Elevated Low-Density Lipoprotein Levels Predict Pseudarthrosis After Posterior Cervical Fusion: Protective Role of Statins but Not Omega-3 Fatty Acids

Sri Tummala, David Gibbs, Joseph Cruz Chavarria, Jason D Alder, Ioannis A Avramis, James Rizkalla

INTRODUCTION: Posterior cervical fusion (PCF) is a critical intervention for complex cervical pathologies including myelopathy, deformity, and instability where neurological decompression and stabilization are paramount. Despite its utility, pseudarthrosis remains a devastating complication exceeding 20% in multilevel constructs, often necessitating revision surgery. While established risk factors like smoking and diabetes are well-documented, the role of dyslipidemia—particularly elevated LDL-C—in impairing spinal fusion remains understudied despite compelling preclinical evidence linking hypercholesterolemia to microvascular dysfunction, suppressed BMP-2 signaling, and disrupted bone remodeling. Pharmacological agents like statins (with dual lipid-lowering and osteogenic properties) and omega-3 fatty acids (with anti-inflammatory effects) offer potential mitigation strategies, yet clinical validation in PCF populations is absent. This study addresses this gap by investigating LDL-C levels, statin use, and fish oil supplementation as predictors of pseudarthrosis after PCF.

METHODS: This retrospective cohort study utilized the TriNetX Research Network (100+ healthcare organizations; 150M+ de-identified patients). Adults undergoing PCF were identified using ICD-10-PCS and CPT codes. Three matched cohorts were constructed: 1) High LDL-C (≥140 mg/dL) vs. low LDL-C (≤66 mg/dL); 2) Statin users vs. non-users; 3) Fish oil users vs. non-users. LDL thresholds were derived from distribution analysis of 24M+ lab records. Medication use required prescriptions within 6 months preoperatively (validated via RxNorm codes). Patients with concurrent anterior instrumentation were excluded. Propensity score matching (1:1, caliper=0.1 SD) adjusted for age, sex, BMI, race, smoking, diabetes, osteoporosis, steroid use, hypertension, malnutrition, and metabolic syndrome. Pseudarthrosis was defined by ICD-10 code M96.0 at 6 months, 1 year, and 3 years. Standardized mean differences confirmed covariate balance (SMD<0.1). STROBE guidelines were followed for patient selection (Figure 1).

RESULTS:

In the matched LDL-C analysis (1,784 patients/group), high LDL-C demonstrated significantly elevated pseudarthrosis rates versus low LDL-C at 6 months (12.8% vs. 9.3%; OR=1.42, 95% CI:1.18-1.71, P<0.001), 1 year (16.7% vs. 12.5%; OR=1.37, 95% CI:1.17-1.61, P=0.002), and 3 years (22.1% vs. 17.3%; OR=1.30, 95% CI:1.11-1.52, P=0.006). (Table 1).

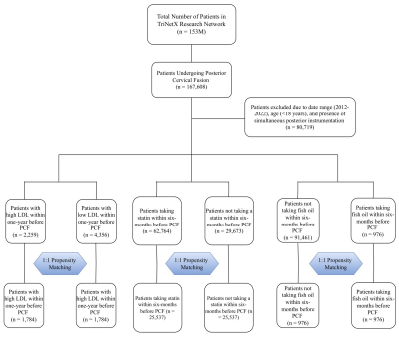
Among 25,537 matched statin users, pseudarthrosis incidence was consistently lower than non-users: 10.2% vs. 11.9% at 6 months (OR=1.20, P<0.001), 13.1% vs. 15.2% at 1 year (OR=1.18, P<0.001), and 17.3% vs. 19.1% at 3 years (OR=1.12, P<0.001). Concomitant LDL-C reductions were significant in statin users at all intervals (e.g., 78.9±32.7 mg/dL vs. 98.0±38.1 mg/dL at 6 months, P<0.001). (Table 2).

