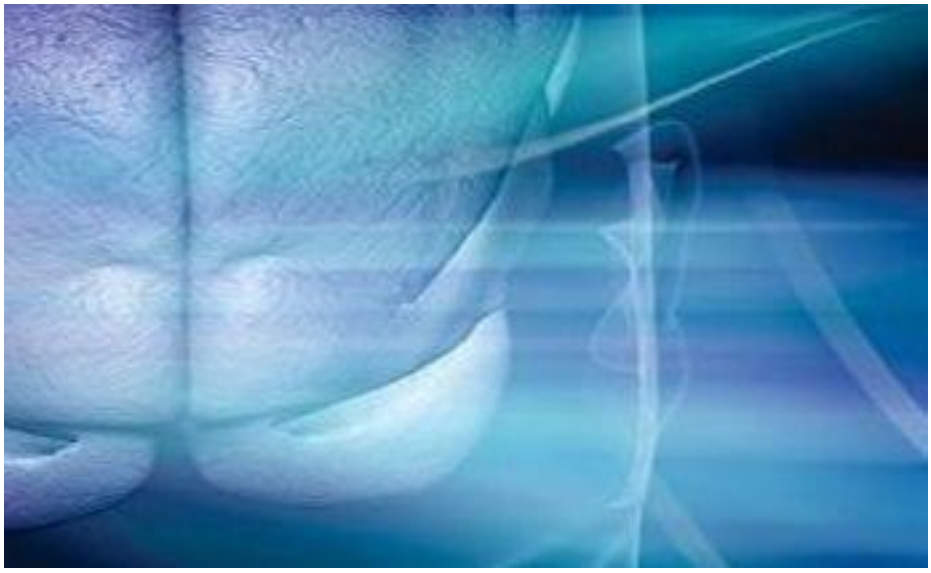

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NEUROLOGICAL SURGEONS AND ACOS NEUROSURGICAL SECTION

VOLUME 1, 2001

INSTRUCTIONS FOR AUTHORS

Papers submitted should be original documentation, including photographs. The papers should be single column, double-spaced. The title should be in title case and bold, followed by Authors, degree, organization and city, state.

The papers should contain an abstract and be separated into sections with bold typing of the section title. The page set-up should be 0-6.5 inches. Paragraphs should be indented 0.5 inches. All tables should be submitted separate from the paper. If possible make the tables up to 3 inches wide so that they could fit into a column. This will allow quicker scanning and preparation.

References should be numbered, tab, name of authors. Title of paper. Journal. Year volume:pages.

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EDITOR'S PAGE

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Welcome to the Journal of the American Organization of Neurological Surgeons and the American College of Osteopathic Surgeons Neurosurgical Section. This volume is composed of the Residents' annual papers that were submitted but not published elsewhere. It is therefore dedicated to the future Neurosurgeons and their education. All papers were reviewed by the peer review committee and selected for awards. The papers submitted are excellent, representing some of our talented colleagues. Issues will be published annually. I hope that this issue will spread the knowledge of our residents and our section. We will continue to solicit annual papers and all papers submitted at the annual meeting. This is your Journal paid for by your annual dues. This issue is available on our website AOANeurosurgery.org. This is your organization; please support it as you can.

Thank you,

Dan Miulli, D.O, F.A.C.O.S
Editor

2007 Annual Resident Paper Awards ACOS Neurosurgery Discipline
The Neurosurgical Resident's Annual Paper Awards are presented by the Neurosurgical Discipline for the best end of year submission. The awards will be presented Wednesday night at the Neurosurgical Discipline Reception 6:00 at the Marriott. The talks are being given Saturday at 1:15 PM during the program.

First Prize:
Boyd Richards, DO,
Providence Hospital of Michigan
Minimally Invasive Transforaminal Lumbar Interbody Fusion and Pedicle Screw Fixation: An Excellent Technique for Treatment of Chronic Lower Back Pain Secondary to Spondylolisthesis or Degenerative Disc Disease With or Without Associated Stenosis

Award: $1500
Presentation Saturday 1:15 PM

Second Prize:
Will Beringer, DO
BroMenn Regional Medical Center
Postoperative CyberKnife Radiosurgery for Single Brain Metastases

Award: $1000
Presentation Saturday 1:25 PM

Minimally Invasive Transforaminal Lumbar Interbody Fusion and Pedicle Screw Fixation: An Excellent Technique For Treatment of Chronic Lower Back Pain Secondary to Spondylolisthesis or Degenerative Disc Disease With or Without Associated Stenosis

Boyd Richards, DO
Department of Neurosurgery, Providence Medical Center, Southfield, MI

Abstract

Object: Minimally invasive lumbar fusion and instrumentation techniques preserve the normal anatomical integrity of the spine while accomplishing the other goals of a more traditional open transforaminal lumbar interbody fusion (TLIF). Minimally invasive TLIF uses a unilateral posterior approach for achieving bilateral decompression and interbody arthrodesis with instrumentation. This article discusses the technical aspect of this procedure and presents outcome results.

Methods: A retrospective review of 51 consecutive patients (28 with spondylolisthesis, 1with retrolisthesis, 1 with spondylolysis and 21 with degenerative disc disease) was conducted with an average of 17 months follow-up. The TLIF in these patients was performed by accessing the disc interspace via a unilateral facetectomy with preservation of the contralateral facet. The $MetR_x$ system was used for exposure of the disc space and completion of the facetectomy. Supplemental percutaneous pedicle fixation with pedicle screws was added for completion of the TLIF procedure

Results: The average length of pre-operative back pain symptoms was 8.3 years. Twenty-two patients had moderate to severe lumbar stenosis. The average total operative time was 256 +/- 47 min and estimated blood loss was 224 cc +/- 63 cc. The average length of hospitalization was 4.2 days. VAS-score was reduced from 7.7 pre-operatively to 2.89, ODI was reduced from 44.4 pre-operatively to 22.4 and SF-36 scores improved greatly. Prolo scores were 76.4% excellent, 21.5% good, 1.96% fair. Fusion rate was 98% at one year follow up. Complications included one patient with a permanent nerve root injury and one graft failure requiring return to OR.

Conclusions: Minimally invasive TLIF can be safely performed in patients with degenerative disc disease and spondylolisthesis with or without foraminal or central stenosis. Fusion rates have been 100% with no pseudoarthroses. The prior disadvantages of accessibility for bilateral radiculopathy have been overcome via a unilateral approach using the tubular retractor system. The procedure is a novel surgical approach to achieve fusion and spondylolisthesis reduction.

Keyword: Spinal Fusion, Transforaminal Lumbar Interbody Fusion, Minimally Invasive spine surgery

Introduction

Low back pain is a major cause of disability in the United States and is the second most common reason for physician visits. About one percent of the total U.S. population is chronically disabled

from low back pain and an additional one percent is temporarily disabled. The yearly prevalence of low back pain in the United States is 15 to 20 percent (1). The mainstay of treatment for the majority of these patients is non-surgical, but of those patients who fail to improve with non-surgical treatments, many will be referred for the evaluation of surgical options. For many patients, surgical stabilization and fusion will be considered as treatment. The last century has seen a tremendous evolution of techniques to obtain neural decompression of the lower spine and subsequently obtain a fusion of individual spinal elements. In the mid 1980's, systems for pedicle screw fixation were developed to augment stabilization constructs and improve fusion rates (4). Over time pedicle screws have been demonstrated to be biomechanically superior to other fixation systems.

Minimally invasive spine (MIS) surgery has recently evolved from traditional open approaches with the aim of reducing approach related morbidity. The standard open exposure for this procedure frequently causes significant dorsal neurovascular, ligamentous and muscular damage, often leading to paraspinal ischemia, denervation, muscular weakness and subsequent atrophy. The described minimally invasive pedicle screw fixation system has been designed to address and minimize these operative morbidities. In addition, the normal ligamentous and muscular attachments are left undisturbed which further hastens post-operative recovery and reduces post-operative pain. The concept of MIS surgery has gradually extended to spinal fusion and pedicle screw instrumentation for treating a variety of degenerative conditions affecting the lumbar spine.

The Minimally Invasive Transforaminal Lumbar Interody Fusion (MITLIF) procedure evolved from the open posterior lumbar interbody fusion and TLIF procedure. Interbody fusion via a posterior approach was first described in publications by Ralph Cloward in 1953 who reported satisfactory results in 85% of his patients (4). The advantages to placing structural interbody graft material include: improved load sharing, restoration of disc and foraminal height, placement of graft material under pressure to promote fusion, and improved sagittal alignment. However, the interbody fusion technique did not gain popularity until the advent of supplemental pedicle screw instrumentation and Thomsen proved that pedicle screw fixation improves fusion rates as well as functional outcomes (28). In 1981, Blume introduced the unilateral transforaminal approach for segmental lumbar interbody arthrodesis to reduce the complications associated with instrumented PLIF (15). In 1997, the TLIF procedure was modified and popularized by Harms, who accessed the disc space *via* a path through the far lateral portion of the vertebral foramen (12). Like PLIF, the TLIF construct rigidity is enhanced when combined with pedicle screw instrumentation. However, the TLIF offers advantages in that it is usually performed *via* a unilateral approach, reduces nerve root retraction and preserves the facet complex on the contralateral side (10). The current study analyzes the results of patients undergoing the MITLIF procedure supplemented with posterior percutaneous pedicle screw fixation. Indications for this minimally invasive pedicle screw system include: degenerative disc

disease, spondylolisthesis, spinal deformities, fractures, pseudoarthrosis, and post tumor resection.

Clinical Materials and Methods

Between September 2003 and July 2005, 51 patients, ages 35 to 81 years old presented to a single neurosurgeon with chronic disabling low back pain refractory to non-operative therapy. All patients had received multi-modality non-operative therapies including physical therapy, injection therapy, and/or chiropractic manipulations. Some patients had undergone prior lumbar diskectomy and or laminectomies. Conditions treated included spondylolisthesis (grade 1, n=15; grade 2, n=11) and degenerative disc disease (n=23). A significant portion of these patients also had severe (n = 12) or moderate (n=6) stenosis that required decompression during the fusion and instrumentation procedure. Average duration of symptoms was 8.3 years.

All patients underwent a unisegmental TLIF **(Figure 1)** and bilateral percutaneous pedicle screw fixation using either the Sextant (Sofamor Danek, Memphis, TN) or Pathfinder percutaneous instrumentation system (Abbott Spine, Austin, TX) **(Figure 2).** Pre-operative imaging using magnetic resonance (MRI) and/or computerized tomographic myelography and plain radiography of the spine was reviewed. All patients had evidence of central or foraminal stenosis, vertebral MODIC end-plate changes showing different degeneration stages, disc space collapse or spondylolisthesis. These findings were correlated with post-operative outcomes using the Prolo Anatomic-Functional-Economic Rating System. Oswestry score, Visual Analogue Scale (VAS), and SF-36 outcome measures were performed pre-operatively and at 2 weeks, 3 months, 6 months and 24 months post-operatively. Other variables evaluated included: post-operative return to work date, analgesic usage, physical therapy usage, pain clinic usage, chronicity of back pain, operative times, blood loss and need for blood transfusion. Fusion rates were determined by independent review of plain dynamic radiographs at 3, 6, 12 and 18 months intervals.

Procedure

The patient is placed in the prone position on a radiolucent table. C-arm fluoroscopy is subsequently positioned in the lateral position. The sterile field is prepped and draped in the normal sterile fashion. Using a radiopaque object (Figure 1A), the lateral border of the pedicles are identified and marked. A 3 cm incision is planned approximately 1 centimeter lateral to these marks, allowing for an appropriate medial vector when cannulating the pedicle screws.

The MetRx dilator system (Medtronic; Memphis, TN) is used to achieve an appropriate operative corridor for performing the decompression and interbody fusion. A K-wire is docked on the facet and dilators are used up to a size of 26 mm, which is secured in place with a pneumatic arm. A unilateral facetectomy is performed under microscope visualization. Remaining soft tissue is removed from the facet complex using monopolar cautery. Using a high speed drill and

Kerrison punch, a complete facetectomy is performed. Drilled bone is collected in a Luken trap, obviating the need to perform an open iliac graft harvest.

In those patients with concomitant central spinal or foraminal stenosis (n=18), a decompression was performed. A unilateral laminectomy is perfomed using a high speed drill. This is followed by an undercutting of the spinous process and contralateral lamina with a high speed drill. The ligamentum flavum is subsequently removed.

The traversing and exiting nerve roots are then identified. The epidural venous plexus is cauterized using bipolar cautery. The disc space was entered and prepared for graft placement using a series of disc space reamers, pituitary ronguers, Kerrison punches, and various shaped long handled curettes. The disc space was then entered with a box chisel while carefully retracting the traversing and exiting nerve roots. Once the disc space was prepared, the bone graft material collected was mixed with a bone graft extender, typically Vitoss (Zimmer spine), or Healos (Depuy) with stem cell iliac crest aspirate at roughly a 1:1 ratio. The mixture was then placed in the interspace, placing it evenly on the contralateral and ipsilateral side. The appropriately sized structural graft, which was packed with the bone graft mixture, was placed into the disc space. A bone decortication and posterolateral fusion was then performed on the ipsilateral side to reconstruct the resected facet complex.

The c-arm is then placed in the AP direction for localization of the pedicle for screw fixation. The best location to acquire the pedicle is in its most lateral and superior quadrant. The entry point will help to avoid the overriding facet and allow the screw to follow the natural pathway of the pedicle providing better screw convergence. A Jamshidi needle is then passed through the skin incision in an oblique lateral to medial trajectory and docked on the bony anatomy. The stylet from the Jamshidi needle is removed a K-wire is advanced through the Jamshidi trochar.

After each pedicle has been localized in a similar fashion, each K-wire is advanced down the pedicle under lateral fluoroscopic guidance. After successful placement of the K-wire, the soft tissue is dilated using the sequential dilating instruments. Once the largest dilator is positioned the smaller dilators are removed. The pedicle is then broached with the cannulated bone awl of the K-wire and through the largest dilator. Tapping the screw placement should be completed with fluoroscopic guidance.

Following successful placement of the pedicle screws, the tissues between the screws are dissected to allow for placement of the rod. EMG testing is subsequently performed to evaluate for pedicle breach. In most cases the threshold ranged from 10 to 35 mAmps. In one case a screw was repositioned due to stimulation less than 10 mAmps.

The length of the rod can be estimated using a rod caliper. Approximately 15 mm is added to the length measure with the caliper when selected an appropriately sized rod. Ensure with fluoroscopy the proper positioning of the rod. Top-locking screws within all pedicle screws are placed and with the use of a counter torque wrench, they are locked in place.

The facia and skin are closed in layers.

Results

In this series of 51 patients, the average duration of pre-operative chronic back pain was 8.3 years. Pre-operative image analysis revealed that 18 patients had stenosis (severe, n = 12; moderate, n=6). In this group, 6 patients had foraminal stenosis, 7 patients had central stenosis and 5 patients had combined foraminal & central stenosis. Nineteen patients had significant end plate MODIC changes. Operative times averaged 256 minutes $\pm$ 47 minutes and estimated blood loss of 224 cc $\pm$ 63 cc. One patient required a blood transfusion. Analgesic usage included morphine or dilaudid PCA pump for an average of 2 days post-operatively followed by oral analgesics. Most patients (76%) were off oral analgesics by post-operative week 3. Thirty-three percent of patients completed a course of physical therapy and less then 10% used the pain clinic post-operatively. Twenty-four (89%) patients showed significant improvement in clinical outcome at average 1 year follow-up. Prolo outcomes score were excellent, good, and fair in 76.4 % (n = 15), 21.5 % (n = 7), and 1.96 % (n = 3) of patients, respectively. At 3, 6 and 12 months follow-up, fusion rates were 96%, 100% and 100% respectively.

Outcomes in the spondylolisthesis group were quantified using the VAS and the Oswestry Disability Index and SF-36. From a preoperative average, the VAS score decreased from 9.07 to 2.32 at 1 year postoperatively. The average Oswestry score decreased from 46.41% preoperatively to 13.14% at 1 year follow-up (Figure 7). SF-36 (Figure 8) with PCS (Physical Component Scale) and MCS (Mental Component Scale) shows great improvement. The preoperative PCS increased from 27.09 to 41.03 at 1 year follow-up. The preoperative MCS increased from 42.06 to 55.22 at 1 year follow-up (Figure 9) Most patients (88%) returned to work or activity of daily living within eight weeks after the surgery. Statistically significant improvements in patient outcomes were observed**.**

Case Example 1

58 year old female suffering from chronic debilitating back and right leg pain who was confined to a wheel chair. The back pain was reported to be 10 of 10 on Visual Analogue Scale (VAS). She also reported associated numbness on the right side and right foot dorsum. Previous conservative treatment included physical therapy; epidural steroid injection provided temporary relief only. MRI of lumbar spine showed multilevel degenerative disc disease, most prominent at L4-L5 level, with a grade II spondylolisthesis and severe stenosis. The patient underwent a minimally invasive procedure, microscopic laminectomy for stenosis, followed by TLIF using

structural allograft, Vitoss bone matrix with autograft harvested from the surgical site. Interbody fusion was further supplemented with percutaneous pedicle screw and rods. Estimated blood loss was 150 cc. The surgery was uneventful. She was discharged in a stable condition on postoperative day 2. Postoperative imaging shows a solid osseus fusion, intact instrumentation and also reduction of the spondylolisthesis with maintenance of disc space height.

Patient was seen in a two week follow up visit and reported a significant right leg pain improvement, objective findings and Visual Analog Scale showed improvement of 74%. The patient was able to ambulate with a walker. Patient regained a full strength in her lower extremities. One year post op visit showed fusion rate of 100%, and objective improvement of symptoms at 90% including Visual Analog Scale and SF36. The patient was ambulating with no difficulties or significant back pain.

Case Example 2

A 52 year old female presented with back pain and bilateral radiation of pain to her legs and feet. The pain has been persistent and causes difficulty sitting, standing and walking. In addition to walking difficulty walking, she reports dragging of her feet, which is consistent with partial foot drop. The preoperative AP and lateral x-rays (Figure 6C) show a grade II spondylolisthesis. She underwent a 360 degree fusion (TLIF) through one incision with percutaneous pedicle screw fixation from L5-S1. The intervertebral disc was replaced with allograft structural bone and also autograft and bone matrix material as postero-lateral fusion. Partial reduction of the spondylolisthesis was achieved with the Abbott Spine reduction device to almost a grade 0. Figure 6D shows the reduction and instrumentation. She was discharged on postoperative day 2. The patient was seen at the clinic in a two week follow up visit and reported significant improvement of both back and leg pain.

Discussion

The minimally invasive TLIF with percutaneous pedicle screw fixation is a novel surgical technique that can be safely used to achieve adequate spinal decompression as well as solid bony fusion in the lumbar spine.

The deleterious effects of the extensive muscle stripping and retraction have been well documented in the medical literature (6, 10, 14, 16, 17, 18). These undesired side effects of lumbar surgery occur so commonly that the term “fusion disease” has been coined to describe their occurrence (9). Therefore the goal of minimally invasive surgery is to preserve normal anatomical structure of the spine while having the same degree of accessibility to the neural elements and make it possible to achieve a complete decompression.

The minimally invasive TLIF procedure described in this series can be safely performed while achieving the goals of a more traditional open TLIF procedure. Fulfilling the need to bridge the

gap for the dearth of outcome studies determining the safety and efficacy of these procedures, our study is the first to determine outcome results on such a large series of patients.

Although technically demanding, minimally invasive spine TLIF offers a number of potential advantages over traditional open, posterior lumbar fusion techniques, and the ability to perform adequate decompression of neural elements and reduction of spondylolisthesis is maintained. However, direct comparison of a single surgeon using open and minimally invasive techniques has not been performed.

A variety of materials have been used for structural interbody support, including cancellous autograft, allograft bone, metal cages, composites and recently introduced nonresorbable and resorbable polymers, with varying degrees of success. In the experience of the senior author (M.P.C), a combination of locally harvested autograft, Healos or Vitoss sponge, bone allograft material and bone marrow stem cells harvested from the iliac crest have yielded 100% fusions in our series of patients and have eliminated the use of any single material with less than optimal results.

The indications for this series of patients for performing minimally invasive TLIF included symptomatic degenerative disc disease at L4-L5 and L5-S1 interspaces secondary to incompetence of degenerated discs. Typical symptoms in these patients ranged from axial back pain and sequelae of neural compression secondary to varying degrees of stenosis of the spinal canal or foraminal stenosis. Patients frequently presented with exercise intolerance from neurogenic claudication and/or radicular complaints. Surgical treatment was used after all conservative non surgical treatment modalities such as pain medications, physical therapy, selective nerve root or epidural steroid injections failed.

In conclusion, we feel that minimally invasive TLIF with percutaneous pedicle screw fixation is a safe and effective technique to adequately achieve bilateral decompression and stabilization of the lumbar spine. Further head-to-head studies comparing minimally invasive techniques with more tradition open techniques of a single surgeon would be of benefit in a future study design.

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Legends

Figure 1. A). Two K-wires are used to identify the entrance point for placement of a percutaneous pedicle screw and plan the overall incision. Note that in the identification of the incision location the superior vertebral body endplates should be aligned and the spinous processes in the midline, as seen for targeting this L4 body. B). For initial localization of the pedicle, the tip of a Jamsheedi needle is placed at the superior-lateral quadrant of the pedicle. Alignment on the AP image of the superior endplates of the corresponding pedicle is essential for this step. C). With the k-wire guide in place the pedicle is then tapped and D,E). screw applied.

Figure 2. Illustration showing wanding of the Jamsheedi needle to the next level for pedicle screw placement.

Figure 3. Once the first screw is in place A). the Jamsheedi is placed to target the next pedicle on the ipsilateral side B). A K-wire is then passed through the Jamsheedi needle which had been seated through the pedicle and into the vertebral body. The first dilator can then be used to aid in rigidity as the k-wire is seated in the vertebral body. This procedure is done under fluoroscopy to prevent passing the k-wire beyond the vertebral body. C). Tissue dilators are then passed over the k-wire followed by D). tapping and E). screw placement.

Figure 4. Illustration showing A). opening of fascial plane with letter opener device to allow B). passage of rod to C.) connect screw heads.

Figure 5. Intra-operative photo showing A). measuring and B). passage of rod to secure C), D) two segment construct seen in AP and lateral plain film x-ray.

Figure 6. Minimally invasive spondylolisthesis reduction using the PathFinder system reduction device. A) Intraoperative photo showing the device secured to the more anterior (ventral) screw head and, B, after reduction with corresponding intraoperative fluoroscopic images. C, preoperative and, D, postoperative images.

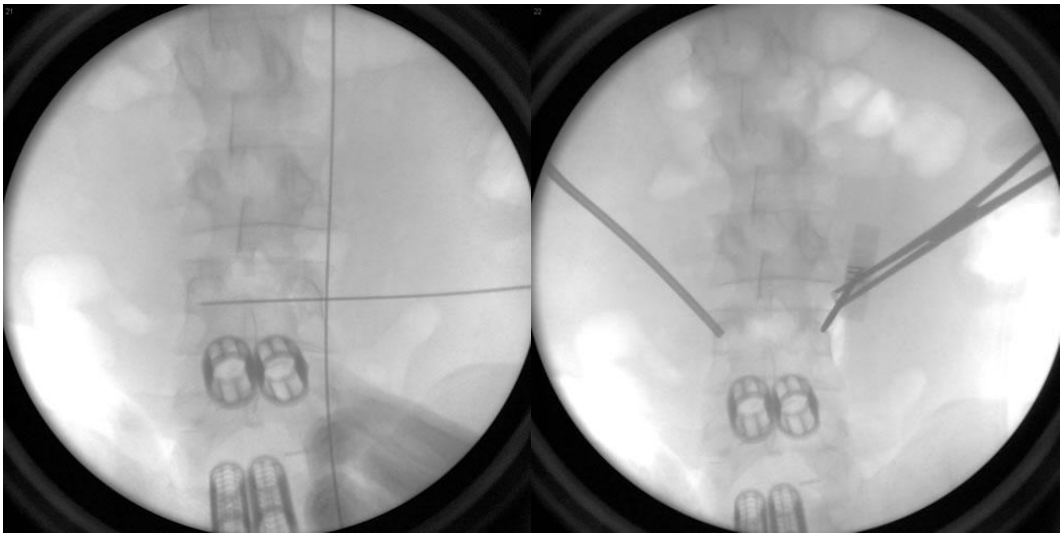
Figure 7. The average Oswestry score decreased from 46.41% preoperatively to 13.14% at 1 year follow-up.

Figure 8. The preoperative PCS increased from 27.09 to 41.03 at 1 year follow-up.

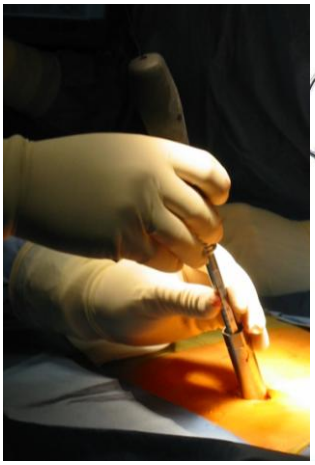
Figure 9. The preoperative MCS increased from 42.06 to 55.22 at 1 year follow-up.

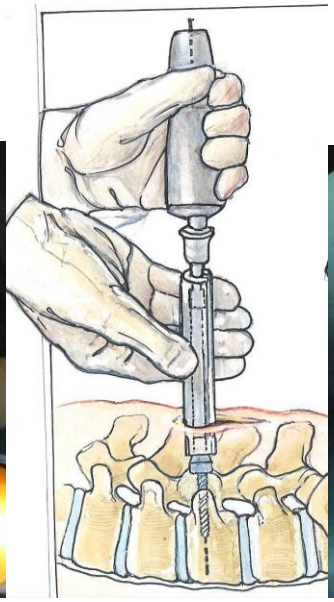
Figure 1.

A. **B.**



C. **D.** **E.**





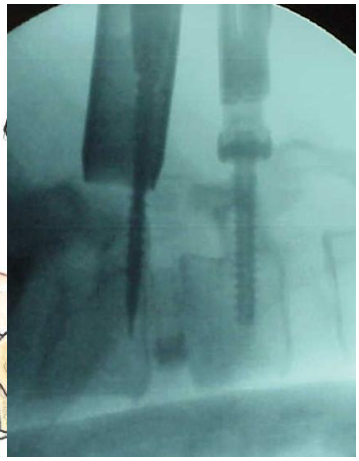


Figure 2.

A. B.

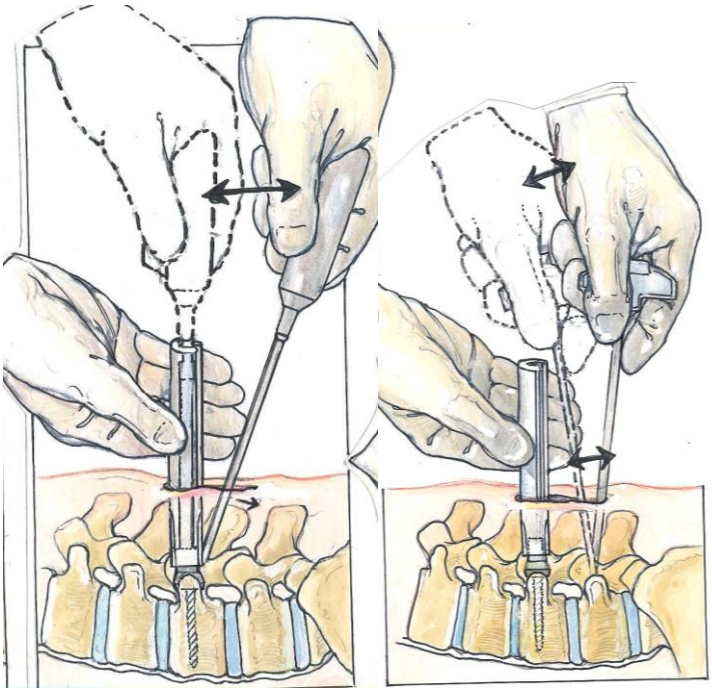
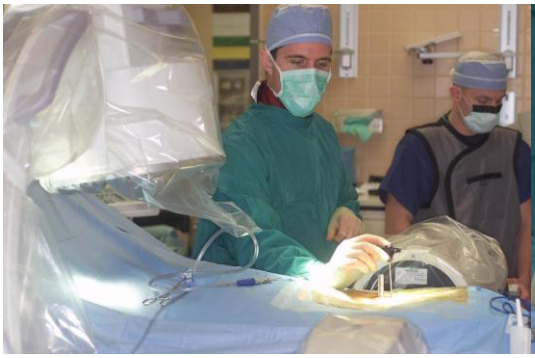


Figure 3.

A. **B.**



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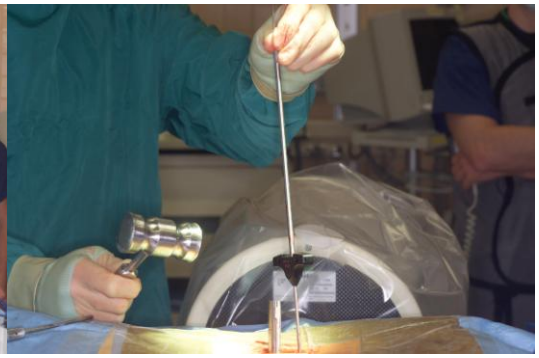
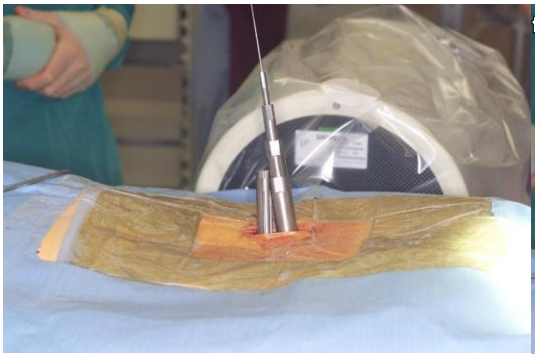


D.



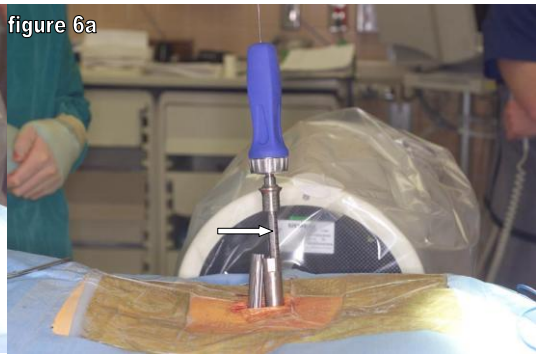
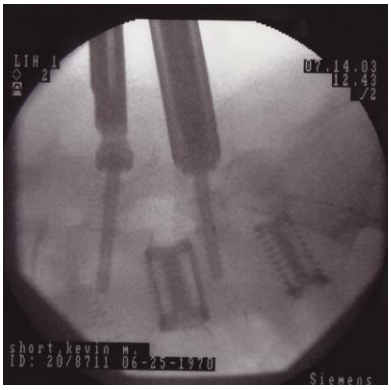


figure 6a

E.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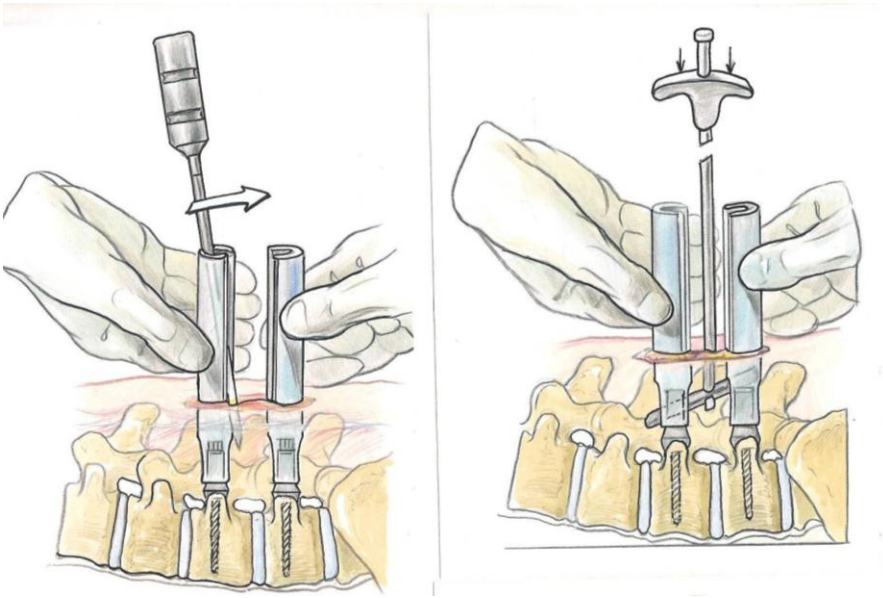
Siemens

Figure 4.

