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MRI- and CT-derived carotid plaque characteristics and stroke: Insights from the ANTIQUE study

Short title: Carotid plaque characteristics and risk of stroke

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WHAT'S NEW?

Intraplaque hemorrhage (IPH) is considered one of the strongest predictors of stroke of all carotid plaque characteristics. However, the presence of IPH varies in individual groups of patients. Of 132 patients (59 symptomatic/157 asymptomatic stable carotid plaques) were included, the presence, age, location, or volume of IPH were not related to the risk of cerebrovascular events. Only stenosis degree and additionally alcohol consumption were independent stroke risk factors. Our findings suggest that a complex evaluation of carotid plaque characteristics and common stroke/atherosclerosis risk factors should be considered rather than focusing only on IPH in high-risk patients needing prospective follow-up, risk stratification, and further treatment, but larger prospective studies are needed.

Abstract

Background: Carotid plaque composition plays a key role in plaque stability and patient risk stratification. Of unstable plaque features, intraplaque hemorrhage (IPH) is considered the main risk factor for stroke development.

Aims: We aimed to assess an association between the presence of IPH and other plaque characteristics detectable by computed tomography (CT) or magnetic resonance imaging (MRI) and stroke.

Methods: Of all consecutive patients from the ANTIQUE study, 132 patients (91 males; aged 70.0 [8.6] years) with 59 symptomatic and 157 asymptomatic stable carotid plaques were included in the retrospective analysis of prospectively collected data. Plaques in the vascular territory of ischemic stroke within 90 days were classified as symptomatic and were diagnosed by CT and MRI after symptoms occurred. Plaques without progression and clinical infarction were classified as asymptomatic stable. Univariate and multivariate logistic regression analyses were performed to identify risk factors.

Results: The presence, age, location, and volume of IPH were not related to stroke risk (P >0.05). Patients with a symptomatic plaque were more likely to consume alcohol (P = 0.005), had more severe stenosis (CT median: 80% vs. 72%; P = 0.005; MRI median: 79% vs. 72%; P = 0.01), lower American Heart Association grade (P = 0.03), and more frequent lipid plaque (89.8% vs. 76.4%; P = 0.04) compared to patients with asymptomatic stable plaques. Stenosis

severity (odds ratio [OR], 1.037; 95% CI, 1.015–1.059) and additionally alcohol consumption (OR, 3.571; 95% CI, 1.694–7.527) were found the only significant predictors of a recent stroke. **Conclusions:** In this cohort, no IPH or other plaque characteristics were associated with stroke risk. The degree of stenosis and alcohol consumption were the only associated with ipsilateral stroke. Larger prospective studies considering plaque characteristics are needed.

Key words: carotid atherosclerosis, computed tomography, intraplaque hemorrhage, magnetic resonance imaging, stroke

INTRODUCTION

Atherosclerosis-induced stenosis occurs most frequently at the site of the carotid bifurcation and the origin of the internal carotid artery (ICA) among all blood vessels that supply the brain, and its most common serious complication is ischemic stroke [1]. Growing atherosclerotic plaques cause stenosis in carotid arteries in up to 75% of men and 62% of women over the age of 65 years, and carotid artery stenosis causes approximately 18%–25% of all strokes [2, 3].

Carotid plaques can be split from the clinical point of view as stable, i.e. asymptomatic with a low chance of rupture and stroke development, and unstable, i.e., potentially symptomatic with a high risk of stroke, or symptomatic which caused acute brain ischemic events [4, 5]. Generally, unstable plaques are characterized by the presence of a thin fibrous cap overlying a large lipid core, show intraplaque hemorrhage (IPH), stenosis >90%, ulceration/fissure, active inflammation, neovascularization, and tend to be a source of silent microemboli [5–7]. Stable plaques are composed mainly of solid fibrous tissue, and show calcification, with lipids either absent or present only in small amounts [4, 8].

IPH in carotid stenosis is considered one of the strongest predictors of stroke of all plaque characteristics in symptomatic and asymptomatic patients and also in patients with low stenosis [9–12]. However, the presence of IPH varied in frequency between symptomatic progressive plaques, symptomatic stable plaques, asymptomatic progressive plaque, and stable asymptomatic plaques [13, 14]. Therefore, problems related to the classification of IPH and stroke risk in individual groups of patients appeared.

For the noninvasive diagnostic imaging of atherosclerotic plaques, carotid artery ultrasound, magnetic resonance imaging (MRI), and computed tomography (CT) are commonly used because they are widely available in developed countries and have high sensitivity and specificity [15].

The aims of this retrospective data analysis from the prospective multicenter observational study were 1) to assess an association between IPH detected by MRI and ipsilateral transient ischemic attack (TIA) and/or stroke, and 2) to compare other atherosclerotic plaque characteristics detectable by CT and MRI between symptomatic and asymptomatic stable plaques in the carotid bifurcation.

