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Biomechanics of Hybrid Anterior Cervical Fusion and Artificial Disc Replacement in 3-Level Constructs: An *In Vitro* Investigation

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: The ideal surgical approach for cervical disk disease remains controversial, especially for multilevel cervical disease. The purpose of this study was to investigate the biomechanics of the cervical spine after 3-level hybrid surgery compared with 3-level anterior cervical discectomy and fusion (ACDF).

Material/Methods: Eighteen human cadaveric spines (C2-T1) were evaluated under displacement-input protocol. After intact testing, a simulated hybrid construct or fusion construct was created between C3 to C6 and tested in the following 3 conditions: 3-level disc plate disc (3DPD), 3-level plate disc plate (3PDP), and 3-level plate (3P).

Results: Compared to intact, almost 65~80% of motion was successfully restricted at C3-C6 fusion levels ($p<0.05$). 3DPD construct resulted in slight increase at the 3 instrumented levels ($p>0.05$). 3PDP construct resulted in significant decrease of ROM at C3-C6 levels less than 3P ($p<0.05$). Both 3DPD and 3PDP caused significant reduction of ROM at the arthrodesis level and produced motion increase at the arthroplasty level. For adjacent levels, 3P resulted in markedly increased contribution of both upper and lower adjacent levels ($p<0.05$). Significant motion increases lower than 3P were only noted at partly adjacent levels in some conditions for 3DPD and 3PDP ($p<0.05$).

Conclusions: ACDF eliminated motion within the construct and greatly increased adjacent motion. Artificial cervical disc replacement normalized motion of its segment and adjacent segments. While hybrid conditions failed to restore normal motion within the construct, they significantly normalized motion in adjacent segments compared with the 3-level ACDF condition. The artificial disc in 3-level constructs has biomechanical advantages compared to fusion in normalizing motion.

MeSH Keywords: **Arthrodesis • Biomechanical Phenomena • Cervical Vertebrae • Total Disc Replacement • Two-Hybrid System Techniques**

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Background

Radiculopathy and myelopathy from degenerative, inflammatory, and traumatic processes have been successfully treated with anterior cervical discectomy and fusion (ACDF) [1,2]. Despite clinical success with fusion treatment, there are concerns regarding the long-term effects of fusion on the cervical spine. Hilibrand et al. [3] reported on the incidence of radiculopathy and myelopathy at adjacent segment to a cervical fusion and found that 25% of ACDF patients will have symptomatic adjacent segment deterioration (ASD) within 10 years of ACDF at a rate of 2.9% each year. It is believed that although some changes in ASD occur naturally, the effects of fusion disturb the biomechanics, most likely increasing the incidence of ASD. *In vitro* studies demonstrated that intradiscal pressures, shear strains, and motion increased in upper and lower segments adjacent to fusion levels [4–7]. Recently, artificial cervical disc replacement (ACDR) has become the alternative to fusion, with the potential to preserve the motion of the instrumented level and to prevent overload of the adjacent levels and subsequent ASD [8]. ACDR has been proven to be beneficial in terms of avoiding the deleterious effects of fusion [9]. Furthermore, these benefits are more explicit in the context of multilevel cervical surgeries [10].

However, indications for ACDR are more stringent and hypermobility of the operative levels may occur, which lead to the limitation of multilevel ACDR [8,11]. Clinical studies regarding hybrid combinations of fusion and non-fusion have been reported, with improved total motion and earlier recovery and return to work [12–15]. Biomechanical studies of 2-level hybrid ACDF and ACDR have demonstrated advantages of the hybrid in reducing compensatory adjacent motion and reduced internal stresses in the construct [4,16–21]. In a clinical study, Kang el al. [15] reported that the hybrid construct is a safe and effective alternative for 3-level cervical disk disease. However, there are few reported *in vitro* biomechanical studies of 3-level hybrid constructs. The hypothesis was that the motion response of disc replacement adjacent to fusion was comparable to a stand-alone disc replacement, and the non-operated segments in a hybrid construct would experience significantly less motion than with a fusion. This study is a progression to 3-level from the 1- and 2-level biomechanical studies because 3 levels of fusion are common and hybrid combinations either performed initially or for revision of ASD are more common today.

