Arthroplasty in the Cervical Spine

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Introduction

Cervical spine consists of seven vertebral bodies with intervening discs. The discs and the unique configuration of the posterior zygoapophyseal joints allow a full 3D positioning of the head in the space, while the vertebral bodies provide a protective passage for the spinal cord and vertebral arteries. Degenerative changes in intervertebral discs due to aging or trauma can alter significantly the biomechanics of the cervical spine and lead to compression of nerve roots (i.e. cervical radiculopathy) or spinal cord (i.e. cervical myelopathy). For many years, the only available treatment option for cervical radiculopathy and/or myelopathy has been either discectomy (*anterior cervical discectomy*, ACD) or discectomy and fusion (*anterior cervical discectomy and fusion*, ACDF). Over the past 15 years cervical disc arthroplasty (or *cervical disc replacement*, CDR) has emerged as a viable alternative to fusion and the development of new artificial disc devices has been an area of intense research. The aim of this chapter is to present the current state of this technique, including the results of the best available outcome studies of the most common devices.

Anterior cervical discectomy and fusion (ACDF) surgery was pioneered by Cloward and Smith—Robinson in early 1950s. Following the early encouraging results, the new technique rapidly became the gold standard in treatment of cervical spondylosis and disc degeneration. Numerous recent studies have reported good to excellent results in 70–90% of patients, and a fusion rate of 89% in single level operation [1]. However, despite being a successful and widely used procedure some important drawbacks of this technique have become apparent as more fusions are performed every year throughout the world.

Adjacent segment degeneration is defined as the radiographic appearance of degenerative changes at a level above or below a fused segment. The reported incidence of this phenomenon varies greatly in literature (ranging from 51.1 to 92%) [2]. Despite the very common occurrence of adjacent segment degeneration, only a minority of patients will require surgery at an adjacent level. For this reason, a clear distinction exists in literature between *adjacent segment degeneration* (*ASDegeneration*) and *adjacent segment disease* (*ASDisease*). Adjacent segment disease is defined as adjacent segment

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Table 10.1 Classification of adjacent segment degeneration

	Disc height	Anterior osteophyte formation
Normal	Same as adjacent disc	No anterior osteophyte
Mild	75–100% of normal disc	Just detectable anterior osteophyte
Moderate	50–75% of normal disc	Clear anterior osteophyte <25% of AP diameter of the corresponding vertebral body
Severe	<50% of normal disc	Clear anterior osteophyte >25% of AP diameter of the corresponding vertebral body

degeneration with clinical symptoms (pain or neurologic disorders or both), whilst *adjacent segment degeneration* (*ASDeg*) only refers to the presence of radiographic degenerative changes in the absence of clinical symptoms (Table 10.1).

In 1999, Hilibrand et al. [3] reported on the long-term outcome of 374 patients after single and multiple-level ACDF surgery and observed a constant yearly incidence of ASDisease of 2.9% (range, 0.0–4.8% per year) during the first 10-years after the operation. The Kaplan-Meier survivorship analysis developed by the authors suggested that 13.6% of patients with ACDF will develop ASDisease within the first 5 years after surgery and that 25.6% will have new disease within 10 years after the index procedure. Although the actual reported figures, 11.7% prevalence of ASDisease at 5 years and 19.2% prevalence at 10 years, are slightly lower they provide a good overview of the real extent of the problem. Other authors [1, 4, 5] have confirmed these findings reporting an incidence of ASDis of 25% at 5–10 years after surgery [2].

Although reported data suggest a strong correlation between ACDF surgery and higher risk of ASDisease, this is most likely a multifactorial process. The incidence of degenerative changes in the cervical spine increases with aging. In a seminal study, Boden et al. [6] studied the prevalence of degenerative changes in the cervical spine of 68 asymptomatic volunteers and found that abnormalities were present in 14% of the subjects less than 40 years old and in 28% of those who were older than 40. In a different study on cervical disc herniation and radiculopathy, Henderson et al. [7] noted new radiculopathy at a different level in 9% of 846 patients after posterolateral foraminotomy without fusion at an average of 3 years after surgery. This study is frequently cited by authors who believe that ASDegeneration/ASDisease is part of the normal aging process of the cervical spine and the higher incidence observed in patients treated with ACDF is to be related to an intrinsic genetic predisposition of these patients.

Other factors can also contribute in determining the risk of ASDegeneration. As shown by Nassr and co-workers [8] the insertion of a marking needle during surgery in a disc at the wrong level determined a threefold increase of risk of disc degeneration at that level. Similarly, placement of an anterior plate within 5 mm from the adjacent segment has been shown to be a significant risk factor for adjacent level ossification and degeneration [9, 10]. On the other hand, intrinsic mechanical factors are also involved in the degeneration process. According to Hilibrand et al. [11] the relative risk of ASDis is 3.2 times higher at the C3–C4 and C4–C5 levels than C2–C3 level and 4.9 times higher at C5–C6 and C6–C7 interspaces. Biomechanical analyses have shown an increase of intradiscal pressure (stress) at the levels adjacent to a previous fusion and led to the concept that levels adjacent to a fusion have to compensate for the loss of motion in the fused segment [12]. Finally, more recently a lot of research efforts have been placed in elucidating the role of spinal sagittal alignment on the incidence of ASDegeneration and ultimately ASDisease. Yang et al. have shown that patients with higher values of the occipito-cervical angle are at increased risk of ASDegeneration [13]. On the other hand, other authors have failed to recognized a clear definitive role of cervical spine sagittal alignment on the risk of ASDegeneration and ASDisease [14, 15].

