

# Comparison of Adverse Events Between the Bryan Artificial Cervical Disc and Anterior Cervical Arthrodesis

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**Study Design.** Randomized controlled study.

**Objective.** To compare the rates of adverse events associated with disc arthroplasty *versus* those of anterior cervical discectomy and arthrodesis with allograft and plate.

**Summary of Background Data.** Cervical disc arthroplasty as a substitute for fusion has been developed to maintain motion and, theoretically, prevent adjacent segment degeneration. Currently, cervical arthroplasty devices are undergoing clinical testing for safety and efficacy. The evaluation of safety is performed by critical analysis of all adverse occurrences following surgery to determine if the new device has a beneficial risk profile for the patient.

**Methods.** Adverse events associated with Bryan Disc arthroplasty and arthrodesis were compared in a prospective randomized study. Four hundred sixty-three (463) patients having cervical radiculopathy and/or myelopathy at a single level were treated at 31 sites. A total of 242 patients received the disc and 221 patients had anterior cervical discectomy and fusion. All patients were evaluated before surgery and at 1.5, 3, 6, 12, and 24 months after surgery. Adverse events were recorded concurrently and categorized by severity and as medically or surgically related.

**Results.** No differences in overall medical events occurred between groups. Surgically related events occurred more frequently in the investigational group secondary to more complaints of postoperative dysphagia and late medical events occurred more frequently in the investigational patients. However, the more severe World Health Organization Grade 3 and 4 events occurred more frequently in the arthrodesis patients related to treatment of pseudarthrosis and persistent symptoms. Significantly, more cervical spine reoperations occurred in the fusion group. Only one spinal cord injury occurred and it was in the arthrodesis group and no patients had deep infection or death related to either procedure.

**Conclusion.** Bryan cervical disc replacement and anterior cervical fusion are both safe procedures with a low incidence of significant adverse events related to the procedure. Statistically, more serious adverse events and reoperations occurred in the fusion group while a greater number of less serious surgically related events were seen in the investigational group.

**Key words:** cervical arthroplasty, cervical radiculopathy, cervical myelopathy, anterior cervical fusion, adverse events, complications, surgical morbidity. **Spine 2008;33:1305–1312**

Anterior cervical discectomy, arthrodesis, and plating is a successful procedure with good outcomes and predictably high patient satisfaction.<sup>1</sup> Additionally, there is a perception that adverse events are rare. However, to our knowledge, a rigorous large-scale, prospective study to assess adverse events following anterior cervical arthrodesis has not been conducted. Knowledge of such events is further limited, as there is a significant difference in the perception of morbidity by the patient compared to the surgeon.<sup>2</sup>

An important component of validation of new technology is the establishment of safety. Independent systematic monitoring of adverse events and early reporting are essential to evaluate patient risk. This requires a rigorous approach and for the evaluation of cervical disc prostheses, prospective randomized trials have been performed.

The purpose of our study is to determine the adverse events associated with the Bryan artificial disc compared to anterior cervical arthrodesis during an Investigational Device Exemption study. Adverse events were defined as those episodes that may affect patient outcome, require intervention, or need further diagnostic tests or monitoring.<sup>3</sup> These can occur or be identified at any time during surgery, initial hospitalization, or follow-up through 24 months.

## ■ Materials and Methods

A prospective, randomized, multicenter Investigational Device Exemption clinical study approved by the Food and Drug Administration (FDA) was conducted to evaluate the safety and effectiveness of the Bryan Cervical Disc. Patients with symptomatic single-level cervical degenerative disc disease, who met inclusion and exclusion criteria, and signed an informed consent were enrolled. After consent, patients were randomized to either arthrodesis or arthroplasty. Both groups were treated by an anterior approach, discectomy, and appropriate decompression. The control patients underwent arthrodesis with a struc-

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tural allograft and a titanium alloy plate and screw construct. In the investigational group, the endplates were prepared and a Bryan Disc inserted.<sup>4</sup> (Medtronic Spinal and Biologics Business, Memphis, TN.) The Bryan Disc is composed of 2 titanium shells, 2 titanium retaining wires, a polycarbonate polyurethane nucleus, a polyurethane sheath, and 2 titanium seal plugs.<sup>5</sup> All study sites were approved by their local IRB and patients voluntarily consented to be enrolled in the study. Post-operative bracing and instruction were at the discretion of the surgeons. Following arthroplasty, 27.1% of patients were immobilized in an orthosis compared with 68% following fusion. In general, arthroplasty patients were allowed to return to normal activities including work in the first several weeks whereas the majority of patients having fusion had limitations until 4 to 6 weeks.

