SWISS MED WKLY 2001;131:610–615 · www.smw.ch

Gender differences in coronary artery size per 100 g of left ventricular mass in a population without cardiac disease

Nils Kucher, Ernst Lipp, Markus Schwerzmann, Marianne Zimmerli, Yves Allemann, Christian Seiler

Cardiology, Swiss Cardiovascular Center, University Hospital, Bern, Switzerland

Summary

Objectives: To determine whether there is a gender difference in coronary artery size normalised for left ventricular (LV) mass.

Background: Small coronary artery caliber may play a role as a risk factor for coronary artery disease in women. However, the existence of a gender difference in coronary artery size is controversial. Furthermore, coronary artery size ought to be normalised for LV mass, since there is a theoretical relation of coronary artery size to LV mass according to the law of minimum viscous energy loss for the transport of blood in the coronary circulation.

Methods: In 200 individuals (100 women) without cardiac disease and with normal Doppler echocardiography, left main (LCA) and right coronary artery (RCA) size were determined using transoesophageal echocardiography. LV mass was assessed by transgastric M-mode echocardiography.

Results: Age (44 ± 15 years in women; 41 ± 16 years in men), the presence of non-cardiac diseases, cardiovascular risk factors and medication were similar in women and men. LV mass in women was lower than in men (148 ± 36 g, 189 ± 45 g; p <0.0001). LCA and RCA cross-sectional areas in women were smaller than those in men (LCA: 10 ± 3 and 16 ± 5 mm^2, p <0.0001; RCA: 4 ± 2 and 7 ± 3 mm^2, p <0.0001, respectively). LCA and RCA cross-sectional areas of women were smaller even after normalisation for LV mass (LCA: 7 ± 3 and 9 ± 3 mm^2/100 g LV mass, p <0.0001; RCA: 3 ± 1 and 4 ± 1 mm^2/100g LV mass, p = 0.002, respectively). LCA caliber of women ranged below the theoretically expected size according to the law of minimum viscous energy loss for the transport of blood in the coronary circulation, whereas those of men tended to be above it.

Conclusions: In a population without cardiac disease, women have smaller coronary artery size even after normalisation for left ventricular mass.

Key words: coronary artery disease; gender; echocardiography

Introduction

The outcome of coronary artery disease (CAD) in women is worse than in men [1–8]. Recently, it has been shown in a large registry that early mortality of women <50 years with myocardial infarction is more than twice as high than that of men [9]. This may be due to the presence of a more unfavourable cardiovascular risk profile at the time women need to be treated for CAD. Primarily, women are older, have a higher incidence of diabetes, hypertension and congestive heart failure and more often undergo non-elective procedures than men. Even after multivariate adjustment of these factors, cardiovascular mortality in women is higher than in men [5, 8, 9]. The possibility has been discussed that men are better cared for than women [7, 11].

The role of coronary artery size as a predictor of mortality in patients with myocardial infarction and with coronary artery bypass grafting is controversial [1–5, 7, 10]. In the Coronary Artery Surgery Study, small body size and coronary artery caliber were the strongest predictors of perioperative mortality [3].

The existence of gender differences in coronary artery size has hitherto not been proven with

Abbreviations

CAD	coronary artery disease
LCA	left main coronary artery
LV	left ventricular
RCA	right coronary artery
TEE	transoesophageal echocardiography

sufficient certainty. Roberts and Roberts examined proximal portions of the three major epicardial coronary arteries in 98 necropsy patients with different coronary events and did not find a significant gender difference [12]. Dodge et al. examined the influence of gender on lumen diameter of normal human coronary arteries using coronary arteriograms and found that women have smaller epicardial arterial diameter than men even after normalisation for body surface area [13]. Concerning gender differences in coronary artery size, these studies are limited due to small sample size, to possible underestimation of coronary artery diameter in non-perfused vessels in postmortem analysis, and to the lack of normalisation for left ventricular (LV) mass.

Coronary artery caliber ought to be normalised for LV mass. According to the law of minimum viscous energy loss for the transport of blood in the coronary circulation, coronary artery size is directly determined by LV mass according to a $^2/_3$ power law [14]. The law of minimum viscous energy loss is a physical law which can be derived from Poisewille's law, and which applies to circulatory systems in different biological species.

