Artificial neural network-based model enhances risk stratification and reduces non-invasive cardiac stress imaging compared to Diamond–Forrester and Morise risk assessment models: A prospective study

Hussain A. Isma'eel, MD,[a,b] George E. Sakr, PhD,[c] Mustapha Serhan, MD,[a] Nader Lamaa, MD,[a] Ayman Hakim, MD,[a] Paul C. Cremer, MD,[d] Wael A. Jaber, MD,[d] Torkom Garabedian, MD,[e] Imad Elhajj, PhD,[b,f] and Antoine B. Abchee, MD[a,b]

[a] Division of Cardiology, Department of Internal Medicine, American University of Beirut, Beirut, Lebanon
[b] Vascular Medicine Program, American University of Beirut Medical Center, Beirut, Lebanon
[c] École Superieurd'Ing. de Beirut (ESIB), St Joseph University, Beirut, Lebanon
[d] Department of Cardiovascular Medicine, Cleveland Clinic Foundation, Cleveland, OH
[e] Department of Internal Medicine, Saint Elizabeth's Medical Center, Boston, MA
[f] Department of Electrical & Computer Engineering, American University of Beirut, Beirut, Lebanon

Received Oct 11, 2016; accepted Jan 19, 2017
doi:10.1007/s12350-017-0823-1

Background. **Coronary artery disease (CAD) accounts for more than half of all cardiovascular events. Stress testing remains the cornerstone for non-invasive assessment of patients with possible or known CAD. Clinical utilization reviews show that most patients presenting for evaluation of stable CAD by stress testing are categorized as low risk prior to the test. Attempts to enhance risk stratification of individuals who are sent for stress testing seem to be more in need today. The present study compares artificial neural networks (ANN)-based prediction models to the other risk models being used in practice (the Diamond–Forrester and the Morise models).**

Methods. **In our study, we prospectively recruited patients who were 19 years of age or older, and were being evaluated for coronary artery disease with imaging-based stress tests. For ANN, the network architecture employed a systematic method, where the number of neurons is changed incrementally, and bootstrapping was performed to evaluate the accuracy of the models.**

Results. **We prospectively enrolled 486 patients. The mean age of patients undergoing stress test was 55.2 ± 11.2 years, 35% were women, and 12% had a positive stress test for ischemic heart disease. When compared to Diamond–Forrester and Morise risk models, the ANN model for predicting ischemia provided higher discriminatory power (DP)(1.61), had a negative predictive value of 98%, Sensitivity 91% [81%-97%], Specificity 65% [60%-79%], positive predictive value 26%, and a potential 59% reduction of non-invasive imaging.**

Conclusion. **The ANN models improved risk stratification when compared to the other risk scores (Diamond–Forrester and Morise) with a 98% negative predictive value and a significant potential reduction in non-invasive imaging tests. (J Nucl Cardiol 2018;25:1601–9.)**

Key Words: Artificial neural networks (ANN) • Diamond–Forrester score • Morise score • stress echocardiography • nuclear stress test

Electronic supplementary material The online version of this article (doi:10.1007/s12350-017-0823-1) contains supplementary material, which is available to authorized users.

The authors of this article have provided a PowerPoint file, available for download at SpringerLink, which summarizes the contents of the paper and is free for re-use at meetings and presentations. Search for the article DOI on https://www.SpringerLink.com.

Reprint requests: Hussain A. Isma'eel, Division of Cardiology, Department of Internal Medicine, American University of Beirut, PO-BOX 11-0236, Riad el Solh, Beirut 11072020, Lebanon; *hi09@aub.edu.lb*

Hussain A. Isma'eel and George E. Sakr—co-authors with equal contribution.

1071-3581/$34.00

See related editorial, pp. 1610–1612.

INTRODUCTION

Coronary artery disease (CAD) accounts for more than half of all cardiovascular events in adults younger than 75 years, and it is the leading cause of death worldwide.[1] Depending on guidelines and local expertise, patients presenting with suspected CAD can be investigated with one of several diagnostic modalities.

According to the 2010 UK National Institute for Health and Care Excellence (NICE) guidelines, patients are assigned a pretest probability score of having obstructive CAD based on risk category, age, sex, and characteristics of chest pain.[2] The European Society of Cardiology (ESC), as well as the American College of Cardiology (ACC), endorse pretest probability with a modified Diamond–Forrester model that includes age, sex, and characteristics of chest pain. Notably, cardiovascular risk factors are not included.[3,4]

In these guidelines, stress testing remains the cornerstone for non-invasive risk stratification for patients with possible or known coronary artery disease (CAD).[4] This risk stratification performs best in patients with an intermediate pretest probability; however, clinical utilization reviews show that most patients who present for evaluation of stable CAD with stress testing are actually at low risk.[5,6] This practice pattern is maintained due to several complex reasons including misinterpretation of pretest risk, current models of reimbursement, and concern for medico-legal consequences from adverse outcomes.[7,8]

In 2009, direct and indirect costs of CAD were estimated to be $195 billion in the United States.[1] Costs of testing include both the direct costs of the procedures and the downstream costs of additional testing, follow-up, and referrals. Much of this cost is related to testing low-risk patients, and inappropriate cardiac testing in such patients has been identified by several professional organizations as one of the most overused clinical practices.[9] Therefore, critical examination of current stress testing practices and the development of improved risk stratification models are imperative.

