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Original Research Article

Comparison of Amritsar scoring system using quantitative contrast enhanced ultrafast magnetic resonance mammography and diffusion technique with conventional Kaiser scoring system

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ABSTRACT

Background: Magnetic resonance imaging (MRI) mammography has been recommended as a problem solving tool in patients with breast lump for which newer imaging protocols like abbreviated, ultrafast MRI and diffusion MRI are now available. For interpretation lexicons like BIRADS and Kaiser score system are available but there is a scope for improvement of results and need for newer lexicons.

Methods: Retrospective study of 175 patients of breast lump who had MRI mammography was done. The lesions were labelled as malignant by Kaiser score system (KSS) and a newer scoring system "Amritsar score system" (AMSS). Final diagnoses was confirmed by histological examination with hormone and Her2neu receptor studies. Statistical analysis was done for correlation, sensitivity, specificity and accuracy along with area under curves and the results compared.

Results: Study comprised 32/175 patients with malignant nodules. Mean age of 47.2 (range: 44.2-49.6) years with mean nodule size of 2.2 cm (range 1.8-5.5 cm). ADC and Ktrans, Kep, TTE, MS and IAUC60 showed high correlation with size of malignant nodule. Sensitivity of detection was 87.4%, 87.5%, 88.6%, 71.8% and 80% respectively for ADC, Ktrans, Kep, TTE, MS and IAUC60 while specificities were 94, 88.7, 88.7% 90% and 90% respectively. The sensitivity, specificity and accuracy for KSS and AMSS were 62.5%, 88.9%, 72% and 96.5%, 90% and 94% respectively.

Conclusions: AMSS is more accurate than KSS and improves the sensitivity and specificity of cancer detection. Ktrans and ADC imaging parameters not only show high sensitivity for cancer detection but also have a good correlation with the size and nuclear grade to be used as imaging biomarkers.

Keywords: Breast cancer, Diffusion imaging, MRI mammography

INTRODUCTION

Breast cancer is the leading cause of death in women worldwide.[1] The prognosis depends on early diagnosis and the stage of disease which influences the patient outcome. Imaging plays an important role in the early diagnosis and staging of disease. Mammography along with ultrasound breast has been the traditional imaging tools to evaluate patients with a breast lump. However, mammography has a wide variation in the sensitivity from 48% to 76% depending upon the density of breast and has reported specificity of 84%.[2-5] Ultrasound also has a reported sensitivity and specificity of 76% and 84% respectively.[6-7] Magnetic resonance imaging (MRI) is recommended as a screening tool in only high-risk patients or as a problem solving tool in the evaluation of a breast lump along with pre operative staging of disease.[8] MRI examination can be conducted using many techniques like the full six minute protocol, abbreviated or ultrafast protocol along with use of diffusion technique. These have become indispensable prior to breast conservative surgery.[9] Two commonly used systems of reporting are Kaiser scoring system and multi para metric reporting using BIRADS.[10-12] Both these have shown a high sensitivity of 90-100% in high risk screening patients but a low specificity of 12-47% which can result in unnecessary mastectomies.[13] So far quantitative dynamic contrast enhanced MRI has been used to define imaging biomarkers to identify high grade malignant lesions.[14,15] In a patient with palpable breast lump the purpose of doing MR is to rule in or rule out malignancy and to stage the extent of disease. This is more valuable in patients with BIRAD IV category on digital mammography or sonography so as to avoid unnecessary biopsies as per EUSOBI guidelines.[18,19] Studies done so far to demonstrate the role of MRI mammography as a diagnostic tool after a prior mammography or ultrasound have shown variable results with cancer detection rate of 5 to 26%.[20,21] Further the use of ACR BIRAD lexicon in breast MRI also shows a higher inter observer variation and lack of flexibility of imaging parameters.[22] The Kaiser scoring system showed improved results over BIRADS for detection of malignant lesions with accuracy of 88% and sensitivity and specificity of 77%, 69% respectively at a cut off score of >7 but still there was scope for improvement.[23,24] We designed a study using ultrafast and diffusion imaging with quantitative evaluation of dynamic contrast parameters labelled as “Amritsar scoring system” (AMSS) and compared the results with Kaiser scoring system (KSS).