The purpose of this study was to determine whether there is a gender difference in coronary artery size normalised for LV mass in a population without cardiac disease, and whether coronary artery size is related to LV mass by a $^2/_3$ power law as predicted theoretically.

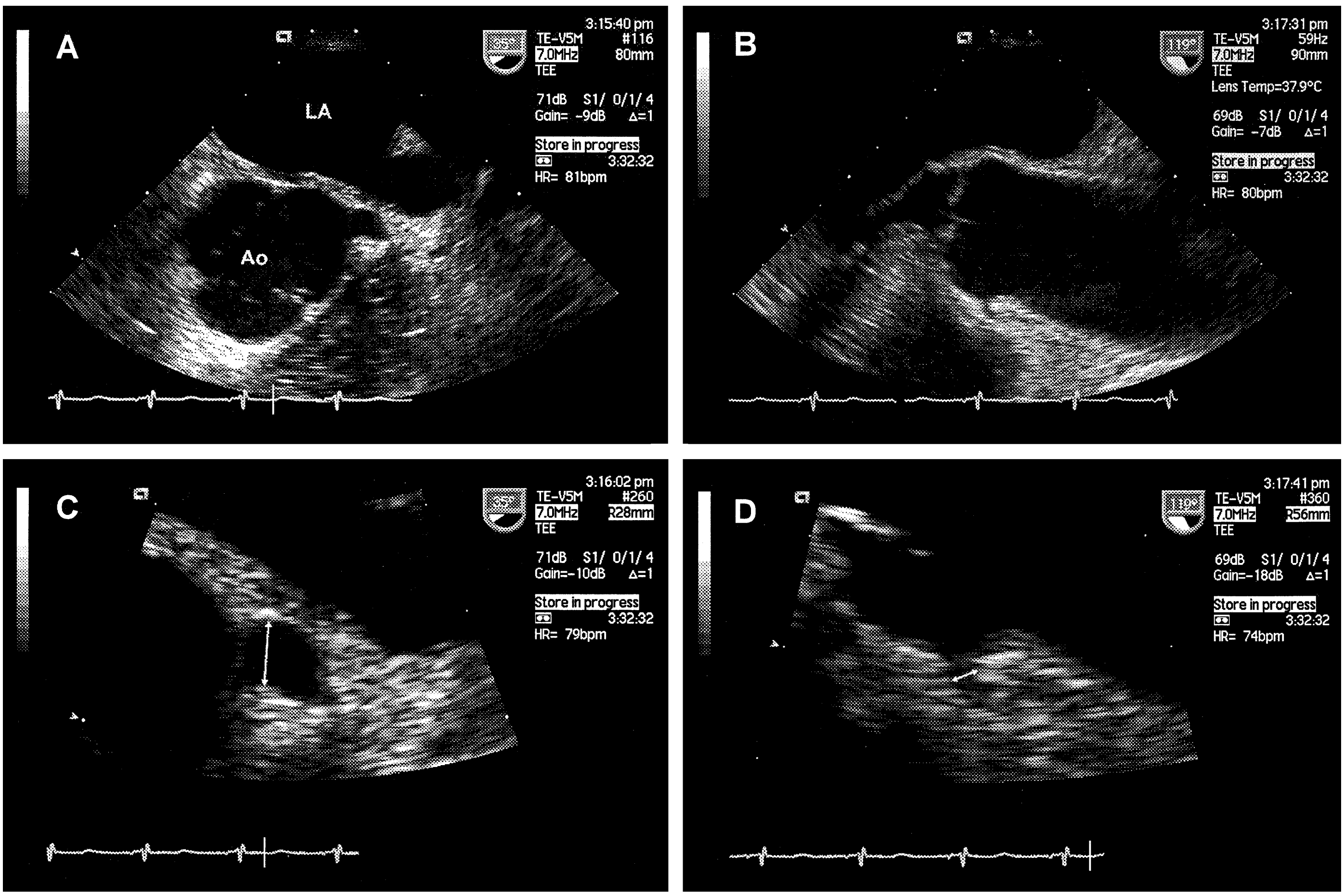
Methods

Study individuals

The study population consisted of 129 patients (48 men), who underwent transoesophageal echocardiography (TEE) for medical reasons and 71 healthy probands (52 men) who had been previously included in a study on diving and cerebral ischaemia in the absence or presence of a patent foramen ovale [15]. A history of any cardiac disease as well as an abnormal Doppler echocardiogram were exclusion criteria. In particular, study individuals with LV mass index above the normal range w >134 g/m^2 for men; >109 g/m^2 for women) were not included [16]. The study individuals gave informed consent to participate in the study.

