Cervical Spine Arthroplasty: Fact or Fiction: The Absence of Need for Arthroplasty

Suzanne Tharin, MD, PhD, and Edward C. Benzel, MD

In the past decade, we have seen significant enthusiasm for the use of total disk arthroplasty (TDA) for the management of spinal disorders.[1-4] Recently published clinical and laboratory studies have introduced conflicting and confusing information.[5,6] Hence, controversy has prevailed. Surgical clinical trials are fraught with methodological inadequacies and bias issues. These include enrollment issues, researcher-related bias (methodological, enrollment, and outcome assessment-related bias), patient-related bias (winner-loser bias), academic bias, and the methodological difficulties associated with the control of the multiple variables and the aforementioned associated biases.

It is our opinion that arthroplasty does not present an incrementally significant breakthrough for the management of degenerative disk disease. Therefore, we address 4 major domains related to the controversy: biomechanics, the rationale for arthroplasty, early laboratory studies and clinical trials, and finally the ultimate conclusion that the available evidence does not support the notion that TDA improves outcome over that expected with alternative surgical approaches. Each is addressed in the following pages.

BIOMECHANICS

When new technologies are applied, it is imperative to consider the mechanisms of action of the technology at hand. It is also imperative to understand the underlying basic science principles that provide the foundation on which further evidence is developed via both basic science and clinical studies. It is in this vein that the attributes of TDA be assessed and carefully considered.

Attributes of TDA

A multitude of attributes are associated with TDA. The predominant attributes of TDA (replication of anatomy, replication of motion, replication of mechanics, replication of the instantaneous axis of rotation [IAR], incidence of complications, adequacy of revision strategies in failed cases, longevity of the implant, ability of arthroplasty to retard degenerative changes, and symptom relief associated with arthroplasty) are considered individually here.

Replication of Anatomy

A TDA should, relatively speaking, replicate normal disk interspace anatomy. Specifically, it should replicate disk interspace height and angle. In general, most TDAs accomplish this. Therefore, one should conclude that anatomy is, in general, adequately replicated.

Of particular note regarding anatomy is the fact that nonspinal artificial joints (eg, hip and knee artificial joints) are "ball-in-socket" joints. The ball-in-socket joint is conceptually similar to the synovial joint (diarthrodial joint). It varies significantly from the intervertebral joint, which in its youthful state is a gel (nucleus pulposus)-filled and tightly (by the annulus fibrosus) amphiarthrodal joint. First-generation TDAs are, to one degree or another, ball-in-socket joints. The application of such a mechanical strategy (ball-in-socket joint) to a clinical environment in which motion is allowed and constrained by a diarthrodial joint presents some theoretical and real clinical challenges. These challenges are discussed in the pages that follow.

Replication of Motion

A TDA should, by virtue of the intent of the surgeon, replicate normal disk interspace motion both quantitatively and qualitatively. Even with the most advanced first-generation TDA implants, motion is not truly replicated. The center of rotation usually deviates from the norm. And although flexion-extension and lateral bending may quantitatively approach the norm, qualitative parameters such as coupled motions and the sequence of component motions often significantly deviate from the norm. Finally, all first-generation TDAs do not allow axial motion because they are either metal-on-metal or metal-on-poly or equivalents.

Replication of Mechanics

To understand TDA mechanics, one must fully appreciate the concepts of stiffness and its subclassifications. Stiffness is a function of both stress (applied load) and strain (motion). It is, in fact, defined by their ratio (stress/strain). For biological tissues, the stress/strain curve is composed of a neutral zone, an elastic zone, a plastic zone, and finally failure (Figure 1). Thus, stiffness is assessed by calculating the slope of the elastic zone of the stress/strain curve.

Stiffness has been arbitrarily subdivided into several categories. One such classification scheme subdivides stiffness into 3 categories: unconstrained, semiconstrained, and
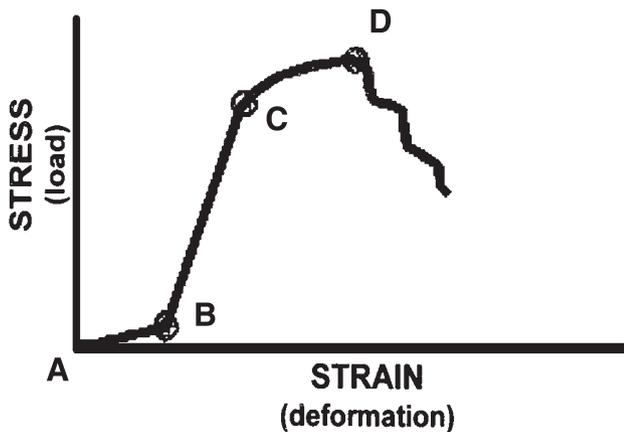
FIGURE 1. The stress/strain curve for biological tissues is composed of 4 zones. The curve is composed of a neutral zone (AB), an elastic zone (BC), a plastic zone (CD), and failure (D and beyond). Stiffness is defined as the slope of the elastic zone of the stress/strain curve.