A total of 463 study patients were enrolled, consisting of 242 Bryan Disc and 221 arthrodesis. Sixty-five (65) investigators from 31 sites in the United States performed the surgeries. The arthrodesis and artificial disc treatments were randomized in a 1:1 manner.

The inclusion criteria were single level cervical degenerative disc disease causing radiculopathy or myelopathy in skeletally mature patients (21 or older) from C3 to C7. Patients had to fail conservative care for 6 weeks (except for myelopathy cases needing immediate attention). Patients required a Neck Disability Index score of equal to or greater than 30%.<sup>6</sup> The most important exclusion criteria were the presence of significant anatomic deformity such as moderate to advanced spondylosis, radiographic signs of subluxation (>3.5 mm) or angulation (>11°), or previous cervical procedures at the operative level.

Patient evaluations occurred before surgery, at the time of operation, and after surgery at 6 weeks ( $\pm 2$  weeks), 3 months ( $\pm 2$  weeks), 6 months ( $\pm 1$  month), 12 months ( $\pm 2$  months), and 24 months ( $\pm 2$  months). At each evaluation, all adverse events, regardless if they appeared related to the surgery or not, were prospectively recorded by research coordinators. The sites were instructed to record all such events so that any possible subtle or rare correlation could be examined later. The composite follow-up rate for the 2 treatment groups was 90% at 24 months.

The severity of each event was classified using a 4-point scale adapted from the World Health Organization (WHO).<sup>7</sup> Grade 1 events did not require treatment and had no effect on outcome. Grade 2 events may have required nonoperative treatment, but had no effect on outcome or health of patient. Grade 3 events required medical treatment or may have had a long-term health effect. Grade 4 events required an operation, were life threatening, permanent disability, or caused death. Adverse events graded as a “3” or “4” were considered “serious” whereas grades “1” or “2” were considered “non-serious.”

Since all adverse events were recorded, it was likely that many had no connection to the study treatment. The case report forms were reviewed by 2 authors and adverse events that were deemed not to meet the above definitions were excluded. Examples of these were traumatic events that resulted in no injury and no pain or patients who had facial cosmetic surgery. No differences in the rates of these excluded events were present between groups.

Two authors further categorized the adverse events as medical or surgical related. Medical events were categorized by organ system and were further divided by timing into those from surgery to 6 weeks and those after 6 weeks. The early

medical adverse events were considered related or possibly related to the operative procedure. Late medical events occurring after 6 weeks following the surgery were categorized for this paper as not related to the procedure, the device, or disease state. The time frame chosen was arbitrary but clinically a meaningful time and consistent with a recent report on complications following total hip arthroplasty.<sup>8</sup> Examples were sinus infection, myocardial infarction, or urinary tract infection occurring after 6 weeks of surgery. Surgical related events were categorized as secondary to anesthesia, the approach, decompression, or the implants. Other surgeries possibly related to the spinal condition were reported separately including decompression of peripheral nerve entrapments, shoulder surgery, and lumbar spine surgery.

### Statistical Analysis

Rates of adverse events between groups were compared using  $\chi^2$  analysis. A *P* value less than 0.05 was chosen as statistically significant. Statistical results are given on a by patient basis, not on a number of occurrences basis. If a patient had more than one event in a similar category then it was scored one time, whereas if the event was a different type then it was analyzed as a separate event.

The data and analyses reported within this study may not always agree with those reported in the FDA Pre-market approval submission. The authors used the same database but analyzed the data in what they felt as a more clinically meaningful manner, which may not have been consistent with the FDA policy. The present analysis was in more detail and used a different criterion (6 weeks) for determining whether or not the event was surgically related. For example, the data reported here were sometimes separated into more columns so the individual complications (such as “other pain” and hematoma) could be further examined and the data analyzed in more detail. Also, the “clearly not meaningful complications” such as those occurring after a postimplantation facelift surgery or being hit with a golf ball were excluded from the analysis unless they affected the clinical result. This was done to give the reader a clearer view of how adverse events from the 2 types of surgery compared in a clinically meaningful manner.

