Systematic Review and Meta-Analysis

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Efficacy and safety of Mobi-C cervical artificial disc versus anterior discectomy and fusion in patients with symptomatic degenerative disc disease

A meta-analysis

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Abstract

Background: Total disc replacement (TDR) using Mobi-C cervical artificial disc might be promising to treat symptomatic degenerative disc disease. However, the results remained controversial. We conducted a systematic review and meta-analysis to compare the efficacy and safety of Mobi-C cervical artificial disc and anterior cervical discectomy and fusion (ACDF) in patients with symptomatic degenerative disc disease.

Methods: PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases were systematically searched. Randomized controlled trials (RCTs) assessing the effect of Mobi-C versus ACDF on the treatment of symptomatic degenerative disc disease were included. Two investigators independently searched articles, extracted data, and assessed the quality of included studies. The primary outcomes were neck disability index (NDI) score, patient satisfaction, and subsequent surgical intervention. Meta-analysis was performed using the random-effect model.

Results: Four RCTs were included in the meta-analysis. Overall, compared with ACDF surgery for symptomatic degenerative disc disease, TDR using Mobi-C was associated with a significantly increased NDI score (Std. mean difference = 0.32; 95% CI = 0.10–0.53; $P = .004$), patient satisfaction (odds risk [OR] = 2.75; 95% confidence interval [CI] = 1.43–5.27; $P = .002$), and reduced subsequent surgical intervention (OR = 0.20; 95% CI = 0.11–0.37; $P < .001$). Mobi-C was found to produce comparable neurological deterioration (OR = 0.77; 95% CI = 0.35–1.72; $P = .53$), radiographic success (OR = 1.18; 95% CI = 0.39–3.59; $P = .77$), and overall success (OR = 2.13; 95% CI = 0.80–5.70; $P = .13$) compared with ACDF treatment.

Conclusion: Among the 4 included RCTs, 3 articles were studying patients with 1 surgical level, and 1 article reported 2 surgical levels. When compared with ACDF surgery in symptomatic degenerative disc disease, TDR using Mobi-C cervical artificial disc resulted in a significantly improved NDI score, patient satisfaction, and reduced subsequent surgical intervention. There was no significant difference of neurological deterioration, radiographic success, and overall success between TDR using Mobi-C cervical artificial disc versus ACDF surgery. TDR using Mobi-C cervical artificial disc should be recommended for the treatment of symptomatic degenerative disc disease.

Abbreviations: ACDF = artificial disc and anterior cervical discectomy and fusion, HO = heterotopic ossification, NDI = neck disability index, NSAIDs = nonsteroidal anti-inflammatory drugs, RCTs = randomized controlled trials, Std. MDs = standard mean differences, TDR = total disc replacement.

Keywords: anterior cervical discectomy and fusion (ACDF), cervical artificial disc, meta-analysis, Mobi-C, symptomatic degenerative disc disease

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1. Introduction

Anterior cervical discectomy and fusion (ACDF) was widely accepted as the standard surgical treatment for symptomatic radiculopathy and myelopathy caused by degenerative disc disease.[1–3] But it could result in adjacent-segment degeneration because of the elimination of natural motion of treated segments and improved intradiscal pressures at adjacent levels.[4–7] Total disc replacement (TDR) was able to preserve treated segment natural motion as well as overall cervical spine biomechanics and might alleviate symptomatic radiculopathy and myelopathy, and avoid exacerbating adjacent segment degeneration.[8,9]

There have been many clinical studies reporting the clinical outcome of cervical TDR versus ACDF. Results showed cervical TDR could produce outcomes similar or superior to ACDF, and the results were consistent ranging from 1 to 5 years of follow-up.[10–14] Cervical TDR was associated with a significantly lower reoperation rate[15] as well as reduced occurrence of adjacent segment degeneration in relative to ACDF.[10,16] But, adjacent segment degeneration was found to have no significant difference between cervical TDR and ACDF.[9]

The Mobi-C cervical artificial disc (LDR Medical; Troyes, France) is a semiconstrained, mobile bearing, bone-sparing TDR consisting of 2 cobalt–chromium–molybdenum alloy endplates and an ultra-high-molecular-weight polyethylene mobile insert facilitating 5 independent degrees of freedom.[17] Clinical studies reported cervical TDR using Mobi-C significantly improved neck disability index (NDI) score, patient satisfaction, overall success, and reduced subsequent surgical intervention compared with ACDF.[9,18]

In contrast, some relevant randomized controlled trials (RCTs) showed that compared with ACDF treatment for symptomatic degenerative disc disease, cervical TDR using Mobi-C failed to significantly improve NDI scores, patient satisfaction, overall success, and decrease neurological deterioration.[9,19] Considering these inconsistent effects, we therefore conducted a systematic review and meta-analysis of RCTs to compare the efficacy and safety of Mobi-C cervical artificial disc and ACDF for the treatment of symptomatic degenerative disc disease.

