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Utilization Patterns and Performance of Commercial Myositis Autoantibody Panels in Routine Clinical Practice

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Identifying idiopathic inflammatory myopathies (IIM), including dermatomyositis (DM), clinically amyopathic dermatomyositis (CADM), and polymyositis (PM), remains clinically challenging. Testing for myositis-associated (MAA) and myositis-specific (MSA) autoantibodies is an increasingly important tool to aid in IIM diagnosis and phenotyping. Data from research cohorts suggest MSA may be found in over 50% of DM and PM patients[1,2]. Commercial myositis autoantibody panel testing is now widely available, but studies evaluating performance of these assays is limited[3–6].

We performed retrospective analysis of all adult patients with myositis autoantibody panels ordered during routine care at all University of Pennsylvania outpatient and two inpatient locations between December 31, 2010 to March 30, 2016. Investigator-assigned diagnoses were determined using all available information except autoantibody profile and based on

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Conflicts of Interest

None

Ethical Standards

The study protocol was approved by the University of Pennsylvania institutional review board (approval #824647). A full checklist documenting adherence to STROBE recommendations for cross-sectional studies is attached separately.

Bohan and Peter criteria for classic DM and PM[7] and Sontheimer criteria for CADM[8]. "Definite CADM" required confirmatory skin biopsy, while "Possible CADM" had typical DM skin lesions without biopsy. Immune-mediated necrotizing myopathy was classified as PM and anti-synthetase as either PM or DM depending on cutaneous involvement. Patients with ILD on CT imaging without at least possible DM/PM/CADM were "ILD without myositis".

Myositis autoantibody panels were performed mostly by ARUP Laboratories (ARUP), RDL Reference Lab (RDL), Quest Diagnostics, or LabCorp. Techniques were reported by lab representatives: ARUP tested Jo-1 by semi-quantitative multiplex bead assay and other MSA by qualitative immunoprecipitation or immunoblot; RDL performed Jo-1 testing by enzyme immunoassay and other MSA by radioimmunoprecipitation assay; Quest tested through a combination of immunoassay and radioimmunoprecipitation assay; LabCorp utilized multiplex flow immunoassay.

We identified 378 patients with available commercial myositis autoantibody panel results (mean age 55 ± 15 years; 66% female; 68% white, 17% black). 76 (20%) were definite/probable IIM (i.e., DM, CADM, or PM), 48 (13%) possible IIM, and 102 (27%) ILD without myositis.

Myositis panel testing increased dramatically over time: 27 panels were sent 2011–2013, 57 in 2014, and 222 in 2015. This trend was seen for all subspecialties and indications. 274 (72%) of panels were performed by ARUP, 50 (13%) by Quest, 33 (9%) by RDL, 5 (1%) by LabCorp, and 16 (4%) through other labs. Included MSA varied by vendor. ARUP and RDL panels included Jo-1, Mi-2, PL-7, PL-12, p155/140, EJ, OJ, and SRP autoantibodies. Quest and LabCorp did not include p155/140 and only some Quest panels included SRP. Anti-HMG-CoA-reductase and MDA-5 were not included.

MSA and MAA positivity rates by diagnosis are shown in Table 1. Among patients with definite/probable IIM, 11/76 (14%) had positive MSA and 16/76 (21%) positive MAA. MSA positivity rates were higher for patients with definite/probable IIM tested through ARUP versus other commercial laboratories [10/46 (22%) vs. 1/30 (3%); $p = 0.04$]. MSA positivity rates did not change over time.

Our study illustrates real-world experience with commercial myositis autoantibody panel testing utilization and performance. Testing rapidly increased over time. Importantly, however, our positive MSA rates in patients with definite/probable IIM (14%) were substantially lower than the >50% rates reported in research-laboratory based cohort testing[1]. Low yields using commercial line blot kits were also reported in two recent small single-hospital clinical experiences where MSA were positive in 7/21 (33%) and 4/22 (18%) of IIM patients[3,4]. Disparity between commercial and research lab testing is likely partially related to differences in testing techniques and included autoantibodies.

