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Review

Fatal Enterovirus Associated Myocarditis: Postmortem Diagnostic Confirmation Patterns and a U.S. Mortality Coding Signal Assessment

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A B S T R A C T

Introduction: Fatal enterovirus-associated myocarditis may be confirmed postmortem using multiple diagnostic approaches, including myocardial RT-PCR, sequencing, VP1 or viral capsid immunohistochemistry, electron microscopy, routine histology, inflammatory immunohistochemistry and non-myocardial viral testing. These methods provide different forms of evidence and published fatal cases vary in whether viral material is demonstrated directly in myocardium or only in extra-cardiac specimens.

Methods: A PubMed-based full-text review was performed to identify fatal myocarditis case reports and case series involving suspected or confirmed enteroviral infection, including coxsackievirus and echovirus where specified. Extracted variables included study type, fatal case count, myocardial tissue testing, RT-PCR, VP1 or viral capsid immunohistochemistry, demonstration of viral material in myocardium and diagnostic notes abstracted from the full text. CDC WONDER Multiple Cause of Death files for the United States (U.S.) were queried to describe myocarditis/viral carditis mortality coding and co-listing of enterovirus code B34.1 across non-overlapping 1999–2017 and 2018–2024 query periods.

Results: The literature-review dataset included 12 studies describing 34 fatal cases. Viral material was demonstrated in myocardium in 24 of 34 cases overall and in 24 of 31 cases in which myocardial tissue-based testing was performed. Myocardial RT-PCR was performed in 14 of 34 cases and VP1 or viral capsid-type immunohistochemistry was performed in 25 of 34 cases. In the U.S. CDC WONDER Multiple Cause of Death files for 1999–2024, myocarditis/viral carditis-coded deaths numbered 38,046 and enterovirus code B34.1 was co-listed in 83 cases, representing 0.22% of myocarditis/viral carditis-coded deaths in the queried dataset.

Conclusion: Fatal enterovirus-associated myocarditis is confirmed inconsistently across the selected published fatal case literature. Direct myocardial testing provides stronger evidence for enteroviral myocardial involvement than non-myocardial viral detection alone, but the available case-report and case-series data do not support formal sensitivity or specificity estimates for the reviewed testing methods. CDC WONDER findings describe mortality coding patterns and rare co-listing of B34.1 among myocarditis/viral carditis-coded deaths, but they do not establish the true national burden of fatal enteroviral myocarditis.

Keywords: Infective myocarditis; Enterovirus infection; Mortality data

Introduction

Fatal myocarditis may be reported with varying degrees of etiologic specificity. In the fatal enterovirus-associated myocarditis cases selected for this review, published reports used multiple diagnostic approaches, including myocardial RT-PCR, VP1 or viral capsid immunohistochemistry, sequencing, electron microscopy, routine histology, inflammatory immunohistochemistry and testing of non-myocardial specimens[1-12]. These methods do not provide identical evidence. Some directly demonstrate viral material in myocardium, while others demonstrate systemic or extra-cardiac viral infection without proving myocardial localization[1-12].

Across the included reports, fatal presentations included neonatal fatal infection or sepsis[2,4], sudden unexpected death in a young athlete or child[5,8], suspected sudden infant death syndrome context[12], progressive myocarditis and multisystem organ failure[9] and fatal or severe myocarditis or heart muscle disease in autopsy and case-series settings[1,6,10-11]. These reports support a tissue-level diagnostic framework rather than a single terminal mechanism: myocarditis was interpreted in relation to direct myocardial viral findings when available, including enteroviral RNA, viral antigen, sequencing evidence or virus-like particles[1-3,5-6,9-12]. Because the selected reports varied in specimen source and testing method, the central diagnostic question becomes whether viral evidence is localized to the myocardium rather than detected only in extra-cardiac specimens[3-4,7-8].

