Original Article
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Re-stooping after Corrective Osteotomy in Patients with Ankylosing Spondylitis

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Background: Corrective osteotomy is an effective surgery for correcting posture in patients with ankylosing spondylitis (AS). Despite satisfactory correction, some patients experience re-stooping during follow-up. However, there have been no studies on re-stooping in AS. We aimed to analyze the factors that affect re-stooping.

Methods: Fifty patients (50 cases) who underwent thoracolumbar corrective osteotomy for AS from March 2006 to April 2018 were analyzed. We defined re-stooping as global kyphosis that recurs after corrective osteotomy. The patients were divided into two groups based on the ratio of correction loss: non-re-stooping group (N group) and re-stooping group (R group). We analyzed the demographic data and radiological parameters, such as modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), sagittal vertical axis, and various angles. We also investigated the factors affecting re-stooping by analyzing the correlation between the ratio of correction loss and various factors.

Results: A significant difference was seen in the change in the mSASSS from before surgery to the last follow-up between the N group (2.87 ± 3.08) and the R group (9.20 ± 5.44). In multivariate analysis, only the change in the mSASSS from before surgery to the last follow-up was significantly correlated with the ratio of correction loss.

Conclusions: Thoracolumbar corrective osteotomy seems to provide high satisfaction among patients with AS but can lead to re-stooping during follow-up. The change in mSASSS was related with re-stooping in the current study. We recommend active rehabilitative exercises and appropriate medication depending on the patient's condition, which may help delay the postoperative progression of AS.

Keywords: *Ankylosing spondylitis, Thoracolumbar, Osteotomy, Modified Stoke Ankylosing Spondylitis Spine Score, Re-stooping*

Ankylosing spondylitis (AS) is a chronic inflammatory disease affecting the spine, including the sacroiliac joint. It induces the ossification of capsules and ligaments, thus progressively limiting joint movements.[1,2] Ankylosis of the whole spine leads to sagittal imbalance and fixed kyphosis that can result in difficulties in staring forward and lying straight supine.[3] Previous studies reported that patients with AS were 2.21 times more likely to have psychological depression than the general population.[4,5] Sagittal imbalance is surgically corrected to reduce problems in daily life and improve quality of life.

Surgical procedures for AS include Smith-Peterson osteotomy (SPO), pedicle subtraction osteotomy (PSO), and vertebral column resection (VCR). Corrective osteotomy is effective for AS accompanied by fixed kyphosis; however, it requires sophisticated technical skills, and complications may occur during or after surgery. A previous study reported that corrective osteotomy corrected sagittal imbalance and improved quality of life in the phys-

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ical and psychological domains.[6)]

However, we experienced recurrence of stooping during a long-term follow-up after successful corrective osteotomy. We coined the term re-stooping to describe global kyphosis that recurs after corrective osteotomy in patients with AS. There are several studies on cases of kyphosis that occurred after spinal fusion of degenerative disease. Most of them were deformities due to junctional problems such as proximal junctional failure and proximal junctional kyphosis. Metal failure due to osteoporosis was also a cause.[7-9)] However, we found specific characteristics different from those of degenerative disease in AS patients, which aroused our curiosity. In our patients, there was no problem at the surgical site, and re-stooping was due to global kyphosis, not a proximal junctional problem. Although the attention on AS is increasing, there is no study on re-stooping that occurs during the follow-up period. In this study, we aimed to investigate the occurrence of re-stooping and analyze the factors that affect re-stooping.

METHODS

The study protocol was approved by the Institutional Review Board of Hanyang University Guri Hospital (No. 2020-06-042) and conformed to the ethical guidelines of the World Medical Association Declaration of Helsinki. The requirement for informed consent was waived by the board.

