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ORIGINAL RESEARCH

RAMA-WeRA Risk Score in Predicting the Ruptured Appendicitis in Emergency Department; a Multicenter Study for External Validation

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Abstract: **Introduction:** Distinguishing between ruptured and non-ruptured acute appendicitis presents a significant challenge. This study aimed to validate the accuracy of RAMA-WeRA Risk Score in predicting ruptured appendicitis (RA) in emergency department. **Methods:** This study was a multicenter diagnostic accuracy study conducted across six hospitals in Thailand from February 1, 2022, to January 20, 2023. The eligibility criteria included individuals aged >15 years suspected of acute appendicitis, presenting to the ED, and having an available pathology report following appendectomy or intraoperative diagnosis by the surgeon. We assessed the screening performance characteristics of RAMA-WeRA Risk Score, in detecting the ruptured appendicitis (RA) cases. **Results:** 860 patients met the study criteria. 168 (19.38%) had RA and 692 (80.62%) patients had non-RA. The area under the receiver operating characteristic curve (AuROC) of RAMA-WeRA Risk Score was 75.11% (95% CI: 71.10, 79.11). The RAMA-WeRA Risk Score > 6 points (high-risk group) demonstrated a positive likelihood ratio (LR) of 3.22 in detecting the ruptured cases. The sensitivity and specificity of score in > 6 cutoff point was 43.8% (95%CI: 36.2, 51.6) and 86.4% (95%CI: 83.6, 88.9), respectively. **Conclusions:** The RAMA-WeRA Risk Score can predict rupture in patients presenting with suspected acute appendicitis in the emergency department with total accuracy of 75% for high-risk cases.

Keywords: Appendicitis; Abdomen, acute; Rupture; Clinical decision rules; Validation study

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1. Introduction

Acute appendicitis (AA) is a common cause of acute abdominal pain encountered in patients seeking care at the emergency department (ED) (1, 2). The Alvarado score stratifies patients into different likelihood categories for AA diagnosis. A score of 1 to 4 indicates a low probability of AA, 5 to 6 suggests a moderate probability where close monitoring of symptoms is advisable, and a score of 7 to 10 signifies a high probability, necessitating surgical intervention (3-6). This scoring system enjoys broad acceptance and usage in Thailand for predicting the presence of AA. However, the Alvarado score is not particularly effective in predicting complications associated with AA, such as ruptured appendicitis (RA).

RA and gangrenous appendicitis are common complications (7, 8) observed in approximately 20-34% of cases (9, 10), with a higher incidence among younger patients and those aged over 50 years. RA represents a significant and serious complication leading to prolonged hospitalization and an elevated risk of mortality. Within the cohort of patients experiencing RA, the mortality rate is estimated to be around 5%, in contrast to the mortality rate of approximately 0.1-0.6% observed in patients with non-RA (1, 11).

Distinguishing between RA and non-RA preoperatively presents a significant challenge (12, 13). There are several factors that have been identified for the prediction of RA. These factors include male sex, presence of a fever > 38 degrees Celsius, anorexia (loss of appetite), prolonged duration

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of pain in the period leading up to admission, elevated heart rate > 130 beats per minute, and the presence of localized rebound tenderness in the right lower quadrant (RLQ) of the abdomen (14).

In 2021, Welawat et al. conducted a study where they developed the Ramathibodi Welawat RA score (Rama WeRA score) to predict RA. Five specific factors were significant indicators of RA: age > 60 years, fever > 37.3 degrees Celsius, the presence of guarding, a polymorphonuclear neutrophil (PMN) count > 75%, and duration of abdominal pain > 24 hours prior to presentation.

The risk scores derived from these factors were stratified into three distinct categories: a score < 2, indicative of low risk; a score between 2 and 6, representing moderate risk; and a score > 6, indicating high risk. It was observed that individuals classified within the high-risk group (score > 6) exhibited a 3.88-fold increased likelihood ratio (LR) of having RA (15).

The Rama WeRA score was developed in the ED of Ramathibodi Hospital and underwent internal validation within the same dataset (15). We plan to implement the Rama WeRA score for use in EDs across Thailand to assist emergency physicians (EPs) in diagnosing RA and facilitating rapid transfer to definitive diagnosis and surgery. Before implementing the Rama WeRA score, temporal and geographic validation is essential. The primary objective of our study was to assess the accuracy of the Rama WeRA score in predicting the likelihood of RA among patients presenting with AA in a multicenter study involving EDs of Thai hospitals.

2. Methods

2.1. Study design and setting

This study was a prospective diagnostic accuracy study conducted in six hospitals, including secondary care hospitals (Warinchamrab Hospital, Kalasin Hospital), tertiary care hospitals (Nakhon Si Ayutthaya Hospital, Maharaj Nakhon Si Thammarat Hospital, and Suratthani Hospital) and Ramathibodi Hospital, a university-affiliated super tertiary care hospital in Bangkok, Thailand.

