



# Survival and Prognostic Factors After Carotid Artery Stenting in Patients with Concomitant Coronary Disease

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## Abstract

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**AIM:** The aim of the study was to analyze the prognostic factors in patients after carotid artery stenting (CAS).

**METHODS:** In 329 patients after CAS, the median survival (MS) and overall survival (OS) were calculated for a follow-up period of 2–101 months. All patients underwent coronary angiography before carotid stenting and, if indicated, coronary revascularization. Four groups of factors were analyzed: Carotid disease, coronary artery disease (CAD), underlying cardiac pathology, and concomitant diseases.

**RESULTS:** MS in all patients was 86 months, OS at 1, 3, 5, and 9 years was - 94%, 85%, 73%, and 51%, respectively. Event free survival was 85 months. Log Rank-Mantel-Cox analysis demonstrated significantly reduced MS in 21 tested factors, most of them related to CAD. Two-step multifactorial Cox regression analysis defined only 7 of them as independent prognostic factors for the survival of patients after CAS: Left main stenosis, complete revascularization, late myocardial infarction, stroke, age over 70 years, valvular disease, and carotid score.

**CONCLUSION:** Survival of patients after CAS is limited mainly by CAD and underlying cardiac pathology. Staged revascularization treatment strategy may improve the prognosis and survival of patients with both carotid and coronary disease.

## Introduction

Carotid atherosclerosis is one of the leading causes of neurological morbidity and mortality. About 87% of strokes are ischemic, 30% of which are caused by atherosclerotic plaque in the carotid arteries resulting in stenosis and/or thrombosis in the aforementioned. Thromboembolism of 50–99% stenosis of the internal carotid artery is the cause of approximately 10–15% of strokes in adults [1], [2], [3]. Carotid stenosis above 50% occurs in a very wide range of people among the general population, but progresses markedly with age: In patients over and under 70 it is, respectively, 12.5% and 4.8% in men, and 6.9% and 2.2% in women [4], [5]. The characteristic localization and predilection site for stenosis is the carotid bifurcation and the ostium of the internal carotid artery. In clinical terms, carotid stenoses (CS) are defined as symptomatic, asymptomatic, and hemodynamically significant (>70% in 2 projections). For about 2 years, high-grade (>70%) asymptomatic CS progressed to thrombosis in 29% of patients, with 60% of them manifesting clinically (symptomatic stenosis) in the form of transient ischemic attack

and stroke [1]. The relative risk of ischemic stroke in asymptomatic CS over 50% is 2.0, and triples in patients with stenosis above 75%. A characteristic feature of the atherosclerotic process is its progression with involvement of various vascular areas [6], [7]. According to the REACH register (Reduction of Atherothrombosis for Continued Health) about 40% of patients with cerebrovascular disease have multifocal vascular involvement, clinically manifested by coronary heart disease (CHD) and/or peripheral artery disease (PAD) [8]. In the studies of Hertzler *et al.* and Cohen *et al.*, on CHD coronary stenosis was reported in 37% of patients with carotid endarterectomy (CEA) [9], [10], and according to Pieniazek *et al.* and Hofman *et al.* in 66–77% [11], [12]. The combination of coronary and carotid atherosclerosis is an unfavorable prognostic factor, and myocardial infarction (MI) and cardiac pathology in general are the most common causes of death after carotid revascularization [8]. Considering all of the above, the prognostic factors for patient survival after carotid and coronary revascularization, as well as the choice of the optimal strategy are a debatable issue. The aim of this study is to analyze the unfavorable prognostic factors for survival in patients with carotid and

concomitant coronary atherosclerosis after stepwise interventional revascularization.

## Patients and Methods

A prospective study followed 329 patients referred for carotid artery stenting (CAS). The average observation period was  $40.9 \pm 27.6$  months (May 2011–Sep 2019). The male:female ratio was 253 (76.9%): 76 (23.1%) with a mean age of 70 years (ranged 45–88 years). Patients with symptomatic carotid stenosis >50% and patients with asymptomatic carotid stenosis >70% were selected, assessed according to the NASCET criteria, with degree of stenosis classified according to a newly proposed score system. All patients underwent one-stage selective coronary and carotid angiography and, if indicated, coronary revascularization before CAS. CHD was assessed by means of Syntax and Gensini score systems. Revascularization procedures - percutaneous coronary intervention (PCI)/coronary artery bypass grafting (CABG) and CAS, including bilateral carotid revascularization were performed in separate step-by-step procedures. In CAS, self-expandable stents with mandatory distal protection device – distal filter were implanted. All patients received dual antiplatelet therapy (Clopidogrel + Aspirin) and statins. Patients were monitored intra- and post-procedurally, on day 30, at the 1<sup>st</sup> year mark, and until the end of the follow-up for the frequency and characteristics of early and late complications, as well as fatal outcome of any cause. The revascularization procedures and the standard panel tests were performed in certified interventional units and laboratories at a university hospital. For the purpose of the study, the relationship between the four groups of factors (carotid disease, CHD, underlying heart pathology, and concomitant diseases) and the registered peri- and post-procedural complications was sought. The data were processed using the statistical programs IBM SPSS, V 26 (2018), MedCalc V 19.0.7 (2019) and Minitab V 18.1 (2017). Two-step Kaplan–Meier, Log rank test, and two-step (2 blocks) multifactor Cox regression analysis were used to assess survival and prognostic factors.

## Results

### General risk profile of patients

With a significant predominance of males (76.9%), 88.8% of patients were over 60 years of

age, and their relative share was highest in the 69–78 age groups (43.2%). The analysis of the main risk factors for atherosclerosis, comorbidity and in particular concomitant cardiocerebral and other vascular pathology shows that 100% of patients were hypertensive, every second patient was overweight (58.1%) or a smoker (56.8%), every third patient had diabetes mellitus (33.4%) or hyperlipidemia (31.1%) (Table 1).

