Internal carotid artery stenosis in patients with degenerative aortic stenosis

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Abstract

Background: In patients with severe degenerative aortic stenosis (DAS) the operative mortality risk is 3% for isolated aortic valve replacement (AVR), but it significantly increases in patients with concomitant coronary artery disease (CAD) and internal carotid artery stenosis (ICAS).

Aim: To assess the frequency of ICAS ≥50% and factors determining its occurrence in patients with severe calcified DAS referred for AVR.

Methods: The study included 104 patients (67 men), aged 63.4±8.4 years, with symptomatic moderate-to-severe DAS (aortic valve area <1.5 cm^2) undergoing coronary angiography prior to valve surgery. In all patients Doppler ultrasound of carotid arteries was performed with the assessment of lumen stenosis.

Results: Significant CAD, defined as at least one lumen reduction ≥50% in a main coronary artery, was found in 44 (42.3%) patients and ICAS ≥50% in 13 (12.5%) patients. Among patients with DAS, 12 (27.3%) out of 44 patients with significant CAD and 1 (1.7%) out of 60 patients without CAD had ICAS ≥50% (p <0.001). The frequency of ICAS ≥50% increased with advancing CAD, occurring in 4 (25%) out of 16 patients with 1-vessel CAD, 3 (25%) out of 12 with 2-vessel CAD and (31.3%) out of 16 patients with 3-vessel CAD (p <0.001). The independent ICAS predictors by multivariate regression analysis were identified as: concomitant CAD (p <0.001), diabetes (p=0.054), cigarette smoking (p=0.08) and decreased left ventricular ejection fraction (p=0.039). ICAS ≥50% was found to be an independent predictor of CAD (p=0.002).

Conclusions: ICAS ≥50% occurs in 13% of patients with isolated DAS and in 27% of those with DAS and CAD. Independent ICAS risk factors were identified as CAD, diabetes and cigarette smoking. Duplex ultrasound of carotid arteries should be considered in patients with DAS and concomitant CAD prior to AVR.

Key words: severe aortic valve stenosis, internal carotid artery stenosis, coronary angiography

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Introduction

Degenerative aortic valve stenosis (DAS) is a common clinical problem affecting approximately 2% to 7% of the European population aged over 65 years [1, 2]. According to the recommendations of the European Society of Cardiology (ESC), symptomatic patients with severe aortic valve stenosis (i.e. aortic orifice area <1 cm^2) (recommendation class I; level of evidence B) and subjects with moderate aortic valve stenosis defined as aortic orifice area between 1 and 1.5 cm^2 requiring coronary artery bypass grafting (recommendation class IIa; level of evidence C) are reffered for aortic valve replacement (AVR) [2].

European Society of Cardiology recommends that before surgery the risk of perioperative mortality should be stratified according to the EuroSCORE classification in all patients with DAS [3]. It has been known that a need for coronary artery bypass grafting doubles mortality risk at surgery compared to isolated AVR (4.3-7 vs. 2.7-3.7%) [2]. Moreover, among risk factors of perioperative mortality are variables such as age of over 60 years, serum creatinine concentration >200 μmol/L, decreased left ventricular ejection fraction (<50%), chronic obstructive pulmonary disease, female gender, unstable angina and history of myocardial infarction within 90 days prior to AVR as well as internal carotid artery stenosis (ICAS) ≥50% [3]. Internal

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carotid artery stenosis is associated with elevated risk of perioperative stroke with all its consequences.

The purpose of this study was to define the prevalence of significant ICAS in patients with DAS as well as search for any potential predictors of ICAS development.

Methods

This study comprised 104 (67 M, 37 F) patients at the mean age of 63.4±8.4 (47 to 80) years admitted to hospital with symptomatic degenerative moderate or severe aortic valve stenosis (aortic valve area <1.5 cm^2) to qualify for AVR. Patients with rheumatic aortic valve disease were excluded.

The prevalence of cardiovascular risk factors, i.e. hypertension, hyperlipidaemia, diabetes mellitus, smoking, male gender and age, was estimated.

In all study participants, echocardiography was performed in accordance with the guidelines of the American Society of Echocardiography as well as carotid ultrasonography according to the recommendations of the Polish Association of Ultrasonography [4, 5].

Echocardiography

The following parameters were evaluated: aortic cusps separation and morphology, presence of valvular calcifications, maximum and mean aortic transvalvular pressure gradient, aortic valve area (AVA) and the left ventricular ejection fraction (LVEF) calculated using Simpson's method.

