

Diagnostic efficacy of optimised evaluation of planar MIBI myocardium perfusion scintigraphy: a probabilistic approach

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Abstract

BACKGROUND: The Bayesian (probabilistic) approach to the results of a diagnostic test appears to be more informative than an interpretation of results in binary terms (having disease or not). The aim of our study was the analysis of the effect of an optimised evaluation of myocardium perfusion scintigrams on the probability of CAD in individual patients.

METHODS: 197 patients (132 males and 65 females) suspected of CAD, with no history of myocardial infarction were examined. Scintigraphic images were evaluated applying two methods of analysis: visual (semiquantitative) and quantitative, and the combination of both. The sensitivity and specificity of both methods (and their combination) in the detection of CAD were determined and optimal methods of scintigram evaluation, separately for males and females, were selected. All patients were subjected to coronary angiography.

The pre-test probability of CAD was assessed according to Diamond (1) and the post-test probability was evaluated in accordance with Bayes's theorem. Patients were divided, according to a pre-test probability of CAD, into 3 groups: with low, medium and high probability of the disease. The same subdivision was made in relation to post-test probability of CAD. The numbers of patients in respective subgroups, before and after the test, were compared. Moreover, in order to test the reliability of post-test probability, its values were compared with real per-

centages of CAD occurrence among the patients under study, as demonstrated by the angiography.

RESULTS: The combination of visual and quantitative methods was accepted as the optimal method of male scintigram evaluation (with sensitivity and specificity equalling 95% and 82%, respectively) and a sole quantitative analysis as the optimal method of female scintigram evaluation (sensitivity and specificity amounted to 81% and 84%, respectively). In the subgroup of males the percentage of individuals with medium pre-test CAD probability equalled 52 and after the scintigraphic study it decreased to 21 ($p < 0.0001$). In the subgroup of females it changed from 60 to 43 ($p = 0.05$). The verification of the values of post-test probability revealed its high concordance with the real frequencies of CAD, with correlation coefficient being 0.98 and the regression line differing only slightly from the line of identity.

CONCLUSIONS: The results confirm the high reliability of the values of post-scintigraphic probability of CAD obtained in this way, and support the Bayesian, probabilistic interpretation of the study outcome and its application in the diagnostic process.

Key words: coronary artery disease, probability of CAD, Bayes's theorem, probabilistic approach, ^{201}Tl -MIBI, planar myocardium perfusion scintigraphy, sex differences

Introduction

The sensitivity and specificity of a diagnostic test are considered the most important indices of its efficacy. Knowledge of these indices, however, does not secure a proper evaluation of the diagnostic usefulness of a test. According to Bayes's theorem, the efficacy of a test, whose sensitivity and specificity are below 100%, depends also on the probability of disease in the population being studied. A direct application of Bayes's theorem to individual patients is also possible, provided one can assess the pre-test probability of a disease and the sensitivity and specificity of a test are also known.

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The pre-test probability of coronary artery disease (CAD) is related to multiple clinical variables such as sex, age, chest pain characteristics and the result of an electrocardiographic test (position of the ST wave). These probabilities were described by Diamond and Forrester in a series of 60 000 patients and their results may be applied to patients suspected of having CAD (1, 2).

The aim of our study was the practical application of Bayes's theorem to individual patients, especially the analysis of the effect of an optimised evaluation of myocardial perfusion scintigram on the probability of CAD.

Material and Methods

One hundred and ninety seven patients (132 males and 65 females) suspected of having CAD, with no history of myocardial infarction, were examined. All patients were subjected to coronary angiography, no later than 3 months after scintigraphic study. The degree of coronary artery stenosis was expressed as a percentage of the normal cross-section of the coronary artery. Stenosis exceeding 70% was accepted as critical. In 85 patients (64 males and 21 females) CAD was diagnosed, based on the detection of critical stenosis of at least one of the three main coronary arteries in angiography. In 112 patients (68 males and 44 females) critical stenoses of coronary arteries were not detected.

