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Simplified Geleijnse score for identifying chest pain features associated with coronary ischemia

Wern Yew Ding[a], Ana Isabel Romero-Aniorte[b], Antonio Tello-Montoliu[b], Pablo Gil-Pérez[b], Cecilia López-García[b], Andrea Veliz-Martínez[b], Miriam Quintana-Giner[b], Gregory Y.H. Lip[a,c], José Miguel Rivera-Caravaca[a,b,d,*], Francisco Marín[b]

[a] *Liverpool Centre for Cardiovascular Science at University of Liverpool, Liverpool John Moores University and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom*
[b] *Department of Cardiology, Hospital Clínico Universitario Virgen de la Arrixaca, University of Murcia, Instituto Murciano de Investigación Biosanitaria (IMIB-Arrixaca), CIBERCV, Murcia, Spain*
[c] *Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark*
[d] *Faculty of Nursing, University of Murcia, Murcia, Spain*

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ABSTRACT

Background: The Geleijnse score, which was proposed to assess for coronary ischemia, has practical limitations.
Objectives: Our aim was to design and evaluate a simplified version of the Geleijnse score.
Methods: We enrolled patients with suspected coronary heart disease but negative troponin T or absence of enzymatic curve, and a non-diagnostic 12-lead ECG. The initial study was performed in a retrospective derivation cohort and the results were subsequently validated in a prospective cohort.
Results: From 109 patients included in the derivation cohort, 33 (30.3%) received a diagnosis of coronary heart disease. Chest pain with both arms radiation (OR 3.54), severe intensity (OR 2.41), improvement by nitroglycerin (OR 1.61), associated dyspnea (OR 1.97) and prior exertional angina history (OR 2.91) were independently associated with an ischemic origin on multivariate logistic regression analysis. ROC curves comparison demonstrated both the original and simplified scores presented modest predictive ability with significant difference when analyzed using dichotomous cut-offs (0.647 [simplified] *vs.* 0.544 [original], $p = 0.042$) but not as a continuous variable (0.670 [simplified] *vs.* 0.621 [original], $p = 0.396$). In 305 patients from the validation cohort, the simplified score presented extensively increased predictive accuracy than the Geleijnse, in the continuous (c-indexes = 0.735 vs. 0.685, $p = 0.040$) and the dichotomic (c-indexes = 0.682 vs. 0.514, $p<0.001$) forms.
Conclusions: A simplified version of the Geleijnse score, including some routine clinical manifestations associated with coronary heart disease, presented significantly better predictive ability compared to the original score.

Introduction

Currently, there are multiple risk scores to determine the prognosis of high-risk patients presenting with an acute coronary syndrome (ACS) to chest pain units or emergency departments. For example, the PURSUIT score predicts the risk of death or death/myocardial infarction (MI) at 30-days after admission in patients with unstable angina and non-ST elevation MI, the TIMI risk score estimates mortality for patients with unstable angina and non-ST elevation MI, and GRACE score predicts mortality among ACS patients.[1] Chest pain is a commonly occurring symptom in these patients, with a lifetime prevalence of between 20% and 40% in the general population,[2] and it is an usual indicator of coronary ischemia. However, the features of chest pain associated with coronary ischemia can be difficult to distinguish from those of other causes.

Contrary to patients already diagnosed with coronary ischemia, there are few risk stratification schemes or tools for patients without ACS (no diagnostic ST-segment deviation or positive biomarkers), and the final diagnosis of such a kind of patient is often complex. The Geleijnse score[3] was described to perform a baseline evaluation to determine the probability of ischemia-related chest pain, to guide the immediate clinical management of such patients. However, the

* Corresponding author at: Faculty of Nursing, University of Murcia, Despacho 6.5, Edificio LAIB, Ctra. Buenavista s/n 30120, Murcia, Spain.
E-mail address: josemiguel.rivera@um.es (J.M. Rivera-Caravaca).

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Geleijnse score has numerous categories and may be difficult to implement in a busy clinical environment.

The aims of this study were to determine the main clinical characteristics of patients admitted to a chest pain unit, and to design and evaluate a simplified version of the Geleijnse score for identifying chest pain of ischemic origin.

