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Opinion paper

Occurrence of discal and non-discal changes after sequestrectomy alone versus sequestrectomy and implantation of an anulus closure device

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ABSTRACT

Sequestrectomy alone represents a procedure for the treatment of lumbar disc herniation. For selected cases, an anulus closure device (ACD) can be implanted which may result in lower reoperation rates. However, comparative magnetic resonance imaging (MRI) changes and their clinical relevance of both procedures are unclear and have not been reported so far.

Clinical and MRI data of patients after limited discectomy with ACD implantation (group ACD; $N = 45$) and patients after sequestrectomy alone (group S; $N = 40$) with primary lumbar disc herniation were compared retrospectively. Pain intensity on the visual analogue pain scale (VAS), oswestry disability index (ODI) or the patient satisfaction index (PSI) were collected. Disc signal intensity, Modic type changes, endplate reactions, anular tears and reherniations were investigated using MRI before and <18 months postoperative. Morphologic changes were correlated with clinical outcome.

There was no difference in VAS back, VAS leg or ODI/PSI after the operation although group S showed significantly more reherniations in MRI. The overall rate of repeated surgery at the same level was similar with a trend in favour of the ACD group ($P = 0.729$). Significantly more patients of the ACD group experienced endplate erosions after surgery ($P < 0.001$). Both groups experienced progression of disc signal intensity, Modic type changes, and anular tears with most MRI signs being without clinical relevance.

ACD implantation is associated with a significantly lower reherniation rate in MRI but showed a significantly higher rate of endplate erosions. The structural changes do not appear to be clinically relevant.

1. Introduction

Patients suffering from symptoms of lumbar disc herniation classically undergo open lumbar microdiscectomy or sequestrectomy alone. Regardless of the operative technique, these operations represent the most common surgical procedures in the United States performed for those patients [1]. Both techniques may lead to immediate relief of symptoms but recurrent disc herniations may cause increased pain and disability, which necessitates repeat surgery. A recent comprehensive review addressing the degree of discectomy concluded that limited discectomy may be associated with a lower incidence of long-term recurrent low back pain at the cost of an increased incidence of reherniations [2].

In order to prevent any further outward migration of nuclear material at the location of tear or rupture and thereby associated unfavourable outcome, anulus closure devices (ACDs) have been developed. They are thought to facilitate the surgeon to preserve the integrity of the entire intradiscal structures and to prevent recurrent reherniations. Preliminary effectiveness of such an ACD has been recently shown in patients at high risk of reherniation based on anular defect size [3].

However, no control group was available and imaging results were focused on the presence or absence of reherniations only. Thus, no information is available on additional pathological changes occurring inside the disc space and/or in the vertebral bodies associated with ACD implantation.

We therefore analyzed discal and non-discal changes occurring in patients of a single prospective patient cohort after limited discectomy and implantation of an ACD. These changes were compared to results of a similar patient cohort that received sequestrectomy alone. As the disc space has not been entered in

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this control group, significant morphologic changes of any kind in the ACD group should be generated by the implant itself. Finally, MRI changes observed in both patient groups were investigated for clinical relevance.

2. Materials and methods

2.1. Patient selection

For the present investigation, a total of 85 patients were retrospectively screened for eligibility. Patients were only included if magnetic resonance imaging (MRI) and clinical datasets were available before and after the operation. Clinical data of the sequestrectomy alone group (Group S) originate from the sequestrectomy arm ($N = 40$) of a previously published trial [4,5], clinical data of the limited discectomy group with implantation of an anulus closure device (Group ACD) are derived from a post marketing surveillance study ($N = 45$), which represents 'Cohort B' of a recently published study [3]. Fig. 1 shows images of the device. For the present investigation, all preoperative and follow-up MRI-data of Group S and Group ACD were newly analyzed by an independent institution (Medical Metrics Inc., Houston, TX, USA). The following variables were recorded: presence and type of MRI confirmed reherniations, anular tears or fissures, disc signal intensity, Modic Changes, and endplate changes/reactions (for details, see Section 2.3). In group S, only 34 complete imaging datasets were available. Additional 5 MRI datasets had to be discarded due to insufficient imaging quality. In Cohort B, no follow-up MRI was available in 3 patients resulting in 42 datasets ready for analysis.

