Peer Review File

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Reviewer A

The objective of this retrospective cohort study was to investigate the radiographic relationship between SSPA and hip extension in a standing position. I have carefully reviewed this interesting paper with great interest. I have some recommendations for improvement:

Major comments

(1) These are selection biases, as 336 of the 398 potential subjects, (84.4%) were excluded. Please state this in the limitations. Also, compare gender, age, etc. between included vs. excluded patients to ensure there are no significant differences.

Response:

We appreciate the reviewer's insightful comment. The articulation of our statement and the substantial number of excluded subjects may have inadvertently given the impression of a biased selection process. The criteria for exclusion were rigorously defined to identify and assess a relatively healthy demographic in terms of spinal and lower extremity health. The exclusion of a large patient cohort was not a result of arbitrary selection; rather, it was due to the high prevalence of fractures and degenerative changes in the spine and lower extremities among the osteoporotic patients who present at our clinic. Additionally, it is worth noting that the patient population at our clinic for osteoporosis predominantly comprises females, which further accounts for the gender distribution in our study sample. In order to clarify the matters above, the statements in Materials and Methods were rewritten as below, "*Subjects capable of maintaining an upright standing posture with healthier spine and lower extremity conditions were chosen for the radiographic assessment of their sagittal alignment, as described below.*" (Line 125-126), and "*Specifically, criteria 2), 3), and 4) were established to minimize biases impacting the spinal alignment, thereby ensuring the selection of subjects with near-normal profiles.*" (Line 132 -134)

As the reviewer astutely highlighted, there was a gender bias towards female subjects in our study. To address the potential implications of this bias with respect to the existing literature, we have included the following elucidation: "*Furthermore, the exclusive inclusion of female subjects may introduce a gender-specific bias in the results pertaining to spinal alignment. Regarding sexual dimorphism, the Pelvic Incidence (PI) has been reported to exhibit negligible or minor differences between*

genders (4). Conversely, Lumbar Lordosis (LL) is documented to be more pronounced in females as compared to males (5,6)." was added. (Line 278-281)

(2) Please specify that the normality test was performed using the Shapiro-Wilk test in JMP. In addition, normally distributed continuous variables should be expressed as mean ± SD and compared using Student's t test. Non-normally distributed continuous variables should be expressed as median (IQR) and compared using the Mann-Whitney U test. Similarly, use Pearson correlation coefficient for normally distributed continuous variables, and Spearman's correlation coefficient for non-normally distributed continuous variables.

Response:

Thank you very much for indicating very important issues. The normality of the distribution of demographic data was analyzed using the Shapiro-Wilk test. A Student's t-test was conducted for the comparison between two groups of variables demonstrating a normal distribution, while the Mann-Whitney U test was applied to variables that did not follow a normal distribution. the Shapiro-Wilk test demonstrated that only the SVA and PI-LL of the malalignment group were not normally distributed: The description *"For the malalignment group, SVA and PI-LL were found to be non-normally distributed (p =0.01 and 0.04, respectively)."* was added. (Lines 187 – 189) The comparison between the two groups for SVA and PI-LL was conducted using The Mann-Whitney U test. The method section was revised as follows: *"The distribution of demographic data, including PI-LL, was assessed for normality using the Shapiro-Wilk test at the significance level of $p<0.05$. For the comparison of the two groups, the Student's t-test and the Mann-Whitney U test were used for parameters with normal and non-normal distributions, respectively. For the assessment of correlation between two variables, the Pearson coefficient and the Spearman's rank correlation were used for parameters with normal and non-normal distributions, respectively."* (Lines162 – 167). The result section was revised as follows: *". As for the comparison between Normal and Malalignment groups, age, SVA, PFA, PI and PT were significantly larger, and LL, PI-LL and TK were significantly lower in Malalignment group, respectively, as shown in Table 2."* (Lines 189 – 191), and "*The Pearson and Spearman's rank correlation coefficients for each parameter are listed in Table 3."* (Lines 193 – 194)

The reviewer's comment "normally distributed continuous variables should be expressed as mean ± SD and non-normally distributed continuous variables should be expressed as median (IQR)" was valid.

(3) Please check whether the test power is sufficient. If the statistical power is insufficient, please state it in the limitation and conclusion section.

