Brief Report

Mean Platelet Volume Does Not Predict Restenosis After Carotid Artery Stenting in Whites

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Background and Purpose—Mean platelet volume (MPV) indicates platelet activity possibly affecting patient's risk for progressive atherosclerotic disease. A recent study identified elevated MPV as a predictor of in-stent restenosis (ISR) after carotid artery stenting (CAS) in a Chinese population. However, the role of MPV on the development of ISR following CAS in whites is yet unknown.

Methods—We retrospectively identified all consecutive patients who underwent CAS for atherosclerotic disease at our center from 2005 to 2017. All patients were followed clinically and by duplex sonography at 1, 3, and 6 months and annually after CAS. ISR was defined as ≥50% stenosis (NASCET [North American Symptomatic Carotid Endarterectomy Trial] criteria) in the treated vessel. MPV was assessed before CAS, at last follow-up and at the time of ISR detection.

Results—Of 392 patients with CAS (mean age 68.5±9.5 years, 26.8% women, 42.3% symptomatic stenosis), 54 had ISR after a mean follow-up time of 32 months. Baseline MPV was not different in ISR compared with non-ISR patients (10.7 versus 10.6 fL, P=0.316). MPV levels did also not change from baseline to ISR detection (P=0.310) and were not associated with recurrent stroke or vascular events (P>0.5). Multivariable analysis identified active smoking as the sole risk factor for carotid ISR (odds ratio, 2.53 [95% CI, 1.21–5.29]).

Conclusions—We did not identify MPV as a risk factor for ISR after CAS in whites. Smoking cessation is an important target to avoid this complication. **(*Stroke*. 2020;51:986-989. DOI: 10.1161/STROKEAHA.119.028180.)**

Key Words: biomarkers ■ carotid artery ■ cerebrovascular disease ■ mean platelet volume ■ population

Carotid artery stenting (CAS) is a well-established treatment option for symptomatic or high-grade extracranial stenosis. The major long-term complication after CAS is in-stent restenosis (ISR), which is associated with recurrent cerebrovascular events.[1] Therefore, the identification of ISR predictors is of clinical importance.

Mean platelet volume (MPV) is a marker for platelet activity and was associated with restenosis after angioplasty/stenting of atherosclerotic coronary artery disease.[2] One recent study also identified elevated MPV as a predictor for ISR after CAS in Chinese patients.[3]

However, differences in vessel structure, plaque biology, and efficacy of preventive medication including antiplatelet therapy have been identified between Asians and whites, supporting the need for ethnic-specific data on the role of MPV on ISR.[4,5]

Moreover, the effect of longitudinal MPV changes on the risk of carotid ISR is unclear thus far.

Therefore, we aimed to investigate the value of MPV at baseline and during follow-up in predicting ISR and vascular re-events after CAS in a central European population.

Methods

Data from this study are available from the corresponding author upon reasonable request. The study was approved by the ethics committee of the Medical University of Graz (written informed consent was not requested).

In this retrospective study, we analyzed all consecutive patients who underwent stenting of atherosclerotic steno-occlusive carotid artery disease (internal or common carotid artery) at our primary and tertiary care University Hospital between 2005 and 2017 (Figure 1).

All patients underwent a predefined standardized follow-up regime including neurological examination and duplex ultrasonography at 1, 3, and 6 months and annually after stenting. The NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria were used to determine the degree of (re-)stenosis.[6] ISR was defined as ≥50% stenosis in the treated artery.[3] Blood parameters at follow-up were analyzed at the day

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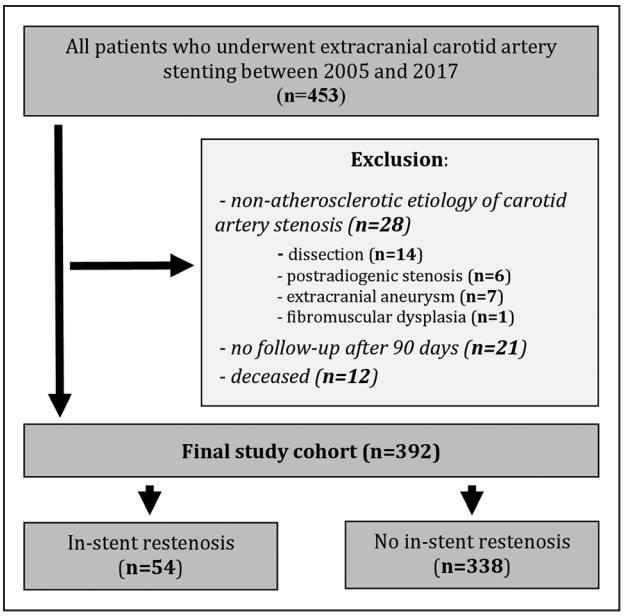

Figure 1. Flow diagram of patient selection.

of ISR detection and at last clinical follow-up. Active smoking was documented if patients continued smoking until last clinical follow-up or ISR detection.

