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FULL RESEARCH ARTICLE

Vascular signs of Kaiser score* on contrast-enhanced breast MRI improve prediction of malignancy in mass and non-mass breast lesions

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ABSTRACT

Introduction: *The modified Kaiser score (KS*) evaluates vascular signs. such as a positive adjacent vessel sign (AVS) and increased ipsilateral breast vascularity, which have independent predictive value for malignancy in breast lesions. The aim of this study was to compare the original KS and the modified KS* for the prediction of malignancy based on the presence of vascular signs in mass and non-mass breast lesions on contrast-enhanced breast magnetic resonance imaging (MRI).* **Material and methods:** *This was a retrospective cross-sectional study of women with breast cancer. Mass and non-mass lesions seen on contrast-enhanced breast MRI were scored using the original KS based on the morphologic and kinetic features of the BI-RADS lexicon. KS* was classified based on positive AVS and increased ipsilateral breast vascularity. The molecular subtypes of breast cancer were also determined.* **Results:** *A total of 476 women with breast cancer were included: 421(88.4%) with mass breast lesions and 55 (11.6%) with non-mass breast lesions. The mean age ± SD was 49.3 ± 10.9 and 51.2 ± 10.9 years, respectively. A positive AVS and increased ipsilateral breast vascularity were found in 176 (41.8%) of 421 mass lesions. The score of these mass lesions was increased by three additional points, and they were reclassified as intermediate and high risk for malignancy on the KS*. In 23 (41.8%) of 55 non-mass lesions, both vascular signs were found. Non-mass lesions were also upgraded by 3 additional points and categorized as intermediate and high-risk on the KS*. Twenty-one (91.4%) of 23 non-mass lesions with both vascular signs were reclassified as high-risk (KS* 8 to 11).* **Conclusion:** *KS* improves malignancy prediction based on vascular signs in mass and non-mass breast lesions by contrast-enhanced breast MRI. This is the first study in Mexico that confirms that the presence of vascular signs improves the KS* diagnostic stratification algorithm in identifying lesions suspicious of malignancy and indicating the need for a breast biopsy.*

Keywords: *Contrast-enhanced breast magnetic resonance imaging. Breast Imaging Reporting and Data System. Kaiser score. Kaiser score*. Adjacent vessel sign. Increased ipsilateral breast vascularity.*

INTRODUCTION

Contrast-enhanced breast magnetic resonance imaging (MRI) is performed as a complementary examination in breast lesion diagnosis, especially in suspected breast cancer[1,2]. Morphologic findings of breast lesions on MRI are described in the Breast Imaging Reporting and Data System (BI-RADS) lexicon[3]. The Kaiser score (KS) algorithm is used to categorize the risk of malignancy based on a specific BI-RADS lexicon with scores

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ranging from 1 to 11. Higher scores are associated with a higher probability of malignancy[4-6]. The KS increases the specificity of contrast-enhanced breast MRI while reducing false-positive results and decreasing the number of unnecessary breast biopsies[7]. However, its diagnostic performance varies depending on the type of lesion, mass or non-mass,[1] and lesion size (< 1 cm)[8].

Malignant angiogenesis, characterized by abnormal, irregular vascular growth and increased capillary permeability, has been described in breast cancer[2]. Tumor blood supply has been shown to correlate with clinical prognosis[1]. The KS* was developed by integrating the original KS with the assessment of breast vascularity, including a positive adjacent vessel sign (AVS) and increased ipsilateral breast vascularity[1].

Breast lesion classification with the KS* improves malignancy prediction of breast lesions initially classified as low risk with the original KS[1,2,9]. Vascular signs are particularly useful for predicting malignancy in the evaluation of non-mass lesions[1]. The aim of this study was to compare the original KS and KS* for the prediction of malignancy based on the presence of vascular signs in mass and non-mass breast lesions on contrast-enhanced breast MRI.

MATERIAL AND METHODS

This retrospective cross-sectional study was conducted from January 2014 to December 2023 in the Breast Imaging Department of San Jose Hospital and Zambrano Hellion Hospital of TecSalud in Monterrey, Nuevo Leon, Mexico. We included all contrast-enhanced breast MRI examinations performed in patients with a breast cancer diagnosis confirmed by percutaneous breast biopsy. Patients with a breast cancer diagnosis by excisional biopsy, a history of mastectomy, radiotherapy, or bilateral breast cancer were excluded. Informed consent was not required for this retrospective analysis of data collected as part of medical care. The Institutional Research and Ethics in Research Committees approved the study.

Study development and variables

Data were obtained from the clinical records of women with a confirmed diagnosis of breast cancer who had undergone contrast-enhanced breast MRI for diagnostic and/or staging purposes within one month or less after a percutaneous breast biopsy. The decision for breast biopsy was based on mammography, ultrasound, and/or MRI findings with BI-RADS categories 4 or 5. KS and KS* classifications were performed retrospectively.

Image acquisition and analysis

A 1.5T Magnetom Aera and a 3.0T Espree MRI scanner (Siemens Medical Solutions, Erlangen, Germany) with a dedicated breast coil were used. The following sequences were acquired: T2-weighted with fat suppression, diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) maps, T1-weighted spin-echo without contrast agent, and Turbo Inversion Recovery Magnitude (TIRM). After contrast administration, T1-weighted gradient echo sequences with fat suppression were performed. A gadolinium-based contrast agent, 0.1 mL/kg, was administered at an injection rate of 2 mL/s. Five T1-weighted post-contrast series with image subtraction were acquired, followed by multiplanar reformatting and maximum intensity projection (MIP). A kinetic curve analysis was performed, and peak enhancement index (PEI) values were determined. The contrast-enhanced breast MRI images were stored in a Picture Archiving and Communication System (PACS) (Carestream, Phillips, Rochester, NY, USA). A radiologist (NGG) with 16 years of experience in breast imaging performed the image analysis.

Mass and non-mass lesions were scored using the KS based on the morphologic and kinetic features of the BI-RADS lexicon. These descriptors were the root sign (presence or absence of spiculations), enhancement curve (type 1, 2, or 3), lesion margin (irregular or circumscribed), internal enhancement pattern, and edema. The KS score was calculated using a virtual calculator available at https://school-of-radiology.com/kaiserscore/[10]. Based on the total score, lesions were classified to define malignancy risk and their relationship to BI-RADS: KS 1 to 4, low risk, BI-RADS 2 or 3; KS 5 to 7, intermediate risk, BI-RADS 4; and KS 8 to 11, high risk, BI-RADS 5.