Ultrasonography of carotid arteries

Flow velocity and atherosclerotic plaques localisation in the common, internal as well as external carotid arteries were assessed. The degree of carotid artery lumen narrowing was assessed according to the criteria of Bluth et al., which are based on measurement of maximum systolic and end-diastolic flow velocity within the stenotic vascular segment [5]. The ICAS stenosis ≥50% was diagnosed if maximal systolic velocity across the atherosclerotic plaque exceeded 1.3 m/s and end-diastolic 0.4 m/s as well as when reduction of carotid artery cross sectional area >75% in the transverse projection was detected. After ICAS stenosis ≥50% was diagnosed with ultrasound, degree of stenosis was verified with carotid angiography performed directly after coronary angiography.

Coronary angiography

Coronary angiography was carried out in all patients using the Seldinger method and routine femoral arterial access. Coronary artery disease (CAD) was diagnosed if angiography (Axiom Artis DFC or Coroscop, Siemens devices equipped with quantitative assessment software – Quantcor QCA V2.0) revealed at least one stenotic lesion with >50% of lumen diameter reduction in the main segments of the coronary arteries.

Statistical analysis

Examined parameters are expressed as means ±SD for the continuous variables and as numbers and percentages for the categorical variables. Differences between distribution and prevalence of the evaluated parameters among groups were verified using non-parametric tests such as Mann-Whitney U and Chi-square test. Differences of ICAS ≥50% prevalence in patients with DAS in relation to the severity of CAD were tested by means of analysis of variance (ANOVA).

Independent predictive factors of ICAS ≥50% were assessed using multivariate analysis by retrograde step-wise logistic regression. Twelve clinical, echocardiographic and angiographic variables including age, gender, cigarette smoking, hypertension, hyperlipidaemia, diabetes mellitus, left ventricular ejection fraction, maximum and mean transvalvular aortic gradients, AVA, and coexistence and severity of coronary artery disease were entered into the analysis. Employing the same statistical method, independent predictors of CAD were sought among the following 11 variables: age, gender, cigarette smoking, hypertension, hyperlipidaemia, diabetes mellitus, LVEF, maximum and mean aortic transvalvular gradient, AVA and ICAS ≥50%.

Statistical analysis was carried out using Statistica 5.5 software. A p value <0.05 was considered statistically significant.

Results

Overall in the group of DAS patients, the mean AVA was 0.81±0.32 cm^2 (range 0.4-1.5 cm^2), maximum and mean transvalvular aortic gradient 82.1±29.5 mmHg (35-178.3 mmHg) and 48.5±19.5 mmHg (16-115.3 mmHg) respectively and separation of the aortic cusps – 10.1±3.4 mm (4-14 mm). Average LVEF was 57.1±11.3% (25-78%), but in 10 (9.6%) subjects LVEF was markedly decreased (<45%). In the latter subset of patients dobutamine stress test was performed to verify the haemodynamic significance of aortic valve disease.

Based on coronary angiography, significant lesions (CAD) were detected in 44 (42.3%) patients, of these single-vessel disease in 16 subjects, two-vessel in 12 individuals and three-vessel disease in 16 patients. In 60 (57.7%) patients normal coronary arteries or with lesions not exceeding 50% were found.

The CAS stenosis ≥50%, confirmed with angiography, was detected in 13 (12.5%) patients, of whom in 9 (8.7%) lesions exceeded 70%. In 4 out of 13 patients ICAS stenosis was estimated to be 50 to 69%; in 6, 70 to 99%; and in 3 total occlusion of the internal carotid artery was noted. Moreover, in 2 patients ICAS stenosis ≥50% was bilateral. In 12 patients, ICAS ≥50% coexisted with significant CAD, and in one case diffuse atherosclerotic coronary artery lesions <50% were visualised. Prevalence of ICAS ≥50% increased proportionally to the severity of CAD. It was detected only in 1 (1.7%) patient among 60 subjects without significant coronary lesions, in 4 (25%) out of 16 patients with single-vessel disease, in 3 (25%) of 12 subjects with two-vessel CAD and in 5 (31.3%) of 16 individuals with three-vessel CAD (p <0.001) (Figure 1).

Patients with ICAS ≥50% significantly more often manifested hypertension and diabetes mellitus and smoked cigarettes than patients without significant atherosclerotic carotid disease (Table I). Likewise, prevalence of hypertension, diabetes mellitus and hyperlipidaemia was higher in patients with significant CAD. However, both groups of patients with and without CAD as well as the groups of subjects with and without ICAS ≥50% did not differ between each other with respect to measured aortic valve echocardiographic parameters (Table I).