constrained. Unfortunately, each subtype is not clearly defined and is often used differentially, depending on the scenario at hand. For example, some may consider a TDA to be a semiconstrained device, whereas others consider it to be an unconstrained device. Hence, for purposes of this discussion, unconstrained is mechanically portrayed by the neutral-zone portion of the stress/strain curve, whereas semiconstrained defines the characteristics associated with the elastic zone of the stress/strain curve. Constrained (or fully constrained) implies no motion and infinite or near-infinite stiffness. A fully constrained construct is depicted mechanically by a vertical orientation of the curve (Figure 2). Such would be characteristic of a solid fusion.
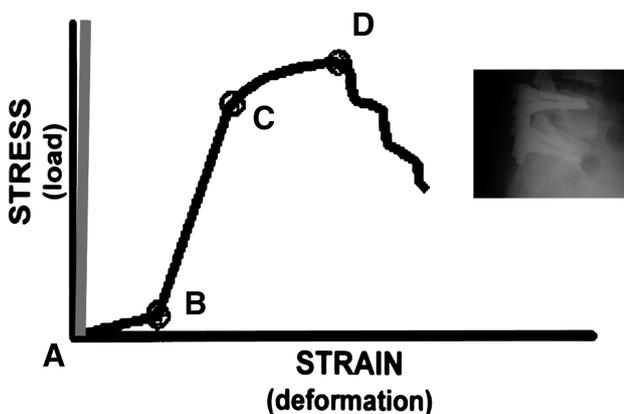
From a biomechanical perspective, a degenerated disk with dysfunctional motion and mechanics is portrayed mechanically by a shift to the right of the stress/strain curve (Figure 3). Thus, the neutral zone is widened and shifted to the right. A "sloppiness" of segmental motion is observed. Such a mechanical scenario may be associated with a mechanical pain syndrome. Mechanical pain is characterized by a clinical triad: pain that is deep in location, agonizing in nature, and worsened with spinal loading and improved with unloading.

One can then assess the function of the various spinal motion-altering devices by noting their stress/strain characteristics. This assessment should compare and contrast those characteristics associated with flexion-extension and axial loading. In both flexion-extension and axial loading, the stress/strain curve is as depicted in Figure 1. In flexion-extension, the first-generation TDA ball-in-socket–like joint is associated with a widened neutral zone until a hard stop is reached at the extreme of motion (Figure 4A). This is quite unlike that observed in the normal in vivo state. An elastomeric disk (elastomer sandwiched between the endplate caps, which is characteristic of the short-lived Acroflex [AcroMed] and, to some degree, new second-generation disks) may have the mechanical characteristics depicted in Figure 4C. This approximates the normal stress/strain relationships in flex-extension more closely than the ball-in-socket–like joint. For reference purposes, a dynamic stabilization device such as the Dynesis implant stiffens the spine and may be expected to shrink or normalize a pathologically widened neutral zone (Figure 4E), whereas a fusion, as already noted, is associated with near-infinite stiffness and an essentially vertical trajectory for the curve (Figure 4G).

In axial loading, the implant loading mechanics are quite different. Metal-on-metal or metal-on-poly implants do not cushion axial loads. Hence, they are near-infinitely stiff
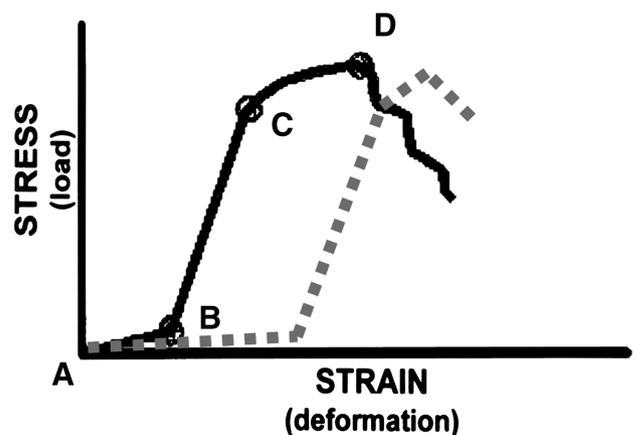

FIGURE 2. A fully constrained construct is depicted mechanically by a vertical orientation of the stress/strain curve. Constrained (or fully constrained) implies no motion and infinite or near-infinite stiffness, as would be characteristic of a solid fusion (inset). The red line represents the stress-strain curve for a fully constrained construct. AB, neutral zone; BC, elastic zone; CD, plastic zone; D and beyond, failure.