The objective of the present study was to compare the 3-level ACDF to combinations of ACDR and ACDF with displacement controlled kinematics at instrumented and adjacent levels.

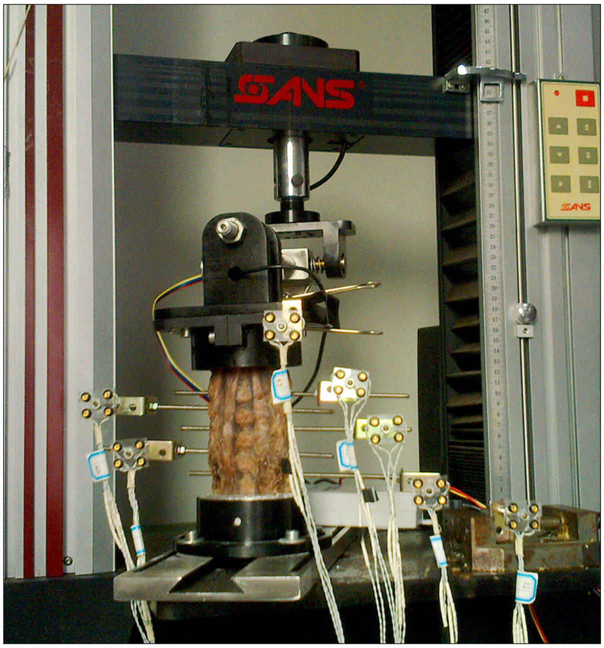

Figure 1. Test set-up for *in vitro* biomechanical testing of cervical specimens.

Material and Methods

Specimen preparation

Eighteen fresh adult human cadaveric cervical spines (C2-T1; age range, 52–73 years) were used for biomechanical testing. All cervical spines were evaluated for bone mineral density (BMD) using dual-energy x-ray absorptiometry scanning and measured BMD values ranged from 0.53 to 0.72 g/cm^2. Ligamentous structures were preserved while the musculature and fascia were carefully removed. Cervical spines with degenerative diseases or traumatic pathology were excluded by anteroposterior and lateral screening radiographs before biomechanical testing. Once harvested, all cervical specimens were immediately conserved in plastic bags and frozen at –20°C. In preparation for biomechanical testing, the required spines were thawed at 4°C for 12 hours. At room temperature on the testing day, the proximal vertebra (C2) and distal vertebra (T1) were separately mounted in a cylindrical container using a low-fusion point (72°C) alloy. And then, the C2 container was attached to the upper fixture while the T1 container was mounted to the lower testing platform. All tested cervical spines were mounted in neutral upright orientation. Markers made of 4 Plexiglas motion detectors were fixed to the anterior aspects of each vertebra from C2 to T1. These markers can be detected by an optoelectronic motion measurement system. The 3-dimensional motion range of each vertebra was obtained with an optoelectronics measurement system (Optotrak, Northern Digital Inc., Waterloo, Ontario, Canada) capable of capturing the motion curve of the markers.

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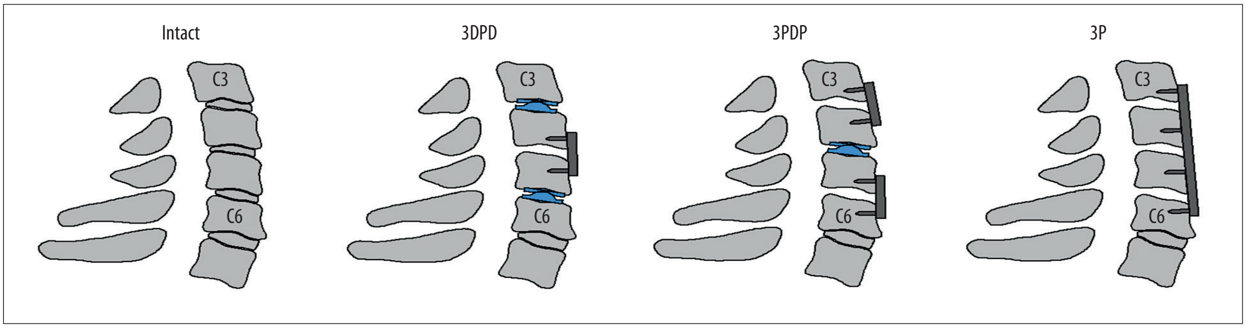

