

# Diagnostic Value of Arterial Blood Gas Measurement in Suspected Pulmonary Embolism

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Pulmonary embolism (PE) is a common and lethal yet treatable condition. Several authors have reported on the diagnostic value of combinations of arterial blood gas (ABG) and other clinical data (i.e., prediction rules), and have claimed that these combinations can be safely used to exclude PE. The purpose of this investigation was to evaluate the diagnostic value of ABG measurement and to attempt to validate the ABG prediction rules published by these various authors for the assessment of patients with suspected PE. Two hundred ninety-three consecutive patients referred for imaging to investigate suspected PE were approached to participate in the investigation. ABG and other clinical data were obtained from consenting and eligible patients before an outcome classification (PE versus non-PE) was performed. None of the ABG data or prediction rules had sufficient negative predictive value, specificity, or likelihood ratios to be useful in the management of patients with suspected PE. We conclude that ABG data alone or in combination with other clinical data are not useful in the assessment of suspected PE.

Pulmonary embolism (PE) is a common clinical condition. It is the third leading cause of cardiovascular mortality in North America, with an age- and sex-adjusted estimated incidence rate of 21 to 69 per 100,000 persons per year in population-based studies (1, 2). PE is also responsible for 5% to 10% of all in-hospital deaths (3–5). It is an important diagnosis to establish, given that undiagnosed PE has a hospital mortality rate as high as 30%, which falls to about 8% if PE is diagnosed and treated appropriately (4, 6, 7).

The diagnosis of PE remains one of the most difficult problems confronting clinicians. PE is considered in the differential diagnosis of many clinical presentations, including chest pain, hemoptysis, and dyspnea, and in a wide variety of clinical settings, such as emergency departments, obstetrics units, surgical wards, and intensive care units. Yet less than 35% of patients suspected of having PE actually have PE (8–11). Simple diagnostic tools, such as arterial blood gas (ABG) analysis, are often used at the bedside by clinicians to assist in making difficult management decisions in patients with suspected PE (e.g., to pursue a diagnosis of PE or not, to presumptively anticoagulate or not). However, a bedside method of evaluation for PE needs to: (1) ensure that patients who have PE are treated

(i.e., the bedside method is safe); and (2) ensure that many of those who do not have PE are not exposed to the hazards and inconveniences of further investigation and presumptive therapy (i.e., the bedside method excludes a large proportion of patients without PE).

One commonly held misconception, in the face of reports to the contrary (12), is that a normal alveolar–arterial oxygen tension gradient (A–a)Do<sub>2</sub> excludes PE (13). Cvitanic and Marino tried to improve on the sensitivity of the (A–a)Do<sub>2</sub> gradient in excluding PE by combining it with a normal arterial carbon dioxide tension (Pa<sub>CO<sub>2</sub></sub>) (i.e., normal [A–a]Do<sub>2</sub> and Pa<sub>CO<sub>2</sub></sub> > 36 mm Hg excludes PE) (14). McFarlane and Imperiale tried to improve the sensitivity of the (A–a)Do<sub>2</sub> gradient in excluding PE by combining it with the absence of a prior history of thromboembolic disease (i.e., a normal [A–a]Do<sub>2</sub> and no prior thromboembolic disease excludes PE) (15). Neither McFarlane and Imperiale's nor Cvitanic and Marino's rules as reported were 100% sensitive. More recently, Stein and colleagues reported that a normal (A–a)Do<sub>2</sub> gradient in the absence of prior thromboembolic disease had a sensitivity of only 89% (16), and that a normal (A–a)Do<sub>2</sub> gradient and a Pa<sub>CO<sub>2</sub></sub> > 35 mm Hg had a sensitivity of only 92% in excluding PE (13). A second limitation to these rules is that their clinical utility, as measured by the proportion of patients correctly excluded, was either not measured (14) or was low (15).