For both studies, informed consents and Ethics Committee approvals were available. Inclusion criteria for both studies were similar: presence of lumbar disc herniation with at least six weeks of failed conservative treatment prior to surgery; no previous surgery at index level; age above 18 and below 60; sufficient knowledge of the German language for completing the questionnaires; MRI confirmed disc herniation; and absence of concomitant spinal disease. Patients were excluded if spondylolisthesis was present at the index level; clinically compromised vertebral bodies in the lumbosacral region due to any traumatic, neoplastic, metabolic, or infectious pathology; scoliosis of greater than ten degrees; or any metabolic bone disease that has not been stabilized for at least three months.

2.2. Operative procedures

In both groups, a standardized microsurgical midline approach was used. In group S, patients received removal of the herniated material only without entering the disc space. Even in cases of transanular herniation, fragments were removed above the anulus-level without entering the disc space. In group ACD, a limited discectomy was performed, and annulus closure device implanted. The implant consists of a flexible woven polyester mesh (Dacron®) attached to a titanium bone anchor (Barricaid®, Intrinsic Therapeutics, Inc., Woburn, USA). Patients with defects larger than 6 mm in height or 10 mm in width were excluded from the study. For detailed surgical description, see Bouma et al. [3].

2.3. Assessment of MRI

The following findings were recorded:

- Type of MRI confirmed reherniations with (1) None, (2) Protrusion, (3) Extrusion, (4) Sequestration, (5) Indeterminate.
- Presence of anular tears or fissures were rated as (1) absent, (2) present, or (3) indeterminate.
- Disc signal intensity was graded according to Pfirrmann [6] with (1) Grade I: bright white disc, homogenous structure, clear distinction between nucleus and anulus, hyperintense signal intensity, isointense to cerebrospinal fluid, normal disc height; (2) Grade II: white disc, inhomogeneous structure with or without horizontal bands, clear distinction between nucleus and anulus, hyperintense signal intensity, isointense to cerebrospinal fluid, normal disc height; (3) Grade III: gray disc, inhomogeneous structure, unclear distinction of nucleus and anulus, intermediate signal intensity, normal to slightly decreased disc height; (4) Grade IV: dark gray disc, inhomogeneous structure, no distinction between the nucleus and anulus, intermediate to hypointense signal intensity, normal to moderately decreased disc height; (5) Grade V: black disc, inhomogeneous structure, no distinction between the nucleus and anulus, hypointense signal intensity, collapsed disc; (6) indeterminate/unable to assess: a reliable determination cannot be made from the available imaging due to technical factors, sub-optimal image quality, obscured anatomy, obstructed view due to parallax effects or other imaging artifacts. The relevant images are missing or unavailable for review, or the relevant anatomy is not visible in the field of view.
- Modic Changes with (0) None: no edematous reaction or vascular congestion induced in the adjacent bone marrow of the endplates; (1) Type I: new or increased hypointense reaction and vascular congestion in the adjacent marrows on T1-weighted MR imaging; hyperintense on T2-weighted images, new or increased relative to the previous time point; (2) Type II: bone marrow converted to a predominantly fatty marrow. Hyperin-

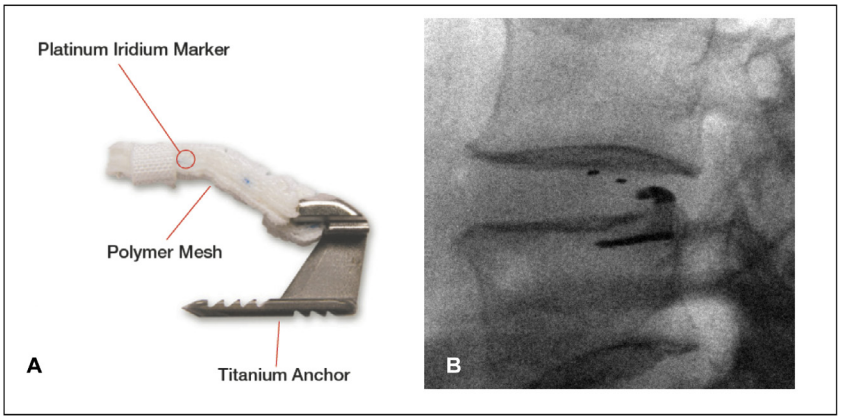

Fig. 1. Illustration of the anulus closure device (ACD). (A) Photography of the device, which consists of a polymer mesh that is attached to a titanium anchor. For better radiographic visibility, platinum iridium markers are incorporated into the mesh. (B) Lateral radiographic view of an implanted ACD.