This study included patients with AS who had severe kyphosis and underwent thoracolumbar corrective osteotomy between March 2006 and April 2018. Of 58 patients, 50 with a follow-up period of > 2 years were retrospectively analyzed. AS was diagnosed using the modified New York criteria and the Assessment of Spondylarthritis International Society classification criteria, which have been increasingly used recently.[10,11)]

We defined re-stooping as global kyphosis that occurs after corrective osteotomy. Re-stooping is related to correction loss: greater correction loss is related to severer re-stooping. We classified the grade of re-stooping using a new method. We calculated the ratio of correction loss based on the magnitude of change in the sagittal vertical axis (SVA). The ratio of correction loss was calculated by taking the difference between the SVA at the last follow-up and the SVA immediately after surgery (i.e., loss of SVA during the follow-up), dividing the difference between the SVA before surgery and that immediately after surgery (i.e., correction of the SVA), and multiplying the result by 100.

Ratio of Correction Loss (%)

Ratio of correction loss (%) = [last SVA – postoperative SVA (Δloss of SVA) / preoperative SVA – postoperative SVA (Δcorrection of SVA)] $\times$ 100

Patients with a ratio of correction loss > 50% were included in the re-stooping group. Re-stooping was classified into three grades: grade I, if the ratio of correction loss was < 50% (Fig. 1); grade II, if it was 50%–100%; and grade III, if it was ≥ 100%. According to the ratio of correction loss, the patients were divided into the non-re-stooping group (N group) and the re-stooping group (R group). Thirty patients were assigned to the N group and 20 patients to the R group. Age, sex, bone mineral density (BMD), length of follow-up, and preoperative blood test parameters were compared between the two groups. The SVA, modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), and various angles were radiologically measured and compared.[12)]

All patients were radiologically examined in the same posture. Long-cassette standing lateral spinal radiographs obtained before surgery, after surgery, and during the follow-up were evaluated. For the radiography of the spine, each patient was asked to stand in an erect but comfortable posture. The hands were placed on the supports, and the knees were held in extension.[13)] To measure spinal sagittal malalignment, the shortest horizontal distance between the posterior-superior edge of the sacral endplate and the plumb line from C7 was measured as the SVA.[14)] The thoracic kyphosis angle (TKA) was measured as the

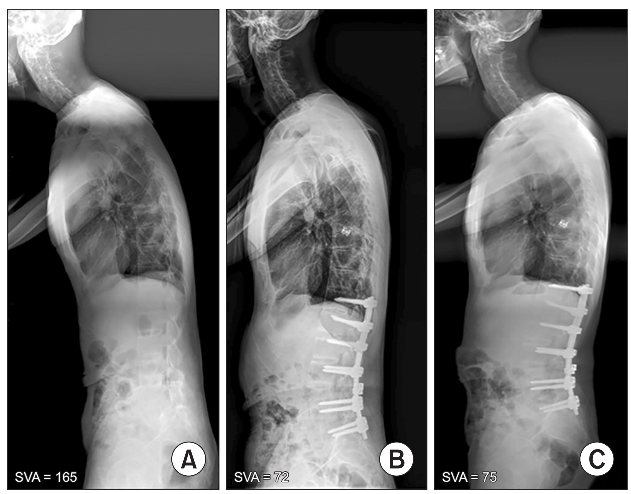

Fig. 1. Entire standing lateral radiographs. (A) The preoperative sagittal vertical axis (SVA) was 165 mm. (B) The SVA was 72 mm immediately after pedicle subtraction osteotomy at L4. (C) The SVA was 75 mm at the 48-month follow-up, and the ratio of correction loss was 3%; accordingly, the patient was categorized into the N group (grade I).

Table 1. Comparison of Demographic Characteristics between N Group and R Group

Variable	N group (n = 30)	R group (n = 20)	*p*-value
Age (yr)	38.8 ± 5.6	40.5 ± 9.0	0.457
Sex (male : female)	25 : 5	17 : 3	0.878
Follow-up (mo)	49.4 ± 33.1	51.5 ± 31.4	0.824
BMD (T-score)	–0.8 ± 1.5	–1.5 ± 1.1	0.126
Preop CRP	0.9 ± 0.7	2.0 ± 2.3	0.039*
Preop ESR	27.1 ± 21.3	29.3 ± 25.1	0.742
Preop mSASSS	46.4 ± 18.0	44.6 ± 16.4	0.717
Last-preop mSASSS	2.87 ± 3.08	9.20 ± 5.44	< 0.001*
Last-postop WA (°)	0.42 ± 2.04	0.07 ± 2.59	0.458
Last-postop AIL (°)	–0.30 ± 3.01	–0.24 ± 3.07	0.951
Last-postop PJA (°)	0.92 ± 0.57	0.87 ± 0.60	0.758

