NuNec™ cervical disk arthroplasty improves quality of life in cervical radiculopathy and myelopathy: a two-year follow-up.

Abstract

BACKGROUND: Anterior cervical disk replacement is an alternative to fusion for the treatment of selected cases of radiculopathy and myelopathy. We report clinical and radiological outcomes after disk replacement with the NuNec™ artificial cervical disk with subgroup analysis.

OBJECTIVE: To review clinical and radiological outcomes after anterior cervical disk replacement with the NuNec™ artificial cervical disk.

METHODS: A consecutive case series of patients undergoing cervical disk replacement with the NuNec™ artificial disk. Clinical outcomes were assessed by questionnaires pre-operatively and up to two years post-operatively including neck and arm pain, Neck Disability Index, Euroqol 5-dimensions, and Short Form-36; x-rays from the same period were analyzed for range of movement and presence of heterotopic ossification.

RESULTS: Forty-four NuNec™ disks were implanted in 33 patients. Clinical improvements were seen in all outcomes; significant improvements on the Neck Disability Index, Euroqol 5-dimensions and physical domain of the Short Form-36 were maintained at two years. There was a mean of 4 degrees range of movement at the replacement disk level at two years, a significant reduction from baseline; there was also progression in levels of heterotopic ossification. Complications included temporary dysphagia (10%) and progression of disease requiring foraminotomy (6%); no surgery for adjacent level disease was required. There was no significant difference in the outcomes of the radiculopathy and myelopathy groups.

CONCLUSION: Clinical outcomes using the NuNec™ disk replacement are comparable with other disk replacements. Although range of movement is reduced, re-operation rate is very low.

Short title: NuNec™ improves quality of life.

Keywords:
Arthroplasty; Cervical; Myelopathy; NuNec; Quality of life; Radiculopathy

Abbreviations

ACDF, Anterior cervical disk fusion
ACDR, Anterior cervical disk replacement
ASD, Adjacent segment disease
EQ-5D, EuroQol 5 Dimension
HO, Heterotopic ossification
NDI, Neck disability index
SF-36, Short form-36
VAS, Visual analogue scale

Introduction

Anterior cervical disk replacement (ACDR) has gained popularity as an alternative surgical option to anterior cervical diskectomy and fusion (ACDF) for degenerative disk disease [1-3]. Studies of post-operative outcomes after ACDR have shown equitable or slightly improved clinical and radiological outcomes, when compared with ACDF at 2-5 years [4-9], together with superior cost-effectiveness [10,11]. There are currently no studies of the efficacy of the NuNec disk replacement, and additionally there is currently little information about whether outcomes are different for patients presenting with myelopathy, as opposed to radiculopathy. Reports have suggested that patients with myelopathy are generally older, have a more advanced condition, but show similar outcomes to those with radiculopathy [12,13].

Cervical disk replacements aim to maintain movement at the symptomatic level, theoretically reducing the risk of adjacent segment disease (ASD) although a causative relationship between ACDF and ASD has not been formally proven [2]. Maintenance of movement has been demonstrated in over 80% of patients [1,14-16]. In ACDR, the prosthesis generates biomechanical conditions closer to physiological parameters by maintaining motion at the affected level, whereas ACDF results in reduced movement of the affected vertebrae, particularly after fusion of more than one level [7]. As a consequence, adjacent joint movement increases and adjacent disk

pressure is greater after fusion [7,17,18].

Range of movement after ACDR is not always preserved in part due to the development of heterotopic ossification (HO) [19]. The development of which has been attributed to a number of factors, including natural progression of degeneration [20], as well an iatrogenic causes [19,21,22], which may be aggravated by reduced movement [23]. Disk replacements vary by material and design, which affect both motion preservation and wear and tear characteristics, and consequently the risk of HO development [24].

The NuNec™ disk replacement (Pioneer® Surgical Technology, Marquette, MI, USA) has a semi-constrained ball and socket design with an integrated cam locking system (see Figure 1). It is largely radio-lucent on x-ray and MRI imaging [25]. The NuNec™ device is made from the polymer, Polyether-ether-ketone (PEEK), which differs from frequently used artificial disks such as the Bryan Disk, Prestige, PCM and ProDisc-C, which use metal alloys and ultrahigh molecular weight polyethylene; it has a hydroxyapatite covering to encourage bony ingrowth. The NuNec™ prosthesis has high radiation, thermal and aging resistance, good mechanical and biological performance and generates smaller wear particles than some other disks, which may reduce the immune response that accelerates osteolysis [26].