Figure 2. Testing conditions. Eighteen human cadaveric spines from C2 to T2 were divided into 3 groups (3DPD, 3PDP, 3P).

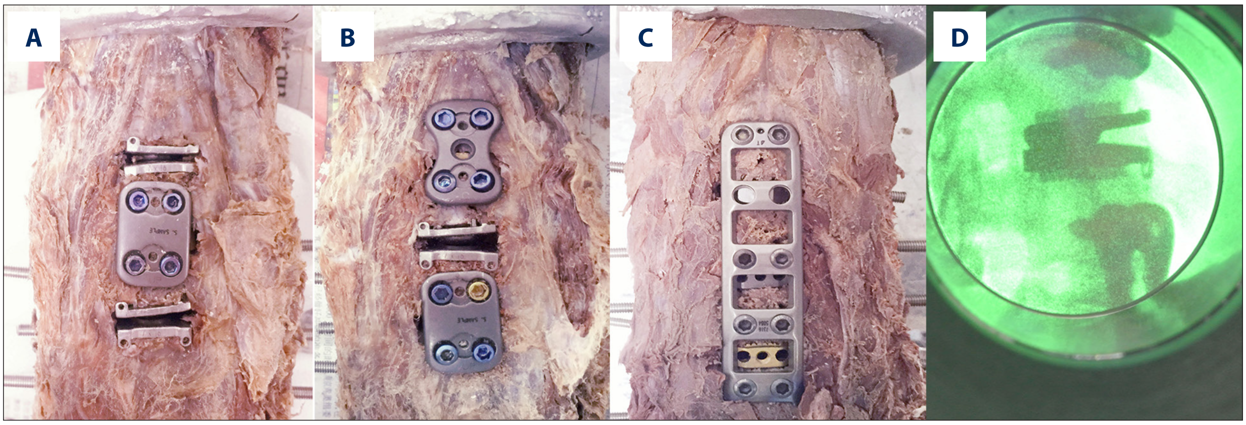

Figure 3. Instrumented cervical specimens: 3DPD (**A**), 3PDP (**B**), 3P (**C**), and X-ray picture (**D**).

Biomechanical tests protocol

Biomechanical tests were performed under displacement control by an MTS machine (CMT6104; MTS Systems (China) Corp., Shenzhen, China) which can replicate physiologic motion with displacement control [22] (Figure 1). The flexion–extension axis of each tested spine was placed eccentric to the load axis of the actuator [23]. Flexion–extension bending moments and a compressive load were applied to the upper container. The bending moments were limited to the upper bound of physiological human bending (4.5 nm). An angular displacement transducer was assembled to measure the global rotation of the cervical spine (C2-T1). A displacement transducer was used to measure the changes in moment arm length between the upper container and the load axis of the MTS machine. All testing specimens were preconditioned by the application of 3 loading cycles. The spine specimens were tested by application of a 50 N preload in flexion-extension and lateral bending circumstances. During the biomechanical tests, all specimens were moistened with 0.9% NaCl physiologic serum spray to avoid tissue dehydration.

Reconstruction procedures

After analysis of the intact spine, each specimen was sequentially reconstructed at C3-C6 3-level) motion segments. The conditions were as follows (Figure 2):

1. ACDR, ACDF, ACDR, or 3-level disc plate disc (3DPD);
2: ACDF, ACDR, ACDF or 3-level plate disc plate (3PDP);
3. Three-level ACDF or 3-level plate (3P).