METHODS

This was a retrospective study of 175 patients who presented to us with a breast lump over a period of sixteen months i.e. April 2021 to July 2022 done at Advanced Diagnostics and Institute of Imaging. Approval was obtained from the institutional review board (IRB/5/22). All the data was anonymized and demographic details of all patients were recorded along with the histopathological and hormone marker details. Patients underwent ultrasound guided Trucut biopsies followed by surgical treatment depending upon the nature of breast lump by coauthors.

Inclusion criteria

Any female patient above the age of 30 years with presentation of breast lump for the first time.

Inclusion criteria

Exclusion criteria included patients with prior history of lumpectomy or unilateral mastectomy, claustrophobia, post lactation or those in the secretory phase of menstrual cycle.

MRI protocol

MRI was done on a 1.5 Tesla system (Amira, Siemens AG) using a 16-element dedicated breast coil. Plain examination was done first using following parameters: T2-weighted imaging (STIR): TR/TE, 4000/65 ms; slice thickness, 5 mm, 0.5 mm gap; field of view (FOV), 340 × 340; matrix, NEX,1. T1WI (FLASH-3D): TR/TE, 3.6/2.1 ms; slice thickness, 1.2 mm, 0.2 mm gap; flip angle, 10°; NEX,0.7. RESOLVE DW with b values of 0 and 800 s/mm2 TR 4200 TE 67. DCE- Ultrafast MRI was performed by the following parameters: TR/TE, 6.6/2.4 ms; flip angle, 10°; slice thickness, 1 mm, 0.3mm gap with temporal resolution of 3 seconds; using pressure syringe with total scan time of 1 minute.

Image analysis

All images were processed on a Siemens syngio via system. Two radiologists with 10 years of experience interpreted the images by consensus and were blinded to histological results. The quantitative DCE-MRI parameters were interpreted using Siemens 4 D software which used a model of Tofts.[16] Quantitative DCE-MRI parameters include volume transfer constant (Ktrans), rate constant (Kep), and extravascular space (Ve). Semi quantitative analysis of mean curve was done using the same software on the region of interest and parameters of time to relative enhancement (TTE), maximum slope (MS), initial area under curve at 60 seconds (IAUC60) were calculated. Measurements of ADC values were done from two sites of the lesion and a mean value calculated on the b 1000 image. KSS system was done using five parameters (lesion type, shape and margins, root sign, edema and enhancement (Table 1) by an online software (available at http://www.meduniwien.ac.at/kaiser-score/). Cutoff score of 6 and above was taken as probably malignant. AMSS system used parameters enlisted in the Table 2. Seven imaging parameters were used i.e. lesion margins, ADC, type of enhancement kinetics, Ktrans, IACU60, TTE and MS. A cut off of 5 and above was labeled as probably malignant (Figures 1a-e).

Table 1: Kaiser score system (KSS).

Kinetics		1-3
Root sign	0-2	
Edema	0-1	
Margin	0-2	
INT enhancement	0-1	
1-2	Benign	BIRAD 2
3-5	Probab benign	BIRAD3
6-7	Probab malign	BIRAD 4
8-11	malignant	BIRAD5

Table 2: AMSS scoring system.

Parameters of imaging		Score
Margin	SMOO	-1
	WELL	0
	LOB	1
	SPIC	2
ENH	Type 1	-1
	2	0
	3	1
ADC	>1.3	-1
	1.2-1.3	0
	<1.2	1
TTE	>15	-1
	13-15	0
	<13	1
MS	<4	-1
	5-6.4%	0
	>6.5	1
Ktrans	<0.2	-1
	0.2-0.34	0
	>0.35	1
IAUC60	<10	-1
	Oct-15	0
	>15	1
Total score		
1-2	Benign	BIRAD 2
3-4	Probab benign	BIRAD3
5-6	Probab malignant	BIRAD 4
7-8	Malignant	BIRAD5