A. **B.**



C.

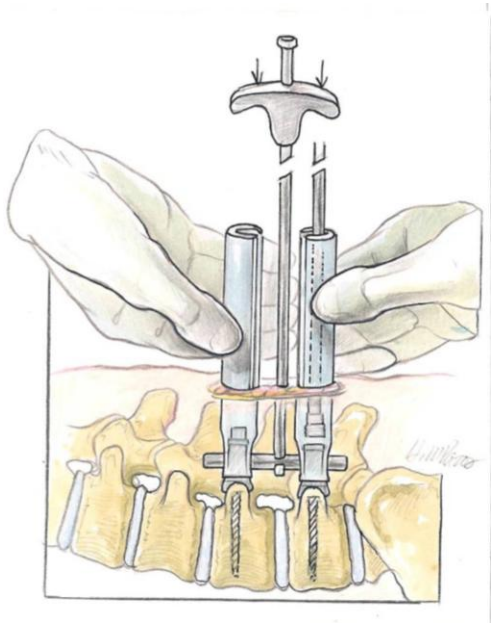
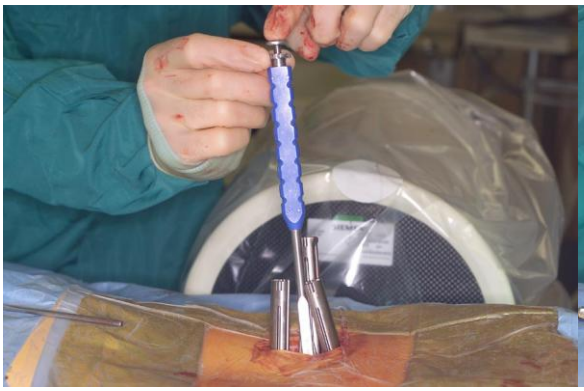


Figure 5.

A.



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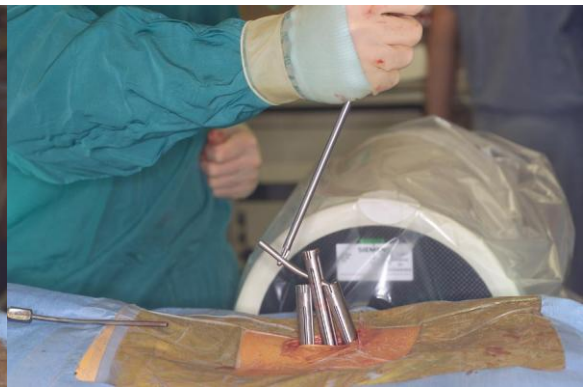

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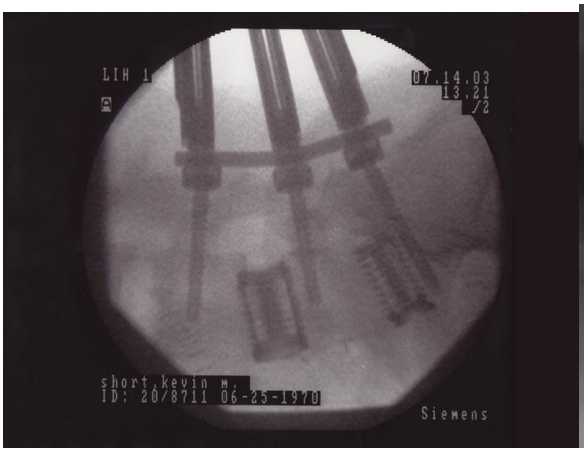

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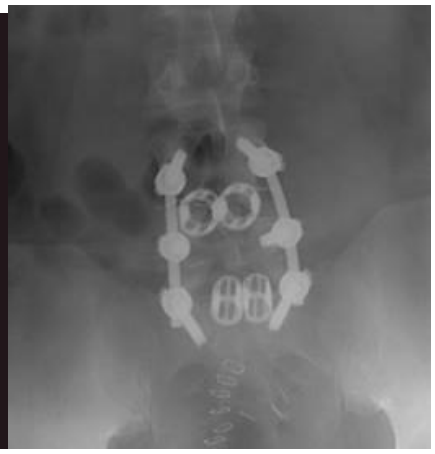
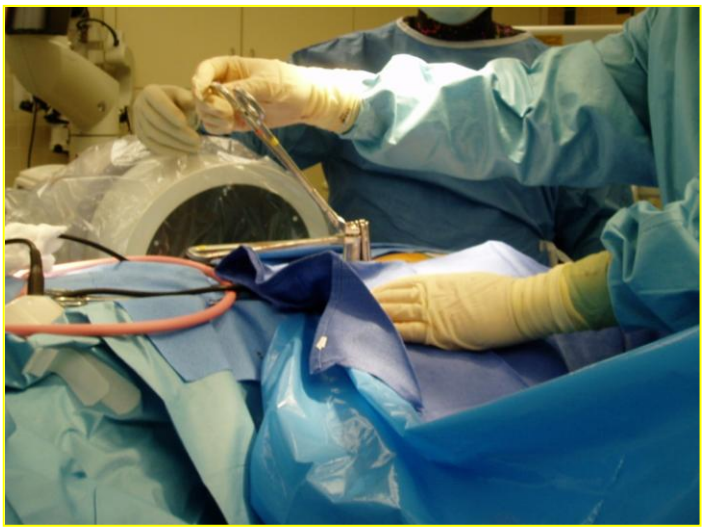


Figure 6

A



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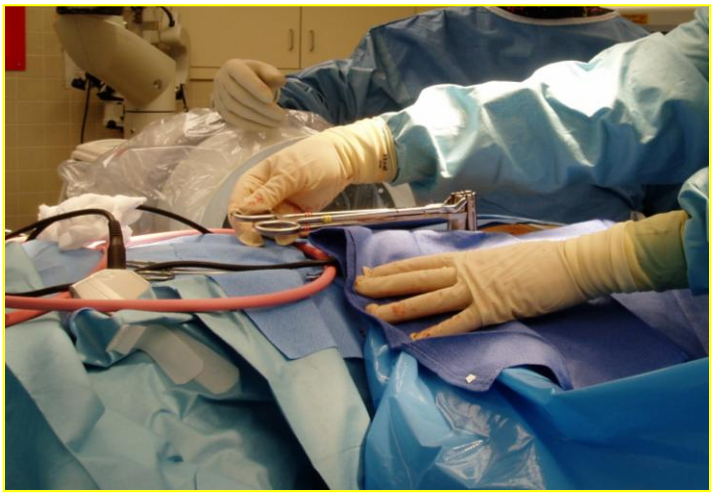

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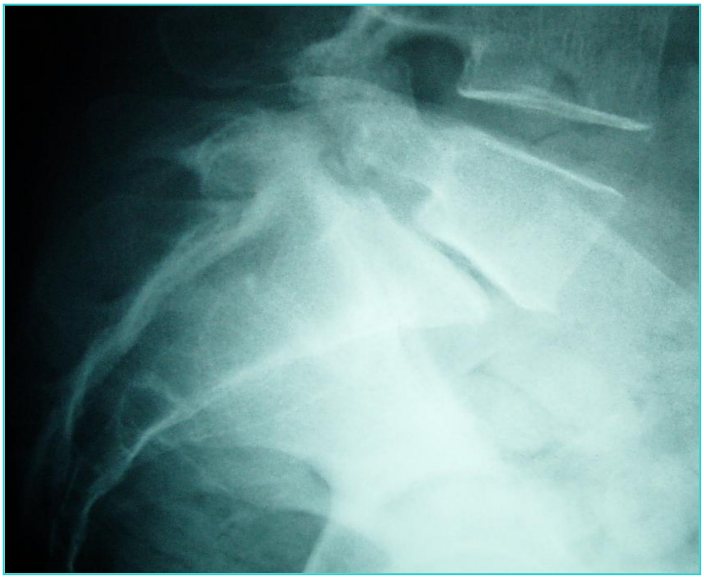

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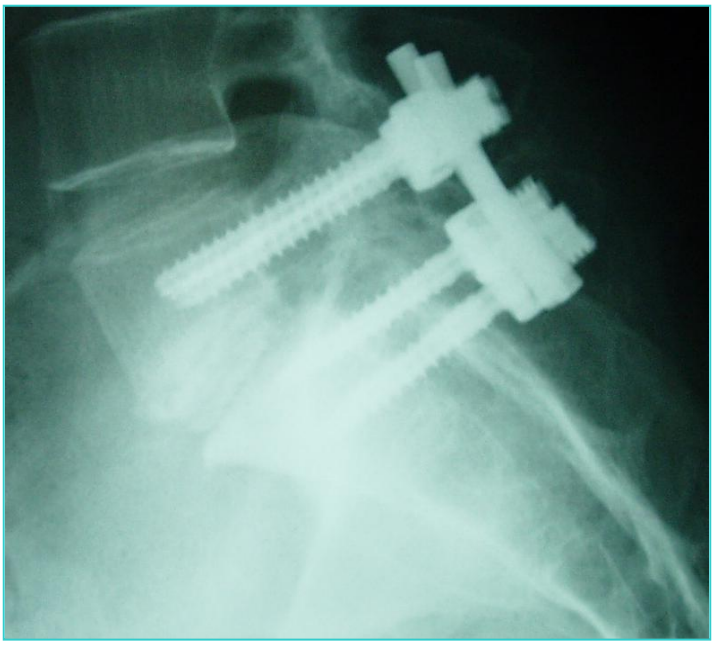


Figure 7

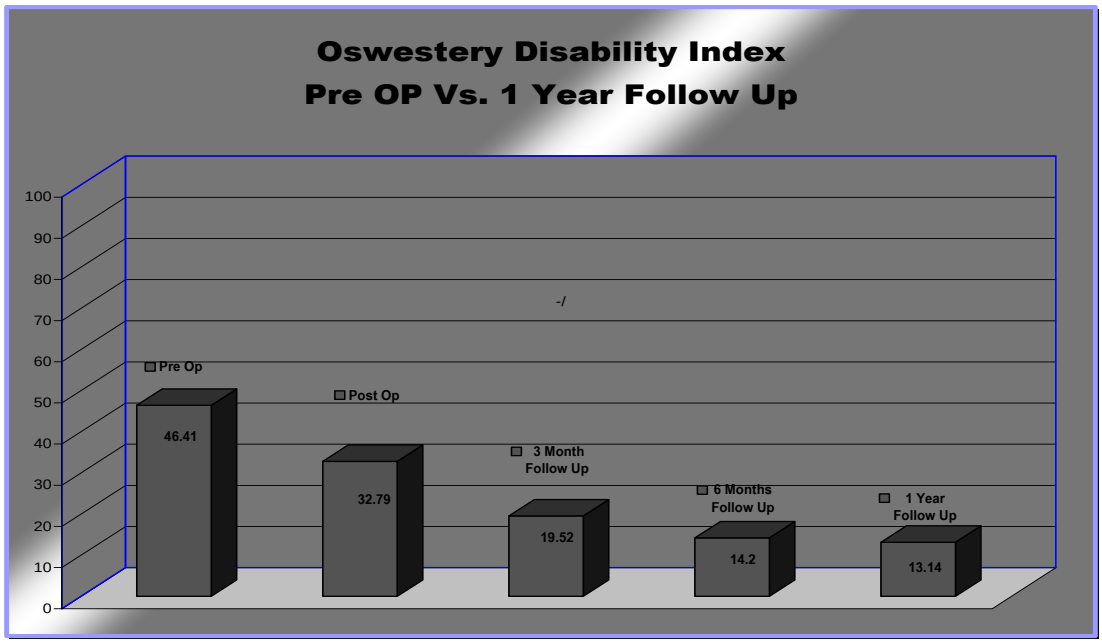

Oswestery Disability Index
Pre OP Vs. 1 Year Follow Up
100
90
80
70
60
50
40
30
20
10
0
-/
Pre Op
46.41
Post Op
32.79
3 Month
Follow Up
19.52
6 Months
Follow Up
14.2
1 Year
Follow Up
13.14

Figure8

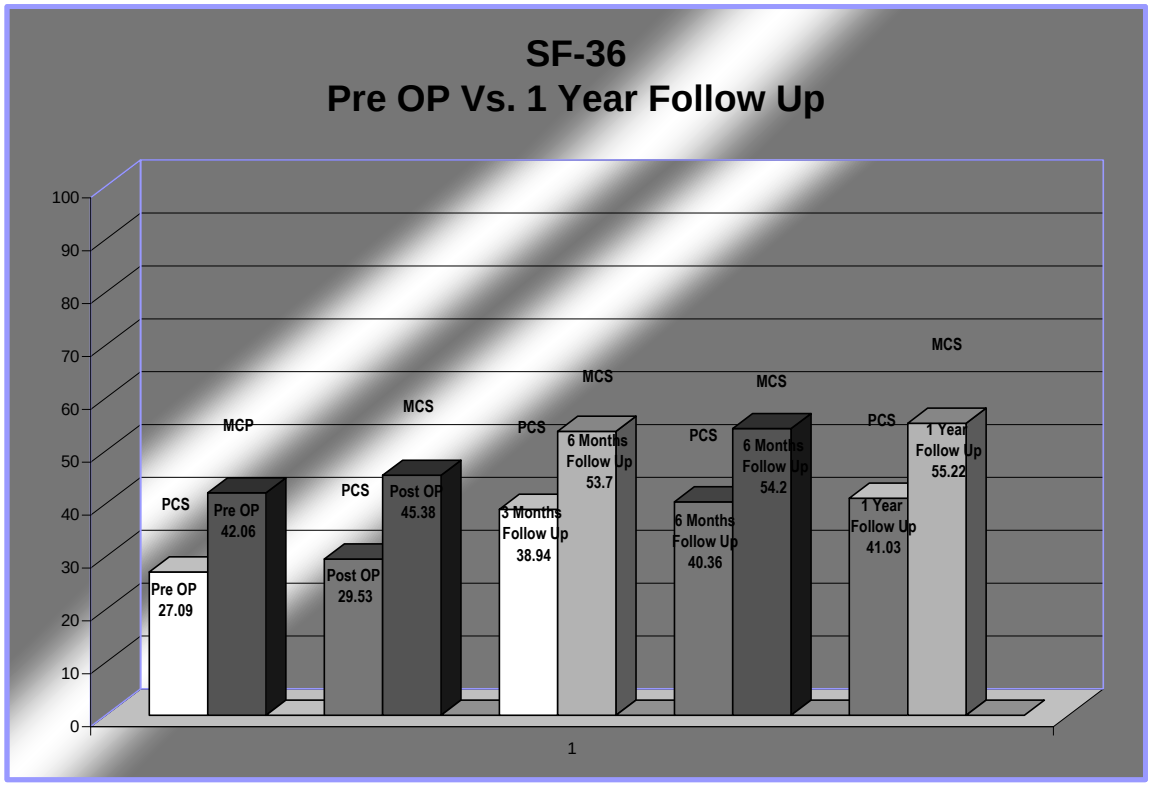
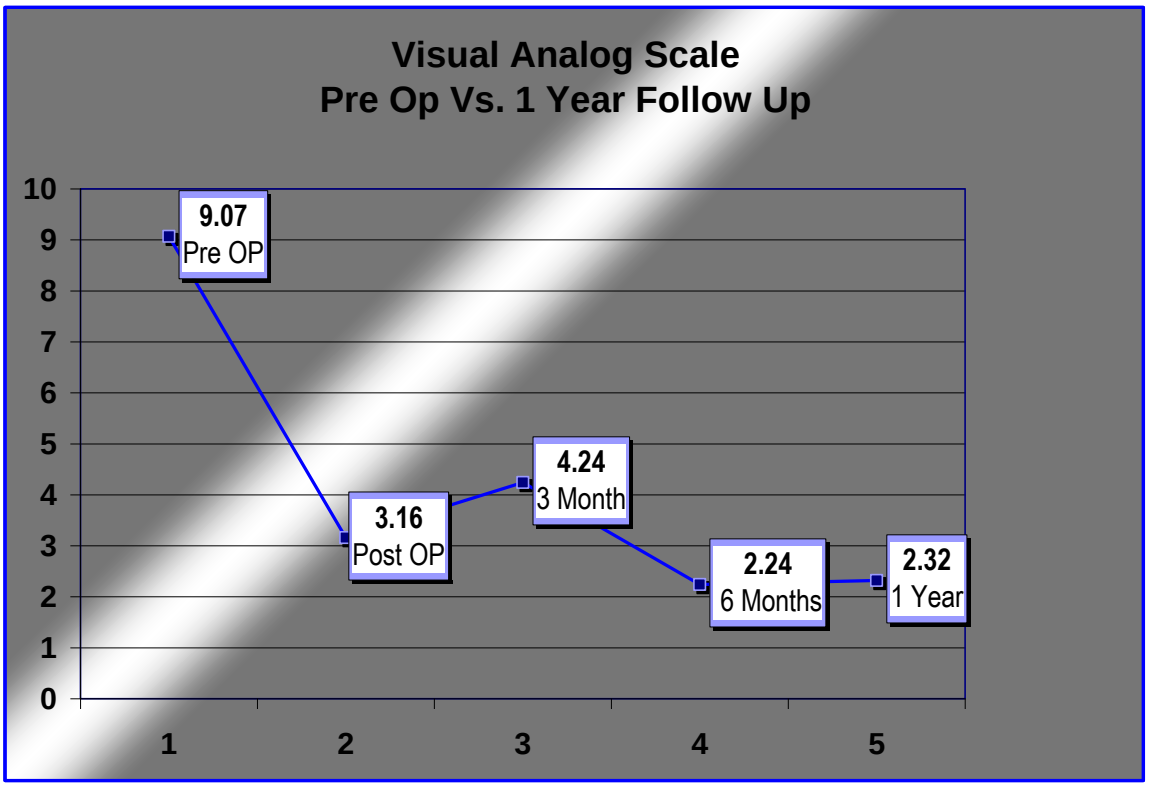

SF-36
Pre OP Vs. 1 Year Follow Up
100
90
80
70
60
50
40
30
20
10
0
MCP
PCS
Pre OP
27.09
MCS
Pre OP
42.06
PCS
Post OP
29.53
MCS
Post OP
45.38
PCS
3 Months
Follow Up
38.94
MCS
6 Months
Follow Up
53.7
PCS
6 Months
Follow Up
40.36
MCS
6 Months
Follow Up
54.2
PCS
1 Year
Follow Up
41.03
MCS
1 Year
Follow Up
55.22
1

FIGURE 9


Visual Analog Scale
Pre Op Vs. 1 Year Follow Up
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
9.07
Pre OP
3.16
Post OP
4.24
3 Month
2.24
6 Months
2.32
1 Year

C

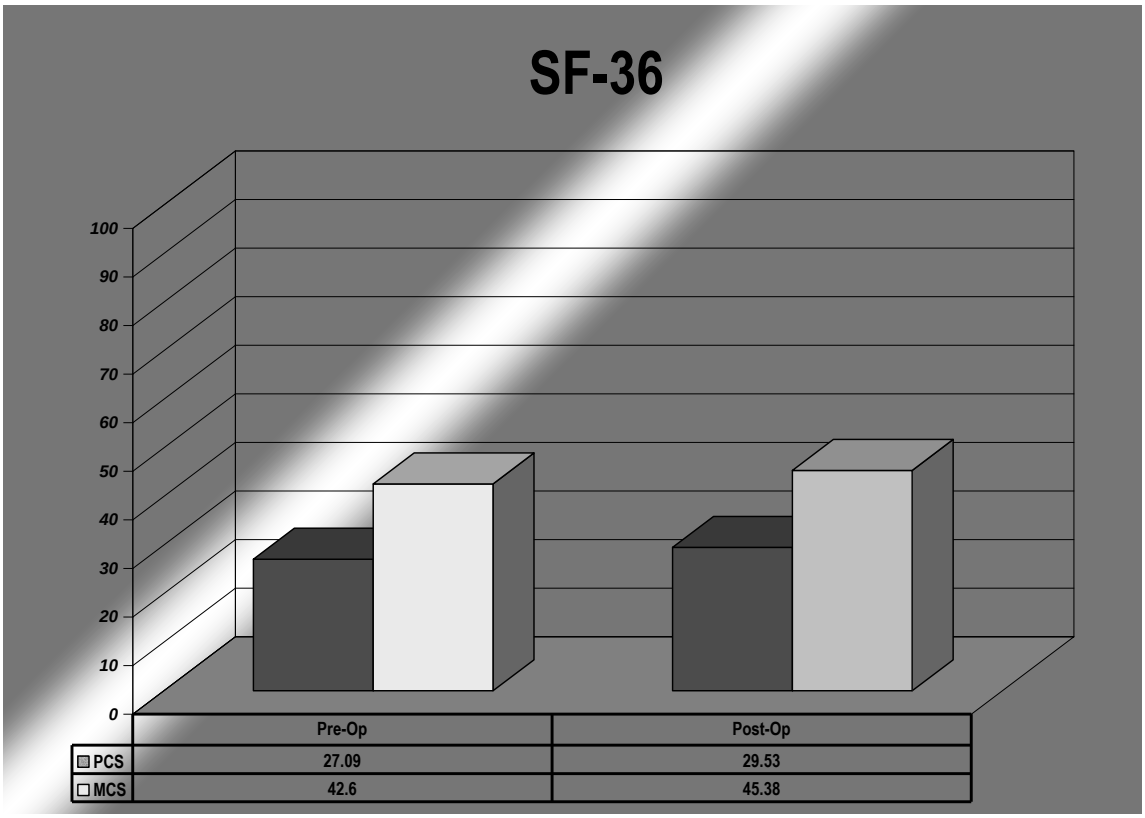


Figure AAA 1

- Screws within L3 vertebral body

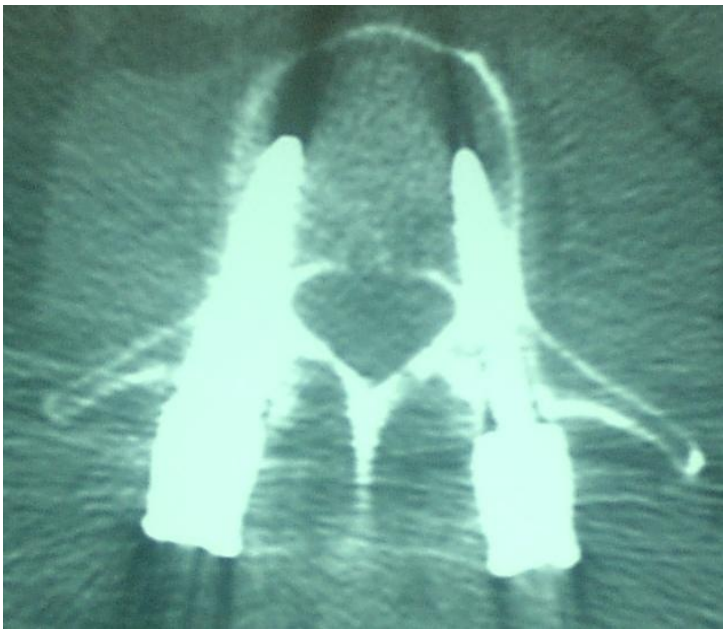
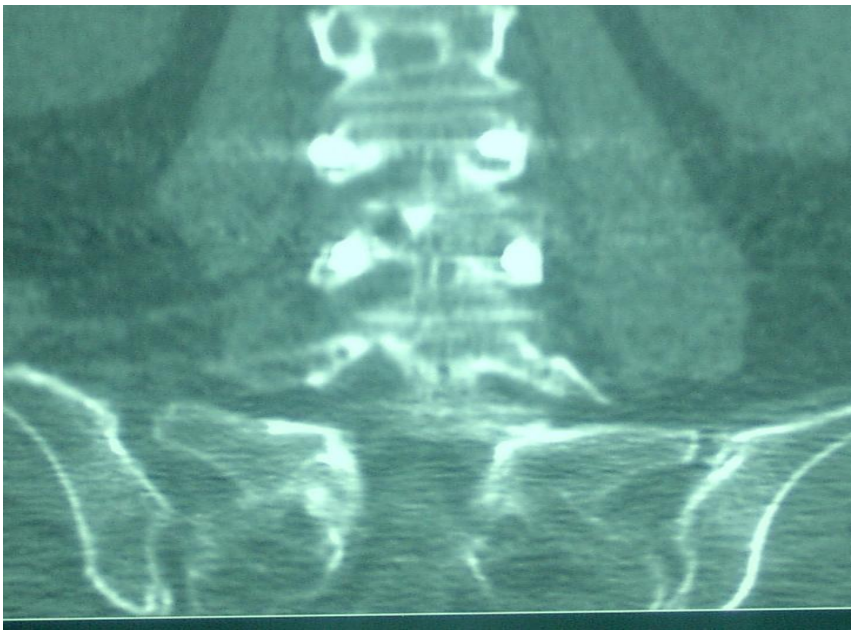


Figure AAA 2

No facet violation notified, all screws in L3 and L4 vertebral bodies were stimulated with EMG response > 25 mAmps



Postoperative CyberKnife Radiosurgery for Single Brain Metastases

Will Beringer D.O., Bromenn Regional Medical Center

Introduction

Over 100,000 Americans suffering from cancer will be diagnosed with brain metastasis this year[1]. While improved treatment of systemic cancer has allowed more patients to live long enough to develop brain metastasis, high resolution multi-planar brain imaging has led to earlier detection of smaller, more treatable brain metastases. Early aggressive treatment of brain metastases can significantly improve quality of life and survival for cancer patients.

Treatment options for brain metastases include surgery, whole brain radiotherapy (WBRT) and stereotactic radiosurgery (SRS) either alone or combined[2,3,4,5]. Each therapeutic option has given risks, benefits and expected efficacy for treating local (at the site of the metastasis) and distant (in the brain but not at the local site) metastases. Local postoperative recurrences are due to residual tumor and undetectable cancer cells at the resection margin not removed at the time of surgery. Distant recurrences are due to both micrometastases undetected at the time of surgery and hematogenously spread metastases to the brain after surgery.

A recent prospective study has shown patients with a single brain metastasis treated with surgery alone have a 46% local and 37% distant recurrence rate[6]. While surgery can be performed for select individuals with easily accessible and life threatening metastases, WBRT can be used on almost all patients with brain metastases[7]. WBRT delivers a series of sublethal radiation treatments to the entire brain to improve both local and distant control. Knowing that most normal brain cells are capable of repairing the inflicted DNA injuries between fractions and that rapidly proliferating cancer cells cannot, the linear quadratic equation predicts each fractional dose will leave fewer viable cancer cells in the radiation field[8]. In essence, WBRT is a race between the tumoricidal capabilities of fractionated radiotherapy and the cancer tissue's rate of proliferation with the constraint of not creating radiation toxicity to the surrounding normal brain. Unfortunately, up to half of patients treated with WBRT alone die from intracranial progression[9]. For this reason, WBRT is often combined with surgery or radiosurgery to improve local control.

Stereotactic radiosurgery is an attractive non-invasive treatment that delivers a single large conformal (the marginal dose closely matches the contours of the targeted lesion and has steep dose gradient peripheral to these contours) dose of ionizing radiation to a well-defined, small intracranial target. Conformal radiation fields allow for a higher dose

to be delivered to the target with minimal exposure to surrounding, non-targeted tissue. This improves local control and reduces the risk of radiation-induced side effects[10,11,12,13,14]. Because SRS delivers a large, conformal radiation dose, it provides better control of radioresistant metastases like renal cell carcinoma and melanoma than fractionated WBRT[15]. However, SRS cannot effectively treat large tumors since the single fraction doses required to destroy them lead to large volumes of normal brain included within high dose margins[16]. Retrospective studies have shown in selected patients radiosurgery alone provides equivalent length of survival when compared to WBRT plus radiosurgery[17]. Furthermore, protocols have been developed to treat local and distant recurrences in radiosurgery alone treated patients with repeat salvage radiosurgery[18].

A new approach to treating tumors has recently evolved that involves using frame-based and frameless SRS devices to deliver precisely focused, conformal radiotherapy [19,20,21,22,23,24,25]. Radiotherapy is performed with these SRS devices by giving higher total doses broken into several fractions thereby giving a lower dose per fraction. This hypofractionated stereotactic radiotherapy (HSRT) can deliver a precise, conformal and therefore, *higher* dose due to its use of SRS devices for dose delivery while hypofractionation of this radiation dose allows for the normal brain tissue adjacent to the metastatic lesion to recover from sublethal DNA injury between each fraction[26]. Since normal brain tissue is given time to recover from sublethal injury between fractions, tumors that would have been too large to be safely treated with SRS can be treated with HSRT.

The current standard for SRS and HSRT uses head pins to attach a confining head frame to the skull. Patients are required to wear this head frame for several days; which is cumbersome and over the course of days has the risk of inadvertently having the head pins slip and induce targeting inaccuracies. Frameless, image-guided robotic SRS and HSRT using the CyberKnife (Accuray, Inc. Sunnyvale, CA) can conveniently deliver single or multiple fractions of highly conformal radiation to lesions with an application accuracy that equals that of conventional stereotactic frames[27]. For HSRT, each fractional dose is delivered within an hour and patients return daily for additional fractions.

While there have been many studies demonstrating the efficacy of postoperative WBRT, WBRT with SRS boost and SRS alone for the treatment of brain metastases, little has been published on postoperative HSRT. Postoperative HSRT may improve local control at the site of resection and also help to control new metastases if they are found on follow up surveillance imaging. We initiated this pilot study investigate the efficacy of adjuvant postoperative HSRT for local control of brain metastases because they may:

1) improve patient comfort
2) confer radiobiologic advantage over WBRT for local control
3) give long term survivors less neurocognitive deficits than postoperative WBRT

Our investigation seeks to determine the survival duration, local and distant control of disease and maintenance of overall functional status in patients treated with postoperative CyberKnife HSRT.

Materials and Methods

Patient Selection:

Patients over the age of eighteen with a recently resected brain metastasis and a Karnofsky Performance score of fifty or greater were chosen by an interdisciplinary team of neurosurgeons, radiation oncologists, oncologists and radiation physicists to receive postoperative HSRT to their resection cavity and SRS for up to three additional small brain metastases. While control of the patient's primary cancer was encouraged, it was not required prior to treatment.

Treatment Protocol:

Between September 2003 and March 2007, fifteen patients underwent craniotomy for resection of a large or life threatening solitary brain metastasis at St. Joseph's Medical Center, Bloomington, IL or Bromenn Regional Medical Center, Normal, IL

All patients received their preoperative CT and MR imaging between two weeks and one month of metastasis resection to allow for expected shrinkage of the tumor resection cavity. CyberKnife HSRT was initiated within ten days of imaging to reduce the likelihood of local tumor enlargement between imaging and treatment. Single fraction SRS and five fraction HSRT were delivered by CyberKnife (Accuray, Sunnyvale, CA). In the event that new distant recurrence developed, SRS or HSRT boost was repeated at the site of the new recurrence.

Radiosurgery Technique:

After comfortably positioning the patient supine on the CyberKnife treatment table, a custom Aquaplast (WFR/Aquaplast Corp., Wykoff, NJ) mask was created. While the patient was immobilized in the form-fitting mask, a zero degree gantry 1.25 mm thin slice high-resolution computed tomographic (CT) image set was obtained with a GE Light Speed Scanner (Milwaukee, WI) after intravenous administration of 125 ml of Omnipaque contrast (iohexol, 350 mgI/ml; Nycomed, Inc., Princeton, NJ). Within a few days of the CT study, a gadolinium (Optimark, Tyco, St. Louis, MO) enhanced 1.25 mm thick slice MR image set was generated with a 1.5 Tesla GE LX MR scanner

(Milwaukee, WI) using a weight-based protocol for the gadolinium and 28 cm field of view with zero degree gantry for the MR protocol. The CT and MR image sets were transferred by network to the CyberkKnife treatment planning workstation. Using the CYRIS In-View (Accuray, Sunnyvale, CA) image fusion and contouring station, CT and MR image sets were fused to provide the maximal soft tissue resolution while maintaining the bony skull anatomy information for CyberKnife real-time patient tracking. The CYRIS In-View planning station was also used for treatment planning where tumor and sensitive structures were delineated as well as dosimetry planned. Non-isocentric, inverse planning allowed for maximally conformal radiosurgical dose to the tumor bed and surrounding 2 millimeters of brain tissue while minimizing the dose to surrounding brain tissue. Dose volume histograms were calculated for the targeted tumor bed or metastasis to assess the quality of the treatment plan. For HSRT, total treatment dose for the postoperative tumor bed and unresected regional brain metastases was 2500 cGy. This dose was broken into five fractions of 500 cGy delivered over a maximum of nine days to allow for weekends and holidays.