Multivariate retrograde step-wise regression analysis showed significant CAD, diabetes mellitus and decreased LVEF to be independent predictors of ICAS ≥50% in patients with moderate to severe DAS. In the case of smoking, a positive trend was observed (Table IIA). Coexistence of significant CAD and DAS was associated with approximately 4 times higher probability of ICAS ≥50% detection, and the risk of significant ICAS was about two times higher in smoking subjects suffering from diabetes mellitus. Meanwhile, ICAS ≥50%, diabetes mellitus, hyperlipidaemia, age and reduced LVEF were found to be predictors of significant CAD in the multivariate analysis (Table IIB). Detection of ICAS ≥50% in patients with DAS was the most powerful predictor of significant CAD. It was associated with over 3 times higher probability of CAD.

Discussion

Rheumatic heart disease has become infrequent in recent decades. At the same time, aging of the human population have resulted in a steadily increasing number of patients with DAS as well as with CAD [2]. Aronow et al. showed that in a group of 1275 individuals at the mean age of 81 years (range 60 to 101 years) 31 (2%) subjects had valvular stenosis of the LV outflow tract with systolic gradient ≥50 mmHg and 45 (4%) patients had asymptomatic CAS exceeding 80% [1]. Moreover, in one in four DAS patients ICAS ≥80% was detected [1].

Significant CAD is seen in approximately half of patients with severe DAS, as reported by other investigators [2]. This is not surprising since DAS and CAD share the same

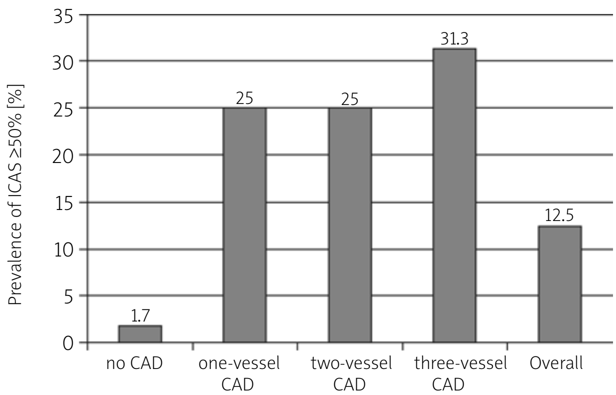

Figure 1. Prevalence of internal carotid artery stenosis (ICAS) ≥50% in patients with symptomatic moderate or severe DAS in relation to coronary artery disease severity (p <0.001)

Table I. Characteristics of the examined groups

	Whole group N=104	CAD free N=60	CAD N=104	p	ICAS <50% N=91	ICAS ≥50% N=13	p
Age [years±SD]	63.4±8.4	62.2 ± 8.4	65.0±8.3	0087	63.1±8.2	64.8±9.6	0.497
Male gender [n]	67 (64.4%)	35 (58.3%)	32 (72.7%)	0.130	59 (64.8%)	8 (61.5%)	0.816
Hypertension [n]	70 (67.3%)	34 (56.7%)	36 (81.8%)	0.007	58 (63.7%)	12 (92.3%)	0.040
Diabetes mellitus, type 2 [n]	17 (16.3%)	5 (8.3%)	12 (27.3%)	0.009	11 (12.1%)	6 (46.2%)	0.001
Hyperlipidaemia [n]	78 (87.9%)	40 (66.7%)	38 (86.4%)	0.022	66 (72.5%)	12 (92.3%)	0.123
Smoking [n]	51 (49.0%)	28 (46.7%)	23 (52.3%)	0.572	41 (45.1%)	10 (83.3%)	0.032
Coronary artery disease [n]	44 (42.3%)	0 (0%)	44 (100%)	<0.001	32 (35.2%)	12 (92.3%)	<0.001
Previous myocardial infarction [n]	11 (10.6%)	0 (0%)	11 (25%)	<0.001	7 (7.7%)	4 (30.8%)	0.014
LV ejection fraction [%±SD]	57.1±11.3	59.0±10.9	55.0±11.0	0.076	60.5±11.5	56.7±6.7	0.150
Aortic orifice area [cm²±SD]	0.81±0.32	0.83±0.34	0.81±0.36	0.724	0.83±0.35	0.79±0.33	0.723
Maximum systolic gradient [mmHg±SD]	82.1±29.5	83.1±31.2	80.3±28.2	0.644	82.2±31	79.8±20	0786
Mean aortic gradient [mmHg±SD]	48.5±19.5	49.8±20.9	46.4±18.2	0.381	49.0±20.510.1	44.0±13.1	0.390
Cusps separation [mm±SD]	10.1±3.4	10.0±3.4	10.3 ±3.5	0.654	10.1±3.3	10.0±4.3	0.911