Methods

Observational study comprised of a retrospective derivation cohort and a prospective validation cohort. The retrospective derivation cohort was composed of patients admitted to the chest pain unit in a tertiary center (Hospital Clínico Universitario Virgen de la Arrixaca; Murcia, Spain) between January 2010 and December 2011. The prospective validation cohort included consecutive patients admitted to the same chest pain unit between January 2012 and December 2015.

To be included in the study, patients from both cohorts shared the same inclusion criteria: equal or more than 18 years of age; chest pain at rest or progressive with minimal effort upon arrival at the Emergency Department suggesting coronary heart disease (*i.e.* heart ischemia) but with non-diagnostic or undetermined electrocardiogram (ECG) and negative troponin(s) or no enzymatic curve. Patients with a diagnosis at discharge of myocarditis, pericarditis, cardiomyopathy, valvular heart disease and Takotsubo cardiomyopathy, as well as non-coronary pathologies such as pulmonary embolism, pneumonia, pleurisy, pneumothorax, seizures of sickle cell anemia, anemia, aortic dissection, cerebrovascular disease, esophageal spasm, esophagitis, peptic ulcer, pancreatitis, cholecystitis, cervical disk disease, rib fracture, muscle injury, costochondritis, and herpes zoster; were excluded.

At inclusion, a complete medical history was recorded for all patients, independent of the cohort, including demographics, history of cardiovascular risk factors and other comorbidities, by staff and research nurses. During the stay in the chest pain unit, the nurses also calculated the Geleijnse chest pain score to assess the probability of pain from cardiac origin. This score classifies pain according to the location (substernal; precordial; neck, jaw, epigastrium; or apical), radiation (one of the arms; shoulders, back, neck or jaw), character (crushing/pressing; heaviness; or stabbing), severity and if it varies by certain factors (severe; moderate; influenced by nitroglycerine; posture; or breathing), associated symptoms (dyspnea; nausea or vomiting; diaphoresis), and history of previous exertional angina (Supplementary Table 1). All data from the derivation cohort were collected by a retrospective evaluation of medical records whereas data from the validation cohort were recorded prospectively.

Patient groups and diagnosis of coronary ischemia

Although all patients included in the chest pain unit had non-diagnostic or undetermined ECG, they were classified into two groups based on the results of their troponin T (TnT): group 1, patients with negative TnT results in all measurements; and group 2, patients with a positive result in at least one of the TnT measurements, but no enzyme curve. The subsequent diagnosis of coronary ischemia during hospitalization was based on current clinical guidelines considering three fundamental pillars: clinical presentation, physical examination and the results of the different specific diagnostic tools, including 12-lead ECG, biomarkers (TnT) and non-invasive imaging techniques. Regarding TnT, the assay used was the fourth-generation TnT in patients from the derivation cohort, and the cut-off applied was 0.035 ng/mL. TnT levels >0.035 ng/mL were considered as positive. High-sensitivity TnT (hs-TnT) was available since 2011 and was used for the assessment of patients from the validation cohort, considering 14 ng/L as the cut-off point. A TnT concentration above the 99th percentile upper reference limit was considered suggestive of MI.

When there were no changes indicating ischemia either in the ECGs or in the results of the enzymatic curve for TnT, a non-invasive ischemia test was requested (mainly stress echocardiography) at the discretion of the responsible cardiologist. If the ischemia test was positive or inconclusive, a diagnostic coronary angiography was subsequently scheduled to confirm the diagnosis. If the ischemia test was clearly negative, the patient was discharged with a diagnosis of chest pain without evidence of ischemia.

Ethical considerations

The study protocol was approved by the Ethics Committee from the Hospital Clínico Universitario Virgen de la Arrixaca, and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Patients were included during hospital admission after being informed of the purpose and procedures of the study. All patients from the prospective cohort gave informed consent to participation.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analysis

Continuous variables were examined for normality with Kolmogorov-Smirnov test. Normally-distributed variables were expressed using mean and standard deviation, and tested for differences with *t*-test while non-normally-distributed variables were expressed using median and interquartile range (IQR), and tested for differences with Mann-Whitney U test. Categorical variables were expressed using absolute frequencies and percentages and tested for differences using chi-squared or Fisher's exact tests, as appropriate.