FIGURE 3. A degenerated disk is depicted mechanically by a shift to the right of the stress/strain curve. The motion and mechanics of a degenerated disk are dysfunctional, resulting in a neutral zone that is widened and shifted to the right. The dashed red line represents the stress/strain curve for a degenerated disc. AB, neutral zone; BC, elastic zone; CD, plastic zone; D and beyond, failure.
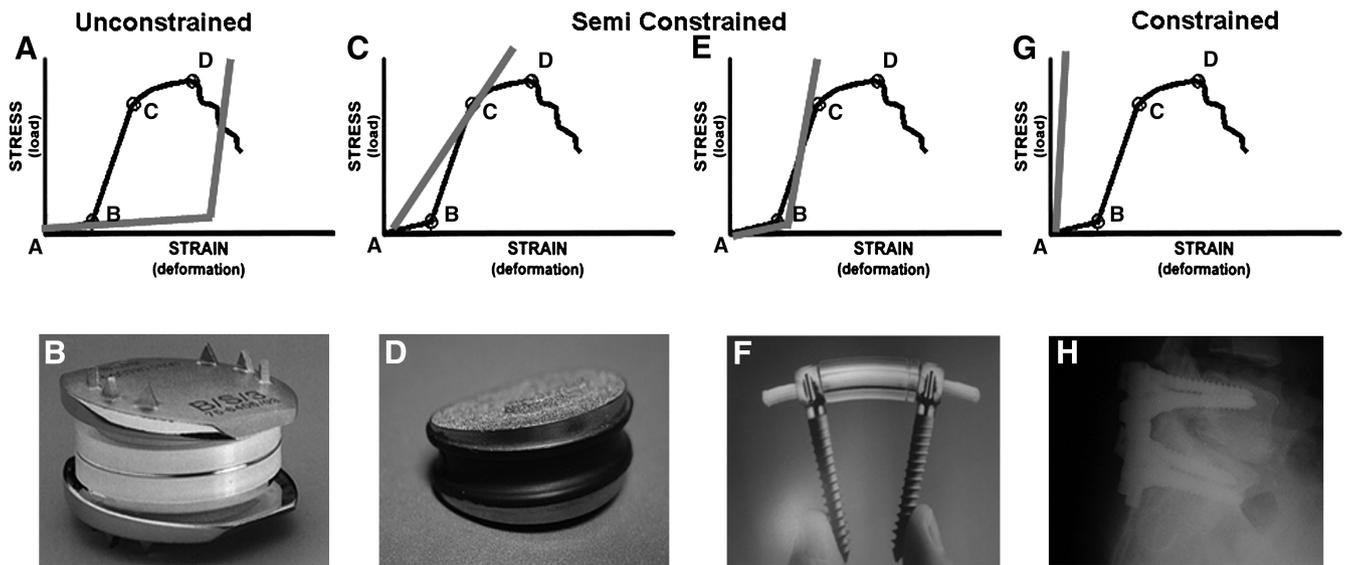
FIGURE 4. The stress/strain characteristics of various spinal motion altering devices in flexion, extension, and lateral bending are different from those of biological tissues. In flexion-extension, the first-generation total disk arthroplasty "ball-in-socket"–like joint (B) is associated with a widened neutral zone until a hard stop is reached at the extreme of motion (A). An elastomeric disk (D) may have the mechanical characteristics that more closely approximate the normal stress/strain relationships (C). A dynamic stabilization device (F) stiffens the spine and may be expected to normalize a pathologically widened neutral zone (E). A solid fusion (H) as already noted is associated with near-infinite stiffness and an essentially vertical trajectory for the curve (G).

(Figure 5A) in axial loading. The elastomeric implant cushions loads and again may have the mechanical characteristics depicted in Figure 5C. Depending on the degree of stiffness and the unique physical attributes of a dynamic spine stabilization implant (Figure 5E and 5F), the slope of the elastic zone would likely be located between that of the metal-on-metal or metal-on-poly implant (Figure 5A) and the normal in vivo state (Figure 1).

The unique loading characteristics associated with first-generation TDAs (eg, near-infinite stiffness in axial loading)
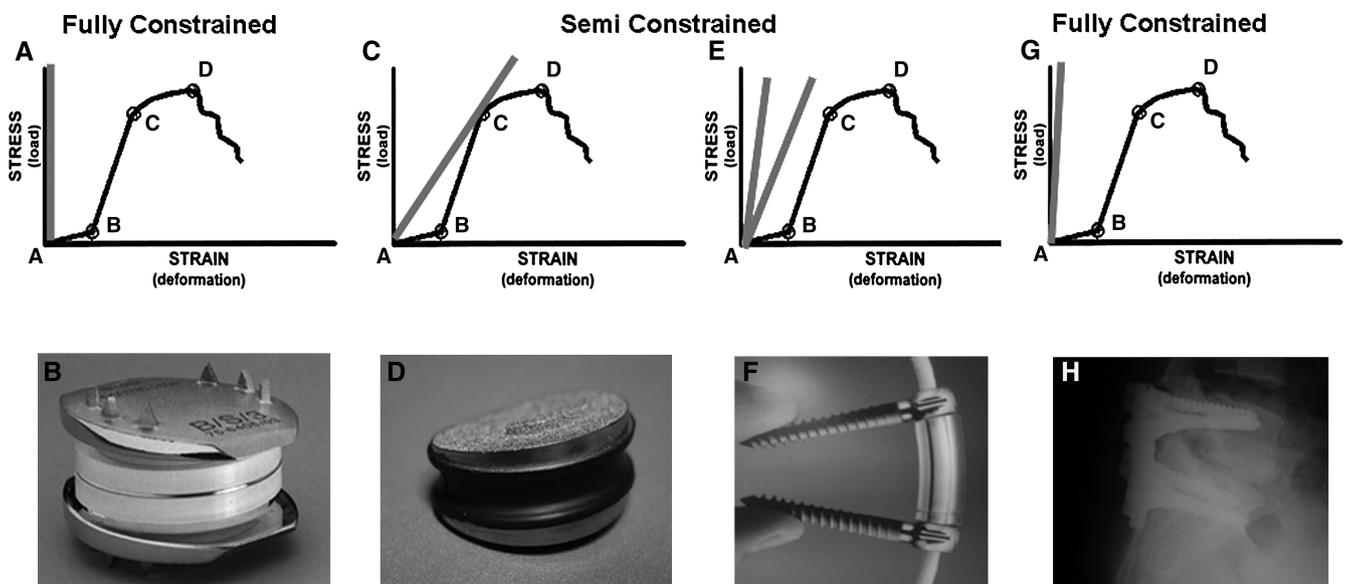