MATERIAL AND METHODS

All consecutive patients from Atherosclerotic Plaque Characteristics Associated With a Progression Rate of the Plaque in Carotids and a Risk of Stroke (The ANTIQUE Study; ClinicalTrials.gov Identifier: NCT02360137) who underwent clinical and diagnostic examinations between October 2016 and March 2019 were included. The patients were recruited into the comprehensive stroke center's sonographic laboratory from those indicated for neurosonology examination in primary or secondary stroke prevention or acute stroke diagnostics [16]. Conservative and/or interventional treatment (carotid endarterectomy or stenting) was indicated according to valid guidelines for all patients [17]. Inclusion and exclusion criteria are shown in Figure 1.

Subsequently, only carotid plaque (the most stenotic lesion when multiple plaques were present) that caused at least 30% stenosis on ultrasound (transition from laminar to turbulent blood flow stated in Reynolds numbers as a critical value: 2000–2400) [18, 19] was analyzed.

Clinical characterization

Extracranial carotid atherosclerotic plaques were divided into two groups: symptomatic and asymptomatic stable plaques. Symptomatic plaques were defined as only carotid plaques in patients with clinical signs of ipsilateral cerebrovascular events (TIA, stroke, amaurosis fugax, and/or retinal infarction) in the carotid artery region in the prior 90 days, excluding patients with other potential stroke etiology (cardioembolic, lacunar, arterial dissection, vasculitis, other rare causes of stroke). Plaques in patients without clinical signs of TIA/stroke in the relevant arterial territory and without progression (changes <20% of plaque width) within the last 3 years were classified as asymptomatic stable plaques.

In case a patient experienced a clinical cerebrovascular event (TIA, stroke, amaurosis fugax, and/or retinal infarction), only ipsilateral carotid plaque to the affected territory was evaluated. In asymptomatic patients with bilateral stable plaques, both plaques of the right and left ICA were analyzed. All other plaques (asymptomatic progressive, with detected silent infarction, etc.) were excluded from the analysis to reach homogeneous groups of plaques.

When a patient had a cerebrovascular event, brain CT and ultrasound examination were performed as soon as possible. The patient was immediately scheduled for CT angiography (CTA) and MRI of carotid arteries (performed within 30 days) in the case of detected carotid stenosis (at least 30%) and enrollment in the study.

Computed tomography

All patients underwent standard multi-detector helical CTA of the cerebral and carotid arteries on different machines with 50–100 ml of intravenous iodine contrast agent (CA). Detailed information is provided in the Supplementary material.

The degree of carotid artery stenosis was evaluated according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria [20]. The plaque structure was evaluated according to the representation of individual components in the plaque by measured density (expressed in HU). A distinction was made among lipid (<60 HU), fibrous (60–130 HU), and calcified components (>130 HU) by measurement on the voxel level using drawn region of interest (2–10 pixels per region) in several sections covering the entire plaque (minimum of three sections) [21]. The plaques were further divided according to their surface morphology: smooth (plaque surface without signs of irregularity), irregular (small changes on plaque surface) or ulcerated (excavation >1 mm depth on plaque surface, visible in at least two planes) [22].

Magnetic resonance imaging

MRI examinations of carotid arteries were performed on different machines. The MRI carotid bifurcation examination protocol consisted of four basic sequences: T1w, 3D MPRAGE, T2w, and 3D TOF. In selected patients, 7.5–10 ml CA was administered (postcontrast T1w). Detailed information is provided in Supplementary material.

The signal intensities of the individual characteristics of the carotid plaques were visually compared with those of the sternocleidomastoid muscle. Intraplaque hyperintensity on MPRAGE sequences signaled the presence of IPH, further divided into acute (fresh, less than 1 week old: hyperintense on TOF and T1w images, and isointense to hypointense on T2w images) and subacute (recent, 1–6 weeks old: hyperintense on TOF, T1w and T2w images; Supplementary material, *Figure S1*). The location of IPH as superficial (juxtaluminal) or deep (saturated plaque) and the volume of IPH compared to the volume of the whole plaque (0%, 20%, 40%, 60% and 80%) were evaluated only visually [23]. Evaluation of other plaque characteristics is available in Supplementary material.

One experienced rater (D.P.) evaluated all plaque characteristics on CT and MRI based on the described methods used in previously published studies. The rater was blinded to the patient's status, medical history, and CT results during MRI evaluation.

Demographic data and clinical examinations

Age and sex were recorded from the patient demographic data. Information on the CT and MRI examinations performed and the side of ICA stenosis were recorded from the imaging data of patients. From the patient anamnestic data, selected past and present diseases associated with atherosclerosis and stroke (arterial hypertension, diabetes mellitus, dyslipidemia, coronary arterial disease, myocardial infarction, atrial fibrillation, chronic kidney disease, and autoimmune disease) were recorded and their definitions are listed in Supplemental material. Data on smoking (number of cigarettes per day) and daily alcohol consumption (1 unit/20 g of alcohol = 0.5 l of beer/2 dl of wine/0.5 dl of spirits) the last year, together with the use of antithrombotic and statin medication were also recorded.