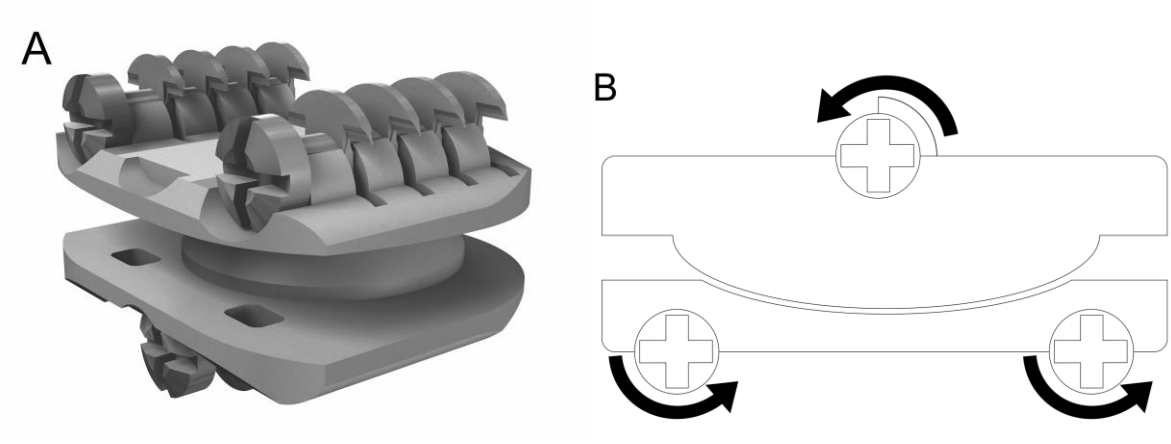

Figure 1: NuNec™ disk replacement A: 3D B: Sagittal plane

The purpose of our study was to evaluate current data from a single site regarding the NuNec™

cervical disk replacement; we present two-year follow-up clinical and radiographic data including subgroup analysis for patients presenting with myelopathy and radiculopathy.

Methods

We prospectively collected data from a consecutive series of patients who presented to a single spinal surgery unit in London, UK with cervical radiculopathy or myelopathy and underwent ACDR, having given written consent, from 2009 to 2016. Patients were considered for cervical disk replacement if symptoms resulted from spondylotic disease; movement at the affected level was evident on dynamic flexion/extension x-rays; and they had undergone at least six weeks of unsuccessful conservative management, which might include anti-inflammatory and analgesic medications, physical therapy and nerve root or epidural injections. Contra-indications to ACDR included rheumatoid arthritis, osteoporosis, trauma, spinal tumour, infection, severe degenerative facet disease, ossification of the longitudinal ligament, and spine instability. Patients were undergoing routine clinical care and follow-up, as a result, ethical approval was not required.

Surgery was performed through a right-side transverse skin-crease neck incision, using a standard anterior cervical retractor system. Subperiostial dissection of the longus colli muscles was performed to expose the disk space. An interbody disk distractor or vertebral body pin distracter was used. Diskectomy was performed under the microscope with a high-speed drill, curettes, and Kerrison rongeurs, and the posterior longitudinal ligament was divided in all cases. After the endplates were decorticated to allow a close fit with the surface of the replacement an appropriately sized disk replacement was inserted.

Prospective clinical outcome measures were collected pre-operatively and by postal questionnaire at 3, 6, 12 and 24 months, including Visual Analogue pain score for neck pain (VAS neck) and for arm pain (VAS arm), Neck disability index (NDI), Euroqol (EQ-5D) health status and Short form 36 (SF-36). Dynamic x-rays were taken as was deemed relevant for clinical follow-up, and were matched to the time points above. X-rays were assessed for affected level range of movement by measuring the angle change between the superior and inferior endplates using lines drawn between bony points anteriorly and posteriorly that were reproducible on each pair of flexion/ extension x-rays pre-operatively, and tips of the radiolucent anterior aspect and the radiolucent marks at the rear of the implant post-operatively; a lordotic

angle was taken as a positive value and kyphotic angle as negative (Figure 2). Each level was measured five times by the same researcher and the average taken; reliability was assessed by using the intra-class correlation coefficient and comparing residuals to mean movement change. <2° of measured movement was considered equal to fusion [1,15,16].

