



Retrospective Study

Type 2 dynamic curves: A diagnostic dilemma

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Abstract

BACKGROUND

Magnetic resonance imaging (MRI) with multiparametric dynamic contrast plays a critical role in the assessment of breast lesions. Dynamic curves are a critical parameter in determining the benign or malignant nature of lesions. Dynamic curves of type 1 are known to represent benign masses, while dynamic curves of type 3 are known to identify malignant masses. Type 2 dynamic curves have a sensitivity of 42.6% and specificity of 75% for malignancy detection.

AIM

To investigate the pathological diagnosis of lesions with type 2 dynamic curves.

METHODS

We evaluated breast MRI examinations performed between 2020 and 2021 retrospectively and included lesions with type 2 dynamic curves. We included 38 lesions from 33 patients. The lesions were evaluated for their pathological diagnosis and morphological characteristics.

RESULTS

Twenty-six lesions were malignant, while twelve were benign. The most frequently encountered benign lesion (7/12, 58.3%) was sclerosing adenosis, while the most frequently encountered malignant diagnosis was invasive ductal cancer. The presence of a type 2 dynamic curve had a sensitivity of 40.2% and specificity of 73.4% for predicting malignancy. By combining type 2 curves and morphological features, the sensitivity and specificity were increased.

CONCLUSION

The high rates of malignancy detected histopathologically among patients with type 2 dynamic curves in our study are remarkable. Type 2 dynamic curves can be detected in benign breast masses, especially in sclerosing adenosis cases. Considering morphological features can increase the diagnostic accuracy in cases

with type 2 dynamic curves.

Key Words: Type 2; Dynamic curve; Benign; Malignant; Breast; Magnetic resonance imaging

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Core Tip: Dynamic contrast-enhanced magnetic resonance imaging (MRI) plays a critical role in the evaluation of breast lesions. The sensitivity and specificity of dynamic curves acquired using MRI are variable. While type 1 curves indicate more benign pathologies and type 3 curves indicate more malignant pathologies, there is a significant overlap in type 2 dynamic curves. We examined the histopathological outcomes of lesions with type 2 curves retrospectively. The histopathology results of lesions with type 2 curves were malignant at a rate of 68.4%. The presence of a type 2 dynamic curve had a sensitivity of 40.2% and specificity of 73.4% for predicting malignancy. By combining type 2 curves and morphological features, the area under the curve, sensitivity, and specificity were increased.

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INTRODUCTION

Breast magnetic resonance imaging (MRI) is a noninvasive technique that is highly sensitive for detecting breast cancer. Breast MRI can be used in situations where mammography is insufficient, in patients with dense breast structure, for preoperative planning in breast cancer, in multifocal and multicentric cases, for detecting contralateral malignancy, for evaluating response to neoadjuvant chemotherapy, and for postoperative control[1-5]. Breast MRI provides morphological information about lesions as well as kinetic features such as perfusion and enhancement of the lesion. Additionally, breast MR imaging is less affected by dense breast tissue than other imaging modalities, allowing for a higher sensitivity in detecting lesions[6-10].

The most frequently used MRI technique for evaluating breast cancer is dynamic contrast-enhanced magnetic resonance imaging (DCE-MR). A low molecular weight contrast agent (gadolinium) is injected intravenously for DCE-MR imaging. Gadolinium uptake and washout, and thus the detection of signal changes on T1-weighted images and the differentiation of cancerous from normal breast tissue, are the foundations of DCE-MR imaging of breast cancer[11].

The enhancement properties are determined by examining changes in signal intensity across multiple images acquired by pre- and post-contrast repeat MRI scans. The time-signal intensity curve, also known as the kinetic curve, can be classified into three types: Type 1 (persistence), type 2 (plateau), and type 3 (washout). Dynamic curve of type 1 (persistent) exhibits a persistent increase in signal intensity following contrast agent injection. Dynamic curve of type 2 (plateau) exhibits an initial slow or rapid increase followed by a flattening. Dynamic curve of type 3 (washout) involves an initial increase and subsequent decrease in signal intensity. Between benign and malignant lesions, there is considerable overlap in dynamic curves. Various noninvasive cancers may lack washout or plateau kinetics, but various benign entities, such as fibroadenomas, fibrocystic changes, scars, sclerosing adenosis, lobular carcinoma *in situ*, focal fibrosis, and atypical ductal hyperplasia, may show malignant curves[9,12,13]. Therefore, dynamic curves should not be evaluated alone without considering lesion morphology.

