Upsala J Med Sci 112 (1): 73–82, 2007

Grade of Aortic Atherosclerosis: A Valuable Adjunct to Coronary Flow Velocity Reserve in the Evaluation of Coronary Artery Disease

Attila Nemes, Attila Thury, Tamás Forster, Krisztina Boda, Miklós Csanády

2nd Department of Medicine and Cardiology Centre, Medical Faculty, Albert Szent-Györgyi Medical and Pharmaceutical Centre, University of Szeged, Hungary

Abstract

Background: Atherosclerosis is a generalized disease of the arterial vasculature; among thus it manifests in the descending aorta and the coronary arteries. We tested whether known risk factors, the coronary flow velocity reserve and the grade of aortic atherosclerosis detected by transoesophageal echocardiography in the course of the same semi-invasive examination is able to distinguish between patients with significant left anterior descending coronary artery (LAD) stenosis or with multivessel disease.

Methods and results: The present study involved 125 consecutive patients (mean age: 56±11 years, range: 22–73) with chest pain undergoing coronary angiography. Grade of aortic atherosclerosis was obtained by means of transoesophageal echocardiography, and the coronary flow velocity reserve was calculated in the left anterior descending coronary artery. The age (ROC area, 63%, $p<0.01$), the gender (ROC area, 63%, $p<0.02$) and the grade of aortic atherosclerosis (ROC area, 64%, $p<0.01$) exhibited good power for the prediction of patients with multivessel disease from among all other patients. Only the grade of aortic atherosclerosis (ROC area, 63%, $p<0.05$) appears useful to distinguish patients with left anterior descending coronary artery disease from those with multivessel disease.

Conclusions: These results demonstrate that grade of aortic atherosclerosis furnishes additional help in the prediction of patients with severe coronary artery disease. It can differentiate patients with multivessel disease from those with significant left anterior descending coronary artery stenosis. Coronary flow velocity reserve has no any prognostic power in this evaluation.

List of abbreviations

AA = aortic atherosclerosis
ANOVA = analysis of variance
AOS = aortic valve stenosis
CAD = coronary artery disease
CFR = coronary flow velocity reserve
CI = confidence interval
CX = left circumflex coronary artery
LAD = left anterior descending coronary artery
MVD = multivessel disease
OR = odds ratio

Received 15 August 2006
Accepted 28 August 2006

RC = right coronary artery
ROC = receiver operator characteristic
TEE = transesophageal echocardiography

Introduction

Atherosclerosis is a generalized disease of the arterial vasculature; among thus it manifests in the descending aorta and the coronary arteries. The detection of atherosclerotic plaques in the descending aorta by multiplane transesophageal echocardiography (TEE) has been found to be indicative of coronary artery disease (CAD) [1,2]. The severity of aortic atherosclerosis (AA) can be classified by TEE by using an echocardiography-based five-grade scale [2]. The absence of atherosclerotic lesions in the thoracic aorta indicates the absence of significant CAD [3]. Few data are available concerning the relation between the grade of AA and the severity of CAD. Khoury et al. found that the combinative plaque score of the extracardiac vessels was significantly higher in patients with multivessel CAD than in patients with single-vessel CAD disease or with normal coronary arteries ($p<0.001$) [4].

Measurement of the coronary flow velocity reserve (CFR) characterizes the reserve capacity of a coronary artery and establishes the functional significance of an epicardial coronary stenosis [5]. This concept was first exploited invasively by measuring the baseline and hyperemic (i.e. after intravenous adenosine administration) average peak velocities with an intracoronary Doppler wire [6]. TEE is capable of measuring the blood velocity in the proximal left anterior descending coronary artery (LAD). TEE Doppler evaluation of the coronary blood flow velocity under baseline conditions and during dipyridamole-induced coronary vasodilation was first described by Iliceto et al. [5]. The sensitivity and specificity of the CFR, assessed by Doppler TEE (TEE-CFR), for the detection of significant obstruction in the LAD proved to be high [7].

During the present study, we tried to find a clinically available risk factor or echocardiographic parameter for the differentiation of multivessel disease from LAD disease before the operation. Regarding to the fact, that TEE allows the parallel evaluation of the CFR and the severity of aortic atherosclerosis, we tested whether known risk factors, TEE-CFR and the grade of AA detected by TEE in the course of the same semi-invasive examination is able to distinguish between significant stenosis of the LAD and MVD. Additionally, we created a prediction model for MVD by using the variables correlating significantly with the presence of MVD, in order to evaluate the advantage of measuring AA, too.

