THE PREVALENCE OF HETEROTOPIC OSSIFICATION AMONG PATIENTS AFTER CERVICAL DISK ARTHROPLASTY AT 5 YEARS

PREVALÊNCIA DE OSSIFICAÇÃO HETEROTÓPICA ENTRE PACIENTES CINCO ANOS DEPOIS DE ARTROPLASTIA DE DISCO CERVICAL

PREVALENCIA DE OSIFICACIÓN HETEROTÓPICA EN PACIENTES CINCO AÑOS DESPUÉS DE ARTROPLASTIA DE DISCO CERVICAL

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ABSTRACT

Objective: This study was designed to evaluate the prevalence and grading of heterotopic ossification (HO) at five years, among patients after cervical disk arthroplasty (CDA). Methods: The CDA procedure with Activ C and M6-C prostheses was performed on 127 patients. The mean age of the cohort of patients was 38.4 years (range 18-49). The mean follow-up time was 58.4 months, ranging from 51 to 66 months. Results: Grade 1 ossifications were present in 11 (8.6 %) levels. A total of 45 (35.4 %) segments showed grade 2 HO. HO that led to restrictions in range of motion were present in 13 (10.2 %) cases. Five years after surgery, 9 (7.0 %) patients with grade 4 ossifications were found only in the M6-C artificial disk prosthesis group. In the analysis of patient survival following the occurrence of HO, all patients showed median survival of 28.3±5.6 months. The group that received the Activ C artificial disk prosthesis showed statistically longer survival (49.5±7.8 months) than the M6-C disk group. Conclusions: In our study 61.4% of patients exhibited HO after a mean follow-up of 58.4 months. In the analysis of patient survival after HO, all patients showed median survival of 28.3±5.6 months. The group that received the Activ C artificial disk prosthesis showed statistically longer survival (49.5±7.8 months) than the M6-C disk group. ***Level of evidence III; Cross-sectional Observational Study.***

Keywords: Diskectomy; Arthroplasty; Heterotopic Ossification; Prevalence; Prosthesis.

RESUMO

Objetivo: Este estudo foi desenhado para avaliar a prevalência e o grau de ossificação heterotópica (HO) entre pacientes depois de cinco anos de artroplastia de disco cervical (CDA). Métodos: O procedimento de CDA com próteses Activ C e M6-C foi realizado em 127 pacientes. A média de idade da coorte de pacientes foi de 38,4 anos (variação de 18 a 49). O tempo médio de acompanhamento foi de 58,4 meses, variando de 51 a 66 meses. Resultados: Ossificações de grau 1 foram encontradas em 11 (8,6%) níveis. Um total de 45 (35,4%) segmentos apresentou HO de grau 2. As HO que levaram à restrição da amplitude de movimento foram verificadas em 13 (10,2%) casos. Cinco anos depois da cirurgia, 9 (7,0%) pacientes com ossificações de grau 4 foram vistas apenas no grupo de prótese do disco artificial M6-C. Na análise de sobrevida depois da ocorrência de HO, todos os pacientes tinham sobrevida mediana de 28,3 ± 5,6 meses. O grupo que recebeu a prótese de disco artificial Activ C tinha sobrevida estatisticamente maior (49,5 ± 7,8 meses) do que a do grupo com disco M6-C. Conclusões: Em nosso estudo, 61,4% dos pacientes apresentaram HO no acompanhamento médio de 58,4 meses. Na análise de sobrevida d*epois de ocorrência de HO, todos os pacientes tinham sobrevida mediana de 28,3 ± 5,6 meses. O grupo que recebeu a prótese de disco artificial Activ C teve sobrevida estatisticamente maior (49,5 ± 7,8 meses) do que o grupo de disco M6-C.* ***Nível de evidência III; Estudo Observacional Transversal.***

Descritores: *Discotomia; Artroplastia; Ossificação Heterotópica; Prevalência; Próteses.*

RESUMEN

Objetivo: Este estudio fue diseñado para evaluar la prevalencia y el grado de osificación heterotópica (HO) entre pacientes después de cinco años de artroplastia de disco cervical (CDA). Métodos: Se realizó el procedimiento de CDA con prótesis Activ C y M6-C en 127 pacientes. La edad promedio de la cohorte de pacientes fue de 38,4 años (rango 18-49). El tiempo medio de seguimiento fue de 58,4 meses, con un rango de 51 a 66 meses. Resultados: Se encontraron osificaciones de grado 1 en 11 (8,6%) niveles. Un total de 45 (35,4%) segmentos presentaron HO de grado 2. Las HO que llevaron a restricciones en el rango de movimiento estuvieron presentes en 13 (10,2%) casos. Cinco años después de la cirugía, se observaron 9 (7,0%) pacientes con osificaciones de grado 4 sólo en el grupo de prótesis de disco artificial M6-C. En el análisis de sobrevida tras la ocurrencia de HO, todos los pacientes presentaron una media de sobrevida de 28,3±5,6 meses. El grupo que recibió la prótesis de disco artificial Activ C presentó una sobrevida estadísticamente más larga (49,5±7,8

