The Application of Proposed Criteria for the Diagnosis and Classification of Lymphocytic Myocarditis to Autopsy Specimens

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Background: Historically, no diagnostic criteria were available for lymphocytic myocarditis in autopsy specimens. In the absence of such, the Dallas criteria has been adapted to postmortem specimens in a non-validated manner. Recently, the Society for Cardiovascular Pathology and Association for European Cardiovascular Pathology (SCVP and AECVP, respectively) are working to rectify this, bringing autopsy into alignment with endomyocardial biopsies. The aim of this study is to evaluate the provisional criteria comparing it with the adapted Dallas criteria.

Design: Institutional autopsy records were queried for cases containing a diagnosis of "lymphocytic myocarditis" (1999-2022). Existing H&E-stained slides were reviewed (by consensus of 3 cardiovascular pathologists) and assigned one of the following classifications based on the proposed criteria (**Figure 1**): Lymphocytic Infiltrate of Undetermined Significance (LIUS), Focal, Multifocal, Diffuse. Cause and manner of death and demographic information were abstracted.

Results: 25 cases (12 women) were available to review. The average decedent age was 58 yrs (range: 14–86 yrs). The manner of death was natural in 22 cases; 3 were accidents. Of 8 cases that had originally been called "borderline," five were re-classified as focal or multifocal myocarditis (**Table 1**). Of 17 cases originally called 'active," three were re-classified as LIUS. Both cases with diffuse patterns of myocarditis had been adjudicated to have infectious/inflammatory causes of death (**Table 2**). 7 cases had multifocal patterns, 4 (57%) of which had been adjudicated to have infectious/inflammatory causes of death, compared to 3 (30%) focal cases and 2 (33%) LIUS cases.

Table. Redistribution of Myocarditis Autopsy Cases using Proposed Criteria

	Proposed Criteria			
LIUS	**Focal**		**Multifocal**	**Diffuse**
Adapted Dallas Criteria	**Borderline**	3	4	1
Active	3	6	6	2

Figure 1: Draft criteria for diagnosis of lymphocytic myocarditis in large specimens

Tissue Source	Technical Requirements	Definition of Myocarditis	Extent of Myocarditis
Autopsy	6 full-thickness sections in 5 or 6 blocks*	Myocardial inflammation with myocyte injury that is not explained by another cause (ischemia, trauma, foreign body, amyloid, etc.). Myocyte injury must be distinct from changes seen in non-inflamed areas and may consist of: · single-cell hypereosinophilia · nuclear karryorrhexis/karyolysis · sarcoplasmic membrane scalloping.	*Focal:* single focus *Diffuse:* ≥50% area of a single block involved by confluent myocarditis *Multifocal:* more than a single focus but <50% area of a single block involved by confluent myocarditis
Explant			
Apical Core	Entirely submitted (to visualize epicardium to endocardium)		
Septal Myectomy	2 blocks of myocardium		
Atrial appendages / Atrioplasty	N/A	N/A	N/A

*Minimum of 1 short-axis slice (taken at mid-ventricular level) should be saved for additional processing

**In the absence of myocyte injury, the term *"lymphocytic infiltrate of undetermined significance"* can be considered.

Figure 2. Distribution of Proposed Myocarditis Classification Amongst Causes of Death

		Proposed Classification			
		LIUS	**Focal**	**Multifocal**	**Diffuse**
Causes of Death	**Infectious/Inflammatory**	2	3	4	2
	Vascular	2	5	1	
	Neoplastic			2	
	Epileptic/Neurodegenerative		1		
	Toxic	1			
	Traumatic	1	1		

Conclusion: Herein, we present a direct head-to-head comparison of adapted Dallas criteria and the recently proposed draft criteria set forth by the SCVP/AECVP for the diagnosis of myocarditis in non-biopsy specimens. This early data shows correlation between the multifocal and the diffuse patterns with previously adjudicated cause of death in our institution. More than half of the cases previously regarded as active myocarditis were "downgraded" to focal or LIUS. This better definition may help practicing pathologist better put into context myocardial inflammation that they encounter in non-biopsy samples.