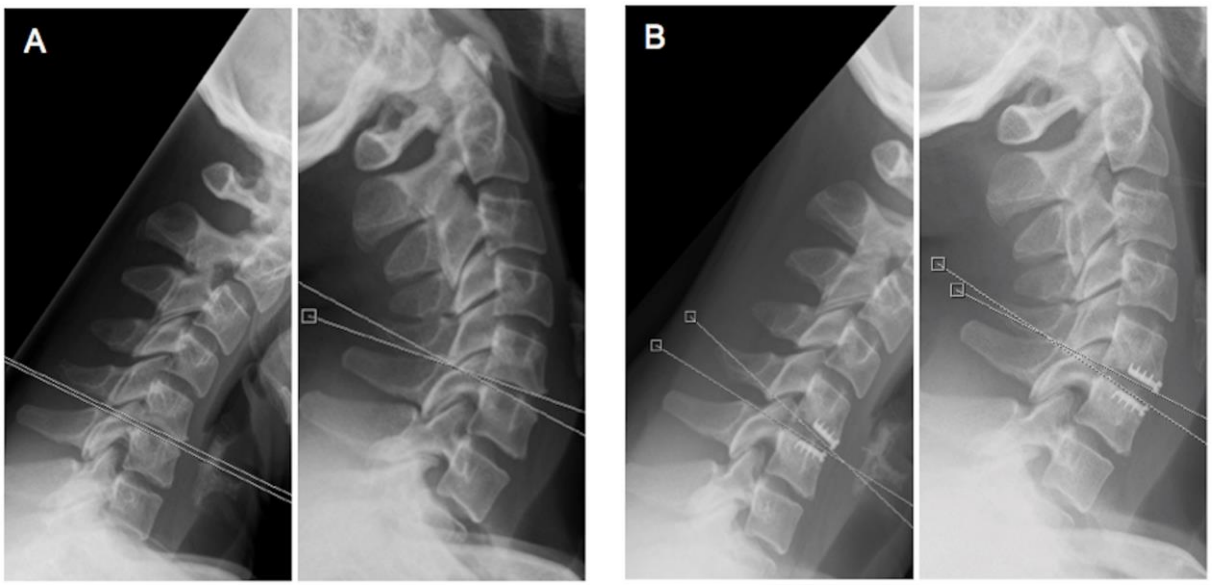

Figure 2: Angular measurements to assess movement at the operated level between flexion and extension. A: pre-operatively, B: post-operatively

Lateral x-rays were also used to assess the presence of HO using the modified McAfee score, which ranges from 0 (no HO) to 4 (fusion) [27], grades 3 and 4 were taken as being clinically significant [14].

Results were explored using descriptive statistics, and hypothesis testing for differences between baseline and 2 years for clinical and radiological data, using the paired t-test for continuous data, Mann-Whitney U test for categorical data and Spearman rank correlation coefficient to investigate relationships; significance was set at P=.05. All analysis was carried out using Stata 13 (StataCorp, College Station, Texas, USA).

Results

From a total of 43 patients, 33 patients had been followed up for two years. 13 were male (39%) and mean age was 48.3 (SD 8.7). 14 presented with radiculopathy, 12 with myelopathy and 4

with a mixed picture. Of patients presenting with an element of myelopathy, 8 presented with soft disk hernia, 3 with osteophytes, and 4 with a mixed picture. Clinical details were unavailable in 3 patients (Table 1).

Gender: male n (%)	13 (39.4%)
Age: mean (SD)	48.3 (8.7)
Underlying problem: n (%)	
Radiculopathy	14 (46.7%)
Myelopathy	12 (40.0%)
Mixed	4 (13.3%)
Number of disks replaced: n (%)	23 (70%)
1	9 (27%)
2	1 (3%)
3	
Level of disk replaced: n (%)	
C3/4	5 (11%)
C4/5	8 (18%)
C5/6	20 (45%)
C6/7	11 (25%)

Table 1: Subject demographics

A total of 44 NuNec™ disk replacements were implanted. The majority of patients had one-level operations (23, 70%), 9 had two-level operations (27%) and 1 patient had a three-level disk replacement operation (3%) according to clinical need and radiological findings. Five (11%) of the replacements were at C3/4, 8 (18%) at C4/5, 20 (45%) at C5/6 and 11 (25%) at C6/7.