Recently, Egermayer and colleagues examined the safety and clinical utility of the SimpliRED D-dimer test, arterial oxygen tension, and respiratory rate (RR) measurement for excluding PE. They determined that the best combination of findings for excluding PE was a negative SimpliRED test (Agen Biomedical Ltd., Acadici Ridge, Australia) and an arterial oxygen tension (Pa<sub>O<sub>2</sub></sub> ≥ 80 mm Hg, which gave a sensitivity and negative predictive value of 100% in their derivation study (17). Egermayer and colleagues concluded that it was safe to exclude PE with a negative SimpliRED D-dimer test result and a Pa<sub>O<sub>2</sub></sub> ≥ 80 mm Hg.

The purpose of the present investigation was to attempt to validate these previously published prediction rules through ABG analysis.

## METHODS

Over a 30-mo period, consecutive inpatients and outpatients at the Ottawa General Hospital who were suspected of having PE and were referred for a ventilation–perfusion (V/Q) scan or pulmonary angiogram were approached for consent to participate in a study being done to develop a clinical prediction rule for excluding PE. Patients were excluded from the study if they: (1) were less than 18 yr of age; (2) were unable to give informed consent; (3) required pulmonary angiography and had a contraindication to pulmonary angiography; (4) were ventilated; or (5) were in the final stages of terminal disease. The study protocol was approved by the institutional review board of the Ottawa General Hospital, and all participants signed informed consent.

A latex D-dimer (Accuclot; Sigma Diagnostics, St. Louis, MO) or whole-blood agglutination D-dimer (SimpliRED) test was performed

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TABLE 1  
DEMOGRAPHIC CHARACTERISTICS, PRESENTING SYMPTOMS, AND TEST RESULTS  
USED IN OUTCOME CLASSIFICATION IN TOTAL STUDY POPULATION CONSISTING  
OF PATIENTS WITH AND PATIENTS WITHOUT PULMONARY EMBOLISM

	All Patients (n = 246)	PE (n = 49)	No PE (n = 163)	Unclassified (n = 34)
Mean age, yr (SD)	53.9 (17.6)	58.9 (14.8)	50.6 (17.8)*	63.0 (15.3)
Female, %	60.6%	40.8%	67.5%*	55.9%
Outcome determined by		Positive angiogram (n = 16) High-probability $\dot{V}/\dot{Q}$ scan with intermediate to high pretest probability (n = 33)	Normal angiogram (n = 28) Normal $\dot{V}/\dot{Q}$ scan (n = 90) Low-probability $\dot{V}/\dot{Q}$ scan with low pretest probability (n = 19) Low-probability $\dot{V}/\dot{Q}$ scan with nor- mal ultrasound examination (n = 26)	Low-probability $\dot{V}/\dot{Q}$ scan with inter- mediate to high pretest prob- ability; no angiogram; no ultra- sound examination (n = 22) Intermediate probability $\dot{V}/\dot{Q}$ scan; no angiogram (n = 10) High-probability $\dot{V}/\dot{Q}$ scan; low pre- test probability; no angiogram (n = 2)
Chest pain or dyspnea	94.9%	95.9%	94.2%	96.6%

Definition of abbreviations: PE = pulmonary embolism;  $\dot{V}/\dot{Q}$  = ventilation/perfusion.

\* p < 0.05.

on venous blood within 24 h after  $\dot{V}/\dot{Q}$  scanning or pulmonary angiography. ABG analyses were performed by collecting blood from a single arterial puncture within 24 h of outcome measurement, and subjecting it to analysis on a CIBA Corning 278 blood gas system (Chiron Diagnostics, Maryland).

The referring physician first assigned an index of clinical suspicion of PE (i.e., gestalt pretest percentage likelihood of PE) on the basis of all available clinical data (i.e., history, physical examination, blood gas analysis, D-dimer test, electrocardiogram, and chest radiograph). Patients were excluded if a pretest probability was assigned after  $\dot{V}/\dot{Q}$  scanning or pulmonary angiography.