Figure 1

Transoesophageal short-axis view of the ascending aorta shows the origin of the left main coronary artery (A and C), and transoesophageal long-axis view shows the origin of the right coronary artery (B and D) at the aortic sinus. Arrows in C and D demonstrate the measurement of coronary artery diameters.



Transoesophageal echocardiography (TEE)

TEE was performed in all study individuals in the left lateral supine position using an Acuson Sequoia™ C256 system (Mountain view, California, USA) with a multiplane 3.5–7 MHz TEE probe. The epipharynx was anaesthetised using lidocaine hydrochloride 10% spray. Before intubation of the TEE probe, 2–5 mg Midazolam (Dormicum®) was given intravenously. A 3-lead ECG and blood pressure were registered during the procedure. M-mode and 2D echocardiographic images as well as Doppler examinations of valves and pulmonary veins were performed as recommended by the the American Society of Echocardiography [17]. M-mode echocardiography of the left ventricle was performed using the transgastric long-axis view, proximal to the papillary muscles. A frequency of 7 MHz was used to image epicardial coronary arteries. The left main coronary artery (LCA) was imaged using the short-axis view, and the right coronary artery (RCA) was examined using both the long-axis and short-axis view (figure 1). For accurate detection of the vessel borders, the region of interest was magnified using the resolution function. Subsequently, the focus was adjusted. Color Doppler flow was not used to measure coronary artery caliber.

Data aquisition

Echocardiographic off-line measurements were performed by reloading data from optical discs to the internal hard disc of the echograph. Two experienced cardiologists from our laboratory performed the measurements of LV mass and coronary artery caliber unaware of gender and clinical data of the study individuals. LV mass was calculated according to the cube formula [16]. LCA- and RCA-calibers were measured close to the origin of the vessels at the coronary sinus of the aorta.

Statistical analysis

All data are expressed as mean values ± 1 SD. Nominal data comparison between men and women was performed using the chi square test. Continuous data were analysed by an unpaired t-test. In order to compare measured with the theoretically expected coronary artery cross-sectional area ($y = 0.4 \times \text{LV mass}^{0.67}$ in mm^2), power equation fitting was performed (Sigmaplot Version 5.0, SPSS Incorporation) [14]. Data were considered significant at $p < 0.05$.

Results

Study population

Age, drug therapy, the presence of non-cardiac diseases, cardiovascular risk factors and medication were similar in men and in women (table 1).

Gender analysis

Haemodynamic and echocardiographic data are listed in table 2. LV mass in women was lower than in men. LCA and RCA cross-sectional areas in women were smaller than those in men. LCA and RCA cross-sectional areas of women were smaller even after normalisation for LV mass. Gender differences in coronary artery cross-sectional areas in relation to LV mass are shown in figure 2 and 3. Power equation fitting of measured LCA cross-sectional areas compares well with the theoretically expected LCA size ($0.4 \times \text{LV mass}^{0.67}$ in mm^2). According to the law of minimum viscous

Table 1

Baseline characteristics.