The standardized protocol for managing patients with suspected AA and RA varied slightly across hospitals. In Nakhon Si Ayutthaya and Kalasin Hospitals, patients suspected of having AA and RA were admitted to the surgical unit with or without an abdominal Computer Tomography (CT) scan or ultrasound. In Maharaj Nakhon Si Thammarat, Warinchamrab, and Suratthani Hospitals, patients suspected of having AA and RA underwent surgeon consultation in the ED with or without a CT scan or ultrasound before admission. In Ramathibodi Hospital, patients suspected of having AA and RA underwent a CT scan or ultrasound in the ED. Patients with officially reported RA were referred for surgical consultation. The definitive management protocol in every hospital included exploration laparotomy for appendectomy. Following the appendectomy procedure, the surgical specimen was submitted for histopathological analysis to validate the definitive diagnosis, or surgical operative findings were documented in the patient's chart.

Our study received ethical approval from the Faculty of Medicine's Committee on Human Rights Related to Research Involving Human Subjects at Ramathibodi Hospital, Mahidol University (Approval Number COA. MURA2022/66), Kalasin Hospital Research Ethics Committee; KLSH REC (Approval Number 020/2022R), Surat Thani Hospital Research Ethics Committee (Approval Number REC 65-0015), Maharaj Nakhon Si Thammarat Hospital Research Ethics Committee (Approval Number A004/2565), Ubon Ratchathani Provincial Health Office Research Ethics Committee (Approval Number SSJ.UB2565-015) and Ayutthaya Hospital Research Ethics Committee (Approval Number 25/2565). Throughout the research process, the investigators strictly adhered to the ethical guidelines outlined in the Helsinki Declaration, ensuring the confidentiality of patients' information.

2.2. Participants

During the study period from 1 February 2022 to 20 January 2023, the eligibility criteria included individuals aged ≥ 16 years presenting with suspected AA or RA who visited the ED in the six mentioned hospitals. The same record form was utilized across six hospitals. The protocol for managing AA and RA varied depending on the hospital's guidelines. Patients suspected of AA and RA who underwent appendectomy but lacked official pathological results from a pathologist or intraoperative diagnosis by a surgeon were excluded. Additionally, patients with AA and RA who received conservative treatment, declined treatment, were referred to another hospital, or had pathological results unrelated to AA were also excluded.

2.3. Data collection and study variables

The development dataset was retrospectively gathered between March 2016 and March 2018 (15), while the validation dataset was prospectively collected from February 2022 to January 2023. Additionally, temporal validation in Ramathibodi Hospital and geographic validation was implemented, incorporating data from multiple hospitals located in Kalasin, Warin Chamrap, Phra Nakhon Si Ayutthaya, Surat Thani, and Maharaj Nakhon Si Thammarat. All pertinent study variables of each eligible patient were systematically documented in the record form by the attending EP. The study variables encompassed baseline characteristics as well as parameters associated with the Rama WeRA score, which was employed for prognosticating the probability of RA based on previously published research (15). These variables included sex, age, RLQ pain, migratory pain, presence of nausea and vomiting, diarrhea, anorexia, body temperature, rebound tenderness, guarding, white blood cell (WBC) count, PMN WBC count, and the duration of pain before the patient's presentation (table 1).

The duration of pain was defined as the time elapsed from the onset of abdominal pain to the patient's arrival at ED.

Furthermore, we collected an additional potential factor in this study, referred to as 'time to surgery,' which was defined as the interval between a patient's arrival at the ED and their subsequent appendectomy procedure. Any missing data in the record form were addressed using a naive approach, wherein no data imputation was employed for other variables.

2.4. Outcomes of interest

The primary outcome of interest involved the presence of a positive pathological report indicating ruptured or perforated appendicitis, as determined by a pathologist's report or surgical operative findings, which were documented in the patient's chart. Subsequently, patients were stratified into two distinct categories: those belonging to the RA group and those comprising the non-RA group.

2.5. Statistical analysis

We conducted all statistical analyses using STATA software version 18.0 (StataCorp, College Station, TX, USA)—the comparative assessment of all study variables between RA and non-RA. Baseline prognostic factors were summarized in a table using descriptive statistics. Categorical data was presented in frequencies and percentages, while continuous data was expressed as the mean and standard deviation. Potential factors were compared utilizing a t-test and exact probability test, which were calculated through univariable analysis to discern differences in clinical characteristics. The results were then depicted as the area under the receiver operating characteristic curve (AUROC) with corresponding 95% confidence intervals (95% CIs).