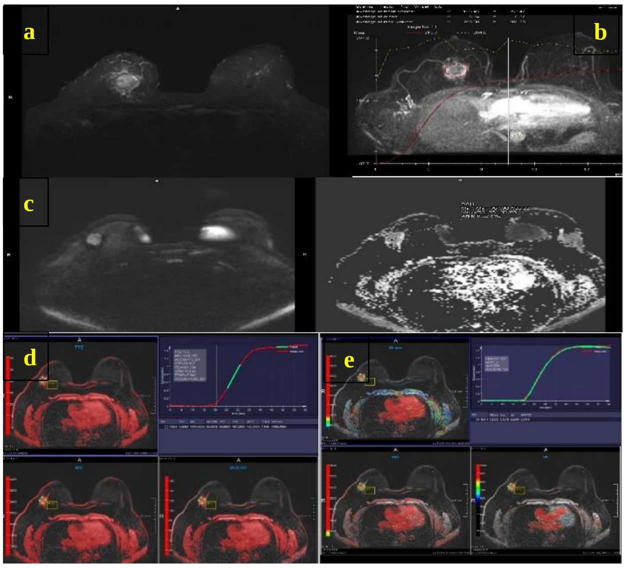


Figure 1: (a) T2W fat supressed axial image with hyperintense nodule with surrounding edema in right breast with KSS score of10 -BIRAD 5 category; (b) post contrast kinetic curve of the nodule; (c) Diffusion axial image showing hyperintense nodule with ADC 0.85; (d,e) Quantitative analysis showing TTE 1.0, MS of 104, iACU 72 and Ktrans of 1.5 KSS score 8- BIRAD V category.

Histological analysis

Histological grading of IDC was performed based on nuclear polymorphic tubular structures and mitotic counts according to the modified criteria of Bloom and Richardson.[17] Historical analysis was performed by surgically resected specimens. A score of 3-5, 6-7, and 8-9 were considered grade I, grade II, and grade III, respectively. Immunohistochemistry of ER, PR, and HER2 was obtained for malignant lumps as molecular markers.

Statistical analysis

Was done using Analyse-IT (Leeds UK) software. The data was assessed by test of normality, and the data corresponding to the normal distribution were expressed as x±s. The data of non-normal distribution were expressed as the median. Spearman correlation test was conducted to calculate the relationships between ADC values or DCE-MRI quantitative parameters and prognostic factors. P<0.05 was considered statistically significant. Diagnostic analysis was done for sensitivity, specificity, likelihood ratio for all imaging biomarkers and KSS and AMSS systems and AUC were obtained.

RESULTS

Study consisted of 175 patients with mean age of 47.2 (range 44.2-49.6) years. Mean size of nodules was 2.2 (range: 1.8-5.5) cm. All patient demographics and imaging markers are enlisted in (Table 3). There 32 (18.2%) patients with malignant nodules confirmed by histopathology out of which IDC were the commonest types. Correlation between the size of nodule and imaging markers done showed a significant inverse correlation between size of the lesion and the ADC value while a statistically significant positive correlation was seen with various imaging biomarkers and the size of lesion i.e. larger breast nodules showed increasingly lower ADC values and had higher TTE, IAUC60, Ktrans and Kep (Table 4). Similarly nodules which were ER and PR positive also showed lower ADC values along with increased values of TTE, IAUC 60, Ktrans and Kep, Her2 positive patients showed similar trends except that Ktrans values did not show statistically significant change. Ve on the other hand did not show any positive correlation with any of the parameters enlisted in (Table 3). Nuclear grades of the tumor also had a positive correlation with all the imaging markers except Ve. Diagnostic analysis for sensitivity and specificity done for all imaging biomarkers showed sensitivities of 87.4, 87.5, 88.6% 71.8 and 80% respectively for ADC, Ktrans, Kep, TTE, MS and IAUC60 while specificities were 94, 88.7, 88.7, 90 and 90% respectively (Table 5). KSS detected 20/32 cases of malignant nodules with a mean KSS score of 9.0. The sensitivity and specificity for KSS in the present study was 62.5% and 88.9% with overall accuracy of 72% with 12(37%) false negatives (Figure 2a-e).

