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ORIGINAL ARTICLE

Outcomes of non-contiguous two-level anterior cervical discectomy and fusion in patients with degenerative cervical myelopathy: a retrospective study

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Abstract

Background Non-contiguous two-level Anterior Cervical Discectomy and Fusion (ACDF) may be a viable option for patients with degenerative cervical myelopathy and imaging-evident spine and radicular compression at two non-contiguous cervical levels. The risk of hastening degeneration and triggering Adjacent Segment Disease at the spine levels located between the fused levels is a putative adverse event, which was assessed in a few studies. The aim of this study is to investigate the clinical outcomes of patients undergoing non-contiguous two levels ACDF and to assess biomechanical modifications at non-fused segments.

Method We retrospectively reviewed all patients with noncontiguous two-level spine and radicular compression, who underwent simultaneous noncontiguous two-level ACDF at our center. We analyzed clinical and radiological outcomes and investigated the rate of adjacent segment disease. Radiographic parameters were calculated on pre- and postoperative images.

Results Thirty-two patients underwent simultaneous noncontiguous two-level ACDF for cervical myelo-radiculopathy between 2015 and 2021 and were followed up for a mean period of 43.3 months. For all patients, the mJOA score significantly improved from 14.57 ± 2.3 to 16.5 ± 2.1 ($p<0.01$) and the NDI score significantly decreased from 21.45 ± 4.3 to 12.8 ± 2.3 ($p<0.01$) postoperatively. Cervical lordosis increased after surgery (from 9.65° ±9.47 to 15.12° ± 6.09); intermediate disc height decreased (5.68 mm ± 0.57 to 5.27 mm ±0.98); the ROMs of intermediate (from 12.45 ± 2.33 to 14.77 ± 1.98), cranial (from 14.63 ± 1.59 to 15.71 ± 1.02), and caudal (from 11.58 ± 2.32 to 13.33 ± 2.67) segments slightly increased. During follow-up assessment, in one patient the myelopathy worsened due to spine compression at the intermediate level.

Conclusions Simultaneous and non-contiguous two-level ACDF is a safe and effective procedure. The occurrence of postoperative adjacent and intermediate segment disease is rare.

Keywords Degenerative Cervical Myelopathy · Non-contiguous ACDF · Cervical biomechanics · Skip ACDF

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Introduction

Anterior Cervical Discectomy and Fusion (ACDF) is an established surgical technique for degenerative cervical myelopathy (DCM) [2, 6]. Worsening myelopathy due to spine degenerative changes and spinal cord compression at the spinal segments adjacent to those fused, known as adjacent segment disease (ASD), is a possible risk of ACDF [14].

Occasionally, patients with myelopathic and radiculopathic signs at two non-contiguous cervical levels require surgical treatment, prompting the decision of whether to fuse the intermediate level. Biomechanical studies using finite element analysis suggest that when cervical segments are fused, the overall mechanical stress increases in adjacent unfused levels [1, 7]. Therefore, avoiding fusion of the intermediate level might decrease surgical time and preserve more mobility but can also exponentially increase mechanical stress on the intermediate level, theoretically accelerating its degeneration.

Conversely, treating also the intermediate level would eliminate the risk of its degeneration but would enhance mechanical stress and the risk of ASD in adjacent cranial and caudal levels. This surgical dilemma is further heightened by the lack of substantial data in literature. In vivo, biomechanical stress on segments adjacent to fused ones can be indirectly estimated by analyzing changes in flexion-extension mobility and intervertebral disc height [7]. Our study, which encompasses the largest monocentric patient cohort in the literature, seeks to evaluate biomechanical alterations of the intermediate and adjacent levels and their clinical implications, with a focus on patient-reported outcomes, neurological recovery, and the incidence of complications and ASD.

Material and Methods

The study received approval from the local ethics committee (approval number 1456614) and adhered to the 1964 Declaration of Helsinki principles and its amendments.

We conducted a monocentric retrospective analysis of consecutive patients treated with two simultaneous non-contiguous levels ACDF for DCM between January 2015 and December 2021 at the Department of Neurosurgery in Humanitas Research Hospital (Milan, Italy).

The inclusion criteria were: 1) age 18 years or older; 2) two non-contiguous levels of DCM and minimal or no spinal canal stenosis with the absence of radiological signs of myelopathy at the intermediate level on MRI (Fig. 1); 3) a minimum clinical and radiological follow-up of 12 months.