Subjects, materials and methods

Study population. The study comprised 125 consecutive patients (mean age: 56±11 years, range: 22–73) with chest pain without a previous myocardial infarction in

whom coronary angiography were planned. AA grade determination and TEE-CFR measurement were undertaken as part of a prospective investigation aimed at establishment of the clinical utility of the TEE-CFR. All 125 patients underwent coronary angiography with the following results: negative, non-significant CAD, significant LAD stenosis or significant multivessel disease (MVD). MVD was defined as significant stenosis of the LAD and/or CX and/or RC, or significant left main coronary artery stenosis. Patients with isolated left circumflex coronary artery (CX) and/or right coronary artery (RC) stenosis were excluded from the study, because the CFR characterizes the functionality of the LAD and the measurements were made on that. Coronary stenosis was assessed by a digital caliper method, with the Siemens HiCor^{TM} biplane angiographic system; a diameter reduction >50% was considered to be significant when the „worst view method" was applied. Fourty-seven patients with anatomically non-significant CAD (group 1), 34 patients with significant LAD disease (group 2) and 44 patients with MVD (group 3) were examined. None of the patients had significant valvular heart disease. Informed consent was obtained from each patient and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in *a priori* approval by the institution's human research committee.

Transesophageal echocardiography. TEE was performed with the ATL® Ultramark 9 HDI echocardiography equipment, using a 5.5 MHz biplane transducer. TEE-CFR measurements were carried out according to the standard protocol proposed by Iliceto et al. [5]). Patients were lying in the left lateral decubitus position, and TEE examinations were made in each patient after sedation with 2.5–5 mg intravenous midazolam. In all patients, the aortic root and the proximal portion of the LAD were visualized in the transversal plane. The biphasic coronary flow waveform was recorded in the LAD by pulsed Doppler. Flow measurements were made under baseline conditions and after the administration of 0.56 mg/kg dipyridamole over 4 minutes. The peak velocities were measured in the 6th minute at maximal vasodilation. All measurements were recorded on super-VHS videotape. In each case, five consecutive cycles were measured and averaged. The CFR was calculated as the ratio of the hyperemic to the basal peak diastolic flow velocity. Blood pressure was monitored under baseline conditions and during stress. At the end of the examination, the AA grading of the thoracic descending aorta at the level of the left atrium was performed as proposed by Fazio et al. [2]: grade 0: no atherosclerosis, grade 1: intimal thickening, grade 2: <5 mm plaque, grade 3: >5 mm plaque, grade 4: plaque with mobile parts. Patients with grade 2, 3 or 4 were grouped together as those in whom the presence of macroscopic atherosclerosis was regarded as proved. Parameters were considered at the „worst place" (2). All TEE examinations proceeded coronary angiography.

Statistical analysis. Data are reported as means±standard deviation; 95% confidence intervals are also given. Analyses were performed with a standard software package (SPSS 9.0, SPSS Inc. Chicago, IL, USA). Variables were compared by a

multiple ANOVA test between patient groups. For dichotomous values, Fisher's exact test was used where needed. To establish the prediction power of the variables, receiver operating characteristic (ROC) curves were constructed and the areas under curves are reported, $p < 0.05$ was considered statistically significant. Binary logistic regression tests were performed to study the correlation of the variables with the results of coronary angiography. Variables showing significant correlations were entered in a multiple regression analysis; a statistical model was created in order to assess the overall predictive value. A likelihood ratio test was performed to evaluate the difference between the model with or without entering the grade of AA.

Results

Correlation of risk factors and the presence of AA with CAD. The mean age and the incidences of arterial hypertension and diabetes mellitus were not significantly different between patient groups (Table 1). The fasting glucose and cholesterol levels did not differ between the groups. The prevalence of male gender was significantly higher in patients with MVD. The prevalence of hypercholesterolemia was significantly lower in patients without major CAD. The mean grade of aortic atherosclerosis was increased in patient with significant CAD (Figure 1). The CFR was significantly decreased in the patients with signifiant LAD stenosis or MVD as compared with the patients without major CAD (Figure 2). The CFR was decreased in aortic intimal thickening (grade 1 AA) and no further decrease could be observed in the presence of aortic plaque (grade 2–3 AA) (Figure 3).