For KS* breast vasculature assessment, AVS was defined as the presence of vessels either entering the lesion or in contact with the edge of the lesion, clearly delineated on the subtraction images[1,11]. Vessels with a length ≥ 3 cm and a diameter ≥ 2 mm were counted for the breast with the lesion and the contralateral breast on the MIP images. If the number of vessels in the lesion-bearing breast was two or more than those in the contralateral breast, this was categorized as increased ipsilateral breast vascularity[1]. In cases where

a breast lesion had a KS ≤ 7 but simultaneously had positive AVS and increased ipsilateral breast vascularity, the KS was increased by 3 points, thereby modifying the final score. The KS* range remained from 1 to 11, aligning with the original KS framework[1].

Molecular breast cancer subtypes

Tumor biopsies were stained for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) using a Ventana BenchMark GX Autostainer with validated internal protocols. An external positive control tissue was included in each run. ER and PR were classified as positive if nuclear staining was >1% according to ASCO/CAP guidelines[12]. HER2 assessment was performed according to the 2023 ASCO/CAP HER2 test update[12].

Histopathologic workup

Breast lesions identified as BI-RADS 4 or 5 that underwent image-guided or surgical breast biopsy were evaluated by a breast pathologist (GGM) with 14 years of experience. The diagnostic criteria for histopathological diagnosis were based on the fifth edition of the WHO classification of breast tumors[13].

Statistical analysis

Measures of central tendency and dispersion were used to summarize numerical variables, and absolute numbers and percentages for categorical variables. The association between unrelated categorical variables was assessed using the chi-square test. The p value < 0.05 was statistically significant. SPSS v.25 (IBM Corp., Armonk, NY, USA) was used for data analysis.

RESULTS

A total of 476 women with breast cancer were included: 421 (88.4%) had mass lesions and 55 (11.6%) had non-mass lesions. The mean age ± SD was 49.3 ± 10.9 and 51.2 ± 10.9 years, respectively.

Contrast-enhanced breast MRI findings in mass lesions with or without vascular signs in women with breast cancer

The contrast-enhanced breast MRI findings in 418 of the 421 mass lesions in women with breast cancer with or without vascular signs are shown in Table 1. Three cases with only increased ipsilateral vascularity without AVS were not included. The shape, margin, type of enhancement, kinetic curve, and root sign of the mass breast lesions with or without vascular signs were not significantly different. Mass lesions with both vascular signs, AVS positive and increased ipsilateral breast vascularity (n = 176/418) had a higher frequency of masses (n = 120/176, 68.1%) with larger size (≥ 21 mm). In contrast, in 44 patients without vascular signs, 68.0% (n = 30/44) had small masses (≤ 20 mm) (p = 0.001). The presence of edema was observed in 23.4% (98/418) of the masses. Absence of edema was significantly more common in cases without vascular signs (n = 40/44, 90.9%) (p = 0.003).

Contrast-enhanced breast MRI findings in non-mass lesions with or without vascular signs in women with breast cancer

The contrast-enhanced breast MRI of 55 non-mass lesions in women with breast cancer with or without vascular signs is shown in table 2. Both vascular signs were found in 23 (42.0%), with a regional distribution pattern (n = 11/23, 47.8%) (p = 0.015) and a size > 51 mm (n = 16/23, 69.6%) (p = 0.001) being more significant. The absence of vascular signs, observed in 9.1% of cases (n = 5/55), was significantly associated with small, non-mass lesions (< 20 mm) (p < 0.001). There were no significant differences in the type of enhancement, kinetic curve, edema, or margin with the presence or absence of vascular signs. An increase in root sign was found in cases with a positive AVS and increased ipsilateral breast vascularity, although this difference was not significant.

Upgrading from KS to KS* based on the presence of vascular signs in women with breast cancer

Both vascular signs, positive AVS and increased ipsilateral breast vascularity, were found in 176 (41.8%) of 421 mass lesions on contrast-enhanced breast MRI (Table 3A). The score of these mass lesions was increased by 3 additional points, and they were reclassified as intermediate-risk and high-risk for malignancy on the KS*. There was no mass lesion in the low-risk category (KS* 1 to 4). Both vascular signs were found in 158 (89.8%) of 176 mass breast lesions with KS* 8 to 11, with a high risk of malignancy.

Table 1. Contrast-enhanced breast MRI findings in 418[a] mass lesions with or without vascular signs in women with breast cancer

Descriptor	Total (n = 418)	Positive AVS (n = 198)	Positive AVS and increased ipsilateral breast vascularity, (n = 176)	No vascular signs (n = 44)	*p*
Shape, n (%)					0.219
Oval	20 (4.8)	9 (4.5)	6 (3.4)	5 (11.4)	
Round	34 (8.1)	14 (7.1)	17 (9.7)	3 (6.8)	
Irregular	364 (87.1)	175 (88.4)	153 (86.9)	36 (81.8)	
Margin, n (%)					0.258
Circumscribed	13 (3.1)	5 (2.5)	5 (2.8)	3 (6.8)	
Spiculated	181 (43.3)	79 (39.9)	85 (48.3)	17 (38.6)	
Irregular	224 (53.6)	114 (57.6)	86 (48.9)	24 (54.5)	
Enhancement, n (%)					0.470
Homogeneous	54 (12.9)	30 (15.2)	16 (9.1)	8 (18.2)	
Heterogeneous	267 (63.9)	123 (62.1)	117 (66.5)	27 (61.4)	
Rim shape	96 (23.0)	45 (22.7)	42 (23.9)	9 (20.5)	
Dark internal septation	1 (0.2)	0	1 (0.6)	0	
Main lesion size, n (%)					0.001
2 to 20 mm	185 (44.3)	99 (50.0)	56 (31.8)	30 (68.2)	
> 21 to 50 mm	210 (50.2)	94 (47.5)	102 (58.0)	14 (31.8)	
> 51 mm	23 (5.5)	5 (2.5)	18 (10.2)	0	
Kinetic curve, n (%)					0.223
Type 1	48 (11.5)	26 (13.1)	18 (10.2)	4 (9.1)	
Type 2	210 (50.2)	94 (47.5)	87 (49.4)	29 (65.9)	
Type 3	160 (38.3)	78 (39.4)	71 (40.3)	11 (25.0)	
Root sign, n (%)					0.211
Yes	181 (43.3)	79 (39.9)	85 (48.3)	17 (38.6)	
No	237 (56.7)	119 (60.1)	91 (51.7)	27 (61.4)	
Edema, n (%)					0.003
Yes	98 (23.4)	40 (20.2)	54 (30.7)	4 (9.1)	
No	320 (76.6)	158 (79.8)	122 (69.3)	40 (90.9)	

[a]Three women with only increased ipsilateral breast vascularity were not included. AVS: adjacent vessel sign. KS: Kaiser score; KS*: modified Kaiser score.

Both vascular signs were found on contrast-enhanced breast MRI in 23 (41.8%) of 55 non-mass lesions (Table 3B). These lesions were upgraded by 3 additional points and were categorized as intermediate- and high-risk groups on KS*. Twenty-one (91.4%) of 23 non-mass lesions with both vascular signs were reclassified with high scores (KS* 8-11). Only one non-mass lesion remained in the low-risk category.