Follow-up Evaluation:
Patients' neurological condition, Karnofsky scoring and disease progression were assessed in the neurosurgical clinic at one month and three month intervals thereafter. Contrast-enhanced 2 to 3 millimeter slice thickness brain MRI was performed for the three and six-month follow-up visits to search for recurrence. Subsequent clinic follow up and MRI studies were performed every three months or as necessary if recurrences were suspected.

Local tumor control was defined as no residual enhancement in the tumor cavity on follow up imaging. Stable disease was indicated by the lack of any significant increase or decrease in enhancing tumor volume (>25%). Distant tumor control was defined by lack of new enhancing brain tumor lesions on follow up imaging. Freedom from local or distant recurrence was calculated from the date of the first fraction of HSRT to the date that a local or distant recurrence was detected on MR imaging; neither calculation was confounded by the effects of new treatment or retreatment. Radiation injury was defined as new MR T 2 weighted hyperintensity in the area of the brain receiving SRS or HSRT.

Statistical Analysis:
The reference point for survival was the date of SRS or the first fraction of HSRT. Endpoints were death and date of detected tumor progression. Actuarial length of survival was estimated using the Kaplan-Meier method. Correlation coefficients were calculated for KPS at the time of HSRT or SRS and length of survival as well as presence of extracranial disease control and survival.

Results:

Patient Characteristics:

All patients in this study had a single brain metastasis resected followed by HSRT to the tumor resection cavity. There were six women and nine men with ages ranging from 45 to 81 years (median 62). Karnofsky Performance Scale score (KPS) at the time of HSRT ranged from 50 to 90 with the median KPS of 80. Ten of the fifteen patients treated had their primary tumor controlled at the time of HSRT. One patient developed a distant metastasis during follow up that was not treated and caused death due to intracranial progression. Patient characteristics, tumor histology and volume of tumor cavity treated are shown in Table 1.

Pt. #	Age / sex	KPS During SRS / HSRT	Solitary Lesion	Control of Extracranial Disease	Primary Histology	Treatment Volume
1	52 M	70	yes	No	NSCLC	19472mm^3
2	64 F	90	yes	Yes	NSCLC	11359mm^3
3	62 F	70	yes	No	Endometrial carcinoma	25236mm^3
4	45 M	80	yes	Yes	NSCLC	12198mm^3
5	56 M	80	yes	Yes	NSCLC	18365mm^3
6	58 M	50	yes	Yes	NSCLC	32783mm^3
7	60 M	80	no	No	Renal cell CA	18535 mm^3
8	51 M	60	yes	Yes	NSCLC	22890 mm^3
9	80 F	80	yes	Yes	NSCLC	35840 mm^3
10	77 F	80	yes	Yes	NSCLC	30200 mm^3
11	58 M	80	yes	Yes	NSCLC	17345 mm^3
12	55 F	90	yes	Yes	Ovarian CA	28325 mm^3
13	81 F	60	yes	No	NSCLC	22750 mm^3
14	62 M	70	yes	Yes	NSCLC	17050 mm^3
15	72 M	60	no	No	NSCLC	28690 mm^3

Table 1: Patient treatment data

Survival: All patients have been followed from the time of their single metastasis resection until their death or the month this pilot study was completed (March 2007). Median survival after HSRT was 5 months. At the time of this analysis six of the fifteen study patients are still living independently. One patient died of intracranial disease progression while eight others died a few months after treatment from progression of their primary cancer. One patient died from unrelated Blastomycosis and hepatitis B infections. For the fifteen study patients, KPS at the time of the HSRT or SRS had a correlation of .59 with survival. Control of extracranial cancer had an even higher correlation of .71 with survival. See chart 1 for Kaplan-Meier survival curve for the six patients in this study.

Freedom From Progression of Intracranial Disease:
Local control of disease was 93.3% for the fifteen patients studied. One of these patients developed a distant metastasis that was decided by the patient not to treat and he subsequently died from progression of his new metastasis. This patient's distant metastasis was detected 3 months after HSRT. Freedom form local progression was 93.3%. Two patients died two months after HSRT and did not live long enough to have follow up brain imaging. Their neurological symptoms at 6 weeks follow up had not worsened after HSRT while their NSCLC primary disease did. These patients were presumed to not have local progression.

Pt. #	**Local / Distant Progression**	**Last Follow up KPS**	**Length of Survival**	**Cause of Death**	**Edema or Radionecrosis**
1	No	50	3 months	Extracranial disease progression	No
2	No	90	8 months+	living	No
3	No	70	2 months	Extracranial progression	No
4	No	90	8 months +	living	No
5	No	50	4 months	Fungal infection (not intra or extracranial progression)	No
6	Distant	40	4 months	Intracranial progression	Edema improved with steroids
7	No	70	5 months	Extracranial progression	No
8	No	60	2 months	Extracranial progression	No
9	No	60	7 months +	living	No
10	Local	60	5 months	Extracranial progression	Yes
11	No	70	11 months	living	No

			+		
12	No	80	18 months+	living	No
13	No	50	3 months	Extracranial progression	No
14	No	60	9 months +	living	No
15	No	60	5 months	Extracranial progression	No

Table 2: Patient Follow up data showing local and distant progression, Karnofsky score on last follow up, cause of death if death occurred and whether edema or radionecrosis was detected on follow up imaging

Treatment Complications:
There was no perioperative mortality with these fifteen patients. Two patients required steroids to reduce edema in the region of HSRT treatment volume. One patient needed steroids for his distant metastasis. This patient (#6) also had neurocognitive deficits that progressed after HSRT.

Discussion:
Radiosurgery or hypofractionated stereotactic radiotherapy to the resected tumor bed can reduce the likelihood of local recurrence and thereby reduce the morbidity and mortality caused by local tumor progression. While our pilot study of fifteen patients had a median follow up of only 5 months due to high mortality from extracranial causes, we do note that there was only one local recurrence in the study patients. We believe this was due to good surgical resection of the metastases as well as the focused tumoricidal HSRT delivered to the tumor bed.

Patchell performed a prospective, randomized trial of surgery alone versus surgery followed by WBRT in 95 patients with single brain metastases[28]. That study demonstrated 70% recurrence in the patients receiving surgical resection alone for their single metastasis compared to 18% recurrence in those randomized to surgical resection followed by WBRT. Postoperative WBRT reduced local progression from 46% to 10% and distant progression form 44% to 14%. We await data on the local and distant control rates for postoperative stereotactic radiosurgery advocated by researchers at the University of Pittsburgh[29]. Hasegawa et al. treated 172 brain metastases patients with SRS alone for a median survival of 8 months with two-year local and distant control rates of 75% and 41% respectively[30].

The survival of our patients in this pilot study reflects our selection criteria allowing treatment of patients without systemic disease control and KPS as low as 50. Our willingness to treat postoperative patients with radiosurgery or HSRT reflected our intent to minimize the likelihood of local recurrence and radiation injury from WBRT. For patients in this study survival was correlated with higher KPS at the time of HSRT and the presence of extracranial cancer control. These correlations would have been stronger if we had more study patients to reduce the effect of patient #5 dieing of a fulminant Blastomycosis infection.

Using recursive partitioning analysis, (RPA) Gaspar and colleagues analyzed prognostic factors for survival after surgical resection of single brain metastasis followed by WBRT and placed patients into three categories according to their preoperative status[31]. In our study of fifteen patients, eight fit into RPA class 1 (age < 65, controlled systemic cancer and KPS greater than or equal to 70), four into RPA class 3 (KPS less than 70), and three in RPA class 2 (those patients not fitting into RPA 1 or 3 classes). Gaspar et al. found RPA class 1 patients treated with surgery plus WBRT have an average survival of 7.1 months while those in RPA class 2 and 3 have an average of 4.2 and 2.3 months respectively. While not statistically significant due to small sampling size, the length of survival seen in our study patients appears to be consistent with that of patients receiving postoperative WBRT. Six of our RPA class 1 patients are still alive while one died of an unrelated Blastomycosis infection at 4 months.

The rate of acute or late complications due to treatment of brain metastases with single fraction radiosurgery has been reported to range from 4.6%-14%[32,33]. Fractionation of WBRT reduces the early complications seen in SRS, however neurocognitive decline in long term survivors has been documented[34,35]. The one patient in our study who developed edema in the area of his tumor bed received 36 Gy of WBRT seven months prior to HSRT. The combination of WBRT plus HSRT to the tumor bed was the likely cause of this patient's vasogenic edema. The high cumulative dose of radiation to the tumor bed could have overwhelmed the normal brain's reparative mechanisms. The edema in the area of the HSRT field was not likely to be due to recurrence as there was minimal enhancement in the resection cavity.

We look forward to enrolling more patients with longer follow up to develop a better understanding of the rate of local and distant recurrence after postoperative HSRT or SRS. More enrollees would give us data to accurately determine the impact of initial KPS and extracranial disease control on survival. Radiation injury was seen in only one of our patients treated with WBRT 7 months prior to surgery and HSRT. More patients and long-term survivors may add depth to our understanding of the incidence of radiation injury in patients treated with HSRT postoperatively. While following KPS is commonly

used in the radiotherapy literature and sheds light on the patient's overall functional status, perhaps a more comprehensive battery of neurological testing taken initially and at follow up could add to our understanding of preservation of neurological function in patients receiving postoperative HSRT.

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LEOPARD Syndrome and Chiari Type I Malformation: A Case Report and Review of the Literature

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Abstract

We present a 31 year-old male with a Chiari Type I Malformation (CMI) occurring in conjunction with LEOPARD Syndrome. He presented with severe dysphagia requiring placement of a percutaneous endoscopic gastrostomy (PEG) tube. Work-up included magnetic resonance imaging (MRI) of the brain and cervical spine which revealed an extensive cervical syringomyelia. The patient underwent a suboccipital craniectomy with C1 laminectomy and duraplasty. His symptoms quickly resolved and his PEG tube was removed. The occurrence of a CMI with LEOPARD syndrome has only been reported once, whereas CMI and Noonan syndrome have been linked in several cases[2, 10]. The similarity between LEOPARD and Noonan syndromes has been reported and many propose they represent two entities along a spectrum[15]. In light of this spectrum, we propose that CMI should be considered in all patients presenting with LEOPARD syndrome.

Key words: LEOPARD syndrome, Noonan syndrome, Chiari type I malformation (CMI), Dysphagia, Syringomyelia, Percutaneous Endoscopic Gastrostomy (PEG) tube

Introduction

LEOPARD syndrome is a rare and complex dysmorphogenetic disorder with variable penetrance and expressivity. Gorlin and colleagues introduced the acronym LEOPARD in 1969 as a way to recognize the primary features of the disorder: (L) Lentigines, (E) Electrocardiac conduction defects, (O) Ocular hypertelorism, (P) Pulmonary stenosis, (A) Abnormalities of genitalia, (R) Retardation of growth, and (D) Deafness[7, 13]. The diagnosis does not require identification of all these features and numerous additional findings have been described, including several skeletal and neurologic abnormalities (Table1). Chiari Type I Malformation (CMI) in association with LEOPARD syndrome has been reported once[2]. Here we report a second case and based on literature review, propose the inclusion of CMI as an associated abnormality of LEOPARD syndrome and related disorder Noonan syndrome.

Clinical History

History: A 31-year-old male previously diagnosed with LEOPARD syndrome presented with a six month history of progressive dysphagia. During his most recent admission he was unable to swallow liquids or solids. He denied neurological complaints such as numbness, weakness or bowel and bladder dysfunction. Additional history revealed he has one functioning kidney and

multiple lentigines over his body consistent with his diagnosis of LEOPARD syndrome. Family history was unremarkable.

Physical exam: On neurologic examination the patient appeared well and in no apparent distress. He was alert and oriented with intact language. Evidence of disconjugate nystagmus was noted bilaterally. However, the remainder of his cranial nerve, motor, sensory and cerebellar examinations were unremarkable. Further physical examination revealed the patient was of short stature with low set ears, multiple lentigines and a misshapen hand.

Management: Initial medical management included a work up for aspiration pneumonia and dysphagia. Computed tomography (CT) of the abdomen revealed a nonvisualized right kidney and the patient's initial swallow evaluation showed general pharyngeal weakness with near absent epiglottic movement. This was followed by a fiberoptic rhino-laryngoscopy revealing a narrow epiglottis, but no clear etiology of his dysphagia. At this point neurologic consultation was pursued and additional studies included a Tensilon test and evoked potentials which were unremarkable. Magnetic resonance imaging (MRI) of the brain and cervical spine were performed revealing a CMI along with extensive syringomyelia (Figure 1). Due to the patient's profound dysphagia, it was elected to proceed with placement of a percutaneous endoscopic gastrostomy (PEG) tube. A neurosurgical evaluation was also requested and a suboccipital craniectomy, C1 laminectomy and duraplasty were performed in an attempt to alleviate the patient's dysphagia.

Postoperative course: Postoperative day one, the patient was able to swallow and tolerate sips of water. A formal swallow evaluation on postoperative day three demonstrated normal oral and pharyngeal phases. The patient was discharged postoperative day four with resolution of his dysphagia. Two weeks following discharge his PEG tube was removed and at six months the patient remained well without evidence of dysphagia.
A follow-up MRI six months post-op was performed secondary to complaints of headache, which revealed a persistent of syrinx (Figure 2). Due to the clinical findings and persistent syrinx, the patient returned to the operating room for an exploration of the previously performed posterior fossa decompression. A fibrous band of tissue was found to be indenting the tonsil which is believed to have developed after the first surgery. This adhesion was released and the duraplasty was revised. Postoperatively, patient continues to do well without complaints of headache or dysphagia. Final imaging, eight months following the revision procedure, shows resolution of the syrinx as well as complete decompression (Figure 3).

Discussion

LEOPARD syndrome is a rare and complex dysmorphogenetic disorder. Gorlin and colleagues introduced the acronym LEOPARD in 1969 as a way to recognize the primary features of the disorder: (L) Lentigines, (E) Electrocardiac conduction defects, (O) Ocular hypertelorism, (P)

Pulmonary stenosis, (A) Abnormalities of genitalia, (R) Retardation of growth, and (D) Deafness[7, 13]. LEOPARD syndrome has little epidemiologic data secondary to the rarity of the disorder. It is believed to be autosomal dominant with variable penetrance and expressivity, which makes the diagnosis difficult[6]. The minimum criteria for diagnosis proposed by Voron et al in 1976 include: multiple lentigines (Figure 4) and features of at least two other categories (other cutaneous abnormalities, structural or electrocardiographic cardiac abnormalities, genitourinary abnormalities, endocrine abnormalities, neurologic defects, cephalofacial dysmorphism, short stature and skeletal abnormalities). Additionally, the diagnosis can be supported without lentigines if an immediate relative is diagnosed with LEOPARD syndrome and the patient has three of the previously described features. Table I describes the associated abnormalities seen in LEOPARD syndrome. The pathophysiology of LEOPARD syndrome remains speculative. The cutaneous and neurologic features are thought to arise from mutations in neural crest stem cells, whereas skeletal abnormalities cannot be explained by the same mechanism due to their mesodermal origin. Some theorize that gene products from mutated neuroectodermal stem cells may interact with cells of mesodermal origin giving rise to the observed skeletal abnormalities[22].

A disorder that shares many features with LEOPARD syndrome is Noonan syndrome. Characteristic features include hypertelorism, congenital heart defects and short stature. Additionally, neurologic, genitourinary, skin and skeletal abnormalities may be present[14]. Holder-Espinasse et al, reported on four cases of CMI in association with Noonan syndrome and argue it should be considered part of the disorder[10].

The syndrome was initially described as a unique disorder in 1963 by Noonan and Ehmke[20]. These patients were originally thought to represent a form of Turner syndrome due to many similar features, however the distinction was made based on a normal karyotype seen in Noonan syndrome[14]. Noonan syndrome may be either sporadic or autosomal dominant with an incidence between 1:1000 and 1:2500[15, 20]. Like LEOPARD syndrome, the diagnosis is based primarily on clinical features[20]. As alluded to earlier, the differentiation between Noonan and LEOPARD syndrome is difficult as there are many overlapping qualities (Table I and II). Many believe that lentigines and deafness distinguish LEOPARD from Noonan syndrome[6]. However, lentigines have been reported in up to three percent of patients with Noonan syndrome[11, 21]. Additionally, cases of lentiginosis sine lentigines have been described in families with LEOPARD syndrome. Therefore some feel the two conditions may be allelic[6]. Interestingly, several studies have linked a missense mutation in the PTPN11 gene to Noonan syndrome in 40-50% of the cases[20]. Missense mutations in the PTPN11 gene have been demonstrated in LEOPARD syndrome patients as well[15, 20].

Chiari malformations describe hindbrain anomalies with three types being classically described. Type I malformations have caudal herniation of the cerebellar tonsils through the foramen

magnum. Type II malformations have caudal herniation of the cerebellar vermis, brainstem, and fourth ventricle, along with myelomeningocele and intracranial anomalies such as hydrocephalus. Type III malformation consists of a posterior fossa encephalocele. Cerebellar aplasia or hypoplasia with aplasia of the tentorium cerebelli has been referred to as a Chiari Type IV malformation. However, herniation is absent and this is no longer considered a Chiari malformation[5, 18].

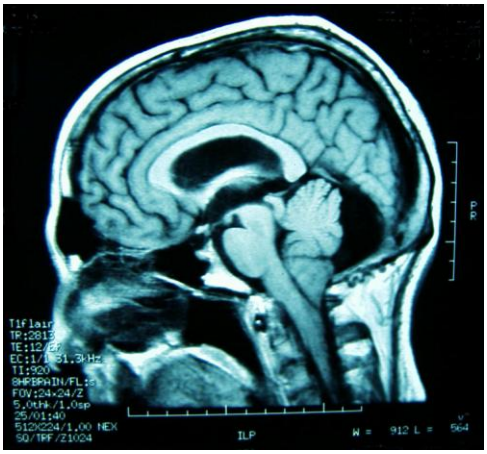
In the past, Chiari malformations I to III were considered a pathological continuum of increasing hindbrain abnormalities. However, evidence is accumulating that CMI is likely of different etiology than types II and III[16]. Although pathogenesis of Chiari malformations has been disputed with no universally accepted theory, the predominant theory accepted by most researchers rests on the thought that CMI represents a disorder of the mesoderm[4, 16-18]. Morphometric anatomic studies have shown that an underdeveloped posterior fossa leads to overcrowding of the cerebellum. This leads to abnormal CSF fluid dynamics as demonstrated by quantitative CINE-mode MRI that is thought to result in tonsillar herniation and formation of a syrinx [3, 4, 16, 17].

The symptomatology of CMI is broad and can be placed into six categories: 1) constitutional symptoms- headache and neck pain, 2) ocular disturbances, 3) neuro-otological disturbances, 4) posterior fossa disturbances, 5) spinal cord disturbances, and 6) MRI abnormalities (Table III). The most common presenting symptom is headaches and/or cervical pain. These headaches classically worsen with any activity that increases intracranial pressures, such as a Valsalva maneuvar[8]. Dysphagia as the sole symptom of CMI occurs rarely. However, several case reports describe patients undergoing extensive work-up and interventions for dysphagia before a neurologic etiology is considered[1, 9, 19].

Conclusion

CMI in association with LEOPARD syndrome has been reported once along with four cases associated with Noonan syndrome[2, 10]. LEOPARD syndrome and Noonan syndrome seem to share a missense mutation in some patients, and have been described by some as allelic[6]. As more information is gained by genetic analysis, the relationship of these disorders will likely be further defined. However, at this time evidence suggests that LEOPARD-Noonan represent two syndromes along a spectrum[15]. There are clear skeletal/mesodermal abnormalities common to both disorders and most experts agree that CMI represents a disorder of the mesoderm[4, 16, 17]. In light of this evidence and the six cases reported to date, we propose that CMI should be considered a diagnostic feature of LEOPARD-Noonan syndromes. Additionally, early imaging in the setting of neurologic criteria, including dysphagia, with LEOPARD-Noonan syndrome patients is recommended.

Figure 1: (a) Preoperative sagittal T1-weighted MRI of brain and (b) sagittal T2-weighted MRI of cervical spine. Revealing compressed, downward herniation of the cerebellar tonsils consistent with a CMI. A syrnix as well as a mega cisterna magna are present.



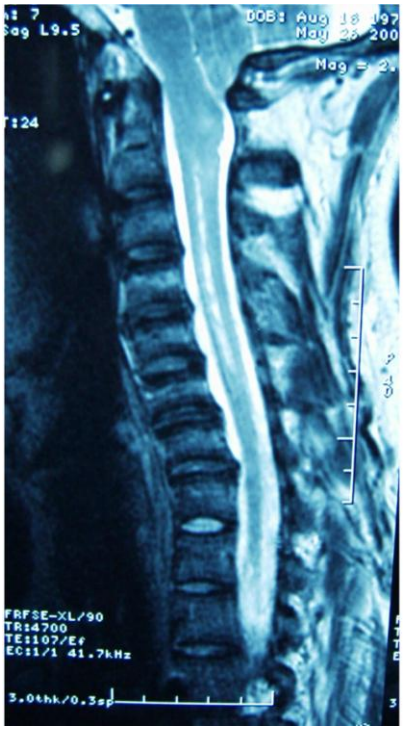
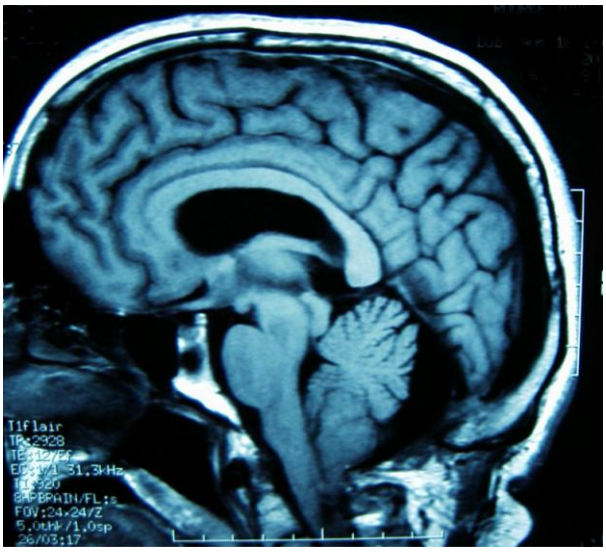


Figure 2: (a) Sagittal T1-weighted MRI of brain and (b) sagittal T2-weighted MRI of cervical spine. Six months status post suboccipital decompressive craniectomy and C1 laminectomy. Revealing decompressed cerebellar tonsils and mega cisterna magna.



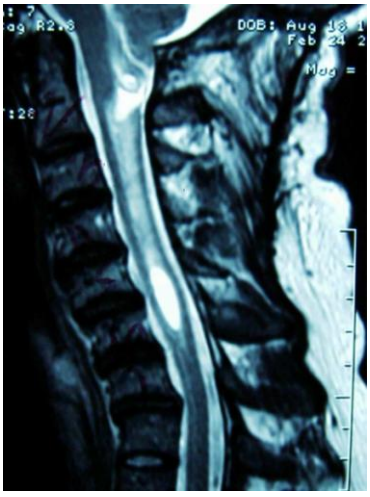


Figure 3: (a) Sagittal T1-weighted MRI of cervical spine. Eight months status post revision suboccipital decompressive craniectomy and C1 laminectomy. Revealing decompressed cerebellar tonsils and mega cisterna magna, as well as resolution of syrinx.

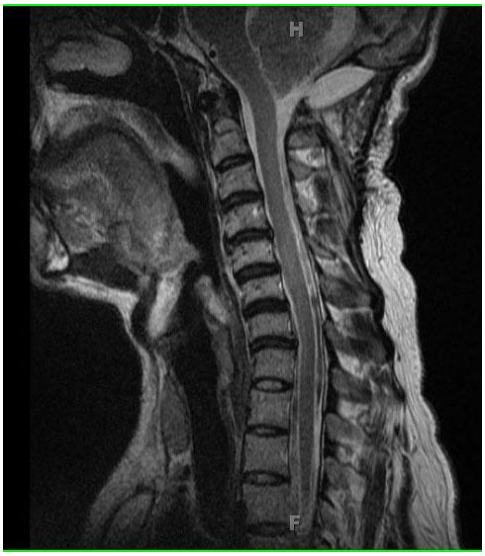


Figure 4: 31 Year-old male with LEOPARD syndrome and a CMI.

Note the multiple lentigines. The patient was also of short stature, had a misshapen hand, low set ears and one functioning kidney.

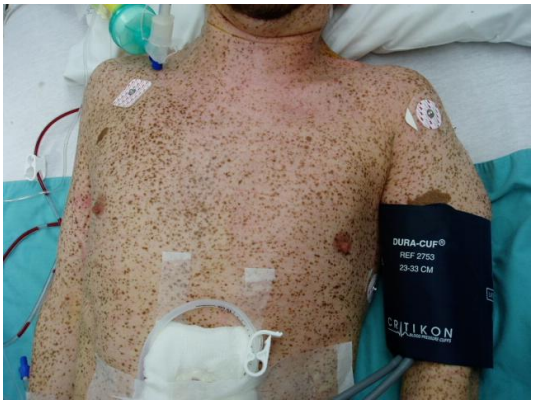


Table I LEOPARD Syndrome [2, 12, 22]

Cutaneous	Lentigines
	Axillary freckling
	Café au lait spots
	Localized hypopigmentation
	Onychodystrophy
	Interdigital webs
	Hyperelastic skin
Cardiac	EKG abnormalities
	Pulmonary stenosis
	Hypertrophic cardiomyopathy
Ocular	Hypertelorism
	Bilateral ptosis
	Retinal pigmentation
	Epicanthial folds
	Colobomas of iris, retina, choroid
Skeletal	Short stature
	Pectus excavatum/carinatum
	Kyphoscoliosis
	Winging of scapula
	Rib anomalies
	Clinodactyly
	Hypermobility of joints
Genitourinary	Hypoplasia/Developmental anomalies
	Aplasia of the kidney
	Cryptorchisim
	Hypospadias
	Delayed puberty
Cephalofacial	Mandibular prognathism
	Broad nasal root
	Dysmorphic skull
	Low-set ears
	Dental abnormalities
Neurologic	Seizures
	Nystagmus
	Hyposmia
	Gertsmann tetrad
	Mental retardation
	Deafness- sensorineural
	Chiari I Malformation

Table II Noonan Syndrome [10, 11, 14, 21]

Cutaneous	Lymphedema
	Prominent pads of fingers and toes (67%)
	Follicular keratosis of face and extensor surfaces (14%)
	Multiple lentigines (3%)
Cardiac	Dysplastic/stenotic pulmonic valve
	Hypertrophic cardiomyopathy
Ocular	Strabismus (48%)
	Hypertelorism
	Ptosis
	Amblyopia (33%)
	Refractive disorders (61%)

	Down-slanting eyes
Skeletal	Short stature (80%)
	Joint laxity (>50%)
	Talipes equinovarus
	Radioulnar synostosis
	Cervical spine fusion
	Pectus carinatum/excavatum
	Scoliosis
	Joint contractures
Genitourinary	Renal abnormalities (not clinically significant) (10%)
	Undescended testes (>50%)
Cephalofacial	Triangular-shaped face
	Low-set ears with thickened helices
	High nasal bridge
	Short webbed neck
Neurologic	Mental retardation
	Hypotonia
	Seizure disorder (13%)
	Peripheral neuropathy
	Sensorineural hearing loss
	Chiari I Malformation
Abdominal	Hepatosplenomegaly (25%)
Other	Bleeding diatheses

Table III Chiari Signs and Symptoms [8]

Symptoms	**Details**
Cranial/Brainstem	
--Headaches	Heavy, severe, suboccipital, posterior with radiation to vertex, common
--Ocular	Eye pressure/pain, photophobia, visual field cuts
--Otoneurological	Dizziness, disequilibrium, vertigo, tinnitus, ear pressure, hearing loss
--Posterior fossa	Dysphagia, hoarseness, hiccups, facial pain, facial numbness, syncope, aspiration, imbalance, clumsiness,
Spinal Cord	
--Motor	Weakness, atrophy, spasticity, incontinence
--Sensory	Tingling, numbness, pain, burning sensation, nonradicular numbness/pain in shoulders and limbs
--Other	Decreased reflexes
Signs	
Cranial/Brainstem	
--Ocular	Decreased visual acuity, visual field cuts, extraocular muscle paresis
--Otoneurological	Nystagmus, hearing loss
--Posterior fossa	Impaired gag reflex (CN IX-X), CN V sensory loss, vocal cord paresis, apnea, ataxia, dysmetria
Spinal Cord	
--Motor	Weakness, hemiparesis, quadriparesis, decreased tone, atrophy
--Sensory	Dissociated sensory loss (loss of pain and temperature, sparing of light touch and proprioception), paresthesias, hyperesthesia, analgesia, dysesthesia, poor position sense, impaired temperature, Charcot's joints
--Other	Hyperreflexia/hyporeflexia, clonus, Babinski sign
Other	
--Miscellaneous	Scoliosis, oscilloscopia, associated skull base anomaly, Klippel-Feil , hydrocephalus, axial skeletal pain, fatigue

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Does Early Administration of Intravenous Magnesium Sulfate after Acute Moderate and Severe Closed Head Injury Improve Neurological Outcome?

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Abstract

Object: Administration of intravenous magnesium salts has been shown to improve neurological outcome in rats using traumatic brain injury (TBI) models. This magnesium had attenuated the secondary injury cascade that occurs within minutes after TBI. Secondary injury events result ultimately in impaired cellular metabolism. Free intracellular magnesium after TBI falls after injury and continues to for several days. As the free (ionized) magnesium is felt to be the active portion of the body's magnesium, our goal was to maintain this in a therapeutic range in the treatment group and then compare this to the total magnesium levels in placebo patients and ascertain whether there was any difference in neurologic outcome. To date, there has not been a prospective study in humans using intravenous magnesium in the early post closed head injury period correlating its effect on neurologic outcome. The aim of this study is to see if the use of IV magnesium sulfate within six hours of closed head injury (CHI) and its continued use for five days will result in better neurologic outcomes in humans sustaining moderate and severe CHI.

Methods: A prospective randomized placebo-controlled single blinded pilot study was performed to examine if early IV magnesium sulfate administration would improve neurologic outcome in patients sustaining moderate and severe CHI. Patients were considered eligible if they were between 14-75 years old, sustained moderate or severe closed head injury (Glasgow Coma Scale Score 3-12) and were able to be enrolled in the study within six hours of the head injury. Ten patients (5 female and 5 male) were enrolled. Five received treatment with magnesium and 5 with placebo. Treatment or placebo was continued for 5 days in each of the patients. Serum *free* magnesium levels were maintained between 0.67-1.2mmol/L in the treatment group over a five day period. In the placebo group, total serum magnesium levels were treated to maintain levels 2-2.5mg/dl as we have been doing routinely after moderate and severe closed head injury.

Results: The mean age for the females was 33 and for males, 24. The mean GCS score in treatment group was 6 and 5 in the placebo group. None of the patients required surgical evacuation of hematoma or craniectomy for ICP control. All patients underwent ICP monitoring using a ventricular catheter. Serum total and free magnesium levels were monitored three times daily in all patients using the NOVA CCx analyzer. This machine gave results of ionized and serum magnesium within 5 minutes. All patients received standard ICP management according to the Guidelines for the management of Severe Traumatic Brain Injury, 3rd edition. Systemic injuries as a result of the trauma were comparable in both groups and had no direct impact on ICP control or outcome. Mean GOS scores were 3.6 and 3.2 in the treatment and placebo groups respectively ($p= 0.75$) at 3 and 9 months after injury. No adverse effects occurred as a result of magnesium treatment.

Conclusion: High dose intravenous magnesium sulfate administration after moderate and severe closed head injury appeared to be safe in our 10 patients. Ionized serum

magnesium levels were easily measured and maintained in the treatment group. There was a trend toward improved GOS scores in treated patients but it was not statistically significant. We will need to enroll a significantly larger volume of patients in a future study to see if this trend persists.

Key Words: Ionized magnesium, closed head injury, magnesium sulfate, excitatory amino acids.