**Table 1: Main risk factors for atherosclerosis**

Risk factors	Males %	Females %	Total %
Hypertension	253 (100.0)	76 (100.0)	329 (100.0)
Age above 70	147 (58.1)	46 (60.5)	193 (58.3)
Overweight	142 (56.1)	49 (64.5)	191 (58.1)
Smoking	151 (65.6)	36 (47.4)	187 (56.8)
Diabetes	78 (30.8)	32 (42.1)	110 (33.4)
Hypertriglyceridemia	73 (28.5)	23 (30.3)	96 (31.1)
Hypercholesterolemia	55 (21.7)	17 (22.4)	72 (22.6)
CKD	51 (20.2)	15 (19.7)	66 (20.1)
COPD	12 (4.7)	8 (10.5)	20 (6.1)
Anemia	8 (3.2)	6 (7.9)	14 (4.4)

CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease.

In 90.9% of patients concomitant CHD was established, 39.8% had heart failure (HF), 38.6% had suffered MI, and 38.0% - ischemic stroke (Table 2).

Given the above information 287 (87.2%), patents were classified as high-risk and 42 (12.8%) standard risk patients refused surgical treatment.

### Median survival (MS) rate

The MS for the entire cohort for the observation period was 86 months (Kaplan–Meier and Log-rank test). High-risk patients had MS of 83 months, while, that is, the standard risk group MS was unattainable -  $\chi^2 = 6.683$ ,  $p = 0.010$  (Figure 1).

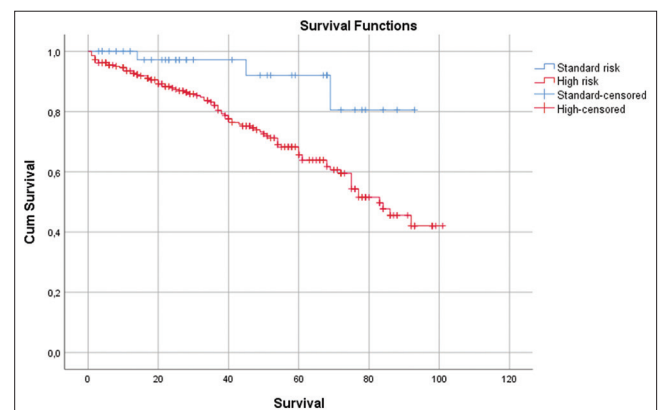


Figure 1: Risk profile and survival rate

### Survival prognostic factors

#### Carotid artery disease

##### Carotid score

The degree of CS was assessed by means of specifically designed carotid score, as a sum of points for the two carotid arteries: 0 points for

**Table 2: Concomitant cardiovascular disease**

Cardiovascular disease	Male (253)			Female (76)			Total (329)
	Total	<70 years	>70 years	Total	<70 years	>70 years	
CHD	237 (93.7)	127 (50.2)	110 (43.5)	62 (81.6)	27 (35.5)	35 (46.1)	299 (90.9)
Ischemic stroke	106 (42.1)	62 (24.6)	44 (17.5)	21 (27.6)	6 (7.9)	15 (19.7)	127 (38.6)
Pacemaker	19 (7.5)	1 (0.4)	18 (7.1)	3 (3.9)	1 (1.3)	2 (2.6)	22 (6.7)
Valvular heart disease	73 (29.0)	25 (9.9)	48 (19.0)	20 (26.3)	5 (6.5)	15 (19.7)	93 (28.3)
FA	32 (12.6)	10 (4.0)	22 (8.7)	6 (7.9)	1 (2.9)	5 (12.2)	38 (11.6)
HF	108 (42.7)	44 (17.4)	64 (25.3)	23 (30.3)	9 (11.8)	14 (18.4)	131 (39.8)
Hypertension	253 (100.0)	133 (52.6)	120 (47.4)	76 (100.0)	35 (46.1)	41 (53.9)	329 (100.0)
Renal stenosis	4 (1.6)	3 (1.2)	1 (0.4)	3 (3.9)	2 (2.6)	1 (1.3)	7 (2.1)
PAD	48 (19.0)	30 (11.9)	18 (7.1)	5 (6.6)	3 (3.9)	2 (2.6)	53 (16.1)
Past ischemic stroke	103 (40.7)	56 (22.2)	47 (18.6)	22 (28.9)	11 (14.4)	11 (14.4)	125 (38.0)

PAD: Peripheral artery disease, HF: Heart failure, CHD: Coronary heart disease, FA: Atrial fibrillation.

plaque of 0–29%, 1 point for low-grade stenosis of 30–49%, 2 points for moderate stenosis - 50–69%, 3 points for high/critical 70–95% stenosis, 4 points for subtotal occlusion - 95–99%, and 5 points for total occlusion - 100%. The mean carotid score of the patients was 4.2 points with a significant predominance of score 3 (40.1%), which corresponds to a high-grade/critical stenosis of 70–95% (Figure 2). The MS for the group with a high carotid score of 5–9 points was 75 months, while in patients with a carotid score of 1–4 points MS was unattainable ( $\chi^2 = 6.731, p = 0.009$ ) (Figure 3).