The purpose of this study was to describe how fatal enterovirus-associated myocarditis has been confirmed in the selected published case-report and case-series literature and to compare those confirmation patterns with United States (U.S.) mortality coding patterns in CDC WONDER Multiple Cause of Death files[1-12]. The study does not attempt to determine the true national prevalence of fatal enteroviral myocarditis. Instead, it evaluates whether the published fatal literature shows heterogeneity in confirmatory methods and whether mortality coding demonstrates limited co-listing of enterovirus among myocarditis/viral carditis-coded deaths.

This distinction is central to the interpretation of the study. The selected case literature can show how published fatal cases documented enteroviral involvement, including whether testing demonstrated viral material directly in the myocardium or only in non-myocardial specimens[1-12]. The CDC WONDER data can identify how often selected ICD-coded myocarditis or viral carditis deaths also list an enterovirus etiology code in the queried files. These data cannot determine how many additional deaths truly resulted from enteroviral myocarditis but were not tested, diagnosed, reported or coded as such. Accordingly, this manuscript describes the CDC WONDER findings as a mortality coding signal rather than proof of the true burden of fatal enteroviral myocarditis.

Materials & Methods

PubMed search strategy and case selection

A PubMed-based full-text review was performed to identify human fatal myocarditis case reports and case series involving suspected or confirmed enteroviral infection, including coxsackievirus and echovirus where specified. The final PubMed search was performed on May 7, 2026, using the following search string: ((enterovirus OR coxsackievirus OR "coxsackie virus" OR "coxsackievirus b" OR CVB) AND myocarditis AND (fatal OR death OR "sudden death" OR autopsy OR postmortem OR forensic)) NOT (review[pt] OR systematic review[pt] OR meta-analysis[pt]). Filters included English, humans, exclude preprints, publication date from 1990 through 2026 and the following article-type filters: case reports, clinical study, comparative study, evaluation study, multicenter study, observational study and validation study. This search returned 51 results.

Records were screened for relevance to fatal enterovirus-associated myocarditis. Articles were eligible for extraction if they described human fatal myocarditis with suspected or confirmed enteroviral infection and included postmortem cardiac findings and/or viral testing. Articles were excluded if they were reviews, systematic reviews, meta-analyses, preprints, non-human studies, non-English articles, did not describe fatal myocarditis, did not include relevant postmortem cardiac findings or viral testing or did not provide case-level information sufficient for diagnostic-method extraction. One PubMed-indexed article was identified during review but was included in the analytic extraction because full text could not be obtained.

For each included report, extracted variables included PubMed identifier, study type, number of fatal cases, whether myocardial tissue testing, RT-PCR, VP1 or viral capsid immunohistochemistry was performed, whether viral material was demonstrated in the myocardium and qualitative notes on the diagnostic approach. The extracted analytic set contained 12 studies describing 34 fatal cases. One additional PubMed-indexed article was identified during review but was not included in the analytic extraction because full text could not be obtained. A structured data extraction spreadsheet was created from the selected PubMed full-text review and served as the primary dataset for the literature-review component of this study.

CDC WONDER multiple cause of death query

CDC WONDER Multiple Cause of Death files were queried to evaluate mortality coding patterns for myocarditis/viral carditis and co-listing of enterovirus etiology code B34.1. Extracted CDC WONDER results combined non-overlapping 1999-2017 and 2018-2024 query periods to generate a 1999–2024 series. The WONDER component was used to describe coding frequency, not to establish the true incidence or prevalence of fatal enteroviral myocarditis.

CDC WONDER Multiple Cause of Death data are based on death certificate information coded using ICD-10. Each death certificate includes one underlying cause of death and may include additional multiple-cause codes for other conditions reported on the death certificate. For this analysis, myocarditis/viral carditis-coded deaths were queried with attention to co-listing of enterovirus code B34.1. Because CDC WONDER reflects coded death certificate data rather than case-level diagnostic review, absence of B34.1 co-listing was interpreted as absence of coded enteroviral attribution in the queried mortality record, not absence of true enteroviral infection.