Introduction

Traumatic brain injury affects tens of thousands of people each year, the majority of which are between 15-40 years old. These patient and their families incur tremendous hospital and rehabilitative costs. Some of the neuronal damage following is caused by primary or mechanical injury that occurs at the time of the traumatic event. However, significant evidence suggests that a considerable amount of neurologic damage is the result of secondary injury involving the release of excessive excitatory amino acids (glutamate and aspartate mostly) leading to a cascade of cerebral cellular swelling and decreased brain energy metabolism. These events are set in motion minutes after closed head injury and can persist for days to weeks. Patients with severe (GCS 3-8) and moderate (9-12) closed head injury suffer the worst neurologic sequelae and have overall poorer neurologic outcomes compared to those with mild head injuries. TBI alters the blood brain barrier resulting in disrupted cerebral autoregulation. Magnesium sulfate IV therapy has been shown to attenuate this effect of head injury[5]. Magnesium is essential for normal cellular functions such as cell membrane integrity, cellular respiration, protein synthesis, glucose and energy metabolism and maintenance of normal sodium and potassium gradients.[19] Magnesium is also a competitive inhibitor of NMDA gated channels in the brain and spinal cord. As an inhibitor of the NMDA channel, magnesium can inhibit or attenuate the unregulated influx of calcium that occurs after head injury thereby minimizing damage to neurons.

A decline in brain and serum free magnesium concentration has been widely reported in experimental animal traumatic brain injury (TBI) models involving focal and diffuse brain injury.[1,7,8] Initiation of intravenous magnesium salts has been shown to significantly improve neuromotor and cognitive outcomes when administered within 6-8 hours after experimental injury.[8,9] Depletion of serum and brain ionized magnesium has also been reported in humans sustaining closed head injury. Research shows that the physiologically active form of magnesium is the free or ionized form and that the total Mg levels were not predictive of functional stores. Magnesium levels begin to drop within minutes after injury and continue to do so for 4-5 days. Since the mid to late 1990's there has been made available laboratory devices that can accurately measure free serum and brain magnesium levels and report results within minutes. Intravenous magnesium therapy has been used safely and in high doses in patients with eclampsia and preeclampsia. Magnesium sulfate has also been used in patients with aneurysmal SAH to help prevent and improve cerebral vasospasm and improve neurological outcome.[2,16,18] To date there has not been a prospective randomized study in humans using intravenous magnesium in closed head injured patients relating to neurologic outcome. Our goal was

to safely administer high dose magnesium sulfate to patients and to show that there is potential for IV magnesium sulfate to improve overall neurologic outcome.

Clinical Material and Methods

A prospective randomized placebo-controlled patient blinded study was performed to evaluate if intravenous magnesium sulfate was safe to administer in high doses and to determine if it would improve neurologic outcome after severe and moderate closed head injury. The study was done at a single institution and was approved by the hospital Institutional Review Board Committee. Patients included were 14-75 years old and sustained moderate or severe closed head injury and arrived to the hospital within 6 hours from injury. Exclusionary criteria consisted of patients known to have any condition that would predispose to adverse affects of magnesium therapy such as congestive heart failure, renal failure with a creatinine clearance less than 30cc/min, serum potassium >5.5 and systolic blood pressure less than 90mmHg that is unresponsive to fluid resuscitation or vasopressors. Also any patient known to be taking chronic diuretics or on digitalis at the time of the injury were excluded because these medications can alter the free and total serum magnesium levels. Consent was obtained by patient's next of kin prior to the initiation of any treatment.

A total of 10 patients were enrolled in this study. Five (3 males and 2 females) were randomized to receive IV MgSO4 and 5(3 males and 2 females) to receive IV normal saline placebo. Mean ages for the treatment and placebo groups were 24 and 33, respectively. Mean initial GCS for the treatment and placebo groups were 6 and 5 respectively. Those treated with MgSO4 were given an initial 2 grams infusion over 2 hours after obtaining initial free and total serum magnesium levels. The MgSO4 infusion was continued at 1-2 grams/hr in normal saline and adjusted based on every 8 hour free magnesium levels. Our goal free magnesium level was 0.67-1.2mmol/L (normal 0.53-.67). The infusion was adjusted up or down by 0.5-1.0 grams/hr. Patients received the treatment protocol for 5 days. Patients in the control received 250cc of IV normal saline over 2 hours once daily followed by a continuous infusion of normal saline of 30cc/hr for 5 days.

All patients were treated in the intensive care unit and intubated. All were treated with ventriculostomies and all were treated equally in regards to head injury and ICP management according to the Brain Trauma Foundation Guidelines, 3d edition. Daily neurological exams were performed by the neurosurgical team any other injuries not related to the head were managed by the trauma team. Enteral nutrition was started in all patients within 2-3 days. All patients received prophylactic phenytoin on admission with one gram loading dose followed by 100mg three times daily. Routine ICU monitoring including cardiorespiratory, hemodynamic and input and output measurements were obtained. Continuous ICP monitoring was done and ICP greater than 15-20cmH20 that was sustained more than 15 minutes was treated according to the Brain Trauma Foundation Guidelines. Initial non contrast CT scan of the brain was performed in the emergency room and then again the morning following the injury in all patients. Subsequent CT scans were dictated by clinical need based on any changes in neurological condition or intracranial pressure control.

All patients had serum total and free magnesium levels checked every 8 hours for 5 days. Daily serum chemistries, calcium, phosphorus, CBC and arterial blood gases were obtained. After transfer from the ICU, patients continued with daily neurological exams and involvement with physical, occupational and speech therapy as appropriate. Most patients went on to inpatient rehabilitation and 3 and 9 month GOS score was assigned. GOS score of 5 = good recovery, 4=independent with moderate disability, 3= severe disability, dependent, 2=persistent vegetative state, 1=death. GOS scores of 4 or 5 were considered good and those with 2 or 3 as poor.

Results

Patient characteristics were similar except for slight older age of control group (33 versus 24). Some of the patient data can be seen in Table 1. Seven of ten patients (4 in treatment group and 3 in control group) had small (<1cm) bilateral cerebral contusions. Of the 4 in the treatment group 2 had less than 5mm right SDH that did not require surgical evacuation. One of the 3 in the control group had ~ 8mm Lt SDH without any significant shift and controlled ICP and did not require surgery. The one remaining treatment group patient had no acute blood on CT scanning but later had MRI evidence of diffuse axonal injury and clinically GCS 5 for first 3 days. The last 2 control patients had a variety of traumatic high convexity SAH and small unilateral punctuate hemorrhages consistent with diffuse axonal injury. No patient required neurosurgical evacuation of any hemorrhage and no one underwent craniectomy for uncontrolled ICP. Overall 4 patients (1 in treatment and 3 in control) had long bone fractures (closed) and they did not require acute operative fixation. One patient in each group was felt to develop aspiration pneumonia, however no hypoxia or hypoxemia resulted and they were treated effectively. Pulmonary contusions occurred in 3 patients (2 control and 1 treatment group). One patient in control group had moderate to severe pulmonary contusions and experienced some arterial oxygen desaturations for several minutes into low to mid 80's. This patient had concomitant ICP problems during this time and subsequent CT scanning revealed no change in the punctuate contusions but a development of diffuse cerebral edema. With prolonged ICP management including pentobarbital coma for several days, this patient stabilized, however his best outcome was GOS score of 2. All ventriculostomies in the treatment group were out by day 5 and in the placebo group by day 6, except for the patient who required pentobarbital coma. Average initial ICP in the treatment and placebo groups was 13 and 15 cmH20, respectively. Over the first 5 days of ICP monitoring the mean ICP for the treatment and placebo groups was 15 and 21, respectively (Table 1). No patient required any other operative intervention during their stay. No patients developed post traumatic hydrocephalus.

Normal values for free serum magnesium are between 0.53-0.67. All except one patient had initial free magnesium levels below 0.53 (0.39-0.57). Initial total serum Mg++ levels for all ranged from 1.6-2.5. We were able to maintain our goal of free Mg++ levels in the treatment group of 0.67-1.2 (mean=0.8) in all patients with adjustments in magnesium infusions. The free Mg++ levels in the control group that were monitored for comparison remained low (0.39-0.58) with a mean of 0.49, despite us keeping the total serum

magnesium in these patients 2-2.5md/dl. This suggested that total serum Mg++ was not predictive of free magnesium stores. Magnesium sulfate therapy did not result in any episodes of lowered blood pressure below 90mmHg systolic at any time. Mean infusion rate was 1 g/hr +/_ 0.5 g/hr. No adverse effects of Mg++ occurred. All patients had been seen in follow up at 3 and 9 months and evaluated using the GOS. Upon leaving the acute hospital care setting, 2 patients in the treatment group were functioning independently and went home with supervision, while the remaining three went to acute rehabilitation. From the hospital the placebo patients were discharged home (one), 2 to acute rehab, 1 to subacute rehab and eventually to acute rehab after 3 weeks, and one went to a long term nursing facility where he remained even at 9 month follow up. At 3 month follow up there were to treatment group patients that went home from rehab with their primary difficulties being short tem memory difficulty and problems concentrating on tasks for more than 5 minutes. In the placebo group at 3 months the one patient in subacute rehab made it to acute rehab and had significant word finding difficulty (the patient with the left SDH) and a very mild right hemiparesis. The other patients (excluding the nursing home patient in the vegetative state) had cognitive difficulties similar to the treatment group. At 9 month follow up 3 patients in the treatment group had a GOS of 4 or 5 and 2 scored a 3. In the placebo group, 2 patients had GOS score of 4, and 2 with a GOS score of 3. The remaining patient continued to be in vegetative state with a GOS score of 2. In both groups, the patients with GOS scores of 4 or 5 also were those who arrived with higher GCS scores initially. Mean GOS scores for treatment and control groups were 3.6 and 3.2 respectively, (p value of 0.63) however this did not reach statistical significance.

TABLE 1

	Placebo	$MgSO_4$ Group	P-Value
Median Age	32	24	N/A
Initial GCS	5	6	0.82
Average ICP (Over first five days)	10-35cmH_2O (mean=21)	8-22cmH_2O (mean=15)	0.5
GOS Score	Mean=3.2	Mean 3.6	0.63

Discussion

In this small study intravenous magnesium sulfate was used to treat a group of randomized moderate and severe head injured patients. Magnesium sulfate has been shown to improve neuromotor and cognitive outcomes in experimental TBI in rats[6,9-11]. In humans it has been shown that the excessive release of excitatory amino acids after head injury ultimately leads to an early depletion of serum and CSF magnesium,

specifically the free magnesium.[3] Free magnesium remains depleted for up to 4-7 days. In animal studies it was found that the ideal time to initiate IV magnesium therapy was before 6-8hours, with less improvements in outcomes the later magnesium therapy was started. Starting magnesium therapy after 24 hours did not result in any improvement in neurologic outcome. Normal serum ionized magnesium levels are within a very narrow range (0.53-0.67mmol/L).[15] Because ionized Mg++ is continuously depleted over days after the injury we wanted to maintain high normal to slightly supranormal levels of ionized serum Mg++ so that levels would more likely not get below normal during the study. We were able to reach our goal free Mg++ levels with the Mg++ infusions. Interestingly, the free Mg++ in the placebo patients remained either low or low normal despite treating the total serum Mg++ to a level of 2-2.5mg/dl. The total Mg++ may be overestimating the amount of physiologically active Mg++. These findings appear to align with Bareyre where they looked at alterations in total and free Mg++ in TBI in rats and witnessed a normalization of ionized serum Mg++ after IV MgCl2 infusion.[1] Furthermore, in their study the total serum Mg++ remained at normal levels just after the TBI while the free Mg++ was low.

In this study the ICP values averaged over the first 5 days trended lower in the Mg++ treated group even if one factors in for the one patient who developed secondary brain insult from worsening pulmonary contusions, however this difference was not statistically significant. It may be that the magnesium therapy attenuated brain edema by binding to NMDA receptors, minimizing calcium influx and blunting some of the excessive excitatory amino acid load thereby limiting neuronal injury and death. Feldman, showed in anesthetized rats randomized to TBI and sham surgery that rats who were treated with IV Mg++ within one hour of injury had significantly higher specific gravity in contused hemispheres and that brain Mg++ concentrations were significantly higher than untreated rats. They concluded that post injury brain edema is attenuated by early Mg++ therapy.[4]

Although IV MgSO4 has been used safely in high doses in pregnant patients with eclampsia, acute ischemic stroke and aneurismal SAH patients there are some serious side effects that can occur.[16] Hypermagnesemia may cause depressed respiratory function (levels > 14mg/dl), cardiac conduction and contractility defects heart block and cardiac arrest. Another effect of elevated serum magnesium or from Mg++ given to quickly inravenously is hypotension. We did not have any adverse events related to Mg++ treatment.

Conclusion

We noted a trend in better neurologic outcomes in patients receiving Mg++ therapy and noticed that mean ICP during the treatment period was lower in the Mg++ group. These did not reach statistical significance. In addition, for a study of this nature to reach statistical significance we would need almost 200 patients in each group. We do feel we can administer high dose IV MgSO4 safely in patients with moderate and severe CHI and that a future larger study perhaps a multicenter one will be needed to achieve numbers needed to determine if indeed maintaining at least normal serum ionized Mg++ levels will have a direct improvement in neurologic outcome.

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Anterior Cervical Discectomy and Fusion Using Bioabsorbable Polymer Plate in the Treatment of Single-Level Cervical Degenerative and Traumatic Disc Disruption

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Abstract
Study Design. Prospective clinical trial.
Objective. The authors present their initial multicenter experience in the surgical management of single-level degenerative and traumatic disc disruption of the cervical spine with anterior cervical discectomy and fusions (ACDF) using a bioabsorbable polymer plate.
Background Data. The introduction of a radiolucent bioabsorbable polymer plate and screws for ACDF presents a novel opportunity to gain the some of the potential added benefit of stabilization with internal immobilization while possibly reducing some of the long-term complications and imaging artifacts associated with titanium instrumentation. We prospectively analyze 54 patients who were treated at Kaiser Fontana Medical Center, Desert Regional Medical Center, and Riverside County Regional Medical Center with bioabsorbable polymer plate and screws for ACDF surgery.
Methods. Patients were prospectively enrolled. A retrospective review of patients' charts and imaging was performed to determine clinical and radiographic outcome following anterior cervical spine surgery. Specifically, the authors looked at need for additional surgeries, local reaction to bioabsorbable polymer, fusion rate, and complications. Surgeries involved the C3-C4, C4–C5, C5–C6, C6–C7, and/or C7–T1 levels. Cadaveric bone was used in 36 patients, polyetheretherketone (PEEK) cages in 12 patients, and iliac crest autograft in 6 patients. The patients were observed for an average of 12.88 months.
Results. Radiographic fusion was achieved in 98.15% (53 of 54 patients) of the cases at 6 months. One patient had evidence of nonunion on flexion-extension imaging but remains asymptomatic. A different patient had persistence of radicular symptoms but refused further surgery. Two patients developed hoarseness after surgery that resolved by 3 months. There were no clinical signs or symptoms of reaction to the bioabsorbable material.
Conclusions. The rates of fusion following single-level ACDF with internal fixation using bioabsorbable polymer plate and screws in this study match those previously reported in the literature with metallic implants and are superior to noninstrumented fusions. Preliminary results suggest that this newly available technology for anterior fusion may be as effective as traditional titanium plating systems in single-level disease. The bioabsorbable material appears to be well tolerated by patients. A larger, randomized, controlled study is necessary to bring the results to statistical significance.
Key words: Anterior cervical discectomy, bioabsorbable plate, cervical, fusion, polymer.
Introduction

Symptomatic cervical spondylosis is a debilitating condition that commonly occurs in patients after the third decade of life. The complete natural history of symptomatic cervical degenerative disc disease is unknown, but the majority of patients present with symptoms of axial neck pain, radiculopathy and/or myelopathy, or a combination of these symptoms. Although symptomatic cervical spondylosis is not uncommon, the majority of patients respond well to conservative therapies. Patients are often instructed to attempt physical therapy and epidural steroids, maintain ideal body weight, and use adequate pain and anti-inflammatory medications for a period of time. If there is no relief of symptoms with conservative therapy, then surgery can be considered. Anterior cervical discectomy and fusions (ACDF) is the most commonly used surgical approach to relieve cervical radiculopathy and spondylosis. Although the need for plating of single-level surgery remains controversial, it allows patients earlier return to normal activities. Questions of advanced degeneration of adjacent levels have been addressed in the literature at length, as have the rates of successful arthrodesis with plating (1-6).

The current state of art in anterior cervical discectomy and instrumented fusion relies on the use of titanium alloy plates and screws. Although the biocompatibility of titanium and its alloys is superior to many other materials, recent evidence suggests that the mismatch in elastic moduli of the metallic constructs and the vertebral bodies and spinal motion segments causes stress shielding (12). Surgeons and engineers have looked to polylmers as a mean to solve this mismatch in mechanical properties. Typical polymers used in orthodedics, such as polyethylene, elicit a strong immune and inflammatory response and may lead to osteolysis when wear debris is generated (16). Bioabsorbable materials, such as poly-(L-lactide) (PLLA) and polyglycolic acid, which degrade predictably and are removed by normal physiologic functions, present an attractive alternative to polymers currently used in orthopedic applications (13).

The introduction of a radiolucent bioabsorbable polymer plate and screws presents a novel opportunity to gain the some of the potential added benefit of stabilization with internal immobilization while possibly reducing some of the long-term complications and imaging artifacts associated with titanium instrumentation. Also, because the material is fully absorbed, if further surgical intervention is necessary at adjacent levels, the need for removal of the prior instrumentation in future surgeries is eliminated. But before this technology can be fully embraced, the bioabsorbable materials must not only be tolerated well *in vivo* but must provide similar fusion rates to currently available instrumentation.

In this study, the authors present their initial multicenter experience in the surgical management of single-level degenerative and traumatic disc disruption of the cervical spine with anterior cervical discectomy and fusions (ACDF) using a bioabsorbable polymer plate.

Materials and Methods

Between January 2005 and June 2006, 54 consecutive patients underwent ACDF with internal fixation using bioabsorbable polymer plate and screws at the C3-C4, C4–C5, C5–C6, C6–C7, and/or C7–T1 levels. Patient demographics are outlined in Table 1. Twenty-three men and thirty-one women (average age of 50.33 years, range 28-68 years) were prospectively enrolled after receiving institutional review board approval from the respective institutions. The surgeries

were performed at Kaiser Fontana Medical Center, Desert Regional Medical Center, and Riverside County Regional Medical Center. Inclusion criteria were failure of conservative treatment for progressive symptoms of cervical myelopathy, radiculopathy or myeloradiculopathy secondary to a herniated nucleus pulposus or spondylosis corresponding with radiographs and magnetic resonance imaging, adequate mental capacity to provide informed consent, consent given within 4 weeks before surgery, age 18 years or more, ability to return for follow-up assessment, and the completion of all enrollment information. Individuals presenting for surgical treatment of tumors, fractures, infections or for revision surgery were excluded from the study.

In all cases, the patients were brought to the operating room, placed in a supine position and underwent general anesthesia. A standard right-sided anteromedial approach to the cervical spine was performed through a transverse incision in all cases. Distraction of the disc space was obtained by using a pin held distracter. A complete intervertebral discectomy was performed and the cartilaginous end plates were removed with a combination of curettage and a high speed burr. Care was taken to ensure that excessive end plate decortication did not occur. Before graft insertion, graft height was fashioned in every patient to obtain approximately 2mm of disc height distraction to establish proper compressive forces on the graft-end plate interface. After each graft was properly prepared, it was impacted with the cortical surface positioned anteriorly and countersunk 2mm from the anterior vertebral border. A 2-mm bioabsorbable plate (Mystique; Medtronic Sofamor Danek, Memphis, TN) was then molded to the anterior spinal elements and fixed in position with 3.0-mm or 3.5-mm diameter and 11 mm, 13 mm, 15 mm, or 17 mm in length bioabsorbable screws (Figure 1). These plates are constructed from an amorphous 70:30 poly (*l*-lactide-co-*d*, *l*-lactide) polymer and, from a biomechanical standpoint, are nonconstrained. The incision was then closed in layers. There were no notable intraoperative complications. All patients were placed in an Aspen cervical collar postoperatively to be worn at all times except for bathing for 2 months.

Age (yr)	**Sex**	**Level**	**Graft Type**	**Follow-up (months)**	**Complication**
37	F	C5-C6	Allograft	12	None
55	M	C3-C4	Allograft	13.5	None
47	F	C6-C7	PEEK	14	None
42	F	C5-C6	Allograft	12.75	None
58	F	C5-C6	Allograft	12	None
66	F	C4-C5	PEEK	12	None
28	M	C6-C7	Allograft	12.25	None
39	M	C7-T1	Allograft	12.5	None
54	F	C5-C6	PEEK	12.75	Hoarseness
42	M	C3-C4	Allograft	13	None
66	F	C6-C7	Autograft	14.25	None

38	F	C5-C6	Allograft	13	None
51	M	C4-C5	Allograft	13.5	None
49	M	C5-C6	Allograft	12	None
58	M	C5-C6	PEEK	12.5	None
45	F	C6-C7	Allograft	15	None
49	F	C6-C7	Allograft	12	None
29	M	C5-C6	PEEK	12.75	None
55	F	C6-C7	Allograft	12	None
39	F	C5-C6	PEEK	13.25	None
57	F	C6-C7	Allograft	12	None
52	F	C3-C4	Allograft	12.75	None
49	F	C5-C6	Allograft	12	None
47	M	C4-C5	PEEK	13.25	None
42	F	C5-C6	Allograft	13	None
45	M	C5-C6	Allograft	12.75	None
41	F	C5-C6	Allograft	12.5	None
63	M	C4-C5	Allograft	12	None
64	F	C6-C7	PEEK	13	Hoarseness
61	F	C5-C6	Allograft	14.5	None
44	F	C7-T1	Autograft	13.75	None
52	M	C5-C6	Allograft	12	None
57	M	C6-C7	Allograft	12.25	None
68	M	C5-C6	Autograft	13.25	None
48	F	C6-C7	Allograft	15	Radiculopathy
35	F	C4-C5	Allograft	13.75	None
67	F	C5-C6	Autograft	12	None
60	F	C6-C7	Allograft	12	None
57	F	C4-C5	PEEK	12.75	None
49	M	C5-C6	PEEK	12.25	None
33	M	C4-C5	Allograft	13	None
61	F	C5-C6	Allograft	13.5	None
55	M	C5-C6	Allograft	14	None
65	F	C6-C7	PEEK	13.75	Nonunion
44	F	C6-C7	Allograft	12	None
49	M	C3-C4	Allograft	12	None
61	M	C5-C6	Autograft	12.5	None
54	F	C6-C7	Allograft	12.25	None
59	M	C5-C6	PEEK	15	None
47	F	C4-C5	Allograft	13.25	None

39	M	C5-C6	Allograft	13	None
55	M	C4-C5	Allograft	12.75	None
42	F	C5-C6	Allograft	12	None
49	M	C6-C7	Allograft	12.5	None

Table 1. Patient Demographics & Results

A retrospective review of patients' charts and imaging was performed to determine clinical and radiographic outcome following anterior cervical spine surgery. Specifically, the authors looked at need for additional surgeries, local reaction to bioabsorbable polymer, fusion rate, and complications. Cadaveric bone was used in 36 patients, polyetheretherketone (PEEK) cages packed with local bone in 12 patients, and iliac crest autograft in 6 patients (Table 1).

Patients' wounds and vital signs were followed closely during their hospitalization and at routine follow-up visits at 2 weeks, 6 weeks, 3 months, 6 months, and 12 months after surgery for any signs of overlying soft tissue infection or systemic inflammatory response. Patients were also asked to provide subjective evaluations of their ability to swallow or speak and of the adequacy of pain relief following the surgeries. Follow-up imaging with plain radiographs was obtained, whenever possible, in all patients immediately after surgery and at 2 weeks, 6 weeks, 3 months, 6 months, and 12 months after surgery.

Figure 1. Mystique (Medtronic Sofamor Danek) bioabsorbable plate and screws constructed from an amorphous 70:30 poly (*l*-lactide-co-*d*, *l*-lactide) polymer.

Results

Fifty-four patients underwent ACDF with implantation of Mystique bioabsorbable plate (Medtronic Sofamor Danek) (Table 1). The average patient age was 50.33 years (range, 28-68 years). The patients were observed for more than 1 year after surgery (average, 12.88 months; range, 12–15 months). Nineteen of the 54 patients were either present or prior smokers. Successful radiographic fusion was achieved in 98.15% (53 of 54 patients) of the cases at 6 months (Figure 2). Fusion was identified by the absence of motion between the spinous processes on flexion-extension lateral radiographs; the absence of a radiolucent gap between the

graft and host vertebral enplates; and the presence of continuous, bridging, bony trabeculae at the graft-host vertebral endplate junction.

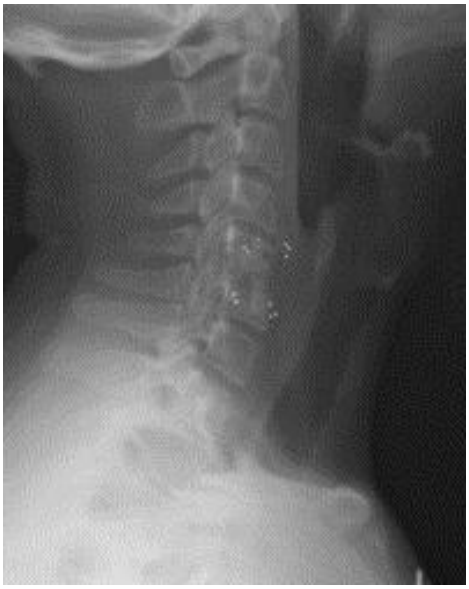

Figure 2. Lateral cervical spine radiograph showing incorporated allograft and cervical plate 6 months after surgery. Radio-opaque markers (appearing as dots) delineate plate and screws.

One patient who smoked cigarettes had evidence of nonunion on flexion-extension imaging but remains asymptomatic. A different patient had persistence of radicular symptoms but refused further surgery. Two patients developed hoarseness after surgery that resolved by 3 months. There were no clinical signs or symptoms of reaction to the bioabsorbable material. There was no incidence of postoperative hematoma, wound infection, or osteomyelitis. All but 1 patient reported symptomatic relief and/or improvement to some degree following surgery.

Discussion

The use of bioabsorbable material has been gaining popularity in many surgical procedures including, recently, spinal surgery. Although this technology is becoming more available to the spine surgeon, it has already been used and examined more extensively in a variety of plastic/reconstructive and orthopedic applications. Extensive series exist in the literature describing the use of bioabsorbable implants for craniofacial and orthopedic repairs (7-12). Eppley *et al* illustrated the effectiveness and safety of similar technology in the repair of 912 pediatric craniofacial deformities (8). All patients followed up to 1 year after surgery had complete absorption of the implants without any instances of infection, overlying soft tissue reactions, or instability, thereby demonstrating the safety of the synthetic material (8).

For the bioabsorbable plate and screws to compete with the currently available metallic instruments, they must prove, at a minimum, to be efficacious and produce similar fusion rates as their titanium counterparts. Numerous sources have demonstrated fusion rates in excess of 90% with internal fixation of single-level ACDFs with metallic plates and screws (1-6). The fusion rate of 98.15% (53 of 54 patients) with a bioabsorbable plate corresponds well with previously

published values. Thus, preliminary results indicate that this system may provide an equivalent value in achieving fusion.

Metallic implants rely on a variety of technical innovations to account for subsidence and continual load sharing over the time required for fusion. Some examples of these designs are the nonlocking, variable angle screw, telescoping plates, and sliding plates and screws systems. Because bioabsorbable plates are slowly absorbed, their strength gradually diminishes over time. The polylactide polymer in the bioabsorbable plates is hydrolyzed into carbon dioxide and water over the course of 2 years (14, 15). At 6 months after implantation, studies report that the plates maintain approximately 90% of initial strength (7). This continues to slowly decrease to 70% after approximately 9 months with complete absorption occurring after 2 years (7, 14, 15). This slow decremental change in plate strength may allow the fusion construct to gradually assume more of the burden of structural support, thus potentially enhancing the rates of fusion while reducing stress shielding (7, 16). The inherent properties of the material provide for subsidence and continual load sharing while maintaining a simple engineering design. The strength of the bioabsorbable plate over time must be sufficient to provide the cervical vertebrae ample opportunity to fuse properly. Bioabsorbable plates appear to confer enough support for the 6 to 12 weeks in which graft-host interface healing begins.

Long-term complications associated with the permanent metallic implants are reduced with the use of the bioabsorbable sheets and screws. Complications from instrumentation are reported to occur in 0% to 14% of instrumentations (2, 4, 6, 17). These can range from screw loosening or back-out, plate migration, or plate and screw breakage and can occur at any stage of the postoperative period. Patients have also reported difficulty with swallowing or foreign body sensations following anterior cervical plating (18). While the authors did not encounter any of these complications during the follow-up period, it is possible that similar short- and intermediate-term complications can still occur with bioabsorbable sheets and screws. However, after the time interval necessary for complete absorption, these complications should be nonexistent.

The lucency and radiolucency of the bioabsorbable plate confers several unique advantages over traditional metallic implants. During surgery, it is possible to visualize the graft and vertebrae during implantation, something that is more difficult to do with metallic plates. This may potentially allow for a more satisfactory construct and a reassurance that proper placement has been achieved without immediate migration. Also, because these plates are radiolucent, there is significantly less artifact on imaging. After surgery with metallic plates and screws, certain imaging methods, most notably CT and MR imaging, are negatively affected by artifact created by the implants (19). Earlier bioabsorbable plates did not possess any radio-opaque markers, resulting in an inability to precisely locate the position of the plate or screws immediately after surgery. Thus, it was impossible for the surgeon to determine if any plate migration or screw loosening or back out had occurred. This problem has since been addressed with the incorporation of radio-opaque markers into the plates, which are readily visible on plain radiographs.

The incidence of progressive adjacent segment disease following cervical fusions can require some patients to undergo additional operations at neighboring levels. During these second instrumentations, the need often arises to remove the previously implanted instrumentation. Given the long time course of adjacent segment disease, it appears more likely that bioabsorbable polymers will eliminate the need for instrumentation removal and, thus, possibly decrease the size of surgical exposure and length and difficulty of the case.

The bioabsorbable materials used in the authors' series are produced by Medtronic Sofamor Danek and are composed of a polylactide polymer. This material is hydrolyzed slowly over time into carbon dioxide and water and leaves no visible residual. Complications associated with bioabsorbable materials in the past have centered on local tissue reaction at the implant site uniformly in material without 70/30 polymerization (20,21). The safety of the polymer has been examined extensively, initially in animal models, and most recently with the use of this technology in craniofacial and orthopedic surgeries (7-12). Also, the degradation products have not been shown to possess any mutagenic or immunogenic properties *in vivo* (16). The authors' results are similar to previously reported studies demonstrating little or no local tissue reaction with the use of the bioabsorbable polymers.

Conclusions

The rates of fusion following single-level ACDF with internal fixation using bioabsorbable polymer plate and screws in this study match those previously reported in the literature with metallic implants and are superior to noninstrumented fusions. Preliminary results suggest that this newly available technology for anterior fusion may be as effective as traditional titanium plating systems in single-level disease. The potential advantages of bioabsorbable materials in spine surgery are significant and include no interference with radiographic studies, predictable resorption through bulk hydrolysis as carbon dioxide and water, and the elimination of long-term residual metal hardware. The bioabsorbable material appears to be well tolerated by patients. A larger, randomized, controlled study is necessary to bring the results to statistical significance.

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Transverse Myelitis as the Initial Manifestation of Systemic Lupus Erythematosus in a 12 year-old African-American Male with Progressive Longitudinal Involvement of the Spinal Cord: A Case Report and Literature Review

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Abstract

Background: Transverse myelitis (TM) is a rare central nervous system (CNS) manifestation of systemic lupus erythematosus (SLE) that can present with weakness, sensory changes and autonomic dysfunction. Furthermore, progression to longitudinal involvement of the spinal Cord is an even rarer phenomenon with only 8 reported cases all involving adult females (8). We describe a progressive case of Acute Transverse Myelitis (ATM) as the initial manifestation of SLE in a patient who would not typically be considered at risk for this disease.

Case Description: A 12-year-old African-American male presented with a 5-month progressive history of weight loss, chronic lower leg pain, unstable gait, and urinary incontinence at the level of the conus. MRI demonstrated abnormal decreased T2 signal intensity with surrounding increased T2 signal intensity. The conus was significantly expanded with near-complete effacement of the thecal sac and a thickened filum terminale.