The ultimate goal of cervical disc arthroplasty is to preserve segmental motion in order

to prevent development of ASDisease, thus reducing incidence of secondary surgery. The typical candidate for cervical disc replacement is the young active adult with single level soft disc herniation and intact zygapophyseal joints. Motion preservation at the index level avoids stress raise at the adjacent levels and prevents later adjacent segment degeneration/disease (ASDegeneration/ASDisease). By not achieving fusion, cervical disc replacement also avoids the morbidity of bone graft harvest and typical complications of ACDF surgery, such as pseudoarthrosis, issues caused by anterior cervical plating, and prolonged cervical spine immobilization.

History and Implant Design

Some basic understanding of the history of CDR is of pivotal importance in interpreting present clinical results and evaluating future devices. Many new implants have been developed in recent years, reflecting an increased interest on non-fusion technologies by industry and clinicians. However, over the last 40 years, three fundamental designs have emerged in TDR [16]. These three design philosophies have led to the development of three different prosthetic devices: the PRESTIGE (Medtronic, Inc.), the BRYAN (Medtronic, Inc.), and the ProDisc-C (Synthes-Spine, Inc.). These three implants will be discussed here and will serve as base knowledge to evaluate other available implants.

Early attempts at developing an artificial substitute of the intervertebral disc with stainless steel balls are credited to Ulf Fernstrom and date back to 1960s. The early clinical follow-up of the new technique, however, showed unacceptably high rates of implant migration (88%) and subsidence and led many surgeons to direct their interest towards fusion procedures [17]. Twenty years later, in 1989, B.H. Cummins at the Frenchay Hospital in Bristol, UK, developed the first model of a modern cervical disc arthroplasty. This new device consisted of two pieces of 316L stainless steel with a metal-on-metal ball-and-socket design. The anchoring system consisted of two anterior screws that fixed the device to the vertebral body. Unfortunately, early implants were plagued by high incidence of screws pull-out, dysphagia and implant mobilization [18].

A second-generation device was developed from the original Cummins prosthesis with the name of Frenchay artificial disc in 1998. The anterior profile of the device, the locking screw system and the articulating surface were all completely redesigned and following acquisition by Medtronic, Inc., renamed PRESTIGE I Disc. Several redesigns of the implants have led to the fourth-generation system, PRESTIGE ST, and more recently to the fifth-generation PRESTIGE LP (low profile) disc. Although the metal-on-metal design has not been modified, the articulating mechanism of the PRESTIGE ST has been changed into a coupled, semiconstrained system. The newer PRESTIGE LP model is made of a titanium-ceramic composite and incorporates two endplate rails for extra fixation strength in the vertebral body.

The BRYAN cervical disc (Medtronic, Inc.) was designed by the American neurosurgeon Vincent Bryan from Seattle in 1990s. The concept and design of the BRYAN disc is completely different from the Bristol/PRODISC series. This device consists of two titanium alloy endplates articulating with a polyurethane core. The two titanium endplates are fixed to the bone by a porous titanium layer and stability is achieved through a tight fit of the prosthesis in the milled cavity. The implant has been extensively tested in Europe and received US FDA approval in May 2009.

The third alternative to metal-on-metal implants is represented by the ProDisc-C device (Synthes, Inc.) which has recently obtained the approval for use in the United States. The ProDisc-C system was developed by Dr. Thierry Marnay in France and consists of two cobalt-chrome-molybdenum (CCM) endplates with an UHMWPE articulating surface. It is a ball-and-socket constrained prosthesis and has a central keel for extra fixation in the vertebral body.

Other devices have recently joined the market of cervical TDR. Kineflex-C disc (Spinal Motion, Inc.) and CerviCore disc (Stryker Spine, Inc.) are metal-on-metal implants, whilst PCM (CerviTech, Inc.), DISCOVER (DePuy Spine, Inc.), and the MOBI-C (LDR, Inc.) are metal-on-UHMWPE implants. More recently, the SIMPLIFY disc (Nuvasive, Inc.) gained FDA approval for single and double level disc replacement procedures.