2. Materials and methods

This systematic review and meta-analysis were conducted according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement[20] and the Cochrane Handbook for Systematic Reviews of Interventions.[21]

2.1. Literature search and selection criteria

PubMed, EMbase, Web of science, EBSCO, and the Cochrane library were systematically searched from inception to December 2016, with the following keywords: Mobi-C, and anterior cervical discectomy, and fusion or ACDF. To include additional eligible studies, the reference lists of retrieved studies and relevant reviews were also hand-searched and the process above was performed repeatedly until no further article was identified.

The inclusion criteria were as follows: the study population were patients with symptomatic degenerative disc disease; intervention treatment was TDR using Mobi-C versus ACDF; and study design was RCT.

The exclusion criteria included any prior spine surgery at operative level, Paget disease, osteomalacia, or any other metabolic bone disease other than osteoporosis.

2.2. Data extraction and outcome measures

The following information was extracted for the included RCTs: first author, publication year, sample size, baseline characteristics of patients, intervention of TDR using Mobi-C, intervention of control, study design, NDI score, patient

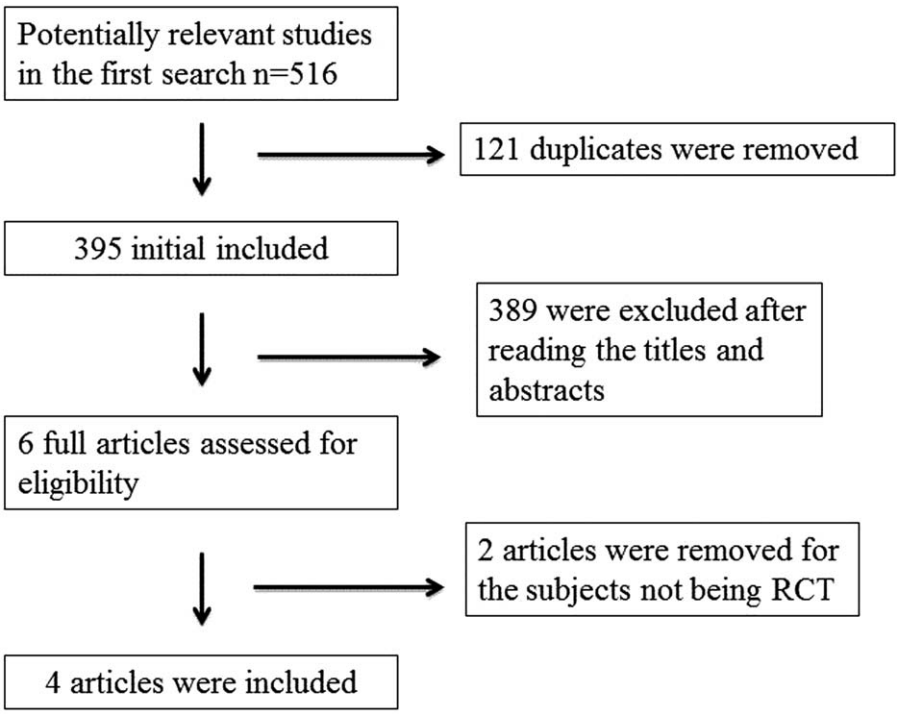

Figure 1. Flow diagram of study searching and selection process.

Table 1

Characteristics of included studies.

		Mobi-C group				ACDF group						
No. author	Number	Age, y	BMI, kg/m^2	Work status (being able to work) No.	Driving status (being able to drive) No.	Number	Age, y	BMI, kg/m^2	Work status (being able to work) No.	Driving status (being able to drive) No.	Type	Follow-up	NASS grades	Jada scores
1 Hou 2016	51	46.3±7.8	21±3.2	–	–	48	48.5±8.3	22±2.5	–	–	1-level	5 y	Level I	3
2 Hisey 2016	164	43.3±9.2	27.3±4.4	108 (65.9%)	155 (94.5%)	81	44.0±8.2	27.4±4.2	46 (56.8%)	79 (97.5%)	1-level	5 y	Level I	4
3 Reginald 2015	225	45.3±8.1	27.6±4.5	141 (62.7%)	210 (93.3%)	105	46.2±8.0	28.1±4.2	64 (61.0%)	102 (97.1%)	2-level	4 y	Level I	4
4 Park 2008	21	45 (31–61)	–	–	–	32	47 (26–63)	–	–	–	1-level	1 y	Level I	3

