Clinical Features of Myositis: Cardiac Manifestations

8

Sangmee Bae and Christina Charles-Schoeman

Key Points to Remember

- Clinically evident heart problems such as symptomatic arrhythmias and congestive heart failure are reported in anywhere from 3% to 10% of patients with IIM, and the incidence of asymptomatic cardiac disease in IIM patients is even higher.
- Initial evaluation of cardiac status with assessment of traditional CV risk factors as well as echocardiogram and EKG, especially if high cardiovascular risk is recommended in IIM patients.
- Cardiac MRI and technetium99m-pyrophosphate scintigraphy are noninvasive imaging tools that can be utilized.
- Comprehensive screening of cardiac function in all IIM patients should be undertaken if patients present with any cardiac or even nonspecific unexplained symptoms.
- cTnI is more specific for myocardial damage and should be used to evaluate the myocardium in IIM, whereas cTnT and CK-MB are nonspecific and elevated with elevation of CK.
- Immunosuppressive therapies in conjunction with traditional cardiac medications and risk mitigation can be used for the treatment of cardiac disease in IIM. Severe cases may require pacemaker or defibrillator placement.

Introduction

Cardiac involvement in idiopathic inflammatory myopathies (IIM) was first reported in the late nineteenth century by Oppenheim [1] but until the late 1970s was considered to be a rare disease manifestation. However, with the introduction of sensitive, noninvasive techniques to assess cardiac involvement, heart disease is now a well-recognized clinical manifestation of IIM [2–4]. In earlier reports, the cardiac manifestations in IIM were primarily described as being occult or subclinical, mostly manifesting as conduction abnormalities [5]. However, as additional data on various noninvasive testing have accumulated, it has become evident that the heart muscle is frequently affected in patients with IIM, and more importantly, cardiovascular events are one of the major causes of morbidity and mortality [6–9]. To date, there have been no large epidemiological studies on cardiac involvement in IIM, and thus, the exact frequency of heart involvement is still unknown. In smaller cohort studies, the reported incidence of cardiac involvement varies between

S. Bae (✉) · C. Charles-Schoeman
University of California, Los Angeles, CA, USA
e-mail: SBae@mednet.ucla.edu; CCharles@mednet.ucla.edu

R. Aggarwal, C. V. Oddis (eds.), *Managing Myositis*, https://doi.org/10.1007/978-3-030-15820-0_8

6% and 72% dependent on patient selection, the definition of heart involvement, and the diagnostic modalities used for screening [10–12]. Clinically evident heart problems are reported in 3–10% of patients with IIM, of which symptomatic arrhythmias and congestive heart failure constitute a large portion [13].

Pathophysiology

Distinct histopathological features are noted in the skeletal muscle of polymyositis (PM) and dermatomyositis (DM) patients [14]. Similarly, autopsy studies of DM and PM patients demonstrate inflammatory infiltration of the myocardium that resembled the inflammation in the skeletal muscle [15]. Diffuse, severe mononuclear inflammatory infiltrates and fibrosis localized to the endomysium and the perivascular areas were reported with associated degeneration of cardiac myocytes. Such findings were also noted in the conduction system including the SA-AV node and His-Purkinje conduction system, suggesting a mechanistic link to the clinically observed conduction abnormalities including complete heart block [15, 16].

A recent case report compared detailed histopathological findings of both the heart and the skeletal muscle of a DM patient undergoing heart transplantation [17]. A distribution of muscle fiber damage/atrophy in the peripheral areas of the cardiac muscle was noted to be similar to the perifascicular distribution in the DM skeletal muscle. Intense perimysial alkaline phosphatase reactivity was also noted in the cardiac and skeletal muscles. Finally, overexpression of membrane attack complex (MAC) on capillaries, another hallmark finding of DM, was present in both the cardiac and skeletal muscles of the same patient further supporting a similar pathogenesis.

- Cardiac muscle shows similar histopathological findings as skeletal muscle in DM.
- Inflammatory infiltrates and fibrosis are seen in the endomysium, perivascular, and perifascicular regions of the cardiac muscle as well as in the conduction system.