Differentiation of patients with MVD from all other patients. Binary logistic regression and ROC curves were utilized to establish the prognostic power of traditional risk factors, aortic grade and the CFR for the to selection of patients with MVD (Table 2). The age (ROC area, 63%, $p < 0.01$), the gender (ROC area, 63%, $p < 0.02$) and the grade of AA (ROC area, 64%, $p < 0.01$) displayed good value for

Table 1. Comparison of risk factors and presence of coronary artery disease

	Group 1	Group 2	Group 3
Patient number	47	34	44
Mean age (years)	53.7±11.0	56.1±11.1	59.0±9.0
Male gender (%)	28 (60)	24 (71)	40 (91)*
Arterial hypertension (%)	23 (49)	21 (62)	29 (66)
Diabetes mellitus (%)	11 (23)	6 (18)	9 (20)
Hypercholesterolemia (%)	15 (32)	18 (53)*	23 (52)*
Fasting serum glucose level (mmol/l)	4.29±1.32	4.35±1.22	4.41±1.38
Serum cholesterol level (mmol/l)	4.12±0.11	5.16±1.19	5.11±0.99
CFR	2.41±1.00	1.78±0.48*	1.87±0.58*

Results of multiple ANOVA; values are expressed as number (%) unless otherwise indicated.
Abbreviation: CFR= coronary flow velocity reserve.
* $p < 0.05$ vs group 1

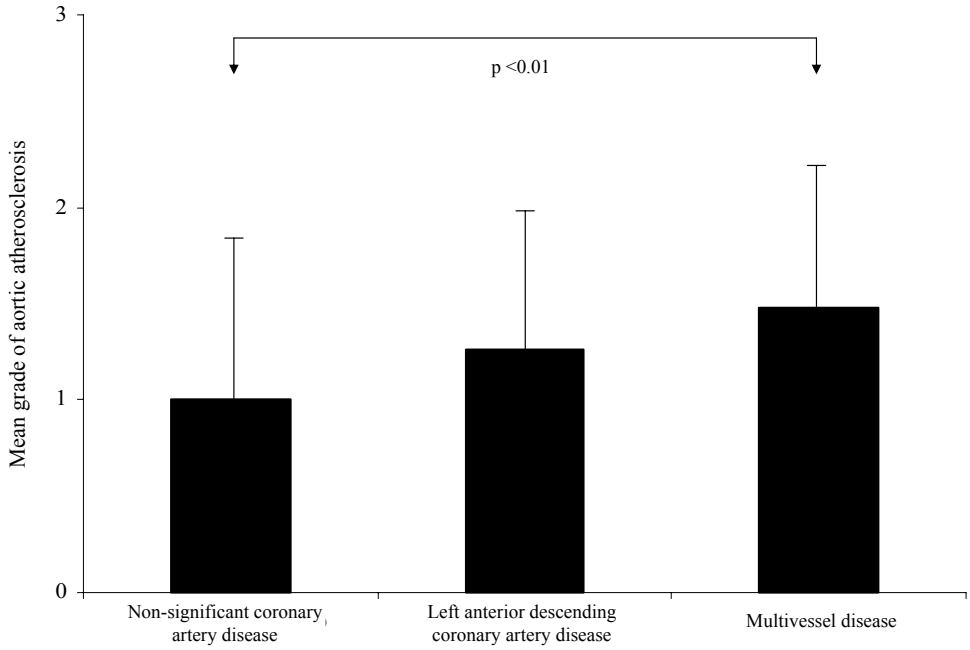

Figure 1. Dependence of mean aortic atherosclerosis grades on the degree of coronary artery disease