Molecular subtypes in mass and non-mass breast lesions in women with breast cancer

The distribution of molecular subtypes was comparable between mass and non-mass breast lesions (Table 4). The luminal A molecular subtype was more common, with 154 (36.6%) of 421 mass lesions and 26 (47.3%) of 55 non-mass lesions. The triple-negative

Table 2. Contrast-enhanced breast MRI findings in 55 non-mass lesions with or without vascular signs in women with breast cancer

Descriptor	Total (n = 55)	Positive AVS (n = 27)	Positive AVS and increased ipsilateral breast vascularity, (n = 23)	No vascular signs (n = 5)	*p*
Enhancement, n (%)					0.601
Homogeneous	3 (5.5)	3 (11.1)	0	0	
Heterogeneous	32 (58.2)	14 (51.9)	14 (60.9)	4 (80.0)	
Clumped	17 (30.9)	8 (29.6)	8 (34.8)	1 (20.0)	
Cluster ring	3 (5.5)	2 (7.4)	1 (4.3)	0	
Distribution, n (%)					0.015
Focal	21 (38.2)	13 (48.1)	4 (17.4)	4 (80.0)	
Lineal	8 (14.5)	5 (18.5)	2 (8.7)	1 (20.0)	
Segmental	12 (21.8)	6 (22.2)	6 (26.1)	0	
Regional	14 (25.5)	3 (11.1)	11 (47.8)	0	
Main lesion size, n (%)					0.001
2 to 20 mm	11 (20.0)	5 (18.5)	1 (4.3)	5 (100)	
> 21 to 50 mm	21 (38.2)	15 (55.6)	6 (26.1)	0	
> 51 mm	23 (41.8)	7 (25.9)	16 (69.6)	0	
Kinetic curve, n (%)					0.416
Type 1	15 (27.3)	8 (29.6)	7 (30.4)	0	
Type 2	24 (43.6)	12 (44.4)	8 (34.8)	4 (80.0)	
Type 3	16 (29.1)	7 (25.9)	8 (34.8)	1 (20.0)	
Root sign, n (%)					0.234
Yes	36 (65.5)	15 (55.6)	18 (78.3)	3 (60.0)	
No	19 (34.5)	12 (44.4)	5 (21.7)	2 (40.0)	
Edema, n (%)					0.317
Yes	17 (30.9)	7 (25.9)	7 (30.4)	3 (60.0)	
No	38 (69.1)	20 (74.1)	16 (69.6)	2 (40.0)	
Margin, n (%)					0.646
Circumscribed	6 (10.9)	2 (7.4)	3 (13.0)	1 (20.0)	
Non-circumscribed	49 (89.1)	25 (92.6)	20 (87.0)	4 (80.0)	

AVS: adjacent vessel sign; KS: Kaiser score; KS*: modified Kaiser score.

molecular subtype was significantly more common in mass lesions (n = 70/421, 16.6%) than in non-mass lesions (n = 1/55, 1.8%) (p = 0.004).

Association of KS and KS with molecular subtypes of mass lesions in women with breast cancer*

Of the 421 mass lesions, 48 (11.4%) were categorized as low risk, 195 (46.3%) as intermediate risk, and 178 (42.3%) as high risk for malignancy by KS (Table 5A). No significant association was found between molecular subtype and malignancy risk in KS. However, the majority of mass lesions of all molecular subtypes were categorized as intermediate (n = 195/421, 46.3%) or high malignancy risk (n = 178/421, 42.3%).

Among the 421 mass breast lesions, a subgroup of 176 showed both vascular signs on contrast-enhanced breast MRI and were classified with KS* (Table 5B).

Table 3A. Upgrade from KS to KS* based on the presence of vascular signs in mass lesions on contrast-enhanced breast MRI in women with breast cancer

KS				KS*			
1 to 4	5 to 7	8 to 11	Total	1 to 4	5 to 7	8 to 11	Total
48 (11.5%)	195 (46.3%)	178 (42.3%)	421	0	18 (10.2%)	158 (89.8)	176[a]

[a]A subgroup of 176 (41.8%) of the 421 mass lesions had both vascular signs; these were upgraded by 3 additional points. As a result, none of the lesions remained in the low-risk category (KS* 1–4). MRI: magnetic resonance imaging; KS: Kaiser score; KS*: modified Kaiser score.

Table 3B. Upgrade from KS to KS* based on the presence of vascular signs in non-mass lesions on contrast-enhanced breast MRI in women with breast cancer

KS				KS*			
1 to 4	5 to 7	8 to 11	Total	1 to 4	5 to 7	8 to 11	Total
9 (16.3%)	26 (47.3)	20 (36.4%)	55	1 (4.3%)	1 (4.3%)	21 (91.4%)	23[a]

[a]A subgroup of 23 (41.8%) of the 55 non-mass lesions had both vascular signs; these were upgraded by 3 additional points on the KS*. As a result, only one non-mass lesion remained in the low-risk category (KS* 1–4). MRI: magnetic resonance imaging; KS: Kaiser score; KS*: modified Kaiser score.

Table 4. Molecular subtypes in mass and non-mass lesions in women with breast cancer

Description	Mass breast lesions, (n = 421)	Non-mass breast lesions, (n = 55)
Luminal A, n (%)	154 (36.6)	26 (47.3)
Luminal B, n (%)	119 (28.3)	13 (23.6)
Luminal B HER2+, n (%)	33 (7.8)	7 (12.7)
HER2+, n (%)	29 (6.9)	5 (9.1)
Triple-negative, n (%)	70 (16.6)	1 (1.8)
HER2-low, n (%)	16 (3.8)	3 (5.5)

HER2+: human epidermal growth factor receptor 2.

These lesions received an upgrade of 3 additional points. As a result, none of the lesions remained in the low-risk (KS* 1 to 4). The high-risk category was elevated in all molecular subtypes (range 75.8% to 94.4%).

Figure 1 shows a contrast-enhanced breast MRI in a 41-year-old woman with a mass lesion with positive AVS and increased ipsilateral breast vascularity. This mass was classified as a BI-RADS category 2 and a KS of 2, corresponding to a low risk of malignancy. In addition, 3 points were assigned based on the presence of vascular signs, resulting in a KS* of 5 corresponding to an intermediate risk of malignancy, BI-RADS category 4. The histopathologic diagnosis was invasive non-special type (NST) carcinoma, molecular subtype luminal A.