Furthermore, we conducted a multivariable logistic regression analysis to evaluate the five potential factors previously identified as significantly associated with RA according to the WeRA score. The outcomes of this analysis were presented in terms of the AUROC, odds ratios, 95% CIs, and calibration plots, comparing the development and validation datasets.

3. Results

3.1. Baseline characteristics of studied cases

From February 1, 2022, to January 20, 2023, a total of 893 patients were included in this study as they presented with symptoms indicative of AA or RA, underwent appendectomy, and had official pathological results provided by a pathologist or intraoperative diagnosis by a surgeon across the six EDs. Thirty-three patients were subsequently excluded from the analysis due to various reasons: receipt of conservative treatment (9 patients), denial of treatment (2 patients), referral to another hospital (6 patients), and pathological results not associated with AA, including reactive lymphoid hyperplasia (8 patients), absence of appendiceal tissue (2 patients), neuroendocrine tumor (2 patients), fecal compaction (2 patients), granulomatous (1 patients), and Omental hemorrhage (1 patients). Finally, 860 patients met the eligibility criteria for this study. 168 (19.5%) patients presented with pathologically confirmed RA or were diagnosed intraoperatively by experienced surgeons. The remaining 692 (80.5%) patients within this group were diagnosed with non-RA (Figure 1). These patients were distributed across multiple medical institutions, with 133 patients (15.47%) from Kalasin Hospital, 189 patients (21.98%) from Phra Nakhon Si Ayutthaya Hospital, 173 patients (20.12%) from Surat Thani Hospital, 119 patients (13.84%) from Maharaj Nakhon Si Thammarat Hospital, and 196 patients (22.79%) from Ramathibodi Hospital.

The demographic and clinical characteristics between the development and validation datasets were not statistically significant except for certain variables: anorexia (41.6% vs. 61.40%, p-value < 0.001), rebound tenderness (70.0% vs. 53.72%, p-value < 0.001), and duration of pain to ED (p-value < 0.001). The category of non-RA in the validation group encompassed various subtypes, including inflamed appendicitis in 298 patients (38.75%), suppurative appendicitis in 266 patients (34.59%), gangrenous appendicitis in 54 patients (7.02%), and appendiceal abscess in 2 patients (0.26%) (Table 2).

3.2. Screening performance characteristics of RAMA-WeRA score

The AUROC of the RAMA-We RA Risk Score was 75.11% (95% CI: 71.10, 79.11) for the geographic validation (Figure 2) and 80.78% (95% CI: 72.72, 88.84) for the temporal validation (Figure 3).

The calibration plots effectively depict the alignment between the observed risk (depicted as circles) and the score-predicted risk (represented by the solid line) pertaining to RA. Notably, the score-predicted risk exhibited a discernible and consistent increase in tandem with the observed risk.

In the subsequent analysis, the risk scores were stratified into three groups: scores < 2 categorized as low risk, scores 2 to 6 indicating moderate risk, and scores > 6 designating high risk. Within the high-risk group, the positive LR for the presence of RA was 3.20 (95% CI: 2.49, 4.13). The sensitivity and specificity of score in > 6 cutoff point was 43.8% (95%CI: 36.2, 51.6) and 86.4% (95%CI: 83.6, 88.9), respectively (Table 3).

4. Discussion

This research has yielded significant findings regarding the accuracy of the RAMA-WeRA Risk Score in diagnosing RA across multiple hospitals in Thailand. The geographic validation conducted in six hospitals observed an overall accuracy rate of 75.11% for predicting RA, which was not statistically significant compared to the development dataset in Ramathibodi Hospital. Furthermore, the RAMA-WeRA Risk Score > 6 points (the high-risk group) demonstrated a positive LR of 3.22 in predicting the ruptured cases. These outcomes closely paralleled the results of the initial development study, affirming the robustness and consistency of the RAMA-We RA Risk Score. This result confirmed the validity

of the RAMA-WeRA Risk Score for predicting RA in the ED of Thai hospitals.

Many studies used the cut point of neutrophil-to-lymphocyte ratio (NLR) to differentiate RA (16); the study of Hajibandeh et al. demonstrated that NLR> 8.8 was strong in the prediction of RA (17). The study of Ahmad et al. used a cut point of 6.17 to predict RA with sensitivity and specificity of 76.32% and 58.72%, respectively (18).

While many studies have incorporated abdominal ultrasound findings as a predictive factor for identifying RA cases, it is noteworthy that the RAMA-WeRA Risk Score exclusively relies on clinical manifestations and ED laboratory data as its primary predictor variables. Interestingly, the accuracy of this approach does not appear to differ significantly compared to other models. For instance, the model TH Kim et al. developed employs four variables, including appendiceal diameter, ascites, fat stranding, and C-reactive protein (CRP). In their investigation, TH Kim et al. reported an AuROC of 77.7% (95% CI: 71.8, 83.5) (19). Similarly, the model proposed by Atema et al. incorporates eight variables, encompassing age, temperature, duration of symptoms, WBC count, CRP, the presence of extraluminal free air, peri appendiceal fluid, and the presence of an appendicolith. In their study, Atema et al. achieved an AuROC of 82.6% (95% CI: 77.4, 87.8) (20).

