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ORIGINAL STUDY

Heterotopic ossification after cervical disc replacement : Clinical significance and radiographic analysis. A prospective study

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Limited data is available regarding heterotopic ossification (HO) after cervical disc replacement (CDR). The goal of this study was to determine the incidence of HO after CDR with the Mobi-C® artificial disc to identify the risk factors for HO, and to investigate whether HO affects clinical outcome and range of motion (ROM). Seventy one patients were included in this study. The mean follow-up was 21 months. Radiological evaluation included grading of HO and assessment of ROM for each level treated. HO was detectable in 23 treated segments (27.7%). The mean ROM was 8.1° preoperatively and increased to 10.2° at the last follow-up visit. Nevertheless, HO did not appear to affect clinical outcomes. HO appears to be a common complication after CDR. No specific risk factors have been clearly identified in our study. Long-term follow-up will be needed to assess the clinical significance of HO.

Keywords : heterotopic ossification ; cervical disc replacement ; spontaneous fusion.

INTRODUCTION

Anterior cervical discectomy and fusion (ACDF) is considered the gold standard for the treatment of cervical spondylosis (*6*). However this very popular surgery may lead to altered motion of cervical segments and increased intradiscal pressure (*11,26*) at adjacent levels, all of which can lead to adjacent segment degeneration (*2,13-15,20*).

Cervical disc replacement (CDR) is an alternative to anterior cervical discectomy and fusion. The goals of CDR are to preserve the normal kinematics of the spine and potentially prevent adjacent segment degeneration. Several authors have reported favourable results after CDR (*4,12,17,23,27*).

The Mobi-C® artificial disc (LDR, Troyes, France) has received approval from the Food and Drug Administration to undergo an Investigational Device Exemption trial in the United States. Preliminary results from a multicenter study

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conducted in France are very encouraging (*3,25*). This prosthesis is a metal-on-polyethylene device and has five degrees of freedom. It is composed of two spinal plates (cobalt, chromium, and 29 molybdenum alloy ISO 583212) and an ultra-high-molecular-weight polyethylene mobile insert.

Heterotopic ossification (HO) occurring after lumbar (*21,24*) and cervical disc replacement is a well-known complication (*19,22*). Data regarding HO after CDR is sparse. Mehren *et al* (*22*) modified and applied the McAfee classification of HO initially developed for lumbar arthroplasty for CDR (*21*). The aims of this study were to determine the incidence of HO after CDR with Mobi-C® prosthesis, to identify associated risk factors for HO, and to investigate whether HO affects clinical outcome and range of motion (ROM).

MATERIAL AND METHODS

Study Design

This is a unicenter, prospective, non-comparative study.

Patients

Seventy one patients were included in this study (32 men, 39 women). Their mean age was 41.2 years (range : 23-53). The mean age for men was 41 years (range : 28-51) and 41 years for women (range : 23-53). Sixty one patients presented with radiculopathy (85.9%) and 10 patients presented with myelopathy (14.1 %). The mean duration of preoperative symptoms prior to cervical disc replacement was 14.9 months (range : 1-120 months). Three patients had an injection before surgery. Two patients had been previously operated (one patient had a C6-7 anterior disk fusion and the other a C5-6 cervical disc arthroplasty). One patient presented with a congenital block at C6-C7 level. Thirty two patients were smokers. The mean follow-up was 20.95 months (range : 12 to 36 – SD : 8.5 month). The last follow-up visit was at 12 months for 29 patients, 24 months for 31 patients and 36 months for 11 patients.

Data collection

All patients were assessed with the same protocol. Surgical data including intraoperative and postoperative blood loss, operative time, size of mobile insert was collected for all patients.

Patients were clinically assessed in a prospective manner by using SF-36 questionnaire (SF-36 PCS and SF-36 MCS), Neck Disability Index (NDI), Visual analogue scale (VAS) neck pain and Visual analogue scale arm pain. All patients were assessed radiographically with cervical spine radiographs and magnetic resonance imaging (MRI). MRI was done in the preoperative period to investigate for herniated discs (level, type), compression of nerve roots and/or spinal cord. Static (neutral position) and dynamic (flexion and extension) cervical radiographs in the pre and postoperative period were done at the following intervals using the same protocol : 1, 3, 6, 12, 24, 36 months.