Artificial neural networks (ANN)-based modeling has emerged as a robust technique that can provide higher accuracy than prediction models that are based on standard multivariable linear and logistic regression analyses.[10] In particular, ANN modeling has been shown to enhance risk stratification and potentially reduce downstream testing for patients with suspected acute coronary syndromes with negative cardiac biomarkers and normal ECGs.[11] However, none of the prior ANN modeling studies have incorporated the quality, area, and type of chest pain, nor the estrogen status in female subjects in their model. Therefore, the aim of this study is to compare ANN-based prediction models to other risk models that are being used in clinical practice to assign the pretest probability of obstructive CAD (i.e., the Diamond–Forrester and the Morise models).[12,13] We hypothesized that if we compare the ANN-based models with other models' scores, they would provide higher discriminatory power (DP) to identify patients that are likely to have inducible ischemia on stress echocardiography, or nuclear stress test. Furthermore, if the ANN models perform better than the Diamond–Forrester and Morise scores, we plan to develop an interactive interface to facilitate the use of these models in a clinical setting.

METHODS

Study Design

In our study, we prospectively recruited 486 patients who were 19 years of age or older, and who were being evaluated for coronary artery disease with exercise radionuclide testing or echocardiographic stress testing. Patients who presented with symptoms suggestive of stable angina, and patients with features of unstable angina but had normal ECGs and at least two negative serial troponin tests were included. We excluded patients who presented with non-ST elevation Myocardial Infarction (NSTEMI), ST elevation Myocardial Infarction (STEMI), and those who presented with unstable angina with any ST changes on ECG. Patients were recruited when they presented for evaluation of chest pain at our institution (American University of Beirut Medical Center). All patients underwent stress exercise according to the Bruce protocol. 89 patients had radionuclide stress testing using Technetium-99m-Sestamibi SPECT myocardial perfusion imaging, and 397 had stress echocardiography. A stress imaging test was considered positive for obstructive CAD if there was reversible perfusion abnormalities (assessed qualitatively by subjective judgement) or new wall motion abnormalities by radionuclide stress testing or stress echocardiography, respectively.

After obtaining informed consent, patients were asked to fill out a questionnaire that included age, sex, smoking status, past medical history of cardiovascular disease and co-morbidities (dyslipidemia, diabetes mellitus, hypertension, and cardiomyopathy), and family history of dyslipidemia and/or CAD at a young age (<60 years old) in a first-degree relative. Patients were also asked about the test being performed (radionuclide stress testing or stress echocardiography), their symptoms, and characteristics of chest pain (onset, quality, anatomic location, exacerbating, and relieving factors). The anatomic location of chest pain was based on prior studies[14,15] (Figure 1) where locations 1, 4, and 7 are the right side of the patient. The questionnaire includes all items assessed by the two commonly used risk scores (updated Diamond–Forrester and Morise scores).

For the purposes of comparing our ANN model to widely used models, we selected the Diamond–Forrester and Morise Scores.

Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines as reflected by a prior approval by the institution's human research review board.

Data Analysis

ANN models. A detailed introduction to ANN has been described by Hagan and Demuth.[16] The architecture design for ANN used a systematic method, where the number of neurons is changed incrementally and bootstrapping is performed to evaluate the accuracy of the models. We derived one model to predict if a patient has ischemia present by stress imaging. The covariates used in the ANN model included age, sex, chest pain, diabetes, hyperlipidemia, hypertension, smoker, family history of CAD, body mass index (BMI), the type of complaint (atypical, angina, and non-anginal), and the area of chest pain as described earlier. The age is represented in years, BMI is a continuous number, the type of complaint is 0 for atypical, 1 for angina, and 2 for non-anginal, and all the other predictors take only one of two values: 1 if the predictor applies to that patient and 0 if not. A multilayer network was used for the predicted outcomes consisting of one input layer one hidden layer and one output layer. The input layer consists of 3 neurons that are connected to all the observed independent variables. The hidden layer consists of 3 neurons and the output layer of 1 neuron. The transfer function in the entire layer is the tangent sigmoid function defined by

$$f(n) = \frac{e^{n} - e^{-n}}{e^{n} + e^{-n}}.$$

The training of the network was done using the Levenberg–Marquardt back-propagation algorithm. This algorithm finds the weights that minimize the error using a variation of Newton's method for minimizing functions.[17] This algorithm was chosen because it is the fastest neural networks training algorithm for moderate size networks[16] as is the case in this study. The details split into a derivation cohort used to derive the prediction model and a validation cohort used to measure the performance of the derived model. Figure 5 shows the neural network used with all the inputs and outputs.