In all patients planar ^{201}Tl -MIBI stress and rest myocardial perfusion scintigraphies were performed, the studies being separated by at least 24 h. The stress test was performed in a standard way, a tracer being injected during a stress test on an ergometric bicycle. An activity of 740 MBq was applied to both studies. An acquisition was performed with a DDC camera by Picker coupled to a Siemens MaxDelta processing system, in 3 typical projections: anterior, LAO 45° and LAO 70°.

Scintigraphic images were evaluated applying two methods of analysis: visual (semiquantitative) and quantitative.

The visual (semiquantitative) method of analysis was based on the visual inspection of tracer uptake in segments assigned to 3 regions of the left ventricle: septum and anterolateral wall, posterolateral wall and inferior wall. The uptake was scored according to a three-grade system: 0 = normal uptake, 1 = moderately reduced and 2 = severely impaired uptake. For scintigraphic detection of CAD an optimised, semiquantitative criterion of regional perfusion reduction, worked out earlier (3), was applied.

A quantitative analysis of scintigrams, presented in earlier publications (3, 4), was based on a transformation of myocardial uptake of the tracer into circumferential profiles, subjected later to normative evaluation, i.e. compared with the profiles of normal patients with no CAD. Multivariate and discriminant analyses were then applied to the obtained quantitative measures of perfusion impairment, resulting in an optimised, quantitative criterion of CAD detection.

In subgroups of males and females, sensitivities and specificities of visual and quantitative methods of scintigraphic detection of CAD were determined, as well as indices of the diagnostic efficacy of the combination of both methods (a result was considered positive in the case of a positive outcome of at least one of the methods of scintigram evaluation).

Probabilistic Bayes's theorem

According to Bayes's theorem, the post-test probability of a disease is a function of its pre-test probability, and the sensitivity and specificity of the detection of the disease by a test. Under the assumption of the independence of test results from the clinical (pre-test) data, post-test probability can be calculated according to the following formula (5):

$$\text{post odds} = \text{prior odds} * \text{Likelihood ratio (LR)}$$

$$\text{where odds} = \text{probability}/(1-\text{probability})$$

$$\text{LR} = \text{sensitivity}/(1-\text{specificity}) \text{ in the case of a positive test result}$$

$$= (1-\text{sensitivity})/\text{specificity} \text{ in the case of a negative test result.}$$

Pre-test probability of CAD was determined making use of tables created by Diamond and Forrester (1), taking into account the patient's age, sex, chest pain characteristics, and the result of the electrocardiographic stress test (position of the ST wave). Post-test probability of CAD was calculated according to the formula presented above.

In the next step, patients were divided, according to a pre-test probability of CAD, into 3 groups: with low (less than 10 per cent), medium (between 10 and 80 per cent), and high (above 80 per cent) probability of the disease. The same subdivision was made in relation to post-test probability of CAD. Numbers of patients in respective subgroups, before and after the test, were compared.

Moreover, in order to test the reliability of the post-test probability, its values were compared with the real percentages of CAD occurrence among the patients under study. Accordingly, the whole probability range was subdivided into 5 subranges: $P \leq 20\%$, $20\% < P \leq 40\%$, $40\% < P \leq 60\%$, $60\% < P \leq 80\%$, and $P > 80\%$. In every subrange the mean probability of CAD for patients falling into this subdivision was calculated and this value was compared with the real frequency of CAD among these patients (percentage of coronarographically positive patients).

Results

The visual method detected 56 of 64 males with CAD (sensitivity — 88%) and 18 of 21 females (sensitivity = 86%). The specificity of the method amounted to 82% (56/68) in the subgroup of males and 59% (26/44) in the subgroup of females. Application of the quantitative method resulted in detection of CAD in 55 males (86%) and 17 females (81%). Its specificity equalled 87% (59/68) and 84% (37/44), respectively.

A combination of both methods resulted in a sensitivity of 95% (61/64) and a specificity of 82% (56/68) in the subgroup of males, whereas in the subgroup of females sensitivity of 95% (20/21) and specificity of 54% (24/44) were attained. Taking these results into consideration the authors decided to accept a combination of both methods as the optimal method of male scintigram evaluation and a sole quantitative analysis as the optimal method of female scintigram evaluation. The combination of visual and quantitative analysis for male scintigrams secured a higher sensitivity ($p < 0.05$) than the optimal (quantitative) method for female scintigram analysis, with no significant differences between the specificities of both methods.