Radiological analysis

All radiographs were digitized using a Vidar radiograph digitizer (Vidar Systems Corp., Hernon, VA). The radiological evaluation of the cervical spine in the pre- and postoperative period included anteroposterior (AP) views and lateral radiographs in neutral position, full flexion and full extension. Range of motion (ROM) was calculated for each level treated. Quantitative measurements were performed with Spineview® software (LBM, LIO, Surgiview Company) (Fig. 1A,B). This software has been previously validated (*20*). HO was classified according to Mehren *et al* (Table I) (*19*). This classification rates the severity of HO based on the extent of ossification in relation to the disc space and the amount of reduction in mobility of the prosthesis.

Statistical analysis

Statistical analysis was performed using SPSS software 17.0 (SPSS Inc., Chicago, IL). Statistical analysis was performed using t tests, Wilcoxon tests, $\chi 2$ and Fisher exact test. The significance was accepted at the 1% level.

RESULTS

Surgical Data

Eighty three levels in 71 patients were treated in this study. Fifty five patients underwent a single cervical disc replacement, 4 patients underwent a hybrid fusion (one-level arthroplasty with an adjacent ACDF), and 12 patients underwent 2-level cervical disc replacement. In the hybrid fusions,

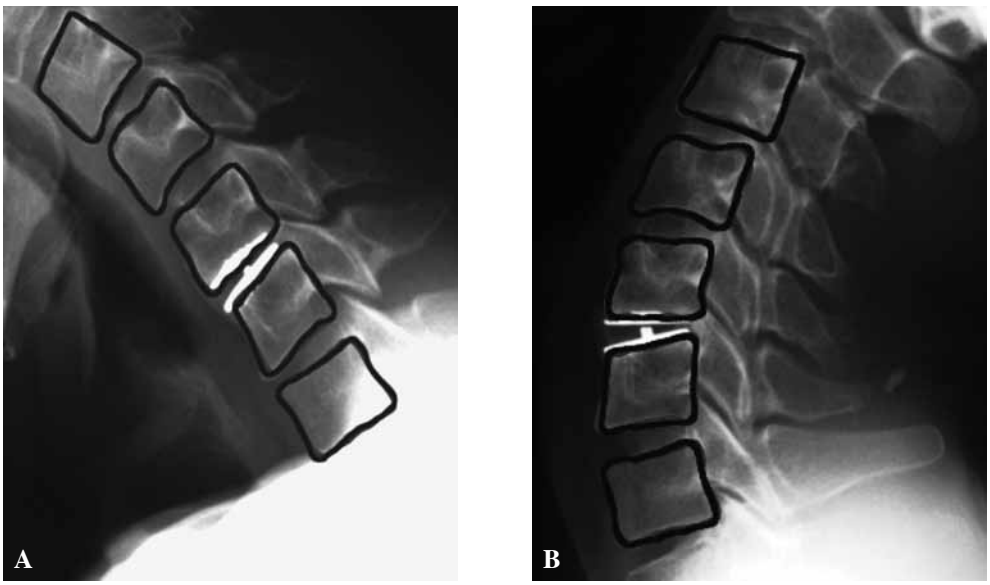

Fig. 1A,B. — ROM analysis with Spineview® software (LBM, LIO, Surgiview Company).
A : Full Flexion ; B : Full Extension.

Table I. — Classification of heterotopic ossification

Grade 0	No HO present
Grade 1	HO is detectable anterior to the vertebral body but not in the anatomic discal space
Grade 2	HO is growing into the disc space. Possible interference with function of the prosthesis
Grade 3	Bridging ossifications noted but motion of the prosthesis persists
Grade 4	Complete fusion of the treated segment without movement of prosthesis in flexion/extension

cervical disc arthroplasty was performed in the upper adjacent level for 3 patients and the lower adjacent level for 1 patient. The mean operative time was 75 min (range : 45-150). The mean blood loss was 82.5 ml (range : 10-450).