Results: Despite corticosteroid therapy, the patient developed progressive paralysis. The patient was taken for T11-LI laminectomy with spinal axis decompression, intramedullary mass biopsy and spinal cord untethering to prevent quadraplegia. Pathology indicated a definite acute inflammatory process with acute neutrophilic vasculitis. The thickened filum was compatible with an underlying developmental cystic lesion with hyperplastic component laboratory evaluation confirmed the diagnosis of SLE and he was treated with corticosteroid and immunosuppressive pulse therapy. Follow-up MRI at 3 months was indicative of longitudinal myelitis from T4-Conus. Although the patient has a neurogenic bladder and remains paraplegic with a sensory level of T7 there has been no progression to involve the upper extremities at 24 months.

Conclusion: A high index of suspicion for SLE in any patient who presents with similar symptoms regardless of sex, age or race is important. However, longitudinal myelitis is an unusual form of SLE myelitis that confers a poor prognosis that is typically refractory to aggressive medical therapy. This case emphasizes the need for controlled multi-center trials to establish guidelines for optimal treatment on this rare hut serious neurological condition.

Key Words: Transverse Myelitis • Systemic Lupus Erythematosus • Longitudinal Myelitis • Tethered Cord • Coitus Medullaris Syndrome • Cyclophosphomide Pulse Therapy • Corticosteroid Pulse Therapy

Introduction

Systemic lupus erythematosus (SLE) is a chronic, multifaceted inflammatory disease that can affect every organ system of the body. SLE is protean in its manifestations and follows a relapsing and remitting course. The most common patients with SLE are white (97.1%), female (90.8%) adults (mean of 37 ± I4 years) (7). Central nervous system involvement has been reported in 24-51% of SLE cases (36). However, transverse myelitis (TM) is a rare but serious initial manifestation of SLE and its prevalence has been estimated to be 1-2% (18). An even more infrequent sequel is the progression to longitudinal involvement of the spinal cord classified as "longitudinal myelitis" (12). We present the case of a 12 year-old African-American male who presented with TM as the initial manifestation of SLE. Despite aggressive medical therapy, the patient's symptoms progressed rapidly with resultant paraplegia. The final MRI findings were consistent with neurological deterioration associated with progressive longitudinal myelitis.

Case Report

History

A 12-year old African American male presented to the emergency department in September 2005 with intermittent lower leg pain, unstable gait, and urinary incontinence. The patient first complained of the pain to his parents in April 2005, but this was the first time seeing a physician for the complaint. Since April, the pain had increased in frequency and intensity. The presenting episode began five days prior to admission and intensified the day before admission to the point where the patient could not ambulate normally. The pain was located in the calf and anterior thigh regions bilaterally. Associated symptoms included a mild headache, intermittent urinary incontinence for five days, and a ten pound weight loss over the last month; in addition, the parents described nonspecific personality and behavioral changes over the preceding five months.

The patient's past medical history was unremarkable with no prior surgeries, no medications, and no known drug allergies. His immunizations were current. His birth history was unremarkable with normal vaginal delivery and no complications. The social history was negative for smoking or second-hand smoke exposure, and there was no history of trauma. The patient attended and did well in school. Family history was unremarkable with no known inherited disorders.

Examination

The patient's vital signs were stable in the emergency department. He was found to be alert with a dull and flattened affect. Gait was reluctantly performed with short, shuffling steps. The patient complained of extreme pain with ambulation, and his motor exam was 3/5 in bilateral lower extremities with hyperreflexic patellar and achilles reflexes. Perianal, sacral, and lateral foot paresthesias were noted with pain in the anterior thighs and calves to palpation bilaterally.

Rectal exam demonstrated good anal sphincter tone with intact anal and cremasteric reflex was intact. No meningeal signs were noted. Cranial nerves II through XII were grossly intact.

Complete blood count, electrolytes, blood urea nitrogen, creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and urinalysis were performed in the emergency department. All were within normal limits with the following exceptions: hemoglobin 9.7 g/dL (normal 11.0-16.0 g/dL); hematocrit 29.7% (35-49%); ESR 97 mm/hr (0-10 mm/hr); CRP 7.28 mg/dL (0-0.9 mg/dL); and l+ proteinuria (none). The following abnormal values were obtained on additional testing: aspartate aminotransferase (AST) 107 U/L (normal 15-40 U/L); creatine phosphokinase (CPK) 2151 U/L (24-195 U/L); total serum protein 9.9 g/dL (5.7-8.0 g/dL); and serum IgG 4640 mg/dL (759-1550 mg/dL). CSF was atypical for: glucose 25 mg/dL (40-70 mg/dL); IgG 98.2 mg/dL (0.4-6.0 mg/dL); albumin 86 mg/dL (13.4-23.7 mg/dL); and protein 261 mg/dL (15-45 mg/dL).

A computerized tomography (CT) of the head without contrast was performed to rule out intracranial pathology**.** There was no evidence of midline shift: the brain was symmetric with an intact grey-white matter interface; and the peripheral sulci, basal cisterns, and ventricular system were within normal limits.

At the level of the conus, MRI (Figure 1) demonstrated abnormal decreased T2 signal intensity with surrounding increased T2 signal intensity. The conus was significantly expanded with near-complete effacement of the theca) sac. Although the conus was in a normal anatomical position, a thickened, tight film terminale was evident. Findings in the region of the conus were suggestive of central hemorrhage, possibly within an edematous neoplastic lesion. Additional possibilities included a vascular malformation with infarction and edema, and an infectious or inflammatory process such as an abscess with myelitis.

Neurosurgical Management

Despite corticosteroid therapy the patient's neurological deficits progressed to complete paraplegia with a T7 sensory level. The patient was taken for T11-L1 laminectomy with spinal axis decompression, intramedullary mass biopsy and spinal cord untethering to prevent quadraplegia. The dura was quite expanded. At T11 to T12 there was loss of ligaments suggestive of increased pressure. As the dura was opened sharply, a soft mass rapidly extruded from the incision. The mass was fluffy, white, "cottage cheese-like" tissue, which was surrounding and compressing the nerves. The mass, which appeared to arise from within the conus medullaris was gently biopsed and sent to pathology. The filum terminale was identified, coagulated, divided and sent to pathology as a separate specimen.

Pathological Findings

Microscopic examination of the biopsy showed fragmented spinal cord tissue with necrosis and

neutrophilic infiltrate (Figure 2). Marked axonal swelling was identified in a neurofibrillary background without recognizable viable neurons or astrocytes. Few small sized vessels with perivascular cuffing of mononuclear cells and intense neutrophilic infiltrate were present.

Microscopic examination of the resected filum demonstrated dense, thickened, and somewhat disorganized collagenous tissue containing nests of glial tissue, focally lined by ependyma, consistent with central canal. Abundant neutrophilic infiltrate, recent hemorrhage, and hemosiderin-laden macrophages were noted throughout. Medium and large vascular channels, some representing small muscular arteries, had neutrophilic infiltrate in their walls associated with necrosis and thrombosis.

The patient's antinuclear antibody titer was positive to 1:2560 (normal < 1:80). Anti-Smith was 184.2 EU/mL, anti SS-A was 155.9 EU/mL, and anti SS-B was 98.6 EU/mL; all were strongly positive (greater than 80 EU/mL). Complement C3 was 40 mg/dL (normal 90-200 mg/dL), and CH 50 total complement was 29 mg/dL (I00-300 mg/dL). These were all consistent with the diagnosis of systemic lupus erythematosus with transverse myelitis.

Postoperative Course

Follow-up MRI at 3 months was indicative of longitudinal myelitis from T4-Conus, demonstrating increases in signal intensity on T2-weighted imaging, and persistent cord edema (Figure 3). Although the patient has a neurogenic bladder and remains paraplegic with a sensory level of T7, there has been no progression to involve the upper extremities at 24 months. Fie remains on chronic corticosteroid and immunosuppressive pulse therapy.

Literature Review

Cases of "acute myelitis" were described as early as 1882 (4). It was not until 1971 that the American Rheumatism Association (ARA) established criteria for the classification of systemic lupus erythematosus (SLE) (9). Prior to 1971, diagnosis of SLE was more subjective. Typically the diagnosis was applied to patients with multi-system disease and a positive lupus erythematosus cell test, a positive antinuclear antibody test, or both (14). This review of literature will focus on cases described after the original ARA criteria was established in 1971.

Patient Demographics

Transverse myelitis (TM) as a manifestation of SLE can occur at almost any age. The youngest case reported was in a 9-year-old child; the oldest patient was 77 years old (18). The median age of onset of TM is 33 years and the median age of onset for SLE is 31 years (34). SLE patients with TM are predominantly female which is consistent with sexual prevalence for SLE in general: in one cohort study of 1000 SLE patients, 90.8% were female. In the same study, the majority of patients were white (97.1%), followed by black (1.9%), and all other races (1%) (7). The prevalence of TM at any time in patients with SLE range from I% to 2%

depending on the source- TM as an initial manifestation of SLE was 1.6% in one study of 315 patients (25).

Clinical Features

Patients with TM can develop motor, sensory, and autonomic dysfunction. The most common presentation is a discrete sensory level with lower leg weakness. The weakness is rapidly progressive; it usually begins with the legs, and sometimes ascends to the arms. The majority of the sensory levels are in the thoracic region, with cervical being the next most common (16). Autonomic symptoms consist variably of increased urinary urgency, bowel or bladder incontinence, difficulty or inability to void, incomplete evacuation, or constipation (28). Optic neuropathy develops in 25% of patients with TM, and 1% of patients with SLE (14, I8).

Some studies have shown a strong association between TM in SLE and antiphospholipid antibodies (aPL); however, the incidence of aPL in SLE patients with TM is only slightly higher than the general SLE patient population (10, 21, 30). In other studies, CSF examination has demonstrated low glucose, high protein, and high pleocytosis (2, 25).

Radiological Features

An MRI will often show evidence of acute inflammation and is the diagnostic tool of choice for TM (10, 33). Most visible lesions are seen as a hyperintensity of the spinal cord on T2-weighted imaging. The majority will be isointense on T1-weighted imagine, while the remainder will be hypointense on T1 (33). Not all cases of acute TM will have visible abnormalities on MRI; between 56-70% will have signal changes (18, 25). One study suggested that patients with an abnormal MRI at presentation tended to have a less favorable outcome than those with a normal MRI at presentation (18).

Pathological Diagnosis

Few studies contain pathological descriptions of TM. Those that do confirm TM as an inflammatory condition associate it with immune-mediated mechanisms. Gray and white matter can be equally affected, and it is not uncommon to have prominent CD4+ and CD8+ lymphocytic artd monocytic infiltration (19). Focal areas of spinal cord ischemia without prominent inflammation are often seen in autoimmune disorders such as SLE (19).

Treatment Outcomes

TM as a manifestation of SLE is rare. Treatment guidelines have not been established, so it is difficult to generalize outcomes between studies. Corticosteroids alone or with cyclophosphamide (CP) are the most common treatments (10). In one review of 86 cases with outcome data available, complete recovery occurred in 50%, partial recovery in 29%, and no improvement or deterioration in 21% (18).

Other recent approaches to treatment include: plasmapheresis in addition to IV steroids and CP; and anticoagulation in addition to immunosuppressive therapy in patients who have APL (10).

Future treatments may involve CSF filtration. This is not yet available in the United States, but in one study of CSF filtration versus plasma exchange in patients with Guillain-Barre syndrome, CSF exchange was better tolerated and at least as effective (24).

Future treatment may focus on specific autoantibodies and the antigens to which they respond. This would allow for the development of specific targets to block the effects of these autoantibodies (19). Another therapy is being aimed at altering the affects of cytokines on the nervous system, although paradoxical demyelination may be caused by TNF-a in the blood (24).

Discussion

Several factors make the presentation of this case exceptional. TM as an initial manifestation of SLE is uncommon (1.6% of SLE patients), the median age of onset for any SLE symptom is 31 years, and the vast majority of SLE patients are female (90.8%) (7, 25, 34). Our patient, a 12-year-old African-American male, with TM as an initial manifestation of SLE is rare.

Because TM in SLE is a very rare manifestation, treatment guidelines for this entity have not been established. A prevalence of 1.6% has been estimated, and only 105 cases are reported in the literature (18). It has been long described as a late complication of lupus (6). However, contrary to what has been reported, Kovacs (18) found that ATM occurring as the initial manifestation of SLE is rather common (5 of 14 cases of lupus-related transverse myelopathy).

The differential diagnosis of TM is patients with SLE includes ATM, medullar compression caused by vertebral fractures, epidural or subdural hematoma, epidural and/or paraspinal abscess complicating disc space infection, disc herniation, and intra- and extramedullary tumor (36). The etiology of ATM includes multiple sclerosis (MS), vasculitis, infection, and autoimmune disorders (27). However, such extensive spinal cord lesions with normal cerebral white matter on MRI would be very unusual in MS. Transverse Myelopathy caused by MS usually presents with lesions of a limited, focal extension (single lesion involving only one level, not continuous, and that do not involve more than one level each) (17,20,3I).

MRI is the diagnostic and follow-up method of choice (12, 27, 29). Provenzale studied 8 episodes of ATM in 4 patients and found increase signal intensities in T1 and T2-weighted images, which is comparable with our case (27). Deodhar reported the first case report of a patient with continuous involvement of the spinal cord, described as "longitudinal myelitis (12)." Owing to its rarity, the reported MRI experience in patients with SLE-related myelopathy is still limited.

This case report is in agreement with the published literature that systemic complement consumption is generally not evident during the acute phase of myelitis (1, 35, 38). Lavelle reported a strong association between SLE and ATM with antiphospholipid syndrome (21). However, this association was not observed in our case. Studies involving a larger number of ATM patients with antiphospholipid syndrome are needed to clarify this discrepancy.

The pathogenic mechanism of spinal cord dysfunction is still uncertain, although 3 types of pathological changes have been postulated in SLE-related myelopathy: vasculitis, ischemic cord necrosis, and peripheral white matter degeneration (27). Immune complex mediated vasculitis causing hemorrhage or ischemic necrosis of the cord may not be the sole mechanism, because complement activation was not present in many previous reports (38). In experimental conditions, tethering of the spinal cord resulted in changes similar to those expected from studies of hypoxemia (37). Furthermore, the impairment of oxidative metabolism and the elongation of the spinal cord in the animal traction model were found only below the attachment of the lowest pair of dentate ligaments (37). This would account for the initial involvement of the conus only unless different types of lesions coexist in higher spinal cord segments. A spinal vessel thrombosis might account for the progression of transverse myelitis to the thoracic spine (18). The longitudinal arterial trunks are largest in the cervical and lumbar regions and are much smaller in the thoracic region. If there were vascular compromise secondary to thrombosis, the thoracic cord would be most vulnerable because of limited blood supply.

Intravenous (IV) pulse methylprednisolone and cyclophosphomide therapy seem to have gained wide acceptance by most rheumatologist in recent years (12, 13, 16, 23). However, Zenteno reported that 5 of 6 patients had poor results despite aggressive treatment (38). Because of the rarity of lupus related transverse myelitis, it has not been possible to conduct controlled trials for treatment. It is unclear whether plasmapheresis has any additional therapeutic benefit (3, 5, 18). The prognosis for transverse myelitis has frequently been considered to include death or severe neurologic sequelae (25). A 1989 review revealed 44 reported cases, but only 26 had sufficient details to enable meaningful comparisons (26). Of these, only 7 (26%) recovered either full or partial neurologic function; others remained static, worsened, or died.

Conclusion

In light of this case. it is important to have a high index of suspicion for SLE in patients who present with acute or subacute spinal cord involvement regardless of age or gender. However, even in aggressively treated cases of longitudinal myelitis, incomplete recovery, significant permanent neurological disability, or death may result. Controlled, multi-center trials to establish guidelines for optimal treatment on this rare but serious neurological condition are

needed.

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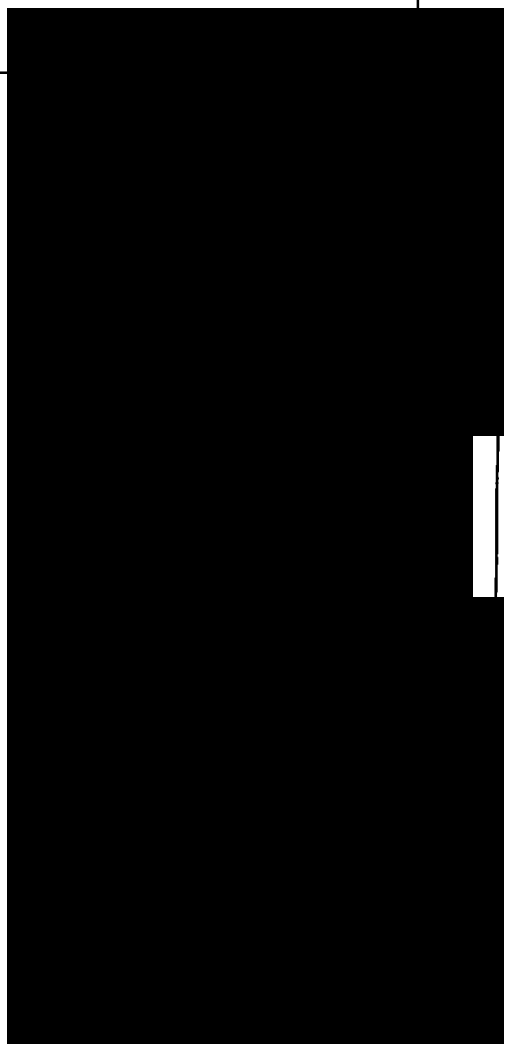
FIGURES

Figure 2: Conus Mass Biopsy-
Fragmented spinal cord tissue with necrosis and neutrophilic infiltrate is present.



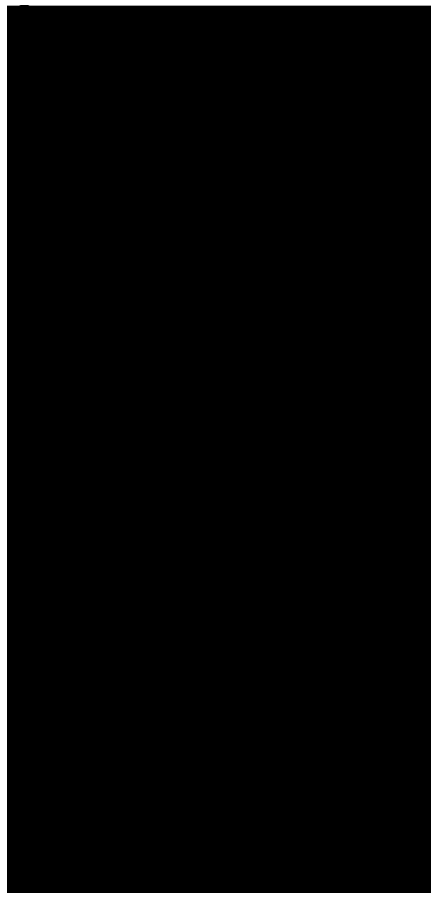


Figure 3: T-2 MRI Spine.
Follow-up MRI at 3 months, indicative of longitudinal myelitis with increased intensity on T2-weighted imaging and persistent cord edema.

Case Report and Literature Review: Extraneural Metastasis of Anaplastic Intracranial Ependymoma

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Abstract
Extraneural metastases of gliomas are rarely reported in the literature. The statement by Bailey and Cushing that gliomas never metastasize outside the CNS was accepted for years until case reports in the last 50 years disproved them. Among these tumors ependymomas have a metastatic incidence of approximately 1%. Extracranial metastases of ependymomas occur most frequently in the lungs and pleural fluid, followed by cervical lymph nodes, vertebral bodies, thorax, and peritoneum. We present a case of an 11 year old male with a recurrent right parietooccipital and cervical lymph node anaplastic ependymoma.

Key Words: Anaplastic Ependymoma, Extraneural Metastasis, Iatrogenic, Blood-Brain Barrier

Introduction
Ependymomas represent a common entity among both adult and pediatric populations. These tumors arise from ependymal cells lining ventricles and central canal of the spinal cord. Presentation varies depending on location. For cerebral pathology, signs and symptoms are related to location of intracranial lesion, presence of hydrocephalus, or assiociated seizures. While typically benign, anaplastic variants, World Health Organization (WHO) grade 3, are the most underrepresented. Treatment usually hinges on surgery and radiation, with little benefit from chemotherapy except occasionally in cases of recurrence.

This is a presentation of a rarely encountered sequela of anaplastic ependymoma, extraneural metastasis.

Case History
Our patient was an 11 year-old male with frontal headaches of one month's duration. The patient had no history of trauma or infection and was otherwise healthy. He described the pain as severe pounding and was associated with increasing nausea and emesis. His cephalgia progressed despite conservative therapy from his pediatrician, prompting imaging one month later.

Computerized tomography and subsequent MRI revealed a 5.5cm right parietooccipital ring enhancing cystic lesion. The patient underwent craniotomy and gross total resection of lesion was achieved. Pathological evaluation demonstrated a WHO Grade III anaplastic ependymoma. He underwent whole-brain radiation at 5900cGy and developed a tumor recurrence requiring repeat craniotomy two years later. The patient again underwent radiation, gamma knife radiosurgery and chemotherapy. A second recurrence was noted in another two years. Additionally, the patient was enrolled in an experimental immunotherapy, consisting of a series of vaccinations. One year after a third repeat

resection the patient developed localized painless swelling to this right neck and a local intracranial tumor recurrence. The neck mass was excised and found to be a posterior cervical lymph node, infiltrated with anaplastic ependymoma. The patient had a CT of his chest performed, revealing pulmonary metastasis with malignant effusion.

Discussion

Ependymomas account for approximately 8% of intracranial tumors in children and 3-4% of intracranial tumors in adults.[1,2] Ependymomas are graded using the World Health Organization (WHO) consensus criteria revised in 1993 as neuroepithelial originating tumors, ependymomas are grouped separately from the embryonal ependymoblastomas.[3] Grade I ependymomas are classified as subependymomas and have unique histology and epidemiology when compared with Grade II and Grade III tumors. Grade II ependymomas are slow growing and well demarcated tumors. They show neoplastic ependymal cells, classically with rosettes and perivascular pseudorosettes. Occasional necrotic foci may be seen, though this is more characteristic of Grade III tumors. These tumors are found along the midline and the fourth ventricle classically.

Anaplastic or malignant ependymomas (Grade III) differ from grade II in that they show high cellurity, marked vascular proliferation, a high mitotic index, and necrosis. Though necrosis has the least diagnostic specificity of these findings it can be seen in Grade II's as well. Grade III ependymomas are more often found in the cerebral hemispheres, leading to the conclusion that as degree of malignancy increases as the distance from midline increases.[1,5] The usage of the WHO grading scale aids in long-term prognostication as the tissue grade is directly related to the survival rates.[1,2,4,5,6]

Our neurosurgical practice serves as a regional tertiary and quaternary referral system in southern California. Additionally, through our affiliation with Kaiser Permanente, we contribute a large number to their tumor database, which was instituted in 1988.[13]

The brain tumor database was queried for all gliomas, numbering over 12,000. Ependymomas represented 5.3 percent (n=657). Ages of patients with ependymomas ranged from 18 months to 63 years, with approximately 11% aged less than 18. The pediatric population had only two percent represented as spinal cord tumors, as compared to 67% of ependymomas in adults.

Of the pediatric population's intracranial ependymomas (98%), infratentorial lesions represented 68%. Anaplastic ependymomas accounted for only eight percent of all grades. There were no other reports of extraneural metastasis of ependymoma or other gliomas, therefore respresenting 0.15% in our population.

The extraneural spread of ependymomas has been examined and appears to be largely related to iatrogenically induced tumor dissemination[4,5,7]. Surgery itself may play the biggest role, as the surgical manipulation of the tumor disrupts the blood brain barrier and communicates tumor cells with systemic circulation. After craniotomy occurs, the rates of metastases increase sharply.[2]

Often patients with ependymomas develop hydrocephalus necessitating a shunt placement. The shunt itself may provide a tract for migration of tumor cells into the peritoneum. This conceptual metastatic route appears to have been confirmed by increased rates of both malignant ascites and peritoneal metastases in patients with ventriculoperitoneal shunts as well as quantitatively significant ependymal cells found in close proximity to the shunts.[8,9] This, however, was concluded to be of little clinical significance, as these patients were studied post mortem. Interestingly, there has been no correlation between the completeness of the surgical resection and the presentation of extraneural metastases.[9] However, the extent of surgical resection does determine ultimate patient outcome in intracranial ependymomas confirming the surgical nature of this disease.[1,2,6]

Our patient's history is consistent with that of previous reports. His metastatic disease was discovered after his third craniotomy. Interestingly, in the interim between his third craniotomy and discovery of his lymphadenopathy, he underwent experimental immunotherapy, which was stopped in its final cycle due to lack of patient's tolerance to the regimen. After his biopsy was consistent with metastasis, he received a CT of his chest, which revealed multiple pulmonary lesions with effusion. His family opted for hospice care, and the patient succumbed soon after.

The paucity of reports for metastatic gliomas, and specifically anaplastic ependymomas, offer potential investigations, such as evaluation of high dose corticosteroid in the perioperative period.[8,9,10,11,12] Theoretically, it would aid in stabilization of cell membranes and blood-brain barrier. Obviously, it would be a difficult inquiry, and likely require multiple centers, multiple surgeons and many years to enroll, operate, and follow enough patients for statistical significance. More likely, radiosurgery for tumor recurrence will be a continued source of growth control which should be further studied for incidence of extraneural metastasis.[6]

Conclusion

Our experience with ependymomas echoes the rarity of extraneural metastasis. This rare occurrence follows the theory of iatrogenically-induced disruption of the blood-brain barrier, thus exposing the systemic circulation to the malignancy. While previously reported in the literature, we believe it to be less that than the documented 1%.[8,10,11] However, with advancing imaging techniques for detection and improved operative technology, radiation dosing, and radiosurgery the diagnosis of metastatic disease will increase. Treatment modalities such as radiosurgery may offer other avenues for treatment of recurrent tumor, without the potential of insult to the blood-brain barrier.

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Pre-Sacral Approach to L5-S1 Fusion: Review of Case Series and Possibilities for the Future

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Abstract

Objectives: We will review our case series of 19 patients, their outcomes, complications, and work status before and after surgery. We will also review the basic biomechanical forces responsible for hardware failure at the lumbosacral junction, and the advantages of an axial screw system over traditional systems. We will discuss some interesting future developments, and present a novel design for dynamic stabilization at L5/S1 using the pre-sacral approach.

Results: In our review of 19 patients we found that patients having lumbosacral fusions via a presacral approach did significantly ($p=0.0034$) better in their Oswestry scores following surgery based on a review of thirteen patients with complete data. We found no neurologic complications attributable to the placement of the axial screw, and there were no infections in our patients either in the paracoccygeal region or the pedicle screw incisions. No visceral injuries occurred in our case series and all post operative imaging showed good placement of the axial fixation device even in the case of spondylolisthesis.

Conclusion: We have reviewed our series of patients undergoing L5-S1 interbody fusion using the presacral approach to the L5/S1 disc space. This is the largest case series of patients reported to date in the literature. The safety and efficacy of this approach has been demonstrated in our small case series, and it clearly has some significant advantages over traditional spinal fusion at L5-S1. These advantages include improved translational stability, no disruption of anatomically important structures, and containment of BMP and other fusion compounds within an intact annulus. Future developments within the framework of this approach will expand it's application range to the L4-L5 level as well as increase it's possibilities as a stand alone system. We have also presented a novel dynamic axial fixation device that can be applied using the same pre-sacral approach. This screw will be useful in stabilizing the lumosacral junction by counteracting shear forces responsible for the development of spondylolisthetic defects, while still allowing full range of motion at the lumbosacral junction. Dynamic stabilization at the lumbosacral junction will decrease the development of adjacent level disease particularly at L4/L5.

Introduction

Spinal fusion is one of the most frequent procedures performed by spine surgeons for axial back pain. A new study by Yuan gives convincing evidence that patients with axial back pain have better outcomes after surgery than patients treated with conservative measures only. There are a number of modalities and methods for accomplishing spinal

fusion and if asking three spine surgeons the best method for accomplishing fusion at a given level, you will likely get three different answers. Posterior spinal fusion and anterior spinal fusion are the two most widely used methods today. Each of these approaches has a given set of risks and benefits that a surgeon must weigh when considering an approach to any given spinal level.

Anterior approaches are well suited for stabilization of the anterior spinal column but have little direct effect on the posterior columns. Posterior fusions have more variability in the types of fusions that can be performed. Pedicle screw instrumentation, although technically providing three column stabilization, has its greatest strength when posterior column stabilization is the main goal. Anterior column stabilization can also be performed via a PLIF or the more popular TLIF. All of these posterior methods require some degree of ligamentous, muscular, and annular disruption which decreases the spines anatomical stability and exposes any instrumentation placed to increased stress. Anterior and posterior approaches, by their very nature, weaken the spine's anatomical methods of stabilization[1]. There are also significant risks to both of these approaches. The posterior approaches risk injury to the nerve roots and the anterior approaches risk injury to vascular, GI, and nervous structures intimately associated with the anterior portion of the lower lumbar segments. There is also a significant amount of pain generated by these procedures due to the amount of soft tissue dissection necessary to perform each procedure.

The Pre- sacral approach for fusion at L5/S1 offers a unique method of fusion that eliminates some of the pitfalls of the traditional anterior and posterior approaches [2-4]. The Pre-sacral approach is a true minimally invasive approach in that it can be performed though a 1-2 cm incision in the paracoccygeal region. Most of the dissection is done in the pre-sacral fat plane, and no spinal ligamentous structures are disrupted in order to perform the procedure.

The system is also well suited for the L5/S1 level due to its high resistance to translational forces, which are the main cause of fusion failure at this level. At the current time the axial screw system is not designed to function as a stand-alone system, but it can easily be supplemented by percutaneous pedicle screw fixation to give the rotational stability which the Axial screw inherently lacks. We will present our case series of patients that have undergone the L5/S1 axial screw procedure and review pre and post work status, pre-surgical and post surgical Oswestry scores, complications, and placement accuracy. We will also discuss the unique biomechanical forces present at the lumbosacral junction, and review some biomechanical comparisons of the axial screw with other interbody devices, some technical notes, and trends for the future. We will also

present a novel dynamic interbody device for stabilizing the lumbosacral junction using the pre-sacral approach.

Biomechanics of L5-S1

In order to fully appreciate the advantages of the pre-sacral approach to the lumbosacral junction, it is necessary to discuss the biomechanics of this part of the spine and briefly look at the forces involved. An in depth review is not necessary to understand the important forces which need to be addressed in any type of instrumentation at this level, and the biomechanics of the lumbosacral junction have been well described in other publications [5].

The lumbosacral junction must resist some of the highest forces applied in the spine. There is an extremely complex interaction of forces at the lumbosacral junction due to it's role as the base of the spine and the sacrum's intimate connection with the pelvis and locomotion anatomy.

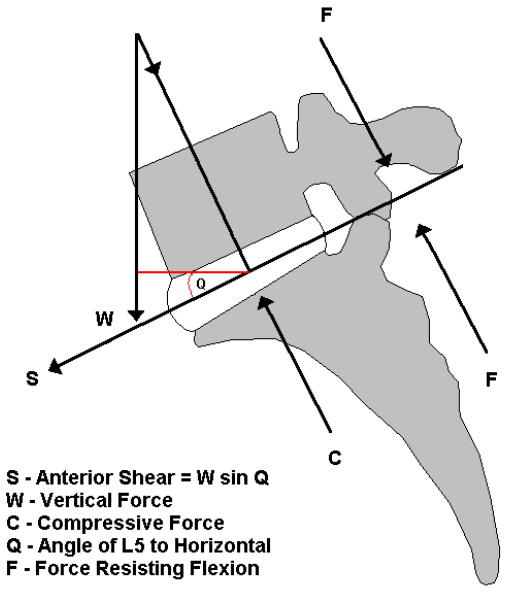


Fig 1: Modified figure from Troup, JD [ref 29]

To simplify the forces that are of primary interest to our discussion we will cover the main four forces that need to be counteracted in dealing with lumbosacral instability. Fig 1 shows the primary forces involved. The most important force applied across the lumbosacral junction is anterior shear. Anterior shear (**S**) is a function of a number of different variables including lumbosacral angle, pelvic incidence, angle of the L5 endplate with the horizontal plane(**Q**), and quantity of vertical force applied across the lumbosacral junction(**W**). Fig 1 shows that the anterior shear can be calculated by knowing the vertical force vector and the angle of the L5 vertebral body with the horizontal (**Q**). **C** represents the compressive forces applied to the disc

space, which is also a function of the amount of vertical force, flexion, and the ability of the posterior ligaments to resist the flexion forces (**F**). The absolute value of any of these forces is not important, however, their interaction is.

