ARTIFICIAL DISC REPLACEMENT FOR DEGENERATIVE DISC
DISEASE OF THE LUMBAR SPINE

INTRODUCTION

The California Technology Assessment Forum has been asked to update its review of the scientific literature on the safety and efficacy of artificial spinal disc replacement for the treatment of low back pain caused by lumbar degenerative disc disease.

This review will update the February 16, 2005 assessment of the Charité Artificial Disc (www.ctaf.org). Since the last review, full details of the pivotal randomized clinical trial have been published in a pair of articles accompanied by two editorials. The largest case series has also been updated with data on patients at least 10 years after artificial disc surgery.

BACKGROUND

Back Pain

Up to 40% of chronic low back pain has been reported to originate from the intervertebral disc (Schwarzer, Aprill et al. 1995), but there is controversy surrounding its diagnosis and management. There is no gold standard for the diagnosis of discogenic pain. In particular, the literature concerning the utility of provocative discography is particularly contentious (Schwarzer et al, 1995). Low back pain caused by intervertebral disc disease may be insidious or sudden in onset. Pain is usually at the center of the back and may radiate to the buttocks or thighs. It is usually increased by sitting and improved by lying down.

The usual treatments for low back pain include structured exercise programs, non-steroidal anti-inflammatory drugs, opioid analgesics, antidepressants and cognitive behavioral therapy. For the minority of patients with persistent pain due to degenerative disc disease, treatment with spinal fusion is sometimes recommended.

Lumbar Spine Fusion Surgery for Degenerative Disc Disease

Patients with clear discogenic pain may benefit from complete surgical removal of the intervertebral disc and vertebral fusion. Measurable decreases in preoperative pain has been noted in over 80% of patients in
various series (Lee, Vessa et al. 1995). One high quality randomized clinical trial reported statistically significant improvements in pain and disability with lumbar fusion compared with conservative management (Fritzell, Hagg et al. 2001). This study has been criticized for the lack of standardized cognitive behavioral therapy combined with structured exercise program in the control group. Two more recent studies compared lumbar fusion to structured exercise programs (Brox, Sorensen et al. 2003; Fairbank, Frost et al. 2005). The first (Brox, Sorensen et al. 2003) found no difference between the two arms, though there was a trend towards better outcomes in the Oswestry Disability Index (ODI) in the surgical group at one year. The second (Fairbank, Frost et al. 2005) found a small, but statistically significant benefit in the ODI at two years in favor of fusion.

Spinal fusions can be performed by an anterior or posterior approach. The majority of spinal fusion operations in the U.S. have been by the posterior approach, which in turn is comprised of three main techniques: a posterior lumbar interbody fusion (PLIF), a posterolateral gutter fusion surgery and a transforaminal lumbar interbody fusion (TLIF). In these procedures, the paraspinal muscles must be detached, thus potentially leading to paraspinal muscle weakness and atrophy in some patients. The PLIF and TLIF allow for placement of bone or a cage in the disc space. There are two types of anterior fusion procedures: the anterior/posterior lumbar fusion and the anterior lumbar interbody fusion (ALIF). The anterior approach preserves the paraspinal musculature and nerves. In addition, bone graft is placed in front of the spine and therefore receives more compression and may fuse more efficiently (Burkus, Gornet et al. 2002). Risks of ALIF surgery include damage to large blood vessels, and in males, retrograde ejaculation in around 1% of cases (Fowler, Dall et al. 1995). Both implantation of the Charité device and use of the BAK cage require greater vascular access and manipulation than other anterior approaches and may be at higher risk for the complications associated with the anterior approach.

Fusing the spine is designed to decrease back pain by limiting the motion at a painful motion segment. Fusion occurs over a three to six months (and up to 18 months) period following surgery. There are concerns that lumbar fusion may accelerate degeneration at other disc levels. Rigid immobilization of one spinal segment can lead to hypermobility of adjacent segments which is thought to accelerate degenerative changes in the adjacent discs (Etebar and Cahill 1999; Chou, Hsu et al. 2002; Gertzbein and Hollopeter 2002). Artificial discs have been developed to allow removal of the diseased disc while preserving normal range of motion at the disc.