## ■ Results

### Baseline Demographics

No differences in baseline demographics (such as age, sex, height, weight, smoking history, and percent workmen’s compensation, or severity of disease as measured by Neck Disability Index score and pain VAS) were present between groups, *P* > 0.05.

### General Medical Events Unrelated to the Operation

Medical events occurring 6 weeks or more after surgery were identified in 35.1% and 31.2% of investigational and control patients, respectively, Table 1. This difference was statistically significant. The majority of the differences between groups were from more frequent gastrointestinal and genitourinary events in the investigational group. These did not seem to be related to the device or cervical spine disease.

None of the investigational patients died during the follow-up period while in the control group, one death (0.5%) occurred following a motor vehicle crash unre-

**Table 1. General Medical Events That Occurred Between 6 Week and 3 Year and Were Thought to be Unrelated to the Operation**

	WHO Grade						P
	Bryan (n = 242)			Control (n = 221)			
	1-2	3-4	Total	1-2	3-4	Total	
Cardiovascular	5	3	8	5	3	9	
Central nervous system	10	4	14	9	2	11	
Dermatologic/allergy	1	0	1	0	0	0	
Endocrine	6	2	8	6	1	7	
Gastrointestinal	6	7	14	2	2	4	
Genitourinary	2	6	7	2	1	3	
Hematologic	2	0	0	0	0	0	
Infection	4	3	7	4	4	9	
Musculoskeletal	12	9	18	10	6	16	
Psychiatric	4	2	6	3	0	3	
Pulmonary	0	1	0	2	2	6	
Cancer	0	2	2	0	0	0	
Death	0	0	0	0	1	1	
<b>Total</b>	<b>52 (21.5%)</b>	<b>39 (16.1%)</b>	<b>85 (35.1%)</b>	<b>43 (19.5%)</b>	<b>22 (10.0%)</b>	<b>69 (31.2%)</b>	<b>0.049</b>

Significantly more events occurred in the investigational patients (primarily gastrointestinal and genitourinary).

lated to his cervical spine. The mortality rate between the 2 groups was not statistically significant.

Two patients (0.8%) receiving the investigational device were diagnosed with cancer in the postoperative period. Neither cancer was deemed to be related to the study treatment. One patient was diagnosed with a metastatic, neuroendocrine carcinoma of the duodenum approximately 7 months following the operation. The second patient was diagnosed with a 2 mm papillary carcinoma of the thyroid. Before enrollment in the study, the patient was known to have a cystic mass on the thyroid. Four weeks following the study operation, the patient complained of difficulty swallowing and the patient was eventually referred for removal of the cystic mass. The rate of cancer between the 2 groups was not statistically significant. Another patient in the investigational

group had a miscarriage, which was felt to be unrelated to the device or cervical spine surgery.

#### **Medical Events Possibly or Directly Related to the Operation**

Medical events occurring within 6 weeks of surgery were present in 14.9% and 15.4% of investigational and control patients, respectively, Table 2. This difference was not statistically significant. The overall (early and late) rate of medical adverse events was similar in the 2 treatment groups,  $P > 0.05$ .

#### **Adverse Events Related to the Operation**

Overall, more adverse events occurred in the investigational group, 33.9% versus 29.0%. These were related to more superficial wound infections, dysphagia and cardiovascular events.

**Table 2. Medical Events Occurring Within 6 Week of Index Surgery**

	WHO Grade						P
	Bryan (n = 242)			Arthrodesis (n = 221)			
	1-2	3-4	Total	1-2	3-4	Total	
Cancer	0	0	0	0	0	0	
Cardiovascular	5	0	5	0	0	0	
Gastrointestinal	4	2	6	1	4	5	
Infection	4	0	4	3	0	3	
Dermatologic/allergy	6	0	6	4	0	4	
Psychiatric	0	0	0	3	1	4	
Pulmonary	5	1	6	3	4	7	
Genitourinary	0	0	0	0	0	0	
Musculoskeletal	1	0	1	4	0	4	
Endocrine	1	0	1	3	0	3	
Central nervous system	5	2	7	2	2	4	
Death	0	0	0	0	0	0	
<b>Total</b>	<b>31 (12.8%)</b>	<b>5 (2.1%)</b>	<b>36 (14.9%)</b>	<b>23 (10.4%)</b>	<b>11 (4.9%)</b>	<b>34 (15.4%)</b>	<b>0.07</b>

These occurred perioperatively or up to 6 wk from the operation. No difference was present between the 2 groups.

