Patterns of Spinal Fusion after Anterior Cervical Discectomy and Fusion with Polyether Ether Ketone Cage Filled Hydroxyapatite

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ABSTRACT

Background Data: ACDF is one of the most commonly performed operations for degenerative spinal diseases. Traditionally, graft was harvested from iliac crest which was associated with donor site morbidity. This has led to the introduction of many synthetic implants such as PEEK cages to overcome this problem.

Purpose: To evaluate the patterns of spinal fusion after ACDF with PEEK cage filled with HA.

Study Design: Retrospective clinical study.

Patients and Methods: Twenty-five patients that underwent ACDF with PEEK cage filled HA were enrolled in this study through the period from January to December 2017. All patients were submitted to pre- and postoperative clinical and radiological follow-up. Postoperative full neurological and images evaluations were done by independent observer on outpatients at 1, 2, 3, 6, and 12 months. Postoperative neck pain was evaluated using VAS. Radiological evaluation was done using cervical X-ray and images were evaluated using software Surgimap™.

Results: The mean age of our patients was 44.4±6.57 with 9 patients being males and 16 patients females. Total numbers of levels reported were 33 in 25 patients, with 17 patients (68%) undergoing single-level ACDF and 8 patients (32%) double-level ACDF. Five patients (20%) suffered from myeloradiculopathy and twenty patients (80%) had radiculopathy. The mean follow-up was 11.04±1.2. The mean preoperative neck pain VAS was 7.8±1.9, while postoperative VAS was 2.9±1.8. Continuous bridging bony trabeculae were reported in 29 levels (87.9 %) (N=21), while they were absent in 4 levels (12.1%) (N=4). Cage migration was reported in two patients (6%) and both showed >2 mm mobility in dynamic cervical X-ray indicating instability and nonunion.

Conclusion: ACDF with PEEK cage filled with HA is a safe and effective method to achieve interbody fusion in patients with cervical disc disease. Although fusion occurred within usual time, remodeling took longer time than that previously reported with iliac graft (2018ESJ171).

Keywords: Cervical disc disease; anterior cervical discectomy; spinal fusion; PEEK; hydroxyapatite.
INTRODUCTION

Prior to 1950, the posterior approach was the main technique to operate on the cervical spine.\textsuperscript{10} The anterior cervical approach was introduced in the 1950s with anterior cervical discectomy (ACD) which is not advised because of the disc space collapse with consequent nerve root compression.\textsuperscript{12} In 1958, Smith and Robinson used this technique to perform ACDF using iliac crest graft.\textsuperscript{28} The success of this procedure relies on thorough decompression and the development of solid osseous fusion.\textsuperscript{11} This procedure was associated with complications such as iliac pain, ilio-inguinal nerve injury, hematoma or seroma formation, wound infection, and fracture iliac bone.\textsuperscript{27}

Bone grafts and bone graft substitutes can be osteoconductive, osteoinductive, or osteogenic or have some combination of these properties. Autologous bone grafts work by all three mechanisms.\textsuperscript{3,2}

To decrease donor site morbidity, many synthetic materials have been used such as titanium cages, carbon cages, and PEEK cages.\textsuperscript{29} Cervical cages give instant stability and enlarge neural foraminal space. The cages are filled with a small amount of cancellous bone harvested from iliac crest by a small incision\textsuperscript{16} to decrease complications.\textsuperscript{29}

PEEK cages were introduced in 1990s and have been used on a wide scale in cervical spine surgeries due to its radiolucency which permits easy evaluation of fusion, significant power, their ability to resist weariness, and equivalent stiffness to bone which decreases stress shielding.\textsuperscript{30} PEEK itself is inactive and has no ability to connect to bone. Thus, PEEK was added to other substances such as HA which is a perfect candidate as its composition is similar to the inorganic constituent in natural bone. Its combination with PEEK encourages new bone formation from bony walls which achieves implant fusion in little time.\textsuperscript{4,23}

A lot of nonsurgical factors affect fusion such as steroid intake, osteoporosis, cigarette smoking, clinical indications, use of cervical orthosis, and patient’s age and general condition. Surgical factors that could affect fusion include surgical modality used, graft properties, extrinsic covering with osteoconductive materials, and endplate preparation.\textsuperscript{22}

Plain X-rays are done postoperatively to assess fusion and implant condition. Advancement of fusion is decided by opacification and connecting trabecular bone at the edges of the graft which usually happens after 6 to 12 weeks.\textsuperscript{6} Pseudoarthrosis is identified when any radiolucent area is present in the intervertebral space, in addition to growing deformity and radiolucency around grafts more than twelve months postoperatively.\textsuperscript{17} Cannada et al.\textsuperscript{6} suggested a distance of >2 mm between any two spinous processes on cervical dynamic X-rays as indicator of non-union with 89% specificity and 91% sensitivity.