It is evident that as **W** increases **C** and **S** will increase. **S** will also increase with flexion, and with increases in the lumbosacral angle. There are a number of structures that are involved in resisting the shear force across the joint. The annulus, facet joints, ligaments and muscles all participate in counteracting the shearing force and quantification of their individual involvement has been well described.

Adams and Hutton have shown that the facet joints resist approximately 16% (12-25% in other studies [6,7]) of the anterior shear in normal lordotic postures but the facet contribution decreases dramatically as the lumbosacral joint is flexed [8]. The normal lumbosacral angle ranges from 20-30 degrees [9,10,11] and the normal pelvic incidence, a fixed parameter, is different in each individual and ranges from 34 to 77 degrees [12]**.** Hanson has shown that as the pelvic incidence increases, so does the incidence of spondylolisthesis due to the increased shear produced at the lumbosacral junction [13].

Physiologic movement at L5/S1 is also important to consider. Flexion/ Extension is the largest degree of motion that occurs at the lumbosacral junction and averages 14-20 degrees, lateral bending ranges from 1.5 to 5 degrees, and axial rotation is minimal at this level and ranges from 1.3 to 5 degrees [14-17,30].

The facts discussed above are important to keep in mind when considering instrumentation for securing the lumbosacral junction. Any instrumentation applied to the lumbosacral junction must be able to adequately resist these forces to allow time for fusion. Traditional methods of fusion, by the very nature of their application, cause ligamentous and annular disruption and weakens the bodies anatomical methods of dealing with these forces.

Two studies have demonstrated the effects of an annulotomy on lumbar joint stability [18,19]. These studies have shown that an annulotomy significantly weakens the motion segment stiffness in the lumbar spine. This is important in that the annulus bears a large portion of the resistance to shearing at L5/S1, particularly in cases where the facet joints are not functioning properly and this is clearly the case in many patients with lumbosacral instability. Ledet have shown that the drilling of the vertebral bodies in the presacral approach has minimal effect on the stability of the motion segment [20]. This is clearly not the case with traditional approaches in which large annulotomies, ligamentous disruption, and muscular dissection weakens normal anatomical resistance to abnormal motion.

The pre-sacral approach has an advantage in that it produces minimal disruption of the spine's anatomical stability and allows the body to more effectively participate in stress shielding the implanted hardware.

Axial Screw Biomechanical Testing

Ledet, using the calf spine model, have completed biomechanical testing of the axial screw system[20]. A number of different motion parameters were tested using a standardized technique, which allowed comparison to previously tested interbody devices. Results from this study are reproduced in Table 1 [20, 21] .

Stiffness (% intact)				
Device	Flexion	Lateral Bending	Torsion	Comp-ression
Non-tapered axial	169	562	134	144
Tapered axial	131	288	116	132
BAK	115	120	115	135
Femoral ring	115	125	155	150
Bone Dowel	105	130	115	115
Brantigan ALIF	100	90	65	90
Ray TFC	95	130	145	135
Brantigan PLIF	95	155	95	110
Infix device	95	200	110	100
Danek TIBFD	90	150	135	105
Single harms	90	80	105	110
BAK Proximity	85	110	110	95
Double Harms	70	115	100	95

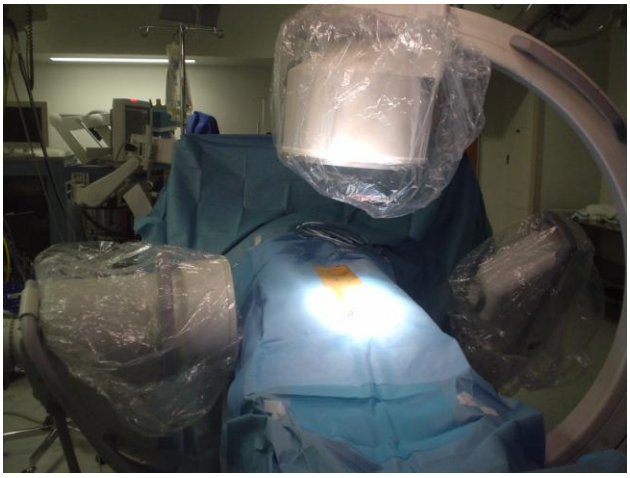
Table 1

As can be seen from the data in Table 1, the axial screw system performs very well in providing overall increases in stiffness at the motion segment when compared to traditional devices. The weakest point with the axial fixation device is in torsion. This is clearly due to the shape of the implant. As has been described in the previous section, flexion/extension is the main motion at the lumbosacral junction, while movement in the axial plane is minimal. Flexion also is a major component in the generation of shear forces at the lumbosacral junction. The axial screw provides excellent resistance to flexion, axial compression, and also sidebending, which provides superior conditions for fusion. As discussed in the previous section, the process of drilling into L5 and S1 did little to affect the stability of the motion segment. This becomes an extremely important issue when considering dynamic stabilization at this level which will be addressed in the future trends section of this article.

Pre-sacral Fusion

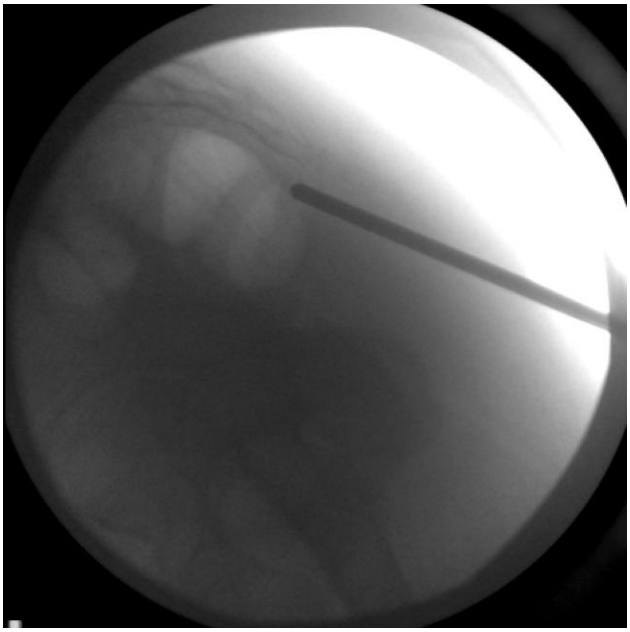
Procedure

The Pre-sacral procedure may be done on a number of different tables with proper patient positioning. Our group uses the Jackson table with a sling. The legs must be lowered in the sling to roughly a 20-30 degree angle with the torso. This allows a reasonable amount of maneuvering of the working tube. Once the patient is properly positioned on the Jackson table, a rectal catheter is placed and the bowel is filled with 60-120cc of air in order to aid in visualization of the bowel during the procedure. AP and lateral fluoroscopes are then brought in and properly positioned (Pic 1).



Pic 1

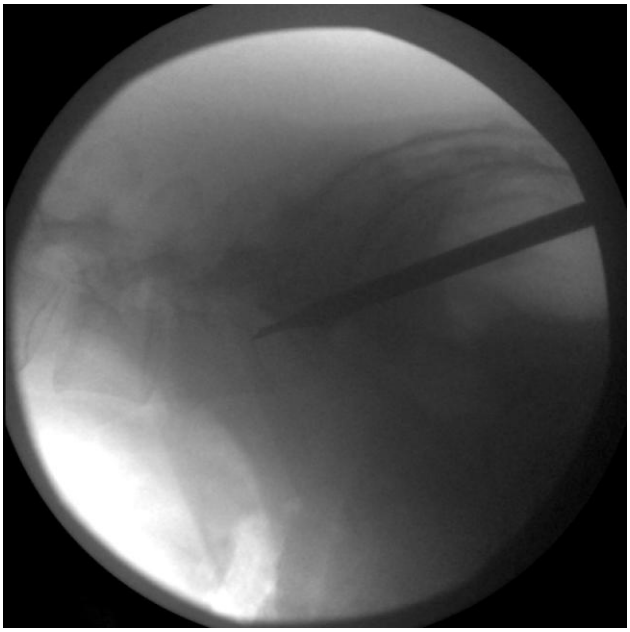
Once the fluoroscopy and the patient are in proper position the paracoccygeal groove is palpated and the surgical site is marked. The patient is then prepped and draped with alcohol and betadine. The surgical site is then infiltrated with 1% Lidocaine with epinephrine. The site is then incised using a 15 blade. Once the skin has been incised through to the fat layer, the introducer is used to "pop" into the pre-sacral, retroperitoneal space (fig 2).



Pic 2

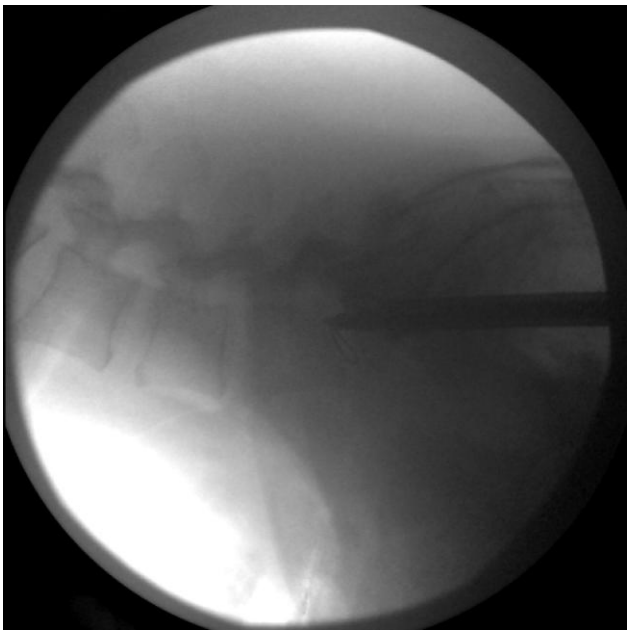
Before advancing the introducer, the AP and lateral fluoroscopy x-ray is taken in order to confirm position. The introducer is kept gently against the sacrum, and AP fluoroscopy is used to confirm that the tip of the introducer is in the midline. The introducer may then be advanced using slight rotational movement with positive pressure on the end of the introducer and gentle upward pressure of the tip against the sacrum. Frequent fluoroscopy is used in order to avoid sliding off the midline and injuring the sacral roots. The introducer is advanced until the midportion of the S1 body is reached. The alignment of L5 and S1, as well as the size of the lip provided by the S1 body determine the best entry site and trajectory.

Once the entry site has been chosen and confirmed on fluoroscopy, the introducer can be used to affix the dilator system to S1 using a sharp guide wire passed through the introducer. This will provide a stable platform for the rest of the case and allow passage of the dilators and working channel. A small mallet may be used to advance the guide wire to the L5/S1 disc space. Once the guide wire is placed, an extension is screwed onto the end so that a number of sequential dilators can be used to dilate the presacral space. The dilators are placed sequentially using a slight twisting motion. Once the final dilator (10mm) and the working tube (Connected to the 10mm dilator) is in position, a slap hammer is used to drive the dilator/working tube combination into the sacral segment (fig 3). Once the working tube is properly countersunk into the sacrum, a 9mm drill is used to drill a channel through S1 into the disc space.



Pic 3

Once the sacral segment has been drilled the disc space loop curettes can then be used to break up the disc and clean the endplates of L5 and S1. A number of different curettes are available in different sizes and with different cutting angles (fig 4).

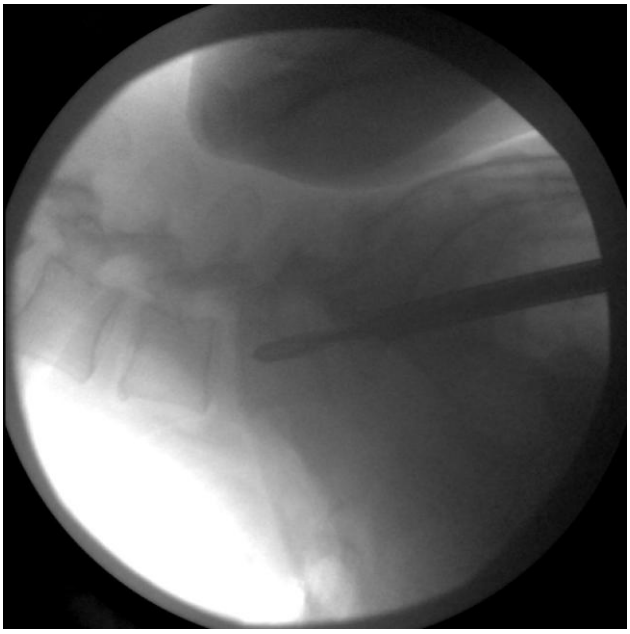


Pic 4

The curettes come in two different sizes, (large and small), and two different angles (straight and down-angled). These loop curettes are used to clean the end plates and break up the disc material.

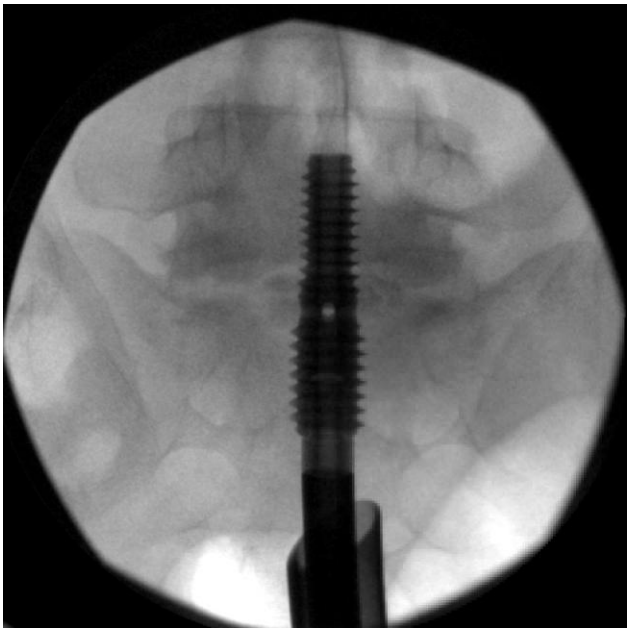
Once the endplates have been cleaned with the curettes and the disc is broken up with the curettes, the brushes are inserted into the disc space and turned 6-7 times counterclockwise to extract the disc material. The process of curettage and disc extraction with the brushes is repeated until the surgeon determines that the disc space has been adequately cleared of disc material. A suction/irrigation unit can also be used to wash out the disc space and remove any remaining small fragments.

Once the disc space has been adequately prepared, the fusion substance (BMP, Vitoss) is placed in the disc space with a special application tube. Once the graft substance is in place, the L5 vertebra is drilled with a 7.5mm drill bit (fig 5).

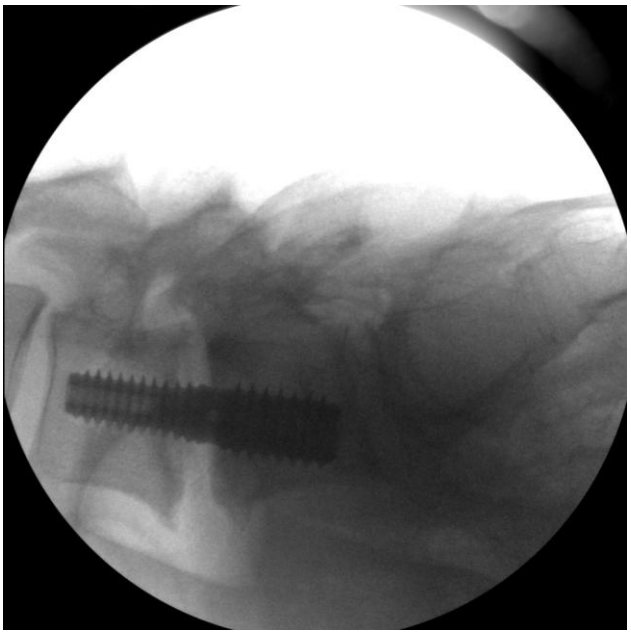


Pic 5

Once the disc space is filled with graft material and the L5 vertebra has been drilled, the axial screw can be placed (Pic 6,7).



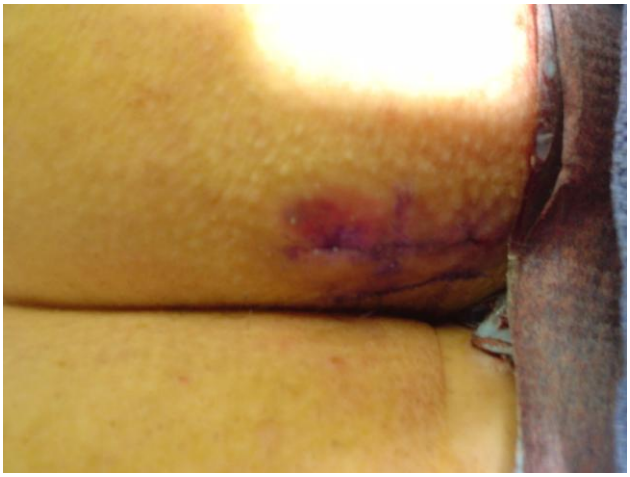
Pic 6



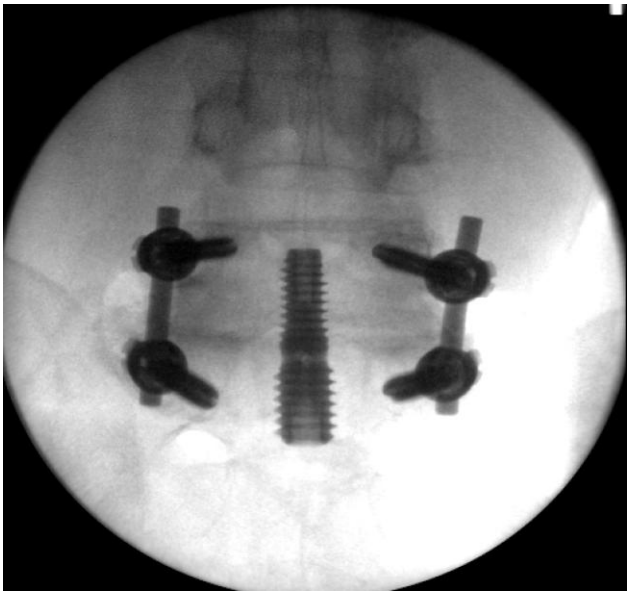
Pic 7

Once the screw has been placed a small screw is available which can be placed in the end of the graft to prevent extrusion of graft substance from leaking out of the disc space through the axial screw.

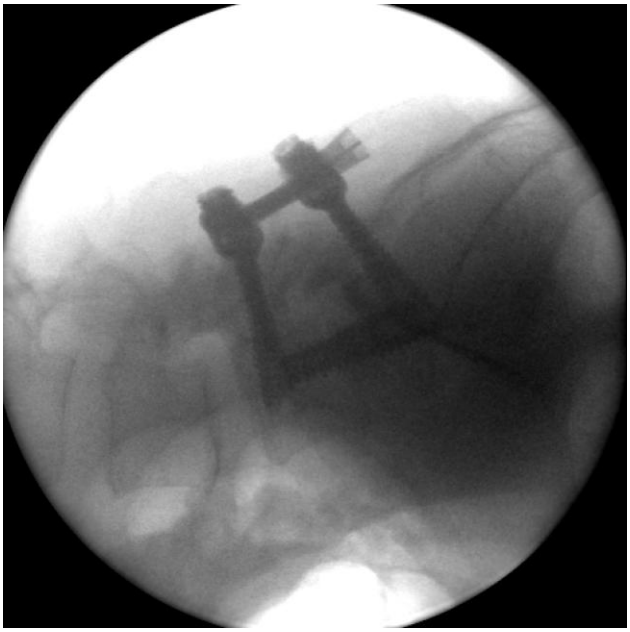
We then close the wound with 3-O vicryl and dermabond (Pic 8). Post placement films are then taken prior to placement of the posterior stabilization system. Once the percutaneous pedicle screws are placed post operative films are taken in the AP and lateral planes (Pic 9,10).



Pic 8

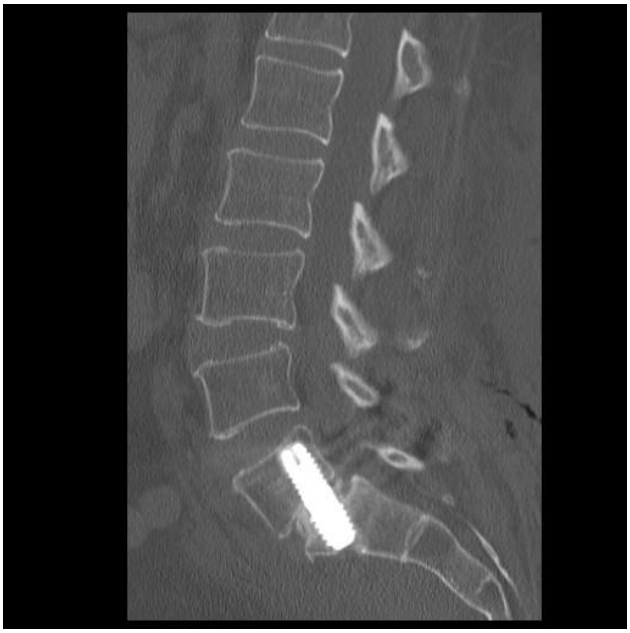


Pic 9



Pic 10

Post-operative CT scans are taken in order to confirm placement and to have baseline comparison for evaluating fusion progress (Pic 11).



Pic 11

Technical Notes

Although the use of a single fluoroscopy x-ray is conceivable it is not recommended. A single fluoroscopy x-ray would require multiple repositioning of the unit from AP to Lateral positions and would add significant amount of time and difficulty to the case.

Air in the bowel has been found to be preferable to radio-opauqe liquids due to it's ability to define the location of the bowel, and not interfere with the visualization of the lumbosacral anatomy and the instruments.

When advancing the introducer a slight twisting motion, upward pressure against the sacrum, and frequent use of fluoroscopy should minimize the risk of injury to the sacral roots or bowel during the placement of the working channel.

When placing the guide wire, the beveled end may be used to slightly guide the wire anterior or posterior while advancing. If advancing with the beveled end anterior the guide wire will tend to advance to a more posterior position and the opposite is true if the bevel is placed posterior while advancing.

When initially drilling S1 it is important to remove the drill bit with clockwise motion as this will remove the drilled bone from the operating canal. This bone can then be used in the fusion mixture. The opposite is true when drilling L5. Counterclockwise removal will leave the drilled bone in the hole and will not remove the already placed interbody fusion compound.

When using the loop curettes it is important to be cautious when turning the curette posterior. Using frequent fluoro and not forcing the curette with excess torsion will keep the operator from damaging the PLL or the thecal sack. Excessive force may cause breakage of the curette and retention of parts of the curette in the disc space.

The irrigation/suction unit is very useful in removing free fragments that are left by the curettes and the brushes. It may also be used prior to closing to irrigate the wound and remove any air left in the surgical tract.

It is important to not over pack the L5/S1 disc space with bone graft material. This could possibly lead to annular bulging and cause compression of the S1 nerve root leading to postoperative radiculopathy. If BMP is used as graft material, it would be best if the retention screw is placed in order to prevent leakage of the BMP outside the confines of the annulus.

We prefer closure of the wound with Dermabond due to it's ability to seal the wound from a part of the body which is inherently infectious. It also does not have to be removed as do sutures and staples, which can cause a significant amount of discomfort to the patient.

Case Series

Our case series consists of 19 patients who received a Lumbosacral fusion during the period of 2006 to 2007 using the Trans 1 axial screw system (Trans 1, Wilmington NC). Eighteen of the cases were fusions due to degenerative disease and one due to congenital pars defect. In 14 patients we were able to obtain pre-fusion and post fusion Oswestry scores. The raw data collected is represented in Table 1. Some patients were not available for interview and thus data on these patients is incomplete. Patients with incomplete data could not be used in our statistical comparisons. One patient in whom data was available was less than a month from surgery therefore, the data was not used in our pre-surgical and post-surgical comparison due to the likelihood of there still being a significant amount of immediate post operative pain.

Table 1

	Posterior instrumentation	**Pre-Oswestry**	**Post-Oswestry**	**Pre work**	**Post work**
1	Pedicle screws	58	50	Yes	No
2	Pathfinder	46	0	Yes	Yes
3	IST percut.	42	36	No	Yes
4	IST percut	74	20	No	Yes
5	Pathfinder	54	62	No	No
6	None	90	**N/A**	**N/A**	**N/A**
7	Pathfinder	62	**N/A**	**N/A**	**N/A**
8	Pathfinder	68	20	No	No
9	Unilateral screws	44	**N/A**	**N/A**	**N/A**
10	Pathfinder	48	14	No	Yes
11	Pathfinder	66	34	Yes	No
12	Pathfinder	51	24	No	Yes
13	Pathfinder	60	28	No	No
14	Sextant	22	**N/A**	**N/A**	**N/A**
15	Pathfinder	50	58	No	No
16	Pathfinder	**N/A**	24	**N/A**	**N/A**
17	Pathfinder	74	6	Yes	No
18	Lanx	58	56	No	No
19	Sextant	54	60	No	No

The average age of the patients treated with pre-sacral fusion was 43.9 yrs. 58% were male, 42% were female. The average pre-surgical Oswestry score was calculated using the data from 13 patients with complete data. The average pre-Oswestry score in the 13 patients with complete

data was 57. The average post surgical Oswestry score was 36 in this same group of patients. Only 31% of patients were working prior to surgery and 38% were working following surgery. A paired t-test was used to evaluate the statistical significance between the pre-surgical Oswestry scores and the post-surgical Oswestry scores. The mean of the pre-surgical group minus the mean of the post surgical group equals 23.93, and the 95% confidence interval of this difference is from 9.48 to 38.38. The standard deviation of the Pre-surgical group was 10.7, and the standard deviation of the post surgical group was 20.84. The calculated two-tailed *p* value for the two groups was .0034. This value using conventional statistical criteria is considered to be very statistically significant.

It is useful to discuss a number of other observations of a less statistical nature in our patient group. There were no complications in the placement of the axial screw in 19 patients. Postoperative radiographs show good placement in all 19 patients with the axial screw totally within the L5 and S1 segments in 100% of the cases. Two patients received posterior instrumentation prior to axial screw implantation in order to use the pedicle screws for reduction of a spondylolisthetic defects.

Only one technical complication was noted. A curette loop broke off leaving a fragment in the L5/S1 disk space. The fragment was able to be removed and no ill effects to the patient occurred.

No bowel injuries or nervous system complaints were directly attributed to placement of the axial screw, however, two patients were taken back to the OR in the following months in order to decompress the S1 nerve root due to a buldging annulus. It is unclear as to why the patients developed a radiculopathy following the procedure, however, the most plausible explanation is that overpacking of the annulus with graft material caused a disc bulge and led to compression of the S1 nerve root.

The lack of any significant technical complications is highly significant in that these were the first cases performed by our group using the pre-sacral technique. We feel that any spine surgeon with adequate operative skills can safely perform this technique. The most important issue in performing the technique is proper pre-surgical evaluation and planning.

Upon review of the patient charts, two patients complained of mild peri-coccygeal pain, however, both patients had a significant improvement in their back pain following surgery. No infections were found in our series either at the pericoccygeal incision site or the percutaneous pedicle screw sites.

A variety of graft materials and posterior pedicle screw systems were used and all seem to have adequate fusion results to date. This data is summarized in Table 1. No comparison of the pedicle

screw system or the type of graft material has been done at this time. One patient had a stand alone axial screw placed and is doing well and has returned to work.

Six month follow up CT scans to evaluate fusion are planned and the data will be presented in the final draft of this paper.

Future Technology

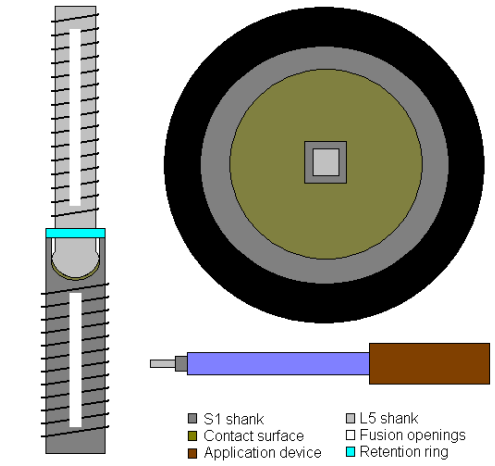
Because of the unique approach to the L5/S1 disc space there are a number of different new technologies being developed for dealing with degenerative and congenital disease of the lumbosacral junction.

The most recent expansion of this approach would be to treat the L4/5 degenerative levels simultaneously while fusing the L5/S1 joint [22] . This approach would clearly be advantageous to patients who need fusions at both levels. This technique is currently being developed and should be the first major expansion of the use of the pre-sacral approach. This approach would allow placement of a screw across the L4/L5 disc space as the initial step prior to fusion at L5/S1. The technique will only be useful in patients that need fusion at both levels and there is an increased chance that anatomical constraints would make this approach unacceptable in a number of patients.

Another developing technology that may also benefit from the presacral approach is the nucleus replacement technologies [23], [24,25]. The pre sacral approach would allow minimally invasive access to the L5/S1 interspace as well as the possibility of accessing the L4/5 interspace and simultaneously repairing both levels. A number of different nucleus replacement systems are currently being developed. Hyaluronan-derived polymeric substitute materials [26], hydrolyzed polyacrylonitrile hydrogel [27] , PVA/PVP hydrogel substances [28] are just a few of the substances currently being tested for use. The presacral approach has the advantage of accessing the L4/5 and L5/S1 disk space without causing annular disruption which makes it a perfect approach for nucleus replacement.

Dynamic stabilization systems are also being developed using the pre sacral approach to L5/S1. The original patent submission for the pre sacral approach showed some ideas that provided dynamic stabilization system. This system primarily provided dynamic motion in axial compression. The primary author also is developing an axial placed dynamic system that would be placed using the presacral approach and would not require any posterior stabilization. This system would be particularly useful in young patients with apars defects and back pain secondary to a spondylolisthesis. The Dynamic axial screw is based on a ball and socket design with either a metal on metal interface or a polymer interface. The screw is designed to offset the shear strain between L5/S1 which normally is the function of an intact pars and facet. The clear advantage to this system is that it should be useful in preserving motion in young patients in whom adjacent level disease would be of particular concern. The screw itself has within it's threaded portion

fusion openings to aid in fusion of the bone/metal interface. The internal portion of both the L5 and S1 shanks can be filled with bone graft material to aid in the fusion of the shanks within the vertebral body (fig 2).



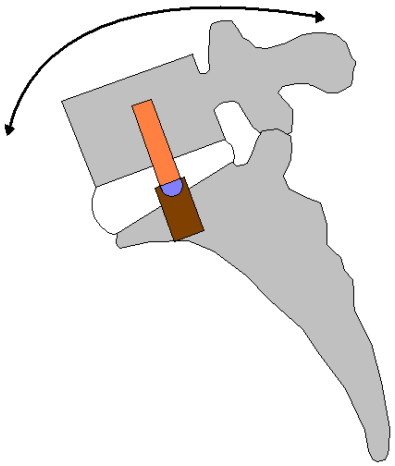


Fig 2*

***Patent Pending**

The system would allow rotation in the axial plane and therefore there should be no movement between the vertebral bodies and the threaded portion of the dynamic screw. The dynamic screw should allow preservation of anatomical motion at the L5/S1 joint minus compression. The screw would also allow restoration of disc height if needed, reduction in the incidence of adjacent level disease at L4/L5, and restriction of abnormal translational forces at L5/S1 which is likely the main source of axial back pain and progressive spondylolisthesis.

When compared to other dynamic systems that could be used at the L5/S1 level such as the Dynesys system there are a number of distinct advantages. Many of the studies looking at the Dynesys system show that a large portion of patients go on to fuse at the level that the system is used. This is unlikely to happen with the dynamic axial screw because most of the disc material will remain in place inhibiting fusion, and motion around the segment will provide far less resistance than the dynesys system. The Dynesys system also requires a significant amount of posterior muscle disection in order to place the system which leads to a significant amount of postopperative pain. The presacral dynamic screw placement only requires a small pericoccygeal incision (fig 2). All dissection is done in the presacral retroperitoneal space to insert the screw and requires no further posterior support leading to a significant reduction in postoperative pain when compared to the posterior applied systems.

Further testing will be needed before any of these systems are put into widespread use. It is clear that the pre-sacral approach opens up new possibilities for static and dynamic fusion systems in dealing with disease at the lumbosacral junction.

Summary

In the previous sections we have discussed the biomechanical advantages of the application of an axial screw system for fusion of the L5/S1 segment. When compared to the ALIF and posterior instrumentation at this level the axial system is stronger in a number of different tested motion parameters. In addition to these advantages the system allows a minimally invasive approach to fusing the lumbosacral segment. With minimal dissection of the lumbosacral ligamentous structures, disc annulus, and supporting Erector spinae musculature, most of the spines own biomechanical stabilization apparatus is left intact. The ability to fuse the L5/S1 segment without having to strip the posterior musculature from the lumbar segments also leads to a significant decrease in the amount of post-operative pain.