In contrast, 976 matched fish oil users showed no pseudarthrosis reduction versus non-users (6mo: 10.7% vs. 9.0%, OR=1.21, P=0.215; 3yr: 17.9% vs. 17.0%, OR=1.07, P=0.612) and no LDL-C differences (P>0.05). (Table 2).

DISCUSSION AND CONCLUSION:

Elevated preoperative LDL-C was found to independently predict increased pseudarthrosis incidence after PCF, substantiating preclinical evidence that hypercholesterolemia may impair osteogenesis via microvascular dysfunction, BMP-2 suppression, and oxidative stress. Statins appeared to confer significant protection, mechanistically attributable to their known dual lipid-lowering and pleiotropic mechanisms including enhanced BMP-2 signaling and anti-inflammatory activity. These findings align with lumbar and anterior cervical fusion studies, confirming hypercholesterolemia as a modifiable surgical risk factor. Conversely, fish oil demonstrated no benefit despite anti-inflammatory properties, potentially due to PCF-specific biomechanical demands or insufficient dosing. Notably, statins' effects were measurable within 6 months, supporting rapid therapeutic utility. While traditional anti-inflammatories like NSAIDs may be linked to impeded fusion, statins emerge as uniquely advantageous for arthrodesis.

In conclusion, elevated preoperative LDL-C levels were significantly associated with increased pseudarthrosis rates following PCF. Statin use emerged as a potentially effective prophylactic intervention, correlating with decreased pseudarthrosis rates and a conferring a modulatory effect in lowering LDL-C levels. In contrast, fish oil supplementation demonstrated no measurable benefit. Clinicians may consider incorporating routine LDL-C assessment and management into preoperative planning for PCF to help optimize fusion outcomes. Notably, patients scheduled to undergo PCF may benefit from being prescribed a statin if they meet established guidelines set by the US Preventive Services Task Force, especially given that the lipid-lowering and anti-inflammatory effects of statins can become evident within four weeks of initiating therapy.



Time Interval	Patient count n (% of cohort)	Patient count n (% of cohort)	Odds ratio (95% CI)	p-value
	High LDL (n = 1,784)	**Low LDL (n = 1,784)**		
Six months	244 (13.75)	186 (10.4)	1.422 (1.158–1.747)	**<0.001**
One year	260 (14.6)	205 (11.5)	1.373 (1.126–1.676)	**0.002**
Three years	298 (16.7)	248 (13.9)	1.299 (1.079–1.565)	**0.006**
	No Statin Use (n = 25,537)	**Statin Use (n = 25,537)**		
Six months	3,188 (12.5)	2,714 (10.6)	1.196 (1.132–1.264)	**<0.001**
One year	3,503 (13.7)	3,030 (11.9)	1.178 (1.117–1.242)	**<0.001**
Three years	3,925 (15.4)	3,542 (13.9)	1.124 (1.069–1.181)	**<0.001**
	No Fish Oil Use (n = 976)	**Fish Oil Use (n = 976)**		
Six months	101 (10.3)	84 (8.6)	1.214 (0.893–1.649)	0.215
One year	111 (11.4)	98 (10.0)	1.137 (0.851–1.520)	0.385
Three years	133 (13.6)	124 (12.7)	1.071 (0.821–1.397)	0.612

CI, confidence interval; LDL, low-density lipoprotein.
Bold *p-value* = Statistically Significant Difference ($p \leq 0.05$)

Time Interval	Mean LDL-C Level (mg/dL) ± SD		p-value
	No Statin Use	**Statin Use**	
Six months	98.0 ± 38.1	78.9 ± 32.7	**<0.001**
One year	101.0 ± 37.9	80.7 ± 33.1	**<0.001**
Three years	99.5 ± 38.7	80 ± 33.6	**<0.001**
	No Fish Oil Use	**Fish Oil Use**	
Six months	89.0 ± 36.7	87.1 ± 40.7	0.279
One year	91.4 ± 37	93.1 ± 39.6	0.327
Three years	91.1 ± 37.2	90.9 ± 38.3	0.907

SD, standard deviation; LDL-C, low-density lipoprotein cholesterol.