Prior to biomechanical tests, positioning of implants was verified before each test by X-rays. Measurements included vertebral motion, applied load, and moment.

In the biomechanical tests, the ACDR was a titanium-ceramic alloy Cervical Disc (Prestige LP Cervical Disc, Medtronic Sofamor Danek USA, Inc.). The arthrodesis was performed using an interbody cage (Telamon TM, Medtronic Sofamor Danek USA, Inc.) combined with an anterior cervical plating (ACP) system (DOC Cervical Plate, Depuy Spine, Inc., Raynham, MA, USA) (Figure 3).

Data and statistical analysis

This biomechanical protocol limited motion to 20 degrees in flexion and extension as well as 15 degrees in lateral bending and axial rotation. The ratio of segmental ROM to the total C2-T1 ROM was applied to evaluate the operation effect by normalization method. One-way ANOVA ($p<0.05$) was used to determine the statistical differences in both C3-C6 motion and adjacent level motion under the 3-level anterior plate fusion (3P), the 3PDP, and 3DPD conditions.

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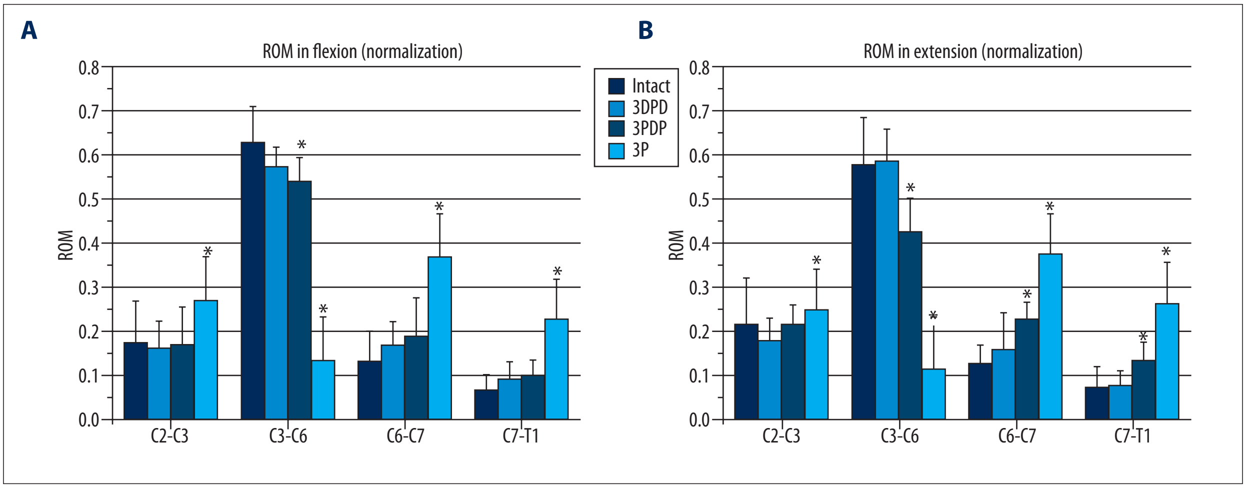

Figure 4. Segmental ROM relative to total C2-T1 ROM (20°) in flexion (**A**) and extension (**B**) (*: statistical significant difference, $p<0.05$, 3DPD/3PDP/3P *vs.* intact; I: Standard Deviation).