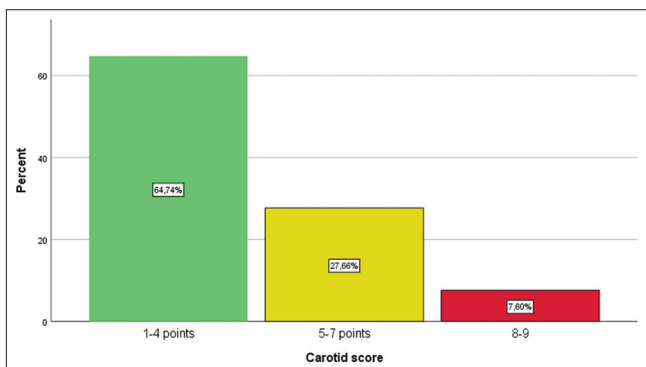


Figure 2: Carotid score distribution

**Bilateral carotid stenosis and symptomatology**

The presence of bilateral CS significantly reduces MS, the aforementioned being unattainable in unilateral stenosis ( $\chi^2 = 6.118, p = 0.013$ ) (Figure 4). The MSR in patients with symptomatic stenosis was 77.0 months and did not significantly differ from the MSR of asymptomatic CS  $p = 0.134$  (Figure 5).

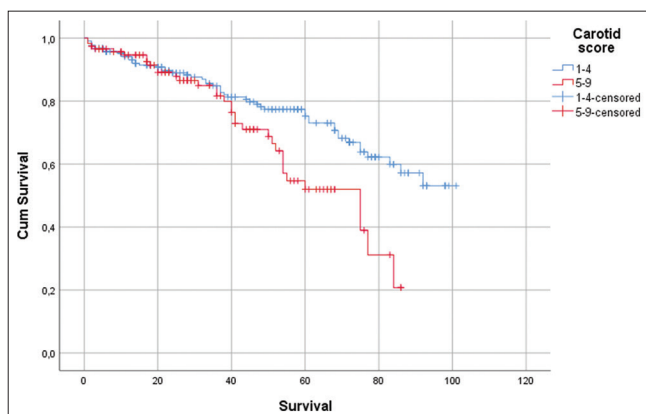


Figure 3: Carotid score and survival rate

**Previous strokes**

A significant factor for reduced survival was a previous stroke before CAS, with MS of 75.0 months compared to unattainable MS in patients without the previous ischemic stroke ( $\chi^2 = 4.762, p = 0.029$ ) (Figure 6).

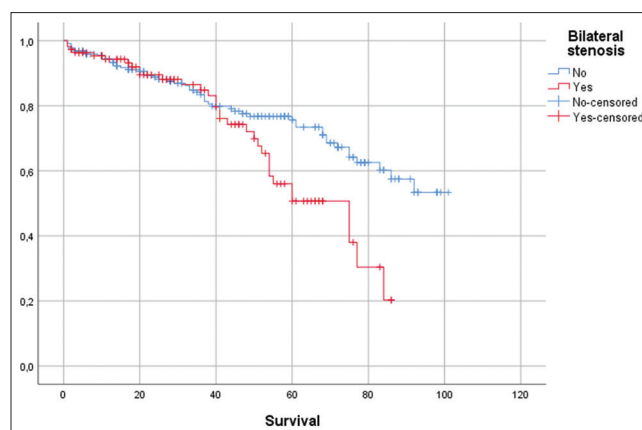


Figure 4: Bilateral carotid stenosis and median survival

**Other factors**

We did not find a relationship between patient survival and the type of implanted carotid stent ( $p = 0.311$ ) or carotid restenosis ( $p = 0.447$ ).

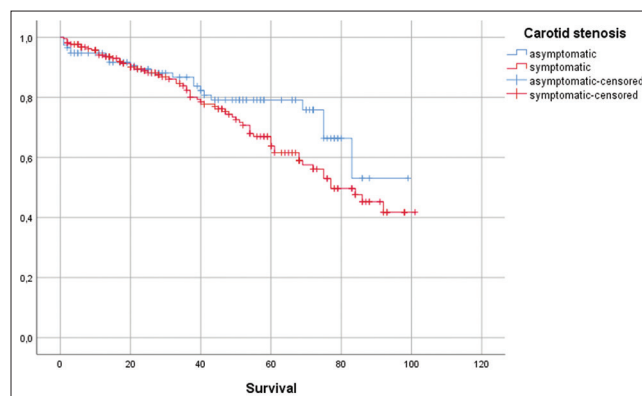


Figure 5: Symptomatic carotid stenosis and median survival

**CHD**

The MS for patients without concomitant CHD was unattainable, compared to 84 months

in the presence of such ( $\chi^2 = 3.121, p = 0.077$ ) (Figure 7).

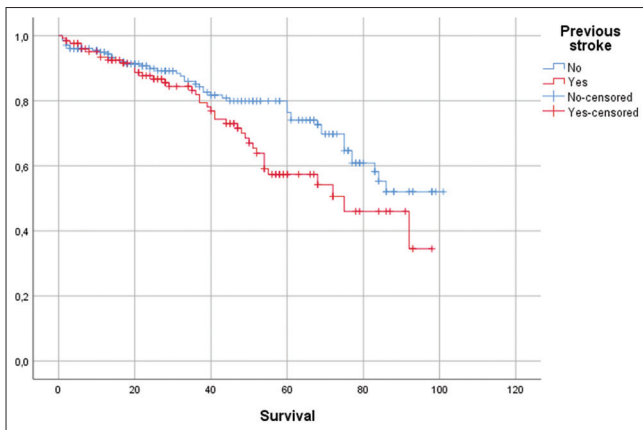


Figure 6: Ischemic stroke and survival

MS was significantly lower in patients with left main (LM) disease - 54.0 months, while in patients without LM disease the MSR was unattainable  $-\chi^2 = 30.188, p < 0.001$  (Figure 8).