To evaluate the relationship between the features of chest pain and underlying coronary ischemia in the derivation cohort, logistic regression analysis was performed. Variables with p-value below 0.15 (SLENTRY = 0.15) in the univariate analysis were included in the multivariate regression model, and a multivariate significance level of 0.05 was required for a variable to stay in the model (SLSTAY = 0.05).

Independent features of underlying coronary ischemia in the multivariate logistic regression model were then used in the design of a simplified Geleijnse score. The points associated with each feature of chest pain were determined as the nearest integer of the odds ratio (OR). The predictive ability of the simplified Geleijnse score was investigated using receiver-operating characteristic (ROC) curves and compared to the original Geleijnse score by the method of DeLong et al.[4] Additionally, the integrated discrimination improvement (IDI) was carried out according to the methods described by Pencina et al.[5] Finally, the clinical usefulness and net benefit of the simplified Geleijnse were assessed using decision curve analysis (DCA).[6,7] The DCA allows assessing the clinical usefulness of the original and simplified Geleijnse scores on a continuum of potential thresholds for a diagnosis of coronary ischemia (*x*-axis) and the net benefit of using the scores to stratify patients at risk (*y*-axis) relative to assuming that no patient will have a diagnosis of coronary ischemia. In this study, each score is represented by color lines. The farther are the prediction scores models from the dashed black line (*i.e.*, assume all patients will have coronary ischemia) and the horizontal black line (*i.e.*, assume no patient will have coronary ischemia), the higher the net clinical benefit.

A two-sided p-value of less than 0.05 was considered statistically significant. Analyses were performed using SPSS software version 25.0 (SPSS Inc., Chicago, Illinois, United States), MedCalc v. 16.4.3

(MedCalc Software bvba, Ostend, Belgium), and STATA v. 12.0 (Stata Corp., College Station, TX, USA) for Windows.

Results

In the derivation cohort of 109 patients, the median age was 59 (IQR 51–73) years and there were 38 (34.9%) females (Table 1). Of these patients, 104 (95.4%) were classified in group 1 (*i.e.* no changes in 12-lead ECG and negative TnT in all determinations) and 5 (4.6%) in group 2 (*i.e.* no changes in 12-lead ECG and at least one positive TnT determination but absence of enzymatic curve).

The majority of chest pains were located in the substernal region (n = 65, 59.6%) with radiation to shoulder, back, neck or jaw (n = 55, 50.5%), of moderate severity (n = 95, 87.2%) and influenced by nitroglycerin (n = 35, 32.1%), described as heaviness/tightness in nature (n = 82, 75.2%), and associated with diaphoresis (n = 53, 48.6%) (Supplementary Table 2).

Following hospitalization, 33 (30.3%) patients were diagnosed with coronary ischemia and discharged (29 [27.9%] from group 1 and 4 [80.0%] from group 2; p = 0.013). Multivariate logistic regression analysis found that independent predictors of coronary ischemia were chest pain with radiation to both arms (OR 3.54 [95% CI, 1.60–7.87]), intensity (severe) (OR 2.41 [95% CI, 1.39–4.16]), improvement by using nitroglycerin (OR 1.61 [95% CI, 1.01–2.58]), dyspnea (OR 1.97 [95% CI, 1.24–3.15]) and history of previous exertional angina (OR 2.91 [95% CI, 1.81–4.67]) (Table 2). Hence, the "simplified" Geleijnse score included the following: radiation to both arms (4 points), severe pain intensity (2 points), pain relieved with nitroglycerin (2 points), associated dyspnea (2 points) and exertional angina history (3 points) (Supplementary Table 3).