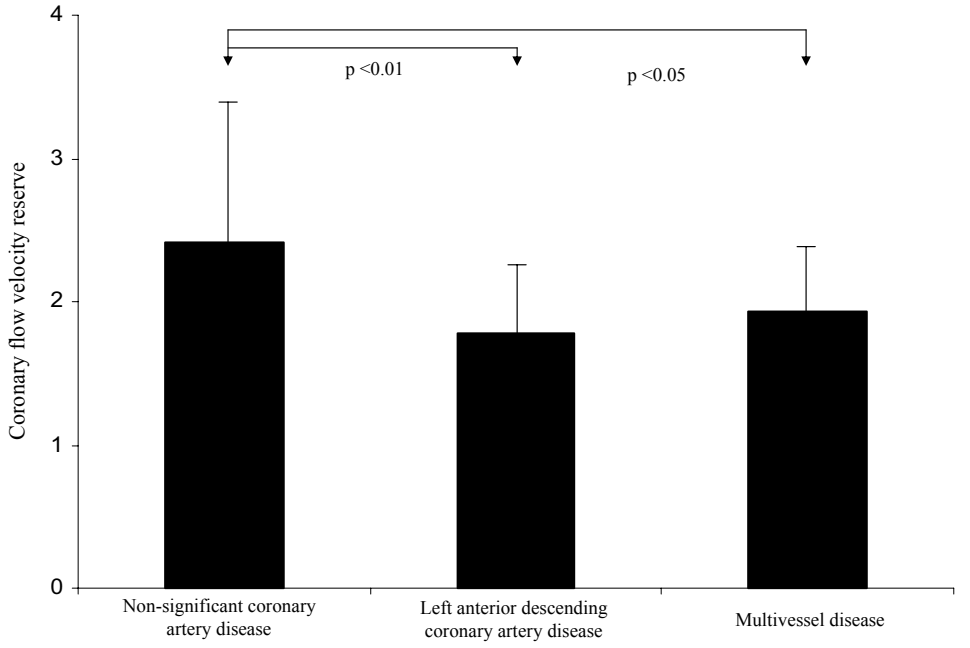

Figure 2. Coronary flow velocity reserve in non-significant coronary artery disease, in left anterior descending coronary artery disease and in multivessel disease

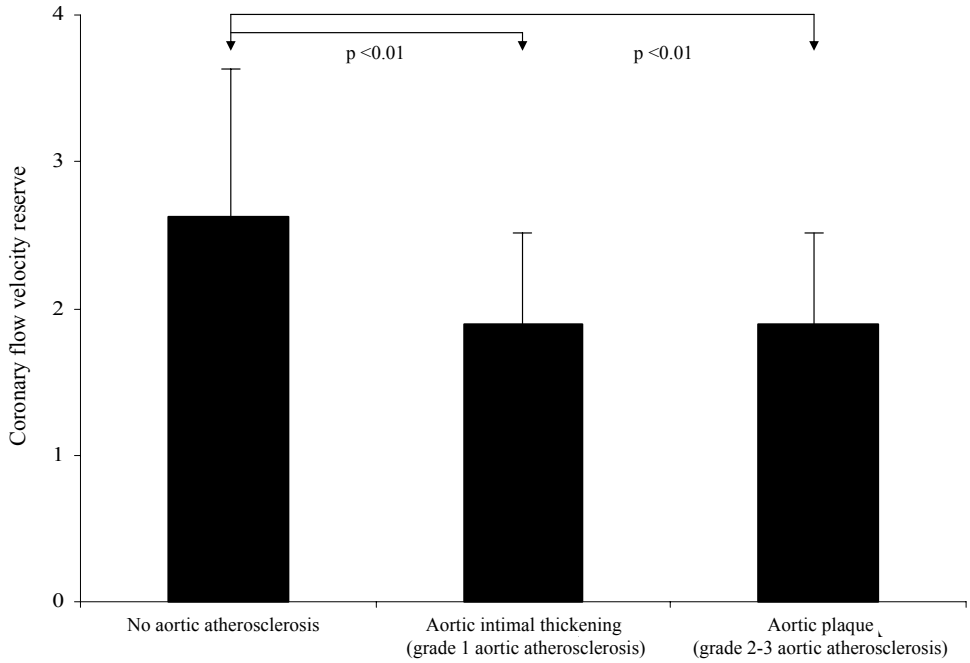

Figure 3. Coronary flow velocity reserve in patients with different grades of aortic atherosclerosis.

Table 2. Differentiation of patients with multivessel disease from all other patients

			Binary logistic regression	
Variable	ROC area (95% CI)	*P*-value of ROC	OR (95% CI)	*P*-value
Hypertension	0.56 (0.46–0.67)	0.46	1.69 (0.78–3.68)	0.18
Diabetes mellitus	0.49 (0.39–0.61)	0.98	0.98 (0.40–2.44)	0.97
Hypercholesterolaemia	0.54 (0.43–0.65)	0.49	1.36 (0.64–2.88)	0.42
Age	**0.63 (0.53–0.73)**	**0.01**	**1.05 (1.00–1.09)**	**0.02**
Male gender	**0.63 (0.53–0.73)**	**0.02**	**4.59 (1.63–12.9)**	**0.01**
Grade of aortic atherosclerosis	**0.64 (0.54–0.74)**	**0.01**	**2.11 (1.22–3.64)**	**0.01**
CFR	0.41 (0.31–0.51)	0.09	0.57 (0.32–1.00)	0.05

Abbreviations: ROC = receiver operator characteristic, OR = odds ratio, CI = confidence interval, CFR = coronary flow velocity reserve.

