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Selection of X-ray *versus* magnetic resonance imaging as a first-line imaging modality for diagnosing axial spondyloarthritis

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Abstract

Introduction: To determine the cut-off values for age and symptom duration that could be used in selecting preferential first-line imaging modality of sacroiliac joints [X-ray *versus* magnetic resonance imaging (MRI)] for diagnosing axial spondyloarthritis (axSpA).

Methods: This retrospective cohort study included 388 patients newly diagnosed with axSpA. Patients were classified into radiographic axSpA (n = 322) and non-radiographic axSpA (n = 66) groups according to the fulfilment of modified New York criteria by X-ray. Patient characteristics of the two groups were compared. Receiver operating characteristic (ROC) curve analysis was conducted to determine the cut-off values for age and symptom duration that best distinguish non-radiographic axSpA from radiographic axSpA.

Results: Compared with patients with radiographic axSpA, those with non-radiographic axSpA were younger at diagnosis (35.7 ± 11.3 years *versus* 26.8 ± 7.8 years, $p < 0.001$) and had shorter symptom duration [5.1 (2.1–12.0) years *versus* 1.0 (0.5–3.2) years, $p < 0.001$]. ROC analysis showed that age > 33.5 years at diagnosis [area under the curve (AUC): 0.734] and symptom duration > 4.1 years (AUC: 0.787) were the cut-off values that best discriminate radiographic axSpA from non-radiographic axSpA.

Conclusion: The best cut-off values for age and symptom duration for predicting radiographic sacroiliitis are 33.5 and 4.1 years, respectively. It is reasonable to use X-ray as a first-line imaging modality in patients older than 33.5 years with a symptom duration longer than 4.1 years, and use MRI as a first-line imaging in patients younger than 33.5 years with a symptom duration less than 4.1 years.

Keywords: axial spondyloarthritis, cut-off value, magnetic resonance imaging, X-ray

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Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease characterized by sacroiliitis, spinal inflammation and bony ankylosis.[1] AxSpA encompasses both patients without structural damage in sacroiliac joints (non-radiographic axSpA) and patients with structural damage in sacroiliac joints (radiographic axSpA).[1,2] Imaging of sacroiliac joints is an important step in the diagnostic workup of axSpA.[3,4]

X-ray of sacroiliac joints is recommended as a first-line diagnostic imaging modality in patients with clinically suspected axSpA.[5] The presence of sacroiliitis grade ⩾ II bilaterally or sacroiliitis grade ⩾ III unilaterally, which is the radiologic criterion of the modified New York criteria,[6] on X-ray is needed to classify a patient as having radiographic axSpA.[7] If these features are not observed on X-ray, and axSpA is still clinically suspected, magnetic resonance imaging (MRI) of

sacroiliac joints is recommended to secure the diagnosis of axSpA.[5] Using MRI, both inflammatory lesions, such as bone marrow oedema and osteitis, and structural lesions, such as bone erosion, sclerosis, ankylosis and fat infiltration, can be detected.[8–10] MRI is advantageous over X-ray in that it can detect active inflammatory lesions before structural damage can be captured by X-ray, enabling earlier diagnosis.[11] A recent study has reported that the accuracy of MRI is superior to that of X-ray in diagnosing axSpA.[12] Given its advantages over X-ray, using MRI as a first-line imaging modality instead of X-ray could be useful.[12] However, MRI is expensive and takes longer time to perform compared with X-ray, and it may not always be readily available. It would be desirable to use MRI as a first-line imaging modality in carefully selected patients who are not likely to show definite sacroiliitis on X-rays. Indeed, MRI is recommended as an alternative first-line imaging modality in certain patients, such as young patients and patients with short symptom duration.[5] However, the cut-off values for age and symptom duration to select patients who may benefit from using MRI as a first-line imaging are unclear. In this study, we aimed to determine the cut-off values for age and symptom duration that could be used to select patients who may benefit from using MRI as a first-line imaging.