Charité Artificial Disc

The Charité Artificial Disc was developed to treat severe, chronic low back pain by replacing a damaged disc in the lower back with an artificial disc. It is made of two metallic endplates and a sliding plastic core.
The disc was designed to restore disc space height, to restore motion segment flexibility, to prevent disc degeneration at adjacent segments, to reduce or eliminate pain from motion or from nerve compression and to improve the patient's functional activities. It was designed to have a life span of 40 years.

The surgical approach is typically through an anterior retroperitoneal route. Meticulous attention to implantation is required to ensure that the articulating surfaces of the endplates are parallel in order to restore normal biomechanics. Patient positioning is important so that radiographic confirmation of the implant position can be seen easily by the surgical team. A spine surgeon (either an orthopedic spine surgeon or a neurosurgeon) uses specially designed instruments to remove the damaged disc, create a space between two vertebrae for the implantation of the artificial disc and fit the Charité disc in between the two vertebrae. The disc replacement procedure is performed with the patient under general anesthesia and typically takes about two hours to complete. During the U.S. clinical trials, the average hospital stay for patients was about four days. Surgeons generally advise restriction of certain activities for a certain time period following the surgery and some surgeons may prescribe a back brace.

Indications for Artificial Disc Replacement

- Lumbar degenerative disc disease confirmed by the patient’s medical history and an x-ray, MRI and/or other diagnostic tests
- Symptoms not relieved with at least six months of non-surgical treatment (pain medications, physical therapy, manipulation, ice and/or heat therapy, etc.)
- The damaged disc is located at either L4-L5 or L5-S1
- No or minimal (< 3 mm) spondylolisthesis

Contraindications for Artificial Disc Replacement

- Multi-level disc degeneration
- Instability in the spine (such as spondylolisthesis, fracture or spinal tumor)
- Osteoporosis or osteopenia
- Prior spine surgery
- Pregnancy
- Facet joint arthritis

Technology Assessment (TA)

TA Criterion 1: The technology must have the appropriate regulatory approval.
On October 26, 2004 the U.S. Food and Drug Administration (FDA) approved the Charité™ Artificial Disc (DePuy Spine, Inc., a Johnson & Johnson Company, Raynham, MA) for use in patients who have severe lower back pain caused by degenerative disc disease and have obtained little or no pain relief after at least six months of non-surgical treatments, such as pain medications, physical therapy, injections and/or manipulation. The FDA clearance for disc replacement is a single level of the lower spine, either L4-L5 or L5-S1.

TA Criterion 1 is met.

**TA Criterion 2:** The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.

The Medline database, Cochrane clinical trials database, Cochrane reviews database and the Database of Abstracts of Reviews of Effects (DARE) were searched using the key words artificial disc or Charité. These were cross-referenced with the keywords lumbar and human. The search was performed for the period from 1966 through September 2005. The bibliographies of systematic reviews and key articles were manually searched for additional references. The abstracts of citations were reviewed for relevance and all potentially relevant articles were reviewed in full.

The updated search identified one new publication of an uncontrolled case-series (Lemaire, Carrier et al. 2005) describing the outcomes after at least 10 years of follow-up for 100 patients at a single center in France. These patients were described in an earlier publication (Lemaire, Skalli et al. 1997) reviewed in the prior assessment.

In the prior assessment, one U.S. study (Geisler, Blumenthal et al. 2004) that randomized 305 patients was identified. Since that time, more detailed data on the same trial have been published (Blumenthal, McAfee et al. 2005; McAfee, Cunningham et al. 2005).

Level of evidence: 1 and 5

**TA Criterion 2 is met.**

**TA Criterion 3:** The technology must improve the net health outcomes.

The benefits of treatment for low back pain include pain relief, decreased disability/restoration of function, cessation of narcotic therapy and return to work. The primary outcome measure used in most studies of
back pain is change in the pain score as measured by a 10-point visual analog scale (VAS). Changes of two points or greater are generally considered clinically significant. Disability is usually measured by the 100-point Oswestry low back pain Disability Index (ODI).

