

# Systematic Review/Meta-analysis

## Echocardiographic Criteria to Differentiate Constrictive Pericarditis From Restrictive Cardiomyopathy: A Meta-analysis

Carlos Diaz-Arocutipa, MD,<sup>a</sup> María Chumbiauca, MS,<sup>b</sup> Hector M. Medina, MD, MPH,<sup>c</sup> Adrian V. Hernandez, MD, PhD,<sup>a,d</sup> and Lourdes Vicent, MD<sup>e,f</sup>

<sup>a</sup>Unidad de Revisiones Sistemáticas y Meta-análisis (URSIGET), Vicerrectorado de Investigación, Universidad San Ignacio de Loyola, Lima, Peru

<sup>b</sup>Facultad de Ciencias de la Salud, Universidad San Ignacio de Loyola, Lima, Peru

<sup>c</sup>Division of Cardiology, Fundacion CardioInfantil-La Cardio, Bogota, Colombia

<sup>d</sup>Health Outcomes, Policy, and Evidence Synthesis (HOPES) Group, University of Connecticut School of Pharmacy, Storrs, Connecticut, USA

<sup>e</sup>Cardiology Department, Hospital Universitario 12 de Octubre and Instituto de Investigación Sanitaria Hospital 12 de Octubre (imas12), Madrid, Spain

<sup>f</sup>Centro de Investigación Biomédica en Red Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain

### Echocardiographic Criteria to Differentiate Constrictive Pericarditis From Restrictive Cardiomyopathy: A Meta-analysis

#### Summary

Mayo Clinic echocardiographic criteria has a good diagnostic accuracy to differentiate constrictive pericarditis and restrictive cardiomyopathy in patients with signs/symptoms of heart failure

#### Data sources

17 studies

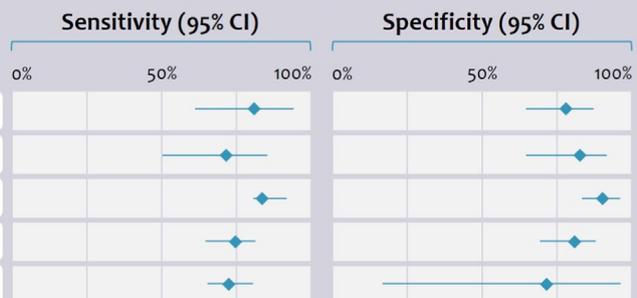
889 participants



#### Results

##### Echocardiographic parameters

Ventricular septal shift
Respiratory variation in mitral inflow $\geq 14.6\%$
Septal e' velocity $\geq 8\text{cm/s}$
Septal e' velocity/lateral e' velocity $\geq 0.88$
Hepatic vein ratio in expiration $\geq 0.79$



## ABSTRACT

**Background:** To assess the diagnostic accuracy of the Mayo Clinic echocardiographic criteria for differentiating between constrictive pericarditis and restrictive cardiomyopathy.

**Methods:** We searched electronic databases for the date range from their inception to July 1, 2022. The index tests were the Mayo Clinic echocardiographic criteria. We performed a bivariate random-effects model to estimate the pooled sensitivity and specificity, each with 95% confidence interval (CI). The area under the curve of the summary receiver operator characteristic curves, with 95% CI, was also calculated.

**Results:** We included 17 case-control studies involving 889 patients. The pooled sensitivity and specificity (95% CI), respectively, were as follows: ventricular septal shift, 82% (60%-94%) and 78% (65%-87%); respiratory variation in mitral inflow  $\geq 14.6\%$ , 71% (51%-85%) and 82% (66%-91%); septal e' velocity  $\geq 8$  cm/s, 83% (80%-87%) and 90% (83%-95%); septal e' velocity/lateral e' velocity  $\geq 0.88$ , 74% (64%-82%) and 81% (70%-88%); and hepatic vein ratio in expiration  $\geq 0.79$ , 73% (65%-81%) and 71% (19%-96%). The area under the curve of the summary receiver operator characteristic curves varied from 0.75 to 0.85, with overlapping CIs across index tests.

**Conclusions:** Our meta-analysis suggests that all echocardiographic parameters from the Mayo Clinic criteria have good diagnostic accuracy for differentiating between constrictive pericarditis and restrictive cardiomyopathy.

## RÉSUMÉ

**Contexte :** Évaluation de l'exactitude diagnostique des critères échocardiographiques de la clinique Mayo visant à faire la distinction entre une péricardite constrictive et une cardiomyopathie restrictive.

**Méthodologie :** Nous avons effectué une recherche dans des bases de données électroniques pour la période s'étendant de leur date de création au 1<sup>er</sup> juillet 2022. Les tests de concordance portaient sur les critères échocardiographiques de la clinique Mayo. Nous avons réalisé un modèle à effets aléatoires et à deux variables afin d'estimer la sensibilité et la spécificité en fonction des données regroupées, chacune avec un intervalle de confiance (IC) à 95 %. L'aire sous la courbe des courbes caractéristiques sommaires de la performance du test, avec un IC à 95 %, a également été calculée.

**Résultats :** Nous avons inclus 17 études cas-témoins comptant 889 patients. Selon les données groupées, la sensibilité et la spécificité (IC à 95 %), respectivement, étaient les suivantes : déplacement du septum interventriculaire, 82 % (60 à 94 %) et 78 % (65 à 87 %); variation respiratoire lors du remplissage mitral  $\geq 14,6$  %, 71 % (51 à 85 %) et 82 % (66 à 91 %); vitesse e' mesurée en septal  $\geq 8$  cm/s, 83 % (80 à 87 %) et 90 % (83 à 95 %); rapport vitesse e' mesurée en septal/vitesse e' mesurée en latéral  $\geq 0,88$ , 74 % (64 à 82 %) et 81 % (70 à 88 %); et rapport veineux hépatique lors de l'expiration  $\geq 0,79$ , 73 % (65 à 81 %) et 71 % (19 à 96 %). L'aire sous la courbe des courbes caractéristiques sommaires de la performance du test variait de 0,75 à 0,85, avec des IC se chevauchant dans les tests de concordance.

