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Radiographic Predictors of Functional Outcome in Degenerative Lumbar Spondylolisthesis Surgery

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Surgery

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Abstract:

Objective: To confirm the importance of sagittal spinal alignment on functional outcome with degenerative lumbar spondylolisthesis (DLS) surgery and to identify the radiographic parameters that predict functional outcomes after DLS surgery.

Methods: Retrospective analysis of the prospectively collected functional and radiographic outcomes of the Canadian Spine Outcomes and Research Network DLS database. All patients underwent either decompression, posterolateral fusion or interbody fusion surgery with a minimum of one-year postoperative follow-up.

Results: Most patients improve or remain unchanged in their sagittal spinal alignment regardless of surgery type with fusion procedures not experiencing statistically significantly improved alignment changes to decompression alone. By multiple linear regression adjusted for baseline patient age, body mass index, gender and preoperative presence of depression, increase of a patient's pelvic incidence (PI) -lumbar lordosis (LL) mismatch with any technique of DLS surgery was associated with a higher one-year postoperative ODI score R^2 0.179 (95% CI 0.080, 0.415, p=0.004), back pain R^2 0.152 (95% CI 0.021, 0.070, p <0.001) and leg pain R^2 0.059 (95% CI 0.008, 0.066, p=0.014) score. Likewise, reduction of LL was associated with a higher ODI score R^2 0.168 (-0.387, -0.024, p=0.027) and back pain R^2 0.135 (95% CI -0.064, -0.010, p=0.007).

Conclusions: This is the first work to examine DLS patients outside of extrapolated sagittal balance parameters from the adult scoliosis literature. Importantly, we show that any worsening in sagittal spinal alignment parameters with DLS surgery regardless of surgery type leads to poorer functional outcomes even among patients who remain within conventionally held appropriate sagittal balance.

Keywords: degenerative lumbar spondylolisthesis; sagittal spinal balance; sagittal alignment; functional outcomes

Summary for Lay Audience:

Degenerative lumbar spondylolisthesis (DLS) is a commonly encountered clinical issue for adult spinal surgeons and results in painful cramping in the legs with activity. These symptoms can be debilitating in patients and when there are signs of damage to the nerves in the lower legs coming from the lumbar spine, surgery has proven beneficial. It is unclear how best to treat patients surgically with DLS. Multiple surgical options exist with the mainstay being a decompression procedure, whereby bone and soft tissue are removed from the involved level of the lumbar spine to free the nerves providing function to the lower legs. Largely the North American spine surgical practice has moved to include fusion procedures alongside decompressions. With fusions, screws are placed in the pedicles, (the bony connection from the back to the front of the spine), stabilized by instrumentation on both sides of the spinal canal. Additionally, the use of artificial spacers placed in the disc space to reestablish collapsed disc heights, called interbody devices, are commonly utilized in DLS surgery. Without proven benefit of fusion procedures over decompression procedures alone, it is important to establish the effect that instrumentation can have on patients with DLS. Much recent interest in the world of DLS surgery has focused on how surgery for DLS can improve the overall alignment of a patient's spine. The work of this thesis project provides a comprehensive and informative analysis of 248 DLS patients, the largest available Canadian DLS patient data set. We demonstrate that a similar proportion of patients undergoing decompression, decompression and fusion and decompression and fusion with interbody device use, improve in their overall spinal alignment regardless of the type of surgery. Furthermore, we have demonstrated that patients who have a worsening of their spinal balance one-year after surgery do predictably worse functionally than those patients who remain unchanged or see an improvement in their spinal alignment with surgery. Our work has

helped to demonstrate the importance of spinal alignment to DLS surgery in addition to highlighting the tendency to perform too much and too invasive of spinal surgery for the average DLS patient.

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Chapter 1: Literature Review of Radiographic Predictors of Degenerative Lumbar Spondylolisthesis

Introduction to Lumbar Degenerative Spondylolisthesis:

The spinal column is comprised of the vertebrae, intervertebral discs and the posterior spinal elements, namely the spinous processes, laminae and facet joints.[1] In addition, a host of associated surrounding ligamentous and soft tissue supports together with their bony attachments combine to perform a multitude of critical functions.[1] In the lumbar spine, these structures protect the neural elements of the lumbar and sacral spinal nerve roots, in addition to assisting with the importance of maintaining balance and overall sagittal spinal alignment, a phenomenon which will be further discussed later in this chapter.[1; 2] Throughout an individual's lifetime, the product of bipedalism can lead to increased strain in the form of degenerative 'wear and tear' preferentially on the lowest segments of the lumbar spine.

Degenerative lumbar spondylolisthesis (DLS) is a well-known and described pattern of arthritic degeneration of the lumbar spine, representing one of the most common presenting pathologies to spinal surgeons worldwide.[3] While DLS has an unclear etiology, it is thought to be caused by a multifactorial degenerative process of the lumbar spine.[3] The degenerative process is characterized by an acquired anterior displacement (anterolisthesis) of one vertebral body on its corresponding subjacent level in the absence of a disruption of the pars interarticularis.[4] Associated with this degenerative process is the concurrent degenerative changes that occur within the aging lumbar spine, namely intervertebral disc degeneration, ligament flavum hypertrophy or buckling, osteophyte proliferation and a corresponding, compensatory facet joint hypertrophy.[4; 5; 6] Unfortunately, the evidence outlining the natural history and evolution of DLS is limited and efforts to develop recommendations based on an expected trajectory of symptoms for a given patient are difficult to establish and are often unsuccessful.[6]

Most frequently however, DLS occurs at the L4-L5 level, typically in women older than age 60.[3; 4] This process is frequently associated with lumbar spinal stenosis and the constellation of symptoms that result from spinal stenosis.[5; 7] Patients presenting with lumbar spinal stenosis typically present with a combination of both low back pain in addition to stereotypical leg pain in a neurogenic claudication and possibly radicular pattern.[3] Typically, patients will describe axial loading dominant back pain, worsened with extension and heavy or cramping buttock and posterior thigh pain exacerbated by ambulation and often improved with forward lumbar flexion or exercise cessation.[3; 4] Differentiating lumbar spinal stenosis and associated neurogenic claudication from vascular claudication is a diagnostic dilemma and can be difficult to parse out clinically.[5] While both patient subsets may describe relief with cessation of activity, the absence of pain triggering with standing alone in addition to symptom relief with not only exercise cessation but also positional changes (specifically sitting) will further delineate neurogenic from vascular claudication.[5] As a result of this progressive lumbar degenerative condition patients may experience severely restricted function via a reduction in exercise capacity, walking tolerance and overall quality of life.[8]

The importance of an adequate history and physical examination is essential to formulating a complete and thorough understanding of each individual patient presenting with DLS.[6] A complete diagnostic workup for DLS includes appropriate noninvasive imaging. The North American Spine Society (NASS) clinical guideline on the diagnosis and treatment of degenerative lumbar spondylolisthesis provides a grade B level recommendation for lateral lumbar plain film radiographs to diagnose DLS.[6] Furthermore, for patients presenting with stenosis accompanying their DLS, a similar grade B level of evidence recommendation supports pursuing a magnetic resonance imaging (MRI) scan or a computed tomography (CT) myelogram if the patient has an MRI contraindication.[6]

Lumbar degenerative spondylolisthesis thus represents a significant economic burden to healthcare owing to the progressive disability afflicted patients may experience and health care costs for both operative and nonoperative treatments.[9] Estimated health care expenditures for the diagnosis and management of back pain and spinal stenosis in the United States of America is estimated to exceed 90 billion US dollars annually, with $10-$20 billion per year in loss of economic productivity among these patients.[10; 11]

Lumbar Degenerative Spondylolisthesis Treatment Options:

Non-operative modalities, which include activity modifications, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, massage and acupuncture treatment remain the first-line treatment for DLS.[4; 6] An important distinction, now well-established is that anterolisthesis (slip) progression does not correlate with clinical symptom worsening particularly when index level intervertebral disc height loss exceeds 80% of native height and associated intervertebral osteophyte formation is present on plain film radiographs.[4; 6] While more invasive non-surgical treatment options exist, the NASS DLS guideline highlights that there is insufficient evidence to recommend for or against the use of injections for the treatment of DLS.[6] However, the nonoperative treatment spectrum for DLS patients frequently does involve a multitude of injection therapy options including lumbar epidural steroid injections, facet injections and therapeutic nerve root blocks among other less conventional injection therapies that are beyond the scope of this review. Importantly, the vast majority of patients with symptomatic DLS in the absence of neurologic deficits do well with conservative, nonoperative treatments.[6; 8] With an ever-increasing average population age, the volume of DLS patients continues to grow and important health care decisions need to be made regarding the most cost-effective treatments for this patient population. Adogwa et al. demonstrate that the cost of maximizing nonoperative treatment for symptomatic DLS patients amounts to $1013 US per patient prior to lumbar spinal fusion, with the bulk of cost directed at lumbar epidural steroid injections.[12] The analysis further indicates the most frequently utilized treatment modality in maximizing nonoperative treatment in this patient cohort is opioid medications, with a well-known and potentially catastrophic side effect and addictive profile. Furthermore, assuming minimal improvement in pain and functional disability after a maximal nonoperative treatment trial over the course of two-years in this patient population, the incremental cost effectiveness for maximizing nonoperative modalities prior to an eventual surgical intervention may be highly cost unfavorable.[12]

As has been highlighted in this review previously, the presentation of DLS follows a spectrum with varied clinical presentations and associated symptomatology. While patients who do not exhibit neurologic symptoms concurrent with their DLS pathology are well-managed via nonoperative modalities, the corollary is that overwhelming evidence supports meaningful clinical and functional improvement with surgical intervention for DLS patients with neurologic features to their presentation.[3; 4; 6; 13] Importantly, patients with lower extremity sensory changes, muscle weakness as a result of their lumbar spinal stenosis or cauda equina syndrome are significantly more likely to develop progressive functional decline in the absence of surgery.[6] The most widely known study on surgical treatment of patients with DLS is the randomized controlled trial entitled the Spine Patient Outcomes Research Trial (SPORT) trial which demonstrated superiority of surgery over nonoperative management of DLS.[13] Of the initial 304 enrolled patients in the SPORT trial, 66% of those randomized to receive surgery actually underwent surgery by the four-year enrolment endpoint whereas 54% of patients randomized to the nonoperative cohort crossed over and received surgery during the same enrolment timeline. Accordingly, the intention-to-treat analysis of the randomized cohort was grossly limited by the volume of noncompliance within the cohorts and has been a source of criticism to the study since its publication.[4; 13] However, an as-treated analysis that combined an observational cohort in which patients (303 total enrolled) selected their preferred treatment with 97% selecting surgery receiving surgery and 33% selecting nonoperative treatment undergoing surgery was performed.[13] From this analysis, patients who underwent surgery in the presence of DLS with associated spinal stenosis and neurologic symptoms fared better with surgery in terms of reduced back and leg pain and improved functional status at the three-months, one- and two-year follow-up timepoints.[13] Weinstein et al. performed further analysis at the four-year follow-up standpoint among surgical patients and found that compared with nonoperatively treated patients, the functional and pain relief findings persisted.[13] Importantly, in this trial 94% of patients treated surgically underwent decompression with instrumented fusion. It is worth noting that the SPORT trial did include a nonoperatively treated patient cohort who fared well at one-year after enrolment in the absence of any neurologic changes or high grade anterolistheses.[13]

Largely based on the findings from the SPORT trial and multiple further supportive evidence pieces (much of which is outlined further in this review) for the benefits of surgical intervention in the DLS population, lumbar spinal stenosis, namely DLS, is now the most common indication for spinal surgery.[8; 9; 13] However, the most efficacious and ideal surgical treatment for these patients remains unclear. For the purposes of this literature review and thesis project, the focus of surgical options will be the three most commonly performed interventions in

North America for DLS surgery: decompression, decompression with pedicle screw instrumentation and posterolateral fusion (decompression with PLF) and decompression with pedicle screw instrumentation and interbody fusion (decompression with IB).[4] With such clinical equipoise, and an increasing patient volume afflicted with neurologic symptoms associated with their DLS, it is imperative among the spine surgical community to establish the most clinically meaningful and cost-effective intervention to appropriately treat these patients. A 2014 United States (US) health care cost report highlights that in 2011, 465,000 hospital-based spinal fusions were performed in the US accounting for the highest aggregate hospital costs of all surgical interventions ($12.8 billion) performed in the US.[14] Despite these increased costs, surgical treatment for symptomatic DLS patients has been shown to be cost-effective with a 0.43 quality adjusted life years (QALYs) gain with surgery.[15]

Decompression Alone for DLS:

As previously highlighted, this review focuses on three surgical treatment options for the appropriately selected patient with DLS. Decompression is an appealing surgical intervention for patients with DLS. The surgery represents the least invasive of the three outlined options. The decompression procedure proceeds to remove any hypertrophied ligamentum flavum, synovial cyst formation and may include microdiscectomy work to alleviate ventral dural compression as well. Both the technique of lumbar decompression and the definition of a lumbar decompression are very heterogenous within the literature. While the above surgical goals exist as commonplace among surgeons pursuing lumbar decompression, vastly different techniques (open versus minimally invasive, versus endoscopic), approaches (unilateral versus bilateral exposures), and volume of lamina +/- spinous process bony removal exists within the literature. Complications unique to decompression procedures include the potential to disturb the facet joints at the index level in addition to the potential of introducing iatrogenic instability or anterolisthesis worsening via damage to the pars interarticularis.[4; 16]

One of the largest available randomized controlled trials outlining decompression as a more favourable treatment option to decompression and fusion in the DLS population comes from the Swedish Spinal Stenosis Study group.[8] A 247 patient cohort with lumbar spinal stenosis, of which 135 patients had an DLS diagnosis, between ages 50-80, were randomly assigned to undergo either decompression alone (decompression group) or decompression with instrumentation and fusion (fusion group). The per protocol analysis included 228 patients (111 fusion group patients and 117 decompression alone group patients). The primary functional outcome measure was the Oswestry Disability Index (ODI), a validated functional outcome score for lumbar spine patient functional assessments.[8] The ODI is scaled from 0-100 with higher scores representing worse functional status and more severe disability. In Forsth et al. there was no significant difference between groups in terms of mean ODI score at two-year postoperative follow-up or in the results of a six-minute walk test.[8] While extended follow-up numbers were limited, among those patients available for five-year follow-up (153, 62% of total participants), there continued to be no significant difference between groups in clinical outcomes. Importantly, mean length of hospital stay was 3.3 days longer in the instrumented fusion group ($p<0.001$), with statistically significant differences for instrumented fusion cases for operative time, blood loss and surgical cost. At a mean 6.5-year additional follow-up, similar rates of revision surgery were found between the decompression alone group (21% revisions) and the instrumented fusion group (22% revisions). Importantly, revisions in the instrumented fusion group were typically performed for adjacent level disease cranial or caudal to the initial index level surgery while revision surgery in the decompression alone group was typically performed at the index level, with revision fusion procedures favoured in both groups.[8] Similarly, Kuo et al. performed a propensity-matched retrospective cohort analysis and demonstrate that among patients with DLS operated via unilateral laminotomy with bilateral decompression, at five-year follow-up the reoperation rate was 10.4% compared to 17.2% in the fusion patient group.[9] Like Forsth et al., it was found that among revision procedures, most commonly they were performed at the index surgical level in the decompression alone group of patients and at the adjacent level in the fusion group.[9] Thus, an important distinction is demonstrated. Among patients with stable DLS, decompression procedures carry lower adverse surgical risk, operative time, blood loss and health care cost and represent a durable option compared to fusion surgery.[9]

Decompression and Fusion for DLS:

Following the findings of the landmark SPORT trial and ensuing long-term follow-up analyses, much research has focused on the outcome of patients with DLS undergoing decompression with pedicle screw instrumentation and posterolateral fusion. Kleinstueck et al. report a 213 consecutive patient series with 56 decompression only patients and 157 decompression and instrumented fusion patients.[3] Patients completed the Core Outcome Measures Index (COMI) preoperatively and at one-year postoperatively and were stratified into 'good' and 'poor' global outcomes. A multiple regression analysis was performed to control for confounding variables and revealed instrumented fusion to be the only significant predictor of improved functional outcome at one-year. It was thus hypothesized that underlying anterolisthesis as the cause of the central spinal stenosis may be better addressed with fusion than decompression alone.[3] In the absence of quality level one evidence to support fusion over decompression alone, Ghogawala et al. performed a randomized controlled trial of 66 patients between age 50-80 undergoing either decompression alone or decompression with instrumented fusion for symptomatic spinal stenosis in the setting of DLS.[16] The authors utilized the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), which is a surrogate functional outcome marker ranging from 0-100, with higher scores indicating better quality of life.[16] The SF-36 was performed two-years postoperatively. Eighty-six percent of patients were available for follow-up at two-years, with 68% of patients followed to the four-year postoperative period. The fusion group had a greater SF-36 score at two-years compared to the decompression alone group (15.2 vs. 9.5, p=0.046), with these differences persisting at the four-year postoperative mark as well (p=0.02). Importantly, the changes in ODI between groups did not differ at the two-year postoperative mark. More blood loss occurred in the fusion group in addition to longer hospital stays (p<0.01 for both variables).[16] While these results seem to sharply conflict with those of the Forsth et al. trial also published in the New England Journal of Medicine, important critiques to the Ghogawala et al. trial exist.[8] Ghogawala et al. had a higher rate of patient dropout in addition to a significantly increased rate of reoperation in the decompression alone group during follow-up (34%) compared to the fusion group (14%), which could have impacted SF-36 outcome scores of overall well-being during the follow-up period of the study.[16] Additionally, Forsth et al. highlight the important notion that the decision to proceed with a revision surgery is not always solely a patient driven decision and may in fact be driven by surgeon discretion.[8] While reported rates of reoperation vary depending on the length of follow-up, one of the longest available follow-up periods from the longitudinal cohort follow-up of surgical patients from the SPORT trial showed a 22% revision rate at eight-year follow-up.[15]

Decompression with Interbody Fusion for DLS:

The use of interbody devices, often colloquially referred to as interbody cages, for DLS treatment continues to be a widely investigated topic.[4] The theoretical potential of an interbody cage to enhance the chance to augment a posterolateral fusion via fusion across the disc space, achieved via either an anterior, lateral or posterior approach carries strong evidence of enhancing fusion rates.[4] However, interbody cages are also associated with increased surgical time, cost, blood loss, adverse event risk and potentially limited clinical outcome improvement compared to posterolateral fusion alone.[4; 17; 18; 19; 20] An prospective cohort investigation performed at our own institution analyzed 87 consecutive DLS patients at baseline and two-years postoperatively undergoing either posterolateral fusion or interbody fusion following decompression in both instances.[17] Ultimately, Urquhart et al. concluded that there were no differences in rates of complications between groups and more importantly no difference in fusion rates or functional outcomes between patients in either surgery group.[17] Challier et al. performed a randomized controlled trial examining 60 patients with DLS randomized to either decompression with posterolateral fusion versus decompression with interbody fusion at two-year follow-up.[18] There was a significant functional improvement observed in both groups for pain and disability. Furthermore, radiographic assessment showed better posterolateral fusion rates in the interbody group without statistically significant superiority, suggesting from both a functional and radiographic standpoint, that interbody fusion may not be indicated.[18] McAnany et al. conducted a meta-analysis of 383 posterolateral fusion patients and 268 interbody fusion patients for DLS concluding that the overall quality of available evidence is moderate to poor.[20] Furthermore, no statistically significant difference was observed between the posterolateral fusion and interbody fusion groups with respect to fusion rates, ODI and SF-36.[20] More recently, Dantas et al.

completed an updated systematic review and meta-analysis comparing the effect of interbody fusion versus posterolateral fusion for DLS.[19] From twelve included articles, they concluded the rates of neural injury was higher in the interbody fusion groups OR 0.28 (95% CI, 0.13-0.60) than in the posterolateral fusion group. However, there were no other differences found between surgery type in terms of functional outcomes of back pain, ODI, SF-36, blood loss or infection.[19] The NASS guidelines previously discussed similarly state that there is insufficient evidence to recommend for or against the use of interbody fusion for DLS.[6] Thus, with clinical equipoise as to the most effective modality to augment instrumentation for DLS patients undergoing decompression and fusion based procedures there has been a significant increase in the focus of the role of spinopelvic alignment and the potential role for interbody devices to assist with this optimization.

A Brief Overview of Spinopelvic and Sagittal Balance:

In 2011, Dubousset coined the term "cone of economy".[21] When standing upright, minimal energy expenditure occurs and maximal comfort is obtained when the C7 vertebrae is centered over the S1 vertebrae. In the sagittal plane this is achieved via a series of corresponding lordotic and kyphotic curvatures. Malalignment be it through scoliosis or loss of normal sagittal curves, such as in degenerative conditions can disturb this balance leading to greater energy expenditure to maintain this cone of economy.[21] As a product of this relatively new and novel approach to understanding the spine much initial focus turned to understanding how best to maximize a balanced spine to minimize energy expenditure and deviation from the cone of economy. Initially this took primary focus in understanding overall spinal alignment as it relates to scoliosis.[2] Eventually, focus shifted to the role of spinopelvic alignment as it pertains to overall spinal balance.[2; 21; 22] With respect to spinopelvic balance, the pelvic incidence is the key parameter.[22] The pelvic incidence (PI) is defined as the angle between the line perpendicular to the sacral superior endplate at its midpoint and a line connecting this point to the midpoint of the femoral head axis on an upright lateral view radiograph.[22] The PI is a fixed parameter unique to each patient and results from the added combination of an individual's pelvic tilt (PT) and their sacral slope (SS). The PT is the angle between the line connecting the midpoint of the superior sacral endplate to the center axis of the femoral heads and a vertical reference line on an upright lateral radiograph. While the sacral slope is the angle formed between the horizontal and a line along the superior sacral endplate surface.[2; 22] The PI is a reflection of the pelvic anatomy and does not change once adolescent maturity is achieved.[2; 22] Importantly, the PI is strongly correlated to the SS.[22] Concurrently, the lumbar lordosis (LL) is strongly correlated to SS. Thus, a high PI by necessity requires a high SS and a high LL.[2; 22] To maintain an appropriate upright posture an individual with a high LL may in turn require a compensatory increased PT and may attempt to flatten their upper thoracic spine (thoracic kyphosis – TK) to accommodate for this.[22] One further sagittal spinal balance parameter that is important to understand is the sagittal vertical axis (SVA). The SVA is defined as the length of a horizontal line connecting the posterior superior aspect of the S1 vertebral body to a vertical plumb line drawn from the centroid of the C7 vertebral body on a lateral three-foot standing radiograph.[2] Multiple investigations have demonstrated poor health related quality of life (HRQOL) measures to correlate with poor spinal sagittal balance, which is now understood contemporarily to refer to patients with an SVA greater than 5cm or a PI minus LL mismatch greater than 10 degrees.[2; 22; 23; 24] It is important to note that no specific SVA measure for the DLS population has been determined nor discussed and this 5cm value comes from the spinal deformity literature and is extrapolated at face value to the DLS papers addressing sagittal balance.

Sagittal spinopelvic balance is involved in a variety of degenerative processes in the lumbar spine with patients with low back pain frequently suffering from an SVA greater than 5cm and a resultant increased amount of hip extension in an effort to augment pelvic retroversion.[22] The degenerative lumbar spine further reduces the compensatory ability to achieve an increased LL. Interestingly, it has been demonstrated that individuals with a constitutionally higher PI are predisposed to the development of DLS, which has led to increased efforts to understand the spinopelvic parameters most important to optimize for patients undergoing surgery for DLS.[22]

Sagittal Balance and Spinopelvic Parameters in Lumbar Degenerative Spondylolisthesis:

Gille et al. discuss the importance of failing to recognize sagittal alignment in surgical treatment of DLS leading to increased rates of revision surgery in their instrumented fusion patients.[7] Furthermore, Gussous et al. outline how DLS negatively affect HRQOLs with low or high-grade anterolistheses and highlight the importance of addressing the overall spinal alignment at the time of surgery in this patient population.[25] However, Gussous et al. included both degenerative as well as lytic spondylolisthesis patients ("high grade spondylolisthesis") which may impact the overall necessity of addressing overall spinal alignment in all patients when most DLS patients typically have low-grade slip angles and associated better average preoperative spinopelvic alignment.[25] Radovanovic et al. report a retrospective cohort of 84 patients surgically treated for DLS with 54% of patients having a postoperative SVA greater than 5cm.[26] Similar to Gussous et al., these patients had significantly worse clinical outcome scores on both the ODI and SF-36 measures at a mean three-year follow-up.[25; 26] Interestingly, what was most frequently determined as a driver of this worsened SVA was a decreased LL postoperatively.[26] From this observation, renewed interest in the role of interbody devices to impart increased lumbar lordosis in patients undergoing DLS surgery has occurred. Currently, limited evidence on this specific area of research exists. Salem et al. outline the difficulties in comparing small cohort series examining the role of interbody cages to restore LL in patients with DLS undergoing surgery given the heterogeneity among the trials.[27] However, among their 84-patient cohort undergoing posterior decompression and interbody fusion for DLS, they found that the bulk of total LL correction achieved postoperatively (4.3 +/- 9.6^0, $p<0.001$) is likely due to decompression alone as the use of bilateral facetectomy and a lordotic interbody cage provided only modest (1.8+/- 6.7^0, $p=0.025$) index level LL correction.[27]

Clinical Equipoise:

Thus, my primary objective will be to define the radiographic parameters that can predict functional outcome within the DLS surgical population. Ultimately this work will allow clinicians to utilize objective, image-based parameters to inform evidence-based treatment decisions. The secondary objective of this thesis project is to establish the magnitude of sagittal spinal alignment change that can occur with each type of surgical intervention for DLS.

The work of this thesis is presented in an integrated article format. The logical flow of this manuscript will follow the path towards our primary objective first by mapping all currently available literature on our topic and the mechanisms of how this research has been conducted thus far via a comprehensive scoping review. With an understanding of the clinical interest in understanding sagittal spinal alignment and the associated changes that can occur through surgery for DLS, chapter three will demonstrate the magnitude of sagittal alignment change occurring with decompression, decompression and posterolateral fusion and decompression and interbody fusion in our patient cohort. Recognizing the magnitude of sagittal alignment correction that can occur via surgical intervention on these DLS patients, chapter four will highlight the most important radiographic parameters that predict functional outcomes for this population.

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Chapter 2: Sagittal Alignment in Operative Degenerative Lumbar Spondylolisthesis: a Scoping Review

Before proceeding with the assessment of our own patient cohort for this thesis project, it is important to assess the available literature on our topic. Through this review, I wanted to map the currently available evidence and the means by which these investigations had been conducted in addition to their primary focus. Understanding the entirety of the available literature was deemed to be best assessed via a scoping review which provides the unique ability to both map the currently available literature in addition to critically assessing current knowledge gaps to direct future investigations.

Introduction:

Degenerative lumbar spondylolisthesis (DLS) is a frequently encountered clinical pathology for adult spine surgeons.[1] While the mechanism of this unique degenerative process is not fully understood, DLS primarily leads to central stenosis with an anterolisthesis of the affected vertebral body on the immediately caudal vertebrae.[2] As a result of this process, patients commonly experience neurogenic claudication and may also suffer from increased back pain and radiculopathy.[3; 4] The benefit of surgical intervention over conservative treatment for DLS patients with neurologic symptoms such as motor weakness and/or sensory changes is well-established.[1; 3; 5] The optimal treatment for this patient population however remains unclear. Treatment options centre on the goal of achieving neurologic decompression, though frequently these interventions are coupled with instrumented fusions, most typically with interbody device use even in the absence of demonstrated efficacy over decompression alone.[4; 6; 7]

Patients with DLS tend to prefer a forward flexed posture to increase intracanal space and minimize claudication symptoms while ambulating.[8] The result of this postural accommodation leads to an energy-inefficient posture, which can lead to worsened health related quality of life (HRQOL).[9] To compensate for sagittal spinal imbalance, individuals with DLS tend to have increased pelvic incidence (PI), pelvic tilt (PT), sacral slope (SS) and lumbar lordosis (LL) compared to healthy individuals in addition to patients with lumbar spinal stenosis without anterolisthesis.[10; 11; 12] The retroversion of the pelvis is the protective mechanism for maintaining sagittal balance in DLS.[13] Unfortunately, PT has a finite accommodation that can occur before segmental and global sagittal spinal imbalance occurs. When sagittal imbalance occurs in DLS patients, spinopelvic compensation reaches a finite accommodation at which juncture there is a corresponding increase in the sagittal vertical axis (SVA) and a reduction in LL.[14]

Appropriately addressing and correcting sagittal spinal imbalance at the time of surgery has been shown to improve HRQOLs and degree of disability in the adult spinal deformity literature.[15] Patients with DLS who have a worse sagittal spinal alignment postoperatively also report greater disability and poorer HRQOL.[3] Unsurprisingly, there has been an increased interest in the literature on understanding the role of surgery for DLS on functional outcomes with respect to focal and global sagittal spinal alignment.[16]

It is currently unclear what breadth of available evidence exists on regional and global sagittal alignment in DLS surgery. Thus, our objective was to conduct a scoping review to map and synthesize the DLS surgical literature regarding the current radiographic assessment of alignment both pre and postoperatively. We sought to identify critical gaps in current knowledge and to provide insight about directions for future research.

Methods:

This study was completed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Review (PRISMA-SCR) protocol.[17]

Eligibility Criteria

To be eligible for inclusion in this scoping review, investigations had to be peer-reviewed, primary studies, with English-language full text available from January 1971-December 2021. Studies needed to examine radiographic parameters related to patients undergoing surgery of any type or indication for DLS and involve human subjects only, with greater than five patients included. Included studies did not have to primarily assess radiographic parameters nor sagittal spinal balance. However, in such instances, secondary outcomes had to include at least one time point analysis of a radiographic parameter either preoperatively or postoperatively related to DLS surgery. Studies reporting outcomes of lumbar spinal stenosis without spondylolisthesis, low-grade spondylolisthesis without a breakdown of isthmic and DLS patient data were excluded. Any study examining functional outcomes only or fusion rates of a specific surgical technique without any measured radiographic alignment parameter were excluded.

Information Sources and Search

To identify relevant studies to our review, we performed a comprehensive search in the MEDLINE, EMBASE and Cochrane databases from January 1971 to December 2021. MeSH and EMTREE headings and subheadings were used to query the databases for appropriate studies for inclusion after agreement upon the highest yield search strategy by the review team. The search terms used were: "spondylolisthesis or degenerative spondylolisthesis or lumbar degenerative spondylolisthesis or spondylolistheses AND surgery or surgical procedure or surgical procedures or decompression or fusion or posterolateral fusion or interbody fusion or interbody device or interbody cage AND radiograph or radiographic parameter or spinopelvic balance or spinopelvic alignment or sagittal balance or sagittal alignment or foraminal height or disc angle or lordosis or segmental lordosis or global lordosis or segmental lumbar lordosis or global lumbar lordosis."