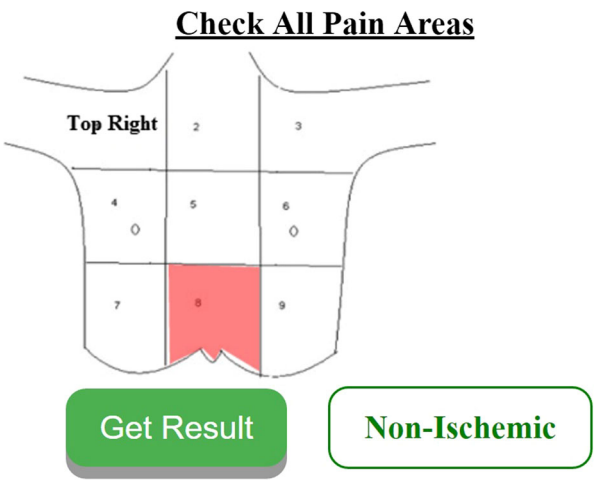

Figure 1. Anatomical location of chest pain according to the patient.

Prediction Model for Ischemia Present by Stress Imaging

Since the data are unbalanced (only 12% with documented ischemia), the derivation cohort was randomly chosen as follows: 30 out of the 59 patients who tested positive were added randomly to the derivation cohort, and 30 out of the remaining 427 patients who tested negative were also added randomly to the derivation cohort. The remaining 426 patients (29 positive, 397 negative) were all added to the testing cohort and in order not to bias the results were used only to test the performance of the models derived using the derivation cohort. In order not to over train the neural network model, during the training phase, the 60 patients that are used for training were split 80% for pure training and 20% for validation. The model that yields the highest accuracy on the validation set is used on the testing set in order to report the accuracy (Table 1).

ANN bootstrapping. ANN is a special type of non-linear regression that presents multiple local minima; hence, every time we run the training algorithm, it will converge in general to a different model. To make the choice of the best model, the training process is repeated 200 times. The 200 repetitions yield a smooth ROC curve that gives us a finer granularity in our choice. In every iteration, the algorithm converges to a point that results in the highest accuracy on the validation set. Then, every model of the 200 generated models is tested on the testing cohort, and the sensitivity and specificity of the models are recorded. Some models presented good specificity but poor sensitivity, some models the opposite, and some presented good specificity and sensitivity. The results of the 200 models are presented as sensitivity versus 1-specificity of each model. However, if 2 models had the same specificity but different sensitivities, then only the model with higher sensitivity was included.

Statistical analysis. Discriminatory power (DP) has been previously used to compare ANN models. Therefore, ANN models were compared to the Morise score and Diamond–Forrester score for predicting the presence of ischemia on stress imaging by deriving DP and the corresponding 95% confidence intervals (CI).[18] Also, as separate independent comparisons of calculated physician and network sensitivities or specificities are not valid due to the reciprocal relationship between sensitivity (Sens) and specificity (Spec), the DP of a test[19] was used to compare physician and network performance:

$$DP = \frac{\sqrt{3}}{\pi}\left[\ln\left(\frac{\text{sens}}{1-\text{spec}}\right) + \ln\left(\frac{\text{spec}}{1-\text{sens}}\right)\right],$$

representing the log of the positive likelihood ratio plus the log of the negative likelihood ratio scaled by the standard deviation (SD) of the logistic normal distribution curve $\sqrt{3}/\pi$. The negative and positive predictive values (NPV and PPV, respectively) of each model were also calculated.[20] The percentage of avoided tests corresponding to each ANN

Table 1. Baseline characteristics

	All patients n = 486	Negative stress imaging n = 427	Positive stress imaging n = 59	*P* value
Female	35% (166)	37% (161)	8% (5)	<.0001
Age	55.2 SD 11.2	54 ± 12.2	64 ± 10	<.0001
Diabetes mellitus	20% (99)	18% (79)	33% (20)	.006
Hyperlipidemia	60% (294)	58% (240)	74% (44)	.01
Hypertension	44% (217)	42% (182)	59% (35)	.01
Smoker	73% (357)	49% (209)	34% (20)	.02
Family history of CAD	22% (108)	20% (87)	35% (21)	.0054
Obesity (BMI > 28)	47% (232)	48% (205)	46% (27)	.77
Complaint				
Anginal	55% (269)	54% (233)	61% (36)	.31
Non-anginal	45% (217)	45% (194)	39% (23)	.31
Chest Pain (Any Area)	55% (270)	55% (235)	59% (35)	.56
Area 1	4% (21)	3% (16)	8% (5)	.05
Area 2	3% (15)	3% (15)	0% (0)	.18
Area 3	15% (71)	14% (62)	15% (9)	.83
Area 4	1% (7)	1.6% (7)	0% (0)	.44
Area 5	26% (127)	26% (112)	25% (15)	.87
Area 6	20% (96)	19% (82)	24% (14)	.46
Area 7	0% (1)	0.3% (1)	0% (0)	.73
Area 8	6% (29)	6% (27)	3% (2)	.35
Area 9	4% (21)	4% (18)	5% (3)	.71
Ischemia present	12% (59)			
Morise score < 9	22.4% (109)			
Average Morise Score	11.4 (SEM 3.77)			
Average DF score	0.124 (SEM 0.086)			

