Computed Tomography (CT) Scan Assessment of Paravertebral Bone After Total Cervical Disc Replacement: Prevalence, Temporal Relationships, and the Effect of NSAIDs

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Study Design

This is a retrospective, cross-sectional computed tomography (CT) scan analysis of paravertebral bone following BRYAN® Cervical Disc replacement.

Summary of Background Data

Despite favorable clinical outcomes at two-year follow-up of the BRYAN® Cervical Disc replacement, some random computed CT scans have demonstrated the unexpected appearance of varying degrees of paravertebral ossification. Literature regarding the presence of heterotopic bone following intervertebral disc replacement remains scant.

Introduction

The advent of intervertebral disc prostheses is the natural consequence of the growing awareness of the shortcomings of spinal arthrodesis. Fusion of a spinal motion segment not only restricts range of motion, but also has the potential to accelerate adjacent segment disc degeneration by altering the physiologic stresses applied to these regions.[1,2] The primary goal of total cervical disc replacement therefore is to maintain motion and function at an operated disc level, without substantially altering the biological or biomechanical milieu of the native spine.

Two-year follow-up of the BRYAN® Cervical Disc replacement indicated favorable clinical outcomes with preservation of motion at the index level.[3] Importantly, however random, late computed tomography (CT) scans of earlier cervical disc designs have shown the unexpected appearance of varying degrees of paravertebral ossification (unpublished data). Complete ankylosis was observed by Pointillart in 8 of 10 patients implanted with a different disc replacement device (Figure 1). Furthermore, heterotopic bone formation has recently been reported following total lumbar disc replacement[4] (Figure 2). The formation of bone at a motion segment that is attempting to keep moving presents a bit of a paradox. After decades of attempting to perfect the anterior cervical discectomy and fusion, we may find ourselves seeking to modulate an unwanted mechanism by which the spine resists increased motion. In light of the knowledge accumulated over the last 30 years regarding the prevention and treatment of heterotopic bone formation following total hip arthroplasty, a pro-active detailed investigation of paravertebral bone formation appeared warranted following cervical spinal arthroplasty.

Figure 1: Photograph of the prototype device implanted by Pointillart (A), which were noted to have spontaneously fused in 8 of 10 patients by two years post-op (B). (Courtesy of V. Pointillart, Bordeaux, France)

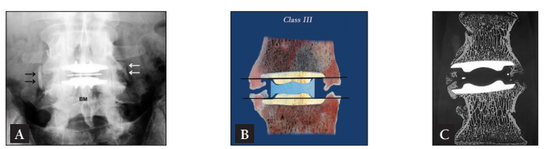

Figure 2: A reformatted CT scan image from a baboon implanted with a Link SB Charite device demonstrating neo-bone formation (A). The pathology is further revealed in this photomicrograph (B) and a microradiograph (C). (Courtesy of P. McAfee, Baltimore, MD)

Purpose

The purpose of this study therefore was to: 1) Devise a qualitative classification scheme for paravertebral bone following cervical disc replacement, 2) Investigate the amount and temporal relationship of paravertebral bone formation to length of follow-up, and 3) Ascertain if the use of post-operative non-steroidal anti-inflammatory drugs (NSAIDs) influenced the quantity of bone observed.

Materials and Methods

CT Scan Assessment

Post-operative thin section (typically 1.0 millimeter) computed tomography (CT) scans and reformations were obtained from 83 willing patients from the practices of 7 European surgeons experienced in the use of the BRYAN® Cervical Disc prosthesis. The operative technique has been previously described.[3] A panel of three masked observers (two fellowship-trained spinal surgeons and one neuroradiologist) evaluated each CT scan using a 5-point scoring system (0 to 4) devised to describe the amount of bone observed lateral or anterior to the operated disc space(s). **Grade 0** indicated no bone present beyond normal vertebral landmarks, whereas **Grade 4** indicated osseous fusion (continuous bridging bone) of the motion segment. Four scores were generated for each motion segment; one for each "corner" (e.g., inferior left and right of the cranial vertebra, and superior left and right of the caudal vertebra) as seen on coronal reformations (Figure 3). The highest grade for each level (0-4) from each reader was employed for subsequent analysis. Scores of 0, 1, and 2 were grouped as "Radiographically Insignificant" and scores of 3 and 4 were grouped as "Radiographically Signigicant" for calculations of prevalence and NSAID effects. Each panel member read each scan independently and the inter-observer variability was assessed. For each subject, the follow-up period from the surgery date until the time of the CT scan was recorded in days. The dose, duration, and NSAID prescribed, if any, for each patient was extracted from their medical records. The scans from subjects receiving a prescribed post-operative regimen of NSAIDs were assigned to the "treatment" group, whereas subjects who were not prescribed NSAIDs or who did not take their medication were assigned to the "control" group. Patients were excluded from the study if reformatted coronal-plane CT images were not available for review or were of such poor quality that they could not be reasonably analyzed.

Statistical Analysis

Figure 3: Schematic illustration of the authors' proposed radiographic scoring system for paravertebral bone formation following total cervical disc replacement.

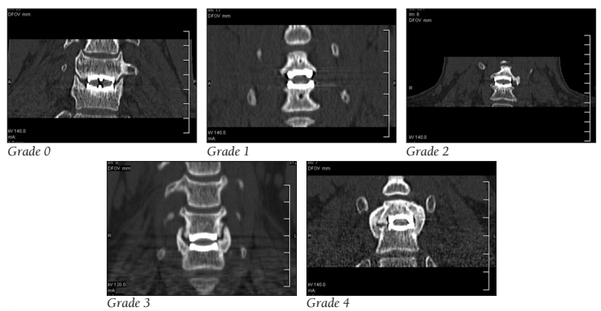

Figure 4: Sample coronal CT scan reformations corresponding to the authors' proposed radiographic scoring system for paravertebral bone formation following total cervical disc replacement.

