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A comparison of post-COVID vaccine myocarditis classification using the Brighton Collaboration criteria versus Centre for Disease Control criteria

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Introduction

Myocarditis associated with coronavirus disease 2019 (COVID-19) vaccines was first reported as an adverse event of special interest (AESI) in early 2021.¹ Whilst endomyocardial biopsy is the gold standard for diagnosing myocarditis, a combination of clinical features and investigations can also confirm a diagnosis.² There is no globally accepted definition for myocarditis post-vaccination, but several groups have developed case definitions (Table 1). The Centres for Disease Control and Prevention (CDC) established case definitions in 2003 for myopericarditis associated with the United States Smallpox Vaccine Immunization Program.³ In 2022, the Brighton Collaboration Myocarditis/Pericarditis working group published updated case definitions in the context of the COVID-19 vaccine-related AESI.³ These definitions are to be used in the appropriate clinical context, where other causes of myopericarditis have been excluded.

Different case definitions used nationally and internationally can create inconsistency and can limit direct comparison between jurisdictions, as well as aggregation of data. Identifying discrepancies in criteria will assist with establishing a consistent global definition for myocarditis and improve understanding of post-COVID vaccine myocarditis. This study aims to compare the classification of reported myocarditis cases post-COVID vaccination in a single patient cohort using both the Brighton Collaboration (BC) and CDC criteria.

Methods

The jurisdiction of Victoria, Australia, has a population of approximately 6.6 million. The state's vaccine safety surveillance service, Surveillance of Adverse Events Following Vaccination In the Community (SAEFVIC), received 460 reports of myocarditis temporally associated with COVID-19 vaccination between 1 February 2021 and 4 May 2022.⁴

As part of clinical safety surveillance, the SAEFVIC team obtained report details including demographic information, clinical presentations, and investigations. Two authors then used the above case definition criteria to classify each case, with any discrepancies in classification verified by a third author.

Follow-up of cases was undertaken as part of public health management of adverse events following immunisation (AEFI). SAEFVIC data is part of a clinical quality registry that forms part of Victoria's vaccine safety surveillance program. All AEFI cases were forwarded to the Therapeutic Goods Administration (TGA), which reports weekly on the national cases.⁵ No external funding was received for this study.

Results and discussion

Of 440 reported myocarditis cases, 225 were classified as confirmed/definitive or probable myocarditis using BC and CDC criteria (Table 1). Of the remaining cases, 37 were excluded due to a more likely alternative cause of myocarditis; 121 because they did not meet

Table 1: Comparison of diagnostic criteria for myocarditis³

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

- a Cardiac magnetic resonance imaging.
- b Transthoracic echocardiogram.
- c Creatine kinase myocardial band.
- d Electrocardiogram
- e Chest X-ray.

any criteria for a myocarditis classification; and 57 because there was inadequate information to make a classification.

The BC criteria classified 79 cases (35%) as level 1 (definitive) and 146 (65%) as level 2 (probable). Using CDC criteria, 60 (27%) were classified as confirmed, and 165 (73%) as probable. All 60 CDC confirmed cases were also classified as definitive using the BC criteria. Of the 165 CDC probable cases, 19 were BC definitive and 146 were BC probable. All 146 BC level 2 (probable) cases also met the criteria for CDC probable cases.

The BC and CDC criteria were largely consistent in categorising myocarditis in our dataset as confirmed/definitive or probable, but the two case definitions did not correlate absolutely. The discrepancies were nineteen cases classified as definitive by BC criteria but probable with CDC criteria. This discrepancy was due to all cases having transthoracic echocardiogram (TTE)

abnormalities but without any cardiovascular magnetic resonance (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.³

While CMR is less accessible than TTE, it is more sensitive in diagnosing myocarditis due to its unique use of late gadolinium enhancement (LGE), which can provide evidence of myocardial injury such as necrosis, oedema, and fibrosis.³ Therefore, the CDC case definition, which places more weight on CMR than the BC criteria, may be more appropriate where CMR has been performed. However, CMR is often not available, even in well-resourced settings. Of note, CMR for diagnosis of post-COVID vaccine myocarditis was not government-subsidised (under the Medicare Benefits Schedule) in Australia until January 2022.⁶ Therefore, BC criteria may potentially be more applicable in locations where CMR is not readily available.

With its large dataset, our study provides a valuable assessment of the utility of different criteria for myocarditis post-COVID vaccination. Local guidelines may consider recommending the CDC case definition where CMR is available and the BC criteria where CMR is unavailable. The study highlights the ongoing importance of refining criteria for AEFI based on evolving data, outcomes and availability of diagnostic tools.

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