Further details on patient selection, baseline assessment, plaque morphology, CAS procedure, and statistical analyses are presented in Methods in the Data Supplement.

Results

Of 453 patients who underwent CAS in the study period, 392 patients (mean age: 68.5±9.5 years, internal carotid artery stenosis: 96.4%) were included in the final study cohort (Figure 1). Baseline characteristics, including laboratory parameters and plaque morphology, are presented in the Table and Table I in the Data Supplement.

During a 60-month mean follow-up period (range: 3–165), ISR was present in 54 patients after a mean period of 32 months (range: 1–135). Of those, ISR was symptomatic in 6 patients.

Compared with non-ISR patients (86.2%), patients who developed ISR (13.8%) were younger (65.6 versus 68.9 years, *P*=0.015) and more often remained active smokers during follow-up (22.2% versus 13.0%; *P*=0.015; Table and Table I in the Data Supplement).

Baseline MPV was similar between ISR and non-ISR patients (10.7 versus 10.6 fL, *P*=0.316). Highest MPV levels (≥10.91 fL, tertile 3) were also not associated with the occurrence of ISR (*P*=0.943; Table).

In multivariable regression analysis, active smoking remained the sole predictor for ISR (odds ratio, 2.53 [95% CI, 1.21–5.29], *P*=0.013; Table II in the Data Supplement).

Table. Demographics, Clinical, and Laboratory Data of CAS Patients at Baseline According to the Occurrence of In-Stent Restenosis During Follow-Up

	All Patients (n=392)	In-Stent Restenosis (n=54)	No In-Stent Restenosis (n=338)	*P* Value
Demographics				
Age, y	68.5±9.5	65.6±8.3	68.9±9.7	0.015
Female (%)	105 (26.8)	13 (24.1)	92 (27.2)	0.628
Risk factors, n (%)				
Hypertension	345 (88.0)	46 (85.2)	299 (88.5)	0.491
Diabetes mellitus	120 (30.6)	20 (37.0)	100 (29.7)	0.270
Hyperlipidemia	341 (87.4)	49 (90.7)	292 (86.9)	0.430
Active smoking	56 (14.3)	12 (22.2)	44 (13.0)	0.015
Preinterventional stenosis, n (%)				
High grade stenosis >80%	49 (12.5)	8 (14.8)	41 (12.1)	0.580
Symptomatic stenosis	166 (42.3)	18 (33.3)	148 (43.8)	0.149
Stroke	103 (26.3)	11 (20.4)	92 (27.3)	0.283
TIA	48 (12.3)	4 (7.4)	44 (13.1)	0.240
Amaurosis fugax	15 (3.8)	3 (5.6)	12 (3.6)	0.479
Recurrent stroke, n (%)	28 (7.1)	6 (11.1)	22 (6.5)	0.223
Platelets				
Total platelet count (×10^9/L)	222.2±70.7	214.3±75.4	221.2±70.0	0.510
Mean platelet volume, fL	10.6±0.9	10.7±0.8	10.6±0.9	0.316
Tertile 1: 8.50–10.20 fL (%)	134 (34.2)	17 (31.5)	117 (34.6)	0.652
Tertile 2: 10.21–10.90 fL (%)	129 (32.9)	19 (35.2)	110 (32.5)	0.701
Tertile 3: 10.91–13.60 fL (%)	129 (32.9)	18 (33.3)	111 (32.8)	0.943

CAS indicates carotid artery stenting; and TIA, transient ischemic attack.

There was also no change in MPV from baseline to ISR detection (P=0.310) or to last clinical follow-up (P=0.710) comparing patients with versus without ISR (Figure 2).

MPV was not influenced by preventive medication such as statins (P=0.574), antidiabetics (P=0.143), or antihypertensive drugs (P=0.619).

Of all 392 patients with CAS, 28 had a recurrent ischemic stroke (mean time after CAS: 39 months, range: 1–156) and another 3 patients had further major cardiovascular events during follow-up (all: myocardial infarction). Recurrent stroke (10.7 versus 10.6 fL, P=0.811) or any recurrent vascular event (10.7 versus 10.6 fL, P=0.651) was not associated with MPV.

Discussion

In this large retrospective study on consecutive patients receiving CAS for atherosclerotic stenosis, we did not find an association between elevated MPV and ISR. Moreover, MPV did not change from baseline to follow-up and did not predict the risk of recurrent stroke or vascular events. Notably, active smoking was the only independent risk factor for ISR after CAS.

