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Neurosurgery concepts: Key perspectives on imaging characteristics of spinal metastases, surgery for low back pain, anesthesia for disc surgery, and laminectomy versus laminectomy and fusion for lumbar spondylolisthesis.

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SNI: Neurosurgery Concepts

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Neurosurgery concepts: Key perspectives on imaging characteristics of spinal metastases, surgery for low back pain, anesthesia for disc surgery, and laminectomy versus laminectomy and fusion for lumbar spondylolisthesis

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Key Words: Laminectomy, low back pain, neoplasm metastasis, spinal cord, spinal fusion, spondylolisthesis

IMAGING CHARACTERISTIC ANALYSIS OF METASTATIC SPINE LESIONS FROM BREAST, PROSTATE, LUNG, AND RENAL CELL CARCINOMAS FOR SURGICAL PLANNING: OSTEOLYTIC VERSUS OSTEOBLASTIC[14]

Study Question: What are the computed tomography (CT) imaging characteristics of common spine metastases?

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The authors of this study retrospectively reviewed CT images for patients treated for metastatic spine disease at their institution from 2009 to 2012.[14] A total of 66 patients were included with primary tumors from breast (n = 17), prostate (n = 14), lung (n = 18),

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and kidney [renal cell carcinoma (RCC), $n = 17$]. Overall, spinal metastases demonstrated an osteolytic pattern (48%), followed by osteoblastic (34%) and mixed lesions (18%). Breast, lung, and RCC metastases to the spine were most often osteolytic (56%, 64%, and 91%, respectively). Prostate metastases to the spine were most often osteoblastic (62%).

Osteolytic lesions demonstrate destructive loss of both cancellous and cortical bone and are often well-demarcated. Osteoblastic lesions are hyperdense, expansile, and also well-demarcated. Osteolytic lesions are associated with spinal instability and pathologic fractures, and may require fusion and instrumentation. Osteoblastic lesions are associated with spinal and foraminal stenosis, and may require decompression. The authors recommend preoperative CT of the spine to facilitate surgical planning.

Perspective: Advances in imaging have enhanced our understanding of the radiologic profiles of pathologies, both outside and within the neural axis. Neurosurgeons use imaging characteristics to focus differential diagnoses and ultimately guide management. In the spine, identification of bony metastases and organization of these lesions into those amenable to fusion versus decompressive surgery becomes increasingly important.

The incidence of spinal metastases remains high in patients with breast, lung, renal cell, and prostate cancer. This study highlights the osteolytic nature of breast, lung, and RCC metastases and the osteoblastic tendency of prostate metastases. Despite the sample size being relatively small, the lesions were evenly distributed among the most common spinal metastases. The retrospective nature of this study is sufficient for characterization of the lesions. However, future studies should aim to validate the trends described here using larger prospective cohorts.

Recent studies investigating the molecular mechanisms underlying osteolytic and osteoblastic lesions have largely focused on breast and prostate cancers, respectively. These studies provide insight into the radiologic patterns observed in this paper. Breast cancer cells are known to secrete parathyroid hormone related protein (PTHrP), tumor necrosis factor α, interleukins, leukemia inhibitory factor, receptor activator of nuclear factor kappa-B ligand (RANKL), and transforming growth factor beta (TGF-β), which can all stimulate osteolysis.[2,5,10] TGF-β1-stimulated RCC bone metastasis has been found to promote tumor growth and osteolysis *in vivo*.[3,12] Endothelin-1 (ET-1) has been shown to stimulate bone formation in murine and human models and is increased in advanced prostate cancers.[5,8] ET-1 regulates expression of proteins involved in bone turnover including IL-6, Wnt5a, connective tissue growth factor, RANKL, and Dickkopf WNT Signaling Pathway Inhibitor 1 (DKK-1).[4,5] Interestingly, prostate cancer cells also express PTHrP, and activation of a different receptor, the ET-1 receptor (ETAR), promotes bone formation.[5,15] Lastly, bone morphogenetic proteins (BMP4 and BMP6) have been found to promote osteogenesis in prostate cancer.[5,9,13] Further elucidation of these molecular mechanisms is imperative in identifying potential targets to impede pathologic bone remodeling that occurs in spinal metastases.