In addition to ischemic stroke, possible TIA, amaurosis fugax, and retinal infarction were recorded among the monitored ischemic disorders. Ischemic stroke was defined as an episode of neurological dysfunction caused by focal cerebral infarction persisting ≥24 hours confirmed by CT and TIA as focal arterial ischemia with transient symptoms lasting <24 hours without evidence of infarction on CT. Retinal infarction was defined as acute painless visual loss (retinal ischemic stroke) and amaurosis fugax as retinal TIA. Updated definitions by expert consensus were used to define cerebrovascular events [24].

Ethics

The study was approved by the Ethics Committee of the University Hospital of Ostrava (no 605/2014) and performed according to the Declaration of Helsinki and its later amendments. All patients provided signed informed consent.

Statistical analysis

A pre-study statistical calculation determined that the minimum sample size of 198 carotid stenoses is required to demonstrate a 10% difference in IPH presence between symptomatic/asymptomatic stable carotid plaques with an alpha level of 5% and power of 80%. Shapiro–Wilk normality tests verified that only age had a normal distribution. A comparison of age samples was performed with a two-sample t-test. For other quantitative and ordinal

variables, the Mann–Whitney U-test was used. Qualitative variables with absolute and relative frequencies were described, and group comparisons were performed with Fisher's exact test.

Multivariate analysis was performed with logistic regression using the backward stepwise (likelihood ratio) method with symptomatic stenosis (ischemic stroke, TIA, amaurosis fugax, and retinal infarction) as dependent variables, and with selected demographic factors (age, sex, and side of stenosis), risk factors (arterial hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, myocardial infarction, atrial fibrillation, chronic kidney disease, smoking, alcohol consumption, antithrombotic therapy, and statin therapy), CT plaque characteristics (percentage of stenosis, lipid plaque, fibrous plaque, calcification, and plaque surface) and MRI plaque characteristics (IPH, age of IPH, location of IPH, volume of IPH, percentage of stenosis, AHA plaque type, lipid-rich necrotic core [LRNC], fibrous cap, and enhancement) as independent factors.

P <0.05 was considered as significant. SPSS Statistics 23 (International Business Machines Corporation, Armonk, NY, US) and STATA 17 (Stata Corp., TX, US) were used for statistical data processing.

RESULTS

Of 1863 patients enrolled in the ANTIQUE study, a total of 132 patients (91 males; mean age 70.0 [8.6] years) passed all inclusion and exclusion criteria and were included in the analysis. Of the 264 total imaged carotid bifurcations, 216 arteries were analyzed (excluded arteries due to carotid occlusion in 17 cases, carotid stenosis <30% in 10 cases, silent but not recent clinically manifested brain ischemia in 21 cases). Finally, a smaller number of carotid plaques was evaluated with MRI than with CT (199 vs. 216, respectively). In 17 carotid plaques evaluated by CT, the MRI image quality was not sufficient to perform an MRI analysis of plaque morphology. The study flow chart is in Supplementary material, *Figure S2*.

A total of 59 atherosclerotic plaques were classified as symptomatic (43 males; mean age 69.7 [9.6] years) and asymptomatic stable plaques were detected in 157 carotid arteries (108 males; mean age 70.1 [8.2] years). Comparing demographic stroke risk factors, patients with symptomatic plaques were significantly more likely to drink alcohol in greater quantities (demographic data in Table 1).

On MRI, we found no significant difference between symptomatic and asymptomatic stable plaque groups in the presence, age, location, or volume of IPH (Table 2). Patients with symptomatic carotid plaques were statistically significantly more often categorized by lower AHA plaque type (IV–V/VI) and exhibited a higher degree of stenosis (median: 79% vs. 72%)

compared to asymptomatic stable plaques. The evaluation of carotid plaque characteristics on CT showed a significant difference between the symptomatic and asymptomatic stable plaque groups in stenosis severity (median: 80% vs. 72%) and lipid plaque (89.8% vs. 76.4%). Other characteristics assessed on CT or MRI did not differ significantly between the groups (Table 3 for MRI, Table 4 for CT).

Age, sex, and the following variables with P <0.20 were included in the logistic regression analysis: coronary arterial disease, smoking, alcohol consumption, lipid part, AHA plaque type, and stenosis measured on CT and MRI (enhancement was not included due to the small number of measured values). Multinomial logistic regression indicated that only alcohol consumption (odds ratio [OR], 3.571; 95% CI, 1.694–7.527) and stenosis severity on MRI (OR, 1.037; 95% CI, 1.015–1.059) were significant predictors of recent TIA/stroke. Detailed logistic regression results including all steps are presented in Supplementary material, *Table S1*. The distribution of carotid stenosis severity in both groups is presented in Supplementary material, *Figure S3*, and probability models of plaque being symptomatic for alcohol abuse and LRNC related to stenosis severity are in Figures 2 and 3, respectively. Finally, an association between daily alcohol consumption and stenosis severity is shown in Figure 4.

DISCUSSION

The results of our study did not confirm that the presence, age, location, or volume of IPH are risk factors for ipsilateral TIA or stroke. In contrast, the significant predictors of stroke were found to be a lower AHA plaque type (IV–V and VI), a higher stenosis degree, lipid plaque on CT, and additionally alcohol consumption.