Our small series of patients demonstrates that the use of the pre-sacral approach to fuse the L5/S1 segment is a viable and safe alternative to other traditional methods of fusing this segment. In our series we had no incidence of bowel injury, and no patient complications directly related to the placement of the axial screw.

We have also reviewed some of the developing technology that will be able to take advantage of the unique features of the pre-sacral approach. We have also introduced a novel dynamic screw which would allow stabilization of the lumbosacral joint by restoring disc height, and counteracting the severe translational forces present at the lumbosacral junction.

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The Decompressive Craniectomy for Traumatic Intracranial Hypertension

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Abstract

Enthusiasm for the use of the craniectomy to address intracranial hypertension has waxed and waned during the past century. The failure and success of this procedure has been attributed to multiple clinical and technical factors. Currently this procedure is used as a salvage or life saving effort in patients with diffuse traumatic brain injury and impending herniation. Its simplicity and effectiveness in lowering intracranial pressure has encouraged many surgeons to use it more readily although it has not been proven to improve neurological outcome in a systematic fashion. The indications and appropriate timing of the procedure remain controversial. A retrospective review of the cases performed at a single center is presented to demonstrate factors which may mask its benefits in severe traumatic brain injury. Further investigation is required to validate its use as an early intervention tool rather than a life saving procedure and to identify appropriate candidates.

Key terms: Decompressive craniectomy, traumatic brain injury.

Introduction

Severe Traumatic Brian Injury (TBI) remains a major cause of morbidity and mortality in the younger and increasingly in the elder patient populations. Although some studies have shown an association of improved outcomes with treatment at a major trauma center and with the use of intra-cranial pressure (ICP) monitoring, this is mostly due to injury prevention and the development of pre-hospital triage systems. Over the past three decades, neurological outcome of severe head injury victims appears to have reached an insurmountable plateau **(45)**. This may be in part due to the fact that available medical and surgical intervention options are incapable of repairing initial damage sustained during injury. Protocols for the treatment of comatose head injury patients have focused on preventing secondary injury. Elevated ICP is commonly associated with severe TBI and has been correlated with poor outcome **(33)**. The Traumatic Coma Data Bank documented a 72% incidence of intracranial hypertension (ICP > 20mmHg) in patients with severe TBI **(32)**. Its normalization and control is hypothesized to optimize the recovery of viable neuronal tissue by balancing the metabolic utilization of oxygen. In the absence of a mass lesion, therapeutic options are frequently ineffective in controlling ICP. The removal of a portion of skull is occasionally utilized to allow for brain swelling and to facilitate ICP control. This is referred to as a decompressive craniectomy.

The first documented use of a craniectomy for the reduction of intracranial hypertension in modern medicine was by Annandale in 1894 **(30)**. It was also advocated by Kocher, Cushing, and Penfield but fell out of favor due to poor outcome. The efficacy of the craniectomy in reducing traumatically elevated intracranial pressure has been documented in multiple laboratory and clinical studies **(38)**. Although intuitively speaking this reduction in ICP should translate to an improved outcome, this has been difficult to validate. Animal studies in the late 1960s demonstrated improved mortality in

dogs but resulted in minimal levels of brain function and recovery. One early theory suggested that the reduction in interstitial pressure resulted in an increase in vasogenic edema which was believed to exacerbate neuronal injury. This theory has been refuted by some, and more recent clinical studies although not randomized, have shown a perceived benefit and good outcome resulting in a resurgence of interest in this procedure. Although there is objective evidence of reduced intracranial pressure and improved perfusion and oxygenation after a decompressive craniectomy, its ultimate effect on outcome has been difficult to demonstrate (**55)**. Therefore, it remains a second tier option, as defined by the Brain Trauma Foundation Guidelines (BTFG), reserved as a therapeutic option for dire situations in which first line measures have failed to control ICP **(7)** in severe TBI.

Head injury is conventionally classified according to the presenting neurological condition and the radiological findings. Severe TBI constitutes nearly 10% of all brain injury patients admitted to the hospital and carries a mortality rate of about 40% **(45)**. This refers to any patient presenting with a Glasgow Coma Score of 8 or less after resuscitation or subsequent decline to this level of consciousness. Despite known limitations the Glasgow Coma score (GCS), as presented by Teasdale in 1974, has been used repeatedly because of its simplicity, reproducibility and it ability to predict long term neurological outcome in severe TBI. (**26,27)**. Although useful for prognosis, this classification of injury is not necessarily specific for the primary injury pattern involved.

Brain injury may also be characterized with regard to the radiological findings of either a focal injury pattern or diffuse involvement, but it is important to recognize that both patterns are usually involved to a certain extent. Diffuse injury is a general term encompassing any wide spread pathological process related to mechanical trauma. Study of data from the Traumatic Coma Databank (TCDB) has uncovered specific CT manifestations of diffuse injury which when used in conjunction with other established prognostic factors accurately predicts patients at risk for intracranial hypertension, subsequent neurological decline, and overall outcome **(fig 1)(fig 2) (35)**. In the face of focal intra or extra axial hematoma, classification of severe TBI by radiological correlates has enabled a more systematic evaluation of affected patients, and the development of a set of recommendations for surgical intervention **(26,27)**. In the absence of a significant focal mass lesion, elevated ICP is typically related to edema associated with diffuse injury. Medical and surgical therapeutic options for treatment of diffuse injury have remained non-specific and with significant limitation. A decompressive craniectomy may reduce evolution of injury related to mass effect and elevated ICP, but its effect on other pathophysiological processes involved is unknown.

Figure 1 – Outcome in relation to CT classification

Outcome @ DC	Diffuse Injury I	Diffuse Injury II	Diffuse Injury III	Diffuse Injury IV	Evacuated Mass	Non evacuated Mass	Brainstem Injury

	%	%	%	%	%	%	%
Good	27	8.5	3.3	3.1	5.1	2.8	0
Moderate	34.6	26.0	13.1	3.1	17.7	8.3	0
Severe	19.2	40.7	26.8	18.8	26.1	19.4	33.3
Vegetative	9.6	11.3	22.9	18.8	12.3	16.7	0
dead	9.6	13.5	34.0	56.2	38.8	52.8	66.7

Figure 2 – CT classification of severe traumatic head injury	
Diffuse injury **I**	No visible pathology seen
Diffuse injury **II**	Visible cisterns, midline shift ≤ 5mm, lesion ≤ 25cc
Diffuse injury **III**	Compressed or absent cisterns, midline shift ≤ 5mm, lesion ≤ 25cc
Diffuse injury **IV**	Compressed cisterns, midline shift ≤ 5mm, lesion ≤ 25cc
V	Surgically evacuated lesion
VI	Mass lesion > 25cc not evacuated
VII	Evidence of 1° brain stem injury

There are two different situations in which a decompressive craniectomy is used in severe head injury. Some authors have suggested a prophylactic role for the decompressive craniectomy as a surgical adjunct in patients undergoing evacuation of a focal lesion with signs of diffuse injury by CT scan (**47**). This is supported by studies demonstrating a significant rate of uncontrolled ICP (31%) after hematoma evacuation **(50)**. The second situation is one in which ICP is unresponsive to medical intervention. In this situation, clinicians' threshold for utilization of surgical decompression varies. The effects of osmotic agents and CSF drainage although valuable, are transient and with real limitation. If first tier options fail, paralysis or chemically induced coma are typically utilized to control intractable intracranial hypertension before surgical decompression is considered. Whether or not this is appropriate has not been studied systematically. Surely these maneuvers, especially if prolonged, carry significant side effects and risks comparable to or even more harmful than a craniectomy. Furthermore, this algorithm may result in delay and possible exacerbation of secondary injury. Gower documented

40 % mortality in patients undergoing subtemporal decompression for intractable intracranial hypertension compared to 82.4% among patients in pentobarbital coma without decompression **(22)**. Outcomes were significantly worse if the procedure was delayed more than 48 hours after admission. This finding was also echoed by Polin and others **(40).** Recent unpublished military data from the Iraqi conflict has demonstrated impressive outcome results with aggressive utilization of the decompressive craniectomy as an early primary procedure or an adjunct to hematoma evacuation **(46)**. It is likely that the potential benefits of surgical decompression may be masked by its current use in a delayed fashion, or in patients with devastating brain injury, brainstem damage, or diffuse axonal injury. Currently, there are two prospective trials in progress that may shed new light on relation to outcome and surgical indication **(25,43)**.

A single institutions experience in the usage of the decompressive craniectomy for severe traumatic brain injury is presented to identify situations of success and failure and associated complications. Although this study does not have the power to make any recommendations for other institutions, evaluation of trends at our hospital will demonstrate held perceptions and, by cross examination of the available literature, will offer a proposition for standardization of its use and will possibly improve outcome.

Method

Patients admitted directly or transferred to Cooper University Hospital in Camden New Jersey to the trauma service formed the patient base for this study. This is a level one regional trauma center servicing an area of 3300 square miles within the state of New Jersey. A search for patients undergoing craniectomy from 2002 through 2006 was conducted by CPT code (61322). Codes for intra and extra-axial hematoma evacuation (61312, 61313) were also reviewed to assure inclusion of all cases. All charts were reviewed by a single entity in a retrospective fashion. Craniectomies performed on patients with presenting GCS > 8 or for reasons other than acute trauma were excluded. Cases from seven neurosurgeons were included. Selection of the appropriate surgical candidates and type of surgery was at their discretion. Patient care was not standardized during the accrual period, but well accepted therapeutic options were generally adhered to. Intracranial pressure monitors were utilized for all patients presenting with a GCS < 9 and an abnormal CT scan or two of the following three criteria - age > 40, systemic hypotension or posturing by examination. Medical intervention used to control intracranial hypertension included head elevation, hemodynamic and respiratory support, fever control, chemical sedation and paralytics, CSF drainage, and chemical diuresis via osmotics or loop diuretics. Pentobarbital coma was utilized up to the middle of 2004 on select cases, and 3% normal saline thereafter rather than mannitol in cases of hemodynamic instability or intravascular depletion. Changes in management trends reflected new staff appointment.

Demographic and clinical factors documented include patient age, presenting GCS and motor score, pre-operative GCS score, pupillary dysfunction, highest sustained ICP, initial CT score **(fig 2)**, time interval from admission to the operation, and the GCS at discharge. Morbidity, complications, and mortality information was also recorded.

Outcomes are compared to historical data collected from the Trauma Coma Data bank as a control group was not obtainable from the patient population included owing to clinical and documentation trends adhered to.

Results

Two hundred forty nine patients underwent a craniotomy or craniectomy for traumatic brain injury during the five year period being reviewed. This included thirty two patients undergoing craniectomy for decompression of diffuse injury related to acute trauma. Seven of these cases were excluded for clinical reasons including one involving a gunshot wound and six other patients presenting with a GCS >8. Patient information was incomplete or unobtainable in sixteen other cases and these were also excluded. The following table represents clinical data collected on the nine remaining cases.

The average age of patients undergoing a decompressive craniectomy was 21. The average presenting GCS was 6 (5.56) and if mortalities are considered a GCS of 3, the average GCS at discharge was 9 (8.89). Patient presenting with a GCS ≥ 7 had an average GCS at discharge of 14.67 whereas patients presenting with lower scores resulted in an average discharge GCS of 6. If a motor score ≥ 4 after resuscitation is used as a cut-off, the average discharge GCS was found to be 13.25 as opposed to 5.4 in patients admitted with signs of posturing or worse.

All patients with pupillary dysfunction remained below a GCS of 10. Three of nine patients in this series died. All mortalities showed evidence of pupillary dysfunction preoperatively and occurred within the first week after admission. Complications associated with surgical intervention included frequent subgaleal and interhemispheric fluid collections, but none required a second surgical intervention, increased hospital stay, or was apparently detrimental to the patient's ultimate neurological outcome.

Figure 3 – Demographic and clinical data of patients undergoing hemicraniectomy

Age/ gender	Presenting GCS	Motor score	Preop GCS	Pupillary dysfunction	CT score	Highest ICP (mmHg)	Time to OR	LOS (days)	GCS @ discharge
26	6	3	3		2	40	4 d	37	9
16	3	1		L	3	80	2 hr	6	-
11	7	4			5		3 hr	6	14
18	8	4	6		3	33	6 d	23	15
16	8	5	7		5		3 hr	26	15

44	3	1		R	5		1 hr	2	-
26	4	2		Bilat	5		1 hr	87	9
20	5	3	3	Bilat	5(7)		1 hr	1	-
10	6	4	3	L	3	51	3 d	26	9

Discussion

The series presented does not offer any new information, but it does exemplify cases that are likely to respond favorably to surgical decompression by craniectomy and others that may not. Evaluation of specific factors involved in each case may help identify a protocol for prospective study of this procedure.

The age of patients undergoing a craniectomy in this series demonstrates a selection bias for aggressive therapy in younger patients. This is relevant for a number of reasons. A vast majority of traumatic brain injuries occur in adolescents and young adults resulting in the highest cause of mortality and a great deal of long-term neurological and cognitive dysfunction. Furthermore, the pathophysiology and potential for recovery from traumatic brain injury vary in children and adults **(21)**.

Although metabolic dysfunction related to traumatic brain injury is not as well understood in the pediatric population, when compared to adult patients, variations in cerebral blood flow and biomarkers have been documented. It is unknown whether this is related to the documented increased incidence of diffuse cerebral edema in the pediatric population **(2)**. Nevertheless, the strongest literature support of a craniectomy for diffuse cerebral edema and the only prospective randomized controlled trial completed to date was conducted by Taylor in patients between the ages of 1 and 18 years **(52)**. In this study, patients randomized to receive maximal medical therapy in conjunction with bitemporal craniectomies showed lower rates of death and poor outcome (46%) when compared to maximal medical management alone (86%). Another issue specific to the young brain is the recovery potential. The human brain continues to develop through the second decade of life, and although immature brains have a higher propensity for plasticity, there is an increasing amount of evidence in the literature suggesting unique vulnerability in younger patients **(21)**. Therefore, it is imperative to evaluate the effects of a decompressive craniectomy in various age groups separately **(12,44)**.

The variable clinical scenarios and timing in which a craniectomy is performed also makes it more difficult to identify subpopulations that may benefit from surgical intervention. Its prophylactic use as a surgical adjunct after evacuating an acute focal hemorrhagic clot is typically done before an ICP monitor is placed and thus referred to as a primary decompressive craniectomy. Five of the 9 cases described above fit this criterion. The other situation is the failure of medical management to control intracranial hypertension related to diffuse edema. This would be considered “therapeutic” as

opposed to "prophylactic" decompression and is termed secondary decompressive craniotomy. Our series is unable to demonstrate a significant difference in outcome, however, since the goal of a prospective study is to determine the ability of decompressive surgery to improve outcome in the face of diffuse cerebral edema and associated intracranial hypertension, it would be reasonable to investigate cases of documented hypertension before including prophylactic procedures.

The high mortality rate observed in patients undergoing a decompressive craniectomy may be related to poor patient selection and irreversible severe primary brain damage occurring at the time of injury. Although intensive care and ICP monitoring have improved outcome, recent epidemiological studies conducted by the European Brain Injury Consortium still show a 40% mortality rate at six months for patients with severe traumatic brain injury and another 20% remaining vegetative or severely disabled. American sources may represent a more appropriate comparison. Studies from the 1980s, although not as grim, still document a relatively high mortality rate of 33% (**34).** The series presented above shows similar results demonstrating neither a benefit nor harm related to the procedure in question. Retrospective series in the literature attributing improved outcome to a decompressive craniectomy routinely exclude patients with what appears to be irreversible brainstem damage. Guerra **(23)** excluded patients with evidence of irreversible brainstem dysfunction or a GCS of 3 and documented satisfactory outcome in about 60% of cases. Polin **(40)** consistently found poor outcome in patients with sustained ICP above 40 mmHg. Our series supports these findings- both patients with an initial GCS of 3 died, and all patients with pupillary dysfunction or an ICP$\geq$ 40 fared poorly. Perhaps better selection of surgical candidates may help reveal benefit conferred to patients without evidence of extreme neuronal damage or brainstem injury.

Interestingly, there are studies that have suggested poor outcome in patients undergoing a decompressive craniectomy early in their course of treatment **(1)**. Whereas Gaab **(20)** and Polin**(40)** attributed good outcome in part to early intervention before intracranial hypertension resulted in irreversible secondary injury. These findings are not necessarily conflicting, rather it may be related to selection bias. It is conceivable that patients presenting in extremis or with rapid neurological decline may represent a category of traumatic edema indicative of more pronounced primary injury that is less responsive to decompression.

The pathophysiology underlying diffuse injury and traumatically induced edema is multifactorial and possibly affects the response to decompression. Edema attributed to hypoperfusion and ischemia is more likely to respond to decompression than edema related to blood brain barrier disruption, interstitial hyperosmolarity, and hyperperfusion states associated with dysautoregulation. All of these processes have been described as contributors to traumatically induced edema and consequent intracranial hypertension. The chronological order in which they occur and how they are interrelated is not clearly defined. Undoubtedly there are other poorly understood mechanisms as well. Theories continue to evolve, and better understanding will allow for the identification of appropriate surgical candidates. Initially it was believed that vasogenic edema was a

major contributing factor to traumatic intracranial hypertension. Experimental animal studies in the 1970s demonstrated an increase in the amount of vasogenic edema indicated by Evans blue dye extravasation after surgical decompression **(13).** Cooper thus concluded that although a craniectomy decreased intracranial hypertension, it also exacerbated secondary neuronal injury by enhancing vasogenic edema. Recent experimental and clinical studies have refuted this by defining a more complex and specific model of traumatic brain edema. Although vasogenic edema may be linked to states of hyperperfusion observed later in the course of traumatic brain injury, MR diffusion studies have demonstrated only small amounts after 48 hrs. Furthermore, post mortem immuno-histochemical study of early brain injury failed to show any plasma protein leakage making vasogenic edema a less likely culprit of early clinical deterioration after severe head injury. Japanese studies have attributed early edema formation to a prolonged hyperosmolar state resulting form contusion necrosis **(28)**. Dysautoregulation and consequent cerebral ischemia may also contribute to early edema formation and subsequent secondary brain damage. Bouma documented an association between poor outcome and a decrease in cerebral blood flow within six hours of injury **(4)**. Proponents of the primary decompressive craniectomy hypothesize better outcome related to intervention before irreversible ischemic damage is caused by elevated ICP **(34).** Perhaps it also decreases secondary injury by reducing edema formation associated with hypoperfusion states early after primary injury **(55)**. Undoubtedly, injury patterns and the extent of involvement of any one of these process varies form patient to patient and it is unknown whether one may respond more readily to decompression depending on the underlying etiology of the intracranial hypertension. Therefore, the temporal aspect of neurological decline and timing of intervention should be considered when evaluating response to a decompressive craniectomy and if possible, blood flow, oxygen tension, and microdialysis should be incorporated into future studies to study association of metabolic parameters to outcome.

A great deal of variability in surgical technique is seen in trials evaluating the decompressive craniectomy. Historically, removal of the temporal squamous bone was advocated by surgeons realizing the importance of mesencephalic decompression. This has been replaced by the creation of large defect involving either a fronto-temporo-parietal or bi-frontal bone flap. These decisions usually depend on the region of injury and surgeon preference. Both have been shown to be effective in decreasing ICP and both have minor specific advantages over the other. All patients in this series underwent a unilateral craniectomy determined by the side of hematoma or increased shift. It is unknown whether a bifrontal or unilateral craniectomy is preferable, but temporal bone removal has been shown to result in decompression of the perimesencephalic cisterns **(55**). This carries intuitive merit in that cisternal compression has been associated with elevated ICP and poor outcome (**53).** A wide decompression is also recommended to decrease the chance of a venous infarct associated with brain herniations through a small bone flap **(42)**. The actual size of the craniectomy has been studied clinically and Burket demonstrated a reduction of 20 – 30 mmHg in experimental models when the radius of the bone flap created was two thirds that of the head **(10)**. A prospective study by Yoo compared ICP before and after dural opening revealing a 15% reduction in ICP and therefore providing evidence to support durotomy **(56).**

In light of the literature reviewed and the clinical results of the series presented, we propose an outline to evaluate the efficacy of the craniectomy in improving functional outcome of severe traumatic brain injury patients at Cooper University Hospital. Patients presenting with a GCS <9 after mechanical blunt injury will be evaluated for ICP monitor indications. This includes an abnormal CT scan, or two of the following three criteria – age > 40, hypotension, or a posturing motor response. Brain tissue oxygen tension monitoring will also be measured when feasible. Patients with a CT score of 2 – 4 and elevated ICP will then be treated with conventional methods of control for 24 hours. At this point patients still requiring intervention to treat intracranial hypertension above 20 mmHg will be randomized to either receive medical management alone or a decompressive craniectomy followed by medical management. Randomization will occur before consent is obtained, and only family members for patients randomized to receive surgery will be approached. This approach is previously described as Zelen randomization and may be appropriate in this situation (**24**). Exclusion criteria will include surgical intervention for hematoma with mass effect or the need for a craniectomy before 24 hours. Patients with GCS of 3 and bilateral pupillary dysfunction should not be considered for randomization on the basis of neurological devastation; this protocol is not intended to evaluate the procedures miracle potential. The surgical technique will include a uni or bilateral craniectomy as seen fit by the surgeon. Middle fossa decompression and durotomy will be performed in all cases and the length and height of the bony defect will be recorded. An ICP monitor will be kept in place for at least 24 hours after the procedure or longer if indicated. Admission CT score, pre and post operative ICP, PbO_2, length of hospital stay, and complications will be documented. Functional outcome will be assessed at hospital discharge and 6 months after injury using the Glasgow Outcome Score.

Conclusion

The decompressive craniectomy is a relatively safe and effective option for treating elevated ICP. The long term benefits suggested by the literature are repeatedly noted in certain subgroups of severe traumatic brain injury patients. We propose a protocol for early intervention to see if this maneuver offers added benefit over medical management alone in regards to length of hospital stay and neurological outcome. Although the results of this study would not be applicable to all situations in which a decompressive craniectomy may be useful, it would elevate its role in the treatment algorithm for traumatic intracranial hypertension to more than just a salvage operation. This initial study may then act as a platform to evaluate the craniectomy in less optimal conditions or when used prophylactically.

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Early abdominal abscess with ventriculoperitoneal shunt infection associated with diabetes mellitus and review of literature

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Abstract
We present a case of early, infected abdominal pseudocyst or abdominal abscess with S*taphylococcus aureus* ventriculoperitoneal shunt infection in an uncontrolled diabetic adult. To the best of our knowledge, a MEDLINE [PubMed] search using the terms "ventriculoperitoneal shunt, infected abdominal pseudocyst, abdominal abscess, *Staphylococcus aureus*, and diabetes mellitus," found no results for similar cases. We relate this early, infected abdominal pseudocyst formation with *Staphylococcus aureus* shunt infection (within the first nine months of the shunt placement) to the patient's immunosuppressed state secondary to uncontrolled diabetes. This case illustrates that comorbidities must be included with history of abdominal surgery, inflammatory process, or infection as etiologies for the early infected abdominal pseudocyst formation in adults.

Key Words: ventriculoperitoneal shunt, infected abdominal pseudocyst, abdominal abscess, diabetes mellitus

Introduction
Ventriculoperitoneal (VP) shunting for hydrocephalus was first introduced in 1905.[14,15] Today, VP shunting has become a common operation for cerebrospinal fluid (CSF) diversion. As the number of VP shunts performed rise, numerous intra-abdominal complications have been reported. Some of these include obstruction (most common at the ventricular end), kinking of distal tube, disconnection and breakage, catheter migration, infection, pseudocyst formation and viscus perforations.[11] The frequency of abdominal CSF pseudocyst (APC) formation is approximately 0.7 to 4.5%.[1,11,19] Since the first case reported by Harsh in 1953, only 204 cases of APC have been documented.[1,13,20,22] The frequency of infected APC has not been reported. The most common etiologies for APC formation are recent abdominal surgery, inflammatory process, or infection.[1,19]

Pseudocyst formation is an uncommon complication of VP shunting. Frequently, APC formation occurs after a late VP shunt infection and then is referred to as an infected APC or abdominal abscess.[2] In early shunt infection, occurring within first nine months of shunt placement or revision, Baird found the most common pathogens are *Staphylococcus epidermidis*/coagulase negative and *Staphylococcus aureus*. In late shunt infections, Staphylococcus aureus is not found to be a causative pathogen. To the best of our knowledge, a MEDLINE [PubMed] search using the terms "ventriculoperitoneal shunt, infected abdominal pseudocyst or abdominal abscess, *Staphylococcus aureus*, and diabetes mellitus," found no results for a diagnosis of early *Staphylococcus aureus* shunt infection complicated by an infected APC or abdominal abscess in an uncontrolled diabetic adult (serum glucose >200mg/dL). In this report, we describe a 46-year-old female with history of uncontrolled diabetes mellitus who presented seven months from her first VP shunt placement for hydrocephalus from neurocysticercosis and one month

from her shunt revision with early *Staphylococcus aureus* shunt infection complicated by infected APC.

Case study

A 46 year-old right-handed Hispanic female presented with a 3-day history of altered mental status, nausea and vomiting, incontinence, and unsteady gait. Her medical and surgical history consisted of three-years of uncontrolled diabetes mellitus and neurocysticercosis with secondary hydrocephalus for which she underwent ventriculoperitoneal shunt placement seven months previous. One month prior to the presentation, the patient's VP shunt valve was replaced due to malfunction. The cerebrospinal fluid analysis at that time was negative, and the abdominal films illustrated no evidence of APC formation. The patient had a cesarean section 12 years ago without complications.

The patient had low-grade temperature of 99.9 degrees; otherwise, vitals signs were within normal limits. Physical examination revealed a dehydrated female. The abdomen was mildly distended with minimal tenderness on palpation. She intermittently followed commands and had difficulty with initiating gait. The shunt valve was patent. There was no overlying erythema throughout the shunt system. The CSF analysis from the valve was consistent with bacterial infection.

A nasogastric tube was inserted for decompression. Abdominal radiograph illustrated a pelvic mass containing the shunt tip displacing bowel loops superiorly (Figure 1). A head and abdominal/pelvis computed tomography (CT) was obtained. The head CT showed moderate hydrocephalus and the abdominal/pelvis CT revealed the tip of the VP shunt catheter in the midline of the lower abdomen (Figure 2). The distal portion and tip appeared to be within a loculated fluid collection that appeared to be the largest of multiple fluid loculations in the upper pelvis. The largest fluid collection measured approximately 11.5 x 6.4 cm (Figure 3). This was percuteneously drained and irrigated under CT guidance and a 10-French locking pigtail catheter was placed (Figure 4). The catheter was connected to a suction bag for continuous aspiration. The diagnosis of an infected APC was confirmed by the purulent aspirate and the cultures grew *Staphlylococcus aureus*. The CSF and urine cultures also grew the same specie. The infected shunt was externalized at the neck with the proximal end draining clear fluid into a ventriculostomy bag titrated to drain 5-10ml per hour. The patient's clinical status improved rapidly. She was placed on intravenous antibiotics until the repeat cultures were negative. The infected APC resolution was complete within three weeks (Figure 5). The externalized shunt was then removed and replaced with ventriculoatrial shunt. On follow a up, the patient had good recovery to baseline.

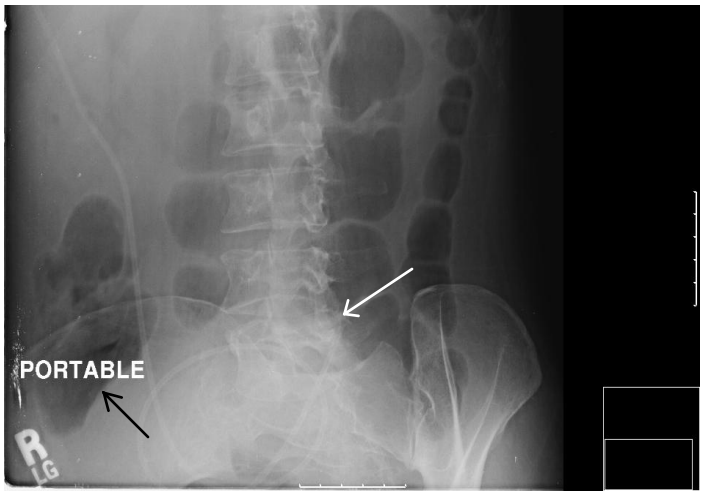

Figure 1. Abdominal radiograph: illustrates a pelvic mass containing a shunt tip (white arrow) displacing the bowel loops (black arrow) superiorly.

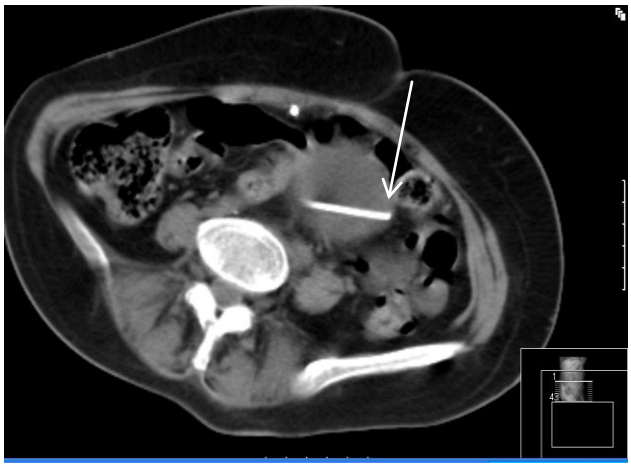

Figure 2. Abdominal CT: reveals the shunt tip (arrow) in the midline of the lower abdomen.

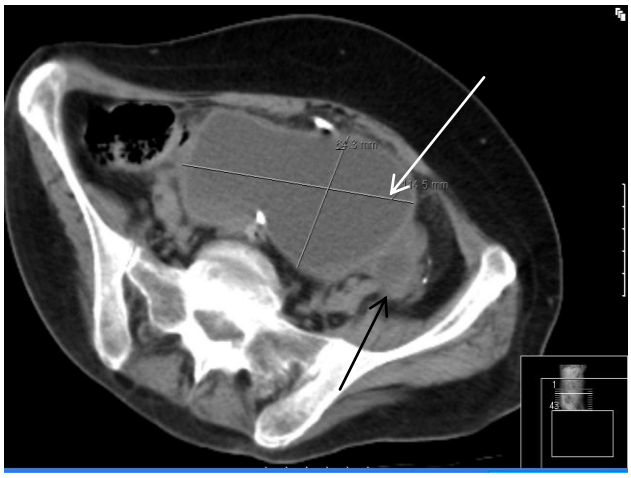

Figure 3. Abdominal CT: illustrates a large fluid filled collection measuring 11.4 x 6.4 cm (white arrow) with adjacent smaller loculations (black arrow).

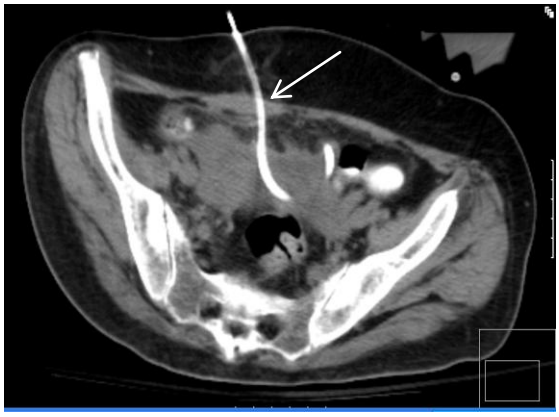

Figure 4. Abdominal CT: showing percuteneous drainage of the abscess with a 10-French locking pigtail catheter (arrow).

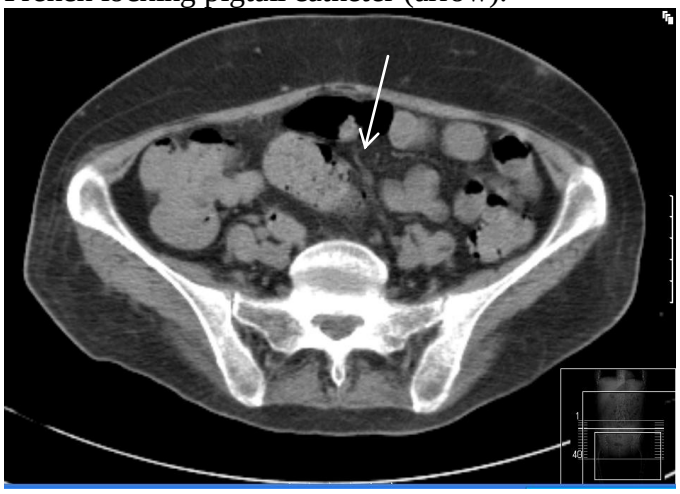

Figure 5. Abdominal CT: reveals almost complete resolution of the abscess (arrow) after the CT guided percuteneous drainage and at two weeks of intravenous antibiotics.