Results

Viral material was demonstrated in myocardium in 24 of 34 cases overall and in 24 of 31 cases in which myocardial tissue-based testing was performed. Myocardial RT-PCR was performed in 14 of 34 cases. VP1 or viral capsid-type immunohistochemistry was performed in 25 of 34 cases.

The reports varied substantially in the type and location of viral testing. Nine reports demonstrated viral material directly in myocardium by RT-PCR, VP1 or capsid immunohistochemistry, sequencing or electron microscopy[1-3,5-6,9-12]. Four reports included viral detection in non-myocardial specimens such as blood, plasma, throat culture, stool, spleen, liver or pancreas[3-4,7-8]. Among these, one report also demonstrated enterovirus RNA in myocardium and was therefore interpreted as myocardial confirmation rather than extra-cardiac positivity alone[3]. Five reports used more than one viral-directed or ancillary diagnostic method, including combinations of myocardial RT-PCR, VP1/capsid immunohistochemistry, sequencing, inflammatory immunohistochemistry and electron microscopy[1-2,5-6,10].

RT-PCR and sequencing

RT-PCR was used to detect enteroviral RNA in several included reports. Myocardial RT-PCR was documented in five reports[1-3,5-6]. One report described enteroviral RNA in myocardium with sequencing confirmation.1 A neonatal autopsy report described enterovirus RNA detected in heart tissue by RT-PCR in two cases, with sequencing identifying echovirus 5 and echovirus 11.2 Another case report described enterovirus RNA detected from myocardium, with additional liver and pancreas involvement noted in the extracted review.3 One report paired RT-PCR performed on heart tissue with VP1 immunohistochemistry[5]. Another reported RT-semi-nested PCR positivity in one of two fatal cases[6].

Sequencing was reported in selected cases and provided additional viral specificity when performed. Sequencing confirmed viral material in one report,1 identified echovirus 5 and echovirus 11 in the neonatal autopsy report[2] and identified echoviruses 6, 13 and 7 in one case series[10]. These sequencing results strengthened etiologic specificity when paired with evidence of myocardial involvement.

The interpretive strength of RT-PCR depended on specimen source. Myocardial RT-PCR positivity was treated as stronger evidence for enteroviral myocarditis than RT-PCR positivity limited to plasma, blood, stool, throat, spleen, liver, pancreas or another non-cardiac specimen. One report described throat culture and plasma RT-PCR without stated myocardial positivity[4]. Another described enterovirus PCR positivity in blood only[7]. A third described enterovirus RNA detected in stool and spleen by PCR, while virus could not be cultured from postmortem stool, spleen or heart[8]. These reports were therefore interpreted differently from reports with myocardial RT-PCR positivity.

The selected reports did not provide enough information to compare RT-PCR sensitivity or specificity across cases. Myocardial RT-PCR was not performed in every fatal case and the reports did not consistently include a uniform comparator group or a standardized reference test. Therefore, RT-PCR was analysed as a method of molecular confirmation when applied to myocardium, not as a method with calculable diagnostic accuracy from the current dataset.

VP1 / Viral capsid immunohistochemistry

VP1 or viral capsid-type immunohistochemistry was one of the most commonly reported tissue-based approaches in the extracted cases. This method detects viral protein in tissue sections and can provide anatomic localization when staining is demonstrated in myocardium. VP1 or related capsid/viral antigen immunohistochemistry was documented in six reports[2,5-6,10-12].

In the neonatal autopsy report, VP1-related testing was reported alongside CD3/CD68 inflammatory immunohistochemistry, myocardial RT-PCR and sequencing[2]. Another report described VP1 immunohistochemistry and RT-PCR performed on heart tissue[5]. One report described VP1 antibody staining, with RT-semi-nested PCR positive in one of two cases[6]. A separate report described a polyclonal marker showing immunolabeled enteroviral antigen in cardiomyocyte cytoplasm[12]. One case series reported enteroviral capsid protein VP1 detected in duplicate myocardial tissue sections from six of nine myocarditis cases and three of four dilated cardiomyopathy cases[11]. Another case series included partial VP1-related testing and sequencing in fatal cases where echoviruses 6, 13 and 7 were identified[10].

