

# Junctional kyphosis and junctional failure after multi-segmental posterior cervicothoracic fusion – A retrospective analysis of 64 patients

## ABSTRACT

**Introduction:** Junctional kyphosis (JK) and junctional failure (JF) are known complications after thoracolumbar spinal deformity surgery. This study aims to define the incidence and possible risk factors for JK/JF following multi-segmental cervicothoracic fusion.

**Methods:** This is a retrospective analysis of 64 consecutive patients undergoing cervicothoracic fusion surgery, including at least five segments. Clinical and radiographic outcome measures were analyzed. A univariate analysis was performed to determine the effect of the level of upper instrumented vertebra (UIV) and lower instrumented vertebra (LIV), fusion status, C2 sagittal vertical axis (SVA), C2–C7 lordotic angle and T1 slope angle on the occurrence of JK/JF.

**Results:** A total of 46 patients were followed up for a median of 1.1 years (range 0.3–4) with a median age of 65.5 years (range 42.2–84.5). Indication for surgery was spinal stenosis in 87%, trauma in 7%, and tumor in 6% of cases. The median number of levels fused was 7; the most frequent UIV was C2, and the most frequent LIV was T2. Solid fusion was achieved in 78% at the last follow-up. Postoperatively, the median C2 SVA was 32 mm (range 7–75), median T1 slope angle was 33 (range 2–57), C2–C7 sagittal Cobb angle was 4 (29–12). JK developed in 4% of cases, no case of JF was observed. No statistically significant impact of bone density, level of UIV, level of LIV or postoperative sagittal parameters on the occurrence of JK/JF was observed, even though fusion status and pathologic T1 slope angle showed a trend toward significance.

**Conclusion:** In this cohort of patients with mildly pathologic sagittal balance, JK was a rare event after multi-segmental fusion, observed in only 4% of cases. Neither level of UIV nor LIV had an influence on its occurrence; however, nonunion and pathologic sagittal alignment showed a nonsignificant trend.

**Keywords:** Cervicothoracic fusion, junctional failure, junctional kyphosis

## INTRODUCTION

Proximal junctional kyphosis (PJK) following thoracolumbar deformity surgery is a major complication reported in up to 46% of patients, with 66% of cases occurring within 3 months of the index surgery.<sup>[1]</sup> Its mechanism is the failure of the upper instrumented vertebra (UIV) as well as the failure of the posterior ligamentous complex. Proximal junctional failure (PJF) is the most severe example of PJK and is clinically characterized by neurologic deficits related to spinal cord compression and/or focal angular kyphotic deformity. Known risk factors for PJK/PJF are: sagittal overcorrection of a deformity,<sup>[2,3]</sup> posterior fusion (versus anterior fusion),<sup>[3-5]</sup>

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high pelvic incidence,<sup>[6,7]</sup> older age,<sup>[4,8,9]</sup> high body mass index,<sup>[8,9]</sup> osteoporosis,<sup>[5,8]</sup> fusion to sacrum,<sup>[3,5]</sup> greater change of sagittal vertical axis (SVA),<sup>[5,10,11]</sup> fusion to lower thoracic spine (versus upper thoracic spine),<sup>[9]</sup> pedicle screws at UIV<sup>[12]</sup> (versus transverse process hooks). Less is known about the occurrence of junctional kyphosis (JK)/junctional failure (JF) after multilevel cervicothoracic junction fusion.

The occurrence of JK/JF after multisegmental cervicothoracic fusions has not been extensively investigated. We speculate that fundamental differences exist between cervicothoracic and thoracolumbar fusion surgeries with regards to JK/JF given the differing biomechanical properties of these two distinct anatomical segments of the spine. One key difference may be that lower body weight and a resulting smaller load/force is implicated in fusion surgery of the cervical spine and upper thoracic spine versus lumbar and lower thoracic spine.

This retrospective single-institution experience of three board-certified neurosurgeons aims to define the incidence rate of JK/JF after multisegmental posterior cervicothoracic fusion surgery. Further, we look to establish possible risk factors that may elucidate vulnerable subpopulations before cervicothoracic fusion interventions.

## METHODS

Local ethics committee approval was obtained (Institutional Review Board 19-1118). A search of our institutional records identified 64 consecutive patients operated in a single institution between January 1, 2015 and June 30, 2019, who underwent posterior spinal fusion of at least 5 motion levels spanning the cervicothoracic junction.