Clinical outcomes

All clinical outcomes had improved at the two-year follow-up, although significant variability was seen. Baseline and two year follow-up data was available for 82%, 82%, 82%, 76% and 85%

of patients who had reached two years post-operatively, for VAS neck, VAS arm, NDI, EQ5D and SF36 respectively. There were no significant differences between changes seen for the radiculopathy or myelopathy groups for any of the clinical variables.

The pattern of pain reduction is shown in Figures 3a and 3b. Broadly, the largest reduction is seen at six months, with some return of pain over a longer time scale. At two-year follow-up, neck and arm pain were no longer significantly improved (P=.28; P=.24). Average reduction in neck pain at two years was -0.58 (95%CI -1.65, 0.49) from a baseline of 3.69, whilst reduction in arm pain was -0.66 (95%CI -1.78. 0.46) from 3.17. When radiculopathy and myelopathy subgroups were analyzed separately, neither demonstrated significant improvements for neck pain (mean change (95% CI) -0.18 (-1.58, 1.94) P=.83; -0.92 (-2.62, 0.77) P=.26) or arm pain (-0.48 (-1.95, 0.99) P=.49; -0.74 (-2.89, 1.42) P=.46).

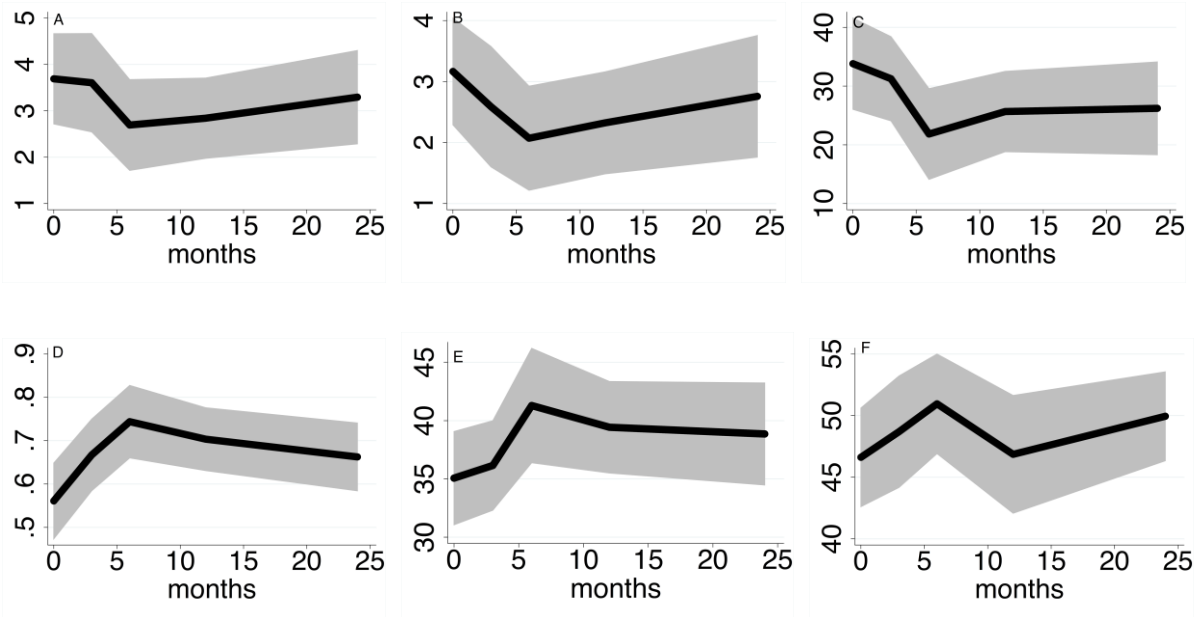

Figure 3: Change in clinical outcomes over time, mean and 95% CIs. A: VAS neck, B: VAS arm, C NDI, D: EQ5D index, E: SF36 PCS, F: SF36 MCS.

