Original Article

Development of a diagnosis model for coronary artery disease

Hongzeng Xu, Zhiying Duan, Chi Miao, Song Geng, Yuanzhe Jin*

Department of Cardiology, The fourth Affiliated Hospital, China Medical University, Shenyang 110032, China

A R T I C L E   I N F O

Article history:
Received 27 September 2016
Accepted 16 February 2017
Available online 29 March 2017

Keywords:
Coronary artery disease
Logistic model
Diagnosis
Risk factors

A B S T R A C T

Background: The purpose of this study was to develop a coronary artery disease (CAD) prediction model that optimally estimates the pre-test probability of CAD for patients suspected of CAD.

Methods and results: This retrospective, multi-centre study included 7360 consecutive patients (4678 men, 57.87 ± 11.42 years old; 2682 women, 61.60 ± 9.58 years old) who underwent coronary angiography for evaluation of CAD. A prediction model was fitted for diagnosis of CAD with the help of eight significant risk factors including sex, age, smoking status, diabetes, hypertension, dyslipidaemia, serum creatinine and angina. All potential predictors were significantly associated with the presence of CAD. The prevalence of CAD was significantly higher in men than in women. The clinical model gives a relatively accurate prediction of CAD with an area under the curve (AUC) of 0.74 (95% CI 0.88–0.96; P < 0.001). Addition of angina to the prediction model improves the predictive precision of the model. The optimal cut-off for predicting CAD in this model was 0.79 with a sensitivity of 0.658 and a specificity of 0.709. Conclusion: A prediction model including age, sex, and cardiovascular risk factors allow for an accurate estimation of the pre-test probability of coronary artery disease in Chinese populations. This algorithm may be useful in making decisions relating to the diagnosis of CAD.

© 2017 Published by Elsevier B.V. on behalf of Cardiological Society of India. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Coronary artery disease (CAD) continues to be the leading cause of death and disability in the Chinese population and worldwide. Early and effective identification and treatment of CAD in high-risk patients are recommended. Coronary artery angiography (CAG) is still widely accepted as the gold standard for diagnosing CAD. However, using coronary angiography routinely as a first choice test is not accepted because of the risk of complications, high costs and the unwillingness of many patients to undergo invasive examinations. Several important non-invasive diagnostic tools, such as computed tomography (CT) and magnetic resonance imaging (MRI), scanning, in cardiovascular risk patients are limited and expensive. In the Chinese population, the reliability of probabilities has not been investigated in patients referred to invasive CAG testing.

It is generally acknowledged that CAD is a multifactorial disease in which various major risk factors, such as age, sex, diabetes, smoking, family history and high cholesterol, are involved in disease development and clinical manifestation. CAD progresses slowly and may develop over a patient’s whole lifetime, and the results of alterations in diet, exercise, living conditions, or drugs may not be seen until many years later. Time and economics are crucial for obtaining the correct diagnosis in the early stage of heart disease. In recent years, considerable research has been conducted and large amounts of money have been spent to determine whether it is possible to alter the incidence of heart disease by altering peoples’ lifestyles. Diagnosing heart disease, in most cases, depends on a complex combination of clinical and pathological data. Because of this complexity, considerable interest exists among clinical professionals and researchers in the efficient and accurate prediction of heart disease. The costs of invasive and non-invasive diagnostic methods, which are used to identify the presence and severity of CAD, are increasing dramatically. Because of the limited resources available in certain areas of the world, finding low-cost strategies for developing a diagnosis model is essential. Developing a model from routine clinical characteristics for the diagnosis of CAD could help physicians refine their knowledge of the stratification of CAD risk with respect to vague information.

There is a growing awareness of the need to apply statistical techniques to develop evidence-based models for enhanced decision-making. Several studies have focused on predicting the risk of CAD in Asian populations. However, few studies have constructed prediction models for CAD in a large cohort of Asian populations.

* Corresponding author.
E-mail address: yzjin@cmu.edu.cn (Y. Jin).

http://dx.doi.org/10.1016/j.ijh.2017.02.022
0019-4832 © 2017 Published by Elsevier B.V. on behalf of Cardiological Society of India. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
patients suspected of CAD who met the diagnostic criteria and underwent coronary angiography. The purpose of this study was to develop a simple diagnostic model that can be used in clinical practice for diagnosis of CAD in the Chinese population.