Indications for Use and Contraindications

The rationale of considering CDR rather than a standard fusion procedure (i.e. ACDF) lies in the aim of maintaining the motion of the treated segment and preventing adjacent-segment degeneration and disease. The typical candidate patient for CDR is the young active adult patient with single level symptomatic disc disease (i.e. radiculopathy) from C3 to T1 with intact posterior facet joints. General contraindications are marked reduction of the disc space (<3 mm or <50% of normal disc height) with loss of motion at that level [19, 20], zygapophyseal joint osteoarthritis, significant deformity in the sagittal and coronal plane, clear segmental instability, and infection. Other relative contraindications include rheumatoid arthritis, renal failure, osteoporosis (T-score values < 1 SD), cancer, and preoperative corticosteroid use [21].

Evaluation of sagittal alignment, presence of zygapophyseal joint osteoarthritis and instability is of paramount importance and should be undertaken as routine preoperative assessment in every patient. Standard X-ray films (i.e. AP and lateral view) of the cervical spine and flexion-extension studies are usually sufficient in clarifying the extent of residual movement at the index level and the presence of osteoarthritic changes in the posterior joints.

The role of CDR in patients with axial neck pain has not been clarified yet and therefore disc pathology with no neurological symptoms should not be considered an indication for CDR. European and US trials have enrolled patients 1- or 2-levels cervical radiculopathy due to disc herniation (soft or hard), foraminal osteophytes as well as cervical myelopathy. In our clinical experience the presence of a hard disc herniation should be considered a relative contraindication to TDR due to frequent need of a more extensive disruption of the endplate for a satisfactory clearance of the canal. In both European and North American trials, there has been a strong prevalence of patients enrolled with radiculopathy (77–93%) rather than cervical stenosis/myelopathy. The role of TDR in cervical myelopathy remains controversial [22–24]. According to the authors' clinical experience cervical TDR should be avoided in patients with cervical myelopathy. Complete clearance of the spinal canal and wide decompression of the spinal cord are top priorities in cervical myelopathy surgery and the achievement of a solid and stable fusion if the best single guarantee for a long term success of the decompression.

A summary of the most common indications and contraindications for cervical TDR is shown in Table 10.2. In a recent analysis of 464 consecutive patients undergoing cervical spine surgery treated at a single center by three surgeons specializing in CDR, the rate of CDR eligible patients was 76.7%. The most common reasons for not performing CDR were: anatomy (i.e. severe compromise of disc height and less than 2° ROM at the index level) that may compromise segmental stability and/or CDR functionality (13.79%), insurance denial of coverage (3.23%), and deformity/kyphosis not addressable with CDR (2.80%). Osteoporosis also was considered a contraindication in 0.43% of cases. Two cases were reported with unplanned intra-operative conversion of CDR to ACDF due to: (1) poor ver-

Table 10.2 List of indications and contraindications for TDR

Indications for cervical TDR	*Relative* indications for cervical TDR	Contraindications for cervical TDR
Radiculopathy caused by soft disc herniation	Radiculopathy caused by hard disc herniation	Osteoarthritis of the zygapophyseal joints
	Myelopathy caused by disc herniation	Sagittal malalignment of the cervical spine
	Radiculopathy caused by foraminal osteophytes	Segmental instability
		Infection
		Previous posterior surgery
		Ossification of the Posterior Longitudinal Legament (OPLL)

tebral body endplate quality, (2) anterior inferior vertebral body bevelling with high risk of implant migration [25].

Clinical Studies

BRYAN Disc

The BRYAN disc has the longest clinical and radiological follow-up among cervical TDR devices. The first multicentre study on this device was published in 2002 by Goffin and co-worker as part of a European prospective multicentre trial [26]. The study enrolled 60 patients with cervical radiculopathy or focal myelopathy non responsive to at least 6-weeks of conservative treatment. Exclusion criteria were the presence of sole axial neck pain, malalignment of the cervical spine, previous neck surgery and cervical instability. Only single level implants were used for this study and clinical success rates at 6 months and 1 year were 86 and 90%. Because of the lack of a control group, the authors assumed from the literature a target level of success rate of 85% for ACDF surgery. The number of patient lost at follow-up was significant with only 30 patients available at the 1-year follow-up. No complications directly related to the implant were detected. However, three patients underwent revision operation for prevertebral hematoma drainage, posterior foraminotomy for residual compression, and posterior laminectomy for residual myelopathy.

In a second study, Goffin and colleagues [27] expanded their original study with a second group of patients treated with two levels TDR. The study reported the results for 103 patients in the single-level group and 43 patients in the two-level group at 2 years follow-up. Success rates for the single-level group were 90%, 86%, and 90% at 6 months, 1 year and 2 years follow-up respectively. Patients in the two-level group had success rates of 82% at 6 months, and 96% at 1 year. No device failure or subsidence was reported in this second study and an average postoperative range of motion of 7.9° per level in flexion-extension was recorded. Movement was maintained in 87.8% of the single-level patients and 85.7% of two-level patients. Four complications were reported including one case of prevertebral hematoma, one case of epidural hematoma, one case of pharyngeal and oesophageal injury, and one case of residual nerve root compression.