**Conclusions :** Notre méta-analyse laisse entendre que tous les paramètres échocardiographiques de la clinique Mayo ont une bonne exactitude diagnostique pour faire la distinction entre la péricardite constrictive et la cardiomyopathie restrictive.

In clinical practice, the diagnostic task of differentiating between constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM) remains a challenge.<sup>1,2</sup> The difficulty is due to the fact that the 2 conditions exhibit similar clinical features consistent with heart failure. Although most patients have preserved ejection fraction, many cases of CP or RCM are accompanied by a slight reduction in left systolic function.<sup>3,4</sup> Despite this overlap between the conditions, their treatment and prognosis differ significantly. Hence, a timely diagnosis is required to provide specific and early treatment, which has the potential to influence the survival of these patients.<sup>5</sup>

Cardiac catheterization with classic and modern hemodynamic criteria is still considered the gold standard for CP.<sup>2,6</sup> However, due to its invasive nature and the expertise required for this procedure, a reliable noninvasive diagnostic technique is needed. Currently, transthoracic echocardiography (TTE) is the first-line diagnostic test when CP is suspected. Nevertheless, other imaging modalities, such

as cardiac magnetic resonance or computed tomography, may be helpful when TTE produces inconclusive results.<sup>1,7</sup>

The Mayo Clinic criteria for the TTE diagnosis of CP have been adopted and described in several studies.<sup>8</sup> These criteria are based on hemodynamic parameters and pathophysiological mechanisms of CP.<sup>1</sup> The pooled analysis of the 5 TTE variables may help clinicians discriminate between CP and RCM.<sup>7</sup> Therefore, the objective of this meta-analysis is to assess the diagnostic accuracy of these criteria in differentiating between these 2 conditions using completely different treatment modalities.

## Methods

This review was reported according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>9,10</sup>

## Search strategy

The search was conducted in 4 electronic databases (PubMed, Embase, Scopus, and Web of Science), including the date range from their inception to July 1, 2022. The following terms were used: “constrictive pericarditis”; “constriction”; “restrictive cardiomyopathy”; and “restriction.” The complete search strategy is available in [Supplemental Table S1](#). No restriction on language or publication year

Received for publication March 2, 2023. Accepted June 4, 2023.

Corresponding author: Dr Carlos Diaz-Arocutipa, Vicerrectorado de Investigación, Universidad San Ignacio de Loyola, Av. La Fontana 550, La Molina, Lima 15024, Peru. Tel.: +51-994-928-488.

E-mail: [cdiazar@usil.edu.pe](mailto:cdiazar@usil.edu.pe)

See page 689 for disclosure information.

was applied to the search. In addition, a hand search of reference lists of included studies was performed.

### Eligibility criteria

The inclusion criteria were as follows: (i) cross-sectional, case-control, and cohort studies that included adult patients (aged  $\geq 18$  years); (ii) studies that assessed any of the Mayo Clinic echocardiographic criteria (ventricular septal shift, respiratory variation in mitral inflow  $\geq 14.6\%$ , septal e' velocity  $\geq 8$  cm/s, septal e' velocity/lateral e' velocity  $\geq 0.88$ , and hepatic vein ratio in expiration  $\geq 0.79$ ) for differentiating between constrictive pericarditis and restrictive cardiomyopathy<sup>8</sup>; and (iii) studies that reported the true positives, false negatives, true negatives, and false positives of each echocardiographic parameter. Case reports, case series, commentaries, systematic reviews, and narrative reviews were excluded.

### Study selection

All articles were downloaded to EndNote X9 software (Thompson Reuters, Philadelphia, PA), and duplicate records were removed. Titles/abstracts and the full text were independently screened by 2 of the review authors for relevance. Any disagreements were resolved by consensus.

### Data extraction

Data from each study were independently extracted by 2 review authors using a standardized data extraction form. The following information was extracted: first author name; publication year; study design; country; sample size; study period; population; age; sex; diagnostic methods for CP and RCM; etiology of CP and RCM; the reference standard for CP; and the number of true positives, true negatives, false positives, and false negatives for each echocardiographic parameter.

### Assessment of methodological quality

The **Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2)** tool was used to assess the methodological quality of all studies.<sup>11</sup> The QUADAS-2 tool is divided into 2 sections (risk-of-bias assessment and applicability concerns) and consists of 4 domains (patient selection, index test, reference standard, and flow and timing). All domains are considered for risk of bias, and the first 3 domains are considered for applicability. Each domain was classified as having "high," "low," or "unclear" quality. Two review authors independently performed this evaluation, and any disagreements were resolved by consensus.

### Statistical analyses

A bivariate random-effects model was used to estimate the summary sensitivity and specificity with the 95% confidence interval (CI) of each echocardiographic parameter.<sup>12</sup> In addition, a summary receiver operating characteristic (SROC) curve was also fitted, and the area under the curve (AUC) of each SROC curve was calculated. The 95% CI for each AUC was estimated using a bootstrapping technique, and the significance of the pair-wise differences of AUCs was evaluated.<sup>13</sup> Heterogeneity between studies was assessed by visually inspecting the SROC curves, by observing the degree of closeness between the 95% predictive region and the 95%

confidence region.<sup>12</sup> Publication bias was not evaluated because of the current uncertainty about how to assess publication bias in diagnostic test accuracy reviews. All meta-analyses were conducted using the *mada* and *dmetatools* packages from R 4.2.0 software (R Foundation for Statistical Computing, Vienna, Austria). A 2-tailed *P*-value  $< 0.05$  was considered statistically significant.