Abbreviations: LV – left ventricular, CAD – coronary artery disease, ICAS – internal carotid artery stenosis

Table II. Independent predictive risk factors for ICAS ≥50% and CAD development in patients with symptomatic severe and moderate degenerative aortic stenosis

Independent predictive risk factor of ICAS ≥50%	Beta	Beta error	ICAS risk	p
Intercept				0.019
Coronary artery disease	0.36	0.09	3.94	<0.001
Diabetes mellitus	0.18	0.09	1.95	0.054
Smoking	0.16	0.09	1.77	0.080
Left ventricular ejection fraction	–0.19	0.09	2.09	0.039
Independent predictive risk factor of CAD	**Beta**	**Beta error**	**CAD risk**	**p**
Intercept				0.051
Age	0.23	0.09	2.52	0.013
Internal carotid artery stenosis ≥50%	0.30	0.10	3.24	0.002
Diabetes mellitus	0.19	0.09	2.06	0.042
Hyperlipidaemia	0.17	0.09	1.96	0.053
Left ventricular ejection fraction	–0.19	0.09	2.17	0.033

Abbreviations: see Table I

predisposing factors [6-8]. The same factors, i.e. advanced age, hypertension, hyperlipidaemia and diabetes mellitus, also contribute to ICAS development [1, 9]. However, prevalence of ICAS among patients with DAS has not been a subject of extensive reports.

We have shown that ICAS ≥50% was present in approximately 13% of patients with advanced DAS, a finding consistent with the observations of other authors, who estimated prevalence of ICAS ≥50% to be 8-13% in such patients [10, 11]. In our study the prevalence of ICAS ≥70% among patients with clinical suspicion of CAD was 8.8%, similar to the rate observed in the group of DAS patients [12]. It is noteworthy that ICAS very rarely involves DAS patients without significant coronary lesions, but is seen often among patients with CAD (in 25%, 25% and 31% among patients with single-, two- and three-vessel CAD, respectively). Similar findings were reported by Terramani et al., who found that prevalence of ICAS ≥50% differed between DAS patients and was related to additional factors, e.g. coexistence of CAD [10]. These authors found that in DAS and CAD patients prevalence of ICAS ≥50% was six times higher than in DAS patients without CAD (2 vs. 12%) [10]. In our study a rate of ICAS ≥50% was 14 times higher among CAD patients than in patients with 'isolated' DAS. Thus, ICAS ≥50% involves predominantly DAS patients with coexisting CAD and in our patient group it was seen in more than one fourth of patients (27%).

When analysing the issue of DAS with CAD and ICAS coexistence, not only common risk factors but also common aetiological pathways should be taken into consideration [13, 14]. In 1986 Roberts suggested that calcifications involving aortic cusps and mitral annulus were a form of atherosclerotic degeneration in elderly patients [13]. Park et al. concluded that in patients at the mean age of 73 years with atherosclerosis of the peripheral arteries expressed as pathological ankle-brachial index (ABI <0.9), prevalence of calcifications in the aortic cusps and mitral annulus was 69 vs. 35% among patients without obliterating arteriosclerosis of the inferior extremities [14]. In spite of the suggested common aetiology of all three aforementioned diseases, the relatively low prevalence of ICAS among patients with advanced DAS and, in contrast, its high incidence in a group of ICAS and CAD coexistence, seems to indicate that special promoting circumstances must be involved in the development of aortic disease. The studies show that excluding atherosclerotic disease of extracardiac vessels (e.g. carotid arteries) with ultrasonography may help to anticipate no significant CAD in DAS patients [15, 16].

Identification of patients with ICAS based on auscultation of carotid arteries is more difficult because systolic murmur of the stenotic aortic valve radiates to the vessels of the neck and both murmurs have similar acoustic characteristics. It is estimated that among patients with murmur over the carotid arteries the prevalence of ICAS ≥50% is 18 to 50% [17, 18].

Detection of ICAS prior to valvular surgery is of paramount importance for perioperative stroke prevention. Edwards et al. have shown the risk of ischaemic stroke associated with AVR to be 1.58% and higher, 3.15%, among patients undergoing simultaneously AVR and CABG [19]. Despite the many mechanisms of perioperative stroke (embolisation, cerebral hypoperfusion, hypotension, low cardiac output syndrome), significant ICAS should be diagnosed before surgery because such a finding may change the therapeutic approach. Moreover, in selected cases simultaneous surgical correction of coexisting disorders is feasible [20, 21].