All patients in the study underwent  $\dot{V}/\dot{Q}$  scanning. Two nuclear medicine physicians independently interpreted all scans, utilizing the criteria of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) (8). In the event of a discrepancy in interpretation, the  $\dot{V}/\dot{Q}$  scan was reinterpreted, with the reinterpretation assigned by consensus. After the  $\dot{V}/\dot{Q}$  scan, patients with a posttest probability of PE of less than 5% were considered for study purposes not to have PE. This group was defined as: (1) patients with normal or nearly normal  $\dot{V}/\dot{Q}$  scans; (2) patients with a low pretest index of clinical suspicion who had low-probability  $\dot{V}/\dot{Q}$  scans (8); and (3) patients with low-

probability  $\dot{V}/\dot{Q}$  scans who had a negative result of leg vein ultrasound examination at presentation (9). After  $\dot{V}/\dot{Q}$  scanning, patients with a posttest probability of 88% or greater for PE were considered for study purposes to have a PE. These patients were defined as patients with a high or intermediate index of pretest clinical suspicion of PE who had high-probability  $\dot{V}/\dot{Q}$  scans (8). All other patients were recommended for subsequent pulmonary angiography, but this decision was left to the patient's treating physician. Those patients with indeterminate scans who did not undergo angiography were excluded from the data analysis.

Continuous data in the PE and non-PE groups were compared with a *t* test for independent groups, with equal variances assumed if Levene's test gave a nonsignificant result. If Levene's test gave a significant result, a *t* test for independent groups with unequal variances was performed. Pearson's chi-square tests were used to compare proportions between the two groups. A value of p < 0.05 was taken as indicating a statistically significant difference. Likelihood ratios, sensitivity, specificity, and positive and negative predictive values were determined for any variable or combination of variables reaching statistical significance, and for the previously published ABG-based rules for excluding PE.

TABLE 2  
PREVALENCE OF ARTERIAL BLOOD GAS, D-DIMER, RESPIRATORY RATE ABNORMALITIES, PRIOR  
DEEP VEIN THROMBOSIS/PULMONARY EMBOLISM, AND COMBINATIONS OF THESE  
ABNORMALITIES IN PATIENTS WITH SUSPECTED PULMONARY EMBOLISM

Clinical Variable	All Patients (n = 212)	
	PE (n = 49)	No PE (n = 163)
Arterial blood gas data		
Pa <sub>O<sub>2</sub></sub> < 80 mm Hg	57.9%	46.6%
Pa <sub>CO<sub>2</sub></sub> < 36 mm Hg	44.4%	39.7%
Abnormal (A-a)D <sub>O<sub>2</sub></sub> gradient	84.2%	72.6%
D-dimer data		
D-dimer positive	83.0%	42.4%*
Prior DVT/PE		
Prior history of DVT or PE	34.7%	13.6%*
Respiratory rate		
Respiratory rate > 20 breaths/min	48.6%	39.3%
Combinations		
Abnormal (A-a)D <sub>O<sub>2</sub></sub> gradient or Pa <sub>CO<sub>2</sub></sub> < 36 mm Hg	91.9%	85.3%
Abnormal (A-a)D <sub>O<sub>2</sub></sub> or prior history of DVT/PE	92.1%	78.9%*
Pa <sub>O<sub>2</sub></sub> < 80 mm Hg or D-dimer positive or respiratory rate > 20 breaths/min	96.9%	78.7%*
Pa <sub>O<sub>2</sub></sub> < 80 mm Hg or D-dimer positive	91.9%	67.6%*

Definition of abbreviations: (A-a)D<sub>O<sub>2</sub></sub> = alveolar-arterial oxygen tension gradient; DVT = deep vein thrombosis; Pa<sub>CO<sub>2</sub></sub> = arterial carbon dioxide tension; Pa<sub>O<sub>2</sub></sub> = arterial oxygen tension; PE = pulmonary embolism.

\* p < 0.05.

## RESULTS

Between January 1996 and August 1998, 293 consecutive patients with suspected PE were approached for participation in the study. A total of 282 patients were eligible, and 246 patients gave consent. Among these 246 patients, 49 had PE (19.9%), 163 did not have PE (66.3%), and 34 (13.8%) could not be classified with acceptable outcome measures (Table 1). ABG analysis was done for 155 of the 212 classified patients, and a D-dimer result was obtained for 196 of the 212 classified patients. The majority of ABG analyses were performed with breathing of room air (135 of 155 patients; 87.1%). Age, sex, and source of referral were not significantly different in comparing unclassified patients and classified patients. Patients with PE were significantly older than those without PE, and were more likely to be male than female. Almost all patients presented with chest pain or shortness of breath (Table 1).