ACDF = artificial disc and anterior cervical discectomy and fusion, BMI = body mass index, NASS = North American Spine Society.

satisfaction, subsequent surgical intervention, neurological deterioration, radiographic success, overall success, and adverse events. The author would be contacted to acquire the data when necessary.

The primary outcomes were NDI score, patient satisfaction, and subsequent surgical intervention. Secondary outcomes included neurological deterioration, radiographic success, overall success, and adverse events.

Patient satisfaction was tested by a questionnaire: very satisfied, somewhat satisfied, somewhat dissatisfied, or very dissatisfied with their treatment. Patients were asked if they would definitely, probably, probably not, or definitely not recommend the same treatment method to a friend with the same symptoms and indications. Subsequent surgical intervention was defined as any secondary surgery at an index-level segment and included removal, revision, supplemental fixation, or reoperation, but did not included adjacent-level subsequent surgeries. Radiographic success for the ACDF group was considered to be fusion of both treated levels—<2° of angular motion in flexion/extension and evidence of bridging bone across the disc space and radiolucent lines at no >50% of the graft vertebral interfaces. Radiographic success for the TDR group was considered to be at least 2° angular motion in flexion/extension or no evidence of bridging trabecular bone across the disc space.

2.3. Quality assessment in individual studies

The Jadad Scale was used to evaluate the methodological quality of each RCT included in this meta-analysis.[22] This scale consisted of 3 evaluation elements: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). One point would be allocated to each element if they have been mentioned in article, and another one point would be given if the methods of randomization and/or blinding had been detailedly and appropriately described. If methods of randomization and/or blinding were inappropriate, or dropouts and withdrawals had not been recorded, then one point was deducted. The score of Jadad Scale varies from 0 to 5 points. An article with Jadad score ≤ 2 was considered to be of low quality. If the Jadad score ≥ 3, the study was thought to be of high quality.[23]

2.4. Statistical analysis

Standard mean differences (Std. MDs) with 95% confidence intervals (CIs) for continuous outcomes (NDI score) and odds risks (ORs) with 95% CIs for dichotomous outcomes (patient satisfaction, subsequent surgical intervention, neurological deterioration, radiographic success, overall success) were used to estimate the pooled effects. All meta-analyses were performed using random-effects models with DerSimonian and Laird weights. Heterogeneity was tested using the Cochran Q statistic ($P < .1$) and quantified with the I^2 statistic, which describes the variation of effect size that was attributable to heterogeneity across studies. An I^2 value >50% indicated significant heterogeneity. Sensitivity analysis was performed to detect the influence of a single study on the overall estimate via omitting one study in turn when necessary. Owing to the limited number (<10) of included studies, publication bias was not assessed. $P < .05$ in two-tailed tests was considered statistically significant. All statistical analyses were performed with Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

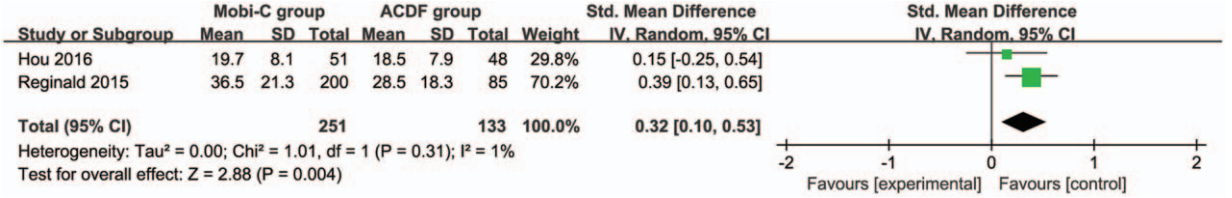

Figure 2. Forest plot for the meta-analysis of NDI score. NDI scores ranged from 0 to 50. NDI = neck disability index.