ROC curves comparison showed that both the original and simplified Geleijnse scores presented modest predictive accuracy for identifying an ischemic origin of chest pain; with numerically higher c-index for the simplified Geleijnse score (0.670 vs. 0.621, p = 0.396). The Youden test showed that a simplified Geleijnse score >3 had the best combination of sensitivity (63.6% [95% CI, 45.1–79.6]) and specificity (65.8% [95% CI, 54.0–76.3]) with a likelihood ratio+ of 1.86 (95% CI 1.2–2–8), a likelihood ratio- of 0.55 (95% CI 0.3–0.9), and an OR of 3.37 (95% CI, 1.43–7.90) for underlying coronary ischemia. ROC curves comparison using dichotomized scores demonstrated that the simplified Geleijnse score was significantly better than the original score (0.647 [95% CI, 0.550–0.736] *vs.* 0.544 [95% CI, 0.446–0.640], p = 0.042) (Fig. 1A).

In the validation cohort of 305 patients (213 [69.8%] were classified in group 1 and 92 [30.2%] in group 2), 120 (39.3%) patients received a final diagnosis of coronary ischemia. Baseline characteristics of the entire validation cohort are shown in Supplementary Table 4. ROC curves established that the simplified Geleijnse score had a significantly higher predictive ability for coronary ischemia than the original Geleijnse score, when assessed as either a continuous (0.735 [95% CI, 0.682–0.784] *vs.* 0.685 [95% CI, 0.630–0.737], p = 0.040) or dichotomic variable (0.682 [95% CI, 0.627–0.734] *vs.* 0.514 [95% CI, 0.456–0.571], p<0.001) (Table 3, Fig. 1B). Patients with a simplified Geleijnse score >3 had a significantly greater risk of coronary ischemia compared to patients with a score ≤3 (OR 5.18 [95% CI, 3.02–8.89], p<0.001). Of note, patients with a Geleijnse score ≥more than 6, *i.e.* the cut-off point in the original score, were not found to have a higher risk of coronary ischemia compared to

Table 2
Association between features of chest pain and underlying coronary ischemia.

	Univariate Analysis OR (95% CI), *p-value*	Multivariate Analysis OR (95% CI), *p-value*
Location		
Substernal	1.36 (0.91–2.04), 0.138	1.51 (0.95–2.40), 0.083
Precordial	0.76 (0.51–1.15), 0.193	–
Neck, jaw, epigastrium	1.27 (0.68–2.36), 0.456	–
Apical	0.80 (0.07–8.89), 0.855	–
Radiation		
Either arm	1.37 (0.90–2.10), 0.146	0.89 (0.50–1.59), 0.694
Both arms	2.74 (1.50–5.04), 0.001	3.54 (1.60–7.87), 0.002
Shoulder, back, neck, jaw	1.15 (0.76–1.74), 0.500	–
Character		
Crushing, pressing, squeezing	1.63 (1.06–2.51), 0.025	1.10 (0.65–1.87), 0.721
Heaviness, tightness	0.79 (0.52–1.20), 0.261	–
Sticking, stabbing, pinprick, catching	0.49 (0.20–1.17), 0.106	0.60 (0.23–1.55), 0.291
Severity		
Severe	2.73 (1.74–4.27), <0.001	2.41 (1.39–4.16), 0.002
Influenced by nitroglycerin	2.23 (1.48–3.37), <0.001	1.61 (1.01–2.58), 0.048
Influenced by posture	0.54 (0.22–1.31), 0.172	–
Influenced by breathing	0.53 (0.26–1.06), 0.071	0.61 (0.29–1.29), 0.196
Associated symptoms		
Dyspnea	1.54 (1.01–2.33), 0.043	1.97 (1.24–3.15), 0.004
Nausea or vomiting	0.66 (0.41–1.07), 0.094	0.58 (0.34–1.00), 0.052
Diaphoresis	1.04 (0.69–1.56), 0.867	–
Previous history of exertional angina	2.97 (1.96–4.52), <0.001	2.91 (1.81–4.67), <0.001

CI = confidence interval; OR = odds ratio.

Table 1
Baseline clinical characteristics of the derivation cohort.