**Table 3. Surgical Related and Neurologic Adverse Events**

	Bryan (n = 242)	Control (n = 221)	P
Anesthesia			0.15
Airway/re-intubation	2	3	
Eye abrasion/symptoms	4	0	
Forearm compartmental syndrome	0	1	
Oral cavity injury	2	1	
Total	8	5	
Medical			0.13
Allergic reaction	6	1	
Cardiovascular	6	0	
Central nervous system	2	2	
Endocrine	1	2	
Gastrointestinal	4	4	
Genitourinary	0	1	
Infection	3	1	
Musculoskeletal	0	1	
Psychiatric	0	2	
Pulmonary	3	6	
Total	25	20	
Technical			0.15
Drill failure	1	0	
Malposition	1	0	
Technical problems	0	1	
Wound contamination	0	1	
Total	2	2	
Surgical			0.06
Cerebral spinal fluid leak	2	3	
Superficial wound infection	7	1	
Deep wound infection	0	0	
Intraoperative bleeding	2	2	
Hematoma	2	3	
Hematoma evacuation	0	1	
Dysphagia/dysphonia	26	16	
Total	39	30	
Acute neurologic change			0.15
Sensory in upper extremities	5	4	
Motor in upper extremities	1	1	
Myelopathy	0	1	
Spinal cord injury	0	1	
Sensory in lower extremities	2	0	
Total	8	7	
<b>Total</b>	<b>82 (33.9%)</b>	<b>64 (29.0%)</b>	<b>0.023</b>

Overall more events occurred in the investigational group primarily from higher incidence of dysphagia, cardiac related events and more superficial wound infections. None of these were rated above WHO grade 2.

### Anesthesia Related

Anesthesia related events were similar between groups, Table 3. However, more patients developed acute airway and pulmonary complications in the control group. Four patients in the investigational group had corneal abrasions or eye discharge and none in the control group.

### Acute Medical Events

No differences occurred in acute medical events between groups. All allergic reactions occurred in the investigational group but were routine and not believed related to the implant.

### Technical Events

One patient having an arthroplasty had to be revised for prosthetic malposition without long-term sequelae. In another arthroplasty patient, the mill to create a cavity in the endplate malfunctioned without harm to the patient.

In the control group, one patient experienced a technical difficulty during plate fixation and one patient had inadvertent wound contamination without infectious complication.

### Surgical

More operative-related adverse events occurred in the investigational group; primarily as a result of a higher incidence of dysphagia/dysphonia and superficial wound infections. Twenty-four patients in the investigational group compared to 16 patients in the control group had at least one complaint of dysphagia/dysphonia. All dysphagia or dysphonia complaints were graded WHO severity 1 or 2. It was not assessed if these symptoms persisted at long-term follow-up. Seven patients in the investigational group had superficial wound infection treated with oral antibiotics. None of these patients had additional operations for chronic infections, although in one case the prosthesis was removed and fusion performed but intraoperative cultures were negative. The cerebrospinal fluid leaks occurred during decompression and not during instrumentation in either group. Two patients in each group had lacerations of large neck veins requiring ligation without sequelae.

Two serious complications occurred in the arthrodesis group. One patient required emergency evacuation of a hematoma and one patient had a spinal cord injury as a result of surgery. No events of this type occurred in the investigational patients.

### Neurologic Events

Perioperative adverse neurologic changes occurred in 8 investigational and 7 control patients, Table 3. In the disc group, 5 patients had upper extremity sensory disturbance, one had upper extremity motor weakness, and 2 experienced sensory changes in the lower extremities without myelopathy or cord injury. In the control group, 4 patients had upper extremity sensory disturbance, one had upper extremity weakness, one a spinal cord injury, and one patient had developed new myelopathic symptoms.