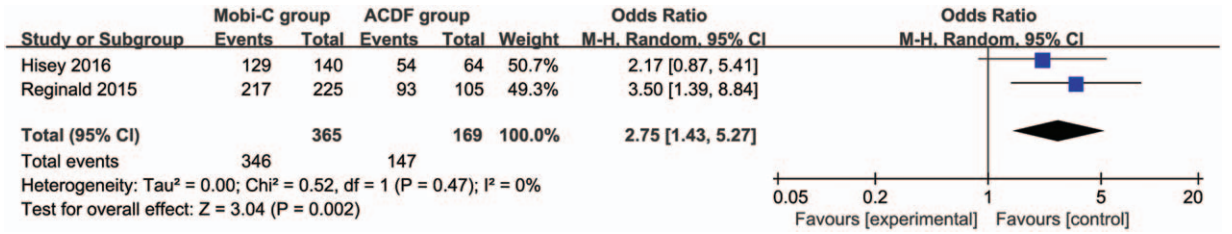

Figure 3. Forest plot for the meta-analysis of patient satisfaction. Patient satisfaction was tested by a questionnaire: very satisfied, somewhat satisfied, somewhat dissatisfied, or very dissatisfied with their treatment.

3. Results

3.1. Literature search, study characteristics, and quality assessment

Five hundred sixteen potential studies were obtained through the initial search of databases. The detailed screening flow was shown in Fig. 1. Three hundred eighty nine studies were excluded after screening the titles and abstracts. Four RCTs were included in the meta-analysis.[9,18,19,24]

Table 1 demonstrated detailed characteristics of 4 included studies in this meta-analysis. Their sample sizes ranged from 53 to 330, and the total number was 727. There were similar age, body mass index (BMI), work status, and driving status in patients at baseline. Of these 4 RCTs, 3 studies reported 1-level disc[9,19,24] and 1 study reported 2-level discs[18] for surgery. The follow-up time varied from 1 year to 5 years.

Among the 4 RCTs, 2 studies reported the NDI score,[18,19] 2 studies reported the patient satisfaction,[9,18] 3 studies reported the subsequent surgical intervention,[9,18,19] 2 studies reported the neurological deterioration, radiographic success, and overall success.[9,18] Jadad scores of the 4 included studies varied from 3 to 4. North American Spine Society (NASS) grades of all included RCTs were level I. These indicated that all 4 studies were considered to be high-quality and well-designed ones.[25]

3.2. Primary outcome: NDI score, patient satisfaction, and subsequent surgical intervention

The random-effects model was applied to analyze these 3 outcome data. These 3 outcome data were analyzed with a random-effects model. Compared with ACDF for symptomatic degenerative disc disease, TDR using Mobi-C could significantly increase NDI score (Std. mean difference = 0.32; 95% CI = 0.10–0.53; $P = .004$) after pooling the results of 2 included RCTs, with low heterogeneity among the studies ($I^2 = 1\%$, heterogeneity $P = .31$) (Fig. 2). TDR using Mobi-C was also found to significantly improve patient satisfaction (OR = 2.75; 95% CI = 1.43–5.27; $P = .002$) than ACDF, with no heterogeneity among the studies ($I^2 = 0\%$, heterogeneity $P = .47$) (Fig. 3). Consistently, the incidence of subsequent surgical intervention was revealed to be significantly lower in Mobi-C group than that in ACDF group (OR = 0.20; 95% CI = 0.11–0.37; $P < .001$) than ACDF, with no heterogeneity among the studies ($I^2 = 0\%$, heterogeneity $P = .87$) (Fig. 4).

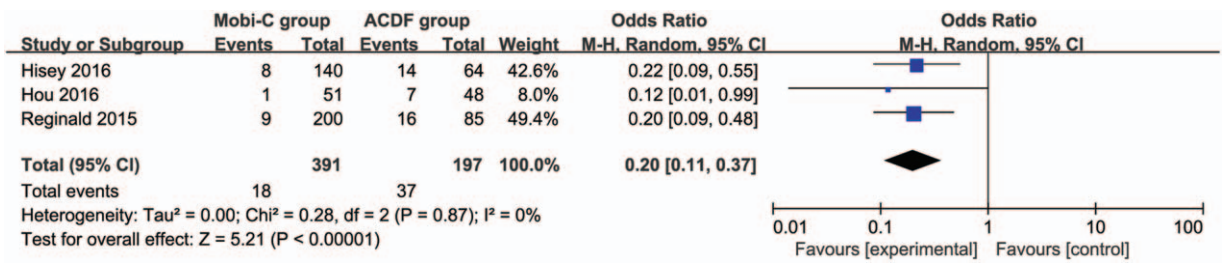

Figure 4. Forest plot for the meta-analysis of subsequent surgical intervention. Subsequent surgical intervention was defined as any secondary surgery at an index-level segment and included removal, revision, supplemental fixation, or reoperation, but did not included adjacent-level subsequent surgeries.

