Treatment for Degenerative Lumbar Spondylolisthesis: Current Concepts and New Evidence

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Published online: 9 October 2017
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Abstract

Purpose of Review Current guidelines for the optimal treatment degenerative spondylolisthesis are weak and based on limited high-quality evidence.

Recent Findings There is some moderate evidence that decompression alone may be a feasible treatment with lower surgical morbidity and similar outcomes to fusion when performed in a select population with a low-grade slip. Similarly, addition of interbody fusion may be best suited to a subset of patients with high-grade degenerative spondylolisthesis, although this remains controversial. Minimally invasive techniques are increasingly being utilized for both decompression and fusion surgeries with more and more studies showing similar outcomes and lower postoperative morbidity for patients. This will likely be an area of continued intense research. Finally, the role of spondylolisthesis reduction will likely be determined as further investigation into optimal sagittal balance and spinopelvic parameters is conducted. Future identification of ideal thresholds for sagittal vertical axis and slip angle that will prevent progression and reoperation will play an important role in surgical treatment planning.

Summary Current evidence supports surgical treatment of degenerative spondylolisthesis. While posterolateral spinal fusion remains the treatment of choice, the use of interbodies

and decompressions without fusion may be efficacious in certain populations. However, additional high-quality evidence is needed, especially in newer areas of practice such as minimally invasive techniques and sagittal balance correction.

Keywords Degenerative spondylolisthesis · Posterolateral spinal fusions · Spinal decompression · Interbody fusion · Sagittal balance · Spino-pelvic parameters · Minimally invasive techniques · Spondylolisthesis reduction

Introduction

Degenerative spondylolisthesis (DS) is an acquired anterior vertebral displacement without a disruption of the pars interarticularis, associated with the degenerative changes of aging, such as intervertebral disc degeneration, ligamentous hypertrophy or buckling, and osteophyte proliferation [1, 2]. Treatment of DS has long been a topic of debate, as multiple modalities are currently utilized. For example, in a recent analysis, 95,647 Medicare patients with a diagnosis of lumbar DS, 40% were treated with corticosteroid injections, 37% were treated with physical therapy, and only 22% were treated surgically [3]. When considering surgical treatment variations with data from the Spine Patient Outcomes Research Trial (SPORT), 7% were treated with decompression alone, 21% were treated with non-instrumented fusion, and 71% were treated with fusion surgery [4]. The reoperation rate is also high at 22% at 8 years after initial surgery. Nevertheless, surgical treatment of DS with symptomatic spinal stenosis has been shown to be cost-effective with gain of 0.43 quality adjusted life years (QALYs), or greater for patients with multilevel disease [4].

Treatment of DS remains a heavily investigated topic, with numerous prospective and retrospective studies being carried

This article is part of the Topical Collection on *Treatment of Lumbar Degenerative Pathology*

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out over the last 20 years, including multiple randomized controlled trials [5•, 6•, 7•, 8•, 9•, 10•]. As a result, the North American Spine Society (NASS) recently released an evidence-based clinical guideline on diagnosis and treatment of DS [1]. The current review describes evidence supporting current guidelines in the context of additional newer research.

Non-operative Management

Non-operative modalities, including activity restriction, non-steroidal anti-inflammatory drugs (NSAIDs), and physical therapy, remain the first-line therapy for patients with DS. In one study of 145 patients non-operatively managed, 76% of patients without neurological deficits remained without asymptomatic at 10 years [11]. However, 83% of patient that did have neurological deficits experienced progression of symptoms over 10 years. Progression of spondylolisthesis was not correlated with progression of symptoms.

The well-known SPORT study also included a non-surgical cohort. These non-operatively managed patients with DS had better outcomes if they had a grade I slip (versus grade II) or had a hypermobile slip (versus a stable slip) [12]. Therefore, in patients with mobile or low-grade spondylolisthesis, without neurological deficits, a trial of non-operative therapy is certainly indicated and generally associated with good clinical outcomes at 1 year.

Surgical Decompression

NASS guidelines state that surgical decompression may be considered for patients with low-grade DS and symptomatic spinal stenosis that is refractory to conservative therapies [1]. In addition, for single-level DS that is symptomatic, low-grade, with only central stenosis (no foraminal stenosis), decompression provides equivalent outcomes compared to decompression with fusion.