The reporting of adverse neurologic symptoms at all time periods is shown in Table 4. Postoperative upper extremity sensory disturbances (such as parathesia, hypesthesia, or anesthesia) occurred in 20.7% and 18.1% of investigational and control patients, respectively. The difference between groups was not statistically significant. New upper extremity motor deficits were seen in 2.1% and 1.8% of investigational and control patients respectively. Again, no statistical difference was present between groups.

New or worsened myelopathy or spinal cord injury was defined as sensory disturbances in the lower extremities, bilateral upper extremity signs and symptoms, or gait disturbance. No differences were observed between the two groups.

### WHO Grade 3 and 4 Events

Significantly more WHO Grade 3 or 4 events occurred in the control compared with the investigational group (Ta-

**Table 4. Adverse Neurologic Events up to 3 Years After Surgery**

	WHO Severity						P
	Bryan (n = 242)			Arthrodesis (n = 221)			
	1-2	3-4	Total	1-2	3-4	Total	
Neurologic							
Sensory in upper extremities	35 (14.5%)	2 (0.8%)	37 (15.3%)	34 (15.4%)	2 (0.9%)	36 (16.3%)	0.14
Upper extremity motor loss	5 (2.1%)	2 (0.8%)	7 (2.5%)	7 (3.2%)	1 (0.4%)	8 (3.6%)	0.12
Myelopathy	1 (0.4%)	0	1 (0.4%)	3 (1.4%)	1 (0.4%)	4 (1.8%)	
Sensory in lower extremities	6 (2.5%)	0	6 (2.5%)	1 (0.4%)	0	1 (0.4%)	0.002
<b>Total</b>	<b>47 (19.4%)</b>	<b>4 (1.6%)</b>	<b>50 (20.7%)</b>	<b>45 (20.4%)</b>	<b>4 (1.8%)</b>	<b>49 (22.2%)</b>	<b>0.125</b>

Sensory includes any complaints of paresthesia, hypesthesia, or anesthesia in upper extremities. Motor changes reflect new or worsened motor function. No differences were present between groups.

ble 5). This was primarily due to more control patients having reoperations for treatment of persistent symptoms and pseudarthrosis.

**Reoperations**

Reoperations on the cervical spine occurred in 5.4% of investigational and 7.7% of control patients (Table 6). This difference was statistically significant. The total number of cervical spine reoperations was also statistically greater in the control group, 21 *versus* 14. Overall reoperations were performed at the index level 12 times and at an adjacent level 11 times in the control group compared with 7 and 8 times in the investigational group. Four patients in the control group and one in the investigational group had more than one reoperation.

Operations occurring in the upper extremity and the thoracolumbar spine are reported as they may have been confounding variables in the diagnosis, outcomes, and the need for further surgical treatment. Although operations in the upper extremity and thoracolumbar spine were frequent, no significant difference was present between groups (Table 6).

**Discussion**

Comprehensive investigations of adverse events following spinal surgery have been rarely performed. Mirza recently described an algorithm for assessing morbidity of lumbar spine surgery.<sup>9</sup> He postulated that the likelihood of an adverse event is a function of patient factors,