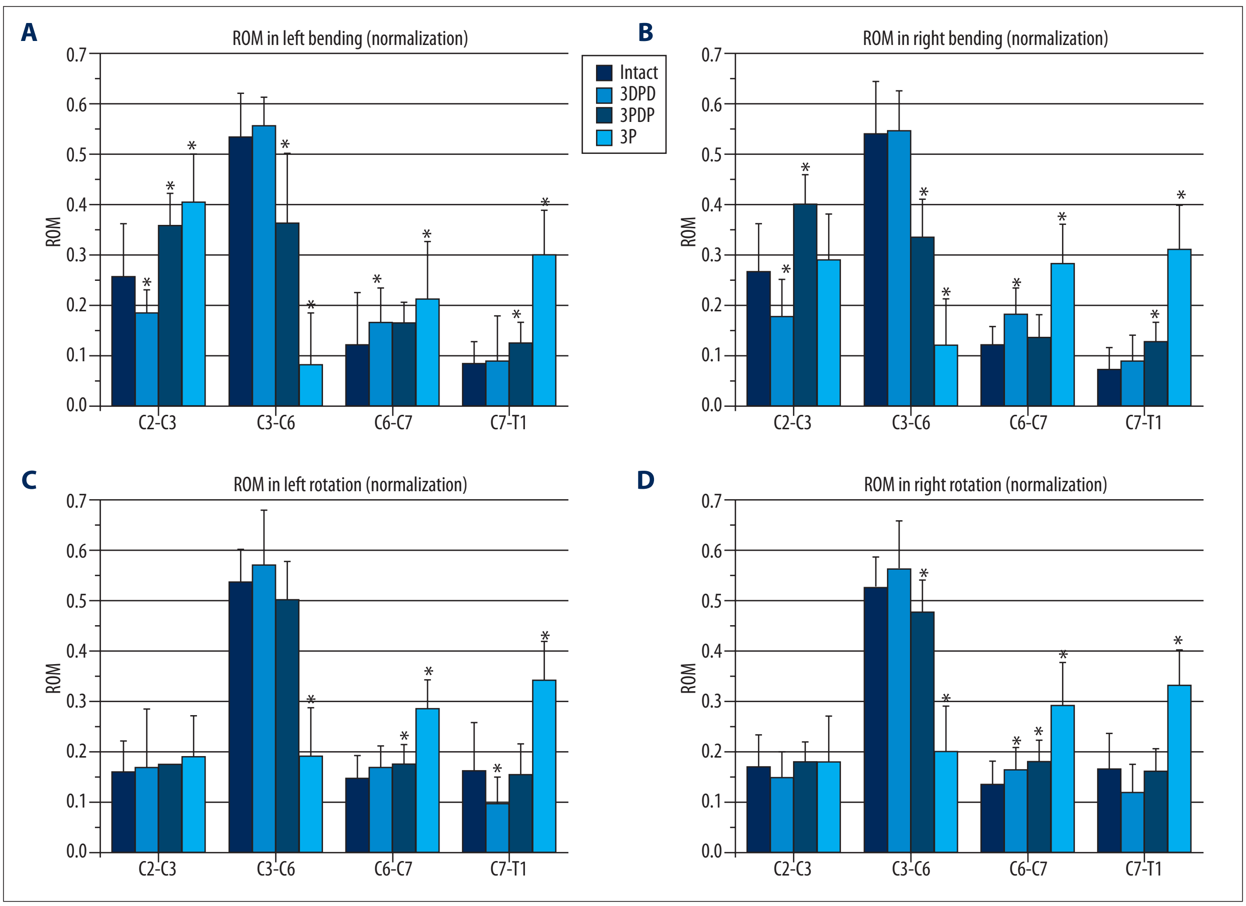

Figure 5. Segmental ROM relative to total C2-T1 ROM (15°) in lateral bending (**A, B**) and axial rotation (**C, D**) (*: statistical significant difference, $p<0.05$, 3DPD/3PDP/3P *vs.* intact; I: Standard Deviation).

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Results

Motion changes at the three instrumented levels

As expected, 3-level arthrodesis resulted in significant reduction of ROM at the three instrumented levels in all 6 loading conditions (flexion, extension, left bending, right bending, left rotation, and right rotation). Compared to intact spines, almost 80% of motion was successfully restricted at C3-C6 fusion levels in flexion, extension, and lateral bending, as well as 65% in axial rotation.

For hybrid constructs, 3DPD construct resulted in slight increase at the 3 instrumented levels in extension, lateral bending, and axial rotation compared to intact ($p>0.05$; maximal variation of +7%). However, the 3DPD condition resulted in a slight decrease at C3-C6 in flexion ($p>0.05$; maximal variation of –9%).

