Original research

SENSITIVITY, SPECIFICITY OF PRE-TEST PROBABILITY AND THEIR USE IN THE RELATION TO SYNTAX SCORE AND CARDIOVASCULAR RISK FACTORS

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ABSTRACT

Overview: *Coronary angiography is the gold standard for definitive diagnosis of obstructive ischemic coronary disease. However, this is an invasive, expensive test, and may have a number of complications. Models of pre-test probability (PTP) in the guideline of the European Society of Cardiology 2013 and 2019 are easy to use and apply even to doctors who are not cardiologists, and can be implemented at the medical facilities. We aim to assess the sensitivity and specificity of different PTP stratification models follow ESC2013 and 2019; and their use in the relation to SYNTAX score and cardiovascular risk factors.*

Materials and Methods: *Patients (n=108) with chest pain had been treated at Ninh Thuan Provincial Hospital from January 2019 to May 2020. The PTP stratification models were calculated according to the recommendations of the European Society of Cardiology (ESC) 2013 and 2019. Coronary angiography was enrolled for the diagnosis, Quantitative coronary analyzed (QCA) - based stenosis assessment was used with a cut-off of ≥ 50% diameter reduction for significant lesions of coronary artery and SYNTAX score were calculated.Diagnostic accuracy was calculated by usingsensitivity, specificitywhich were analyzed by using statistical software SPSS version 20.0.*

Results: *In the 2013 pre-test probability model,group withmedium PTP andhigh PTPhad the sensitivity of 57.14%, 100% respectively; the overall sensitivity for both groups (the medium and high pre-test) was 59.36%; and the specificity was 58.33%. In the 2019PTP model, group withmedium PTP and high PTP had the sensitivity of 41.67%, of 67.57% respectively;the overall sensitivity for both groups (the medium and high scores PTP) was 61.22%; and the specificity was 80%. The group of low SYNTAXscore (<23) had at most 93 cases, accounting for 86.1%; the lowest was the group of high SYNTAX score (≥ 33 points) accounting for 2.8%. There were statistically significant differences in patients with and without smoking, history of hypertension for both PTP model 2013 and 2019.*

Conclusion: *Sensitivity and specificity of the 2013 and 2019 PTP were quite high in the relation to the severity of coronary artery which were evaluated by SYNTAX score.*

Keywords: *Pre-test probability, European Society of Cardiology, Coronary angiography, coronary artery disease, electrocardiogram, computed tomography*

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I. INTRODUCTION

Chest pain is a common symptom of coronary artery disease. In clinical practice, the diagnosis of coronary artery disease (CAD) still faces many difficulties, which can be underestimated or overestimated, leading to inadequate treatment indications [1]. Invasive coronary angiography (CA) is the gold standard for definitive diagnosis of ischemic heart disease [2]. However, this is an invasive, high-cost, and potentially complicated, therefore, ischemic heart disease is often indicated for coronary angiography in the presence of revascularization or non-response medical treatment. The pre-test probability (PTP) in the guideline of the European Society of Cardiology (ESC) 2013 and 2019 is easy to use and apply even to doctors who are not cardiologists, and can be implemented at the medical facilities [3,4]. Therefore, we aimed to compare the ability of risk factors and different PTP stratification models to predict obstructive CAD.

II. METHODS

2.1. Study Design

Patients (n=108) with chest pain had been refered to invasive coronary angiography (CA) at Ninh Thuan Provincial Hospital from January 2019 to May 2020. All patients had a systematic interview to assess risk factorsand symptoms, and, based on this information and medical recordreviews, the PTP stratification models were calculatedaccording to the recommendations of the ESC 2013 and 2019. Coronary angiography was enrolled for the diagnosis, QCA-based stenosis assessment was used with a cut-off of ≥ 50% diameter reduction for significant stenosis lesions of coronary artery [1,5] and SYNTAX score were calculated [6].

Exclusion criteria were (i) previous coronary revascularization; (ii) patients with chest pain suffer from acute diseases or have contraindications to coronary angiography.

2.2. Statistical Analysis

Continuous variables were presented as mean (± standard deviation) andcategorical variables as n (%). Correlations were calculated withPearson's formulation. Calibration of the PTP models wereevaluated according to models of ESC 2013 and 2019. Diagnostic accuracy was evaluated usingsensitivity, specificitywhich were analyzed by using statistical software SPSS version 20.0.