Summary Written by: Carlito Lagman, MD

THE ROLE OF SURGERY FOR TREATMENT OF LOW BACK PAIN: INSIGHTS FROM THE RANDOMIZED CONTROLLED SPINE PATIENT OUTCOMES RESEARCH TRIALS[1]

Study Question: In patients with low back pain, what is the role of surgical intervention for disc herniation, degenerative spondylolisthesis and spinal stenosis?

The authors reviewed recent findings from the Spine Patient Outcomes Research Trial (SPORT) I–III, randomized clinical trials from 13 sites across the country over a 5-year period, which investigated the clinical efficacy of surgery for three common causes of low back pain (i.e., disc herniation [DH], degenerative spondylolisthesis [DS], and spinal stenosis [SS]).[1] Eligibility criteria included persistent, incapacitating back pain, or neurogenic claudication after 6–12 weeks of nonoperative care (physical therapy, counseling, epidural injections, chiropractic therapy, and opioid analgesics). Exclusion criteria included prior surgery, cauda equina syndrome, segmental spinal instability, spinal fractures, infections, tumors, and inflammatory spondyloarthropathies. Primary outcome measures were health-related quality of life, as measured by the SF-36 health status questionnaire, and secondary outcome measures included patient satisfaction with symptoms, work status, care, and the sciatica bothersomeness index (SBI).

SPORT I investigated surgical efficacy for lumbar DH for 501 patients with image-confirmed lumbar intervertebral DH and persistent radiculopathy for at least 6 weeks. Patients were randomly assigned to either open discectomy or nonoperative care. Although adherence to assigned treatment was poor, intention-to-treat analysis showed substantial improvement in all primary and secondary outcomes. However, when comparing between treatment groups, primary outcomes were not significant, while some secondary outcomes (SBI and self-reported progress at 1 year) were significantly improved for the surgical group. As-treated analyses showed significant improvement with surgery in all primary outcomes. These differences persisted at 8-year follow-up.

SPORT II investigated surgical efficacy for DS of 304 patients in a randomized cohort and 303 patients in an observational cohort for patients with image-confirmed DS and persistent symptoms for at least 12 weeks. Treatment was either decompressive laminectomy (with or without fusion) or nonoperative care. Similar to SPORT I, a high crossover rate was observed. Intention-to-treat analysis showed no difference in primary outcomes. As-treated analyses showed significant improvement for surgery in all primary and secondary outcomes up to 2 years that persisted up to the 4-year follow-up.

SPORT III investigated surgical efficacy for SS for 289 patients in a randomized cohort and 365 patients in an observational cohort for patients with image-confirmed SS without spondylolisthesis and persistent symptoms for at least 12 weeks. Treatment was either decompressive laminectomy or nonoperative care. Similar to SPORT I and II there was a high rate of crossover. Intention-to-treat analysis showed significant improvement on the SF-36 bodily pain index of 7.8 (95% CI: 1.5–14.1) for surgery, but not on the SF-36 physical function index or ODI. As-treated analyses showed a significant improvement for surgery in all primary and secondary outcomes up to 2 years, with the differences in primary outcomes persisting up to the 4-year follow-up.

Perspective: Back pain remains a common cause of morbidity in the United States. The Center for Disease Control and Census Bureau data indicate that back and spine disorders are the second most common cause of disability in the United States. There is significant controversy regarding the role of surgical management of these disorders, particularly in the face of rapidly rising health care cost causing increased scrutiny on the number of spine surgeries performed. The results from the SPORT trials indicate that appropriate surgery remains an effective treatment for select patients with DH, DS, and SS, and that these results were both statistically and clinically significant. However, the extensive crossover that was seen in each trial (approaching 50% in certain cases) indicates that offering a previously noneffective, nonoperative management essentially negated the randomization within the study. If a randomized trial were to be attempted in the future, care must be chosen to establish a viable alternative nonsurgical treatment. Despite the surgical efficacy that was demonstrated in the SPORT studies, these findings should not be misapplied to the general patient seeking evaluation. The SPORT trials had strict inclusion and exclusion criteria that may limit their applicability. Nevertheless, these studies represent a significant attempt at elucidating the surgical efficacy for common spine disorders and reducing public stigmas against spine surgery.