2. Methods

2.1. Subject selection

This study was performed as a retrospective, case-control study in the south and north of China (Fourth and First Affiliated Hospital of Chinese Medical University, Zhongda Hospital of Southeast University and the First Affiliated Hospital of Soochow University). A total of 8297 consecutive patients were studied in the Department of Cardiology between 2008 and 2014. All patients in the study were consecutive referrals for coronary angiography because of a clinical suspicion of CAD. The patients had no known prior myocardial infarction according to their medical history or electrocardiographic findings, no presence of heart failure and cardiomyopathy, and no known serious valve diseases, prior percutaneous cardiac catheterizations or coronary artery bypass grafts. Other exclusion criteria were chronic kidney disease, apparent infectious disease, chronic inflammatory disorders, and malignancy. All patients received a general health questionnaire survey. The questionnaire covered demographic background and medical history. This study and the consent process were approved by our local ethics committee (Ethics Committee of The Fourth Affiliated Hospital of Chinese Medical University) and were conducted in accordance with the principles of the Declaration of Helsinki. We adhere to the statement of ethical publishing as it appears in the International Journal of Cardiology.8

2.2. Data collection

All patients received routine blood sample tests before coronary angiography. The blood samples were drawn after overnight fasting for laboratory tests. All of the laboratory tests were conducted by certified experimental specialists using standard protocols at the hospital’s Laboratory Department. We selected biomarkers from the routine health check-up, including low-density lipoprotein (LDL) and serum creatinine. Other data were collected from the patient records and were used as clinical variables. The variables used for predicting CAD or non-CAD were age (years), sex (men/women), type of angina, history of hypertension, smoking history and history of diabetes.

2.3. Clinical definitions

The type of angina was classified as typical or atypical. Typical angina was defined as all of the following criteria: (1) characterized by squeezing or crushing, (2) substernal in location, with or without arm/neck radiation, and (3) provoked by stress and promptly relieved by rest and/or nitroglycerine. If two or none of the criteria was present, the symptoms were classified as atypical angina. Hypertension was defined as systolic blood pressure \( \geq 140 \text{ mm Hg} \) and/or diastolic blood pressure \( \geq 90 \text{ mm Hg} \) or use of antihypertensive drugs. Diabetes mellitus was defined as fasting glucose levels of \( \geq 7 \text{ mmol/L} \) or treatment with insulin or oral hypoglycaemic medications.9 Cigarette smoking was defined as smoking at least one cigarette per day for one or more years.10

2.4. Coronary angiography

All patients suspected of CAD in this study had undergone coronary angiography. Multiple projections were obtained to assess the maximal coronary artery luminal narrowing. Angiograms were analyzed in each institution by consensus opinion of two experienced interventional cardiologists. Each major coronary vessel, such as the right coronary, left main, left anterior descending and circumflex artery or their major branches, was assessed, and the visual estimation of the percent grades of luminal stenosis was reported. CAD was defined as the presence of at least one major epicardial coronary artery with \( \geq 50\% \) lumen diameter narrowing.

2.5. Derivation of the probability algorithms and validation

Logistic regression is a type of regression analysis used for statistically predicting the outcome of a categorical dependent variable from a set of predictor or independent variables.11 Because many factors are related to the diagnosis of coronary disease, multivariate methods have been extensively applied to the diagnostic evaluation process. The logistic regression equation allows us to easily calculate the predicted probability of an outcome. We used the logistic model to evaluate individual contributions of clinical characteristics to determine the presence of coronary artery stenosis in a large segment of the Chinese population. The maximum likelihood method was applied to derive formulas in this model. The Wald test-statistic was used to test the significance of the logistic regression co-efficient.

The model developed in the training sample was used to predict the probability of severe CAD for each patient in the test sample. The accuracy of the model to separate CAD from non-CAD was assessed by using the means of the area under the receiver operating characteristic (ROC) curve, and Youden’s index was applied to establish the optimal cut-off value.

2.6. Statistics

All values are reported as the mean \( \pm \) SD (standard deviation). All tests of significance were two-tailed, and statistical significance was defined as \( P < 0.05 \). All statistical analyses and the multivariable logistic regression analysis were performed using Stata/SE software programme, version 12 (STATA Corp).