Response:

Thank you for important comment. Three additional statements about power analysis have been added. The statements are as follows:

1. The description "*A post hoc power analysis was conducted for the correlation coefficient*." was added in the Materials and Methods section (Line 175-176)
2. The result of post hoc power analysis was described in the Result section. The statements in Line 206: *"The power was revealed to be 0.68 by the power analysis".*
3. The insufficient power was attributed to the small number of cases, which was noted as a limitation in Lines 274 - 278: "*First, the sample size particularly in the malalignment group was small which made the power insufficient. Further studies with a larger number of patients with spinal sagittal malalignment of greater severity are needed to establish the clinical applicability of this parameter, and to investigate whether this concept can be applied to patients with symptomatic spinal kyphosis."*

Minor comments

(4) Please add citation of the sentences "In clinical practice, some older individuals with large PI-LL can stand upright for a long time. In contrast, others with a minor spinopelvic mismatch can barely stand for less than a minute with anterior trunk inclination."

Response:

The citation was added, and the description were amended to clarify the topic as in line 110 - 112: *"Even among elderly patients with kyphosis, the degree of anterior trunk inclination varies. While some exhibit minimal anterior trunk inclination during walking, some demonstrate a significant anterior trunk inclination"*

(5) This study focuses on female. Therefore, please add "female" to the title and explain the differences of SSPA by gender in the background.

Response:

I agree with the reviewer's suggestion. The title was amended to "*Harmony between spinopelvic mismatch and sagittal hip alignment contributes to upright standing in females: a cross-sectional study*" as indicated by the reviewer (Line2). The differences in sagittal plane spinal-pelvic alignment by gender were described in the Introduction section. The statements of the differences of spinopelvic alignment by gender in the background were added as follows.

1. *There is no difference in PI based on gender, or if there is, it is minor (4). It has been reported that LL is greater in female than in male. (Lines 92 – 94)*
2. *As compensation for the reduction in lumbar lordosis, the pelvis was retroverted. However, the pelvic tilt (PT) to PI ratio shows no difference between males and females, indicating that this compensatory mechanism is the same across genders. (Lines 95 – 98)*

(6) Please indicate the ICC evaluation criteria.

Response:

The ICC evaluation criteria were added in Lines 150 – 152: *"The values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 are indicative of poor, moderate, good, and excellent reliability, respectively."*

(7) The SSPA is also strongly influenced by the acetabular anteversion angle. Please read below for further insight.

Kobayashi T, Morimoto T, Yoshihara T, Sonohata M, Rivière C, Mawatari M. The significant relationship among the factors of pelvic incidence, standing lumbar lordosis, and lumbar flexibility in Japanese patients with hip osteoarthritis: A descriptive radiographic study. Orthop Traumatol Surg Res. 2022 Apr;108(2):103123.

Rivière C, Lazennec JY, Van Der Straeten C, Auvinet E, Cobb J, Muirhead-Allwood S. The influence of spine-hip relations on total hip replacement: A systematic review. Orthop Traumatol Surg Res. 2017 Jun;103(4):559-568.

Response:

Thank you very much for your insightful comments. The provided literatures were cited as shown in Lines 268. The current study focuses on the evaluation of images during static standing. However, the literature you provided indicates that changes in the mobility posture of the lumbar spine significantly affect pelvic tilt.

It is crucial to analyze the dynamic changes in the hip joint, particularly during walking or posture transitions, as documented in Lines 262 - 273: *" It has been reported that there is an appropriate LL for PI (3). This study presents a novel finding that spinopelvic mismatch significantly influences hip positioning in the erect posture. However, the dynamics of the hip joint undergo substantial changes during ambulation or in the transition from sitting to standing. Notably, the variation in sagittal pelvic tilt between the standing and sitting positions has been the subject of extensive research. It has been observed that individual variations in pelvic tilt adjustments, due to changes in posture, are closely associated with the range of motion in the lumbar spine (20,21). Furthermore, studies have shown that among Japanese women aged over 50 years,*

there is a notable reduction in both LL and lumbar mobility as a function of aging (22). In our investigation, the group with spinal malalignment was significantly older, suggesting a potential disparity in lumbar mobility between the examined groups. It is imperative for future research to delve into the examination of alterations in lumbar mobility and the positional dynamics of the hip joint during physical activities, such as walking or the transition from a seated to a standing posture.

(8) Please add clinical significance and applications.