Values are presented as mean ± standard deviation or number.
N group: no re-stooping group, R group: re-stooping group, BMD: bone mineral density, Preop: preoperative, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, WA: wedge angle, AIL: angle of instrumented levels, PJA: proximal junctional angle.
*Statistically significant.

angle between the upper endplate of T1 and the lower endplate of T12. The lumbar lordosis angle (LLA) was measured as the angle between the upper endplate of L1 and the lower endplate of L5. The chin-brow vertical angle (CBVA, an index of forward-looking ability) was measured as the angle between the chin-brow line and the line vertical to the ground. The angle of instrumented levels (AIL) was the Cobb angle between the upper endplate of the proximal fixed segment and the lower endplate of the distal fixed segment.[15] The angle between the upper endplate and the lower endplate of the osteotomized vertebra was measured as the wedge angle (WA). The proximal junctional angle (PJA) was determined as the angle between the caudal endplate of the upper instrumented vertebra and the cranial endplate of the two vertebrae above.[16] Three researchers (JSP, BJK, HSA) each performed two measurements.

Statistical Analyses

The independent *t*-test and chi-square test were used to compare demographic characteristics between the N group and the R group. Pearson correlation analysis was used to determine correlations between the ratio of correction loss and various factors. Multivariate logistic regression analysis was used to analyze affecting factors while minimizing the effect of confounding factors. Interobserver and intraobserver accuracy was determined by measuring the SVA, mSASSS, and the various angles on radiographs, using an intraclass correlation coefficient (ICC) model. Statistical analysis was performed using IBM SPSS software ver. 22.0 (IBM Corp., Armonk, NY, USA). The *p*-values < 0.05 were considered statistically significant.

RESULTS

Among the patients, 30 (60%) were assigned to the N group and 20 (40%) to the R group. In the N group and the R group, the mean age of the patients was 38.8 ± 5.6 and 40.5 ± 9.0 years, respectively; the mean BMD (T-score) was –0.8 ± 1.5 and –1.5 ± 1.1, respectively; and the mean length of follow-up was 49.4 ± 33.1 and 51.5 ± 31.4 months, respectively. The preoperative C-reactive protein (CRP) level and preoperative erythrocyte sedimentation rate (ESR) were 0.9 ± 0.7 and 27.1 ± 21.3, respectively, in the N group and 2.0 ± 2.3 and 29.3 ± 25.1, respectively, in the R group (Table 1). With respect to the grade of re-stooping, 30 patients (60%) had grade I, 14 (28%) had grade II, and 6 (12%) had grade III. Four of those with grade III had reoperation (Fig. 2).

Radiologic Evaluation

In the N group, the mean preoperative mSASSS was 46.4 ± 18.0, the mean change in WA from immediately after surgery to the last follow-up was 0.42° ± 2.04°, the mean change in AIL was –0.30° ± 3.01°, and the mean change in PJA was 0.92° ± 0.57°. In the R group, the mean preoperative mSASSS was 44.6 ± 16.4, the mean change in WA from immediately after surgery to the last follow-up was 0.07° ± 2.59°, the mean change in AIL was –0.24° ± 3.07°, and the mean change in PJA was 0.87° ± 0.60°. No significant differences were found in these measurements between the two groups (p = 0.717, p = 0.951, and p = 0.758, respectively, for the mSASSS, AIL, and PJA). However, a significant difference was seen in the change in the mSASSS from before surgery to the last follow-up between the N group (2.87 ± 3.08) and the R group (9.20 ± 5.44) (p < 0.001) (Table 1).