The aim of this study was to examine the histopathological outcomes of lesions with type 2 dynamic curves, in which there is a high degree of overlap between benign and malignant entities in the kinetic analysis performed using dynamic contrast MR imaging.

MATERIALS AND METHODS

Between January 2020 and January 2021, dynamic contrast enhanced breast MRI scans were evaluated retrospectively. In the research conducted from the hospital information system, there were 560 patients who underwent dynamic contrast MR examinations between January 2020 and January 2021. In the results of these patients, type 2 dynamic curve was detected in 48 lesions of 41 patients. Ten lesions in eight patients were excluded from the study due to a history of radiotherapy within the previous 6 mo, previous surgery or tru-cut biopsy, lack of histopathological results, and imaging artifacts. As a result,

38 lesions in 33 patients were included in the study.

Dynamic contrast enhanced breast MR images of the lesions included in the study were reviewed retrospectively with a consensus formed by two radiology specialists. The evaluators had more than 8 years of experience in interpreting breast MRI images. The patients' anamnesis, previous mammography, and ultrasonography examinations were re-examined using the hospital information system. The radiologists who performed the retrospective evaluation were blinded to the lesions' histopathological findings. Enhancement dynamic curves were calculated using the region of interest (ROI) method. Evaluators checked for type 2 dynamic curves by reconstructing dynamic curves from high temporal resolution dynamic images of the included lesions. Additionally, the evaluators classified the lesions according to their morphological characteristics using the American College of Radiology (ACR)'s Breast Imaging Reporting and Data System (BI-RADS) classification[14], which ranges from 0 to 5. Additionally, the histopathological findings of the patients were retrieved and recorded retrospectively from the hospital information system.

The data used for this study were collected anonymously and local ethics committee approval was obtained for this study (ethics committee number: 34336249-604.01.02-E.30236). This study adhered to the Declaration of Helsinki. Because the study was retrospective, informed consent was not obtained.

The same device and protocol were used for dynamic contrast-enhanced breast MRI examinations. One 1.5-T whole-body MRI scanner was used for breast MRI with dynamic contrast (Magnetom Avanto; Siemens Healthineers). The vendor-supplied receive-only 4-channel circularly polarized breast array coil was used. A standard protocol includes a T2-weighted rapid (fast or turbo) spin-echo (TR: 4000 ms; TE: 90 ms; ≤ 4 mm thickness) acquisition and 3D T1-weighted GRE (20/4.5; flip angle, 30°–45°; ≤ 3 mm thickness) acquisitions before and after the administration of gadolinium, with the usual dose of 0.1 mmol/kg injected as a bolus and followed by a 10–20-mL saline flush. For sagittal plane, an image matrix of 256 \times 192 can be used with zero-filled interpolation to 512 \times 512, a small field of view (16–18 cm), and chemical fat suppression. For bilateral axial imaging, the field of view is increased to approximately 30 cm, and high-resolution matrices (between 256 and 512) are used.

Statistical analysis

The sample size was calculated using G power analysis (alpha error: 0.05; power: 80%); the minimum number of patients was thus defined as 31. The Statistical Package for Social Sciences (SPSS) for Windows 20 software was used to analyze the data (IBM SPSS Inc., Chicago, IL, United States). The Kolmogorov-Smirnov test was used to determine whether the age data conformed to a normal distribution. Age is represented as the mean \pm SD and categorical variables as number (*n*) and percentage values (%). To define the diagnostic efficacy of type 2 dynamic curves alone and along with morphological characteristics, receiver operating characteristic analysis was used. The chi-square test was used to compare two groups of categorical variables. Statistical significance was defined as a two-tailed value of $P < 0.050$.

RESULTS

A total of 38 lesions in 33 patients were included in the study. The mean age of the patients was 53.7 \pm 10.1 years (range, 43–87 years).

The 38 lesions included in the study showed a dynamic contrast enhancement curve of type 2 (plateau) on their dynamic contrast imaging (Figures 1 and 2). The histopathological diagnoses of these lesions are shown in Table 1. As a result, 12 lesions were determined to be benign, while 26 lesions were determined to be malignant. While sclerosing adenosis was the most frequently encountered benign pathology, invasive ductal carcinoma was the most frequently encountered malignant pathology (Table 1).