III. RESULTS

Of the 108 patients included, totally completed the PTP and refered to CA. Patient demographics and imaging characteristics are presented in **(Tables 1)**.

Table 1: Patient demographics

Characteristics	Total	
	n	%
Sex,male	48	44.4
Age (years)	60.82 ± 11.65	-
Obesity and overweight	51	47.2
Smoking, yes	33	30.6
Hypertension	78	72.2
Diabetes type 2	33	30.6
Hypercholesterolaemia	87	80.6
Chest pain type		
Non-specific	36	33.3
Atypical chest pain	40	37
Typical chest pain	32	29.7

Values are presented as n (%) or mean ± SD

3.1. The sensitivity and specificity of the pre-test probability

The sensitivity and specificity of 2013 PTP were described in **(Table 2)**. The sensitivity was high with 57.14% and 100% in the group of medium and high scores, respectively.

Table 2: Evaluating the sensitivity and specificity

Results of coronary angiography	Scores of pre-test probability (n=108) (n,%)			Total
	Low	Medium	High	
Stenosis	5	52	5	62
Myocardial bridging	5	21	0	23
No stenosis	2	18	0	23
Total	12	91	5	
Sensitivity	Se	Se 57,14%	Se 100%	Se 59,38%
Specificity	Sp 58,33%	Sp	Sp	Sp 58,33%

In **(Table 3)**, the group of medium and high scores of 2019PTP, the sensitivity was at 61.22%. The specificity of the 2019 PTP was 80.00%.

Table 3: Evaluating the sensitivity and specificity

Results of coronary angiography	Scores of pre-test probability (n=108) (n,%)			Total
	Low	Medium	High	
Stenosis	2	10	50	62
Myocardial bridging	5	7	11	23
No stenosis	3	7	13	23
Total	10	24	74	
Sensitivity	Se	Se 41.67%	Se 67.57%	Se 61.22%
Specificity	Sp 80.00%	Sp	Sp	Sp 80.00%

3.2. The relationship between the pre-test probability and the Syntax score

The relationship between the 2013 PTP and the SYNTAX score were described in **(Table 4)**, it can be seen from the table that the majority of patients with the medium scores of PTP was at (15-85%) 91 cases, accounting for 84.3%. Out of 93 cases with low SYNTAX scores (<23), the medium PTP was mainly with 78 cases, accounting for 72.2%. Similarly, patients with medium (23-32) and high (≥ 33) SYNTAX scores also had the medium scores of PTP (15-85%). This difference is not statistically significant, p> 0.05.

Table 4: The relationship between the 2013 pre-test probability and the SYNTAX score

Scores of Pre-test probability	Syntax scores (n,%)				p
	<23	23 - 32	≥ 33	Total	
Low (< 15%)	12 (11.1)	0	0	12 (11.1)	> 0.05
Medium (15-85%)	78 (72.2)	10 (9.3)	3 (2.8)	91 (84.3)	
High (> 85%)	3 (2.8)	2 (1.8)	0	5 (4.6)	
Total	93 (86.1)	12 (11.1)	3 (2.8)	108 (100.0)	

The relationship between the 2019PTP and the SYNTAX scorewere described in **(Table 5)**, it was seen in the table that the majority of patients with high scores of PTP (> 15%) was 74 cases, occupying 68.5%. The proportion of patients with medium (23-32) and low (<23) PTP were 22.2% and 9.3%, respectively. It was noted that cases with medium and high SYNTAX scores also had high scores of PTP. These differences were statistically significant with p <0.05.