Case Series

The new case series (Lemaire, Carrier et al. 2005) reported outcomes on 107 French patients who received disc replacement with the 3rd generation Charité artificial disc between February 1989 and December 1993. To be eligible for the study, patients were required to have had intractable pain at one or two levels. Patients were excluded if they were obese, had prior fusion, suffered from radicular pain, or had evidence of spondylolisthesis or facet arthrosis. Seven patients in the series were not available for evaluation: six had moved away and were unable to be contacted; the seventh died from lung cancer. The remaining 100 patients were an average of 40 years old at the time of surgery (range 24 to 51 years) and 59% were women. The artificial disc was implanted at one level in 54 patients, two levels in 45 patients and three levels in one patient. The average length of follow-up was 11.3 years and all patients were followed for at least 10 years. The primary outcome was reported as the relative gain in the Modified Stauffer Coventry scale. The relative gain was defined as (post-operative score - preoperative score) / (maximum possible score - preoperative score), expressed as a percentage. It is not clear from the report when the “post-operative score” was assessed and if it was assessed in a standard fashion with blinded evaluators. A relative gain of at least 70% was defined as excellent, 60-69% as good and less than 60% as poor. Using this definition, 62% of patients had excellent results, 28% good results and 10% poor results. Among the 95 patients who had not retired, 87 (92%) returned to work after the surgery. Radiologically, no subluxation of the prosthesis or the polyethylene core was found. The mean increase in interspace height was preserved during follow-up (51.5% post-operatively, 51.3% at latest follow-up), although when the last radiographic evaluation was obtained it was not reported. Mean range of motion was within the normal range: 10.3° flexion/extension and 5.4° lateral bending. Perioperative complications reported included vascular injury in two patients, neurologic injury in two patients, sexual dysfunction in one patient and leg ischemia in one patient. Long-term complications included the need for secondary arthrodesis in five patients, symptomatic facet joint disease in four patients, periprosthetic ossification in two patients, adjacent level degeneration in two patients and subsidence in two patients.

The primary value of this new report is that it gives some evidence in support of the long-term viability of the Charité artificial disc. The number of device failures and additional surgeries appears to be low. Unfortunately, it is unclear from the report whether there was any systematic follow-up for clinical outcomes and no data was given on when the outcomes presented were measured. Standard outcome measures
such as the VAS and ODI were not reported, nor were the scores on the Modified Stauffer Coventry scale. Complications were described in detail, but it was not possible to evaluate how many patients were free from complications during follow-up. Furthermore, as noted by Dr. Deyo in his letter to the Coverage and Analysis Group of the Centers for Medicare & Medicaid Services “Case series are an inadequate study design to determine the degree to which an observed patient improvement (in this case, pain relief or improved function) is a result of natural healing processes, regression to the mean, or placebo effects, or is affected by other factors.”

Randomized Clinical Trials

Updated data from the pivotal randomized trial of the Charité artificial disc has been published in two journal articles (Blumenthal, McAfee et al. 2005; McAfee, Cunningham et al. 2005) accompanied by two commentaries (Mirza 2005; Zindrick, Lorenz et al. 2005). As noted in our prior review, the study recruited 375 patients at 14 spine centers in the U.S. The initial five patients treated with an artificial disc at most centers (71 patients) were considered training cases and were not included in the randomized comparisons. Randomization was done with a 2:1 ratio. 205 patients received the Charité lumbar artificial disc and 99 patients received the control surgery (ALIF with BAK threaded fusion cages and bone graft). The study was designed as a non-inferiority study assuming that 70% of both arms would achieve “clinical success” (defined below) with a 15% difference between success rates considered not clinically significant. In other words, the study was designed to demonstrate that the success rate with the artificial disc would be at least 55%, assuming that the success rate of fusion was 70%.