Patients and methods

Patients

Patients who were newly diagnosed with axSpA at a tertiary referral hospital in Seoul, South Korea, between January 2010 and December 2020 were retrospectively reviewed for inclusion. The inclusion criteria were as follows: (1) patients who fulfilled the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axSpA[2] and (2) patients who underwent X-ray as a first-line modality for sacroiliac joint imaging, followed by MRI if the radiographic features of X-rays did not fulfil the modified New York criteria.[6] The decision to order an X-ray or MRI as a first-line imaging was at the discretion of physicians. For patients who underwent X-ray as a first-line imaging modality and did not have definite radiographic sacroiliitis (i.e. did not fulfil the modified New York criteria[6]), an MRI was ordered as a second-line imaging modality. For patients who underwent X-ray as a first-line imaging modality and had definite radiographic sacroiliitis, additional MRI was not ordered. Patients lacking documentation on the onset of symptoms were excluded because symptom duration could not be calculated. Patients who underwent MRI as a first-line modality for sacroiliac joint imaging and did not undergo X-ray were also excluded. These patients were excluded because it was not possible to judge whether these patients could have been diagnosed with axSpA using X-ray alone. Data on the following variables at diagnosis were reviewed: age, age at the onset of symptom, symptom (back pain) duration, sex, HLA-B27 positivity, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), results of the X-ray and MRI of sacroiliac joints, and presence of syndesmophyte.

This study was approved by the Institutional Review Board (IRB) of Gangnam Severance Hospital (IRB No. 3-2021-0328). Owing to the retrospective nature of this study, the requirement for informed consent was waived. All patient details were de-identified. The reporting of this study conforms to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.[13]

Image assessment

The X-rays and MRIs of sacroiliac joints were interpreted by expert musculoskeletal radiologists or rheumatologists at the time of imaging studies. Based on the results of X-ray, patients were classified into two groups. Patients who fulfilled the radiologic criterion of the modified New York criteria[6] were classified as patients with radiographic axSpA, and patients who did not fulfil the radiologic criterion of the modified New York criteria[6] but fulfilled the ASAS classification criteria for axSpA[2] were classified as patients with non-radiographic axSpA.

Statistical analysis

Normally and non-normally distributed continuous variables are expressed as mean ± standard deviation and median (interquartile range), respectively. Categorical variables are expressed as number (%). Student's t-test or Mann–Whitney's U-test was performed to compare continuous variables between the two groups, and chi-square test or Fisher's exact test was used to compare categorical variables between the two groups. Receiver operating characteristic (ROC) curve analysis was conducted to determine the cut-off values for the age and symptom duration that best predict radiographic sacroiliitis. The best cut-off values were the values at which the

Youden index was maximum.[14] The predictive accuracy of each cut-off value was assessed by estimating the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under the curve (AUC). We also evaluated the predictive accuracy of two composite parameters: (1) combination of age > cut-off value OR symptom duration > cut-off value and (2) combination of age > cut-off value AND symptom duration > cut-off value. A *p*-value of less than 0.05 was considered statistically significant. All analyses were performed using SPSS software (version 25.0; IBM Corporation, Armonk, NY, USA), and all graphs were generated using GraphPad Prism (version 7.0; GraphPad Software Inc., San Diego, CA, USA).

Sensitivity analysis

Considering that X-rays have a low specificity and may result in a considerable number of false positive detections, we conducted a sensitivity analysis using an increased threshold of X-ray positivity. Instead of using radiologic criterion of the modified New York criteria,[6] we used sacroiliitis > grade II unilaterally as the positive criteria for X-ray, and assessed the predictive performance of the cut-off values for the age and symptom duration.

Results

Patient characteristics

A total of 466 patients were newly diagnosed with axSpA between January 2010 and December 2020. Of which, 42 patients who lack documentation of the onset of symptoms and 36 patients who underwent MRI as a first-line modality for sacroiliac joint imaging were excluded. The remaining 388 patients with axSpA were included for analysis. The mean age and median symptom duration of the study population were 34.2 ± 11.3 years and 5.0 (2.0–10.1) years, respectively. The number of patients diagnosed with radiographic axSpA and non-radiographic axSpA was 322 (83.0%) and 66 (17.0%), respectively. Detailed clinical characteristics of the patients at the time of diagnosis are summarized in Table 1.