Written by: Lawrance K. Chung, BS and Luke Macyszyn, MD, MA

GENERAL ANESTHESIA VERSUS COMBINED EPIDURAL/GENERAL ANESTHESIA FOR ELECTIVE LUMBAR SPINE DISC SURGERY: A RANDOMIZED CLINICAL TRIAL COMPARING THE IMPACT OF THE TWO METHODS UPON THE OUTCOME VARIABLES[11]

Study Question: How do intraoperative and postoperative factors differ after general anesthesia (GA) and combined general/epidural anesthesia (CEG) for elective lumbar spine disc surgery?

The authors performed a prospective, randomized controlled trial enrolling a total of 88 patients undergoing elective spine disc surgery.[11] Patients were randomly assigned to one of two anesthesia arms, GA or CEG. Patients in the GA group received Thiopental (4–5 mg/kg), fentanyl (2 μg/kg), midazolam (0.05 mg/kg), and atracurium (0.5 mg/kg) by a single anesthesiologist. Patients in the CEG group received the above GA protocol plus a single injection of 0.25% bupivacaine (18 ml, 45 mg) plus fentanyl (2 ml, 100 μg in 18 ml of distilled water). Intraoperative variables recorded included vital signs (heart rate and mean arterial blood pressure), estimated blood loss, and anesthetic delivered. Postoperative variables recorded included visual analog scale (VAS) scores, total analgesic used, and complications. All intraoperative and postoperative variables were found to be less in the CEG versus the GA group.

Mean intraoperative blood loss was less in the CEG group ($p = 0.002$), which led to less blood being transfused ($p = 0.006$), when compared to the GA group. Mean percentage of isoflurane used was less in the CEG group ($p < 0.001$) when compared to the GA group. Mean pain scores were less in the CEG group ($p < 0.01$). In the CEG group, analgesia requirements, time to first rescue analgesia, and total amount of morphine used were also less ($p < 0.001$), longer ($p = 0.001$) and less ($p = 0.001$), respectively, when compared to the GA group. This data suggests that CEG may reduce intraoperative blood loss and anesthesia requirements, provide better pain control, and decrease the risk of postoperative complications.

Perspective: Lumbar spine disc surgery is most often performed under GA, with the primary advantage being airway patency. This study highlights the potential advantages of CEG in patients undergoing the aforementioned procedures. The sample size and randomized nature of the study support the conclusions. Furthermore, the authors performed multivariate analyses to control for confounders such as age, sex, and weight, particularly in their analysis of intraoperative blood loss. However, it is unclear whether these same analyses were performed for the other outcome measures. It is also possible that some patients may be better suited for

GA, such as those on chronic anticoagulation therapy, for whom there is a high risk of epidural hematoma. Moreover, it is unclear whether the reported benefit of less intraoperative blood loss (with CEG) outweighs the risk of epidural hematoma. Prudent cost-benefit analyses are necessary to determine whether the cost of added epidural anesthesia justifies the advantages described. Comparison of GA versus spinal anesthesia would be valuable because this approach is very important to older patients who may experience more complications (related to multisystem disease) under general anesthesia compared to spinal anesthesia. Moreover, the fear of complications related to general anesthesia is ever present in patients suffering from spinal stenosis, disc disease, and/or foraminal stenosis, and this has the potential to influence patient preference regarding anesthesia.

Summary Written by: Winward Choy, BA and Zachary A. Smith, MD

LAMINECTOMY PLUS FUSION VERSUS LAMINECTOMY ALONE FOR LUMBAR SPONDYLOLISTHESIS[7] AND A RANDOMIZED, CONTROLLED TRIAL OF FUSION SURGERY FOR LUMBAR SPINAL STENOSIS[6]

Study Question: Is lumbar decompression a sufficient operation for patients with lumbar spinal stenosis in the setting of degenerative spondylolisthesis?