The study had 11 inclusion criteria and 23 exclusion criteria (Table 2, Blumenthal, McAfee et al., 2005). To be eligible for the study, patients had to be 18 to 60 years old with single-level L4-5 or L5-S1 symptomatic degenerative disc disease confirmed by discography. They were required to have an ODI score >30, a VAS score >4/10, failed more than six months of non-operative care, back and/or leg pain without nerve compression, less than three prior abdominal surgeries and compliance with the follow-up schedule. Exclusion criteria included previous fusion, multilevel degeneration, prior fracture in the lower lumbar spine, non-contained disc herniation, osteoporosis or metabolic bone disease, spondylolisthesis >3 mm, positive straight leg raise, scoliosis >11 mm, spinal tumor, infection, facet joint arthrosis, psychological disorder and morbid obesity. Additional exclusions were metal allergy, bone growth stimulator elsewhere in the spine, participation in another study, arachnoiditis, pregnancy, chronic steroid use or presence of an autoimmune disease. The number of criteria severely restricts the population that these results apply to. Unfortunately, the investigators did not report the number of individuals screened to accrue the 305 patients randomized in the study.
Patients were randomized in a 2:1 ratio stratified by site in blocks of six. Allocation concealment was maintained with sequentially numbered envelopes opened the day prior to surgery. Neither investigators, study staff, nor patients were blinded after this point. Unfortunately, this approach effectively unblinds every sixth patient. If the prior five patients included two patients randomized to the investigational device and three patients randomized to fusion, both investigators and staff could know that the next patient would be randomized to the investigational device. This could affect their interpretation of the inclusion and exclusion criteria as patients are evaluated, allowing selection bias to creep into the study.

Participants were an average of 40 years old and most were Caucasian (90%). There were trends towards the control group having more women (56% vs. 45%, p=.09), being heavier (82 kg vs. 78 kg, p=.03) and having a lower baseline activity level (6% vs. 17% moderate or active, p=.06), although only weight achieved statistical significance. The majority of the patients were treated at the L5-S1 level (69%).

The number of patients screened for enrollment in the study was not described. However, the flow of patients from randomization through two years of follow-up was described in detail. Follow-up was comparable and good in both groups. At one year, follow-up was available for 96% of patients randomized to the artificial disc and 94% of patients in the fusion group. At two years, the percentage follow-up results were 92% and 89%, respectively.

There were no differences between the two groups in operative time (111 vs. 114 minutes, p=.63) or blood loss (205 vs. 209 ml, p=.89). Length of hospitalization was significantly shorter in the artificial disc group (3.7 vs. 4.2 days, p=.004).

Clinical and radiologic outcomes were described in detail. The primary outcome was “clinical success,” defined as patients meeting all of the following four criteria: at least 25% improvement in the ODI score at 24 months, no device failure, no major complications and no neurologic deterioration. A strict intention-to-treat analysis was used. Clinical success at two years was attained by 57% of patients randomized to the artificial disc and 46% of patients in the fusion group (p<.0001 by one-sided Blackwelder non-inferiority test; p=.087 by two-sided Fisher exact test).

For both patient groups, the VAS and ODI scores improved significantly after surgery (p<0.001 at all time points). The mean ODI score decreased from 51 to 26 at two years (-25) in the artificial disc group and from 52 to 30 (-22) in the fusion group. The change scores did not differ between groups (p=0.27). However, the percentage of patients experiencing at least a 25% reduction in ODI was greater in the Charité group (64% vs. 50%, p=0.04). Similarly, the VAS score decreased from 7.2 to 3.1 at two years (-4.1) in the Charité group and from 7.2 to 3.7 (-3.6) in the control group. The VAS change scores were not different between groups at
two years (p = 0.11). However, improvements in both the ODI and VAS were more rapid in the artificial disc group than in the fusion group: the differences between groups for both the ODI and VAS were statistically significant at six weeks (p=.02) and remained significant through the 12 month evaluation (p=.04). These results were mirrored by patient satisfaction self-reports. At 24 months, more patients in the artificial disc group reported being satisfied with their treatment (74% vs. 53%, p=.001) and more patients in the artificial disc group would have the same treatment again (70% vs. 50%, p=.006).