FIGURE 5. The stress/strain characteristics of various spinal motion-altering devices in axial loading are different from those of biological tissues. In axial loading, first-generation "ball-in-socket" metal-on-metal or metal-on-poly implants (B) are nearly infinitely stiff (A). An elastomeric disk (D) cushions loads and may have the mechanical characteristics depicted (C). A dynamic stabilization device (F) has an elastic zone slope (E) between that of the metal-on-metal and the normal in vivo state. A solid fusion (H) is associated with near-infinite stiffness in axial loading and an essentially vertical trajectory for the curve (G).

cause axial and combined bending/axial loads to be transferred to adjacent levels and to the facet joint complex at the index surgery level. Although not likely evident in early clinical series, this increase in mechanical stress transfer may take its toll over time.

Finally, one must remember that normal varies, depending on patient age and the extent of degeneration. A youthful disk is well hydrated and essentially is composed of a fluid-filled nucleus pulposus and a tough constraining functional annulus fibrosus. It is associated with a high pressure across the entirety of the disk in loaded conditions (Figure 6A). As degeneration occurs, the internal pressure in the loaded disk begins to drop, while the majority of the load (specifically axial load) is borne by the perimeter of the disk in the region of the annulus fibrosus that has been transformed into a fibrocartilaginous scar (Figure 6C and 6E).

TDAs are designed to mimic the youthful disk. Unfortunately, as portrayed here, they fail miserably in that quest from a mechanical perspective. These mechanics and mechanical relationships are further altered as the spine ages. The altered loading patterns that occur with aging (Figure 6)

further muddy the waters regarding the quest for the perfect motion preservation implant.

Replication of the IAR

The IAR of the intervertebral motion segment varies with motion. It is maintained in the region of the disk interspace. Some TDA implants have a fixed IAR; others may have a variable IAR. None of the currently available implants replicate the normal or natural IAR motion characteristics. The clinical implications of this are not yet known but will likely become more significant as time passes after implantation.

Incidence of Complications

It was predicted that TDAs would be associated with a significant complication rate. Although the initial complication rates were high, including fatalities associated with dislodgement, improvements in implant design and surgical technique have minimized both the incidence and significance of complications.[7-10]
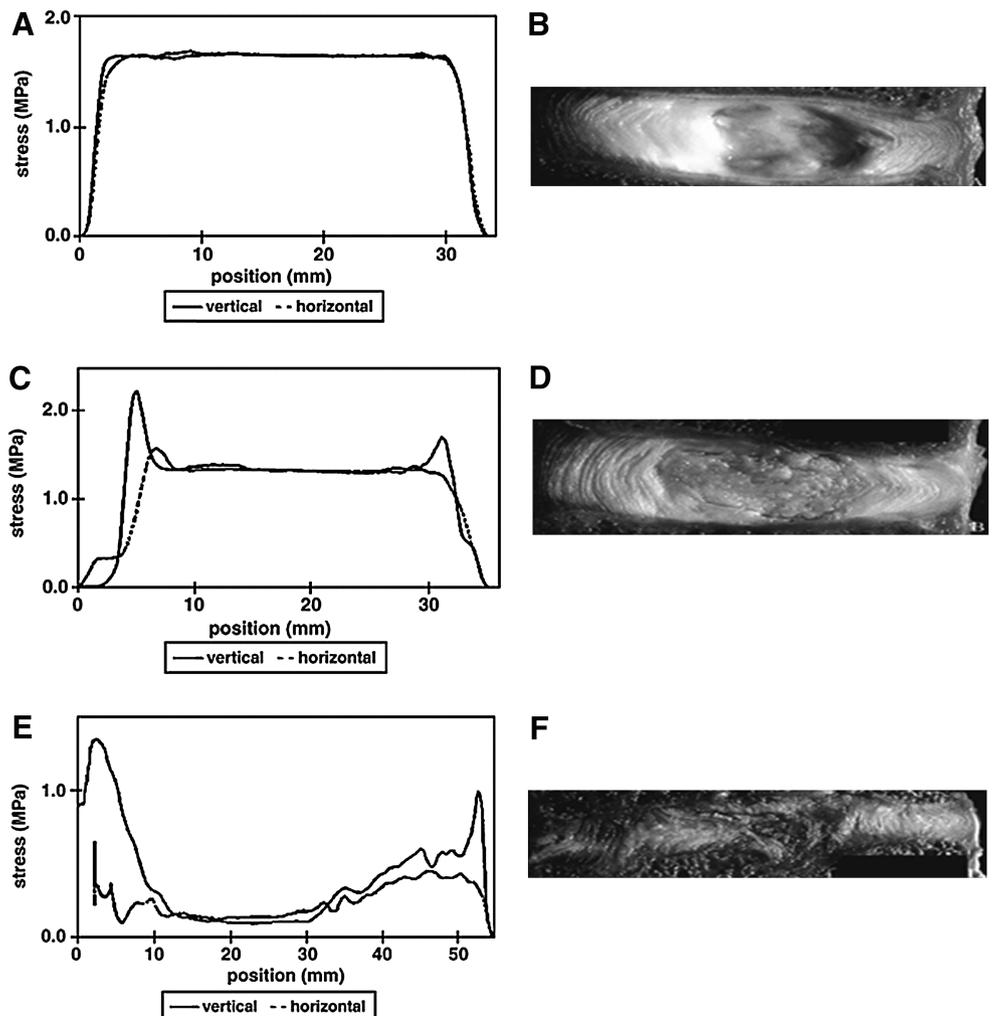
FIGURE 6. The distribution of stress over the intervertebral disk changes with degeneration. A youthful disk (B) is well hydrated and is associated with a high pressure across the entirety of the disk in loaded conditions (A). As degeneration occurs, the internal pressure in the loaded disk begins to drop (C and E), while the majority of the load (specifically axial load) is borne by the perimeter of the disk in the region of the annulus fibrosus that has been transformed into a fibrocartilaginous scar (D and F).

