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A comparison of post-COVID vaccine myocarditis classification using the Brighton Collaboration criteria versus (United States) Centers for Disease Control criteria: an update

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Introduction

Myocarditis associated with coronavirus disease 2019 (COVID-19) vaccination is a known adverse event following immunisation (AEFI). The lack of a singular diagnostic marker or test for myocarditis, besides the now infrequently undertaken histological diagnosis from biopsy, means that a combination of criteria is often needed to confirm a diagnosis.

We have previously compared various international case definitions used to support accurate diagnosis and therefore standardise treatment and management of myocarditis.¹ As more information about this important AEFI has come to light, some case definitions have been refined to provide greater sensitivity. Since our initial findings,² the Brighton Collaboration (BC) Myocarditis/ Pericarditis working group have published updated diagnostic criteria.³ An important specific update is that a reported case with symptoms consistent with myocarditis, combined with abnormal cardiac medical resonance imaging (CMR), is now classified as a 'probable' case using the BC criteria – even in the absence of a raised troponin level. This therefore brings the BC definition for a Level 2 or 'probable' case in line with a 'probable case' using the United States Centers for Disease Control and Prevention (CDC) criteria (Table 1).⁴

Given these edits, this paper aims to refine our previous findings using updated diagnostic criteria, and to evaluate if there remain discrepancies in diagnosis and data reporting between the CDC (June 2021) and BC (June 2022) criteria.

Methods

Between 1 February 2021 and 4 May 2022, Victoria's vaccine safety surveillance system (Surveillance of Adverse Events Following Vaccination In the Community (SAEFVIC)) received 460 reports of myocarditis temporally associated with COVID-19 vaccination.² Every AEFI case was also reported to the Therapeutic Goods Administration (TGA), the body that aggregates national AEFI cases on a weekly basis.

The SAFEVIC group obtained information and findings for each case to allow for diagnostic certainty classification. Two authors used the updated case definition criteria to classify each case, with any discrepancies in classification verified by a third author. No external funding was received for this study.

Results and discussion

Of 440 reported cases of myocarditis, 225 were classified as either 'confirmed' or 'probable' cases according to CDC or BC criteria (Table 1). There were no Level 3 or 'possible' cases as per BC criteria. Of the remaining cases, 37 were excluded due to a more likely alternative cause of myocarditis; 121 because they did not meet any criteria for a classification of myocarditis; and 57 because there was inadequate information to make a classification.

Even with the updated criteria, there was no change in classification level of any of the 225 cases. The BC criteria defined 79 cases (35%) as level 1 (definitive) and 146 (65%) as level 2 (probable). The CDC criteria

defined 60 (27%) as confirmed, and 165 (73%) as probable. All 60 level 1 or confirmed CDC cases were also categorised as level 1 or definitive using the BC criteria. Of the 165 level 2 or probable CDC cases, 146 were BC probable and 19 were BC definitive. All 146 BC level 2 (probable) cases also met the criteria for CDC probable cases.

The authors believe the identical distribution, despite updated BC criteria, demonstrates that it was rare for myocarditis cases to have an isolated abnormal CMR without a corresponding elevated troponin in our cohort. This is most likely due to resource access, with troponin more widely available as a first line biomarker for all cases, whereas CMR was only used in a much smaller proportion.

The discrepancies between the two criteria were 19 cases classified as definitive by BC criteria but probable by CDC criteria. This discrepancy was due to all cases having echocardiogram abnormalities but without any CMR imaging; CDC-confirmed cases require positive CMR findings if there is no histopathology, while echocardiogram abnormalities and elevated troponin alone are sufficient to classify a case as BC definitive.

While CMR may be less accessible than echocardiography, it is often more sensitive in diagnosing myocarditis due to its identification of late gadolinium enhancement (LGE), which provides evidence of myocardial injury such as necrosis, oedema, and fibrosis.³ It remains paramount as an investigation contributing to diagnosis in both the CDC and updated BC criteria, particularly because of its effectiveness and non-invasive methodology. This is important as myocarditis AEFI is predominant in the adolescent and young adult cohort, where the alternative gold-standard cardiac biopsy is less frequently performed due to its invasive nature.

If CMR is not available, echocardiography can be useful for functional assessment of the heart. Transoesophageal echocardiography is considered gold-standard when transthoracic views are limited. In settings where CMR or echocardiography are both unavailable, the BC criteria may prove more sensitive in diagnosis of myocarditis. This is because it includes a Level 3 or 'possible case' definition, which relies on more easily accessible investigations such as a chest X-ray or an electrocardiogram (ECG). A corresponding possible case definition does not exist in the CDC criteria.

Table 1: Comparison of diagnostic criteria for myocarditis

Brighton Collaboration criteria	CDC criteria ^a
Level 1 (definitive) Abnormal histopathology OR Elevated troponin AND abnormal CMR ^b OR Elevated troponin AND abnormal echocardiography	Level 1 (confirmed) Symptoms consistent with myocarditis and at least one of: Abnormal histopathology OR Elevated troponin AND abnormal CMR
Level 2 (probable) Symptoms consistent with myocarditis and at least one of: Abnormal CMR OR Elevated troponin or CKMB ^c OR Abnormal ECG ^d OR Abnormal echocardiography	Level 2 (probable) Symptoms consistent with myocarditis and at least one of: Abnormal CMR OR Abnormal troponin OR Abnormal ECG OR Abnormal echocardiography
Level 3 (possible case) Symptoms consistent with myocarditis AND Enlarged heart on CXR ^e OR non-specific ECG abnormalities	

a United States Centers for Disease Control and Prevention.

b Cardiac magnetic resonance imaging.

c Creatine kinase myocardial band.

d Electrocardiogram.

e Chest X-ray.

Conclusion

Our findings continue to provide a valuable assessment of the utility of different criteria for myocarditis cases following COVID-19 vaccination. Local guidelines may consider recommending BC criteria where CMR or echocardiography is unavailable, as it demonstrates increased sensitivity for the diagnosis of myocarditis. The current study highlights the importance of refining criteria for AEFI based on evolving data, outcomes and availability of diagnostic tools.

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