These findings in favor of the Charité device may be biased due to the lack of blinding. The primary outcome measures were subjective, based on patient self-report of pain and disability. Clearly, the investigators eliciting the responses had an interest in a positive result. As noted in the paper, “All authors have a financial interest in subject matter contained in this manuscript.” More importantly, the participants may have been led to believe that the new device was better. They were participating in a trial of a new technology with a 2:1 randomization design in favor of the new device. This suggests that the high likelihood of receiving the new device may have attracted patients to the trial. Those patients who were randomized to the artificial disc were likely to be delighted, while those randomized to standard therapy were likely to be disappointed.

Other clinically relevant outcomes were reported. Narcotic use was lower in the artificial disc group (72% vs. 86%, p=.008). However, narcotic use at the 24-month follow-up remained remarkably high (64%) even in patients receiving an artificial disc who were categorized as a “clinical success.” Improvements in employment rates were low in both groups. Before surgery, 53% of the artificial disc group and 58% of the control group were employed. 24 months after surgery, 62% of the artificial disc group and 65% of the control group were employed.

Radiographic findings showed an average range of motion of 7.4° for patients in the Charité group compared with 1.1° in the fusion group. At 24 months, range of motion increased 14% in the artificial disc group, but decreased 82% in the fusion group (p<0.05). No data were presented about whether this difference correlated with a reduction in degenerative disease in adjacent discs or with clinical outcomes. Patients in the artificial disc group had improved disc height (p<0.05 vs. fusion) and less subsidence (p<0.05 vs. fusion).

Placement of the disc was assessed radiographically. Most of the subjects had ideal placement of the artificial disc (83%), but 11% had suboptimal placement and 6% had poor placement. Clinical outcomes correlated with the technical accuracy of surgical placement. Both improvements in the ODI and pain VAS were better in patients with ideal placement (p<0.05 for both).
Adverse neurologic events were similar in both groups (16.6% vs. 17.2%, p=.32). Major neurologic events (nerve root injury, motor deficits, neuropathic pain) were also similar in both groups (4.9% vs. 4.0%). Significant device failure occurred in 5% of patients in the artificial disc group and 8% of patients in the fusion group (p=.45). Surgical complications associated with the anterior approach (venous injury, retrograde ejaculation, ileus, DVT, incisional hemia, epidural hematoma, dural tear) occurred in 10% of patients in both groups. One patient in the artificial disc group died from narcotic use. No patients in the fusion group died. The overall complication rate was equivalent in the two groups (p=.68). Further details about the complications are to be published in future papers.

Two additional articles (Mirza 2005; Zindrick, Lorenz et al. 2005) that comment on this randomized clinical trial were published in the same issue of Spine. Both expressed significant reservations about the study. The first commentary (Mirza 2005) argues that the reference procedure, anterior fusion with BAK cage, has fallen out of favor among surgeons because of frequent failures and thus, gives an inappropriate control group. Dr. Mirza points out that the clinical success rate was low for both groups in the trial and that narcotic use was common even among patients who met criteria for “clinical success”. He notes that data from the FDA website indicate that 39% of patients in the artificial disc group had less than 5° of motion at the implantation site, which is within the FDA’s definition of fusion. He concludes that “contrary to optimistic marketing, the data provided to the FDA and published in this issue of Spine argue for caution by patients and surgeons.”

Zindrick et al. (2005) also question whether the BAK cage with iliac crest bone graft is the optimal comparison group by today’s standards. They express concern that sub-optimal placement of the artificial disc, which occurred in 17% of patients, would result in abnormal loading of the facet joints and other aspects of the spinal structure. This may lead to poor short-term outcomes, as noted in the study report (McAfee, Cunningham et al. 2005), as well as increased degeneration over time. They also express concern about potential bias in outcomes due to patient expectations that the Charité artificial disc was better than standard fusion. Their greatest concern was that two years follow-up was too short to fully assess harms from particle debris and to assess whether the artificial disc offered any advantages over fusion in terms of slowing degeneration at adjacent levels of the spine. They conclude that surgeons should “proceed cautiously in incorporating this new technology into their clinical armamentarium.”