Compared to another study that similarly relied on clinical manifestations and ED laboratory data, the RAMA-WeRA Risk Score exhibited a commendable discriminative performance, achieving an accuracy rate of 81.23% within the development dataset. Notably, this discrimination performance was found to be comparable to that of the model proposed by Kang et al., which integrated five variables, including temperature, abdominal pain score, WBC count, NLR, and C-reactive protein (CRP). In their study, Kang et al. reported an AuROC of 77.2% (95% CI: 70.6, 83.9) (21).

Furthermore, the model introduced by Bröker et al., which relied solely on two variables, including the duration of symptoms and CRP, and the RAMA-WeRA Risk Score, demonstrated a comparable discriminative performance. Bröker et al. reported an AuROC of 77.8% (95% CI: 71.9, 83.7) in their investigation. These comparative findings underscore the robustness and effectiveness of the RAMA-We RA Risk Score in predicting RA, even when utilizing a simplified set of clinical and laboratory variables (22).

In the present study, our methodology included intraoperative diagnoses made by attending surgeons to diagnose RA. This approach diverged from the methodology employed in the development study, which excluded patients lacking official pathological reports following appendectomy. The rationale behind this deviation stemmed from the fact that, apart from Ramathibodi Hospital, several other participating hospitals did not possess comprehensive pathological results for all appendectomy cases. This pragmatic modification in our study design allowed us to accommodate the limitations inherent in the availability of pathological data across different medical institutions. By incorporating intraoperative diagnoses made by experienced surgeons, we sought to provide a more comprehensive and inclusive assessment of RA, enhancing the generalizability and applicability of our findings in real-world clinical settings.

In our study conducted at Ramathibodi Hospital, we employed temporal validation for appendicitis patients. The development dataset was retrospectively gathered between March 2016 and March 2018, while the validation dataset was prospectively collected from February 2022 to November 2022. Additionally, geographic validation was implemented, incorporating data from multiple hospitals located in Kalasin, Warin Chamrap, Phra Nakhon Si Ayutthaya, Surat Thani, and Maharaj Nakhon Si Thammarat.

The analysis revealed a reduction in the AuROC for the validation dataset compared to the development dataset. This decline in accuracy can be attributed to several factors, including disparities in patient characteristics, the proficiency of medical history-taking and physical examination, and variances in diagnostic procedures. One notable divergence is the protocol employed at Ramathibodi Hospital, which mandates the acquisition of imaging studies such as ultrasound or CT scans to confirm suspected AA in all patients before surgical consultation. In contrast, other hospitals may selectively utilize imaging, depending on individual cases. This dissimilarity in diagnostic approaches across institutions underscores the complexity of patient populations under study.

Consequently, it is imperative to exercise caution when employing the RAMA-We RA Risk Score as a diagnostic tool outside the confines of Ramathibodi Hospital. The patient demographics and diagnostic practice variations necessitate a nuanced and judicious interpretation of the score's outcomes in different clinical settings. These findings underscore the importance of considering local factors and clinical context when applying this risk score to ensure its effective utilization as part of a comprehensive diagnostic strategy.

This study has underscored the utility and broad applicability of the RAMA-WeRA Risk Score for predicting the risk of RA in patients suspected of AA across various hospital settings. Notably, this risk assessment tool is characterized by its user-friendliness, relying solely on information derived from history-taking, physical examination, and basic laboratory tests, all readily available in virtually every healthcare facility. In cases where the calculated risk score exceeds 6, prudence suggests caution regarding the potential presence of RA. In such instances, timely consultation with a surgeon is advisable, or, in scenarios where no surgical expertise is immediately accessible, consideration should be given to patient transfer to a facility equipped to handle surgical interventions. Additionally, close monitoring of clinical signs and symptoms, coupled with the initiation of early therapeutic measures such as empirical antibiotic administration or fluid resuscitation, can be instrumental in mitigating

potential complications associated with RA. These recommendations are based on the robust findings of this study and hold valuable implications for clinical practice.

4.1. Limitations

One notable divergence is the protocol employed at Ramathibodi Hospital, which mandates the acquisition of imaging studies such as ultrasound or CT scans to confirm AA in all patients before surgical consultation. In contrast, other hospitals may selectively utilize imaging, depending on individual cases. This dissimilarity in diagnostic approaches across institutions may underscore the complexity of patient populations under study.

5. Conclusions

The RAMA-We RA Risk Score can be implemented to predict RA in patients presenting with suspected AA in the ED across Thai hospitals with 75% total accuracy.