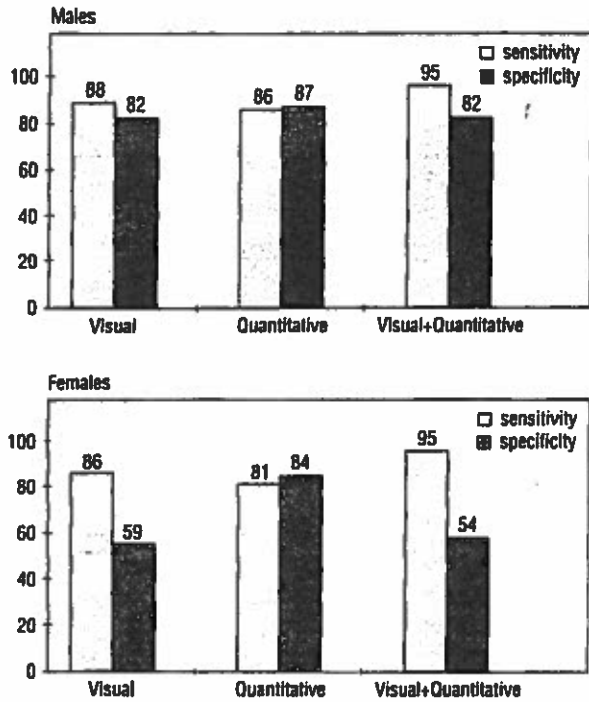


Figure 1. Diagnostic efficacy of visual, quantitative, and the combination of both methods of scintigram evaluation in the detection of CAD in males and females.

The numbers of males and females in the three subranges (below 10%, between 10% and 80% and above 80%) of pre-test and post-test probabilities are presented in Fig. 2. In the subgroup of males the percentage of individuals with medium pre-test CAD probability equalled 52 and after the scintigraphic study it decreased to 21 ($p < 0.0001$) and in the subgroup of females it changed from 60 to 43 ($p = 0.05$). Although the difference between the percentages of male and female patients in pre-test medium probability was non-significant (52% v. 60%, $p = 0.26$), after the scintigraphic study a significantly smaller part of males remained within this sub-range of probability (21% vs 43%, $p < 0.01$).

Figure 3. presents the results of a comparison of the mean post-scintigraphic-study probabilities of CAD, in five subranges, in all patients (males and females pooled together), with real frequencies of CAD occurrence among these patients. The correlation coefficient for these two variables equalled 0.98.

Discussion

In most published studies, the outcome of the test is reported in the 'classical' way in terms of sensitivity, specificity and predictive accuracy. Although this approach provides important information on the diagnostic quality of the test, one should remember that the sensitivity and specificity of any diagnostic test rely, among other factors, on the characteristics of the study population. It appears more informative to express the results of the test in probabilistic (Bayesian) rather than binary (6, 7) terms (having disease or not).

In our material 41 of 107 patients with medium pre-test probability (Fig. 2) were shifted, as a consequence of the negative

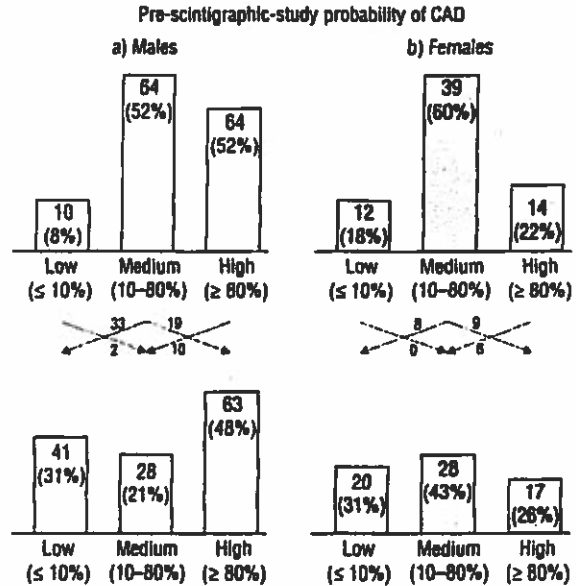


Figure 2. Numbers of males and females (percentages in brackets) in three ranges of probability of CAD: low, medium and high, before and after the myocardium perfusion scintigraphy.