Response:

Thank you very much for your important suggestion. There are two clinical significant points in this results. First, the optimal PFA could be calculated from PI-LL. Second, ΔPFA could objectively indicate the compensatory mechanism of the hip joints. I added the two crucial points in the Discussion section: *"It is clinically crucial that an optimal PFA could be calculated from PI - LL, and the difference between the optimal PFA and the measured PFA, in other words ΔPFA, could be expressed as an objective numerical value. The compensatory mechanism of the hip joints in response to spinopelvic mismatch could be objectively evaluated by using ΔPFA."* (Lines 254 - 257)

(9) Define your research design in the title and methods section.

Response:

The definition of this study was described in the title and the Methods section.

The words "*a cross-sectional study* "were added in the title (line 2). The statement *"This study is a retrospective, cross-sectional study."* was added in the Methods section (line 121).

(10) There was a significant difference in age between the two groups. Also, consider the influence of age.

Response:

Thank you very much for your insightful comment. Lumbar mobility is reported to affect sagittal spinopelvic alignment, and also varies with age. These reports were added as citations. (Citation 20 - 22). In this regards, descriptions were added as below: " *It has been observed that individual variations in pelvic tilt adjustments, due to changes in posture, are closely associated with the range of motion in the lumbar spine"* (Lines 266 - 268) and *"studies have shown that among Japanese women aged over 50 years, there is a notable reduction in both LL and lumbar mobility as a function of aging"* (Line 268 - 269) In the Malalignment group, there is a possibility of reduced

lumbar mobility due to significantly higher age. However, in this study, spinal mobility was not assessed. Therefore, in the discussion section, it was noted that a dynamic assessment is considered necessary for future research. The statement was that "*In our investigation, the group with spinal malalignment was significantly older, suggesting a potential disparity in lumbar mobility between the examined groups. It is imperative for future research to delve into the examination of alterations in lumbar mobility and the positional dynamics of the hip joint during physical activities, such as walking or the transition from a seated to a standing posture.*" (Lines 269 - 273)

(11) Please add an explanation of a representative case.

Response:
–The detailed explanation has been added. Fig. (A) to (C) were presented as examples demonstrating the relationship between ΔPFA and SVA. While the mismatch could be compensated for the hip joints, ΔPFA remained negative and SVA was within normal (Case A). When the hip joints could not compensate adequately, ΔPFA becomes positive, showing a positive correlation with SVA. As showed in Case B and C, ΔPFA in Case C was larger than in Case B, resulting larger SVA. The added explanations were as follows:

（A）*She had a PI-LL mismatch, however, the hip joints were sufficiently extended. SVA was negative, and the trunk was not leaning anteriorly. (Lines 209 – 210, 390 - 391)*

（B）*ΔPFA indicated that the hip joints were not sufficiently extended. SVA was exceeded 40 mm. The trunk was leaning slightly anterior. (Lines 213 – 214, 394 - 395)*

（C）*She had PI-LL mismatch. The extension of the hip joints was insufficient. ΔPFA was larger than case (B). Certainly, SVA also becomes larger compared to case (B), as the ΔPFA and SVA are correlated. (Lines 217 – 219, 398 - 400)*

(12) Please revise your conclusion. First, summarize the notable results for each parameter. Next, summarize in one sentence what you can say from it.

Response:
Thank you very much for your suggestions. I had revised the conclusion divided into two parts: firstly, the key points of this study were summarized, and secondly, the significant findings were described in one sentence.

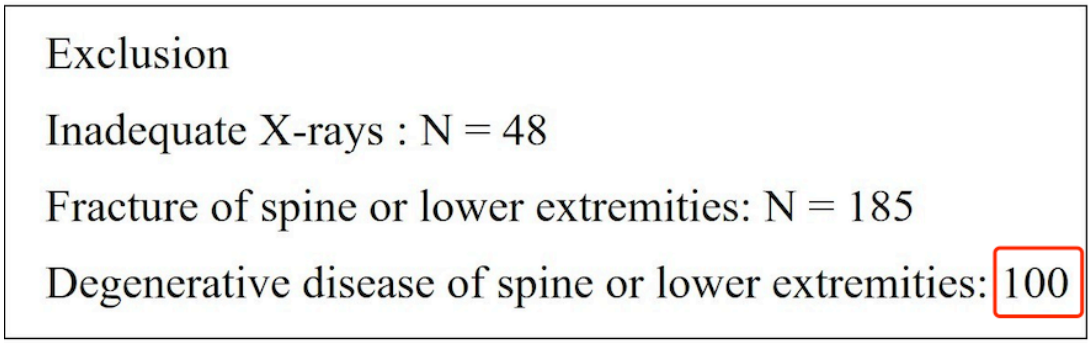
The summary of this report was as follows: "*The ΔPFA, which is the difference between the optimal and actual PFA, may indicate a compensatory insufficiency of the hip joints for spinal sagittal malalignment. In individuals with normal spinal sagittal alignment, a small PI-LL can be adjusted by the thoracic spine and hip joints to maintain a certain range of trunk inclinations.*" (Lines 290 – 293)
The significant finding of this study was that *"The relationship between the sagittal alignment of the hip joints and spinopelvic mismatch is closely related to upright standing in humans."* (Lines 293 – 294)

