Cervical Intervertebral Cages: Past, Present, Innovations, and Future Trends with Review of the Literature

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ABSTRACT

Background Data: Anterior cervical discectomy and fusion (ACDF) has been the standard treatment for degenerative conditions of the cervical spine. Since the introduction of the procedure in the fifties, ACDF has become quite popular and a gold standard procedure. Autologous iliac crest bone grafts were used for fusion with associated drawbacks that mandated the introduction of new metallic substitutes with various fillers. Many improvements and enhancements to these cages were implemented with rising controversial issues.

Purpose: To review the available data of cervical cages and the recent status of ACDF using standalone cages.

Study Design: A narrative literature review.

Patients and Methods: We reviewed the English literature through the last two decades for the most up-to-date available data of the cervical cages and reported the current status of ACDF outcomes using standalone cages. We ran a search using PubMed, Cochrane, and Google Scholar using different relevant keywords and extracted the most relevant researches according to our study aim. We focused on special titles that we thought were most relevant to the spinal surgeon's daily practice.

Results: A great number of cervical cages with different shapes and designs are available for ACDF. Spinal surgeons are confronted with a huge array of cervical cages introduced every day by many medical industry competitors. Clinical and radiological outcomes are generally very satisfactory regardless of the type and material of cages used. Composite or titanium-coated PEEK cervical cages and 3D-printed and porous titanium cages are under evaluation. Self-locking standalone cages showed great advancement and development with promising outcomes.

Conclusion: ACDF is a well-established surgical technique in the management of cervical spondylotic radiculopathy and/or myelopathy. Large numbers of cervical cages with different shapes, designs, and compositions are available in the market with generally satisfactory clinical and radiological outcomes.

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Spinal surgeons should be aware of the available cervical cages and choose the most suitable to their patient’s medical and socioeconomic status. New industrial technology has the potential to improve the load-bearing surface, lower cage dislocation and subsidence, and osteointegration. Composite cages, self-locking cages, and absorbable cages are fairly newly introduced cages and still under evaluation. Multicenter long-term prospective randomized controlled trials are mandatory for obtaining first-class evidence-based medical data on ACDF. (2020ESJ213) 

**Keywords:** Cervical spine, Cages, ACDF, Standalone, Spondylosis, Cervical disc, Myelopathy, Radiculopathy, Fusion, Titanium, PEEK, Iliac bone graft.

### INTRODUCTION

Anterior cervical discectomy and fusion (ACDF) has been the standard treatment for degenerative conditions of the cervical spine including cervical disc disease and cervical spondylotic myelopathy. Since the introduction of the procedure by Smith and Robinson (1958), Cloward (1958), Bailey and Badgley (1960), and Simmons and Bhalla (1969), ACDF has become quite popular with generally good clinical outcomes (Figure 1). Despite the introduction of simple anterior cervical discectomy (ACD) by Hankinson and Wilson and recently motion-preserving disc arthroplasty procedures, ACDF remains the gold standard procedures especially for elderly patients. Autologous iliac crest bone grafts (ICBG) were used for fusion; however, harvesting ICBG was associated with problems such as pain, infection, hematoma, neural injury, and fracture iliac bone. To avoid these morbidities, synthetic grafts or cages were introduced using carbon fiber, ceramics, titanium (Ti), and polyether ether ketone (PEEK). Different materials were used to fill cages including hydroxyapatite (HA), tricalcium phosphate (B-TCP), homologous bone bank, demineralized bone matrix (DBM), or even empty cages. The clinical and radiological outcomes were generally good with some problems including adjacent segment disease, pseudoarthrosis, and subsidence. Improvement in cages technology included 3D-printed cages, anchored cages, self-locking cages, porous titanium cages, and biodegradable cages. With increasing options and alternatives in this field, lots of controversial issues caught our attention to the importance of demonstrating a global and collective view of this subject.

In this review, we reviewed the literature to demonstrate the most important controversial issues with ACDF and highlighted the most up-to-date data in this field to broaden the technical and knowledge spectrum and armamentarium of spinal surgeons.

**Figure 1.** History of ACDF with iliac crest bone graft: (A) Cloward dowel graft; (B) Smith–Robinson-based rectangular graft; (C) Simmons–Bhalla keystone graft; (D) Bailey–Badgley onlay strut.

### ANATOMICAL CONSIDERATIONS

The cervical spine is probably the most distinct spinal region, comprising 76 separate joints and allowing for a range of motion more than any other region in the spine. This region carries unique anatomical and biomechanical features that should be considered while performing cage insertion. The typical cervical vertebra is almost
rectangular in shape with a smaller anteroposterior diameter than the transverse diameter (17.1 ± 0.2 and 15.2 ± 0.3 mm versus 24.6 ± 2.4 and 23.0 ± 2.4 mm in males and females, resp.). These dimensions increase from C2 to C7, with more increase in the transverse than the anteroposterior diameter allowing for more support to the greater axial loads at lower vertebrae. The sex- and level-related differences in dimensions should be considered when selecting the appropriate cage diameter to be inserted. Similarly, the cage height is important that must be selected carefully to achieve a proper foraminal decompression without excessive facet distraction. Facet joint distraction equal to 3 mm or more was associated with worse Neck Disability Index (NDI) and pain Visual Analogue Scale (VAS) following anterior cervical fusion procedures.

The superior and inferior surfaces of the vertebral body are typically described as being saddle-shaped. The superior surface is concave from right to left (by the effect of uncinate processes) but convex and sloping upwards from front to back (by the effect of beveling of its anterior aspect). On the contrary, the inferior surface is convex from right to left but concave from front to back where much of this concavity is created by the anterior lip of this surface and is greatest at C3 and C4, getting shallower as we go down to C5 and C7. Anatomical cages are supposed to be designed in such a way that respect these surface characteristics. Typically, an anatomical cage is slightly convex superiorly when seen from the side and convex inferiorly when seen from the front. This provides a better fitting of the cage for the disc space with adequate coaptation at the implant-endplate interface.