tense on T1 and isointense to hypointense on T2. The exact signal intensity depends on the degree of T2-weighting; (3) Type III: Dense sclerosis of the vertebral endplates. Reflected on MR imaging as hypointensity on both T1 and T2-weighted images; (4) Indeterminate: Insufficient information to conduct the assessment (missing T1 or T2 images)

- Endplate Changes/Reactions with (0) Absent: absence of new endplate changes, including fracture or chipping, or endplate reactions including scalloping, erosions, cysts or other irregularities; (1) Present: presence of new endplate changes since before the operation, including fracture or chipping, or reactions including scalloping, erosions, cysts or other irregularity adjacent to the implant; (2) Regression: regression of known endplate changes, including fracture or chipping, or reactions including scalloping, erosions, cysts or other irregularities.

2.4. Assessment of outcomes

Clinical outcomes were assessed in the context of follow-up visits not less than 18 months after the operation. Patients received a questionnaire, in which they had to rate their low back and leg pain intensities on the visual analogue scale (VAS) ranging from 0 to 10. Patients of the ACD group completed a 10-item oswestry disability index (ODI). A formal ODI has not been requested from patients of group S at two years after the operation. Instead, the patient satisfaction index (PSI) was available with (1) operation met my expectations, (2) I did not experience the expected improvement, but would undergo surgery again, (3) operation helped, but I would not undergo surgery for the same results again, (4) my condition is unchanged/worse compared preoperative. Although there is no example for comparison of both indices in the literature, a rough comparison has been attempted by dichotomization of the ODI into 4 classes. ODI from 0 to 20% was considered as PSI 1, 21–40% to PSI 2, 41–60% to PSI 3, and 61–100% to PSI 4.

2.5. Assessment of reoperations

Assessment of the reoperation rate was carried out by including also those patients that had no complete pre- and postoperative MRI datasets.

2.6. Statistical analysis

Statistical analysis was done by the authors using GraphPad Prism 5 (GraphPad Software Inc., La Jolla, CA, USA). For comparison of qualitative, nominal scaled data between the study groups D and S, the Fisher test has been used. Askew distributed or ordinal scaled data with multiple traits were analyzed using the Mann–Whitney-*U*-Test. Patient characteristics and clinical outcome parameters are given as *n* (%), mean values ± standard deviation (SD) or median values (minimum/maximum), as applicable. For correlation analyzes, a Spearman correlation was used. A *P*-value < 0.05 was considered as significant.

3. Results

3.1. Patient characteristics

Complete datasets with clinical and MRI data before and at least 18 months after the operation were available for 29 patients (72.5%) of group S and for 42 patients (93.3%) of the ACD group. There was no significant difference in patient characteristics, which are summarized in Table 1. MRI follow-up time ranged from 18 to 22 months in group S and from 21 to 27 months in group ACD.

3.2. Outcome

The self-rated patient variables such as the VAS back, the VAS leg and the ODI/PSI did not differ significantly between groups (for details, see Table 1).

3.3. MRI findings

Detailed statistical results of MRI findings are listed in Table 2. In the ACD group significantly less MRI confirmed reherniations occurred. There was a protrusion in one patient and an extrusion

Table 2
Radiological results.

	Group S *N* = 29	Group ACD *N* = 42	*P*
Disc signal intensity			
Before the operation	4 (3/4)	3 (1/4)	<0.001
After the operation	4 (3/5)	3 (2/4)	<0.001
Progression	0 (0/3)	0 (0/3)	0.964
Modic type			
Before the operation	1 (0/2)	0 (0/2)	0.114
After the operation	2 (0/2)	1 (0/2)	0.263
Progression	0 (−1/1)	0 (−1/1)	0.197
Anular tears			
After the operation	1 (0/1)	0 (0/2)	<0.001
MRI confirmed reherniations			
After the operation	14 (50)	2 (4.9)	<0.001
New Endplate Changes/Reactions			
After the operation	3 (10.3)	22 (52.4)	<0.001

Given values are the median and the min/max in parenthesis or *N* and (%), as applicable; group S, sequestrectomy only; group ACD, anulus closure device.

Table 1
Patient characteristics and clinical results.