Harms

Harms related to placement of the artificial disc have been poorly described in the published literature. In addition to usual perioperative complications like myocardial infarction and venous thromboembolic disease, important complications with the anterior approach to the spine include vascular injury and damage to the
paraspinous sympathetic chain. These risks may be increased with this procedure due to the instrumentation needed to restore disc space height and the need to precisely position the artificial disc. Another unstudied concern is that device failures 10 to 15 years after implantation will require very difficult procedures to remove the device.

A Dutch group (van Ooij, Oner et al. 2003) described the possible short- and long-term unsatisfactory results of disc prosthesis surgery. They note that most patients receiving artificial discs are between the ages of 30 and 50 years. In these active patients, complications can be expected to increase with longer follow-up, similar to total joint replacements in the extremities. They report a series of 27 patients who presented to a tertiary university referral center with unsatisfactory results or complications after Charité disc replacement. Their mean age was 40 years (range 30-67 years) at the time of operation. The mean time from disc replacement surgery was 53 months (range 11-127 months). Early complications were as follows: in one patient, an anterior luxation of the prosthesis after one week necessitated removal and cage insertion, which failed to unite. In another patient with prostheses at L4-L5 and L5-S1, the prosthesis at L5-S1 dislocated anteriorly after three months and was removed after 12 months. Abdominal wall hematoma occurred in four cases. Retrograde ejaculation with loss of libido was seen in one case and erection weakness in another case. A temporary benefit was experienced by 12 patients, while 14 patients reported no benefit at all. Main causes of persistent complaints were degeneration at another level in 14, subsidence of the prosthesis in 16 and facet joint arthrosis in 11. A combination of pathologies was often present. Slow anterior migration was present in two cases, with compression on the iliac vessels in one case. Polyethylene wear was obvious in one patient 12 years after operation. In eight cases, posterior fusion with pedicle screws was required. In this relatively small group of patients receiving the Charité disc prosthesis, most problems arose from degeneration of other lumbar discs, facet joint arthrosis at the same or other levels and subsidence of the prosthesis. The first two complications represent the problems that the device was designed to avoid. The major difficulty with interpretation of this report is the lack of knowledge about the total number of artificial discs implanted. The implications are quite different if the 27 patients represent failures from 100 surgeries or failures from 10,000 surgeries.

As noted above, wear debris, a concern with polyethylene implants in the peripheral joints, is a concern with artificial intervertebral discs due to their proximity to the spinal canal and nerve roots. According to the manufacturer, in a long-term laboratory test of cyclical motion simulating >11 years of use, no wear debris particles were identified. As described in the French series, no unexpected complications were found in 100 patients at least 10 years after placement of the device (Lemaire, Carrier et al. 2005). Finally, in the randomized clinical trial, complication rates were almost identical in the artificial disc and spinal fusion groups (Blumenthal, McAfee et al. 2005).
It is worth considering the history of the development of artificial hip and knee joints. Early prototypes had unrecognized design problems that were corrected iteratively over 10 years of careful clinical research. There is approximately 18 years of clinical experience with the Charité implant in Europe and the current device represents the 3rd generation in its development. However, the published literature on the Charité device is sparse, raising concerns about the quality of the follow-up data.

There are also concerns about late complications. Osteoporosis is a contraindication to placement of the artificial disc. However, a substantial proportion of women will develop osteoporosis as they age. It is unclear if these patients will be at risk for subsidence or device migration as their bone fragility increases.

Summary

The case series suggest that outcomes following placement of the Charité device are similar to those reported in the literature from case series of lumbar fusion. However, selection bias and the lack of controls make such interpretation weak. The case series are most useful in providing some data on the types of complications that can be expected, though these are incompletely reported.