## Results

### Study selection

The electronic search retrieved 1597 citations. After the removal of duplicates, 909 citations were screened by title/abstract, and of those, 855 were excluded. After a full-text assessment of the 54 remaining articles, 37 were excluded for the following reasons: being a case report ( $n = 11$ ); having incomplete data ( $n = 6$ ); being a conference abstract ( $n = 12$ ); and being an editorial ( $n = 8$ ). Finally, 17 studies were selected (Fig. 1).<sup>8,14-29</sup>

### Study characteristics

The main characteristics of the 17 included studies are summarized in Table 1. All studies had a case-control design involving a total of 889 patients. Eleven studies were performed in the US and the rest in Germany, South Korea, China, or Italy. The range of sample sizes was 13-166 patients. The mean age ranged from 26 to 66 years across studies, and 74% were men. In nearly all studies, the sample of patients was consecutive. In 12 studies, patients presented with signs and/or symptoms of heart failure, whereas in the rest, this information was not reported. The reference standard for CP was surgical findings in 8 studies, and cardiac catheterization, computed tomography, or cardiac magnetic resonance imaging in the remaining studies. In 6 studies, the reference standard for RCM was biopsy, and in the rest, it was cardiac catheterization or cardiac magnetic resonance imaging. The most common etiologies of CP were idiopathic and postcardiac surgery in 44% and 35% of patients, respectively. For RCM, the most common etiology was cardiac amyloidosis in 71% of patients.

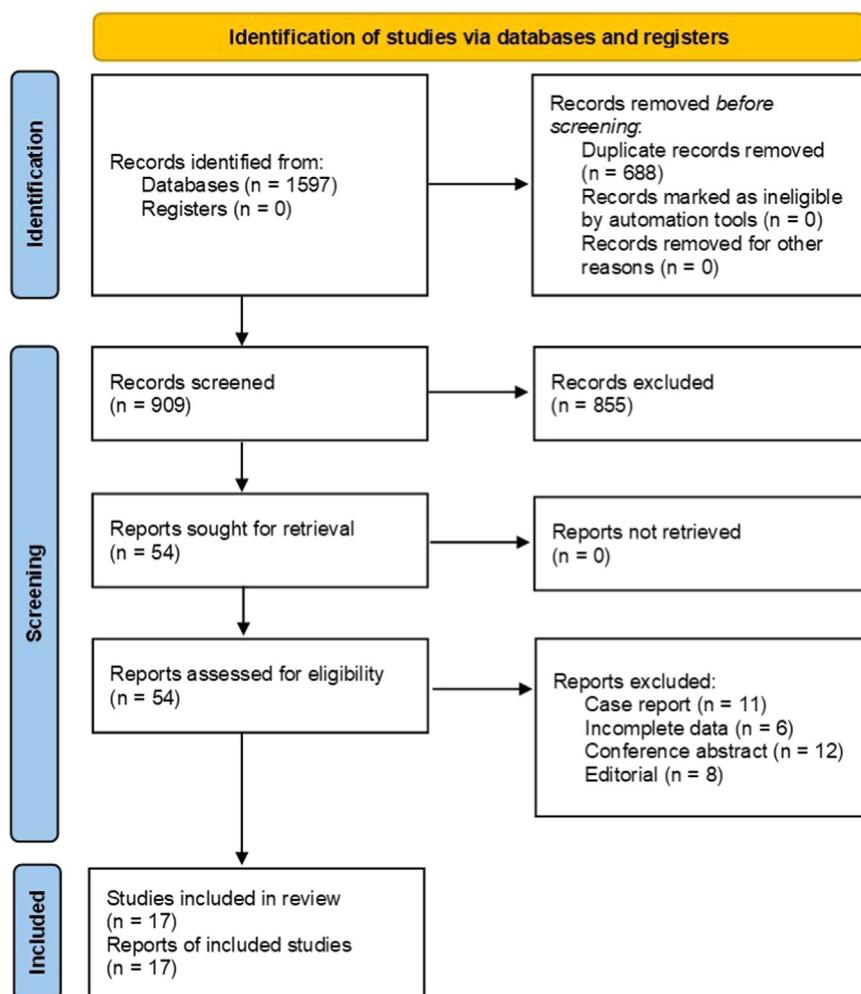
### Quality assessment

The methodological assessment using the QUADAS-2 tool is available in Figure 2. Overall, most studies had a high risk of bias, owing mainly to the patient selection domain. The domains of index tests, reference standard, and flow and timing mostly had either a high or an unclear risk of bias. In contrast, most studies had a low risk of poor applicability.

### Echocardiographic parameters

**Ventricular septal shift.** In 4 studies ( $n = 383$ ), the sensitivity varied from 62% to 93%, and the pooled sensitivity was 82% (95% CI 60%-94%). The specificity varied from 69% to 94%, and the pooled specificity was 78% (95% CI 65%-87%). The AUC of the SROC curve was 0.84 (95% CI 0.72-0.91; Fig. 3).

**Respiratory variation in mitral inflow  $\geq 14.6\%$ .** In 5 studies ( $n = 365$ ), the sensitivity varied from 38% to 94%,



**Figure 1.** Flow diagram of study selection.

and the pooled sensitivity was 71% (95% CI 51%-85%). The specificity varied from 72% to 96%, and the pooled specificity was 82% (95% CI 66%-91%). The AUC of the SROC curve was 0.84 (95% CI 0.66-0.88; [Fig. 3](#)).

**Septal e' velocity  $\geq 8$  cm/s.** In 12 studies (n = 705), the sensitivity varied from 75% to 79%, and the pooled sensitivity was 83% (95% CI 80%-87%). The specificity varied from 71% to 98%, and the pooled specificity was 90% (95% CI 83%-95%). The AUC of the SROC curve was 0.85 (95% CI 0.81-0.92; [Fig. 3](#)).

**Septal e' velocity/lateral e' velocity  $\geq 0.88$ .** In 3 studies (n = 375), the sensitivity varied from 67% to 87%, and the pooled sensitivity was 74% (95% CI 64%-82%). The specificity varied from 73% to 86%, and the pooled specificity was 81% (95% CI 70%-88%). The AUC of the SROC curve was 0.85 (95% CI 0.70-0.90; [Fig. 3](#)).

**Hepatic vein ratio in expiration  $\geq 0.79$ .** In 2 studies (n = 303), the sensitivity varied from 70% to 76%, and the

pooled sensitivity was 73% (95% CI 65%-81%). The specificity varied from 43% to 89%, and the pooled specificity was 71% (95% CI 19%-96%). The AUC of the SROC curve was 0.75 (95% CI 0.55-0.91; [Fig. 3](#)).

### Comparisons between echocardiographic parameters

Statistical tests for pair-wise comparisons between echocardiographic parameters show that the AUCs of all echocardiographic parameters have no significant differences ([Supplemental Table S2](#)).