The morphological evaluation results obtained using the ACR BI-RADS classification system for the lesions are given in Table 2. Histopathological examinations of eight lesions classified as BI-RADS 3 revealed that the vast majority (5 of them) were sclerosing adenosis. One lesion in the BI-RADS 3 category was histopathologically diagnosed as invasive ductal carcinoma. The remaining two lesions were benign. Sixteen of the 18 BI-RADS 4 lesions with type 2 dynamic curve were malignant, while two were benign. All 12 lesions classified as BI-RADS 5 were found to be malignant on histopathology (Table 2).

The presence of a type 2 dynamic curve had a sensitivity of 40.2% and specificity of 73.4% for predicting malignancy. By combining type 2 curves and morphological features, the area under the curve, sensitivity, and specificity were increased (Table 3, Figure 3).

DISCUSSION

In our study, we investigated the histopathological results of type 2 dynamic curves obtained from dynamic contrast magnetic resonance imaging, which plays a critical role in the evaluation of breast

Table 1 Histopathological results of lesions with type 2 curves

	Histopathological diagnosis	n (%)
Benign 12/38 (31.6%)	Sclerosing adenosis	7 (18.4)
	Fibroadenoma	3 (7.9)
	Intraductal papilloma	1 (2.6)
	Usual ductal hyperplasia	1 (2.6)
Malignant 26/38 (68.4%)	Ductal carcinoma in situ	7 (18.4)
	Invasive ductal carcinoma	15 (39.5)
	Invasive lobular carcinoma	4 (10.5)
Total		38 (100)

Table 2 Breast Imaging Reporting and Data System categories of lesions

BI-RADS category	n (%)
BI-RADS-0	0
BI-RADS-1	0
BI-RADS-2	0
BI-RADS-3	8 (21)
BI-RADS-4	18 (47.4)
BI-RADS-5	12 (31.6)
Total	38 (100)

BI-RADS: Breast Imaging Reporting and Data System.

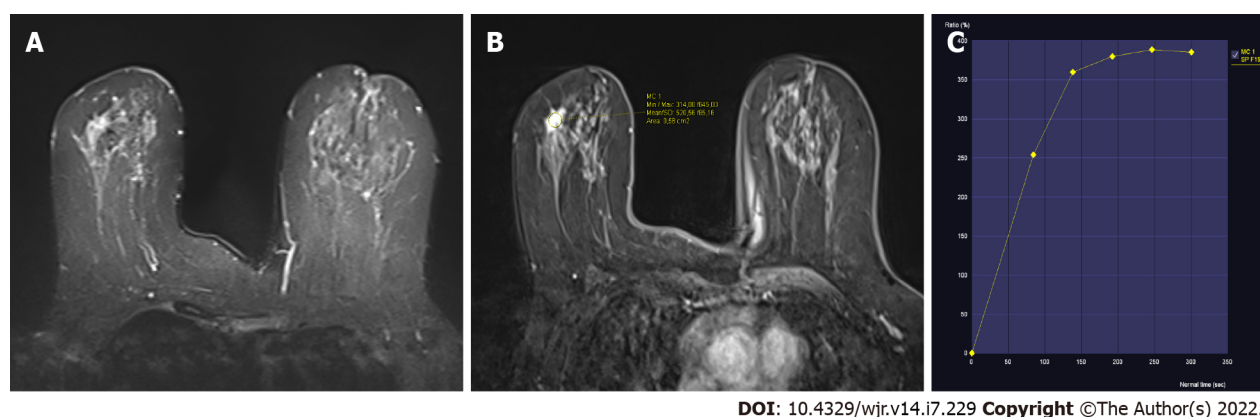
Table 3 Sensitivity and specificity values obtained by combining type 2 curves and morphological features for predicting malignancy

	Sensitivity	Specificity
Type 2 dynamic curve	40.2	73.4
Type 2 dynamic curve + BI-RADS 3 category	41.9	75.8
Type 2 dynamic curve + BI-RADS 4 category	95.3	97.7
Type 2 dynamic curve + BI-RADS 5 category	100	100

BI-RADS: Breast Imaging Reporting and Data System.

