A Comparative Study of Radiographic Results Using HEALOS Collagen-Hydroxyapatite Sponge with Bone Marrow Aspiration versus Local Bone Graft in the Same Patients Undergoing Posterolateral Lumbar Fusion

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Background: *Autologous bone harvested from the iliac crest is the gold standard for lumbar spinal fusion. However, postoperative donor site pain and morbidity have been reported. Local bone graft is insufficient and contains some soft-tissue attachment. Therefore, Healos (DePuy Spine, Raynham, MA, USA) is currently bone graft substitute that was introduced for spinal fusion with good results but radiographic fusion rate has not been clearly defined yet.*
Objective: *To assess the radiographic fusion rate of HEALOS with bone marrow aspiration versus autologous bone graft in the same patients undergoing posterolateral lumbar fusion.*
Material and Method: *A retrospective radiographic outcome study of radiographic fusion rate from plain radiographs in 55 patients indicated for posterolateral lumbar fusion in Lerdsin General Hospital between April 2005 and December 2006 was done. The patients were implanted with HEALOS collagen-hydroxyapatite sponge with bone marrow aspiration and local bone graft on each side of Posterolateral Lumbar Fusion. Twenty-seven patients were included in the present study according to the authors' inclusion criteria. Plain radiographs were collected and radiographic fusion rate was assessed for at least two years follow-up.*
Results: *The two years post operative radiographic fusion rate was 29.63% (8/27) in Healos/BMA group and 62.96% (17/27) in LBG group. At three-years follow-up, radiographic fusion rate of 36.84% (7/19) was achieved in the Healos/BMA group and 78.93% (15/19) in the LBG group.*
Conclusion: *In the present study, Healos collagen-hydroxyapatite sponge with bone marrow aspiration had lower radiographic fusion rate when compared to local bone graft in posterolateral lumbar fusion at two years post operative. The results of the Healos/BMA group was increased fusion rate with time but remained lower than LBG group at three and four years follow-up.*

Keywords: *Healos, Collagen hydroxyapatite sponge, Bone marrow aspirate, Autologous bone graft, Radiographic fusion rate, Posterolateral lumbar fusion*

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The demand for surgical treatment of certain spinal disorders and lumbar spinal fusion in particular appear to be increasing[1]. This may be related to an increased prevalence of lumbar spinal disorders that require fusion as part of their management. These include degenerative scoliosis, degenerative spondylolisthesis, spinal fractures, and certain categories of metastatic disease[2,3].

Autologous bone harvested from the iliac crest is the gold standard in grafting materials for lumbar spinal fusion[1]. However, significant rates of postoperative donor site pain and morbidity have been reported in the literature[4,5]. Local autologous bone available after a posterior decompression is an alternative to iliac crest graft. Yet, local autologous bone graft is often infiltrated with soft-tissue material[6,7].

In an effort to reduce the morbidity of these autograft harvest-related complications, bone graft substitutes with acceptable fusion rates have been the subject of intense research. The ideal bone graft substitute for spinal fusion would have the following characteristic, osteoconductivity, osteoinductivity, or osteogenicity, easily formed to custom shapes and sizes, resorbable, easily transported (does not require refrigeration), non-immunogenic, and provides

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equivalent rates of fusion when compared with iliac crest bone graft[8].

HEALOS (DePuy Spine, Raynham, MA, USA) is a type I bovine collagen scaffold with a 5- to 200-mm pore size that has been coated with hydroxyapatite. This minimally immunogenic collagen-hydroxyapatite sponge (CHS) is intended for use as an osteoconductive matrix for new bone growth. The hydroxyapatite coating provides protein binding capability similar to the composition of immature human bone. In addition, it is being osteoconductive and resorbable. This mineralized collagen meets all of the criteria for an ideal bone graft replacement with the exception that is had no inherent osteoinductive or osteogenic properties.

Bone marrow, an osteogenic component of iliac crest bone graft, can play an important role during bone healing by supplying the stem cells responsible for bone formation. Furthermore, unlike iliac crest bone graft, minimal postoperative pain or morbidity results from harvesting bone marrow[9-11]. Combining Healos with bone marrow would add an osteogenic property to the bone graft substitute[10].

"Combining Healos with BMA" was mentioned as a potential ideal bone graft. It has been reported to have high radiographic fusion rate (80-95%)[12,13] as the gold standard ICBG. The present study was designed to assess the radiographic fusion rate of Healos/BMA as compared to local autologous bone graft in posterolateral lumbar fusion (PLF).