Classification of heterotopic ossification

The classification for each treated level is shown in table II. HO was detected in 23 treated segments (27.7%). HO was present in 9 males and 11 females. Of the71 patients treated with CDR, 5/11 patients had HO at 36 months, 12/31 patients at 24 months, 3/29 patients at 12 months. Two patients had grade 1 HO (n = 2 for 1-level arthroplasty) , 12 had grade 2 HO (n = 7 for 1-level arthroplasty, n = 3 for 2-level arthroplasty, n = 2 for 1-level arthroplasty + ACDF), 5 had grade 3 HO (n = 4 for 1-level arthroplasty, n = 1 for 2-level arthroplasty) and 4 had grade 4 HO (n = 2 for 1 level arthroplasty, n = 2 for 2 levels arthroplasty). Mean HO – free period was 12.6 months (range : 3-30).

HO was anterior in 7 segments, posterior in 8 segments and antero-posterior in 8 segments. Fourteen patients were treated with indomethacin in the postoperative period. Among these patients, none developed HO at the last follow-up visit (p = 0.034 – Fisher exact test).

Range of motion

The mean preoperative ROM was 8.1° (min -3.6 – max 22.3 ; SD 4.2) in the preoperative period and increased to 10.2° (min -2.9° – max 25.3° – SD 5.7°) in the postoperative period at the last follow-up visit (p = 0.001). Range of motion according to