Table 3. Differentiation of patients with multivessel disease from those with single-vessel left anterior descending coronary artery disease

			Binary logistic regression	
Variable	ROC Area (95% CI)	*P*-value of ROC	OR (95% CI)	*P*-value
Hypertension	0.52 (0.38–0.65)	0.68	1.14 (0.44–2.97)	0.78
Diabetes mellitus	0.50 (0.37–0.63)	0.98	1.01 (0.33–3.08)	0.98
Hypercholesterolaemia	0.48 (0.35–0.61)	0.79	0.87 (0.35–2.17)	0.77
Age	0.60 (0.46–0.73)	0.15	1.05 (0.10–1.10)	0.07
Male gender	0.59 (0.46–0.73)	0.17	3.30 (1.00–10.88)	0.05
Grade of aortic atherosclerosis	**0.63 (0.50–0.76)**	**0.05**	**2.15 (1.02–4.52)**	**0.04**
CFR	0.54 (0.41–0.67)	0.53	1.01 (0.41–2.5)	0.99

Abbrevations: ROC = receiver operator characteristic, OR = odds ratio, CI = confidence interval, CFR = coronary flow velocity reserve.

the prediction of MVD. Hypertension, hypercholesterolemia, diabetes mellitus and CFR failed to distinguish the patients with MVD. By binary logistic regression analysis, the age, the gender and the grade of AA were found to correlate significantly with the prevalence of MVD (Table 2). These variables were entered into multiple logistic regression analysis. In order to differentiate patients with MVD from all others, the age and gender were entered as the first covariates: the model gave X^2= 15.214 (df = 2, p = 0.0005). When the grade of AA was entered, the power of the model increased significantly: X^2 = 21.888, df = 4, p = 0.0001; assessment by the likelihood ratio test gave X^2 = 6.674, df = 2, p = 0.036.

Differentiation of patients with MVD from those with LAD disease. Only the grade of AA (ROC area, 63%, $p < 0.05$) was found to exhibit good prognostic value in predicting patients with MVD. All other traditional risk factors, such as hypertension, hypercholesterolemia, diabetes mellitus, age, gender and CFR, were without prognostic power (Table 3).

Discussion

The main finding of the current study is that the grade of aortic atherosclerosis exhibits good prognostic power for the differentiation of LAD disease patients from those with MVD but CFR has no any predictive value in this evaluation. Addition-

ally the age, the gender, and the grade of AA is suitable for the prediction of patients with multivessel disease from all others. Moreover, a new prediction model was created which verified that the grade of AA exhibits an important additional value for predicting MVD.

Stress transesophageal echocardiography allows the evaluation of coronary blood flow velocity reserve of LAD. The CFR is reduced in patients with significant LAD disease, in case of proximal location or more severe stenosis, further impairment can be observed [5,7–11]. When significant stenosis of right coronary artery and/or left circumflex coronary artery is associated, no further CFR impairment can be found [8]. The CFR is reduced in patients with even minimal grade of AA in case of aortic intimal thickening relative to cases without relevant AA. Interestingly, no further decrease can be observed in patients with frank higher grades of AA (in the presence of different grades of aortic plaque) [12].

The presence of aortic atherosclerotic plaques evaluated by means of the widely available TEE appears to be a marker for the presence of significant CAD in general population [1–3,13–21]. Acarturk et al. reported that the sensitivity and specificity of AA in the detection of CAD were 75.9% and 67.7% [1]. The predictive value of atherosclerotic lesions of thoracic aorta was verified in young patients [13,14]), in women [15] and in patients with valvular heart disease, even in the elderly [16,17]. Triboulloy et al. found that the presence of aortic plaque revealed by TEE identified significant CAD in aortic stenosis patients with a sensitivity of 90.5%, a specificity of 72.5%, and positive and negative predictive values of 75.0% and 89.3%, respectively [18]. Khoury et al. found a strong correlation between the presence of significant CAD and periferial arterial atherosclerosis [4]. The sensitivity and specificity of the presence of AA for the detection of CAD were the highest from among all the sites measured. The AA "score" (the sum of the plaque thickness in millimetres at distinct locations in the descending aorta) was significantly higher in patients with CAD than without it, though this variable did not distinguish patients with one-, two- or three-vessel disease.