Clinical Manifestations

Clinically significant cardiac involvement constitutes a small portion of patients with DM/PM. Table 8.1 represents proportions of clinical symptoms in compiled IIM cohorts in a systematic review. The most commonly reported cardiac problem is congestive heart failure seen in 5–12% of patients [2, 4, 5, 16, 18]. Symptoms such as dyspnea, orthopnea, and palpitations are reported in 5–20% of IIM patients [4, 12, 16], but it is difficult to differentiate between a primary cardiac cause and concurrent respiratory muscle weakness due to skeletal muscle involvement [19].

Ischemic heart disease is important in IIM, and angina pectoris has previously been reported in 4–18% of IIM patients [4, 5]. Interestingly, autopsy studies have demonstrated significantly more coronary artery disease than reported clinically as angina, with coronary atherosclerosis including intimal proliferation, medial sclerosis, luminal narrowing, and evidence of remote infarction in up to 44% of patients [5, 15, 18]. In prospective IIM cohorts, MI was seen in 4.6–6.8%, which is similar to the reported age-matched prevalence in the US population [13]. However, a

Table 8.1 Clinically evident cardiac involvement

Prospective cohort	$n = 195$ patients (%)	Retrospective cohort	$n = 290$ patients (%)
Dyspnea	21 (10.8)	Combined dyspnea, chest pain, edema, and palpitations	14.8 (5.1)
Angina	15 (7.7)		
Palpitations	10 (5.1)		
Peripheral edema	13 (1.5)		
Systolic murmur	227 (13.8)	Systolic murmur	3 (1)
S4 gallop	15 (7.7)		
S3 gallop	1 (0.5)	S3 gallop	4 (1.3)
Arrythmia	27 (13.8)	Arrhythmias	7 (2.4)
CHF	11 (5.6)	CHF	34 (11.7)
MI	9 (4.6)		
Myocarditis	5 (2.6)		
Complete heart block	1 (0.5)		
Pericarditis	2 (1)	Pericarditis	2 (0.6)

Reprinted from Gupta et al. [13], Copyright (2011) with permission from Elsevier

recent large Canadian population study noted an incidence rate of MI being significantly higher than in the general population (22.5 vs. 5.5 events per 1000 person-years) with hazard ratios being the highest within the first year of IIM diagnosis [20]. Vasospastic angina has also been reported to be associated with signs of generalized vasculopathy such as Raynaud phenomenon [21].

Symptoms of arrhythmias and conduction defects such as palpitations, dizziness, and syncope have also been reported in up to 13.8% of IIM patients in prospective cohorts [13]. Such signs may suggest developing fibrosis of the conduction system and should be monitored carefully. Although the mild rhythm disorders do not commonly have clinical significance, there are several reports of patients requiring permanent pacemaker placement and others having fatal arrhythmias [4, 18]. Taken together, this data reinforces the need for increased awareness and monitoring of cardiac involvement in IIM patients. Comprehensive screening of cardiac function in all IIM patients should be undertaken if patients present with any cardiac or even nonspecific unexplained symptoms.

Subclinical Heart Involvement

Subclinical cardiac involvement is reported much more commonly than clinically evident cardiac manifestations, and the reported incidence varies between 13% and 72% of IIM patients depending on the selected noninvasive testing [22]. However, the clinical and prognostic significance of these subclinical cardiac abnormalities are not well known such that routine screening is not recommended beyond initial cardiac evaluation in the asymptomatic patient. Abnormal EKG findings are the most commonly observed findings including atrial or ventricular premature beats, atrial/ventricular tachycardia, atrial fibrillation, A-V conduction block, high-grade heart block, bundle branch block, PR prolongation, abnormal Q waves, nonspecific ST-T wave changes, and left ventricular hypertrophy [4, 18]. Echocardiography is useful in detecting structural heart disease and cardiac function even in the absence of clinical symptoms. In patients with IIM, there are reports of atrial enlargement, ventricular hypertrophy, valvular changes such as thickening and stenosis, global or segmental hypokinesis, reduced systolic or diastolic function, and pericardial involvement [22]. Newer techniques such as tissue Doppler imaging [23] allow detection of earlier manifestations such as left ventricular diastolic dysfunction (LVDD) when conventional measurements may be unremarkable [24]. The incidence of LVDD seems to be significantly higher in IIM patients compared to the general population [25].

