Defining cardiac involvement in idiopathic inflammatory myopathies: a systematic review

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Abstract

Objective: Recent advances in cardiac magnetic resonance imaging (CMR) and other diagnostic techniques have made it easier to identify subclinical cardiac inflammation and dysfunction in the idiopathic inflammatory myopathies (IIM). Herein, we systematically review the literature regarding cardiac involvement in IIM.

Methods: We searched Medline and EMBASE from 1990-2020 using keywords related to IIM and cardiac disease. We included English language studies in adults with any immune-mediated, inflammatory muscle pathology.

Results: We identified 10425 potentially relevant abstracts, of which 29 were included. Most frequently these included patients with polymyositis or dermatomyositis without symptomatic myocarditis. Five categories of cardiac investigation were used in these patients: cardiac enzyme testing, electrocardiography (ECG), transthoracic echocardiography (TTE), CMR and nuclear medicine testing. Patients with clinical myocarditis had universally abnormal cardiac troponin levels and ECG. Elevated cardiac troponin T was more common than troponin I (cTnI) and may correlate with disease activity, whereas cTnI was more specific for cardiac involvement. Non-specific ECG changes were common. The major finding on TTE was abnormal ejection fraction. Gross systolic dysfunction was unusual, but subclinical systolic dysfunction was reported in several studies. Abnormal diastolic function was common and may be associated with disease duration. Late gadolinium enhancement (reflecting regional necrosis or scar) and abnormal myocardial mapping parameters (reflecting myocardial inflammation, fibrosis and oedema) were frequently identified on CMR, suggesting significant subclinical myocardial pathology (despite typically normal ejection fraction).

Conclusion: Abnormal cardiac investigations are commonly found in asymptomatic IIM patients, which has potential prognostic and treatment implications.

Key words: myositis, cardiac involvement, cardiac investigation, troponin, echocardiography, cardiac magnetic resonance imaging

Key Messages

- Cardiac involvement is a comorbidity of idiopathic inflammatory myopathies, but has no clear consensus definition.
- Transthoracic echocardiography and cardiac MRI may reveal abnormalities in asymptomatic patients.
- Further data are required to understand clinical and prognostic implications of these abnormalities.

Introduction

Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune diseases characterised by chronic muscle inflammation. In adults, IIM encompasses polymyositis (PM), dermatomyositis (DM), immune-mediated necrotising myopathy (IMNM), anti-synthetase syndrome (ASyS), overlap myositis and inclusion body myositis (IBM). Recent advances include the discovery of myositis-specific antibodies (MSA) which provide insight into clinical subsets of IIM(1). Profound disability owing to muscle weakness is common in these patients(2), however the most common causes of death are malignancy and internal organ involvement(3, 4).

Clinically apparent cardiac involvement is present in up to 9% of IIM patients in the Euromyositis registry(5). Recognised cardiac involvement in IIM is heterogeneous, including heart failure(6), conduction defects(7), arrhythmias(7), and inflammatory infiltrates(8). Autopsy studies in IIM have demonstrated myocarditis (diffuse interstitial mononuclear inflammatory cell infiltrates, similar to skeletal muscle infiltrates), coronary artery disease, myocardial ischaemia, conduction system abnormalities, small vessel disease and replacement fibrosis(8, 9). Typically, inflammatory infiltrates are thought to respond to immunosuppressive therapy and so this finding may alter treatment decisions. However, asymptomatic patients with subclinical cardiac involvement may go unrecognised(3). Advances in diagnostic techniques especially cardiac magnetic resonance imaging (CMR) have made it easier to identify these patients(10), although the implications of these findings are poorly understood. To our knowledge, the literature regarding cardiac involvement in IIM has not been systematically reviewed since 2012(6). Accordingly, we performed this systematic review to summarise current knowledge about subclinical or undiagnosed cardiac involvement in IIM.

Methods

MEDLINE and EMBASE were searched electronically from 1990 to August 2020. We used keywords and MeSH terms related to myositis and cardiac involvement (Supplementary Figure S1, available at *Rheumatology* online). We hand-searched articles from reference lists for additional studies of potential relevance. One author (JF) screened abstracts for potential relevance, with assistance from additional author (JD). If consensus was not reached, a third author (IW) was consulted. One author (JF) performed data extraction, which was reviewed by two authors (JD and SP). This review protocol was not registered.

Inclusion/Exclusion Criteria

We included English language clinical trials or observational studies investigating any form of cardiac involvement in IIM in adults. We only included case series of 10 or more patients. We excluded case reports, reviews, comment or letters to the editor.

Population

We included studies involving symptomatic and asymptomatic patients with IIM, excluding non-inflammatory causes of myopathy. We included necrotising myopathies (e.g. statin-associated myositis) only when patients were demonstrated to have immune-mediated disease, as evidenced by the presence of MSA, specific use of the terms “immune-mediated” or “autoimmune” myopathies, or immunosuppressive treatments. We excluded studies involving muscular dystrophy, metabolic myopathies, mitochondrial myopathies and non-immune causes of necrotising myopathies.

Diagnostic Modalities

We included all forms of investigation for cardiac involvement, including cardiac enzyme testing, electrocardiography (ECG), echocardiography, CMR and nuclear medicine.

Outcomes

Our primary outcome was any prespecified measure of cardiac involvement including clinical characteristics and investigation results. We extracted whatever variables and investigation results were presented, most commonly frequency of abnormalities and average values. We extracted demographic data and clinical profile including disease subtype and manifestations. When available, we extracted data regarding mortality, quality of life, and serologic profiles.

Statistical Analysis

The heterogeneity of included studies in terms of study design, investigative technique, reporting of investigation results and patient populations precluded meta-analysis. As such, we have provided a qualitative synthesis of data extracted. All data extracted are available within this manuscript, or the Supplementary Material, available at *Rheumatology* online.

Risk of Bias Estimation

Risk of bias assessments were performed using the National Heart, Lung and Blood Institute quality assessment tool for Observational Cohort and Cross-Sectional Studies. Each domain was identified as present, absent or unclear. Studies were deemed “Low” risk of bias if all criteria were present, “Moderate” risk of bias if up to two criteria were absent and up to two criteria were unclear, or “High” risk of bias if more than two criteria were absent and/or more than two criteria unclear. Risk of bias assessments were performed by one author (JF) with uncertainties addressed by an additional author (JD).

Results

Description of included studies

Our search identified 10425 studies, of which 3033 were removed as duplicates, and 7201 excluded for other reasons(Figure 1). One hundred and eighty-six publications were reviewed, and 157 excluded (Figure 1), resulting in 29 studies being selected for inclusion (Table 1). These studies included predominantly patients with PM or DM(11-32), with or without overlap or connective tissue-disease (CTD)-associated IIM(11, 13-16, 20, 23, 31), or ASyS(13, 14, 16, 33). Other primary diagnoses included IMNM(13, 14, 16, 23), IBM(13, 17, 23, 34), malignancy-associated(20), statin-induced myositis(30) and immune-mediated myositis not otherwise specified(18, 23, 35).

All studies were observational, involving relatively small numbers of patients (range 11-123). Presence of concomitant cardiovascular risk factors, including hypertension, were variably reported (Table 1). The majority of studies examined screening investigations in unselected IIM patients(12, 16-18, 20, 22, 25, 26, 29, 31, 32, 34, 35) or specifically IIM patients without clinical evidence of cardiac disease(6, 11, 15, 19, 21, 23, 24, 27, 28, 30). Two studies selected patients with IIM and elevated cardiac troponin T levels (cTnT)(13, 14). Two studies included patients with confirmed myocarditis(33, 36). For clarity, we separated the results of general "screening" investigations in patients with confirmed or suspected myocarditis from other studies. All studies were assessed as being of moderate or high risk of bias (supplementary Table S1, available at *Rheumatology* online).

Five main investigative methods were used to define cardiac involvement; cardiac enzyme testing(11, 12, 15-19, 30, 34, 37-39), ECG (including ambulatory monitoring)(12, 13, 20, 22, 25-27, 29, 31, 34, 37), transthoracic echocardiography (TTE)(12, 15, 21, 22, 24-26, 28, 29,

31-35), CMR(13, 14, 18, 19, 23, 33) and nuclear medicine testing(12, 20, 22). Variable definitions of clinically evident cardiac involvement were used, including elevated cardiovascular visual analogue scale (VAS) score(16), a component of the Myositis Disease Activity Assessment Tool (MDAAT)(16, 40).