Objective

To assess the radiographic fusion rate of Healos with bone marrow aspiration versus autologous bone graft in the same patients undergoing posterolateral lumbar fusion

Material and Method

Hospital records between April 2005 and December 2006 were retrospectively reviewed to identify all patients who underwent PLF with Healos collagen-hydroxyapatite sponge with bone marrow aspiration and local bone graft on each side by the same surgeon (Dr. Sombat Kunakornsawat). The study was approved by the institutional review board. Identified patient's data were then analyzed with our inclusion and exclusion criteria.

The criteria for inclusion were patients with spinal disorders who were indicated for posterolateral lumbar fusion (PLF) and spinal stenosis, degenerative scoliosis, and spondylolisthesis.

The criteria for exclusion were other vertebral diseases and included adolescent idiopathic scoliosis, TB spine, trauma, cannot follow-up for two years post-operative, and had previous spinal surgery.

Data collected included preoperative diagnosis, patient age, sex, underlying, operative procedures, level of fusion, and postoperative complications/re-operations rates.

Radiographic data included AP and Lateral plain film taken at every year post operatively. All films were reviewed in a blinded manner for fusion and device-related complications based on the basis of the IDE criteria (details in results section).

Operations

All patients had preoperative physical examination, checked for routine laboratory results, and received consulting as indicated. The only surgeon was "Dr. Sombat Kunakornsawat". Each patient had the same sequence, method of operations, and interventions. a) The midline approach was used based on their corresponding pathology level and disease. b) The decompression and instrumentation was performed in standard fashion dependent upon the pathology. c) After bilateral placement of the transpedicular screw fixation, the patients had Healos placed with BMA graft (Strips of Healos were soaked in bone marrow aspirate from iliac crest in ratio 1:1 by using two strips of Healos per level of fusion as Fig. 1-3) randomly to the left or right side. Then the other side had the local graft as for process of posterolateral fusion. d) Then, the operation was finished as usual.

Results

Patients data

Between April 2005 and December 2006, 55 patients underwent posterolateral lumbar fusion with HEALOS collagen-hydroxyapatite sponge with BMA on one side and local bone graft on the other side. Sixteen patients were excluded from the present study because they were not diagnosed as our inclusion diseases. Furthermore, we excluded another 12 patients that could not follow-up for at least two years. Finally, 27 patients were included in the present study. They included seven men and 20 women with an average age of 61 years (range 48-73 years). Follow-up time was at least two years for 27 patients, at least three years for 19 patients, at least four years for 14 patients, and at least five years for three patients. Primary diagnosis included spinal stenosis (20 patients), spondylolisthesis

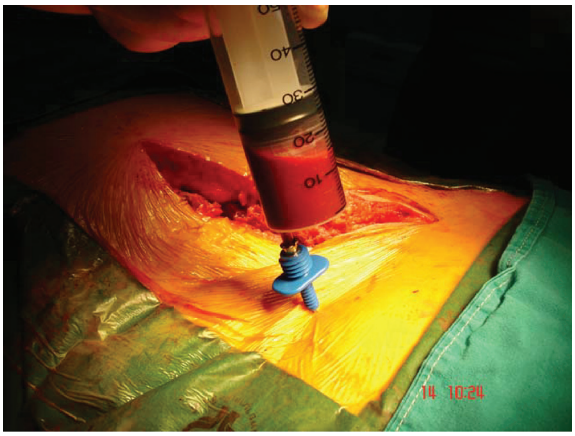

Fig. 1 Aspiration of bone marrow from iliac crest was performed in 2 cc increments to a volume of 10 cc.

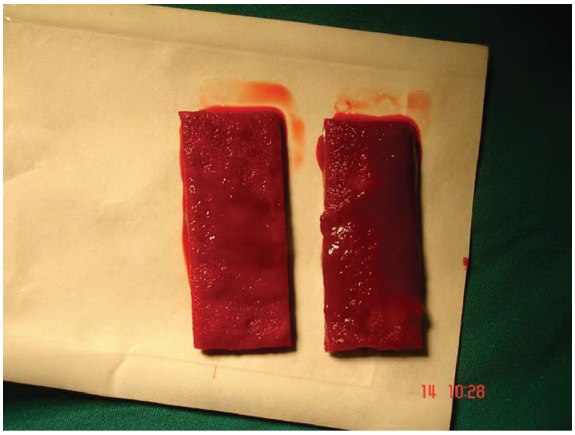

Fig. 2 Strips of Healos were soaked in bone marrow aspirate before used as a bone graft substitute. 2 strips of Healos were used per level of fusion. Each strip (5 cc) was soaked with BMA 5 cc (ratio 1:1).