In a study exploring the effect of the cage design that matches adjacent endplates on the subsidence rate, the authors used a newly designed Ti mesh cage with modified 2 endcaps. The upper endcap of the new cage was convex superiorly in an anterior-posterior fashion to better match the inferior endplate morphology. The lower endcap was sloping upwards and backwards with a 10° angle that conforms to the shape of the adjacent upper-end plate. After a minimum follow-up of 30 months, the authors found significantly lower rates of subsidence, lower height loss at fused segments, and lesser neck pain VAS with the newly designed cages compared to traditional ones. This concept may not apply to segments with higher grades of disc degeneration where the vertebral endplates undergo morphological changes due to subchondral sclerosis resulting in their flattening with osteophytes formation. In such instances, the use of cages with more flat endplates may be easier, achieving better implant-endplate surface matching. The implant-vertebral endplate angular mismatching was found to increase the incidence of subsidence significantly for each 10-degree increase in mismatch angle.

It is a better practice to meticulously select the cage morphology having the best fit rather than to overprepare the vertebral endplate for the available unfit cage. Trials to lessen the mismatch angle by burring during endplate preparation can result in a significant loss of endplate integrity even with the removal of as little as 1 mm of the endplate.

Another important anatomic consideration is the surface area of the cage that comes in contact with the vertebral endplate, known as the cage footprint. Both clinical and finite element studies reported better performance of cages with larger footprints due to the distribution of stresses over a wider surface area of the endplate resulting in lower subsidence rates and better clinical improvements. The contribution of the cage footprint area was reported to be 40 times greater than that of cage material to subsidence. One more concern in cage selection is its lordotic angle. It is generally recommended to avoid fusion in regional or global kyphosis in patients with cervical pathologies as this may enhance adjacent segment degeneration. Kyphotic fused segments worsen forward imbalance, thus increasing the force required to maintain horizontal gaze and the intradiscal pressures in adjacent segments. However, normal asymptomatic cervical spines are not always lordotic. The
The cervical spine was found to take one of 5 distinct sagittal profiles in significant proportions among functioning asymptomatic individuals.\textsuperscript{175,79} The sagittal alignments of cervical spines were not significantly different when compared between symptomatic and asymptomatic cohorts\textsuperscript{202}, nor were the pain scores among different cervical alignment subgroups\textsuperscript{71}. This discrepancy may be because the overall cervical alignment is not the function of regional angle only, but rather the contribution of both angular and translational parameters, and is related to and affected by the global spine balance.\textsuperscript{178} These anatomical and biomechanical facts should be kept in mind during the preoperative evaluation for an adequate personalized correction target for every patient.

**PATHOLOGICAL CONSIDERATIONS**

The most prominent clinical manifestations associated with cervical spine degeneration are neurological compromise and pain. These manifestations can be clearly explained and better addressed by understanding the pathology of cervical degenerative changes. Although cervical degenerative changes can affect any element in the cervical spine\textsuperscript{64}, the disc and facet joint develop the most clinically significant changes. The disc, which is essentially an avascular structure,\textsuperscript{131,77} can perform nutrient-waste exchange primarily via diffusion across the capillary beds in the adjacent vertebral endplates.\textsuperscript{190} With aging, the endplate calcification limits the nutrient-waste exchange, resulting in the death of the inner disc cells (nucleopulpocytes) and contributing to a shift from tissue homeostasis to a state of catabolism that further leads to disc deterioration.\textsuperscript{60} The events triggering this catabolism are thought to have a genetic basis or be related to unnoticed subclinical injuries.\textsuperscript{62,182} Concomitantly, upregulation of proinflammatory cytokines including TNF\textsubscript{α}, IL-1\textbeta, and IL-6 occurs within the disc, promoting further loss of native cells and replacement with fibroblast-like cells.\textsuperscript{60} This results in reduced production of the hydrophilic proteoglycans and gradual disc desiccation that shifts the biomechanical loads from the nucleus pulposus to the annulus, whose yield strength is being concomitantly lowered by the secondary upregulation of matrix metalloproteinases by resident cells of the disc.\textsuperscript{150}

This combined reduced strength with load shifts puts the annulus at risk of fissuring with subsequent nucleus herniation causing potential root and cord impingement. Moreover, desiccation of the disc reduces its height, resulting in foraminal narrowing that adds to root compression. These load shifts not only affect the annulus and disc height but also affect and induce parallel degenerative changes in both the uncovertebral (UVJ) and facet joints (FJ). The UVJs develop osteophytic spurring that project laterally to impinge surrounding structures including the nerve root, spinal cord, radicular artery, vertebral artery, and cervical sympathetic trunk.\textsuperscript{119} Similarly, the FJs, which normally provide load-bearing support and stabilize the spine during flexion-extension and axial rotation, become subjected to more load-bearing stresses that induce degeneration and destabilization of the joints.\textsuperscript{64} These degenerative changes include the following: joint-space narrowing, osteophyte formation, and subchondral sclerosis like any other diarthrodial joint resulting in further foraminal stenosis, canal narrowing, and limited mobility.\textsuperscript{181} Adding the associated ligamentous redundancy and buckling to these effects, the final outcome is the progressive neural compromise associated with degenerative cervical spondylosis. All these changes should be put into consideration and addressed during decompression/fusion surgeries of the cervical spine.

Pain, another hallmark associated with cervical spondylosis, occurs due to various factors. The discogenic component of pain is a result of structural failure of the disc and annular fissures producing mechanical stimuli that lead to peripheral sensitization.\textsuperscript{20} Pathological studies of discs of patients suffering from discogenic
pain also revealed zones of extensive vascular and neural ingrowth from outer annular layers into the nucleus pulposus along torn fissures. These annular and nuclear nociceptive nerve fibers become sensitized by the cytokine environs inside the degenerated disc contributing to the development of pure discogenic pain syndrome. Similarly, the FJs innervated by nociceptive fibers and their degeneration in the context of disc degeneration make them a putative source of cervical pain. Moreover, other factors such as central sensitization and distortion of surrounding soft tissues, including ligaments and muscles, have been suggested as potential sources of pain. These sources of pain should be dealt with during the stabilization/fusion techniques including adequate removal of disc remnants, proper stabilization, effective fusion techniques, and achievement of optimal alignment.