Demographics of the patients who underwent either stress echocardiography or nuclear stress test. Only 12% (59) of the patients had ischemia. Negative and positive results are shown along with their *P* values

model to predict ischemia presence was then plotted against the sensitivity of the prediction model. The number of tests avoided was calculated assuming that the results of the ANN model were respected. The %Avoided was then calculated as

$$\%\text{Avoided} = 100 \times \frac{N \text{ not sent to stress echo}}{\text{Total}}.$$

Percentage ordered is 100 − % avoided.

RESULTS

Most of the risk factors in our risk models (gender, age, diabetes mellitus, hyperlipidemia, hypertension, smoking, and family history of CAD) were predictive of ischemia with stress imaging (P value $\leq .01$). Conversely, the type of chest pain was not significantly associated with ischemia ($P > .1$). In addition, the only area of chest pain that may be associated with ischemia was area 1.

Even though ischemia was seen in only 12% of patients, most patients were classified as intermediate or high risk according to DF (54%) and Morise (78%) scores. The discretization of Morise and DF scores from pretest probabilities to positive/negative outcomes entailed using the cut-points that yielded the highest discriminatory power to compare their corresponding performance to the ANN models (Table 3, ''Appendix''). The Morise and DF scores that yielded the highest DP were then compared to the ANN models (Figure 2). A good discriminatory power is reflected as greater than one, and a poor one is reflected as less than one.[19] The ANN model performed best with a DP 1.61 to predict ischemia by stress imaging (Table 2). The ANN model with the best DP for predicting ischemia has a negative predictive value of 98% [96-99], Sensitivity 91% [81-97], Specificity 65% [60-79], and PPV 26% [17-35]. In addition, the performance of ANN model in both diagnostic modalities was similar. The sensitivity and specificity of the ANN model when used in stress echo were 80% [67-89] and 73% [66-79], respectively, and when used in radionuclide stress test

Table 2. Classification of patients being tested into risk group category according to DF and Morise risk scores

	Low risk	Intermediate risk	High risk
DF score	221 (46%)	157 (32%)	108 (22%)
Morise score	109 (22%)	313 (65%)	64 (13%)

Table 3. Performance of DF, Morise* scores, and ANN models to assess for inducible ischemia by stress imaging

	Sensitivity % with 95% CI	Specifiicity % with 95% CI	PPV % with 95% CI	NPV % with 95% CI	LR+	LR−	DP	Stress imaging avoided
Morise	65 [48-79]	55 [51-59]	8.2 [1-18]	96 [93-99]	1.44	0.63	0.45	54% [51-57]
DF	69 [53-83]	59 [55-62]	9.5 [2-19]	96.9 [94-99]	1.68	0.52	0.64	57% [53-60]
ANN	91 [81-97]	65 [60-69]	26 [17-35]	98 [96-99]	2.6	0.14	1.61	59% [56-61]

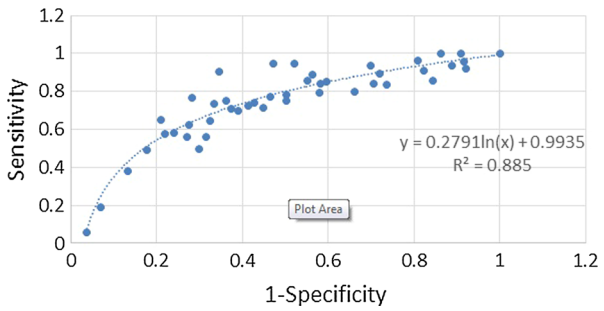

Figure 2. Plot of the sensitivity of each ANN model vs 1-specificity to predict ischemia by stress imaging.

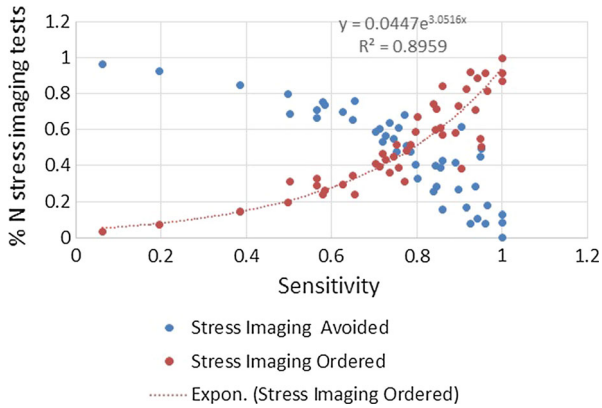

Figure 3. Percentage stress imaging ordered and sensitivities of ANN model used.

were 70% [54-84] and 68% [58-79], respectively. Furthermore, Figures 6 and 7 show the ROC for Morise score and DF score, respectively. The area under the curve for Morise score is 0.59 and the area under the curve for DF is 0.55 compared to 0.7 for ANN ($P < .01$).