Cardiac Enzymes: cTnI is more specific than cTnT for cardiac involvement

Twelve studies measured cardiac enzymes in unselected patients or those without clinical myocarditis(11, 12, 15-19, 30, 34, 37-39)(Table 2).

Elevated cardiac troponin T (cTnT) levels in IIM patients were common (Table 2), correlating with various markers of IIM disease activity/severity. cTnT was associated with weakness(16), patient-reported muscle disease activity(16), neuromuscular symptom scores(16), reduced patient functioning(15, 16) and CMR evidence of inflammation in the skeletal muscles adjacent to the scanned myocardium(39). Several studies observed strong correlations between cTnT and creatine kinase (CK)(17, 41, 42) or the creatine kinase iso-enzyme CK-MB(15, 17, 42). One study demonstrated that 40% (29/73) of patients with a normal total CK had an elevated cTnT(16). In these cases the abnormal cTnT was not associated with an increased risk of cardiac involvement but rather was associated with increased muscle weakness(16). Two studies performed serial cTnT measurements(30, 34): one found cTnT levels were stable in IBM patients over time(34). The other noted temporal discordance between CK and cTnT levels in newly diagnosed IIM (n = 11)(30), with cTnT peaking later and taking longer to normalise following immunomodulation. While this pattern may reflect subclinical myocarditis(30), elevated cTnT in IIM could arise from muscle(15, 17, 42), as cTnT isoforms may be re-expressed in regenerating skeletal

myofibres(43). Numerous studies reported no association between abnormal cTnT and cardiac involvement detected using ECG or TTE(15, 34, 42), or CMR(19, 39).

Conversely, abnormal cTnI levels were uncommon in unselected IIM cohorts (0-29%)(15, 16, 18, 34, 37, 41, 44)(Table 2). cTnI levels did not differ from healthy controls in one large study(44); others reported that IIM patients with raised cTnI levels had abnormalities on other cardiac investigations(34, 37). One study reported that both cTnT and cTnI were associated with increased risk of cardiac involvement (MDAAT cardiac domain), but only cTnI was independently associated after adjustment for overall disease activity(16). While the sensitivity of an elevated cTnI for cardiac involvement was lower than cTnT in this study (44% vs. 83%), it had greater specificity (95% vs. 46%) and positive predictive value (62% vs. 21%) (16). High sensitivity (97%) and specificity (84%) of cTnI for cardiac involvement was also reported in studies using CMR-confirmed myocarditis(36). NT-pro-brain natriuretic peptide (NT-proBNP) also demonstrated a high sensitivity (95%) and specificity (93%)(36), correlating with CMR features of cardiac disease in several other reports(19, 39), although not all(18).

The predictive value of abnormal cardiac enzymes for symptomatic myocardial involvement is unclear. One study found IIM patients with raised cTnT (82%) and/or cTnI (2.5%) but without clinical features of cardiac disease remained symptom free over 24.5 months follow up(11).

ECG: non-specific ECG changes are common in IIM

Eleven studies reported ECG findings in patients with IIM(12, 20, 22, 25-27, 29-31, 34, 37). ECGs were abnormal in 24-85% of unselected IIM patients(20, 22, 26, 29-31) (Table 3), most commonly demonstrating non-specific ST changes (58-64%) (22, 26, 31). ECG criteria for left

ventricular hypertrophy (LVH) were met in 3-22% of PM/DM patients(20, 22, 26, 27, 29, 31), higher than in healthy controls(27). No significant differences were seen in the frequencies of abnormal rhythm(27), repolarisation abnormalities(27) or conduction block(27) compared with healthy controls in one study. A second study showed longer QRS duration and corrected QT interval(QTc) interval in IIM patients than healthy controls(12). Sinus tachycardia was found in 20-36% of IIM patients in small studies(20, 30, 31). One study demonstrated a longer duration of IIM in those with abnormal ECG findings, but this was not adjusted for age(29).

Data were mixed from 3 studies examining ambulatory ECG monitoring(12, 22, 29). One reported an increased frequency of supraventricular tachycardia (SVT) in IIM patients compared with healthy controls(12), while two reported abnormalities in 77-78% of IIM patients (PVCs, atrial premature complexes and paroxysmal SVT)(22, 29).

Echocardiography: ejection fraction in IIM patients is frequently normal, but subclinical LV systolic dysfunction can be detected using advanced echocardiography techniques.

Sixteen studies investigated TTE in IIM patients(12, 21, 22, 24-26, 28, 29, 31-38)(Table 4). Multiple techniques were used and different parameters were measured across the studies.

Overt systolic dysfunction was rare, evidenced by a reduction in LV ejection fraction (LVEF) (Table 4). Multiple studies of PM/DM showed normal LVEF or fractional shortening (FS) in most/all patients(22, 31, 32), and no difference in LVEF compared with healthy controls(12, 21, 28, 35).

However, while LVEF is an important prognostic marker, it cannot identify more subtle degrees of systolic dysfunction. Newer echocardiographic techniques, such as global longitudinal strain (GLS) which measure local myocardial fibre shortening, are more sensitive at detecting subclinical systolic dysfunction, and have important negative prognostic value in multiple settings(45, 46). Interestingly, subclinical LV systolic dysfunction was detected in several myositis studies when more sensitive TTE techniques were employed. One study used systolic tissue doppler imaging (TDI) and mitral annular plane systolic excursion (MAPSE) to demonstrate subclinical reductions in LV systolic function in IIM patients at baseline(24). These abnormalities normalised after 3 months of corticosteroid therapy(24). Two studies used 2D speckle-tracking GLS, and both reported clear reductions in strain values in IIM patients compared to controls; 57% vs. 21% (p=0.006), RR =4.9 (95%CI 1.5-15.8, p=0.006) (35); 47% vs. 3% (p<0.001) (25, 47).

RV systolic dysfunction was rarely identified, but one study demonstrated reduced RV systolic TDI (RVS') and tricuspid annular plain systolic excursion (TAPSE) which normalised after 3 months of corticosteroid therapy(24). Two studies assessed RV GLS, and demonstrated subclinical reductions in RV systolic function (RR = 3.4, 95%CI 1.1-11.7, p=0.04(25, 35).

Echocardiography: features of LV diastolic dysfunction are common in IIM and may correlate with disease duration and/or treatment.

Echocardiographic parameters indicative of LV diastolic dysfunction were frequently reported in patients with IIM(29) when compared to healthy controls (12, 21, 24, 28). However, in most studies, isolated diastolic measurements were used and few studies graded patients using a combination of parameters, as recommended by the American

Society of Echocardiography (ASE)(48). Most studies did not adjust for age, gender or presence of comorbidities, which may influence diastolic function(49). However, one study showed that abnormal E/A and E/E' parameters were associated with age at disease onset, disease duration and female gender(21), and another showed that diastolic parameters significantly correlated with disease duration (but not disease activity scores) in DM(28). The causative role that immunosuppressive therapy might play was explored in only one study, which found that diastolic dysfunction (abnormal E/A and E'), was not present in IIM patients at baseline but was detected after three months of corticosteroid therapy(24).

Left and right heart size

Structural abnormalities including ventricular and atrial enlargement and hypertrophy were uncommon. Two studies reported larger LA size in IIM patients than controls, although still within normal limits(11, 36). This finding may reflect elevated filling pressures associated with diastolic dysfunction.

Pulmonary pressures

In general, no studies found evidence of pulmonary hypertension without concomitant lung disease. Two studies reported abnormalities in pulmonary valve doppler, suggestive of pulmonary hypertension(25, 30). However, the echocardiographic techniques used have since been adapted and therefore cannot be easily interpreted.

Valvular abnormalities

No clinically significant valvular abnormalities were reported, though mild valvular regurgitation was sometimes detected(15, 21, 31).

CMR: CMR evidence of subclinical myocardial pathology is common in IIM.

CMR enables detailed assessment of cardiac structure and function, as well as tissue characterisation with late gadolinium enhancement (LGE) and myocardial mapping techniques (T1, T2, T2* and extracellular volume(ECV)). Ten studies investigated CMR in IIM patients(13, 14, 18, 19, 23, 33, 36-39)(Table 5). Three studies included patients with IBM(17, 34, 38).