	N	Group S	Group ACD	*P*
MRI after the operation	71	29	42	
Male: Female	71	14:15	22:20	0.811
Age [years]	71	40.1 (9.1)	42.3 (11.3)	0.391
BMI	71	26.3 (4.8)	26.1 (3.8)	0.879
Operated level	71			
L3/4		0	1	
L4/5		10	21	0.265
L5/S1		19	20	
VAS back		1 (0/8)	0.5 (0/9)	0.653
VAS leg		0 (0/8)	0 (0/9)	0.310
Mod. ODI/PSI		1 (1/3)	1 (1/4)	0.916

Given values are *N*, mean (SD), or median (minimum/maximum) when appropriate; VAS pain intensity values and ODI /PSI refer on the time point 2 years after surgery. BMI, body mass index; VAS, visual analogue scale; ODI, oswestry disability index; PSI, patient satisfaction index; group S, sequestrectomy only; group ACD, anulus closure device.

in another patient compared to 11 protrusions and 3 extrusions in group S. In addition, group S showed significantly more anular tears. Disc signal intensity was significantly different between groups before and after the operation. However, there was a similar progression of signal intensity in both groups.

In regard to Modic type changes, there were no significant differences between groups before and after the operation. Both groups showed an insignificant degree of progression ($P = 0.197$).

Endplate changes such as small cysts or erosions were detectable before surgery in 12 patients of group S and 7 patients of the ACD group ($P = 0.029$). While these findings remained stable in group S, prevalence of new endplate erosions after surgery was significantly higher in the ACD group ($P < 0.001$). More than half of all patients of the ACD group ($N = 22$; 52.4%) showed new endplate erosions compared to 3 patients of group S (10.3%). Based on the location of the titanium anchor of the implant, the majority of patients had new lesions in the opposite endplate ($N = 15$), some in the adjacent endplate ($N = 3$), and 5 patients at both locations. An example of typically occurring endplate changes is shown in Fig. 2.

3.4. Correlation analysis

To assess the correlation of clinical outcome with a certain MRI feature, data of both groups were pooled. None of the 4 variables disc signal intensity, anular tears, Modic-type changes, and endplate erosions showed a significant correlation with low back or leg pain intensity, or ODI/PSI after the operation. For detailed analysis, see Table 3. Spearman correlation analysis of Modic-type changes with other MRI variables showed no significant correlations (each $P > 0.1$).

3.5. Reoperations

By considering all initially included patients, the reoperation rate for true reherniations (identical level and side) showed a trend in favour of the ACD group (Table 4). Only one patient of group ACD suffered a true reherniation (2.2%) compared to 5 in group S (12.5%, $P = 0.095$). The device of this single ACD patient has been explanted followed by monosegmental fusion. After reviewing of the postoperative images by the data safety monitoring board, this implantation was classified as surgical technique error, since the implant has been implanted too far anteriorly and thus permitting nuclear extrusion.

By including all recurrent surgeries at the index level, no difference exists between groups. All patients of group S that received repeated surgery, underwent again sequestrectomy. No additional surgeries were performed. Three additional patients of group ACD had to undergo repeated surgery. One patient suffered reherniation at the opposite side of the index level and received sequestrec-