This is based on existing evidence including a retrospective study of 18 patients undergoing decompressive laminoplasty for grade I DS after a 3-month period of conservative therapy [13]. Patients were compared with similar cohorts of 16 patients undergoing non-operative treatment and 19 patients undergoing laminectomy and posterolateral instrumented fusion. Clinical outcomes improved with both surgical options but there was no significant difference between groups. However, in the non-operatively managed group, there was no clinical improvement in outcomes.

A second retrospective study compared 55 patients with grade I DS that underwent non-operative treatment, laminectomy, or laminectomy and posterolateral fusion [13]. There was no significant improvement in symptoms with non-operative treatment. Symptoms did significantly improve in

both surgical cohorts. However, there was no significant difference in clinical improvement between the two groups. The degree of slip was seen to progress in both laminectomy and non-operative groups; however, this was not specifically associated with patient outcomes.

A more recent prospective study followed 84 patients undergoing bilateral surgical decompression with a unilateral approach for grade I DS and neurogenic claudication [14]. Patients were initially treated with 6 months of conservative therapy. After surgery, both the Oswestry Disability Index (ODI) and Neurogenic Claudication Outcomes Score (NCOS) improved over 24-month follow-up. However, this cohort was never compared to a control population. The authors still concluded that surgical decompression is a safe and effective alternative to conservative management.

Another prospective comparative study enrolled 17 consecutive patients to undergo decompression with fusion versus 33 patients to undergo microscopic decompression [15]. Overall, there was more improvement in Japanese Orthopaedic Association (JOA) Back Pain Evaluation Questionnaire with fusion. However, for patients with less than 20% slipping, outcomes were equivalent. In addition, decompression was associated with lower estimated blood loss (EBL) and hospital length of stay (LOS). Therefore, authors concluded that with less than 20% slippage, decompression is indicated due to lower surgical morbidity and invasiveness.

In addition, a number of newer studies also demonstrate evidence supporting the use of spinal decompression over spinal fusion procedures in certain patient populations. One recent randomized controlled trial of decompression versus fusion for spinal stenosis included a cohort of patients with DS [5•]. A total of 133 patients with DS and spinal stenosis were randomized to either decompression or fusion surgery. At 2-year follow-up, there was no significant difference in ODI or 6-min walk test. In addition, operative time and hospital LOS were lower for decompression patients. In the decompression population, 21% of patients required additional spinal surgery within 6.5 years, compared to 22% of fusion patients. A total of 14 patients did not receive the assigned treatment and were not included in this per protocol analysis.

A similar more recent retrospective study of 60 patients undergoing decompression for DS, compared to 80 patients undergoing decompression and fusion, found that clinical improvements were similar between populations [16]. In decompression patients, greater than 5-mm translation was associated with slip progression, but this did not cause increased instability in patients.

In cost-effectiveness analysis, decompression has also been shown to have significant advantages over fusion surgery. One cost-utility analysis compared 57 patients undergoing decompression and 58 patients undergoing decompression and fusion, all for symptomatic DS [17]. It was found that

there was a slight advantage in clinical outcomes for fusion patients. However, fusion surgery was associated with an additional \$185,878 per QALY compared to decompression surgery. A more recent cost-utility analysis compared 25 spinal decompression patients with 25 patients with spinal decompression and posterolateral fusion and 25 patients with posterolateral fusion with additional interbody fusion [18]. Decompression had the lowest cost-effectiveness by a large margin (\$57,000 compared to \$117,000 and \$110,000 per QALY for decompression compared to fusion groups).

Finally, three recent non-comparative cohort studies have also demonstrated safety and efficacy of spinal decompression in populations with low-grade spondylolisthesis with spinal stenosis [19–21]. In these studies at long-term follow-up, patients had improvements in ODI, EuroQol Five Dimensions (EQ-5D), or visual analogue scale (VAS) for back and leg pain scores. Additionally, the rate of revision surgery after decompression varied from 11 to 12.5% in the three studies.

