# Cervical Disc Arthroplasty

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## Introduction

The 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 or spinal cord. For many years, the only available treatment option for cervical degenerative disc disease has been either discectomy (*anterior cervical discectomy*, ACD) or discectomy and fusion (*anterior cervical discectomy and fusion,* ACDF). In recent years cervical disc arthroplasty (or *cervical total disc replacement,*TDR) 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 spread out and 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, and it is a matter of intense debate among spinal surgeons. It is worth noting that a clear difference exists in the meaning of the terms *adjacent segment degeneration (ASDeg)* and *adjacent segment disease (ASDis)*.

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Adjacent segment disease is defined as adjacent segment 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. This distinction is not always clear in literature, and often leads to unclear estimates of the real extent of the phenomenon.

In 1999, Hilibrand et al. [2] reported on the long-term outcome of 374 patients after single and multiple-level ACDF surgery and observed a constant yearly incidence of ASDis 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 ASDis 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 of 11.7 % prevalence of ASDis 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 [3, 4] have confirmed these findings reporting an incidence of ASDis of 25 % at 5–10 years after surgery. On the other hand, reported incidence of ASDeg is much higher as shown by many studies available in literature. In 2004, Goffin et al. [5] studied the long-term outcome of 108 patients after ACDF surgery and observed a 92 % rate of ASDeg at 5 years after surgery. More recently, Matsumoto et al. [6] conducted a prospective 10-year follow-up study on 64 patients who underwent ACDF and 201 asymptomatic volunteers and found progression of degenerative changes to be significantly more frequent in the ACDF group.

Although reported data suggest a strong correlation between ACDF surgery and higher risk of ASDis, this is most likely a multifactorial process. The incidence of degenerative changes in the cervical spine increases with aging. In a seminal study which is both beautiful in its simplicity and informative in its results, Boden et al. [7] 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. [8] noted new radiculopathy at a different level in 9 % of 846 patients after postero-lateral foraminotomy without fusion at an average of 3 years after surgery. This study is frequently cited by authors who believe that ASDeg/ASDis 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 are also important in determining the risk of ASDeg. As shown by Nassr and co-workers [9] the insertion of a marking needle during surgery in a disc at the wrong level determined a 3-fold increase of the 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 [10, 11]. On the other hand, intrinsic mechanical factors are also involved in the degeneration process. According to Hilibrand et al. [2] 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 recent studies have also focused their attention of the effects of spine sagittal alignment on the incidence of ASDeg and ultimately ASDis. Many studies have shown a direct correlation between postoperative spinopelvic parameters (i.e. mismatch between lumbar lordosis and pelvic incidence) and higher risk of degenerative changes at adjacent levels to a lumbar fusion [13–15]. The effects of sagittal balance on ASDeg have been much less studied in the cervical spine, but it is reasonable to think that similar relationships can be identified between cervical sagittal imbalance and incidence of ASDeg [16].

The aim of cervical disc arthroplasty is to preserve segmental motion after removing local pathology that is deemed to be the cause of patient's symptoms. 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 (ASDeg/ASDis). 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 TDR 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 [17]. 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. However, the early clinical follow-up of the new technique showed unacceptably high rates of implant migration (88 %) and subsidence and led many surgeons to direct their interest towards fusion procedures [18]. 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 316 L 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 pullout, dysphagia and implant mobilization [19].

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 (Fig. 16.1).

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 (Fig. 16.2). 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.

**Fig. 16.1** *Left*, PRESTIGE® ST cervical disc prosthesis; *Right*, PRESTIGE® LP prosthesis (Image provided by Medtronic, Inc)

**Fig. 16.2** BRYAN® Cervical Disc prosthesis (the BRYAN® Cervical Disc incorporates technology developed by Gary K. Michelson, MD. Image provided by Medtronic, Inc)

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.

## Indications for Use and Contraindications

The rationale of considering TDR rather than a standard fusion procedure (i.e. ACDF) lies in the aim of preserving motion of the treated segment and preventing adjacent-segment degeneration. The typical candidate patient for TDR 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 with loss of motion at that level, 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, cancer, and preoperative corticosteroid use [20].

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

**Table 16.1** List of commonly accepted indications and contraindications to cervical total disc replacement

| 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) |

and the presence of osteoarthritic changes in the posterior joints.

