Preliminary Clinical Outcome of One-level Mobi-C Total Disc Replacement in Japanese Population

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Abstract:

Introduction: In 2018, the first Mobi-C® total disk replacement (TDR) case was performed in Japan. In this study, we examined the preliminary clinical outcome of Mobi-C® for degenerative cervical spine disease.

Methods: We examined 24 consecutive patients who underwent 1-level TDR after 2018 and followed up for more than 6 months after surgery. The evaluation criteria included age, gender, diagnosis, follow-up period, surgical level, implant size, surgery time, intraoperative bleeding volume, complications, revision surgery, imaging findings, JOA score, and various questionnaires.

Results: The mean age was 52.7 years, 13 males and 11 females. There were 15 cases of cervical disk herniation and 9 cases of cervical spondylosis. The mean follow-up period was 17.4 months. Surgical levels were C3/4 in 4 cases, C4/5 in 2 cases, C5/6 in 16 cases, and C6/7 in 2 cases. The mean operation time was 138.5 minutes, the amount of intraoperative bleeding was 32.1 ml, and there were no serious intraoperative complications. The range of motion of the affected level increased significantly, from 6.6 degrees preoperatively to 12.2 degrees at final follow-up. No patients required revision surgery at final follow-up, and there were no cases of heterotopic ossification or adjacent segment disease. One patient exhibited radiculopathy due to mild subsidence 1 year after surgery, and 1 had asymptomatic contact of device plates. Preoperative and final JOA scores improved from 11.7 to 15.8 points, and NRS improved from 4.3 to 1.3 points for neck pain and 4.3 to 1.7 points for arm pain. Preoperative and final NDI improved from 39.7% to 14.0%, and EQ-5D improved from 0.602 to 0.801.

Conclusions: The short-term treatment outcomes of Mobi-C® TDR were generally favorable. Spine surgeons should comply with guidelines when introducing this procedure and strive to adopt this new technology in Japan.

Keywords:

Total disc replacement (TDR), Cervical spine, Clinical outcome, Cervical disc herniation, Cervical Spondylosis

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Introduction

Anterior cervical discectomy and fusion (ACDF) was reported in the 1950s[1)] and developed into a gold standard procedure for symptomatic radiculopathy and myelopathy caused by cervical degenerative disorders as cervical disk herniation (CDH), or cervical spondylosis[2,3)]. ACDF has a high rate of bony fusion with good clinical outcomes[4)]. However, adjacent segment disease (ASD) was often reported due to the elimination of movements at treated segments and increased intradiscal pressure[5-8)].

Cervical total disk replacement (TDR) became an alternative to ACDF to prevent ASD by maintaining mobility between affected disks. Although TDR was first reported in 1966, there were no satisfactory clinical outcomes[9)]. The Cummins-Bristol TDR, a metal-on-metal type implant, was

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Table 1. TDR Inclusion and Exclusion Criteria in Japan (Excerpted Version).

Inclusion Criteria
1. Radiculopathy and/or myelopathy due to cervical disc herniation or cervical spondylosis with bony spur (no indication for neck pain alone)
2. Two contiguous levels between C3/4–C6/7 (two levels only available at a proctoring facility during the post marketing surveillance)
3. Unresponsive to nonoperative, conservative treatment for at least 3 months or presence of progressive symptoms or signs of nerve root/spinal cord compression despite continued nonoperative treatment
Exclusion Criteria
1. Active infection at the cervical spine
2. Cervical spine tumor
3. Trauma with fracture and/or ligamentous injury
4. Allergy to device materials such as cobalt, titanium alloy, or polyethylene
5. Severe bone fragility
6. Marked instability at the affected level
7. Immovability at the affected level such as bridging spur formation
8. Severe injury and/or deformity at the vertebral body and/or cervical posterior element
9. Marked anatomical abnormality
10. Involuntary movements of head and neck
11. Severe cervical deformity including severe narrowing of disc space and/or facet joint
12. Marked abnormal alignment at the cervical spine such as segmental kyphosis
13. Severe cervical stenosis at multiple levels