Table 5: The relationship between the 2019 pre-test probability and the Syntax score

Scores of Pre-test probability	Syntax scores (n,%)				p
	<23	23 - 32	≥ 33	Total	
Low (< 15%)	10 (9.3)	0	0	10 (9.3)	< 0,05
Medium (15-85%)	24 (22.2)	0	0	24 (22.2)	
High (> 85%)	59 (54.6)	12 (11.1)	3 (2.8)	74 (68.5)	
Total	93 (86,1)	12 (11,1)	3 (2,8)	108 (100,0)	

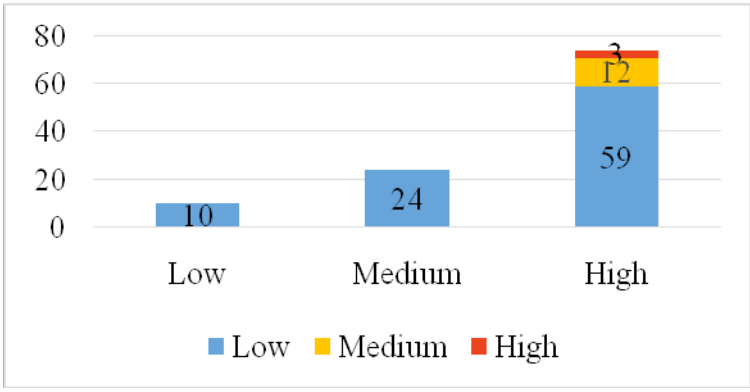

Figure 1: The relationship between the 2019 pre-test probability and the Syntax score

3.3. The relationship between the pre-test probability and cardiovascular risk factors

In patients with a history of smoking, having the scores of 2013 PTP over 15%, there were 33/33 cases accounting for 100% while there were 63/75 cases, accounting for 84% (p <0.01) in non-smoking patients having the scores of PTP over 15%. In the group of patients with other cardiovascular risk factors such as: hypertension, diabetes, dyslipidemia, obesity, there was no difference between the group with risk factors and no risk factors due to p > 0.05 **(Table 6)**.

Table 6: The relationship between the 2013 pre-test probability and cardiovascular risk factors

Risk factors		Scores of pre-test probability			Total	p
		(< 15%)	(15-85%)	(> 85%)		
Smoking	Yes	0	29	4	33	< 0,01
	No	12	62	1	75	
Hypertension	Yes	8	65	5	78	> 0,05
	No	4	26	0	30	
Diabetes	Yes	1	31	1	33	> 0,05
	No	11	60	4	75	
Overweight and obesity	Yes	3	44	4	51	> 0,05
	No	9	47	1	57	
Dyslipidemia	Yes	8	75	4	87	> 0,05
	No	4	16	1	21	

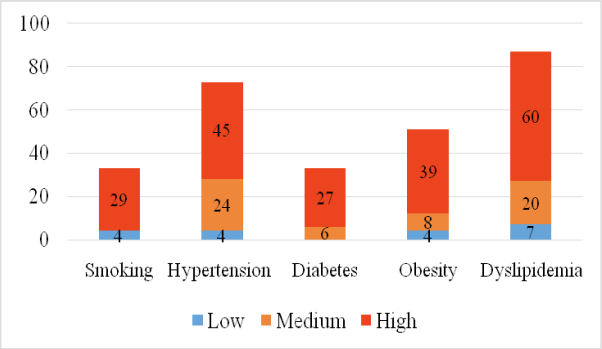

Figure 2: Relationship between the 2013 pre-test probability and cardiovascular risk factors

With the 2019 PTP in **(Table 7)**, patients with a history of smoking and the PTP scores>15%, there were 29/33 cases, accounting for 87.9%, whereas there were 45/75 cases, occupying 60% (p<0.05) in non-smoking patients. In group of patients with hypertension having high scores of PTP, there were 60/78 cases, holding 76.9%. By contrast, in patients without hypertension, there were 14/30 cases with the proportion of 46.7% (p <0.05).There were 27/33 cases with the rate of 81.8% in group of patients with diabetes and high scores of PTP, whereas there were 47/75 cases with the proportion of 62.7% (p<0.05) in patients without diabetes.