The role of TDR 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 TDR. European and US trails have enrolled patients with 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 has been recently investigated by different authors. Sekhon and coworkers [21] from Australia reported on 11 patients with single level myelopathy treated with TDR and average follow-up of 18 months. Although significant improvement was reported in clinical outcome measures, two complications were noted. One patient developed heterotopic ossification, and another patient developed progression of myelopathic compression due to postoperative oedema. Moreover, worsening of sagittal alignment of the cervical spine was noted in three patients. On the other hand, other authors have reported their positive experience of TDR in myelopathic patients. Fay et al. [22] reported on the results of a comparative study of TDR in 151 consecutive patients with cervical radiculopathy and cervical myelopathy. At the average follow-up of 36 months, no differences were identified in the two groups in terms of clinical and radiographic outcomes. However in our opinion 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 Table16.1. Although a thorough discussion on the indications of TDR is not possible due to the recent introduction into clinical practice of this technique, indications and contraindications listed in the table are widely accepted by most authors.

## 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 [23]. 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 [24] 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 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.

Although enrolment criteria for the European study included patients with focal myelopathy, the actual number of patients with myelopathy enrolled in the study was minimal. In a separate study, Sekhon et al. [21] reported the results of BRYAN disc in treatment of 11 patients with cervical myelopathy with average follow-up from 1 to 17 months. No complications were reported and improvement of Nurick grade of 0.72 points and NDI scale of 51.4 points was noted. In contrast to these observations, Lafuente et al. reported on clinical results of 37 patients with cervical radiculopathy and 9 patients with cervical myelopathy. Analysis of the results showed that radiculopathy patients were doing better than myelopathy patients. Moreover, patients with myelopathy were also more likely to experience residual symptoms [25].

The first extensive report on North American experience with the BRYAN disc has been published by Sasso and co-workers in 2007 and 2008 [26, 27]. 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 h vs 1.1 h) but a significantly lower NDI for the disc replacement group at 12 and 24 months (11 vs 20, $p = .005$). Analysis of arm pain at 1 and 2 years also favoured the arthroplasty group with significantly lower VAS scores (14 vs 28, $p = .014$). 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 2 patients in the BRYAN group. Four patients (2 in the control group and 2 in the BRYAN group) underwent a new ACDF surgery for adjacent segment degeneration.

The most recent and comprehensive study on BRYAN disc has been published by Heller and colleagues in 2009 [28]. This was part of the US IDE trial for FDA approval of the device and consisted of a prospective, randomized, controlled trial on 463 patients with minimum follow-up of 24 months. Inclusion criteria and outcomes measures were similar to the studies published by Sasso and co-workers [26, 27]. A total of 242 patients were enrolled in the BRYAN group and 221 patients in the control group (ACDF with

plating). Fusion occurred in 94.1 % of the ACDF patients at the final follow-up. Although both groups showed improvement of the outcome measures, analysis of the data favoured the BRYAN group in several outcomes, including NDI, neck pain and return to work. Overall success rate was 82.6 % for the disc replacement group and 72.9 % for the ACDF group at 2 years. Complications occurred in 75 patients (31.0 %) of the disc replacement group and 61 (27.6 %) of the fusion group. Almost all complication were related to general medical conditions, secondary procedures were needed in only 6 patients for the BRYAN group (1 revision, 3 removals of the implant, and 2 re-operations) and in 8 patients for the fusion group (3 removals, 1 re-operation, and 4 supplemental fixations). Total revision rate for the BRYAN group was 2.9 and 3.2 % for the ACDF group. The average range of motion at 24 months for the arthroplasty group was 8.1°.

## 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 Murray and colleagues [29]. An earlier study by Bertagnoli et al. [30] 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 [29]. 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 ($p = .033$).

## 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. 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 PRESTIGE II implant was studied by Porchet and Metcalf on 55 patients. Standard clinical and radiographic evaluation was undertaken by the authors and the results showed a substantial overlap between the artificial disc and the ACDF surgery group.

The best available data on clinical safety and efficacy of the PRESTIGE ST disc has been

published in 2007 by Mummaneni and colleagues. 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.

In a recent meta-analysis, 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 [31].

