

# Carotid Plaque-RADS, a novel stroke risk classification system

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# **ORIGINAL RESEARCH**

# **Carotid Plaque-RADS**

# A Novel Stroke Risk Classification System

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### ABSTRACT

**BACKGROUND** Carotid artery atherosclerosis is highly prevalent in the general population and is a well-established risk factor for acute ischemic stroke. Although the morphological characteristics of vulnerable plaques are well recognized, there is a lack of consensus in reporting and interpreting carotid plaque features.

**OBJECTIVES** The aim of this paper is to establish a consistent and comprehensive approach for imaging and reporting carotid plaque by introducing the Plaque-RADS (Reporting and Data System) score.

**METHODS** A panel of experts recognized the necessity to develop a classification system for carotid plaque and its defining characteristics. Using a multimodality analysis approach, the Plaque-RADS categories were established through consensus, drawing on existing published reports.

**RESULTS** The authors present a universal classification that is applicable to both researchers and clinicians. The Plaque-RADS score offers a morphological assessment in addition to the prevailing quantitative parameter of "stenosis." The Plaque-RADS score spans from grade 1 (indicating complete absence of plaque) to grade 4 (representing complicated plaque). Accompanying visual examples are included to facilitate a clear understanding of the Plaque-RADS categories.

**CONCLUSIONS** Plaque-RADS is a standardized and reliable system of reporting carotid plaque composition and morphology via different imaging modalities, such as ultrasound, computed tomography, and magnetic resonance imaging. This scoring system has the potential to help in the precise identification of patients who may benefit from exclusive medical intervention and those who require alternative treatments, thereby enhancing patient care. A standardized lexicon and structured reporting promise to enhance communication between radiologists, referring clinicians, and scientists. (J Am Coll Cardiol Img 2024;17:62-75) © 2024 by the American College of Cardiology Foundation.

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oninvasive carotid imaging modalities have demonstrated their ability to characterize plaque features as predictors of future events, offering a significant contribution to risk stratification and patient management.<sup>1</sup> Translation of the present knowledge on plaque vulnerability into routine clinical practice requires a standardized reporting system.

The 2017 European Society of Cardiology clinical practice guidelines have recognized these developments and recommend evaluating the presence of plaque imaging characteristics that may indicate an increased risk of ipsilateral stroke additionally to the degree of carotid stenosis in asymptomatic individuals.<sup>2</sup> These include, among others, intraplaque hemorrhage (IPH) or lipid-rich necrotic core (LRNC) on magnetic resonance imaging (MRI) and large or echolucent plaques or increased juxtaluminal black (hypoechoic) areas on carotid ultrasound.<sup>2</sup> Similarly, the European Society for Vascular Surgery clinical practice guidelines emphasize the importance of plaque vulnerability assessment.<sup>3</sup> Although scoring systems for singular modalities have been suggested (eg, American Heart Association [AHA] lesion-types, modified AHA lesion-types for MRI, carotid plaque score for ultrasound, etc), there is still no universal classification system for various imaging modalities that scores the severity of an atherosclerotic lesion based on plaque morphology and composition.<sup>4-6</sup> The proposed Plaque-Reporting and Data System (RADS) score aims to create an intuitive, accurate,

reliable, and standardized scoring system that can be used with various imaging modalities to provide risk estimates for first-time or recurrent large artery cerebrovascular events.

#### ABBREVIATIONS AND ACRONYMS

<b>CEA</b> = carotid endarterectomy
CTA = computed tomography angiography
FC = fibrous cap
IPH = intraplaque hemorrhage
LRNC = lipid-rich necrotic core
MRI = magnetic resonance imaging
<b>MWT</b> = maximum wall thickness
RADS = reporting and data system

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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# THE RATIONALE OF NEW IMAGE-BASED CLASSIFICATION

As shown with previous scores, such as the Lung-RADS, BI-RADS, PI-RADS, LI-RADS, and CAD-RADS score for lung, breast, prostate, liver, and coronary artery imaging, respectively, the use of a standardized reporting system improves communication and patient selection by reducing differences in terminology, harmonizing classification formats between different institutions, and facilitating the exchange of clear and systematic information between imaging and referring physicians and researchers.<sup>7-11</sup>

To date, there is no such system for a standardized classification of atherosclerotic carotid plaque. Instead, most clinical reports of computed tomography angiography mention the degree of carotid stenosis, but despite their increasingly recognized value, specific plaque features are accounted for in only a minority of cases.<sup>12</sup> This lack of reporting may be at least partly due to gaps in knowledge of high-risk plaque features and their associated risk and possible therapeutic consequences.