In some studies, IPH remained the strongest predictor of future stroke[9, 10, 25] and is currently considered one of the at-risk characteristics where intervention is recommended by guidelines [17]. Carotid IPH is considered the strongest predictor of stroke than any known clinical risk factor by a recent meta-analysis[9]. Moreover, juxtaluminal, fresh, and larger IPH volume were presented significantly more in symptomatic patients compared to asymptomatic, but no differences were found for the presence of IPH and recent IPH [26]. Our study did not find a significant difference between the presence, age, location, or volume of IPH in symptomatic and asymptomatic stable plaques. However, the result of our study shows a trend of the more frequent presence of IPH in symptomatic patients, but it did not reach statistical significance because, in the sample size calculation, we assumed a difference of at least 10% but the result was 3.1%. Nevertheless, we found that large IPH volume (>50% of the plaque) was more often present in symptomatic patients compared to asymptomatic stable (58.6% vs.

36.4%). Several blinded studies achieved the same results, although no clinicopathological correlation between various types of IPH was found in symptomatic versus asymptomatic patients [27, 28]. The persistent popularity of publishing only positive results of studies may bias the number of studies with positive and negative results. A systematic review concluded that the reliable interpretation of IPH in the production of cerebral ischemia was severely undermined by poor methodological quality, substantial heterogeneity, and suspicious publication bias [29]. Similar to our study results, more than half of the included studies in the mentioned systematic review showed no significant increase in symptoms based on IPH. Their findings indicate that studies with minor heterogeneity and high quality tended to yield negative results. Only more recent meta-analyses and recalculations of results show a strong association between IPH and stroke. According to the AHA classification, complicated type VI plaque was associated primarily with developing symptoms in the carotid arteries [30]. This result was confirmed in our study, where not only AHA plaque type VI but also plaque type IV–V were significantly more common than type VII and VIII in symptomatic plaques. However, plaque type IV–V appeared less often (type VI more often) in symptomatic plaques than in asymptomatic stable plaques in another study [26].

The finding that a higher degree of carotid stenosis poses a higher risk of stroke than a lower degree was demonstrated by the NASCET study [20]. Several studies [13, 31] showed that even mild stenosis can lead to cerebrovascular events, suggesting that plaque composition likely plays a key role in stroke risk. In addition, recently published studies[32, 33] revealed that patients with a higher stenosis degree had a higher stroke risk compared to those with a lower degree and agreed with our study results (for both CT and MRI). However, according to recent valid guidelines, stroke risk associated with carotid plaques is attributable not only to stenosis degree but also to plaque composition [17].

Our results demonstrated a marginally significant association of lipid plaque on CT with symptomatic plaques. In a different study, a significant difference was found between the presence of lipid plaques detected by CT and brain ischemic changes, which confirms our results [9]. LRNC and fibrous cap are considered the most important components of vulnerable plaques, characterized by the presence of a thin fibrous cap that covers a large LRNC containing macrophages and inflammatory cells [15]. Previous studies confirmed an association of both characteristics with the risk of cerebrovascular events [10, 30]. Statins represent the first-choice treatment in patients with atherosclerosis, aiming for low-density lipoprotein cholesterol reduction recommended by guidelines [17]. The stabilizing anti-inflammatory effects of statins

on carotid plaque composition, including LRNC, have already been proven [34]. In our study, 76% of all patients used statins, with no significant difference between both groups.

Other carotid plaque characteristics evaluated in this study did not show significant differences between the symptomatic and asymptomatic stable plaques. However, the presence of plaque surface irregularities and ulceration [20, 22], enhancement [35], and fibrous cap rupture [10, 26] have been associated with plaque vulnerability. The main reasons for the difference in our study results are the definition of vulnerable/symptomatic plaques, which differs between studies, and changes in plaques over time after stroke occurrence.

Finally, in terms of clinical and demographic factors, alcohol consumption was found to be closely related to stroke risk. Unlike heavy drinking (>4 units per day), the consumption of <1 unit of alcohol per day is associated with a lower risk of ischemic stroke [36]. We showed that even light to moderate regular alcohol consumption (1 unit per day/140 g of alcohol per week) was a significant predictor of recent TIA/stroke, which stands towards the mentioned meta-analysis, and another study claimed that 1–2 drinks per day could be associated with protection against stroke [37]. This result is very alarming for our population due to very high alcohol consumption in the Czech Republic, one of the highest globally [38]. When we compared daily alcohol consumption with stenosis degree on CT (Figure 4), we found that mild alcohol consumption was associated with a lower stenosis degree (no effect on atherogenesis) compared to either heavy drinkers or abstainers. Those results are following the results of large prospective studies (J-shaped curve) [39, 40].