	men	women	p
Number	100	100	
Age (years)	44 ± 15	46 ± 16	0.39
Body surface area (m^2)	1.9 ± 0.2	1.7 ± 0.2	<0.0001
Cardiovascular risk factors			
Systemic hypertension	16	18	0.49
Smoking	15	15	0.31
Familiy history	5	9	0.61
Hypercholesterolaemia	13	8	0.05
Diabetes mellitus	2	5	0.22
Drug therapy			
Calcium channel blocker	3	2	0.41
ACE-inhibitor	6	8	0.95
Beta-blocker	3	5	0.79
Aspirin	35	41	0.26
Coumarine	3	6	0.05
Thiazide	1	2	0.58
Statins	6	2	0.05

	men	women	p
Diagnosis			
Ischaemic cerebrovascular insult	21	30	0.26
Transient ischaemic attack	15	15	0.31
Arterial embolism (other)	6	6	0.95
Bacteraemia	5	5	0.94
Local bacterial infection	2	2	0.84
Bone marrow malignancy	0	4	0.03
Decompression illness	1	1	0.93
Cerebral vasculitis	1	1	0.93
Carotid dissection	1	0	0.59
Encephalitis	0	1	0.59
PFO (device occluded)*	6	10	0.61

* Patients with previously diagnosed paradoxical embolism in whom a residual shunt of a device occluded PFO was ruled out using TEE.
Abbreviations: ACE = angiotensin converting enzyme; NS = not significant; PFO = patent foramen ovale; TEE = transoesophageal echocardiography.

Table 2

Haemodynamic and echocardiographic data.

	men	women	p
Number	100	100	
Blood pressure (mm Hg)	128/72	125/72	0.43
Heart rate (beats per minute)	74 ± 18	72 ± 16	0.39
Interventricular septal end-diastolic thickness (mm)	11 ± 2	10 ± 2	0.36
Posterior wall end-diastolic thickness (mm)	10 ± 2	9 ± 1	0.32
Left ventricular end-diastolic diameter (mm)	47 ± 7	42 ± 6	<0.0001
Left ventricular ejection fraction (%)	68 ± 6	67 ± 5	0.51
Left ventricular mass (g)	160 ± 42	178 ± 45	0.004
Left ventricular mass index (g/m²)	89 ± 19	97 ± 23	0.01
Left main coronary artery cross sectional area (mm²)	16.4 ± 4.6	9.6 ± 3.0	<0.0001
Right coronary artery cross sectional area (mm²)	6.6 ± 3.0	4.3 ± 1.9	<0.0001
Left main coronary artery cross sectional area per 100 g of left ventricular myocardium	9.4 ± 3.2	6.7 ± 2.4	<0.0001
Right coronary artery cross sectional area per 100 g of left ventricular myocardium	3.6 ± 1.5	3.0 ± 1.4	0.002

Figure 2

Gender differences of left main coronary artery cross-sectional area (vertical axis) in relation to left ventricular mass (horizontal axis). Thin solid curve: theoretically expected left coronary artery caliber according to the law of minimum viscous energy loss for the transport of blood in the coronary circulation ($y = 0.40 x^{0.67}$). Thick solid curve: power equation fitting to compare measurements in all study individuals with theroretically expected left coronary artery size ($y = 0.47 x^{0.65}$, r = 0.4, p <0.0001, SEE [standard error of estimate] = 4.8 mm²). Dashed curve: power equation fitting to compare measurements in men with theoretically expected coronary artery size ($y = 5.8 x^{0.20}$, r = 0.17, p = 0.1, SEE = 4.6 mm²). Dashed-dotted curve: power equation fitting for measurements in women ($y = 2.2 x^{0.29}$, r = 0.20, p = 0.04, SEE = 2.97 mm²).

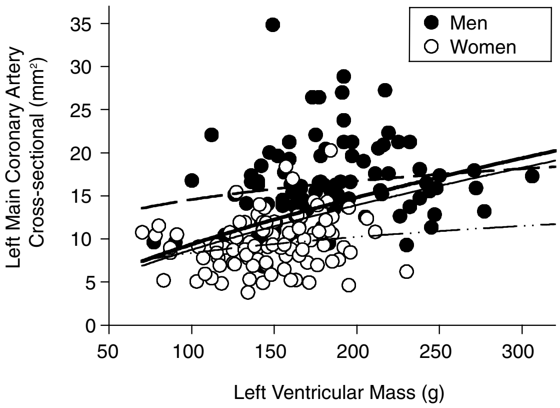
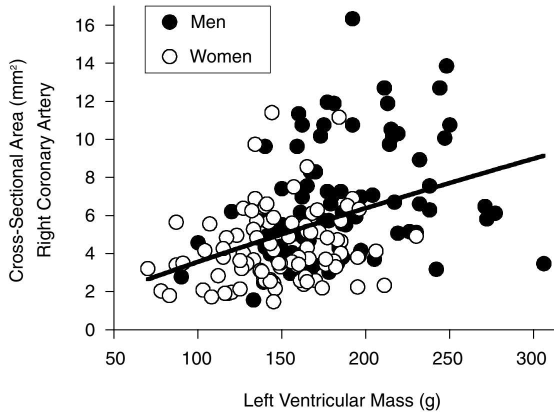