Of the individual clinical variables that formed the focus of this investigation, only a positive D-dimer test result and a history of previous deep-vein thrombosis or PE were predictive of PE (Table 2). An RR > 20 breaths/min, a PaO<sub>2</sub> < 80 mm Hg, a PaCO<sub>2</sub> < 36 mm Hg, or an abnormal (A-a)DO<sub>2</sub> gradient were not predictive of PE in patients suspected of having PE (Table 2). The mean (A-a)DO<sub>2</sub> gradient and RR were, however, statistically significantly different in the PE (75.7 mm Hg and 23.6 breaths/min, respectively) and non-PE groups (49.3 mm Hg and 21 breaths/min, respectively). However, there was no difference between the two groups in either the mean PaO<sub>2</sub> or the mean PaCO<sub>2</sub>.

In patients presenting with dyspnea, neither the mean PaO<sub>2</sub> nor the mean PaCO<sub>2</sub> were statistically significantly different in the PE (81.6 mm Hg and 35.6 mm Hg) and non-PE groups (84.6 mm Hg and 36.9 mm Hg). There was also no difference in mean PaO<sub>2</sub> and PaCO<sub>2</sub> in the subgroup without dyspnea of the PE group as compared with the same subgroup of the non-PE group.

Of the previously published combinations of the foregoing clinical predictors for excluding PE, only Egermayer and colleagues' combinations (a negative D-dimer test result, PaO<sub>2</sub> > 80 mm Hg, and RR < 20 breaths/min exclude PE; and a negative D-dimer test result and PaO<sub>2</sub> > 80 mm Hg exclude PE) had negative predictive values over 90%. The remaining combinations had negative predictive values of less than 90% (Table 3). Egermayer and colleagues' combinations had likelihood ratios of less than 1.5 (Table 3).

## DISCUSSION

ABG analysis either alone or in combination with other clinical variables is of very limited diagnostic utility in suspected PE.

When faced with a patient with suspected PE, clinicians seek clinical clues that will enable them to increase or decrease the pretest probability of PE. For example, the finding of a normal (A-a)DO<sub>2</sub> gradient has been suggested as excluding PE. However, as we and others have shown, a normal (A-a)DO<sub>2</sub> gradient is equally likely to be found in patients with and without PE who were initially suspected of having PE. Hence, in our study patients, the finding of a normal (A-a)DO<sub>2</sub> gradient did not offer the clinician any additional diagnostic information.

When determining whether to perform a diagnostic test, clinicians must determine whether the results of studies of the test are valid, whether the results of these investigations are applicable to their patients, and whether the results of the test are likely to change patient management (18, 19). Previous investigations of the diagnostic value of ABG analysis in suspected PE have been limited by patient selection and by failure to compare the results of ABG analysis to an appropriate reference standard (14, 15). In McFarlane and Imperiale's study (13), patients without high probability V/Q scans were excluded from investigation, thereby introducing a significant selection bias. Cvitanic and Marino's investigation (14) was limited by their having studied only patients with confirmed PE and not examining patients with suspected PE. Hence, the diagnostic value of the combination of a normal (A-a)DO<sub>2</sub> and normal PaCO<sub>2</sub> could not be described in the Cvitanic and Marino study. Further, their study population was also a highly selected group of patients with PE (with positive angiograms only).

In our investigation, patient selection was minimized by including consecutive inpatients and outpatients referred for imaging done to exclude or diagnose PE. Ideally, all patients would have had the reference standard (pulmonary angiography or a normal V/Q scan). Unfortunately, it is not uncommon in clinical practice that clinicians do not pursue pulmonary angiography or other tests in patients with indeterminate V/Q scans (20, 21). Clinicians' reluctance, to use the "gold standard" of pulmonary angiography even in the setting of a clinical trial (as we experienced), obligates investigators to use imperfect outcome measures. Even if a group of investigators were able to convince clinicians to obtain pulmonary angiograms of all