**Table 5. WHO Grade 3 and 4 Adverse Events**

	Bryan (n = 242)			Arthrodesis (n = 221)			P	
	Early ≤6 wk	Late >6 wk	Total	Early ≤6 wk	Late >6 wk	Total		
Medical								
Cardiovascular	0	3	3	0	3	3	0.09	
Central nervous system	2	4	6	2	2	4		
Endocrine	0	2	2	0	1	1		
Gastrointestinal	2	7	9	4	2	6		
Genitourinary	0	6	6	0	1	1		
Infections	0	2	2	0	3	3		
Musculoskeletal	0	8	8	0	7	7		
Psychiatric	0	2	2	1	1	2		
Respiratory	1	0	1	4	1	5		
Cancer	0	2	2	0	0	0		
Death	0	0	0	0	1	1		
<b>Total</b>	<b>5 (2.1%)</b>	<b>36 (14.9%)</b>	<b>41 (17.0%)</b>	<b>11 (5.0%)</b>	<b>22 (10%)</b>	<b>33 (14.9%)</b>		
Surgical related								
Technical	2	0	2	1	0	1		0.12
Hematoma	0	0	0	1	0	1		
Prolonged anesthesia	1	0	1	0	0	0		
<b>Total</b>	<b>3 (1.2%)</b>	<b>0</b>	<b>3 (1.2%)</b>	<b>2 (0.9%)</b>	<b>0</b>	<b>2 (0.9%)</b>		
Outcome related								
Severe neck/arm symptoms	5	11	16	6	22	28	0.0003	
Thoracolumbar pain	1	9	10	2	6	8		
Headaches	1	2	3	2	1	3		
Pseudoarthrosis	0	0	0	0	6	6		
<b>Total</b>	<b>7 (2.9%)</b>	<b>22 (9.1%)</b>	<b>29 (12.0%)</b>	<b>10 (4.5%)</b>	<b>35 (15.8%)</b>	<b>45 (20.4%)</b>		
<b>Total grade 3 and 4</b>	<b>15 (6.2%)</b>	<b>58 (24.0%)</b>	<b>73 (30.2%)</b>	<b>23 (10.4%)</b>	<b>57 (25.8%)</b>	<b>80 (36.2%)</b>	<b>0.012</b>	

Statistical results are given on a patient basis.

**Table 6. Reoperations Following Cervical Arthroplasty or Arthrodesis**

	Bryan (n = 242)		Arthrodesis (n = 221)		P
	Patients	Total Operations	Patients	Total Operations	
Cervical spine					
Index	6	6	8	10	0.056
Adjacent	6	7	7	9	0.08
Both levels	1	1	2	2	
Total	13 (5.4)	14 (5.8)	17 (7.7)	21 (9.5)	0.045
Thoracolumbar spine					
Upper extremity	10 (4.1)	10 (4.1)	8 (3.6%)	9 (4.1)	0.13
Shoulder	2	4	6	7	
Carpal tunnel	4	4	2	2	
Ulnar nerve transposition	1	1	1	1	
Thoracic outlet release	0	0	1	1	
Total	7 (2.9)	9 (3.7)	10 (4.8)	11 (5.0)	0.56
<b>Total</b>	<b>17 (7.0)</b>	<b>19 (7.8)</b>	<b>18 (8.1)</b>	<b>20 (9.0)</b>	<b>0.15</b>

All values inside parentheses indicate percentages.

The sum total of reoperations at treated and adjacent levels are greater than overall total as some patients had surgery at both index and treated level.

disease attributes and treatment intensity. Additionally, he recommended that adverse events be categorized by type, their severity assessed, and the effect on outcome measured. Finally, the etiology or cause of the adverse event should be independently determined. Only using independent assessments and a quantitative system can the true significance of adverse events be determined and then the effectiveness of abatement strategies measured. His model was reliable for lumbar spine procedures, but has not been evaluated for the cervical spine. We examined adverse events and categorized them similar to Mirza.<sup>9</sup> We did not attempt to determine the etiology although this data were reported by the clinical research coordinator. We had no way to independently verify this and therefore we chose not to include that information in our study. The effect of having an adverse event on outcome will be examined in a separate study.

The severity of adverse events is rarely reported in spine literature.<sup>10-12</sup> We used the WHO method, which was devised to assess morbidity of cancer treatments.<sup>7</sup> In their guidance document, they noted that adverse events will occur that are not covered in their examples and that criteria for these should be established. This was done *a priori* in this study. Our method was similar to that recently reported by Parvisi *et al* who examined major complications following total joint arthroplasty.<sup>8</sup> They defined major complications as those that were life threatening, required complex medical intervention or surgical treatment, or were associated with temporary or permanent disability. These are identical to the WHO categories 3 and 4 as used in the current study. They similarly categorized adverse events into systemic and local, which corresponds to our medical and surgical groupings. Furthermore, they concluded that most perioperative complications required a minimum of 6 weeks follow-up, which is identical to how we divided the medical morbidities into late unrelated and early possibly related groups.