Selection of Sources of Evidence

Title and abstract screening were performed in duplicate with review among the two screeners (PT and CO) performed after the first 50 studies were screened to standardize and amend the screening process. Discrepancies and disagreements in the screening process were resolved via discussion and consensus upon inclusion and exclusion. Inter-observer agreement for assessment by the reviewers was calculated via Cohen's kappa coefficient of agreement.[18] Full text screening was performed through an agreed upon data extraction method that was determined ad hoc by the review team to assess the salient features of our included studies.

Data Charting Process, Data Items and Synthesis of Results

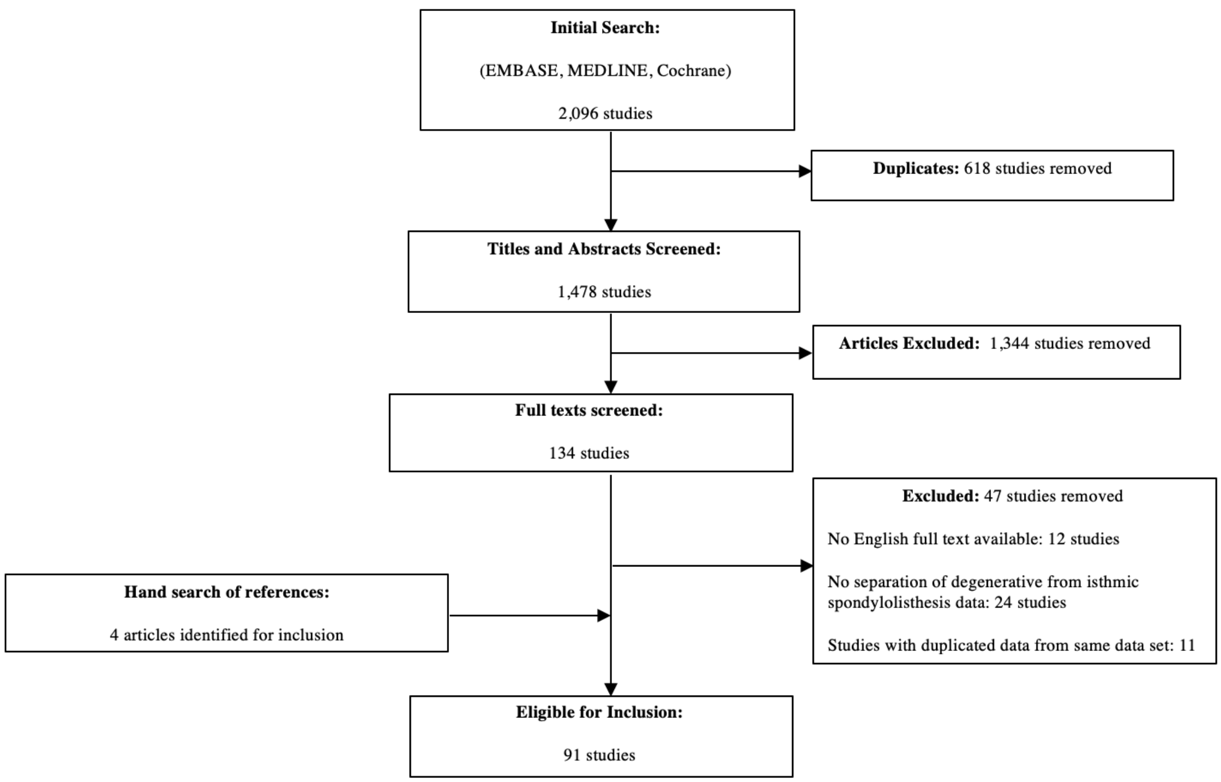
A data charting form was developed prior to beginning data extraction, with agreed upon variables to extract from included studies. We abstracted data on study characteristics such as date of publication, origin of investigation, type of study and the level of evidence. Additionally, we assessed the primary objective of the investigation, surgical procedure type(s), the number of patients, average age and follow-up length. We also extracted the type of radiographic parameter(s) measured and if these were compared preoperatively to postoperative values and/or to a comparative group. Furthermore, we assessed any functional outcomes examined among the studies. We grouped the studies by their primary investigational objective (radiographic alignment; functional outcome/radiographic alignment secondary; adjacent segment disease; new device/technique; adequacy of surgery; classification development).

Results:

Literature Search Results and Selection

From our initial search, 2,096 studies were returned for review (Figure 1). After removal of 618 duplicate studies, 1,478 titles and abstracts were available for screening. Duplicate screening provided a substantial Cohen's kappa correlation coefficient of 0.73.[19] Ultimately, full text screening of 134 studies identified 87 studies for inclusion with an additional four studies identified via included full text study reference lists, for a total of 91 included studies.

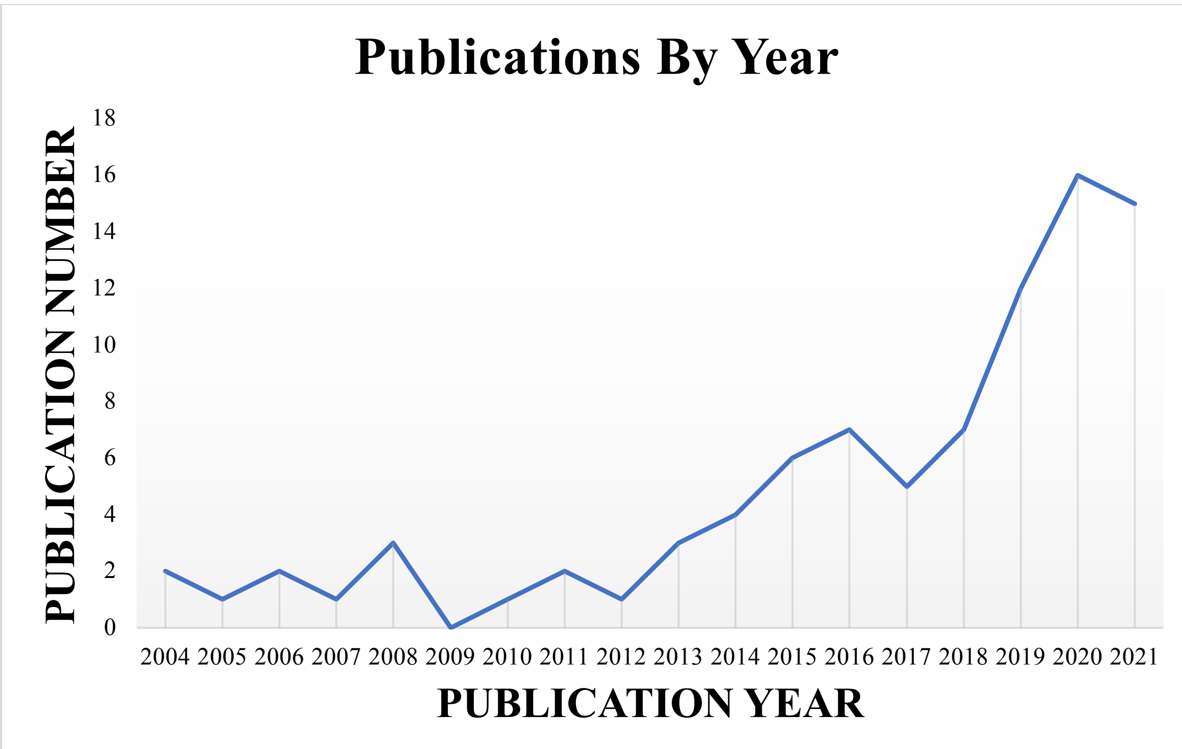
Figure 1: Flowchart outlining the systematic scoping review process.



Study Characteristics

The included studies contained 7,870 patients with an average age of 62.3 years old at the time of surgery. Average follow-up was performed 36.9 months postoperatively. Analysis of the included studies by year of publication demonstrated a strong increasing prevalence of recent investigations examining radiographic alignment with surgery in DLS (Figure 2). The last decade (2012-2021) represented 84% (76/91) of all included studies.

Figure 2: Publications by Year



** 1 publication each from 1990[20], 2001[21] and 2002[22] excluded from graph above for display purposes.*

Included studies were largely retrospective cohorts 56 (62%) or case series 21 (23%) (Figure 3). Overall, the level of evidence among the included studies was low, with 60 (65%) studies graded level three evidence and an additional 23 (25%) included studies comprising level four evidence. Only two investigations (2.2%) provided level one evidence[23; 24]. There was a predominance of publications from Asia 59 (65%) studies, Europe 15 (16%) studies and North America 14 (15%) studies (Figure 4).

Figure 3: Overview of Included Study Type

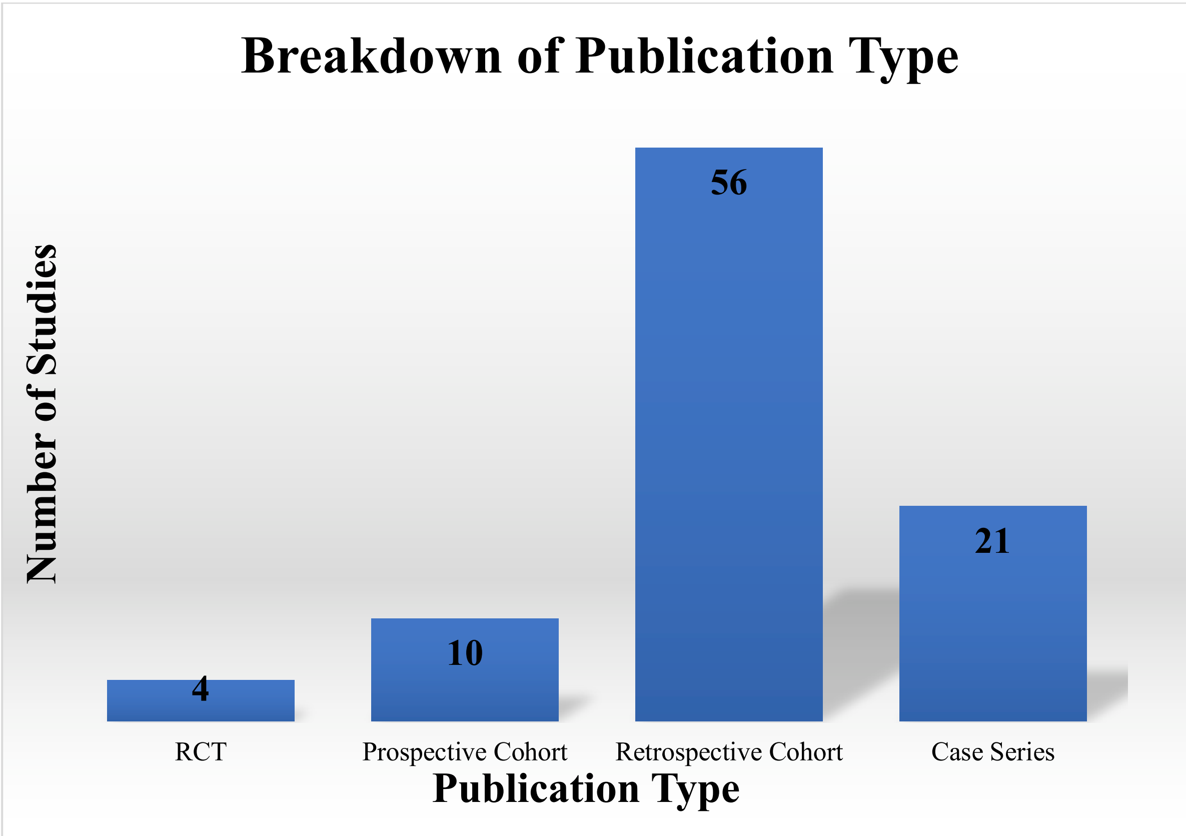
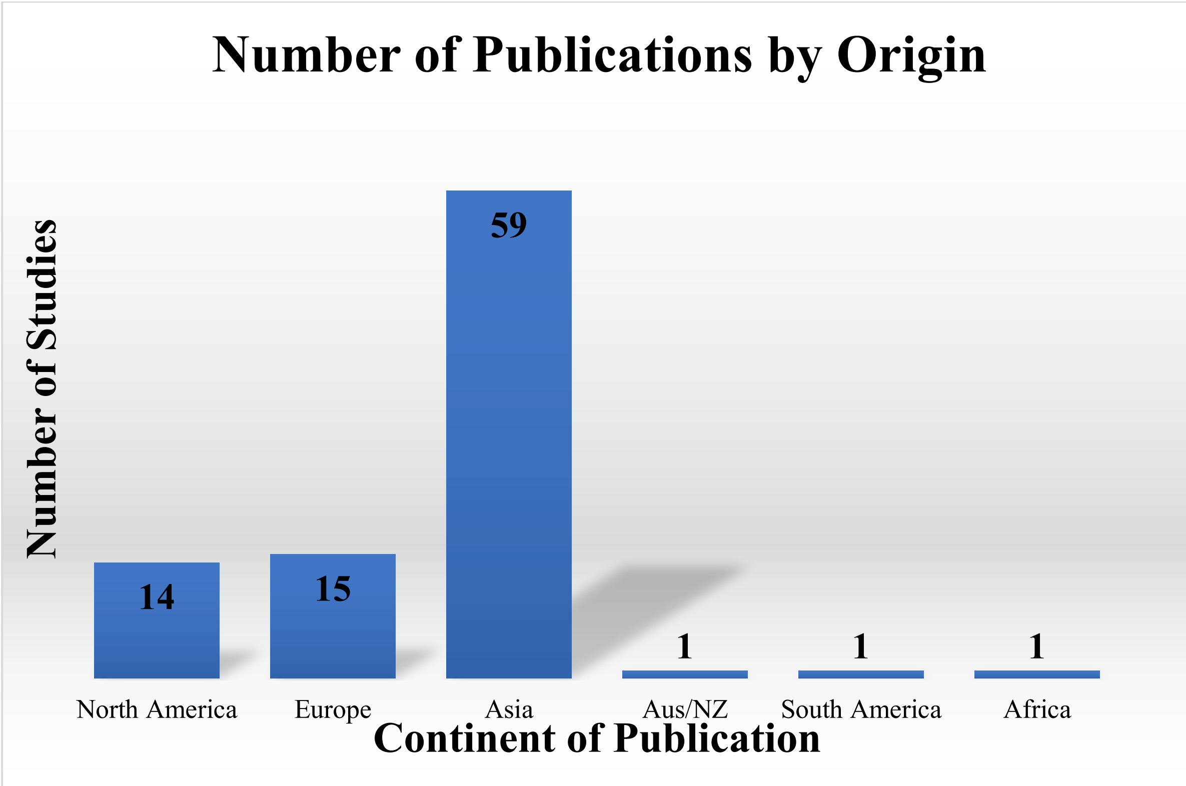