Adequacy of Revision Strategies

It was predicted during the early implementation of TDAs that revision strategies for the management of TDA-related complications were inadequate and fraught with risk. It turns out that this has not been commonplace. Revision strategies that either directly involve implant removal or replacement or involve simple fusion from a dorsal approach have proven to be relatively safe and to provide adequate backup strategies.[7,8]

Longevity of the Implant

Although some first-generation devices have been in place and have remained functional for > 2 decades, data are sparse. The TDA does not alter its mechanics as the patient and his/her spine degenerate. All other joints have an evolving mechanical pattern that is characteristic of senescence (Figure 6). This evolving mismatch between the motion preserving device and the adjacent aging motion segments must be considered carefully.

Retarding of Same- and Adjacent-Segment Degenerative Changes

Although published data suggest that TDAs diminish adjacent-level stresses and degeneration,[11-14] this information is sparse and relatively unconvincing in terms of long-term clinical outcomes and reoperation rates.[1] The near-infinite stiffness observed in axial loading and the near-zero stiffness in flexion-extension cause adjacent- and same-segment mechanics to be substantially altered and "stressed." In fact, mounting laboratory evidence suggests an increased facet joint force at the treated level associated with TDA.[15,16] Moreover, the most recent clinical data reveal no difference in the incidence of symptomatic adjacent-level disease after TDA compared with anterior cervical diskectomy and fusion (ACDF).[5,17]

Symptom Relief

Symptom relief or improvement associated with cervical TDA use as a spacer after an anterior cervical diskectomy (ACD) is based on clinical trials that are associated with significant bias and results that are often conflicting.[1,18-22]

Although greater improvements in neck pain after TDA compared with ACDF might be expected by some, such was not observed in early clinical studies. This finding also was not borne out in the long term. Studies revealing greater improvements in arm pain in TDA vs ACDF trials need to be interpreted with great caution because the index operation for radiculopathy (and therefore arm pain) is the diskectomy. This is common to both TDA and ACDF. In fact, this finding when present raises serious concerns about the validity of the aforementioned studies. Reports of greater improvement in neurological function after TDA vs ACDF raise similar concerns for the same reason: The decompression, common to both TDA and ACDF, is the portion of the operation understood to be responsible for the neurological outcome. Setting aside these concerns, the clinical data as a whole suggest that TDA offers equivalent, but not superior, clinical outcomes compared with ACDF in terms of relief of neck and arm pain and stabilization or improvement in neurological status.

ADJACENT SEGMENT DISEASE AS A RATIONALE FOR ARTHROPLASTY?

The predominant rationale for TDA has focused on the notion that an arthroplasty diminishes adjacent-segment and same-segment stresses and thus diminishes adjacent-segment degeneration and adjacent-segment disease (ASDis; symptomatic degeneration). First and foremost, as already addressed, the loads transferred to adjacent levels and to the facet joints at the same level after implantation of a TDA, by virtue of motion segment stiffness alternations, are increased, not decreased. Second, it has been assumed that fusion alters adjacent-level mechanics to such an extent that adjacent-segment degeneration and ASDis are significantly and adversely affected. The transfer of loads has already been addressed. To explore the effects of a variety of surgical approaches on adjacent-segment degeneration and ASDis, a review of the existing literature is in order.

Bohlman et al,[23] Bore and Sepic,[24] and Cauthen et al[25] have shown the incidence of ASDis to vary from 1.5% to 4.5% per year after cervical fusion. Hilibrand et al[26] published a large series of ACDF patients (409 patients) in 1999. They observed an annual incidence ASDis of 3%. In a compilation of 3 studies, Hilibrand and Robbins[27] corroborated the low incidence of ASDis (1.5%-4.5%).