The present study was created on the analogy of our previous observation in patients with aortic valve stenosis (AS) [22]. The CFR was similarly decreased in AS patients with or without severe LAD disease, and could not be used to distinguish between these patient populations. Neither the age, the gender, the hypertension, the diabetes mellitus and the hypercholesterolemia nor the CFR, only the grade of AA was suitable for the prediction of AS patients with significant LAD stenosis from those without it.

In this study, our aim was to examine the role of CFR and the grade of AA evaluated by the same semi-invasive TEE examination in cases of suspected LAD disease for the prediction of the severity of CAD. In comparison with known risk factors and the CFR, the grade of AA could help in this differentiation and its predictive value for MVD was also verified. The authors did not want to suggest that all patients with possible CAD should undergo TEE. The results of the present study hinted that patients undergone TEE on other indications were found to have significant aortic atherosclerosis, the probability of severe CAD is very high. It is

important to be stated that these data are useful on the level of the whole group but aggravated on the individual level due to overlapping problems in the absence of evident cut-off points. Hence, overlapping makes it difficult to comment on single cases.

Study limitations. This approach measures blood flow velocities, and not the blood flow itself. The measurement of coronary blood flow requires an evaluation of the luminal cross-sectional area. Further, there is an angle between the ultrasound beam and the vessel direction, as a result of which blood flow velocities measured by this approach can be lower than the actual values. However, both the numerator and the denominator in the formula for the CFR are measured at the same angle, and thus the ratio is not appreciably influenced by the angle or the vessel direction. The analysis of wall motion abnormalities was not the aim of the present study. Previously the interobserver variability was found to be high. According to this fact, we could not examine the interobserver variability during this study.

Conclusions. Our results confirm that the grade of AA furnishes additional help in the prediction of patients with severe CAD. The grade of AA can differentiate patients with MVD from those with significant LAD stenosis. The CFR has no any prognostic power in this evaluation.

Acknowledgement

We gratefully acknowledge the skilled assistance of the nursing staff of our Stress Echocardiographic Laboratory and Cardiac Catheterization Unit. This study was supported by an ETT grant (408 06/2003; Budapest, Hungary).

References

1. Acarturk E, Demir M, Kanadasi M (1999) Aortic atherosclerosis is a marker for significant coronary artery disease. Jpn Heart J 40: 775–781.
2. Fazio GP, Redberg RF, Winslow T, Schiller NB (1993) Transesophageal echocardiographically detected atherosclerotic aortic plaque is a marker for coronary artery disease. J Am Coll Cardiol 21: 144–150.
3. Parthenakis F, Skalidis E, Simantirakis E, Kounali D, Vardas P, Nihoyannopoulos P (1996) Absence of atherosclerotic lesions in the thoracic aorta indicates absence of significant coronary artery disease. Am J Cardiol 77: 1118–1121.
4. Khoury Z, Schwartz R, Gottlieb S, Chenzbraun A, Stern S, Keren A (1997) Relation of coronary artery disease to atherosclerotic disease in the aorta, carotid, and femoral arteries evaluated by ultrasound. Am J Cardiol 80: 1429–1433.
5. Iliceto S, Marangelli V, Memmola C, Rizzon P (1991) Tranesophageal Doppler echocardiography evaluation of coronary blood flow velocity in baseline conditions and and during dipyridamole-induced coronary vasodilation. Circulation 83: 61–69.
6. Bach RG, Kern MJ (1997) Practical coronary physiology. Clinical application of the Doppler flow velocity guide wire. Cardiol Clin 15: 77–99.
7. Galati A, Greco G, Goletta C, Ricci G, Serdoz R, Richichi G, Ceci V (1996) Usefulness of dipyridamole transesophageal echocardiography in the evaluation of myocardial ischemia and coronary artery flow. Int J Cardiovas Imaging 12: 169–178.