Surgery was performed under electrophysiologic monitoring, consisting of somatosensory evoked potential and motor evoked potential. Patients were placed prone with the head fixed in a Mayfield head holder in neutral position. Standard midline incision was followed by subperiosteal dissection and laminectomies, as indicated by the pathology. Placement of C3–C6 lateral mass screws was done under fluoroscopy or free-handed. C1 lateral mass screws and C2 pedicle screws were placed using computed tomography (CT)-guided navigation or fluoroscopy. Occipital plates were placed free-handed and T1–T3 pedicle screws were placed with free-handed or CT-guided technique. In all cases, lordotic titanium rods were used. After decompression and hardware placement, decortication of the remaining lateral masses and transverse processes was performed. Depending on surgeon's preference, either morselized autograft with or without demineralized bone matrix was used around the decorticated

posterior elements. Postoperative imaging consisted of CT scan and X-ray c spine with additional cross-sectional imaging if deemed necessary by the operating surgeon.

Baseline demographic data, as well as details of the surgery, were extracted from the electronic patient files. The occurrence of intraoperative or postoperative complications was noted. Postoperative sagittal parameters were evaluated using a standing cervical X-ray in neutral position. C2 SVA, T1 slope and C2–C7 lordotic angle were measured and documented.

Bone density was assessed by measurement of a mean Hounsfield unit (HU) value in the lower instrumented vertebra (LIV) on preoperative CT scan. A region of interest (ROI) was defined in the axial plane in the mid-body of the LIV and the mean HU value of the same ROI was then noted.

The sagittal parameter C2-SVA, T1 slope angle and C2–C7 angle were correlated with age-adjusted normative values.<sup>[13]</sup>

A univariate analysis was performed to compare the effect of fusion status, level of UIV, level of LIV, bone density assessed by HU measurements in the LIV, C2-SVA, T1 slope angle, C2–C7 lordotic angle on the occurrence of JF/JK.

For the statistical analysis, patients with the above-mentioned variables were categorized as follows: bone density in 3 three groups, HU <150, 150–250, >250; fusion status yes/no/inconclusive; the level of UIV either C0, C1, C2, C3 or C4; level of LIV either T1, T2 or T3; C2-SVA pathologic yes/no; T1 slope angle pathologic yes/no; C2–C7 angle pathologic yes/no.

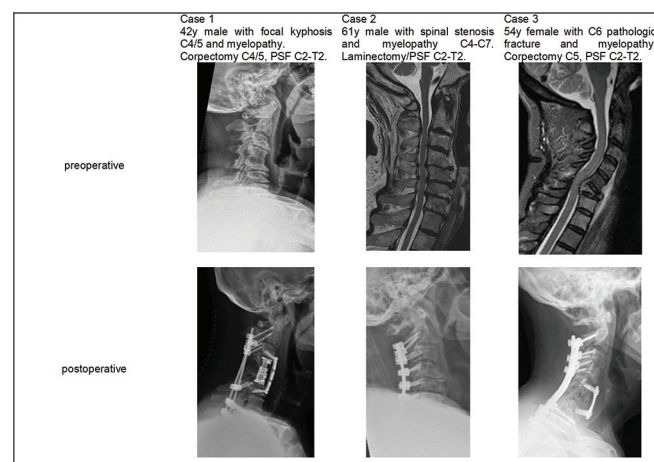
## RESULTS

Out of 64 patients who underwent a surgical procedure at our institution between January 1, 2015 and June 30, 2019 who met inclusion criteria, 46 had sufficiently long follow-up of at least 3 months. An outline of baseline patient characteristics as well as surgical details are given in Table 1. Median follow-up in 46 patients undergoing 47 procedures was 1.1 years. The median patient age was 65.5 years and 74% of patients were female. Indications for surgery were multilevel spinal stenosis (87%), fracture (6.5%), and neoplastic lesions (6.5%). Figure 1 shows three illustrative cases from our cohort. A median of 7 levels were fused with the UIV being C2 (59%), C3 (30%), occiput (4%), and C4 (4%). The LIV included T2 (63%), T1 (35%), and T3 (2%). A total of nine patients had additional anterior cervical discectomy and fusion (ACDF), 5 had additional corpectomy, and one patient had corpectomy plus Ponte osteotomy for fixed focal kyphotic deformity.