CAGE MATERIAL

Since the use of autografts in cervical surgeries in the 1950s to replace disc material and promote fusion, several steps have been taken to introduce new materials into the field of cervical surgeries as follows: starting with stainless steel cages in the 1960s, passing through Ti and alloys in the 1980s, reaching the carbon fiber PEEK and silicon nitrides in the 1990s, and finally the introduction of the nitinol, cobalt-chromium-molybdenum, and tantalum implants in the 2000s. When interbody spacer reaches the optimal bone integration, it aids the fusion process and limits complications such as subsidence and pseudoarthrosis. Cage materials selection is based on how they effectively promote osteoconduction and osteoinduction and facilitate early biological fusion between endplates. During the last 20 years, PEEK and Ti have been the most common materials for cervical cages. However, in unprocessed forms, both materials are not highly bioactive. Consequently, surface compositions are used to improve bioactivity and enhance osteointegration with the body.

Ti is a highly biocompatible material in spine surgeries due to its strong nature, resistance to corrosion, and less density. In contrast to natural bone, Ti has a higher stress load around the implant site leading to higher rates of subsidence, bone atrophy, and failure. Also due to its radiodensity, it is difficult to assess fusion after using Ti implants. Modifications to Ti-based implants are processed mainly on their surface, to enhance the osseointegration and bone-implant fusion. The increase in porosity areas in Ti implants allows for bone growth within the implant. Hydroxyapatite coatings to Ti implants improve the ontogenetic effects during the fusion process. De Groot et al., in their study, concluded that HA-coated Ti implants combine the best of the two materials.

While Ti enhances osteointegration and cell adhesion, PEEK, being chemically inert, lacks that ability. Due to the high modulus elasticity of Ti (which far exceeds that of bone), it provides long-term stabilization with rigid support. As PEEK’s modulus is the same as that of cortical bone, postoperative assessment of continuity and fusion is much easier than that with Ti. In addition, Ti carries a higher risk of subsidence and metal allergy. Recent cages have been designed in such a way that promotes osseointegration and fusion by modifying cage surfaces. Plasma beam and electron spray techniques are used to increase the surface roughness of Ti cages and its alloys, which was found during in vitro studies to be associated with an elevation in alkaline phosphatase and total protein levels, thus increasing osteogenic cell differentiation. On the other hand, the elastic modulus of PEEK cages are close to that of bone, which helps decrease the stress shielding and promote bony fusion. Additionally, the radiolucency of PEEK cages allows for better fusion assessment and better MRI compatibility. Trials to combine the improved bioactivity of Ti with the elastic modulus and radiolucency of PEEK resulted in the creation of composite Ti/PEEK cages thought to have
enhanced biological properties.\textsuperscript{84} The clinically available composite cages with PEEK bodies and Ti endplates can augment the bone-implant fusion. Similarly, composite cages combining beta-tricalcium phosphate (beta-TCP) to make use of its osteoconductivity with a plastic material like lactic acid polymer (PLLA) resulted in the creation of a resorbable cage that has an elastic modulus close to the natural cortical bone with a high breaking strength, higher ability to tolerate plastic and elastic strain compared to pure TCP, and better osteogenic properties.\textsuperscript{13} The results of its clinical use were promising, with long-term fusion, no loss of correction, and no inflammatory reactions.\textsuperscript{51} Probably, the future will witness more use of these composite cages than pure materials, making use of the bioactivity of different materials in one construct.

A meta-analysis compared the results of 107 and 128 patients in the PEEK cage group and Ti cage group, respectively, and concluded that there was “no significant difference in functional and radiographic performance” between both cages. However, they noted a higher subsidence rate with the Ti cage group.\textsuperscript{115} Another meta-analysis compared the results of 182 and 228 patients in the PEEK cage group and Ti cage group, respectively, and demonstrated the same results, although the Ti group was “associated with an increased risk of subsidence.”\textsuperscript{161} Chou et al.\textsuperscript{42} compared the results of 55 patients who underwent ACDF using Ti cage (N = 27), PEEK (N = 9), and tricortical iliac crest graft (N = 19) and concluded that both PEEK cages and iliac crest grafts “yielded similar fusion rates,” while Ti was associated with a higher complication and a lower fusion rate.

The Brantigan cage, introduced early in the 1990s by AcroMED, had been widely used in the spine field.\textsuperscript{27} It is made of biocompatible, radiolucent material; when reinforced with carbon fibers and engineered in a specific design, it mimics the structure of cortical bone graft.\textsuperscript{147} PEEK was thought to be a breakthrough in the field of implants to overcome the drawback of Ti, especially stress shielding. However, Pelletier et al. concluded that there is no difference between PEEK and Ti in the biomechanics of animals.\textsuperscript{142} Sagomonynats et al.\textsuperscript{155} favored PEEK for bone growth in vitro compared to Ti; however, Olivares-Navarrete et al.\textsuperscript{135} concluded the opposite. Wu et al.\textsuperscript{195} manufactured Ti-PEEK composite implants and concluded a double bone volume when compared to standard PEEK implants. Han et al.\textsuperscript{84} had improved cellular proliferation with Ti-PEEK implants.

In a 5-years follow-up study, Marotta et al.\textsuperscript{122} reported the outcomes of 167 patients who underwent ACDF using carbon fiber cages filled with HA and reported a good fusion rate in accordance with the literature and a 13% nonfusion rate without clinical significance. Zhou et al.\textsuperscript{204} compared standalone PEEK cage versus tricortical iliac bone graft and plate and reported that PEEK is a good substitute that restores curve and disc height and facilitates fusion follow-up. Chen et al.\textsuperscript{39} compared Ti versus PEEK cage in 3-level ACDF with more than a 7-year follow-up and reported that PEEK is superior to Ti in the maintenance of disc height and cervical lordosis with better clinical outcomes.