The exclusion criteria were: 1) prior cervical spine surgeries and 2) other neurological conditions that could alter clinical evaluation. In our center, ACDF is performed using a standard technique [16]. Fusion is achieved using titanium or PEEK intersomatic cages with a mini-plating integrated system.

We collected demographic information (age, sex), surgical details (operative time, treated cervical levels, length of hospital stay), and clinical parameters (modified Japanese Orthopedic Association [mJOA] score, Neck Disability Index [NDI] Italian version questionnaire [10], Nurick scale, Numeric Pain Rating Scale [NPRS]).

Clinical outcomes were evaluated both in terms of Delta (difference between postoperative value and preoperative value) and MCID (Minimal Clinically Important Difference). The MCID for mJOA is 3 points for severe (mJOA 11 or lower), 2 points for moderate (12-13-14), and 1 point for mild myelopathy (over 15) [17]. MCID for NDI is 7.5 points, for NPRS is 2 points, while for Nurick can be considered 1 point.

Radiological analysis was performed independently by two authors (AB, MDR) and it was conducted on the preoperative and last follow-up static and dynamical cervical radiographs. We assessed intermediate disc height (IDH), functional spinal unit (FSU) angle, and the range of motion (ROM) of the intermediate level. IDH was measured using a perpendicular line from the middle of the inferior endplate to the superior endplate in the same disc space. The ROM was calculated as the sum of the Cobb angle at maximum flexion and maximum extension (Fig. 2). We also calculated the ROM of the cranial and caudal adjacent levels and the global C2-C7 ROM and cervical lordosis angle.

The type and number of observed complications were collected. Pseudoarthrosis and ASD rates were calculated. ASD was defined as radiological degeneration of the intermediate or the adjacent levels with symptomatic spinal cord compression.

Statistical analysis used Stata/MP® 13.1 for Mac (StataCorp LP, College Station, TX). Descriptive statistics were utilized to summarize the demographic characteristics of the patient cohort, including mean, standard deviation, and range for continuous variables, while categorical variables were expressed as frequencies and percentages. Descriptive statistics were also used to summarize radiographic parameters. Repeated measures analysis of variance or paired t-test was used to assess continuous clinical and radiographic data between time points. $p < 0.05$ was considered statistically significant.

Results

Of the total 1523 cases of ACDF collected from January 2015 to December 2021, we identified 32 consecutive patients treated at two non-contiguous levels for DCM.