Wang reported the complications and mortality following cervical spine operations for degenerative conditions from 1991 to 2001.<sup>10</sup> The study used ICD-9 codes from an administrative database of discharges from over 1000 hospitals in the United States including over 932,000 admissions. Overall, the hospital mortality for treatment of cervical spine disease was 0.14%. They found a 3.9% complication rate and 0.14% mortality. Risk factors were age greater than 74, myelopathy, multilevel disease, and posterior or anterior-posterior approaches. Because the definitions of complications are different, and they are likely underreported in the administrative database, we cannot compare results. Many of the risk factors identified by Wang were not present in the majority of our patients enrolled in this randomized control study.

The present study was undertaken to evaluate the safety of a new device by comparing adverse events between disc arthroplasty and anterior cervical arthrodesis as part of the premarket approval process monitored by the Food and Drug Administration. Safety is a critical component of this process and therefore the requirements to report all adverse occurrences are stringent, even though they may not seem to have any relationship to the drug or device being evaluated. This is appropriate as there may be occurrences that are not anticipated that only can be identified through a comprehensive compilation of all such occurrences. An example is the identification of cardiac valvular insufficiency associated with diet medications.<sup>13</sup> In this study, we are reporting both medical and surgical adverse events that occurred to patients, including those which were unrelated, possibly related, or directly related to surgery. These events included those associated with poor outcome or the requirement for additional treatment or monitoring.

The results demonstrate equal safety of the Bryan Cervical Disc arthroplasty and arthrodesis using an anterior cervical plate and allograft for treatment of single-level

radiculopathy or myelopathy. Total medically related events, which the authors felt to be unrelated to surgery, occurred equally between groups. Similarly, although differences between medical events related to surgery were present between groups, these were not severe and had no long-term consequences.

Surgically related events were more common in the investigational group primarily from dysphagia and superficial wound infections. Higher incidences of dysphagia may be from longer operating times, the use of a special frame, which is attached to the operating table, a higher sensitivity of researchers in reporting this in the experimental group, or a true difference between groups. Unfortunately, assessment of these symptoms was not standardized and was most likely inconsistently reported.<sup>14</sup> All dysphagia symptoms were less severe (rated WHO Grade 1 or 2). It is unknown if these symptoms were different between groups at 24 months. No differences between groups occurred in neurologic complications with the majority being sensory disturbances in both groups. The majority occurred after 6 weeks, and therefore were likely related to outcome or alternative diagnosis such as peripheral nerve entrapment than directly attributable to the index operation. Only one major spinal cord injury occurred and this was in the control group. Four patients in the investigational group had perioperative corneal abrasions or eye discharge. We are aware of no theoretical difference in risk of such injury in arthroplasty patients. This demonstrates the importance of careful anesthesia care of the eyes before draping and maintaining protection during the procedure. None of these events had any long-term consequences.

The more serious WHO Grade 3 or 4 adverse events were more common in the control group. These were largely from the need for treatment of pseudarthrosis or recurrent symptoms. Overall, cervical spine reoperations were significantly different between groups. This was true for both the treated and for the adjacent levels. The overall reoperation rate at adjacent levels at 2 years in the control group was similar to that reported by Hili-brand.<sup>15</sup>

Our results are difficult to compare to historical controls as they are more comprehensive, have a high percent of follow-up at 2 years, and were concurrently obtained. Most of the adverse events we are reporting did not result in harm to the patient and in most studies would not have been reported. These data should provide a good benchmark from which to compare future studies. Other studies are based on administrative databases, which likely under represent adverse events and are subject to miscoding.<sup>10,11</sup>

We reported an outcome related adverse event defined as patients having further surgery for symptoms that may have been related to their initial presentation. These include release of entrapment syndrome, shoulder surgery, and lumbar surgery. High rates of these procedures occurred in both groups. Despite strict inclusion and exclusion criteria, the high rate of additional surgeries in

both groups is worrisome, indicating that surgeons should be comprehensive in their preoperative assessment no matter what surgical procedure is being contemplated. It also confirms that spine pathology may occur in patients having a systematic degenerative process, alterations in pain neurophysiology, or who have abnormal biopsychosocial factors making persistent symptoms more likely.