- Initial evaluation of cardiac status with assessment of traditional CV risk factors, echocardiogram, and EKG is recommended in IIM patients.
- No routine follow-up screening is currently recommended beyond initial cardiac evaluation in an asymptomatic patient.
- Comprehensive cardiac workup is recommended in a patient with cardiac or nonspecific, unexplained symptoms.

Diagnostic Modalities

Clinically relevant cardiac manifestations may be present even without overt symptoms, which is why noninvasive testing is recommended at the time of diagnosis.

1. *Electrocardiogram (EKG)*

EKG or Holter abnormalities are detected in 32–72% of IIM patients, which is significantly more frequent than the general population. The most well-described finding is a conduction abnormality, with the most frequently observed being left anterior hemi-block and right bundle branch block [18]. SA or AV nodal dysfunction related to extensive fibrotic damage of the conduction system can be seen and may even result in high-

Table 8.2 ECG abnormalities in IIM patients

Prospective cohort	*n* = 243 patients (%)	Retrospective cohort	*n* = 433 patients (%)
First-degree AV block	9 (3.7)	First-degree AV block	6 (1.4)
Second-degree AV block	1 (0.4)		
Third-degree AV block	3 (1.2)	Third-degree AV block	8 (1.8)
Bundle branch blocks	3 (1.2)	Bundle branch block	12 (2.7)
Left anterior fascicular block	5 (2)		
Conduction abnormality, not specified	38 (15.6)	Arrhythmias, nonspecific	7 (1.6)
Supraventricular tachycardia	8 (3.3)	ECG abnormalities, nonspecific	28 (6.4)
Atrial fibrillation/flutter	3 (1.2)		
Premature atrial contraction	6 (2.5)		
Premature ventricular contraction	46 (18.9)		
Nonsustained ventricular tachycardia	1 (0.4)		
ST-T abnormalities	11 (4.5)	ST-T abnormalities	64 (14.7)
Q waves	2 (0.8)	Q waves	3 (0.7)
Left ventricular hypertrophy	18 (7.4)		
Left atrial hypertrophy	4 (1.6)	Left atrial hypertrophy	2 (0.4)
Right ventricular hypertrophy	2 (0.8)	Right ventricular hypertrophy	1 (0.2)

Reprinted from Gupta et al. [13], Copyright (2011) with permission from Elsevier

degree heart block, which has been reported in 1–2% of patients. Other rhythm abnormalities include premature atrial or ventricular contractions, atrial dysarrhythmias, ventricular tachyarrhythmias, longer QRS, and supraventricular tachycardia [25]. Nonspecific ST-T wave changes are also seen frequently in 4–15% of patients [22] (Table 8.2).

As rhythm and conduction abnormalities are the most commonly reported cardiac manifestations in IIM patients, experts recommend routine ECG at time of diagnosis. ECG and telemetry monitoring should also be done when patients present with symptoms such as palpitations or syncope. Findings such as high-degree heart block or tachyarrhythmias may require therapeutic intervention such as a permanent pacemaker or defibrillator placement.

- Baseline EKG should be done in all patients diagnosed with IIM.
- EKG abnormalities are common in IIM patients, but most are not clinically significant.
- No association between myositis disease activity and EKG abnormalities has been found in the studies to date.
- Severe arrhythmias in IIM patients may occur and require telemetry for diagnosis and pacemaker/defibrillator placement.

To date, the degree of systemic disease activity does not seem to correlate with the presence of ECG abnormalities [15, 16]. In a cohort of 77 IIM patients, there was no association between the presence of ECG abnormalities and CK levels, severity of IIM, presence or absence of various clinical phenomenon (i.e., arthritis, Raynaud phenomenon, rash, ILD, malignancy), disease duration, or treatment. Furthermore, ECG findings frequently progressed during clinical remission [18].