Comparison between patients with radiographic axSpA and non-radiographic axSpA

Compared with patients with radiographic axSpA, patients with non-radiographic axSpA were younger at diagnosis (35.7 ± 11.3 years *versus* 26.8 ± 7.8 years, $p < 0.001$) and at the onset of symptom (26.9 ± 8.9 years *versus* 24.3 ± 7.5 years, $p = 0.013$) and had shorter symptom duration [5.1 (2.1–12.0) years *versus* 1.0 (0.5–3.2) years, $p < 0.001$], lower ESR [25.5 (10.8–46.0) mm/h *versus* 12.5 (6.0–37.3) mm/h, $p = 0.004$], lower CRP [5.5 (1.3–17.6) mg/L *versus* 2.7 (0.8–12.5) mg/L, $p = 0.035$] and syndesmophyte less commonly (30.1% *versus* 3.0%, $p < 0.001$) (Table 2).

Cut-off values for age and symptom duration to predict radiographic sacroiliitis

The cut-off values for age and symptom duration that best predicted radiographic sacroiliitis were determined by ROC analyses. Age > 33.5 years at diagnosis [AUC: 0.734, 95% confidence interval (CI): 0.676–0.792] [Figure 1(a)] and symptom duration > 4.1 years (AUC: 0.787, 95% CI: 0.730–0.844) [Figure 1(b)] best predicted radiographic sacroiliitis.

The predictive performances of the parameters using the cut-off values determined are reported in Table 3. Age > 33.5 years as a predictor of radiographic sacroiliitis had a sensitivity, specificity, PPV and NPV of 0.57 (95% CI: 0.51–0.62), 0.83 (95% CI: 0.72–0.91), 0.94 (95% CI: 0.91–0.97) and 0.28 (95% CI: 0.25–0.32), respectively. Symptom duration > 4.1 years as a predictor of radiographic sacroiliitis had a sensitivity, specificity, PPV and NPV of 0.61 (95% CI: 0.56–0.67), 0.83 (95% CI: 0.72–0.91), 0.94 (95% CI: 0.91–0.97) and 0.31 (95% CI: 0.27–0.34), respectively. The combination of age > 33.5 years OR symptom duration > 4.1 years as a composite parameter had the highest sensitivity (0.76, 95% CI: 0.71–0.81), and the combination of age > 33.5 years AND symptom duration > 4.1 years as another composite parameter had the highest specificity (0.97, 95% CI: 0.89–1.00).

Sensitivity analysis

When using sacroiliitis > grade II unilaterally as the positive criteria for X-ray, the predictive performances of the cut-off values for age and symptom duration for predicting radiographic sacroiliitis were as follows. Age > 33.5 years had a sensitivity, specificity, PPV and NPV of 0.58 (95% CI: 0.52–0.65), 0.76 (95% CI: 0.68–0.83), 0.82 (95% CI: 0.77–0.87) and 0.49 (95% CI: 0.44–0.53), respectively. Symptom duration > 4.1 years had a sensitivity, specificity, PPV and

Table 1. Characteristics of the patients.

	MRI as first-line imaging (N = 36)	Study population (N = 388)	*p*-value
Age, years, mean (±SD)	22.7 (±4.9)	34.2 (±11.3)	< 0.001
Age at the onset of symptom, years, mean (±SD)	20.2 (±5.6)	26.5 (±8.7)	< 0.001
Symptom duration, years, median (IQR)	1.8 (0.6–4.0)	5.0 (2.0–10.1)	< 0.001
Male sex, n (%)	29 (80.6)	293 (75.5)	0.499
HLA-B27 positive[a], n (%)	30 (83.3)	307 (83.2)	0.983
ESR, mm/h, median (IQR)	18.0 (5.3–36.8)	22.5 (9.0–44.0)	0.223
Elevated ESR, n (%)	17 (47.2)	229 (59.0)	0.170
CRP, mg/L, median (IQR)	5.3 (1.8–16.5)	5.1 (1.1–17.0)	0.959
Elevated CRP, n (%)	15 (41.7)	179 (46.1)	0.607
Radiographic axSpA[b], n (%)	N/A	322 (83.0)	N/A
Sacroiliitis grade II bilaterally, n (%)	N/A	73 (22.7)	N/A
Sacroiliitis > grade II unilaterally, n (%)	N/A	249 (77.3)	N/A
Non-radiographic axSpA[c], n (%)	N/A	66 (17.0)	N/A
Sacroiliitis grade 0 bilaterally, n (%)	N/A	23 (34.8)	N/A
Sacroiliitis > grade 0 unilaterally, n (%)	N/A	43 (65.2)	N/A
Presence of syndesmophyte, n (%)	2 (5.6)	99 (25.5)	0.007