Overall, recent evidence including one high-profile randomized controlled trial supports the current NASS recommendation that spinal decompression is a good option for certain patients with DS. After a trial of conservative management, patients with low-grade spondylolisthesis and symptomatic central stenosis have been shown to have good improvement in their symptoms. Multiple series have demonstrated a progression rate of about 10%, necessitating eventual fusion surgery. However, with the significantly lower cost-benefit ratio, spinal decompression may be considered prior to fusion in certain patients.

Posterior Spinal Fusion

Current NASS guidelines recommend that surgical decompression with fusion is the suggested treatment of patients with symptomatic spinal stenosis and degenerative lumbar spondylolisthesis with improved clinical outcomes compared with decompression alone and non-operative management [1]. This recommendation is based on multiple prior studies comparing outcomes after fusion with decompression and non-operative treatment.

Likely, the most well-known study establishing the benefit of spinal surgery for DS, including spinal fusion, compared to non-operative management is the SPORT study. In the analysis of patients with DS, 204 patients were randomized to surgical treatment (decompression with or without fusion) or non-operative treatment [6•]. In this 2-year cohort, there was a high degree of crossover between groups (~40% crossover from both groups), resulting in no significant difference between cohorts in the intention-to-treat analysis. However, in the as-treated analysis, surgical treatment showed clinical benefits in pain and functioning at 3 months, 1 year, and 2 years. While the SPORT study considered both spinal

decompression and spinal fusion together in the analysis, the vast majority of patients treated operatively (94%) were treated with spinal fusion.

In the follow-up study looking at long-term outcomes of SPORT patients, improvements in pain, physical function, and ODI were maintained though 4 years postoperatively [22]. An additional retrospective post hoc analysis found that patients with DS and single-level spinal stenosis had better outcomes postoperatively compared to patients with DS and multilevel stenosis [23]. Finally, a post hoc analysis of obese patients in the SPORT study found that patients with obesity who are non-operatively managed had significant deterioration in pain level and function at long-term follow-up [24]. Obese patients that were treated surgically had clinical improvement, but also had higher rates of reoperation compared to non-obese patients.

While the benefits of spinal fusion surgery over non-operative treatment were largely established by the SPORT results, additional research has further demonstrated improved outcomes specifically with fusion surgery for DS compared with surgical decompression alone. Mardjetko et al. conducted a meta-analysis of outcomes after spinal decompression compared to spinal fusion for DS [25]. Nine case series including 239 fusion patients were compared to 11 case series including 216 decompression patients. Overall, patient satisfaction was significantly better after fusion surgery rather than decompression. However, the grade of DS or the severity of preoperative symptoms was not compared.

Martin et al. conducted a systematic review of previous studies comparing posterolateral spinal fusion for DS with decompression [26]. It was found that in the eight studies included, satisfactory clinical outcomes were more likely with spinal fusion than with decompression alone. In an additional six studies comparing instrumented and uninstrumented fusion, it was found that there was not a significant difference in clinical outcomes; however, the likelihood of achieving a solid fusion was greater with instrumented fusion.

One older prospective cohort study compared 25 patients with DS and spinal stenosis that underwent spinal decompression surgery with 25 similar patients that underwent spinal fusion surgery. Patients were followed for a mean follow-up period of 3 years. In the fusion group, 44% of patients report “excellent” improvement in back and leg pain, while in the decompression group, only 8% reported excellent outcomes [27].

More recently, a randomized controlled trial of 66 patients was conducted comparing laminectomy with spinal fusion surgery for treatment of symptomatic DS [7•]. There was significantly more improvement in Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) scores with spinal fusion surgery at 2, 3, and 4 years of follow-up compared to decompression alone. However, there was no difference in ODI between the two cohorts. Additionally, the rate of

reoperation was 14% in the fusion cohort, compared to 34% in the laminectomy cohort.

Another large study from the Norwegian Registry for Spine Surgery retrospectively compared 260 patients undergoing surgical decompression versus 260 patient undergoing decompression and spinal fusion, for DS with spinal stenosis [28]. They found no difference in ODI at 12 months between the groups. However, the fusion group did experience a significant greater improvement in back and leg pain. In addition, 74% of fusion patients had a clinically significant improvement in back pain versus 63% of patient undergoing decompression.