To date, only one study in Chinese patients addressed the association between MPV and carotid ISR and showed that elevated MPV at baseline (before stenting) was an independent risk factor for postinterventional ISR.[3] However, risk is a dynamic process limiting their results as they did not measure MPV during the follow-up period.[3] In contrast, our study in a larger European population provides additional data on MPV at the time of ISR detection and during follow-up. Despite these repeated measurements, a comparable rate of ISR and a similar regime of antiplatelet therapy, neither baseline nor follow-up MPV levels were associated with ISR in our study. Importantly, we were also able to exclude a major influence of drugs (eg, statins) that were thought to affect MPV in previous investigations.[7]

Notably, patients with ISR in the Asian study more often had concomitant diabetes mellitus, while vascular risk factors were comparable between ISR and non-ISR groups in our study population.[3] Diabetes mellitus has been associated with higher MPV and with a nonresponsiveness rate to clopidogrel,[8] which is generally more prevalent in Asians compared with whites.[5] Apart from presumed ethnic-specific pathways in carotid plaque development,[4] this might also explain the missing link between MPV and ISR after CAS in our cohort.

In the present study, active smoking was the only independent predictor for ISR. Contradicting pathophysiological assumptions, earlier studies did not report an association between smoking and ISR after CAS.[9] This difference might be explained by the fact that our thorough outpatient follow-ups performed by vascular neurologists allowed us to differentiate between persistent smokers after CAS from those who stopped smoking. Our results once more underline the necessity of patient education and immediate smoking cessation in patients with carotid atherosclerosis, especially after CAS.

Because of the available long-term follow-up (at mean about 5 years), we were also able to analyze the impact of MPV on the occurrence of recurrent (cerebro)vascular events after CAS. Data on this important aspect is scarce. Our results support those of a recent study suggesting that MPV has no predictive value for the occurrence of ischemic stroke in

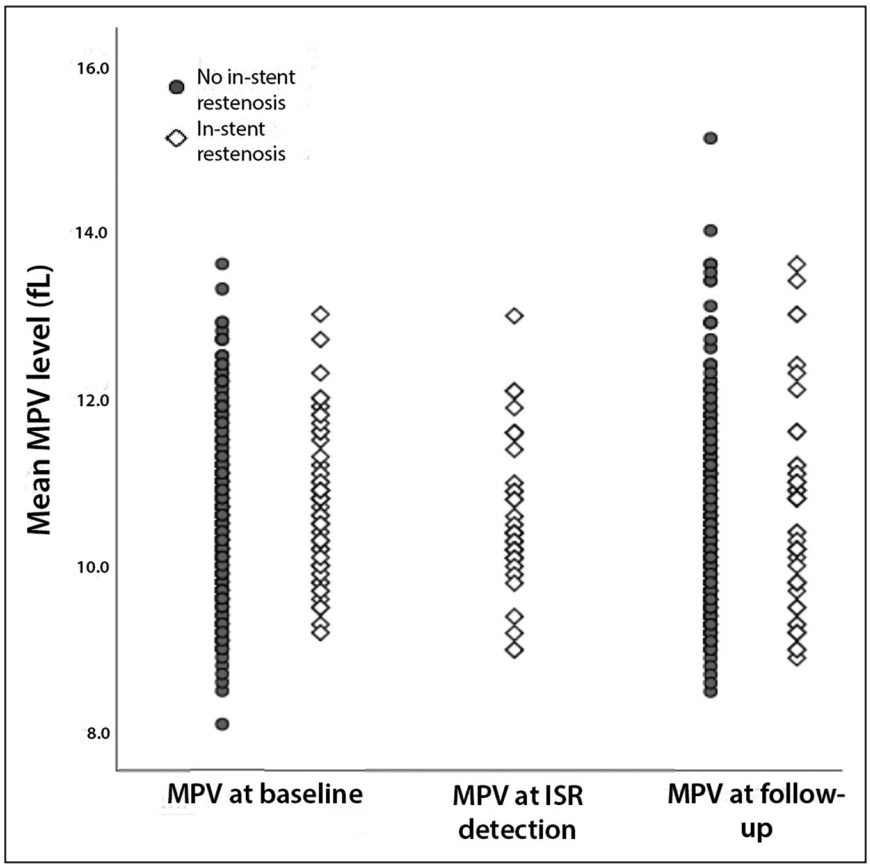

Figure 2. Mean platelet volume (MPV) at baseline, at detection of in-stent restenosis and at last follow-up. ISR indicates in-stent restenosis.

patients with carotid steno-occlusive disease.[9] However, in both studies, sample size may have been too small to detect such differences.

Another limitation of our retrospective study is that certain laboratory parameters were not documented at baseline (eg, immature platelets) or during follow-up (hemoglobin A1c, LDL [low-density lipoprotein] cholesterol) consistently. However, as all included patients underwent repeated follow-up by cerebrovascular experts, the number of patients with insufficient risk factor control should have been low and might not have affected our results to a major extent.

Disclosures

Dr Deutschmann reports personal fees and other from Stryker and Medtronic outside this work. Dr Gattringer reports grants from Austrian Neurological Society outside this work. The other authors report no conflicts.

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