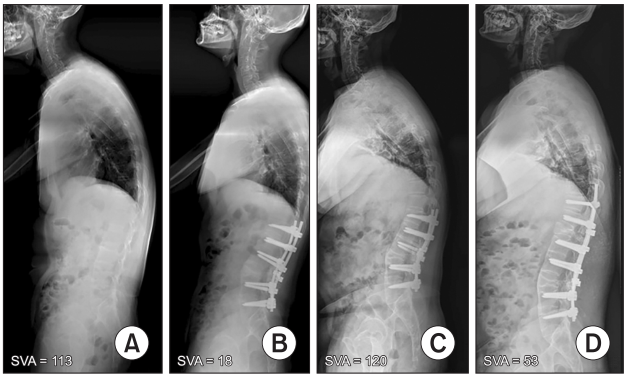

Fig. 2. Entire standing lateral radiographs. (A) The preoperative sagittal vertical axis (SVA) was 113 mm. (B) The SVA was 18 mm after pedicle subtraction osteotomy at L3. (C) Correction loss was observed at 40-month follow-up; the patient was classified as R group (grade III). (D) After revision surgery, the SVA was 53 mm.

In the N group, 25 patients had one-level PSO and 5 patients had two-level PSO. Of the 35 PSO cases, osteotomies were conducted in 2 cases at T12, in 5 cases at L1, in 3 cases at L2, in 15 cases at L3, and in 10 cases at L4. In the R group, 17 patients had one-level PSO and 3 patients had two-level PSO. Of the 23 PSO cases, osteotomies were conducted in 2 cases at T12, in 3 cases at L1, in 3 cases at L2, in 8 cases at L3, and in 7 cases at L4. There was no significant difference in osteotomy method between the two groups. The mean fusion level was 5.8 ± 1.4 in the N group and 5.3 ± 1.6 in the R group, and no significant difference between the two groups was observed. Radiological parameters such as preoperative and postoperative mean LLA, TKA, SVA, and CBVA did not show significant differences between the two groups (Table 2).

Table 2. Comparison of Surgical Methods and Radiological Parameters between N Group and R Group

Variable	N group (n = 30)	R group (n = 20)	*p*-value
Osteotomy method			0.875
PSO (1-level)	25	17	
PSO (2-level)	5	3	
Fusion level	5.8 ± 1.4	5.3 ± 1.6	0.232
Radiological parameter			
Pre-LLA (°)	–5.5 ± 11.1	–9.3 ± 16.8	0.347
Post-LLA (°)	–38.5 ± 6.4	–38.3 ± 10.2	0.922
Pre-TKA (°)	45.4 ± 10.8	47.1 ± 10.9	0.606
Post-TKA (°)	42.2 ± 8.4	46.2 ± 6.1	0.089
Pre-SVA (mm)	134.3 ± 53.6	128.2 ± 44.2	0.685
Post-SVA (mm)	46.2 ± 21.3	54.6 ± 19.1	0.176
Pre-CBVA (°)	30.6 ± 8.5	30.1 ± 6.6	0.862
Post-CBVA (°)	8.5 ± 3.8	7.3 ± 5.3	0.363

Values are presented as number or mean ± standard deviation.
N group: no re-stooping group, R group: re-stooping group, PSO: pedicle subtraction osteotomy, LLA: lumbar lordosis angle, TKA: thoracic kyphosis angle, SVA: sagittal vertical axis, CBVA: chin-brow vertical angle.

Table 3. Analysis of Factors Affecting the Ratio of Correction Loss

Factor	ICC	*p*-value
Age	0.157	0.276
Sex	0.147	0.310
Follow-up	0.244	0.088
BMD	–0.243	0.089
Preop CRP	0.258	0.070
Preop ESR	0.026	0.858
Preop mSASSS	–0.054	0.711
Last mSASSS	0.135	0.349
Last-Preop mSASSS	0.594	< 0.001*
Last-Postop WA (°)	–0.195	0.174
Last-Postop AIL (°)	–0.128	0.377
Last-Postop PJA (°)	0.127	0.378

Pearson's correlation test was used.
ICC: intraclass correlation coefficient, BMD: bone mineral density, Preop: preoperative, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, Postop: postoperative, WA: wedge angle, AIL: angle of instrumented levels, PJA: proximal junctional angle.
*Statistically significant.