Two studies documented reduced LVEF in 9/52 (17%) and 2/15 (13%) of IIM patients(37, 38); most studies demonstrated normal LVEF(14, 19, 23, 39, 50). The most common finding was presence of LGE suggestive of regional necrosis or scar. Four studies evaluating LGE in IIM patients without known/suspected myocarditis demonstrated LGE in 20-62% of patients(19, 23, 38, 39) and 0% of age- and sex-matched healthy controls(19, 39). Early gadolinium enhancement suggestive of myocardial oedema was detected in 44% of IBM patients in the only study that used this technique(38). One study performed CMR on a pre-selected group of IIM patients with elevated cTnT. The proportion of LGE was similar in IIM patients with a raised cTnT and in unselected IIM patients (7/20, 35%), with no LGE evident in unmatched controls(13). The location of LGE was mostly in a non-ischaemic distribution(14, 23).

Elevated T1, T2 and ECV mapping parameters are novel CMR techniques indicating subclinical myocardial oedema, inflammation and fibrosis. All CMR studies using these mapping techniques found abnormalities in IIM patients, indicating subclinical cardiac disease(13, 14, 19, 23, 37, 39).

Taken together, the prevalence of LGE and elevated T1, T2 and ECV mapping parameters reported in these studies suggests significant subclinical LV myocarditis in IIM despite normal systolic function.

Studies using nuclear medicine

Three studies reported different nuclear medicine investigations in IIM (Supplementary Table S2, available at *Rheumatology* online). One study showed no difference in ^{99m}Tc-PYP (Technetium pyrophosphate) scans between IIM patients and controls(44). Another demonstrated abnormal ^{99m}Tc-PYP uptake in 17/30 (57%) and abnormal ^{67}Ga uptake in 3/20 (15%) of IIM patients(20). This study demonstrated an association between ^{99m}Tc-PYP uptake and frequency and severity of ECG abnormalities ($p<0.01$)(20). One study found 4/26 (15%) PM patients had regional wall motion abnormalities on radionuclide ventriculography (^{99m}Tc-pertechnetate), despite a normal EF(22).

Studies including IIM patients with clinical myocarditis

Two studies investigated IIM patients with clinically manifest myocarditis. One study compared 31 IIM patients with and without myocarditis(36), and another reported results of cardiac investigations in ASyS patients with myocarditis(33). The prevalence of myocarditis in ASyS was 3.4% (n=12) within the ASyS registry (n=352)(33). cTnI and NT-proBNP levels were elevated in myocarditis patients(33, 36); on average 19-fold(33). ECG abnormalities were common: atrial arrhythmias (17%-53.3%), ventricular arrhythmias (76.7%) and conduction block (42%-63.3%)(33, 36). TTE demonstrated reduced LVEF in 58-74% patients with myocarditis and in none without myocarditis(33, 36). In contrast, diastolic dysfunction was common in those with (46%) and without (36%) myocarditis(36). CMR demonstrated LGE in 50-64% of those with IIM and myocarditis(33, 36). Antimitochondrial antibody M2-subtype (AMA-M2) positivity was more common in those with myocarditis (25.8% vs. 3.2%, $p<0.05$); and AMA-M2 positive patients exhibited more diffuse LGE(36).

Discussion

This review identified 29 studies describing cardiac involvement in IIM patients. Despite heterogeneity in cardiac investigations and patient populations, common themes emerged (Figure 2). Cardiac enzymes are often abnormal in IIM(11, 15, 17, 41, 42); cTnI appears most specific for cardiac involvement(16, 36), while cTnT elevation is more common, correlating with muscle disease activity(16, 39). Whether cTnT elevations are due to re-expression of foetal cTnT in regenerating myofibres(51) or true myocardial injury remains contentious(52). ECG abnormalities are common(20, 22, 26, 29), particularly ST-T wave changes(22, 26). Typically, TTE studies demonstrate normal LVEF(12, 21, 28, 35), but subclinical systolic dysfunction may be detected using advanced echocardiographic techniques including GLS(25, 35). Importantly, reduced GLS has been shown to be associated with worse outcomes in other conditions(45, 46, 53); further research is required in IIM patients. While abnormal diastolic parameters were commonly reported in IIM patients, the use of only single indices of diastolic dysfunction and lack of adjustment for known diastolic dysfunction risk factors in many cases, make these findings difficult to interpret(12, 21, 24, 28). Whether diastolic dysfunction constitutes the first sign of fibrotic transformation of the myocardium in IIM or results from some other factor such as corticosteroid therapy or comorbid hypertension needs further evaluation. Corticosteroids are associated with diabetes and hypertension, both with clear correlations with heart failure with reduced ejection fraction(54), but there is a paucity of evidence to suggest a direct link between corticosteroids and diastolic dysfunction(55). There was also a high rate of LVH on ECG(20, 22, 26, 27, 29, 31), out of keeping with the proportion of LVH on TTE or CMR. Most studies did not document criteria used to define LVH, which makes this difficult to interpret. Interestingly however, recent studies have suggested that ECG LVH carries

independent negative prognostic information distinct from anatomic LVH, so documenting LVH on ECG in these patients may still be relevant(56, 57). CMR in asymptomatic patients frequently demonstrates possible subclinical LV myocarditis despite normal systolic function, including LGE positivity (suggestive of regional necrosis or scar) and abnormal T1, T2 and ECV mapping parameters (suggestive of myocardial inflammation and oedema)(18, 19).

In patients with overt myocarditis, cardiac enzyme elevation and ECG changes were almost universal(33, 36). The key difference was reduced LVEF on TTE, which is common in those with clinical myocarditis, but uncommon in asymptomatic IIM patients(36).

The definition of cardiac involvement in IIM may evolve over time with increasingly sophisticated diagnostic modalities. For example, several TTE studies revealed abnormal diastology in IIM patients(12, 21, 24, 28). However, the diagnosis of abnormal diastology has changed, with the most recent ASE guidelines emphasising the use of multiple parameters(48). Generally, early IIM studies used single measurements of diastolic dysfunction, which are difficult to interpret in isolation. The true prevalence of abnormal diastology in IIM may therefore be lower. Likewise, two older studies reported prevalent pulmonary hypertension but did not use contemporary parameters, limiting the interpretability of these results(26, 31). Similarly, novel CMR mapping techniques are now considered the most accurate markers of myocarditis(58). The Lake Louise Criteria for myocardial inflammation have recently been updated to include mapping techniques(59), but earlier CMR studies did not include these(37, 60). Additional studies using current, comparable TTE and CMR techniques are required to understand these patterns.

Our review highlighted the prevalence of abnormal cardiac investigations, particularly CMR, in asymptomatic IIM patients(18, 19). This substantiates other data demonstrating that up to 50% of PM/DM patients may have “silent” cardiac involvement on CMR(61). Indeed, asymptomatic abnormalities on CMR may exist in systemic lupus erythematosus, systemic sclerosis and sarcoidosis; up to 40% of whom may have an abnormal CMR(10). The clinical implications of these findings are unknown and require investigation with longitudinal studies. However, LGE is associated with poor outcomes and increased mortality in systemic amyloidosis(62), hypertrophic cardiomyopathy(63) and dilated cardiomyopathy(64).

Cardiac involvement in IIM has no consensus definition, with multiple different methods of investigation. Due to the poor sensitivity and specificity of most biochemical tests and ECG, we propose that a diagnosis of cardiac involvement in IIM should be reserved for those patients with elevated cTnI, subclinical or overt systolic or diastolic dysfunction on TTE or CMR, or tissue abnormalities (including LGE) on CMR. Until we understand more about the prognostic implications of these findings, we cannot recommend a specific panel of cardiac investigations be performed empirically in asymptomatic patients with IIM. Further data are required to better understand those IIM patients at highest risk of cardiac involvement, particularly using autoantibody profiles. Some early reports of anti-signal recognition particle (SRP) myopathies suggested a predilection for myocardial involvement(65, 66). While this association has not been reproduced in larger studies, some experts still recommend routine cardiac screening in SRP-positive patients(67). AMA positivity has been associated with increased frequency of cardiac involvement in IIM patients(36) which may precede muscle involvement(68), including risk of arrhythmias and reduced EF(69). An increased frequency of supraventricular arrhythmias has been identified in patients with abnormal hepatobiliary enzymes and AMA positivity(70). Furthermore, while we did not

include patients with drug-induced myopathies in this review, patients with immune checkpoint inhibitor (ICI) induced myopathies may have an increased risk of myocarditis (16-32%)(71, 72). Further research is required to understand the factors which predict risk of cardiac involvement in IIM.