6. Declarations

6.1. Acknowledgments

None.

6.2. Conflict of interest

The authors declare that they have no competing interests.

6.3. Funding

We secured funding from the Faculty of Medicine at Ramathibodi Hospital, with registry number RF_65082, to conduct data collection across six hospitals.

6.4. Authors' contribution

All contributors to this work have substantially participated in its development, encompassing the concept formation, study design, implementation, data collection, data analysis, and interpretation. Each author has been involved in the drafting and revision process, providing critical feedback on the manuscript. They have unanimously approved the final version for publication, concurred on the choice of journal for submission, and collectively accept responsibility for the integrity of all aspects of the work.

6.5. Ethical considerations

Our study received ethical approval from the Faculty of Medicine's Committee on Human Rights Related to Research Involving Human Subjects at Ramathibodi Hospital, Mahidol University (Approval Number COA. MURA2022/66), Kalasin Hospital Research Ethics Committee; KLSH REC (Approval Number 020/2022R), Surat Thani Hospital Research Ethics Committee (Approval Number REC 65-0015), Maharaj Nakhon Si Thammarat Hospital Research Ethics Committee (Approval Number A004/2565), Ubon Ratchathani Provincial Health Office Research Ethics Committee (Approval Number SSJ.UB2565-015) and Ayutthaya Hospital Research Ethics Committee (Approval Number 25/2565).

Throughout the research process, the investigators strictly adhered to the ethical guidelines outlined in the Helsinki Declaration, ensuring the confidentiality of patients' information.

6.6. Conflict of interest

The authors declare that they have no competing interests.

6.7. Using artificial inteligence chatbots

During the preparation of this work the author(s) used ChatGPT3.5 in order to check and correct grammatical error during the manuscript writing process. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Table 1: The RAMA-WeRA ruptured appendicitis risk score for the diagnosis of ruptured appendicitis

Predictors	**Assigned score**
Age > 60 (years)	1
Fever > 37.3 (Celsius)	1.5
Guarding	2
Polymorphonuclear neutrophil count > 75%	1.5
Duration of abdominal pain (hours)	
< 12	0
12-13	1
≥ 24	3

Risk categories: Low (<2), Moderate (2-6), High (>6)