All of the data was entered into STATISTICA software from STATSOFT (Tulsa, Oklahoma). Assessment of inter-observer reliability was performed using a correlation test. Maximum score for bone formation was plotted with regard to follow-up time. Relationships between NSAID use and paravertebral bone were investigated using ANOVA with Bonferroni's adjustment for multiple comparisons. Statistical significance was established at a P value less than 0.05.

Results

Sixty-four coronal views were available for interpretation, with 54 single-level (of the 64) and 10 two-level (of the 64) procedures. The follow-up interval ranged from 1 to 749 days. The inter-observer correlation coefficient was 0.7496. There was no statistically significant relationship between the length of follow-up and the maximum score ($r^2 = 0.02$). While longitudinal data was not available, the data suggest that if new bone was formed, it tended to be present within the first 100 post-operative days. Anterior bone scores of 4 were observed as early as 77 days post-operative (Figure 5a). Similar amounts of anterior bone were observed following one-level and two-level procedures, p=0.87.

When bone formation was grouped as "Radiographically Insignificant" (Score of 0, 1 or 2) versus "Radiographically Significant" (Scores of 3 or 4), less bone was observed among the NSAID treatment group subjects compared to controls (p=0.00085) (Figure 5b). The effect was less striking when analyzed separately for COX-1 (p=0.173) and COX-2 (p=0.002) specific drugs (Figure 5c).

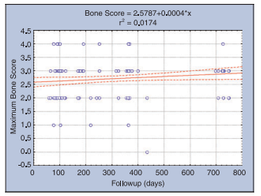

Figure 5a

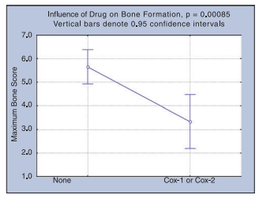

Figure 5b

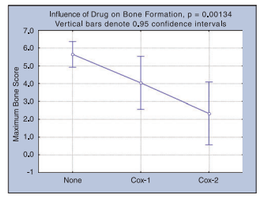

Figure 5c

Discussion

As the primary objective of intervertebral disc replacement is to maintain physiologic range of motion and biomechanics, the existence of bridging bone anterior to the implant could potentially dramatically impact this function. Published data regarding heterotopic or paravertebral bone formation following disc arthroplasty remain scant. Therefore, a detailed, pro-active investigation of this phenomenon would seem critical prior to further prospective, randomized trials. We believe that the data presented in this study met the objectives which were to: Devise a reliable classification scheme for paravertebral bone formation, investigate the prevalence and temporal relationship of anterior paravertebral bone with length of follow-up, and establish the potential role of non-steroidal anti-inflammatory medications in suppressing bone formation following BRYAN® Cervical Disc replacement.

The inter-observer correlation coefficient of 0.7496 indicates a moderate level of consistency between observers, and validates this observational method. A correlation coefficient of 1.0 is not expected, as the scores are non-continuous data. Whether the five-part (0-4) classification system presented here can be further simplified remains open to further evaluation. We chose to categorize bone formation that did not cross the disc space (Scores of 0, 1, or 2) as "Radiographically Insignificant" because it seemed unlikely that these small amounts of bone would have any clinical impact in comparison to bone which was observed to be either partially or completely bridging the disc space (Scores of 3 or 4).

There was no observed relationship between the length of follow-up and the maximum amount of anterior bone ($r^2 = 0.02$). If bone was observed anterior to the implant, it tended to be present in the first 100 post-operative days. These data would suggest that neo-bone formation in these subjects did not progress with time. We qualify this conclusion, however, because serial CT scans for the same patients over time were not available in this retrospective analysis.

The finding that significantly (p=0.00085) less bone was observed among patients treated with post-operative NSAIDs compared to the control group suggests that these medications have a suppressive effect. This is perhaps not surprising given the known prophylactic effects of indomethacin and other non-steroidal anti-inflammatory medications on heterotopic ossification after total hip replacement or acetabular fractures.[5] Importantly, however, the use of NSAIDs following hip and acetabular surgery is aimed at patients with known risk factors such as the previous development of heterotopic ossification, ankylosing spondylitis, revision surgery, and surgical exposures requiring large amounts of muscle dissection.[5] While post-operative NSAID use would seem to be an appropriate means of prophylaxis in cervical disc replacement, this decision needs to be based not only upon the potential benefits, but also on their associated costs and well-known clinical risk profile (e.g., gastro-intestinal bleeding). A clearer understanding of the mechanism of paravertebral bone formation will likely yield the most rationale strategies of its prevention.

Conclusion

Based on the radiographic findings reported here, the authors recommend that future clinical investigations employ serial CT scans to assess bone formation in study subjects over their pre-operative and follow-up intervals. Correlation of paravertebral bone formation with patient outcomes, range of motion, and adjacent segment affects will help establish the clinical relevance of this phenomenon. Our data supports the need for a placebo-controlled, randomized clinical trial of perioperative NSAID use after total cervical disc replacement.

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Figure 1 images courtesy of Vincent Pointillart, Bordeaux, France.

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Disclosure

Note that the BRYAN® Total Cervical Disc replacement is not commercially available for clinical use in the United States, Japan or Korea. An Investigational Device Exemption (IDE) study that is regulated by the Food and Drug Administration is underway in the United States for single level applications. (CAUTION – Investigational Device. Limited by Federal [United States] law to investigational use.)

The senior author (JGH) hereby discloses a potential conflict of interest based on his consulting and other services provided to Medtronic Sofamor Danek USA, Inc. (Memphis, TN).