Table 7: The relationship between the 2019 pre-test probability and cardiovascular risk factors

Risk factors		Scores of pre-test probability			Total	p
		(< 5%)	(5-15%)	(> 15%)		
Smoking	Yes	4	0	29	33	< 0,001
	No	6	24	45	75	
Hypertension	Yes	4	14	60	78	< 0,01
	No	6	10	14	30	
Diabetes	Yes	0	6	27	33	< 0,05
	No	10	18	47	75	
Overweight and obesity	Yes	4	8	39	51	> 0,05
	No	6	16	35	57	
Dyslipidemia	Yes	7	20	60	87	> 0,05
	No	3	4	14	21	

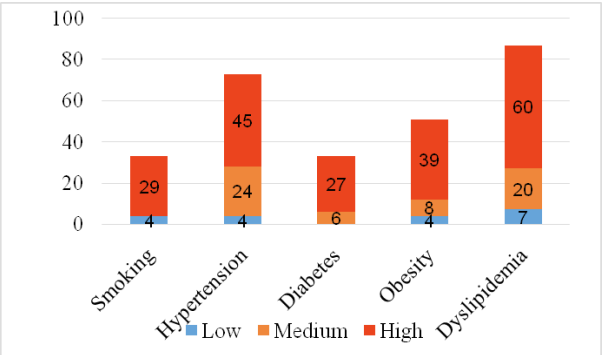

Figure 3: Relationship between the 2019 pre-test probability and cardiovascular risk factors

IV. DISCUSSION

4.1. The sensitivity and specificity of the pre-test probability

In our study, we evaluated the 2013 PTP, and then compared with the results of CA. In the group with the medium and high scores ofPTP (> 85%), the sensitivity of PTP was quite high, nearly 60%. Specifically, in the group withmedium PTP, the sensitivity was 57.14% (52/91) while high PTP group had a sensitivity of 100% (5/5). The specificity of the 2013 PTP was 58.33% (7/12).

Regarding the sensitivity and specificity of the 2019 PTP when being addedthe symptom of dyspnea, there were small differences compared to the 2013 one: in the group of medium scores of PTP, the sensitivity was 41.67% while the sensitivity of high PTP group was 67.57%. The overall sensitivity for both groups (the medium and high PTP) was 61.22%; and the specificity of PTP was 80% higher than2013 PTP model.

Univariate analysis has shown an important relationship between clinical symptoms; risk factors (age, gender) and CAD. This means that if having a detailed, clear and careful medical history, it has correctly diagnosed approximately 60% of clinical coronary stenosis cases [3,4]. Our findings were similar to other previous domestic and foreign studies, which have proven that a good clinical medical history provides valuable information to suggest patients with or withoutCAD.

The results of Thuong Nghia Nguyen's study, in regard to the value of some diagnostic methods of CAD compared with CA in 224 patients, showed diagnostic value of CAD of typicaldiagnostic methods: typical angina had a sensitivity of 89.2%, a specificity of 72.9%; the resting ECG had sensitivity from 9%-51%, specificity from 34%-92%; signs of wall motion abnormalities on the echocardiogram had a sensitivity of 61.9%, specificity of 57.6%; exercise ECG had a sensitivity of 82% and a specificity of 36%. This author's study also indicated that, when diagnosing CAD based only on the clinical symptoms of typical chest pain, the sensitivity and specificity do not change much when incorporating additional cardiovascular risk factors. But when combined with the resting ECG markers and routine echocardiography, the specificity increased to 82% [5].

The results of Phuoc Hoang Le's study, in group of chest pain generally (typical and atypical chest pain), the sensitivity and the specificity of the PTP was at 56% and 80%, respectively. In the typical chest pain group, the sensitivity and the specificitywas at 58% and 80%, respectively. Atypical chest pain group had a sensitivity of 53% and a specificity of 80%. Compared our study with this one, it shows that the sensitivity of our study was equivalent, the specificity was lower, this can be explained that in our study there was an additional factor called myocardial bridge in our subjects [7].

The study of Lan Viet Nguyen et al, when comparing non-invasive methods with CA showed that: routine ECGhad sensitivity of 42.7% and specificity of 75.4%. The exercise ECG treadmill test had a sensitivity of 85.7% and a specificity of 63.6%. Multislice CT with 64-slice technology was performed at 3 levels including patients, coronary (artery) and segment coronary (segment), had sensitivity respectively: 93.8%, 89.9% and 83.2%; and the corresponding specificity were 88.5%, 92.3% and 98.8%, respectively [8].