reported in Europe in the 1980s with treatment results[10]. In 1992, Bryan developed a new type of artificial disk consisting of metal endplates and polyethylene, and the US Food and Drug Administration (FDA) approved it in 2007[11]. To date, there have been eight models that have been FDA-approved. Many studies have reported the clinical outcome of cervical TDR versus ACDF. A meta-analysis, with eight independent studies, showed TDR was superior to ACDF for treating symptomatic cervical disk disease in terms of overall success, neck disability index (NDI) success, neurological success, implant/surgery-related serious adverse events, secondary procedure, functional outcomes, patient satisfaction and recommendation, and adjacent segment degeneration[12]. In Japan, TDR was first approved in 2017 with two models (Mobi-C®, Zimmer Biomet Holdings, Inc.; Prestige LP®, Medtronic, Inc.) introduced in clinical practice, generating great expectations for their clinical potential. The Mobi-C® cervical artificial disk is a semi-constrained, mobile bearing, bone-sparing TDR consisting of 2 cobalt-chromium-molybdenum alloy endplates with an ultra-high-molecular-weight polyethylene mobile insert facilitating 5 independent degrees of freedom[13].

Compared to ACDF, clinical studies reported cervical TDR using Mobi-C® significantly improved NDI score, patient satisfaction, overall success, and reduced subsequent surgical intervention and ASD[14,15]. A seven-year follow-up evaluation of a randomized, prospective, multicenter clinical trial in 1-level Mobi-C® TDR was previously reported[16]. There were no statistically significant differences in NDI, visual analog scale (VAS) neck pain, VAS arm pain, and 12-item Health Survey (SF-12) between TDR and ACDF seven years after surgery. The composite success analysis did not demonstrate inferior results for 1-level TDR compared to ACDF[16]. The rate of secondary surgery for ASD was significantly lower in 2-level TDR patients compared to ACDF patients[16].

To our knowledge, the preliminary clinical outcome of TDR for the Japanese population is not well known. In this study, we conducted a prospective observational study and investigated the short-term clinical outcome of 1-level Mobi-C® TDR in the Japanese population.

Materials and Methods

Patient population

We performed a prospective observational study using the clinical records of 24 consecutive patients who underwent a 1-level Mobi-C® TDR at a single institute for cervical degenerative diseases since 2018. Surgical decision-making in TDR was in strict accordance with the established Japanese TDR guideline (Table 1). All patients showed radiculopathy and/or myelopathy due to CDH or cervical spondylosis with bony spurs. None of the patients revealed neck pain alone. Conservative treatment was adequately applied for at least three months except in patients with progressive nerve palsy due to nerve root/spinal cord compression. The mean follow-up duration was 17.4 (range: 6.7-29.3) months. Evaluation criteria included age, gender, body mass index (BMI), symptoms, diagnosis, the affected disk level, surgical time and estimated blood loss, and implant size (depth, width, and height). Pre- and post-operative assessments used the following outcome measures: Japanese Orthopedic Association (JOA) scores; JOA recovery rates (JOA RR)[17]; JOA cervical myelopathy evaluation questionnaire (JOACMEQ) consisting of 1) cervical spine function, 2) upper extremity

Table 2. Subject Demographics.

No. of patients	24
Age (years)	52.7 (30–84)
Sex:	13 male, 11 female
BMI (kg/m^2)	22.9 (18.7–28.7)
Follow-up period (months)	17.4 (6.7–29.3)
Diagnosis	
CDH (R, M, RM)	15 (3, 10, 2)
CSR	4
CSM	3
CSRM	2
Affected level	
C3.4	4
C4/5	2
C5/6	16
C6/7	2
Surgical time (minutes)	138.5 (94–174)
Estimated blood loss (ml)	32.1 (5–183)

CDH: Cervical disc herniation,
CSR: Cervical spondylotic radiculopathy,
CSM: Cervical spondylotic myelopathy,
CSRM: Cervical spondylotic radiculomyelopathy,
R: Radiculopathy
M: Myelopathy
RM: Radiculomyelopathy

function, 3) lower extremity function, 4) bladder function, 5) quality of life (QOL); numerical rating scale (NRS) at the neck and arm; NDI; EuroQoL 5 dimensions 5-level (EQ-5D-5L); imaging findings, complications, and need for reoperation. The JOA, JOA RR, and JOACMEQ were used for clinical evaluation in patients with myelopathy. The authors' affiliated institution IRB approved this research, and the study participants provided informed consent.