	Overall (n = 109)	Group 1 (n = 104)	Group 2 (n = 5)	*p-value*
Age (years), median (IQR)	59.0 (51.0–53.0)	58.5 (51.0–73.0)	66.0 (48.5–78.5)	0.653
Female sex, n (%)	38 (34.9)	35 (33.7)	3 (60.0)	0.227
Comorbidities, n (%)				
Diabetes mellitus	27 (24.8)	25 (24.0)	2 (40.0)	0.419
Hypertension	67 (61.5)	62 (59.6)	5 (100.0)	0.070
Dyslipidemia	55 (50.5)	53 (51.0)	2 (40.0)	0.632
Current smoking habit	39 (35.8)	37 (35.6)	2 (40.0)	0.840
Stroke/TIA	4 (3.7)	4 (3.8)	0 (0)	0.655
Previous coronary artery disease	29 (26.6)	26 (25.0)	3 (60.0)	0.084
Familial history of coronary artery disease	1 (0.9)	1 (1.0)	0 (0)	0.826
Peripheral artery disease	3 (2.8)	3 (2.9)	0 (0)	0.700
Renal impairment	13 (11.9)	13 (12.5)	0 (0)	0.400
Previous use of aspirin	40 (36.7)	37 (35.6)	3 (60.0)	0.268
Original Geleijnse score, median (IQR)	9 (7.5–11.5)	9 (7.3–12.0)	9[8,-10]	0.737

Group 1 = patients with non-diagnostic or undetermined ECG and negative TnT results in all measurements. Group 2 = patients with non-diagnostic or undetermined ECG and a positive result in at least one of the TnT measurements but no enzyme curve.
ECG = electrocardiogram; TnT = troponin T; IQR = interquartile range; TIA = transient ischemic attack.

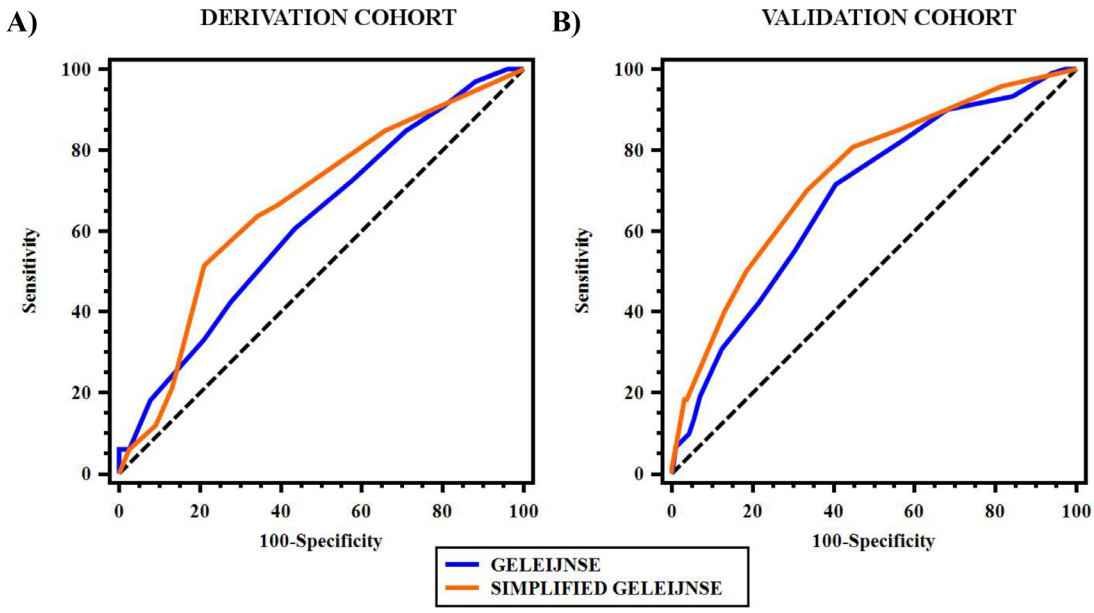

Fig. 1. Receiver-operating characteristic curves for Geleijnse *vs.* simplified Geleijnse scores in a prospective validation cohort.

Table 3
Comparison of receiver-operating characteristic curves and integrated discriminatory improvement of the simplified and original Geleijnse scores in the validation cohort.