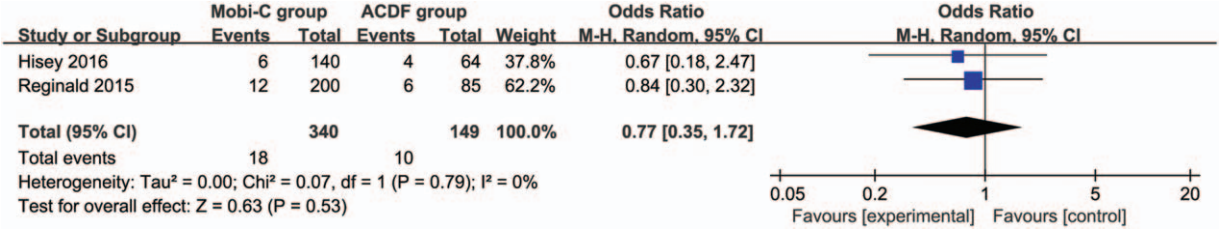

Figure 5. Forest plot for the meta-analysis of neurological deterioration.

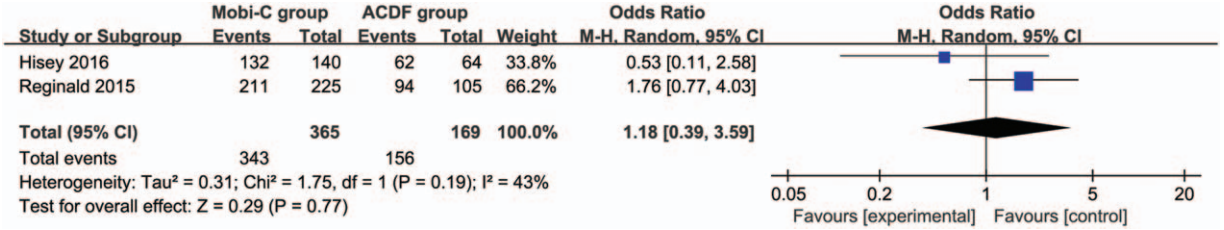

Figure 6. Forest plot for the meta-analysis of radiographic success.

3.3. Sensitivity analysis

Low heterogeneity or no heterogeneity was observed among the included studies for NDI score, patient satisfaction, and subsequent surgical intervention. Thus, we did not perform sensitivity analysis by omitting one study in each turn to detect the source of heterogeneity.

3.4. Secondary outcomes

Compared with ACDF treatment, TDR using Mobi-C cervical artificial disc resulted in comparable neurological deterioration (OR = 0.77; 95% CI = 0.35–1.72; $P = .53$; Fig. 5) and achieve comparable radiographic success (OR = 1.18; 95% CI = 0.39–3.59; $P = .77$; Fig. 6), and overall success (OR = 2.13; 95% CI = 0.80–5.70; $P = .13$; Fig. 7).

3.5. Adverse effects

Device-related adverse events were defined as any clinically adverse sign, symptom, syndrome, or illness that occurred or worsened during or after the initial surgery, and were caused by TDR using Mobi-C artificial disc or ACDF. These adverse events mainly included malpositioned implant, cage subsidence, heterotopic ossification, wound infection, non-union, etc. There was no significant difference of device-related adverse events between Mobi-C group and ACDF group after pooling the results of 3 included studies (OR = 0.61; 95% CI = 0.18–2.10; $P = .43$; Fig. 8).

4. Discussion

Our meta-analysis clearly suggested that compared with ACDF treatment for symptomatic degenerative disc disease, TDR using Mobi-C cervical artificial disc was associated with a significantly improved NDI score, patient satisfaction, and reduced subsequent surgical intervention, and resulted in comparable neurological deterioration, radiographic success, and overall success. Similar device-related adverse events were found between Mobi-C group and ACDF group. This was the first meta-analysis to study the treatment efficacy of TDR using Mobi-C cervical artificial disc versus ACDF in patients with symptomatic degenerative disc disease.