This study is one of the ongoing clinical efforts to validate and evaluate the patterns of spinal fusion after ACDF using PEEK cage augmented with HA.

PATIENTS AND METHODS

This study has been conducted on 25 patients who had been presented with cervical disc disease (CDD) and documented both clinically and radiologically. All failed adequate conservative therapy and operated with ACDF with PEEK cage filled with HA through the period from January to December 2017 in Neurosurgery Department, Suez Canal University Teaching Hospital. Inclusion criteria included patients with single- or double-level symptomatic CDD, confirmed radiologically, failing adequate conservative therapy, and ageing from 18 to 70 years in both genders. Exclusion criteria included patients not candidate for surgery, having other pathology such as osteoporosis, infection, trauma, and tumors, suffering previous cervical spine surgeries, having >2 level surgeries, patients with redo, or those having plate-augmented ACDF.

Preoperative evaluation included detailed history and clinical examination, cervical X-ray AP, lateral and dynamic views, and MRI T1 and T2 weighted images. Postoperative evaluation
included clinical and radiological follow-up at 1, 3, 6, and 12 months. Clinical and full neurological evaluations were done by independent observer. Postoperative neck pain was evaluated using VAS. Radiological evaluation was done using cervical X-ray AP and lateral views and dynamic study. Images were evaluated for fusion, disc height, cage migration, and segment mobility by measuring the distance between interspinous processes of the fused segment on dynamic study using software Surgimap™.

Fusion was evaluated according to absence of a radiolucent gap between the cage and endplates and presence of continuous bridging bony trabeculae at the graft-endplate interface and movement of the interspinous process on cervical dynamic X-rays less than 2mm. Disc height was measured as the distance between midpoint of upper and lower end plate of the disc on pre- and postoperative X-ray.21

Surgical Technique:

During the surgical procedure according to our hospital operative filling system, patients were positioned supine on the operating table; a transverse skin incision was made at the right side of the neck at the appropriate level guided by anatomical landmarks and fluoroscopy. The skin incision extended medially from the anterior border of sternocleidomastoid muscle; the platysma was exposed and then divided. The anterior triangle was then dissected, developing a plane between carotid sheath laterally and the larynx and esophagus medially. The carotid pulse should be confidently palpated inside the wound. The midline structures were retracted to avoid retraction on the recurrent laryngeal nerve. An avascular plane is dissected down to the longus colli muscles, which were then undercut bilaterally; self-retaining retractors were inserted under the longus colli fibers to provide a clear surgical view. Fluoroscopy was always used to confirm the operating level and the position of the cage afterwards. Any anterior osteophytes may be removed using electrical drill or Kerrison punch; Caspar pins were used to distract adjacent levels.32

Discectomy was performed using a scalpel, rongeurs, and curettes under the operating microscope. Posterior osteophytes were removed. The posterior longitudinal ligament was carefully opened and the ligament was resected to enable good visualization of the dura and the nerve root origins. A PEEK cage (Velofix™: U & I corporation, Uijeongbu-si, Gyeonggi-do, South Korea) filled with HA (G-Bone Cement: GSurgiwear Ltd., Shahjahanpur, India) was used as graft material for interbody fusion then closure was done in layers.18

RESULTS

A total of 25 patients, 9 males (36 %) and 16 females (64%), were enrolled in this study. The mean age of the studied patients was 44.4±6.57 (range 31–57) years. Seventeen patients (68%) underwent single-level ACDF representing 17 levels and 8 patients (32%) double-level ACDF representing 16 levels, with a total number of 33 disc levels per 25 patients. C5/6 ACDF was the most frequently involved level with 18 levels/cages representing 54.5% of the total number, followed by C6/7 level with 8 levels/cages (24.2%), then C4/5 level with 5 levels/cages (15%), and lastly C3/4 level with 2 levels/cages (6.3%) (see Table 1).

Five patients were complaining of myeloradiculopathy (20%) and twenty patients had radiculopathy (80%). Twenty-one patients had no motor deficit (84%), while 4 patients suffered from motor weakness (16%), and 3 patients had sphincter affection (12%).

Reported comorbidities included the following: 2 patients (8%) suffered from HTN and 3 patients (12%) suffered from DM; 2 patients (8%) were smokers, one of them was also diabetic.