A smaller retrospective study compared 20 patients that underwent unilateral laminectomy and bilateral decompression with 25 patients who underwent spinal decompression and fusion [29]. Minimum follow-up was 3 years and the primary outcome measures were numeric rating scale (NRS) for back and leg pain, SF-36, and ODI. While functional outcomes were similar between groups, a significantly greater decrease in back pain was seen in the fusion group. Another previous smaller prospective study followed 9 patients treated with laminectomy, 10 patients treated with laminectomy and uninstrumented fusion, and 24 patients treated with laminectomy and instrumented fusion [30]. All patients had DS with symptomatic spinal stenosis. Progression of spondylolisthesis was noted in 44% of patients treated with laminectomy and in 70% of patients treated with uninstrumented fusion, but only in 4% of patients treated with instrumented fusions.

In conclusion, the existing body of evidence supports spinal fusion surgery for patients with symptomatic DS that have failed a course of conservative treatment. Multiple studies have demonstrated improved long-term outcomes of fusions compared with decompression surgery alone, however, at the cost of higher surgical morbidity and extended hospital LOS.

Interbody Fusion

The use of interbody fusion (IBF) in addition to standard posterolateral spinal fusion for treatment of DS continues to be a widely debated topic. The additional benefits of a potentially more stable fusion are curtailed by increased surgical morbidity and potentially limited improvement in clinical outcomes compared to posterior fusion. Current NASS guidelines state that there is insufficient evidence to recommend for or against interbody fusion for DS. This is based on the two preexisting studies comparing the two procedures in small cohorts.

Rousseau et al. conducted a retrospective review of 16 patients that underwent posterolateral fusion (PLF) and 8 patients that underwent posterior lumbar interbody fusion (PLIF) [31]. All patients had a successful fusion postoperatively. However, PLIF patients had greater improvement in

Beaujon scoring system outcome measure. Of note, only 2 patients had completed 2-year follow-up in this study.

Ha et al. retrospectively compared 21 patients with DS at L4-L5 that underwent PLF with 19 patients that underwent PLIF [32]. Patients were additionally divided based on whether or not they had a stable slip (defined as less than 4-mm translation or 10° angulation). In the stable group, there was no difference in clinical outcomes between PLF and PLIF groups, although slip angle and disc height had better improvement with PLIF. However, in the unstable group, both radiological and clinical outcomes (ODI and VAS pain) had greater improvement in the PLIF group.

While these two studies together do not present a significant body of evidence, a significant amount of newer recent research has been conducted on the topic of interbody fusion for DS. One multicenter randomized controlled trial compared 30 patients undergoing PLF with 30 patients undergoing transforaminal lumbar interbody fusion (TLIF) [8•]. All patients had one-level DS and symptomatic spinal stenosis. At 2-year follow-up, there was no significant difference in pain, disability, or radiological segmental lordosis. However, fusion rate was greater in the TLIF cohort.

Another retrospective cohort study compared 65 patients undergoing PLF and 80 patients that underwent TLIF [33]. At 24-month follow-up, VAS back pain, ODI, global outcome, and fusion rate were greater in the TLIF cohort. However, operative time and EBL were greater in the PLF population. Two additional smaller recent retrospective studies also demonstrate no difference in clinical outcomes at long-term follow-up between PLF and either TLIF or PLIF [34, 35].

Two recent cost-effectiveness analyses have also compared PLF and IBF for treatment of DS. Kim et al. compared costs and outcomes for 37 patients treated with PLF and 62 patients treated with TLIF [36]. The investigators found no significant difference in patient-reported outcomes, complications, reoperation rate, gain in QALYs or cost per QALY. Additionally, Carreon et al. retrospectively compared 101 PLF patients with 101 TLIF patients [37]. While the authors demonstrated greater improvement in ODI and Short-Form-6D (SF-6D) at 12 months in the TLIF population, it was at the high cost of an additional \$4830. This was determined to be prohibitive based on cost thresholds of \$100,000 per QALY and the 2014 US per capita gross domestic product of \$53,042.

