Unsupervised Machine Learning Can Group Synovial Fluid Samples into Disease-Relevant Clusters: AI Diagnosis of PJI is Near

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INTRODUCTION: The diagnosis of periprosthetic joint infection (PJI) in clinical practice remains complex, requiring the clinician to order, interpret, and combine several tests using a multiple-criterion definition such as that of the 2018 ICM. The existing literature suggests that there is poor adoption and implementation of authoritative definitions of PJI in practice, suggesting a need for alternate methods that can be more easily used by practicing clinicians.
Machine learning can be applied to evaluate multidimensional biomarker datasets, extracting previously unappreciated relationships that are useful for diagnostic classification. The purpose of this study was to determine whether unsupervised machine learning (ML) techniques could leverage rapidly available synovial fluid (SF) tests to group joint arthroplasty samples into diagnostically relevant clusters.

METHODS: SF samples were collected at a centralized clinical laboratory from 67,551 hip and knee arthroplasties across 2,359 institutions in the United States from 2017 to 2023. All rapidly available results including age, SF-CRP, alpha-defensin, SF-WBC count, SF-PMN%, SF-RBC count, SF-absorbance (A280), and microbial antigen test results were used as inputs for this study. Delayed results such as culture were not included as inputs. Principal component analysis (PCA) reduced input dataset complexity to five components, which were then used for K-means clustering. These unsupervised cluster results were then compared to a modified 2018 International Consensus Meeting (ICM) classification, which included both biomarker and culture results.
RESULTS: Unsupervised clustering, based on the rapidly available data from each SF-sample, yielded three naturally occurring groups of synovial fluid samples (Table 1). Cluster 1 (N=15,425) was characterized by 56.9% SF-culture positivity along with markedly elevated biomarker results. Clusters 2 (N=33,324) and 3 (N=18,802) yielded 0.3% and 1.2% SF-culture positivity respectively and were characterized by low biomarker values. When labelling Cluster 1 as "Infected" and Clusters 2 and 3 as "Not-Infected", concordance with the modified 2018 ICM definition of PJI yielded a sensitivity and specificity of 98.7% (95% CI: 98.5-98.9%) and 98.7% (95% CI: 98.6-98.8%), respectively.
DISCUSSION AND CONCLUSION: Unsupervised machine learning techniques can effectively simplify and analyze multidimensional data from rapidly available SF fluid tests to accurately classify samples, matching a modified 2018 ICM criteria for PJI. Artificial intelligence applied in the clinical laboratory could improve and simplify the diagnostic process by matching complex, criteria-based diagnostic systems, thus reducing the likelihood of human error and democratizing expert-level diagnostic capabilities across a broader range of clinicians.

	Culture Positive %	MID Positive %	Mean SF-CRP	Mean AD	Mean WBCs	Mean PMNs	Mean RBCs
Cluster 1	56.9%	79.6%	14.9	2.45	17,276	91.8	23,000
Cluster 2	0.3%	0.5%	0.6	0.08	391	29.2	8,000
Cluster 3	1.2%	6.8%	1.9	0.11	764	43.5	49,000