Several narrative reviews describe cardiac involvement in IIM(73, 74), and possible investigative strategies(75). Previous systematic reviews of this topic are more than 5 years old(6, 76). This review has several strengths. We have provided a current and comprehensive summary of cardiac investigations in patients with a range of inflammatory myopathies. We have included both symptomatic and asymptomatic patients to facilitate screening and diagnostic evaluation of IIM patients. In summarising the results of different investigative modalities, we have provided the clinician with a framework for correlating and comparing results of investigative techniques.

However, this review also has limitations. Studies were small, observational in nature and all assessed as being of moderate or high risk of bias. Our subgroup analysis is incomplete due to the lack of data in the literature, particularly around patients with IBM and MSA. Furthermore, we did not include drug-induced myopathies, including ICI-induced myositis. The heterogeneity of the included studies precluded meta-analysis or pooled effect size estimates. Finally, data pertaining to certain subjects may be duplicated(13, 14, 37, 44), but due to differences in study design and because we were unable to perform a meta-analysis, we elected to include all data.

Conclusion

Cardiac involvement in IIM has no consensus definition. cTnI appears to be specific for cardiac involvement and may have utility in screening these patients for subclinical disease, although more data are needed. ECGs are frequently abnormal but changes are non-specific and of uncertain prognostic value. TTE is generally normal, though advanced techniques including GLS may reveal subclinical disease. Likewise, CMR often reveals myocardial inflammation and scar, although the clinical significance of these changes in asymptomatic patients is uncertain. Further research is required to better understand the results and implications of CMR and advanced TTE techniques in IIM, and particularly their prognostic significance.

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Data Availability Statement: The data underlying this article are available in the article and in its online supplementary material.

Figure Legend	
Figure 1	PRISMA Flowchart
Figure 2	Key Points
Table 1	Description of included studies
Table 2	Findings of cardiac enzymes in idiopathic inflammatory myopathies
Table 3	Findings of ECG/Holter in idiopathic inflammatory myopathies

Table 4	Transthoracic echocardiography findings in idiopathic inflammatory myopathies
Table 5	Cardiac MRI findings in idiopathic inflammatory myopathies

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Table 1: Description of included studies

Studies of an unselected population of IIM patients*						
Author (Year) Country	**N**	**Characteristics of IIM patients examined**	**Study design**	**IIM Criteria**	**Exclusions**	**Cardiac Outcome**
Buchpiguel (1996) Brazil	30 IIM	PM (8) DM (14) Malignancy-associated IIM (2) JDM (4) OM (2) Age (mean): 35 years (range 8-59); Female: 77%	Cross-sectional	B&P	NR	ECG, 99mTc-PYP Scintigraphy, Gated blood pool scan.
Byrnes (1991) USA	13 IIM	PM (7) DM (5) OM (1) Age (mean): 47 years (range 21-78); Female: 77% Disease duration (mean): 47 months (range 1-131) Exertional dyspnoea 15%, cough 15%, orthopnoea 23%, peripheral oedema 15%, syncope 8%, HTN 46%, murmur 31%, ILD 62%	Cross-sectional	B&P	NR	ECG, TTE
Diederichsen (2015) Denmark	14 IIM 14 HC	PM (8) DM (4) Malignancy-associated IIM (2) Age (mean): 59.5 +/- 18.8 years; Female 57% Disease duration (median): 0.0 years (Range 0-0.5 years) Dyspnoea 57% (NYHA II 37.5%, NYHA III 62.5%), palpitations 21%	Cross-sectional	B&P	OM, IBM.	cTnI, ECG, Holter monitor (48 hours), TTE, 99mTc-PYP SPECT/CT, CMR
Diederichsen (2016) Denmark	76 IIM 48 HC	PM (52) DM (24) Age (mean): 60 +/- 11.2 years; Female: 64% Disease duration (mean +/- SD): 9.0 +/- 8.3 years Dyspnoea 57%, palpitations 34%, chest pain 5%, syncope 3%, HTN 71%, diabetes mellitus 13%, hyperlipidaemia 88%	Cross-sectional	B&P	OM, IBM, malignancy-associated IIM.	cTnI, ECG, Holter monitor (48 hours), TTE, 99mTc-PYP Scintigraphy, 99mTc-PYP SPECT/CT
Erlacher (2001) Austria	39 IIM	PM (22) DM (15) OM (2) Age (mean): 40 +/- 23 years; Female: 90% Disease duration (mean +/- SD): 20 +/- 22 months	Cross-sectional	B&P	NR	cTnT, cTnI, CK-MB, β-type of myosin heavy chain, myoglobulin level
Gonzalez-Lopez (1996) Mexico	32 IIM	PM (6) DM (26) Age (mean): 44 years (range 16-76); Female: 78% Disease duration (mean): 6 years (range 0.25– 23) Cardiac symptoms 6%, HTN 12.5%, ILD 3%	Cross-sectional	B&P	OM, other causes of myopathy, cyclophosphamide therapy.	CK-MB, ECG, Holter monitor (duration not specified), TTE
Hebert (1990) USA	11 IIM	PM (7) DM (4) Age (mean +/- SD): 46 +/- 16 years; Female: 64% Disease duration (mean +/- SD): 42 +/- 38 months HTN 27%, diabetes mellitus 18%, ILD 36%	Cross-sectional	B&P	OM, inability to exercise.	ECG, TTE, CXR, PFTs, Multistage incremental exercise test
Lilleker (2018) UK	123 IIM	DM (39) PM (34) ASyS (37) IMNM (8) OM (5) Age (mean +/- SD): 58 +/- 14 years; Female: 66% Disease duration (median, IQR): 4.3 (1.1-10.2) Cardiac involvement 15%	Cross-sectional	B&P	If an alternative explanation for elevations in serum muscle damage markers was known prior to assessment.	cTnT, cTnI, cardiac domain of MDAAT
Mugii (2018) Japan	23 IIM	DM (12) Amyopathic DM (10) PM (1) Age (median): 60 years (range 27-80); Female: 57% ILD 83%	Cross-sectional	B&P; S	JDM, OM, manual muscle test score <4 in extremities, leg discomfort during 6MWT, active myositis.	TTE, Noninvasive impedance cardiography , PFTs
Rosenbohm (2015) Germany	53 IIM	PM (34) DM (13) MNOS (4) Granulomatous myositis (2) Age (mean, IQR): 55.3 years (45-66); Female: 57%	Cross-sectional	H	IBM, contraindication for CMR, gadolinium allergy, pregnancy, unknown contraception.	CK-MB, NT-proBNP, CMR