As another 3-level hybrid construct, 3PDP construct resulted in significant decrease of ROM at the C3-C6 instrumented levels in all 6 loading conditions except for left rotation (mean variation of –21%; maximal variation of –38%).

Although 3PDP and 3P conditions produced significant motion decrease at the 3 instrumented levels, there was significant difference within the instrumented levels between 3PDP and 3P conditions in all 6 loading conditions ($p<0.05$). On the other hand, there were also significant differences within the C3–C6 levels between 3DP D and 3PDP conditions in all 6 loading conditions except for flexion and left rotation ($p<0.05$) (Figures 4, 5).

More normal motion with ACDR within construct

For each instrumented level, 3DPD and 3PDP hybrid constructs caused significant reduction of ROM in all 6 loading conditions at the arthrodesis level compared to intact ($p<0.05$) and produced motion increase at the arthroplasty level.

For the 3DPD hybrid construct, implantation of upper-level (C3-C4) ACDR resulted in significant increase of ROM only in right rotation ($p<0.05$; maximal variation of +36%), while implantation of lower-level (C5-C6) ACDR resulted in significant increase of ROM in all 6 loading conditions except for flexion ($p<0.05$; maximal variation of +41%).

For 3PDP hybrid construct, implantation of middle-level (C3-C4) ACDR resulted in significant increase of ROM in extension, left rotation, and right rotation compared to intact ($p<0.05$; maximal variation of +67%) but produced motion increase in flexion, left bending, and right bending, without significant difference ($p>0.05$) (Figure 6, Table 1).

Motion changes at adjacent levels

As suspected, 3-level arthrodesis resulted in an increased contribution of upper and lower adjacent levels. Significant changes were noted at the lower adjacent level in all 6 loading conditions as well as upper adjacent level in flexion and left bending ($p<0.05$; maximal variation of +197%).

Concerning 3DPD hybrid construct, significant changes of motion increase were only noted at lower adjacent level in left bending, right bending, and right rotation ($p<0.05$; maximal variation of +57%). Importantly, there was a significant decrease toward normal in adjacent segment motion adjacent to an ACDR.

Concerning 3PDP hybrid construct, significant changes of motion increase were noted at both upper and lower adjacent levels and the largest motion increase was noticed at lower adjacent level in extension ($p<0.05$; maximal variation of +79%) (Figures 4, 5).

Discussion

This study demonstrated that the motion response of an ACDR adjacent to a fusion maintains normal motion at the ACDR level and normalizes adjacent segment motion in 3-level hybrid constructs. In longer fusions, the intradiscal pressures and the compensatory hyper-mobility are increased for all adjacent segments compared to 1-level fusion [10]. This study confirms the work of Lee et al. and others [4,13–21] that a longer fusion affects all adjacent levels with hyper-mobility. This study shows that an ACDR normalized the adjacent level motion in a 3-level construct.

ACDF remains the criterion standard in surgical management of multilevel cervical degenerative conditions. ACDR is the accepted alternative to anterior cervical fusion for single-level disc disease [24]. Favorable outcomes and the prospect of a lower incidence of adjacent-level disease have encouraged surgeons to expand current ACDR indications to multilevel disc disease [25]. However, the evidence in multilevel ACDR is not as well established as its role in single-level disease, and some levels may be too degenerative for ACDR. With that in mind, authors are reporting combinations of fusion and arthroplasty as an alternative to multi-level ACDF or ACDR. Barbagallo et al. [12] described 2-level, 3-level, and 4-level hybrid surgery results as safe and reliable without revision. Shin el al. [11] compared hybrid construct to ACDF in 2 levels, with improved NDI, pain, return of motion, and reduced ASD. Kang el al. [15] confirmed these findings in 3-level hybrid treatments, with improvement in recovery of total motion and maintenance of adjacent segment motion. Jia et al. [26], in a systematic review