The NDI demonstrated significant improvement at two year follow-up (P<.01), with

improvements seen by six months and maintained at two years (Figure 3c); the mean reduction in score was -9.0 points (95%CI -14.2, -3.9) from a pre-operative score of 33.81. Separate subgroup analysis demonstrated significant improvements in both the radiculopathy and myelopathy subgroups (mean change (95% CI) -9.86 (-18.56, 1.15) P=.03; -10.36 (18.55, 2.17) P=.02 respectively).

EQ5D also demonstrated significant improved health status at follow-up (P<0.01), some improvement was seen initially, peaking at six months (Figure 3d). The mean improvement was 0.12 (95% CI 0.04, 0.20) from a pre-operative mean of 0.56. In the subgroup analysis, significant improvement was seen in the radiculopathy group (mean change (95% CI) 0.18 (0.06, 0.31) P<.01), but not in the myelopathy group (0.08 (-0.02, -0.19) P=.11).

The physical sub-score (PCS) of the SF36 demonstrated a similar pattern to the other outcome measures, improving to six months and then plateauing, whilst the mental sub-score (MCS) demonstrated more variability after six months (Figure 3e and f). At two-year follow-up, the improvement in PCS was significant (P=.02), which was not demonstrated in the MCS (P=.17). The average improvement in the PCS was 4.01 (95% CI 0.64, 7.38) from a baseline score of 35.06, the MCS improvement was 3.69 (95% CI -1.67, 9.06) from 46.62. In the subgroup analysis the PCS remained significant improved in the radiculopathy group but not the myelopathy group (mean change (95% CI) 6.05 (1.15, 10.94) P=.02; 3.68 (-2.70, 10.07) P=.23), whilst both groups were not significantly improved on the MCS scale (7.11 (-0.79, 15.02) P=.07; 5.18 (-3.06, 13.42) P=.19).

Radiological outcomes

Radiological data was available for 17 (52%) patients at one year and 12 (36%) at two years, and for 23 (52%) operated levels at one year and 15 (34%) at two years post-operatively; flexion/ extension xrays were not considered clinically necessary in a number of cases, accounting for the low follow-up rate. Repeated measures of each x-ray resulted in residuals of less than 1° across all measurements (0.99, 95% CI 0.92, 1.06), and individual ICC was greater than 0.76 at all time points, demonstrating good intra-rater reliability.

Average movement between flexion and extension at the index level was 6.6° preoperatively, and 4.0° after two years. Paired baseline and follow-up data available from 13 levels

demonstrated that average angle change was -3.38° (95% CI -6.00, -0.75), a statistically significant reduction (P=.02). 72.7% of operated levels demonstrated >2° of movement at follow-up, the progression can be seen in Figure 4. Subgroup analysis did not demonstrate a significant reduction in range of movement in the radiculopathy group, but was significant in the myelopathy group (mean (95% CI) -3.72° (-10.14, 2.70) P=.18; -3.07 (-6.03, -0.11) P= .04 respectively).There was no significant difference in the group changes, P=.76.

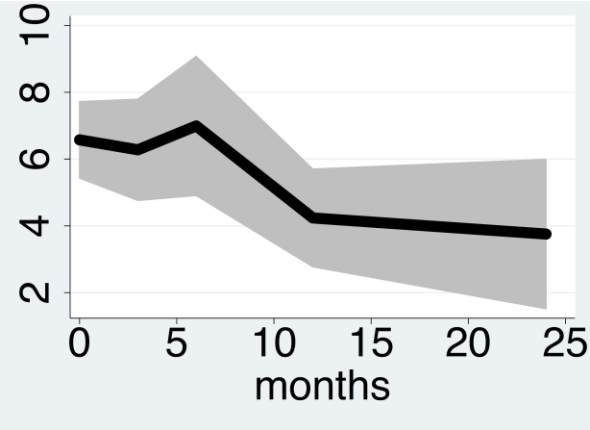

Figure 4: Range of movement at the index level over time, mean with 95% confidence intervals.

Clinically significant HO was seen at five levels (10.8%) pre-operatively, all with level 3 HO. There was significantly more HO at follow-up (P<.01); 53.3% of levels demonstrated clinically significant HO at two years post-operatively, split evenly between levels 3 and 4 (Figure 5). There was a significant relationship linking increased HO with reduced movement at the index level (r=-0.25, P<.01) (Figure 6). There was no significant trend seen in either the radiculopathy or myelopathy subgroups (r=-0.23, P=.07; r=-0.15. P=.24 respectively).