Figure 2 shows a contrast-enhanced breast MRI of a 41-year-old woman with a non-mass lesion, BI-RADS category 2, and a KS of 1, corresponding to a low risk of malignancy. Three points were assigned based on the positive AVS and increased ipsilateral breast vascularity, resulting in a KS* of 4, corresponding to a low risk of malignancy, BI-RADS category 2. A breast biopsy was ordered due to calcifications in the right breast detected by mammography (not shown). The histopathologic diagnosis of the non-mass lesion in the right breast was invasive NST carcinoma, molecular subtype luminal B, with an associated *in situ* carcinoma.

Figure 3 shows a contrast-enhanced breast MRI in a 52-year-old woman with a mass lesion with positive AVS and increased ipsilateral breast vascularity. This mass was classified as BI-RADS category 2, with a KS of 2, corresponding to a low risk of malignancy. Three points were assigned based on the presence of vascular signs, resulting in a KS* of 5, corresponding to an intermediate risk of malignancy, BI-RADS category 4. The histopathologic diagnosis was invasive NST carcinoma with basaloid features, molecular subtype triple-negative.

Table 5A. Association of KS with molecular subtypes of mass lesions in women with breast cancer

Description	Total, n	KS			*p*
		1 to 4	5 to 7	8 to 11	
Luminal A, n (%)	154	16 (10.4)	80 (51.9)	58 (37.7)	0.374
Luminal B, n (%)	119	10 (8.4)	58 (48.7)	51 (42.9)	0.577
Luminal B HER2+, n (%)	33	4 (12.1)	13 (39.4)	16 (48.5)	0.720
HER2+, n (%)	29	2 (6.9)	11 (37.9)	16 (55.2)	0.351
Triple-negative, n (%)	70	13 (18.6)	25 (35.7)	32 (45.7)	0.080
HER2-low, n (%)	16	3 (18.8)	8 (50.0)	5 (31.3)	0.531

HER2+: human epidermal growth factor receptor 2; KS: Kaiser score.

Table 5B. Association of KS* with molecular subtypes of mass lesions[a] in women with breast cancer

Description	Total, n	KS*			*p*
		1 to 4	5 to 7	8 to 11	
Luminal A, n (%)	54	0	3 (5.6)	51 (94.4)	0.257
Luminal B, n (%)	54	0	3 (5.6)	51 (94.4)	0.257
Luminal B HER2+, n (%)	18	0	2 (11.1)	16 (88.9)	0.902
HER2+, n (%)	13	0	2 (15.4)	11 (84.6)	0.539
Triple-negative, n (%)	33	0	8 (24.2)	25 (75.8)	0.008
HER2-low, n (%)	4	0	0	4 (100)	0.500

[a]A subgroup of 176 (41.8%) of the 421 mass lesions had both vascular signs; these were upgraded by 3 additional points. As a result, none of the lesions remained in the low-risk category (KS* 1 to 4). HER2+: human epidermal growth factor receptor 2; KS*: modified Kaiser score.

Association of KS and KS with molecular subtypes of non-mass lesions in women with breast cancer*

Nine (16.4%) of 55 non-mass lesions were categorized as low risk, 26 (47.3%) as intermediate risk, and 20 (36.3%) as high risk in KS (Table 6A). Only luminal A, luminal B, and HER2+ molecular subtypes had low-risk KS lesions. No significant association was found between the molecular subtype and risk of malignancy categorized by KS.

Of 55 non-mass breast lesions, 23 (41.8%) had both vascular signs on contrast-enhanced breast MRI (Table 6B). Twenty-one (91.3%) of the 23 were categorized in the high-risk category (KS* 8 to 11), similar to the mass lesions. Figure 4 shows a contrast-enhanced breast MRI of a 67-year-old woman with a non-mass lesion enhancement classified as BI-RADS category 3 and a KS of 4 with a low risk of malignancy. Three points were assigned based on the presence of vascular signs, resulting in a KS* of 7, corresponding to an intermediate risk of malignancy, BI-RADS category 4. The diagnosis was high-grade DCIS of the solid, comedo, and cribriform type, with a HER2-positive molecular subtype.

DISCUSSION

Our study showed that KS* improved malignancy prediction by contrast-enhanced breast MRI based on the presence of vascular signs in both mass and non-mass breast lesions. This is the first study in Mexico to confirm that the presence of vascular signs optimizes the