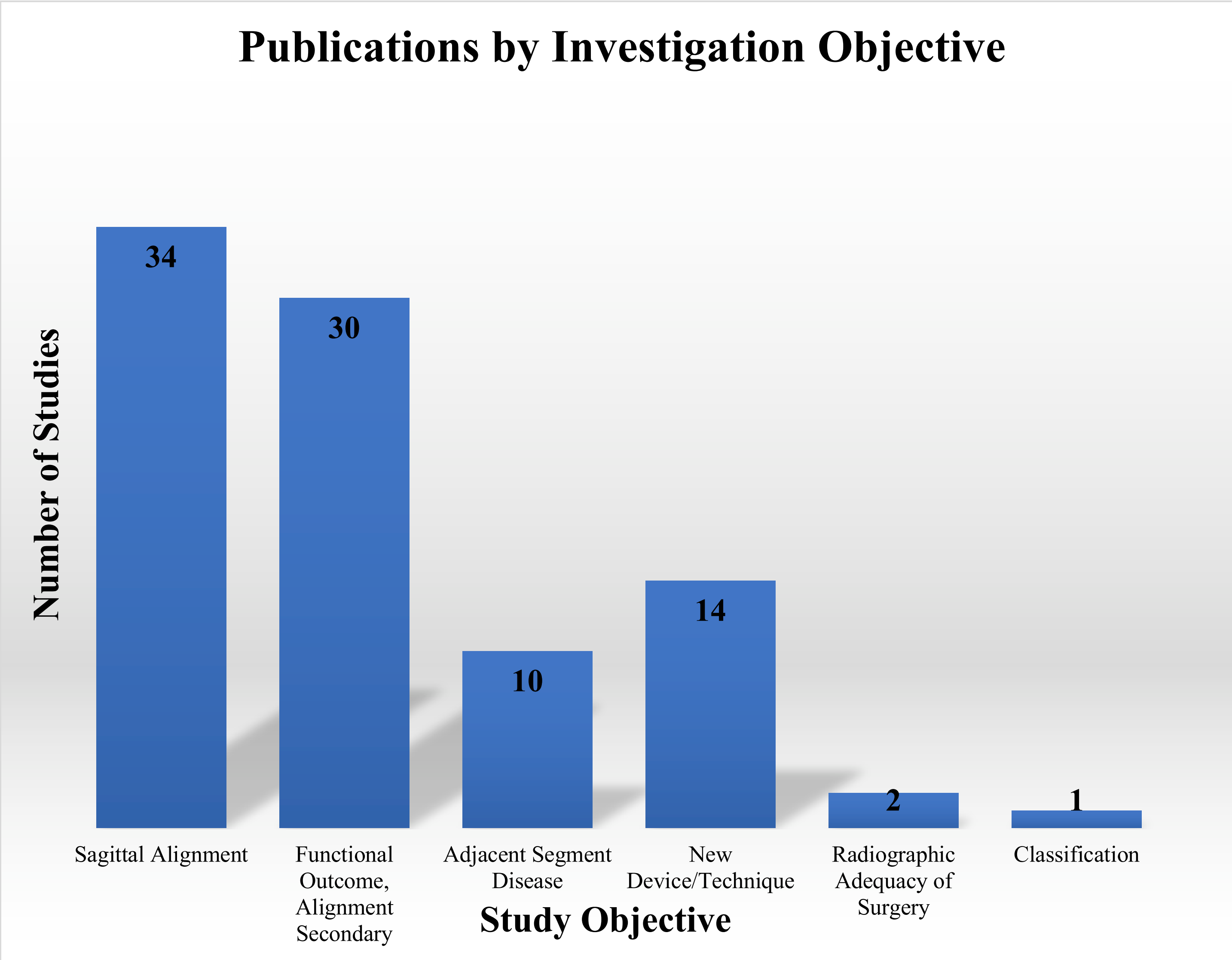
Figure 4: Included Studies by Continent of Investigation



Primary Objective of Included Investigations

There was wide variability among included studies with respect to primary objectives of investigation (Figure 5). Thirty-four (37%) studies primarily assessed sagittal spinal alignment in patients undergoing DLS surgery. A similar proportion, 30 (33%) studies, primarily sought to assess the functional outcomes of DLS surgery with a secondary objective of sagittal spinal alignment outcomes and/or correlation to functional outcomes. There were also 14 (15%) studies that examined either new surgical techniques or new devices in DLS surgery and their role in sagittal alignment changes.

Figure 5: Primary Study Objective

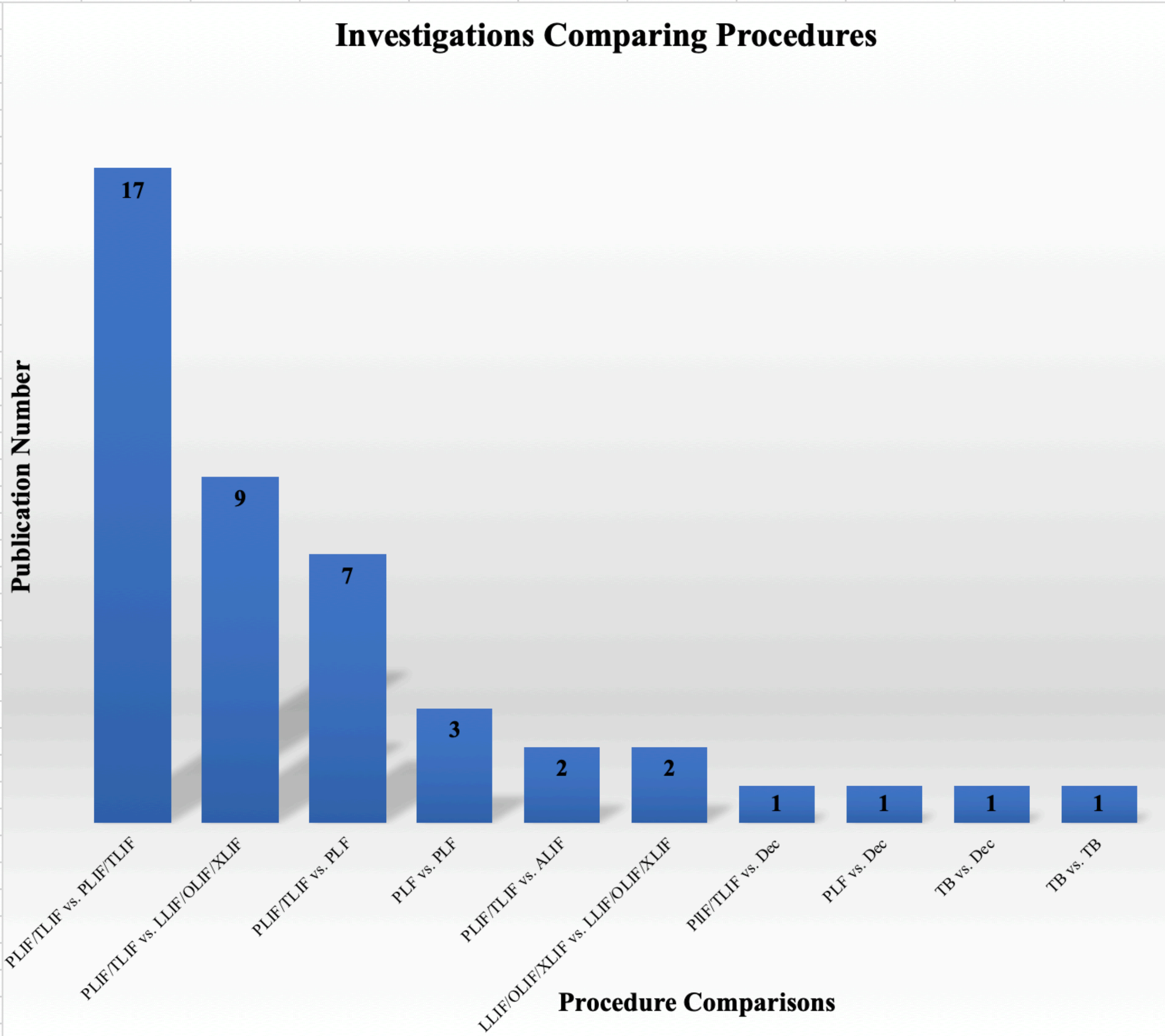


Primary Procedure Types and Comparative Analysis Among Included Studies

The most frequently investigated primary procedure types were posterior lumbar interbody fusion (PLIF) and transforaminal lumbar interbody fusion (TLIF), with 62 (68%) of studies reporting results of PLIF/TLIF. Eleven studies (12%) assessed lateral lumbar interbody fusion (LLIF), extreme LIF (XLIF) or oblique LIF (OLIF), with 7 (7.7%) of studies assessing posterolateral fusion (PLF). Only four (4.4%) studies primarily assessed decompression alone with 3 (3.3%) reporting on tension band device use, two (2.2%) studies examining anterior lumbar interbody fusion (ALIF). Finally, one (1.1%) investigation assessed lumbar disc replacement, with an additional investigation combining reports of ALIF/PLIF/PLF without stratification by procedure type. Of all studies included, 23 (25%) reported on the use of minimally invasive techniques.

The majority of investigations (47 (52%) studies) did not report a comparative arm of either differing patient types compared to each other with the same surgical techniques, nor a comparison of two different surgical techniques and their corresponding radiographic and/or functional results. Of the included studies (44 (48%) studies) that did report a comparative arm, the greatest number of investigations (17/44 (39%) studies) compared PLIF/TLIF to PLIF/TLIF (Figure 6). There was additionally higher emphasis in the included investigations on comparing PLIF/TLIF to LLIF, 9/44 (20%) studies and PLIF/TLIF (7/44 (16%) studies) to PLF.

Figure 6: Investigations Comparing Procedure Types or Procedure Groups



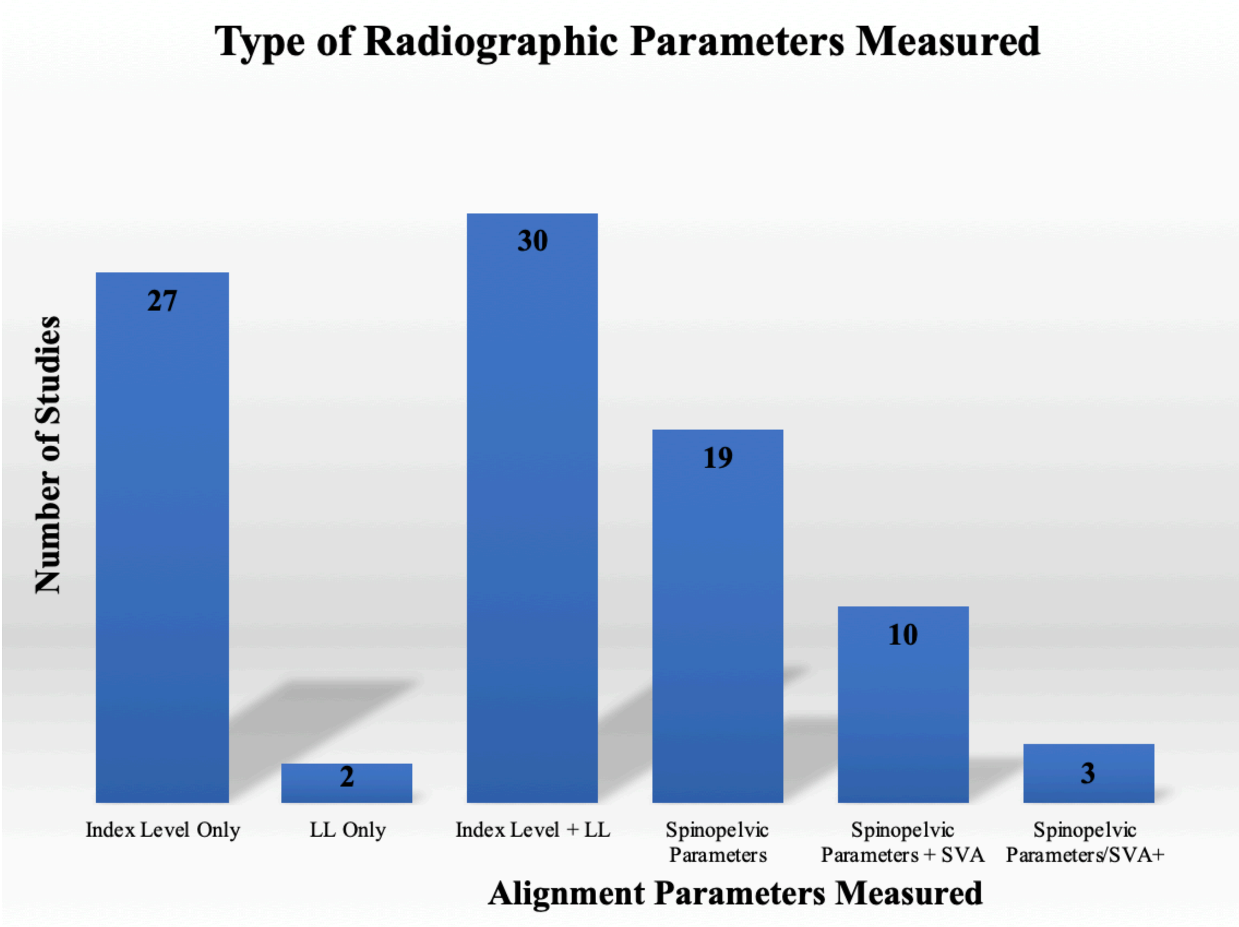
PLIF: posterior lumbar interbody fusion; TLIF: transforaminal lumbar interbody fusion; LLIF: lateral lumbar interbody fusion; OLIF: oblique lateral interbody fusion; XLIF: extreme lateral interbody fusion; PLF: posterolateral fusion; ALIF: anterior lumbar interbody fusion; Dec: decompression only; TB: tension band device

Radiographic Measures Reported

There was a marked degree of variation among the studies with regards to which radiographic parameters were reported (Figure 7). Eighty-four (91%) studies compared the same preoperative to postoperative measurements of their patient cohorts. Of the 47 studies which reported a comparative arm, 44/47 (94%) assessed the radiographic parameters preoperatively and postoperatively between groups. A common theme among the reporting of radiographic parameters in the included investigations was the assessment of the magnitude and/or maintenance of a radiographic change postoperatively, with 79 (87%) studies reporting these findings.

The majority of studies focused on index DLS level (27 (30%) studies) or lumbar spine radiographic imaging (32 (35%) studies) only. Thirty-two (35%) studies reported spinopelvic parameters inclusive of PI, PT and SS, with only 13 (14%) of all included studies assessing 36-inch standing lateral radiographs and associated overall alignment.