Our study was not intended to assess the performance of any one assay or vendor and, indeed, commercial testing continues to evolve with changing testing methodology and tested autoantibodies (including at the laboratories included here) even since 2016. Rather, our study highlights the variability in commercial testing and need for standardization as

commercial MSA and MAA testing becomes increasingly widespread. Clinicians must recognize that included autoantibodies and assay methodology in a “myositis panel” may vary greatly between commercial laboratories, and that commercial MSA testing may be negative in many patients with IIM.

For limitations, diagnoses were based on chart review but used stringent criteria to identify a subset of patients with IIM with a high degree of confidence. Clinicians may not have ordered myositis autoantibody panels in patients with a clear diagnosis or if patients were tested only for particular MSA instead of the full commercial panel. Our study design did not allow assessment of false positive rates or comparison of commercial testing to a gold-standard assay.

In conclusion, commercial myositis autoantibody panel testing has dramatically, but clinicians should recognize the substantial heterogeneity in methodology and included autoantibodies in commercial panels. Negative commercial MSA testing is common even in patients with clinically confirmed IIM.

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Table 1:

Rates of myositis panel positive autoantibody testing by final diagnosis

	Myositis Panel		MSA from Myositis Panel							
	Any MSA	***Any MAA***	***Jo-1***	***Mi-2***	***PL-7***	***PL-12***	***p155/140***	***EJ***	***OJ***	***SRP***
Definite/Probable PM	**2**	**1**	0 / 16	0	0	0	0 / 13	0	0	2 / 14
n = 17	**(12 %)**	**(6 %)**	(0 %)	(0 %)	(0 %)	(0 %)	(0 %)	(0 %)	(0 %)	(14 %)
Definite/Probable DM	**6**	**6**	0 / 25	3	1	0	2 / 19	0	0	0 / 22
n = 26	**(23 %)**	**(23 %)**	(0 %)	(12 %)	(4 %)	(0 %)	(11 %)	(0 %)	(0 %)	(0 %)
Definite CADM	**3**	**9**	1 / 32	0	0	1	1 / 24	0	0	0 / 28
n = 33	**(9 %)**	**(27 %)**	(3 %)	(0 %)	(0 %)	(3 %)	(4 %)	(0 %)	(0 %)	(0 %)
Possible PM/DM/CADM	**9**	**11**	2	1	2	2	1 / 36	0	1	0 / 37
n = 48	**(19 %)**	**(23 %)**	(4 %)	(2 %)	(4 %)	(4 %)	(3 %)	(0 %)	(2 %)	(0 %)
Overlap Autoimmune Disease	**5**	**14**	1	1	1	1	0 / 22	1	1	0 / 22
n = 26	**(19 %)**	**(54 %)**	(4 %)	(4 %)	(4 %)	(4 %)	(0 %)	(4 %)	(0 %)	(0 %)
ILD without myositis	**10**	**18**	2	1	1	5	0 / 95	0	0	1 /98
n = 102	**(10 %)**	**(18 %)**	(2 %)	(1 %)	(1 %)	(5 %)	(0 %)	(0 %)	(0 %)	(1 %)
None of the above	**3**	**12**	1	1	0	0	0 / 82	0	0	1 / 90
n = 103	**(3 %)**	**(12 %)**	(1 %)	(1 %)	(0 %)	(0 %)	(0 %)	(0 %)	(0 %)	(1 %)

Definite/Probable PM or DM = 3–4 Bohan and Peter's Criteria; Possible DM or PM = 2 Bohan and Peter's Criteria; Definite CADM = consistent rash and skin biopsy; Possible CADM = consistent rash without biopsy; Overlap Autoimmune Disease = myositis due to non-IIM systemic autoimmune disease. MSA = myositis specific antibody; MAA = myositis associated antibody [Ku, PM-Scl, Ro-52, Ro-60, u1-RNP, or u2-RNP]; PM = polymyositis; DM = dermatomyositis; CADM = clinically amyopathic dermatomyositis; ILD = interstitial lung disease