The limitations of the study should also be described. First, due to the multicenter nature of the study, multiple diagnostic devices were used, potentially leading to small differences in the evaluation of individual characteristics. Diagnostic devices were calibrated on five atherosclerotic plaques in vitro to minimize this error. Second, most of the patients in the ANTIQUE study (approx. 90%) were not included in our study because of stenosis <30 %, missing CT/MRI scans, and particularly because they could not be assigned to one of our groups (symptomatic/asymptomatic stable) so that there is no overlap between them. Third, not all MRI examinations were performed with CA, so enhancement evaluation was not possible in a larger sample size. Therefore, other characteristics recommended for evaluation on postcontrast MRI sequences needed to be evaluated in other sequences in which the characteristics were more difficult to distinguish, thus, potentially leading to errors in the evaluation. Moreover, not the same number of plaques were evaluated by MRI and CT. Fourth, ultrasound and histology evaluation of plaque characteristics would have been advantageous in addition to CT and MRI to obtain a comprehensive picture of unstable characteristics. Fifth, the carotid plaque

composition of symptomatic patients was detected by imaging modalities after the cerebrovascular event occurrence. Thus, plaque composition may have changed in the time gap between event occurrence and plaque imaging. Sixth, the evaluation of CT and MRI-derived plaque characteristics was based on a single rater and rating, so intra-rater and inter-rater reliability are not available. Seventh, the exclusion of patients with clinically silent cerebral infarction(s) [24] led to homogenous study groups but reduced the study power in testing an association between carotid plaque morphology and stroke risk. Finally, laboratory markers were not measured in all patients as we were purely focused on the imaging-based carotid plaque composition and its association with stroke risk.

Our study results suggest that a complex evaluation of carotid plaque characteristics and common stroke/atherosclerosis risk factors should be considered rather than focusing only on IPH in high-risk patients in need of follow-up, risk stratification, and further treatment. A harmonized multi-specialty approach to multi-morbidity prevention in carotid stenosis patients was recently stressed in evidence-based expert consensus [41]. However, large follow-up imaging studies using basic noninvasive diagnostic modalities and considering all plaque characteristics with their uniform evaluation are needed.

CONCLUSIONS

We did not find any relationship between IPH (presence, age, location, volume) and the risk of cerebrovascular events in our study as only stenosis severity and additionally alcohol consumption were found to be independent risk factors for recent TIA/stroke in carotid stenosis territory. We showed that multiparametric and multimodal plaque assessment should be considered in stroke risk assessment. Larger follow-up studies considering all plaque characteristics are needed.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

Conflict of interest: None declared.

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Table 1. Demographic data of patients enrolled in the study

	Asymptomatic stable carotid plaque	Symptomatic carotid plaque	*P*-value
Subjects, n	157	59	NA
Age of patients, years, mean (SD)	70.1 (8.2)	69.7 (9.6)	0.75
Male sex, n (%)	108 (68.8)	43 (72.9)	0.62
Right side of stenosis, n (%)	82 (52.2)	25 (42.4)	0.22
Ischemic stroke; n (%)	0 (0)	37 (62.7)	NA
Transient ischemic attack, n (%)	0 (0)	15 (25.4)	NA
Retinal infarction, n (%)	0 (0)	2 (3.4)	NA
Amaurosis fugax, n (%)	0 (0)	4 (6.8)	NA
Hemorrhagic stroke, n (%)	1 (0.6)	1 (1.7)	NA
Arterial hypertension, n (%)	147 (93.6)	52 (88.1)	0.25
Diabetes mellitus, n (%)	68 (43.3)	24 (40.7)	0.76
Dyslipidemia, n (%)	116 (73.9)	46 (78.0)	0.60
Coronary arterial disease, n (%)	50 (31.8)	13 (22.0)	0.18
Myocardial infarction, n (%)	30 (19.1)	7 (11.9)	0.23
Atrial fibrillation, n (%)	22 (14)	8 (13.6)	1.00
Chronic kidney disease, n (%)	9 (5.7)	5 (8.5)	0.54
Autoimmune disease, n (%)	0 (0)	0 (0)	1.00
Smoking, n (%)	49 (31.2)	24 (40.7)	0.20

Number of cigarettes per day, median (IQR)	0 (0–5)	0 (0–10)	0.23
Alcohol consumption, n (%)	54 (34.4)	33 (55.9)	**0.005**
Number of alcohol units per day, median (IQR)	0 (0–1)	1 (0–1)	**0.003**
Antithrombotic therapy, n (%)	140 (89.2)	51 (86.4)	0.63
Statin therapy, n (%)	122 (77.7)	43 (72.9)	0.48

Abbreviations: IQR, interquartile range; NA, not applicable; SD, standard deviations

Table 2. MRI-detected IPH

	Asymptomatic stable carotid plaque	Symptomatic carotid plaque	*P*-value
Subjects, n	145	54	NA
IPH, n (%)			
None	116 (80.0)	43 (79.6)	0.73
Acute	17 (11.7)	8 (14.8)	
Subacute	12 (8.3)	3 (5.6)	
IPH location, n (%)			
None	116 (80.0)	43 (79.6)	0.47
Superficial	11 (7.6)	2 (3.7)	
Deep	18 (12.4)	9 (16.7)	
IPH volume, n (%)			
0%	116 (80.0)	43 (79.6)	0.83
20%	8 (5.5)	1 (1.9)	
40%	9 (6.2)	3 (5.6)	
60%	6 (4.1)	4 (7.4)	
80%	6 (4.1)	3 (5.6)	