2. *Echocardiogram*

Few prospective, detailed echocardiographic studies are available in the literature, which report echocardiographic abnormalities in 14–62% of myositis patients [4, 11, 23, 26]. Left

ventricular diastolic dysfunction (LVDD) by tissue Doppler imaging (TDI) is the most frequently reported abnormality, noted in up to 48% of IIM patients, which is significantly higher than in the general population (30%) [24, 25, 27]. LVDD may be reflective of increased chamber stiffness due to fibrosis and is usually the first sign of systolic and diastolic heart failure. TDI estimates the velocity of contraction and relaxation of myocardial segments during a cardiac cycle. The use of TDI has increased sensitivity and specificity for systolic and diastolic dysfunction when compared to traditional echocardiography [28] and has been shown to be a useful tool to detect preclinical cardiac impairment in several studies [24, 25, 27, 29]. Two prospective controlled studies of echocardiographic measurements on 46 IIM and 51 DM patients with age- and gender-matched healthy controls confirmed a higher frequency and/or severity of LVDD in IIM [24, 27]. In contrast to diastolic dysfunction, compromise of systolic function noted by decreased LV ejection fraction on echocardiogram is rarely noted except when severe cardiac involvement and typical CHF symptoms are present.

Finally, other observed findings noted on echocardiography include mitral valve prolapse (7–23%), hyperdynamic LV function, left atrial and/or left ventricular enlargement, left ventricular hypertrophy, septal hypertrophy, thickened valve leaflet, valve prolapses/stenosis/regurgitation (most frequently in the mitral and aortic valve), pericardial effusions (which were all hemodynamically insignificant), and pulmonary hypertension [30]. However, reported incidences are observational from prospective patient cohorts, and it is unclear if such findings are more common in IIM compared to healthy controls.

- Left ventricular diastolic dysfunction (LVDD) is reported more frequently in IIM patients compared to matched healthy controls.

3. *Cardiac Magnetic Resonance (CMR)*

CMR provides not only anatomical imaging but also the ability to detect features of myocardial tissue such as inflammatory edema, irreversible necrosis or scarring, and contractile dysfunction [31]. Contrast-enhanced MRI technique using gadolinium diethylene-triaminepantaacetic (Gd-DTPA) is able to differentiate between myocardial infarction and inflammatory tissue from myocarditis. Early contrast enhancement with high signal intensities detected within the first minutes of injection indicates myocardial hyperemia; however, late gadolinium enhancement (LGE) [32] is highly sensitive for irreversible injury demonstrated as areas with high signal intensity in the equilibrium phase (>10 min post injection) [33]. The pattern and regional distribution of LGE is helpful in distinguishing the etiology of myocardial disease, whereas the severity or extent of LGE is associated with a worse prognosis [34, 35]. Inflammatory myocarditis may have a patchy distribution and can be subepicardial, sparing the subendocardium, which is distinct from ischemic lesions that always involve the subendocardium [36]. As IIM patients have an increased risk of both inflammatory myocarditis and ischemic events, CMR can be considered to differentiate between the two with the differences in regional distribution. This suggests CMR as a useful tool in diagnosis as well as monitoring of myocardial inflammation in IIM [37–39].

CMR may also be a useful tool in early detection of subclinical cardiac involvement in IIM by determining the extent of unrecognized myocardial scarring [39]. CMR is also sensitive to changes in the cardiac muscle following treatment. In a study of four patients with IIM and myocarditis, after 6 months of treatment with glucocorticoids, the area of early and delayed contrast enhancement on CMR was substantially reduced and correlated with improvement of cardiac symptoms [38].

- Cardiac MRI is a useful noninvasive tool for detection of inflammation vs. myocardial damage in IIM.