Interestingly, an annual incidence of ASDis of 3% has been observed in another study examining ACD with and without fusion; in the 1980s, Lunsford et al[28] demonstrated an annual incidence of ASDis for patients undergoing ACD with or without fusion to be 2.5% per year. In fact, they observed no difference regarding the incidence of ASDis between those undergoing fusion and those not undergoing fusion. This observation is strongly suggestive of the notion that single-level fusion does not significantly alter adjacent-segment mechanics to a clinically relevant extent.

A particularly revealing study of > 800 patients from the 1980s by Henderson et al[29] demonstrated an annual incidence of ASDis of about 3% in patients undergoing posterior laminoforaminotomy. As one peruses the literature, this 3% per year incidence becomes a recurrent theme, independent of approach (anterior vs posterior) and fusion.

Even more revealing is the observation that the incidence of ASDis was less with multiple-level fusions compared with single-level fusions. This counterintuitive observation truly de-emphasizes and in fact negates the association between fusion and ASDis. Indeed, if such a relationship existed, a longer fusion with an associated greater bending moment would be expected to cause a greater ASDis incidence, not a lesser incidence. In reality, such an observation likely results from the fact that the majority of ACDFs are performed at the most degeneration-prone levels (C5-6 and C6-7), thus leaving more degeneration-resistant levels in which the incidence of degenerative changes occurring after surgery or occurring naturally is diminished.

EARLY TDA STUDIES

Laboratory Studies

Early biomechanical studies of TDA kinematics in cadaveric models supported the hypothesis that TDA retained native range of motion (ROM) at the operated and adjacent levels. This is unlike ACDF, which decreases ROM at the operated level and consequently increases motion and stresses at adjacent levels. Puttlitz et al[11] compared Prodisc-C arthroplasty and native disk at C4-5 in 6 cadaveric spines. Using a pure moment bending methodology, they measured flexion, extension, lateral bending, and axial rotation, as well as coupled motion (lateral bending during axial rotation and axial rotation during lateral bending), at the operated level only. The authors observed no differences in ROM in any of the 3 rotation planes or in coupled motion between TDA and native disk. They concluded, without direct measurement, that motion at adjacent levels is replicated by TDA. In a similar study, DiAngelo et al[12] compared the Bristol cervical joint (similar to Prestige) arthroplasty, native disk, and graft with plate at C5-6 in 4 cadaveric spines. Using a displacement control method, they measured flexion, extension, and lateral bending at the operated and adjacent levels. The authors found no differences between arthroplasty and native disk at the operated and adjacent levels, whereas they found decreased ROM at the operated level and increased motion at adjacent levels with graft and plate. Chang et al[13] compared Prodisc-C (metal on polymer), Prestige (metal on metal), ACDF, and native disk at C6-7 in 18 cadaveric spines. They measured flexion, extension, lateral bending, and axial rotation at the operated and adjacent levels. As expected from prior studies, those authors found that ACDF decreased ROM at the operated level and increased ROM at the adjacent level. Curiously, they actually observed an increased ROM at the operated level in the arthroplasty compared with native spines, although these findings were not statistically significant at all levels and in all modes. A concordant decreased ROM at adjacent levels was observed in the arthroplasty group compared with the native spine. The significance of this regarding adjacent-level degeneration is unclear. Of note, no differences were found between Prodisc-C and Prestige.[13]

A primary mechanism contributing to adjacent-segment degeneration is thought to be related to increases in adjacent segment intradiskal pressure, causing altered metabolism in the nucleus pulposus. Dmitriev et al[14] studied the operated-level ROM in all modes and adjacent-level intradiskal pressure in arthroplasty vs native vs allograft dowel vs allograft dowel and plate at C5-6 in 10 cadaveric spines. At the operated level, the authors observed no ROM differences between arthroplasty and native spine under any conditions (axial loading was not studied), whereas the expected decreased ROM was observed in both arthrodesis constructs. Adjacent-level intradiskal pressures were unchanged in the arthroplasty vs native spines, whereas they were increased at the superior adjacent level and trended toward increased at the inferior adjacent level in the arthrodesis constructs compared with native and arthroplasty.

Clinical Studies

Early clinical studies on cervical TDA demonstrated similar improvements in pain and disability outcomes in cervical TDA vs ACDF, the overall safety of the devices, and the maintenance of sagittal-plane motion in TDA. Most did not address ASDis, and when such data were available, no statistically significant reduction in ASDis requiring reoperation was demonstrated. Goffin et al[19] published an early study of the Bryan cervical disk prosthesis. This prospective multicenter trial of 146 patients with 1- or 2- level disease and radiculopathy and/or myelopathy examined ROM (plain radiographs), Short Form-36, and neurologic status with 2-year follow-up for single-level and 1-year follow-up for 2-level treatment. The study included no control subjects, instead relying on a review of the ACDF literature to establish an anticipated success rate. The authors reported neurological function (and success) similar to that after ACDF and maintenance of motion at the operated level(s) in TDA. Although this short-term study does not contain significant data on ASDis, it is worth noting that 1 of 103 patients (1%) in the single-level study developed ASDis requiring an adjacent-level implantation at 21 months.[19] A subsequent study of Bryan TDA outcomes from Coric et al[20] reported the results from a single site (33 patients) participating in a prospective, randomized, controlled, multicenter trial of Bryan TDA vs ACDF in patients with single-level disease and radiculopathy and/or myelopathy assessing ROM (plain radiographs), Neck Disability Index (NDI), Visual Analog Scale, Short Form-36, and neurological status at intervals up to 2 years. The authors reported excellent outcomes in both groups, with no significant differences and maintenance of motion in the arthroplasty group. No data on ASDis were reported in this short-term study.