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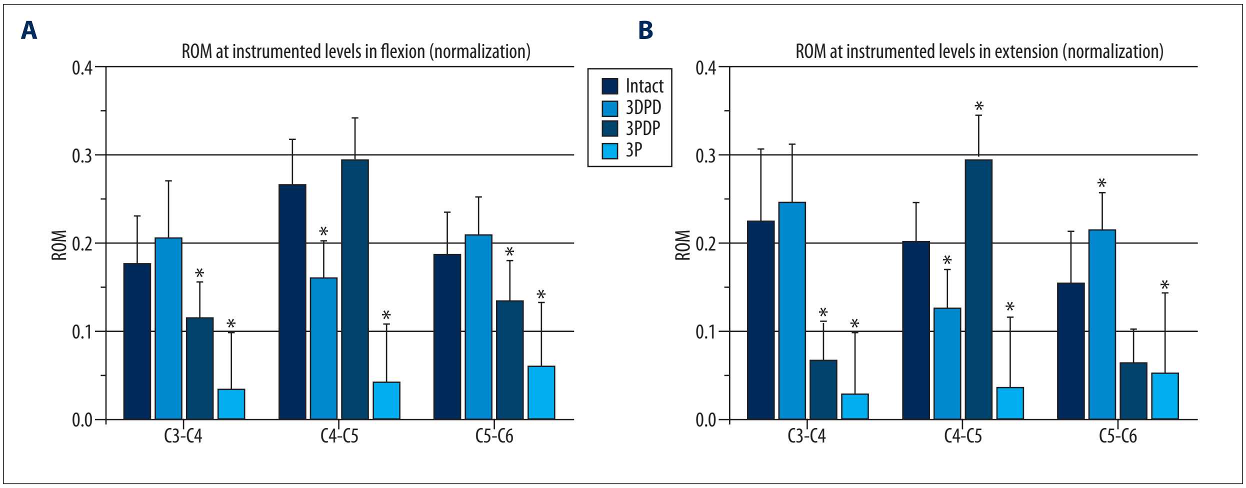

Figure 6. ROM at instrumented levels relative to total C2-T1 ROM (20°) in Flexion (**A**) and Extension (**B**) (*: statistical significant difference, p<0.05, 3DPD/3PDP/3P *vs.* intact; I: Standard Deviation).

Table 1. ROM at instrumented levels relative to total C2-T1 ROM (15°) in lateral bending and axial rotation: mean ± standard deviation (* no statistical significant difference, p>0.05, 3DPD/3PDP/3P *vs.* intact).

	Intact	3DPD	3PDP	3P
Left bending				
C3-C4	0.227±0.07	0.265*±0.062	0.103±0.083	0.037±0.103
C4-C5	0.159±0.083	0.092±0.084	0.158*±0.057	0.017±0.093
C5-C6	0.149±0.094	0.201±0.069	0.103±0.061	0.029±0.081
Right bending				
C3-C4	0.231±0.059	0.248*±0.045	0.062±0.079	0.061±0.096
C4-C5	0.167±0.048	0.101±0.060	0.161*±0.048	0.016±0.102
C5-C6	0.142±0.042	0.198±0.053	0.112±0.075	0.043±0.085
Left rotation				
C3-C4	0.185±0.045	0.214*±0.051	0.093±0.041	0.084±0.091
C4-C5	0.170±0.049	0.106±0.062	0.285±0.075	0.049±0.102
C5-C6	0.181±0.043	0.251±0.050	0.124±0.059	0.058±0.084
Right rotation				
C3-C4	0.177±0.040	0.241±0.043	0.089±0.047	0.050±0.104
C4-C5	0.180±0.044	0.091±0.054	0.260±0.082	0.071±0.079
C5-C6	0.171±0.051	0.233±0.049	0.129±0.052	0.077±0.098

of 8 biomechanical and 7 clinical papers, found a paucity of quality evidence to support hybrid surgeries and recommended prospective randomized trials.