4. *Technetium99m-Pyrophosphate (99mTc-PYP) Scintigraphy*

Cardiac uptake of ^{99m}Tc-pyrophosphate (99mTc-PYP) in particular has been suggested as a mode of detecting inflammatory activity of the myocardium in IIM patients. A study of 30 DM/PM patients reported abnormal 99mTc-PYP uptake in 57% of patients suggesting that it may assist in early detection of cardiac involvement [40]. Patients with high uptake scores had poor cardiac outcome, and autopsy showed perivascular and interstitial mononuclear infiltrates and degenerative muscle fibers within the myocardium [40]. Smaller studies also have used 99mTc-PYP in the detection of cardiac outcome in IIM and reported uptake in 50–76% of patients [41–43]. However, without large comparative studies with a control group, the clinical usefulness of scintigraphy in IIM-related myocarditis is yet to be proven, and further studies are warranted. False-positive results may be seen with hyperparathyroidism, prior myocardial infarction, dystrophic cardiac calcification, and ventricular aneurysms.

5. *Endomyocardial Biopsy*

Endomyocardial biopsies allow histologic confirmation of inflammatory myocarditis and are the gold standard for diagnosis. However, biopsies are rarely performed in routine clinical practice given the invasive nature and concern for complications such as vascular injury, puncture site complications, or prolonged bleeding [44] and should only be considered at a center where it is performed routinely. A case of endomyocardial biopsy in a patient with abnormal contrast enhancement on Gd-DTPA CMR showed interstitial fibrosis, edema, cellular cluster, and hypertrophy, suggestive of inflammatory damage [45].

- Endomyocardial biopsy is the gold standard for myocarditis due to connective tissue disease, but is not commonly done due to the risk of complications related to an invasive procedure.

6. *Biochemical Markers*

Cardiac enzymes in patients with IIM must be interpreted with caution, as elevations may be from damaged or regenerating skeletal muscle. Creatine kinase isoenzymes include the CK-MM form, which is mainly from the skeletal muscle, and the CK-MB isoform, which is thought to be restricted to the myocardium. Although cardiac enzymes are reported to be specific for myocardial damage and ischemia, there have been reports of elevated CK-MB levels and CK-MB/CK ratios in IIM patients even in the absence of cardiac symptoms or ECG changes [46–48]. This is also true for cardiac troponins, which are typically thought to be highly specific for myocardial ischemia [49, 50]. It is thought that as regenerating muscle fibers resemble fetal muscles and express similar genes, CK-MB and cTnT isoforms (which are known to be expressed in the skeletal muscle during fetal development) are re-expressed in damaged or regenerating skeletal muscle. Hence, elevated CK-MB and cTnT may be misleading in IIM patients and result in unnecessary investigations for coronary artery disease.

Cardiac troponin isoform I (cTnI) is only expressed in the heart during fetal development and unlikely to be found in a noncardiac muscle [51, 52]. In a study of 49 patients with IIM, CK elevations had a high correlation with cTnT but not with cTnI, suggesting cTnI is the most reliable serum marker to detect myocardial damage in patients with IIM [53, 54]. A study by Erlacher and colleagues also measured various "cardiac" enzymes in IIM patients without clinical evidence of cardiac involvement and showed CKMB elevation in 51%, cTnT in 41%, and cTnI in only 2.5% of patients. CTnT, but not cTnI, was correlated with disease severity scores and skeletal muscle damage markers [55].

- CK-MB and cTnT may be elevated in myositis without cardiac involvement
- cTnI is more specific for myocardial damage and should be used to evaluate the myocardium in IIM

Management

1. *Glucocorticoids and Immunomodulatory Agents*

There are no randomized trials to evaluate the treatment effects for DM/PM-specific heart disease. Glucocorticoids and immunosuppressive therapy are used to control the underlying disease process as active disease is thought to be driving the cardiac disease. However, reports of response in the cardiac manifestations to immunosuppressive therapy are conflicting. In a study of four patients with IIM-related myocarditis, two of four (50%) patients who presented with symptoms of heart failure had resolution of their symptoms after 2 months of immunosuppressive therapy, and cardiac MRI normalized in all four patients after 6 months, suggesting a beneficial role for systemic immunosuppression [38]. In contrast, other studies assessing abnormal EKGs, complete heart block, and abnormalities on autopsy in IIM cohorts suggested that cardiac involvement was independent of skeletal muscle disease activity or treatment [16, 18, 56].