Figure 3

Gender differences of right coronary artery cross-sectional area in relation to left ventricular mass. Thick solid curve: power equation fitting for measured RCA sizes ($y = 0.07 x^{0.84}$, r = 0.41, p <0.0001, SEE [standard error of estimate] = 2.5 mm²).



energy loss for the transport of blood in the coronary circulation, LCA sizes of women tended to range below the theoretically expected size, whereas those of men tended to be above it (see the dashed and dashed-dotted curves in figure 2).

Discussion

Taking into account the basic structure-function relations of the coronary vascular tree, this study demonstrates that there is a significant gender difference in coronary artery size in a population without cardiac disease, whereby coronary artery cross-sectional areas normalised for LV mass in women are smaller than those in men.

Determinants of coronary artery caliber

To examine the influence of coronary artery size on clinical variables such as outcome of coronary artery disease, one should keep in mind its main determinants. Coronary artery caliber strongly depends on wall shear stress which is related to blood flow, and on myocardial bed size [14, 18–20]. Using quantitative coronary angiography in patients with and without stenotic lesions, a curvilinear relation (²/₃ power equation) between coronary artery lumen area and regional myocardial mass has been described which is in accordance with the law of minimum viscous energy loss for the transport of blood in the coronary circulation [14]. Our data on left main coronary artery size and LV mass seem to comply with this principle of minimal viscous energy dissipation, since the observed relation very closely matches the theoretical prediction following the ²/₃ power law ($y = ax^b$; observed data: b = 0.65, predicted data: b = 0.67) (see figure 2).

Coronary artery size should not be assessed in symptomatic patients using angiographically measured cross-sectional lumen area, since it may be underestimated in patients with diffuse coronary artery narrowing, where the luminal area is significantly smaller than would be expected in the absence of CAD [14]. In patients with LV hypertrophy and dilated cardiomyopathy, coronary artery caliber is larger than in patients with normal LV mass, but may be too small in relation to myocardial bed size [13, 21]. Thus, patients with an elevated LV mass index were not included in the present study [16].

Literature data on gender-related coronary artery size

To our knowledge there is no study which has examined gender-related coronary artery size normalised for LV mass in a sizeable population without cardiac disease. In 98 patients with CAD, there was no gender difference in coronary artery size; however, those necropsy findings were presented without normalisation for LV mass [12]. Dodge et al. found significantly smaller coronary artery caliber in women even after normalisation for body surface area using carefully selected coronary angiograms without arteriosclerosis, but the sample size was limited (10 women) [13]. Studies including larger sample sizes provided mortality data of patients undergoing coronary artery bypass surgery [1, 3, 22]. The Northern New England Cardiovascular Disease Study Group found a significantly smaller mid left anterior descending coronary artery after correction for body surface area [22]. The main limitation of this study was that LV mass data were not available.

Study limitations

TEE has been shown to be reliable for the examination of proximal coronary arteries [23]. However, the follwing limitation of this approach for measuring coronary artery caliber should be mentioned: although the problem with reduced lateral resolution for the measurement of horizontal distances can be managed with optimal echograph settings (ie, high transducer frequency, lowest possible gain), this may still be relevant for the measurement of coronary artery caliber using TEE [24]. However, it is not relevant in left coronary artery caliber measurement since this is obtained in a perpendicular projection. Conversely, the origin of the right coronary artery is directed parallel to the ultrasonic beam causing reduced image quality of the vessel wall due to deminished lateral resolution. Thus, the measurement of the right coronary artery caliber in our study population was probably less precise than left coronary artery measurements. Moreover, for calculation of the cross-sectional area, errors in the measurement of dimensions are increased by a power of two. However, the intima-media border of the left main coronary artery was precisely identified in all cases due to the orthogonal direction of the ultrasound beam relative to the imaged artery. Coronary arteries were measured by image magnification. However, although the frequency of image aquisition is increased when the region of interest is made smaller, the number of pixels remains the same. Thus, in study individuals with poor vessel delineation, the accuracy of coronary artery caliber measurement was not improved by image magnification.