The first extensive report on North American experience with the BRYAN disc has been published by Sasso and co-workers in 2007 and 2008 [28, 29]. The authors conducted a prospective, three-center, randomized trial on 115 patients randomized in a 1:1 ratio to disc

replacement and ACDF and plate surgery. Inclusion criteria were similar to the European studies and included patients with cervical radiculopathy and focal myelopathy due to single-level disc degeneration with symptoms non responsive to conservative treatment. Follow-up was 2 years for 99 patients. The authors reported a longer operative time for the arthroplasty group (1.7 vs. 1.1 h) but a significantly lower NDI for the disc replacement group at 12 months and 24 months (11 vs. 20, p = 0.005). Analysis of arm pain at 1 and 2 years also favoured the arthroplasty group with significantly lower VAS scores (14 vs. 28, p = 0.014). The reported average range of motion per level in the disc replacement group was 7.9° in flexion-extension at 24 months, whilst it was 0.6° in the fusion group. No complications related to the implants were noted, as well as no heterotopic ossifications. Six patients underwent additional operations during the follow-up period, four patients in the control group and two patients in the BRYAN group. Four patients (two in the control group and two in the BRYAN group) underwent a new ACDF surgery for adjacent segment degeneration.

Results of the FDA IDE approval trial of the BRYAN disc was published by Sasso et al. in 2011 [30]. The study was designed as a non-inferiority trial and randomized a total of 582 patients into two arms (i.e. ACDF vs. CDR). Overall success rate at 4 years was significantly better for BRYAN disc (85.1%) vs. ACDF surgery (72.5%, p = 0.004). Also, neck disability index improvement was higher for BRYAN disc (mean NDI at 4 years, 13.2) than ACDF (mean NDI at 4 years, 19.8, p < 0.001). Up to 48-months follow-up, nine patients (3.7%) in the arthroplasty group and ten patient (4.5%) in the fusion group had to undergo secondary surgical procedures; the difference between the two groups was not statistically significant. Interestingly, the rate of adjacent segment surgery in the two groups was also similar and not statistically significant (4.1%) [30]. Ten-years outcomes of the same group of patients were reported by Lavelle et al. in 2019, although only 232 patients out of the initial 582 patients were available. Overall success rate was significantly higher for the BRYAN group (81.3 vs. 66.3%, p = 0.005), and the rate of secondary surgery at adjacent levels was lower for the BRYAN group (9.7 vs. 15.8%, p = 0.146). ROM at the index level in the BRYAN group was 8.7° [31].

In a more recent work, 18-year follow-up data for BRYAN disc were reported by a single center [32]. At the time of the latest follow-up, residual movement at the index level was noted in 56% of patients, the average range of motion decreased from 10.1° preoperatively to 6.1° at the time of the last follow-up. Rate of ASDegeneration and heterotopic ossification was 77.1% and 73%, respectively, at the time of the latest follow-up; no data is provided in terms of reoperation rate in this cohort [32].

ProDisc-C

The ProDisc-C implant has received the US FDA approval for use in single-level disc arthroplasty due to the good results reported by the IDE study by Murrey and colleagues [33]. An earlier study by Bertagnoli et al. [34] reported on the results of 27 patients treated with single-level ProDisc-C implantation at 1 year follow-up. Patients experienced sustained improvement of their symptoms at 1 year follow-up with decrease of NDI and VAS scores. No device complications were reported.

The actual FDA approval study was published in 2009 [33]. It was a prospective, multicenter, randomized controlled trail conducted on patients with single-level pathology. A 1:1 randomization scheme was adopted, 106 patients were randomized into the ACDF group and 103 patients in the arthroplasty group. VAS, NDI, and SF-36 scores were recorded at 3, 6, 12, 18, and 24 months after surgery. Clinical outcome measures significantly improved in both groups after surgery and results were maintained at final follow-up. Arthroplasty

group maintained range of motion at the index level in 84.4%. Overall, the ProDisc-C group showed results equivalent or slightly superior to the ACDF group although there was a statistically significant difference in the complication rates. In the fusion group, 8.5% of the patients needed re-operation, revision, or supplemental fixation compared with 1.8% of the ProDisc-C group ($p = 0.033$).

Long term results with ProDisc-C prosthesis have been recently published by two independent groups [35, 36]. Zhao et al. reported results of 27 patients treated with single-level ProDisc-C arthroplasty at 10-year follow-up. The average range of motion at the index level was 6.6° ± 3.5° at final follow-up. Seventy-four percent of patients developed heterotopic ossification (12 levels were classified at grade III according to McAfee's classifications). Three patients (11.1%) developed ASDisease with recurrent radiculopathy and/or myelopathy and underwent reoperations (i.e. two cases of CDR surgery and one case of cervical laminoplasty) [35]. Zigler et al. reported reoperation rate of 535 patients who underwent single-, two-level, and hybrid (i.e. ACDF and adjacent level CDR) with a median follow-up of 77 months. Reoperation occurred in 30 out of 535 patients (5.6%) and included 3 conversions to ACDF, 1 arthroplasty repositioning, 21 ASDisease, 1 non-union, 1 wound infection, 1 hematoma, and 2 patients who received stimulators for pain control. No reoperations were performed for issues related to device failure [36].