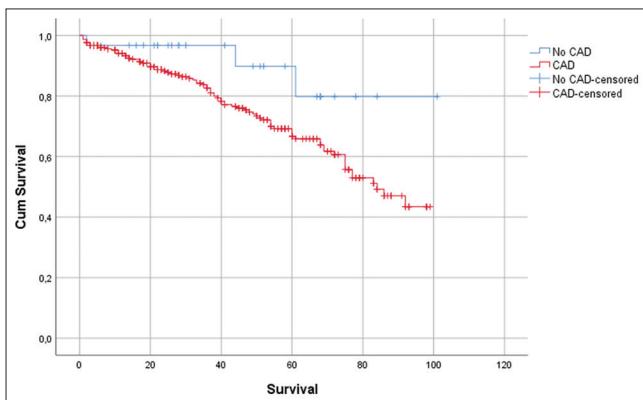


Figure 7: Coronary heart disease and median survival

### Coronary score systems

The two score systems are generally not used as indicators of survival, but rather to assess coronary stenosis and select a revascularization strategy. However, the MS of patients with Gensini score  $>70$  was 68 months, while in patients with Gensini score  $<70$  MSR was unattainable ( $\chi^2 = 17.860, p = 0.000$ ) (Figure 9). The MSR for Syntax score  $>32$  was only 55 months compared to a MSR of 83 months for Syntax score  $<23$  (Log Rank Mantel-Cox  $p < 0.000$ ) (Figure 10). What felt surprising was data on the discontinuity of the curves in patients with intermediate Syntax score 23-32 and the most favorable Syntax score  $<23$ , which turned out to have a lower survival rate. In this group the incidence of death from other causes, mainly malignant diseases, was the highest - 26 (21.3%).

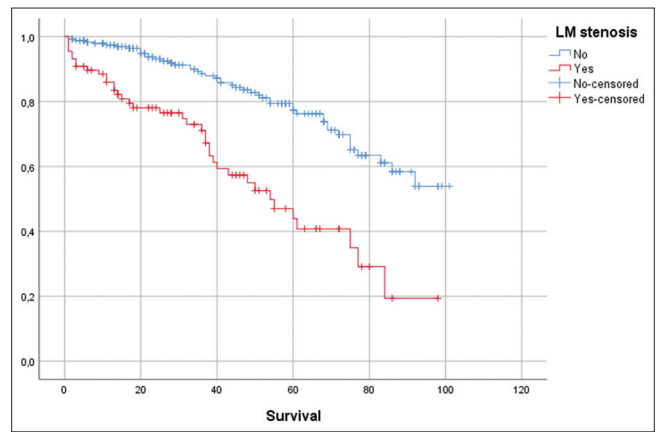


Figure 8: Left main disease and median survival

### Quality/degree of revascularization and re-intervention

MSR in patients with repeat coronary revascularization and without re-PCI did not show

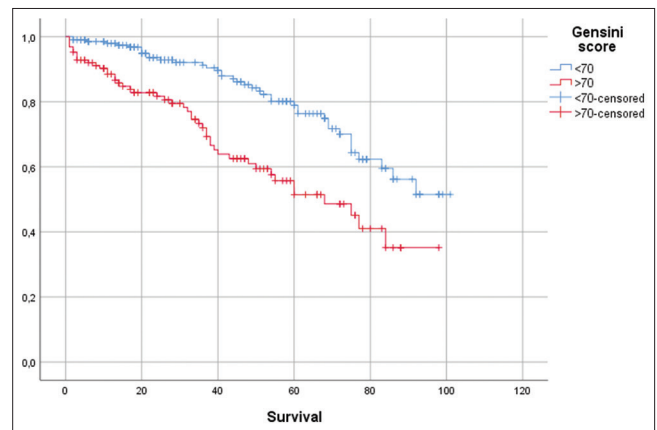


Figure 9: Gensini score and survival

statistically significant difference, 80.3 months survival in the re-intervention group compared to 69.9 months in patients with a single procedure (Figure 11).

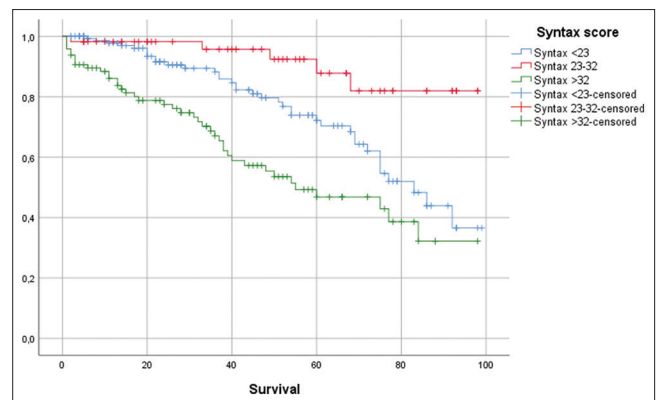


Figure 10: Syntax score and survival

It is important to point out that MS in patients with complete coronary revascularization was unattainable compared to the group with incomplete revascularization with MS of only 38 months ( $\chi^2 = 28.215, p < 0.000$ ) (Figure 12).

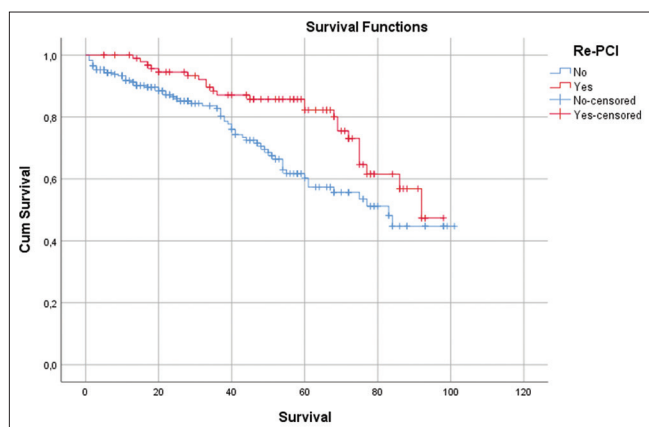


Figure 11: Re-do revascularization and survival

Coronary revascularization before or after carotid stenting?