Bertagnoli et al[21] reported early clinical results for ProDisc-C in a prospective, uncontrolled study of 16 patients with 1- or 2-level disease and axial neck pain either with or without radiculopathy. ROM (plain radiographs), Oswestry Disability Index, and Visual Analog Scale scores were reported with 1-year follow-up. The authors reported a significant reduction in neck and arm pain compared with before surgery and increased ROM at the operated level from an average of 4° preoperatively to 12° postoperatively. They also reported no spontaneous fusions and no device-related complications. Interestingly, 2 of their 16 patients had prior adjacent-level Bryan TDA presenting with symptomatic adjacent-level disease 2 to 2.5 years later who were treated with ProDisc-C TDA as part of this study.[21] Nabhan et al[22] reported a prospective, randomized, controlled study of 33 patients who underwent either ProDisc-C TDA or ACDF. The authors reported clinical results at the 6-month follow-up in the form of Visual Analog Scale for arm and neck pain and ROM as assessed by radiostereometric analysis. Both groups showed significant decreases in Visual Analog Scale score for arm and neck pain 6 months postoperatively with no significant differences in pain relief between the ProDisc-C and ACDF groups. Decreased segmental motion was observed at follow-up compared with immediately postoperatively in both groups. A significantly greater decrease in ROM was

observed in ACDF patients. These radiostereometric analysis measurements (by their nature) compared immediate postoperative states with later time points but not with preoperative ROM or with adjacent levels. A strength of the study is that it described segmental motion in TDA and ACSDF under physiologic loads.

Initial clinical outcomes for the Prestige TDA were reported in a prospective, randomized, controlled, multicenter Food and Drug Administration trial.[1] Five hundred forty-one patients (at 32 sites) with single-level degenerative disk disease and radiculopathy and/or myelopathy were randomized to either the Prestige TDA or ACDF. ROM, NDI for neck pain and arm pain, neurological success (maintenance or improvement in sensory, motor, and reflex examination), return to work, and Short Form-36 were assessed at 1.5, 3, 6, 12, and 24 months. NDI scores improved significantly in both groups compared with preoperatively, and although the TDA group demonstrated significantly greater improvement in NDI at 3 months, the difference disappeared at 24 months. There was a trend toward earlier return to work in the TDA group, but it was not statistically significant. Curiously, neurologic success was statistically significantly greater in the TDA than in the ACDF group at 12 and 24 months, which is difficult to explain in light of the fact that the index operation for sensory/motor/reflex examination is the microdiskectomy, which is common to both groups. As expected, segmental motion of 7.5° was maintained in the TDA group and decreased in the ACDF group. At 2 years, the TDA group showed a statistically significantly decreased rate of adjacent segment reoperation; however, this difference was no longer significant at the 5-year follow-up in the same group of patients.[18] Overall success, defined as ≥ 15-point improvement in NDI, maintenance or improvement in neurological status, no adverse event, and no second surgery, was significantly greater in TDA compared with ACDF at 12 months (77.6% vs 66.4%) and 24 months (79.3 vs 67.8%). The study should be interpreted in light of the potential for bias because neither patients nor surgeons were blinded and in light of the disclosure stating that the authors received benefits from Medtronic in relation to use of the device. The longer-term 5-year follow-up study of the same group of patients revealed no statistically significant difference at 5 years in NDI, neck pain, arm pain, Short Form-36 scores, return to work, and implant removal/reoperation.[18] Overall neurologic success was higher in the TDA group at 2, 3, and 5 years. Importantly, surgery for symptomatic ASDis was not statistically significantly different between the 2 groups.[18]

ARTHROPLASTY DOES NOT PROVIDE AN ADVANTAGE OVER TRADITIONAL SURGICAL TECHNIQUES

"History repeats itself." One does not need to look too far back in the spine surgery archives to see the rapid rise and then fall of popularity of new technologies. The rapid rise and fall of threaded interbody fusion cages (TIBCs) provides a very relevant example. As a result of the controversies and medicolegal storms surrounding the use of pedicle screws for lumbar spine stabilization in the early 1990s, TIBCs were introduced as an alternative to pedicle screws as an adjunct for fusion. Initial biomechanical studies demonstrated improvements in stiffness, and clinical trials showed promise. What then transpired is both extremely interesting but also disheartening.

Biomechanical studies demonstrated significant increases in stiffness associated with the TIBC-associated distraction that tensioned the annulus fibrosus and ligamentum flavum and resulted in extraordinarily stiff constructs, ie, in the equivalent of the first day postoperatively. Unfortunately, the suboptimal endplate contact associated with the TIBC resulted in subsidence and a diminished tensioning of the annulus fibrosus and ligamentum flavum. This, in turn, resulted in motion, which in turn would be expected to result in pseudoarthrosis.[30-33]

Initial clinical trials (industry funded and associated with significant methodological, surgeon, and patient biases) demonstrated positive short-term results.[34,35] Reality, however, then set in. Longer follow-up and nonbiased reporting demonstrated a much greater clinical failure rate than previously reported.[36-38] TIBCs soon fell into disfavor, and their use, except in unique circumstances, plummeted. We should have similar concerns regarding TDAs. We are likely in the midst of a similar "rise and fall" scenario with TDAs.