Study conducted at the Irkutsk State Medical University, Irkutsk, Russia.
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meses) que el grupo del disco M6-C. Conclusiones: En nuestro estudio el 61,4% de los pacientes presentaron HO en el seguimiento medio de 58,4 meses. En el análisis de sobrevida tras la ocurrencia de HO, todos los pacientes presentaron mediana de sobrevida de 28,3±5,6 meses. El grupo de prótesis de disco artificial Activ C tuvo una sobrevida estadísticamente más larga (49,5±7,8 meses) que el grupo de disco M6-C. ***Nivel de evidencia III; Estudio observacional transversal.***

Descriptores: *Discectomía; Artroplastia; Osificación Heterotópica; Prevalencia; Prótesis.*

INTRODUCTION

Anterior cervical diskectomy and fusion (ACDF) is the gold standard for surgical treatment of cervical degenerative disk disease, and has shown long-term clinical success.[1,2] In recent years, cervical disk arthroplasty (CDA) has become widely used in patients as a substitute for ACDF.[3] The introduction of CDA to treat cervical disk degenerative disease is based on the concept of preserving the patient's range of motion. Motion preservation most closely mimics the natural motion of the cervical spine, and CDA is believed to preserve the adjacent segments from degeneration over the long term, compared with ACDF.[4] Randomized controlled trials have reported good outcomes and high patient satisfaction after CDA.[5-7]

However, heterotopic ossification (HO) and spontaneous fusion after CDA have been reported, and maintenance of motion following arthroplasty can be hindered by the development of HO.[8] HO is defined as the formation of bone outside the skeletal system. It is a well-known phenomenon in the field of total hip or knee arthroplasty and immobilized the activity of patients after surgery.[9] McAfee et al.,[10] have already described and classified the phenomenon of HO in lumbar total disk arthroplasty. The rate of HO following CDA is unclear, but reported rates vary drastically, creating further debate and concern around the true rate and impact of HO. The long-term effects of HO resulting in unintended fusion have not been sufficiently studied.

The purpose of this study was to evaluate the prevalence and graduation of HO among patients after cervical disk arthroplasty at 5 years.

METHODS

Patient population

The CDA procedure with Activ C (B. Braun, Sheffield, UK) and M6-C (Spinal Kinetics, Sunnyvale, CA, USA) prostheses was performed from January 2009 to June 2011, on 127 patients, including 65 (51.1 %) women and 62 (48.8 %) men with symptomatic cervical disk degenerative disease but who had not responded to conservative treatment. All patients included in our study were below 50 years old. The mean age of the cohort of patients was 38.4 years (range 18-49). There were no statistically significant differences in baseline characteristics between patients with low- and high-grade HO. (Table 1)

Eligibility criteria and follow-up

The enrollment inclusion criterion was symptomatic cervical disk herniation at levels C3-C4 to C6-C7 with preserved mobility (> 30 and < 110) within 1 affected segment. The exclusion criteria were trauma, kyphotic deformity, ossification of the posterior longitudinal ligament, and instability of the cervical spine. Other exclusion criteria were advanced osteoporosis, rheumatoid arthritis, and ankylosing spondylitis (Bekhterev's disease). The mean follow-up time was 58.4 months, ranging from 51 to 66 months. The study protocol was approved by the local ethics committee, in accordance with the Declaration of Helsinki.[11]

Table 1. Baseline characteristics of the patients with low- and high-grade HO 5 years after CDA.

	Low-grade HO group (n = 56)	High-grade HO group (n = 22)	p
Mean age, years	39.2±7.3	38.6±6.6	0.81
Female sex, n (%)	11 (19.6 %)	16 (72.2 %)	0.07
Height, cm	173.5±11.3	175.5±11.2	0.26
Weight, kg	75.2±10.8	79.3±17.4	0.08
BMI*	25.4±2.5	25.7±3.8	0.74
Level operated C5-C6, %	16 (28.5 %)	12 (54.5 %)	0.19

*– The body mass index is weight in kilograms divided by the square of the height in meters.