### Discussion

This meta-analysis, including 17 case-control studies and 889 patients, to evaluate the accuracy of differentiation between CP and RCM using echocardiographic assessment, shows that the following: (i) all echocardiographic parameters from the Mayo Clinic criteria have good diagnostic accuracy; (ii) used separately, each one of the echocardiographic criteria has a good discriminative capacity for the differential diagnosis of CP and RCM; and (iii) echocardiographic criteria reflect

**Table 1. Main characteristics of included studies**

Study	Country	Diagnosis of CP	Diagnosis of RCM	Etiology of CP	Etiology of RCM	Sample size	Age, y	Male, %
Butz et al. <sup>14</sup> (2008)	Germany	Surgery	Cardiac biopsy and clinical features	Post-cardiac surgery: 8; inflammatory: 6; idiopathic: 6	Cardiac amyloidosis: 12; idiopathic: 2	CP: 20; RCM: 14	58 ± 12	71
Butz et al. <sup>15</sup> (2010)	Germany	Surgery	Cardiac biopsy	Post-cardiac surgery: 13; chest irradiation: 3; idiopathic: 18	Cardiac amyloidosis: 26	CP: 34; RCM: 26	CP: 58 ± 12; RCM: 65 ± 9	57
Choi et al. <sup>16</sup> (2007)	South Korea	Clinical or radiologic or hemodynamics	Echocardiography or cardiac biopsy	Post-cardiac surgery: 8; tuberculosis: 4; idiopathic: 5	Cardiac amyloidosis: 2; idiopathic: 10	CP: 17; RCM: 12	CP: 55.2 ± 12; RCM: 51.9 ± 20	79
Choi et al. <sup>17</sup> (2011)	South Korea	Echocardiography and CT or surgery or cardiac catheterization	Cardiac biopsy	Tuberculous pericarditis: 11; post-cardiac surgery: 9; idiopathic: 17	Cardiac amyloidosis: 32; endomyocardial fibrosis: 3	CP: 37; RCM: 35	CP: 49 ± 17; RCM: 58 ± 9	60
Garcia et al. <sup>18</sup> (1996)	US	Surgery or CMR	Cardiac biopsy or CMR	Postpericardiectomy: 6; idiopathic: 2	Cardiac amyloidosis: 4; nonspecific fibrosis: 1; diabetic small vessel disease: 1; post-heart transplantation: 1	CP: 8; RCM: 7	CP: 61 ± 11; RCM: 63 ± 12	87
Ha et al. <sup>19</sup> (2004)	US	Surgery	Echocardiography and/or systemic biopsy	Post-cardiac surgery: 8; undetermined: 15	Cardiac amyloidosis: 38; idiopathic: 14	CP: 23; RCM: 52	CP: 59 ± 13; RCM: 66 ± 10	71
Hatle et al. <sup>20</sup> (1989)	US	Surgery	Echocardiography or cardiac catheterization or CT or cardiac biopsy	Unknown: 3; post-cardiac surgery: 2; previous radiation therapy: 2	Systemic infiltrative disorder (amyloidosis, Fabry's disease): 3; charcot-Marie-tooth disease: 1; previous radiation: 1; previous cardiac transplantation: 5; unknown: 2	CP: 7; RCM: 12	CP: 52 ± 11; RCM: 49 ± 16	NR
Himelman et al. <sup>21</sup> (1989)	US	Clinical or surgery or autopsy or CT or CMR or cardiac catheterization	Clinical or echocardiography or cardiac biopsy or cardiac catheterization	Post-cardiac surgery: 18; malignancy: 8; end-stage renal failure: 6; purulent pericarditis: 2; tuberculosis: 1; radiation: 1; collagen-vascular disease: 1; unknown: 2	Cardiac amyloidosis: 6; interstitial myocardial fibrosis: 6; endomyocardial fibrosis associated with eosinophilia: 2; radiation cardiomyopathy: 2	CP: 39; RCM: 16	NR	NR
Liu et al. <sup>22</sup> (2018)	China	Echocardiography or CT or surgery	Biopsy	Viral: 11, unknown: 13	Cardiac amyloidosis: 24	CP: 24; RCM: 24	CP: 53 ± 12; RCM: 54 ± 9	75
Mancuso et al. <sup>23</sup> (1991)	Italy	Surgery or cardiac catheterization	Clinical or echocardiography or cardiac biopsy or cardiac catheterization	Tuberculosis: 5; post-cardiac surgery: 1; recurrent pericarditis: 1	Cardiac amyloidosis: 1; thalassemia major: 1; idiopathic: 4	CP: 7; RCM: 6	CP: 50 ± 10; RCM: 54 ± 9	85

Qamruddin et al. <sup>24</sup> (2019)	US	Surgery	Cardiac biopsy	Viral or idiopathic or rheumatologic: 75%, post-cardiac surgery: 13%, post-radiation: 7%	Cardiac amyloidosis: 30	CP: 107; RCM: 30	CP: 58.9 ± 13.8; RCM: 69.7 ± 9.9	82
Rajagopalan et al. <sup>25</sup> (2001)	US	Surgery or CMR or cardiac catheterization	Echocardiography or cardiac catheterization or cardiac biopsy	Post-cardiac surgery: 3; chronic infection: 2; radiation: 1, idiopathic: 13	Cardiac amyloidosis: 8; hypertension: 1; diabetic small vessel disease: 1; idiopathic: 1	CP: 19; RCM: 11	CP: 56 ± 13; RCM: 66 ± 12	90
Reuss et al. <sup>26</sup> (2009)	US	Unspecified	Cardiac biopsy or fat biopsy	Idiopathic: 10; post-CABG: 4	Cardiac amyloidosis: 10	CP: 14; RCM: 10	CP: 63 (25–75); RCM: 69 (47–88)	NR
Sengupta et al. <sup>28</sup> (2004)	US	Surgery	Echocardiography or cardiac biopsy	Tuberculosis: 26; pyogenic: 2; post-radiation: 2; unknown: 15	Biventricular endomyocardial fibrosis: 9; idiopathic myocardial fibrosis: 1; cardiac amyloidosis: 1	CP: 45; RCM: 11	CP: 24 ± 12; RCM: 29 ± 8	55
Sengupta et al. <sup>27</sup> (2008)	US	Surgery	Extracardiac biopsy and echocardiography	Post-cardiac surgery: 7; radiotherapy: 2; idiopathic: 7	Cardiac amyloidosis: 15	CP: 16; RCM: 15	CP: 61.8 ± 13; RCM: 60.5 ± 9	74
Tei et al. <sup>29</sup> (1983)	US	Surgery or cardiac catheterization	Autopsy or biopsy	NR	Cardiac amyloidosis: 12	CP: 13; RCM: 12	CP: 47 (29–67); RCM: 49 (15–74)	72
Welch et al. <sup>8</sup> (2014)	US	Surgery	Echocardiography or catheterization or endomyocardial biopsy	Idiopathic or related to rheumatologic disease: 77; post-cardiac surgery: 39; post-chest radiation: 14	NR	CP: 130; RCM: 36	CP: 62 ± 12.2; RCM: 61.3 ± 13.3	75