### CAGE SUBSIDENCE

ACDF was first introduced in the 1950s and autologous osseous grafts were used then to preserve the intervertebral height and promote fusion between adjacent vertebrae.\textsuperscript{24} However, multiple complications have arisen from this technique such as graft collapse and harvested graft site complications such as iliac crest, pseudoarthrosis, and cage subsidence.\textsuperscript{36} These complications have been the step for the invention of synthetic cervical implants. Made up of stainless steel, polymethyl-methacrylate (PMMA), Ti, and PEEK, cages were used in ACDF surgeries. It was hypothesized that these synthetic material cages will preserve the intervertebral height and improve fusion, consequently overcoming autologous graft complications.\textsuperscript{121} The main aim...
of the intervertebral cage is to advocate segment immobilization and maintain foraminal patency. Subsidence of cages on the other hand affects these aims dramatically, promoting pseudoarthrosis and nearby osteophytes formation, finally leading to segmental kyphosis and root compression.\textsuperscript{180} To confirm the occurrence of cage subsidence, it is stated that a loss >3 mm of intervertebral height compared to the direct postoperative image at the final follow-up visit has to be reported.\textsuperscript{7} (Figure 2). The mean incidence of cage subsidence is 20.2%.\textsuperscript{133} Subsidence has a direct proportion relation with axial load pressure and inverse proportion relation with cage area of interface with the endplate.\textsuperscript{83} Etiology of cage subsidence has not been well established, but several hypotheses have been published. Borm et al.\textsuperscript{26} suggested that subsidence is a natural process of fusion itself between bone resorption and remodeling. Some surgeons have correlated cage subsidence with cage material, especially Ti cages.\textsuperscript{34,39} Endplate damage or poor surgery could be directly correlated with cage subsidence but yet to be confirmed.\textsuperscript{201} Multiple-level ACDF, more than two levels, and lower cervical level surgeries had higher rates of subsidence.\textsuperscript{18,99} Bone pathologies like osteoporosis could be a risk factor of subsidence occurrence.\textsuperscript{199} Finally, cervical cage subsidence is less likely to affect the general alignment of the cervical spine, but it affects the neural foramen.\textsuperscript{99} There are several hypothesized techniques to decrease the incidence of cage subsidence. Igarashi et al.\textsuperscript{94} in a prospective study proposed that the greater the cage height, the higher the risk of subsidence in cervical fusion. They also proposed that PEEK cages are better to preserve intervertebral height than Ti ones. Yang et al.\textsuperscript{200} in their study have found that the larger the AP diameter with no intraoperative anterior overdistraction, the less likely the occurrence of subsidence. Xu et al.\textsuperscript{196} also discovered that cage with plate or iliac graft with plate has lower subsidence rate than cage alone or iliac graft alone. Finally, the cage or graft intended for fusion must cover most of the surface area of the intervertebral space to decrease the incidence of subsidence.\textsuperscript{83}

### PSEUDOARTHROSIS

In their systematic review, Oshina et al.\textsuperscript{136} reported that the most common fusion criteria, bridging trabecular bone between end plates, and absence of a radiolucent gap between endplates and graft, are subjective (Figure 2). They recommend using <1 mm of motion between the spinous processes on dynamic X-ray to confirm fusion. Pseudoarthrosis is the failure of fusion after spinal fusion surgery.\textsuperscript{163} It accounts for 50% of revision spinal cases.\textsuperscript{118} Zhu et al.\textsuperscript{205} reported that 62% of complications of ACDF cases are pseudoarthrosis. Although the true incidence of pseudoarthrosis is not well established yet, it is estimated in the literature that 30% of cases may pass asymptatically.\textsuperscript{118} With more intended fusion levels, fusion becomes very challenging, and the more caudal the levels, the higher the risk for pseudoarthrosis. This is due to the increased axial load and stress applied between the graft and vertebral body.\textsuperscript{25} There are several factors hypothesized to address the pseudoarthrosis problem. Age is of great importance as younger patients are at high risk of symptomatic pseudoarthrosis, possibly due to the increased activity and greater expectations on the implants used.\textsuperscript{25} Smoking is one of the strong factors associated with pseudoarthrosis, which was proved to be an independent factor in literature.\textsuperscript{90} Patient comorbidities such as diabetes, hypertension, osteoporosis, and other chronic debilitating illnesses are associated with pseudoarthrosis.\textsuperscript{25,118,146} A meta-analysis showed that plate fixation improved fusion in single- and multiple-level cervical fusion surgeries.\textsuperscript{65} Recombinant human bone morphogenetic protein-2 (rhBmP-2) has shown slight superiority over autografts in fusion in one prospective study.\textsuperscript{33} Aside from clinical data to suspect pseudoarthrosis, the lack of radiological evidence of fusion is the key for the diagnosis,
that is, the absence of bridging trabecular across the fused levels on static radiographs, excessive motion on dynamic lateral radiographs, and thin-cut MSCT scans, which have a more advanced role in identifying the fusion state. Pseudoarthrosis is diagnosed if a radiolucent gap across the fusion levels is found. The diagnosis of pseudoarthrosis is very complex and is controversial. When patients have persistent, recurrent, or new neurological symptoms or pain, the surgeon tends to seek a firm diagnosis for this condition. Several methods of dynamic cervical radiography were hypothesized to have an objective diagnosis for pseudoarthrosis. Simmons’ method, 2 fixed points on the anterior surface of the superior and inferior vertebral bodies are marked, then the lines are passed through them in the dynamic views. When the angle subtended via these lines is more than 2 degrees in extension, nonunion is diagnosed. In Hutter’s method, both flexion and extension films are put together and motion is detected between the 2 films. Moreover, in this method, the motion of the spinous process is observed; however, it may enlarge the overall motion and bias the fusion. Multislice CT offers an advanced modality in diagnosing pseudoarthrosis. Especially in cases of locked pseudoarthrosis when the graft is fused with the adjacent intervertebral bodies but fails to fuse within the cage. MSCT shows solid proof of fusion; however, it has limited abilities when devices contain metallic components. In a prospective study, MSCT was statistically significant in correlation with intraoperative findings compared to dynamic radiographs. Lin et al. in their review reported that no single method is perfect for the diagnosis of pseudoarthrosis and using dynamic lateral cervical films in 150% magnification. If the interspinous motion is <1 mm and superjacent interspinous motion is ≥4 mm, fusion is confirmed. In ambiguous cases, MSCT scans are superior in evaluating extragraft bone bridging with the highest sensitivity and specificity diagnostic criteria of pseudoarthrosis. The management of pseudoarthrosis depends on clinical conditions, comorbidities, and other factors. The revision surgery is mainly indicated when pseudoarthrosis is accompanied by clinical findings. The aim is to ensure proper arthrodesis. Other factors need to be addressed such as smoking, obesity, osteoporosis, and malnutrition before aiming directly for revision surgery. Lee et al. studied the fate of pseudoarthrosis one year after ACDF and reported that those patients may be observed because approximately 70% of them will eventually fuse by 2 years. They recommended early revision if pseudoarthrosis was associated with considerable neck pain.