Previous biomechanical studies have investigated the operative- and adjacent-level kinematic properties of 2-level ACDF and combined ACDR/ACDF. Faizan et al. [16] demonstrated that 2-level ACDR had a better motion distribution than 2-level ACDF. ACDF plus ACDR had less severe biomechanical effects on adjacent levels when compared to 2-level ACDF procedure. Cunningham et al. [20] reported that the ACDF at C6-C7 and ACDR at C5-C6 produced increased segmental motion at the arthroplasty level, particularly in axial rotation and flexion-extension. Barrey et al. [18] analyzed the biomechanics of ACDR placed above ACDF and found similar kinematics to single-level ACDR and adjacent to a previously implanted ACDR. Lee et al. [4] compared the biomechanics of 2-level ACDF and hybrid; the hybrid construct had a better biomechanical performance

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than the fusion and the hybrid avoided excessive increase of adjacent level motion and loads. Lee et al. [4] found that the location of the fusion (cephalad or caudad) did not affect the behavior of the disc replacement.

Biomechanical studies investigating the kinematic properties of 3-level hybrid arthroplasty-arthrodesis reconstruction are limited. However, multilevel cervical surgeries, such as 3-level anterior surgeries, are more common in clinical practice. Hanai et al. [27] reported that there was excellent clinical success and a 100% union rate for 3-level and 4-level cervical corpectomy and autograft strut graft reconstruction. Swank et al. [28] revealed that the likelihood of pseudarthrosis was 10% for 1-level surgery, 44% for 2-level surgery, and 54% for 3-level surgery. So the rational procedure for 3-level cervical surgery is worthy of attention. One study investigated ACDR as a promising treatment for symptomatic adjacent level after prior 2-level cervical fusion. Martin et al. [19] characterized ACDR kinematics above 2-level fusion and found that ACDR placed adjacent to a 2-level fusion was subjected to a more challenging biomechanical environment as compared to a stand-alone ACDR. Two groups reported both 2-level and 3-level hybrid surgeries are comparable to ACDF and ACDR in terms of safety and feasibility with a minimum follow-up of 2 years [14,15]. Ding et al. stated that hybrid surgeries may be an alternative to ACDF for 3-level cervical disease due to the equivalent or improved early clinical outcomes, better overall C2-C7 range of motion, and less impact at adjacent levels [13].

We found that ROM in instrumented levels after 3P condition was systematically reduced in all planes. In contrast, the 3DPD condition appeared to preserve motion at adjacent intact levels to the ACDR segments. Compared to 3DPD condition, ROM in instrumented levels after 3PDP condition was slightly reduced but the difference was not significant. In addition, we did not observe an abnormal increase of motion for 3DPD and 3PDP conditions.

At the adjacent levels, 3P condition resulted in increased adjacent segment motion, especially in the caudal adjacent segment, which may potentially result in accelerated adjacent segment degeneration. On the contrary, and as expected, although 3DPD and 3PDP conditions did not fully restore motion within the instrumented levels, they did not demonstrate hyper-mobility, and in fact induced only minimal changes in ROM at adjacent levels. This confirmed the finding that the hybrid construct could avoid large motion increase in adjacent levels and clinically may reduce the risk of adjacent segment degeneration. The 3DPD construct did produce a smaller motion change in adjacent segments compared with 3PDP construct.

This study has the limitations of any cadaveric biomechanical study of cervical fusion in that it allows only observation of the immediate effects of the intervention. It did not remove all motion in the fusion segments and cannot represent the long-term effect of increasing stiffness as the fusion progresses.

Conclusions

This study analyzed the biomechanics of cervical spine after 3-level hybrid treatment. ACDF eliminated motion within the construct and greatly increased adjacent motion. ACDR normalized motion of its segment and adjacent segments. These biomechanical findings suggest that while hybrid conditions failed to restore normal motion within the construct, they significantly normalized motion in adjacent segments compared with the 3-level ACDF condition. The artificial disc in 3-level constructs has biomechanical advantages compared to fusion in normalizing motion.

Conflict of interest

None.

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