Regarding this debatable but practically important question, we found that patients with coronary revascularization before CAS (74 months) had a higher

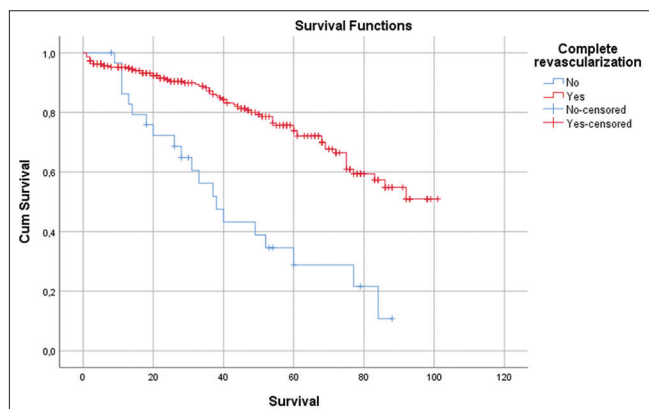


Figure 12: Degree of revascularization and survival

survival rate than those with revascularization after CAS (60 months) ( $\chi^2 = 5.306, p = 0.018$ ) (Figure 13).

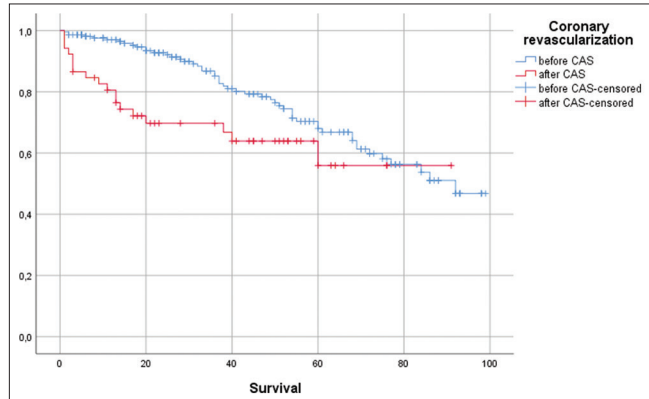


Figure 13: Percutaneous coronary intervention before/after carotid artery stenting – survival rate

Concomitant heart disease. Ejection fraction (EF) and HF

Depending on the value of EF, patients were divided into three groups: With normal EF  $\geq 55\%$ ,

slightly to moderately reduced EF 36–54%, and severely reduced EF  $\leq 35\%$ . There was a statistically significant difference ( $\chi^2 = 21.349, p = 0.000$ ), namely, a progressively decreasing MSR in the three groups, respectively: Unattainable MS in normal EF, 69 with moderately reduced EF and 43 months in patients with severely reduced EF (Figure 14).

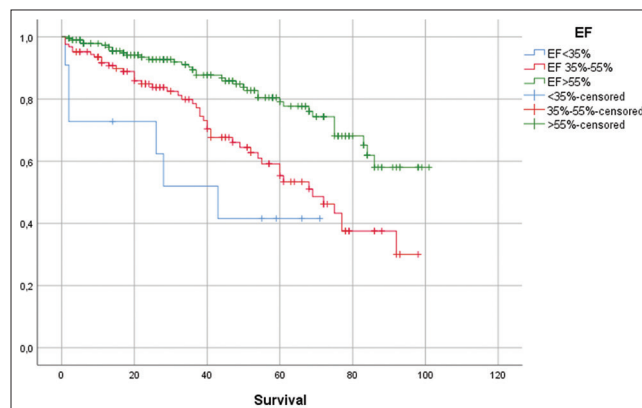


Figure 14: Ejection fraction and survival rate

The results are similar when analyzed in terms of HF: MSR in patients with HF was 60 months, and MSR in those without CH is unattainable ( $\chi^2 = 35.539, p = 0.000$ ) (Figure 15).

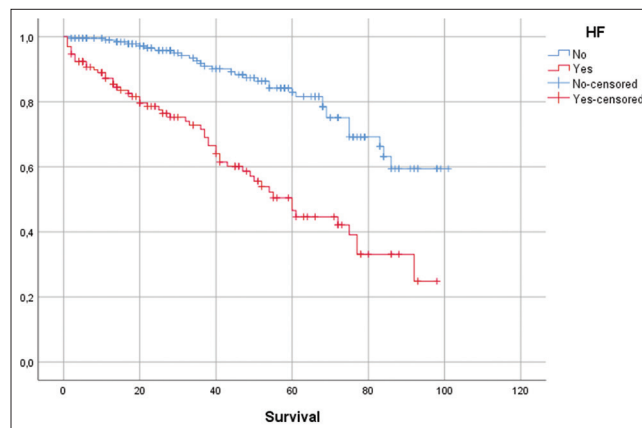


Figure 15: Heart failure and survival rate

Valvular heart disease, permanent pacemaker, and atrial fibrillation (FA)

In patients with concomitant severe valvular heart disease, MSR was only 61 months, and in the group without valvular pathology - unattainable ( $\chi^2 = 27.237, p = 0.000$ ) (Figure 16). An interesting fact was that patients with implanted pacemaker had a two-fold reduction in MSR - 41 months, compared to MSR without a permanent pacemaker - 92.0 months ( $\chi^2 = 13.132, p = 0.000$ ) (Figure 17). The most common arrhythmia in the monitored group of patients - FA did not show a significant influence on survival.