Figure 7: Radiographic Parameters Analyzed Among Studies

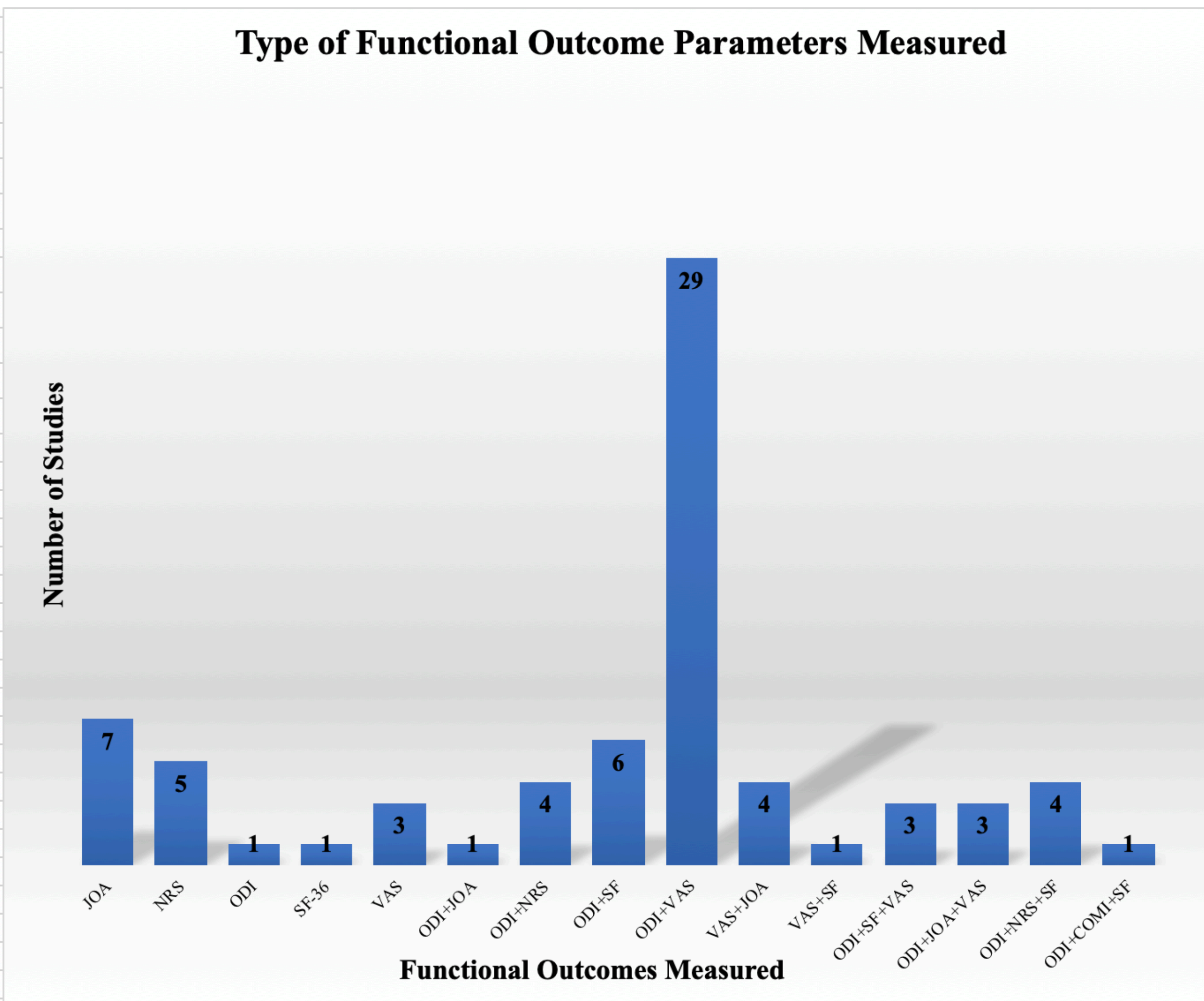


Index level only: facet angle, disc angle measurement, slip angle; LL only: Lumbar lordosis only; Spinopelvic Parameters: includes index level only measurements, LL and pelvic incidence (PI), pelvic tilt (PT), sacral slope (SS); SVA: sagittal vertical axis; Spinopelvic parameters/SVA+: additionally includes thoracic kyphosis, T1 spinopelvic inclination, T9 spinopelvic inclination

Functional Outcomes Reported

A total of 71 (78%) studies reported at least one functional outcome in addition to radiographic measurements (Figure 8). The most frequent patient reported outcome (PROM) was the Oswestry Disability Index (ODI), with 51 (72%) investigations reporting PROMs utilizing the ODI. Similarly, the Visual Analog Scale (VAS) (38 (54%) studies) and the Japanese Orthopaedic Association (JOA) back pain score (15 (21%) studies) were heavily emphasized in the PROMs reported.

Figure 8: Functional Outcomes Reported



JOA: Japanese Orthopaedic Association back pain evaluation; NRS: numeric rating scale (back and/or leg pain); ODI: Oswestry Disability Index; SF-36: Short Form survery-36; VAS: Visual Analog Score; COMI: Core Outcomes Measures Index

Discussion:

In this scoping review, we identified 91 primary studies addressing sagittal radiographic parameters in DLS surgery from 1990 to 2021. Our findings indicate a recent increasing trend of interest in the importance of sagittal spinal balance among patients undergoing DLS surgery. The predominant number of investigations are being pursued in Asia with the largest number of investigations providing level three and four evidence. Primarily, retrospective cohort studies and case series dominate the literature included in this scoping review. Among our included studies, we were able to map the primary objective of each investigation in addition to the types of radiographic parameters most frequently being reported. From this synthesis, we have identified significant heterogeneity among the sagittal spinal alignment parameters being reported in these investigations. Largely the focus of our included studies centre on segmental and regional sagittal alignment parameters, with fewer studies pursuing whole spine sagittal alignment measurements. The current variability of reporting among our included studies limit the ability to meaningfully synthesize and amplify the potential effect of these smaller investigations.

While the demonstrated functional benefits of surgery for DLS have been definitively established, it has not been established what radiographic alignment parameters both preoperatively and postoperatively are most important for DLS patients. The important sagittal spinal alignment parameters demonstrated in the adult spinal deformity literature have widely permeated to degenerative lumbar spine and DLS investigations. It is unclear which surgical intervention in DLS can most affect regional and global sagittal alignment. Furthermore, different investigations outline differing effects of decompression, posterolateral fusion and interbody fusion based techniques.[23; 25]

Varied reports exist in the literature surrounding the regional and global sagittal alignment changes that can occur with single-level DLS surgery and importantly how this relates to functional outcomes. It has been shown that patients with greater SVA postoperatively suffer worsened functional outcome improvements than individuals with an SVA under five centimetres.[3] Similarly, a PI-LL mismatch after TLIF for DLS is associated with worsened functional outcomes.[26] While not borne out in the postoperative literature, there does appear to be unique patients within the DLS population who suffer from sagittal imbalance versus those who have DLS but no radiographic imbalance and these patients likely need to be treated differently.[27] Kobayashi et al. have attempted to demonstrate that distinct sagittal spinal alignment patterns exist among DLS patients, normal SVA <40mm, high SVA >95mm, with associated differences in PI.[28]

Unfortunately, as demonstrated, small cohort studies largely dominate the available literature on this topic. Small scale cohort studies have been shown to exaggerate or mislead with results.[29] There are a corresponding number of conflicting results which muddy the signal of alignment effect and importance from DLS surgery. Attempts at systematic reviews and meta-analyses in the DLS population with respect to radiographic alignment outcomes have struggled to achieve meaningful effect given heterogeneity within the available literature and have focused on only a limited number of DLS surgical techniques.[16; 30] As such, it is currently unclear what degree of sagittal balance restoration if any, correlates to improved functional outcomes in patients undergoing DLS surgery. Furthermore, Rhee et al. have demonstrated that both those patients deemed to be conventionally sagitally balanced and those determined to be imbalanced postoperatively have not been shown to have meaningful clinical functional differences in outcome.[16] With existing clinical equipoise surrounding the most efficacious surgical treatment option for the DLS population it is important to identify which patients will most benefit from more invasive, expensive and higher risk surgical interventions.

Limitations

Our scoping review has several limitations. Firstly, we were unable to retrieve 12 non-English studies to assess in full text. This potentially limits some of the mapping of the available evidence on our topic and may have produced an underestimation of the contributions of investigations from Europe and Asia.[31] However, large scale investigations such as multi-centre randomized controlled trials and high-impact prospective cohorts most commonly achieve publication in high-impact English language journals, which should help to minimize this limitation.[31] Additionally, we intentionally excluded some studies which reported including patients with DLS when their results sections did not stratify the DLS patient outcomes from the isthmic or "low grade spondylolisthesis" or lumbar stenosis populations.

Conclusion

There is an increasing prevalence of studies investigating sagittal spinal alignment parameters in DLS surgery. The currently available literature on this topic is of overall low quality evidence and largely retrospective in nature. There is limited analysis of global sagittal spinal alignment in DLS . Future investigational emphasis on longitudinally followed large prospective cohort or multi-centre randomized controlled trials should be prioritized. Attempts at standardizing the radiographic and functional outcome reporting techniques across multi-centre investigations and prospective cohorts will allow for more robust, reproducible analyses of significance to be conducted on DLS patients.

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Chapter 3: Decompression is Equivalent to Posterolateral or Interbody Fusion for Sagittal Balance Correction in Degenerative Lumbar Spondylolisthesis

There is clearly a strong interest in assessing sagittal spinal alignment and how it relates to degenerative lumbar spondylolisthesis surgery. However, the overall magnitude of effect in sagittal spinal alignment change that can result from decompression or decompression and fusion in degenerative lumbar spondylolisthesis is unclear. To better understand this objective, we sought to assess the magnitude of postoperative alignment based on each type of surgical intervention for patients with degenerative lumbar spondylolisthesis. As such, we conducted an analysis to assess the effect of decompression versus posterolateral fusion versus interbody fusion on spinal alignment among patients undergoing surgery for degenerative lumbar spondylolisthesis.

Introduction:

Degenerative lumbar spondylolisthesis (DLS) is characterized by an acquired displacement of a lumbar vertebrae on the immediately adjacent caudal vertebra with associated degenerative compensatory changes.[1; 2] Most commonly DLS occurs in women over the age of 50 at the L4-L5 level, with patients typically presenting with complaints of primarily neurogenic claudication and/or radiculopathy with or without low back pain.[1; 2; 3] Among DLS patients with intractable symptoms unresponsive to nonoperative modalities or in the presence of neurological findings, such as weakness, sensory changes or radiculopathy, surgical intervention has unequivocally been shown to provide clinically meaningful improvement.[4; 5; 6; 7; 8] However, the most optimal surgical intervention for individuals with DLS is still unclear.[4; 5; 6; 7; 8]

Sagittal spinopelvic balance is involved in a variety of degenerative processes in the lumbar spine with patients with low back pain frequently suffering from a sagittal vertical axis (SVA) greater than five centimetres and a resultant increased amount of hip extension in an effort to augment pelvic retroversion.[5] Patients with DLS are known to frequently take on a forward flexed posture when ambulating to effect neural decompression.[9] The maintenance of balanced spinopelvic alignment is important to achieve an optimized energy-efficient posture in both normal and diseased states.[5] Multiple investigations have shown spinopelvic changes in DLS to be unique among other degenerative lumbar spine conditions.[10; 11; 12; 13; 14; 15; 16] Individuals with DLS have a significantly increased pelvic incidence (PI) as well as lumbar lordosis (LL) when compared to healthy individuals and those with degenerative spinal stenosis.[10; 11; 12; 13; 14; 15; 16] The increased PI among those with DLS has been correlated to increasing the propensity for vertebral listhesis, particularly anterolisthesis of L4.[14]

It has been shown that surgical correction of sagittal spinal imbalance independently predicts satisfaction and degree of disability among patients.[17] These findings have been echoed in the DLS literature with regards to sagittal correction and improved health related quality of life (HRQOL) measurements, with worsened postoperative sagittal balance correlating to poorer patient reported outcomes.[2; 18] The ideal surgical intervention to achieve both sagittal alignment correction and HRQOL in patients with DLS has not been definitively determined. Interestingly, despite evidence not supporting clinical significance of superiority over decompression alone, national treatment patterns have dramatically transitioned to largely incorporate interbody fusion techniques over decompression in isolation over the last twenty years.[19]

The overall effect of differing surgical intervention type for patients undergoing interventions for DLS is not known. Specifically, to this investigation, the magnitude of postoperative alignment effects based on a particular surgical intervention for DLS is not established. The objective of this investigation was to assess the effect of decompression versus posterolateral fusion versus interbody fusion on spinal alignment among patients undergoing surgery for DLS.

Methods:

Patient population

A retrospective review of the prospectively collected data from the Canadian Spine Outcomes Research Network (CSORN) longitudinal cohort study on the assessment and management of degenerative spondylolisthesis was performed. Eligible patients for inclusion demonstrated radiographic evidence of degenerative spondylolisthesis with symptoms of neurogenic claudication or radiculopathy with or without back pain, unresponsive to non-operative management over at least three months who underwent surgical treatment between

January 1, 2015 and August 31, 2020 at any of the seven CSORN contributing academic spine centres. Patients were included if they underwent decompression, decompression and posterolateral fusion or decompression and interbody fusion. Open or minimally invasive techniques were eligible for inclusion and regardless of surgical technique were grouped according to procedure type. For this analysis, patients who had multilevel decompressions for spinal stenosis in the same procedure were included if the instrumented fusion was limited to one segment. Patients with greater than 10 degrees of scoliosis were excluded. Any patient undergoing surgery for an isthmic spondylolisthesis, spinal fracture, concomitant cervical or thoracic myelopathy, multilevel fusion procedures or had previous lumbar fusion procedures were excluded. Furthermore, all patients with symptoms from concomitant hip and/or knee osteoarthritis were excluded from the analysis. All patients provided written consent to participate in the study. Study approval was provided by University Health Science Research Ethics Boards at each institution.

Among all contributing centres, standardized CSORN preoperative demographic and radiographic data sheets were completed. Additionally, a standardized surgical data sheet was completed for all procedures performed. Captured patient demographics included patient age, body mass index (BMI), sex, smoking status, primary preoperative complaint and surgical indication, American Society of Anesthesiology (ASA) score, spondylolisthesis grade and comorbidities. Operative data recorded included procedure type: decompression, decompression and posterolateral fusion or decompression and interbody fusion. Additionally, operative time, estimated blood loss and intraoperative adverse events were recorded.

All surgical procedures were performed by academic, fellowship-trained adult spine surgeons at each contributing centre from a posterior approach either open or through minimally invasive techniques. The primary goal of each intervention among this patient cohort was obtaining an adequate decompression and was not necessarily a sagittal spinal deformity correction. Postoperative adverse events were captured to the one-year postoperative follow-up time point of this investigation, including return to the operating room within a year of surgery.

Radiographic Measurements

All enrolled patients had a complete radiographic evaluation immediately preoperatively, with the same measurements performed 12-months postoperatively. The standardized radiographic evaluation across all contributing centres included a 36-inch standing lateral radiograph in addition to a standing lateral lumbar radiograph, which included the femoral heads. All radiographic evaluations were completed according to the CSORN radiographic outcomes standardized evaluation form. The grade of spondylolisthesis, sagittal vertical axis (SVA), lumbar lordosis (LL), pelvic tilt (PT), sacral slope (SS) and pelvic incidence (PI) were determined at each timepoint. Furthermore, the PI-LL was recorded for each patient pre- and postoperatively. Slip percentage at the listhesis level was determined by dividing the length of the slip in millimeters by the width of the superior endplate of the immediately caudal vertebrae below the listhesis level to give a percentage of the slip. A standard Meyerding classification was then utilized to grade the degree of anterolisthesis. Global lumbar lordosis was measured via a cobb angle from the superior endplate of L1 to the superior endplate of S1 on the standing lateral lumbar spine radiograph. The pelvic parameters of PI, PT and SS were measured using a standing lateral lower lumbar view which included the femoral heads. Per previously described standards, the PT was measured by the angle formed between a vertical reference line from the centre of the femoral head and a line from the centre of the femoral head to the midpoint of the superior S1 endplate.[20] Sacral slope was measured via the angle formed between the slope of the

S1 superior endplate and an intersecting line parallel to the horizontal plane.[20] The PI was measured by the angle formed from a line connecting the midpoint of the S1 superior endplate and midpoint of the femoral head and a line perpendicular to the S1 superior endplate.[21] Sagittal vertical axis was measured from the 36-inch standing lateral radiograph with a midpoint C7 vertebral body plumb line dropped vertically and the distance between the plumb line and the posterior superior corner of the S1 endplate recorded.[20] Per previously reported standards, an SVA greater than 50mm was understood to reflect a high SVA.[20] The grade of spondylolisthesis, SVA, lumbar lordosis, pelvic tilt, sacral slope and pelvic incidence were determined at each timepoint. Furthermore, the PI-LL was recorded for each patient pre and postoperatively.

Statistical Analysis

Data were analyzed using SPSS software version 26 (SPPS Inc., Chicago, Il, USA). In order to quantify the patients who experienced an improvement in their spinopelvic alignment the radiographic measure at the one-year postoperative mark was subtracted from the preoperative value for each patient. The patients were then grouped by improved or worsened alignment for SVA, LL and PI-LL based on these values. An improved alignment was understood to represent a reduction in SVA, an increase in LL and a decrease in the PI-LL mismatch. Conversely, a worsened alignment reflected an increased SVA, a reduction in LL and an increased PI-LL mismatch. For continuous parametric variables between group comparisons were made using a one-way analysis of variance (ANOVA). Between groups analysis was performed via student's t test. A p-value of less than 0.05 was considered to indicate statistical significance.

