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

Oh Chan Kwon and Min-Chan Park

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 fulfillment 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
sacroiliac joints is recommended to secure the diagnosis of axSpA. 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. 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. A recent study has reported that the accuracy of MRI is superior to that of X-ray in diagnosing axSpA. Given its advantages over X-ray, using MRI as a first-line imaging modality instead of X-ray could be useful. 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. 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 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. Indeed, MRI is recommended as an alternative first-line imaging modality in certain patients, such as young patients and patients with short symptom duration. 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.

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. 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, 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
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. 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

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**Table 1.** Characteristics of the patients.

| Characteristic                                      | 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*, 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*, 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*, 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.

*Patients (N = 19) with missing data were excluded.

bPatients who fulfilled the radiologic criterion of the 1984 modified New York criteria were classified as patients with radiographic axSpA.

cPatients who did not fulfill the radiologic criterion of the 1984 modified New York criteria were classified as patients with non-radiographic axSpA.
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. 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. 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 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, 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.

*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.
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 \& 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

### 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.
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%,\textsuperscript{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%.\textsuperscript{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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