Consequently, the introduction of a standardized classification system for carotid atherosclerotic plaque (Plaque-RADS): 1) will level the differences across the various institutions regarding the use of terminology and patient evaluation criteria, serving as a reference format in everyday clinical practice; 2) facilitates data mining and allows researchers across different institutions to collect information in a more homogenous and synergistic way; eg, in the course of time stratified prognostic data could be collected for each Plaque-RADS category and help clinicians design agreed-upon treatment flowcharts; and 3) draws attention to imaging findings representative of plaque morphology and composition beyond the mere degree of stenosis underscoring a paradigm shift.

# PLAQUE-RADS REPORTING SYSTEM

Plaque-RADS categories are based on specific imaging features of plaque composition and other characteristics. The score is applied on a per-vessel basis and can be established by ultrasound, computed tomography angiography, and MRI. Figure 1



and the **Central Illustration** provide a flowchart and schematic overview of the Plaque-RADS categories. Categories range from Plaque-RADS 1 (absence of atherosclerosis) to Plaque-RADS 4 (plaque with features of complicated plaque) and should represent the clinically most relevant finding per vessel. Further subspecifications (a, b, c) can be provided for Plaque-RADS categories 3 and 4. Not all imaging modalities

Plaque-RADS Score	Attributable Risk of Ipsilateral Cerebrovascular Events	Imaging Findings
1	Absent	Normal vessel wall
2	Low	MWT <3 mm
3	Moderate	MWT $\geq$ 3 mm or Healed ulcerated plaque
3a	Moderate	LRNC with intact thick FC (MWT $\ge$ 3 mm)
3b	Moderate	LRNC with thin FC (MWT $\ge$ 3 mm)
3c	Moderate	Healed ulcerated plaque
4	High	Complicated plaque (irrespective of MWT)
4a	High	IPH
4b	High	Ruptured FC
4c	High	Intraluminal thrombus
Ancillary features: inflammation, n presence of a stent ("Stent"), previ	eovascularization, positive plaque remodeling, plaque progra ous carotid endarterectomy ("CEA").	ession, calcifications. Modifiers: limited diagnostic study ("L"),



are currently equally suited to identify the individual categories. Therefore, the modality used to obtain the score should always be provided.

In addition, the Plaque-RADS categories may be supplemented by "ancillary features" of carotid plaque vulnerability, namely, plaque inflammation and neovascularization, positive carotid artery remodeling, plaque burden, progression of stenosis, and carotid plaque calcifications (see Supplemental Methods, Supplemental Table 1, Supplemental Figures 1 to 4). Table 1summarizes the characteristic imagingfeatures of the Plaque-RADS categories and theattributable risk of developing symptoms.

# PLAQUE-RADS CATEGORIES

**PLAGUE-RADS 1.** This category represents the normal vessel wall with no evidence of localized atherosclerotic plaque (Figure 2). Population-based cohort studies including the Rotterdam Study, the Tromsø Study, and the MESA (Multi-Ethnic Study of



Atherosclerosis) study have shown that patients without carotid plaque are not at risk of atherosclerosis-related cardiovascular or cerebrovascular events.<sup>13-16</sup> Vessels of this category are consistent with AHA lesion-type I/II plaques.

**PLAQUE-RADS 2.** This category is defined by an eccentric plaque with a maximum wall thickness (MWT) <3 mm and the absence of complicated plaque features such as IPH, fibrous cap (FC) rupture, and intraluminal thrombus (**Figure 3**).

Plaques in this category may consist mainly of fibrous tissue, small lipid pools, a small LRNC, calcifications, or a combination of these tissue types.