Taylor (1993) USA	26 IIM	PM (22) DM (4) Age (mean +/- SD): 48 +/- 14 years; Female: 58% Disease duration (mean +/- SD): 31 +/- 41 months Cardiovascular symptoms 62%	Cross-sectional	B&P	OM	ECG, Holter monitor (24 hrs), CXR, TTE, Radionuclide ventriculography
Studies of IIM patients without clinical features of cardiac disease						
Author (Year) Country	**N**	**Characteristics of IIM patients examined**	**Study design**	**IIM Criteria**	**Exclusions**	**Cardiac Outcome**
Aggarwal (2009) USA	49 IIM	PM (23) DM (16) OM (10) Age (mean +/- SD): 45.8 +/- 8.8 years; Female: 67% Follow up duration (mean +/- SD): 9.3 +/- 6.5 years	Retrospective	B&P	Renal failure, myocardial ischaemia or damage as determined by clinical exam, ECG, TTE or left heart catheterisation.	cTnI, cTnT, CK-MB
Deveza (2016) Brazil	112 IIM 86 DC	DM (78) PM (34) Age (mean): 48.9 +/- 15.4 years; Female: 71% Disease duration (mean): 5 years (range 2-12) HTN 46%, diabetes mellitus 15%, ILD 33%	Cross-sectional	B&P	Amyopathic DM, OM, malignancy-associated IIM, other causes of myopathy, clinical cardiac disease.	ECG
Fisher (2010) ** UK	11 IIM	PM (5) DM (3) Statin-induced myopathy (2) IBM (1) Age (mean): 70.4 years (range 59-87 years); Female: 73%	Retrospective	B&P	Clinical myocardial involvement defined by history, ECG and/or TTE.	cTnT, ECG
Guerra (2017) Italy	28 IIM 29 HC	PM or DM (numbers not specified) Age (mean): 61.3 +/- 13.1 years; Female: 78.6% Time from diagnosis (median): 44 months (IQR 3-65) Smoking 7%, HTN 60%, diabetes mellitus 7%	Retrospective	B&P	IBM, IMNM, OM, juvenile myositis, significant cardiac disease.	cTnI, TTE
Khoo (2019) Australia	19 IIM	DM (4) PM (4) MNOS (4) IBM (2) IMNM (2) OM (3) Age (mean): 59 +/- 10.3 years; Female: 63% Disease duration (mean): 8.4 years (range 1-25 years) Smoking 16%	Retrospective	H	Known cardiac involvement, coronary artery disease, hypertension or secondary cause of myositis.	CMR
Lu (2013) China	46 IIM 21 HC	PM (11) DM (35) Age (mean): 31.1 +/- 12.1 years; Female: 67% Disease duration (mean): 4.78 +/- 13.19 months ILD 35%	Cross-sectional	B&P	Overt cardiac manifestations, malignancy, overlap syndromes, IBM, >50 years, underlying cardiac disease, severe renal disease, anaemia, HTN, diabetes mellitus, thyroid dysfunction.	TTE
Peter (2015) Hungary	30 IIM HCs	PM (23) DM (7) Age (mean): 42.3 +/- 1.6 years; Female: 90% ILD 37%	Prospective	B&P	Systemic autoimmune disease, malignancy, OM, congenital heart disease, HTN, rheumatic fever, coronary or valvular heart disease, cardiomyopathy, arrhythmias, diabetes mellitus, chronic renal failure, anaemia, AF, severe MR	TTE
Wang (2014) China	51 DM 51 HC	DM (51) Age (mean): 44.06 +/- 11.8 years; Female: 84% Disease duration (mean): 8 months (range 0.3-48 months) ILD 53%	Prospective	B&P	Cardiac disease, diabetes mellitus, HTN, chronic renal failure, other CTD.	TTE
Xu (2020) China	44 IIM 30 HC	IIM (44) Age (mean): 49.0 ± 12.0; Females 50% Disease duration (mean): 0.5 years (range 0.2-2.0 years) HTN 13.6%, diabetes 2.3%	Prospective	ENMC	Other autoimmune/inflammatory disease, pre-existing IIM, known cardiac disease or poorly controlled HTN/DM, contraindications to CMR, GFR <30, CMR with incomplete/poor quality images.	CK-MB, cTnT, NT-pro-BNP, CMR
Yu (2018) China	25 IIM 25 HC	PM (13) DM (12) Age (mean): 50 +/- 13 years; Female: 48% Disease duration (median): 6 months (IQR 2.4-30 months) HTN 28%, hyperlipidaemia 64%, Smoking 24%, ILD 36%	Prospective	ENMC	Known cardiac disease, clinical heart failure, reduced LVEF, contraindications to CMR.	CK-MB, cTnT, NT-proBNP, CMR

Zhong (2018) China	60 IIM 30 HCs	PM or DM (numbers not specified) Age (mean +/- SD): 51.1 +/- 12.6 years; Female: 73% Disease duration: >1y in 41/60 (68%) HTN 27%, hyperlipidaemia 48%, diabetes mellitus 60%, ILD 48%	Cross-sectional	B&P	Other autoimmune disease, OM, IBM, malignancy-associated myositis, reduced LVEF, congenital heart disease, valvular heart disease or ischaemic heart disease.		BNP, ECG, TTE
Studies of IIM patients with raised cTnT and suspected myocardial involvement							
Author (Year) Country	**N**	**Characteristics of IIM patients examined**	**Study design**	**IIM Criteria**	**Cardiac selection criteria**	**Exclusions**	**Cardiac Outcome**
Huber (2018) France	20 IIM 20 viral myocarditis 20 HCs	IMNM (7) ASyS (5) OM (2) PM (3) DM (2) IBM (1) Age (mean): 45 +/- 16 years; Female: 40% Dyspnoea 30%, AF or AV block 25%, heart failure 5%, chest pain 10%, HTN 15%, diabetes mellitus 10%	Retrospective	C, H	cTnT > 50ng/mL	Coronary artery disease on angiogram	cTnT, NT-proBNP, CMR
Huber (2019) France	20 IIM 20 HCs	IMNM (7) ASyS (5) PM/DM/OM (8) Age (mean): 54 +/- 18 years; Female: 45% HTN 15%, hyperlipidaemia 25%, diabetes mellitus 10%	Retrospective	H	cTnT > 50ng/mL	>2 week lapse between CMR and blood test, prior cardiac events.	cTnT, NT-proBNP, CMR
Studies of IIM patients with clinical features of myocarditis							
Author (Year) Country	**N**	**Characteristics of IIM patients examined**	**Study design**	**IIM Criteria**	**Cardiac selection criteria**	**Exclusions**	**Cardiac Outcome**
Dieval (2015) France	12 ASyS	Age (median): 54 years (range 17-67); Female: 67% Follow-up (median): 11 months (range 0-84) Patients selected from a nation-wide registry of ASyS LV and/or RV dysfunction 83%, ICU required 50%, chest pain 25%, normal cardiac exam 67%, relapsing episodes 25%	Retrospective	C	Acute (<72 hours) cardiac symptoms with abnormal cardiac enzymes, CMR or cardiac biopsy in the absence of other causes.		cTnT, cTnI, ECG, TTE, CMR
Liu (2020) China	31 IIM with myocarditis 31 IIM without myocarditis	PM (34), DM (28) Age (mean): 47.2±13.8 years; Female 59.7% Disease duration (median): 3.5 years (range 1.4-9.0 years) HTN (11%), DM (8.1%), dyslipidaemia (6.5%)	Case-control	EULAR	TnI, ECG and TTE with CMR and/or endomyocardial biopsy as required.	IBM, IMNM, muscular dystrophy, metabolic myopathy, long-term excessive alcohol, GFR <60 mL/min, malignancy, coronary heart disease, flu-like syndrome in the past 6 months.	cTnI, NT-proBNP, CK-MB, ECG, TTE, CMR
Studies examining an unselected* cohort of IBM patients							
Author (Year) Country	**N**	**Characteristics of IIM patients examined**	**Study design**	**IIM Criteria**	**Exclusions**		**Cardiac Outcome**
Cox (2010) Netherlands	51 IBM	Age (mean): 67 +/- 9 years; Female: 33% Disease duration (mean): 11 +/- 6 years Cardiac symptoms in 24%	Cross-sectional	ENMC	NR		CK-MB, cTnT, cTnI, ECG, TTE
Lindberg (2006) Sweden	42 IBM	Age (mean): 68.1 +/- 9.5 years; Female: 21% Previous MI 10%; cardiac symptoms 0%	Retrospective	C, H	Other causes of myocardial damage to explain abnormal cardiac enzymes.		cTnT, CK-MB

Rosenbohm (2020) Germany	20 IBM 20 HC	Age (mean): 61.4 +/- 12 years (IBM); Female 35% HTN IIM 65% (vs. 25% HC), diabetes mellitus 10%	Prospective	ENMC	Contraindication to CMR, pregnancy.	CK, CK-MB, NT-proBNP, TTE, CMR

*unselected with respect to the presence or absence of cardiac involvement. ** This study actively selected for patients with elevated cTnT but no evidence of cardiac disease.

Abbreviations: 99mTc-PYP = 99m Technetium pyrophosphate; AF = atrial fibrillation; AR = aortic regurgitation; ASyS = anti-synthetase syndrome; AZA = azathioprine; BBB = bundle branch block; bpm = beats per minute; B&P = Bohan and Peter; C = clinical; CI = confidence interval; CK = creatine kinase; CTD = connective tissue disease; cTnI = cardiac troponin I; cTnT = cardiac troponin T; DC, disease controls; DM = dermatomyositis; E' = early diastolic filling wave on tissue doppler imaging; E/A = early diastolic filling velocity compared to late diastolic filling velocity; EDV = end-diastolic volume; ESV = end-systolic volume; ECG = electrocardiograph; ENMC = European Neuromuscular Centre; FAC = fractional area change; GCBPS = gated cardiac blood pool scan; GLS = global longitudinal strain; H, histological, HC, healthy controls; HR = heart rate; HTN = hypertension; IBM = sporadic inclusion body myositis; ICU = intensive care unit; IIM = idiopathic inflammatory myopathy; IVIG = intravenous immune globulin; LV = left ventricle; LVH = left ventricular hypertrophy; LVEF = left ventricular ejection fraction; MDAAT = Myositis Disease Activity Assessment Tool; ug = micrograms; MMF = mycophenolate; MI = myocardial infarction; MR = mitral regurgitation; MTX = methotrexate; MNOS = myositis not otherwise specified; NR = not reported; NYHA = New York Heart Association Classification; OM = overlap myositis; PM = polymyositis; PYP = pyrophosphate; RA = right atrium; RBBB = right bundle branch block; RR = relative risk; S' = peak systolic annular velocity on tissue doppler imaging; S = Sontheimer's; SPECT = single-photon emission computed tomography; SR = sinus rhythm; TAPSE = tricuspidal annulus plane systolic excursion; TR = tricuspid regurgitation; TLC = total lung capacity; TLCO = diffusing capacity for carbon monoxide.