Abbreviations: IPH, intraplaque hemorrhage; MRI, magnetic resonance imaging

Table 3. Characteristics of carotid plaque evaluated on magnetic resonance imaging

	Asymptomatic stable carotid plaque	Symptomatic carotid plaque	*P*-value
Subjects, n	145	54	NA
Severity of stenosis in %, mean (SD)	66.5 (19.6)	74.8 (18.6)	**0.005**
Lipid part, n (%)	112 (77.2)	45 (83.3)	0.27
Type according to the AHA, n (%)			
IV–V	43 (34.7)	23 (46.9)	**0.03**
VI	35 (28.2)	17 (34.7)	
VII	22 (17.7)	5 (10.2)	
VIII	24 (19.4)	4 (8.2)	
Fibrous cap, n (%)			
None	46 (40.7)	14 (30.4)	0.22
Thick	37 (32.7)	14 (30.4)	
Thin	19 (16.8)	8 (17.4)	
Rupture	11 (9.7)	10 (21.7)	
Examination with CA, n (%)	56 (38.6)	28 51.9)	NA
— Enhancement, n (%)	14 (25.0)	12 (42.9)	0.13

Abbreviations: AHA, American Heart Association; CA, contrast agent; other — see Table 1

Table 4. Characteristics of carotid plaque evaluated on computed tomography

	Asymptomatic stable carotid plaque	Symptomatic carotid plaque	*P*-value
Subject, n	157	59	NA
Severity of stenosis in %, mean (SD)	67.6 (18.9)	74.4 (18.5)	**0.01**
Lipid part, n (%)	120 (76.4)	53 (89.8)	**0.04**
Fibrous part, n (%)	89 (56.7)	34 (57.6)	1.00
Calcification, n (%)	136 (86.6)	48 (81.4)	0.39
Plaque surface, n (%)			

Smooth	9 (5.7)	4 (6.8)	0.88
Irregular	75 (47.8)	27 (45.8)	
Ulcerated	73 (46.5)	28 (47.5)	

Abbreviations: see Table 1

Inclusion criteria
• Age 30–90 years
• Location of the atherosclerotic plaque in the carotid bifurcation or the proximal part of the internal carotid artery (ICA)
• Carotid plaque thickness of ≥2 mm in the transverse plane of the ultrasound B-mode measurement
• Sufficient image quality of the atherosclerotic plaque in the carotid bifurcation and ICA with computed tomography (CT) / magnetic resonance imaging (MRI)
• Patient self-sufficiency (modified Rankin scale score 0–2)
• Provision of signed informed consent by the patient
Exclusion criteria
• CT or MRI of the neck not performed
• Insufficient CT and MR image quality
• Patient non-cooperation
• Detected carotid artery occlusion
• Stent implementation in the carotid bifurcation
• Invasive treatment (carotid endarterectomy or angioplasty and stenting) of the ipsilateral carotid artery