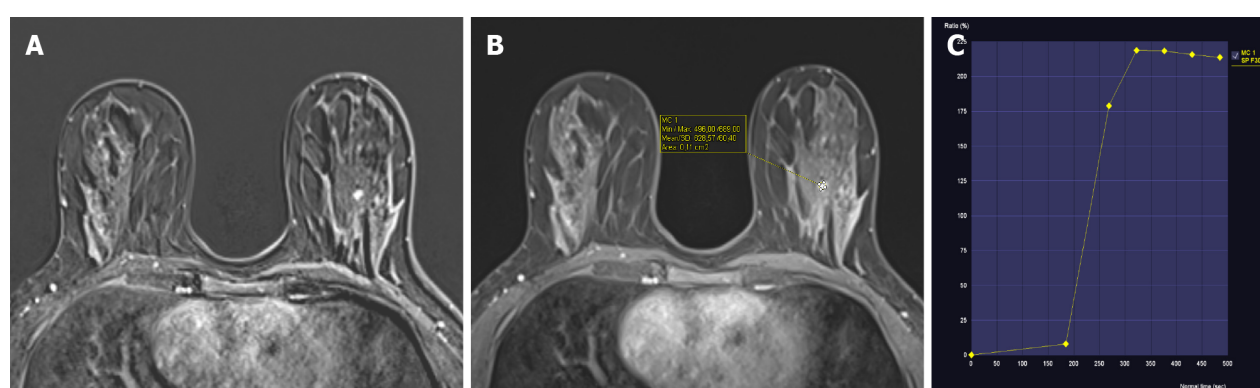
lesions. We found that the type 2 dynamic curve had a sensitivity of 40.2% and specificity of 73.4% in predicting malignancy. Additionally, we found that combining type 2 dynamic curve with morphological findings increased the sensitivity and specificity.

The type 1 (persistent) dynamic curve obtained from breast MRI with dynamic contrast indicates a higher rate of benign pathologies, while the type 3 (washout) dynamic curve indicates a higher rate of malignant pathologies according to the literature[9,11]. However, it has been reported in the literature that time-signal intensity curves have a high sensitivity but relatively low specificity for breast cancer diagnosis[15-20]. It is critical to keep in mind when evaluating these kinetic images that there is considerable overlap between benign and malignant lesions[9,12,13,21]. Schnall *et al*[20] reported in a multicenter study of evaluating 995 breast lesions that a lesion with type 3 curve has a five times higher relative risk of cancer than a lesion with type 1 curve. According to the same study, 76% of lesions with type 3 curves were associated with malignancy. In other studies in the literature, a significant correlation was reported between malignancy and type 3 washout dynamic curve[15,16,22,23]. Durhan *et al*[24] in their study on young women under 40 years of age, stated that 25 of 27 malignant lesions had type 2 and type 3 dynamic curves. In contrary to the majority in the literature, Williams *et al*[25] found no significant difference between dynamic curves and benign and malignant lesions in their study with



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Figure 1 A 63-year-old patient. A: Hyperintense lesion on T2 weighted image (WI) in the right breast; B: The lesion is enhanced on post-contrast T1WI; C: The dynamic curve of the lesion is type 2. Pathological diagnosis is invasive ductal carcinoma.



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Figure 2 A 37-year-old patient. A: Hyperintense lesion on T2 weighted image (WI) in the right breast; B: The lesion is enhanced on post-contrast T1WI; C: The dynamic curve of the lesion is type 2. Pathological diagnosis is fibroadenoma.

41 malignant and 113 benign lesions. They stated that the reason for lack of significant difference may be due to the lower temporal resolution in their study and the different MR imaging protocols compared to other studies. Macura *et al*[26] stated in support of this in the literature that due to the low temporal resolution, washout may not be visible in the signal intensity-time curve because the first contrast images are acquired too late after peak formation. When these data in the literature are reviewed, it is understood that the results of dynamic curves, especially type 2 dynamic curves, may be contradictory. For this reason, we conducted a study investigating the histopathological results of type 2 curves. Our findings show that type 2 dynamic curve can be an important finding in demonstrating malignancy and supports other data in the literature in contrary to the study of Williams *et al*[25].