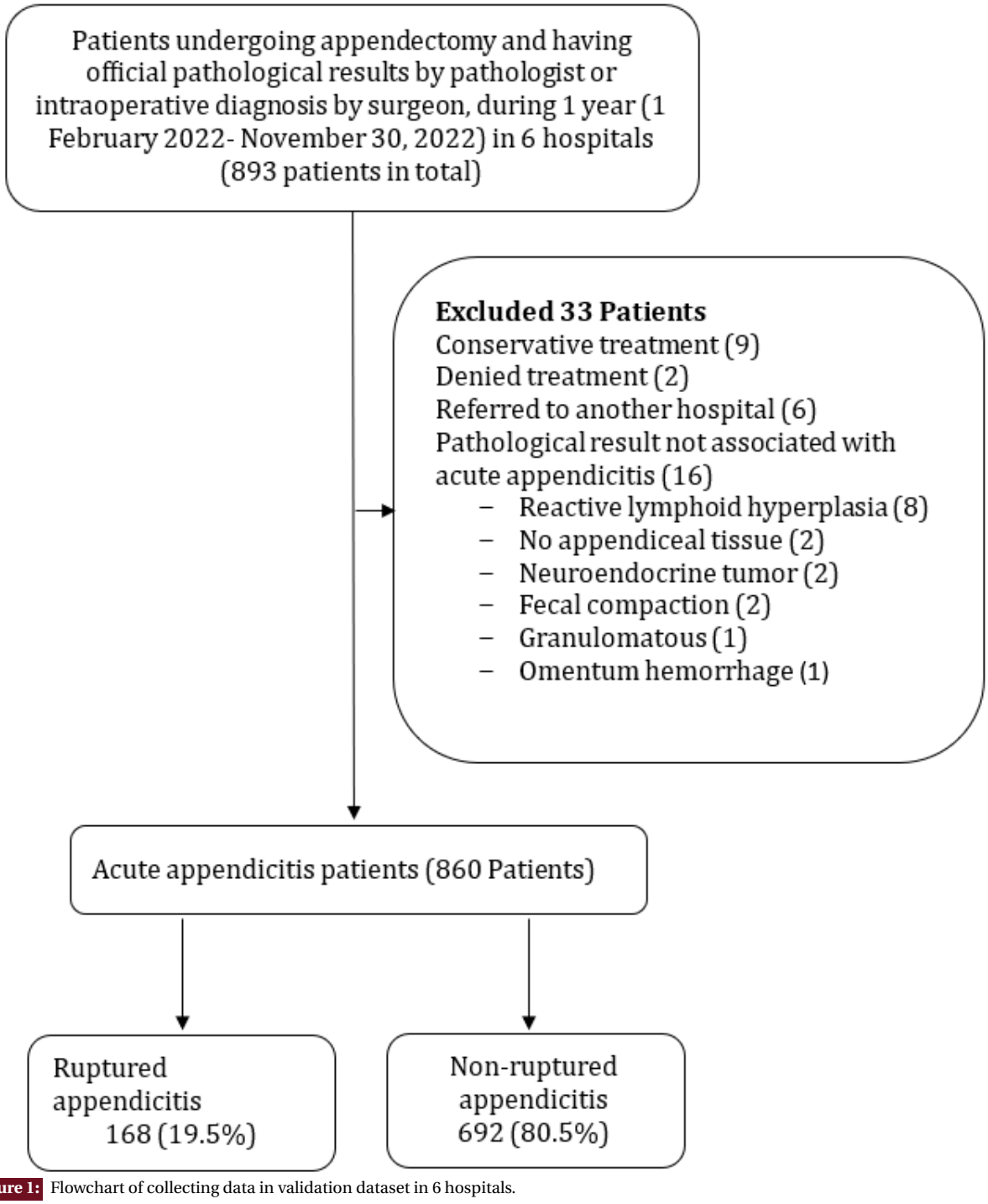

Figure 1: Flowchart of collecting data in validation dataset in 6 hospitals.

Table 2: Comparing the demographic and clinical characteristics of patients in the development and validation datasets

Characteristics	Development (N=480)	Validation (N=860)	P-value
Demography			
Male	197 (41.04)	399 (46.40)	0.067
Age > 60 years	88 (18.33)	172 (20.00)	0.472
Sign and symptom			
RLQ pain	479 (99.79)	854 (99.42)	0.429
Migratory pain	282 (58.75)	499 (58.02)	0.817
Nausea and vomiting	285 (59.38)	541 (62.91)	0.219
Diarrhea	105 (21.88)	191 (22.21)	0.945
Anorexia	199 (41.46)	528 (61.40)	< 0.001
Fever > 37.3 C	220 (45.83)	337 (39.19)	0.021
Rebound tenderness	336 (70.00)	462 (53.72)	< 0.001
Guarding	151 (31.46)	304 (35.35)	0.166
White blood cell count			
< 10000	69 (14.37)	132 (15.35)	
10000-15000	222 (46.25)	401 (46.63)	0.846
> 15000	189 (39.38)	327 (38.02)	
PMN > 75%	367 (76.46)	625 (72.67)	0.135
Duration of pain to ED			
< 12 hours	102 (21.25)	306 (35.58)	
12-23 hours	64 (13.33)	134 (15.58)	< 0.001
≥ 24 hours	314 (65.42)	420 (48.84)	
Pathology results			
Ruptured	77 (16.04)	168 (19.53)	0.122
Inflamed	403 (83.96)	331 (38.49)	NA
Suppurative		294 (34.19)	
Gangrenous		64 (7.44)	
Abscess		3 (0.35)	
Hospital			
Kalasin		133 (15.47)	NA
Warin Chamrap, Ubonratchathani		50 (5.81)	
Phra Nakhon Si Ayutthaya		189 (21.98)	
Surat Thani		173 (20.12)	
Maharaj Nakhon Si Thammarat		119 (13.84)	
Ramathibodi, Bangkok	480 (100)	196 (22.79)	
Time from ED to surgery (hours)			
median (IQR)		7 (5, 9)	NA

Data are presented as number (%). RLQ: Right Lower Quadrant; PMN: Polymorphonuclear; ED: Emergency department; IQR: interquartile range; NA: not applicable.

Table 3: The area under the receiver operating characteristic curve (AuROC)of RAMA WeRA risk score in predicting the presence of ruptured appendicitis

Characteristics	
AuROC (Total)	75.11 (71.10, 79.11)
AuROC (Subgroup by hospital)	
Kalasin	73.00 (63.10, 82.90)
Warin Chamrap, Ubonratchathani	81.12 (68.39, 93.85)
Phra Nakhon Si Ayutthaya	73.18 (61.47, 84.89)
Surat Thani	79.42 (71.53, 87.30)
Maharaj Nakhon Si Thammarat	66.13 (56.32, 75.94)
Ramathibodi, Bangkok	80.78 (72.72, 88.84)
Positive likelihood ratio	
Low (<2)	0.18 (0.09, 0.39)
Moderate (2-6)	0.81 (0.69, 0.95)
High (>6)	3.20 (2.49, 4.13)
Performance in the best cutoff point (score > 6)	
True positive	74
True negative	597
False positive	94
False negative	95
Sensitivity	43.8 (36.2, 51.6)
Specificity	86.4 (83.6, 88.9)
Positive predictive value	44.0 (36.4, 51.9)
Negative predictive value	86.3 (83.5, 88.7)
Negative likelihood ratio	0.65 (0.57, 0.75)
Positive likelihood ratio	3.22 (2.50, 4.15)
Total accuracy	75.11 (71.10, 79.11)