8. Nemes A, Forster T, Palinkas A, Vass A, Borthaiser A, Unig I, Thury A, Litvai E, Nadaskay M, Csanady M (2000) The value of coronary flow reserve in ischaemic heart disease measured by dipyridamole stress transoesophageal echocardiography. Orv Hetil 141: 1517–1521.
9. Nemes A, Forster T, Gruber N, Csanady M (2004) Coronary flow velocity reserve and indices describing aortic distensibility in patients after coronary angiography. Int J Cardiol 96: 29–33.
10. Hutchinson SJ, Soldo SJ, Gadallah S, Kawanishi DT, Chandraratna PA (1997) Determination of coronary flow measurements by transesophageal echocardiography: Dependence of velocity reserve on the location of stenosis. Am Heart J 133: 44–52.
11. Stoddard MF, Prince CR, Morris GT (1995) Coronary flow reserve assessment by dobutamine transesophageal Doppler echocardiography. J Am Coll Cardiol 25: 325–332.
12. Nemes A, Forster T, Csanady M, Gruber N (2004) Indices of aortic distensibility and coronary flow velocity reserve in patients with different grades of aortic atherosclerosis. Int J Cardiovasc Imag 20: 271–277.
13. Parthenakis FI, Kochiadakis GE, Skalidis EI, Kanakaraki MK, Mezilis NE, Kanoupakis NE, Vardas PE, Nihoyannopoulos P (2000) Aortic atherosclerotic lesions in the thoracic aorta detected by multiplane transesophageal echocardiography as a predictor of coronary artery disease in the elderly patients. Clin Cardiol 23: 734–739.
14. Matsumura Y, Takata J, Yabe T, Furuno T, Chikamori T, Doi YL (1997) Atherosclerotic aortic plaque detected by transesophageal echocardiography: its significance and limitation as a marker for coronary artery disease in the elderly. Chest 112: 81–86.
15. Tribouilloy C, Peltier M, Senni M, Colas R, Rey JL, Lesbre JP (1997) Multiplane transesophageal echocardiographic detection of thoracic aortic plaque is a marker for coronary artery disease in women. Int J Cardiol 61: 269–275.
16. Tribouilloy C, Shen WF, Peltier M, Lesbre JP (1994) Noninvasive prediction of coronary artery disease by transesophageal detection of thoracic aortic plaque in valvular heart disease. Am J Cardiol 74: 258–260.
17. Tribouilloy C, Peltier M, Colas L, Rida Z, Rey JL, Lesbre JP (1997) Multiplane transesophageal echocardiographic absence of thoracic aortic plaque is a powerful predictor for absence of significant coronary artery disease in valvular patients, even in the elderly. A large prospective study. Eur Heart J 18: 1478–1483.
18. Tribouilloy C, Peltier M, Rey JL, Ruiz V, Lesbre JP (1998) Use of transesophageal echocardiography to predict significant coronary artery disease in aortic stenosis. Chest 113: 671–675.
19. Khoury Z, Gottlieb S, Stern S, Keren A (1997) Frequency and distribution of atherosclerotic plaques in the thoracic aorta as determined by transesophageal echocardiography in patients with coronary artery disease. Am J Cardiol 79: 23–27.
20. Ben Halima A, Kachboura S, Selmi K, Makoddem A, Makni H, Bachraoui K, Fradi I, Boujnah MR (2002) Evaluation of thoracic aortic atherosclerosis by transesophageal ultrasonography: value and limits as predictive factor of coronary disease. Tunis Med 80: 703–713.
21. Sekoranja L, Vuille C, Bianchi-Demicheli F, Dorsaz BA, Kalangos A, Trindade PT, Lerch R (2004) Thoracic aortic plaques, transoesophageal echocardiography and coronary artery disease. Swiss Med Wkly 134: 75–78.
22. Nemes A, Forster T, Thury A, Kovacs Z, Boda K, Csanady M (2003) The comparative value of aortic atherosclerosis and the coronary flow velocity reserve evaluated by stress transesophageal echocardiography in the prediction of patients with aortic stenosis with coronary artery disease. Int J Cardiovasc Imag 19: 371–376.

Corresponding author:
Dr. Attila Nemes,
2nd Department of Medicine and Cardiology Center,
Medical Faculty,
Albert Szent-Györgyi,
Medical and Pharmaceutical Center,
University of Szeged,
Hungary, H-6720 Szeged,
Korányi fasor 6, P.O. Box 427,
Fax: 36-62-544568,
Tel.: 36-62-545220,
E-mail: nemes@in2nd.szote.u-szeged.hu

Upsala J Med Sci 112 (1): 83–93, 2007

Dosin® – A New Pump Device. Its Construction and Function

Andreas Wahlberg[1], Uno Erikson[1], Laszlo Fuchs[2], Anders Andersson[3], Anna Attefall[1]

[1]*Department of Diagnostic Radiology, Akademiska Sjukhuset, Uppsala University, Sweden,* [2]*Department of Heat and Power Engineering, Lunds Institute of Technology, Lund University, Sweden and* [3]*Swedish National Testing and Research Institute, Borås, Sweden*

Abstract

The cyclic flow of the Dosin® is useful in interventional radiology since it prevents clotting and increases the mixing with the blood. The flow rate varies from 0.03 mL/s to 5 mL/s and it is recommended to use fluid with a viscosity lower than 3 mPa.s. The outlet pressure is recommended below 300 mm Hg. The Dosin® must be replaced after each patient, alternatively after maximum 24h continuous use.