**Table 1: Characteristics of patients and surgical procedures**

	Median	Mean	SD	Minimum	Maximum	Proportion (%)
Age (year)	65.5	66.2	10	42.2	84.5	
Sex						
Female						16 (35)
Male						30 (65)
Etiology						
Stenosis						40 (87)
Fracture						3 (6.5)
Tumor						3 (6.5)
UIV						
C0						2 (4)
C1						1 (2)
C2						27 (59)
C3						14 (30)
C4						2 (4)
LIV						
T1						16 (35)
T2						29 (63)
T3						1 (2)
Number of levels fused	7	6.3	1.1	5	9	
ACDF						
1 level						5 (11)
2 level						1 (2)
3 level						3 (7)
ACCF						
1 level						1 (2)
2 level						4 (9)
Ponte osteotomy						1 (2)
Follow-up (years)	1	1.2	0.7	0.3	4	

ACDF: Anterior cervical discectomy and fusion, SD: Standard deviation, LIV: Lower instrumented vertebra, UIV: Upper instrumented vertebra, ACCF: anterior cervical corpectomy and fusion

**Figure 1: Three illustrative cases with pre- and post-operative imaging studies**

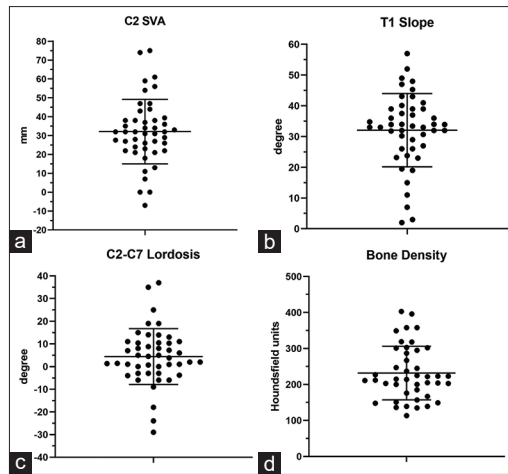
As outlined in Table 2 and Figure 2a-c, sagittal alignment above or below age-adjusted normative values,<sup>[13]</sup> as assessed on standing cervical x rays, was observed in a portion of the cohort: C2-SVA in 29 out of 46 patients (63%), T1 slope angle in 31 out of 46 patients (67%) and C2–C7 lordotic angle global in 35 out of 46 patients (76%). The average values above

and below age-adjusted cutoffs for patients with pathologic sagittal alignment were: mean C2 SVA +15 mm, standard deviation (SD) 11 mm, range +1 mm ± 42 mm; mean T1 slope angle +10°, SD 6°, range +1° ± 22°; mean C2C7 lordotic angle -14°, SD 10°, range 48°–0° [Table 2].

Summative values of bone density, as assessed by HU measurements in the LIV, is given in Figure 2d. Directly procedure-related complications have been observed in 10 patients [Table 3].

At the last follow-up, 36 patients showed solid fusion as assessed on standing cervical X-rays, for which 3 cases were equivocal and 7 showed no solid fusion. Screw loosening in either UIV or LIV was found in two patients. Proximal junction kyphosis was found in two patients, while PJF, Distal JK and Distal JF were not observed [Table 4].

The results of the univariate analysis are given in Table 5. As shown, no variable tested, including fusion status, bone density, level of UIV, level of LIV, C2 SVA, T1 slope, C2 C7 lordosis, correlated with the occurrence of JK or JF. However,



**Figure 2:** Distribution of postoperative sagittal parameters (a) C2 sagittal vertical axis, (b) T1 slope angle, (c) C2C7 lordotic angle) as well as baseline bone density as assessed by hounsfield unit measurements in the lower instrumented vertebra, inlet, (d) individual inlets show median, average, standard deviation, minimum and maximum value

**Table 2: Postoperative complications**

Complication	Incidence (%)
Infection or wound dehiscence	1 (2)
Epidural hematoma or seroma	2 (4)
CSF leak	1 (2)
Dysphagia	2 (4)
C5 palsy	1 (2)
New neurologic deficits	1 (2)
Respiratory failure (most likely due to laryngeal swelling after intubation)	1 (2)
Brisk perivertebral venous plexus bleeding, leading to abortion of the surgery	1 (2)

CSF: Cerebrospinal fluid

two variables, fusion status and T1 slope angle were shown to have a tendency toward significance.

## DISCUSSION

JK and JF after multi-segmental cervicothoracic posterior fusions spanning a median of seven segments occurred in only 4% of patients. Notably, another 4% of patients showed screw loosening in either UIV or LIV, which could progress to JK/JF. This incidence rate is markedly lower than for PJK/PJF of the lower thoracic spine after thoracolumbar fusions. No statistically clear risk factors were identified.