McAnany et al. conducted a meta-analysis of five prior studies, including 383 patients treated with a PLF and 268 treated with IBF [38]. It was concluded that there was no difference in rates of fusion, operative time, EBL, and ODI, SF-36, and VAS outcome measures between procedures. Similarly, Baker et al. completed a more recent systemic review including 13 studies, mostly graded as level III evidence [18, 32, 39–49]. The authors concluded that there was not sufficient evidence to recommend for or against interbody fusion. Two of the included studies were graded as level II evidence. One, a retrospective

subgroup analysis of 380 patients from the SPORT study with 4-year follow-up concluded that there was no difference in clinical outcomes over 4 years between PLF and IBF [40]. The second was a prospective cohort study of 46 patients comparing PLF with anterior lumbar interbody fusion (ALIF), concluding that low back pain had greater improvement after ALIF; however, at a cost of greater hospital stay and bed rest [47]. Overall, while there have been several recent studies published analyzing outcomes for IBF to treat DS, there remains no clear evidence that outcomes are indeed improved with addition of IBF to spinal fusion procedures.

The minimally invasive lateral interbody fusion (XLIF) is an alternative technique for IBF that utilizes a lateral transposas approach. It is being increasingly used for IBF as it avoids disruption of posterior structures and the hazards of thecal sac and nerve root retraction. It also allows for a larger interbody cage to be inserted. A recent multicenter prospective randomized trial of 55 patients compared the XLIF and the TLIF procedures for treatment of symptomatic DS [9, 10]. Both populations showed similar improvements in back pain, leg pain, and ODI at 2-year follow-up. Additionally, XLIF had lower rates of cage subsidence and improved indirect decompression of the neural foramina while TLIF patients had improved central canal decompression. There was also no significant difference in fusion rates. Based on these findings, further investigation of the XLIF procedure for treatment of DS may be warranted, especially in DS patients with primarily lateral foraminal stenosis.

Minimally Invasive Techniques

Minimally invasive techniques (MIS) for spine surgery are increasingly being utilized as ways to reduce surgical morbidity and maintain posterior midline structures such as the multifidus muscle, which play a role in spine stability. As this new field grows, investigation of MIS techniques for treatment of DS has also been increasingly studied. The most current NASS guidelines state that there is conflicting evidence regarding whether MIS techniques or traditional spinal fusion leads to better outcomes.

This report was largely based on four prior studies.

Harris et al. compared 21 patients undergoing standard PLF using a midline approach with 30 patients undergoing fusion with a mini-open technique, all for treatment of symptomatic DS. They demonstrated no significant difference in improvements in ODI or VAS pain score between groups or any differences in operative time, EBL, or LOS [50]. Kotani et al. conducted a prospective cohort study of 80 patients with DS and spinal stenosis. Forty-three patients underwent MIS-PLF with a percutaneous pedicle screw system, while 37 underwent open PLF [51]. They demonstrated more rapid improvements in ODI and Roland-Morris Disability Questionnaire (RMQ) at

3, 6, 12, and 24 months, but no difference in JOA score or VAS pain score. Mori et al. compared 26 patients that underwent conventional open PLF for treatment of DS with 27 patients that underwent PLF utilizing a spinous process-splitting (SPS) approach, which preserves the midline attachment of the multifidus [52]. While there was no difference in JOA or RMQ, VAS low back pain scores were significantly lower in the SPS group. They also demonstrated reduced multifidus muscle atrophy on postoperative magnetic resonance imaging at 1-year follow-up. Finally, Adogwa et al. compared 15 patients that underwent open TLIF for grade I DS with 15 patients that underwent MIS-TLIF for grade I DS [53]. There was similar improvement in VAS back pain, VAS leg pain, ODI, and EQ-5D at 2 years between both groups. However, the MIS-TLIF group had significantly reduced hospital LOS, postoperative narcotics usage, and length of time to return to work.

Since the most recent NASS guidelines, Cheng et al. conducted a prospective cohort study comparing 43 patients undergoing bilateral decompression via a unilateral midline-sparing approach (BDUA) and TLIF with 40 patients undergoing laminectomy and open PLIF, all for treatment of symptomatic DS [54]. At 2-year follow-up, there was no difference in fusion rates, but greater improvement in ODI and VAS back pain with the BDUA + TLIF group. BDUA + TLIF was also associated with less EBL, shorter hospital LOS, and few complications. Finally, one recent meta-analysis analyzed 37 studies and 1156 patients, comparing outcomes after laminectomy and MIS-laminectomy for treatment of spinal stenosis associated with DS. It was determined that MIS-laminectomy was associated with improved patient satisfaction, and reduced complications, slip progression, and secondary fusion [55]. In conclusion, there is a growing body of evidence that supports that MIS techniques may have some long-term benefits for patients with DS, compared to more traditional open techniques. However, little high-quality evidence exists, making it difficult to draw definitive conclusions.