Surgical procedure

Here, we briefly describe our Mobi-C® surgical procedure[18]. All surgeries were performed by one surgeon (K. I.). Patients are placed in a supine position. The patient's neck should be positioned and maintained in neutral lordosis to avoid hyperextension. A C-arm is prepared to capture the true A/P and lateral views during patient positioning and before final draping. An anterior cervical approach through a 4-cm skin incision is performed that is nearly identical to that of a traditional ACDF. Bilateral longus colli muscles are separated to expose vertebral bodies' anterior aspect and the affected intervertebral disk. Casper pins are inserted at the center of the midline of the vertebrae in the coronal plane. A Caspar distractor is attached to obtain the desired height. Under the microscope, discectomy is performed between the uncinate processes and the back to the posterior ligament. All posterior osteophytes on the superior and inferior vertebral endplates are manually removed. Distraction forceps (paddle distractors) are useful to gain the desired disk height to release the disk space. A release of the posterior longitudinal ligament may help to obtain parallel distraction. The release should be bilaterally symmetrical. The endplate's width is typically small in Asian patients, so flattening the caudal vertebral body's endplate should be needed to fit the device to the endplate. A 3 mm diameter pneumatic drill should flatten the caudal endplate's posterolateral aspects to preserve the bony endplates. Significant endplate disruption may cause post-operative implant subsidence into the vertebral body. In patients with radiculopathy due to bony spurs, the bony spurs should be removed to decompress the nerve roots' shoulder bilaterally. An adequate width should cover the flat area of the endplate to the largest extent possible, and the use of a depth gage should determine the depth. Trialing should begin with the smallest height first (5 mm) and should not exceed the height of healthy adjacent disks. Then, the TDR prosthesis (Mobi-C®, Zimmer Biomet, Austin, TX, USA) is implanted into the intervertebral disk. Before the Casper pins are removed, compression force should be applied until the lateral teeth tightly bite into the endplates.

Radiographic examinations

Plain radiographs of the cervical spine, including lateral flexion and extension angles at the surgical level and C2-7 angle, were measured before surgery and during the follow-up period. The range of motion (ROM) at the surgical level and the ROM of the cervical spine (C2-7 ROM) were assessed over time. The clear zone between the endplate and prosthesis, migration of the implant, the prevalence of heterotopic ossification, and ASD were analyzed.

Statistical analysis

The Mann-Whitney test evaluated statistical differences and one-way ANOVA, followed by Fisher's PLSD post hoc test and Fisher's exact probability test. Statistical analysis was performed using SPSS Statistics 21.0. Statistical significance was defined as $P<.05$.

Results

All patients presented with neck pain and cervical radiculopathy with/without myelopathy and underwent conservative treatment for a mean period of 4.5 months. All patients fulfilled the inclusion criteria, as defined by the Japanese Guideline for Medical Devices, Spinal Disk Prosthesis (Pharmaceuticals and Medical Devices Agency: PMDA) (Table 1: excerpted version)[19].