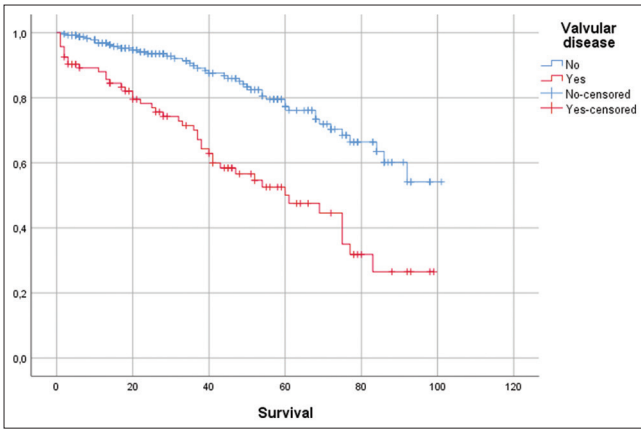


Figure 16: Valvular heart disease and survival rate

Late MI and late stroke

Our results show that the impact on survival of late-onset cardiac events such as MI and stroke is very different. MSR in patients without late MI was unattainable, while in case of MI MSR was significantly reduced - 60 months ( $\chi^2 = 11.118$ ,  $p = 0.001$ ) and is almost 2 years shorter than MSR of the whole group (Figure 18). However, a late ischemic stroke with MSR of 75 months did not have a significant effect on MSR ( $\chi^2 = 1.978$ ,  $p = 0.160$ ) (Figure 19).

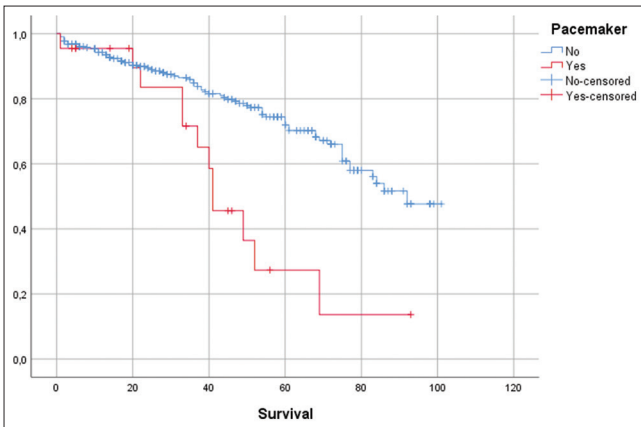


Figure 17: Permanent pacemaker and survival rate

Sex, age, concomitant diseases, and laboratory abnormalities Table 3 are shown in Table 3 (Table 3).

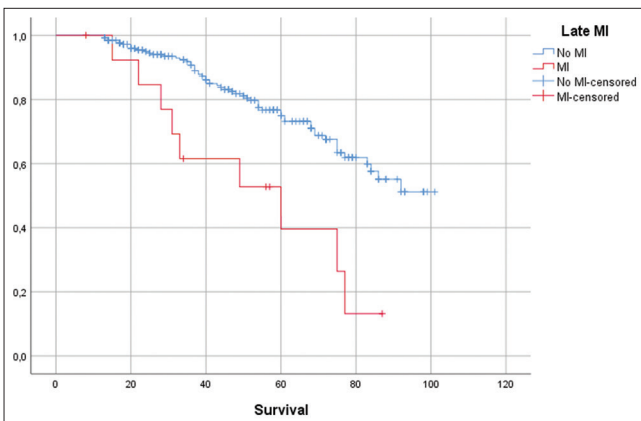


Figure 18: Late miocardial infarction and survival rate

In the analysis of these heterogeneous indicators, the significant risk factors in the prognosis turned out to be CKD ( $p < 0.000$ ), diabetes mellitus

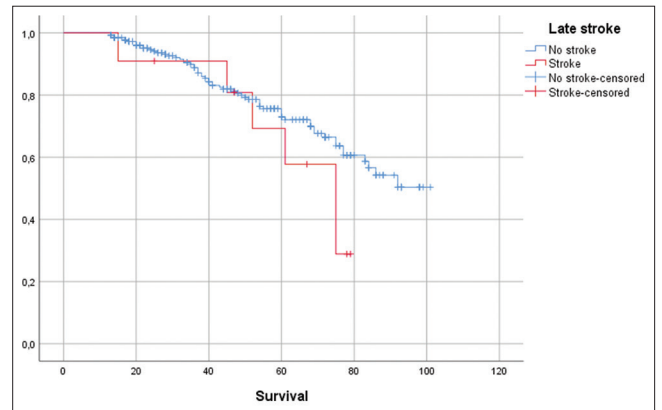


Figure 19: Late ischemic stroke and survival rate

( $p = 0.004$ ). Of particular interest is a group of 11 patients with residual elevated troponin levels  $\geq 0.1$  to 1.0 in whom carotid stenting was performed <14 days after acute coronary syndrome (ACS). MSR in the group without elevated troponin was unattainable compared to significantly lower in patients with elevated troponin - 20 months ( $\chi^2 = 15.985$ ,  $p < 0.000$ ). Similarly there was lower MSR in patients with hyperfibrinogenemia ( $\chi^2 = 4.164$ ,  $p = 0.041$ ).

Combinations with unfavorable prognostic significance

While, in general, FA had no effect on survival, the combination of FA and male gender turned out to lead to a significant reduction in MSR ( $\chi^2 = 6.656$ ,  $p = 0.010$ ). Similarly, anemia in a female patient resulted in MSR of 54 months ( $p = 0.023$ ).