AxSpA, axial spondyloarthritis; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HLA, human leukocyte antigen; IQR, interquartile range; MRI, magnetic resonance imaging; SD, standard deviation.
[a]Patients (n = 19) with missing data were excluded.
[b]Patients who fulfilled the radiologic criterion of the 1984 modified New York criteria were classified as patients with radiographic axSpA.
[c]Patients who did not fulfil the radiologic criterion of the 1984 modified New York criteria were classified as patients with non-radiographic axSpA.

NPV of 0.69 (95% CI: 0.63–0.74), 0.75 (95% CI: 0.67–0.82), 0.84 (95% CI: 0.80–0.88) and 0.56 (95% CI: 0.50–0.61), respectively. The combination of age > 33.5 years OR symptom duration > 4.1 years as a composite parameter had the highest sensitivity (0.79, 95% CI: 0.74–0.84), and the combination of age > 33.5 years AND symptom duration > 4.1 years as another composite parameter had the highest specificity (0.93, 95% CI: 0.88–0.97) (Table 4).

Discussion

In this study, we determined the best cut-off values for age and symptom duration to predict radiographic sacroiliitis in patients with newly diagnosed axSpA. Age > 33.5 years at diagnosis and symptom duration > 4.1 years best predicted radiographic sacroiliitis. The composite parameters using a combination of these two parameters yielded higher sensitivity or specificity according to the method of combination.

Imaging is crucial for the diagnosis of axSpA as it is the only method that can objectively detect inflammatory changes in the axial skeleton.[4] In some patients, sacroiliitis can be detected by X-ray as well as by MRI, whereas in other patients, sacroiliitis can be detected only by MRI. In other words, X-ray may be sufficient to diagnose axSpA in some patients (radiographic axSpA), whereas in others, X-ray alone is insufficient, and MRI is

Table 2. Comparison between patients with radiographic axSpA and patients with non-radiographic axSpA.

	Radiographic axSpA (N = 322)	Non-radiographic axSpA (N = 66)	*p*-value
Age, years, mean (±SD)	35.7 (±11.3)	26.8 (±7.8)	< 0.001
Age at the onset of symptom, years, mean (±SD)	26.9 (±8.9)	24.3 (±7.5)	0.013
Symptom duration, years, median (IQR)	5.1 (2.1–12.0)	1.0 (0.5–3.2)	< 0.001
Male sex, n (%)	249 (77.3)	44 (66.7)	0.066
HLA-B27 positive[a], n (%)	266 (84.2)	51 (78.5)	0.261
ESR, mm/h, median (IQR)	25.5 (10.8–46.0)	12.5 (6.0–37.3)	0.004
Elevated ESR, n (%)	203 (63.0)	26 (39.4)	< 0.001
CRP, mg/L, median (IQR)	5.5 (1.3–17.6)	2.7 (0.8–12.5)	0.035
Elevated CRP, n (%)	158 (49.1)	21 (31.8)	0.010
Presence of syndesmophyte, n (%)	97 (30.1)	2 (3.0)	< 0.001

AxSpA, axial spondyloarthritis; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HLA, human leukocyte antigen; IQR, interquartile range; SD, standard deviation.
[a]Patients (n = 19) with missing data were excluded.