3. Results

3.1. Baseline characteristics

Our study collected the data from 7360 consecutive asymptomatic and symptomatic patients (4678 men, 2682 women) with suspected CAD who underwent coronary angiography from the 4 participating centres. A total of 937 patients were excluded from the study because of incomplete or absent data according to our study protocol. Table 1 shows the demographic and clinical characteristics of the various patient groups. The mean age was 59 years, ranging from 19 to 90 years.

A total of 4860 consecutive patients were diagnosed with CAD (at least 1 coronary stenosis \( \geq 50\% \) in the major epicardial arteries), and the remaining 2500 patients with normal coronary arteries were categorized as control subjects. All eight characteristics of the patient population showed statistically significant variation between CAD and non-CAD patients. The prevalence of CAD was significantly higher in men than in women. All variables were significantly different between CAD patients and non-CAD patients. The prevalence of diabetes was substantially higher in CAD patients. Of these characteristics, the incidence of angina, smoking and serum creatinine were higher in males than in females, while age and prevalence of diabetes, LDL and hypertension were higher in females than in males.
3.2. Identification of determinants of CAD using multivariate logistic regression

Stepwise multivariate logistic regression analysis was used to calculate a function model for evaluating the association between CAD and risk factors. The risk factors—variables $x_i$ and the coefficients $\beta_i$—are shown in Table 2. Eight risk factors—age, sex, chest pain, diabetes mellitus, smoking and lipids—were considered to be significant risk factors associated with CAD in the model. The meaning of each variable is shown in Table 2 and Appendix A. Among these factors, age, LDL, and serum creatinine were treated as continuous variables, while sex, diabetes, hypertension, angina and smoking were treated as binary variables.

The results of the logistic regression analysis enabled us to determine which characteristics were independently associated with the presence of CAD. Among these characteristics, age has an odds ratio of 1.0564, which indicates that with an increase of 1 year in age, the associated risk of CAD will also be increased by 1.0564 times. CAD develops slowly, so if this odds ratio is perceived in the context of a 10-year period, then the odds ratio for a 10-year period would be 1.73, which indicates that the risk of CAD increases by 1.73 times with an increase of 10 years in age, while the other factors remain constant. The male sex has an odds ratio of 1.96, which means that a male patient has a 1.96 times higher risk of CAD, while other factors remain the same. Diabetes mellitus has the highest odds ratio of 2.37, while angina has an odds ratio of 1.73.

3.3. Receiver-operating characteristics curve analysis of logistic regression analysis

Fig. 1 depicts the area under the curve (AUC) with sensitivity, specificity and the cut-off points of 0.792 using our logistic model. Employing age, sex, serum creatinine, smoking, LDL factors, history of diabetes and hypertension, the AUC was 0.727 ($P < 0.01$, Fig. 1A). After adding angina, the AUC was increased to 0.738 ($P < 0.01$, Fig. 1B). Therefore, angina was added as a risk factor for predicting CAD.

We also investigated the model performance in different subgroups. Fig. 1 depicts receiver operating characteristic curves for men and women that show good discrimination for the model. The area under the ROC curve was 0.7297 (95% CI, 0.7137–0.7456; $P < 0.001$) in males (Fig. 1C) and 0.7415 (95% CI, 0.7227–0.7602; $P < 0.001$) in females (Fig. 1D), suggesting that this model had a superior performance for identifying subjects with or without CAD among Chinese people.

4. Discussion

Using the recently collected clinical data, we developed a diagnosis model that performed well in predicting the presence of CAD. We first evaluated the ability of CAD to predict the prevalence of the anatomic disease in 7360 patients who were referred subsequently for invasive coronary angiography. This study is the first to apply a large sample from routine coronary angiography check-ups in Asia. The main findings suggest that a model developed from 8 routine clinical variables can classify patients with and without CAD.

Several personal cardiovascular risk characteristics, such as male sex, tobacco use, diabetes, high-level LDL, peripheral vascular disease, cerebrovascular disease, and hypertension, have been shown to be related to CAD risk, and none has been found to be strictly determinative. These risk factors take one of two forms. Some are qualitative factors, such as sex and diabetes. Others are quantitative factors, such as age, blood pressure or serum cholesterol. The angiographic assessment of coronary stenosis is a widely accepted and clinically useful method for risk stratification in patients with CAD. In our study, we construct an integrated appreciation model of CAD and compared it with the invasive CAG method. We found that age and diabetes are the most important CAD risk factors for the presence of angiographic CAD among the Chinese population. Regarding the screening of CAD, the lipid profile and type of chest pain constitute important factors in the diagnosis. The data from the 18-year Framingham Study showed that the relative risk for CAD in diabetic men and women, aged 45 to 74 years, is 2.4 and 5.1 times greater, respectively, than for age-