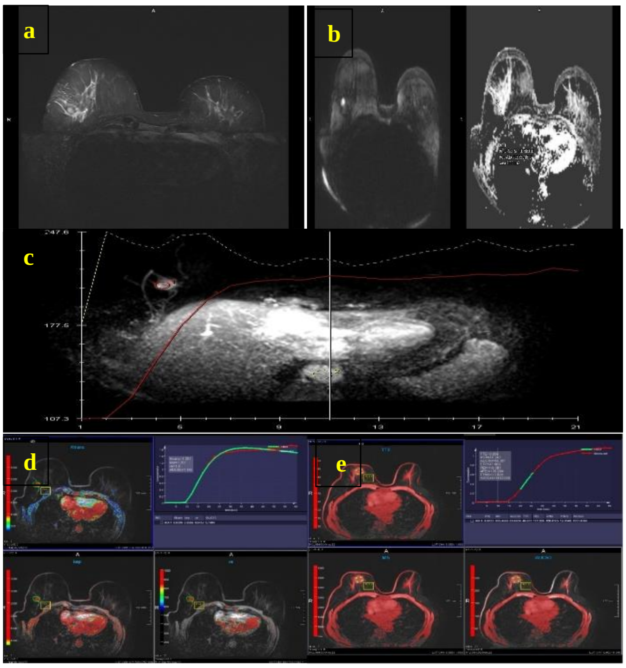


Figure 2: (a) T2W STIR axial image showing 1.5x1.5 cm smooth marginated nodule in right breast with absent edema with KSS score of 4-BIRAD III; (b) DW and ADC images showing hyperintense nodule with ADC of 0.73; (c) type II enhancing kinetic curve of lesion; (d, e) quantitative analysis showing TTE 8.6 sec, MS of 6.1, IAUC60 of 64 and Ktrans of 1.29 AMSS score of 8 BIRAD 5.

Table 3: Imaging and patient characteristics.

Characteristics	Mean	SD
Age	47.2	44.2-49.6
Size of lump	2.2	1.8-5.5 cm
<2 cm	7	
2-4 cm	37	
>4 cm	6	
IDC	18	
ILC	6	
ADH	2	
DH	3	
FCD	7	
Abscess	3	
Fibroadenoma	9	
Phylloides	1	
Mastitis	3	
HG (histolog. grade)		
<5	3	
6-7	13	
8-9	8	
ER	24	
PR	18	
Her 2	6	
Luminal A	20	
Luminal B	4	
BCL	4	
Her 2	2	

DH (ductal hyperplasia), ADH (atypical ductal hyperplasia), FCD (fibrocystic disease), ILC (intralobular carcinoma).

Table 4: Correlation between imaging parameters of DCE and diffusion.

Parameters	ADC	TTE	MS	IAUC60	Ktrans	KEP	Ve
Size	0.019	0.035	0.07	0.004	0.033	0.01	0.7
ER	0.002	0.01	0.001	0.01	0.0001	0.004	0.16
PR	0.0002	0.01	0.001	0.01	0.0001	0.001	0.16
HER2	0.02	0.04	0.05	0.06	0.09	0.08	0.11
HG grade	0.0001	0.001	0.0001	0.0002	0.0001	0.0001	0.12

Table 5: Diagnostic analysis of imaging parameters.

Percentage	ADC	TTE	MS	IAUC	Ktrans	Kep	KSS	AMSS
Sensitivity	87.4	75	71.8	80	87.5	88.6	62.5	90.6
Specificity	94.4	88.75	90	90	88.7	65.5	100	100
Positive LR*	15.7	6.7	7.8	8	7.8	2.5	#	#
Negative LR*	0.13.3	0.28	0.31	0.2	0.14	0.16	0.3	0.09
Accuracy	90	80	78.85	84	92	88	76	94

*LR: Likelihood ratio

9/12 false negative cases on KSS had absence of perilesional edema while 3 cases had smooth non spiculated margins. AMSS had a higher sensitivity and specificity of 96.5% and 90% respectively with 1 (3%) false positive of breast abscess and 2 (6%) false negative cases with central necrosis which showed reduced enhancement with false high ADC (Figures 3a-d, 4a-f). AMSS had an overall accuracy of 94%. The AUC's for KSS and AMSS were 0.93 and 0.97 while for individual biomarkers of IAUC60, Ktrans, ADC and MS AUC's were 0.92 (Figure 5).