These plaque features are hallmarks of relatively stable plaques, although they are also potential precursors of more advanced lesions. The presence of these features results in an increase in wall thickness that has been shown to be associated with increased cerebrovascular and cardiovascular risk, but less than that associated with complicated plaque features.<sup>17</sup> In this regard, total plaque thickness, as determined by ultrasound, has been shown to improve the prediction of future atherosclerotic cardiovascular events over and above that provided by traditional risk factors alone.<sup>18,19</sup> The risk of Plaque-RADS 2 lesions is higher than Plaque-RADS 1 lesions, but it is still relatively low. This category contains plaques of AHA-lesion types III, IV/V (small), VII, and VIII. The rationale of choosing a cutoff of MWT <3 mm is discussed in the Supplemental Methods.

**PLAQUE-RADS 3.** This category represents a carotid plaque with an MWT of  $\geq$ 3 mm which may consist of a moderate to large LRNC, calcifications, healed ulcerations, and fibrous tissue. Complicated plaque features, such as IPH, thrombus, and plaque



rupture are absent. Further subclassification may be undertaken with dedicated imaging. This category contains plaques of AHA lesion-types IV/V, VII, and VIII.

**PLAQUE-RADS 3A.** This subcategory represents a carotid plaque with a moderate to large LRNC, a thick FC, and an MWT of  $\geq$ 3 mm in the absence of complicated plaque features (Figure 4).

Currently, data on the risk of LRNC is limited. Nonetheless, a meta-analysis by Gupta et al<sup>20</sup> showed an increased risk for future ipsilateral cerebrovascular events when LRNC is present with an HR of 3.00 (95% CI: 1.511-5.945; P = 0.002).<sup>2</sup> Besides an increased downstream cerebrovascular risk, the presence of an LRNC is also associated with an increase in cardiovascular risk.<sup>21</sup> **PLAQUE-RADS 3B.** This subcategory contains carotid plaque with an MWT  $\geq$ 3 mm with a moderate to large LRNC with thin and intact FC (Figure 5).

It must be emphasized that the capability of contemporary imaging to accurately assess thin FCs lacks evidence. Thus, for assigning a score 3b in the Plaque-RADS classification system, the thin FC may be either directly visualized (if the spatial resolution of the modality in use allows that) or inferred by the presence of an LRNC without visualization of a thick and intact FC. Most importantly, what distinguishes this class from higher-risk class 4 is the absence of complicated plaque features.

Regarding FC integrity, several studies have emphasized its determinant role in plaque stability.<sup>20,22</sup> A thick FC is associated with a low risk of



plaque rupture, whereas the risk of rupture increases for a thin FC. $^{20,23}$ 

**PLAQUE-RADS 3C.** The defining feature of this category is plaque ulceration regardless of plaque thickness in the absence of IPH, FC-disruption, or intraluminal thrombus (Figure 6).

Thus, for what pertains to the designation of score 3c in the Plaque-RADS classification system, the term ulceration must be intended as ulceration not associated with the presence of IPH (score 4a), visible FC disruption (score 4b) or intraluminal thrombus (score 4c); rather, the term ulceration in this context refers to a surface cavity most likely secondary to previous extrusion of atheromatous material in the context of a healed plaque rupture.

**PLAQUE-RADS 4.** Plaque-RADS score 4 is assigned in the presence of at least one of the following findings independent of plaque thickness: IPH, a ruptured FC, or an intraluminal thrombus. When feasible, a further subclassification can be used, differentiating IPH, ruptured FC, and intraluminal thrombi into classes

4a, 4b, and 4c, respectively. Subclasses may provide important information in future studies to better understand statistical correlations between such specific entities and clinical events. This category contains plaques of AHA lesion-type VI.

**PLAQUE-RADS 4A.** The defining feature of this category is IPH (Figure 7).

In the CAPIAS (Carotid Plaque Imaging in Acute Stroke) study, IPH was the most common feature of complicated plaques and present in 89% of all complicated plaques ipsilateral to acute ischemic stroke.<sup>24</sup> In the recent prospective PARISK (Plaque At RISK) study of 244 patients with a recent symptomatic mild-to-moderate carotid stenosis during a mean follow-up period of 5.1 years, the presence of IPH was associated with recurrent cerebrovascular events (HR: 2.12; 95% CI: 1.02-4.44).<sup>25</sup> Along the same lines, pooled individual patient data from 7 cohort studies of 560 patients with symptomatic and 136 patients with asymptomatic carotid stenosis found MRIdetected IPH in 51.6% of the symptomatic and