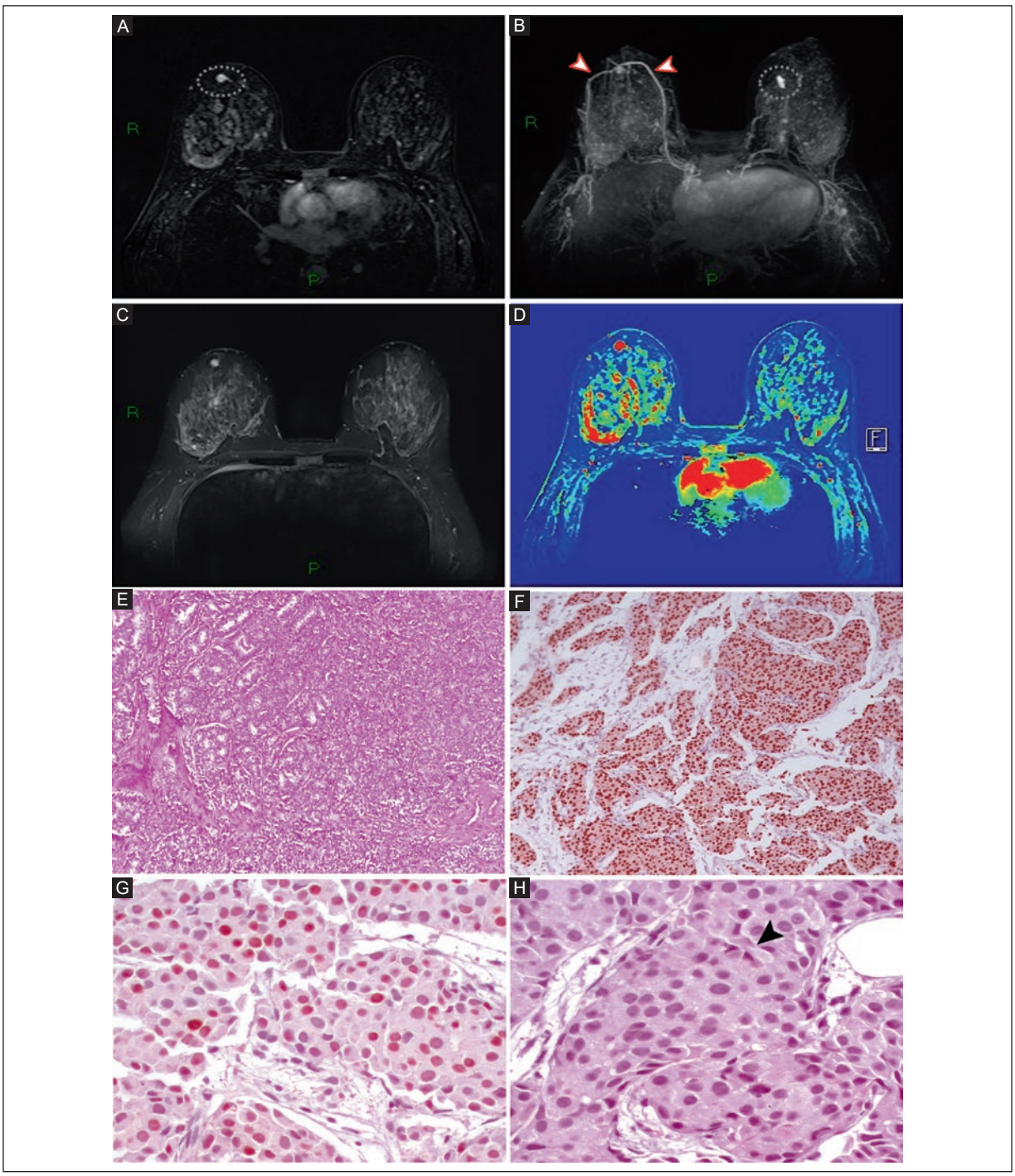

Figure 1. Contrast-enhanced breast MRI of a 41-year-old woman. **A:** T1 DCE sequence with gadolinium demonstrates a round mass with circumscribed margins and ring enhancement in the upper outer quadrant of the right breast (dotted circle). **B:** MIP image demonstrates a right breast mass with a positive AVS and increased ipsilateral breast vascularity (red arrowheads). In the left breast, a hyperenhanced solid mass without vascular signs is also observed, corresponding to a previously diagnosed fibroadenoma confirmed by histopathology (dashed circle). **C:** there is no perilesional edema on the TIRM sequence. **D:** PEI and the correlation of time–signal intensity curves of the main lesion in the right breast shows a type 2 plateau curve (not shown). This mass breast lesion was classified as BI-RADS category 2, and KS 2, with a low risk of malignancy. Three points were assigned based on the presence of vascular signs, resulting in a KS* of 5, with an intermediate risk of malignancy, BI-RADS category 4. **E:** H&E 10X, nests of neoplastic cells with sparse lumen formation. The cells have nuclear pleomorphism and frequent mitoses. **F:** ER (5X) 100% nuclear expression, with strong intensity. **G:** PR (10X) 100% nuclear expression, with strong intensity. **H:** HER-2 (10X) negative membrane staining (0+) (black arrowhead). The histopathologic diagnosis was invasive NST carcinoma, luminal A molecular subtype.

AVS: adjacent vessel sign; KS: Kaiser score; KS*: modified Kaiser score; BI-RADS: Breast Imaging Reporting and Data System; DCE: dynamic contrast-enhanced; Gd: gadolinium; MIP: maximum intensity projection; MRI: magnetic resonance imaging; PEI: positive enhancement integral; TIRM: turbo inversion recovery magnitude; NST: non-special type; H&E: hematoxylin and eosin; ER: estrogen receptor; PR: progesterone receptor; HER-2: human epidermal growth factor receptor 2.