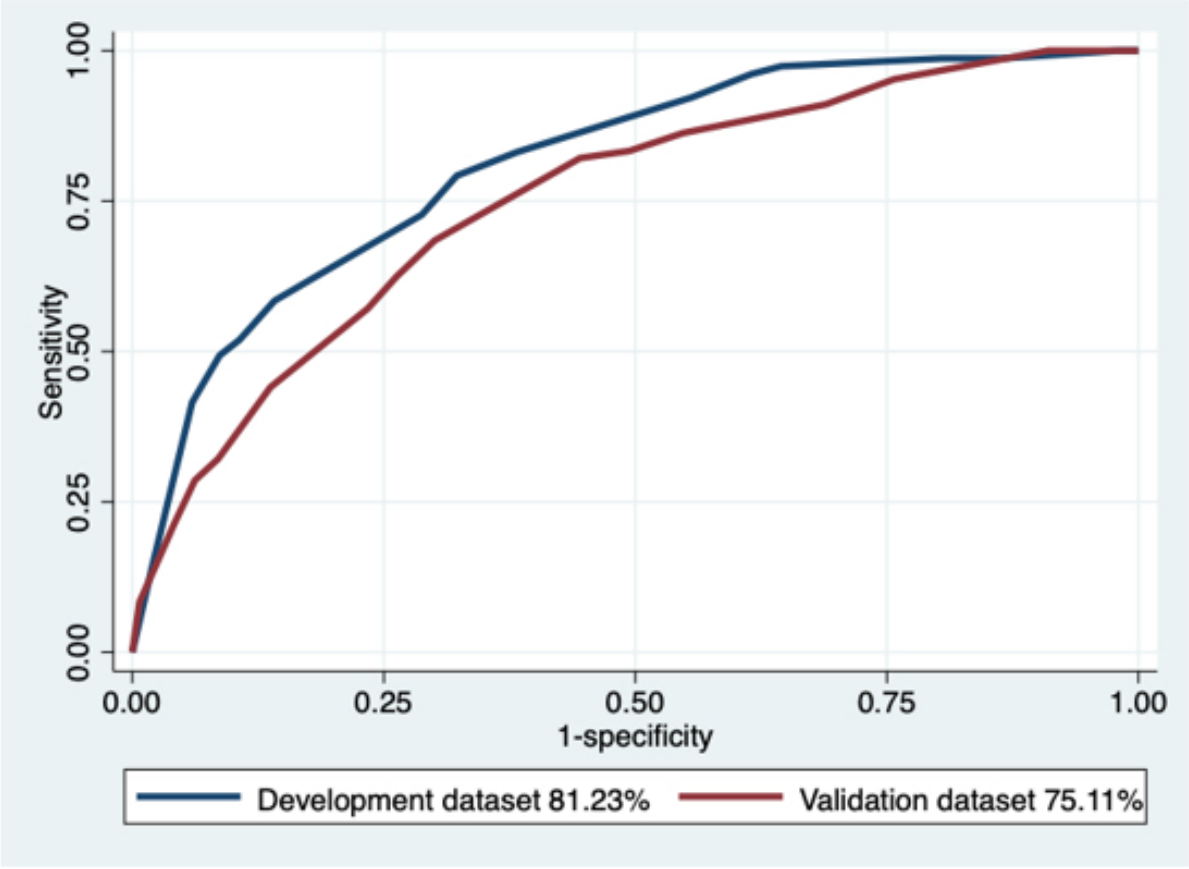

Figure 2: The areas under the receiver operating characteristic curves (AuROCs) of RAMA-WeRA RA risk score for the prediction of ruptured appendicitis in the development and validation datasets.