CABG, coronary artery bypass grafting; CT, computed tomography; CMR, cardiac magnetic resonance; CP, constrictive pericarditis; NR, not reported; RCM, restrictive cardiomyopathy.



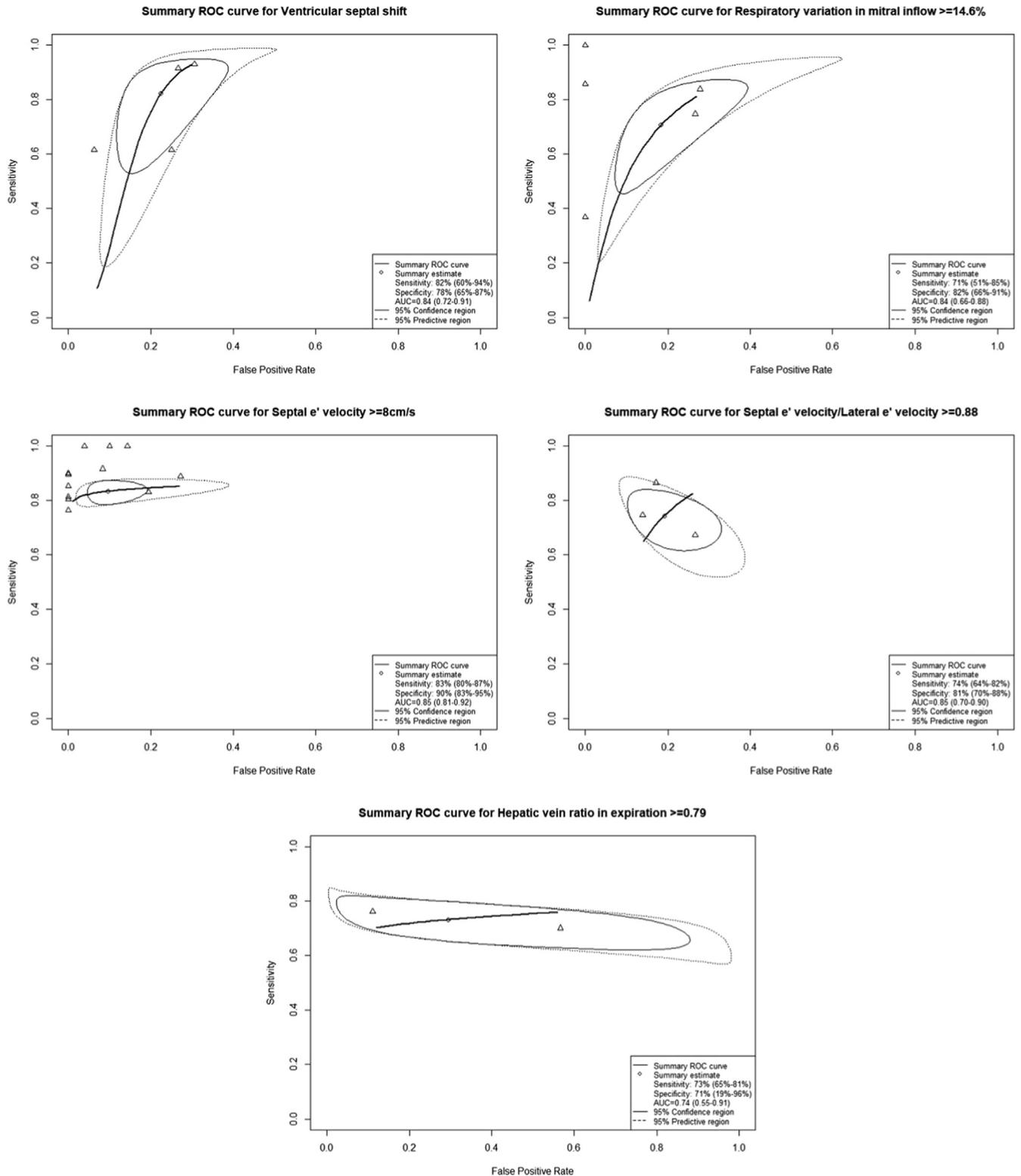
**Figure 2. Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) summary items for risk of bias and applicability concerns for all studies.**

the pathophysiological changes underlying the pericardial involvement of CP.