Review of literature

Since the first case of an abdominal cerebrospinal fluid pseudocyst as a complication of VP shunt described by Harsh in 1954, the frequency has been reported between 0.7 to 4.5%. [1,19] Grosfeld reported only three cases with APC of 185 patients (1.6%) with VP shunts.[11] APCs have been identified in the age range from two months to 76 years.[22,24] However, most of the literature is based on the pediatric population. Fischer and Shillito described the abdominal pseudocyst as a thick-walled fibrous capsule containing CSF.[9] The words "infected pseudocyst" and "abscess" are used interchangeably in this paper, but both are different from APC.

APC formation has multiple risk factors. The history of abdominal surgery, inflammatory process, or infection is more likely to precipitate pseudocyst formation.

Previous abdominal surgeries cause development of peritoneal fibrous adhesion formation via an inflammatory process, which leads to minimal CSF absorption resulting in an APC development.[9] APC formation tends to occur on average 15.1 months from the last abdominal surgery.[14,25] The smaller cysts tend to be infected and larger cysts to be sterile, most likely due to the host's defenses or antibiotics.[1] In addition, Roitberg's analysis of 27 patients with APCs illustrated that the patients with recent revisions were more predisposed to shunt infections, rather than an APC formation.[23]

Another main risk factor for an APC formation is an infection. Early shunt infection occurs in the first nine months from shunt placement or revision.[2] Baird reported a review of 94 shunt infections in 87 patients over a 10-year period. 86 of the 94 shunt infections (91%) occurred in the first nine months. The most common microorganism isolated was the *Staphylococcus epidermidis*/coagulase negative (63%). *Staphylococcus aureus*, the second most common, was cultured in 12 of 94 infections (13%). They found that *Staphylococcus aureus* was not a pathogen in any of the late occurring infections and not associated with APC formation. Furthermore, APC formation was more common in the late infection than in the early infection. APC was found in 63% of the late occurring shunt infection and only 14% of the patients diagnosed with the early shunt infection.

Abdominal complications tend to present with abdominal discomfort, nausea and vomiting, and may lead to central nervous system (CNS) signs and symptoms days or weeks after, if the peritoneal catheter becomes obstructed.[18] These CNS signs and symptoms include lethargy, headache, and visual disturbances, due to the inability of the abdominal cavity to absorb CSF.[24,25] Early shunt infection presents with fever, seizure, high serum C-reactive protein, and abnormal CSF analysis (leukocytosis, low glucose level and high protein level).[16]

Ultrasound and CT are the imaging modality of choice for diagnosis of APC. Ultrasound shows a sonolucent mass with uniform echotexture. If septa with possible fluid levels are identified, then an infected cyst is suspected.[12] Computed tomography examination of the APC demonstrates homogenous fluid collection around the catheter tip. For these studies, it is important to identify the tip in the fluid collection to differentiate from pancreatic or ovarian cystic lesions.[20] Other tests including plain films, shunt contrast studies, and nuclear medicine studies may also be used for evaluation.[1]

The treatment of infected APC is controversial. Treatment includes removal of abscess (percutaneous drainage or exploratory laparotomy), intravenous antibiotics, externalization of the shunt, and replacement and internalization of the shunt once the infection is cleared.[1,17] In majority of cases the shunt can be reinserted into the abdominal cavity.[23] In Roitberg's analysis of 27 consecutive pediatric patients with APC [out of unknown total], 12 patients (44%) had positive cultures (none were positive for *Staphylococcus aureus*) on presentation. This is unlike early shunt infection where *Staphylococcus* aureus infection is common. 10 of these 12 patients (83%) had prior history of shunt revision within the previous year from the current presentation. After the infection cleared, the shunt was safely reinserted into the abdomen without further complications in half of the patients. In the remaining six patients there were further

complications. Three patients with the revised VP shunts (25%) needed further revisions within seven months. The last three patients had their shunt revised to ventriculoatrial (VA) shunt (17%) and ventriculopeural (VPL) shunt (8%) because of ascites and acute abdomen. One of the two patients with a VA shunt required even more revisions. Salomano and Leibinger reported that three patients out of 18 APC patients (17%) underwent VA shunting for reoccurrence of APC after revision of a VP shunt into the abdomen.[24] Similarly, Fischer and Shillito described three case reports, where the VP shunts were inserted into another part of the abdomen after clearance of infection and APC, all three shunt malfunctioned within three months secondary to obstruction.[9] They explained that the recent shunt infection must have propagated the body's inflammatory process, and in turn, caused fibrous adhesion formation limiting the function of the revised shunt. All three patients underwent a ventriculoatrial shunt placement. Despite, the severe complications of VA shunting such as atrial thrombi, emboli and endocarditis, to prevent reoccurrence, some prefer VA shunt insertion once the infection is cleared.[1,6,9,11,21]

Regardless of the treatment plan considered, one must take in account the patient's comorbidities to maximize the postoperative outcome. According to Erman, a study of 503 patients who underwent various neurosurgeries over a one year period, the overall infection rate was 6.2%.[7] The presence of diabetes mellitus played a significant role with a 24.3-fold increase in infection risk. Hyperglycemia causes malfunction of the innate immune system. It impairs phagocytosis and migration of polymorphonuclear neutrophils causing the patient to become more vulnerable to infections.[4] In addition, in 100 patients who underwent elective surgery, the patients with early postoperative high (>220mg/dL) serum glucose had 2.7 times higher infection rate and risk for serious nosocomial infection (i.e. urinary tract infection) was 5.7 times higher than those who had lower serum glucose levels postoperatively.

Discussion

A diagnosis of early shunt infection with *Staphylococcus aureus* complicated by infected APC in an uncontrolled diabetic adult has never been reported to the best of our knowledge. The presentation of this patient makes this a unique case. First, the microorganism identified in our case, *Staphylococcus aureus*, is not associated with infected APC formation, and second, the development of infected APC is not commonly an early finding. We speculate during the shunt revision the system may have been inoculated leading to shunt infection and making the patient susceptible to rapid infected APC formation secondary to patient's altered immune system from uncontrolled diabetes mellitus. In this case, we contemplate if we had continued the prophylactic antibiotic for a longer period of time secondary to the underlying comorbidities and enforced a more stringent serum glucose control, then the infected APC formation may have not occurred.

Conclusion

To the best of our knowledge, this is the first case of an adult patient with an early infected APC with *Staphylococcus aureus* associated shunt infection. We relate the early *Staphylococcus aureus* shunt infection with infected APC formation to the patient's immunocompromised state secondary to uncontrolled diabetes. This case illustrates that

underlying comorbidities play an important role in severity of developing shunt complications. The previous main etiologic agents for early, infected APC formation included recent abdominal surgery, inflammatory process and infection, but now must contain comorbidities.

Summary

As the popularity of ventriculoperitoneal shunting for hydrocephalus grows with time, and with prolonged life expectancy of shunted patients due to advances in medicine, these patients will present later in life and with once-thought to be uncommon complications. The development of early shunt infection with abscess has multifactorial etiologies, including comorbidities that may alter patient's natural immune response. If patients with comorbidities such as, in our case, uncontrolled diabetes mellitus require shunt revision, we speculate extending the course of antibiotics and maintaining stringent serum glucose control may prevent the early shunt infection with infected APC formation. All physicians, not just neurosurgeons, need to become more cognizant of abdominal complication when evaluating shunted patients.

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Vertebral Artery Injury after Acute Cervical Spine Trauma

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Abstract
A retrospective analysis of 59 patients with Stage I or Stage II cervical spine trauma was evaluated. The Vertebral artery injury (VAI) was evaluated using computed tomographic angiography (CTA) or magnetic resonance angiography (MRA). Our primary focus was to study VAI after fracture through foramen transversarium (FT). Out of 59 patients there were 24 who had fractures through foramen transversarium. Our results indicate that 3 out of 24 (12.5%) patients had VAI. These fractures, however, did not result in spinal cord dysfunction or vertebro-basilar insufficiency. The VAI is statistically correlated with comminuted fracture through FT. A linear, non displaced fracture through FT does not correlate with VAI. Also there is no VAI in just unilateral sublaxation without fracture through FT. Therefore, we conclude that a CTA is warranted to evaluate VAI after comminuted fractures through FT.

Key words: foramen transeversarium (FT), vertebral artery injury (VAI), computed tomographic angiography (CTA), magnetic resonance angiography (MRA), catheter angiography(CA).

Introduction
Vertebral artery is divided into five common segments: origin (V0); origin to entry in the C6 transverse foramen (V1); mid cervical intraforaminal componentC6-C2 (V2); exit transverse foramen C2 to dural penetration at the skull base (V3); and intracranial course to formation of the basilar artery (V4). In general, the V2 segment that runs through the vertebral foramen is more prone to injury. The most frequent site of vertebral artery injury was reported to be at C5-6 level (Veras, Willis).

Injury to vertebral artery was studied by most invasive method of catheter angiography (CA), and the largest study was done in 766 patients (Cothren). The benefit of ultrasound has also been previously studied. In a 2006 report, Eastman established that CTA is as 100% specific as CA in detecting cervical vascular injury. The use MRA has been studied (Taneichi, Simcha), however, its co-relation with CA has so far not been established. In this study we focused on the use of CTA or MRA to detect VAI.

Cervical deformities were classified into four stages by Allen-Ferguson classification in 1982 and Sim in 2000, studied vertebral artery injury corresponding to each stage of cervical deformity. Stage I is associated with subluxation with in the physiological range of cervical flexion, without significant rotational displacement. Stage II is associated with flexion-distraction (unilateral dislocation), stage III is bilateral dislocation and stage IV is associated with complete disruption of ligaments and paracervical muscles.

Methods
This study included adult patients with suspected neck injury during the past 18 months at Arrowhead Regional Medical Center. All of them received plain x-rays followed by

CT for evaluation of fractures. There were a total of 104 cervical fractures which include of all four stages of spine injuries. Out of 104, only 59 patients had Stage I and Stage II fractures. There were 16 had stage III and 9 had stage IV fractures and 20 patients had fractures that do not fit the above criteria. Of 59 patients with stage I and II, only 24 had fractures through FT.

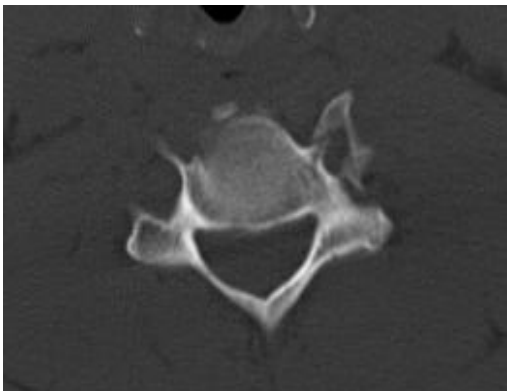
Overall there were 24 patients included in this study. There were16 males (66%) and 8 females (33%). The age range was between 18 and 71. Cervical spine injury was recognized by the Allen-Ferguson classification. In this study, we examined VAI after fractures involving foramen transversarium, especially those in Stage I and stage II of cervical injuries. Stage III and IV fractures are not included due to obvious significant impact on VA secondary to severe vertebral rotation, translation and distraction associated with such injuries.

Injuries to cervical spine were due to automobile accidents (12), fall from motor cycle (4), auto vs. pedestrian (3), sports related injury (1), fall from ladders (2) fall from horse (1), gun shot wound (1). Any patient who is deemed to have high risk for vertebral artery injury had subsequent angiographic study. However not all patients automatically received angiograms. When there was a fracture though FT, the patient was randomly selected to undergo either CTA or MRA. Out of 24 patients with fractures through FT, 17 had CTA, and 7 had MRA. Among the 35 patients with no fractures through FT, only 20 received either CTA or MRA.

Results

There were a total of 104 spine fractures in last 18 months. These fractures included in all groups. Only 59 out of 104 had stage I and II cervical spine injuries. Among those who had stage I and II cervical injuries, 24 had fractures through FT, and 35 patients had no fracture through FT. All 24 patients with fractures through FT received noninvasive angiographic studies, however, among those with intact FT, 20 received CTA or MRA and no VAI was associated in these 20 patients. Four out of 24 had comminuted fractures and 20 had linear fractures. Out of 24 patients, 17 had randomly chosen to have CTA and 7 patients had MRA.

Three patients out of 17 who had CTA showed VAI. Figure 1 is a cervical CT that shows fracture through Left FT. Figure 1A is a CTA, that shows occlusion of left Vertebral artery. In Seven patients, who had MRA there was no injury to vertebral artery. We believe that MRA is sensitive, however, these patients randomly had MRA and they just did not have any VAI. Therefore, out of a total 24 patients, only 3 had injury VAI. This corresponds to approximately 12.5% of VAI in association with fractures of FT.



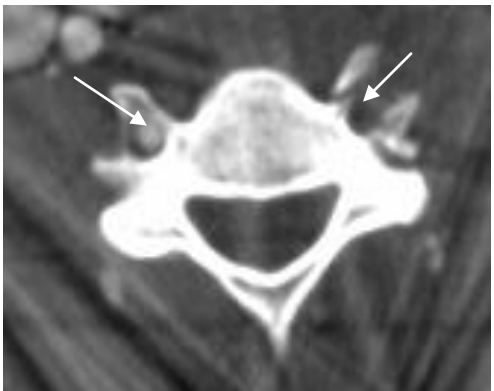
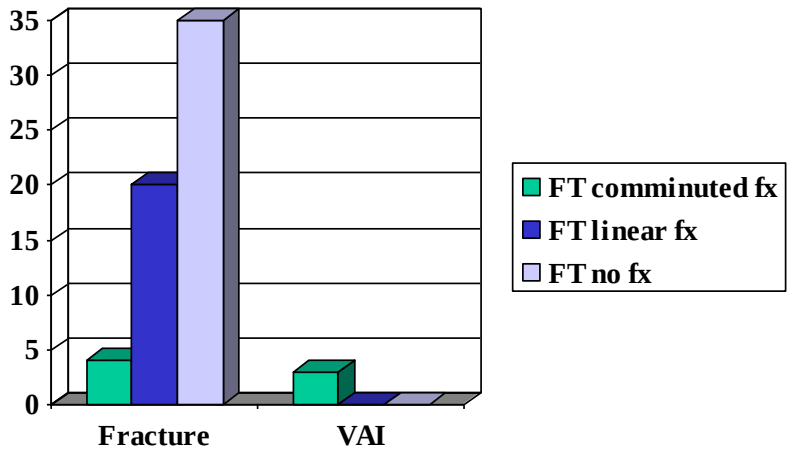


Figure 1: axial CT
Fracture through left C5 FT

Figure 1A: axial CTA
Left Arrow: occlusion of left VA
Right Arrow: intact Right VA



None of these patients developed injury to spinal cord. In those patients who had VAI, it was unilateral and no patient had bilateral vertebral artery injuries. No patient developed symptoms of vertebro-basilar insufficiency. In certain cases, there was an association of a single nerve root injury secondary to facet dislocation.
Graph 1: VAI after fracture through foramen transversarium
Fischer exact analysis $p<0.001$ for VAI vs comminuted fx through FT

The association between vertebral artery injury was compared with the following factors: a comminuted fracture through foramen, or a linear fracture through foramen, or a unilateral facet dislocation and or neurological deficit. Because of the small sample size in this study, we used Fischer Exact Test for statistical analysis. The correlation between VAI and fractures through FT is shown in graph 1.

Of 24 patients who had fractures through FT, 20 of those had linear fractures, and 4 had comminuted fractures. No patient had spinal cord injury. Nine patients had unilateral facet dislocation, but only one had associated VAI. Isolated nerve root injury was involved in 3 of 9 patients with unilateral facet dislocation, however none of these patients had VAI. There was no VAI detected in MRA. In VAI that were detected with

CTA, VAI did not statistically correlate with spinal cord injury, or unilateral facet dislocation and a linear fracture though. Only a comminuted fracture through FT has statistical correlation with VAI. ($p<0.001$), however, the association between linear fracture and VAI is not significant ($p<0.06$).

Discussion

In this retrospective analysis we studied VAI associated with spine fractures: Our main goals were to analyze: 1.which cervical spine fractures require screening to exclude vertebral artery injury; 2. which patients mandate screening to rule in a vertebral artery injury; 3. In which patients the time and money is unnecessary to perform angiograms; 4. which test would be a rapid and reliable to confirm VAI.

We concluded that the incidence of VAI in Cervical fractures through FT is 12.5%. In Stage I and II cervical fractures, we primarily focused on fractures through foramen transversarium. There is a significant association between comminuted fractures through FT and vertebral artery injury ($p<0.001$). Stage I and II cervical injuries that do not involve fracture through FT were not associated with VAI. We did not include stage III and IV spine fractures, which could have resulted in higher incidence of VAI.

A high index of clinical suspicion is the most important step in making the diagnosis of vertebral artery injury. Vertebro-basilar ischemia presents with one or all of the following symptoms: altered consciousness, dysphagia, dysarthria, vertigo, nystagmus and blurred vision. Vertebral artery injuries, remain occult because of bilateral occlusion of vertebral artery may be required to present the above symptoms.

Without any suspicion of clinical signs, radiological imaging may reveal VAI, when there is instability with subluxation, facet fractures or fractures through FT. Abnormal flow or lack of flow can be identified by CTA, or MRA or more invasive study using catheter angiography. Recent studies indicate that CTA is as sensitive and specific as Catheter angiography in detecting VAI (Eastman).

The recognition of specific fracture pattern that is associated with VAI will reduce imaging requirements. For example, in a large study of 776 patients, catheter angiography was performed, and Cothren reported 56% VAI in vertebral subluxation. Catheter angiography was also performed by Willis in 4 all types of cervical fractures and concluded a total of 46% of VAI. Taneichi used MRA and reported VAI in of 17% in cervical dislocation injuries alone. Severe cervical fractures involving body fractures were associated with 89% of VAI as studied both by CTA and CA (Eastman). However, there were only 19% VAI after fractures through FT alone (Cothren). Our current study is comparable to the last report by Cothren. The great discrepancy in the above studies is due to a large variety of fractures that included in each study.

Conclusion

In this study we concluded that there is siginificant co-relation between VAI and comminuted fractures through foramen transverarium. Approimately 12.5% of fractures through FT result in VAI. CTA is an economic, efficient and a reliable study to detect

VAI. However, a prospective study with more patients would further provide the importance of CTA and or MRA in detecting such injuries. The goal of identification of VAI is prompt anticoagulation, which would result in significant reduction in ischemic neurologic events. Preemptive treatment may be reasonable is some patients who have high risk of VAI.

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Diagnosis and Correction of Coagulopathy in Patients Presenting with Intracerebral Hemorrhage and Taking Anticoagulant and/or Antiplatelet Agents

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Abstract

Introduction: Intracerebral hemorrhage (ICH) is only a small percentage of strokes. There are many predictors of mortality after spontaneous ICH some of which may be addressed by reducing the risk of hematoma expansion in the period following the initial hemorrhage. Patients having ICH and taking oral anticoagulation and platelet inhibiting agents may have reduced risk of hematoma expansion and thus better outcome if coagulopathy is rapidly corrected. Treatment options for management of coagulopathy from oral anticoagulation include administration of vitamin K, fresh frozen plasma (FFP), prothrombin complex concentrates (PCC), and recombinant activated factor VII (rFVIIa). The purpose of this study is to evaluate the management of ICH patients in the emergency department and during the early period of their hospital course.

Methods: This is a retrospective review of data collected from four large Southern California facilities from January 2006 to June 2007. The clinical history, laboratory values, radiology reports, blood bank forms, ambulance reports, and physician and nursing emergency department reports of patients with intracerebral hemorrhage from January 2006 to June 2007 was systematically reviewed. The primary outcome was 1) diagnosis of coagulopathy in ICH patients, and 2) coagulopathy reversal within 24 hours. Mean time intervals were calculated from the time the patient was accessed by emergency medical services (EMS) through the time the patients coagulopathy was corrected.

Results: 111 patients were identified as taking platelet inhibiting agents in coagulopathy inducing doses and had laboratory values which corroborated having a coagulopathy, received platelets. 113 patients were identified as taking platelet inhibiting agents in coagulopathy inducing doses, but had no laboratory values drawn to evaluate platelet function, and did not receive platelets. The time from diagnosis to correction of coagulopathy at the four institutions were 18.0 hours, 29.75 hours, 15.0 hours, and 19.75 hours. Collectively the time from diagnosis to correction of coagulopathy was 20.63 hours.

Conclusions: Only 49.5% of the patients having platelet inhibitor-induced coagulopathy were transfused platelets. Collectively the institutions meet the goals of the study and disprove the null hypothesis, however one institution had a correction time of 29.75 hours. Perhaps the national guidelines for rapid correction of coagulopathy in patients having ICH should be more aggressive.

Keywords: stroke, intracerebral hemorrhage, antiplatelet therapy, oral anticoagulation

Introduction

Intracerebral hemorrhage (ICH), hemorrhagic stroke, accounts for approximately 15% of strokes. Predictors of mortality after spontaneous ICH include size, location of the hemorrhage, midline shift on computed tomography, intraventricular hemorrhage, low Glasgow Coma Scale (GCS) score on admission, and high blood glucose and blood pressure on admission.[1] Anticoagulation and platelet inhibition also increases both the risk of developing ICH and its

morbidity and mortality rates. The effect of anticoagulants and platelet inhibitors on ICH severity is related to variables which increase the patients risk of hematoma expansion. Flibotte report in their study on hematoma expansion and outcome of intracerebral hemorrhage that when compared with ICH patients not on anticoagulants and platelet inhibitors, patients on anticoagulants and platelet inhibitors are at increased risk of hematoma expansion.[2]

The acute phase of ICH, the time during which ongoing bleeding is most likely, occurs during the pre-hospital time interval (prior to activation of the emergency medical system) and during the pre-correction time interval (in the emergency department).[3] There is a population of ICH patients that are not treated for coagulopathy that take antiplatelet agents. Few ICH patients on oral anticoagulation go untreated, however the time interval in which their coagulopathy is corrected varies significantly.

The volume of blood that extravasates from ruptured vessels is an important determinant of outcome; it increases significantly in 18 % to 38% of patients during the first 24 hours of their hospital admission. More than 50% of patients with ICH that are taking anticoagulants have risk of hematoma expansion.[4] Therefore early diagnosis of coagulopathy and intervention to minimize hematoma expansion has a significant impact on outcome.

Proper management of ICH patients having coagulopathy in the emergency department is critical. Treatment options for management of coagulopathy from oral anticoagulation include administration of vitamin K, fresh frozen plasma (FFP), prothrombin complex concentrates (PCC), and recombinant activated factor VII (rFVIIa). Current practice is to administer a combination of vitamin K and either FFP or PCC; due to the extremely high price of rFVIIa, its use so far is limited. Platelets are transfused for coagulopathy resulting from the use of platelet inhibiting agents.[5]

The purpose of this study is to evaluate the management of ICH patients in the emergency department. This involves the diagnosis of a coagulopathy (resulting from oral anticoagulants and/or antiplatelet agents) and the time interval from diagnosis to correction of the coagulopathy. It is hypothesized that 1) coagulopathy resulting from antiplatelet agents are frequently not diagnosed or treated, and 2) there is a significant time interval between the time of coagulopathy diagnosis and the of coagulopathy correction.

Methods

This is a retrospective review of data collected from four large Southern California facilities from January 2006 to June 2007. Patients were identified by systematic review of databases maintained by the Department of Neurosurgery from each facility.

Coagulopathy was defined as: 1) INR greater than or equal to 1.5, 2) platelet function test EPI greater than 184 and ADP greater than 102, or 3) bleeding time greater than 8 minutes.

Patients defined as taking oral anticoagulation were taking doses of warfarin from 2 mg to 10 mg daily or every other day. Patients defined as taking antiplatelet inhibitors were taking 81 mg to 325 mg of aspirin daily, 1600 mg to 3200 mg of ibuprofen daily, 440 mg to 660 mg of naproxen

sodium daily, celecoxib 200 mg to 400 mg daily, aspirin/dipyridamole 50 mg/400 mg daily, or 75 mg of clopidogrel daily.

The clinical history, laboratory values, radiology reports, blood bank forms, ambulance reports, and physician and nursing emergency department reports of patients with intracerebral hemorrhage who presented to Desert Regional Medical Center (1150 North Indian Canyon Drive, Palm Springs, CA 92262), Kaiser Permenente Fontana Medical Center (9961 Sierra Avenue, Fontana, CA 92335), Arrowhead Regional Medical Center (400 North Pepper Avenue, Colton, CA 92324), and Riverside County Regional Medical Center (26520 Cactus, Moreno Valley, CA 92555) from January 2006 to June 2007 was completed.

The patients clinical history was reviewed and medications were noted, specifically whether or not the patient was taking antiplatelet agents or oral anticoagulation agents. The report of the computed tomography (CT) of the patients head was reviewed to identify intracerebral hemorrhage. Laboratory values were reviewed during the time the patient was first admitted to the hospital until the coagulopathy was corrected. The protime (PT) and international normalized ratio (INR) were observed for patients taking oral anticoagulation. Platelet function test and bleeding time were observed for patients taking platelet-inhibiting agents. Blood bank forms were used to note the time that fresh frozen plasma (FFP) or platelet transfusions were started and ended.

Ambulance reports and physician and nursing emergency department reports were used to identify the time it took the patient to arrive at the hospital (the pre-hospital time interval), whether or not the ICH patient had been diagnosed with a coagulopathy, the time interval from the time of diagnosis to the time to begin treatment, the time interval from the time to begin treatment to the time of coagulopathy correction.

Exclusion criteria was 1) unobtainable past medical history especially regarding current medications or medical conditions (e.g. warfarin for atrial fibrillation), 2) non-spontaneous ICH (e.g. trauma, ischemic stroke with hemorrhagic transformation, brain tumor, vascular malformation, or vasculitis), 3) patients whose power of attorney had given do-not-resuscitate orders (DNR) during the period when the patients coagulopathy was being corrected and all subsequent aggressive management of the patients coagulopathy ceased, 4) patients that had ICH but were not taking antiplatelet agents and/or oral anticoagulation, and 5) patients having ICH and who were taking antiplatelet agents and/or oral anticoagulation, but whose INR, platelet function test, or bleeding time values did not indicate therapeutic levels.

The primary outcome was 1) diagnosis of coagulopathy in ICH patients, and 2) coagulopathy reversal within 24 hours. Determination of the 24-hour end point was based on previous studies; efforts were made to model the design of prior studies as much as possible to allow for comparison of data.

Mean time intervals were calculated for the time of arrival of emergency medical services (EMS) to the time of arrival at the emergency department, the time of arrival at the emergency department to the time of diagnosis of ICH with coagulopathy, the time of diagnosis of ICH with

coagulopathy to the time to begin treatment, and the time to begin treatment to the time the coagulopathy was resolved.

Results

There were 148 ICH patients from Desert Regional Medical Center, 127 patients from Kaiser Permenente Medical Center Fontana, 131 patients from Arrowhead Regional Medical Center, and 118 patients from Riverside County Regional Medical Center evaluated for enrollment in the study. The institutions were assigned random identification numbers for purposes of anonymity.

Of 524 patients having ICH, 13 were excluded due to unobtainable past medical history regarding current medications or medical conditions, 15 were excluded due to having non-spontaneous ICH, and 37 were excluded due to the patient's power of attorney having given do-not-resuscitate orders (DNR). 113 patients having ICH and being on platelet inhibitors were excluded from the correction portion of the trial because they did not have any laboratory studies ordered to diagnose for coagulopathy. Also, 2 patients on oral anticoagulation having ICH and having a coagulopathy were excluded due to being statistical outliers; their coagulopathies took 36 hours and 42 hours to correct.

This left 457 patients having proper documentation and information (clinical history, laboratory values, radiology reports, blood bank forms, ambulance reports, and physician and nursing emergency department reports) available in the patient's medical records.

Of the 457 patients evaluated, and not excluded based on the above criteria, 281 patients had coagulopathy resulting from the use of platelet inhibiting agents (123 patients), oral anticoagulation (57 patients) or both platelet inhibiting agents and oral anticoagulation (101 patients); 156 patients had spontaneous ICH not associated with a coagulopathy, and 20 patients having ICH and who were taking antiplatelet agents and/or oral anticoagulation had laboratory values (INR, platelet function test, or bleeding time values) that did not indicate therapeutic levels.

281 patients were enrolled in the diagnostic phase of the trial and 167 patients were enrolled in the correction phase of the trial.

Diagnosis of Coagulopathy

Coagulopathy was diagnosed by reviewing the patient's clinical history and by evaluation of laboratory studies. Medications were noted, specifically whether or not the patient was taking antiplatelet agents or oral anticoagulation agents. Laboratory values were reviewed, specifically the protime (PT) and international normalized ratio (INR), platelet function test, and bleeding time.

At institution #1 111 patients were identified as taking platelet-inhibiting agents in coagulopathy-indusing doses and had laboratory values which corroborated having a coagulopathy, received platelets. At institutions #2, #3, and #4 113 patients were identified as taking platelet inhibiting agents in coagulopathy-indusing doses, but had no laboratory values drawn to evaluate platelet function, and did not receive platelets.

Correction of Coagulopathy

Correction of coagulopathy was initiated in all four study institutions using 5 mg to 10 mg vitamin K, and administering FFP until the coagulopathy was resolved. Mean time intervals were calculated for the time of arrival of emergency medical services (EMS) to the time of arrival at the emergency department (pre-hospital time interval), the time of arrival at the emergency department to the time of diagnosis of ICH with coagulopathy (diagnostic time interval), the time of diagnosis of ICH with coagulopathy to the time to begin treatment (therapeutic time interval), and the time to begin treatment to the time the coagulopathy was resolved (corrected time interval).

Mean pre-hospital time interval at institution #1 was 5.25 hours, institution #2 was 4.5 hours, institution #3 was 5.75 hours, institution #4 was 5.5 hours. The diagnostic time interval at institution #1 was 0.75 hours, at institution #2 was 0.5 hours, at institution #3 was 0.5 hours, and at institution #4 was 0.5 hours. The therapeutic time interval at institution #1 was 1.75 hours, at institution #2 was 3.25 hours, at institution #3 was 0.75 hours, and at institution #4 was 1.0 hour. The corrected time interval at institution #1 was 16.25 hours, at institution #2 was 26.5 hours, at institution #3 was 14.25 hours, and at institution #4 was 18.75 hours. Collectively the mean pre-hospital time interval 5.25 hours, the diagnostic time interval was 0.56 hours, the therapeutic time interval was 1.69 hours, and the corrected time interval was 18.94 hours.

The time from diagnosis to correction of coagulopathy at institution #1 was 18.0 hours, at institution #2 was 29.75 hours, at institution #3 was 15.0 hours, and at institution #4 was 19.75 hours. Collectively the time from diagnosis to correction of coagulopathy was 20.63 hours.

Conclusions

Only 49.5% of the patients having platelet inhibitor-induced coagulopathy were transfused platelets. Furthermore, all of these (49.5%) patients were seen at the same institution; the other facilities did not treat for platelet inhibitor-induced coagulopathy. Pertti reported that the use of platelet inhibiting agents doubled the 3-month mortality of ICH patients compared with patients having ICH that did not use platelet-inhibiting agents. The use of antiplatelet agents predisposes patients to hematoma expansion.[6, 7] Given most hospitals do not have a trauma rating, one would anticipate that the above statistic would translated to the majority of hospitals in the United States. National guidelines should be changed to reflect this emergency as one recognizes that oral anticoagulation in patients having ICH requires emergent therapy.

Collectively the institutions meet the goals of the study and disprove the null hypothesis, however one institution had a correction time of 29.75 hours. It is anticipated that this discrepancy arises as the consequence that blood banks are forced to triage blood to the most critical locations; trauma centers have better correction times due to the availability of blood products from the local blood banks.

Efforts were made to model the design of prior studies as much as possible to allow for comparison of data. However, this may not be optimal treatment for ICH associated with coagulopathy. Perhaps correction of coagulopathy within 24 hours is too conservative of a goal. Perhaps the national guidelines for rapid correction of coagulopathy in patients having ICH and taking oral anticoagulation and/or platelet-inhibiting agents should be more aggressive.

Reference

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