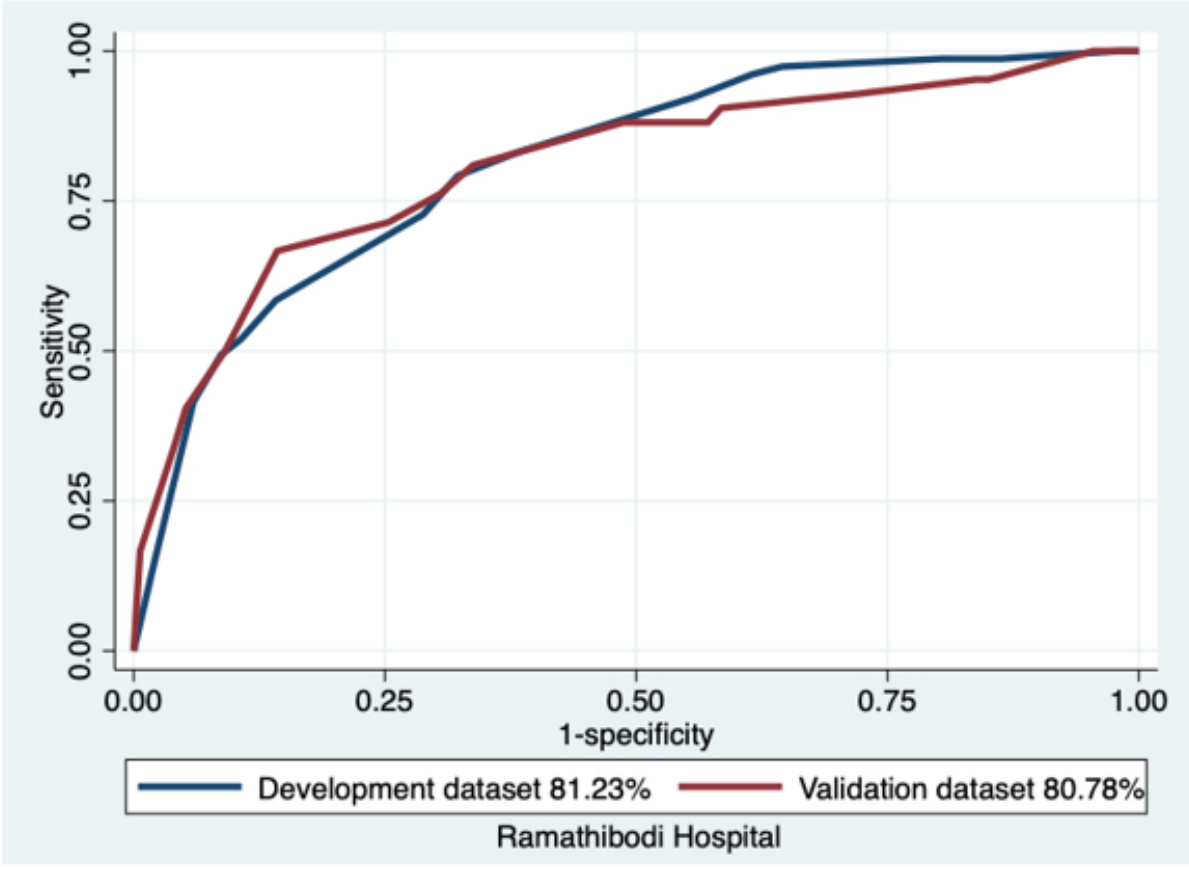

Figure 3: The areas under the receiver operating characteristic curves (AuROCs) of RAMA-WeRA RA risk score for the prediction of ruptured appendicitis in the development and validation datasets (Ramathibodi hospital).

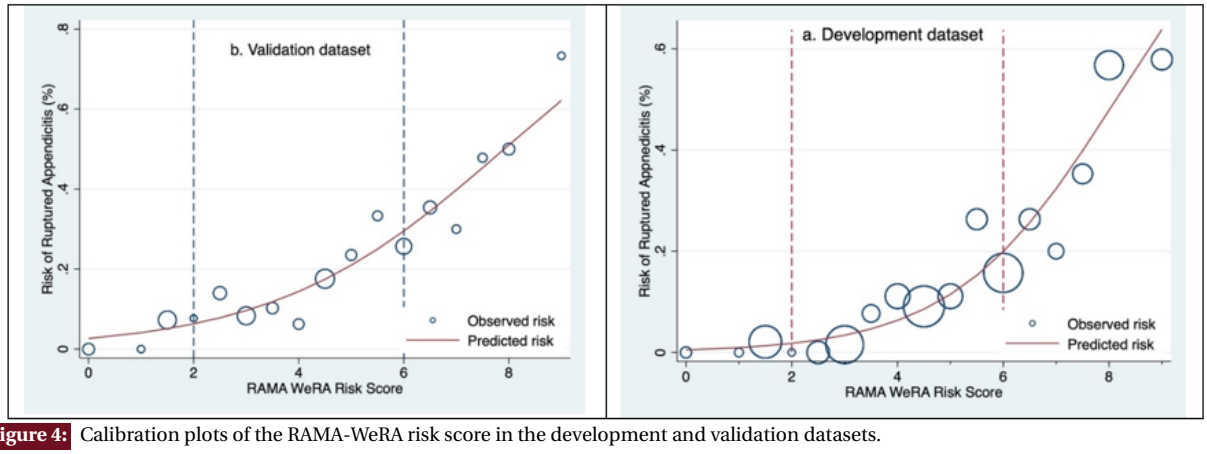

Figure 4: Calibration plots of the RAMA-WeRA risk score in the development and validation datasets.