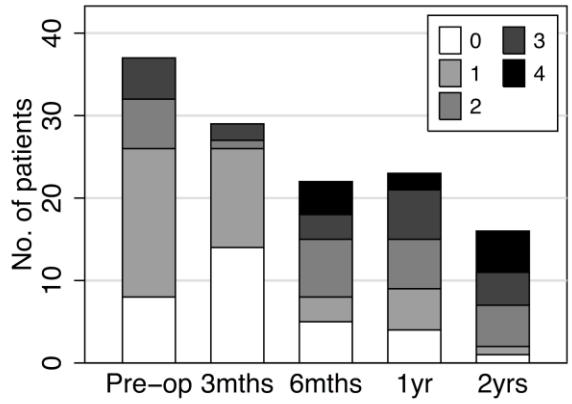

Figure 5: Level of HO at the index level over time.

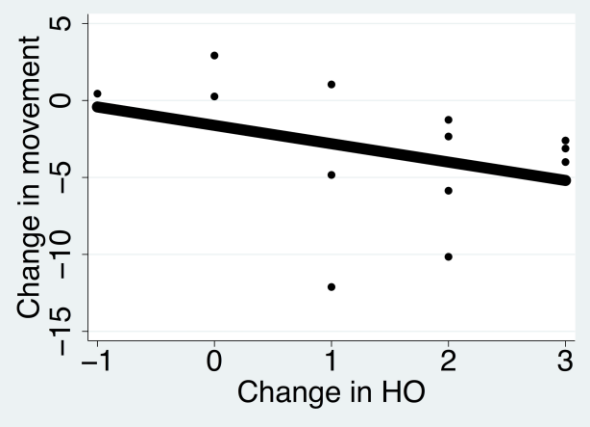

Figure 6: Relationship between the change in level of HO and change in range of movement at the index level. r=-0.25, P<.01

Complications

A cohort of 30 patients was followed up at the surgical hospital. Three patients (10.0%) had temporary dysphagia lasting less than three months and none required further treatment. Two patients required foraminotomy at the index level for recurrence of symptoms, beyond 18 months after the initial operation. No operations were carried out for adjacent segment disease.

Discussion

This report details the clinical and radiographical outcomes of a cohort of patients who underwent ACDR at a single spinal center, and is the first published clinical data for the

NuNec™ disk replacement including subgroup analysis of radiculopathy and myelopathy patients.

Clinical benefits

Equitable or improved clinical outcomes have been demonstrated when comparing ACDR to fusion, using various other disk prostheses [4-8,28]. The two-year post-operative scores from our patient group demonstrate clinical improvements in line with recent large-scale studies [4-8,28-30]; however the percentage improvement is not as large. The results here are likely to be impacted by a lower operating threshold: pre-operative VAS neck scores of 3.7 in this group demonstrate less impairment than seen in the study by Burkus et al [4], in which patients demonstrated an average VAS of 6.8. This pattern is repeated across the other clinical outcome measures; similar reduced impairment is seen with VAS arm at 3.2 pre-operatively compared to 5.91 in the study by Burkus et al., NDI 33.8 and 55.7, EQ5D 0.56 and 0.42, SF36 PCS 35.1 and 31.9, lastly SF36 MCS 46.6 and 42.3, the values for EQ5D and SF36 MCS are taken from studies by Heller et al. and Schluessmann et al. [6,31].

Following neck surgery for radiculopathy or myelopathy, short term improvement in symptoms is frequently seen immediately after surgery for patients with radiculopathy, and by six months for patients with myelopathy, whilst ongoing degenerative disease processes or long term surgical sequelae may impede further improvement [20]. Our results suggest that both groups of patients may clinically benefit from ACDR, and that there is a trend to these benefits being maintained for longer in patients with radiculopathy. This is in line with a large retrospective review of 5256 patients by Lukasiewicz et al [13], who suggests that myelopathy is a more advanced condition, and that these patients may generally be older, less healthy and have significantly greater risk of morbidity, although this was not found in smaller series [12].