## ■ Conclusion

This prospective randomized study demonstrated small differences in adverse medical events between the Bryan Cervical Disc arthroplasty and arthrodesis groups. More surgically related adverse events occurred in the investigational group, mostly related to more complaints of dysphagia and more superficial wound infections. However, the more serious WHO Grade 3 and 4 events and the only severe neurologic injury occurred in the control group. While the rate of device-related complications of anterior cervical patients was low in both treatment groups, the arthrodesis patients had more serious complications and more additional surgical procedures. Thus, we believe this study demonstrates that the overall safety was clinically similar between the investigational and control groups.

## ■ Key Points

- In a randomized controlled study, adverse events were categorized and graded following cervical decompression and fusion or arthroplasty.
- Comparison between fusion and arthroplasty showed minimal clinical differences in adverse events between groups.
- Both the Bryan cervical disc replacement and anterior cervical fusion are safe procedures with a low incidence of severe adverse events related to the procedure.

## References

1. Bohlman HH, Emery SE, Goodfellow DB, Jones PK. Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathy. Long-term follow-up of one hundred and twenty-two patients. *J Bone Joint Surg Am* 1993;75:1298–307.
2. Edwards CC, Karpitskaya Y, Cha C, Heller JG, Laurysen C, Yoon ST, et al. Accurate identification of adverse outcomes after cervical spine surgery. *J Bone Joint Surg Am* 2004;86-A(2):251–6.
3. Rampersaud YR, Moro ER, Neary MA, White K, Lewis SJ, Massicotte EM, et al. Intraoperative adverse events and related postoperative complications in spine surgery: implications for enhancing patient safety founded on evidence-based protocols. *Spine* 2006;31:1503–10.
4. Goffin J, Van Calenbergh F, van Loon J, Casey A, Kehr P, Liebig K, et al. Intermediate follow-up after treatment of degenerative disc disease with the Bryan Cervical Disc Prosthesis: single-level and bi-level. *Spine* 2003;28:2673–8.
5. Anderson PA, Sasso RC, Rouleau JP, Carlson CS, Goffin J. The Bryan Cervical Disc: wear properties and early clinical results. *Spine J* 2004;(4):3035–9S.
6. Hains F, Waalen J, Mior S. Psychometric properties of the neck disability index. *J Manipulative Physiol Ther* 1998;21:75–80.
7. World Health Organization. *Toxic effects. WHO Handbook for Reporting Results of Cancer Treatment. Offset Publication No. 48.* Geneva Switzerland: World Health Organization; 1979:14–22.

8. Parvizi J, Mui A, Purtill JJ, Sharkey PF, Hozack WJ, Rothman RH. Total joint arthroplasty: when do fatal or near-fatal complications occur? *J Bone Joint Surg Am* 2007;89:27–32.
9. Mirza SK, Deyo RA, Heagerty PJ, Turner JA, Lee LA, Goodkin R. Towards standardized measurement of adverse events in spine surgery: conceptual model and pilot evaluation. *BMC Musculoskelet Disord* 2006;7:53.
10. Wang MC, Chan L, Maiman DJ, Kreuter W, Deyo RA. Complications and mortality associated with cervical spine surgery for degenerative disease in the United States. *Spine* 2007;32:342–7.
11. Romano PS, Campa DR, Rainwater JA. Elective cervical discectomy in California: postoperative in-hospital complications and their risk factors. *Spine* 1997;22:2677–92.
12. Bertalanffy H, Eggert HR. Complications of anterior cervical discectomy without fusion in 450 consecutive patients. *Acta Neurochir (Wien)* 1989;99:41–50.
13. Ryan DH, Bray GA, Helmcke F, Sander G, Volaufova J, Greenway F, et al. Serial echocardiographic and clinical evaluation of valvular regurgitation before, during, and after treatment with fenfluramine or dexfenfluramine and mazindol or phentermine. *Obes Res* 1999;7:313–22.
14. Bazaz R, Lee MJ, Yoo JU. Incidence of dysphagia after anterior cervical spine surgery: a prospective study. *Spine* 2002;27:2453–8.
15. Hilibrand AS, Carlson GD, Palumbo MA, Jones PK, Bohlman HH. Radiculopathy and myelopathy at segments adjacent to the site of a previous anterior cervical arthrodesis. *J Bone Joint Surg* 1999;81A(4):519–28.