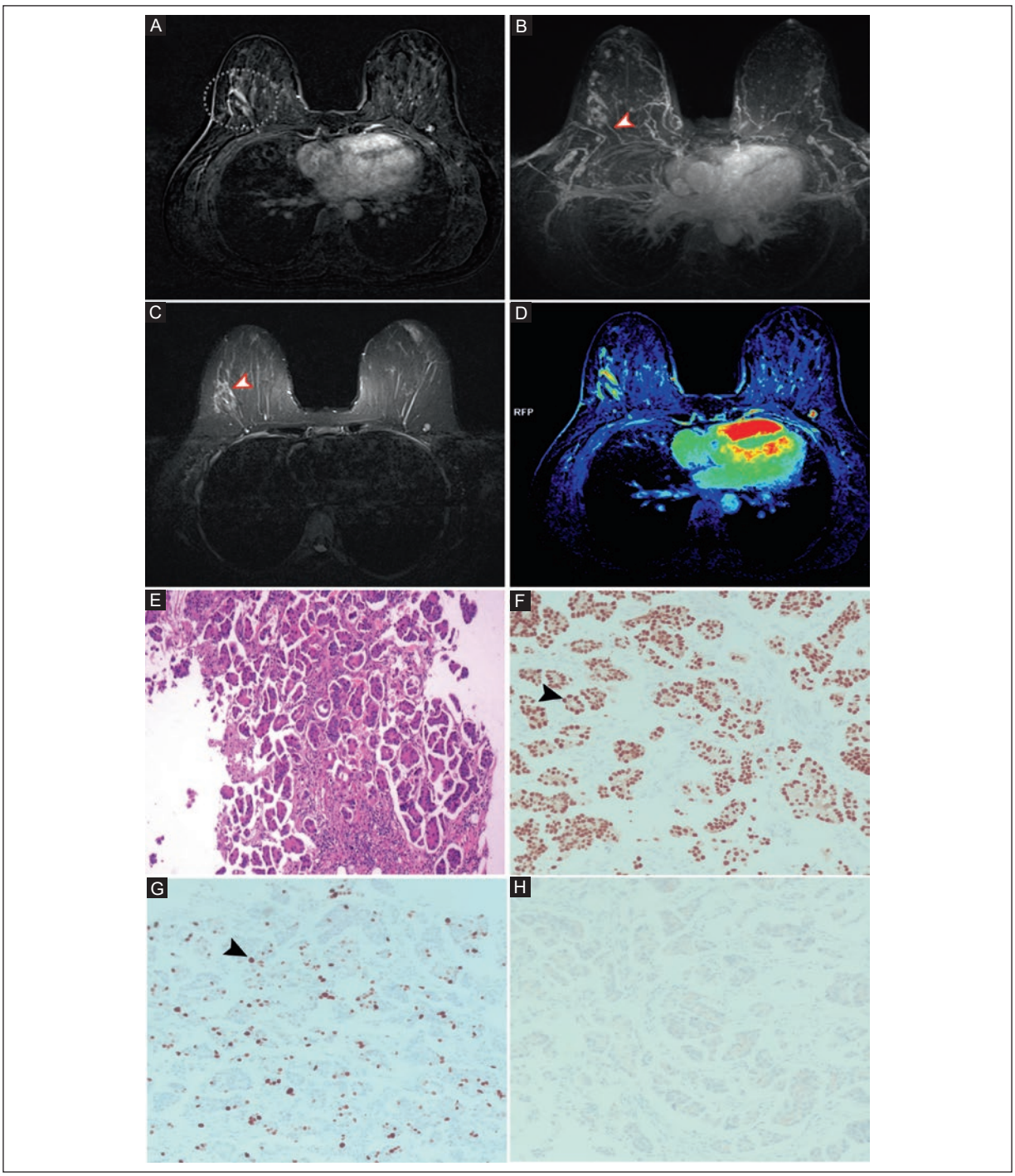

Figure 2. Contrast-enhanced breast MRI of a 41-year-old woman. **A:** T1 DCE sequence with Gd shows a non-mass lesion with a circumscribed margin and cobblestone enhancement in the upper outer quadrant of the right breast (dotted circle). **B:** MIP shows a non-mass lesion in the right breast with positive AVS and increased ipsilateral breast vascularity (red arrowhead). **C:** perilesional edema is seen on the TIRM sequence (red arrowhead). **D:** PEI and the correlation of time–signal intensity curves of the main lesion with a persistent type 1 curve (not shown). This non-mass lesion was classified as BI-RADS category 2, KS 1, with a low risk of malignancy. Three points were assigned based on the positive AVS and increased ipsilateral breast vascularity, resulting in a KS* of 4 with a low risk of malignancy, BI-RADS category 2. Breast biopsy was indicated due to calcifications in the right breast detected by mammography (not shown). **E:** H&E 5X, nests of neoplastic cells with reversed polarity and stromal retraction. **F:** ER 5X, 100% nuclear expression with strong intensity (black arrowhead). **G:** PR 5X, 100% nuclear expression with strong intensity (black arrowhead). **H:** HER-2 5X, partial and weak membrane staining (1+). The histopathologic diagnosis of the non-mass lesion in the right breast was invasive NST carcinoma, luminal B molecular subtype, with associated in situ carcinoma.

AVS: adjacent vessel sign; KS: Kaiser score; KS*: modified Kaiser score; BI-RADS: Breast Imaging Reporting and Data System; DCE: dynamic contrast-enhanced; Gd: gadolinium; MIP: maximum intensity projection; MRI: magnetic resonance imaging; PEI: positive enhancement integral; TIRM: turbo inversion recovery magnitude; NST: not-special type; H&E: hematoxylin and eosin; ER: estrogen receptor; PR: progesterone receptor; HER-2: human epidermal growth factor receptor 2.

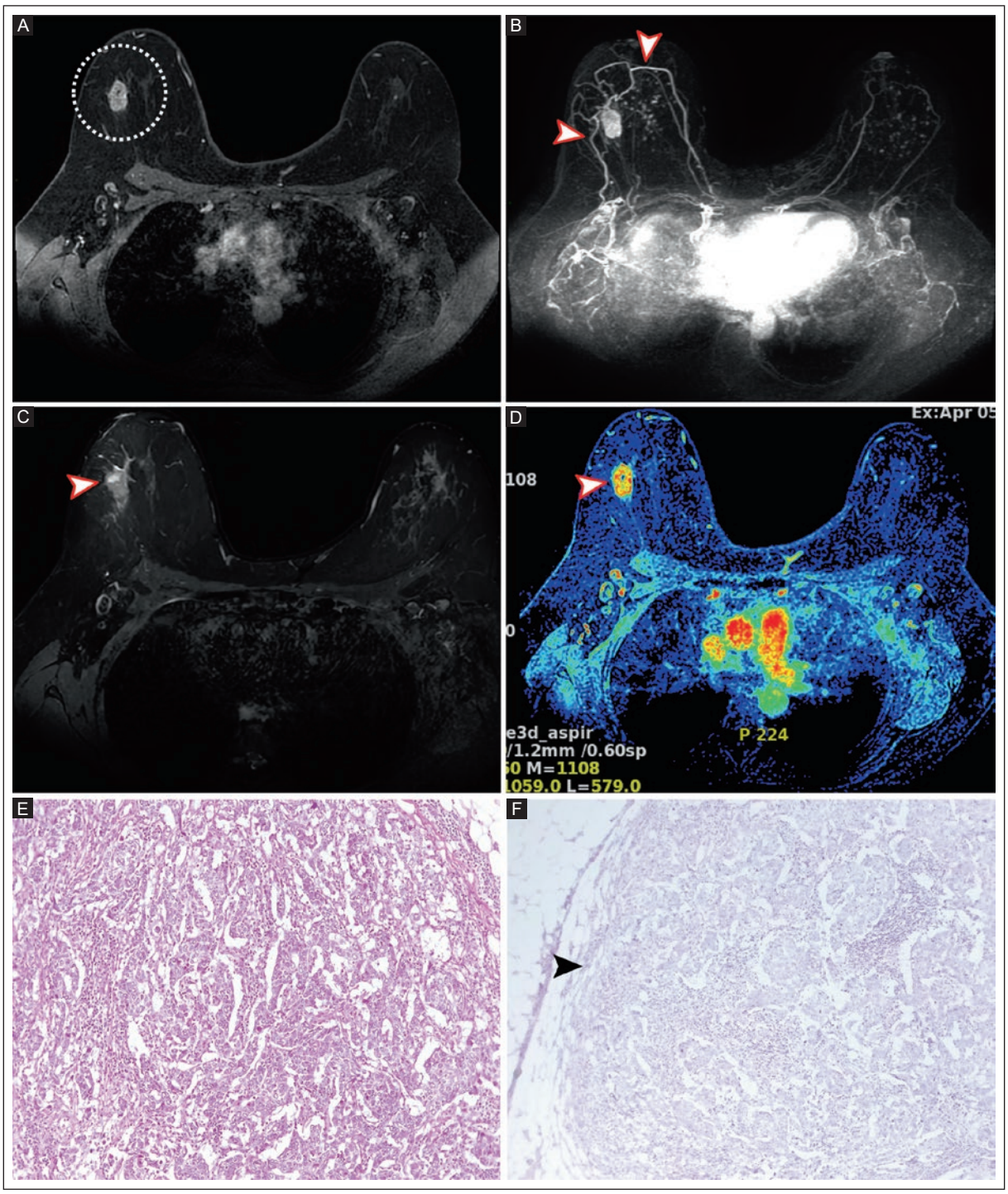

Figure 3. Contrast-enhanced breast MRI of a 52-year-old woman. **A:** T1 DCE sequence with Gd shows a round mass lesion, with circumscribed margins and homogeneous enhancement in the upper outer quadrant of the right breast (dotted circle). **B:** MIP shows a mass lesion of the right breast with positive AVS and increased ipsilateral breast vascularity (red arrowheads). **C:** there is no perilesional edema in the TIRM sequence (red arrowhead). **D:** PEI and the correlation of time–signal intensity curves of the breast lesion with a type 2 plateau curve (not shown). This mass was classified as BI-RADS category 2, KS 2, with a low risk of malignancy. Three points were assigned based on the presence of vascular signs, resulting in a KS* of 5, with an intermediate risk of malignancy, BI-RADS category 4. **E:** H&E 10X, nests of neoplastic cells with sparse lumen formation, nuclear pleomorphism, and frequent mitoses. **F:** ER 5X, negative expression. PR 5X, negative expression. HER2 5X, negative expression (black arrowhead). The histopathologic diagnosis was invasive NST carcinoma with basaloid features, triple-negative molecular subtype.