The sample's demographic characteristics were as follows: mean age, 52.7 years (30-84); sex, 13 males and 11 females; BMI, 22.9 (range: 18.7-28.7) kg/m^2. The following conditions were diagnosed: CDH, 15 cases (radiculopathy: 3, myelopathy: 10, radiculomyelopathy: 2 cases); cervical spondylotic radiculopathy (CSR), 4 cases; myelopathy (CSM), 3 cases; radiculomyelopathy (CSRM), 2 cases. The surgical levels were C3/4 in 4 cases, C4/5 in 2 cases, C5/6 in 16 cases, and C6/7 in 2 cases. The mean surgical time was 138.5 (94-174) minutes, and the mean estimated blood

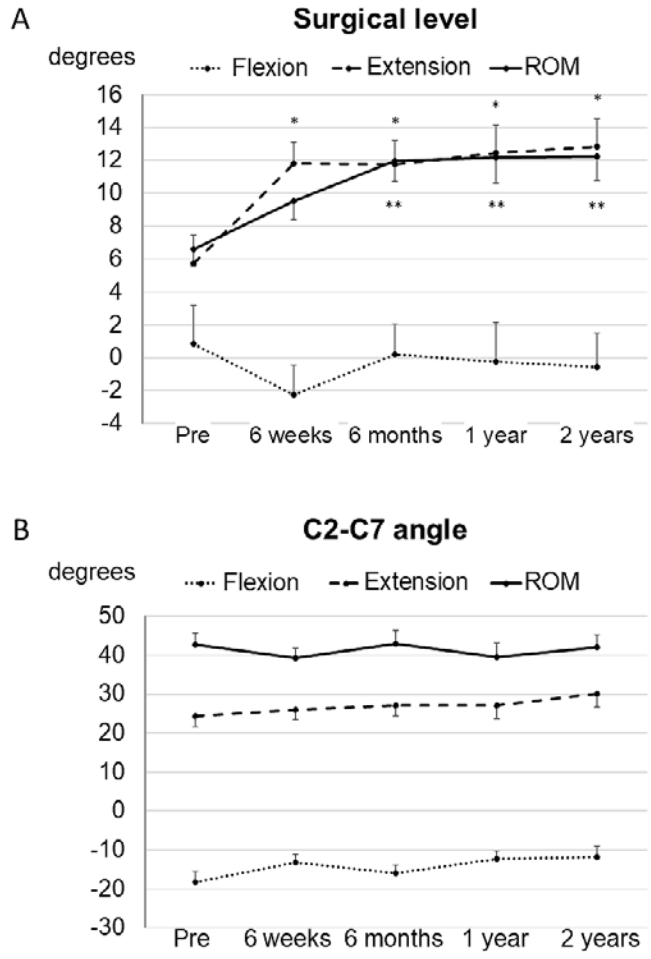

Figure 1. A: Range of motion (ROM) at the affected level at the pre- and post-operative period. Increases in extension and ROM are significantly regained after six months. B: The C2-7 angles of flexion and extension positions during the pre- and post-operative period. The C2-7 ROM were maintained at the final follow-up.

loss was 32.1 (5-183) ml (Table 2). The implant sizes (depth × width × height [mm]) were 13×15×5 in 1, 13×17×5 in 1, 15×15×5 in 7, 15×17×5 in 2, 15×17×6 in 1, 17×17×5 in 6, 17×17×6 in 2, 17×19×5 in 3, and 17×19×6 in 1 case(s). In all cases, no serious complications, such as vascular and neurologic injuries, were encountered. The preoperative C2-7 angle was 6.5 degrees, followed by 13.1 degrees one year after surgery, and maintained at 14.7 degrees two years after surgery. The mean ROM at the affected level recovered significantly from 6.6 degrees preoperatively to 12.0 degrees at six months after surgery and maintained at 12.2 degrees two years after surgery (Fig. 1 A). The ROM at the cervical spine (C2-7) was 42.7 degrees, followed by 43.1 degrees at six months after surgery, and maintained at 42.1 degrees at two years after surgery (Fig. 1 B).

At the final follow-up, the JOA score increased from a mean of 11.7 (6-16) points before surgery to a mean of 15.8 points showing a JOA RR of 72.2% (Fig. 2A). The mean NRS for neck pain recovered from 4.3 (0-10) points to 1.3 (0-4) points. The mean NRS for arm pain recovered from 4.3 (0-10) points to 1.7 (0-4) points. The mean NDI score also improved from 39.7 (18-86)% before surgery to 14.0 (0-28)% (Fig. 2B). The EQ-5D-5L improved from 0.602 (0.264-0.871) to 0.801 (0.733-1.000) (Fig. 2C). All functions except bladder function in the JOACMEQ significantly recovered at final follow-up compared to preoperative scores (Fig. 2D).