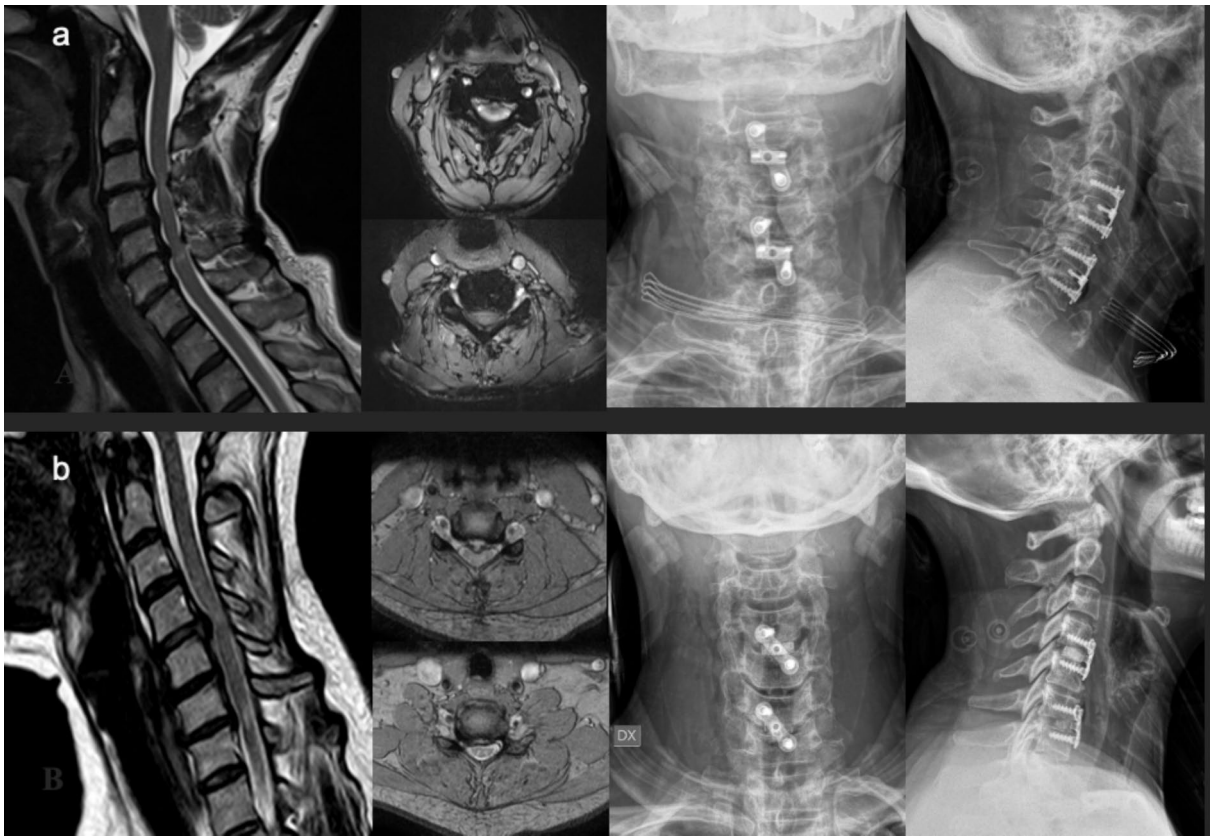

Fig. 1 Example of two patients ("**a**" and "**b**") who presented non-contiguous 2-level myelopathy. On the left of each line, there is the preoperative MRI, while on the right there are the postoperative X-rays. Patient "**a**" was treated for C3C4 and C5C6 myelopathy, while patient "**b**" was treated for C4C5 and C6C7 myelopathy

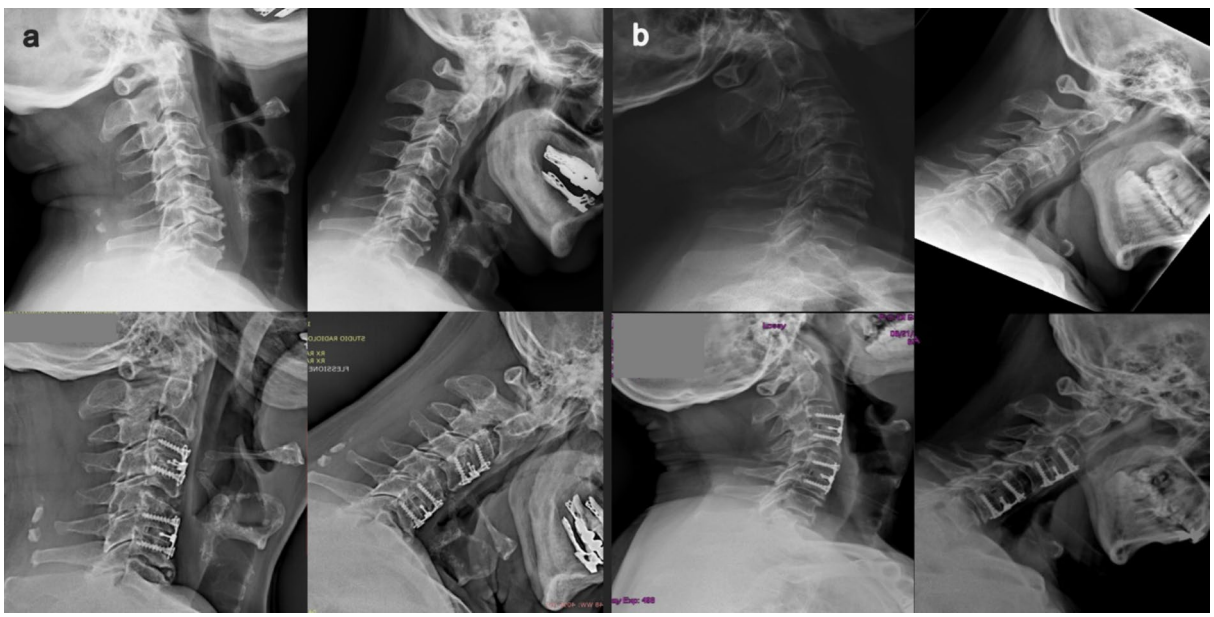

Fig. 2 Example of two different patients "**a**" and "**b**" who performed dynamic radiographs before surgery and at last follow-up

Among them 22 were males. Mean age was 57.3 years old (range 37-78). All patients presented with myelopathy, while 14 patients had also adjunctive radiculopathic symptoms. The most common non-contiguous levels were C3C4-C5C6 (24/32, 75%), followed by C4C5-C6C7 (25%). The mean follow-up was 43.3 months (range 14-60). This part of the results is summarized in Table 1. Complication rate was 9.3% (3/32) and ASD at the intermediate level was observed in only 1 patient (3.1%).