PRESTIGE Disc

The Cummins/Bristol device was the precursor of the PRESTIGE series of disc arthroplasty. The Cummins disc was developed to address the problem of disc degeneration in patients with previous fusions or with Klippel-Feil syndrome. The first study on this device enrolled 20 patients and showed, at 5 years, significant clinical improvement and preservation of the movement in 88.9% of the patients. Unfortunately, a high rate of complications was reported, including screw loosening, mobilization of the implant, dysphagia and transient hemiparesis.

The PRESTIGE I and II discs were developed as an evolution of the original Cummins disc. Clinical results of the PRESTIGE I disc were published by Wigfield and coworkers in 2002. A total of 15 patients were enrolled in a prospective non randomized trial [37]. Inclusion criteria encompassed patients with cervical radiculopathy or single level myelopathy secondary to cervical disc herniation or foraminal osteophytes. No significant complications were reported by the authors and all patients showed preservation of motion at the index level at 2 years after surgery. Mean flexion-extension ROM was 6.5° and mean antero-posterior translation was 2 mm. Clinical improvement was documented by ODI, NDI, and SF-36 but no valuable statistical analysis was undertaken because of the small number of patients.

The best available data on clinical safety and efficacy of the PRESTIGE ST disc has been published in 2007 by Mummaneni and colleagues [38]. Data from this report have also served as the basis for the current FDA approval of this device in the United States. The study consisted in a prospective 1:1 randomized trial with patients undergoing either single level disc arthroplasty or single level ACDF. A total of 541 patients were enrolled, 276 patients in the PRESTIGE ST group and 265 patients in the ACDF group. The study showed a two-point greater improvement of NDI in the investigational group at 12 and 24 months. Improvement in SF-36 questionnaire scores was higher in the arthroplasty group at 12 and 24 months, as well as the VAS score. The rate of revision surgery was lower for the interventional group (5 revision surgeries) vs. the fusion group (23 revision surgeries). No device failures or complications were reported, the average motion preservation at 2 years was 7°. The PRESTIGE LP disc

arthroplasty has received FDA approval for use in patients in July 2014.

Outcomes at 10 years of the PRESTIGE LP disc arthroplasty were reported by Gornet et al. in 2019 [39]. Scores of patient reported outcomes and neurological function remained stable for the CDR group. The rate of revision surgery at the index level was 10.3% (nine patients), while four patients (7.8%) reported serious implant adverse events. The rate of secondary surgery at adjacent level was 13.8% for the CDR group, and incidence of heterotopic ossification increased from 1.2% at 2 years to 9.0% at 10 years [39].

McAfee and colleagues have summarized best available evidences about the use of cervical total disc replacement in clinical practice. The authors looked at the reported results of four prospective randomized controlled FDA IDE trials using BRYAN, PRESTIGE, ProDisc-C, and PCM implants. Data from 1226 patients at 24 months were available for the analysis. Results showed an overall success rate of 70.8% in the ACDF patients and 77.6% in the arthroplasty group ($p = 0.007$), thus favouring this last treatment. The analysis of all clinical subcomponents (i.e. neck disability index, neurological status, and survivorship) also favoured arthroplasty over ACDF surgery at 24 months. Survivorship ranged from 90.9% in the PRESTIGE group to 98.1% in the ProDisc-C group. Survivorship was achieved by 96.6% of the cervical arthroplasty group on average and by 93.4% of the ACDF patients. Some criticism has been raised regarding the poor results of the ACDF surgery (70.8% overall success rate) in the reported FDA IDE trials. As pointed out by the authors of the study a common perception of a much higher success rate in fusion patients undermines confidence in the results of these trials. FDA criteria for definition of *success* are much more stringent than what has been traditionally reported in observational studies on ACDF surgery. This may account for the lower than expected results of the control fusion groups; taken together these data suggest that cervical disc arthroplasty is at least as clinically successful as fusion at 24 months [40].

Complications

Complications following CDR surgery can be grouped as: surgery related; implant related; or changes in physiological biomechanics of the cervical spine. CDR surgery shares with ACDF surgery the same risks related to the surgical approach. In a recent meta-analysis by Hui et al. including a total of 3223 patients the pooled prevalence of post-operative complications following CDR was low, ranging from 0.8 to 4.7% [41]. The most commonly reported complications included, intraoperative dural tear (0.9%), post-operative dysphagia (5.4%), neurological adverse events (5.0%), and intraoperative vascular injury (1.1%) [41]. In a retrospective review by Fountas et al. of 1015 cases of primary one, two, and three level ACDF and plating, reported mortality was 0.1%; 9.5% of the patients suffered from postoperative dysphagia, 3.1% had recurrent laryngeal nerve palsy, 2.4% prevertebral hematoma, 0.5% had dural perforation, 0.1% hardware failure, and 0.1% wound infection [42]. Most recent evidence suggests that the rate of surgery related complications between ACDF and CDR surgery is similar [43].