The current dataset supports VP1/capsid immunohistochemistry as a tissue-localizing method used in published fatal and severe myocardial disease cases. It does not support a pooled estimate of sensitivity or specificity. The reports did not consistently describe standardized staining protocols, antibody selection, interpretation thresholds, controls or blinded review and VP1/capsid staining was not uniformly applied across all cases.

Electron microscopy

Electron microscopy was reported less frequently than RT-PCR or VP1/capsid immunohistochemistry. One case report described electron microscopy findings as consistent with coxsackievirus myocarditis in a fatal case with an enlarged, dilated heart, cardiac and pericardial fibrinous adhesions and death attributed to progressive myocarditis and multisystem organ failure[9]. Another report described enteroviral RNA and virus-like particles in myocardium, with sequencing confirmation[1].

In this review, electron microscopy was treated as supportive tissue-based evidence when reported. It was not analysed as a routine diagnostic method because it was rarely used in the extracted fatal cases and was not systematically applied across the study set. The available data does not permit estimation of diagnostic sensitivity or specificity for electron microscopy.

Routine histology and inflammatory immunohistochemistry

Routine histology was central to establishing myocarditis as the pathologic substrate in the reviewed fatal cases. Viral-directed testing was interpreted in relation to myocardial inflammation and injury when those findings were described. Inflammatory immunohistochemistry, including CD3 and CD68 staining, was specifically noted in the neonatal autopsy report, where frozen myocardial sections showed CD3/CD68-positive inflammatory infiltrates in two cases[2]. In that report, inflammatory immunohistochemistry was paired with enterovirus RNA detected in heart tissue by RT-PCR and sequencing that typed the viruses as echovirus 5 and echovirus 11[2].

Other reports established myocarditis or myocardial disease in combination with viral-directed evidence. One report paired heart-tissue RT-PCR with VP1 immunohistochemistry[5]. A second report paired VP1 antibody staining with RT-semi-nested PCR positivity in one of two cases[6]. One additional report described immunolabeled enteroviral antigen in cardiomyocyte cytoplasm[12]. A separate case report described autopsy findings of an enlarged, dilated heart and fibrinous cardiac/pericardial

adhesions, with electron microscopy interpreted as consistent with coxsackievirus myocarditis[9].

CD3 and CD68 immunohistochemistry does not identify enterovirus. Their value in the reviewed reports was contextual: they helped characterize myocardial inflammation, while viral-directed methods such as RT-PCR, sequencing or VP1/capsid immunohistochemistry supported etiologic attribution when viral material was demonstrated. This distinction was maintained throughout the analysis.

Non-myocardial viral testing

Several reports identified enterovirus in non-myocardial specimens. One report described a virus detected by throat culture and RT-PCR in plasma, but myocardial positivity was not stated in the extracted review.4 Another described enterovirus PCR positivity in blood only[7]. A third described enterovirus RNA detected in stool and spleen by PCR, while virus could not be cultured from postmortem stool, spleen or heart.8 One report described enterovirus RNA detected from myocardium, with liver and pancreas also noted; because myocardium was positive in that report, it was interpreted differently from cases with only extra-cardiac positivity[3].

These non-myocardial findings were considered supportive of enteroviral infection but were not considered equivalent to myocardial confirmation. This distinction affected the interpretation of cases where myocarditis was present but viral testing was positive only outside the heart or where myocardial positivity was not stated. These cases remained relevant to the descriptive review but were interpreted as having weaker evidence for direct enteroviral myocardial involvement than cases with viral RNA, viral antigen, sequencing evidence or virus-like particles demonstrated in myocardium **(Table1)**.

Table 1: Included Studies and Diagnostic Features Extracted from Full-Text Review.