Clinical Outcomes

Clinical outcomes are presented in Table 2. The mean preoperative mJOA was 14.57. The majority of patients had a substantial clinical improvement. The mJOA score improved from 14.57 ± 2.3 to 16.5 ± 2.1 postoperatively (p-value< 0.01) and the NDI score decreased from 21.45 ± 4.3 to 12.8 ± 2.3 postoperatively (p-value <0.01). Nurick score improved from 2.55± 0.9 to 1.27±0.7, by an average of 1.27 points (p-value <0.01). NPRS improved from 5.3±1.3 to 1.2±0.8 (p-value <0.01). MCID was, respectively for the four measured outcome parameters, 81%, 66%, 78%, and 87%.

Radiological Outcomes

Radiographic evaluation on static radiograph showed improvement of cervical lordosis (from 9.65° ±9.47 to 15.12° ± 6.09), a slight reduction of the IDH (5.68 mm ± 0.57 to 5.27 mm ±0.98), and substantially similar intermediate FSU angle (2.41° ± 4.23 to 3.01°±2.89). On flexion-extension radiographs, we observed an evenly distributed increase of intermediate (from 12.45 ± 2.33 to 14.77 ± 1.98), cranial (from 14.63 ± 1.59 to 15.71 ± 1.02), and caudal (from 11.58 ± 2.32 to 13.33 ± 2.67) ROMs.

Table 1 General Characteristics and Surgical Details of Patient Population

Variable	Details
No. Of patients	32
Age (range), years	57.31 (37-78)
Sex (m/f)	22/10
Symptoms	
Myelopathy	18
Myeloradiculopathy	16
Levels	
C3C4 C5C6	24
C4C5 C6C7	8
Operative time (range), min	98.2 (63-149)
Lenght of hospital stay (range), days	4 (2-16)
Follow-up (range), months	43.3 (14-60)

Table 2 Clinical Outcomes

Variable (N. 32)	Preop	Last followup	Delta	p value	MCID
mJOA	14.57 ± 1.3	16.5 ± 1.1	+1.93	< 0.01	81%
NDI	21.45 ± 3.8	12.8 ± 2.7	-8.65	< 0.01	66%
Nurick	2.55 ± 0.6	1.27 ± 0.5	-1.28	< 0.01	78%
NPRS	5.3 ± 1.3	1.2 ± 1.0	- 4.1	<0.01	87%

Overall cervical ROM decreased from 39.87°±10.82 to 34.66°±9.63. For this part of the results refer to Table 3.

Complications and ASD

Among complications we observed 1 case of hematoma, which was drained with no permanent neurological injury; 1 case of pseudoarthrosis with screws pull out and plate dislocation two years after surgery causing mild dysphagia; and 1 case of progressive worsening of myelopathy at the ACDF levels, that required a posterior multilevel laminectomy with fusion.

Only 1 case of intermediate-level ASD was observed in a 49-year-old male with no comorbidity, who was firstly treated with a C3C4-C5C6 ACDF for myeloradiculopathy (mJOA 15), skipping the intermediate level (Suzuki grade II on preoperative MRI) because no significant canal stenosis or spinal cord compression was observed. After significant initial clinical improvement, 38 months later he presented new myelopathic symptoms and left-sided brachialgia. ASD was diagnosed and the patient was treated with a C4C5 ACDF. (Fig. 3)

Table 3 Radiographic Parameters

Variable (N. 32)	Pre-op	Last follow-up
Cervical Lordosis	9.65 ± 9.47	15.12 ± 6.09
Disc Height Intermediate Level	5.68 ± 0.57	5.27 ± 0.98
FSU angle Intermediate Level	2.41 ± 4.23	3.01 ± 2.89
ROM Intermediate Level	12.45 ± 2.33	14.77 ± 1.98
ROM Cranial Level	14.63 ± 1.59	15.71 ± 1.02
ROM Caudal Level	11.58 ± 2.32	13.33 ± 2.67
ROM C2-C7	39.87 ± 10.82	34.66 ± 9.63