Table 2: Cardiac enzyme studies in idiopathic inflammatory myopathies

Cardiac Enzymes							
Study	**Population**	**Results**					**Notes**
		CK	**CKMB**	**cTnT**	**cTnI**	**Other**	
Studies of an unselected* population of IIM patients, or those without clinical cardiac disease at inclusion							
Aggarwal (2009)	49 IIM No clinical cardiac disease at inclusion	↑ in 59%	↑ 57%	↑ in 64% (n = 28)	↑ in 2% (n = 41)	NR	cTnT correlates strongly with CK and CK-MB. Patients with cTnT elevation had no clinical, ECG or TTE evidence of cardiac disease after median 24.5 months follow up. The single patient with raised cTnI was found to have an abnormal TTE.
Diederichsen (2015)	14 IIM, 14 HC Unselected*	↑ in 86% IIM	NR	NR	↑ in 29% IIM	NR	Patients with raised cTnI also had other abnormal cardiac findings.
Diederichsen (2016)	76 IIM, 48 HC Unselected*	↑ in 33% IIM	NR	NR	↑ in 8% IIM	NR	cTnI levels did not significantly differ from HCs.
Erlacher (2001)	39 IIM Unselected*	NR	↑ in 51%	↑ in 41%	↑ in 2.5%	βMHC ↑ in 60%	cTnT, CK-MB, βMHC (but not cTnI) were associated with IIM disease severity scores. No patient had evidence of cardiac involvement on TTE or ECG.
Fisher (2010)	11 IIM No clinical cardiac disease at inclusion	↑ in 100%	NR	↑ in 100%	NR	NR	cTnT peaked after CK. One patient developed myocarditis, confirmed on autopsy.
Lilleker (2018)	123 IIM Unselected*	↑ in 40% (n = 121)	NR	↑ in 71% (n = 121)	↑ in 10% (n = 121)	NR	Abnormal cTnI has the highest specificity (95%) and positive predictive value (62%) for cardiac involvement.
Rosenbohm (2015)	53 IIM Unselected*	See note	See note	NR	NR	NT pro BNP 79 pg/mL (38 – 262)	Patients with LGE on CMR had increased CK-MB and CK compared with those without LGE, but equivalent NT pro BNP. Patients with and without early myocardial enhancement had equivalent serum levels of all markers.
Xu (2020)	44 IIM 30 HC Unselected*	316 U/L (range 79-2202)	20.6 ng/mL (5.3–54.0)	96g/L (range 40-269)	NR	NT pro BNP 226pg/ml (85–747)	CMR was used to analysis both myocardium and adjacent skeletal muscle in this study. Skeletal muscle T2 relaxation times correlated positively with cTnT, CK and CK-MB. Conversely NT Pro BNP correlated with myocardial T1, T2 and ECV.
Yu (2018)	25 IIM No clinical cardiac disease at inclusion	↑ in 64%	↑ in 68%	↑ in 88%	NR	NT pro BNP ↑ in 32%	CMR mapping parameters (ECV and native T1) correlated with NT pro BNP but not cTnT or CK.
Studies of IIM patients with confirmed myocarditis							
Dieval (2015)	12 ASyS	↑ in 100%	NR	↑ in 100%	↑ in 100%	NR	
Liu (2020)	31 IIM with myocarditis 31 IIM without myocarditis**	NR	Higher in those with myocarditis	NR	↑ in 100% of those with myocarditis	NT pro BNP higher in those with myocarditis	NT pro BNP: sensitivity 95%, specificity 93% for cardiac involvement. cTnI: sensitivity 97%, specificity 84% for cardiac involvement. CK-MB: sensitivity of 69%, specificity of 62% for cardiac involvement.
Studies of an unselected* population of patients with IBM							

Cox (2010)	51 IBM Unselected*	↑ in 82%	↑ in 82%	↑ in 78%	↑ in 2%	NR	The single patient with raised cTnI had a severe cardiomyopathy. No correlation between cTnT or CKMB and pathological ECG or TTE.
Lindberg (2006)	42 IBM Unselected*	Correlates with cTnT	Correlates with cTnT	↑ in 81%	NR	NR	Strong correlation of cTnT with CK and CK-MB. cTnT rlevels remained stable on serial measurements (up to 17 months). No patients had clinical cardiac disease. Thorough cardiac evaluation was not performed.
Rosenbohm (2020)	20 IBM 20 HC Unselected*	↑ in 90%	↑ in 55%	NR	↑ in 0% (n = 11)	NT pro BNP ↑ in 20%	No correlation between any laboratory values and the presence of LGE on CMR.

* Unselected with respect to the presence or absence of cardiac involvement. *** IIM patients pre-selected for normal cardiac function prior to study. Abbreviations: AF = atrial fibrillation; AR = aortic regurgitation; ASyS = anti-synthetase syndrome; AZA = azathioprine; BBB = bundle branch block; bpm = beats per minute; B&P = Bohan and Peter; C = clinical; CI = confidence interval; CK = creatine kinase; CTD = connective tissue disease; cTnI = cardiac troponin I; cTnT = cardiac troponin T; DC, disease controls; DM = dermatomyositis; E' = early diastolic filling wave on tissue doppler imaging; E/A = early diastolic filling velocity compared to late diastolic filling velocity; EDV = end-diastolic volume; ESV = end-systolic volume; ECG = electrocardiograph; ENMC = European Neuromuscular Centre; FAC = fractional area change; GCBPS = gated cardiac blood pool scan; GLS = global longitudinal strain; H, histological, HC, healthy controls; HR = heart rate; HTN = hypertension; IBM = sporadic inclusion body myositis; ICU = intensive care unit; IIM = idiopathic inflammatory myopathy; IVIG = intravenous immune globulin; LV = left ventricle; LVH = left ventricular hypertrophy; LVEF = left ventricular ejection fraction; ug = micrograms; MMF = mycophenolate; MI = myocardial infarction; MR = mitral regurgitation; MTX = methotrexate; MNOS = myositis not otherwise specified; NR = not reported; NYHA = New York Heart Association Classification; OM = overlap myositis; PM = polymyositis; PYP = pyrophosphate; RA = right atrium; RBBB = right bundle branch block; RR = relative risk; S' = peak systolic annular velocity on tissue doppler imaging; S = Sontheimer's; SR = sinus rhythm; TAPSE = tricuspidal annulus plane systolic excursion; TR = tricuspid regurgitation; TLC = total lung capacity; TLCO = diffusing capacity for carbon monoxide.