The new publications describing the pivotal clinical trial in detail help assess the quality of the trial. Appropriate randomization and allocation concealment were used, follow-up was good through two years and a strict intention to treat analysis was used. However, no one was blinded in the study. The use of a fixed block size for stratified randomization in combination with unblinding of staff raises the possibility of selection bias for every sixth patient randomized. The trends toward the control group being heavier, less active and more likely to be female may be evidence that selection bias did influence randomization, although the investigators report that adjustment for these co-variants did not affect the results. The lack of blinding in a study with subjective measures as the principal outcomes (self reported disability and pain) is a much more important potential source of bias in the results. There is no way to adjust for this potential bias. The VAS and ODI scores suggest a trend towards better outcomes with the artificial disc after two years of follow-up. However, no data are presented on development or progression of disc degeneration at adjacent levels, the main theoretical benefit from the improved range of motion afforded by the artificial disc. Adverse events appear to be comparable in the two groups. On balance, there was no trend towards increased device failure or other adverse events in the artificial disc and all clinical outcomes either were significantly better or showed a trend towards better outcomes in the artificial disc group, compared with the spinal fusion group at all time points over two years of follow-up.

If we accept that spinal fusion improves net clinic outcomes in patients with intractable pain from degenerative disc disease, the case-series and clinical trial data suggest that the use of an artificial disc, in
the highly selected population meeting the inclusion and exclusion criteria of the trial, also improve net outcomes.

TA Criterion 3 is met.

TA Criterion 4: The technology must be as beneficial as any established alternatives.

There is controversy surrounding the established treatment for refractory symptoms from degenerative disc disease. However, since the publication of the meticulously performed and reported Swedish randomized trial (Fritzell, Hagg et al. 2001), many back specialists consider spinal fusion to be the standard treatment. Indeed, all four of the U.S. trials of artificial disc replacement have spinal fusion as the control arm. Unfortunately, there is no consensus on the best technique for fusion. The Swedish trial (Fritzell, Hagg et al. 2002), which was underpowered to compare the three surgical approaches used, reported no significant differences in outcomes between the three arms, although the anterior approach had higher fusion rates and higher rates of early complications. Each of the four U.S. trials assessing artificial disc technologies has a different fusion technique (BAK cage with autograft, 360° fusion with anterior femoral ring, LT-CAGE with infuse bone graft, 360° fusion with posterior approach) as the reference procedure.

One randomized trial directly compared use of the artificial disc to spinal fusion (see details under TA Criterion 3). In the randomized trial (Geisler, Blumenthal et al. 2004; Blumenthal, McAfee et al. 2005; McAfee, Cunningham et al. 2005), complication rates appear equivalent in the artificial disc and spinal fusion groups; two year clinical outcomes favored the artificial disc group. While, long-term outcomes are still uncertain with this novel device, the 10-year results in the French series are reassuring (Lemaire, Carrier et al. 2005). The primary advantage over fusion offered by an artificial disc is the preservation of range of motion at the affected joint. This is intended to prevent hypermobility and accelerated degeneration at adjacent spinal levels. None of the published trials to date presented any evidence of a reduction in degeneration in adjacent discs.

TA Criterion 4 is met.

TA Criterion 5: The improvement must be attainable outside the investigational setting.
The Charité artificial disc is also currently used in disc replacement surgery in more than 30 countries throughout Europe, Asia, North America, Africa and Latin America. According to the manufacturer, worldwide experience with this disc replacement device is now greater than 10,000 cases. However, there is clearly a learning curve to surgery using the Charité disc. In recognition of that fact, the U.S. clinical trial allowed for five device implantations at each surgical center prior to initiating randomization.

There are currently no well-defined, accepted standards for the training of surgeons wanting to employ the use of new technology. The manufacturer of the Charité artificial disc, DePuy Spine, has stated that prior to doing any surgery with the Charité disc, surgeons must undergo extensive training sponsored by DePuy Spine. This mandatory training includes a combination of participating in artificial disc surgery procedures with other trained surgeons, consultation and visitation with spine surgeons, lectures and educational materials.

In addition, the Spinal Arthroplasty Society has set a goal of establishing standardized training programs for physicians prior to their using any new artificial disc replacement technology. It is intended that the training be similar to that required for participation in the FDA clinical trials. Once surgeons have undergone training as recommended by the manufacturer, they should be able to achieve results comparable to those obtained in the investigational studies.

TA Criterion 5 is met.