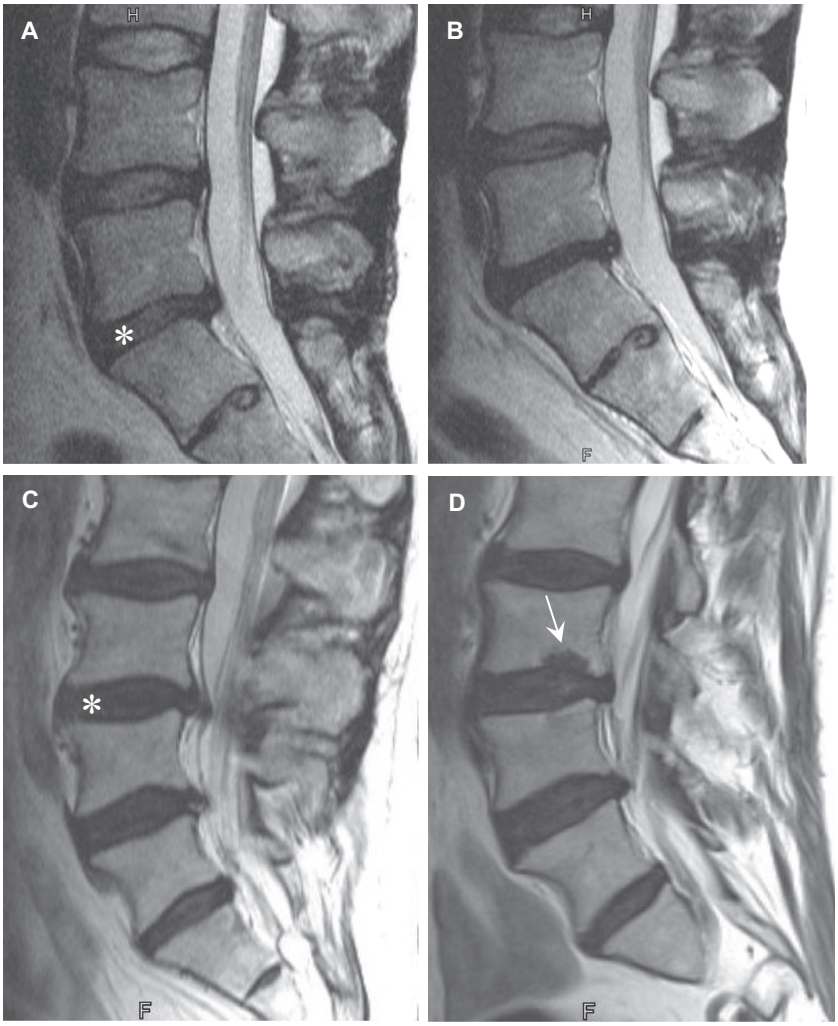

Fig. 2. Development of endplate changes in MRI. Examples of typically occurring endplate changes are shown. (A) and (B) show T2-weighted sagittal images of a patient of group S before and after surgery without endplate changes. (C) and (D) show corresponding images of a patient of the ACD group. The asterisk in both preoperative images indicates the index level. The white arrow points onto the newly developed endplate erosion which occurred at the opposite side of the titanium anchor.

Table 3
Correlation analysis.

	VAS low back pain		VAS leg pain		modODI/PSI	
	r	*P*	*r*	*P*	*r*	*P*
Disc signal intensity	0.032	0.801	−0.182	0.143	0.014	0.914
Anular tears	0.143	0.242	−0.047	0.701	0.092	0.455
Modic-type changes	0.056	0.668	−0.003	0.984	−0.054	0.675
Endplate erosions	0.168	0.168	0.170	0.163	0.023	0.852

Given values represent Spearman correlation coefficient (*r*) and the P value (*P*). VAS, visual analogue scale; ODI, oswestry disability index; PSI, patient satisfaction index.

Table 4
Number of recurrent operations.

	N	Group S	Group ACD	*P*
No. of initially included patients	85	40	45	
Recurrent surgery initial cohort	85	5 (12.5%)	4 (8.9%)	0.729
Recurrent surgery initial cohort at index level/side	85	5 (12.5%)	1 (2.2%)	0.095

Given values are *N*, mean (SD), or median (minimum/maximum) when appropriate; VAS pain intensity values and ODI/PSI refer on the time point 2 years after surgery. Group S, sequestrectomy only; group ACD, anulus closure device.

tomy. Another patient received reoperation at the index side and level due to recurrent pain and a MRI suspected reherniation. Intraoperative, only scar tissue could be found. The third patient had to be revised due to dorsal protrusion of the ACD-mesh. In this patient, only the mesh was removed while the titanium-anchor remained within the vertebral body.

4. Discussion

The present comparison of two studies indicates that the addition of an ACD does not seem to result in a clinically meaningful advantage. Clinical outcome variables of both study groups did not show a statistically significant difference. In addition, the overall reoperation rates were similar in both groups. There were significantly less reherniations detectable in the ACD group. Conversely, this group showed significantly more endplate lesions which were mainly located at the opposite side of the titanium anchor.

However, reoperation rates should be considered in more detail. In the present analysis, all patients of the initial cohort and all spinal reoperations at the index level were included. Reoperations may occur due to a new herniation at a different level, a true reherniation at the same side, a reherniation at the opposite side, and as a result of complications associated with the implant itself or an irregularly performed implantation. Important for the evaluation of the efficacy of this specific implant is the analysis of the number of reoperations due to true reherniations (same level, same side) and due to implant associated complications. Thus, in the present investigation 1 patient of the ACD group suffered a true reherniation, and another patient suffered a Mesh-protrusion. In contrast, 5 patients of group S suffered true reherniations. However, the power of our study is too low due to limited patient numbers to elucidate statistical differences in reherniation rates. A definite answer on this crucial question will be available from a randomized multicenter trial, which has currently closed enrollment with over 550 patients included (http://www.clinicaltrials.gov/ct2/show/NCT01283438).