![Figure 2](image)

**Figure 2.** Lateral cervical radiographs showing (A) C5/6 ACDF with sound bone fusion and bone formation in and around the cage; (B) C6/7 ACDF with sound bone fusion and cage subsidence; (C) C5/6 ACDF with pseudoarthrosis and lucent line in and around the cage.

### ADJACENT SEGMENT DISEASE

Adjacent segment disease (ASD) is believed to occur secondary to altered spine biomechanics after fusion surgery. It is believed that supraphysiologic motion over the adjacent mobile segments is associated with increased stress and increased intradiscal pressure. This increased load on mobile segments either cranial or caudal by the fusion segment is being investigated to be the cause of ASD. ASD is observed radiologically in 50% to 60% of patients with prolonged follow-up periods, whereas the
prevalence of symptomatic ASD ranges from 7% to 15%. Following cervical fusion, 5.6% of symptomatic ASD patients required a second surgery. Furthermore, young males tend to receive a second revision surgery due to ASD more than older females. The stepladder process of ASD formation following cervical arthrodesis is the formation of osteophyte spurs that may initially form a degree of stabilization to the excessive motion on the adjacent segments followed by anterior longitudinal ligament calcifications and disc space narrowing. The site of osteophytes plays a key role in the clinical presentation if it is anterior or anterolateral neurological symptoms. Motion-preserving devices implanted after cervical discectomy may help to preserve the motion segment and thus diminish the ASD formation; however, up till now no strong evidence supports this hypothesis.

Even though ASD may be caused by various risk factors such as surgical maneuver, age, and comorbidities. Studying the risk factors and etiologies of ASD is challenging because ASD usually takes a long period of time to occur and long-term follow-ups are not available in many places. Literature can identify patients with ASD as those who had to undergo second revision surgery due to ASD; however, it cannot identify those asymptomatic or radiologically proved to have ASD. In a prospective study, scientists performed magnetic resonance imaging (MRI) for the patients preoperatively and then another one is done in a short follow-up period with a range of 10–48 months; they radiologically discovered an accelerated degenerative change to the adjacent vertebrae in 75% of patients. This could prove that cervical fusion surgery accelerates the rate of degeneration to the adjacent levels.

Many risk factors have been hypothesized to be causes of ASD following cervical fusion surgeries. There was a higher incidence in multilevel surgery than a single-level surgery. Other studies have hypothesized the absolute contrary that single-level surgeries have a high possibility of ASD incidence compared to multilevel fusion. Some surgeons have regarded ASD to surgical technique, as annulus puncture during the leveling process, plate proximity to the adjacent endplate, and poor alignment after fusion surgery. Different studies have reported that cervical plates should be at least 5 mm away from adjacent disc space as there is strong evidence that proximity to disc space increases the possibility of ASD. To reduce the incidence of ASD, Alhashash et al. recommended restoration and preservation of the sagittal profile of the cervical spine during cervical spine surgery. The only independent risk factors found in the literature were young age and patients with psychiatric disorders. Those were the higher group who required a second surgery due to ACDF.

### CAGE FILLERS

Filling cages with materials to facilitate the fusion process has been the gold standard procedure decades ago. Autologous bone has been used widely to fill cages due to its availability, biocompatibility, and ability to provide a mixture of properties such as being osteoconductive, osteoinductive, and osteogenic. However, autologous bone supply is usually limited on many occasions due to graft site morbidity and bone diseases limiting the use of autologous bone. It was mandatory to seek a different substitute to the autologous bone to facilitate the fusion process.

Chang-Jung et al. used xenograft to fill PEEK cages and reported that a cage incorporated with xenograft prevented donor site and provided successful fusion. Sugawara et al. used B-TCP- and HA-packed Ti cages and reported a satisfactory fusion rate that was higher with B-TCP in the early stages after surgery. Demineralized bone matrix (DBM) is processed from the human allograft bone. It is osteoconductive with little osteoinductive ability. In combination with PEEK cages, DBM represents an acceptable replacement to the autologous bone. Park et al. used
PEEK cages with DBM and reported satisfactory results similar to literature data.

Ceramic, a material that has been used along with interbody devices, works as a scaffold to assist bone growth along with its osteoconductive property. Its low shear strength limits its use as a standalone substitute that needs to be added to autologous bone or bone marrow aspirate. Ceramic materials in spinal fusion use are as follows: B-TCP, calcium sulfate, hydroxyapatite (HA), B-calcium pyrophosphate (B-CPP), and silicate-substituted calcium phosphate (Si-CaP). B-TCP showed good results in cervical radiculopathy and myelopathy patients and good fusion results later in follow-ups. B-TCP showed superior results over HA in fusion in 6-months and 1-year follow-up; however, both results were similar in a 2-year follow-up. Studies showed similar results with autologous bone grafts.

HA is made from corals, which are inert materials and have similar properties to ceramic; in a previous study, HA was demonstrated to be inferior to autologous iliac crest grafts structurally, whereas their fusion rates were nearly equal. Calcium sulfate when mixed with bone marrow aspirate showed good fusion results but strong evidence to support the use of calcium sulfate is yet to be published. Si-CaP is a newer ceramic subclass and generally raises the negative charge on the ceramic scaffold, thus allowing for more osteoblasts to be attracted to the fusion surface, and has high resorption rate than HA. HA is made from corals, which are inert materials and have similar properties to ceramic; in a previous study, HA was demonstrated to be inferior to autologous iliac crest grafts structurally, whereas their fusion rates were nearly equal.

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Bone morphogenic proteins (BMPs) are osteoinductive products, related to transforming growth factor beta (TGF-B). There are approximately 20 types of BMPs: rhBMP-2 and rhBMP-7 are widely studied and used. BMPs are soluble proteins that spread and diffuse into tissues. Basking et al. reported improvement in neck disability index and pain scores in the BMPs group compared to the control group. Butterman et al. reported similar results with iliac crest grafts in ACDF. Despite the high advancement in the field of bone substitutes, studies still lack strong evidence for the selection of the autologous bone alternative. Data is still limited for evidence of superiority over the autologous grafts. Ceramics are promising products, especially when combined with bone marrow aspirate. Recently, stem cell-based products are being thoroughly and widely studied.