Systemic immunosuppressive agents other than glucocorticoids that have been used in treating cardiac disease in IIM include cyclophosphamide, cyclosporine, methotrexate and azathioprine, but the impact of individual agents remains unknown. Intravenous immunoglobulin (IVIG) has shown good immunomodulatory effects in IIM and is frequently used for cutaneous and skeletal disease. There are no studies of its use in IIM cardiac disease, but in pediatric acute myocarditis, IVIG was shown to improve LV function and survival in the first year after treatment [57]. When considering IVIG in patients with IIM cardiac involvement, it is important to consider co-management with cardiology and close monitoring of their volume status with appropriate adjustments in their diuretics given the risk of volume overload with IVIG. Subcutaneous immunoglobulin also may be of benefit with lower risk of volume overload in such cases [58].

2. *Traditional Cardiac Medications*

For clinically evident cardiac involvement, patients are managed similarly to non-IIM patients in regard to their cardiac manifestations. Antiarrhythmics, antianginals, and heart failure medications are considered depending on the clinical presentation. When there is myocardial involvement with clinically significant CHF, pharmacological treatment includes beta-blockers, aspirin, diuretics, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin-II receptor blockers (ARBs) [59]. IIM patients also have a higher risk of vascular involvement leading to ischemic episodes in which case anti-anginals such as calcium channel blockers and nitrates may be used.

3. *Pacemaker and Cardiac Implantable Cardiac Defibrillator*

Conduction abnormalities including high-degree heart block are seen in IIM patients with cardiac involvement, and there are several reports of patients requiring a temporary or permanent pacemaker placement (PPM) with variable outcomes [18, 56, 60]. In the general population, PPM success rates are reported between 88% and 92%, but success rates in IIM patients are yet to be determined [59]. Some reports have shown a successful outcome, whereas others have noted mortality from progressive conduction abnormalities resulting in sudden cardiac death (SCD) despite PPM placement. Most cases that require PPM placement were below the AV node with SA node dysfunction noted infrequently [60].

Cardiac resynchronization therapy with an implantable cardiac defibrillator (ICD) may be considered in patients with symptomatic ventricular tachycardia or ventricular fibrillation which can be fatal. In non-IIM patients, cardiac resynchronization therapy with ICD is indicated for patients with impaired LV function (LV ejection fraction <35%) and left bundle branch block in NYHA functional classes II to IV [61]. There are no studies regarding ICD placement in patients with

IIM-related myocarditis, and further investigation is needed to address the benefits and timing of ICD placement in IIM-related cardiomyopathy.

4. *Management of Traditional Cardiovascular Risk Factors*

There is increasing evidence of a higher prevalence of traditional cardiovascular risk factors (obesity, hypertension, dyslipidemia) in patients with IIM [62–65]. One retrospective study of 344 patients with IIM reported a high prevalence of hypertension (62%) and diabetes (49%) [62], and other cross-sectional studies have shown an increased frequency of dyslipidemia, glucose intolerance, and obesity [63–65]. A Canadian population study showed an increased myocardial infarction frequency but not ischemic stroke in DM and PM patients compared to age-/gender-matched control group selected from the general population [66]. Age/sex/entry time-matched hazard ratios (HR) for MI among PM and DM patients compared with the control cohort were 5.2 and 3.5, respectively. For stroke, the HR for PM was 2.46 and for DM was 1.81 (not statistically significant). The incidence of MI and stroke were highest in the first year of diagnosis.

Several contributing factors have been proposed to explain the increased atherosclerosis in patients with IIM. Long-term use of glucocorticoids is known to increase glucose intolerance and dyslipidemia and accelerate the development of atherosclerosis. The Danish study demonstrated that present use of glucocorticoids correlated with severe coronary artery calcification [65]. Physical inactivity caused by the disease itself as well as the constant low-grade inflammation may also lead to increased development of atherosclerosis and metabolic syndrome, as suggested in patients with RA and SLE [67, 68].