In the present study, gender analysis was performed in a population without known cardiac disease. The incidence of asymptomatic coronary artery lesions could have been larger than expected in a normal population due to the relatively high presence of cardiovascular risk factors and cerebrovascular disease (table 1). However, there were no gender-related differences in cardiovascular risk profile, drug therapy, nor in the prevalence of non-cardiac diseases among our study individuals.

Conclusions

Coronary artery caliber is related to LV mass by a $^2/_3$ power law as predicted by the law of viscous energy loss for the transport of blood in the coronary circulation. In a population without cardiac disease, women have smaller coronary artery caliber normalised for LV mass than men. Left main coronary artery sizes of women tended to range below the theoretically expected size, whereas those of men tended to be above it.

Correspondence:
Prof. Dr. Christian Seiler, MD
Cardiology
Swiss Cardiovascular Center Bern
University Hospital
CH-3010 Bern
e-mail: christian.seiler.cardio@insel.ch

References

1 Christakis GT, Weisel RD, Buth KJ, et al. Is body size the cause for poor outcomes of coronary artery bypass operations in women? J Thorac Cardiovasc Surg 1995;110:1344–56; discussion 1356–8.

2 Edwards FH, Carey JS, Grover FL, Bero JW, Hartz RS. Impact of gender on coronary bypass operative mortality [see comments]. Ann Thorac Surg 1998;66:125–31.

3 Fisher LD, Kennedy JW, Davis KB, et al. Association of sex, physical size, and operative mortality after coronary artery bypass in the Coronary Artery Surgery Study (CASS). J Thorac Cardiovasc Surg 1982;84:334–41.

4 Hendricks AS, Goodman B, Stein JH, Carnes M. Gender differences in acute myocardial infarction: the University of Wisconsin experience. Wmj 1999;98:30–3, 36.

5 Melgarejo-Moreno A, Galcera-Tomas J, Garcia-Alberola A, Rodriguez-Garcia P, Gonzalez-Sanchez A. Clinical and prognostic characteristics associated with age and gender in acute myocardial infarction: a multihospital perspective in the Murcia region of Spain. Eur J Epidemiol 1999;15:621–9.

6 Pagley PR, Yarzebski J, Goldberg R, et al. Gender differences in the treatment of patients with acute myocardial infarction. A multihospital, community-based perspective. Arch Intern Med 1993;153:625–9.

7 Wong CC, Froelicher ES, Bacchetti P, et al. Influence of gender on cardiovascular mortality in acute myocardial infarction patients with high indication for coronary angiography. Circulation 1997;96:II-51–7.

8 Malacrida R, Genoni M, Maggioni AP, et al. A comparison of the early outcome of acute myocardial infarction in women and men. N Engl J Med 1998;338:8–14.

9 Vaccarino V, Parsons L, Every NR, et al. Sex-based differences in early mortality after myocardial infarction. N Engl J Med 1999;341:217–25.

10 Abramov D, Tamariz MG, Sever JY, et al. The influence of gender on the outcome of coronary artery bypass surgery. Ann Thorac Surg 2000;70:800–5; discussion 806.