Steflox et al[39] and Choudhry et al[40] were perhaps the first to bring to light the impact of conflict of interest and bias in the performance of clinical trials. They observed that researchers with financial interests in the drug being studied had a statistically significant propensity to find positive results compared with nonvested physicians. Such bias is inevitable. Industry influence, patient bias (winner-loser bias), and methodological complexities cast surgical trials into the highly suspect subset of clinical evidence.[41]

Accuracy describes the closeness of a measured result to the true value; precision describes the reproducibility of the measurement. To be valid, a measurement must be both accurate and precise. Accuracy and precision are sometimes illustrated by an analogy in which repeated measurements are represented by arrows shot at the bull's-eye (true value) of a target. Accuracy describes the closeness of the arrows to the bull's-eye, and precision the closeness of the arrows to each other. A cluster of arrows very close to each other but far from the bull's-eye are precise but inaccurate. Bias is a nonrandom effect on the measured results caused by factors unrelated to the independent variable. In this analogy, bias could cause the arrows to land systematically to 1 side of the bull's-eye. An outcome measure that should not differ between groups, but is found to differ systematically and reproducibly, suggests that bias is afoot (Robert Harbaugh, personal communication). A reproducibly greater improvement in radiculopathy after TDA vs ACDF is an example of such an outcome measurement. The index operation for improvement in radiculopathy is the microdiskectomy, which does not differ between the groups, and not the choice of spacer, which does.

If an outcome variable does not make sense, something indeed may be wrong. If what should be an independent variable (no expected differences between groups) such as

improvement of radiculopathy after either TDA or fusion as a spacer after diskectomy occurs at a statistically greater rate in 1 group over another, other variables (including dependent variables) may be, and probably are, skewed as well. This clustering of variables may represent precision but not accuracy. The skewing of the results in clusters is likely a manifestation of bias and should result in a failed "sniff test." However, such is the fate in general of prospective surgical trials. They indeed are very difficult, if not impossible, to rid of bias.

Bartels et al[6] went so far as to state, in their meta-analysis of randomized clinical trials for cervical disk arthroplasty, that "A clinical benefit for the cervical disk prosthesis is not proven. Because none of the studies were blinded, bias of the patient or researcher is a probable explanation for the differences found. Therefore, these costly devices should not be used in daily clinical practice." They observed that the development of ASDis is equivalent after both ACDF and cervical TDA. However, they also observed a significantly higher incidence of ASDis in patients with concurrent lumbar degenerative disk disease. Perhaps this finding is much more than a casual observation. It adds further credence to the notion that the cause of ASDis is not related to fusion. Patients who develop ASDis are evidently more likely to be arthropaths (patients harboring multiple sites of degenerative joint pathologies) as exhibited by the presence of lumbar degenerative disk disease. Hence, their risk for ASDis is greater than that for nonarthropaths.

Posture and alignment of the spine after an ACDF or cervical TDA may strongly influence degenerative changes as spinal levels adjacent to the index operation. Mounting evidence exists that a kyphotic posture significantly stresses adjacent segments.[42,43]

Finally, the relative cost of implantable devices for the management of cervical disk herniation is greater for TDA than for ACDF. Bhadra et al[44] analyzed the cost-effectiveness of ACDF vs cervical TDA in England and determined that the implant cost for plate, cage, and bone substitute was £960; that for cage only was £550; and that for TDA was £1100. Interestingly, the authors determined that for the same groups the average total cost of the procedures (including hospital stay and operating room time) was comparable in plate/cage/bone-substitute ACDF (£2520) and TDA (£2435) and less expensive in the cage-only group (£1930). A double-blind, randomized, controlled, multicenter study (the Netherlands Cervical Kinematics [NECK] Trial) comparing the cost-effectiveness of ACD, ACDF, and cervical TDA is currently underway in the Netherlands.[45]

CONCLUSION

ASDis may be more related to the vulnerability of spinal level (particularly C5-6 and C6-7), the presence of degenerative disease elsewhere in the spine (particularly the lumbar spine), and spinal alignment and posture after fusion. There is little support for the notion that short-segment fusions substantially increase the risk of ASDis. Therefore, cervical TDA cannot be rationalized on the basis of ASDis

prevention. In addition, the evident clinical equivalence of cervical TDA to ACDF, the unknown long-term effects of TDA, and the cost of implantation lead us to agree, at least until further evidence is acquired, with Bartels et al[6]: "A clinical benefit for the cervical disk prosthesis is not proven. Because none of the studies were blinded, bias of the patient or researcher is a probable explanation for the differences found. Therefore, these costly devices should not be used in daily clinical practice."

Disclosure

Dr Benzel is on the board for OrthoMEMS, is a consultant for AxioMed, has received grants from Stryker, has patents with AxioMed, and receives royalties from DePuy and stock options from OrthoMEMS and AxioMed. Dr Tharin has no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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