

Background

- Complete cytoresduction is the strongest modifiable predictor of survival in advanced high-grade serous ovarian carcinoma (HGSOC). Despite improvements in imaging and surgical assessment, accurately predicting incomplete cytoresduction before surgery remains challenging.
- Reliable preoperative biomarkers could improve patient selection, optimize referral to high-volume surgical centers, and support individualized treatment planning.

Objective

- To develop and internally validate a preoperative serum proteomic model capable of predicting incomplete cytoresduction following primary debulking surgery in advanced HGSOC.

Why This Matters to the MHS

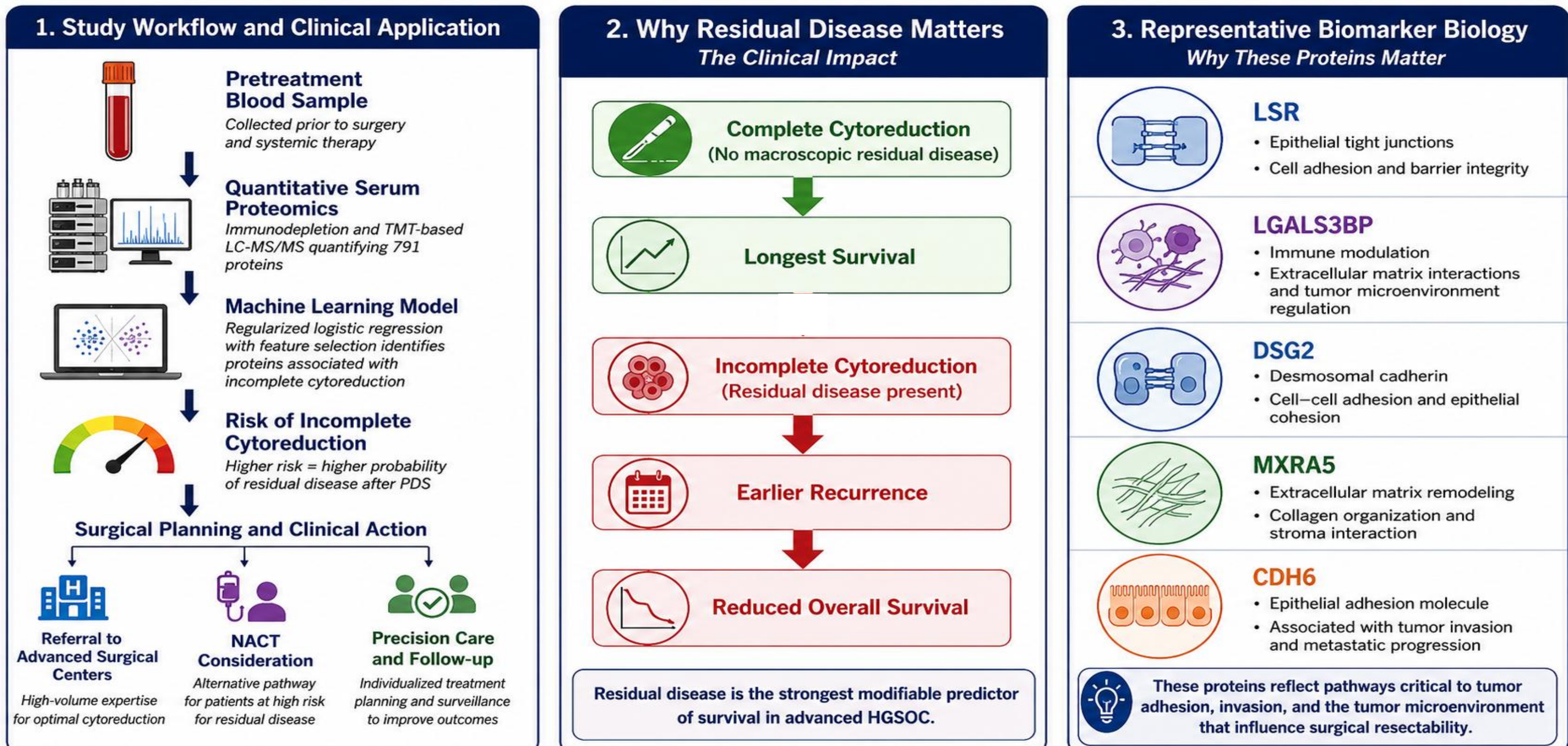
- Supports referral of complex patients to centers with advanced cytoreductive expertise.
- Improves allocation of surgical resources across geographically distributed Military Treatment Facilities.
- May reduce unnecessary operative morbidity through better patient selection.
- Advances precision surgical oncology using minimally invasive serum biomarkers.