Study Type	Fatal cases, n	Myocardial Tissue Testing	RT-PCR	VP1/ capsid IHC	Sequencing	Electron Microscopy	Non-myocardial Viral Testing	Viral Material Demonstrated in Myocardium	Extracted Diagnostic Notes
Case report[1]	2	Yes	Yes	No/unclear	Yes	Virus-like particles reported	Not stated	Yes	Enteroviral RNA and virus-like particles were reported in myocardium, sequencing confirmed viral material
Case report[2]	2	Yes	Yes	Yes, also CD3/CD68	Yes	Not stated	Not stated	Yes	Two neonatal autopsy cases, myocardial inflammatory infiltrates were evaluated with CD3/CD68, enterovirus RNA was detected in heart by RT-PCR, VP1 sequencing typed echovirus 5 and echovirus 11
Case report[3]	1	Yes	Yes	Unclear	Not stated	Not stated	Yes, liver/pancreas also noted	Yes	Enterovirus RNA was detected from myocardium, with liver and pancreas also noted in the extracted review
Case report[4]	1	No/unclear	No myocardial RT-PCR, plasma only	No	Not stated	Not stated	Yes, throat culture and plasma RT-PCR	Unclear	Virus was detected by throat culture and RT-PCR in plasma, myocardial positivity was not stated in the extracted review
Case report[5]	1	Yes	Yes	Yes	Not stated	Not stated	Not stated	Yes	VP1 immunohistochemistry and RT-PCR were performed on heart tissue
Case report[6]	2	Yes	Partial, 1 of 2 cases	Yes	Not stated	Not stated	Not stated	Yes	VP1 antibody staining was performed, RT-semi-nested PCR was positive in one of two cases
Case report[7]	1	No	No	No	Not stated	Not stated	Yes, blood PCR	No	Enterovirus PCR was positive on blood only in the extracted review
Case report[8]	1	No	No myocardial PCR	No	Not stated	Not stated	Yes, stool and spleen PCR	No	A 10-year-old girl died suddenly with myocarditis at postmortem examination, virus could not be cultured from postmortem stool, spleen or heart, but enterovirus RNA was detected in stool and spleen by PCR

Case report[9]	1	No direct myocardial viral molecular/IHC testing recorded	No	No	Not stated	Yes	Not stated	Partial, EM visualization only	Autopsy showed an enlarged, dilated heart with cardiac and pericardial fibrinous adhesions, electron microscopy was reported as consistent with coxsackievirus myocarditis, death was attributed to progressive myocarditis and multisystem organ failure
Case series[10]	8	Yes	Partial	Partial	Yes	Not stated	Not stated	Yes	Enterovirus was identified in 5 of 27 cases in the source series, among the extracted fatal cases, enterovirus was detected by the 5-prime non-translated region in three cases and VP1 sequencing identified echoviruses 6, 13 and 7
Case series[11]	13	Yes	No	Yes	Not stated	Not stated	Not stated	Yes	Enteroviral capsid protein VP1 was detected in duplicate myocardial tissue sections from six of nine myocarditis cases and three of four dilated cardiomyopathy cases
Case report[12]	1	Yes	Partial	Partial, polyclonal marker	Not stated	Not stated	Not stated	Yes	A polyclonal marker revealed immunolabeled enteroviral antigen in cardiomyocyte cytoplasm

CDC WONDER mortality coding findings

In the CDC WONDER Multiple Cause of Death files for 1999–2024, myocarditis/viral carditis-coded deaths numbered 38,046. Enterovirus code B34.1 was co-listed in 83 cases, representing 0.22% of myocarditis/viral carditis-coded deaths in the queried dataset. Co-listing was higher in the 2018-2024 query period than in the 1999-2017 query period, based on the extracted results.

These findings describe the frequency of enterovirus co-listing in mortality coding among the queried myocarditis/viral carditis-coded deaths. They do not establish the true number of fatal enteroviral myocarditis cases in the U.S. They also do not determine whether cases lacked testing, lacked diagnosis, lacked documentation or were coded differently. Therefore, the WONDER findings are best interpreted as a coding observation that may be consistent with incomplete etiologic capture, not as proof of under-ascertainment.