Table 1

| Parameters | With or without CAD | Sex |  |
| --- | --- | --- | --- |
|  | CAD ($n = 4860$) | Non CAD ($n = 2500$) | $P$ value | Male ($n = 4678$) | Female ($n = 2682$) | $P$ value |
| Male, n (%) | 3328 (68.47%) | 1350 (54.02%) | $<0.001$ | 4678 (100%) | 0 | $<0.001$ |
| Age (years) | 61.67 ± 9.93 | 55.61 ± 10.65 | $<0.001$ | 57.87 ± 11.42 | 61.60 ± 9.58 | $<0.001$ |
| Diabetes, n (%) | 1011 (22.65%) | 245 (9.80%) | $<0.001$ | 819 (17.5%) | 527 (19.65%) | $<0.001$ |
| Hypertension, n (%) | 65.90 ± 1.85 | 49.33 ± 1.15 | $<0.001$ | 58.14% | 64.01% | $<0.001$ |
| Angina, n (%) | 84.58% | 72.27% | $<0.001$ | 82.09% | 81.21% | $<0.001$ |
| Smoke, (%) | 44.46% | 31.56% | $<0.001$ | 59.06% | 69.7% | $<0.001$ |
| Serum creatinine (μmol/L) | 84.15 ± 23.11 | 76.88 ± 19.63 | $<0.001$ | 87.45 ± 20.61 | 71.59 ± 21.39 | $<0.001$ |
| LDL (mmol/L) | 2.79 ± 0.85 | 2.65 ± 0.76 | $<0.001$ | 2.66 ± 0.80 | 2.86 ± 0.85 | $<0.001$ |

CAD, coronary artery disease; ≥50% main coronary artery stenosis; LDL, low density lipoprotein.

Table 2

| Variables | Units | $\beta$ | OR | [95% Conf. Interval] | $P$ |
| --- | --- | --- | --- | --- | --- |
| Age | Years | 0.0549 | 1.0564 | [1.0507, 1.0622] | 0.000 |
| Sex | Male/female | 0.6743 | 1.96274 | [1.7045, 2.2500] | 0.000 |
| Scr | μmol/L | 0.0070 | 1.0070 | [1.0039, 1.0102] | 0.000 |
| Smoke | No = 0, yes = 1 | 0.0776 | 1.0776 | [1.0716, 1.0836] | 0.000 |
| Angina | Unypical = 0, typical = 1 | 0.5516 | 1.7360 | [1.5199, 1.9381] | 0.000 |
| Diabetes | No = 0, yes = 1 | 0.8641 | 2.3728 | [2.0282, 2.7760] | 0.000 |
| LDL | mmol/L | 0.2651 | 1.3036 | [1.2195, 1.3935] | 0.000 |
| Hypertension | No = 0, yes = 1 | 0.4663 | 1.5941 | [1.4300, 1.7769] | 0.000 |
| Constant | | –5.2782 | 0.0051 | [0.0032, 0.0079] | 0.000 |

OR, odds ratio; Scr, serum creatinine; LDL, low density lipoprotein.
matched nondiabetic men and women. In our model, angina is less of a risk factor than diabetes and age, because the identification of angina symptom can be interfered by coronary artery spasms, myocarditis and gastrointestinal tract disease factors. However, angina is still an important risk criterion for the diagnosis of CAD; and the strictly identification of typical angina is conducive to further optimize this model.

Previously, Diamond and Forrester showed the importance of age, sex, and symptoms in the prediction of CAD. However, the model tends to overestimate the probability of CAD, mainly in women, and does not consider cardiovascular risk factors associated with the disease. The Framingham risk score, which has been widely adopted in clinical guidelines, enables clinicians to estimate the 10-year individual risk of developing CAD. However, no study showed that the Framingham risk score could predict the presence of CAD compared with coronary angiography, and some risk markers are not incorporated. Several studies have demonstrated that the use of the Framingham risk score in other populations resulted in an overestimation of the CHD risk. While acknowledging the limitations to prediction accuracy in some European and Asian populations, several studies have compared the Framingham predictions with locally produced estimates in diverse populations and have found that the Framingham model either over- or under-estimates the CHD risk in these populations. This study extended the findings of previous studies by adding new clinical characteristics to the CAD prediction model.