Methods

- Study Design**
 - Multisite cohort of stage III-IV HGSOC (2012-2021) from the prospective Tissue and Data Acquisition Network.
 - Patients treated with primary debulking surgery followed by platinum-taxane chemotherapy, and salvage therapy as needed.
- Biospecimen and Proteomic Analysis**
 - Pre-treatment serum, collected prior to surgery and therapy, underwent immunodepletion followed by tandem mass tag (TMT)-based quantitative LC-MS/MS proteomics, identifying 791 quantified proteins.
 - Machine learning using regularized logistic regression with feature selection was performed to identify proteins independently associated with residual disease.
- Endpoints**
 - Incomplete cytoresduction was defined as the presence of macroscopic residual disease following primary debulking surgery
- Statistical Analysis**
 - Associations with incomplete cytoresduction were evaluated using logistic regression.
 - Multivariable models adjusted for stage were reported as adjusted odds ratios (aOR) with 95% confidence intervals. Predictive performance was assessed using ROC analysis.

Results: Serum-Based Proteomic Profiling and Machine Learning Identify Clinically Relevant Biomarkers for Aggressive and Deadly Cancer

Figure 1. Translational Framework for Pretreatment Serum Prediction of Residual Disease.



Key Findings: Pretreatment serum proteomics may enable precision surgical triage by identifying patients at high risk for incomplete cytoresduction before entering the operating room, facilitating optimal referral, individualized treatment planning, and improved resource utilization across the Military Health System.