Implant related complications are specific to CDR and have been reported by several authors. Goffin and colleagues reported a total of four implant complications (three cases of subsidence and one case of implant migration) in a series of 146 patients. Implant failures were related to an improper milling of the endplates and implant positioning [27]. General advice is to avoid CDR in osteoporotic patients because of the increased risk of implant subsidence and supposedly stress shielding effect of the implant on adjacent bone. The largest available and possible implant footprint should also be used in each patient in order to increase the load sharing area of the implant. It is important to notice that no cases of posterior migration and neurological compromise due to cervical arthroplasty have been reported so far to our knowledge. On the other hand, some keeled implants, carry the risk of vertebral body fracture during implant insertion. Datta and co-workers reported a case of C6

Table 10.3 McAfee grading of heterotopic ossification (HO) in cervical disc arthroplasty [46]

Grade 0	Absence of HO
Grade 1	Presence of HO in front of vertebral body but not in the anatomic disc space
Grade 2	Presence of HO in the disc space, possibly affecting the prosthesis's function
Grade 3	Bridging HO with prosthesis's motion still present
Grade 4	Complete fusion of the segment with absence of motion in flextion/extension

vertebral body fracture during insertion of a keeled implant [44]. Similarly Shim and colleagues described a case of an avulsion fracture [45]. In a more recent meta-analysis involving 3223 patients implant related complications between Prestige-LP (2.0%, range 0–4.1%), Bryan (1.3%, range 0–2.9%), Discover (5.1%, range 2.2–8.1%), ProDisc-C (0.9%, range 0–2.6%), and Mobi-C (2.0%, range 0.4–3.6%) arthroplasties were compared. Pooled implant related complications at short term (i.e. <2 years) was 2%, at mid-term (i.e. >2 years, and <5 years) was 1.5%, and at long-term (i.e. >5 years) was 1.7%. Overall, no significant differences were noted between different types of implant.

Heterotopic ossifications (HO) and anterior ankylosis is a known and dreaded complication of cervical disc replacement surgery. HO is commonly classified according to McAfee et al. in four grades (Table 10.3) [46]. Early reports from Leung et al. showed an incidence of 17.8% (16 patients) of HO in a multicentre study on BRYAN disc arthroplasty [47]. Similarly, Mehren et al. reported an incidence of moderate (grade III) HO of 10.4% at 4 years after surgery in a case series of 54 patients treated with ProDisc-C, whereas seven cases (9.1%) had spontaneous fusion of the treated segment at 1 year after surgery [48]. According to more recent meta-analysis the cumulative incidence of HO following CDR is 32.5% [49]. Prevalence of grade 1 HO was estimated at 5.4%, grade 2 at 8.4%, grade 3 at 5.6%, and grade 4 at 3.8%. Kineflex-C (pooled prevalence 62.4%) and Secure-C (pooled prevalence 74.2%) prostheses demonstrated higher overall rates of HO. In contrast, M6-C (pooled prevalence 1.7%), Prestige ST (pooled prevalence 1.7%), and PCM (pooled prevalence 0.4%) exhibited lower rates of HO compared to the overall prevalence of HO. An overall increasing prevalence of HO with length of follow-up was also reported [49]. Aetiology of this complication of CDR remains unknown. Some authors speculate that the extensive dissection of the longus colli muscle could be a contributing factor, while others think that extensive endplate milling should be taken into account. Risk factors for development of HO include male sex, single level CDR, and age [47]. The influence of age on the risk of HO is still controversial. Hui et al. in a meta-analysis involving a total of 3223 patients reported an inverse relationship between age and risk of HO [41]. Non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to be effective in preventing HO in hip arthroplasty and similarly some authors have advised their use for prevention of this complication in cervical TDR as well. Standard protocol requires administration of NSAIDs for 2 weeks after surgery although this practice is still not supported by solid evidence [50, 51].

"Aseptic loosening" or failure of a total joint arthroplasty is a very well-known phenomenon of polymer-bearing implants in general orthopaedics. Peri-implant osteolysis has been reported for CDR surgery as well [52–55]. The aetiology is most likely multifactorial, such as chronic infection, immune-mediated inflammation, vascular compromise, and stress shielding. Most patients showing post-operative peri-implant osteolysis are asymptomatic. A minority of patients though can present with new onset of pain, neurological deficit, and or spinal deformity (e.g. kyphosis at the index level). Reported incidence of cervical osteolysis following CDR ranges from 4.2 to 63.7%, and incidence seems to be higher with a larger number of operated levels [53, 54, 56]. In a recent meta-analysis, two clinical patterns of cervical osteolysis were identified. A first pat-