AVS: adjacent vessel sign; KS: Kaiser score; KS*: modified Kaiser score; BI-RADS: Breast Imaging Reporting and Data System; DCE: dynamic contrast-enhanced; Gd: gadolinium; MIP: maximum intensity projection; MRI: magnetic resonance imaging; PEI: positive enhancement integral; TIRM: turbo inversion recovery magnitude; NST: non-special type; H&E: hematoxylin and eosin; ER: estrogen receptor; PR: progesterone receptor; HER-2: human epidermal growth factor receptor 2.

Table 6A. Association of KS with molecular subtypes of non-mass lesions in women with breast cancer

Description	Total, n	KS			*p*
		1 to 4	5 to 7	8 to 11	
Luminal A, n (%)	26	6 (23.1)	11 (42.3)	9 (34.6)	0.437
Luminal B, n (%)	13	2 (15.4)	7 (53.8)	4 (30.8)	0.856
Luminal B HER2+, n (%)	7	0	4 (57.1)	3 (42.9)	0.456
HER2+, n (%)	5	1 (20.0)	2 (40.0)	2 (40.0)	0.939
Triple-negative, n (%)	1	0	0	1 (100)	0.410
HER2-low, n (%)	3	0	2 (66.7)	1 (33.3)	0.677

HER2+: human epidermal growth factor receptor 2. KS: Kaiser score.

Table 6B. Association of KS* with molecular subtypes of non-mass lesions[a] in women with breast cancer

Description	Total, n	KS*			*p*
		1 to 4	5 to 7	8 to 11	
Luminal A, n (%)	9	0	0	9 (100)	0.495
Luminal B, n (%)	5	1 (20.0)	0	4 (80.0)	0.138
Luminal B HER2+, n (%)	4	0	0	4 (100)	0.794
HER2+, n (%)	3	0	1 (33.3)	2 (66.7)	0.030
Triple-negative, n (%)	1	0	0	1 (100)	0.951
HER2-low, n (%)	1	0	0	1 (100)	0.950

[a]A subgroup of 23 (41.8%) of the 55 non-mass lesions had both vascular signs; there were upgraded by 3 additional points in the KS*. As a result, only one non-mass lesion remained in the low score category (KS* 1 to 4). HER2+: human epidermal growth factor receptor 2; KS*: modified Kaiser score.

KS* diagnostic stratification algorithm that identifies lesions with suspected malignancy and indicates the need for breast biopsy. The breast lesion scores were initially categorized as low risk, with the KS* increased due to positive AVS and increased ipsilateral breast vascularity. They were subsequently reclassified as intermediate and high risk for malignancy with KS*.

Positive AVS and increased ipsilateral breast vascularity improve the diagnostic performance of KS* in predicting breast lesion malignancy[1,10,14]. In our study, the presence of both vascular signs was associated with significantly higher KS* scores in both mass and non-mass lesions. Dietzel et al.[14], in a retrospective study in German women, analyzed 1,084 breast lesions. A positive AVS was significantly associated with malignancy ($p < 0.001$). Lesions larger than 20 mm were more likely to have a positive AVS than those smaller than 20 mm ($p < 0.0001$). Zhou et al.[1] examined 223 breast lesions with suspected malignancy by contrast-enhanced breast MRI with a histopathologic diagnosis. There were 119 (53.4%) benign and 104 (46.6%) malignant lesions. Eighty-five (51.8%) of 164 mass lesions and 19 (32.2%) of 59 non-mass lesions were malignant. In the ROC curve, the AUC of KS* was 0.877 and of KS, 0.858 ($p = 0.016$). In non-mass lesions, the AUC was 0.793, and KS was 0.725 ($p = 0.029$). The combination of KS with vascular signs (KS*) significantly improves the diagnostic performance in differentiating benign and malignant breast lesions, especially in non-mass lesions. Positive AVS and increased ipsilateral breast vascularity were significantly associated with malignancy. Our study of 476 women with breast cancer evaluated with contrast-enhanced breast MRI with histopathologic confirmation and reclassification of breast lesions into