TABLE 3  
DIAGNOSTIC VALUES ASSOCIATED WITH COMBINATIONS OF  
ABNORMALITIES IN SUSPECTED PULMONARY EMBOLISM

Variable Do <sub>2</sub>	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)	Likelihood Ratio*
Abnormal (A-a)DO <sub>2</sub> gradient	84.2% (32/38)	27.4% (32/117)	27.4% (32/117)	84.2% (32/38)	1.16
D-Dimer positive	83.0% (39/47)	57.6 (83/144)	39% (39/100)	91.2% (83/91)	1.96
Abnormal (A-a)DO <sub>2</sub> gradient or PaCO <sub>2</sub> < 36 mm Hg	91.9% (34/37)	14.7% (17/116)	25.6% (34/133)	85.0% (17/20)	1.08
Abnormal (A-a)DO <sub>2</sub> gradient or prior DVT/PE	92.1% (35/38)	21.1% (24/114)	28.0% (35/125)	88.9% (24/27)	1.17
PaO <sub>2</sub> < 80 mm Hg or D-dimer positive or respiratory rate > 20 breaths/min	96.9% (31/32)	21.3% (19/89)	30.7% (31/101)	95.0% (19/20)	1.23
PaO <sub>2</sub> < 80 mm Hg or D-dimer positive	91.9% (34/37)	32.4% (34/105)	32.4% (34/105)	91.9% (34/37)	1.36

Definition of abbreviations: (A-a)DO<sub>2</sub> = alveolar-arterial oxygen tension gradient; DVT = deep vein thrombosis; PaCO<sub>2</sub> = arterial carbon dioxide tension; PaO<sub>2</sub> = arterial oxygen tension; PE = pulmonary embolism.

\* Likelihood ratio = sensitivity/1 - specificity.

patients with suspected PE, as was done in the PIOPED study, it is likely that a highly selected study group would remain, as occurred in the PIOPED study (1,493 patients consenting, among 3,016 eligible patients) (8). This degree of selection almost certainly results in a biased study sample. In our study, we attempted to minimize selection bias and maximize the accuracy of diagnosis by utilizing the reference standard whenever possible (normal  $\dot{V}/\dot{Q}$  and pulmonary angiograms) and by otherwise using validated combinations of  $\dot{V}/\dot{Q}$  scan results and pretest probability of PE or leg vein imaging. All imaging was interpreted by physicians unaware of patient presentation and outcomes, thereby minimizing interpretation bias.

An abnormal (A-a)DO<sub>2</sub> gradient, tachypnea, a PaO<sub>2</sub> < 80 mm Hg, and a PaCO<sub>2</sub> < 36 mm Hg in patients with suspected PE appears to have no diagnostic or discriminatory value. In our population, McFarlane and Imperial's rule (a normal [A-a]DO<sub>2</sub> and no previous venous thromboembolism exclude PE) and Cvitanic and Marino's rule (a normal [A-a]DO<sub>2</sub> gradient and PaCO<sub>2</sub> < 36 mm Hg exclude PE) both gave specificities, sensitivities, negative predictive values, positive predictive values, and likelihood ratios that were too low to be clinically useful, and consequently should not be used in the assessment of patients with suspected PE.

In 1998, Egermayer and colleagues found that the combination of a negative D-dimer test result and a PaO<sub>2</sub> ≥ 80 mm Hg had a negative predictive value of 100% in patients with suspected PE. However, in our study population, we were able to demonstrate a negative predictive value of only 91.9% for this clinical prediction rule. Egermayer further showed that a negative D-dimer, test result, a PaO<sub>2</sub> of ≥ 80 mm Hg, and an RR < 20 breaths/min also had a negative predictive value of 100% in patients with suspected PE. Yet in our study population we were able to demonstrate a negative predictive value of only 95% with this rule. Although Egermayer's rules had negative predictive values above 90%, their ability to correctly exclude PE in large proportions of patients with suspected PE was limited (i.e., the specificity with these rules was low). This is further demonstrated by the small (less than 1.5) likelihood ratio with these rules.

In summary, it is very unlikely that the pretest probability of PE would be raised above the treatment threshold or below the further test threshold with any of the ABG findings suggested in the earlier studies described here, or with ABG-based prediction rules. Invariably, further testing of the value of ABG analysis in confirming or excluding PE will be required. In other words, ABG analysis should not be ordered to either rule in or rule out PE.