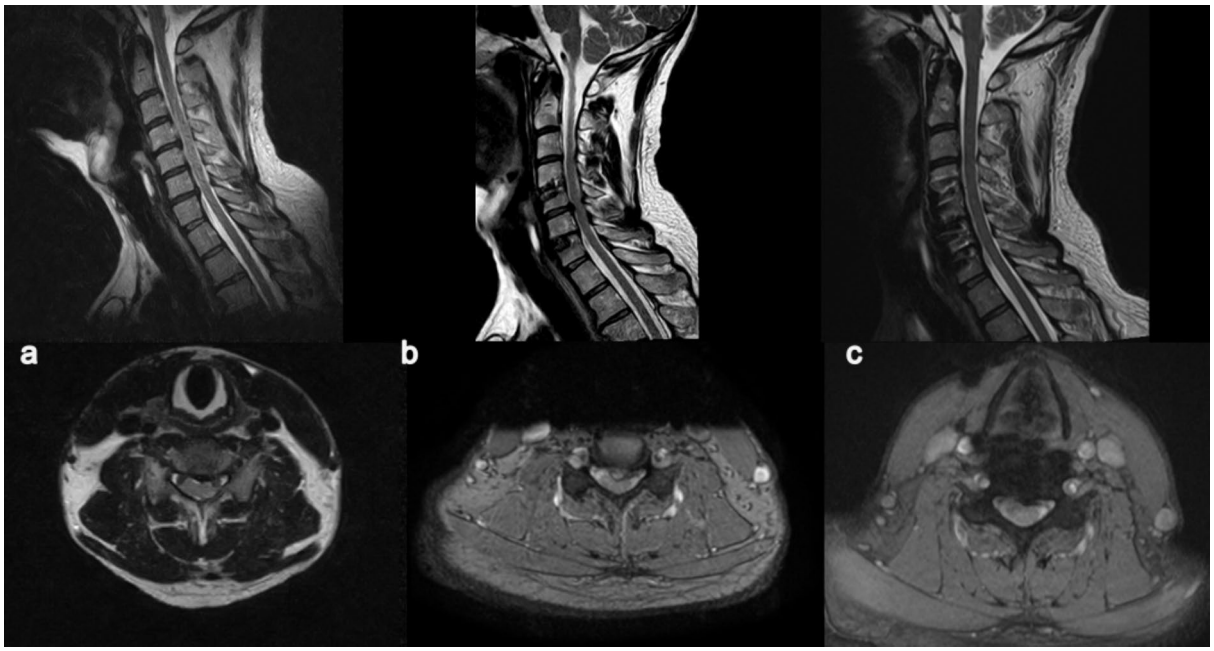

Fig. 3 The only patient who developed ASD during followup. "**a**" before index surgery. "**b**" 38 months after C4C5 and C6C7 ACDF, where new myelopathy signal at C5C6 can be seen. "**c**" last followup after C4C5 ACDF. No residual compression on the spinal cord can be detected

Discussion

In this retrospective study, we observed that simultaneous and non-contiguous two-level ACDF is a safe and effective procedure for most patients. ASD at the intermediate level was rare, and adverse events were uncommon. Ultimately, we found that the ROM, an indirect measure of segment-wise stress, was only slightly increased at both the adjacent and intermediate spinal levels.

The technique of fusing two non-contiguous spine segments with ACDF, while sparing the intermediate level in cases of spine compression at two non-adjacent spinal levels, was introduced to reduce biomechanical stress and potentially prevent degeneration at the upper and lower spinal levels relative to the fused segment. This technique is based on the studies by Park et al. [11] and Dmitriev et al. [5], who observed that a longer fused cervical spinal segment correlated with greater compensatory biomechanical stress on adjacent levels compared to a single-level ACDF. To date, only a few studies have investigated the outcomes and risk of ASD in patients undergoing simultaneous ACDF of two non-contiguous levels. Qizhi et al. presented a case series of 17 patients treated with zero-profile cages, demonstrating favorable clinical outcomes with only one case of clinical ASD 52 months post-operation [12]. Similarly, Bisson et al. reported positive clinical outcomes in 17 patients without any ASD cases. However, the follow-up was limited to 26 months, and the instrumentation and graft type were heterogeneous [3]. Wang et al., using self-locking stand-alone cages, achieved comparable clinical results, with radiological but not clinical evidence of three ASDs observed at 2 inferior adjacent levels and 1 intermediate segment [18]. Recently, in another case series limited to 19 patients treated with zero-profile cages, Shi et al. achieved good clinical outcomes with no evidence of clinical ASD at 24 months follow-up [15]. Our results are comparable with those studies, as we observed significant improvement in all clinical outcomes in most patients and a low rate of symptomatic ASD at an intermediate to long follow-up (mean 43.3 months).