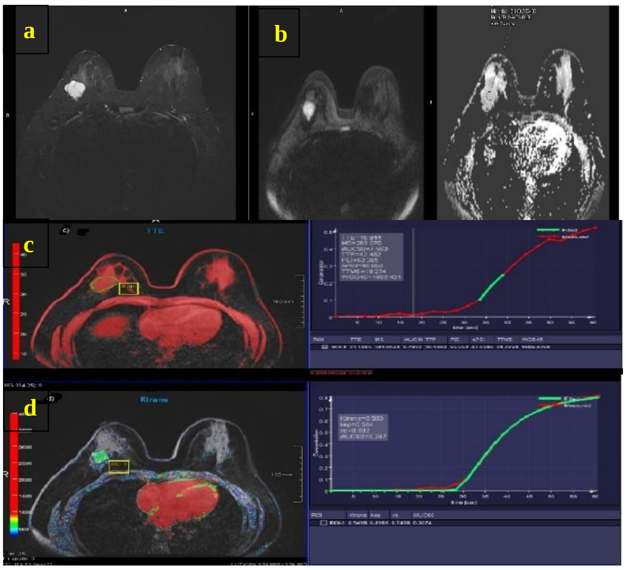


Figure 3: (a) T2W axial image showing hyperintense nodule with well-defined margins and absent surrounding edema with false negative score of KSS score of 2 BIRAD II; (b) DW axial image with hyperintense nodule (c) ADC image with nodule having ADC of 1.44; (d) post contrast analysis showing increased TTE 0f of 18.9 seconds and MS of 2.69 and low IAUC60 of 7.5 with false negative AMSS score of -1 BIRAD II.

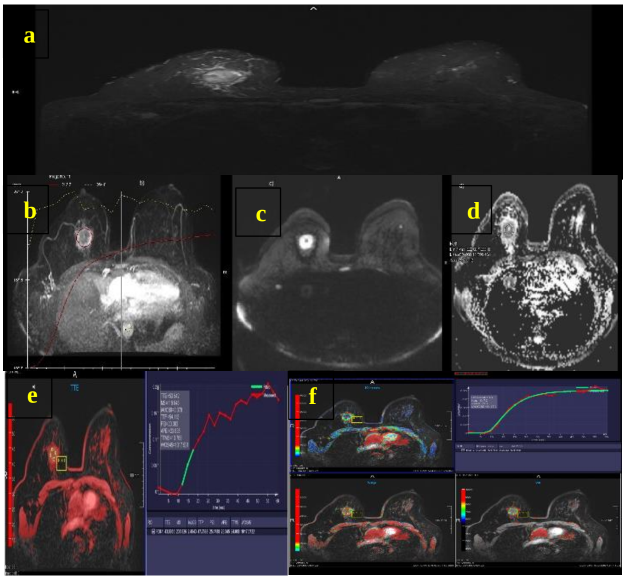
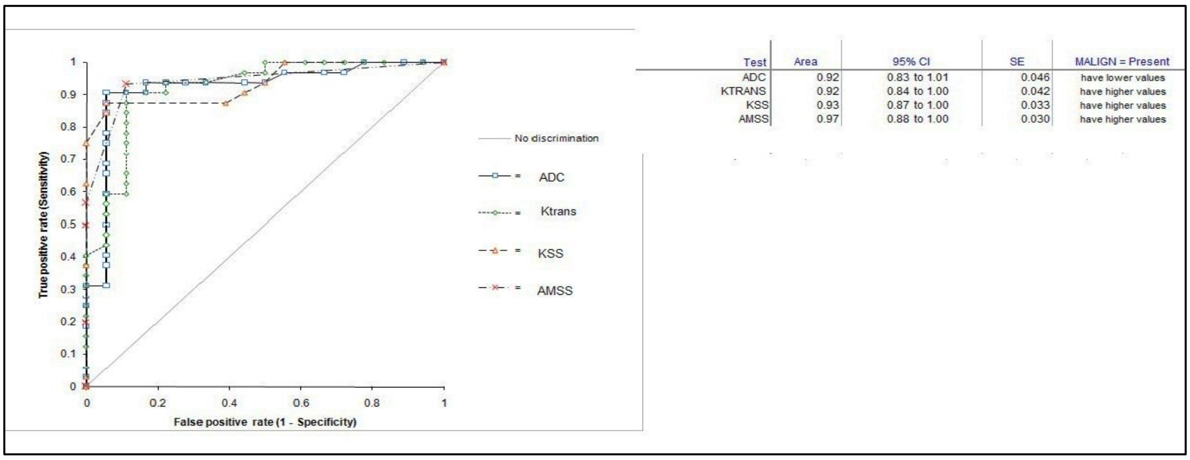


Figure 4: (a) T2WI axial image showing a nodular hyperintense lesion in right breast with KSS score of 11- BIRAD5; (b) post contrast type II kinetic curve; (c) diffusion image with hyperintense nodule; (d) ADC image showing ADC of 0.90; (e) qualitative enhancement curve parameters showing reduced AMSS scores; (f) False negative AMSS score of 2-BIRAD 2 lesion with low Ktrans in same patient.