Discussion

Diagnostic methods were grouped analytically into myocardial RT-PCR and sequencing, VP1 or viral capsid immunohistochemistry, electron microscopy, routine histology and inflammatory immunohistochemistry and non-myocardial viral testing[1-12]. These categories were not laboratory procedures performed for the present study; rather, they were interpretive categories used to describe and compare how the selected published fatal cases documented enteroviral involvement.

Detection of enterovirus in blood, plasma, throat culture, stool, spleen, liver, pancreas or other extra-cardiac sites may support enteroviral infection or exposure, but it was not considered direct myocardial confirmation unless the report also demonstrated viral material in myocardium[3,4,7,8]. This distinction was used because non-myocardial viral detection does not, by itself, localize viral material to the myocardium.

This review demonstrates heterogeneity in how fatal enterovirus-associated myocarditis has been confirmed in the selected published case-report and case-series literature[1-12]. The included reports used multiple diagnostic methods, including myocardial RT-PCR, sequencing, VP1 or viral capsid immunohistochemistry, electron microscopy, routine histology, inflammatory immunohistochemistry and non-myocardial viral testing[1-12]. These approaches provide different types of evidence and should not be treated as interchangeable.

The strongest evidence for enteroviral myocarditis in this review came from reports that demonstrated viral material directly in myocardium.1-3,5-6,9-12 Myocardial RT-PCR provided molecular evidence of enteroviral RNA in cardiac tissue.1-3,5-6 Sequencing increased etiologic specificity when performed[1,2,10]. VP1 or capsid immunohistochemistry provided tissue localization of viral antigen[2,5,6,10-12]. Electron microscopy, when reported, provided supportive ultrastructural evidence[1,9]. Routine histology and inflammatory immunohistochemistry established or characterized myocarditis but did not identify enterovirus by themselves[2,9].

Non-myocardial viral testing had a different evidentiary role. Detection of enterovirus in blood, plasma, throat culture, stool, spleen, liver or pancreas supported infection but did not prove viral localization to the heart[3,4,7,8]. In fatal myocarditis, this distinction is important because the causal question depends on whether viral material is linked to myocardial injury. The reviewed reports therefore support separating direct myocardial viral confirmation from extra-cardiac viral detection[1-12].

This review also shows why sensitivity and specificity cannot be defensibly assigned from the current dataset. The included

reports were not diagnostic accuracy studies[1-12]. They were selected fatal case reports and case series with variable testing strategies, variable specimen sources and variable reporting detail[1-12].

The CDC WONDER findings add a separate mortality coding perspective. Enterovirus code B34[1]. was rarely co-listed among myocarditis/viral carditis-coded deaths in the queried MCOD files. This observation may raise the possibility of incomplete etiologic capture, particularly when considered alongside the heterogeneous confirmation methods in the published fatal literature[1-12]. However, the current design cannot determine the true national rate of fatal enteroviral myocarditis or prove that all uncoded cases represent missed enteroviral disease. The appropriate interpretation is therefore cautious: mortality coding rarely specifies enterovirus among myocarditis/viral carditis-coded deaths in the queried data, while the case literature shows that confirmation depends on whether and how myocardial tissue is tested[1-12].

Limitations

This study is limited by the nature of the selected literature. The included reports were primarily case reports and case series rather than prospective or standardized diagnostic studies[1-12]. Methods were not uniformly applied across cases and reports varied in the level of detail provided about specimen source, testing platform, antibody selection, sequencing, controls and interpretation criteria[1-12]. These limitations prevent direct comparison of test performance.

This review did not calculate pooled sensitivity, specificity, positive predictive value or negative predictive value for any diagnostic method. Since the included reports were primarily case reports and case series, they were not designed as diagnostic accuracy studies[1-12]. They did not apply a uniform test panel across all cases, did not use a consistent reference standard and did not include the comparison groups required to estimate test performance.