Table 3: MS rate in patients with concomitant disease and biochemical marker deviations

Indicator	MSR	p	Indicator	MSR	p
Hypertriglyceridemia	83.0	0.278	Anemia	54.0	0.135
Increased LDL levels	93.0	0.955	PAD	84.0	0.746
Residual increase in troponin levels	20.0	0.000	COPD	86.0	0.846
CKD	55.0	0.000	Hypertriglyceridemia	83.0	0.278
Diabetes	69.0	0.004	Hyperfibrinogenemia	72.0	0.041

PAD: Peripheral artery disease, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, LDL: Low-density lipoprotein.

Prognostic model for survival in patients with carotid stenosis and interventional revascularization

The great number of diverse statistically significant relations in a huge panel of over 40 indicators cannot contribute to a clear prognostic model. Through a two-step (2 blocks) multifactorial Cox regression analysis, we looked for "independent" prognostic factors for patient survival. In block 1, we included 12 factors with expected significant impact on survival, and in block 2-8 factors with probable prognostic significance. Seven of them turned out to be independent prognostic risk factors (Table 4).

**Table 4: Independent survival prognostic factors in patients after CAS and preceding coronary artery revascularization**

Factor	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
LM_disease	-0.844	0.278	9.198	1	0.002	0.430	0.249	0.742
Complete revascularization	0.682	0.331	4.258	1	0.039	1.978	1.035	3.782
Late MI	-1.112	0.408	7.419	1	0.006	0.329	0.148	0.732
Previous stroke	-0.921	0.268	11.856	1	0.001	0.398	0.236	0.672
Age above 70	-1.027	0.300	11.747	1	0.001	0.358	0.199	0.644
Valvular heart disease	-1.001	0.267	14.014	1	0.000	0.367	0.218	0.621
Carotid score	-0.535	0.271	3.915	1	0.048	0.585	0.344	0.995

CAS: Carotid artery stenting, MI: Myocardial infarction, LM: Left main.

## Discussion

In specialized literature, the effectiveness of CAS and its complications have been analyzed for decades in numerous randomized clinical trials (RCTs) among a huge cohort of patients. Almost all older RCTs and national registries, as well as meta-analyses from the CREST, EVA-3S, SPACE, ICSS studies, generally documented a higher incidence of periprocedural stroke by day 30, especially in adult patients over 70 years of age treated with CAS [13]. In recent years, in parallel with the improvement of interventional methods, data from similar studies show comparable results and no difference in long-term follow-up [14], [15]. In 2017 Sardar *et al.* in a meta-analysis - CAS versus CEA of 5 RCTs including 6526 patients, found no differences between the two revascularization methods (OR 1.22; 95% CI: 0.94–1.59) in terms of periprocedural complications and ipsilateral stroke on follow-up for 5.3 years [16]. CAS is established as an effective procedure with strict indications and generally accepted intervention protocols [17], [18]. All studies, both earlier and present lead to one conclusion: It is not the neurological complications but rather CHD and cardiovascular pathology that influence early and late complications and lead to reduction in survival following CAS and CEA [19], [20], [21].

Taking into account the literature data, the systemic nature of the atherosclerotic process and the characteristics of the studied group of patients, we analyzed the risk factors in patients with indications for CAS and concomitant coronary stenosis. All our patients underwent one-stage selective coronary and carotid angiography and in indications - PCI/CABG before CAS, as an attempt to minimize the negative role of CHD and cardiac pathology, that is, to increase the benefits of CAS in the short and long term. Pre-carotid angiography, according to a series of publications by Illuminati *et al.*, is the only independent variable that not only predicts the occurrence of post-operative coronary ischemia, but also reduces the likelihood of cardiac ischemia 4-fold after CEA [22], [23]. Similar protocol, officially Class IIb in recommendations, was found appropriate in our patients, 87.2% of whom were assessed as complex high-risk mainly due to

cardiocerebral and other cardiovascular pathology, and last but not least pronounced comorbidity (Tables 1 and 2). Our incidence of accompanying CHD was higher than this cited in literature. According to Kallikazaros *et al.*, the incidence of carotid stenosis >50% increases from 5% in patients with single-vessel coronary artery disease (CAD) to 40% in the presence of LM disease [24]. According to Hoffman *et al.*, coronary stenosis  $\geq 50\%$  in patients indicated for elective carotid stenting is 77.1% [12], and according to Enomoto *et al.* 49.1% [25]. Predictive correlations between the presence of carotid stenosis and high Syntax and Gensini scores were also sought. Avci *et al.* found a positive correlation between Syntax score I, three-vessel disease, and carotid stenosis [26]. A similar correlation between the intima-media thickness of the carotid artery and Syntax score I and II was reported by the teams of Saedi *et al.*, Ikeda *et al.*, Aksu *et al.*, and Korkmaz *et al.* [27], [28], [29], [30]. The results of Ozturk and Sahin and Costanzo *et al.* and col [31], [32], [33] are opposing. Despite the various incidences cited above, the combination of carotid and coronary atherosclerosis is an indisputable clinical fact. It is no coincidence that CS >50% show increased risk for CHD and are considered equivalent to the above [34], [35]. In patients with symptomatic or asymptomatic carotid stenosis, the presence of CHD increases the risk of vascular cardiocerebral complications during long-term follow-up [21], [36], [37].