There were no cases with heterotopic ossification, ASD, or requiring revision surgery, and three patients experienced complications (12.5%). Post-operative radiculopathy due to subsidence and asymptomatic contact of device plates were observed in each case. Another case demonstrated an issue during device insertion, which had a device disassembling from the insertor during prosthesis placement into the disk space. However, it was not unbeneficial for the patient.

Case presentation

Case: A 43-year-old male.

The patient suffered from neck pain in addition to pain and weakness on the left arm and leg for 10 months. Preoperative magnetic resonance image revealed spinal compression due to disk herniation at the level of C5-6 (Fig. 3A). Because the myelopathy was progressing, a Mobi-C® cervical TDR was performed. There were no complications, and the ROM at C5-6 regained from 6.9 degrees preoperatively to 18.8 degrees at one year follow-up (Fig. 3B-D). The preoperative JOA score improved from 12 to 15 points (JOA recovery rate: 60%).

Discussion

TDR was initially implemented in Japan by the Guidance for Evaluation of Medical Devices with Emerging Technology, Spinal Implant Working Group, in 2015. Spinal surgeons, medical material experts, and representatives from the Ministry of Health, Labor and Welfare and PDMA discussed the status quo in spinal implants abroad and usage guidelines for their potential introduction to the Japanese market[20]. Subsequently, the Working Group for Guideline Development for Cervical TDR was organized to facilitate further discussion between orthopedic surgeons, neurosurgeons, and PMDA to complete the Japanese guideline[19,21]. We were fortunate to be involved as contributors for both working groups for Guideline Development and creating the Guidance for Evaluation. Table 1, 2 show the inclusion and exclusion criteria (excerpted version) in the guidance development of the FDA[22,23], and PMDA-approved TDR[19]. There are several differences between the two criteria. First, provided that there are no progressive neuroparalytic symptoms, the PMDA criteria require at least three months of conservative treatment, while the FDA criteria only require six weeks. Over-indication for surgery is a concern for those undergoing conservative therapy for a relatively short period of six weeks. Second, several inclusion criteria in the FDA criteria are described with specific values (i.e., range of age [18 to