From a biomechanical viewpoint, fusing multiple cervical spine segments redistributes mechanical stress on the remaining unfused levels. Therefore, sparing the intermediate segment between two fused levels is supposed to limit the increase of biomechanical stress on the remaining cervical spine segments. This would consequently prevent degeneration of further levels and, ultimately, worsening of spine compression and myelopathy. In our study, the ROM, which was considered a surrogate for segment-wise mechanical stress, was increased on all unfused intermediate and adjacent levels, even if only slightly, compared to the preoperative level. This result contrasts with those of Shi et al., who found no difference in intermediate-level ROM between preoperative and 3- and 24-month postoperative dynamic radiographs [15]. This difference might be explained by the fact that their study sample was limited to 15 of the 19 total patients, and their follow-up extended to only 24 months, not analyzing medium and long-term effects. However, the lack of a control group of patients undergoing three contiguous levels ACDF doesn't

allow us to make direct comparisons in terms of ROM variations in the postoperative period at the adjacent non-fused levels, and therefore to draw conclusions on the superiority of fusing or sparing the intermediate level. In this regard, a single study in the literature by Finn et al. using finite element analysis demonstrated that an intermediate segment flanked by two fused segments doesn't experience additional strain due to its position [7]. Indeed, compared to a three-level fusion, a two-level non-contiguous fusion conserves an additional motion segment, with all other preserved levels experiencing less stress. Additionally, Fuller et al. demonstrated that one, two, and three levels ACDF do not increase stress forces only on the adjacent level but rather uniformly across all unfused segments [8]. Based on our findings and the results of these studies, we believe that, even without a control group, sparing the intermediate level whenever possible leads to better and more balanced force redistribution across all unfused levels.

Finally, we noted that the overall cervical spine lordosis angle was higher after surgery compared to the preoperative level. Increased cervical lordosis might reduce degenerative changes occurring at the non-fused cervical spine levels, as Hwang et al. demonstrated in their study showing that increasing lordosis during anterior cervical fusion decreases adjacent segment motion [9]. The increased lordosis observed in our patients, likely related to the use of lordotic cages for interbody fusion, may have slowed degenerative changes and contributed to the low rate of ASD occurrence.

Limitations

The results of this study should be interpreted in the context of several limitations. The retrospective design and single-center nature of this study limit its power and generalizability. The lack of a control group undergoing ACDF of the intermediate segment between two levels with spine compression doesn't allow for direct comparison. The small number of patients included in the study doesn't allow for cohort-wise analyses. Additionally, the follow-up period, while intermediate, may not be sufficient to capture all cases of ASD, which typically occurs over several years [4, 13]. Finally, our definition of ASD as symptomatic spinal cord compression requiring surgery is stringent and may contribute to a lower observed rate of ASD. An additional focus on radiographic ASD would enhance the study's value. Future studies should include longer follow-up periods and consider a more inclusive definition of ASD.

Conclusions

Performing a non-contiguous two-level ACDF is safe and effective for patients with myeloradicular symptoms at two non-adjacent levels. Over a medium-term follow-up period, the development of clinical ASD at the intermediate or adjacent segments is rare.

Author Contribution Conceptualization: Ali Baram, Marco Riva, Mario De Robertis; Methodology: Maurizio Fornari; Formal analysis and investigation: Ali Baram, Mario De Robertis; Writing - original draft preparation: Ali Baram, Gabriele Capo, Carlo Brembilla; Writing - review and editing: Andrea Franzini, Zefferino Rossini; Supervision: Franco Servadei, Federico Pessina.

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Declarations

Ethics Approval The study received approval from the local ethics committee (approval number 1456614) and adhered to the 1964 Declaration of Helsinki principles and its amendments

Competing interests All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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