It has been established that PJK/PJF is a much more frequently observed problem in the thoracic spine after thoracolumbar fusion.<sup>[14]</sup> Nicholls *et al.*<sup>[15]</sup> conducted a series in which 440 patients<sup>[15]</sup> underwent thoracolumbar deformity correction and 36% of patients developed PJK, with 41% of these requiring revision surgery. We speculate that the reason for the marked difference between PJK following

thoracolumbar fusion versus cervicothoracic fusions is explained by the different biomechanical properties of the two fusion procedures. The loads concentrated on the fixation points in UIV and LIV are significantly lower in the cervical spine and upper thoracic spine as compared to the lower thoracic levels.

The importance of achieving proper sagittal balance following spinal surgery has been intensively investigated in recent years. You *et al.*<sup>[16]</sup> showed that adjacent segment disease (ASD) following ACDF was more frequent in patients with higher C2-SVA as well as higher T1 slope angle. Many authors recognize that a C2-SVA of more than 40–50 mm correlates with adverse clinical outcomes and should thus be addressed if surgery of the cervical spine is planned.<sup>[17–19]</sup> Further, the C2–C7 lordotic angle has to match the T1 slope angle to keep the C2-SVA within the normal limits.<sup>[20]</sup> Hyun *et al.*<sup>[20]</sup> demonstrated that a mismatch of  $>26^\circ$  is considered pathologic. The study cohort had sagittal parameters outside of the age-adjusted normative values as defined by Attiah *et al.*<sup>[13]</sup> However, the misalignment was mild, as shown in Table 2 and Figure 2. The average C2-SVA was 32 mm for the cohort, lower than the threshold definition of significant deformity for previous studies.<sup>[17–20]</sup> This lower CS-SVA may explain why a statistically significant correlation was found between the occurrence of JK/JF and the sagittal parameters.

As shown by Karikari and Metz<sup>[21]</sup> nonunion can be a contributing factor in the development of JF. Similarly, the results of our study suggest that nonunion may play a role in the development of JK/JF in the cervicothoracic spine. After a median follow-up of 1.1 years in our series, the fusion rate was 78% and it could be assumed that this rate further increases with longer follow-up. The potential link between nonunion and JK/JF should lead the surgeon to ensure that fusion is indeed established, either by optimizing the surgical strategy or by eliminating risk factors such as postoperative nonsteroidal anti-inflammatory drugs,<sup>[22]</sup> steroids,<sup>[23]</sup> or proton-pump inhibitors.<sup>[24]</sup>

Reduced bone density is known to be a major contributor to worse clinical outcomes after spinal fusion.<sup>[25]</sup> Interestingly, reduced bone mineral density did not seem to have an effect on the development for JK/JF in our study. Since DEXA scans were not available for all patients in our study, we chose to use the mean HU measured in the LIV on preoperative CT as a surrogate. It has been shown in previous studies that vertebral HU correlates to DEXA measurements of the spine. For instance, Meredith *et al.* have shown that HU values below 199 indicated an increased risk for osteoporosis-related fractures.<sup>[26]</sup> The fact that lower vertebral HU values did not affect the primary endpoint of this study could be due to

**Table 3: Outcome at last follow-up**

	Patients (%)
Bony fusion	
Yes	36 (78)
No	7 (15)
Undetermined	3 (7)
Screw loosening	2 (4)
PJK	2 (4)
DJK	0
PJF	0
DJF	0

PJK: Proximal junctional kyphosis, PJF: Proximal junctional failure, DJK: Distal junctional kyphosis, DJF: Distal junctional failure

**Table 4: Result of univariate analysis**

	dF (between groups)	dF (within group)	F	P
Fusion status	1	43	3.84	0.057
Bone density	1	43	1.6	0.213
UIV	3	46	0.83	0.483
LIV	1	46	1.76	0.191
C2 SVA	1	46	0.31	0.582
C2C7	1	46	1.36	0.25
T1 slope	1	45	0.355	0.066

LIV: Lower instrumented vertebra, UIV: Upper instrumented vertebra, dF: Degree of freedom

**Table 5: Radiographic parameters**

	C2C7 lordosis (°)	C2 SVA (mm)	T1 slope (°)
Whole cohort			
Mean	4.4	32	32
SD	12.2	16.9	11.8
Range	-29-37	-7-75	2-57
Fraction of patients with pathologic alignment (%)	76	63	67
Subgroup with pathologic alignment			
Mean	-14	15.2	9.7
SD	10.4	10.7	5.8
Range	-48-0	1-42	1--22

SD: Standard deviation

the moderately decreased average bone density in this study population. Furthermore, we speculate that fewer forces and loads are transferred to the fixation points in the case of cervicothoracic fusions versus thoracolumbar fusions.