Results:

A total of 248 patients were available for analysis, with 69 (28%) patients receiving an isolated decompression (D), 32 (13%) patients undergoing decompression and posterolateral fusion (PLF) and 147 (59%) receiving decompression with interbody fusion (IB). At the one-year postoperative mark a PI-LL measurement was available for 243/248 (98%) patients (D: 69 (28%), PLF: 32 (13%), IB: 142 (58%)) and 192/248 (77%) patients (D: 52 (27%), PLF: 26 (14%), IB: 114 (59%)) had an SVA measurement available for analysis.

Baseline patient characteristics

The baseline demographic characteristics are shown in Table 1. There was a statistically significant difference among patient age for individuals undergoing decompression (70 years ± 8.9) compared to PLF (69.1 ± 7.2) and IB (64.1 ± 8.7), p<0.001. Similarly, there was a statistically significant difference between procedures in the proportion of female sex: D 36 (52%), PLF 21 (66%) and IB 102 (69%), p=0.048. There was no statistically significant difference among the patient groups with respect to BMI (p=0.140), smoking status (p=0.350), spondylolisthesis level (p=0.062) and comorbidities (p=0.567).

Table 1: Preoperative patient characteristics

	Decompression n=69	**Posterolateral Fusion n=32**	**Interbody Fusion n=147**	**P-Value**
Age, years Mean±SD	70.0 (8.9)	69.1 (7.2)	64.1 (8.7)	**<.001**
Body mass index, kg/m^2 No. of patients Mean±SD	28.6 (5.1)	28.9 (4.8)	30.2 (6.4)	.140
Sex, Female, n (%)	36 (52%)	21 (66%)	102 (69%)	**.048**
Current smoker, n (%)	7 (10%)	3 (9%)	24 (16%)	.350
Primary Complaint, n (%)				

Neurogenic claudication **Radiculopathy**	57 (83%) 12 (17%)	23 (72%) 9 (28%)	133 (90%) 14 (10%)	**.010**
ASA score **1** **2** **3** **4**	 3 (4.3%) 34 (49%) 32 (46%) 0 (0%)	 0 (0%) 12 (38%) 20 (63%) 0 (0%)	 5 (3.4%) 84 (57%) 55 (37%) 3 (2.0%)	.145
Grade Spondylolisthesis, n (%)	Grade 1: 60 (87%) Grade 2: 9 (13%)	Grade 1: 25 (78%) Grade 2: 7 (22%)	Grade 1: 94 (64%) Grade 2: 53 (36%)	**.001**
Level **L1-L2** **L2-L3** **L3-L4** **L4-L5** **L5-S1**	 0 (0%) 5 (7.2%) 9 (13%) 54 (78%) 1 (1.4%)	 0 (0%) 2 (6.3%) 6 (19%) 24 (75%) 0 (0%)	 1 (0.7%) 12 (8.1%) 19 (13%) 114 (78%) 1 (0.7%)	.062
Previous Surgery, n (%)	2 (2.9%)	0 (0%)	4 (2.7%)	.632
Number of Comorbidities Mean±SD	3.4 (1.8)	3.0 (2.0)	3.3 (1.8)	.567

Overall the average preoperative lumbar lordosis among all patients was 45.2^0 (± 12.8^0), with an average PI-LL of 12.6^0 (13.3^0) and an average SVA of 30.5 (± 39.9) mm. Preoperative radiographic analysis among patients showed no statistically significant difference for any measure other than SVA (Table 2). The average preoperative SVA was significantly higher in the PLF group 47.2 (± 53) mm compared to D 34.3 (± 47) mm and IB 25.1 (± 33.7) mm, p=0.018.

Table 2: Average preoperative radiographic measures

	Decompression n=69	**Posterolateral Fusion n=32**	**Interbody Fusion n=147**	**P-Value**
Sacral Slope (degrees)	34.7 (8.6)	32.3 (9.3)	33.5 (8.4)	.393
Pelvic Tilt (degrees)	24.5 (8.4)	25.6 (8.6)	23.7 (8.3)	.480

Pelvic Incidence (degrees)	59.6 (10.6)	58.1 (12.5)	56.8 (11.2)	.234
Lumbar Lordosis (degrees)	47.7 (10.6)	43.4 (16.0)	44.4 (13.2)	.159
PI-LL (degrees)	11.9 (12.6)	14.7 (14.1)	12.4 (13.5)	.596
Sagittal Vertical Axis (mm)	34.3 (47.0)	47.2 (52.8)	25.1 (33.7)	**.018**

Proportion of Patients experiencing improved or worsened postoperative radiographic parameters

Sagittal Vertical Axis:

With respect to SVA, a similar proportion of patients improved/remained unchanged (D: 50%, PLF: 58%, IB: 66%) and worsened (D: 50%, PLF: 42%, IB: 34%) with surgery across the three interventions, p=0.148 (Table 3). On average, the SVA improved by 23.4 mm (05% CI, -29.5mm, -17.3mm), p=0.004, for the patient cohort demonstrating a one-year postoperative improvement. The greatest magnitude of SVA improvement was seen with PLF 49 (51.8) mm compared to IB 18.1 (23.2) mm. For patients experiencing an improved SVA, the mean difference in magnitude of change for PLF compared to IB was 30.9 mm (95% CI, 52.5, 9.4), p=0.003, and compared to D was 24.9 mm (95% CI, 49.6, 0.2), p=0.048. Across surgery type for the patient cohort that demonstrated a worsened SVA, postoperatively there was no statistically significant difference in the type of surgery to worsened SVA, with an average SVA increase in these patients of 14.6 (95% CI, 10.5, 18.9) mm, p=0.805. Further, there were no between group differences between D, PLF and IB with respect to worsened postoperative SVA.

Table 3: Proportion of patients with one-year postoperative improvement or worsening of sagittal vertical axis (SVA) and magnitude of worsening or improvement at one-year after surgery according to surgery type.

Sagittal Vertical Axis (SVA), change 12 months	Decompression N=52	Posterolateral Fusion N=26	Interbody Fusion N=114	P-Value
% Improved, n (%)	26 (50)	15 (58)	75 (66)	
% Worsened, n (%)	26 (50)	11 (42)	39 (34)	.148
Improved, Mean ± SD (mm)	-24.1 (39.5)	-49.0 (51.8)	-18.1 (23.2)	-23.4 (-29.5, -17.3) **P=0.004**
Worsened, Mean ± SD (mm)	13.9 (16.3)	18.0 (19.4)	14.2 (19.2)	14.6 (10.5,18.9) p=0.805

A negative change in score from baseline indicates an improvement in SVA. Worsening SVA is denoted by a positive change in score from baseline.

Lumbar Lordosis:

Lumbar lordosis improved with similar proportions across all surgery types at the one-year postoperative mark regardless of surgical type, p=0.385 (Table 4). The proportion of patients experiencing improved postoperative LL was D: 62%, PLF: 62%, IB: 71%. Across surgery types, D: 38%, PLF: 38%, IB: 29% had a worsened postoperative LL. However, for patients gaining an increased LL with surgery, the magnitude of LL improvement was greatest among IB fusion 9.7^{0} ($\pm 7.6^{0}$) compared to decompression 6.5^{o} ($\pm$ 6.1^{0}), p=0.05. There was no difference with regards to improved LL between IB and PLF, p=0.934. For the patient cohort that experienced a decrease in LL postoperatively, surgery type did not statistically significantly affect the magnitude of LL loss, with an average decrease across this cohort of 6.1^{0} (95% CI, 7.4^{0}, 4.9^{0}), p=0.426. Between group analysis comparing surgery type did not reveal any statistically significant relation to decrease of LL with any surgery type.

Table 4: Proportion of patients with one-year postop improvement or worsening of lumbar lordosis (LL) and magnitude of worsening or improvement at one-year after surgery according to surgery type.

Lumbar Lordosis (LL),	Decompression n=69	Posterolateral Fusion n=32	Interbody Fusion n=147	P-Value

change 12 months				
% Improved, n (%)	43 (62%)	20 (62%)	104 (71%)	0.385
% Worsened, n (%)	26 (38%)	12 (38%)	43 (29%)	
Improved, Mean ± SD (degrees)	6.5 (6.1)	9.1 (7.0)	9.7 (7.6)	8.8 (7.7,9.9) P=0.05
Worsened, Mean ± SD (degrees)	-5.8(7.4)	-4.4 (2.3)	-6.8 (5.1)	-6.1 (-7.4, -4.9) p =0.426

A positive change in score from baseline indicates an improvement in lumbar lordosis. Worsening lumbar lordosis is denoted by a negative change in score from baseline.

PI-LL:

The proportion of patients who experienced an improvement (D: 64%, PLF: 56%, IB 66%) or worsening (D: 36%, PLF: 44%, IB: 35%) of their PI-LL postoperatively did not differ among surgery type, p=0.617 (Table 5). For patients experiencing an improvement of their PI-LL, the average improvement was 11.1^0 (95% CI, 12.5^0, 9.6^0), p=0.522. There were no between group differences with respect to magnitude of improved PI-LL across surgery types. Similarly, no statistically significant difference was found among surgery type for patients who had a worsened postoperative PI-LL, with an average worsening of 7.1^0 (95% CI, 5.9^0, 8.4^0), p=0.108.

Table 5: Proportion of patients with one-year postop improvement or worsening of pelvic incidence minus lumbar lordosis (PI-LL) and magnitude of worsening or improvement at one-year after surgery according to surgery type.

PI-LL change 12 months	Decompression N=69	Posterolateral Fusion n=32	Interbody Fusion n=142	P-Value
% Improved, n (%)	44 (64%)	18 (56%)	93 (66%)	
% Worsened, n (%)	25 (36%)	14 (44%)	49 (35%)	.617
Improved, Mean ± SD	-10.6 (9.3)	-9.1 (7.3)	-11.7 (9.4)	-11.1 (-12.5, -9.6) p=.522
Worsened, Mean ± SD	6.8 (7.6)	4.3 (2.9)	8.1 (5.5)	7.1 (5.9, 8.4) p=.108

A negative change in score from baseline indicates an improvement in PI-LL. Worsening PI-LL mismatch is denoted by a positive change in score from baseline.

Discussion:

Our results reflect a large multicentre longitudinal prospectively collected cohort investigation of patients undergoing treatment for degenerative lumbar spondylolisthesis. Among this cohort of patients undergoing decompression, decompression with posterolateral fusion or decompression with interbody fusion for degenerative lumbar spondylolisthesis we have demonstrated that the majority of patients experience an improvement in their sagittal spinal alignment one-year postoperatively. Furthermore, no statistically significant difference existed among surgery types with regard to the proportion of patients who improve or worsen with respect to their sagittal balance at one-year postoperatively when undergoing surgery for DLS. However, the magnitude of improvement in SVA was greatest for both type of fusion groups compared to decompression. Additionally, among patients with an improved postoperative LL, the magnitude of LL correction was greatest for IB compared to D. Importantly, for those patients experiencing a worsening in their post-operative radiographic parameters, the magnitude of this change did not differ between surgery type.

The degenerative lumbar spinal stenosis literature has shown decompression in isolation can improve sagittal balance in greater than 70% of patients postoperatively, with worsened postoperative sagittal balance correlated with poorer functional outcomes.[22; 23; 24; 25] Our investigation demonstrated that among the 50% of DLS patients experiencing an improved LL with decompression alone, the magnitude of improved LL is 6.5^0. Likewise, patients undergoing decompression alone with an improved SVA postoperatively saw a reduction in SVA of 24.1mm. The magnitude of lumbar lordosis increase after decompression alone in DLS patients mirrors the findings of Salimi et al. who have previously shown that minimally invasive decompression improves LL an average of 5.5 degrees at five years postoperatively, in their 110 patient cohort of lumbar spinal stenosis patients.[26] Interestingly, despite this improvement in LL, Salimi et al. showed that there was an initial statistically significant worsening of SVA at 2-years postoperatively of 15.4mm, which eventually normalized to no change in SVA from baseline at five year follow-up. Alternatively, a retrospective review of 87 patients with degenerative lumbar spinal stenosis undergoing microendoscopic laminotomy (40% of the patient sample having a DLS) found that preoperative spinopelvic sagittal imbalance correlated with improved sagittal balance postoperatively with a significantly increased LL and decreased SVA postoperatively in the DLS population.[27] Our investigation showed equal proportions of patients having an improvement and worsening of their SVA at one-year postoperatively; representing relatively small magnitudes of mean change (13.9mm and 24.1mm respectively); which is consistent with the known differences in sagittal balance expected among lumbar spinal stenosis and DLS patients.

The greatest magnitude of improvement in radiographic parameters was within the fusion cohorts, with the greatest improvement in SVA seen in patients undergoing PLF and similar LL improvement for PLF and IB fusions (9.1^0 and 9.7^0 respectively). A retrospective cohort by Kong et al. was one of the first investigations focusing specifically on sagittal spinal alignment to show that PLIF for DLS can lead to statistically significant postoperative improvement in LL in addition to a corresponding improvement of functional outcome.[28] Our result echoes the findings of Challier et al. from their 60 patient even sized group randomized investigation of PLF vs. transforaminal lumbar interbody fusion (TLIF) for DLS in which no difference in segmental lordosis was found postoperatively between groups.[29] Our findings are unique in that we have highlighted the sagittal alignment changes that can occur with either D, PLF or IB for DLS and furthered this to demonstrate by what magnitude such correction or worsening can be expected by each surgery type.

Aoki et al. have shown that single level TLIF for degenerative lumbar spinal stenosis and/or DLS is associated with worsened functional outcomes postoperatively in patients with a poor PI-LL mismatch.[30] Tempel et al. described a 159 patient cohort undergoing single level TLIF and highlight the importance of a high PI-LL mismatch.[16] The findings note that for a one degree increase of PI-LL mismatch postoperatively, there was an associated increase by 1.4 fold of adjacent segment disease occuring.[16] Thus, emphasis must be placed on the appropriate indication for interbody fusion in the setting of DLS considering that sagittal alignment correction was shown for half of our cohort with decompression alone. Clinical equipoise around the most ideal surgical intervention for DLS patients persists.[1; 31] The decision to decompress only or decompress and fuse a patient is widely variable.[3; 32] Recent evidence in the DLS literature has focused on the role of preoperative sagittal spinal imbalance concomitantly occurring in patients presenting with the classic findings of neurogenic claudication and/or radiculopathy and back pain. Our findings are therefore important in that the magnitude of significant sagittal correction that can be achieved with decompression alone compared to more invasive, lengthy and higher-risk surgical procedures.

Limitations

The results of our study are limited to the quality of our large, multi-centre database. Strong working relationships and full-time research assistants to care for and curate the database minimizes errors of entry in addition to frequent reviews for logic within the database. We did not report functional outcomes for our patients in this paper as we only wanted to focus on magnitude of sagittal alignment correction. The primary goal of surgical intervention in all of the enrolled patients was not a deformity correction but rather treating the stenosis causing neurologic symptoms. However, with a common surgical goal among all contributing surgeons and similar surgical techniques, bed frames and hardware utilized, some degree of variance has been removed. Given that sagittal spinal alignment parameters specific to the DLS patient population have not been clearly established, we chose to analyze our patient's radiographic parameters by those who improved or worsened in each measurement with surgery. This was performed to capture any patient who saw an improvement or worsening in their sagittal alignment despite potentially remaining within or outside of accepted sagittal spinal alignment parameters derived from the adult spinal deformity literature. Kobayashi et al. have previously described three distinct presenting sagittal alignment patterns among DLS patients with those individuals having a normal SVA <40mm compared to patients with a high SVA >95mm demonstrating marked differences in PI and a higher risk for deterioration of their sagittal balance.[33] Our patient sample size was not amenable to further divisions by high and low PI with regard to surgery type and potentially the magnitude of effect of correction or worsening may have been altered.