In conclusion, ABG analysis is of limited diagnostic value in patients with suspected PE.

## References

- Anderson FA, Wheeler HB, Goldberg J, Hosmer DW, Patwardan NA, Jovanovic B, Forcier A, Dalen JE. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. *Arch Intern Med* 1991;151:933-938.
- Silverstein MD, Heit J, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. *Arch Int Med* 1998;158:585-593.
- Dismuke SE, Wagner EH. Pulmonary embolism as a cause of death. The changing mortality in hospitalized patients. *JAMA* 1986;255:2039-2042.
- Dalen JE, Alpert JS. Natural history of pulmonary embolism. *Prog Cardiovasc Dis* 1975;17:257-270.
- Nordstrom M, Lindblad B. Autopsy-verified venous thromboembolism within a defined urban population—the city of Malmo, Sweden. *APMIS* 1998;106:378-384.
- Carson JL, Kelley MA, Duff A, Weg JG, Fulkerson WJ, Palevsky HI, Schwartz JS, Thompson BT, Popovich J Jr, Hobbins TE. The clinical course of pulmonary embolism. *N Engl J Med* 1992;326:1240-1245.
- Alpert JS, Smith R, Carlson J, Ockene IS, Dexter L, Dalen JE. Mortality in patients treated for pulmonary embolism. *JAMA* 1976;236:1477-1480.
- PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism: results of the prospective investigation of pulmonary embolism diagnosis study (PIOPED). *JAMA* 1990;263:2753-2759.
- Wells PS, Ginsberg JS, Anderson DR, Kearon C, Gent M, Turpie AG, Bormanis J, Weitz J, Chamberlain M, Bowie D, et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism. *Ann Intern Med* 1998;129:997-1005.
- Hull RB, Hirsh J, et al. Pulmonary angiography, ventilation lung scanning, and venography for clinically suspected pulmonary embolism with abnormal perfusion lung scan. *Ann Intern Med* 1985;98:891-899.
- Hull RD, Raskob GE, Coates G, Panju AA, Gill GG. A new noninvasive management strategy for patients with suspected acute pulmonary embolism. *Arch Intern Med* 1989;149:2439-2455.
- Stein PD, Goldhaber SZ, Henry JW. Alveolar-arterial oxygen gradient in the assessment of acute pulmonary embolism. *Chest* 1995;107:139-143.
- McFarlane MJ, Imperiale TF. Use of the alveolar-arterial oxygen gradient in the diagnosis of pulmonary embolism [published erratum appears in *Am J Med* 1998;105:458]. *Am J Med* 1994;96:57-62.
- Cvitanic O, Marino PL. Improved use of arterial blood gas analysis in suspected pulmonary embolism. *Chest* 1989;95:48-51.
- McFarlane MJ, Imperiale TF. Use of the alveolar-arterial oxygen gradient in the diagnosis of pulmonary embolism. *Am J Med* 1994;96:57-62.
- Stein PD, Goldhaber SZ, Henry JW, Miller M. Arterial blood gas analysis in the assessment of suspected acute pulmonary embolism. *Chest* 1996;109:78-81.
- Egermayer P, Town GI, Turner JG, Heaton DC, Mee AL, Beard ME. Usefulness of D-dimer, blood gas, and respiratory rate measurements for excluding pulmonary embolism. *Thorax* 1998;53:830-834.
- Jaeschke R. Users' guides to the medical literature: III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. *JAMA* 1994;271:703-707.
- Jaeschke R. Users' guides to the medical literature: III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group. *JAMA* 1994;271:389-391.
- Schluger N, Henschke C, King T, Russo R, Binkert B, Rackson M, Hayt D. Diagnosis of pulmonary embolism at a large teaching hospital. *J Thorac Imag* 1994;9:180-184.
- van Beek EJR, Buller HR, Brandjes DP, Rutten GC, ten Cate JW. Diagnosis of clinically suspected pulmonary embolism: a survey of current practice in a teaching hospital. *Neth J Med* 1997;44:50-55.