11 Kindwall KE. Therapy for coronary heart disease in women. Cardiovasc Clin 1989;19:195–203.

12 Roberts CS, Roberts WC. Cross-sectional area of the proximal portions of the three major epicardial coronary arteries in 98 necropsy patients with different coronary events. Relationship to heart weight, age and sex. Circulation 1980;62:953–9.
13 Dodge JT Jr, Brown BG, Bolson EL, Dodge HT. Lumen diameter of normal human coronary arteries. Influence of age, sex, anatomic variation, and left ventricular hypertrophy or dilation. Circulation 1992;86:232–46.
14 Seiler C, Kirkeeide RL, Gould KL. Basic structure-function relations of the epicardial coronary vascular tree. Basis of quantitative coronary arteriography for diffuse coronary artery disease. Circulation 1992;85:1987–2003.
15 Schwerzmann M, Seiler C, Lipp E, et al. Relation between directly detected patent foramen ovale and ischemic brain lesions in sport divers. Ann Intern Med 2001;134:21–24
16 Devereux RB, Lutas EM, Casale PN, et al. Standardization of M-mode echocardiographic left ventricular anatomic measurements. J Am Coll Cardiol 1984;4:1222–30.
17 Beyer RW, Ramirez M, Josephson MA, et al. Recommendations for continuous quality improvement in echocardiography. American Society of Echocardiography. J Am Soc Echocardiogr 1995;8:S1–28.
18 Hutchins GM, Bulkley BH, Miner MM, Boitnott JK. Correlation of age and heart weight with tortuosity and caliber of normal human coronary arteries. Am Heart J 1977;94:196–202.
19 Lewis BS, Gotsman MS. Relation between coronary artery size and left ventricular wall mass. Br Heart J 1973;35:1150–3.
20 Koiwa Y, Bahn RC, Ritman EL. Regional myocardial volume perfused by the coronary artery branch: estimation in vivo. Circulation 1986;74:157–63.
21 Kaufmann P, Vassalli G, Lupi-Wagner S, Jenni R, Hess OM. Coronary artery dimensions in primary and secondary left ventricular hypertrophy. J Am Coll Cardiol 1996;28:745–50.
22 O'Connor NJ, Morton JR, Birkmeyer JD, Olmstead EM, O'Connor GT. Effect of coronary artery diameter in patients undergoing coronary bypass surgery. Northern New England Cardiovascular Disease Study Group. Circulation 1996;93: 652–5.
23 Samdarshi TE, Nanda NC, Gatewood RP Jr, et al. Usefulness and limitations of transesophageal echocardiography in the assessment of proximal coronary artery stenosis. J Am Coll Cardiol 1992;19:572–80.
24 Latson LA, Cheatham JP, Gutgesell HP. Resolution and accuracy in two dimensional echocardiography. Am J Cardiol 1981;48:106–10.

Swiss
Medical Weekly

Official journal of
the Swiss Society of Infectious disease
the Swiss Society of Internal Medicine
the Swiss Respiratory Society

The many reasons why you should choose SMW to publish your research

What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising, to the current 1.537
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website http://www.smw.ch (direct link from each SMW record in PubMed)

- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses

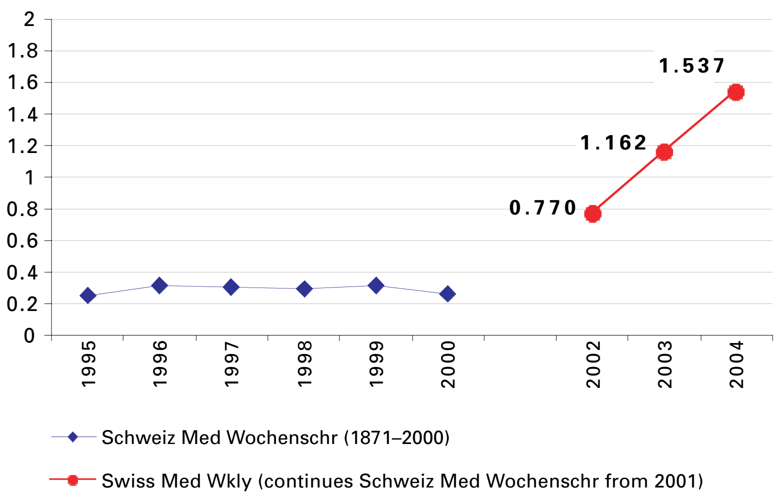
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:
http://www.smw.ch/set_authors.html

Impact factor Swiss Medical Weekly



EMH FMH Schwabe
Editores Medicorum Helveticorum

All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.
SMW Editorial Secretariat
Farnsburgerstrasse 8
CH-4132 Muttenz

Manuscripts: submission@smw.ch
Letters to the editor: letters@smw.ch
Editorial Board: red@smw.ch
Internet: http://www.smw.ch