Figure 1. Study inclusion and exclusion criteria

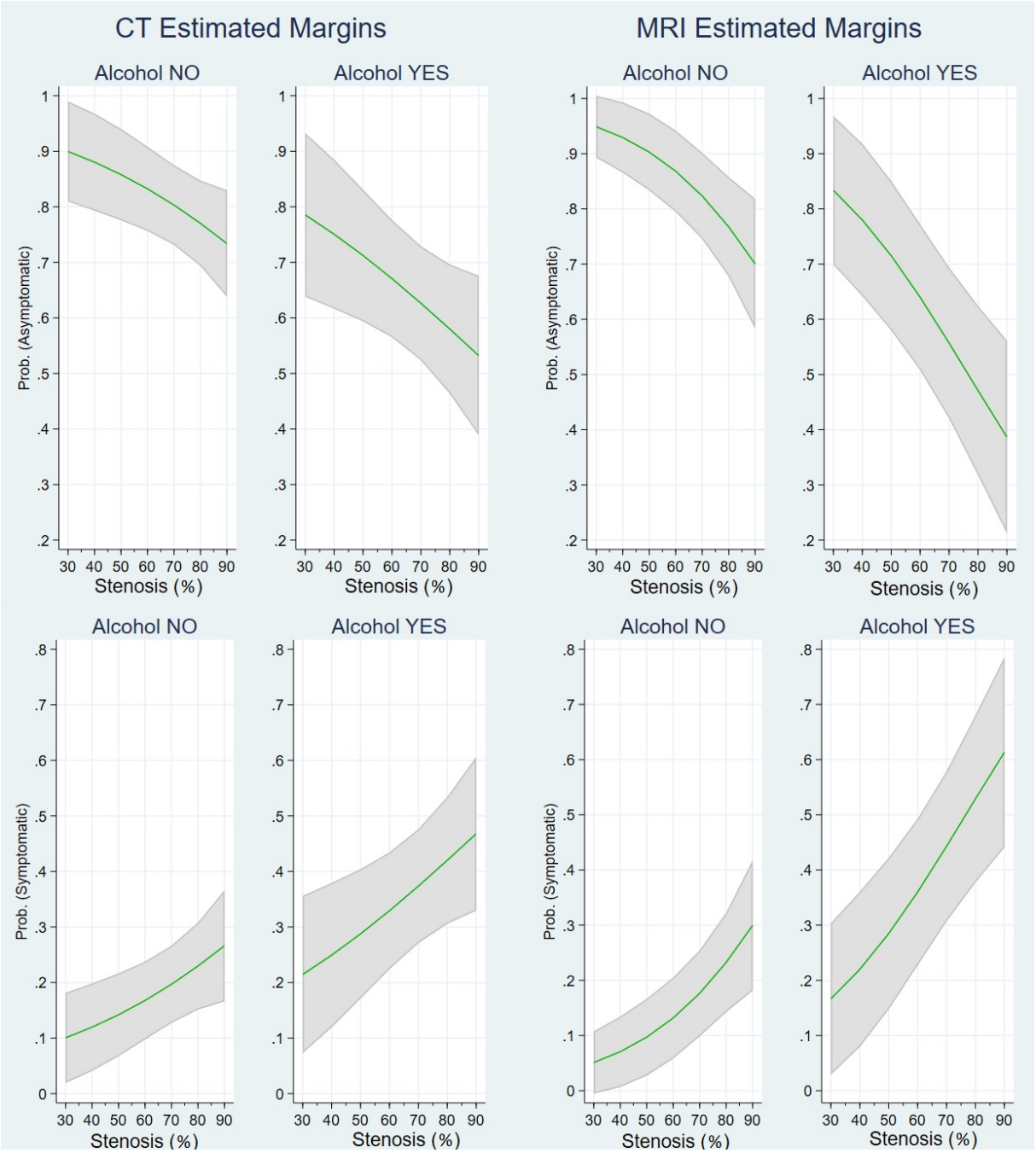

Figure 2. Probability model of carotid plaque to be symptomatic according to alcohol abuse and stenosis severity assessed by CT/MRI