Table 4. Multivariate Analysis for Factors Affecting the Ratio of Correction Loss

Factor	ICC	*p*-value
Age	0.222	0.056
Follow-up	0.225	0.052
BMD	–0.171	0.146
Preop CRP	0.120	0.149
Preop mSASSS	0.211	0.095
Last mSASSS	0.195	0.095
Last-Preop mSASSS	5.010	< 0.001*
Last-Postop PJA (°)	0.120	0.149

Values are presented as non-standardized constant (B) under the linear regression analysis.
ICC: intraclass correlation coefficient, BMD: bone mineral density, Preop: preoperative, CRP: C-reactive protein, mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, Postop: postoperative, PJA: proximal junctional angle.
*Statistically significant.

Correlations between Various Factors and the Ratio of Correction Loss

Age, sex, follow-up, BMD, preoperative CRP, and preoperative ESR did not affect the ratio of correction loss statistically. In preoperative CRP, there was a significant difference between N group and R group, but no correlation with the ratio of correction loss was confirmed. The change in the mSASSS from before surgery to the last follow-up showed a significant correlation, and the other radiographic factors had no significant effect (Table 3). In multivariate analysis, only the changes in the mSASSS from before surgery to the last follow-up was significantly correlated with the ratio of correction loss (Table 4). All parameters were measured two times each by three researchers. The ICC for interobserver agreement was 0.963, and the ICC for intraobserver agreement was 0.991 for observer A, 0.981 for observer B, and 0.989 for observer C.

DISCUSSION

Corrective osteotomy is the best treatment option for AS accompanied by severe kyphosis.[17] The surgical procedures for AS include SPO, PSO, and VCR, and the appropriate procedure is selected according to the patient's condition. Liu et al.[18] reported that SPO and PSO had high postoperative patient satisfaction rates and similar complication risks. Cho et al.[19] recommended SPO of one or two levels for patients with an SVA of 6–8 cm and PSO for those with an SVA ≥ 12 cm. We used Surgimap Spine software (Nemaris Inc., New York, NY, USA) to perform an effective and simple computer-based simulation before performing a corrective osteotomy and predicted the postoperative degree of correction and alignment to choose the appropriate surgical method.[4] We experienced many successful results after corrective osteotomy in AS patients. However, occurrence of re-stooping during long-term follow-up despite the successful corrective osteotomy has been reported in some cases. Although several reports have been published on the recurrence of kyphosis after corrective osteotomy for degenerative spinal diseases, few studies have reported that re-stooping occurs after corrective surgery in patients with AS.

Recurrence of kyphosis after spinal fusion in patients with degenerative spinal disease is mostly associated with junctional problems including PJK and proximal junctional failure according to several studies. However, patients with AS were relatively young with an average age of 40 years in the current study. They showed different characteristics from older patients who underwent spinal fusion for degenerative spinal disease. Contrary to patients with degenerative spinal conditions, patients with AS have ossification and stiffness in most of their spinal segments.

We analyzed re-stooping with an interest in these AS characteristics. In this study, no junctional problem was observed in radiographic analysis, and re-stooping was not localized and was observed as round global kyphosis.

We classified re-stooping in patients with AS into three grades according to the ratio of correction loss and examined the cases of reoperation for each grade. Based on our classification, 30 patients (60%) had grade I, 14 (28%) had grade II, and 6 (12%) had grade III. Four patients underwent reoperation, all of whom had grade III AS. On the basis of these results, we recommend conservative treatment in grade I and II. Reoperation can be considered according to patient satisfaction in grade III.

In the current study, when meaningful re-stooping was defined as grade II or III with the ratio of correction loss of 50% or more, 20 of the total 50 patients were included in the R group. When the N group and the R group were compared, there was a significant difference in preoperative CRP. In the R group, it was high with an average of 2.0. It can also be used as a baseline datum to estimate the severity of AS in the absence of infection-related symptoms before surgery. There was also significant difference in the change of mSASSS before surgery and at the last follow-up between the two groups. This can be interpreted as an indicator of disease progression during the follow-up period because AS is a progressive disease. Among our patients, AS was more advanced in the R group than in the N group (Table 1).