Currently, both CP and RCM are underdiagnosed conditions.<sup>30,31</sup> As these entities share common clinical manifestations,<sup>31,32</sup> diagnosis poses a challenge in daily clinical practice. With the evolution of multimodality cardiac imaging techniques (mainly cardiac computed tomography and cardiac magnetic resonance imaging), the diagnosis of both these diseases has improved.<sup>7</sup> However, we must not forget that these exams are not first-line tests for patients with suspected CP,<sup>7,33,34</sup> as they entail a high cost and are not universally available, which can further delay the correct diagnosis, especially in low-resource healthcare systems. These multimodal imaging techniques provide mainly an anatomic analysis of the pericardium and cardiac chambers.<sup>35</sup> However, a point to note is that among anatomic abnormalities, pericardial calcification or thickening may be absent in about

20% of CP cases, and therefore, a noncalcified and nonthickened pericardium does not exclude CP.<sup>7,36</sup> In this respect, the Doppler hemodynamic assessment provided by TTE presents a significant advantage over other imaging techniques that offer only an anatomic evaluation of the pericardium.<sup>7,8,34</sup>

Although each echocardiographic parameter described had acceptable individual sensitivity and specificity, the combination of all 5 echocardiographic criteria may have higher diagnostic accuracy, as shown in studies that combined 2-dimensional imaging and Doppler echocardiographic parameters.<sup>8,33</sup> Qamruddin et al. found that the combination of ventricular septal shift and septal e' velocity had the best overall sensitivity and specificity, of 80% and 92%, respectively.<sup>24</sup> Although addition of the hepatic vein ratio in expiration to the previous 2 criteria increases specificity (97%), it reduces sensitivity (70%). Our review does not allow us to



**Figure 3.** Summary receiver operating characteristic (ROC) curve for the Mayo Clinic echocardiographic criteria to differentiate between constrictive pericarditis and restrictive cardiomyopathy. The **black curve** corresponds to summary ROC. The **open black triangles** are sensitivity and specificity estimates per study. The **open black circle** is the pooled estimate of sensitivity and specificity.

report the diagnostic accuracy of the 5 combined echocardiographic parameters, owing to the lack of individual data per study. Similarly, this accuracy also was not assessed in previous studies, including the only 2 studies that provided information on hepatic vein ratio in expiration.<sup>8,24</sup> Although a reasonable proposal would be that the combined use of the 5 criteria could improve diagnostic performance, this possibility should be assessed further in an individual patient-data meta-analysis. In CP, the main physiological mechanisms that explain the subsequent echocardiographic findings are as follows: (i) a noncompliant pericardium, with a fixed volume; and (ii) dissociation between thoracic and intracardiac pressure. Both phenomena entail an exaggerated ventricular interdependence.<sup>37</sup> The adherence of the noncompliant pericardium to the lateral wall of both ventricles impedes the displacement of the heart valve annulus during cardiac contraction,<sup>22</sup> and the interventricular septum motion is normal or even increased.<sup>8</sup> This effect is the underlying explanation for the echocardiographic parameters of increased/normal septal  $e'$  wave velocity, as well as the reduction of the lateral  $e'$ , which has been called "annulus reversus."<sup>26</sup> In contrast, in patients with RCM, the displacement of the myocardium during cardiac contraction is globally reduced.<sup>22,24</sup> In CP, dynamic respiratory changes reflecting an exaggerated ventricular interdependence are evidenced by the anomalous displacement of the septum with respiratory movements (respiration-related ventricular septal shift), which can be best evaluated using the M-mode,<sup>24</sup> as well as the exaggerated variability of transmitral inflow velocities, which are significantly reduced on inspiration, owing to the increase in the volume of the right cavities within the constricted pericardium and the decreased gradient between the pulmonary capillaries and the left-sided chambers, leading to a reduction in the capacitance of the left ventricle.<sup>38</sup> About one third of patients with constriction may have no respiratory variation, especially when left ventricular filling pressure is markedly elevated. In this situation, maneuvers to reduce preload may unmask respiratory variation.<sup>39</sup> Besides, the exaggerated reversal flow in the hepatic vein during expiration is also a consequence of the dissociation of intrathoracic and intracardiac pressures.<sup>8</sup> A hepatic vein ratio in expiration  $\geq 0.79$  has been described as the most specific echocardiographic finding for CP, although this is the most difficult Doppler finding to obtain and analyze.<sup>8,24</sup> However, in our meta-analysis pooling almost 900 patients, we found similar sensitivity and specificity for all 5 addressed parameters.

This work has relevant implications and applicability in daily clinical practice. Based on these results, we can conclude that TTE is a reliable diagnostic technique for the differential diagnosis of CP and RCM. Several advantages favour the use of TTE. The test is easily accessible and is the first complementary examination performed on patients with symptoms of heart failure,<sup>8,32,40,41</sup> although its interpretation requires expertise during performance and interpretation. Another advantage of echocardiography in detecting constriction is that CP can be diagnosed even in patients without clinical consideration of CP, by showing these diagnostic features of constriction, as ventricular septal motion abnormalities can be detected during the initial portion of echocardiography, which can prompt further Doppler evaluation. However, a point to consider is that the septal shift observed in CP follows a

respiratory pattern and should be differentiated from the paradoxical septal motion present after cardiac surgery.<sup>42</sup> The individual parameters of the Mayo Clinic diagnostic criteria may occur in patients without constriction. For example,  $e'$  velocity may not be useful in young patients, as  $e'$  is expected to be well preserved in such patients, so greater reliance on other parameters is required. Therefore, we need to know the sensitivity and specificity of the diagnostic criteria as a whole, rather than that of individual parameters. Also, a point that needs to be clarified is whether constriction can be diagnosed when 2 or 3 of the criteria are met, or whether all of them are required. These questions need to be addressed in future studies.

In this meta-analysis, the addressed echocardiographic parameters have shown to have adequate reliability for differentiating between CP and RCM. Although the 2 entities have similar clinical features, they have very different etiology, prognosis, and treatment.<sup>43,44</sup> A surgical pericardiectomy is curative in CP, when it is performed on a timely basis,<sup>32</sup> so a prompt diagnosis is decisive. Given the increasing availability of tests for the assessment of the myocardium and the pericardium, from both a functional and a morphologic/structural perspective, each technique has potential applicability and utility.<sup>7,32</sup> Hemodynamic evaluation with cardiac catheterization is the gold-standard diagnostic test and is recommended to confirm the diagnosis when noninvasive tests are inconclusive, or if further evaluation is needed (ie, mixed cardiac pathology, or hemodynamic significance).<sup>32,37</sup> Other anatomic tests, such as cardiac magnetic resonance imaging, and computed tomography are complementary, and they are particularly useful when TTE is not diagnostic or for preoperative planning in patients with suspected CP.<sup>7,35</sup>