Table 1. Outcomes Risk for the Top 10 Favorable Prognostic Serum Biomarkers

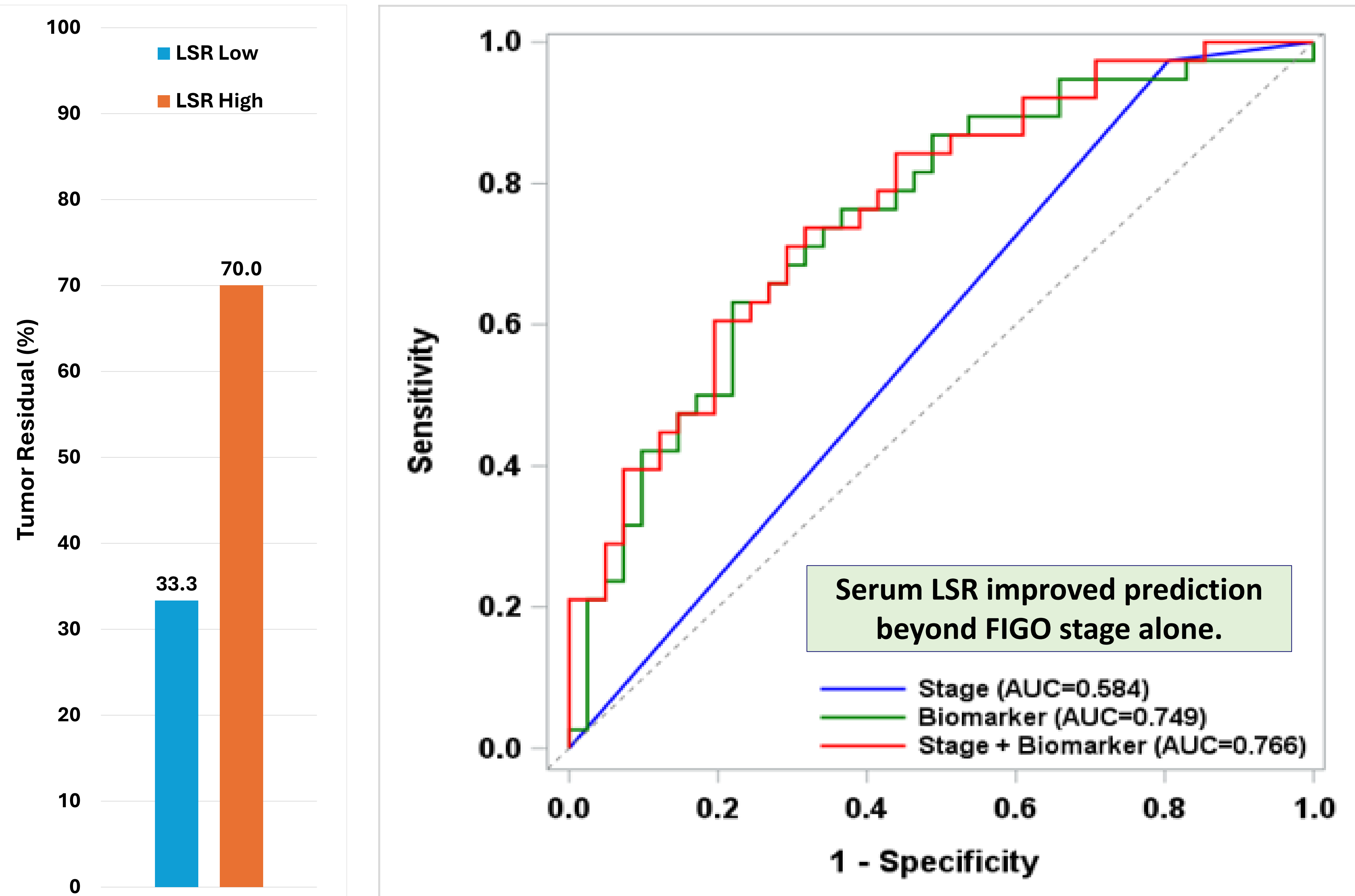
Top 10 Proteins Associated with Residual Disease				
	Continuous Variable Analysis		Categorical Variable Analysis	
Gene Name	aOR (95% CI)	P value	aOR (95% CI)	P value
LSR	2.59 (1.40 – 4.78)	0.002	4.15 (1.57 – 10.99)	0.004
LGALS3BP	2.35 (1.25 – 4.41)	0.008	3.57 (1.36 – 9.33)	0.009
DSG2	2.26 (1.23 – 4.12)	0.008	3.26 (1.25 – 8.48)	0.015
OIT3	2.15 (1.22 – 3.81)	0.009	2.82 (1.09 – 7.25)	0.032
MXRA5	2.06 (1.19 – 3.56)	0.010	3.85 (1.45 – 10.21)	0.007
CPB2	0.49 (0.29 – 0.84)	0.010	0.29 (0.11 – 0.75)	0.011
CD14	2.05 (1.18 – 3.55)	0.011	3.26 (1.25 – 8.48)	0.015
VCL	2.05 (1.17 – 3.59)	0.012	2.69 (1.03 – 7.06)	0.044
MUC1	2.05 (1.16 – 3.64)	0.014	3.26 (1.25 – 8.48)	0.016
CDH6	2.17 (1.17 – 4.04)	0.014	2.58 (1.01 – 6.62)	0.049

Pretreatment serum proteomic profiling identified multiple proteins independently associated with incomplete cytoresduction, with LSR demonstrating the strongest predictive performance. Nine proteins were associated with increased odds of residual disease, whereas CPB2 demonstrated a protective association with reduced odds.

MHS Impact

- Accurate preoperative identification of patients unlikely to achieve complete cytoresduction could improve referral pathways, optimize surgical resource utilization, reduce operative morbidity, and support precision oncology across geographically distributed Military Health System facilities.

Figure 2. Predictive Performance of Pretreatment Serum LSR for Incomplete Cytoresduction.



Higher pretreatment serum LSR concentrations nearly doubled the observed frequency of residual disease (33% vs 70%), supporting its potential utility as a clinically actionable biomarker, and outperformed stage in predicting residual disease and incomplete cytoresduction following primary cytoreductive surgery.

Take-Home Message: Pretreatment serum proteomics may enable accurate preoperative prediction of incomplete cytoresduction, supporting precision surgical planning in advanced ovarian cancer.

Conclusions

- Pretreatment serum proteomics identified reproducible biomarkers associated with incomplete cytoresduction in advanced HGSOC.
- LSR and several extracellular matrix- and adhesion-related proteins demonstrated strong independent predictive value after adjustment for stage.
- Blood-based prediction models may complement imaging and clinical assessment to improve surgical planning and patient selection.
- Prospective external validation is warranted before clinical implementation.