Postoperative NSAID Prophylaxis is Associated with Decreased Rates of Heterotopic Ossification following Cervical Disc Arthroplasty

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INTRODUCTION:
Cervical disc arthroplasty (CDA) has become a common procedure for the treatment of cervical degenerative disc disease that preserves range of motion (ROM) at the operative segment. However, CDA patients are at risk of heterotopic ossification (HO), which can compromise the intended benefits of this procedure. Numerous demographic and technical variables have been explored as factors influencing its incidence in the cervical spine but have remained inconsistent. HO has also been extensively studied within the context of total hip arthroplasty (THA). THA literature has highlighted non-steroidal anti-inflammatory drugs (NSAIDs) prophylaxis as a protective factor against HO formation. Limited data assessing this relationship following CDA exists. Therefore, this study aims to further define the predisposing factors that lead to HO formation after CDA and to investigate the effect of NSAID prophylaxis on the development of HO.
METHODS:
A retrospective review at a single academic center was conducted using a surgical registry. Demographic data (age, sex, BMI) and surgical factors (NSAID use within 48 hours, reason for NSAID use, implant type, operative levels) were collected. Implants were categorized by HO risk(high vs low) per prior studies. Radiographs at the latest time point from 1–2 years post-op were graded for HO using the McAfee grading system. Patient reported outcome measures (PROMs), including neck disability index (NDI), visual analog scale for neck and arm (VAS-N and VAS-A) and 12-item short form, physical component scale (SF-12 PCS), were recorded at pre-op, <6 months, and ≥6 months, along with complications and reoperations. Two regression models were performed based on NSAID use: any reason vs HO prophylaxis. Paired t-tests and minimal clinically important difference (MCID) were used to assess PROM improvement from baseline. HO+ vs HO– groups were compared using t-tests or chi-square tests. Subgroup analysis comparing PROMs by McAfee grade (1, 2, 3+) was also conducted.
RESULTS:
140 patients met inclusion criteria (HO+: 61; HO–: 79). HO+ patients were older (44.2 vs. 40.9 yrs, p=0.025), had higher BMI (27.5 vs. 25.0, p=0.002), and had less NSAID usage both for any reason (16.4% vs. 34.2%, p=0.018) and for HO prophylaxis (9.8% vs. 29.1%, p = 0.005). On logistic regression (NSAIDs for any reason), BMI (OR=1.12, p=0.007) predicted HO, while NSAID use was protective (OR=0.36, p=0.023) (Table 1). Results were similar when NSAIDs were prescribed for HO prophylaxis (BMI OR=1.12, p=0.008; NSAID OR=0.24, p=0.008) (Table 2). No other variables were significant. Both groups showed improvement from baseline by the early time point for all PROMs, with no differences at any time point (Table 3). There was no difference in MCID between groups, with a majority of patients in both groups reaching achievement for all proms by the early time point (Table 3). Complication (2.5% vs. 3.3%, p = 1.0) and reoperation rates were also similar between groups (3.8% vs. 0%, p = 0.26). On subgroup analysis, all groups showed improvement by the early time point for all PROMs, except for VAS-A, which improved by the late time point. ANOVA showed differences in pre-op VAS-N (Grades 1 and 2, p = 0.036) and late VAS-A (Grade 1 and 3, p = 0.020). No other differences in PROMs, including magnitude of improvement, complication, or reoperation rates were found across HO grades.
DISCUSSION AND CONCLUSION:
This study highlights postoperative NSAID use as a potential protective factor and elevated BMI as a significant risk factor for HO within 1–2 years following CDA. We also note a lack of differences in clinical outcomes, consistent with prior literature. To our knowledge, this is the first reported evidence of a significant relationship between early postoperative NSAID use and a lower rate of HO development in the context of cervical disc arthroplasty. Further research involving larger cohorts and longer follow-up periods are needed to validate these findings, define the optimal NSAID agent, dose, and duration of HO prophylaxis following CDA.