	C-index	95% CI	*p-value	IDI	95% CI	p-value
vs. Geleijnse (continuous)						
Simplified Geleijnse	0.735	0.682–0.784	0.040	0.0698	0.0347–0.1049	<0.001
vs. Geleijnse (categorical)						
Simplified Geleijnse	0.682	0.627–0.734	<0.001	0.1165	0.0786–0.1546	<0.001

CI = confidence interval; IDI = integrated discriminatory improvement.
* for C-index comparison.

patients with a score lower than 6 (OR 0.97 [95% CI, 0.95–1.00], $p = 0.069$).

Sensitivity of the simplified Geleijnse score was significantly better as compared to the original score when assessed using IDI. This ability increased by about 7.0% according to the continuous form of the score, and by about 11.7% according to the categorical (*i.e.* dichotomic) form (Table 3). Additionally, DCA also confirmed the higher diagnostic performance of the simplified Geleijnse score. Thus, for a large threshold of probabilities (40% to 70%, approximately), the continuous form of the simplified Geleijnse score demonstrated higher net benefit than the original score, with an overall improvement of 17.07% (Fig. 2, Table 4). This was even more evident in the categorical forms for the threshold of probabilities comprised between 30% and 60% (Fig. 2). Overall, the simplified Geleijnse scoreprovide an improvement in the net benefit for the prediction of coronary ischemia of 24.75% (Table 4).

Discussion

In this study, we found that a substantial proportion of patients who were admitted to the chest pain unit with suspected but unproven coronary ischemia, as assessed by ECG and cardiac enzymes,

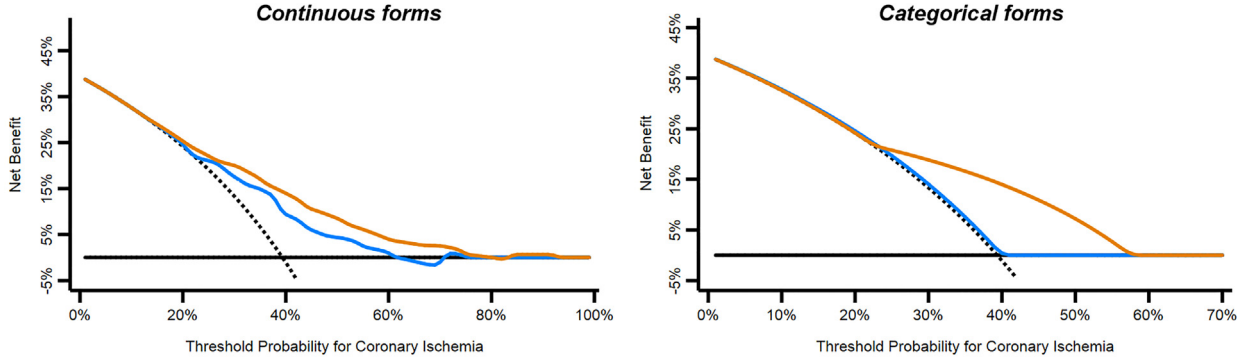

Fig. 2. Decision Curves Analysis.
X-axis demonstrates threshold values for the probability of diagnosis of coronary ischemia at discharge, whereas y-axis represents net benefit for the different threshold values for diagnosis of coronary ischemia at discharge. Prediction models that are farthest from the slanted dashed gray line (*i.e.*, assumes that all patients had coronary ischemia) and the horizontal solid black line (*i.e.*, assumes that no patient had coronary ischemia) demonstrated the highest net benefit. Blue line denotes the original Geleijnse score, and orange line denotes the simplified Geleijnse score.

Table 4
Net benefits for continuous and categorical forms of the original and simplified Geleijnse scores at different threshold probabilities.