The percentage of stress imaging studies that could be avoided with this model was 59%. By comparison, the Morise score had lower performance with a DP 0.45 to detect ischemia, and DF had a DP of 0.64. The percentage of stress imaging studies that could be avoided with the optimal Morise score was 54% and was 57% with the optimal DF score.

A comparison of the predicted sensitivity of the ANN models with predicted downstream testing revealed an exponential increase in expected testing with increasing sensitivity to predict ischemia by stress imaging (Figure 3, % stress imaging tests ordered = $0.0447^{*}\ e^{3.05^{*}\ \mathrm{Sens}}$, $R^2 = 0.9$). This relationship also highlights the decrease in the positive predictive value when a high sensitivity is imposed on a population with a low probability of disease.

DISCUSSION

The current study is the first that employs ANN for the prediction of ischemia by stress imaging in a cohort of 486 patients. We have demonstrated a higher discriminatory power with an ANN-based model compared to Morise and Diamond–Forrester (DF) scores. If this ANN model was employed to select patients for

testing, stress imaging studies would be reduced by 59% with an incremental 2% and 5% increase in savings compared to DF and Morise score, respectively. Furthermore, we showed an exponential increase in downstream testing with increased ANN model sensitivity to predict ischemia. Finally, we incorporated the ANN models with the highest DP into a user-friendly interface that can be integrated by researchers for future studies to further validate and explore the utilization of this modeling method (Figure 4).[21]

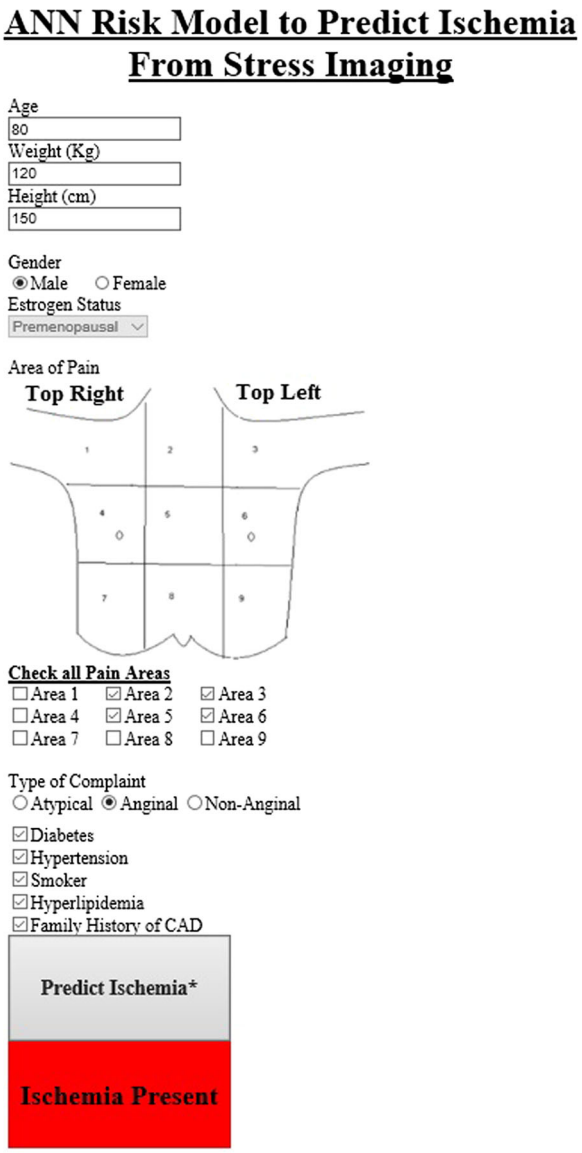

Figure 4. Screenshot of ANN-based models' application to predict ischemia, accessed at http://www.aub.edu.lb/fm/vmp/Documents/StressImaging/index.html.

Advantages of Artificial Neural Networks and Use in Previous Studies

In many studies, ANN has improved outcome prediction in clinical decision-making. Our group has previously shown improved accuracy in anti-coagulant required dosage prediction using ANN in comparison to linear regression analysis.[22] Our group also showed that ANN models have improved risk stratification when compared to the TIMI (thrombolysis in Myocardial Infarction) score in predicting ischemia with myocardial perfusion imaging.[11] Similarly, Wise et al showed that the use of ANN improves outcome prediction of in-hospital mortality after ruptured abdominal aortic aneurysm,[23] Freeman et al demonstrated improvement of in-hospital death prediction after coronary angioplasty, and Purwanto et al have developed ANN-based prediction models for early risk detection of cardiovascular events.[10,24]

This improvement in outcome prediction is primarily attributed to the ability of ANN to incorporate non-linear relationships between predictors and outcomes. It is worth noting that the use of computer-assisted models is not new and Diamond et al, in 1983 showed in the CADENZA trial that computer-assisted modeling relying on Bayes' theorem did provide an accurate method to predict the prevalence of coronary disease and prognosis.[25] However, to our best knowledge, no previous studies have tested the use of ANN to predict the outcome of non-invasive cardiac tests including stress echocardiography and nuclear stress tests.