Introduction

To the many pump inventions already in existence and circulation, we wish to add a whole new concept called *Dosin®* (Figure 1). This Dosin® is based on the principle of continuous flow, in this case with optional, controlled pulsation. The research and development of the Dosin® and the (medical) pump system, in which it is used (*Octapump® Injection System*) was initiated in response to a demand for a new and improved method of delivering fluids to patients. The key requirement was to make the use of refillable syringes obsolete in a cost-effective and user-friendly alternative.

Most syringes, despite their accurate delivery quotas, have a limited volume that necessitates frequent monitoring and filling or changing. This very act is time consuming and potentially dangerous in inexperienced hands.

The new principle, Dosin®, is capable of delivering (medical) fluids of various consistencies in extremely precise amounts regardless of the fluid viscosity. The outlet of the Dosin® goes through another innovation, the bubble detector, which detects any change in direction of a light beam that passes through the content of the outlet. Thus, should an air bubble enter the outflow of the Dosin® and hence be about to enter the blood stream of a patient, the flow of fluid will halt immediately and an alarm will notify the user of the problem.

Basically, the Dosin® is designed to allow adjustable flow rate, up to certain volumes. This pumping effect is achieved by utilizing the internal structure of the cylinder of the Dosin® so as to function as directional valves during the pumping cycle. At recommended flow rates the Dosin® construction is rigid enough to allow a continuous (or pulsed) and accurate (less than 5% deviation) flow rate per pump

Received 26 July 2006
Accepted 14 September 2006

Figure 1. The Dosin®.

cycle. By controlling the rotation rate, together with the well defined pump volume at the operational range, one is able to maintain accurate volume delivery.

Design Inside the Dosin® cylinder (Figure 2), a piston rotates and thereby produces a continuous flow of, in the case of this report, a stroke volume of 3 mL/s. At the same time as the Dosin® rotates, it also reverses back and forth. The design parameters of the Dosin® allow it to achieve a flow rate of between 360 mL/h and 12000 mL/h depending on the application for which it has been programmed.

The Dosin® consists of 5 main parts, a shell, a plunger (above called piston), an axle, a steering notch and a closing lid. The shell, the plunger and the closing lid are together called the cylinder. The housing has connections for an inlet and an outlet. On the outlet is a long straight piece with flat parallel walls which slides into the bubble detector. Both the inlet and outlet have Luer Lock connections to fluid lines. The pumping action is achieved within two cavities that contain the plunger in its housing. The plunger has a semi-helical groove that forces the plunger back and forth as the plunger rotates. Simultaneously, there are two cut-outs on the plunger that are connected hydraulically to either end of the plunger. These cut-outs are situated so as to control the flow. When the volume of the cavity decreases, its cut

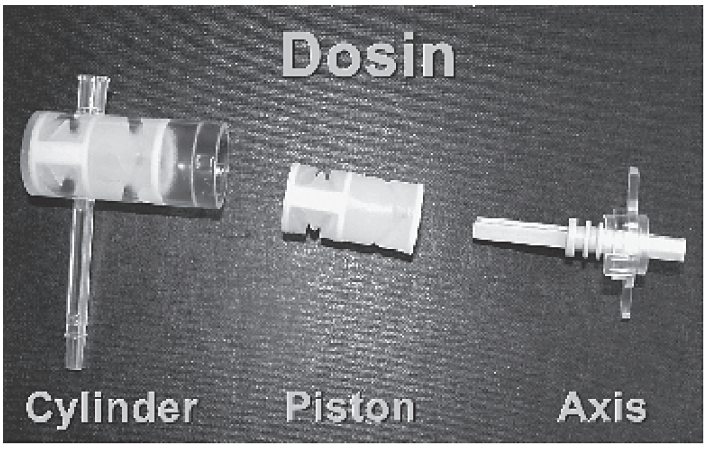

Figure 2. Three of the Dosin®'s 5 parts.