The mean preoperative neck pain VAS was 7.8±1.9 (range 4–10), while the mean postoperative neck pain at the last follow-up VAS was 2.88±1.8 (range 1-7). In patients with good fusion, the mean preoperative VAS was 7.8±1.74 (range 4–10) and the mean final postoperative VAS was 2.5±0.9 (range 1–5). While, in patients with nonunion, the mean preoperative VAS was 8±1.4 (range 7–10) and the mean final postoperative VAS was 4.75±1.5 (range 4–7).
The total number of operated disc levels was 33 levels per 25 patients; of these, 29 levels (87.9%) showed sound bony fusion according to study criteria, while 4 operated disc levels (12.1%) showed nonunion. These nonunion 4 disc levels were single-level patients. Sound bony fusion was reported in 16 out of 18 C5/6 levels (88.9%), 7 out of 8 C6/7 levels, one out of 2 C3/4 levels, and all of the 5 C4/5 disc levels (100%). Although sound bony fusion was completed in patients with sound fusion in 8–12 weeks postoperatively, bone remodeling and osteophytes resorption took ≤12 months postoperatively in majority of patients.

Cage migration was reported in 2 patients (6%) and both of them were females with single-level ACDF. Their images showed minimal bony trabeculae and showed >2mm mobility on dynamic X-ray. We suggested surgery revision which they refused, although they have some neck pain.

The mean preoperative interbody height was 5.2±0.71 mm, while the mean postoperative interbody height was 7.7±0.48 mm. Inserted PEEK cage height ranged between 5 and 7 mm according to disc level and preoperative disc height. One patient (4%) complained of hoarseness of voice postoperatively that improved later over the course of 2 months with no other patient having related perioperative complications and no patients underwent revision surgeries during the follow-up period.

Correlation between presence of fusion and demographic and clinical characteristics showed that there was no statistical significance between patients with fusion and age (P=0.86), gender (P=0.89), presence of comorbidities (P=0.55), clinical picture (P=0.9), motor power grade (P=0.92), sphincter affection (P=0.9) or level of prolapse (P=0.27), and preoperative mean VAS (P=0.2452). However, there was statistical significance between patients with fusion and postoperative VAS (P=0.0141).

Table 1: Clinical characteristics of the study population (N=25).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operated levels (N=33)</td>
<td></td>
</tr>
<tr>
<td>Single level</td>
<td>17 patients (68%)</td>
</tr>
<tr>
<td>Double level</td>
<td>8 patients (32%)</td>
</tr>
<tr>
<td>C5-6</td>
<td>18 cages (54.5%)</td>
</tr>
<tr>
<td>C6-7</td>
<td>8 cages (24.2%)</td>
</tr>
<tr>
<td>C 4-5</td>
<td>5 cages (15%)</td>
</tr>
<tr>
<td>C 3-4</td>
<td>2 cages (6.3%)</td>
</tr>
<tr>
<td>Clinical picture</td>
<td></td>
</tr>
<tr>
<td>Myeloradiculopathy</td>
<td>5 patients (20%)</td>
</tr>
<tr>
<td>Radiculopathy</td>
<td>20 patients (80%)</td>
</tr>
<tr>
<td>Motor weakness</td>
<td>4 patients (16%)</td>
</tr>
<tr>
<td>Affected sphincter</td>
<td>3 patients (12%)</td>
</tr>
</tbody>
</table>

Table 2: Correlation between presence of fusion and VAS.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Fusion</th>
<th>Test value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fused (N=21)</td>
<td>Nonfused (N=4)</td>
<td></td>
</tr>
<tr>
<td>Preoperative mean VAS</td>
<td>7.8</td>
<td>8</td>
<td>1.44</td>
</tr>
<tr>
<td>Postoperative mean VAS</td>
<td>2.5</td>
<td>4.75</td>
<td>5.17</td>
</tr>
</tbody>
</table>

*p-values are based on paired t-test. *Statistical significance at P<0.05.
This study reported 25 patients with cervical disc disease treated with ACDF using hydroxyapatite to fill the fusion cages to evaluate and validate the fusion pattern. HA is a fairly new material used as cage filler in ACDF with fusion pattern, to some extent differing from commonly used iliac bone. The mean age was 44.48 with 42.9 years for males and 45.4 years for females. This was close to the findings reported by Rochester study\cite{26} which included 561 patients where the mean age of males was 47.6 and females was 48.2 years. We included 9 males (36 %) and 16 females (64%) with a male to female ratio 1:1.8 which was different from the Rochester study\cite{26} ratio (1.7:1.1). It was also different from another study by Kelsey et al.\cite{15} which was 1:1.