The role of bone substitutes in cervical arthrodesis in comparison to empty cervical cages has been under study and the available results are controversial. Feng et al. performed a prospective study to compare the results of fusion between PEEK cage with bone substitute and empty PEEK cages. Surprisingly, there was no statistically significant difference in fusion rates between the control and the study groups at 24-month follow-up. This supports the use of empty cages in cervical arthrodesis. Schils et al. compared empty carbon fiber cages with tricortical iliac graft and reported that both gave the same clinical and radiological outcomes and avoided donor site morbidity. An interesting study compared the efficacy of empty PEEK with empty Ti-coated PEEK cages in ACDF and reported that partial PEEK coating does not improve fusion rate and recommend a randomized prospective study with fully coated PEKK cages.

CAGE IN SPONDYLODISCITIS

Although cervical spondylodiscitis has a rapidly progressive course and carries mortality rates of up to 21%, there is no agreement about the optimal timing and ideal surgical technique. Given the improved imaging modalities, some believe that early diagnosis can now be established and recommend conservative management for up to 6 weeks. On the contrary, others consider
early surgical intervention followed by systemic antibiotics to be the standard of care to avoid neurological deterioration during antibiotic treatment.\textsuperscript{158,174,185,32} Several reports found that cervical infections were associated with faster neurological deterioration than lumbar and thoracic infections, justifying the early surgical intervention for tissue sampling, debridement, decompression, and stabilization.\textsuperscript{158,174,185,32}

Several earlier concerns about the use of synthetic implants in infection have been raised due to the lack of antibiotic penetration, glycocalyx formation, bacterial adherence, and immune reaction.\textsuperscript{134,19} This concept justified the practice of some authors who reported treatment of their patients with cervical spondylodiscitis and epidural empyema via anterior single-level discectomy without the interbody implant or bone graft, achieving spontaneous fusion in all patients.\textsuperscript{129} Although being a cost-effective strategy, this results in a reduction in disc space height with subsequent foraminal stenosis. On the other hand, several recent reports challenged this concept and demonstrated a lack of association between using PEEK and Ti implants and chronic infections.\textsuperscript{106,186,32}

Generally, management of spinal infections using nonallogenic implants in thoracolumbar infections preceded this practice in cervical infections with the use of Ti implants before PEEK cages.\textsuperscript{59,106,154} However, during the last decade, several reports demonstrated successful management of cervical discitis using PEEK cages in single-stage debridement and anterior fusion with eventual bony fusion, inflammatory regression, minimal change in alignment, and slight subsidence.\textsuperscript{127,186}

The biomechanical properties of PEEK are closer to the vertebral body owing to closer elastic modulus to the natural bone, making it a good choice for reconstruction and fusion particularly in the setting of reduced bone quality like in the case of spondylitis.\textsuperscript{87} The concerns with the use of PEEK cages in infection are related to the theoretical high potential for biofilm formation compared to Ti. However, the current evidence suggests that biofilm formation on the surface of PEEK is similar to or less than other materials like zirconia and Ti.\textsuperscript{82} In clinical setting, comparing PEEK to Ti cages in management of pyogenic spondylodiscitis in various spinal regions revealed that the material of cage does not influence radiological outcome or the risk of reinfection.\textsuperscript{160}

**POSTOPERATIVE EXTERNAL ORTHOSIS**

The use of a rigid cervical collar has long been considered a standard of care following cervical surgeries. In a questionnaire study exploring the postoperative bracing patterns among spine surgeons, most of the respondents reported routine bracing of their patients for a period of up to 3–8 weeks, with a more bracing tendency among fellowship-trained surgeons and in multilevel constructs.\textsuperscript{22} However, despite the reported increased chance of focal kyphosis and disc space height loss in nonbraced patients after anterior cervical fusions, the same results failed to demonstrate any significant difference between the collar and no-collar practice in terms of fusion rates and clinical outcomes.\textsuperscript{96} Moreover, the short-term use of cervical collars that was supposed to help patients get through the initial postoperative disability and pain\textsuperscript{1} was contradicted by other studies that reported worse NDI scores of braced patients at 2 and 6 weeks.\textsuperscript{35,137}

On the other hand, the routine use of cervical collars has documented drawbacks and complications. First, the cervical collar is an additional cost that may be high enough in certain types adding much to the cost of the procedure.\textsuperscript{137} In the absence of sufficient scientific evidence for the benefit of postoperative bracing, this additional cost may not be economically and ethically justified. Second, swallowing and breathing discomfort, skin- and wound-related complications, coughing, restricted range of motion, residual pain, and muscular atrophy are complications associated with collar use.\textsuperscript{187,111} Third, the overlooked limiting effect of
The cervical collar on daily routine activities and socioeconomic impacts raises special concern. Driving while wearing a cervical collar was found to be associated with potential hazards, resulting from an increase in the number of blind spots in those wearing cervical collars, in addition to a significantly restricted cervical axial rotation causing suboptimal performance at intersection traffic. Fourth, the theoretical biomechanical benefit of cervical bracing was debated by the neck pivot-shift phenomenon raised by Lador and colleagues. In this cadaveric study, computed tomography (CT) scans were used to measure intervertebral movements in cervical spines with induced unstable fractures. The authors surprisingly documented an increase in the craniocaudal and axial intervertebral motions in the one-piece rigid cervical collar compared to nonbraced cervical spines. This was explained by the creation of pivot points at the sites of contact between the collar and the mandible or the shoulders, which caused a shift of the center of rotation lateral to the spine worsening the intervertebral motion and putting stress on the cervical spine. These results were supported by the biomechanical analysis of 9 prehospital extrication techniques including conventional equipment like short extrication jackets and neck collars to determine the best technique causing minimal deviation of the spine from the neutral inline position. The results revealed that conventional equipment-assisted extrication techniques were associated with four times more cervical spine motion than controlled self-extrication. Finally, the close contact between the collar edge and neck veins may raise some issues related to the possible reduction of venous return and theoretically an increase in intracranial pressure. A study by Stone et al. reported a 37% increase in the jugular vein cross-sectional area in healthy volunteers after the application of cervical collars. This explains a previous report that found an increase in CSF pressure by about 25 mmH2O in a group of patients undergoing lumbar puncture with a cervical collar in place compared to preapplication of the collar.