While previous studies have shown that long cervical fusions should include the cervicothoracic junction (versus stopping at C7),<sup>[27]</sup> our study found no evidence that LIV at either T1, T2 or T3 had an impact on the occurrence of JK/JF. In clinical practice, the motion segment C2/C3 usually is not involved in significant degenerative changes. Consequently, surgeons must decide whether or not to include C2 into a multilevel fusion. While our study did not investigate the occurrence of ASD, we

can conclude that there is no difference in the development of JF/JK between UIV C2 and UIV C3 based on our analysis.

Limitations of the study are the rather short follow-up period. However, we maintain that a conclusion can be drawn given previous literature on PJK/PJF following thoracolumbar deformity surgeries, showing that JK/JF occurs in most cases within 3 months after the index surgery. For example, in a literature review on PJK and PJF after thoracolumbar surgery, Lau *et al.*<sup>[1]</sup> found that 66% of events took place within 3 months after the index surgery. Furthermore, the study population showed only a moderately pathologic sagittal profile. The greater sagittal imbalance may increase the rate of JK/JF and explain why a higher T1 slope angle showed a trend toward significance in our analysis.

Future research may aim at better defining the impact of sagittal imbalance and decreased bone density on the development of JK/JF by analyzing a larger cohort. The extent of generalizability would also be enhanced with a population that is characterized by more heterogeneous values in sagittal alignment and bone density.

## CONCLUSION

In this retrospective single-institution investigation, JK was a rare event observed in only two patients (4%), while another two patients showed signs of screw-loosening in the LIV (4%). This finding is contrary to the high incidence rate of JK/JF after thoracolumbar fusions. Neither bone density, fusion status or level of UIV or LIV had an influence on its occurrence, even though there was a tendency toward significance for nonunion and pathologic T1 slope angle.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Lau D, Clark AJ, Scheer JK, Daubs MD, Coe JD, Paonessa KJ, *et al.* Proximal junctional kyphosis and failure after spinal deformity surgery: A systematic review of the literature as a background to classification development. *Spine (Phila Pa 1976)* 2014;39:2093-102.
2. Lowe TG, Kasten MD. An analysis of sagittal curves and balance after Cotrel-Dubousset instrumentation for kyphosis secondary to Scheuermann's disease. A review of 32 patients. *Spine (Phila Pa 1976)* 1994;19:1680-5.
3. Yagi M, Akilah KB, Boachie-Adjei O. Incidence, risk factors and classification of proximal junctional kyphosis: Surgical outcomes review of adult idiopathic scoliosis. *Spine (Phila Pa 1976)* 2011;36:E60-8.
4. Kim YJ, Bridwell KH, Lenke LG, Glatte CR, Rhim S, Cheh G. Proximal