Clinical Implications

From a clinical perspective, the prevalence of CAD will accelerate in the next decade due to aging of the population, increases in the prevalence of obesity and type II diabetes, and increases in cardiovascular risk factors among younger generations. Therefore, appropriate testing to identify patients with CAD is essential, yet current testing is often low-risk yield.[26]

Similarly, our results showed that only 12% of patients demonstrated ischemia, and this low yield is consistent with previous studies.[27,28] This low yield highlights the need for improved risk stratification prior to referral for non-invasive cardiac testing. As healthcare costs continue to increase, the focus of care has transitioned to providing testing that maximizes benefit while minimizing risks and expense.[29]

Moreover, the numerous algorithms that ANN modeling generates provide flexibility in terms of discussing suitable cut-points for sending patients for further non-invasive testing. As shown in Figure 3, a comparison of the predicted sensitivity of the ANN

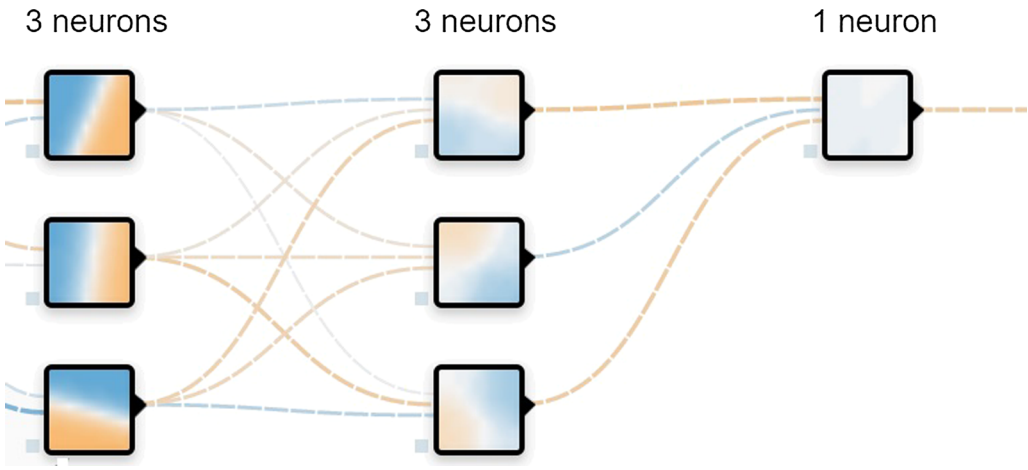

Figure 5. ANN model.

models with predicted downstream testing revealed an exponential increase in the number of expected tests with increasing sensitivity to predict ischemia by stress imaging. This relationship also highlights the decrease in the positive predictive value when a high sensitivity is imposed on a population with a low probability of disease. As total cost is directly related to the number of studies performed, total costs are also likely to increase exponentially with increasing ANN model sensitivity. Therefore, this technique offers stakeholders the opportunity to select model sensitivity that best corresponds to the desired balance between the number of tests ordered, false positive results, and risk of missing obstructive CAD.

Despite the fact that the ANN model selected delivered a higher discriminatory power compared to other models, this translated into marginal added absolute reduction in testing (2%-5%). We hypothesize that this is primarily because we are testing a low-risk population. Even though this absolute reduction is marginal, we believe that at a community level, a 2%-5% reduction in ordered stress imaging tests represents a significant amount of money and resources that can be redirected to more needed areas (Figure 5).

LIMITATIONS AND FUTURE DIRECTIONS

Our study has several notable limitations. Our study lacks external validation, and data were collected from a single medical center. Although the sample size in this study is substantial for this particular population, a larger sample size from multiple centers would be better to validate our results. All the variables we incorporated in the ANN model were based on the updated Diamond–Forrester and Morise risk scores in addition to area of chest pain.

The reason these 2 models were chosen are because

1. DF model is a very widely used model.
2. Morise model incorporates hormonal status in women which is thought to contribute to CAD protection and is also related to symptoms.

Nonetheless, other variables and parameters could be added to improve risk stratification.

Finally, since no risk model can be 100% accurate, this ANN model should not substitute clinical judgment. Rather, the ANN model should be used as an adjunct to clinical assessment.