Such results support increased vigilance in cardiovascular prevention and aggressive treatment of modifiable CV risk factors in IIM. Structured exercise programs have been well established as beneficial to skeletal muscle disease in IIM [69, 70], but the increased physical activity and improvement in aerobic capacity may also be beneficial in improving cardiovascular outcomes. Statins are completely contraindicated in patients with immune-mediated necrotizing myopathy related to the anti-HMGCR antibodies [71, 72]. Approximately 10% of patients developed some worsening muscle symptoms associated with statin use with the majority of symptoms improving after holding therapy, suggesting that particular attention should be paid to statin use in some myositis patients.

5. *Cardiac Transplantation*

Severe cardiac involvement in IIM requiring cardiac transplantation is rare, and only a few cases of cardiac transplant in IIM have been reported. Successful cardiac transplantation was first reported in 1999 in a patient with dilated cardiomyopathy related to polymyositis [73]. A recent report described a case of a patient with treatment refractory DM with severe cardiomyopathy with cardiogenic shock who underwent a successful orthotropic heart transplant doing well at 25 months post-transplant [17].

Cardiac Management

- Immunosuppressive/immunomodulatory therapies
  - Glucocorticoids
  - Other immunosuppressive agents including cyclophosphamide, cyclosporine, methotrexate, azathioprine, etc.
  - IVIG or SQIG
- Traditional cardiac medications
  - Beta-blockers, aspirin, diuretics, ACE inhibitors, or ARBs
  - Antiarrhythmic drugs
- Risk factor modification
  - Smoking
  - Obesity
  - Diabetes/insulin resistance
  - Hypertension
  - Dyslipidemia
  - Steroids
- Pacemaker and cardiac implantable cardiac defibrillator
- Cardiac ablation
- Cardiac transplantation[1]

[1]Angiotensin-converting enzyme (ACE), angiotensin-II receptor blockers [74].

Prognosis

Patients with DM/PM have increased mortality compared to the general population with cardiopulmonary disease as the leading cause of death, ranging between 5% and 20% [8, 10, 12, 75]. Congestive heart failure and/or myocarditis, myocardial infarction, and complete heart block were most frequently noted in a systematic review including 33 retrospective and prospective IIM cohorts (30%, 18%, and 10%, respectively) (Table 8.3) [13]. Unlike viral myocarditis, which leads to spontaneous recovery with minimal or no sequelae, cardiac involvement in IIM portends an overall poor prognosis of the disease [59]. Prospective studies are needed to evaluate the effect of various cardiac and immunomodulatory therapies/strategies on survival in IIM patients.

Conclusions and Recommendations

Cardiac involvement is increasingly recognized in patients with IIM as a poor prognostic factor as well as a major cause of morbidity and mortality. When clinically evident, patients may present with congestive heart failure, arrhythmias, or coronary artery disease, but most patients will have subclinical involvement that is only evident on further testing. Experts recommend that all patients with a diagnosis of IIM undergo a detailed cardiac history and a screening EKG and echocardiogram on initial evaluation. Tailored cardiac therapy should be used in conjunction with immunosuppression, and patients require continued monitoring even when the skeletal disease is in remission (Fig. 8.1.).

Table 8.3 Causes of cardiac mortality

Prospective cohort	$n = 102$ patients	Retrospective cohort	$n = 550$ patients
CHF	4	CHF	3
MI	7	MI	2
Myocarditis	4	Myocarditis	1
Pericarditis	2	High-degree AV block/bundle branch block	5
Endocarditis	1	Arrhythmia	4
		Cardiac arrest	2
		Nonspecific cardiac cause of death	9
		HOCM	1