Mollet et al (2004) performed 16-slice MSCT in 128 patients (89% of men at the average age 58.9 ± 11.7) who were indicatedCA to compare when the stenosis ≥50%. The results of the MSCT to detect a significant narrow lesion had the sensitivity and the specificity of 92% and 95%, respectively, a positive predictive value of 79%, and a negative predictive value of 98% [9].

Cademartiri et al (2006), investigated in 120 patients with suspected CAD were performed withcomputed tomography (CT) of the heart andCAfor comparison. The sensitivity of the CT were 90% and 93% with low and high brightness, respectively, and its specificity were at 95% and 97%, respectively [10].

From the results of studies, it can be seen that although in the era of high-tech applications in medicine has been increasingly implanted in this day and age, the classical methods was simple, but effective if understanding of the basic knowledge and know how to apply scientifically. The combination of classic diagnostic methods of CAD will provide physicians an effective weapon in screening and accurately assessing CAD on each individual patient.

Therefore, it can be confirmed that the 2013 and 2019 PTP are valuable scales in predicting the risk of CAD with higher sensitivity and specificity than ECG, almost equivalent to the exercise ECG

treadmill, but the assessment method is simpler, even it can be applied anywhere, anytime and easily applied at the medical facilities, where high-tech facilities have not been fully implemented.

4.2. Relationship between pre-test probability and the SYNTAX score

We found that there was a difference between the PTP of 2013 and 2019 specifically. For the PTP in 2013, the majority of patients had the medium scores (15-85%) with 91 cases, accounting for 84.3%.Among 93 cases (86.1%) with low SYNTAX score, the medium PTP was mainly with 78 cases, accounting for 72.2%. Similarly, patients with medium (23-32) and high (≥ 33) SYNTAX scores were most likely to have a medium PTP (15-85%). This difference was not statistically significant, p> 0.05.For the PTP in 2019, patients with high score (>15%) were the majority, 74 cases, accounting for 68.5%.Among 93 cases with low SYNTAX score, the high PTP was mainly with 59 cases, accounting for 54.6%. The cases with medium and high SYNTAX scores all had high PTP. This difference was statistically significant, p <0.05.

4.3. Relationship between pre-test probability and cardiovascular risk factors

Relationship between the PTP and cardiovascular risk factors. Through our study we found statistically significant differences in patients with and without smoking for both the 2013 and 2019PTP. The 2013 PTP of more than 15% in patients with history of smoking was 33/33 cases, accounting for 100%, while that in non-smoking patients was 63/75 cases, constituting at 84%, the difference was statistically significant with p<0.01. In the group of patients with other cardiovascular risk factors such as: hypertension, diabetes, dyslipidemia, and obesity and overweight, there was no difference between risk factorsand non-risk factors one due to p>0.05.

The relationship between the 2019 PTP and the cardiovascular risk factors can be seenwith a history of smoking, the PTP was high (> 15%) with 29/33 cases, accounting for 87.9%. The difference was statistically significant with p <0.05. Similarly, in the group of hypertensive patients, the high PTP was 60/78 cases, with p <0.05. However, there was no statistically significant difference on the 2013 PTP. The group of patients with diabetes had high PTP with 27/33 cases, at the rate of 81.8%, difference was statistically significant with p <0.05.

In the study of Thuong Nghia Nguyen (2010) on the value of some diagnostic methods of CAD compared with CA on patients with suspected CAD examined and admitted to cardiology and intervention cardiology department inCho Ray hospital during a study period of nearly 2 years showed that in the group of patients with more than 2 cardiovascular risk factors, the risk of CAD would be two-fold higher than the group of patients with less than 2 cardiovascular risk factors. The author also found that smoking and other cardiovascular risk factors such as: elderly, male sex and dyslipidemia were important indicators of CAD with a statistically significant difference [5].

In summary, our study indicated that: the enhancement of non-invasive measures has helped clinicians to decide whether or not to indicate CA, the variables were evaluated as typical angina with cardiovascular risk factors, especially gender, advanced age, smoking and dyslipidemia, which has been found to be beneficial in distinguishing patients with or without CAD.

V. CONCLUSION

Sensitivity and specificity of the pre-test probability were quite high, can be applied to initial diagnosis for chest pain cases at medical facilities. There are strong relationship between two models of PTP and the severity of coronary artery disease by using SYNTAX score and cardiovascular risk factors.

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