Surgical procedure

After a standard microsurgical anterior Cloward's approach, the midline was marked under fluoroscopic control. Diskectomy and decompression were performed, and the segment was distracted and held in distraction by retaining screws. After testing the intervertebral disk height and width by fluoroscopy, appropriate prosthesis was implanted. Patients were asked to get off the bed 24 hours later. A neck collar was required to wear no > 1 week.

Radiological assessment

Cervical lateral radiographs obtained at scheduled time points before and after surgery were used to identify HO. (Figure 1) HO in some cases was confirmed using computed tomography (CT). (Figure 2) The HO was graded according to the McAfee et al. classification. Occurrence rate, occurrence-free period, location, and grade of HOs were investigated according to the different prosthesis types. The performance of the HO was observed by two independent spine surgeons.

Statistical analysis

Data analyses were conducted in Microsoft Office Excel 2016 and IBM SPSS 21. A significance level of 0.05 was adopted for all the tests. Statistical analysis was performed using the t test and Wilcoxon test.

RESULTS

In 49 (38.5 %) treated segments, no HO was detectable. Grade 1ossifications were present in 11 (8.6 %) levels. A total of 45

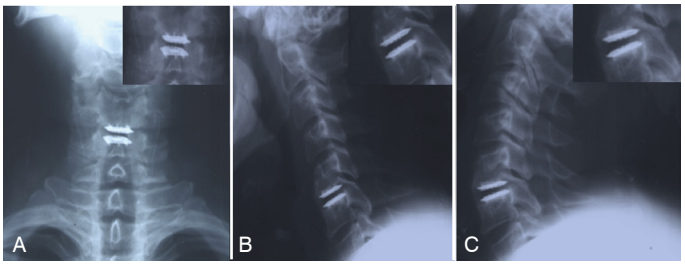

Figure 1. A 41-year-old male patient with C5-C6 intervertebral disk degenerative disease treated by CDA. Clear signs of HO grade III can be seen, with no significant reduction in motion of the prosthesis on flexion and extension at 5-year follow-up: A – frontal radiography, B – lateral radiography with flexion, C – lateral radiograph with extension.

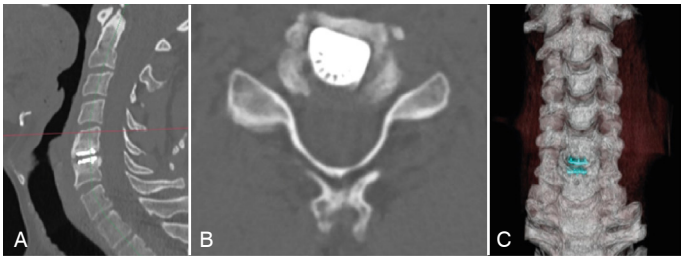

Figure 2. CT scans of HO grade III (previous clinical case): A – sagittal CT scan, B – axial CT scan, C – 3-dimensional CT scan.

(35.4 %) segments showed grade 2 HO. HO that led to restrictions of the range of motion were present in 13 (10.2 %) cases. Five-year postoperatively, 9 (7.0 %) patients with grade 4 ossifications were found only in the M6-C artificial disk prosthesis group.

Anterior ossification was more frequent than posterior, though the difficulty in detecting posterior ossification on plain radiographs should be considered. The distribution of the different grades of HO according to prosthesis type is shown in Table 2.

In the analysis of survival after HO, all patients showed median survival of 28.3±5.6 months. The Activ C artificial disk prosthesis group showed statistically longer survival (49.5±7.8 months) than the M6-C disk group (p=0.003). (Figure 3)

Table 2. Distribution of the different grades of HO according to the prosthesis type.

	Grade 1	Grade 2	Grade 3	Grade 4
Activ C	5 (3.9 %)	27 (21.3 %)	8 (6.3 %)	7 (5.5 %)
M6-C	6 (4.7 %)	18 (14.1 %)	5 (3.9 %)	2 (1.5 %)
All prostheses	11 (8.6 %)	45 (35.4 %)	13 (10.2 %)	9 (7.0 %)