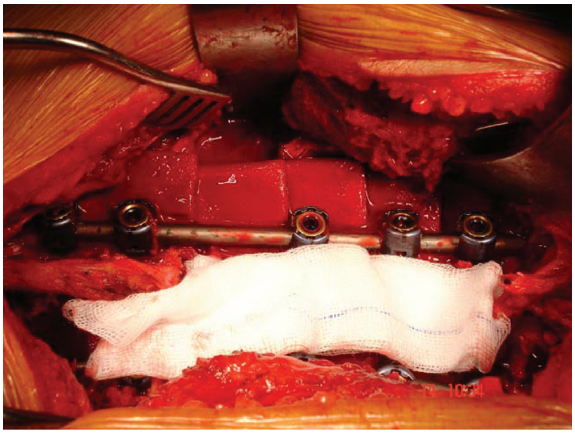

Fig. 3 Healos/BMA were placed either left or right side randomly.

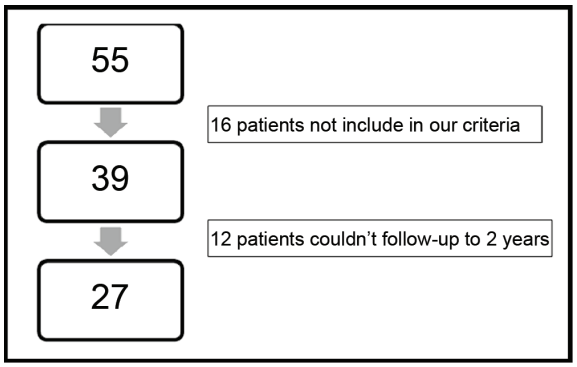

Fig. 4 Patients data.

(4 patients), and degenerative lumbar scoliosis (3 patients). The number of PLF level was one in nine patients, two in ten patients, three in four patients, four in three patients, and five in one patient (Fig. 4).

Radiographic outcomes

A successful fusion was defined, on the basis of the IDE criteria, which was A) solid trabecular bridging bone between the transverse processes, B) absence of radiolucent lines through the fusion mass, and C) no loss of internal fixation.

From the above criteria, we could classify quality of radiographic PLF into three groups, (1) fused, when all of the criteria were met, (2) partial fused when some of the criteria were met, and (3) not fused when none of the criteria were met.

At one-year follow-up, a fusion rate of 11.11% (3/27) was achieved for the Healos with bone marrow aspiration (Healos/BMA) group and 25.93% (7/27) for local bone graft (LBG) group. At two-years, the Healos/BMA group had a fusion rate of 29.63% (8/27) while LBG group had a fusion rate of 62.96% (17/27). At three-years, the number of patients who could follow-up was decreased to 19 patients. A fusion rate was 36.84% (7/19) in the Healos/BMA group and 78.93% (15/19) in the LBG group. Finally, at four-years, we got 14 patients on our research and the fusion rate was 50% (7/14) in the Healos/BMA group and 85.71% (12/14) for the LBG group. Other data was reported in Table 1.

Discussion

The present study described a case series of 27 patients with Healos/BMA on one side, and local bone graft on the contralateral side, in the presence of posterolateral lumbar fusion. Radiographic outcomes were collected and analyzed to describe fusion rate.

Table 1. Radiographic fusion rate

	Healos with BMA			Local bone graft		
	Fused	Partial	Not fused	Fused	Partial	Not fused
1 years	11.11% (3/27)	40.74% (11/27)	48.15% (13/27)	25.93% (7/27)	55.56% (15/27)	18.52% (5/27)
2 years	29.63% (8/27)	40.74% (11/27)	29.63% (8/27)	62.96% (17/27)	18.52% (5/27)	18.52% (5/27)
3 years	36.84% (7/19)	31.58% (6/19)	31.58% (6/19)	78.93% (15/19)	5.26% (1/19)	15.79% (3/19)
4 years	50.00% (7/14)	21.43% (3/14)	28.57% (4/14)	85.71% (12/14)	7.14% (1/14)	7.14% (1/14)

BMA = bone marrow aspiration

Iliac crest bone graft (ICBG) is the accepted standard for promoting.

Reported rates of lumbar fusion were ranged from 89% to 98.9%[12-16]. In Lerdsin General Hospital, we used the local autologous bone graft as a fusion material of choice in order to avoid morbidity of ICBG donor site. However, LBG is often infiltrated with soft-tissue material. Thus, bone graft substitute was emerged as a new material to obtain a fusion. HEALOS (DePuy Spine, Raynham, MA, USA) was one with a promising result.