We assessed the prognostic prospect of four groups of risk factors which are among the most frequently cited in the specialized literature with regards to complications in revascularization procedures [20], [38]. They were pre-tested by single-factor and multi-factor analysis, through which we confirmed a reliable correlation or predictive correlation between them and the most important adverse events in the course of follow-up. Through the adopted stepwise revascularization protocol (CAS after PCI), we did not find a significant difference in MSR among 287 comprehensively assessed high-risk patients compared to the others at standard risk and between a group with angiographically proven CHD (299 patients) and A group without CHD. There is not much difference in the number of patients - CHD is the most common comorbidity in high-risk patients with concomitant disease, organ dysfunction and biochemical abnormalities. Respectively, the MSRs are similar and insignificantly lower than the MSRs (86 months) for the whole group - 83 months for the high-risk group and 84 months for the patients with previous coronary intervention. In the absence of coronary revascularization, Arif *et al.* stated that "the presence of CHD was accompanied by 22% mortality after CAS, compared to 0% in the group without CHD at follow-up of  $71.9 \pm 31.7$  months" [36]. In a significant group of patients The European Carotid Surgery Trial study also shows that coronary heart death in patients with carotid stenosis reaches 30% over a period of 10 years [39].

Our findings also support the idea of the main role of cardiac pathology in the long run regarding patients with carotid and CAD: Unlike late MI, late stroke does not have a significant effect on survival.

In terms of prognosis, among the various indicators characterizing carotid pathology, it turned out that a high carotid score of 5–9 points, stroke and bilateral carotid stenosis correlate with lower MS. In the CREST study, perioperative stroke was also associated with three times worse long-term survival [40] as far as other indicators are concerned, symptoms, the type of implanted carotid stent and carotid restenosis did not show statistical significance.

In the second group of tested indicators, characterizing CHD, significantly lower survival was registered in LM disease (54 months), in Gensini score >70 (68 months), and Syntax score >32 (55 months). An important result and indirect proof of the importance and necessity of preliminary revascularization of CHD is the high statistical significance of low MSR - 38 months in patients with incomplete coronary revascularization ( $\chi^2 = 28.215$ ,  $p < 0.000$ ). The presence of coronary pathology, especially untreated, compromises the results of CAS. Even among the general population stroke patients and the presence of CHD, indicate an incidence of 24% for cardiovascular events over a period of 2 years, according to Amarenco *et al.* Cardiac pathology (exception granted for AF) such as HF, low EF, valvular heart disease, and permanent pacemaker also turned out to be negative prognostic factors in terms of survival.

Concomitant diseases and biochemical abnormalities with prognostic significance for survival were only CKD, diabetes mellitus and residual elevated troponin in patients with previous PCI up to 14 days after ACS. CKD and DM are known and discussed in the literature negative prognostic conditions due to critical organ dysfunction and their frequent combinations with other risk factors [20]. The first positive results of preliminary coronary revascularization in atherosclerotic changes in other vascular areas subject to surgery were reported more than 40 years ago by Hertzler *et al.* [41]. Despite reasonable remarks on patient selection, two studies CARP [42] and DECREASE-V [43] not only did not reveal perioperative and long-term benefit from preliminary coronary revascularization, but also had a serious negative impact worldwide. Only in 2009 Monaco *et al.* in a prospective study refute the negative trend and point out that routine preoperative coronary angiography and selective PCI provide better long-term and event-free survival in patients needing vascular surgery [44]. Optimal behavior in patients with both carotid and CAD is still controversial. Four possible strategies are applied - simultaneous or stepwise CABG and CAS, CABG and CEA, PCI and CEA, and PCI and CAS. The results, however, are very confusingly different: The risk of stroke/death in simultaneous CEA and CABG is highest and lowest in a stepwise approach [45], [46]; in a registry of 27,084 patients in the CAS-CABG versus CEA-CABG strategies, the incidence of postoperative stroke was

2.4% versus 3.9% ( $p < 0.001$ ) and of stroke/death 6.9% versus 8.6% ( $p = 0.1$ ) [47]; according to Versaci *et al.* CAS immediately before CABG gives promising results with a low incidence of death/stroke [48]; 132 patients treated with CAS and CABG on the same day had an in-hospital stroke rate of 0.75% and a 5- and 10-year period free from neurological events of 95% and 85%, respectively; analysis in 350 patients with staged CEA, followed up to 90 days after CABG showed the worst results for MI between revascularization stages [49]. In recent studies by the teams of Sulženko [19] (2019), Kumar *et al.* [50] (2020), Shen *et al.* [51], Manthey *et al.* [52] (2020), Tzoumas *et al.* [53] (2020) results and opinions are mixed, but the need to utilize the effect of CEA/CAS in underlying coronary stenosis by revascularization of both vascular areas is a common opinion. Addressing this problem, our results in high-risk patients show that stepwise PCI before CAS yields significantly better MS than revascularization after CAS ( $\chi^2 = 5.306$ ,  $p = 0.018$ ). Please add strengths and limitations of this study.

## Conclusion

In the study, we focus mainly on the importance of risk factors for the prognosis and survival of patients with carotid and coronary disease after interventional revascularization. In practice, this is the final assessment of the efficiency and effectiveness of any revascularization procedure in any vascular pool. Unfortunately, RCTs are missing so far, and the assessment of each of the risk factors for survival is rare. Insufficient literature data and a very heterogeneous patient population in the individual publications make it difficult to correctly compare our results, which we present cautiously. In modern times, it is still difficult to determine the “ideal” revascularization strategy for carotid and coronary stenosis. Our results show not only the frequent combination between them, but also the possibility of increasing the benefit of CAS by minimizing the effects of concomitant CHD and vascular pathology. The proposed survival model identified by multivariate Cox regression analysis identified the following independent prognostic factors: LM disease, complete revascularization, late MI, stroke, age above 70 years, valvular heart disease, and carotid score. They require a complex therapeutic approach, both before and after the revascularization procedure during the follow-up period.

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