- junctional kyphosis in adult spinal deformity after segmental posterior spinal instrumentation and fusion: Minimum five-year follow-up. *Spine (Phila Pa 1976)* 2008;33:2179-84.
5. Yagi M, King AB, Boachie-Adjei O. Incidence, risk factors, and natural course of proximal junctional kyphosis: Surgical outcomes review of adult idiopathic scoliosis. Minimum 5 years of follow-up. *Spine (Phila Pa 1976)* 2012;37:1479-89.
  6. Lonner BS, Newton P, Betz R, Scharf C, O'Brien M, Sponseller P, *et al.* Operative management of Scheuermann's kyphosis in 78 patients: Radiographic outcomes, complications, and technique. *Spine (Phila Pa 1976)* 2007;32:2644-52.
  7. Maruo K, Ha Y, Inoue S, Samuel S, Okada E, Hu SS, *et al.* Predictive factors for proximal junctional kyphosis in long fusions to the sacrum in adult spinal deformity. *Spine (Phila Pa 1976)* 2013;38:E1469-76.
  8. O'Leary PT, Bridwell KH, Lenke LG, Good CR, Pichelmann MA, Buchowski JM, *et al.* Risk factors and outcomes for catastrophic failures at the top of long pedicle screw constructs: A matched cohort analysis performed at a single center. *Spine (Phila Pa 1976)* 2009;34:2134-9.
  9. Bridwell KH, Lenke LG, Cho SK, Pahys JM, Zebala LP, Dorward IG, *et al.* Proximal junctional kyphosis in primary adult deformity surgery: Evaluation of 20 degrees as a critical angle. *Neurosurgery* 2013;72:899-906.
  10. Cammarata M, Aubin CÉ, Wang X, Mac-Thiong JM. Biomechanical risk factors for proximal junctional kyphosis: A detailed numerical analysis of surgical instrumentation variables. *Spine (Phila Pa 1976)* 2014;39:E500-7.
  11. Kim HJ, Yagi M, Nyugen J, Cunningham ME, Boachie-Adjei O. Combined anterior-posterior surgery is the most important risk factor for developing proximal junctional kyphosis in idiopathic scoliosis. *Clin Orthop Relat Res* 2012;470:1633-9.
  12. Wang J, Zhao Y, Shen B, Wang C, Li M. Risk factor analysis of proximal junctional kyphosis after posterior fusion in patients with idiopathic scoliosis. *Injury* 2010;41:415-20.
  13. Attiah M, Gaonkar B, Alkhalid Y, Villaroman D, Medina R, Ahn C, *et al.* Natural history of the aging spine: A cross-sectional analysis of spinopelvic parameters in the asymptomatic population. *J Neurosurg Spine* 2019;32:63-8.
  14. Hyun SJ, Lee BH, Park JH, Kim KJ, Jahng TA, Kim HJ. Proximal junctional kyphosis and proximal junctional failure following adult spinal deformity surgery. *Korean J Spine* 2017;14:126-32.
  15. Nicholls FH, Bae J, Theologis AA, Eksi MS, Ames CP, Berven SH, *et al.* Factors associated with the development of and revision for proximal junctional kyphosis in 440 consecutive adult spinal deformity patients. *Spine (Phila Pa 1976)* 2017;42:1693-8.
  16. You J, Tang X, Gao W, Shen Y, Ding WY, Ren B. Factors predicting adjacent segment disease after anterior cervical discectomy and fusion treating cervical spondylotic myelopathy: A retrospective study with 5-year follow-up. *Medicine (Baltimore)* 2018;97:e12893.
  17. Cho SK, Safir S, Lombardi JM, Kim JS. Cervical spine deformity: Indications, considerations, and surgical outcomes. *J Am Acad Orthop Surg* 2019;27:e555-e567.
  18. Virk S, Passias P, Lafage R, Klineberg E, Mundis G, Protopsaltis T, *et al.* Intraoperative alignment goals for distinctive sagittal morphotypes of severe cervical deformity to achieve optimal improvements in health-related quality of life measures. *Spine J* 2020;20:1267-75.
  19. Nemani VM, Derman PB, Kim HJ. Osteotomies in the Cervical Spine. *Asian Spine J* 2016;10:184-95.
  20. Hyun SJ, Kim KJ, Jahng TA, Kim HJ. Relationship between t1 slope and cervical alignment following multilevel posterior cervical fusion surgery: Impact of T1 slope minus cervical lordosis. *Spine (Phila Pa 1976)* 2016;41:E396-402.
  21. Karikari IO, Metz LN. Preventing pseudoarthrosis and proximal junctional kyphosis: How to deal with the osteoporotic spine. *Neurosurg Clin N Am* 2018;29:365-74.
  22. Lumawig JM, Yamazaki A, Watanabe K. Dose-dependent inhibition of diclofenac sodium on posterior lumbar interbody fusion rates. *Spine J* 2009;9:343-9.
  23. Leven D, Cho SK. Pseudarthrosis of the cervical spine: Risk factors, diagnosis and management. *Asian Spine J* 2016;10:776-86.
  24. Mangan JJ 3<sup>rd</sup>, Divi SN, McKenzie JC, Stull JD, Conaway W, Casper DS, *et al.* Proton pump inhibitor use affects pseudarthrosis rates and influences patient-reported outcomes. *Global Spine J* 2020;10:55-62.
  25. Rometsch E, Spruit M, Zigler JE, Menon VK, Ouellet JA, Mazel C, *et al.* Screw-related complications after instrumentation of the osteoporotic spine: A systematic literature review with meta-analysis. *Global Spine J* 2020;10:69-88.
  26. Meredith DS, Schreiber JJ, Taher F, Cammisa FP Jr., Girardi FP. Lower preoperative Hounsfield unit measurements are associated with adjacent segment fracture after spinal fusion. *Spine (Phila Pa 1976)* 2013;38:415-8.
  27. Truumees E, Singh D, Geck MJ, Stokes JK. Should long-segment cervical fusions be routinely carried into the thoracic spine? A multicenter analysis. *Spine J* 2018;18:782-7.