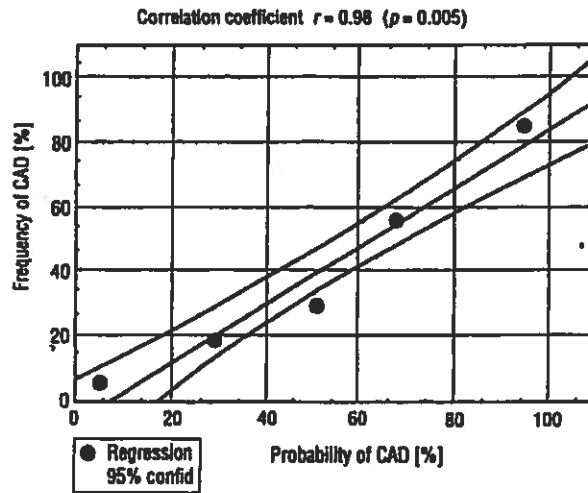


Figure 3. Frequencies of CAD v. mean post-scintigraphic-study probabilities (p) of CAD in 5 subranges: $p \leq 20\%$, $20\% < p \leq 40\%$, $40\% < p \leq 60\%$, $60\% < p \leq 80\%$, $p > 80\%$.

result of the perfusion study, to the low post-test probability range, and 28 patients were displaced to the high probability range. However, in 16 individuals with a high pre-test probability of CAD the negative outcome of the test decreased the probability and shifted them to the medium probability range, but apparently, it could not be a sufficient reason for exclusion of CAD in these patients. Some patients with low pre-test probability of CAD also happened to respond positively to the scintigraphic test. Two patients were displaced from the low to the medium probability range as a result of this positive response. These examples point to some diffi-

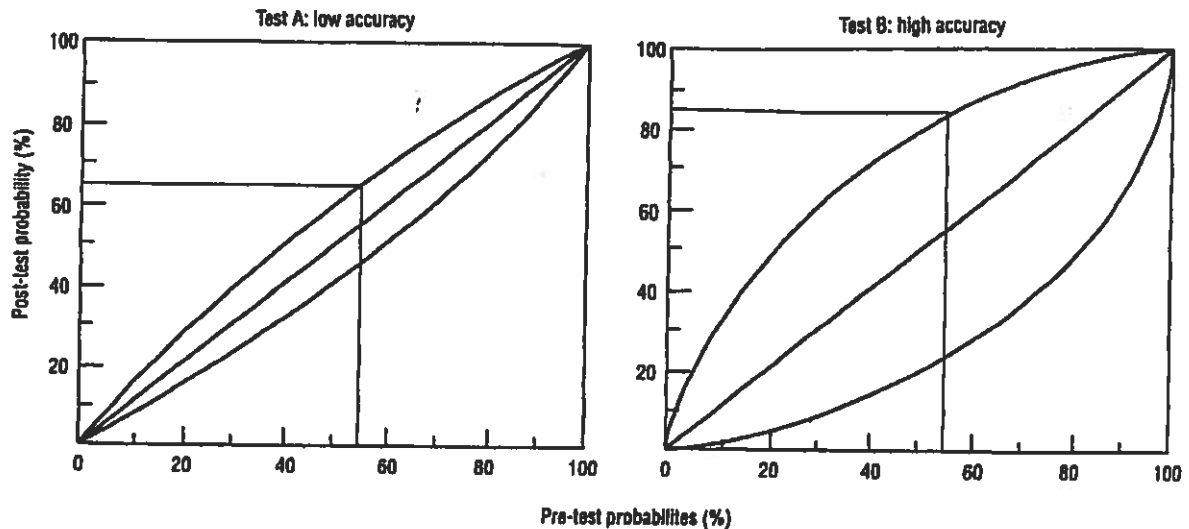


Figure 4. Schematic representation of the effect on post-test probability of two different diagnostic procedures (test A and B) with different diagnostic accuracies. See text for explanations.