Given the documented drawbacks of cervical collars and concomitant inconsistency in its clinical benefits, various review articles and meta-analyses were conducted to investigate the clinical benefit of bracing patients after single- or double-level ACDF. None of these studies recommended the routine bracing of patients postoperatively as no scientific evidence supporting this practice was found. After highlighting the lack of evidence supporting the use of collar following cervical fusions, Demetriades and Tessitore concluded their “letter to the editor” by raising the following questions: “What more do we need as a scientific community before we universally incorporate this into our practice? Is another RCT necessary? Is this question still worthy of the rising costs of running a trial nowadays?”

INNOVATIONS AND FUTURE RESEARCH

The surgical practice has enormously changed during the last few decades. The innovation in technology and the combination between bioengineering and the medical field has brought to us the use of various technological procedures like 3D printing (3DP) in the field of spine surgery. The aim is to obtain and maintain excellence in spine surgeries along with improving the safety of the patients. Since its first introduction to the world by Hull in 1980, 3DP has evolved to reach many fields of our daily practice. Medicine is one of these fields. 3DP is a processing procedure where materials such as metals, biological materials, and ceramics are deposited in layers to form a 3D structure based on a predefined architecture. 3DP has different terminologies such as rapid prototyping, solid free-form technology, or additive manufacturing. Due to the evolving field of radiology and the state-of-the-art CT and MRI machines, acquiring precise structural layout for 3DP is accessible. The main idea is to obtain
multiple reconstructed images in different planes and then fuse them together to acquire a 3D model on a computer that will transfer it to a 3D machine and applies it. In 1999, D’Urso et al. were the first to publish data about the use of 3DP in the spine field. 3DP also invaded the implant manufacturing area. Specific implants designed to be installed in specific spine parts perfectly designed for each patient allow for a better fit and better bone-implant integration. Several authors reported positive outcomes with 3DP implants. Producing individualized implants for patients is a state-of-the-art process, where patients receive a specific implant designed for them, thus improving the alignment and biomechanics process with no excessive stress of strain on the implant or the adjacent spinal segments. Ti alloy powder is melted by laser processing, and the printed Ti porous cage is manufactured to enable osseous incorporation. Animal studies have proved rapid bone incorporation using porous 3DP Ti cages, which showed high biocompatibility and osseointegration and have potential clinical value as implants. Arts et al. found that patients managed with 3DP porous Ti cages had improved NDI, and the results were similar to PEEK cages and autografts. Fusion rates were superior at 6 months for the 3DP porous Ti cages. Literature has proved that bony fusion is an ongoing process and nearly 70% to 90% of surgeries achieve total fusion; however, 30% of spinal fusion surgeries may result in pseudoarthrosis. 3DP porous Ti cages achieved 89% fusion at 6 months. Rapid fusion may change the way we react to traditional PEEK cages. Finally, the suitable bearing-load surface interaction between 3DP implants and adjacent segments of the spine is hypothesized to reduce the rate of pseudoarthrosis, subsidence, and ASD. Manufacturing of individualized cervical fusion cages using specific patients data was proposed by Spetzger et al. and they reported that the improved load-bearing surface will lower the rate of implant dislocation and subsidence. Since ACDF procedures are widely accepted, research and innovations have concentrated on improving and simplifying the fusion part of this procedure, in turn improving its outcome and decreasing its drawbacks. There is a large array of technological and biomechanical advances of many of these devices offering a great number of options in the armamentarium of spinal surgeons (Figure 3).

Increasing the surface roughness of Ti alloy through plasma beam and electron spray technique proved to promote early osteointegration and thus fusion. Improved bioactivity of Ti in combination with elastic modulus and radiolucency of PEEK is represented in composite space such as Combo® cage (A-SPINE Asia, Taiwan), combined PEEK body with Ti-endplate. Data in the literature documenting the efficacy of the spacers is sparse. Research has explored the development of an absorbable design using polylactic acid (PLLA) polyglycolic acid (PGLA) copolymers and poly(L-lactidecoD, L-lactide). Theoretically, these exhibit immediate necessary rigidity and gradual degradation promoting bone formation and arthrodesis and at the same time improving radiological assessment; however, they are not as effective as a standalone device.

An in vitro biomechanical testing study showed that absorbable cages demonstrated equal or superior properties and may be a viable alternative to metallic cages. They also recommended in vivo studies. Another in vivo research using a bioabsorbable polylactide implant in an ovine model to validate tissue reaction reported that fusion was achieved in an animal model without collapse, extrusion, or adverse tissue reaction. Several cervical cages offered by the 3DP technology mimic the anatomy of the disc, whereas the size and design of the cages are adapted to the average shape and sizes of patients’ disc. The philosophy is adapting the implant anatomy to the patients’ individual anatomy and not adapt patients’ anatomy to the available implant. Additive manufacturing (AM) is a powerful new industrial tool and, according to ASTM F42 Committee, is defined as “the process that allows the realization of artifacts from a 3D virtual model, realized by
overlapping of layers fused between them (layer by layer).” With this technology, we can create cages with controlled porosity with a solid part that is characterized by high purity and rough surface enhancing osteointegration.153 A biomechanical experimental study demonstrated 3 different cages (standard PEEK cage and two innovative Ti alloys made by electron beam melting (EBM) technology by MT Ortho) subjected to static compression test with encouraging results. It showed that mechanical and functional failure of the innovative cages occurred due to the load value greater than the physiological one of the cervical spine.153

A different array of standalone cages was evaluated as follows:45 a composite Ti/PEEK integral fixation cages which offered efficacy in ACDF procedures,145 another standalone system; Zero-P cervical cage with a zero-profile plate and Ti cages with promising clinical results;159 the ROI-C cage (LDR Medical, France), one of the devices developed to increase immediate spinal stability and avoid anterior plating and iliac crest bone grafting;74 zero-profile cages made of PEEK with VerteBRIDGE™ double anchoring system and self-locking plate (Figures 4 and 5).