In 2006, Scott H Kitchel et al reported a 25-patient case series assessing Healos/BMA versus ICBG for posterolateral fusion (PLF) in an instrumented posterior lumbar interbody fusion model[12]. They found that the fusion rate was similar. In their series, 80% fusion rate was achieved in the Healos/BMA group while the ICBG group had 85% fusion rate. In another series[13], 20 patients (22 interbody levels) were implanted with Healos/BMA via TLIF/PLF with interbody cages and posterior pedicle screws. The overall fusion rate at two years in this series was 95% (21/22 levels, 19/20 patients).

When comparing to our study, the Healos/BMA group shows fusion rate (at 2 year- 29.63%, 3 year- 36.84%) that is lower than the previous reports (80-95%). Several hypotheses were pointed out to explain the low fusion rate in our study. The first reason is due to our limitation in investigations. Plain film was the only instrument in determining radiographic outcome instead of combined with computed tomography (CT) scans or other advanced imaging. Plain radiographs alone have been used to assess lumbar spine fusion with an accuracy of no more than 70[4,17]. CT evaluations are thought to be superior to plain radiographs for interbody and posterolateral fusion assessments[18-20].

Seconded hypothesis is the dilution effect of nucleated cells in bone marrow aspiration. In 1997, Muschler et al[9] reported that if volumes of BMA was taken greater than 2 cc per aspiration site, then the number of osteoprogenitor cells populating in graft will be significantly reduced and bony ingrowth may be hindered. Generally, one strip of Healos (5 cc) would be soaked with BMA 5 cc (ratio Healos: BMA = 1: 1). We used two strips of Healos for each level of PLF, so BMA had to be drawn five times (increment of 2 cc) to obtain a volume of 10 cc. Due to multiple aspirations, errors could be occurred easily especially in the process of drawing of BMA to exactly of 2 cc and then the dilution effect could happen.

Furthermore, we had found that the fusion rate of Healos might be declined with increasing number of fusion level. Final fusion rate in short fusion group (1-2 level) was 42.1% (8/19), while long fusion group (≥3 level) was 25% (2/8).

Regarding partial fused group, we could recognize a value in this group. Our data showed that partial fused mass could turn to be a fused mass with longer time follow-up. Fifteen partial fuse mass in first year follow-up from both Healos/BMA and LBG group progress to be fused mass in the second year. Moreover, we could detect three partial fuse mass in two years follow-up turned to be fused mass at third year follow-up. Interestingly, we could not find any progression of partial fused mass after three years follow-up. They remained partial fuse through their last follow-up.

There are several limitations to the present study. This study is a retrospective radiographic outcome report of a small group of patients. The study design itself is unusual in that the study protocol was created before patient selection (prospective), but the surgical intervention was performed before study implementation with much of the information being gathered in a retrospective manner. Twenty-seven patients were finally included in the present study. To our knowledge, this is the largest number of patients for Healos study. Regarding the small sample size, it was necessary to eliminate variables that could affect

the overall results. Difference in demographic data between the Healos/BMA group and the LBG group was then eliminated by using the same patient.

Due to the nature of retrospective data, we could not gather all data. Some data such as underlying disease, and smoking may have a role in affecting radiographic outcome. Furthermore, we could not analyze clinical data from this research because we used the same subject between the intervening groups. Therefore, other designs of study providing clinical data and other factors may be a point in future research.

In conclusion, Healos collagen-hydroxyapatite sponge with bone marrow aspiration had lower radiographic fusion rate when compared to local bone graft in posterolateral lumbar fusion at two years post operative. The results of the Healos/BMA group was increased fusion rate with time but remained lower than the LBG group at three and four years follow-up. This result was done with only plain films, next research included more delicate imaging, prospective control and clinical outcome would be recommended.

Potential conflicts of interest

None.

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การศึกษาเปรียบเทียบภาพถ่ายรังสีของผู้ป่วยที่ได้รับการผ่าตัดเชื่อมกระดูกสันหลังด้วยชิ้นกระดูกทดแทนเปรียบเทียบกับกระดูกสังเคราะห์ HEALOS ผสมกับไขกระดูกในผู้ป่วยคนเดียวกัน

สมบัติ คุณากรสวัสดิ์, อาทิทัต คิรินทร์ภาณุ, ชัยวัฒน์ ปิยะสกุลแก้ว, วีระ สถิรอังกูร