Reduction Maneuvers

Current NASS guidelines report that there is insufficient evidence to recommend for or against the use of reduction maneuvers with spinal fusion for DS [1]. This statement is based largely on three previous, non-comparative case series, which demonstrate that spondylolisthesis reduction and spinal fusion together are safe and effective improving symptoms [56–58]. However, these studies do not make a comparison with spinal fusion without reduction (in situ fusion). More recently, a retrospective study compared 41 patients with DS that underwent TLIF surgery with slip reduction with 37 patients with DS that underwent TLIF without reduction [59]. At final follow-up, mean slip angle was 6.3° after reduction compared

with 19.9° with in situ fusion. However, they found that there was no difference in JOA, ODI, or VAS at mean follow-up of over 2 years. While this suggests the benefits of reduction may be limited, further comparative studies are needed.

Sagittal Balance

Sagittal balance and spinopelvic parameters are increasing becoming an important consideration for correction of spinal deformity. A sagittal vertebral axis (SVA) of less than 50 mm has been correlated with optimal health-related quality of life (HRQOL) outcomes in adult spinal deformity patients [60]. Poor sagittal alignment has also been associated with development of DS [61–64] and incorporated into the well-established Spinal Deformity Study Group classification system of lumbosacral spondylolisthesis [65, 66]. One recent retrospective cohort study analyzed postoperative sagittal balance in patients with DS. Eighty-four patients surgically treated for DS were reviewed and 54% of patients had a postoperative SVA > 50 mm [67]. These patients also had significantly worse clinical outcomes as measured by back pain scoring, ODI, and SF-36 physical component summary (PCS) score, over a mean follow-up of 3 years. This association remained significant after controlling for the number of levels fused and the number of levels of spondylolisthesis. Therefore, there is a potential relationship between sagittal balance and postoperative outcomes after surgical treatment of DS. However, the optimal degree of reduction remains to be seen.

There has also been more recent investigation on the specific relationship between use of interbody fusion and restoration of sagittal balance in patients with degenerative spondylolisthesis. One case series of 41 consecutive patients with low-grade degenerative spondylolisthesis treated with single-level ALIF demonstrated a statistically significant improvement in lumbar lordosis of 50.8° to 54.6°.

[68]. Another study compared patient with degenerative spondylolisthesis preoperative SVA of greater than or less than 5 cm. All patients underwent either one- or two-level PLIF. Patients with lower starting SVA had minimal postoperative change in SVA (− 0.3 cm) compared to patients with greater preoperative SVA (− 5.4 cm). Additionally, PLIF at L5-S1, with or without an additional level of fusion, was associated with poor SVA correction (+ 0.1 versus − 2.8 cm) [69]. While interbody fusion appears to have a positive effect on restoration sagittal balance, further investigation in this area is warranted.

Conclusion

Current NASS Evidence-Based Clinical Guidelines for treatment of DS largely support operative treatment of patients

refractory to conservative measures. However, the optimal manner of operative treatment remains poorly established. There is some moderate evidence that decompression alone may be a feasible treatment with lower surgical morbidity and similar outcomes to fusion when performed in a select population with a low-grade slip. Similarly, addition of IBF may be best suited to a subset of patients with higher grade DS, although this remains to be established. MIS techniques are increasingly being utilized for both decompression and fusion surgeries with more and more studies showing equivalent outcomes and lower postoperative morbidity for patients. This will likely be an area of continued intense research. Finally, the role of spondylolisthesis reduction will likely be determined as further investigation into optimal sagittal balance and spinopelvic parameters is conducted. Future identification of ideal thresholds for SVA and slip angle that will prevent progression and reoperation will play an important role in surgical treatment planning.

Compliance with Ethical Standards

Conflict of Interest Andre M. Samuel and Harold G. Moore declare that they have no conflict of interest. Matthew E. Cunningham reports grants from K2M and RTI, outside of the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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