tern has reported in which mild osteolysis is observed early after surgery but rarely progresses beyond 1 year. A second pattern is observed whereby osteolysis is more pronounced and can progress up to 4 years after surgery. Cavanaugh and co-workers reported a case where a revision of CDR was performed and a local chronic inflammatory reaction was noted, the patient also developed a delayed hypersensitivity reaction to metal ions [57]. More recently, Guyer and colleagues reported on four cases of early failure of metal-on-metal CDR presenting with worsening pain and/or radicular symptoms. There were three cases of lumbar CDR and one case of cervical CDR, all patients underwent posterior decompression and anterior removal of the implant. In the cervical case the authors observed the presence of a gray-tinged soft-tissue surrounding the implant suggestive of metallosis [58]. Goffin also reported on a similar case with a BRYAN prosthesis where a chronic inflammatory reaction led to osteolysis and loosening of the implant. Lebl et al. recently published a case series of 30 ProDisc-C implants removed and analysed using light stero-microscopy, scanning electron microscopy and x-ray. Posterior endplate-endplate impingement was present in 80% of the implants. Although no backside wear was observed, third-body wear occurred in 23% of the implants [59]. Based on current evidence, in cases of asymptomatic early osteolysis following CDR surgery, a watchful approach should be used and no surgery performed. In cases on symptomatic (i.e. neck pain, cervical radiculopathy) and progressive CDR osteolysis, revision surgery should be performed with removal of the implant and ACDF or corpectomy with definitive fusion.

The aim of cervical arthroplasty is to preserve movement at the index level and avoid mechanical overloading of adjacent segments. Sagittal alignment of the spine is of paramount importance in determining load distribution on discs and posterior joints. Multiple studies have reported post-operative kyphosis as an adverse event of cervical CDR [60, 61]. Troyanovich and co-workers have shown that adjacent segments to a kyphotic level develop compensating hyperlordosis and accelerated degeneration [62]. Kyphosis may be caused by preoperative loss of physiological lordosis of the cervical spine but also by asymmetric milling of the endplates, wrong insertion angle of the implant, or undersizing of the prosthesis [63]. Several meta-analysis comparing the rate of ASDegeneration and ASDisease between ACDF and CDR sugery have been performed in recent years with contrasting results. Two recent meta-analysis have shown that CDR is superior to ACDF in reducing the rate of ASDegeneration at short and midium-term follow-up [64, 65], while other authors have found that CDR can significantly reduce the rate of ASDisease compared to ACDF [66, 67]. The reported prevalence at 5 years follow-up of ASDegeneration following CDR is 36% and pooled prevalence of secondary surgery of the cervical spine at long follow-up (i.e. >5 years) is 4.5%. Main indications for surgery at the index level are pseudoarthrosis, and new onset myelopathy or radiculopathy; whereas indication for adjacent level surgery is manly ASDisease [41]. The overall risk of reoperation at the index or adjacent level is lower for CDR surgery (6%) than ACDF (12%), accounting for a 50% reduction of reoperations [68].

Biomechanics

The main aim of cervical CDR is maintenance of segmental motion at the index level and avoidance of adjacent segment degeneration. Several studies have shown that segments adjacent to a fusion develop increased compensatory movement and higher intradiscal pressure [12, 69, 70]. These changes are thought to be the basis of increased incidence of ASDeg/ASDis after fusion. Therefore, the most important aim of cervical CDR is to restore the physiological segmental motion of the treated level. Each cer-

vical motion segment consists of three joints, the disc in the front and the two zygapophyseal joints in the back. Ligaments provide extra stability to the motion segment and help prevent extreme motions. The normal cervical spine exhibits flexion-extension movement as well as some anterior translation. The centre of motion is mobile during flexion-extension in order to accommodate for the anterior and posterior translation. Motion constraints also change with flexion-extension. In flexion, load is applied to the disc and posterior joints "unlock" reducing their constraining effects. In extension, load is applied on the posterior joints which also "lock" and limit the amount of possible movement. Therefore, from a mechanical point of view, it is extremely important to achieve a correct balance between posterior joints and intervertebral disc.

In vivo and in vitro studies have confirmed these ideas on the motion of the cervical spine. TDR has been shown to maintain index-level sagittal motion, translation, coupled motion in lateral bending with rotation, disc-space height, and centre of rotation, as compared with preoperative or intact states [71]. However, many artificial discs are available for CDR and not all artificial disc designs will behave the same mechanically because of the distinctiveness of each implant design. Disc designs vary widely in terms of translation of the axis of rotation (constrained vs. semiconstrained vs. unconstrained), range of motion (flexion/extension, rotation and lateral bending), materials (titanium, hydroxyapatite coating, cobalt-chrome alloy, ultra-high molecular weight polyethylene, and polyurethane), number of moving pieces, and encapsulation of the overall design (open vs. closed). Biomechanical studies have shown some important differences in the design of the implants that can significantly affect the in vivo biomechanical behaviour of the prostheses. The three most common and widely studied designs are: (1) the Prestige LP, an open two-piece, semi-constrained design with metal-on-metal articulation, (2) the ProDisc C, an open two-piece, semi-constrained design with polymer-on-metal articulation, and (3) the Bryan disc, a closed one-piece, unconstrained (no fixed core or center of rotation) design with a saline-lubricated polyurethane core. In a recent in silico study all three designs were compared [72]. Prestige LP and ProDisc C were shown to increase motion to a supraphysiologic range and increase facet joint forces at the index level. In contrast, the Bryan disc was shown to reduce forces in the facet joints at the index level but also a reduced flexion movement compared to a physiologic disc at the index level and supraphysiologic movement at the adjacent levels [72].