Two randomized control studies were recently published in the New England Journal of Medicine that compared decompression only to decompression and fusion in patients who harbor lumbar spinal stenosis in the setting of a stable degenerative spondylolisthesis.

The first study by Ghogawala *et al*. randomized a total of 66 patients with lumbar spinal stenosis and spondylolisthesis.[7] Thirty-three patients were randomized in the laminectomy only group, and 31 patients were randomized into the laminectomy and fusion group. Ultimately, 29 patients completed the 2-year follow-up in the laminectomy group and 28 in the fusion group. The rate of follow-up was 68% at 4 years. The primary outcome was the Short form-36 (SF-36) physical component summary score and the secondary outcome was the Oswestry Disability Index (ODI). The increase in the SF-36 physical component summary score was significantly higher at 2, 3, and 4 years for patients receiving laminectomy and fusion compared to laminectomy only. Moreover, the changes in ODI scores were significantly higher at 4 years for patients receiving laminectomy and fusion surgery. The rate for reoperation for patients who received decompression only was 34% as compared to 14% in patients who underwent laminectomy and fusion. Surgical time, blood loss, and hospital stay was increased in patients receiving laminectomy and fusion.

The second study by Forsth *et al*. included 247 patients who had lumbar stenosis.[6] One hundred and twenty-three patients were randomized to receive decompression (laminectomy) and fusion, and among those 67 patients had spondylolisthesis, and 124 were randomized to receive decompression-alone. Among those patients, 68 had spondylolisthesis. There was no significant difference between the groups in the mean score on the ODI at 2 years (27 in the fusion group and 24 in the decompression-alone group, $p = 0.24$) or in the results of the 6-minute walk test (397 meters in the fusion group and 405 meters in the decompression-alone group, $p = 0.72$). Results were similar between patients with and those without spondylolisthesis. Among the patients who had 5 years of follow-up and were eligible for inclusion in the 5-year analysis, there were no significant differences between the groups in clinical outcomes at 5 years. The mean length of hospitalization was 7.4 days in the fusion group versus 4.1 days in the decompression-alone group ($p < 0.001$). Operating time was longer, the amount of bleeding was greater, and surgical costs were higher in the fusion group than that in the decompression-alone group. During a mean follow-up of 6.5 years, additional lumbar spine surgery was performed in 22% of the patients in the fusion group and in 21% of those in the decompression alone-group. The type of fusion was determined by the surgeon.

Perspective: The conclusion from the Ghogawala study was that decompression and fusion surgery for patients with lumbar spinal stenosis in the setting of stable spondylolisthesis is superior than decompression only, whereas the conclusion from the Forsth study was that fusion surgery is unnecessary for patients with stenosis and spondylolisthesis because decompression has similar outcomes and is sufficient. The Ghogawala study was difficult to follow and was less clear in its results. The Forsth paper was an excellent study with good long-term follow-up in almost all patients.

The conflicting results between these two randomized studies are a reflection of the heterogeneity of degenerative lumbar spondylolisthesis. Patients with stable spondylolisthesis on flexion and extension X-rays may have predisposition to biomechanical instability in the presence of a healthy preserved intervertebral disk and bilateral facet edema. Patients with spondylolisthesis who have disk collapse and bridging osteophytes are not predisposed to biomechanical instability following decompression. Moreover, in both the studies, the laminectomy and fusions were performed utilizing traditional open techniques. At present, the use of minimally invasive spinal surgery techniques has minimized blood loss, surgical time, and hospital length of stay.

In conclusion, patient specific factors should be taken into consideration when deciding between decompression or decompression and fusion surgery for lumbar stenosis and degenerative spondylolisthesis.

Summary Written by: Nader S. Dahdaleh, MD and Isaac Yang, MD

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Conflicts of interest

There are no conflicts of interest.

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