CONCLUSION

In summary, this study showed that an ANN model has a higher discriminatory power than Diamond–Forrester and Morise risk scores in predicting ischemia with stress echocardiography and radionuclide stress testing. If employed, these models could significantly decrease downstream testing. Furthermore, we have shown an exponential increase in downstream testing as sensitivity increases in a population where the majority of patients at are low risk.

NEW KNOWLEDGE LEARNED

We learned from this study that in a Middle Eastern Cohort

1. Neither chest pain location nor quality were found to be independently predictive of obstructive CAD by stress imaging,
2. The widely used Diamond–Forrester and Morise Models to predict obstructive CAD performed poorly, and

3. Using artificial neural network modeling enhances the accuracy of prediction of positive stress imaging test compared to logistic regression.

Disclosure

The authors have indicated that they have no financial conflict of interest.

APPENDIX: DISCRETIZATION OF MORISE AND DF SCORES FROM PRETEST PROBABILITIES TO POSITIVE/NEGATIVE OUTCOMES

Table 4 allows us to compute Morise score.[14,15] The Morise score represents a pretest probability of stenosis. We picked a cutoff point for the total score and assumed that if the total score is higher than this cutoff then the result is positive, otherwise, it is negative. This cutoff point was varied over all possible values, which yielded the ROC curve below. Similar to our group's previous work,[30] the cutoff point that yielded the highest DP was then used (Table 5).

The same was applied to DF.[14]

$$\text{Score} = 0.04 * \text{age} + 1.34 * \text{Male} + 1.91 * \text{Typical} + 0.64 * \text{Atypical} - 4.37$$

$$\text{Probability} = \exp(\text{score})/(1 + \exp(\text{score}))$$

A cutoff probability was chosen and we assumed that if the current probability is higher than the cutoff then the result is positive otherwise it is negative. This cutoff varied between 0 and 1 with a step of 0.01 which led to the ROC below (Figures 6, 7). The area under the curve for Morise score is 0.59 and the area under the curve for DF is 0.55 compared to 0.7 by ANN ($P < .01$).

Table 5. Method of transforming Diamond-Forrester risk score into a numerical probability

Predictor	Coefficient
Age	0.04
Male sex	1.34
Typical chest pain	1.91
Atypical chest pain	0.64
Non-specific chest pain	-
Intercept	−4.37

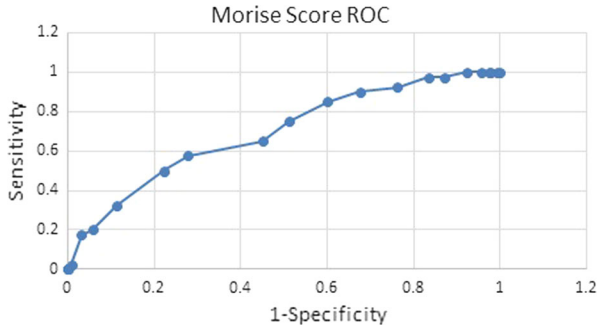

Figure 6. AUROC for Morise.

Table 4. Morise score calculation: how to calculate the pretest score and assigned risk groups

Variable			Choose response sum
Age	Men	Women	
	<40	<50	3
	40-54	50-64	6
	>54	>64	9
Estrogen status (women Only)			Positive = −3
			Negative =+3
Angina history (diamond method)			Typical = 5
			Atypical = 3
			Non-anginal = 1
Diabetes			2
Hyperlipidemia			1
Hypertension			1
Smoking (any)			1
First-degree family history of CAD			1
Obesity BMI > 27			1
			Total score

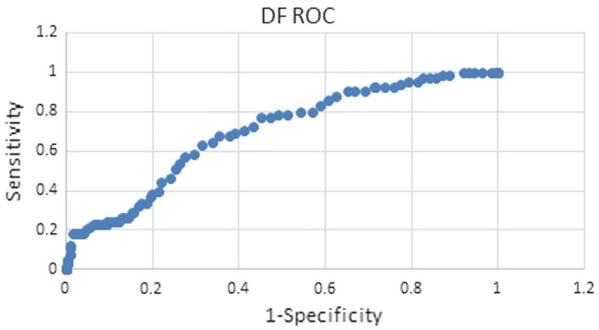

Figure 7. AUROC for DF.