## Complications

Cervical disc replacement surgery shares with standard anterior cervical fusion surgery the same risks related to surgical approach. In a recent 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 [32]. Access related complications for cervical arthroplasty are in the same range. In the two European studies on BRYAN disc, 0.97 % of patients (1 out of 103) required evacuation of prevertebral hematoma, and 2.91 % (3 out of 103) required additional surgery to decompress the neural canal. Dural tear was noted in 2.33 % of patients, and one patient required oesophageal tear repair [23, 24]. Analysis of complications in one FDA IDE trail showed more general medical complications in patients who underwent total disc replacement than the fusion group. Dysphonia/dysphagia was noted in 10 % of patients in the arthroplasty group, and 2.8 % of patients developed wound infection [28].

Heterotopic ossifications (HO) and anterior ankylosis is a known and dreaded complication of cervical disc replacement surgery. Leung and colleagues reported an incidence of 17.8 % (16 patients) of HO in a multicentre study on BRYAN disc arthroplasty [33]. 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 7 cases (9.1 %) had spontaneous fusion of the

treated segment at 1 year after surgery [34]. Other studies have reported similar figures in the range of 11–44 % with concomitant adjacent segment degeneration [35, 36]. Identified risk factors for heterotopic ossifications are pre-existing spondylosis, male gender and increased age [33]. Nevertheless, the aetiology of this complication of TDR 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. 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 any evidence [28, 37].

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 TDR [38, 39]. Troyanovich and co-workers have shown that adjacent segments to a kyphotic level develop compensating hyperlordosis and accelerated degeneration [40]. 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 [41].

Implant subsidence and/or migration have been also reported by some authors. Goffin and colleagues reported a total of 4 implant complications (3 cases of subsidence and 1 case of implant migration) in a series of 146 patients. Implant failures were related to an improper milling of the endplates and implant positioning [24]. General advice is to avoid TDR 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 vertebral body fracture during insertion of a keeled implant [42]. Similarly Shim and colleagues described a case of an avulsion fracture [43]. A specific disadvantage of keeled implants is the bone defect created in the vertebral body and the need of extra bone graft in case of revision of the implant. Although no specific reports have been published in literature, the decreased bone stock may be a problem if a salvage fusion is needed.

"Aseptic loosening" or failure of a total joint arthroplasty is a very well-known phenomenon of polymer-bearing implants in general orthopaedics. Failure of the implants in these cases is related to the local inflammatory response induced by the wear debris released by the prosthesis. Macrophages and inflammatory cells incorporate wear debris and release inflammatory cytokines which induce a progressive bone resorption and eventually mechanical failure of the implant. The amount and type of local response varies with the size, shape, amount and surface chemical reactivity of the released particles [44]. There is some concern that this effect may lead to aseptic loosening and chronic inflammatory reaction in cervical TDR as well. Cavanaugh and co-workers reported a case where a revision of TDR was performed and a local chronic inflammatory reaction was noted, the patient also developed a delayed hypersensitivity reaction to metal ions [45]. More recently, Guyer and colleagues reported on 4 cases of early failure of metal-on-metal TDR presenting with worsening pain and/or radicular symptoms. There were 3 cases of lumbar TDR and 1 case of cervical TDR, 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

[46]. 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 [47].

Anderson published two seminal studies on *in vitro* behaviour of the BRYAN prosthesis [48, 49]. The authors showed that wear debris by this implant is produced at a rate of 1.2 mg/1 million cycles with decrease of implant height of 0.02 mm/1 million cycles. The average size of debris particle was 3.9 μm, larger than the particles observed with hip and knee arthroplasty (1–1.8 μm). In a second study the same authors confirmed the linear relationship between the number of cycles and loss of prosthesis height. Observed wearing of the BRYAN polymeric nucleus was uniform and particulate diameter was on average 3.89 μm. The authors also tested the same device in an animal model of goats sacrificed at 3, 6, and 12 months after implantation of the artificial disc. A trend of increased local inflammatory reaction was noted with later sacrifices in the prosthesis group, however the amount of inflammatory reaction and local debris was higher in the control group treated with fusion and anterior plating. As clinical experience of cervical TDR expands over time, more studies will be needed to fully assess the long-term risks of wear debris released by the implants.