Table 3. ECG and Holter studies in idiopathic inflammatory myopathies

Study	Buchpiguel (1996)	Byrnes (1991)	Diederichsen (2015)	Diederichsen (2016)	Deveza (2016)	Fisher (2010)	Gonzalez-Lopez (1996)	Hebert (1990)	Liu (2020)*	Taylor (1993)	Cox (2010)
N	**30 IIM**	**13 IIM**	**14 IIM**	**76 IIM**	**112 IIM**	**11 IIM**	**32 IIM**	**11 IIM**	**31 IIM**	**26 IIM**	**51 IBM**
Normal	18 (60%)	2 (15%)	8 (57%)	58 (76%)	76 (67%)	6(55%)	15 (47%)	1 (9%)		4 (15%)	39(76%)^
Conduction abnormalities											
Short PR interval	1 (3%)										
1st degree AV block			3 (25%)	4 (5%)	3 (3%)					4 (15%)	
2nd degree AV block										1 (4%) H	
RBBB	2 (6%)	0 (0%)			1 (1%)			1 (9%)		1 (4%)	
LBBB		0 (0%)			1 (1%)				0 (0%)		
Incomplete BBB											5 (10%)
QRS > 120ms		0 (0%)	1 (7%)	3 (4%)					0 (0%)		2 (4%)
Prolonged QTc			3 (25%)	4 (5%)							0 (0%)
NS conduction anomalies					19 (16%)		8 (25%)			4 (15%)	
LAFB									0 (0%)	1 (4%)	
Paced rhythm		1 (8%)									
Rhythm disturbances											
Sinus bradycardia		1 (8%)	0 (0%) H	0 (0%) H				1 (9%)			
Sinus tachycardia	6 (20%)	3 (23%)				4(36%)					
SVT			4 (29%) H	34 (47%) H	1 (1%)		3 (13%) H		0 (0%)	3 (12%) H	
AF/flutter			1 (7%)	1 (1%) H	1 (1%)	1 (9%)			0 (0%)		3 (6%)
PAC			19 (0 – 1558)** H	15 (0 – 5622)**H	2 (2%)		6 (26%) H				
PVC			31 (1 – 3901)** H	11 (0 – 1994)**H	3 (3%)		16 (50%) H			18(69%) H	
NSVT			0 (0%) H	1 (1%) H						1 (4%) H	
Ischaemic changes											
Q waves/Old MI	1 (3%)	2 (15%)					1 (3%)	1 (9%)	0 (0%)		7 (14%)
Poor R wave progression		1 (8%)							2 (7%)	3 (12%)	
Chamber hypertrophy											
LVH	1 (3%)	2 (15%)			12(11%)		7 (22%)	1 (9%)		4 (15%)	9 (18%)
RVH					0 (0%)		1 (3%)			1 (4%)	
LAH		1 (8%)			5 (4.5%)			1 (9%)		4 (15%)	
RAH		1 (8%)			0 (0%)			1 (9%)		1 (4%)	

Table 4: Transthoracic echocardiography findings in idiopathic inflammatory myopathies

Author (Year)	Population	TTE parameters	Positive findings	Notes
Studies of an unselected* population of IIM patients, or those without clinical cardiac disease				
Byrnes (1991)	13 IIM	2D. Valves. FS. PV dop.	Abnormal PV doppler in 9/12	Abnormal PV doppler can signal pulmonary hypertension but contemporary measures of PH were not performed on this study. Further, 8 patients had parenchymal lung disease on CXR
Diederichson (2015)	15 IIM vs. 15 HC	LA and LV vol. LVEF. MVinf dop. MV TDI.	LA size increased in IIM vs. HC.	Average LA size increased in IIM vs. HC but remained within normal limits. Can signal diastolic dysfunction but in absence of significant changes in MVinf dop and TDI this is non-specific.
Diederichson (2016)	76 IIM vs. 48 HC	LA and LV vol. LVEF. MVinf dop. MV TDI. TV dop.	LA size increased in IIM vs. HC. MV TDI E' increased in IIM vs. HC.	Average LA size increased in IIM vs. HC but remained within normal limits. E' <10msec more prevalent in IIM vs. HC. This, combined with the increased LA size, may represent more diastolic dysfunction in this group though E/E' ratio was not significant between groups.
Gonzalez-Lopez (1996)	32 IIM	MVinf dop.	Abnormal E/A ratio in 11 (42%)	Abnormal E/A may represent some diastolic dysfunction but no control group and no other diastolic parameters measured.
Guerra (2017)	28 IIM* vs. 29 HC	LVEF. TAPSE, RVS' and RV FAC. MVinf dop. MV TDI. LV GLS, RVLS.	LV GLS and RVLS reduced in IIM vs. HC.	Reduction in LV GLS and RVLS in IIM group vs. HC suggestive of subclinical systolic dysfunction, though note absolute values in IIM group are just above the 'normal limits' for strain values. No differences in diastology noted.
Herbert (1990)	11 IIM	2D. LVEF. PV dop.	Abnormal PV doppler in 7/11	Abnormal PV doppler can signal pulmonary hypertension but contemporary measures of PH were not performed in this study.
Lu (2013)	46 IIM* vs. 21 HC	2D. LVEF. MVinf dop. MV TDI. TV dop.	Abnormal E, A, E/A and E/E' in IIM vs. HC.	Abnormal E/A and E/E' suggestive of abnormal diastolic function in IIM vs. controls.
Mugii (2018)	23 IIM	LVEF. TV dop.	None.	
Peter (2015)	30 IIM	2D. LVEF. MVinf dop. MV TDI. RV FAC. MAPSE. TAPSE. TV dop. TV TDI	Reduced LV lateral S' and RV S' and MAPSE/TAPSE returned to normal after 3 months of corticosteroid therapy. Normal E/A and E/E' at baseline became abnormal after 3 months of corticosteroid therapy.	Subclinically reduced LV and RV function noted on TDI at baseline. Reduced MAPSE/TAPSE compared to controls but within normal limits. All systolic parameters returned to normal with corticosteroid therapy at 3 months, suggesting that treatment may improve subclinical myocarditis. Normal diastolic parameters that became abnormal after 3 months of corticosteroid therapy suggestive that corticosteroids may independently cause abnormal diastology.
Taylor (1993)	26 IIM	2D. MV dop, TV dop.	None	Minor abnormalities not reaching clinical significance reported.
Wang (2014)	51 IIM* vs. 51 HC	2D. LVEF. MVinf dop. MV TDI.	Abnormal E/A ratio, E/E' and deceleration time in IIM vs. HC.	Abnormal diastolic parameters in IIM group suggestive of diastolic dysfunction in this group.
Zhong (2018)	60 IIM* vs. 30 HC	2D. LVEF. LA vol. MVinf dop. MV TDI. TAPSE. RVS'. TV dop. LV GLS. RVLS.	Reduced LV GLS and RVLS in IIM vs. HC. Elevated E/E' ratio in IIM vs. HC.	Reduction in LV GLS and RVLS in IIM group vs. HC suggestive of subclinical systolic dysfunction, though note absolute values in IIM group are just above the 'normal limits' for strain values. Elevated E/E' suggestive of abnormal diastology.
Studies including IIM patients with clinical features of myocarditis				
Dieval (2015)	12 ASyS	Parameters not described	Pericarditis in 50%. Reduced LVEF in 58%. Possible pulmonary HTN in 33%. No valvulopathy.	
Liu (2020)	32 IIM* vs. 32 IIM + confirmed myocarditis	2D. FS. LVEF. MVinf dop. MV TDI. PV dop. TV dop.	Abnormal diastolic function in 36% IIM vs. 46% IIM+myocarditis.	Abnormal diastolic function (independent measures not reported) in both groups but higher in IIM+myocarditis group. Significant

			Abnormal LVEF in 74% IIM+myocarditis vs. 0% IIM.	prevalence of LV systolic dysfunction in myocarditis group with no LV systolic dysfunction in IIM group.
Studies of an unselected cohort of IBM patients				
Cox (2010)	51 IBM	M-mode dimensions. LVEF. MVinf dop. Valves.	Reduced LVEF (<50%) in 4/51. 14/51 had LVH (from M-mode).	No details of 4 patients with reduced LVEF though note that cohort was relatively old (ave age 67) and a significant proportion had underlying cardiovascular disease. 14/51 had LVH on M-mode which can be inaccurate, however 25% of the cohort also had hypertension which can cause LVH. Overall, these are nonspecific findings.
Rosenbohm (2020)	20 IBM vs. 20 HC	2D. FS. Diastology	None	

* IIM patients pre-selected for normal cardiac function prior to study.

Abbreviations: 2D = 2 dimensional measurements; FS = fractional shortening; IIM = idiopathic inflammatory myopathy; LA vol = left atrial volume; LVEF = left ventricular ejection fraction; LV GLS = left ventricular global longitudinal strain; LV vol = left ventricular volumes; MAPSE = mitral annular plane systolic excursion; MVinf dop = mitral valve inflow doppler; MV TDI = mitral valve tissue doppler imaging; PV = pulmonary valve continuous/pulse wave doppler; RV FAC = right ventricular fractional area change; RVS' = Right ventricular systolic velocity; RV GLS = right ventricular global longitudinal strain; TAPSE = tricuspid annular plane systolic excursion; TTE = transthoracic echocardiography;TV dop = tricuspid valve continuous wave doppler; Valves = colour doppler valvular assessment.