References

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics—2013 update: A report from the American Heart Association. Circulation 2013;127:e6-245.
2. Chest Pain of Recent Onset. Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. London: National Clinical Guideline Centre for Acute and Chronic Conditions; 2010.
3. Demir OM, Alfakih K, Plein S. Current international guidelines for the investigation of patients with suspected coronary artery disease. Eur Heart J Cardiovasc Imaging 2014;15:1422-4.
4. Miller TD, Askew JW, Anavekar NS. Noninvasive stress testing for coronary artery disease. Heart Fail Clin 2016;12:65-82.
5. Cubukcu A, Murray I, Anderson S. What's the risk? Assessment of patients with stable chest pain. Echo Res Pract 2015;2:41-8.
6. Cotarlan V, Ho D, Pineda J, Qureshi A, Shirani J. Impact of clinical predictors and routine coronary artery disease testing on outcome of patients admitted to chest pain decision unit. Clin Cardiol 2014;37:146-51.
7. Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. N Engl J Med 2000;342:1163-70.
8. Herren KR, Mackway-Jones K. Emergency management of cardiac chest pain: A review. Emerg Med J 2001;18:6-10.
9. Chou R. Cardiac screening with electrocardiography, stress echocardiography, or myocardial perfusion imaging: Advice for high-value care from the American College of Physicians. Ann Intern Med 2015;162:438-47.
10. Freeman RV, Eagle KA, Bates ER, Werns SW, Kline-Rogers E, Karavite D, et al. Comparison of artificial neural networks with logistic regression in prediction of in-hospital death after percutaneous transluminal coronary angioplasty. Am Heart J 2000;140:511-20.
11. Isma'eel HA, Cremer PC, Khalaf S, Almedawar MM, Elhajj IH, Sakr GE, et al. Artificial neural network modeling enhances risk stratification and can reduce downstream testing for patients with suspected acute coronary syndromes, negative cardiac biomarkers, and normal ECGs. Int J Cardiovasc Imaging 2015;32:687-96.
12. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. N Engl J Med 1979;300:1350-8.
13. Morise AP, Detrano R, Bobbio M, Diamond GA. Development and validation of a logistic regression-derived algorithm for estimating the incremental probability of coronary artery disease before and after exercise testing. J Am Coll Cardiol 1992;20:1187-96.
14. Genders TSS, Steyerberg EW, Alkadhi H, Leschka S, Desbiolles L, Nieman K, et al. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension. Eur Heart J 2011;32:1316-30.
15. Fox K, Garcia MA, Ardissino D, Buszman P, Camici PG, Crea F, et al. Guidelines on the management of stable angina pectoris. Executive summary. Rev esp Cardiol 2006;59:919-70.
16. Hagan MT, Demuth HB, Beale MH. Neural network design. Boston: PWS Publishing Co.; 1996.
17. Scales LE. Introduction to non-linear optimization. London: MacMillan, City and Guilds; 1985.
18. CaEP Clopper. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 1934;4:404-13.
19. Blakeley DD, Oddone EZ, Hasselblad V, Simel DL, Matchar DB. Noninvasive carotid artery testing. A meta-analytic review. Ann Intern Med 1995;122:360-7.
20. Altman DG, Bland JM. Diagnostic tests 2: Predictive values. BMJ 1994;309:102.
21. Isma'eel H, Sakr, G. ANN risk model to predict ischemia from stress imaging. Université Saint-Joseph. 2016. https://cimti.usj.edu.lb/files/VMP/StressImaging/index.html.
22. Isma'eel HA, Sakr GE, Habib RH, Almedawar MM, Zgheib NK, Elhajj IH. Improved accuracy of anticoagulant dose prediction using a pharmacogenetic and artificial neural network-based method. Eur J Clin Pharmacol 2014;70:265-73.
23. Wise ES, Hocking KM, Brophy CM. Prediction of in-hospital mortality after ruptured abdominal aortic aneurysm repair using an artificial neural network. J Vasc Surg 2015;62:8-15.
24. Purwanto E, Eswaran C, Logeswaran R, Abdul Rahman AR. Prediction models for early risk detection of cardiovascular event. J Med Syst 2012;36:521-31.
25. Diamond GA, Staniloff HM, Forrester JS, Pollock BH, Swan HJ. Computer-assisted diagnosis in the noninvasive evaluation of patients with suspected coronary artery disease. J Am Coll Cardiol 1983;1:444-55.
26. Rozanski A, Gransar H, Shaw LJ, Kim J, Miranda-Peats L, Wong ND, et al. Impact of coronary artery calcium scanning on coronary risk factors and downstream testing the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) prospective randomized trial. J Am Coll Cardiol 2011;57:1622-32.
27. Cremer PC, Khalaf S, Agarwal S, Mayer-Sabik E, Ellis SG, Menon V, et al. Myocardial perfusion imaging in emergency department patients with negative cardiac biomarkers: Yield for detecting ischemia, short-term events, and impact of downstream revascularization on mortality. Circ Cardiovasc Imaging 2014;7:912-9.
28. Cremer PC, Mentias A, Newton D, Menon V, Wazni O, Tchou PJ, et al. Low yield of myocardial perfusion imaging in asymptomatic patients with atrial fibrillation. JAMA Intern Med 2015;175:1854-5.
29. Nawar EW, Niska RW, Xu J. National Hospital Ambulatory Medical Care Survey: 2005 emergency department summary. Adv Data 2005;2007:1-32.
30. Isma'eel HA, Serhan M, Sakr GE, Lamaa N, Garabedian T, Elhajj I, et al. Diamond-Forrester and Morise risk models perform poorly in predicting obstructive coronary disease in Middle Eastern Cohort. Int J Cardiol 2016;203:803-5.