## Biomechanics

The main aim of cervical TDR 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, 50, 51]. These changes are thought to be the basis of increased incidence of ASDeg/ASDis after fusion. Therefore, the most important aim of cervical TDR is to restore the physiological segmental motion of the treated level. Each cervical 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 [52, 53]. However, 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. DiAngelo and colleagues compared motion of two different implants on human cadaveric cervical spines. The PRESTIGE disc was chosen as a typical semiconstrained implant, whilst the ProDisc-C implant was chosen as typical constrained implant. Results of the study were in support of a semiconstrained implant because of a better restoration of normal kinematics in all movements, most importantly the anterior translation movement of the normal cervical spine [50, 54].

Sasso and colleagues have also studied the long-term outcome in terms of motion preservation in a cohort of prospectively enrolled patients [55]. Longest follow-up available for the study was at 24 months. Data showed that motion is preserved at 24 months in the prosthesis group.

Average flexion-extension was 7.95° and postero-anterior translation 0.36 mm. Interestingly, the authors reported no statistically significant difference with regard to adjacent segment motion in the investigational group vs the fusion group. In contrast with these findings, Chang and colleagues have shown a net and significant decrease of adjacent segment motion in patients treated with two cervical TDR (PRESTIGE and Prodisc-C), whilst increased motion was observed in the ACDF control group [56].

## Cost Analysis

A great deal of discussion in the cervical arthroplasty field revolves around the increased costs of this procedure and the short and long-term technological and economical impact of widespread usage of this new technique. Average cost of a single-level cervical total disc replacement implant is about $4000 in the US, whilst the cost for a cervical interbody cage and anterior plate is $2500 [57]. The target market of disc arthroplasty 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 dollars in 2010 [57].

Early cost-analysis studies have only focused on the simple comparison of raw costs of ACDF surgery vs cervical disc replacement surgery. Increased costs were justified by a supposedly decreased number of adjacent-segment operations and earlier return to work and active life. Interest in motion preservation technologies has increased in recent years, and more in depth analyses of costs have been published. Qureshi and co-workers conducted a cost-effectiveness analysis comparing single-level disc arthroplasty vs ACDF surgery. 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 %. Costs of the two procedures were estimated using the 2010 Medicare database. Supported by a recent meta-analysis of 4 randomized trials on disc arthroplasty vs ACDF the authors also assigned a utility value to TDR of 0.9 (scale 0–1) as compared to ACDF which was assigned a slightly lower value, 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 [58]. A similar analysis by Warren and colleagues showed an average cost for ACDF of $16,162 and TDR of $13,171. QALY increase at 2 years was better for ACDF than TDR using NDI results (0.37 vs 0.27), but better for the disc replacement group when comparing SF-36 results (0.47 vs 0.32) [59].

Although real cost estimation is extremely difficult and varies greatly in different health care systems and settings, the more recently published studies are more positive about the clinical utility of cervical arthroplasty. However, although figures seem to support the use of cervical arthroplasty in clinical practice, it must be kept in mind that these studies are based on some fundamental assumptions. Sensitivity analysis by Qureshi and co-workers showed that TDR is a cost-effective strategy once survival time of the prosthesis approaches 11 years. A survival time of the prosthesis less than 9.75 years means that ACDF is a better and more convenient strategy [58]. At the present time, the longest term clinical data on disc arthroplasty available in literature are at 6 years follow-up [31]. These observations call for more long-term studies of clinical efficacy of cervical disc arthroplasty.

### Conclusions

Cervical disc arthroplasty has progressed over the last three decades from a merely hypothesis to a clinical reality. Although it is still far from being a commonly accepted standard for treatment of cervical disc herniation and related conditions, the concept of artificial substitution of cervical discs has been adopted 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. Finally, wear analysis seems to confirm the safety of the implants with regard to tissue reaction and aseptic mobilization at least at medium-term follow-up. Available short and medium-term clinical studies show that cervical arthroplasty offers similar, and in some cases, better results than the commonly accepted "golden standard" of fusion. This has been confirmed by short and medium-term studies reporting survivorship rates for cervical arthroplasty superior to ACDF surgery. Nevertheless only long-term studies can fully validate this hypothesis and prove clinical utility of cervical TDR. 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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