TTE is also very useful for the periodic monitoring and follow-up of patients with pericardial disease.<sup>7</sup> For example, TTE can be used to evaluate the response to treatment of patients with pericardial inflammation and to identify, early, those who develop constrictive physiology. Additionally, in patients with CP who underwent surgical pericardiectomy, the echocardiographic follow-up shows normalization of lateral/medial mitral  $e'$  velocities.<sup>45</sup> Some CP findings may present transiently in the context of pericardial inflammation, and in this regard, cardiac magnetic resonance has value in detecting active pericardial inflammation, which would imply a favourable response to anti-inflammatory treatment.<sup>7,46</sup> The diagnosis of transient constriction should be made retrospectively, once the constrictive physiology has resolved.<sup>47</sup>

This review should be interpreted with caution, and with consideration of some limitations. First, the design of the included studies (case-control) may be subject to some degree of bias, overestimating the value of diagnostic accuracy parameters. Second, clinical heterogeneity was present among the studies, owing to variation in the etiology of CP and RCM, and variability in the gold standard. A point to note is that cardiac biopsy remains the gold standard for the definitive histologic diagnosis of cardiac amyloidosis, yet it has been considered the main criterion in only 6 of the 17 included studies. Therefore, this difference in the gold standard for RCM could result in a measurement error. Third, providing information on mixed constriction and restriction disease was not possible. Fourth, as individual-patient data were not available for each study, evaluation of diagnostic accuracy by

combining echocardiographic parameters was not possible. Therefore, we cannot evaluate the Mayo Clinic echocardiographic criteria as a whole, but rather each criterion can be evaluated separately. Fifth, some patient characteristics may limit the usefulness and interpretation of echocardiographic parameters for the diagnosis of CP. Mitral annular velocities tend to be high in young patients, so this parameter should be applied with caution in this population group. The hepatic vein expiratory diastolic inversion ratio is difficult to obtain accurately, especially in patients with obesity, pulmonary disease, thoracic deformity, and previous thoracic surgery, among other conditions. Sixth, TTE is a very operator-dependent study, which requires an adequate level of training for its correct use in different clinical scenarios. Seventh, although we conducted a comprehensive search for studies in 4 electronic databases, we did not search for unpublished literature. Thus, a publication bias could have been introduced into our results. Finally, the profile of the included patients could be somewhat heterogeneous and not fully representative of daily clinical practice, so a desirable study design is to assess the reliability of these TTE criteria prospectively.

## Conclusion

Our review suggests that TTE can be used to differentiate reliably between CP and RCM. The 5 echocardiographic parameters of the Mayo Clinic criteria have good diagnostic accuracy in patients with suspicion of pericardial constriction.

## Acknowledgements

The authors thank Sergio Moreno and Mario Vargas for their comments on the manuscript.

## Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

## Patient Consent

The authors confirm that patient consent is not applicable to this article.

## Funding Sources

The authors have no funding sources to declare.

## Disclosures

The authors have no conflicts of interest to disclose.

## References

1. Chetrit M, Natalie Szpakowski N, Desai MY. Multimodality imaging for the diagnosis and treatment of constrictive pericarditis. *Expert Rev Cardiovasc Ther* 2019;17:663-72.
2. Geske JB, Anavekar NS, Nishimura RA, Oh JK, Gersh BJ. Differentiation of constriction and restriction: complex cardiovascular hemodynamics. *J Am Coll Cardiol* 2016;68:2329-47.
3. Kyrouac D, Schiffer W, Lennep B, et al. Echocardiographic and clinical predictors of cardiac amyloidosis: limitations of apical sparing. *ESC Heart Fail* 2022;9:385-97.
4. Porta-Sánchez A, Sagristà-Sauleda J, Ferreira-González I, et al. Constrictive pericarditis: etiologic spectrum, patterns of clinical presentation, prognostic factors, and long-term follow-up. *Rev Esp Cardiol (Engl Ed)* 2015;68:1092-100.
5. Welch TD, Oh JK. Constrictive pericarditis: old disease, new approaches. *Curr Cardiol Rep* 2015;17:20.
6. Welch TD, Oh JK. Constrictive pericarditis. *Cardiol Clin* 2017;35:539-49.
7. Alajaji W, Xu B, Sripariwuth A, et al. Noninvasive multimodality imaging for the diagnosis of constrictive pericarditis. *Circ Cardiovasc Imaging* 2018;11:e007878.
8. Welch TD, Ling LH, Espinosa RE, et al. Echocardiographic diagnosis of constrictive pericarditis Mayo Clinic criteria. *Circ Cardiovasc Imaging* 2014;7:526-34.
9. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
10. McInnes MDF, Moher D, Thombs BD, et al. Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. *JAMA* 2018;319:388-96.
11. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529-36.
12. Deeks JJ, Bossuyt PM, Leeflang MM, Takwoingi Y. *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy*. 1st edition. Chichester, UK: John Wiley & Sons, 2023.
13. Noma H, Matsushima Y, Ishii R. Confidence interval for the AUC of SROC curve and some related methods using bootstrap for meta-analysis of diagnostic accuracy studies. *Commun Stat Case Stud Data Anal Appl* 2021;7:344-58.
14. Butz T, Faber L, Piper C, et al. Tissue Doppler imaging in the differential diagnosis of constrictive pericarditis and restrictive cardiomyopathy. *Dtsch Med Wochenschr* 2008;133:399-405.
15. Butz T, Piper C, Langer C, et al. Diagnostic superiority of a combined assessment of the systolic and early diastolic mitral annular velocities by tissue Doppler imaging for the differentiation of restrictive cardiomyopathy from constrictive pericarditis. *Clin Res Cardiol* 2010;99:207-15.
16. Choi E-Y, Ha J-W, Kim J-M, et al. Incremental value of combining systolic mitral annular velocity and time difference between mitral inflow and diastolic mitral annular velocity to early diastolic annular velocity for differentiating constrictive pericarditis from restrictive cardiomyopathy. *J Am Soc Echocardiogr* 2007;20:738-43.
17. Choi JH, Choi J-O, Ryu DR, et al. Mitral and tricuspid annular velocities in constrictive pericarditis and restrictive cardiomyopathy: correlation with pericardial thickness on computed tomography. *JACC Cardiovasc Imaging* 2011;4:567-75.
18. Garcia MJ, Rodriguez L, Ares M, et al. Differentiation of constrictive pericarditis from restrictive cardiomyopathy: assessment of left ventricular diastolic velocities in longitudinal axis by Doppler tissue imaging. *J Am Coll Cardiol* 1996;27:108-14.
19. Ha J-W, Ommen SR, Tajik AJ, et al. Differentiation of constrictive pericarditis from restrictive cardiomyopathy using mitral annular velocity by tissue Doppler echocardiography. *Am J Cardiol* 2004;94:316-9.