ภูมิหลัง: ชิ้นส่วนกระดูกทดแทนจากบริเวณขอบกระดูกสะโพก (iliac crest bone graft) นั้นเป็นมาตรฐานในการผ่าตัดเชื่อมกระดูกสันหลังส่วนล่าง แต่เรื่องความเจ็บปวดและเสียรูปร่างของกระดูกส่วนที่นำมาใช้นี้นับเป็นข้อเสียที่สำคัญของกระดูกทดแทนชนิดนี้ มีการนำกระดูกทดแทนที่ได้จากบริเวณที่ทำการผ่าตัด (local bone graft) มาใช้แทนเป็นวัสดุในการผ่าตัดเชื่อมสันหลัง แต่วัสดุชนิดนี้ยังมีปัญหาที่สำคัญคือการปะปนของเนื้อเยื่อเกี่ยวพัน ดังนั้นกระดูกทดแทนสังเคราะห์จึงถูกผลิตและพัฒนาขึ้นมา กระดูกทดแทนสังเคราะห์นั้นมีหลายแบบ Healos (DePuy Spine, Raynham, MA, USA) นับเป็นกระดูกทดแทนสังเคราะห์ตัวหนึ่งซึ่งมีรายงานผลการใช้งานเป็นที่น่าพอใจ แต่อย่างไรก็ตามอัตราการเชื่อมของกระดูกชนิดนี้ยังไม่ได้มีการศึกษาอย่างชัดเจน

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบอัตราการเชื่อมต่อของกระดูกสันหลังในภาพรังสีของผู้ป่วยที่ได้รับการผ่าตัดเชื่อมกระดูกสันหลังด้วยชิ้นกระดูกทดแทนที่ได้จากบริเวณที่ทำการผ่าตัดกับกระดูกสังเคราะห์ Healos ผสมกับไขกระดูก

รูปแบบการศึกษา: การศึกษาภาพถ่ายทางรังสีแบบย้อนหลัง

ประชากรตัวอย่าง: ผู้ป่วยที่มีข้อบ่งชี้ให้ได้รับการผ่าตัดเชื่อมกระดูกสันหลังส่วนข้าง (posterolateral lumbar fusion) ในโรงพยาบาลเลิดสิน ตั้งแต่เดือนเมษายน พ.ศ. 2548 ถึง เดือนธันวาคม พ.ศ. 2549

การวัดผล: อัตราเชื่อมของกระดูกสันหลังที่ได้จากภาพถ่ายรังสี

วัสดุและวิธีการ: จากเดือนเมษายน พ.ศ. 2548 ถึง เดือนธันวาคม พ.ศ. 2549 ผู้ป่วยจำนวน 55 ราย ได้รับการผ่าตัดเชื่อมกระดูกสันหลังด้วยกระดูกทดแทนสังเคราะห์ Healos ผสมกับไขกระดูกและกระดูกทดแทนที่ได้จากบริเวณที่ทำการผ่าตัด (local bone graft) ในแต่ละข้างของการเชื่อมกระดูกสันหลัง จากเกณฑ์การคัดเลือกของการศึกษาทำให้สามารถคัดแยกผู้ป่วยเหลือ 27 ราย ภาพรังสีของผู้ป่วยในทุก ๆ หนึ่งปีหลังการผ่าตัด จะถูกเก็บนำมาวิเคราะห์เพื่อประเมินอัตราการเชื่อมของกระดูกต่อไป

ผลการศึกษา: อัตราการเชื่อมต่อของกระดูกที่ 2 ปีหลังการผ่าตัด ในกลุ่มกระดูกทดแทนสังเคราะห์ Healos ผสมกับไขกระดูกเท่ากับ 29.63% (8/27) ในขณะที่กลุ่มชิ้นกระดูกทดแทนที่ได้จากบริเวณที่ทำการผ่าตัดเท่ากับ 62.96% (17/27) และอัตราการเชื่อมต่อของกระดูกที่ 3 ปีหลังการผ่าตัดเท่ากับ 36.84% (7/19), 78.93% (15/19) ตามลำดับ

สรุป: อัตราการเชื่อมต่อของกระดูกทดแทนสังเคราะห์ Healos ผสมกับไขกระดูกในภาพถ่ายรังสีมีค่าที่ต่ำกว่าอัตราการเชื่อมต่อของกระดูกทดแทนที่ได้จากบริเวณที่ทำการผ่าตัด ที่การติดตามหลังการผ่าตัด 2 ปี และเมื่อศึกษาต่อไปที่ระยะเวลา 3 และ 4 ปี พบว่าอัตราการเชื่อมต่อของกระดูกทดแทนสังเคราะห์ Healos ผสมกับไขกระดูกมีค่าเพิ่มขึ้นตามลำดับ แต่ยังต่ำกว่าในกลุ่มของกระดูกทดแทนที่ได้จากบริเวณที่ทำการผ่าตัดที่ระยะเวลาเท่ากัน