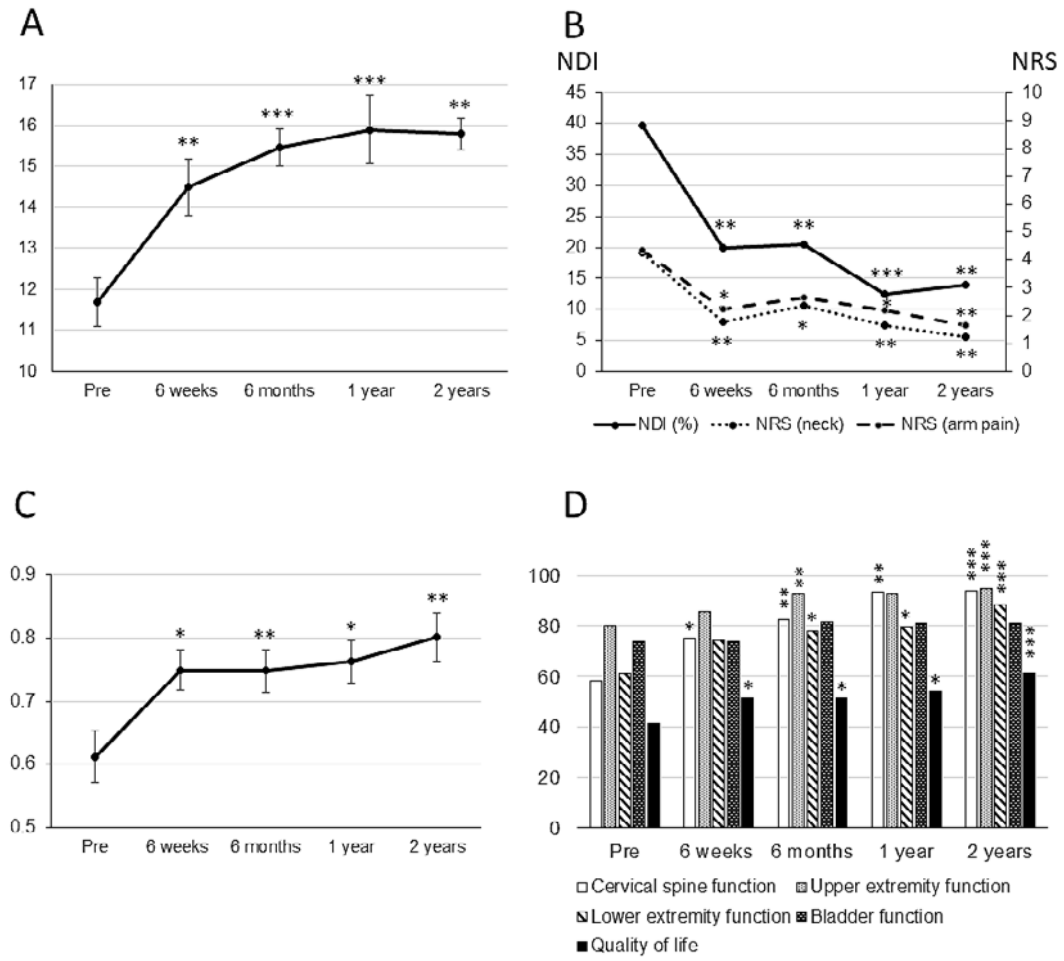

Figure 2. A: Japanese Orthopedic Association (JOA) score. The JOA scores recovered at the follow-up period. B: Neck disability index (NDI) and numerical rating scale (NRS) at the neck and arm. Three indices improved over time compared to preoperative levels. C: EuroQoL 5 dimensions 5-level (EQ-5D-5L). EQ-5D-5L recovered at six weeks after surgery and was maintained at two years after surgery. D: JOA cervical myelopathy evaluation questionnaire (JOACMEQ). All functions except bladder function recovered at 2-year follow-up compared to preoperative scores.
Data represent the mean±SD. Significant differences from control: *P<0.05, **P<0.01, ***P<0.001.