Novel osteoinductive ceramic implants have anti-infective properties, higher fracture resistance, and semiradiolucent with promising results in spine fusion surgeries. However, there were no enough published data to support their use.28,10,72,188 A transition metal, when pretreated with heat and alkali, had shown better osseointegraton.100 Sinclair et al. had great bone volumes in the animal model study over the standard PEEK implants.165 Tantalum implants showed osseointegration results similar to carbon fiber reinforced PEEK.207 Nitinol alloy, a half nickel and half Ti alloy, has a superelastic property and is mainly used in motion-preserving implants.177 Theoretical advancements for bioabsorbable cages, novel state-of-the-art implants, have been proposed to reduce the effects related to stress shielding and implant radiological drawbacks.144

Figure 3. 3D-printed cages. (A) Titanium-C cervical cage, Strykers. (B) A MATRIXX 3D-printed cervical interbody cage (photo via Nexxt Spine). (C) Tiger-shark-C, ChoiceSpine™. (D) EIT Cellular Titanium cervical cage. (E) TirboLOX, Titanium Reinforced Bone cages, Captiva Spine. (F) Cervical interbody fusion cage, CeSPACE® 3D, Aesculap®, Germany.

Figure 4. Self-locking cages. (A) The Zero-P implant, Synthes GmbH Switzerland (Oberdorf, Switzerland). (B) The NEXXT MATRIXX® Standalone Cervical System. (C) CoreLink F3D-C2 standalone Cervical Spine System. (D) ROI-C Cervical Cage. (E) Scorpn II cervical cages, zero-profile Shanghai Reach Medical Instrument CO., Ltd. (F) Redmond (A-Spine, Asia, Taiwan, China).

Figure 5. Self-locking cages. (A) HiJAK AC Expandable Cervical Interbody Fusion Device (IBFD), Atlas Spine, Inc. (B) HiJAK SA Expandable Cervical Standalone
Interbody system with low-profile plate, Atlas Spine, Inc. (C) 3D Printed Non-Screw Based Cervical Standalone Cage, Genesys Spine. (D) Aero-C, Anterior Cervical Interbody and Fixation System, Aerofoil™, Stryker.

CONCLUSION

ACDF is a well-established surgical technique in the management of cervical spondylotic radiculopathy and/or myelopathy. Large numbers of cervical cages with different shapes, designs, and compositions are available in the market with generally satisfactory clinical and radiological outcomes. Spinal surgeons should be aware of available cervical cages and chose the most suitable to their patient’s medical and socioeconomic status. 3DP, AM, and EMB have the potentials of improving load-bearing surface, lowering the rates of cage dislocation and subsidence, and enhancing osteointegration. Composite cages, self-locking cages, and absorbable cages are fairly introduced cages and still under evaluation. Future trends in cage manufacturing will be individualized forms and shapes adapted to the patient’s anatomical features using modern computer-based simulation. Multicenter long-term prospective randomized controlled trials are warranted for obtaining first-class evidence-based medical data on ACDF.

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الملخص العربي

أقفاص الفقرات العنقية: الماضي والحاضر والابتكارات والاتجاهات المستقبلية مع مراجعة الأدبيات

البيانات الخلفية: أصبحت جراحة استئصال الغضاريف وحماء الفقرات العنقية الأدمية هو العلاج القياسي لحالات امراض العمود العنقية التنكسي، منذ ادخال جراحة استئصال الغضاريف وحماء الفقرات العنقية الادمية في الخمسينيات أصبحت منهجية كبيرة واجراء القياسية. تم إجراء ترتيب عموم الراحفي ذاتي المنشأ للحماء الفقرات ولكن هذه الطريقة لها أضرار وعيوب كثيرة مما أدى إلى داخل عالم حديث جديد من البدائل المحدثة مع حرشات مختلفة. يوجد الكثير من التطورات والتحسينات لهذه الاقفاص ولكن هناك اثار للذين من الفضائح الجدلية.

الفقد: مراجعة البيانات والمعلومات المتوفرة عن الاقفاص العنقية والحالة الحدثية لجراحة استئصال الغضاريف وحماء الفقرات العنقية الادمية باستخدام الاقفاص القائمة ذاتها.

تقييم الدراسة: مراجعة الأدب السردي

المريض والطريق: قمنا بمراجعة الأدب الإنجليزي للحصول على أحدث البيانات المتاحة لأقفاص الفقرات العنقية وأبلغنا عن الحالة الحالية للنتائج جراحة استئصال الغضاريف وحماء الفقرات العنقية الادمية باستخدام أقفاص ذات صلة واستخدنا الأبحاث الأكثر صلة وفقًا لهدف دراستنا. ركزنا على العناوين الخاصة التي اعتقداولها الأكثر صلة بالدراسة اليومية لجراحة العمود الفقري

النتائج: يتوفر عدد كبير من أقفاص العنقية ذات الأشكال والتصميمات المختلفة لجراحة استئصال الغضاريف وحماء الفقرات العنقية الادمية يتم تقديمها يومياً من مختلف المصادر الطبية، مثلاً بين من الأقلاع، الأدقاع، ومصادر الإنتاج الصناعي. النتائج السريرية والإشعاعية مرضية بشكل عام، وبعض النظير عن نوع وطبيعة الأقفاص المستخدمة، يتم تقييم أقفاص الفقرات العنقية المركبة أو المطلية بالتيتانيوم بالإضافة إلى الطباعة ثلاثية الأبعاد وأقفاص التيتانيوم المماسية. أظهرت الأقفاص القائمة بذاتها ذاتية الإنسان توفر جملة بنتائج واعدة.

الخلاصة: جراحة استئصال الغضاريف وحماء الفقرات العنقية الأدمية هي تقنية جراحية راسخة في إدارة اعتلال الجدران العقلية القائمة على عمود الفقري أو اعتلال الدماغ الشوكي. تتوفر أعداد كبيرة من أقفاص الفقرات العنقية ذات الأشكال والتصميم والتركيبات المختلفة في السوق مع نتائج سريرية وإشعاعية مرضية بشكل عام، يجب أن يكون جراح العمود الفقري على دراية بأقفاص الفقرات العنقية المتاحة، واختيار الأنساب حسب حالة المريض الطبية والاجتماعية والاقتصادية، وتمتى التكنولوجيا الصناعية الجديدة لإمكانية تسهيل سطح التحميل، وخلع ومسحيف العظام الحالي، وتحسينية إحداثي الاصطناعية، أقفاص مركبة، أقفاص ذاتية الإغلاق، أقفاص قابلة، استخدام كلها أقفاص تم إدخالها إلى حد ما ولا تزال قيد التقييم. تعد التجارب العشوائية المتعددة من الأجل المائي المتعدد المراكز الامرامية للبيانات الطبية القائمة على الأدلة من الدرجة الأولى في جراحة استئصال الغضاريف وحماء الفقرات العنقية الأدمية.