According to the level, 54.5% of the cages were at C5/6, 24.2% of cages at C6/7, and 15% of cages at C4/5, while 6.3% of cages were at C3/4 level. These results correspond to the majority of literature as in the work of Faldini et al.\cite{13} who...
reported that 48% of his patients were at C5/6 level, 32% of patients at C6/7 level, and 20% of patients at C4/5 levels. C5-6 was also the most frequently involved level (35.7%) in a study by Chen et al. The following levels had lower rates: at C6/7 level, 29.1% of patients; C4/5 level, 23% of patients; C3/4 level, 11% of patients; C2-3 level, 1.2% of patients (i.e., one patient). In the study by Niu et al. similar results were found as C5/6 level had a rate of 45.7% among study population, followed by C6/7 level with a rate of 23.3%, then C4/5 level with a rate of 20%, followed by C3/4 level with 11% rate among study group. These results also correspond to another study by Park et al. who reported 51% for C5/6 level, followed by a 28% for C6/7, then 15% for C4/5 level, and 6% for C3/4 level.

Our study included 17 patients who underwent single-level ACDF (68%) and 8 patients who underwent double-level ACDF (32%). These numbers correspond to the study by Niu et al. who had 35 patients who underwent single-level ACDF representing 66% of total study population and 18 patients who underwent double-level ACDF (34%). Our findings also correspond to a study by Park et al. who had a study population of 31 patients. Twenty-one of the study’s patients underwent single-level ACDF (68%), while 9 patients underwent double-level ACDF (29%) with one patient undergoing three-level ACDF (3%).

We included twenty patients with radiculopathy (80%) and 5 patients with myeloradiculopathy (20%). In a study by Yi et al. they included a total number of 77 patients, where there were 49 patients with radiculopathy (64%), 17 patients with myelopathy (22%), and 11 patients of myeloradiculopathy (14%). In another study by Chang et al. a total number of 24 patients were studied which included 10 patients with radiculopathy (42%), 9 patients of myelopathy (37%), and 5 patients of radiculomyelopathy (21%). Radiculopathy was also the most frequently presented manifestation in another study by Feng et al. (45%), followed by myeloradiculopathy (28%) and finally myelopathy (27%). On the contrary, Park et al. found equal ratio between radiculopathy and myelopathy (45%), followed by myeloradiculopathy (10%).

We had 2 patients who were smokers in our sample (8%) which was a significantly lower rate than other studies like the study by Park et al. where the rate of smokers to nonsmokers was 23% and 77%, respectively. In another study by Buttermann GR, 3% of the patients were smokers, while 57% of the patients were nonsmokers. This difference was attributed mainly to the significantly higher number of female patients in our study.

Mashhadinezhad et al. compared PEEK cage filled with autologous bone graft with PEEK cage filled with HA; they reported bridging bony trabeculae across the fused segment in 54% and 47% of their patients, respectively. This was much lower than our study (87.9%) and might reflect their interpretation of bridging bone trabeculae. In their group of PEEK cage with HA, clinical improvement was detected in 95% of patients, while in our study we had improvement in 100% of patients. In a study by Chang et al. to compare PEEK cage with bone graft to HA, clinical improvement was detected in 100% of patients who underwent PEEK cage with HA that is similar to our results with no record of cage extrusion or breakage. Out of the 22 of their patients who underwent PEEK cage with HA, one patient had temporary postoperative dysphagia representing 4.5% of study group which was close to the rate of procedure related complications in our study (4%). Fusion rates were more or less similar between both groups (98% to 96%, resp.). In the PEEK cage with HA group, fusion rate was 96% which was slightly higher than that in our study (87.9%).

Although sound bony fusion was completed in 87.9% of our patients with sound fusion in 8–12 weeks postoperatively, bone remodeling and osteophytes resorption took ≤12 months postoperatively in the majority of patients. This pattern reflects a delay in comparison to other studies previously reported. That why we can see that although HA avoids patients from any local graft harvesting problem, it allows this delay in remodeling. However, this has no significant effect on the clinical and radiological outcome.
parameters in this study which was comparable to any previous report.

Regarding procedure related complications, we had one patient (4%) of postoperative hoarseness of voice that improved gradually over a course of 2 months. There were no other procedure related complications reported in this study. This was lower than what was reported in the literature as in the work of Mastronardi et al.\textsuperscript{19} who studied a total of 36 patients and recorded postoperative complications in 5 patients (14%). Two patients (6%) suffered from temporary hoarseness of voice and 3 patients (8%) temporary dysphagia.