In our study, we evaluated lesions with a type 2 (plateau) dynamic curve and discovered that approximately 68% of these lesions were malignant. According to the literature, Kuhl *et al*[15] in their study including 101 malignant and 165 benign cases, found that the type 1 dynamic curve was observed in 83% of benign lesions and 9% of malignant lesions, type 2 dynamic curve was observed in 13% of benign lesions and 34% of malignant lesions, and type 3 dynamic curve was observed in 6% of benign lesions and 57% of malignant lesions. Bluemke *et al*[16] in their study including 404 malignant and 366 benign cases, found that the type 3 dynamic curve had a 20.5% sensitivity and 90.4% specificity, type 2 dynamic curve had a 42.6% sensitivity and 75% specificity, and type 1 dynamic curve had a 52.2% sensitivity and 71% specificity for detecting benignity. According to these results[15,16], our study's malignancy rate was higher than those reported in the literature, but the sensitivity and specificity rates were similar. As supported by our findings and the literature, the type 2 dynamic curve indicates an increased risk of malignant lesions. These results led us to believe that in the presence of a type 2 dynamic curve, we should exercise caution in terms of suspicion of malignancy.

Numerous studies have demonstrated that combining use of both morphological and enhancement kinetics improves the sensitivity and specificity of MRI[27-29]. Lee *et al*[21] stated in their study that as a reasonable strategy, the morphological features of the lesion should be evaluated before evaluating the enhancement kinetics, and in case of suspicious morphological features, further evaluation including histopathological diagnosis should be made. They also stated that if the lesion is morphologically

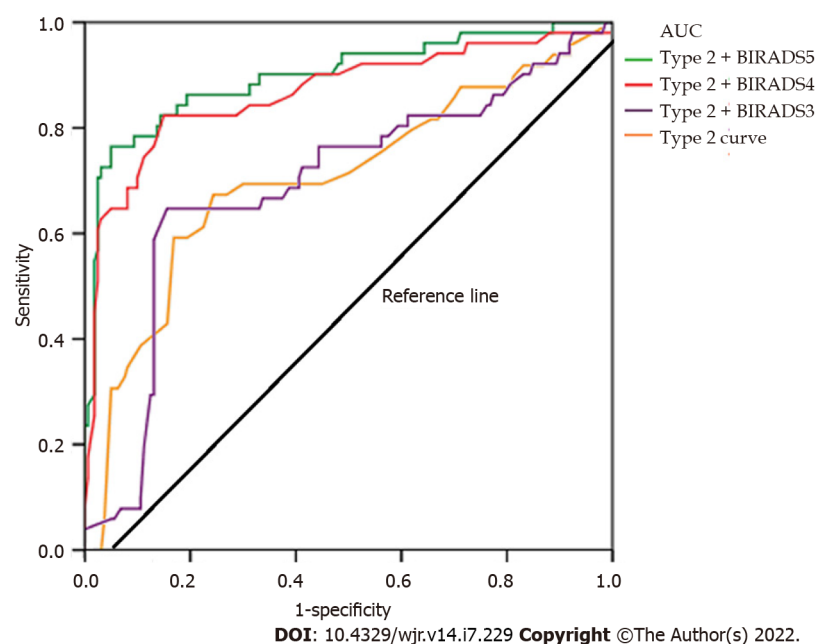


Figure 3 Receiver operating characteristic analysis graph by combining type 2 curves and morphological features for predicting malignancy. AUC: Area under the curve.

benign or indeterminate, evaluation of the enhancement kinetics can help differentiate lesions that may require biopsy. Additionally, it should be emphasized at this point that the MR examination should be correlated with mammographic and sonographic findings to increase the accuracy of the result. According to these data, we also examined the sensitivity and specificity of type 2 dynamic curves for detecting malignancy both alone and in combination with the BI-RADS classification. Accordingly, while the sensitivity and specificity values of the type 2 dynamic curve increased significantly when combined with BI-RADS 4 and 5, no significant increase was observed when combined with BI-RADS 3. According to the ACR, radiological follow-up is recommended instead of histopathological correlation in BI-RADS 3 lesions[14]. In our study, histopathological correlation was performed on eight lesions with type 2 dynamic curves in BI-RADS 3 lesions, and one of them was found to be malignant. At this point, although there is a possibility of unnecessary histopathological correlation to BI-RADS 3 lesions, the fact that even one malignancy was detected in our results suggests that histopathological correlation may provide additional benefit in the presence of type 2 dynamic curve in BI-RADS 3 lesions. There is a need for studies examining the type 2 dynamic curve and BI-RADS 3 classification in a larger patient population.