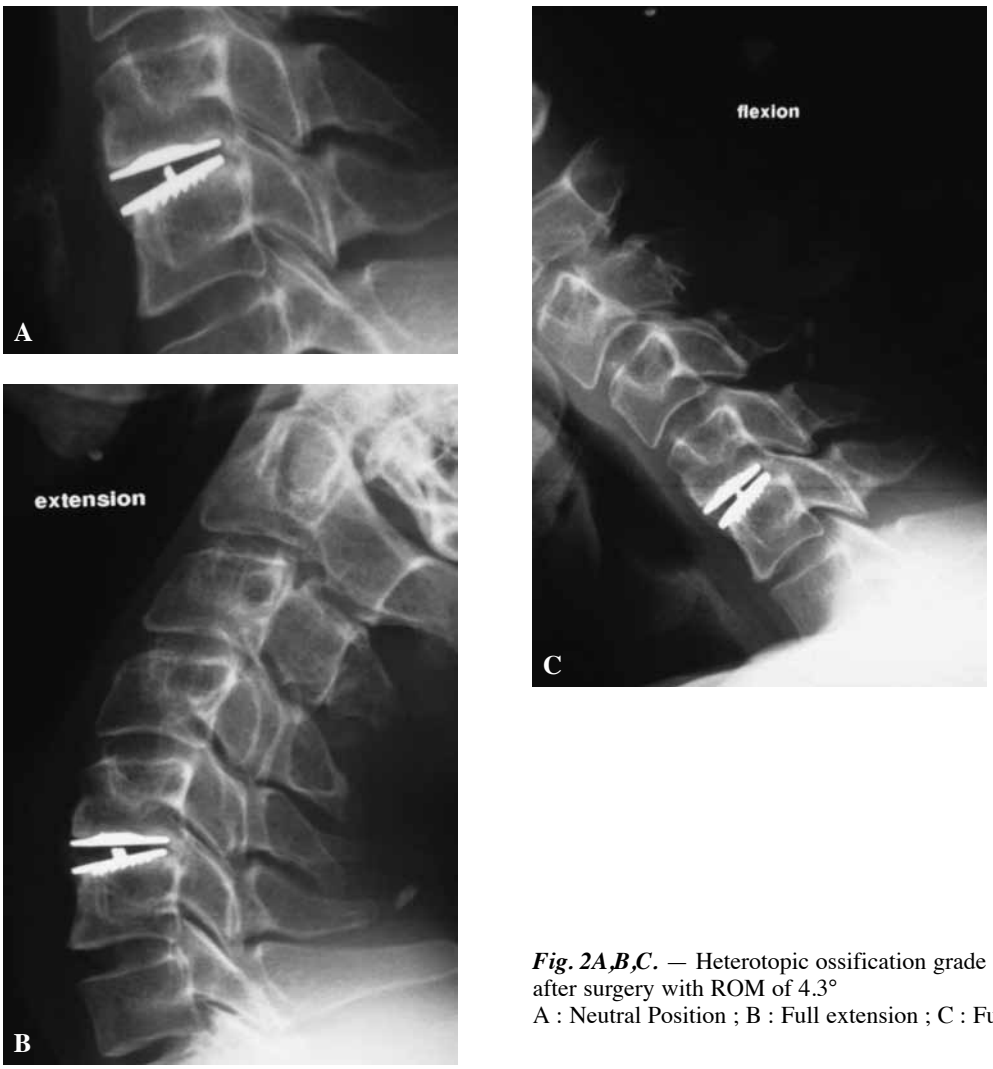

Fig. 2A,B,C. — Heterotopic ossification grade 3 at 24 months after surgery with ROM of 4.3°
A : Neutral Position ; B : Full extension ; C : Full flexion

the grade of heterotopic ossification is shown in table III. ROM was reduced in grade 3 HO (Fig. 2A,B,C) and grade 4 HO. Four prostheses were immobile, all of them with grade 4 HO.

Risk Factor analysis

No factor was found to be associated with the development of HO including age ($p = 0.592$), gender ($\chi2 = 0.059$ $p = 0.808$), tobacco ($\chi2 = 0.644$ $p = 0.422$), type of herniated disk ($\chi2 = 0.155$ $p = 0.694$), height of prosthesis ($\chi2 = 1.087$ $p = 0.297$), operative time ($p = 0.904$), and perioperative blood loss ($p = 0.459$).

Clinical outcomes analysis

The mean preoperative VAS neck pain value was 54.9 (min 1 – max 100 – SD 27.9) preoperatively and significantly decreased to 19.4 (min 0 – max 74 – SD 21.1) postoperatively ($p < 0.0001$).The mean preoperative VAS arm pain value was 69.6 (min 0 – max 100 – SD 22.4) and significantly decreased to 20.7 (min 0 – max 85 – SD 25.2) in the postoperative period ($p < 0.0001$). The mean SF-36 Physical Component Sub score (PCS) was 36.9 (min 26.2 – max 56 – SD 6.4) preoperatively and significantly increased to 46.4 (min 20.6 – max 60 – SD 8.7) in the postoperative period ($p < 0.0001$). The mean

Table II. — Classification and topography of heterotopic ossification

	N	Grade 0	%	Grade 1	%	Grade 2	%	Grade 3	%	Grade 4	%
		N		N		N		N		N	
Total	83	60	72.3	2	2.4	12	14.5	5	6	4	4.8
Treated Level											
C3C4	2	2	2.4	–	–	–	–	–	–	–	
C4C5	9	6	7.2	–	–	2	2.4	1	1.2	–	–
C5C6	39	25	30.1	–	–	8	9.7	4	4.8	2	2.4
C6C7	33	27	32.6	2	2.4	2	2.4	–	–	2	2.4
	N	Grade 0		Grade 1		Grade 2		Grade 3		Grade 4	
Topography											
A	7	–		1		4		1		1	
AP	8	–		1		2		4		1	
P	8	–		–		6		0		2	

(A : Anterior, AP : Antero-posterior, P : Posterior).

SF-36 MCS was 35.7 preoperatively (min 17.8 – max 59.2 – SD 11) and significantly increased to 46.3 (min 12.3 – max 64.5 – SD 11.6) postoperatively ($p < 0.0001$). HO did not alter clinical outcome. The presence and grade of heterotopic ossification did not correlate with any clinical parameters. There was no statistically difference between patients with HO and patients without HO for SF-36 PCS ($p = 0.480$), SF-36 MCS ($p = 0.788$), postoperative NDI($p = 0.748$), VAS neck pain($p = 0.649$) and VAS arm pain ($p = 0.369$) . None of our patients required revision surgery due to the presence of HO.