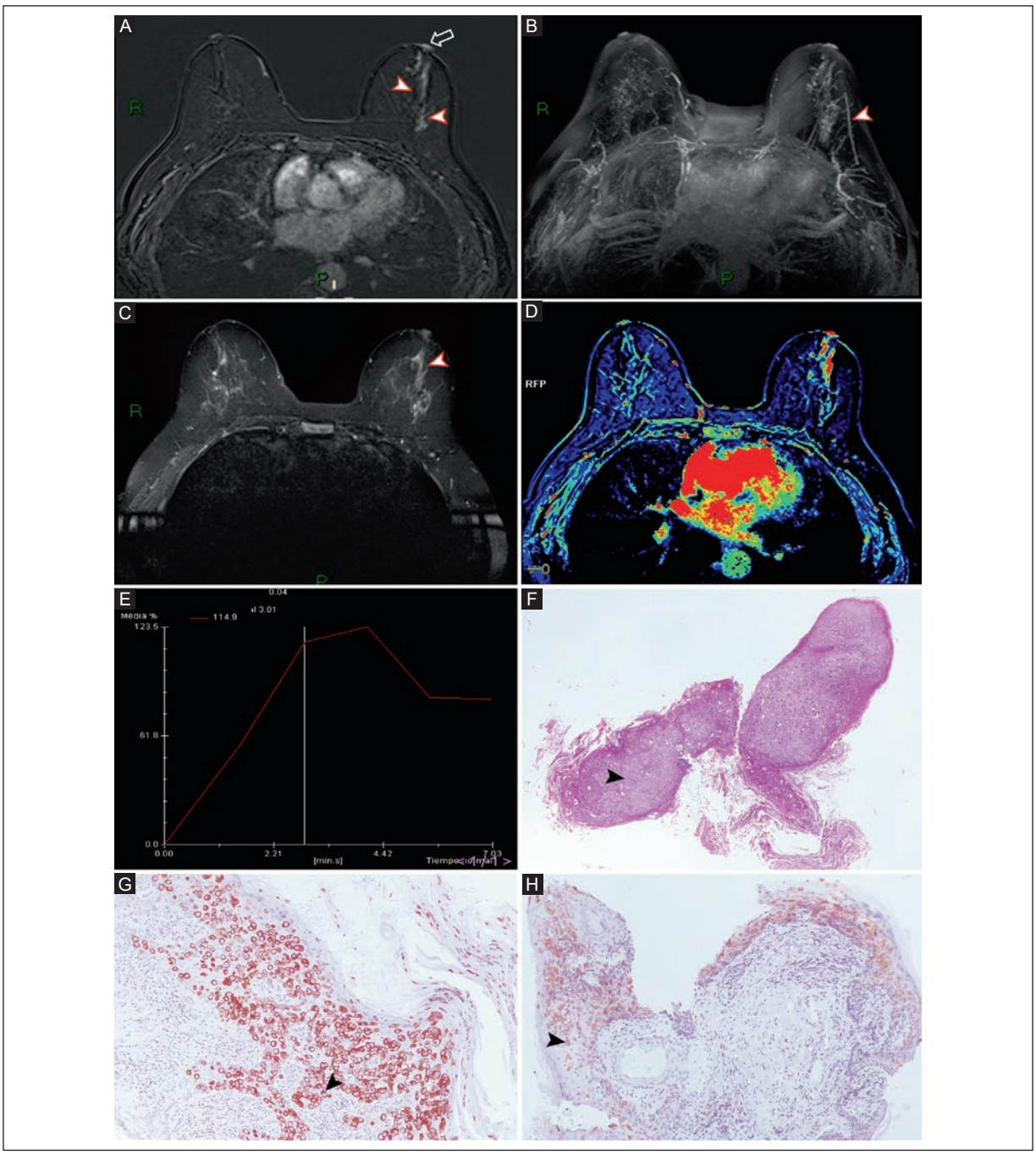

Figure 4. Contrast-enhanced breast MRI of a 67-year-old woman. **A:** T1 DCE sequence with Gd shows non-mass enhancement with a circumscribed margin and cobblestone-like enhancement with linear distribution in the retroareolar region of the left breast (red arrowheads). Note the nipple enhancement (white arrow). **B:** MIP image shows a non-mass lesion in the left breast with positive AVS and increased ipsilateral breast vascularity (red arrowhead). **C:** there is no perilesional edema in the TIRM sequence (red arrowhead). **D-E:** dynamic post-contrast image with time–signal intensity curve analysis of the primary lesion shows a type 3 washout curve. This non-mass lesion was classified as KS 4 with a low risk of malignancy. Three points were assigned based on the presence of vascular signs, resulting in a KS* of 7, with an intermediate risk of malignancy, BI-RADS category 4. A left breast mastectomy revealed a high-grade DCIS with solid, comedo-like, cribriform architecture, classified as a HER2-positive molecular subtype. There is no dermal infiltration. Paget's disease was present on the nipple. **F:** H&E 5X, proliferation of malignant intraepidermal glandular epithelial cells. Cells with abundant eosinophilic cytoplasm and pleomorphic nuclei (black arrowhead). **G:** ER: CK7 (5X), positive membranous expression (black arrowhead). **H:** HER2 (5X), positive membranous expression (black arrowhead).

AVS: adjacent vessel sign; KS: Kaiser score; KS*: Kaiser score*; BI-RADS: Breast Imaging Reporting and Data System; DCE: dynamic contrast-enhanced; Gd: gadolinium; MIP: maximum intensity projection; MRI: magnetic resonance imaging; PEI: positive enhancement integral; TIRM: turbo inversion recovery magnitude; NST: non-special type; DCIS: ductal carcinoma in situ; H&E: hematoxylin and eosin; ER: estrogen receptor; PR: progesterone receptor; CK7: cytokeratin 7; HER-2: human epidermal growth factor receptor 2.

intermediate- and high-risk KS* based on positive AVS and increased ipsilateral breast vascularity increased the prediction of malignancy in lesions originally classified as low-risk. These results highlight the importance of evaluating not only the morphological and dynamic features of breast lesions on contrast-enhanced breast MRI, but also vascular signs, since these provide additional information about their malignant behavior.

Benign and malignant breast lesions may show non-mass enhancement on MRI. KS is less accurate in predicting malignancy in non-mass lesions. Therefore, the addition of vascular signs indicative of abnormal vascularity guides the diagnosis of malignancy[1]. In our study, the presence of vascular signs in the KS* algorithm significantly increased the risk classification of malignancy. In mass lesions with both vascular signs, 158 (89.8%) of 176 mass breast lesions with KS* of 8 to 11 were at high risk of malignancy. None of these KS* lesions were classified as low risk. Twenty-one (91.4%) of 23 non-mass lesions with both vascular signs were reclassified as high risk (KS* 8 to 11), and only one non-mass lesion remained in the low-risk category. KS* with assessment of vascular signs increases the accuracy in predicting the malignancy of mass and non-mass breast lesions, especially lesions that could initially be underestimated with BI-RADS category 2 or 3 morphologic criteria. KS* can reduce false-negative results and support the indication for a breast biopsy in lesions with vascular signs.

Angiogenesis is critical in the development and spread of breast cancer and can vary depending on the molecular subtype[15]. Çetinkaya et al.[16], in a retrospective study of 124 Turkish women examined with contrast-enhanced breast MRI 1.5T with positive AVS, found 105 (78.9%) of 133 breast lesions suspicious for malignancy. No significant association was found between positive AVS and molecular subtypes. Bujor et al.[17] showed that the more aggressive molecular subtypes, HER2-positive and triple negative, had more blood vessels in the tumor compared to the luminal A and B molecular subtypes. In contrast, the luminal A molecular subtype, which has a better prognosis, has less angiogenic activity[17]. In our study of mass and non-mass breast lesions, the absence of vascular signs was predominant in the luminal A molecular subtype. This observation is consistent with a previous report indicating less angiogenesis and less prominent vascular patterns in luminal A tumors[17]. This finding contrasts with more aggressive molecular subtypes that exhibit greater vascularity. Our results reinforce the hypothesis that vascular signs may act as different functional biomarkers depending on the molecular tumor profile, especially in aggressive molecular subtypes that tend to show distinct vascular patterns.

One of the major strengths of this study is the sample size, which included 473 lesions in women with breast cancer and allowed for a robust and stratified analysis. This study also addressed the association between KS* and molecular subtypes, an aspect that has been scarcely explored. The weaknesses of this study are related to its single-center retrospective design. The sample size of non-mass lesions (n = 55) was small. In addition, only malignant cases were included, so it was not possible to determine the diagnostic performance of the KS* and its accuracy in distinguishing between benign and malignant lesions. Intraobserver and interobserver agreement were not assessed.

CONCLUSION

In our study, KS* increased the prediction of malignancy compared to KS, based on the presence of vascular signs in mass and non-mass breast lesions by contrast-enhanced breast MRI. Systematic evaluation of breast lesions with the KS* is recommended to optimize clinical decision making, especially the indication for a breast biopsy. The KS* is based on visual signs for assessing contrast-enhanced breast MRI. These signs are easily applicable in daily clinical practice without specialized software.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical

Association and the Declaration of Helsinki (1964). The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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