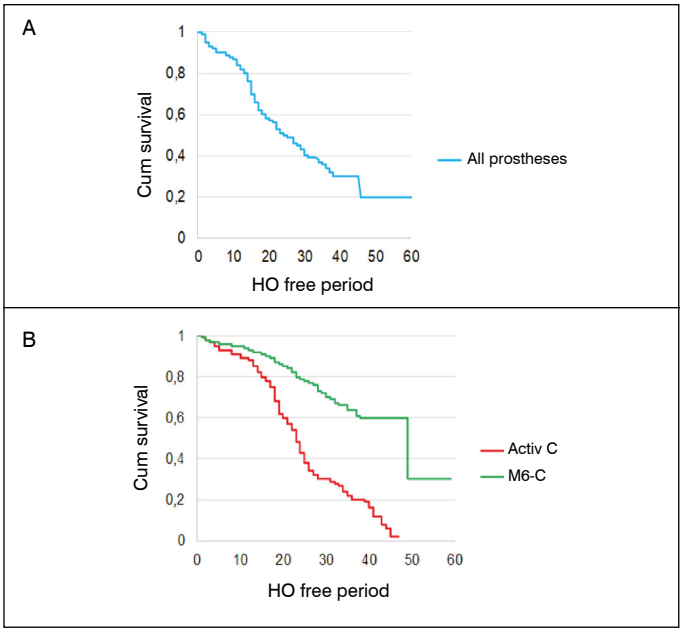

Figure 3. Analysis of survival after the occurrence of HO: A – all patients showed median survival of 28.3±5.6 months, B – the Activ C artificial disk prosthesis group showed statistically longer survival (49.5±7.8 months) than the M6-C prosthesis group (p=0.003).

DISCUSSION

It is common knowledge that the occurrence of HO is an inevitable postoperative complication after CDA, and can decrease the range of motion of the operated segment, which goes against the fundamental goal of inserting an artificial disk[12,13] Previous studies have reported various results in relation to the occurrence of HO. Lee et al.,[14] reported that 78.6 % patients exhibited HO after a mean follow-up of 43.4 months, but Leung et al.,[15] reported 17.8% of HO occurrence at 12 months of follow-up. In the study conducted by Yang et al.,[16] the prevalence of HO was 90%, but their results were based on a 30-year follow-up. In our investigation, only 38.5% of patients did not show any signs of HO after CDA. There is a hypothesis that HO is not a static, but rather a dynamic and progressive phenomenon that is affected by environment.[17] If this is the case, different follow-up times would definitely affect the final results.

The factors associated with HO occurrence have not been clarified. According to Nunley et al.,[18] odds ratios indicated that follow-up visit, male sex, and preoperative Visual Analogue Scale neck pain are related to the development of HO, whereas hazard ratios indicated male sex, obesity, endplate coverage, levels treated, and preoperative Visual Analogue Scale neck pain. Yi et al.,[19] found that the occurrence of HO varies according to the different types of prosthesis used. The Bryan Disk, which has the most unconstrained motion, showed significantly lower incidence of HO compared to other prostheses. The authors proposed that differences in design, biomechanical properties, and prosthesis-specific endplate articulation could contribute to the formation of HO. In our study, the M6-C prosthesis also showed significantly lower occurrence of HO compared to the Activ C artificial disk. Park et al.,[20] found that CDA influences the development of HO. In that study, two spine surgeons performed all the CDA procedures. However, they used different techniques for trimming the endplates; one spine surgeon used a fluted ball-type burr, while the other used a diamond-type burr. The study showed that the use of a fluted ball-type burr resulted in significantly higher levels of HO.

Several other possible causal factors of HO have been discussed, such as not treating patients with nonsteroidal anti-inflammatory drugs (NSAIDs) after different surgical procedures. The use of NSAIDs to prevent HO after total hip replacement has been reported previously.[21] The study protocols of clinical trials for CDA conducted by the US Food and Drug Administration included perioperative use of NSAIDs aimed at preventing the occurrence of HO. One study has reported a trend toward decreased HO formation in patients who used NSAIDs after CDA compared with those who did not, but the difference was not statistically significant.[22] NSAIDs were not used routinely in the present investigation, and further studies are needed to assess the role of NSAIDs in the development of HO after CDA.

Other predisposing factors that have been discussed are age and sex. Male sex has been reported to correlate with HO formation[23] and could be a contributing factor to the differences in HO occurrence observed, compared with other reports. However, the male-to-female ratio reported in our study was not very different from that reported in other studies. There was no relationship between high- and low grade HO and age or sex in our study.

Limitations

Some limitations of this study are that only two types of artificial disk were investigated, the relatively small patient population, and the fact that HO was determined based only on the McAfee classification alone.

CONCLUSIONS

In our study, 61.4% patients exhibited HO after a mean follow-up of 58.4 months. In the analysis of survival after HO, all patients showed median survival of 28.3±5.6 months. The Activ C artificial disk prosthesis group showed statistically longer survival (49.5±7.8 months) than the M6-C disk group. This information should be useful to enable surgeons and patients to gain a better understanding of HO during follow-up. Randomized controlled trials with even longer follow-up times are needed to obtain more definite answers concerning HO occurrence, the factors associated with its occurrence and its impact on mobility, as well as clinical outcomes.

All authors declare no potential conflict of interest related to this article.

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