The need to consider the cost of clinical decisions is becoming important. Cost-effectiveness analyses of CAD allow for more efficient use of health resources and rationalize the use of new technologies. It is believed that major risk factors such as smoking, high cholesterol, hypertension and sedentary lifestyle can be changed. Information about patient age, sex, smoking status, history of diabetes and hypertension are always available. Our model can provide an early diagnosis strategy for patients with possible CAD. The early prognosis of cardiovascular disease can aid in determining lifestyle changes in high-risk patients and, in turn, reduce their complications. High-risk patients should be considered candidates for more aggressive management that may include cardiac catheterization.

In most developing countries, cardiovascular specialists are not widely available to diagnose patients with CAD. Estimating the pre-test likelihood of angiographically significant CAD is a fundamental component in the initial evaluation of symptomatic patients presenting with suspected CAD. Using an automated system can assist the physician in making the accurate diagnosis well in advance. Heart disease diagnosis is a challenging task that can offer automated prediction about a patient’s heart disease so that additional treatment can be facilitated. The clinical value of estimating the likelihood of severe CAD depends on how this calculation might affect a physician’s management decisions. Our logistic regression $\beta$ coefficients can be published in scientific journals and then any end user with a hand-held calculator can
calculate the predicted probability of CAD. This model was easy to apply and was clinically relevant. Our model had fewer variables for CAD risk prediction compared with the Framingham score to fit for the more information availability in developing countries. It calculates a person's percentage risk of having CAD based on sex, age, history of hypertension and diabetes, LDL and smoking status.

This paper presents a reliable computational model for aiding the diagnosis of people with CAD. This model can calculate an individual's risk using patient data input by a clinician, and this model can also be used by healthcare personnel in remote rural hospitals for quick risk assessment. Further research is warranted for the development of more accurate strategies in the diagnosis of coronary disease using new biomarkers and artificial algorithms.

5. Conclusion

This study presents a multivariable risk factor model that can be conveniently used to assess patients with a risk of CAD. The estimated absolute CAD rate can be used to quantify risk and guide preventative primary care. The validity of the proposed general CAD risk model should be evaluated in future studies.

6. Study limitations and future directions

The present study has several limitations. First, the subjects in this study were patients who underwent coronary angiography for clinically suspected CAD. Therefore, the prevalence of CAD (66%) was high, and it is impossible to avoid a selection bias in diagnosis. Second, other risk factors not included in our model should be considered in evaluating risk, such as body mass index, electrocardiogram, C-reactive protein, indications of insulin resistance, triglycerides and a strong family history of premature CVD. However, we limited the number in order to simplify this model. Other variables will be added to future versions of this algorithm. Finally, the heterogeneity of data and the level of physician experience differed between hospitals. Some clinical data, such as duration and severity of chest pain, should be refined. Despite these limitations, our model presented a generally good discrimination (via the c statistic) and calibration.

To reduce cost and improve clinical efficiency, the next step is to develop a computer programme for simplifying the process of calculating the probability of CAD with our model. This approach can be applied by inputting the results of basic clinical assessments into a computer. It will assist the practitioner in deciding when additional treatment is appropriate, thus ensuring the patient access to essential care.

Conflicts of interest

The authors have none to declare.

Acknowledgments

This work was supported by the Doctor Start-up Fund in Liaoning Province, China [Grant No. 201601119]. The authors would like to thank the doctors of the hospitals for their assistance in the data collection.

Appendix A.

The following example illustrates the direct application of the logistic model to estimate CAD. The probability of CAD in a patient was calculated by the following equation:

\[ P = \frac{\exp(f(x))}{1 + \exp(f(x))} \]

where \( P \) is the probability of CAD, \( f(x) \) denotes the discriminant vector estimated by logistic regression, where \( f(x) = a_0 + \sum_{i=1}^{8} \beta_i x_i \). The \( \beta_i \) are the regression coefficients, and \( x_i \) are the eight clinical risk variables used to create the algorithms. \( a_0 \) is intercept; the values for \( \beta_i \) are shown in Table 2.

Age is a continuous number, male sex is coded as 1 and female is coded as 0, typical angina is coded as 1 and atypical angina is coded as 0, hypertension history is coded as 1 and no hypertension history is coded as 0.