During the follow-up period in our study, no revision surgeries were performed which was close to the results of Mastronardi et al.\textsuperscript{19} who had one patient undergoing second operation (2.7%) in their study group. They had no patients with implant related complications, while in our study we had 2 levels with cage extrusion (6%) of the total levels. Four levels in 4 patients in our study were considered nonfused, representing 12.1% of total levels with a fusion rate of 87.9% through our follow-up period. Mastronardi et al.\textsuperscript{19} found 61% fusion rate after 6 months and 100% fusion rate after one year. After 6-month follow-up period, they discovered fusion in 85.7% of nonsmokers and 45.4 % of smokers. In our case, we discovered fusion after 6 months in 100% of smokers, but it was not a significant result as we only had 2 smokers (8.3%) of total study population. All patients in our study have improved clinically postoperatively (100%) that is equal to the results of Mastronardi et al.\textsuperscript{19} Concerning patient related complications, Mashhadinezhad et al.\textsuperscript{18} studied 124 patients with PEEK cage filled with HA. They had a lower patient-related complications than our study (2 patients), representing 2% of study group. They reported one patient of procedure related complications in the form of temporary hoarseness of voice and one patient of cervical hematoma that was managed conservatively. They did not report any cage extrusion, being much lower than our study (6%). Similar to our study, no revision surgeries were performed.

This study as a trial to evaluate the pattern of fusion after ACDF has some limitations including the small sample size and the short follow-up period. These drawbacks need to be addressed in future studies.

**CONCLUSION**

ACDF with PEEK cage filled with HA is a safe and effective method to achieve interbody fusion in patients with cervical disc disease. Although fusion occurred within usual time, remodeling took longer time than previously reported with that iliac graft.

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الملخص العربي

أنماط لحام الفقرات بعد إستئصال الغضروف العنقى و لحام الفقرات من الأمام بإستخدام قفص بولي إيثير كيتون و هيدروكسى أبتيت

البيانات الخلفية: جراحة إستئصال الغضروف العنقى من الأمام مع لحام الفقرات واحدة من أكثر جراحات العمود الفقري شعبًا. تقليديًا، كان يتم أخذ رقعة عظمية من الحوض مما ارتبط مع ظهور مضاعفات في المكان المانع وللتغلب على هذه المضاعفات ظهرت العديد من المواد الصناعية مثل البولي إيثير كيتون.

الغرض: تقييم لحام الفقرات بعد إستئصال الغضروف العنقى من الأمام و لحام الفقرات بإستخدام قفص بولي إيثير كيتون و الهيدروكسى أبتيت.

تصميم الدراسة: دراسة سريرية أثر رجعي.

المرضى و الطرق: اشتملت هذه الدراسة على عدد 25 مريض خضعوا لإستئصال الغضروف العنقى و لحام الفقرات من الأمام بإستخدام قفص بولي إيثير كيتون و هيدروكسى أبتيت في الفترة من يناير إلى ديسمبر 2017 و خضع جميع المرضى للمتابعة بعد الجراحة اكلينيكيا و استخدام الأشعة. و تم إجراء التقييم العصبي و الاكلينيكي بواسطة ملاحظ مستقل. تم تقسيم الام الرومية بواسطة المؤشر البصري لقياس الألم و تم إجراء التقييم الاكلينيكي باستخدام النشاط العاجي، على الفقارات العنقية باستخدام برنامج كمبيوتر. تم تقييم اللحام بناءً على غياب فجوة شفافة بين الرقعة و بين الطرف النهائي للفرقة و وجود ترابي عظمية متصلة بين الرقعة و الطرف النهائي للفرقة و المسافة بين الزائدتين الشوكيتين على الأشعة العادية المتحركة على الفقارات العنقية أقل من 2 مللي متر.

النتائج: كان عدد الكل 33 مستويًا 17 مريض خضعوا للجراحة في مستوى واحد بينما خضع 8 مرضى للجراحة في مستوىين. 5 مرضى كانوا يعانون من الاعتلال النخاعي بينما 20 مريض كان يعانون من اعتلال الجذور. كان متوسط المؤشر البصري لقياس الألم قبل الجراحة 7.8 بينما كان متوسط المؤشر البصري لقياس الألم بعد الجراحة 2.88. الترابي عظمية المتصلة كانت موجودة في 29 مستوى (87.9%) بينما كانت غائبة في 4 مستويات (12.1%). نزوح القفص كان ظاهراً في حالتين و بالنسبة للحركة في الأشعة العادية المتحركة على الفقرات العنقية فقد كانت موجودة في هاتين الحالتين.

الاستنتاج: إستئصال الغضروف العنقى مع لحام الفقرات من الأمام باستخدام قفص البولي إيثير كيتون و الهيدروكسى أبتيت يعد وسيلة مؤثرة و آمنة لتحقيق اللحام بين الفقرات.