DISCUSSION

Heterotopic ossification is a frequent complication following primary total hip arthroplasty (*7*). The exact causes of HO remain unknown. A series of inflammatory processes including an array of specific mediators and growth factors is probably involved in the formation of HO. This leads to the recruitment of mesenchymal stem cells capable of differentiating into bone (*9,16*). Soft tissue injury, trauma of the longus colli and residual bone at the operative site are factors that may facilitate the formation of HO. Hence, irrigation of the operative site during drilling of the endplates and gentle retraction of the longus colli should be done to prevent HO formation (*19*).

Our results show a 27.7% incidence of HO after cervical disc replacement, which is relatively high.

Mehren *et al* reported a much higher rate of HO and fusion after cervical disc replacement with the Prodisc C® device (Synthes Inc., Paoli, PA). In their study only 33.8% of the patients did not present with HO at one year postop (*22*). Leung *et al* reported a rate of 17.8% one year after implantation of the Bryan® cervical prosthesis (Medtronic Sofamor Danek, Memphis, TN) (*19*). Recently, Yi *et al* (*29*) reported differences in HO occurrence following disk arthroplasty with three different types of prosthesis in 170 patients : Bryan® – 81 patients ; Mobi-C® – 61 patients and ProDisc-C® – 28 patients. They reported an overall HO rate of 40.6% (69 patients). HO occurrence rate by prothesis was 21% in the Bryan group, 52.5% in the Mobi-C® group and 71.4% in the Prodisc-C® group. Moreover, the Bryan® group showed statistically longer survival than the other groups. They suggested that differences in the design, biomechanical characteristics, endplate articulation component and surgical procedure could be contributing factors for the different rates of HO (*29*).

No statistically significant pre and postoperative patient characteristics were found in this study to be

Table III. — Range of motion according to grade of heterotopic ossification

		Range of motion			
Ossification	N	Mean	Min	Max	Sd
Grade 0	60	10.7°	-2.7°	25.3°	5.7°
Grade1	2	12.0°	10.1°	14°	2.8°
Grade 2	12	11.8°	8°	24.8°	4.5°
Grade 3	5	6.9°	6°	8°	0.9°
Grade 4	4	0.8°	-2.9°	2°	2.5°

associated with the development of HO. Similar to Boehm *et al* concerning primary shoulder arthroplasty, we did not find any significant difference between males and females (*5*). Our results diverge from those of Leung *et al*, who found that age was a possible risk factor for the development of HO (*19*). These findings were in line with those of other previous studies (*1,28*).

The conventional surgical treatment of patients who have cervical disc disease and cervical spondylosis is anterior cervical discectomy and fusion. Cervical disc replacement is an alternative to this standard procedure. The objectives of total disc replacement are motion preservation and avoidance of long-term complication of fusion procedures. Adjacent segment degeneration, modification of motion at adjacent levels, and increased intradiscal pressure at adjacent levels frequently occur after anterior cervical discectomy and fusion (*11,14,15*). Grade 3 and 4 HO were associated with the loss of disk mobility. In our study, no adjacent segment disease was observed in the HO group. Nevertheless these patients potentially lose the theorical advantage of adjacent segment preservation.

According to our study heterotopic ossification following cervical disc replacement is common but does not affect clinical outcome. Mehren *et al* did not find any correlation between the grade of heterotopic ossification and the clinical parameters (VAS, NDI) (*22*). Leung *et al* came to a similar conclusion in their Bryan® prosthesis study (*19*).

Nonsteroidal anti-inflammatory drugs are effective in the prevention of HO after total hip arthroplasty ; they may also be recommended for prevention of HO after cervical disc replacement (*10,18*). Among the 14 patients who were treated with indomethacin in our study, none developed HO. However, the preventive role of NSAIDs cannot be reliably assessed because the data was not collected prospectively.

Limitations of the present study include the lack of a control group, the small number of patients and the limited follow-up.

CONCLUSION

Heterotopic ossification appears to be a common complication after cervical disc replacement and was not found to affect the clinical outcome in our study. The preventive role of NSAIDs and the risk factors associated with HO must be ascertained. Long-term follow-up will be needed to assess the clinical significance of HO after CDR.

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