20. Hatle LK, Appleton CP, Popp RL. Differentiation of constrictive pericarditis and restrictive cardiomyopathy by Doppler echocardiography. *Circulation* 1989;79:357-70.
21. Himelman RB, Lee E, Kircher B, Schiller NB. Plethora of the inferior vena cava with blunted respiratory response: a useful echocardiographic sign of pericardial disease. *Echocardiography* 1989;6:159-68.
22. Liu S, Ren W, Zhang J, et al. Incremental value of the tissue motion of annular displacement derived from speckle-tracking echocardiography for differentiating chronic constrictive pericarditis from restrictive cardiomyopathy. *J Ultrasound Med* 2018;37:2637-45.
23. Mancuso L, D'Agostino A, Pitrolo F, et al. Constrictive pericarditis versus restrictive cardiomyopathy: the role of Doppler echocardiography in differential diagnosis. *Int J Cardiol* 1991;31:319-27.
24. Qamruddin S, Alkharabsheh SK, Sato K, et al. Differentiating constriction from restriction (from the Mayo Clinic echocardiographic criteria). *Am J Cardiol* 2019;124:932-8.
25. Rajagopalan N, Garcia MJ, Rodriguez L, et al. Comparison of new Doppler echocardiographic methods to differentiate constrictive pericardial heart disease and restrictive cardiomyopathy. *Am J Cardiol* 2001;87:86-94.
26. Reuss CS, Wilansky SM, Lester SJ, et al. Using mitral 'annulus reversus' to diagnose constrictive pericarditis. *Eur J Echocardiogr* 2009;10:372-5.
27. Sengupta PP, Krishnamoorthy VK, Abhayaratna WP, et al. Comparison of usefulness of tissue Doppler imaging versus brain natriuretic peptide for differentiation of constrictive pericardial disease from restrictive cardiomyopathy. *Am J Cardiol* 2008;102:357-62.
28. Sengupta PP, Mohan JC, Mehta V, et al. Accuracy and pitfalls of early diastolic motion of the mitral annulus for diagnosing constrictive pericarditis by tissue Doppler imaging. *Am J Cardiol* 2004;93:886-90.
29. Tei C, Child JS, Tanaka H, Shah PM. Atrial systolic notch on the interventricular septal echogram: an echocardiographic sign of constrictive pericarditis. *J Am Coll Cardiol* 1983;1:907-12.
30. Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases: the Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) endorsed by: the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2015;36:2921-64.
31. McKenna WJ, Maron BJ, Thiene G. Classification, epidemiology, and global burden of cardiomyopathies. *Circ Res* 2017;121:722-30.
32. Syed FF, Schaff HV, Oh JK. Constrictive pericarditis—a curable diastolic heart failure. *Nat Rev Cardiol* 2014;11:530-44.
33. Ardhanari S, Yarlagadda B, Parikh V, et al. Systematic review of non-invasive cardiovascular imaging in the diagnosis of constrictive pericarditis. *Indian Heart J* 2017;69:57-67.
34. Klein AL, Abbara S, Agler DA, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. *J Am Soc Echocardiogr* 2013;26:965-1012. e1015.
35. Kamdar AR, Meadows TA, Roselli EE, et al. Multidetector computed tomographic angiography in planning of reoperative cardiothoracic surgery. *Ann Thorac Surg* 2008;85:1239-45.
36. Senapati A, Isma'eel HA, Kumar A, et al. Disparity in spatial distribution of pericardial calcifications in constrictive pericarditis. *Open Heart* 2018;5:e000835.
37. Doshi S, Ramakrishnan S, Gupta SK. Invasive hemodynamics of constrictive pericarditis. *Indian Heart J* 2015;67:175-82.
38. Hurrell DG, Nishimura RA, Higano ST, et al. Value of dynamic respiratory changes in left and right ventricular pressures for the diagnosis of constrictive pericarditis. *Circulation* 1996;93:2007-13.
39. Welch TD. Constrictive pericarditis: diagnosis, management and clinical outcomes. *Heart* 2018;104:725-31.
40. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2016;29:277-314.
41. Omar AM, Bansal M, Sengupta PP. Advances in echocardiographic imaging in heart failure with reduced and preserved ejection fraction. *Circ Res* 2016;119:357-74.
42. Hudson CC, Hudson JK. The interventricular septum: measurement and motion. *Anesth Analg* 2013;116:788-92.
43. Szabó G, Schmack B, Bulut C, et al. Constrictive pericarditis: risks, aetiologies and outcomes after total pericardiectomy: 24 years of experience. *Eur J Cardiothorac Surg* 2013;44:1023-8; discussion 1028.
44. Bertog SC, Thambidorai SK, Parakh K, et al. Constrictive pericarditis: etiology and cause-specific survival after pericardiectomy. *J Am Coll Cardiol* 2004;43:1445-52.
45. Veress G, Ling LH, Kim KH, et al. Mitral and tricuspid annular velocities before and after pericardiectomy in patients with constrictive pericarditis. *Circ Cardiovasc Imaging* 2011;4:399-407.
46. Haley JH, Tajik AJ, Danielson GK, et al. Transient constrictive pericarditis: causes and natural history. *J Am Coll Cardiol* 2004;43:271-5.
47. Oh JK, Hatle LK, Mulvagh SL, Tajik AJ. Transient constrictive pericarditis: diagnosis by two-dimensional Doppler echocardiography. *Mayo Clin Proc* 1993;68:1158-64.

### Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjopen.ca/> and at <https://doi.org/10.1016/j.cjco.2023.06.002>.