Although we reported the incidence of re-operation according to grade, it is more important to identify the affecting factors and prevent its occurrence. In our study, when comparing the two groups, there was a significant difference in preoperative CRP and change of mSASSS before surgery and the last follow-up. However, only the change of mSASSS before surgery and the last follow-up showed a significant correlation with the ratio of correction loss in Pearson analysis. In multivariate analysis, only the change in the mSASSS from before surgery to the last follow-up was significantly correlated with the ratio of correction loss.

The mSASSS is related to the progression of AS, so we focused on the pathophysiology in AS patients. Patients with AS undergo spinal ossification that leads to the formation of syndesmophytes, which induce spinal stiffness.[20] van der Heijde et al,[21] radiologically measured the mSASSS to determine the severity and progression of AS. Ramiro et al.[22] reported that the mSASSS was the best radiographic scoring method for determining disease progression in patients with AS. An increase in the mSASSS indicates increased bone union, which limits joint movements. In our study, an increase in the mSASSS was associated with the change in the SVA. In multivariate analysis, only the change in the mSASSS from before surgery to the last follow-up was identified as the factor affecting re-stooping. In a long-term cohort study, Sari et al.[23] defined a change of 2 mSASSS units in 2 years as a sign of progression and identified risk factors by classifying the progressors: the mSASSS was associated with the disease activity of AS, male sex, baseline spinal damage, high disease activity, and elevated levels of inflammatory markers. Even according to their criteria, the patients in the R group can be considered as progressors. We also interpreted the change in the mSASSS as the activity of AS.

Poddubnyy et al.[24] performed radiologic examination and blood testing in patients with AS every 6 months to measure the CRP-based AS Disease Activity Score (ASDAS). Consistently high disease activity according to the ASDAS and a high mSASSS were found to be associated with the progression of axial spondylarthritis on radiographs.[24-26] In the current study, the R group showed high preoperative CRP levels. Although preoperative CRP was not a significant affecting factor for re-stooping in multivariate analysis, a close postoperative observation may be needed in patients with high preoperative CRP levels, considering disease activity. In our study, disease activity could not be monitored according to CRP levels during the follow-up period because a blood test was not regularly performed. Additional studies using regular blood tests to examine disease activity are needed.

Based on our results, patients with AS need to be managed after a successful corrective osteotomy considering the characteristics of AS. Considering AS is a progressive disease, treatments and management that lower disease activity and delay disease progression are necessary. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the first-line drugs for AS. Although studies have reported that consistent use of NSAIDs can delay ossification, some studies do not recommend long-terms use due to the risk of gastrointestinal problems.[27,28] Other medications for AS include biological agents that exert therapeutic effects by regulating the levels of inflammatory cytokines, as well as tumor necrosis factor inhibitors and interleukin-17A inhibitors. Although these agents cannot inhibit spinal stiffness, they can alleviate the progression of stiffness.[29,30] Therefore, postoperative pharmacotherapy appropriate to the patient's condition may help delay the progression of AS. It may reduce disease activity and the ratio of correction loss, thereby lowering the risk of re-stooping.

In this study, the change in mSASSS was the only factor influencing the ratio of correction loss, which is shown to affect re-stooping, which is considered a pathophysiological problem rather than a mechanical problem. Appropriate pharmacotherapy after successful surgery may help delay the disease progression, and active rehabilitative exercise may promote a good standing posture, thereby preventing re-stooping.

We were also interested in the timing of surgery before this study. Since AS is a progressive disease, it is necessary to carefully determine the timing of surgery in cases where there are many nonunion segments remaining or in young patients who have the potential to progress in the future. However, rather than considering prophylactic fixation up to the upper thoracic level, it is important to maintain periodic evaluation of postoperative disease activity and medication to reduce disease progression. Although age and the follow-up periods did not show a significant correlation in the current study, further studies with a longer follow-up and a larger number of patients are needed.

In conclusion, thoracolumbar corrective osteotomy seemed to provide high satisfaction among patients with AS but can lead to re-stooping during long-term follow-up, even after a successful treatment procedure. This study showed that the change in the mSASSS was related with re-stooping. We recommend active rehabilitative exercises and appropriate medication depending on the patient's condition, which may help delay the postoperative progression of AS.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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