29.4% of the asymptomatic patients. Multivariate analysis identified IPH (HR: 11.0; 95% CI: 4.8-25.1) and severity of stenosis (HR: 3.3; 95% CI: 1.4-7.8) as independent predictors of recurrent ipsilateral stroke. The presence of IPH increased the risk for first-time stroke in asymptomatic patients with carotid stenosis by almost 8-fold (HR: 7.9; 95% CI: 1.3-47.6).<sup>26</sup>

**PLAQUE-RADS 4B.** The defining feature of this category is a ruptured FC, usually accompanied by juxtaluminal plaque hemorrhage (Figure 8).<sup>27</sup>

Disruption of the FC, with the resultant exposure of thrombogenic subendothelial plaque constituents, can precipitate thromboembolic complications both in the carotid and coronary vascular bed.<sup>28</sup> It appears that plaque ruptures represent a dynamic process of rupture, thrombus formation, healing, and remodeling of the plaque.<sup>29</sup> A meta-analysis of 363 carotid arteries from asymptomatic and symptomatic patients showed that a thin or ruptured FC (HR: 5.93 [95% CI: 2.65-13.29]; P < 0.01) is associated with future cerebrovascular events.<sup>20</sup>

**PLAQUE-RADS 4C.** This category is characterized by carotid plaque with an intraluminal thrombus (**Figure 9**). Other features such as IPH or FC rupture may also be present.

Intraluminal carotid artery thrombi are associated with neurologic symptoms in up to 92% of cases and are recognized predictors of stroke of carotid origin.<sup>17,30-33</sup> McNally et al<sup>17</sup> conducted a retrospective cross-sectional study of 726 carotid-brain MRI examinations in patients undergoing stroke work-up. After the exclusion of noncarotid-plaque stroke, occlusions, and near-occlusions, the strongest predictor of carotid-source stroke was intraluminal thrombus (odds ratio: 103.6 [95% CI: 8.64-710.8]; P < 0.001).<sup>17</sup>

Supplemental Table 2 provides an overview of previous studies examining carotid plaque



characteristics according to Plaque-RADS categories and attributable risk for symptom development.

## REPORTING THE PLAQUE-RADS SCORE

For the structured reporting of a Plaque-RADS score, we recommend using the following syntax, which will be further detailed in the paragraphs below: side of carotid: stenosis degree/imaging modality Plaque-RADS score/MWT/ancillary features/modifiers.

STENOSIS DEGREE. The Plaque-RADS score is not meant to replace the measurement of stenosis but rather to integrate synergistically with it. The independent association between the degree of carotid stenosis in both symptomatic and asymptomatic patients is well known.<sup>34-38</sup> The degree of luminal stenosis should be reported using the NASCET (North American Symptomatic Carotid Endarterectomy Trial) protocol as it is widely used and already harmonized across modalities: stenosis [%] = (diameter of the normal distal internal carotid artery - narrowest ICA diameter in the stenotic segment) / diameter of the normal distal ICA, where ICA represents the internal carotid artery.

**IMAGING MODALITY.** The imaging modality used to obtain the Plaque-RADS score should be indicated. In the final evaluation, all modalities used should be listed, with the one leading to the highest score mentioned first. The Supplemental Methods contains suggestions regarding which imaging modalities should be used for optimal assessment of each Plaque-RADS category. Supplemental Table 3 summarizes key plaque features across different imaging modalities.

However, a detailed discussion of ideal imaging practice of the atherosclerotic plaque is beyond the purpose of this paper but can be found in the consensus document by the American Society of Neuroradiology Vessel Wall Imaging Study group.<sup>1</sup>

**MWT.** The MWT (mm) is derived via a linear measurement of the greatest thickness of the vessel wall as measured on axial images perpendicular to the vessel's long axis and includes the arterial vessel wall and both calcified and noncalcified components of the plaque.

**ANCILLARY FEATURES.** To accommodate the variety of other imaging vulnerability markers that have been well studied and validated in the



scientific published reports, and with an open mind for future advancements, we propose an optional subclassifier of Plaque-RADS: AnFe. We suggested reporting each assessed individual AnFe in the final score.