The review is also limited by selection and publication bias. Published fatal cases may overrepresent diagnostically unusual, severe or well-confirmed cases[1-12]. Conversely, fatal myocarditis cases without viral testing, without myocardial tissue testing or without full reporting may not appear in the literature captured for this review[1-12]. Therefore, the proportions reported here describe the selected literature sample and should not be interpreted as population-level rates[1-12].

The CDC WONDER analysis is limited to coded mortality data. Death certificate coding depends on diagnosis, documentation, certifier language and ICD-10 coding rules. Each mortality record reflects what was certified and coded, not an independent review of the decedent's clinical, autopsy or laboratory materials. The absence of B34.1 co-listing does not prove absence of enteroviral infection and the presence of myocarditis/viral carditis coding does not indicate which diagnostic tests were performed. Therefore, the WONDER data can describe coding patterns but cannot establish true disease prevalence or quantify under-ascertainment. The case literature reviewed here further demonstrates why coding data cannot be assumed to reflect uniform diagnostic workup, because the included reports used heterogeneous myocardial and non-myocardial confirmation methods **(Table2)**[1-12].

Table 2: Diagnostic Method Interpretation.

Testing Category	Primary Contribution	Strongest Interpretation Supported by This Review	Limitation
Routine myocardial histology[1-12]	Establishes myocarditis and myocardial injury	Supports the pathologic diagnosis of myocarditis	Does not identify enterovirus etiology
CD3/CD68 or inflammatory IHC[2]	Characterizes inflammatory infiltrates	Supports inflammatory characterization of myocarditis	Not virus-specific
Myocardial RT-PCR[1-3,5-6]	Detects enteroviral RNA in cardiac tissue	Supports molecular evidence of viral material in myocardium	Not uniformly performed; no sensitivity/specificity estimate possible[1-12]
Sequencing[1-2,10]	Identifies viral type or strain when performed	Strengthens specificity of viral attribution	Not performed in all reports[1-12]
VP1/capsid IHC[2,5-6,10-12]	Detects viral protein in tissue sections	Supports tissue localization of viral antigen in myocardium	Protocols and interpretation vary; no sensitivity/specificity estimate possible from this dataset[1-12]
Electron microscopy[1,9]	Identifies virus-like particles or ultrastructural findings when reported	Provides supportive tissue-based evidence in selected cases	Rarely reported and not systematically applied[1-12]
Non-myocardial PCR/culture[3,4,7,8]	Detects enterovirus outside the heart	Supports systemic or extra-cardiac infection	Does not directly demonstrate myocardial viral involvement

Conclusion

In the selected fatal enterovirus-associated myocarditis literature, postmortem diagnostic confirmation methods were heterogeneous. Direct myocardial testing by RT-PCR, sequencing, VP1 or viral capsid immunohistochemistry and occasionally electron microscopy provided stronger evidence for enteroviral myocardial involvement than non-myocardial viral testing alone. Routine histology and inflammatory immunohistochemistry remained important for establishing and characterizing myocarditis but were not enterovirus specific.

The available case-report and case-series data support descriptive conclusions about diagnostic method use and evidentiary strength. They do not support formal sensitivity or specificity estimates for the testing methods reviewed. The CDC WONDER MCOD findings show rare co-listing of enterovirus code B34[1]. among myocarditis/viral carditis-coded deaths in the queried dataset, but these data should be interpreted as a mortality coding observation rather than proof of the true national burden of fatal enteroviral myocarditis.

Overall, this review supports cautious, method-focused conclusions: fatal enterovirus-associated myocarditis can be confirmed postmortem when myocardial tissue is directly tested,

but published reports vary in how confirmation is performed and reported. Future work would require standardized myocardial sampling, consistent application of viral-directed testing and clearly defined reporting criteria to compare diagnostic methods more directly.

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