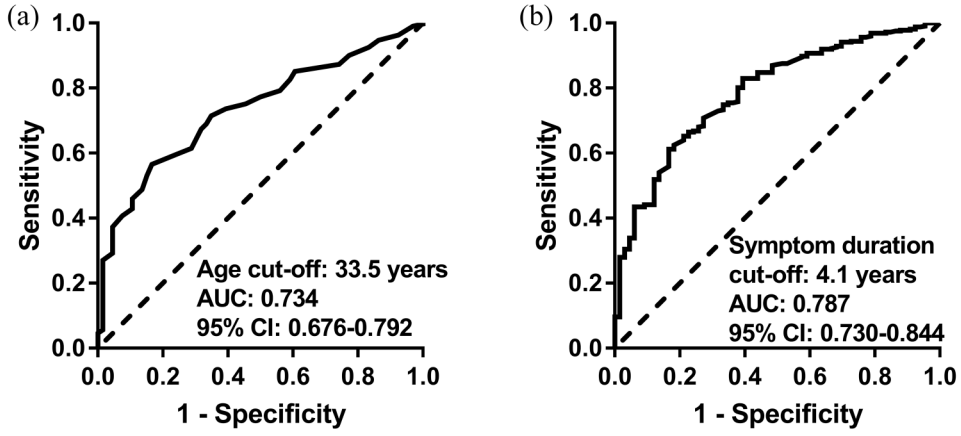

Figure 1. Receiver operating characteristic curve analysis of (a) age and (b) symptom duration to determine the best cut-off values for predicting radiographic sacroiliitis.
AUC, area under the curve; AxSpA, axial spondyloarthritis; CI, confidence interval.

necessary for the diagnosis of axSpA (non-radiographic axSpA). Understanding the differences in clinical characteristics of patients with radiographic axSpA and non-radiographic axSpA may help in preferential selection of imaging modality in individual patients. Previous study has reported that the shorter the duration of back pain, the higher the ratio of patients with non-radiographic axSpA to those with radiographic axSpA.[15] Moreover, a pooled analysis of 60 studies showed that patients with non-radiographic axSpA were younger and had shorter symptom duration than those with radiographic axSpA.[16] Similar findings were also observed in our study population. These differences in patient characteristics support the use of MRI, instead of X-ray, as a first-line

Table 3. Performance of age and symptom duration for predicting radiographic sacroiliitis.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Age > 33.5 years	0.57 (0.51–0.62)	0.83 (0.72–0.91)	0.94 (0.91–0.97)	0.28 (0.25–0.32)
Symptom duration > 4.1 years	0.61 (0.56–0.67)	0.83 (0.72–0.91)	0.94 (0.91–0.97)	0.31 (0.27–0.34)
Age > 33.5 years OR symptom duration > 4.1 years	0.76 (0.71–0.81)	0.70 (0.57–0.80)	0.92 (0.89–0.95)	0.37 (0.32–0.43)
Age > 33.5 years AND symptom duration > 4.1 years	0.42 (0.36–0.47)	0.97 (0.89–1.00)	0.99 (0.94–1.00)	0.25 (0.24–0.27)

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

Table 4. Sensitivity analysis: performance of age and symptom duration for predicting sacroiliitis > grade II unilaterally.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Age > 33.5 years	0.58 (0.52–0.65)	0.76 (0.68–0.83)	0.82 (0.77–0.87)	0.49 (0.44–0.53)
Symptom duration > 4.1 years	0.69 (0.63–0.74)	0.75 (0.67–0.82)	0.84 (0.80–0.88)	0.56 (0.50–0.61)
Age > 33.5 years OR symptom duration > 4.1 years	0.79 (0.74–0.84)	0.58 (0.49–0.66)	0.78 (0.75–0.82)	0.59 (0.52–0.66)
Age > 33.5 years AND symptom duration > 4.1 years	0.48 (0.42–0.54)	0.93 (0.88–0.97)	0.93 (0.88–0.96)	0.48 (0.45–0.51)

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

imaging modality in young patients and in patients with short symptom duration. This is in line with the guideline that recommends using MRI as an alternative first-line imaging modality in young patients and in those with short symptom duration.[5] Our finding is noteworthy in that it provides specific cut-off values for age and symptom duration, which have not been determined previously.

