[11], who demonstrated the dose-response relationship between exercise and cardiovascular health outcomes[9]. Our results also support the concept of: "exercise as medicine," in cardiovascular care, as discussed by Lavie et al.[20]. The protective effect of increased walking distance underscores

the potential of exercise-based interventions in modifying cardiovascular risk beyond traditional pharmacological approaches.

Perhaps the most significant contribution of our study is the identification of modifiable institutional factors that can reduce the risk of severe arrhythmias. The protective effects of staff experience (OR=0.51, p-value=0.037), specialized training (OR=0.39, p-value=0.010), and emergency equipment readiness (OR=0.45, p-value=0.020) provide actionable insights for improving patient safety. These findings align with the recent emphasis on the importance of healthcare system factors in patient outcomes: as discussed by Briggs et al.[12] in their work on quality improvement in cardiac care. The strong protective effect of specialized training highlights the critical role of continuous medical education in cardiac rehabilitation settings. This finding supports the implementation of regular, targeted training programs for healthcare professionals involved in cardiac rehabilitation: as recommended by Supervia et al.[13] in their international survey of cardiac rehabilitation practices. The significance of emergency equipment readiness underscores the importance of institutional preparedness in managing potential adverse events. This finding has implications for resource allocation and hospital policies, particularly in settings with limited resources. It aligns with recent recommendations by the American Heart Association on systems of care for cardiac rehabilitation. Our study also provides empirical evidence supporting these recommendations; potentially influencing policy decisions and resource allocation in cardiac rehabilitation programs globally.

The use of MSEM in our study represents a methodological advancement in this field. By simultaneously analyzing individual and institutional factors, we provide a more comprehensive understanding of the complex interplay between patient characteristics and healthcare system attributes. This approach responds to the call for more sophisticated analytical methods in healthcare research: as advocated by Kim et al.[5] in their recent methodological paper. Our MSEM approach allowed us to disentangle the effects of individual-level factors (such as age and comorbidities) from institutional-level factors (such as staff training and equipment readiness). This multi-level perspective is crucial for developing comprehensive strategies to reduce arrhythmic risk that address both patient-specific and system-wide factors. The application of MSEM in cardiac rehabilitation research opens new avenues for understanding the complex interactions between patient outcomes and healthcare delivery systems.

The implications of our findings extend beyond immediate clinical settings, and contribute significantly to global health initiatives. By demonstrating the importance of institutional factors, our study provides evidence to support policy decisions regarding resource allocation and staff training in cardiac rehabilitation programs. This is particularly relevant in the context of global efforts to strengthen healthcare systems: as outlined in the World Health Organization's global action plan for the prevention and control of noncommunicable diseases[1]. Our findings can inform the development of guidelines for the 6MWT administration in diverse healthcare settings; particularly in resource-limited environments. The identification of both patient-level and institutional-level risk factors allows for a more nuanced approach to risk stratification and management, which can be adapted to different healthcare contexts globally. This aligns with the recent call by Babu et al.[16] for context-specific cardiac rehabilitation models in low- and middle-income countries.

Our study contributes to the ongoing discussion about the safety and efficacy of the 6MWT in various patient populations. While confirming its overall safety, our results highlight the need for personalized risk assessment and tailored monitoring strategies. This aligns with the trend towards precision medicine in cardiovascular care: as

discussed by Krittanawong et al.[15] in their review of artificial intelligence applications in cardiology. The development of our predictive model, which incorporates both individual and institutional factors, represents a step towards more personalized risk assessment in cardiac rehabilitation. Future research could focus on validating and refining this model in diverse populations and healthcare settings, potentially incorporating genetic and biomarker data for even more precise risk stratification. This approach is in line with recent advancements in precision cardiology: as reviewed by Antman and Loscalzo[17].

Despite its strengths, our study has limitations that should be addressed in future research. The single-center design may limit the generalizability of our findings, necessitating multi-center studies across different healthcare settings. Additionally, the retrospective nature of the study may introduce potential biases, calling for prospective studies to confirm our findings. Future research should also explore the long-term outcomes of patients having experienced arrhythmias during a 6MWT. In addition to the impact of different cardiac rehabilitation protocols on arrhythmic risk, and the cost-effectiveness of implementing the suggested institutional measures for risk reduction. Longitudinal studies examining the relationship between functional capacity improvements and arrhythmic risk over time would provide valuable insights into the dynamic nature of cardiovascular risk in rehabilitation settings.

Conclusion

In conclusion, this study not only advances our understanding of arrhythmic risk during the 6MWT but also provides a framework for improving patient safety and care quality in cardiac rehabilitation programs worldwide. By bridging the gap between individual patient factors and institutional characteristics, our findings offer a holistic approach to risk management that can be adapted to diverse healthcare settings globally. The implications of our study extend from bedside care to health policy, contributing to the global effort to reduce the burden of cardiovascular disease and improve patient outcomes in cardiac rehabilitation programs. Our work underscores the importance of a systems approach to cardiac rehabilitation, considering both patient-specific and institutional factors in risk assessment and management. As the global burden of cardiovascular disease continues to grow, particularly in low- and middle-income countries, the insights from our study can inform the development of safe, effective, and context-appropriate cardiac rehabilitation programs worldwide.

This research not only fills academic gaps but also has the potential to create extensive, positive impacts on Thailand's healthcare system; from operational to policy levels. By focusing on the safety and efficacy of the 6MWT in early outpatient cardiac rehabilitation, particularly in a provincial hospital setting, our findings address a critical aspect of cardiovascular care that has been understudied in the Thai context. The developed prediction model and identified risk factors can contribute to the development of more tailored and effective cardiac rehabilitation protocols Furthermore, these could potentially improve outcomes for patients with coronary artery disease and other cardiovascular conditions across various healthcare settings in Thailand and similar developing countries.

Ethics approval

This research project has been approved by the Human Research Ethics Committee of Uttaradit Hospital (Approval Number: REC No.49/2564, Approval Date: August 2, 2021, Expiry Date: August 1, 2022). All data will be kept confidential, using codes instead of names for patients and personnel in analysis and reporting.

Acknowledgement

This study was made possible through the collective efforts and support of numerous individuals and institutions. We extend our heartfelt gratitude to all those who contributed to the successful completion of this research. Firstly, we would like to express our sincere appreciation to the administration and staff of Uttaradit Hospital for their cooperation and support throughout the study period. Their commitment to advancing cardiac care and rehabilitation has been instrumental in the realization of this project. We are deeply grateful to all the patients that participated in this study. Their willingness to contribute to medical research, despite personal health challenges, is commendable and has been crucial to our understanding of cardiac rehabilitation outcomes. Our thanks also go to the cardiac rehabilitation team at Uttaradit Hospital, including the nurses and physiotherapists, whose expertise and dedication ensured the safe and effective implementation of the 6MWT protocols. Finally, we would like to thank our colleagues and family members for their unwavering support and encouragement throughout the research process. This study represents a collaborative effort aimed at improving cardiac care, and we are grateful to all those whom have contributed to this important work.

Conflict of interest

There are no conflicts of interest to declare.

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