There are some limitations to our study. The most significant limitations are the study's retrospective design and small patient population. Additionally, when the ROI method is used to create a dynamic curve, inter-rater variability may occur. In our study, two radiologists evaluated the images retrospectively with a consensus and there was no assessment of interobserver variability. Finally, the study was designed to assess only the type 2 dynamic curve in contrast-enhanced dynamic series; lesions with type 1 or type 3 dynamic curves were not included and early phase (initial) enhancement was not assessed.

CONCLUSION

In conclusion, the high rates of malignancy detected histopathologically among patients with type 2 curves in our study are remarkable. However, it is possible to detect type 2 dynamic curves in benign lesions as well. Compared to the evaluation made with only the type 2 dynamic curve, the combined evaluation with the BI-RADS categories increases the sensitivity and specificity of the type 2 dynamic curve.

ARTICLE HIGHLIGHTS

Research background

Dynamic contrast-enhanced magnetic resonance imaging (MRI) is the most frequently used MRI

technique for evaluating breast cancer. Changes in signal intensity across multiple images acquired by pre- and post-contrast repeat MRI scans are used to determine the enhancement patterns. The time-signal intensity curve, also known as the kinetic curve, can be classified into three types: Type 1 (persistence), type 2 (plateau), and type 3 (washout). A higher rate of benign pathologies is indicated by the type 1 dynamic curve, while a higher rate of malignant pathologies is indicated by the type 3 dynamic curve. However, there is a dilemma with the type 2 curve. The aim of this study was to investigate the histopathological outcomes of lesions with type 2 dynamic curves, which have much overlap in the kinetic analysis between benign and malignant entities.

Research motivation

There have been several studies on type 3 and type 1 dynamic curves, but studies on type 2 dynamic curves are not sufficient. More research on type 2 dynamic curves, which have much overlap in kinetic analysis between benign and malignant entities, is needed.

Research objectives

The aim of this study was to examine the histopathological outcomes of lesions with type 2 dynamic curves, in which there is a high degree of overlap between benign and malignant entities in the kinetic analysis performed using dynamic contrast MRI.

Research methods

Two experienced radiologists retrospectively re-evaluated lesions with type 2 dynamic curves. The included lesions were re-examined for type 2 dynamic curves by the evaluators. Additionally, the evaluators classified the lesions according to their morphological characteristics using the American College of Radiology's Breast Imaging Reporting and Data System classification. The histopathological findings of the patients were retrieved and recorded retrospectively from the hospital information system. Receiver operating characteristic analysis was done to determine the diagnostic efficacy of type 2 dynamic curves alone and in combination with morphological characteristics.

Research results

Thirty-eight lesions in 33 patients were included in the study. As a result, 12 lesions were determined to be benign, while 26 lesions were determined to be malignant. While sclerosing adenosis was the most frequently encountered benign pathology, invasive ductal carcinoma was the most frequently encountered malignant pathology. The presence of a type 2 dynamic curve had a sensitivity of 40.2% and specificity of 73.4% for predicting malignancy. By combining type 2 curves and morphological features, the area under the curve, sensitivity, and specificity were increased.

Research conclusions

In our investigation, the significant rates of malignancy discovered histopathologically among patients with type 2 curves are remarkable. In the presence of a type 2 dynamic curve, we should exercise caution in terms of suspicion of malignancy.

Research perspectives

Studies with larger patient populations focusing on the histopathological results of lesions with type 2 dynamic curves are needed.

FOOTNOTES

Author contributions: Karavas E participated in design and oversight of the study, and drafted the manuscript; Ece B participated in design of the study and drafted the manuscript; and Aydin S participated in design of the study, drafted the manuscript, and performed statistical analysis.

Institutional review board statement: The study was reviewed and approved by the Erzincan University Institutional Review Board (ethics committee number: 34336249-604.01.02-E.30236).

Conflict-of-interest statement: All authors report no relevant conflicts of interest for this article.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at bunyaminece@hotmail.com. Informed consent was not obtained since the presented data are anonymized and risk of identification is low.

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