Conclusion:

Overall spinal alignment either remains the same or improves with the majority of patients undergoing surgery for DLS regardless of surgical intervention. However, the largest magnitude of sagittal correction change occurred in the patients receiving fusion, with interbody fusion providing the greatest increase in lumbar lordosis among patients seeing an improvement in their postoperative lumbar lordosis. In this large, longitudinally followed multi-centre patient cohort, more invasive surgical intervention in the form of interbody or posterolateral fusion for

DLS was associated with a greater magnitude but not statistically significant between group alignment improvement compared to decompression alone.

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Chapter 4: A Canadian Spine Outcomes and Research Network Study of Functional Outcomes after Surgery for Lumbar Degenerative Spondylolisthesis

We now understand the magnitude of sagittal alignment correction that can occur with near equivalence between decompression and fusion based procedures for degenerative lumbar spondylolisthesis. It is thus imperative to understand the radiographic parameters that most predict functional outcome after surgery for these patients to ensure the appropriate surgery and amount of surgical intervention is being performed for patients. Thus, all patients with radiographic and functional outcome parameter measurements at one-year postoperatively were included in the investigation of this as outlined below.

Introduction:

Spinal stenosis associated with degenerative lumbar spondylolisthesis (DLS) represents one of the most common spine surgical indications among adults, particularly females, over the age of 65.[1] While the pathogenesis of DLS is not completely understood, this unique degenerative condition of the lumbar spine occurs in the setting of displacement of a lumbar vertebrae on the immediately adjacent caudal vertebrae commonly associated with clinical symptoms of neurogenic claudication.[2; 3; 4] For patients with DLS and neurologic symptoms, the benefits of surgical intervention over nonoperative treatment are well established in both functional and health related quality of life improvements (HRQOL) [3; 5; 6]; in addition to cost benefit analyses.[7; 8; 9; 10]

The alignment of the lumbar spine has important impacts on segmental motion and the corresponding changes to a degenerative lumbar spine in the presence of DLS has recently been shown to have implications upon HRQOL.[3; 11] Maintenance of spinopelvic alignment as a contributor to an energy-efficient posture when standing and ambulating is well-established.[12] Individuals with DLS tend to prefer a forward flexed posture when ambulating to unload neurologic elements and effect an increased walking tolerance via relief of neurogenic claudicant symptoms.[13] Furthermore, with lumbar spine degeneration and corresponding hypo-lordosis, the pelvis will attempt to accommodate for these postural changes by retroverting or increasing the tilt of the pelvis. However, these compensatory mechanisms are finite and when maximized lead to knee flexion and hip extension to further augment one's balance.[12] The spinopelvic changes that occur when patients have DLS are unique and are associated with a marked increase from normal values for healthy individuals and those with lumbar spinal stenosis for both pelvic incidence (PI) as well as lumbar lordosis (LL).[11; 12; 14; 15; 16; 17; 18; 19; 20; 21] Further, the increased PI among these patients has been correlated to increasing the propensity for vertebral listhesis, particularly of L4, the most commonly affected listhesis level in DLS.[18]

The most optimal surgical intervention for patients with DLS is not clearly defined. DLS is commonly treated posteriorly via an open or minimally invasive technique through a decompression and may be augmented with posterolateral or interbody fusion.[22] Significant discrepancy in preferred surgical procedures for DLS patient presentations exist.[4; 22; 23] For example, Canadian spinal surgeons have been demonstrated to prefer employing the most extensive posterior procedure (interbody fusion) in the majority of patients with DLS.[4; 22] Similarly, US national trends show marked increase in the use of interbody fusions in the DLS surgical population over the past decade, in the absence of proven superiority over more cost-effective techniques, which carry a lower intra- and postoperative side effect profile.[24; 25; 26]

The adult spinal deformity literature supports improved postoperative HRQOL outcomes including satisfaction and degree of disability in patients receiving sagittal spinal balance correction at the time of surgery.[27] Recent retrospective cohort studies on DLS has demonstrated worsened HRQOL among patients with poor sagittal spinal balance following surgery specifically for DLS.[3; 28] However, there does exist heterogeneity within the DLS literature on functional outcomes and their correlation to sagittal radiographic alignment parameters as other prospective cohort studies have shown no functional difference between patients receiving anterolisthesis reduction and corresponding improved sagittal balance.[29] There remains relatively little investigating the importance of radiographic parameters as they pertain to predicting improved functional outcomes among patients undergoing surgery for DLS.

Thus, the objective of this study was twofold: first, we sought to confirm the importance of sagittal spinal alignment on functional outcome with DLS surgery and second, to identify the radiographic parameters that predict functional outcomes after DLS surgery.

Methods:

A retrospective analysis of the prospectively collected Canadian Spine Outcomes Research Network (CSORN) longitudinal cohort study on the assessment and management of degenerative spondylolisthesis was performed. Eligible patients for inclusion demonstrated radiographic evidence of degenerative spondylolisthesis with symptoms of neurogenic claudication or radiculopathy with or without back pain, unresponsive to non-operative management over at least three months, who underwent surgical treatment between January 1, 2015 and August 30, 2020 at any of the seven CSORN contributing academic spine centers. Included patients underwent either decompression, decompression and posterolateral fusion or decompression and interbody fusion. Open or minimally invasive techniques were both eligible for inclusion and were grouped according to procedure type. Patients who had multilevel decompressions for spinal stenosis in the same procedure were included if the instrumented fusion was limited to one segment. All included patients had to have completed preoperative and postoperative functional outcome scores in addition to at least one radiographic measured parameter available at one-year postoperatively.

Patients undergoing surgery for an isthmic spondylolisthesis, spinal fracture, concomitant cervical or thoracic myelopathy, multilevel fusion procedures or had previous lumbar fusion procedures were excluded. Furthermore, all patients with concomitant symptomatic hip and/or knee osteoarthritis were excluded from the analysis. All patients provided written consent to participate in the study. Study approval was provided by Western University Health Science Research Ethics Board, approval number 103079.

For all contributing centres, standardized CSORN preoperative demographic, radiographic and functional data sheets were completed. The radiographic and functional outcome analyses were repeated at one-year postoperatively. Additionally, a standardized surgical data sheet was completed for all procedures performed. Captured patient demographics included patient age, body mass index (BMI), sex, smoking status, primary preoperative complaint and surgical indication, American Society of Anesthesiology (ASA) score, spondylolisthesis grade and comorbidities. Operative data recorded included procedure type: decompression, decompression and posterolateral fusion or decompression and interbody fusion. Additionally, operative time, estimated blood loss and intraoperative adverse events were recorded.

All surgical procedures were performed by academic, fellowship-trained adult spine surgeons at each contributing centre. All procedures were performed via a posterior approach either open or through minimally invasive techniques. Postoperative adverse events were captured to the one-year postoperative follow-up time point of this investigation, including return to the operating room within a year of surgery.

Patient-Rated Functional Outcome Measurements

The patient-rated functional outcome measures collected preoperatively and at one-year postoperatively included, the Oswestry Disability Index (ODI) and the numeric rating scale (NRS) for back and leg pain. The ODI is a validated functional outcome score for lumbar spine patient functional outcome assessments.[30] The ODI evaluates physical disability secondary to back and/or leg pain from 0 (no dysfunction) to 100 (severe impairment).[3; 31] The NRS for back and leg pain are ten point pain scores from 0 to 10 with higher scores indicating more severe symptoms.[3]

Radiographic Measurements

All enrolled patients had a complete radiographic evaluation immediately preoperatively, with the same measurements performed 12-months postoperatively. The standardized radiographic evaluation across all contributing centres included a 36-inch standing lateral radiograph in addition to a standing lateral lumbar radiograph, which included the femoral heads. All radiographic evaluations were completed according to the CSORN radiographic outcomes standardized evaluation form. The grade of spondylolisthesis, sagittal vertical axis (SVA), lumbar lordosis (LL), pelvic tilt (PT), sacral slope (SS) and pelvic incidence (PI) were determined at each timepoint. Furthermore, the PI-LL was recorded for each patient pre- and postoperatively. Slip percentage at the listhesis level was determined by dividing the length of the slip in millimeters by the width of the superior endplate of the immediately caudal vertebrae below the listhesis level to give a percentage of slip. A standard Meyerding classification was then utilized to grade the degree of anterolisthesis. Global lumbar lordosis was measured via a cobb angle from the superior endplate of S1 to the superior endplate of L1 on the standing lateral lumbar spine radiograph. The pelvic parameters of PI, PT and SS were measured using a standing lateral lower lumbar view which included the femoral heads. Per previously described standards, the PT was measured by the angle formed between a vertical reference line from the center of the femoral head and a line from the center of the femoral head to the midpoint of the superior S1 endplate.[32] Sacral slope was measured via the angle formed between the slope of the S1 superior endplate and an intersecting line parallel to the horizontal plane.[32] The PI was measured by the angle formed from a line connecting the midpoint of the S1 superior endplate and midpoint of the femoral head and a line perpendicular to the S1 superior endplate.[33] Sagittal vertical axis was measured from the 36-inch standing lateral radiograph with a midpoint C7 vertebral body plumb line dropped vertically and the distance between the plumb line and the posterior superior corner of the S1 endplate.[32] Per previously reported standards, an SVA greater than 50mm was understood to reflect a high SVA.[32]

Statistical Analysis

Data were analyzed using SPSS software version 26 (SPPS Inc., Chicago, Il, USA). Patients were analyzed according to overall outcomes with surgery and outcomes per type of surgery (decompression, posterolateral fusion or interbody fusion). For continuous parametric variables between group comparisons were made using a one-way analysis of variance (ANOVA). Pearson correlation coefficient was used to assess the association between radiographic parameters and patient-reported functional outcomes, with spearman correlation coefficients utilized for any non-parametric variables. A multiple linear regression was further performed to assess for patient reported outcome measure correlation to postoperative radiographic parameters controlling for age, BMI, sex and preoperative patient health questionnaire-9 (a depression measure score). A weak correlation, that which is most commonly seen in human studies given multiple etiologic factors contributing to events, was understood to represent an R^2 value less than 03.9 with moderate 0.40-0.69 and strong greater than 0.70.[34] A p-value of less than 0.05 was considered to indicate statistical significance.

Results

A total of 363 DLS patients were entered within the CSORN prospective registry database at the time of data extraction. Of this patient cohort, 241 patients had completed surgery and a minimum one-year postoperative follow-up functional and a minimum of one, one-year postoperative radiographic analysis.

Baseline patient demographic and clinical characteristics

Among the included cohort, the average patient age was 66 (+/-8.9) years, with 153 (63%) females (Table 1). The vast majority of patients endorsed symptoms lasting greater than two years, with 209 (86%) patients having symptoms for a minimum of one year or greater at time of enrolment prior to surgery. The bulk of index level listheses were at L4/L5, with 197 (81%) of patients undergoing surgery for a primary indication of neurogenic claudication. Importantly, only 13 (5.3%) of all included patients had a previous remote lumbar spine decompression/fusion, with a smaller proportion of these patients 4 (1.1%) having had the surgery at the DLS level.

Table 1: Patient demographic, clinical and surgical characteristics

Parameters	Value, n=243
Age, years, Mean ± SD	66 ± 8.9
Sex, female	153 (63%)
Body mass index, kg/m^2, Mean ± SD	30 ± 6.0
Current smoker, n (%)	34 (14%)
Work Status, n (%)	
Working	59 (24%)
Employed but not working	17 (7.0%)
Not employed	14 (5.8%)
Retired	133 (55%)
Other	19 (7.8%)
Duration with Symptoms at enrollment, n (%)	
6 to 12 weeks	3 (1.2%)
3 months to 6 months	8 (3.3%)
6 months to 1 year	22 (9.1%)
1-2 years	56 (23%)
Over 2 years	153 (63%)
Spondylolisthesis Grade, n (%)	
Grade I	175 (72%)
Grade II	65 (27%)
Grade III	3 (1.2%)
Listhetic Segment Involved	
L1-2	1 (0.4%)
L2-3	1 (0.4%)
L3-4	48 (20%)
L4-5	181 (74%)
L5-S1	4 (1.6%)
L3-4-5	7 (2.9%)
L4-5-S1	1 (0.4%)
Multilevel Spondylolisthesis	
L3-L5	5 (2.1%)
L2-S1	1 (0.4%)
Principal Complaint, n (%)+	
Back Pain	7 (2.9%)
Neurogenic Claudication	197 (81%)
Radiculopathy	39 (16%)
Comorbidities	
None	4 (1.7%)
<3 comorbidities	138 (57%)
>3 comorbidities	99 (41%)
ASA Score	
1	10 (4.1%)
2	127 (52%)
3	103 (42%)
4	3 (1.2%)
Previous Surgery*, n (%)	13 (5.3%)

Previous Surgery at Level of DLS	4 (1.1%)

SD = standard deviation
*, 1 other, 3 Decompression + Fusion; 9 Decompression only
+ all patients had some degree of neurogenic claudication and/or radiculopathy

Baseline patient radiographic (Table 2) and functional outcome measures (Table 3) were stratified by surgery type (Decompression: D; Posterolateral Fusion: PLF; Interbody Fusion: IF). There were no statistically significant baseline differences among all included patient's preoperative radiographic (sagittal spinal alignment) parameters with respect to SS, PT, LL, PI, nor PI-LL. Of note, there was a statistically significant baseline difference among the included cohort with respect to preoperative SVA, with a significantly higher preoperative SVA in the PLF group.

Table 2: Average preoperative radiographic measures

	Decompression N=65	Posterolateral Fusion N=30	Interbody Fusion n=146	P Value
Sacral Slope (^{0}) (+/-SD)	34.4 (8.8)	32.0 (10.0)	33.3 (8.3)	0.448
Pelvic Tilt (^{0}) (+/-SD)	24.6 (8.5)	26.0 (8.6)	23.5 (8.2)	0.268
Pelvic Incidence (^{0}) (+/-SD)	59.3 (10.6)	56.4 (11.2)	58.7 (12.3)	0.175
Lumbar Lordosis (^{0}) (+/-SD)	47.0 (10.1)	43.8 (16.9)	45.0 (13.9)	0.469
PI-LL (^{0}) (+/-SD)	12.1 (12.3)	15.1 (14.2)	11.6 (14.0)	0.454
Sagittal Vertical Axis (mm) (+/-SD)	33.8 (46.1)	50.8 (54.0)	24.4 (33.2)	**0.006**

Baseline patient reported outcome measures among all patients revealed significant preoperative impairment (table 3). The average baseline ODI among patients was 45.3 indicating severe disability, making activities of daily living difficult. Similarly, the average preoperative NRS leg pain and back pain scores were 7.1 and 7.5 respectively, reflecting moderately severe daily leg and back pain levels. There was a statistically significant difference in preoperative reported back pain among patients undergoing decompression versus those patients undergoing IF, which was maintained following a Bonferroni multiple-comparison post hoc analysis.

Table 3: Average preoperative patient reported outcome measures

	Decompression N=65	Posterolateral Fusion N=30	Interbody Fusion n=146	P Value
NRS Pain Scale Back (+/-SD)	6.3 (2.7)	7.0 (2.6)	7.5 (1.8)	**0.002**
NRS Pain Scale Leg (+/-SD)	7.1 (2.3)	7.6 (2.0)	7.6 (1.9)	0.262
ODI (+/-SD)	41.6 (15.7)	46.5 (13.9)	46.7 (14.0)	0.056

Surgical Details

Among all patients undergoing DLS surgery in this cohort, 178 (83%) underwent instrumented fusion, with the bulk of patients receiving an interbody cage at the index level of surgery, 148 (61%) (Table 4). One third of patients had surgery via minimally invasive techniques, with the remainder undergoing open posterior-based surgery.