For example, a 60-year-old man has an LDL of 1.95 mmol/L and serum creatinine of 129.1μmol/L, without hypertension, with typical angina and is a current smoker but is not diabetic.

The CAD diagnosis based on the model is computed as follows:

\[ f(x) = -5.2782 + 0.0549 * \text{age} + 0.6743 * \text{sex} + 0.007 * \text{Scr} + 0.4776 * \text{smoke} + 0.5516 * \text{angina} + 0.8641 * \text{diabetes} + 0.2651 * \text{Idl} \]

\[ = 1.5802. \]

\[ P = \frac{\exp(f(x))}{1 + \exp(f(x))} = \exp(1.5802)/(1 + \exp(1.5802)) = 0.8292. \]

The probability of the presence of CAD is larger than the cut-off value of 0.79, and this patient can be considered as a patient with CAD. A more aggressive diagnostic or therapeutic strategy is required.

References

1. He J, Gu D, Wu X, et al. Major causes of death among men and women in China. N Engl J Med. 2005;353:1124–1134.
2. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:576–599.
3. Goff Jr. DC, Jr., Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2935–2959.
4. Mauvourich-Horvat P, Ferencik M, Voros S, Merkely B, Hoffmann U. Comprehensive plaque assessment by coronary CT angiography. Nat Rev Cardiol. 2014;11:390–402.
5. Genders TS, Steyerberg EW, Alkadhi H, et al. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension. Eur Heart J. 2011;32:1316–1330.
6. Jee SH, Jang Y, Oh DJ, et al. A coronary heart disease prediction model: the Korean Heart Study. BMJ Open. 2014;4:e005025.
7. Zhu Z, Liu Y, Zhang C, et al. Identification of cardiovascular risk components in urban Chinese with metabolic syndrome and application to coronary heart disease prediction: a longitudinal study. PLOS ONE. 2013;8:e84204.
8. Shewon LG, Rosano G, Henein M, Coats AJ. A statement on ethical standards in publishing scientific articles in the International Journal of Cardiology family of journals. Int J Cardiol. 2014;170:253–254.
9. Genders TS, Steyerberg EW, Hunink MG, et al. Prediction model to estimate presence of coronary artery disease: retrospective pooled analysis of existing cohorts. BMJ. 2012;344:e3485.
10. Chiue SE, Cook NR, Shay CM, et al. Lifestyle-based prediction model for the prevention of CVD: the healthy heart score. J Am Heart Assoc. 2014;3.
11. Amir M, Kelushadi R. Comparison of models for predicting outcomes in patients with coronary artery disease focusing on microsimulation. Int J Prev Med. 2012;3:522–530.
12. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. N Engl J Med. 1979;300:1350–1358.
13. Hense HW, Schulte H, Lowel H, Assmann G, Keil U. Framingham risk function overestimates risk of coronary heart disease in men and women from Germany—results from the MONICA Augsburg and the PROCAM cohorts. Eur Heart J. 2003;24:937–945.
14. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013;34:2949–3003.
15. D’Agostino Sr, RB, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117:743–753.
16. Berger JS, Jordan CO, Lloyd-Jones D, Blumenthal RS. Screening for cardiovascular risk in asymptomatic patients. J Am Coll Cardiol. 2010;55:1169–1177.
17. Hemann BA, Bimson WF, Taylor AJ. The Framingham Risk Score: an appraisal of its benefits and limitations. Am Heart Hosp J. 2007;5:91–96.
18. Empana JP, Ducimetiere P, Arveiler D, et al. Are the Framingham and PROCAM coronary heart disease risk functions applicable to different European populations? The PRIME Study. Eur Heart J. 2003;24:1903–1911.

19. Kotseva K, Jennings CS, Turner EL, et al. ASPIRE-2-PREVENT: a survey of lifestyle, risk factor management and cardioprotective medication in patients with coronary heart disease and people at high risk of developing cardiovascular disease in the UK. Heart. 2012;98:865–871.

20. Lewandowski M, Szwed H, Kowalik I. Searching for the optimal strategy for the diagnosis of stable coronary artery disease. Cost-effectiveness of the new algorithm. Cardiol J. 2007;14:544–551.

21. Tuso P, Stoll SR, Li WW. A plant-based diet, atherogenesis, and coronary artery disease prevention. Perm J. 2014;.