CONCLUSION

Four case series have been published describing the clinical outcomes for 215 patients who received the Charité artificial disc and followed for a minimum of 18 months. Satisfactory clinical outcomes were reported for 63% to 79% of patients, which is comparable to reported success rates for lumbar fusion. One of the four case series reported data on 100 patients with at least 10 years of follow-up: there were no late device failures or unexpected neurologic syndromes. Only 5/100 had subsequent fusion. However, uncontrolled case-series are the weakest form of evidence and detailed outcomes and complications were not systematically assessed or fully reported.

Data from one randomized clinical trial of 304 patients comparing the artificial disc to spinal fusion have been published in detail. While there were some methodologic flaws, the overall quality of the trial was fair to good. Improvements in self-reported pain and disability scores favored the artificial disc, but were of borderline statistical significance and may have been biased due to the complete lack of blinding in the study. Complication rates were similar in the two groups. Neither group had excellent overall results:
average reductions in pain and disability were less than 50% and most patients still required narcotics for pain two years after surgery. The authors stated primary motivation for artificial disc replacement was to maintain range of motion in order to avoid initiating or accelerating degeneration in adjacent segments. Range of motion, as expected, was significantly greater in the artificial disc group. However, they explicitly state that adjacent level degenerative disease would not be detectable with just 24 months of follow-up and did not report any data on adjacent level disease. There remains controversy regarding the efficacy of fusion surgery for this indication. One of the major criticisms of the trial was that the comparison procedure, fusion with the BAK cage, is now considered a failed procedure. These critics argue that the study demonstrated equivalence to another procedure that is not efficacious for the treatment of degenerative disc disease.

In summary, randomized clinical trial evidence demonstrated that two-year outcomes for patients receiving the Charité artificial disc were not inferior to outcomes for patients treated with spinal fusion. Great uncertainties remain concerning the long-term viability of the device. Data from a case series of 100 patients presented evidence that the outcomes are preserved for at least 10 years, although patients who receive an artificial disc will be relatively young, which means that the disc prosthesis must last 40 to 50 years.

RECOMMENDATION

It is recommended that the use of the Charité artificial disc meets Technology Assessment Criterion 1 through 5 for safety, effectiveness and improvement in health outcomes when used in the following patient population:

- Age 18 to 60 years old
- Single-level L4-5 or L5-S1 symptomatic degenerative disc disease
- ODI score \(\geq 30\)
- VAS score \(\geq 4/10\)
- Failed \(\geq 6\) months of non-operative care
- No evidence of radiculopathy

Exclusion criteria

- Prior spinal fusion
- Multilevel degenerative disease
- Prior fracture in the lower lumbar spine
- Non-contained disc herniation
- Spondylolisthesis \(>3\) mm
- Scoliosis \(>11\) mm
- Facet joint arthrosis
- Osteoporosis or metabolic bone disease
- Chronic steroid use
- Presence of an autoimmune disease
After a review of expert testimony and substantial discussion, the CTAF panel voted unanimously against the consultant's recommendation. The CTAF panel's decision was that TA criteria 3-5 were not met.
RECOMMENDATIONS OF OTHERS

Blue Cross Blue Shield Association (BCBSA)
The BCBSA Technology Evaluation Center Medical Advisory Panel reviewed this technology in February 2005 and found that it did not meet criteria.

Centers for Medicare and Medicaid Services (CMS)
On August 16, 2005 the CMS opened a national coverage determination request to review the coverage of the lumbar artificial intervertebral disc.

California Association of Neurological Surgeons (CANS)
The CANS provided an opinion statement in support of the use of this technology as a treatment alternative for appropriate patients with DDD and the need for further post-marketing studies. A representative of CANS attended the meeting.

California Orthopaedic Association (COA)
A COA representative was not available to participate at the meeting. A formal position is not available.

Spine Arthroplasty Society (SAS)
The SAS provided comment in support of the use of this technology.

ABBREVIATIONS USED IN THIS ASSESSMENT:

PLIF: Posterior Lumbar Interbody Fusion
TLIF: Transforaminal Lumbar Interbody Fusion
ALIF: Anterior Lumbar Interbody Fusion
VAS: Visual Analog Scale
ODI: Oswestry Disability Index
References