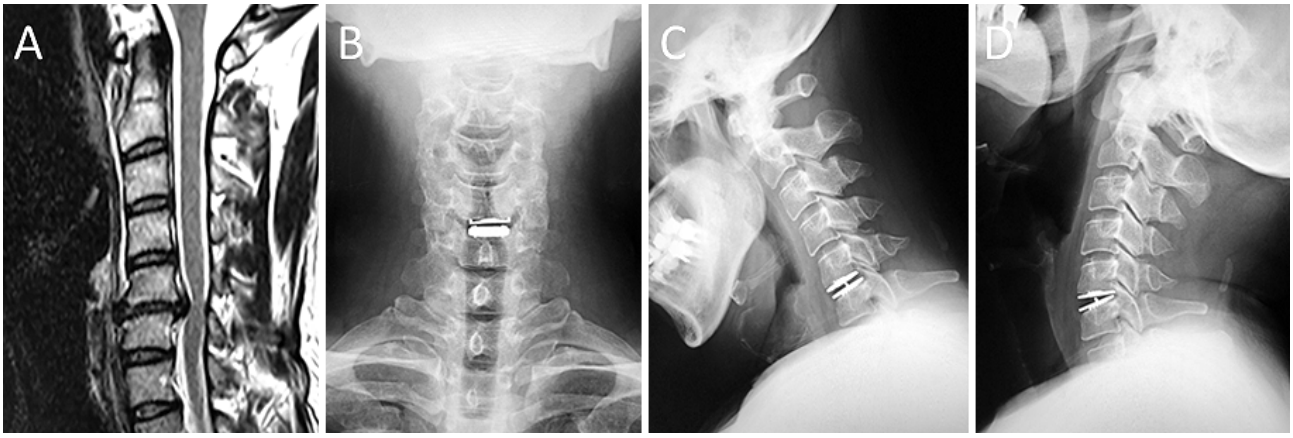

Figure 3. Case: A 43-year-old male with radiculomyelopathy at C5-6 due to cervical disk herniation.
A: Magnetic resonance image shows spinal compression due to disk herniation at C5-6. B: Post-operative A-P view shows adequate implantation of Mobi-C® TDR at 5-6. C and D: Post-operative lateral flexion and extension radiographs are shown. At the implanted level of the TDR, range of motion (ROM) is maintained due to prosthesis movement.

Table 3. TDR Inclusion and Exclusion Criteria in the United States (excerpted Version).

Inclusion criteria
1. Age 18–69 years
2. Symptomatic cervical degenerative disc disease in one or two levels between C3-C7 with:
◦ Myelopathy or myeloradiculopathy and/or
◦ Decreased muscle strength and/or
◦ Abnormal sensation and/or abnormal reflexes
3. NDI Score of ≥ 30/100
4. Unresponsive to non-operative treatment for at least 6 weeks or presence of progressive symptoms or signs of nerve root/spinal cord compression despite continued non-operative treatment; radiculopathy and/ or myelopathy due to cervical disc herniation
5. No prior surgical procedures at the operative level and no prior fusions at any cervical level
6. Willingness to discontinue all use of non-steroidal anti-inflammatory drugs (NSAIDs) from one week before surgery until 3 months after surgery
Exclusion criteria
1. More than two vertebral levels requiring treatment
2. Immobile levels between C1 and C7 from any cause
3. Any prior surgery at the operative level or any prior fusion at any cervical level
4. Disc height less than 3 mm
5. T-score less than −1.5 (osteoporosis evaluation)
6. Paget's disease, osteomalacia, or any other metabolic bone disease other than osteoporosis
7. Active infection of surgical site or history of or anticipated treatment for systemic infection, including HIV and/or Hepatitis C
8. Marked cervical spine instability on resting lateral or flexion-extension radiographs
9. Known allergy to device materials, including cobalt, chromium, molybdenum, or polyethylene
10. Segmental kyphosis of greater than 11^0 at treatment or adjacent levels
11. Rheumatoid arthritis, lupus, or other autoimmune disease
12. Daily, high-dose oral and/or inhaled steroids or a history of chronic use of high dose steroids
13. Morbid obesity (BMI>40)
14. Pending litigation relating to spinal injury (worker's compensation not included)
15. Smoking more than one pack of cigarettes per day
16. Reported to have a mental illness or belonging to a vulnerable population

69 years old], NDI Score of ≥ 30/100, T-score of more than 1.5, or segmental kyphosis of smaller than 11 degrees) but not in the PMDA criteria. While the quantified FDA criteria is easy to understand, there are parameters that can fluctuate, and some items may be difficult to determine as fixed values. In fact, there are reports that 57% of TDRs conducted in the US did not meet the FDA criteria[21]. Nonetheless, when implementing TDR in Japan, surgeons should refer to the FDA criteria, strictly observe the PMDA criteria, and prevent incidents or accidents to the best of their ability.