Two included study also showed that TDR using Mobi-C cervical artificial disc demonstrated statistically better results of SF-12 PCS scores, pain alleviation, and adjacent-segment degeneration than ACDF treatment.[9,18] These results were consistent with trials comparing TDR using other cervical artificial disc with ACDF.[13,26] Adjacent-segment degeneration was the major concern for patients undergoing surgery for degenerative disc disease. ACDF resulted in higher rates of

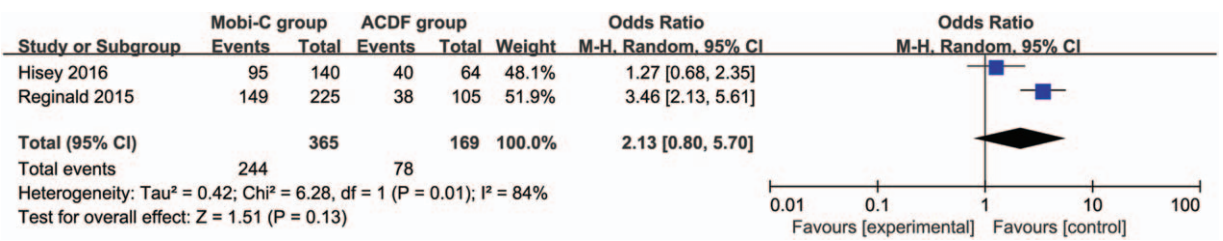

Figure 7. Forest plot for the meta-analysis of overall success.

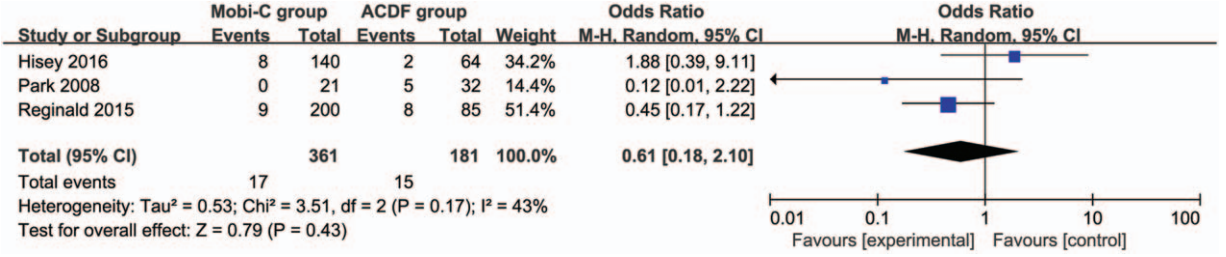

Figure 8. Forest plot for the meta-analysis of adverse events.

adjacent-segment degeneration, and TDR could not entirely prevent adjacent-segment degeneration, but these underlying mechanisms were elusive. It was still widely debated whether the preservation of the adjacent-segment with TDR was due to the preserved biomechanics at the index and adjacent levels.[18]

The stable flexion/extension mean range of motion at the operated segment was of significant difference for TDR surgery. Clinically relevant heterotopic ossification (HO) (Grades III and IV) occurred in 16.6% of segments and 25.6% of patients treated with TDR using Mobi-C artificial disc, which was similar to or less than the rates in other cervical artificial disc.[14,18,27] Severe HO was found to significantly limit motion in patients after TDR surgery. Considering that severe HO resulted in essentially fusion, the clinical results may also be similar to ACDF. Various approaches to avoid HO included complete endplate coverage, meticulous surgical technique minimizing uncovered bleeding bone, and prophylactic use of nonsteroidal anti-inflammatory drugs (NSAIDs).[9,14]

There were some potential limitations. Firstly, the test power was limited by sample size. Only 4 RCTs were included in this meta-analysis and 2 of them had a relatively small sample size ($n < 100$). The follow-up time in the included studies ranged from 1 year to 5 years, and longer follow-up time was needed to evaluate some index including motion and stability of segments, the incidence of HO etc. Different follow-up time and 1 or 2 level symptomatic degenerative disc diseases might affect the pooling results. Next, the mechanisms mediating TDR to reduce adjacent-segment degeneration remained ill clear. Finally, it was unavailable to compare the efficacy and safety of TDR using Mobi-C cervical artificial disc versus ACDF when treating ≥3 level symptomatic degenerative disc diseases.

5. Conclusions

TDR using Mobi-C cervical artificial disc could significantly increase NDI score, patient satisfaction, and decrease subsequent surgical intervention, and obtained comparable neurological deterioration, radiographic success, and overall success compared with ACDF treatment for symptomatic degenerative disc disease. TDR using Mobi-C cervical artificial disc was recommended to be administrated in patients.

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