Reviewer B

1. Abstract
Please revise Background in your abstract. It's not allowed to only describe objectives in the Background. Please expand the content.
→ Background information was inserted in Abstract as in line 39-41.
2. Figure 1
Please define PT in the legend.
→ The definition of PT was added in legend (line 358-359).

3. Figure 2
a) Please provide an editable version of the flow chart (figure 2) in DOC/PPT.
→ The flow chart in PPT file is attached by this email. The file name is "Fig 2 flow chart.pptx".

b) Here should be N=100, please revise.



→ Fig. 2. was revised as indicated.

4. Figure 4
Please define PFA and PI-LL in the legend.

→ The definition of PFA and PI – LL was added in line 384– 389.

5. Figure 5

Please define PFA and SVA in the legend.

→ The definition of PFA and SVA in line 393 – 396.

6. Figure 6

a) Please also add ABC in the figure.

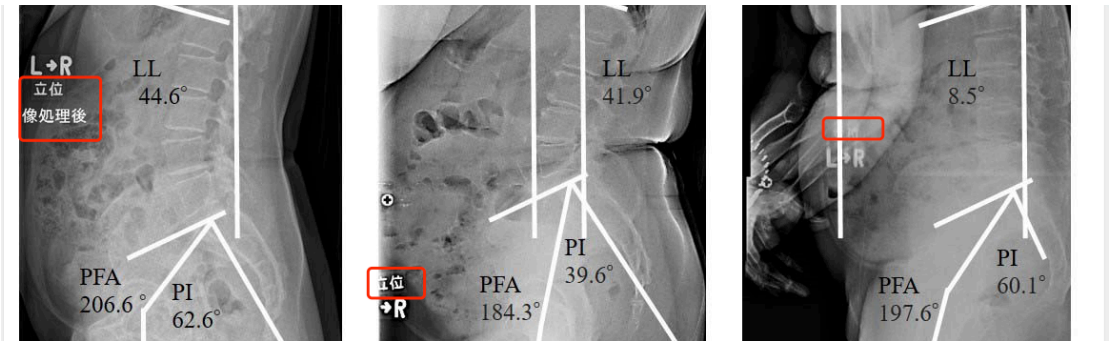
→ The alphabetical labels were added in Figure 6 as indicated.

(A) Case 1. A 61-year-old woman with a negative ΔPFA. She had a PI-LL mismatch, however, the hip joints were sufficiently extended. SVA was negative, and the trunk was not leaning anteriorly. The parameters were as follows: SVA, -2.7 mm; PI-LL, 18°; PFA, 206.6°; optimal PFA, 202.8°; and ΔPFA, -3.8°.

(B) Case 2. A 77-year-old woman with a positive ΔPFA. ΔPFA indicated that the hip joints were not sufficiently extended. SVA was exceeded 40 mm. The trunk was leaning slightly anterior. The parameters were as follows: SVA, 52.2 mm; PI-LL, -2.3°; PFA, 184.3°; optimal PFA, 190.7°; and ΔPFA, 6.3°.

(C) Case 3. A 79-year-old woman with a positive ΔPFA. She had a PI-LL mismatch. The extension of

b) Please translate these words to English in the figure.



→ The word means “Standing”. The word, “Standing” was inserted in Fig.6. The JPEG and PPT files were attached. The file name is “Fig.6”

c) Please define PFA, PI-LL, and SVA.

→The definition of PFA and SVA were added in line 411 – 414.

7. Tables 1 and 3

Please revise table 1, 2 groups should share the same headers. Two headers are not allowed.

→ Table 1 and 3 were revised as indicated, and sent in the Word and Excel files. The file names are “Table 1” and “Table 3”.

8. Table 2

Please provide a header of the first column.

Table 2. Demographic data

	All	Normal group	Malalig
Numbers of patients	62	43	

→ A header “Variables” was provided in Table 2.