Threshold probability	Net Benefit for Continuous forms			Net Benefit for Categorical forms		
	Original Geleijnse	Simplified Geleijnse	Difference in net benefit (simplified *vs.* original)	Original Geleijnse	Simplified Geleijnse	Difference in net benefit (simplified *vs.* original)
20%	24.75%	25.33%	0.57%	24.59%	25.00%	0.41%
30%	17.56%	20.14%	2.58%	14.05%	20.14%	6.09%
40%	9.40%	13.99%	4.59%	0%	13.66%	13.66%
50%	4.60%	8.52%	3.92%	0%	4.59%	4.59%
60%	1.15%	3.93%	2.79%	0%	0%	0%
70%	0%	2.62%	2.62%	0%	0%	0%
80%	0%	0%	0%	–	–	–
100%	0%	0%	0%	–	–	–
Overall improvement			17.07%			24.75%

had chest pain of moderate severity in the substernal region with radiation to the shoulder, back, neck or jaw that was described as a heaviness or tightness and with associated diaphoresis. Subsequently, one-third of these patients had confirmed coronary ischemia. Independent predictors of coronary ischemia were chest pain associated with radiation to both arms, severe intensity, improvement by nitroglycerin, dyspnea, and a background of previous exertional angina. The use of these parameters in a simplified Geleijnse score demonstrated modest predictive performance for identifying chest pain of ischemic origin. Furthermore, the simplified Geleijnse score was found to be significantly more accurate compared to the original, more complex Geleijnse score in a prospective validation cohort.

Implementation of the simplified Geleijnse score as described in this study provides a tool for rapid assessment of patients with suspected ischemic chest pain but with non-diagnostic results using contemporary methods of assessment. The management of these patients often represents a clinical dilemma for health care providers and various methods of evaluation have previously been proposed. In 1979, Diamond and Forrester utilized Bayes' theorem of conditional probability to estimate the pretest likelihood of coronary artery disease in a historical cohort of patients according to age, sex and symptoms (typical angina, atypical angina or non-anginal chest pain).[8] However, this classification system was developed in the outpatient setting and has not been well studied in acute centers. Contemporary studies have found that this model is not useful as it vastly overestimates the true prevalence of obstructive coronary artery disease.[9,10]

Several other scores have been described in the context of suspected chest pain. For example, the HEART (History, ECG, Age, Risk factors and Troponin) score aimed to facilitate diagnostic and therapeutic choices in patients with chest pain in the emergency room.[11] However, it was not derivate based on multivariate regression analysis but on the decision-making clinical factors according to expert opinion. In a study investigating consecutive patients admitted to the chest pain unit with an ECG not showing significant changes in repolarization, the presence of typical chest pain, aspirin use, diabetes, and age >64 years was associated with an increased probability of coronary artery disease.[12] Unfortunately, the final score reported was not tested in terms of predictive ability (using c-index or other tests).

The aim of another research was to develop a risk score for patients with chest pain presenting non-ST-segment deviation ECG and normal troponin levels. The model included a chest pain score ≥10, ≥2 pain episodes in last 24 h, age ≥67 years, insulin-dependent diabetes mellitus, and prior percutaneous transluminal coronary angioplasty. Despite the accuracy of the score was appropriate, the primary composite outcome was mortality or MI at one year,[13] which may raise doubts about its usefulness for immediate management and diagnosis in the chest pain unit or the emergency department.

Another clinical prediction rule was designed to detect patients with chest pain in the emergency department who may be suitable for discharge, combining the following variables: ischemic ECG changes not known to be old, history of coronary artery disease, pain typical for ACS, initial or 6-hour troponin level >99th percentile, and age >50 years. The primary adjudicated outcome was acute MI, revascularization, or mortality at 30-days, and the proposed tool aid in the identification of patients at very low short-term risk for a cardiac event for whom additional investigations might be unnecessary.[14]

Similarly, the EDACS-ADP (age, sex, symptoms and signs [diaphoresis; pain radiates to arm, shoulder, neck, or jaw; pain occurred or worsened with inspiration; pain is reproduced by palpation]) was aimed to safely increase the proportion of patients suitable for early discharge. This rule identified patients presenting to the emergency department with possible cardiac chest pain as having low-risk of short-term major adverse cardiac events (MACEs), with high sensitivity.[15] However, the specificity was low, so there is a high probability that the rule will identify as low risk someone who is actually at high risk. Aligned with this, a score consisting of age >55 years, gender, chest pain quality (typical *vs.* atypical), history of coronary artery disease, shortness of breath, diabetes, smoking, and abnormal ECG, demonstrated strong a good ability to predict hospital admission attending to emergency departments chest pain units.[16]