Table 5: Cardiac MRI findings in idiopathic inflammatory myopathies

Author (Year)	Population	CMR parameters	Positive findings	Notes
Studies of an unselected* population of IIM patients, or those without clinical features of cardiac disease				
Diederichson (2015)	15 IIM vs 15 HC	EF, T2	2 IIM with reduced LVEF	
Khoo (2019)	19 IIM*	LGE, T1 mapping	9/19 (47%) with LGE. 7/15 with elevated T1 mapping.	Presence of LGE in 47% and elevated T1 mapping parameters suggestive of subclinical LV necrosis and myocardial edema.
Rosenbohm (2015)	53 IIM	EF, EGE, LGE	Reduced EF in 9/53 (17%). LGE in 33/53 (62%).	Reduced LVEF in 17% and LGE in 62% suggestive of significant undiagnosed cardiac involvement.
Xu (2020)	44 IIM vs 30 HC	EF, volumes, LGE, T1 mapping, T2 mapping, ECV	LGE in 11/44 (25% of IIM patients, 0% HC). Elevated T1, T2 and ECV in IIM	LGE in 25% and elevated mapping parameters in IIM group vs. HC suggestive of subclinical myocardial LV necrosis and myocardial edema
Yu (2018)	25 IIM* vs. 25 HC	EF, volumes, LGE, T1 mapping, ECV	5/25 (20%) LGE in IIM vs. 0/25 controls. Elevated ECV and T1 mapping in IIM vs. controls.	19% LGE and elevated mapping parameters in IIM group vs. HC suggestive of acute myocardial necrosis and edema.
Studies of IIM patients with suspected myocardial involvement				
Huber (2018)	20 IIM~ vs 20 AVM vs 20 HC	EF, volumes, LGE, T1 mapping, T2 mapping, ECV	LGE in 7/20 IIM, 0/20 HC, 20/20 AVM. Elevated T1 native, T1 contrast and T2 mapping IIM vs. HC.	IIM patients pre-selected for suspected cardiac involvement with elevated troponin T >50ng/ml (note troponin T not specific). Elevated LGE suggests acute necrosis and elevated mapping parameters suggestive of subclinical myocardial edema.
Huber (2019)	20 IIM~ vs 20 HC	T1 mapping, T2 mapping, ECV	Elevated T1 native, T1 contrast and T2 mapping IIM vs. HC	IIM patients pre-selected for suspected cardiac involvement with elevated troponin T >50ng/ml (note troponin T not specific). Elevated mapping parameters suggestive of subclinical myocardial edema.
Studies including patients with clinical features of myocarditis				
Dieval (2015)	12 ASyS with myocarditis	T1, LGE	Spontaneous T2 hypersignal 3/11 (27%); T1-gadolinium late signal (suggestive of myocarditis) 7/11	
Liu (2020)	32 IIM* vs. 32 myocarditis	LGE, T2 mapping	50% IIM with LGE. 20% IIM with elevated T2	IIM without myocarditis compared to IIM with known myocarditis (biopsy proven). 50% LGE and 20% elevated T2 mapping in IIM without myocarditis suggestive of LV necrosis and myocardial edema.
Studies of an unselected* cohort of IBM patients				
Rosenbohm (2020)	20 IBM vs. 20 HC	EF, volumes, EGE, LGE	Reduced stroke volume in IBM vs. HC. EGE in 8/18 (44%) IBM and 1/19 (5%) HC.	Reduced stroke volume but normal EF and mass between groups, of uncertain significance. Elevated EGE in IBM suggestive of myocardial edema. No significant difference in LGE between groups.

Abbreviations: AVM – acute viral myocarditis; ECV – extracellular volume; EF – ejection fraction; EGE – early gadolinium enhancement; LGE – late gadolinium enhancement.

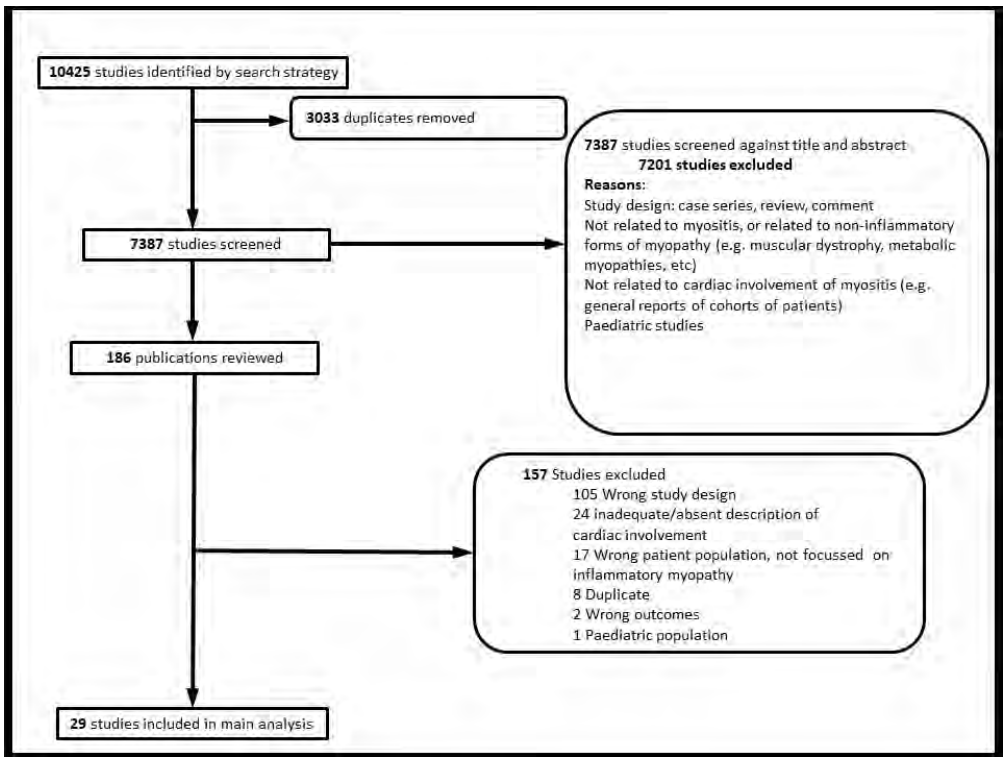

Figure 1

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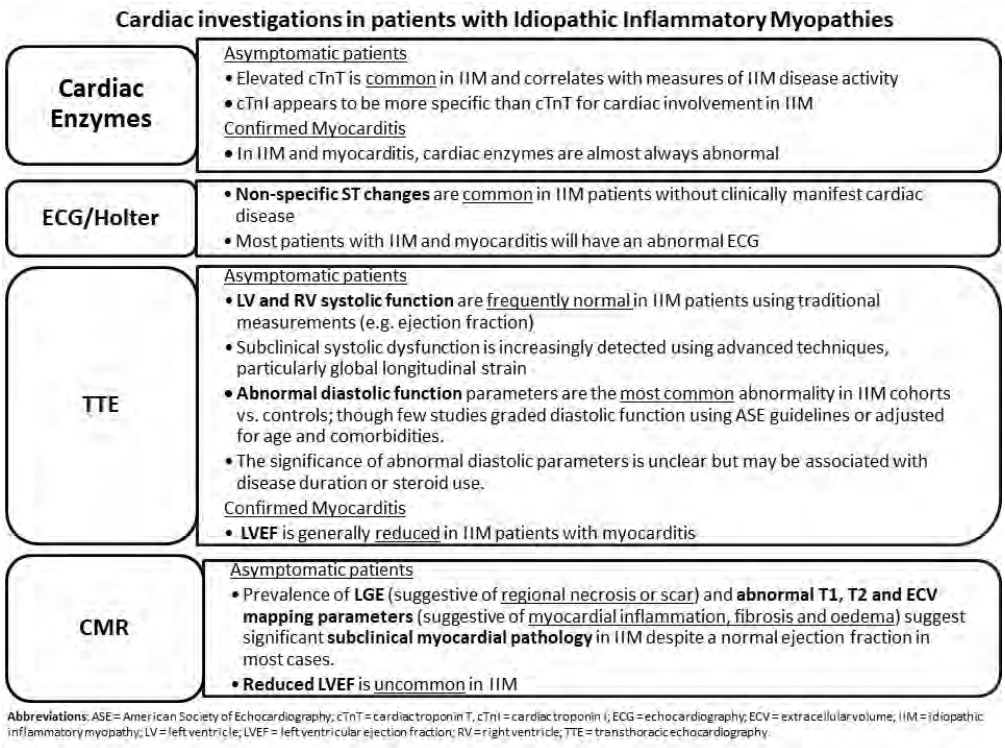

Figure 2

254x190mm (96 x 96 DPI)