Table 4: Overview of surgery details

Parameter	**Value, n=241**
Type of Surgery, n (%)	
Decompression	65 (25%)
Interbody Fusion	146 (61%)
Posterolateral Fusion	30 (12%)
Minimally Invasive Approach, n (%)	78 (32%)
Operating Time, minutes	
Mean ± SD	157 ± 66
Median (min – max)	150 (37 – 403)
Estimated blood loss, ml	
Mean ± SD	339 ± 337
Median (min – max)	300 (5 – 3500)
Length of Stay, days	
Mean ± SD	4 ± 3
Median (min – max)	3 (0-31)
Stepdown Unit Admission, n (%)	8 (3.3%)
Intraoperative Adverse Event, n (%)	25 (6.9%)
Perioperative Adverse Event, n (%)	51 (21%)
Postoperative Adverse Event 6-18 weeks, n (%)	56 (15.4%)

Postoperative Adverse Event >18 weeks, n (%)	35 (9.6%)

There were statistically significant differences for patients undergoing D vs. PLF and IF, with marked reductions in operating time of 94.9 and 89.1 minutes respectively, p<0.001 (Table 5). Similarly, there was a statistically significant difference in length of stay and estimated blood loss between D and PLF and IF.

Table 5: Surgical details by type of surgery

	Decompression N=65	Posterolateral Fusion N=30	Interbody Fusion n=146	P Value
Operating Time (minutes)	91.1 (34.9)	186 (68.2)	180.2 (55.8)	**<0.001**
Length of Stay (days)	1.4 (1.9)	4.5 (2.3)	3.9 (2.2)	**<0.001**
EBL (mL)	63 (76.8)	469.6 (334.5)	405.4 (299.0)	**<0.001**

Postoperative radiographic and functional outcomes

Among all patients regardless of surgery type, the measured preoperative to postoperative radiographic change did not meet statistical significance except for preoperative to postoperative SVA and LL change, which demonstrated an average improvement (reduction in SVA, increase in LL) overall of 8.8 (2.7,14.9; p=0.005) mm and 2.6^0 (4.7^0,0.5^0; p=0.015) respectively. However, there was a statistically significant improvement in all functional outcomes from pre- to postoperative for ODI, NRS back and leg pain scales, p <0.001. Importantly, the ODI improved an average of 20.4 postoperatively, meeting the minimum clinically important difference (MCID) of 12.8 points.[35] Likewise the MCID was met for overall postoperative NRS back (MCID 1.2 points) and leg (MCID 1.6 points) pain average improvements, with average improvements of 4.2 and 4.2 respectively.[35] The average postoperative radiographic parameters remained similar across patients regardless of surgery type with respect to amount of improvement. All surgery types showed postoperative average increases in SS, LL and corresponding decreases in PT and SVA. Except for SVA, which had the only residual statically significant differences between surgery type cohorts postoperatively (Table 6).

Table 6: Average postoperative radiographic measures

	Decompression N=65	Posterolateral Fusion N=30	Interbody Fusion n=146	P Value
Sacral Slope (^{0}) (+/-SD)	35.7 (8.9)	34.4 (11.0)	34.7 (8.2)	0.717
Pelvic Tilt (^{0}) (+/-SD)	22.8 (8.2)	24.8 (8.6)	23.2 (8.2)	0.557
Pelvic Incidence (^{0}) (+/-SD)	57.4 (10.7)	58.6 (13.6)	56.1 (11.39)	0.521
Lumbar Lordosis (^{0}) (+/-SD)	48.5 (11.8)	47.0 (14.3)	49.1 (12.5)	0.698
Sagittal Vertical Axis (mm) (+/-SD)	24.8 (34.2)	33.2 (31.4)	17.7 (26.8)	**0.038**
Change in PI-LL (^{0}) (+/-SD)	-3.6 (11.9)	-2.9 (8.7)	-4.9 (12.6)	0.613

**a negative change represents a reduction in the PI-LL value (a return to more normal sagittal balance)*

Marked postoperative improvement was similarly seen across all surgery cohorts as outlined above (Table 7). Only NRS leg pain scale showed a statistically significant between group difference. However, on post hoc analysis with a Bonferroni correction, no statistically significant difference existed between groups.

Table 7: Average postoperative patient reported outcome measures

	Decompression N=65	Posterolateral Fusion N=30	Interbody Fusion n=146	P Value
NRS Pain Scale Back	2.6 (2.9)	3.2 (2.2)	3.6 (2.6)	0.058
NRS Pain Scale Leg	3.1 (3.1)	1.6 (2.1)	3.1 (3.1)	**0.043**
ODI	23.0 (19.6)	21.9 (17.3)	26.3 (18.4)	0.321

Postoperative radiographic and functional outcome correlations

Analysis of correlation between patient-rated outcome measures and postoperative radiographic measures at one-year postoperatively was performed (Table 8). With an increase in the PI-LL postoperatively, there was a statistically significant increase in postoperative ODI (0.134; $p<0.05$), worsened NRS back pain ($r=0.189$; $P=0.001$) and worsened NRS leg pain ($r=0.143$; $p<0.001$) scores. Overall, no correlation with postoperative SVA and patient-rated outcome measures was observed. However, there was a correlation with the change in SVA ; represented by an increase in the postoperative to preoperative SVA value correlating with significantly higher ODI ($r=0.202$; $p<0.001$) and NRS leg pain scores ($r=0.186$; $P<0.05$).

Table 8: Correlation between patient-rated outcome measures and radiographic measures at one-year postoperatively.

	ODI		NRS Back Pain		NRS Leg Pain	
	n	r	n	r	n	r
SS (^{0})	241	**-0.135***	241	-0.124	239	-0.109
PT (^{0})	239	**0.162***	239	**0.230****	237	**0.164***
PI (^{0})	239	0.011	239	0.060	237	0.037
SVA (mm)	201	0.037	201	0.058	199	0.063
LL (^{0})	234	-0.111	234	**-0.138***	232	-0.118
PI-LL (^{0})	232	**0.134***	232	**0.189****	230	**0.143***
Δ SVA (mm)	182	**0.202****	182	0.145	180	**0.186***

*SS= sacral slope; PT=pelvic tilt; PI=pelvic incidence; SVA=sagittal vertical axis; LL=lumbar lordosis; NRS = numerical rating scale, range 0 to 10, with higher scores indicating worse pain ODI= Oswestry Disability Index, range 0 to 100, with higher scores indicating worse disability and pain. Values are Pearson's correlation coefficients (r) except SVA, T1SPI, and PI, which are Spearman's rho coefficients (ρ). * = p < 0.05; **, P<0.001*

When a multiple linear regression was performed adjusted for baseline patient age, BMI, gender and preoperative presence of depression, worsening of PI-LL was associated with a higher one-year postoperative ODI score R^2 0.179 (95% CI 0.080, 0.415; $p=0.004$), back pain R^2 0.154 (95% CI 0.021, 0.070; $p<0.001$) and leg pain R^2 0.059 (95% CI 0.008, 0.066; $p=0.014$) score (Table 9). Likewise, reduction of LL was associated with a higher ODI score R^2 0.168 (-0.387, -0.024; $p=0.027$) and back pain score R^2 0.135 (95% CI -0.064, -0.010; $p=0.007$). A change to SVA, was found to be significantly associated with higher rated ODI, NRS leg and back pain scores. Subgroup analysis of decompression alone versus instrumented fusion groups only did not reveal statistically significant differences across groups with respect to functional outcomes and postoperative radiographic parameters on the multiple linear regression.

Table 9: Summary of Multiple Linear Regression Outcomes at 12 months and radiographic parameters at 12 months

Leg Pain	R^2	R^2 Adj.	Unstandard. Coefficient β ± Std. error	95% CI of β	P-value
Δ SVA	0.063	0.035	0.015 ± 0.007	0.002, 0.028	0.024
LL	0.052	0.031	-0.034 ± 0.016	-0.065, -0.002	0.038
PI-LL	0.059	0.037	0.037 ± 0.015	0.008, 0.066	0.014
SVA	0.058	0.033	0.013 ± 0.007	-0.001, 0.028	0.062

Back Pain	R^2	R^2 Adj.	Unstand. Coeff. β ± Std. error	95% CI of β	P-value
Δ SVA	0.134	0.109	0.012 ± 0.006	0.001, 0.023	0.037
LL	0.135	0.116	-0.037 ± 0.014	-0.064, -0.010	0.007
PI-LL	0.154	0.135	0.046 ±0.013	0.021, 0.070	<0.001
SVA	0.131	0.108	0.011 ± 0.006	-0.002, 0.023	0.088

ODI	R^2	R^2 Adj.	Unstand. Coeff. β ± Std. error	95% CI of β	P-value
Δ SVA	0.218	0.195	0.086 ± 0.037	0.013, 0.159	0.022
LL	0.168	0.150	-0.205 ± 0.092	-0.387, -0.024	0.027
PI-LL	0.179	0.160	0.247 ± 0.085	0.080, 0.415	0.004
SVA	0.207	0.186	0.074 ± 0.041	-0.007, 0.155	0.073

Adjusted for Age, BMI, Sex, PHQ9

Discussion:

In our large, multi-centre prospectively followed DLS cohort study, we have further demonstrated that patients achieve clinically meaningful improvement in their functional outcomes postoperatively, which is consistent with previous reported outcomes of DLS surgery.[5; 6; 30; 36; 37] Regardless of surgery type, patients showed statistically significant and clinically meaningful functional improvement which met the MCID for ODI as well as NRS leg and back pain; consistent with the findings of Ulrich et al. and Miyauchi et al., we observed no significant difference in decompression versus instrumented fusion for DLS surgery functional outcomes postoperatively, also consistent with previous findings.[30; 38; 39] Importantly, when adjusted for potential confounding variables of age, BMI, sex and preoperative depression presence, post-operative worsening of key spinopelvic (LL and PI-LL) and sagittal balance (Δ SVA) parameters was correlated to worsened patient rated outcomes.

Much spinal deformity and recent DLS sagittal spinal balance literature has focused on functional outcomes of patients within and outside of recognized accepted normal or balanced spinal parameters.[27; 40; 41] Widely accepted spinal deformity parameters describe a PI-LL mismatch of less than 10 degrees and an SVA under 5cm representing acceptable sagittal spinal balance.[27; 42] Concurrently, these accepted sagittal alignment parameters have largely been adopted by the DLS literature examining sagittal balance.[27] Gille et al. have even proposed a classification of differing types of DLS patients based on their sagittal alignment parameters utilizing the accepted balanced and unbalanced parameters of PI-LL mismatch of greater or less than 10 degrees as an extension from the adult spinal deformity literature.[27; 42; 43; 44]

It is known that a reduction in LL in the absence of a corresponding pelvic accommodation leads to a worsened sagittal spinal balance and increased SVA. Radovanovic et al. report on a cohort of DLS patients with worsened functional outcome scores including higher ODI and back pain scores three years postoperatively when the SVA was more than 5cm postoperatively. In our analysis, worsened functional outcome scores were only related to an increase in SVA from preoperative baseline among patients. This likely reflects the fact that most patients with DLS are within a normal range for SVA preoperatively and that it is imperative with surgery in this population to cause no increase of SVA postoperatively. Unique to our analysis is a deviation from analysis of patients within previously extrapolated standards for sagittal balance and imbalance in the deformity literature with a specific focus on individual patient alignment change characteristics with DLS surgery. Through our analysis, we have demonstrated that patients who experience poorer functional outcomes with DLS surgery have worsening of their LL, PI-LL and/or SVA postoperatively. Importantly, the worsening of these radiographic parameters does not necessarily have to include a patient deviating from accepted normal values for sagittal balance but rather the mere change to a patient-specific worsening of sagittal alignment.

The results of our linear regression analysis demonstrated a small but statistically significant effect size showing that patients report worsened functional outcomes postoperatively when a reduction in LL occurs. These findings are corroborated by a previous small cohort study by Liow et al.[45] In their investigation, conventionally sagittally balanced DLS patients experience reduced postoperative back pain, with fusion surgery when they had higher preoperative SS and a corresponding maintained or increased LL postoperatively.[45] Given the clinical equipoise that exists within the DLS literature surrounding most effective intervention, it is important to understand the appropriate indication for more invasive and expensive surgical intervention. Ohyama et al. have suggested that patients with sagittal imbalance that demonstrate a preoperative increase in LL when supine compared to standing have a greater chance of achieving an increased postoperative LL after interbody fusion. While our analysis did not assess standing and supine radiographic differences, recognizing patients who are at risk for a reduction in LL with DLS surgery is important to prevent poorer postoperative functional outcomes.[46]

Short-segment transforaminal lumbar interbody fusion (TLIF) has been shown to have worsened postoperative functional outcomes for both back pain and ODI in patients with a postoperative PI-LL mismatch >11 degrees.[47] While this finding is an intuitive step from the adult spinal deformity literature, our findings of any worsening of PI-LL and poorer ODI, leg and back pain scores are unique. It appears from our cohort that patients with DLS have a unique sagittal balance that typically responds exceptionally well to surgery. However, in our investigation, among those patients who undergo surgery for DLS and have poorer postoperative functional outcomes, it is not the movement of a patient to a position of PI-LL mismatch but rather the change to an individual's baseline PI-LL that portends a worsened postoperative outcome.

Limitations

The results of our investigation are limited to the quality of our large, multi-centre database. Strong working relationships and full-time research assistants to care for and curate the database minimizes errors of entry in addition to frequent reviews for logic within the database. There were two important baseline characteristics that were unable to be explained between the different patient groups with a higher average preoperative SVA in the PLF group and significantly lower preoperative back pain reported by the D group. It was not possible to determine the cause of these discrepancies but this could be related to surgeon bias. While we examined a number of radiographic parameters we did not investigate reduction of anterolisthesis in our cohort and thus were unable to show if reduction of listhesis was significant as this was not measured. Though conflicting results have shown this may[48] or may not[49] have significant functional improvement outcomes in the DLS population. The primary goal of surgery for all patients in this cohort was neurologic decompression not deformity correction. However, with a common surgical goal among all contributing surgeons and standardized surgical techniques, bed frames and hardware utilized, some degree of variance has been removed. As our database grows, further longitudinal follow-up will allow re-examination of our data at longer follow-up intervals to assess for the durability of our radiographic and functional findings.

Conclusion:

Preoperative emphasis on regional and global spinal alignment parameters must be considered in order to optimize surgical procedure indication and functional outcome in lumbar degenerative spondylolisthesis treatment. Recognizing and avoiding increasing a patient's sagittal vertical axis and decreasing lumbar lordosis is imperative to achieving reproducible, positive surgical outcomes in degenerative lumbar spondylolisthesis.

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Chapter 5: Concluding Statements

The work of this thesis project has demonstrated that there is an ever-increasing emphasis in the degenerative spine literature on the role of sagittal alignment and functional outcomes in patients with degenerative lumbar spondylolisthesis (DLS). It has been highlighted that largely, including in our own included Canadian patient cohort, surgeons are selecting the most invasive and highest cost and risk procedures for these patients. However, it has been demonstrated that a similar proportion of patients improve or worsen in their sagittal spinal balance with decompression alone or with fusion based procedures for DLS. Furthermore, it has been shown that the widely held and accepted measurements for a balanced spine extrapolated from the adult spinal deformity literature is not necessarily applicable to DLS patients. That is, in patients who remain within conventionally held sagitally balanced parameters, if they experience a reduction in their lumbar lordosis or a change in their sagittal vertical axis or a worsening in their pelvic incidence, lumbar lordosis mismatch, they will experience inferior functional outcomes postoperatively with surgery for their DLS.

The work of this thesis will require further longitudinal follow-up through the Canadian Spine Outcomes Research Network. However, this thesis has laid the ground work for an important and critical reflection upon current surgical practice of DLS patients and will lead to incorporation in clinical decision-making guidelines and health care system cost savings for adult spine surgeons.