

# **Increased Perioperative Blood Low-Density Lipoprotein Cholesterol Level is Associated with Decreased Levels of Anti-Inflammatory Synovial Fluid Biomarkers in Patients Undergoing Knee Surgery**

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# Faculty Disclosures

## **Eric Strauss:**

- AAOS (Board or committee member)
- American Orthopaedic Association: Board or committee member
- Arthrex, Inc: Paid consultant; Paid presenter or speaker
- Arthroscopy Association of North America: Board or committee member
- Better PT: Stock or stock Options
- Cartiheal: Research support
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# Background

- Low-density lipoprotein (LDL) cholesterol, one of the key drivers of atherosclerotic cardiovascular disease, has been shown to be a systemic mediator of inflammation
- The biomechanical role of body mass index in the progression of degenerative joint disease has been described
- However, the possible linkage between an unfavorable metabolic state and knee inflammation/degeneration has not been explored

**Purpose:** to determine associations between **LDL blood levels** and **synovial fluid biomarker concentrations** in the knee joint. This understanding may help elucidate the possible mechanism of **LDL as an inflammatory mediator of osteoarthritis.**

# Methods

- Patients undergoing knee surgery were prospectively enrolled
- Synovial fluid was aspirated from the operative knee prior to surgical incision
- The concentrations of 10 biomarkers of interest (RANTES, IL-6, MCP-1, MIP-B, VEGF, TIMP-1, TIMP-2, IL-1RA, MMP-3, and bFGF) were measured by immunoassay
- Patients with LDL cholesterol levels available in the electronic health record were identified
- The LDL value nearest to the time of surgery was used
- LDL and biomarker concentrations were log-normalized
- Multivariable linear regression analysis: each biomarker vs. LDL
  - Covariates: age, sex, BMI

# Results: Cohort Demographics

Demographics	N = 119
Age (years)	45.3 ± 14.3
Sex (% male)	58 (48.7%)
Body mass index (kg/m <sup>2</sup> )	28.39 ± 5.82
ACL injury	41 (34.5%)
Meniscal injury	92 (77.3%)
Cartilage injury	17 (14.3%)
Other injury	12 (10.1%)

# Results: Biomarkers vs. LDL

Multivariable Linear Regression: Biomarkers vs. LDL level

Biomarker	p-value	Beta (standardized)
RANTES	0.970	0.003
IL-6	0.671	0.039
MCP-1	0.999	0.000
MIP-B	0.530	0.057
VEGF	0.372	0.084
<b>TIMP-1</b>	<b>0.014*</b>	<b>-0.232</b>
<b>TIMP-2</b>	<b>0.018*</b>	<b>-0.224</b>
IL-1RA	0.191	0.124
MMP-3	0.603	-0.050
bFGF	0.741	0.031

# Perioperative Blood LDL is Inversely Associated with Anti-Inflammatory Synovial Fluid Biomarker Levels in Knee Surgery Patients



We measured levels of 10 synovial fluid biomarkers pre-operatively in 119 knee surgery patients



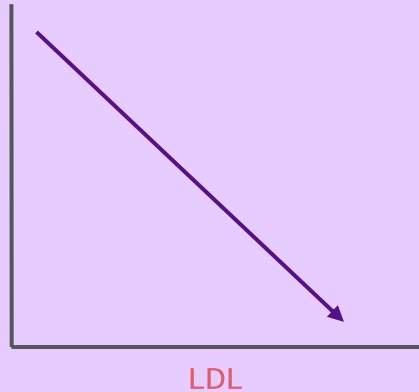
The blood LDL value measured nearest to the time of surgery was retrospectively identified



Log-normalized LDL and biomarker concentrations were regressed pairwise controlling for age, sex, and BMI.

Blood LDL levels were negatively associated with two anti-inflammatory biomarkers: TIMP-1 and TIMP-2

TIMP-1,  
TIMP-2



## KEY INSIGHTS AND FUTURE DIRECTIONS



LDL levels were inversely associated with the levels of two known chondroprotective, anti-inflammatory knee biomarkers



LDL is a known driver of systemic inflammation



LDL may be indirectly involved in intra-articular inflammation and joint degeneration through downregulation of TIMP signaling pathways

# References

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