On the other hand, the Vancouver Chest Pain Rule was found to be useful for the identification of low-risk patients presenting to the emergency department with symptoms of possible ACS.[17] The study was focused on the identification of patients who were suitable for early discharge based on an outcome of ACS occurring within 30 days of presentation. Furthermore, it relied heavily on the use of troponins for initial screening.[17] More recently, the SVEAT score (Symptoms, history of Vascular disease, Electrocardiography, Age, and Troponin) has shown to predict MACE at 30-days in subjects presenting to the emergency department (c-index: 0.98%, 95% CI 0.97–0.99) .[18] Finally, the Bosner Chest Pain Decision Rule was previously validated as a tool (c-index: 0.90 [95% CI, 0.87–0.93]) to predict coronary artery disease as a cause of chest pain.[19] However, the study was performed in the primary care setting and may not be applicable to patients presenting with acute chest pain to the emergency department. In this regard, only half of the patients in the study had chest pain at the time of consultation.[19] As acknowledged by the authors, the diagnosis of coronary artery disease was often on the basis of limited data because there was no requirement for health care providers to use defined investigations.

Summarizing the previous evidence, several current tools include a larger list of variables and are therefore more complex. In addition, most of these tools were designed to predict cardiac events at 30-day or 1-year later, and therefore they do not assist enough regarding the current hospital admission or emergency department consultation. Of note, many of the risk scores include troponins and ECG results to rule in clinical decisions, but the real concern are those patients who already had non-diagnostic or undetermined ECG and negative troponins. In this case, our simplified Geleijnse score presents appropriate predictive ability with a good balance in terms of sensitivity and specificity and more importantly, a high clinical usefulness and net benefit.

However, future research should deepen in some aspects that could be relevant. For example, the issue of sex regarding the clinical presentation of chest pain needs to be clarified. It is known that females and males differ in their presentation for ischemic disease. Thus, females usually refer a different location of pain and more commonly shortness of breath.[20, 21] In our simplified Geleijnse score, pain location is not included so this will not modify the overall score for males or females. In addition, dyspnea is one of the associated symptoms of the simplified Geleijnse score so this important feature of ischemic-related chest pain in females is already recognized. We, therefore, consider that the simplified Geleijnse score could be a reliable tool for clinical decision-making independently of sex, although our results require further investigations and validations, particularly using a larger sample size and a multicenter design.

Limitations

The limitations of this study include the use of a relatively small sample size. Furthermore, patients were recruited from a single tertiary center in Spain and as such the results need to be tested in other populations. Importantly, the simplified Geleijnse score was only validated in a cohort of patients admitted to our chest pain unit. External validations in larger cohorts from other departments are warranted. Hence, the implementation of this score in other clinical context might not be supported with the current data, and we consider that our results should be interpreted with caution and only in an exploratory way or as hypothesis-generating.

Conclusion

The present study introduces a “simplified” version of the Geleijnse score including only common clinical manifestations of *ischemic-suspected* chest pain, which presented higher predictive accuracy and clinical usefulness than the original Geleijnse score for the identification of patients with coronary ischemia among those with non-diagnostic results from contemporary tests.

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Ethical considerations

The study protocol was approved by the Ethics Committee from Hospital Clínico Universitario Virgen de la Arrixaca (code: FMO-2012) and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Patients were included during hospital admission after being informed of the purpose and procedures of the study. All patients from the prospective cohort gave informed consent to participation.

Declaration of Competing Interest

WYD, AIR-A, AT-M, PG-P, CL-G, AV-M, MQ-G: None declared. GYHL: Consultant and speaker for BMS/Pfizer, Boehringer Ingelheim and Daiichi-Sankyo. No fees are received personally. JMR-C: Consultant for Idorsia Pharmaceuticals LTD. FM: Speaker from BMS/Pfizer, Boehringer Ingelheim; research grants from Bayer and Ferrer.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hrtlng.2023.01.010.

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