Specific scoring systems have been developed to stratify perioperative risk of AVR [3, 22-27]. The EuroSCORE (www.euroscore.org) and STS (*Society of Thoracic Surgeons classification*; www.sts.org) scales and that proposed by Amblera et al. are the most commonly used [3, 23-26]. Only in the EuroSCORE system is stenosis of ICAS ≥50% taken into account during perioperative risk stratification [2, 25]. Other models did not include stenosis of ICAS in the scoring system development, which reflects in general the still low awareness of an association of severe DAS with atherosclerosis of the peripheral arteries, including internal carotid ones.

Ultrasound Doppler examination of the carotid arteries is a routine diagnostic procedure performed before referring a patient with multi-vessel CAD for coronary artery bypass grafting, particularly in subjects with left main stem involvement, smokers, aged over 65 years, with history of cerebrovascular events, with murmur over the carotid artery and/or obliterating atherosclerosis [28]. Based on our findings it seems that ultrasound of the carotid arteries should be performed especially in patients with concomitant CAD and/or other cardiovascular risk factors such as diabetes mellitus and in heavy smokers.

Conclusions

1. Prevalence of ICAS ≥50% in unselected patients with degenerative aortic valve stenosis is 13% and 27% in subjects with coexisting CAD.
2. Risk factors of ICAS ≥50% include severe CAD, diabetes mellitus and smoking.
3. Doppler carotid ultrasound examination in DAS patients presenting with CAD, referred for aortic valve replacement, is indicated.

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Zwężenie tętnicy szyjnej wewnętrznej u chorych z degeneracyjną stenozą zastawki aortalnej

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Streszczenie

Wstęp: Zwężenie tętnicy szyjnej wewnętrznej (ICAS) u chorych poddawanych operacji wymiany zastawki aortalnej (AVR), niekiedy połączonej z operacją pomostowania aortalno-wieńcowego (CABG), istotnie zwiększa ryzyko okołozabiegowego udaru mózgu.

Cel: Celem pracy było określenie częstości występowania ICAS ≥50% u chorych kwalifikowanych do AVR z powodu zaawansowanej degeneracyjnej stenozy zastawki aortalnej (DAS).

Metodyka: Badaniem objęto 104 chorych (67 mężczyzn) w średnim wieku 63,4±8,4 roku (zakres 47–80 lat) z symptomatyczną zaawansowaną DAS (powierzchnia zastawki aortalnej <1,5 cm^2) kierowanych do koronarografii przed operacją AVR. U wszystkich chorych wykonano badanie ultrasonograficzne tętnic szyjnych metodą *doppler duplex* z oceną hemodynamiczną stopnia zwężenia ICAS wg kryteriów Blutha. U chorych z podejrzeniem ICAS obecność zwężenia potwierdzano w angiografii.

Wyniki: U 44 (42,3%) chorych stwierdzono chorobę wieńcową (CAD), tj. obecność co najmniej jednego zwężenia ≥50%, u pozostałych 60 (57,7%) chorych nie obserwowano istotnych zmian miażdżycowych w tętnicach wieńcowych. ICAS ≥50% stwierdzono u 13 (12,5%) chorych, w tym u 1 (1,7%) bez CAD, oraz u 12 (27,3%) spośród 44 chorych z CAD (χ^2 p <0,001). Częstość ICAS ≥50% wzrastała wraz z zaawansowaniem CAD, występowało ono u 4 (25%) spośród 16 chorych z jednonaczyniową CAD, u 3 (25%) z 12 chorych z dwunaczyniową CAD oraz u 5 (31,3%) spośród 16 chorych z trójnaczyniową CAD (ANOVA, p <0,001). Wieloczynnikowa analiza metodą wstecznej regresji krokowej wykazała, że niezależnymi czynnikami zwiększającymi prawdopodobieństwo występowania ICAS ≥50% u chorych z DAS są: CAD (p <0,001), cukrzyca (p=0,054), frakcja wyrzutowa lewej komory (p=0,039) oraz palenie papierosów (p=0,08). Natomiast niezależnym czynnikiem ryzyka CAD u chorych z DAS okazało się ICAS ≥50% (p=0,002).

Wnioski: Częstość ICAS ≥50% wśród chorych z DAS wynosi 13%, wzrasta do 27% przy współistniejącej CAD. Czynnikami ryzyka wystapienia ICAS ≥50% są CAD, cukrzyca i palenie papierosów. U chorych z DAS i CAD kwalifikowanych do AVR powinno się rozważyć wykonanie badania doplerowskiego tętnic szyjnych.

Słowa kluczowe: degeneracyjna stenoza aortalna, zwężenie tętnicy szyjnej, koronarografia

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