Cost Analysis

A total of seven cervical disc replacement (CDR) systems have been FDA approved following completion of the FDA investigational device exemption (IDE) studies, and CDR is becoming an increasingly popular technique for treatment of cervical radiculopathy [16, 73]. A common criticism is that novel surgical techniques and devices tend to be more expensive than traditional techniques, while their efficacy is unproven. Ideally, the best interventions will not only optimize outcomes but will also help curb health care spending in the long term. Average cost of a single-level cervical total disc replacement implant is about $4000, whilst the cost for a cervical interbody cage and anterior plate is $2500 in the US [74]. The target market for CDR technologies is huge. In US only, a total of 450,000 cervical and lumbar fusion procedures are performed every year and conservative estimations are that 47.9% of these patients would be good candidates for a motion preservation procedure. The estimated yearly revenue from this segment of the market was $2.18 billion in 2010 [74].

Since the length of hospital stay, therapy protocol, medication usage, imaging, perioperative

complications, and readmission rates are comparable between ACDF and CDR, the largest driver of cost savings in CDR surgery is the reduced rate of secondary surgery due to adjacent segment disease [75]. Early cost-analysis studies comparing ACDF and CDR used data gathered from difference sources. In 2013, Qureshi et al. conducted a cost-effectiveness analysis of single-level CDR vs. ACDF surgery using outcomes data from the Nationwide Inpatient Sample and Medicare reimbursement data. The authors assumed an average failure rate (pseudoarthrosis or hardware failure) of ACDF at 1 year of 5%, and incidence of ASDis of 3%. Failure rate of disc arthroplasty at 1 year was assumed in the range of 0–2%. Supported by a recent meta-analysis of four randomized trials on CDR vs. ACDF the authors also assigned a utility value to CDR of 0.9 (scale 0–1) as compared to ACDF which was assigned a slightly lower value of 0.8. According to the authors disc replacement surgery generated a total lifetime cost of $11,987, whilst ACDF lifetime cost was $16,823. Cervical disc replacement resulted in a generation of 3.94 QALY, whereas ACDF resulted in 1.92 [76]. On the other hand, Warren et al. using data from the ProDisc C IDE study found ACDF surgery to be more costly than CDR ($16,162 vs. $13,171) but more effective in terms of QALY increase at 2 years [77].

Although real cost estimation is extremely difficult and varies greatly in different health care systems and settings, cost-effectiveness studies comparing CDR vs. ACDF have become increasingly sophisticated in the past decade. In 2016, Radcliff et al. conducted a cost-minimization analysis using a single dataset from a health care payer (Blue Health Intelligence). The authors found reduced rates of expenditure by the payer on the index surgery costs and the posthospital health care resource use in CDR vs. ACDF patients ($29.679 vs. $42.486, $p < 0.05$ through 7 years). Even excluding index-level surgery costs, the expenditure per member per month was lower in CDR patients through 36 months. Additionally, the reoperation rate was lower in CDR patients [78]. Additionally, interventional pain procedures and postoperative physical therapy outside of the normal course of treatment were also documented. The authors found that the cumulative costs of ACDF and CDR at 7 years were $42.486 and $29.697, respectively. Utility score measurements demonstrated an improvement in QALY in CDR over ACDF (4.36 ACDF vs. 4.52 CDR) at 7 years. Thus, CDR was a dominant strategy, as it was found to be less expensive but also more effective [78]. As it becomes clear that the largest driver of cost savings of CDR is the reduced rate of secondary surgery; it is likely that with longer-term follow-up study, the financial benefits of CDR will likely be magnified.

Conclusions

Cervical disc arthroplasty has progressed over the last three decades from a merely hypothesis to a clinical reality. The concept of artificial substitution of cervical discs has been embraced by many spinal surgeons and centres throughout the world. Early failures and complications have fostered more research in cervical spine biomechanics and design of better implants. Biomechanical studies have also confirmed that disc replacement decreases the amount of stress posed on adjacent motion segments and on this observation is based the promise of this technique of reducing the incidence of adjacent segment degeneration and disease. Available long term clinical studies have shown that cervical arthroplasty offers similar, and in some cases, better results than the commonly accepted "gold standard" of fusion. Nevertheless, debate is still open as to whether the impact of CDR on reduction of adjacent segment surgery is significant in the long term. As interest for non-fusion technologies from spinal surgeons, industry, and patients increases, cervical total

disc replacement will remain an active and fruitful area of research of spinal surgery in the years to come.

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