Test	Area	95% CI	SE	MALIGN = Present
ADC	0.92	0.83 to 1.01	0.046	have lower values
KTRANS	0.92	0.84 to 1.00	0.042	have higher values
KSS	0.93	0.87 to 1.00	0.033	have higher values
AMSS	0.97	0.88 to 1.00	0.030	have higher values

Figure 5: Comparison of the AUCs for ADC, TTE, IAUC60 and K trans.

DISCUSSION

Our study showed that the use of Ultrafast MRI mammography along with the diffusion imaging had a high sensitivity and specificity of individual parameters of ADC, Ktrans, TTE and IAUC60. Even when used alone the accuracies were higher (84-90%) than the accuracy of KSS which was 72% in our study. Comparison of the individual parameters in our study showed the highest correlation of ADC and Ktrans with size and the grade of lesion. Similar results have been reported in the study by Koo et al in which Ktrans had the highest correlation with tumors >2 cm in size.[25] Unlike the current study which had an equally good correlation of ADC with the size of nodule Koo et al could not demonstrate a good correlation of ADC with the size of nodule.[25] Boulogianni et al also suggested that combining diffusion with quantitative perfusion improved the accuracy of the results as has been observed in the present study where the accuracy increased from 72% by Kaiser scoring to 94% by AMSS using the above parameters.[26] Our study showed a positive correlation of both Ktrans and ADC with histological grade of malignant lesions and lesions with higher grade had higher K trans and a lower ADC. Kim et al in their study of 50 patients of ductal carcinoma found no significant correlation of the above two parameters while Liu et al found a positive correlation of both the above parameters with the grade of lesion similar to findings of current study.[27,28] The probable reason for the above difference is likely due to the more heterogeneous nature of lesions in the present study and in the study by Liu et al whereas Kim et al studied only patients of intraductal carcinomas which may have depicted a uniform tumor biology.[27,28] Our study showed a good correlation of all the perfusion parameters with ER, PR status of lesions however since there were only two Triple negative patients we could not elucidate the differences in the correlation from the majority of ER, PR positive lesions. All the studies in literature so far have used the above technique to evaluate these biomarkers individually for both prognosis and detection. KSS and BI-RADS are the two lexicons which are used on traditional six minute dynamic contrast breast MRI protocols so far.[27,29] This is the first study which used AMSS as a new lexicon using ultrafast breast MRI and diffusion protocol and compared with KSS. Current study showed that with the use of AMSS the accuracy of detection of malignant nodules increased to 94% from 72% seen by KSS which was a desirable goal. KSS system showed higher false negatives i.e. 12 (37%) patients out of which 9 patients had no significant perilesional edema and all were less than 3 cm in size which lead to reduced scores by KSS of less than the cut off score of 7. There were only two false negative cases in AMSS which showed poor enhancement and were type A patients with central necrosis. The only false positive patient was that with breast abscess. The likely reason for improved results by AMSS were a) inherent high sensitivity and specificity of all individual parameters used b) AMSS used seven imaging parameters out of which five were based on quantitative analysis of perfusion and diffusion properties of the lesion and only two were morphologic parameters compared to five morphological parameters used by KSS.

There are few potential limitations of study i.e. we did not do Ki-67 labelling of the tumor cells and compared with imaging biomarkers, the authors were not blinded to prior investigation reports of patients which may have biased the observations on MRI and lastly the total number of malignant breast cancer patients in this cohort was a modest one.

CONCLUSION

The study concludes that AMSS with the use of diffusion and QCE MRI mammography using ultrafast protocol is more accurate than Kaiser scoring using conventional MRI mammography and improves the sensitivity and specificity of cancer detection. Ktrans and ADC imaging parameters when used individually also show a high sensitivity and have a good correlation with the size of lesion and nuclear grade and can be used as prognostic markers.

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Ethical approval: The study was approved by the Institutional Ethics Committee (IRB/5/22)

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