To our best knowledge, this is the first report to present the short-term clinical outcome of 1-level Mobi-C® TDR in the Japanese population. Various studies from abroad have reported on the treatment outcomes of Mobi-C® TDR in the past literature. In the present study, indications, symptoms, and surgical level were comparable to those of previous reports[16,24]. The ROM at the operated level recovered significantly, from 6.6 degrees preoperatively to 12.0 degrees at six months post-operatively, and remained at 12.2 degrees at two years after surgery. The NDI, NRS neck pain, NRS arm pain, and QOL improved significantly. In patients with myelopathy, the JOA score, JOA RR, and four functional domains of the JOACMEQ (cervical spine function, upper extremity function, lower extremity function, and QOL) were significantly recovered. These are short-term data, but the results are similar to those reported previously and tended to stabilize six months after surgery[16,24-26]. There were no serious complications such as nerve injury, vascular injury, or abduction. At the final follow-up, there were no heterotopic ossification and ASD. On the other hand, there was one case of radiculopathy due to subsidence and one case of excessive ROM with asymptomatic plate contact of the prosthesis, but none required revision surgery. Since the excessive ROM may cause instrumentation failure, which is a serious long-term complication, careful observation is required. According to the 1347 TDR complications in the FDA medical device reports from January 2005 to March 2020, TDR complications included 1) migration of the implant (338 entries, 25.2%), 2) insertion problem/failure (312 entries, 23.3%), 3) neck pain (203 entries, 15.2%), 4) heterotopic ossification (108 entries, 8.1%), and 5) radiculopathy (90 entries, 6.7%). Among them, Mobi-C® complications are 1) insertion problem/failure (209 entries, 59.4%), 2) migration of implant (105 entries, 29.8%), 3) heterotopic ossification (16 entries, 4.6%), 4) malposition of device (13 entries, 3.7%), 5) instability (5 entries, 1.4%)[27]. According to our experience, a human technical error caused the insertion problem; there was an insufficient connection between the

prosthesis and the insertor. Migration of the implant is a serious complication, and careful post-operative follow-up will be required in the future. FDA medical device reports showed the incidence of heterotopic ossification was relatively lower than those observed in other prostheses[27]. A meta-analysis of the prevalence of heterotopic ossification revealed a rate of 24.8% (95% CI 16.5% to 33.2%) and 45.3% (95% CI 24.9% to 65.7%) in a 1-2 year and >6 year follow-up period, respectively[28]. The type of prosthesis (Kineflex-C and Secure-C: over 60% of a high rate of prevalence heterotopic ossification), long-term follow-up, and single-level as opposed to 2-level TDR were reported to be risk factors[28]. A composite success analysis of the long-term, seven-year clinical outcomes for Mobi-C® TDR demonstrated that ASD rates of superior and inferior levels were 65.1% and 63.0% in ACDF, while 40.4% and 43.8% in TDR[28]. Although there have been no cases of ASD in our short-term study, we believe that it is important to recognize that its incidence following TDR is not low.

Regarding the surgical procedure, we found that Mobi-C®, which is relatively easy to manage, is similar to that of ACDF. Surgical insertion of Mobi-C® disk prosthesis is very simple, safe, and reproducible. Because the Mobi-C® does not have a keel, it may not be necessary to prepare a groove in the vertebral body during implantation. Also, the implant itself has several advantages, including its dome-shaped superior plate, lateral teeth to aid sufficient initial fixation, and hydroxyapatite and titanium coating with high bone affinity. On the other hand, the Mobi-C® TDR does not, in principle, use pneumatic drills to prevent subsidence since they may damage the bony endplate. However, since the size of the implant is to some extent oversized for Japanese patients, the plate may form a gap when the TDR is implanted into the caudal vertebral body. The caudal Luschka joint's convex area required flattening with a pneumatic drill, which could potentially cause post-operative subsidence.

There are several limitations to this research. First, the sample size was small. Second, the clinical outcome was the result of surgeries that one operator performed. Third, only short-term outcomes were reported. Understanding the complications will require a careful long-term follow-up, especially in ASD, heterotopic ossification, and implant migration. More cases and long-term follow-up are needed to offer conclusions on the efficacy of cervical arthroplasty.

Conclusions

The preliminary clinical outcome of 1-level Mobi-C® TDR for Japanese population from a prospective observational study was reported in the present study. The preliminary clinical outcomes were good and similar to those observed in the previous reports. The surgical procedure of Mobi-C® disk prosthesis is very simple, safe, and reproducible. However, as TDR is a new technology and reports of implant migration in the USA are not uncommon, spine surgeons should fully comply with guidelines when introducing the procedure and strive for its safe adoption in Japan.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

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Informed Consent: Informed consent was obtained by all participants in this study.

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