**MODIFIERS.** Similar to CAD-RADS, categories can be complemented by modifiers including limited-diagnostic study ("L"), the presence of a stent ("Stent"), and previous carotid endarterectomy (CEA).<sup>11</sup> The Modifier L can be applied if the study is not fully diagnostic, eg, in case of blooming artifacts on computed tomography (CT) or motion artifacts or metal-induced artifacts on CT or MRI. Overestimation of restenosis using noninvasive imaging is a potential risk in stented carotid arteries and assessment of plaque morphology is limited in stented vessels.

Therefore, the application of the modifier "Stent" may be useful in clinical practice.

Following the logic described earlier, a plaque in a symptomatic patient with ipsilateral 50% stenosis with IPH with positive remodeling would be classified as "Right carotid: 50%/MRI Plaque-RADS 4a/MWT = 5 mm/Positive Remodeling." AnFE do not determine the main Plaque-RADS score. Therefore, the assessment of the AnFe is not mandatory in the Plaque-RADS score but rather serves as a complementary tool when available and is also for research purposes.

Finally, it is fundamental to consider the appropriateness of the modality used for each Plaque-RADS score. Whenever practitioners find that the study could not definitively exclude the possibility of a relevant score upgrade, further investigation should



be considered. By means of example, the identification of a Plaque-RADS score 3a on CT may require further investigation on MRI to rule out the presence of IPH (which would upgrade to score 4a). Rather than adding a classification category dedicated to the imaging modality, we suggest that "consider MRI examination" is reported in the score and further information is provided in the impressions; in this case, a plaque in an asymptomatic patient with 70% carotid stenosis and an MWT of 5 mm, a positive rim sign, and positive remodeling would read as "Left carotid: 70%/CT Plaque-RADS 3a/MWT = 5 mm/Positive rim sign AND Positive Remodeling/Consider MRI examination."

# INTEROBSERVER AGREEMENT

A score is only helpful if it is straightforward and reliable. As confirmation of applicability and reliability, Plaque-RADS categories were assigned by blinded experts in the field of plaque imaging to 100 vessels on ultrasound, CT, and MRI, each. The 74

interobserver agreement was retrospectively assessed based on Cohen k test to investigate the reproducibility of Plaque-RADS categories (0.00 = poor, 0.00-0.20 = slight, 0.21-0.40 = fair,0.41-0.60 = moderate, 0.61-0.80 = substantial, and 0.81-1.00 = almost perfect).<sup>39</sup> The analysis was based on data from previously published studies approved by the institutional review boards, and informed consent was waived because of its retrospective nature. Interobserver agreement for ultrasound, CT, and MRI images was excellent ( $\kappa = 0.804$ ; P < 0.001;  $\kappa = 0.868; P < 0.001; \text{ and } \kappa = 0.876; P < 0.001;$ respectively). Additionally, the overall inter-reader agreement among the readers across different modalities was excellent ( $\kappa = 0.856$ ; P < 0.001). The results are presented in more detail in Supplemental Table 4.

## CONCLUSIONS

Plaque-RADS is a standardized cross-modality system for reporting carotid plaque composition and morphology. This structured system aims to provide in-depth insight into carotid imaging markers of vulnerability to better evaluate carotid artery disease and predict the risk of cerebrovascular events. The main purposes of the Plaque-RADS score are to create a standardized lexicon and structured reporting for carotid artery disease and to improve communication between those interpreting images, referring clinicians, and researchers by providing a clear and reproducible, personalized risk stratification of patients.

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#### PERSPECTIVES

# COMPETENCY IN MEDICAL KNOWLEDGE:

Plaque-RADS is an intuitive and reliably assessable tool which enables standardized description of a given atherosclerotic carotid lesion in symptomatic and asymptomatic patients. The system, which can be applied by readers of any experience, helps to detect critical hallmarks of atherosclerotic plaques and translates the findings into the attributable risk. This facilitates interpretation of findings in both clinical routine and research. This may allow improvement in diseases risk stratification and adequate therapy.

**TRANSLATIONAL OUTLOOK:** The introduction of the Plaque-RADS classification and its broad application will facilitate communication in clinical routine and may serve as basis for studies, which advance the management of carotid atherosclerotic disease.

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KEY WORDS atherosclerosis, carotid plaque, carotid stenosis, complicated plaque, plaque imaging, Plaque-RADS, reporting and data system, stroke

**APPENDIX** For an expanded Methods section as well as supplemental figures, tables, and references, please see the online version of this paper. Saba et al

Carotid Plaque-RADS Classification