In accordance with a previous meta-analysis,[16] patients with non-radiographic axSpA had lower ESR, lower CRP, and less syndesmophyte than did patients with radiographic axSpA. Therefore, these parameters could also be used for selecting the first-line modality for sacroiliac joint imaging. However, laboratory test or X-ray of the spine must be performed to determine the values of these parameters. Therefore, data on these parameters are not available at the initial visit. This limits the use of these parameters for selecting the first-line method for sacroiliac joint imaging at the initial visit. Therefore, these parameters were not pursued for investigating cut-off values.

Age > 33.5 years (sensitivity 57%, specificity 83%, PPV 94% and NPV 28%) and symptom duration > 4.1 years (sensitivity 61%, specificity 83%, PPV 94% and NPV 31%) had a similar accuracy in predicting radiographic sacroiliitis when used as individual parameters. Notably, the specificity for predicting radiographic sacroiliitis was very high (97%) when a combination of age > 33.5 years AND symptom duration > 4.1 years was used as a composite parameter. In other words, patients older than 33.5 years with a symptom duration longer than 4.1 years are highly likely to have radiographic axSpA rather than non-radiographic axSpA. Therefore, for these patients, using X-ray as a first-line imaging modality could be sufficient to make a diagnosis, saving time and expense of performing an MRI. However, the composite parameter using

combination of age > 33.5 years OR symptom duration > 4.1 years had the highest sensitivity (76%) for predicting radiographic sacroiliitis. For patients who do not fulfil this composite parameter (i.e. patients younger than 33.5 years with a symptom duration shorter than 4.1 years), using MRI as a first-line imaging modality could be desirable. If X-ray is used as a first-line imaging modality in these patients, the patients are likely to undergo additional imaging study with MRI because definite radiographic sacroiliitis would not be identified on X-ray. Hence, it is reasonable to use MRI instead of X-ray as a first-line imaging modality in these patients. In the sensitivity analysis where the threshold of X-ray positivity was increased, the results were comparable to the main analysis (only slight decrease in specificity and modest increase in sensitivity). The similar results from the sensitivity analysis add robustness to our findings.

This study has several limitations. First, this study was conducted in a single-centre tertiary hospital. The pre-test probability of axSpA in a broad population with chronic back pain is only 5%,[17,18] whereas in a referral hospital setting where patients with chronic back pain are more selected, the pre-test probability of axSpA increases up to 30–40%.[19] Therefore, our results may not be generalized to a primary care setting. Second, our study does not fully capture the clinical problems as controls without axSpA were not included. However, those without axSpA would probably have to undergo additional imaging such as MRI of the spine or hip joints, regardless of the first-line imaging modality of the sacroiliac joints. This is in contrast to the patients with radiographic axSpA and those with non-radiographic axSpA, who may benefit from using X-ray and MRI, respectively, as a first-line imaging modality of the sacroiliac joints. Thus, determining the cut-off values of age and symptom duration for selecting first-line imaging modality of sacroiliac joints, with inclusion of patients without axSpA, may not be as clinically relevant. Third, the images were not interpreted by a single reader. The possible influence of inter-reader variability should be considered while interpreting our data. Fourth, the readers were not blinded to the clinical characteristics.

In conclusion, we demonstrated that the best cut-off values for age and symptom duration for predicting radiographic sacroiliitis in a tertiary referral hospital setting are 33.5 years and 4.1 years, respectively. These two parameters could be considered when selecting the first-line imaging modality for diagnosing axSpA. It would be reasonable to use X-ray as a first-line imaging modality in patients older than 33.5 years with a symptom duration longer than 4.1 years, and to use MRI as a first-line imaging in patients younger than 33.5 years with a symptom duration less than 4.1 years.

Author contributions

Oh Chan Kwon: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Min-Chan Park: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Conflict of interest statement

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Data availability statement

All data are incorporated into the article.

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