culties in the interpretation of the test outcome in the Bayesian approach, but these problems are due to taking into account more information about a patient and reflect the more complex nature of a proper diagnostic process than a simple interpretation of a test result in binary terms (having disease or not). These examples also justify the statement that a group of patients that can benefit most from this kind of study are patients with medium probability of CAD. A positive result of the study causes the increase of CAD probability to high range and a negative result decreases it to low range, provided the test is highly discriminant, i.e. the value of the 'likelihood ratio' is high enough in the case of a positive response to the test and low enough when the result of the test is negative. The effect of test discriminant power on its diagnostic efficacy (6) is presented in Fig. 4, where the changes of probability of the disease after two tests are as follows: with low accuracy (sensitivity and specificity equal 60%) and a more accurate one (sensitivity and specificity equal 80%). Application of the first test in a patient with medium pre-test probability (55%) would not change the probability significantly (it would increase to about 65% in the case of a positive test result and decrease to about 40% if the result was negative). But if, in the same patient, a more accurate test was performed, he would benefit more, both in the case of the positive test result (the probability of disease would increase to 80%) as well as when the result was negative (a decrease of probability to about 20%). However, it should be emphasised, that to apply Bayesian analysis, the dependency of test results on clinical variables (information about the patient) must be excluded.

In the case of our test its lower sensitivity in females than in males resulted in a lower discriminant power of the test in female patients (especially, when the result of the test was negative). That was probably the reason for a greater part of females than males remaining in medium post-test probability range. The higher sensitivity of the study for males was reached owing to the application of the combination of two methods, visual and quantitative for the evaluation of scintigrams. In the case of male patients, the application of the quantitative assessment of scintigrams made a detection of CAD possible in 5 more patients (an increase of sensitivity from 88% to 95%) without a decrease of specificity. In the case of female patients, the reason for rejection of the visual method was its low specificity (59%) and thus the only method that remained at our disposal was the quantitative analysis of scintigrams. The sensitivity of this method, although high (81%), remained significantly lower than the sensitivity of the combination of the two methods applied in male patients (4).

The verification of the values of post-test probability, in the form of the real frequencies of CAD occurrence in five subranges of probability, revealed a high concordance of these variables, with the correlation coefficient being as high as 0.98 and the regression line differing only slightly from the line of identity. These results confirm the high reliability of the values of post-scintigraphic probability of CAD obtained in this way, and support the Bayesian, probabilistic interpretation of the study outcome and its application in the diagnostic process.

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References

1. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary artery disease. *N Eng J Med* 1979; 300: 1350-1358.
2. Diamond GA, Forrester JS, Hirsch M et al. Application of conditional probability analysis to the clinical diagnosis of coronary artery disease. *J Clin Invest*. 1980; 65: 1210-1221.
3. Kuśmierk J, Plachcińska A, Bieńkiewicz M., Kośmider M. Quantitative, multivariate analysis-based assessment of MIBI planar heart perfusion studies. In: Bergman H, Kohn H, Sinzinger H. Eds: *Radioactive Isotopes In Clinical Medicine and Research XXIII*. Basel, Switzerland: *Birkhauser Verlag* 1999; 487-490.
4. Plachcińska A, Kuśmierk J, Kośmider M, Bieńkiewicz M, Lniecki J. Quantitative assessment of technetium-99m methoxyisobutylisonitrile planar perfusion heart studies: application of multivariate analysis to patient classification. *Eur J Nucl Med* 1995; 22: 193-200.
5. Altman X. *Practical Statistics for Medical Research*. London: *Chapman and Hall*, 1991: 414-417.
6. Geleijnse ML, Marwick TH, Boersma E, Deckers JA, Melin JA, Fioretti PM. Optimal pharmacological stress testing for the diagnosis of coronary artery disease: a probabilistic approach. *Eur Heart J*, 1995; 16 (Supplement M): 3-10.
7. Beller GA. Detection of coronary artery disease. In: *Clinical Nuclear Cardiology*. Saunders WB Comp.: Philadelphia, 1995: 82-138.

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