With regard to MRI changes, the present study seems unique since it compares discal and non-discal variables over time in two similarly treated patient groups except for the fact of ACD implantation. In both groups sequestrectomy alone or limited nucleus removal has been performed without additional injuring of the cartilage endplates.

With regard to non-discal changes, the most striking finding represents the significantly higher incidence of new endplate lesions in the ACD group. These lesions represent bony erosions, occurring adjacent to the ACD mesh in most instances. To our opinion, they do not represent structures that are known as Schmorl Nodes (SN). Recently, an interesting MRI study [7] has been published on the prevalence of SN in a population of 2449 volunteers (mean age 40.4, range 9.7–88.4 years). In this study, a SN was defined as localized vertebral endplate irregularity. SN were most common at the upper 2 lumbar levels and showed no tendency to increase with advancing age. This finding is in line with results of group S, where no secondary increase of endplate irregularities was detectable. Therefore, the morphologic changes observed in the ACD group most probably do not represent SN, they rather represent new erosions potentially caused by the implant. Unfortunately, no information is available on the clinical relevance of SN or other endplate changes such as erosions or bony cysts in the literature. In the present study population, no correlations were found between endplate changes and outcome variables. Certainly, these findings have to be closely followed in the present population for a longer period of time.

Other non-discal pathologies include Modic-type changes. Compared to other MR-variables investigated, there are an increasing number of studies available investigating Modic-type changes in relation to clinical outcome. According to a recent systematical review on Modic findings on the prediction of future low back pain, no consistent association could be identified [8]. Nevertheless, Modic-type changes seem to be highly prevalent in clinical populations associated with LBP, they are not consistently present over time and a change in the size is not associated with clinical deterioration [9]. This seems consistent with the present investigation, where correlation of Modic-type changes also showed progression or regression over time. Similar to the previously cited study [8], Modic-type changes showed no correlation with clinical outcome parameters. Another study investigating 108 surgical patients with lumbar degenerative disease failed also to demonstrate a relation between Modic Changes and surgical outcomes [10]. In contrast to our results, this group could demonstrate a significant correlation between disc signal intensity grades and Modic-type changes. The reason for this discrepancy remains unclear and may point to the fact, that interpretation of MRI changes may considerably differ between observers [11].

With regard to discal changes, several morphologic changes were taken into account such as homogeneity of signal intensity, presence of horizontal clefts, distinction between the anulus and nucleus pulposus, disc height and the presence of anular tears. Although differences between groups with regard to disc signal

intensity and the presence of anular tears were present in the preoperative MRI, both groups showed progression of discal degeneration over time. Correlation analysis failed to show a link from these intradiscal changes to clinical outcome or clinical deterioration. In the literature, little information is available on the clinical significance of intradiscal changes. There are reports supporting the theory of anular tears being present in the early stages of disc degeneration with an association with a faster subsequent nucleus degeneration [12] and others negating this theory [13]. However, none of these studies related these findings to clinical outcome variables. Likewise, clinical significance of disc signal intensity characteristics have been reported only sporadic. Only one study is available which found a similar result compared to the present study with higher grades of disc signal intensity not being associated with low back pain or ODI [10].

The current study contains several limitations. First, this is a comparison of two independently performed studies. However, inclusion criteria and clinical patient characteristics were similar between study groups, which favour comparability. Second, results of both study populations have already been published in part. For the present investigation, only the clinical information from these studies has been used. The main focus of the present study was on MRI changes. The complete pre- and postoperative MRI data of both study groups have been newly collected by an independent institution and have not been published so far. Third, the comparison between PSI and the modified ODI is unusual and not validated in the literature. However, other clinical variables were also included, e.g. VAS values, which were collected in both studies that likewise showed no significant difference. For future investigations, certainly similar scores should be used. Fourth, the follow-up time for MRI is slightly different between groups within the range of 18–24 months. However, within the ongoing prospective trial, occurrence of new endplate erosions is clearly present already at 12 months after surgery and slowly increases over time (personal communication). Therefore, the incidence of those changes should not be substantially influenced by a 6 month time gap between study groups.

5. Conclusion

In MRI, the addition of an ACD leads to significantly lower reherniation rates at the expense of a significant higher rate of new endplate erosions. Clinically, both groups did not differ significantly after the operation.

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