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging

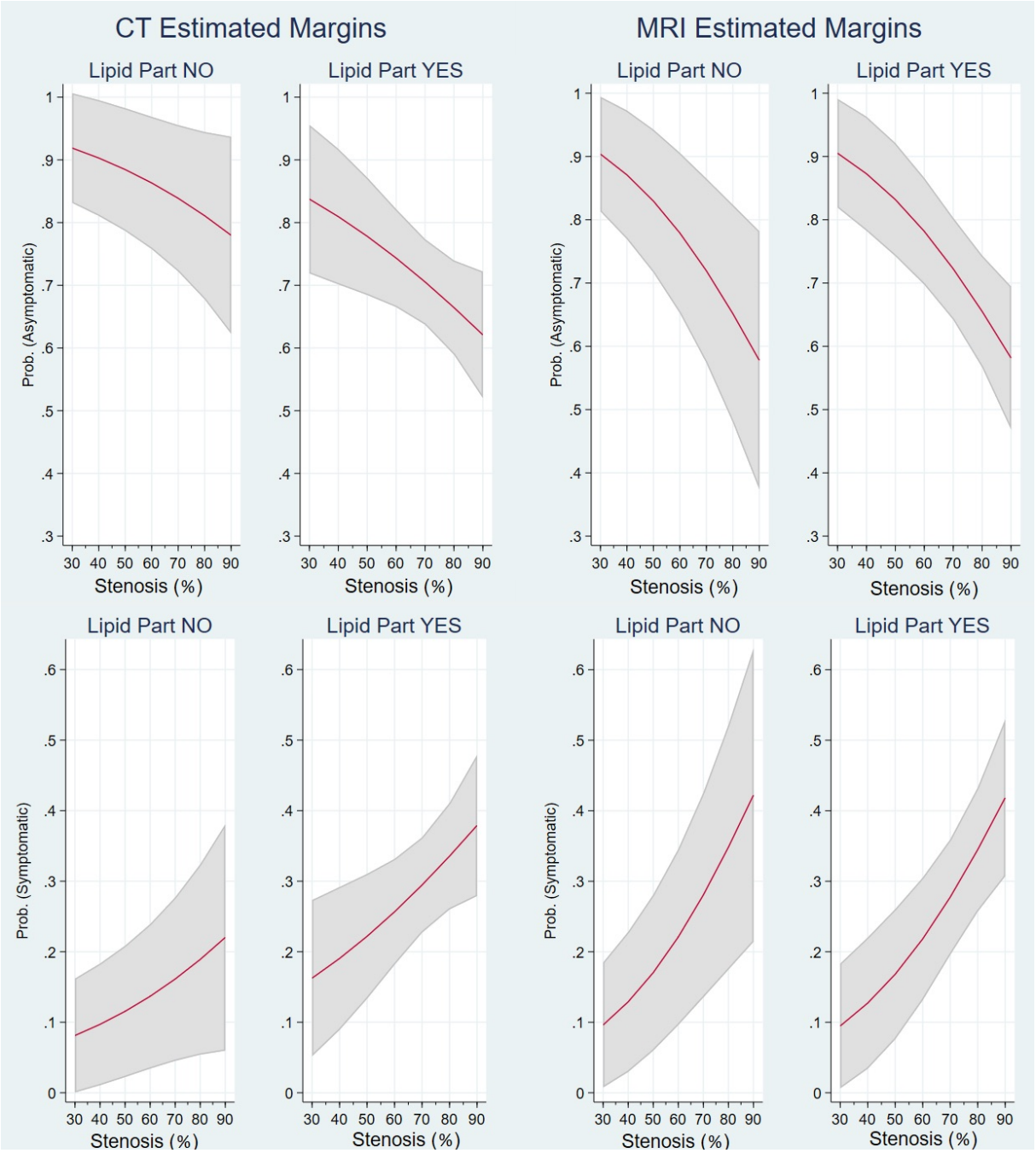

Figure 3. Probability model of carotid plaque to be symptomatic according to present lipid plaque and stenosis severity assessed by CT/MRI

Abbreviations: see Figure 2

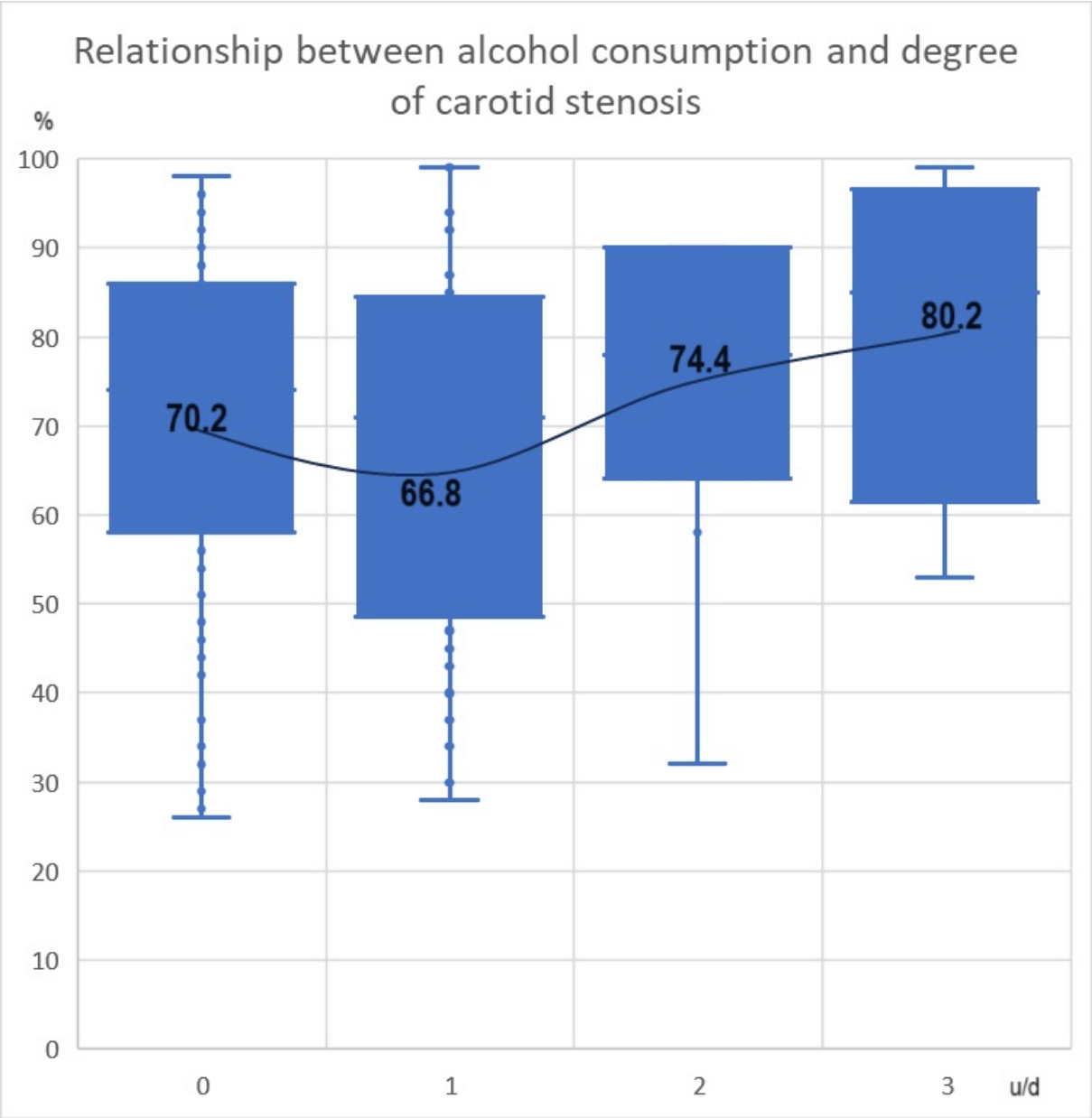

Figure 4. An association between daily alcohol consumption and the degree of stenosis measured on CT

Abbreviations: see Figure 2