Variable	B	SE	OR	95% CI Lower	95% CI Upper	p-value
(Constant)	-4.88	1.45	0.01			**< 0.001***
Age	0.04	0.02	1.04	1.00	1.09	0.08
Sex (Male)	0.22	0.42	1.25	0.55	2.82	0.60
BMI	0.12	0.04	1.12	1.03	1.22	**0.007***
NSAID Use (Any reason)	-1.03	0.45	0.36	0.15	0.87	**0.023***
Operated Levels (2)	-0.41	0.41	0.66	0.30	1.48	0.31
High Risk HO Implant	0.25	0.38	1.29	0.61	2.71	0.51

Table 1. Logistic Regression Results for NSAIDs prescribed for any reason. Significance is p < 0.05 and indicated by bolded and *. B, unstandardized regression coefficient; SE, standard error of B; OR, odds ratio; CI, confidence interval; HO, heterotopic ossification; BMI, body mass index; NSAID, Non-steroidal anti-inflammatory drug.

Variable	B	SE	OR	95% CI Lower	95% CI Upper	p-value
(Constant)	-4.85	1.46	0.01			**< 0.001***
Age	0.04	0.02	1.04	0.99	1.09	0.09
Sex (Male)	0.32	0.42	1.38	0.61	3.14	0.44
BMI	0.11	0.04	1.12	1.03	1.22	**0.008***
NSAID Use (HO prophylaxis)	-1.42	0.53	0.24	0.09	0.69	**0.008***
Operated Levels (2)	-0.40	0.41	0.67	0.30	1.51	0.33
High Risk HO Implant	0.28	0.38	1.32	0.62	2.80	0.47

Table 2. Logistic Regression Results for NSAIDs explicitly prescribed as HO Prophylaxis. Significance is p < 0.05 and indicated by bolded and *. B, unstandardized regression coefficient; SE, standard error of B; OR, odds ratio; CI, confidence interval; HO, heterotopic ossification; BMI, body mass index; NSAID, Non-steroidal anti-inflammatory drug.

PROM	Timepoint	HO - N	HO - Values	HO + N	HO + Values	*p* - value
		N	Values	N	Values	-
NDI	Pre-Op	64	42.4 ± 19.6	49	40.2 ± 18.1	0.55
	Early	60	22.6 ± 16.2 (**p < 0.001**) 71.4%	47	22.8 ± 20.2 (**p < 0.001**) 76.7%	0.94
	Late	52	20.5 ± 19.9 (**p < 0.001**) 77.6%	38	21.3 ± 21.4 (**p < 0.001**) 80.0%	0.87
VAS-N	Pre-Op	65	6.4 ± 2.5	53	5.6 ± 2.4	0.08
	Early	60	2.8 ± 2.3 (**p < 0.001**) 58.9%	45	2.8 ± 2.5 (**p < 0.001**) 61.4%	0.94
	Late	50	2.9 ± 2.9 (**p < 0.001**) 62.5%	37	2.6 ± 2.8 (**p < 0.001**) 58.3%	0.65
VAS-A	Pre-Op	65	5.0 ± 3.1	52	4.7 ± 3.0	0.56
	Early	57	1.7 ± 2.2 (**p < 0.001**) 53.7%	44	2.2 ± 2.7 (**p < 0.001**) 53.5%	0.31
	Late	47	2.0 ± 2.5 (**p < 0.001**) 55.6%	38	1.7 ± 2.3 (**p < 0.001**) 48.6%	0.67
SF-12 PCS	Pre-Op	59	37.6 ± 8.6	45	37.5 ± 9.9	0.97
	Early	49	42.2 ± 10.8 (**p = 0.002**) 56.8%	40	42.6 ± 11.5 (**p < 0.001**) 62.2%	0.89
	Late	48	41.4 ± 10.9 (**p < 0.001**) 54.8%	37	45.2 ± 11.9 (**p < 0.001**) 64.7%	0.13

Table 3. Comparison of PROMs and MCID by HO presence. Values in each cell are presented as: *mean ± SD*, followed (in parentheses) by the *p*-value for change from the pre-operative baseline, and lastly the percentage of patients who achieved MCID. A bold *p*-value in parentheses marks a statistically significant improvement from baseline ($p < 0.05$). Entries that are bold and starred (*) in the final "*p*-value" column indicate a statistically significant difference between HO- and HO+ groups ($p < 0.05$). *N* is the number of patients in each cohort; HO, heterotopic ossification; PROM, patient-reported outcome measure; MCID, minimal clinically important difference; NDI, Neck Disability Index; VAS, Visual Analogue Scale; SF-12 PCS, 12-Item Short Form Survey Physical Component Score.