Movement maintenance and radiological changes

The ability to maintain movement at the operated level is key to the theoretical benefit of ACDR when compared to ACDF [32] however, a recent systematic review did not identify a relationship between post-operative range of movement, or HO development and clinical outcomes [33]; nevertheless, theoretically the reduction in symptoms or need for future re-operations for adjacent segment disease would represent a significant benefit.

In our patient group, maintained or improved movement is seen at the operated level up to the six month follow-up; after this there is a gradual but significant reduction in movement to a mean of 4.0° at two years (P= .02), demonstrated in Figure 4; at this stage 72.7% of operated levels showed greater than 2° of movement. Other studies have demonstrated movement in 82.9- 88% of operated levels at two years [1,14,15]. This may be a result of clinical bias from loss to follow-up, as the small cohort of patients with 24 month dynamic x-rays are more likely to be those with greater impairment. Interestingly, range of movement at baseline, 6.6°, is lower when compared to other recent studies, which reported range of movement of 7.5-12.8°[7,14,34]. Whilst this could be a difference in x-ray methodology and ability to ellicit full range of movement for imaging, this difference may suggest that our cohort had greater mechanical impairment preoperatively which could influence the results, Ahn [35] suggested that fear of extremes of movement may limit neck range of movement on dynamic x-ray.

The development of clinically significant HO is reported in 0- 33% of cases at 2 years after surgery [1,21,36,37] and has been implicated as a factor in the reduction of range of movement [24], this is supported by our results (Figure 6). The objectivity of HO measurement has come under scrutiny, Choi [38] suggested that 'the more you look, the more you see', and variability in measurement has also been linked to bias from conflicts of interest [2]; many studies have formalized this by using the McAfee scale [14]. Yi et al.[24] report that there is a trend toward progression in HO, as measured by the McAfee scale, from a mean of 0.9 at baseline to 1.5 at three years. Our patient group demonstrated greater HO at both baseline (mean 1.2) and follow-up (mean 2.6), (Figure 5), with 10.8% of operated levels showing grade 3 or 4 HO at baseline, and 53.3% after two years. This progression is statistically significant and whilst this may be a result of the mechanical features of the NuNec™ device or an iatrogenic response to bone drilling, it may also be due to clinical bias as noted above, ongoing disease processes [20], or greater baseline impairment: Yi et al. [24] report that greater degrees of HO at follow-up are seen in patients with greater HO at baseline. Of note, in our myopathy cohort, 47% had an element of osteophyte formation that contributed to the surgical indication. Future research may identify if maintaining movement in this patient group, even if short term, is beneficial.

The development of HO and reduction of range of movement is only of interest if it is clinically significant. The clinical outcome measures in our patient group largely plateau after six months, whereas this is the time point of reduction in range of movement and development of HO, suggesting the two are not closely related. The re-operation rate at two years in this cohort, 6.7%, is marginally higher than seen in the literature for ACDR at two years (2-6%) [1,4-8,28-30], and may be a consequence of the small sample size, as this only related to two patients. Notably this is no higher than the range of re-operation rates from recent large studies for ACDF (4-9%) [1,4-8,28-30] and whilst there may be concerns about late-failure of devices, the small cohort of 21 patients in the study by Quan et al. [23], did not require any re-operations at eight years. Of note in our cohort, there was no need for surgery of the adjacent segment, and no significant, long-term complications, which have been seen in 3-8% and 9-39% of patients in recent large studies of ACDR [1,4-8,28-30].

Limitations

Small sample size and low follow-up rates, particularly for dynamic x-rays, may bias our results, however, as there is minimal data regarding the outcomes of NuNec™ disk replacement, we considered it helpful to report. Furthermore, this patient group was only followed up to two years, and there has been some concern of late device failures, as seen in large-joint arthroplasty [3], although this hasn't been documented in ACDR studies to date [23].

Conclusion

This is the first publication of clinical and radiological results following ACDR using the NuNec™ disk replacement. In this cohort, clinical outcomes have been comparable with other studies of ACDR and show a beneficial effect on quality of life, and whilst range of movement is decreased at the two-year follow-up and HO is common as with other disk replacements, re-operation rate was favorable. Furthermore, we have demonstrated no significant difference in outcome for patients presenting with radiculopathy or myelopathy, suggesting that ACDR is appropriate for both.

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