Reprinted from Gupta et al. [13], Copyright (2011) with permission from Elsevier

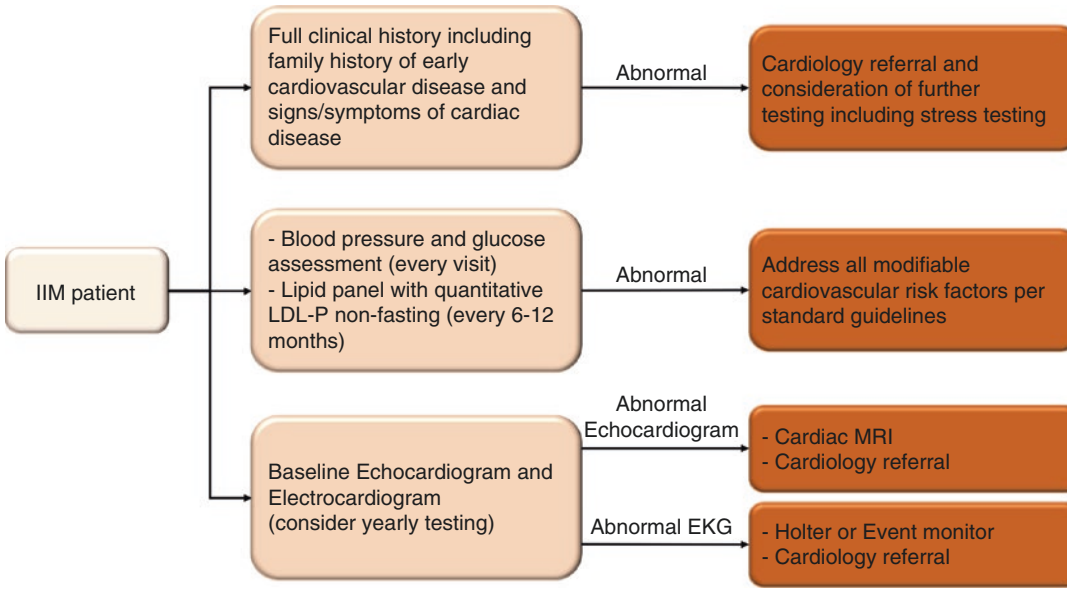

Fig. 8.1 Evaluation of cardiac involvement in IIM. * Co-management by Cardiology and Rheumatology for all IIM patients with cardiovascular disease

References

1. Oppenheim H. Zur dermatomyositis, vol. 36. Berl Klin: Wochenschrift; 1899. p. 805–7.
2. Bohan A, Peter JB, Bowman RL, Pearson CM. Computer-assisted analysis of 153 patients with polymyositis and dermatomyositis. Medicine (Baltimore). 1977;56(4):255–86.
3. Henriksson KG, Sandstedt P. Polymyositis--treatment and prognosis. A study of 107 patients. Acta Neurol Scand. 1982;65(4):280–300.
4. Taylor AJ, Wortham DC, Burge JR, Rogan KM. The heart in polymyositis: a prospective evaluation of 26 patients. Clin Cardiol. 1993;16(11):802–8.
5. Oka M, Raasakka T. Cardiac involvement in polymyositis. Scand J Rheumatol. 1978;7(4):203–8.
6. Danieli MG, Gambini S, Pettinari L, Logullo F, Veronesi G, Gabrielli A. Impact of treatment on survival in polymyositis and dermatomyositis. A single-centre long-term follow-up study. Autoimmun Rev. 2014;13(10):1048–54.
7. Airio A, Kautiainen H, Hakala M. Prognosis and mortality of polymyositis and dermatomyositis patients. Clin Rheumatol. 2006;25(2):234–9.
8. Sultan SM, Ioannou Y, Moss K, Isenberg DA. Outcome in patients with idiopathic inflammatory myositis: morbidity and mortality. Rheumatology (Oxford). 2002;41(1):22–6.
9. Limaye V, Hakendorf P, Woodman RJ, Blumbergs P, Roberts-Thomson P. Mortality and its predominant causes in a large cohort of patients with biopsy-determined inflammatory myositis. Intern Med J. 2012;42(2):191–8.
10. Danko K, Ponyi A, Constantin T, Borgulya G, Szegedi G. Long-term survival of patients with idiopathic inflammatory myopathies according to clinical features: a longitudinal study of 162 cases. Medicine (Baltimore). 2004;83(1):35–42.
11. Gonzalez-Lopez L, Gamez-Nava JI, Sanchez L, Rosas E, Suarez-Almazor M, Cardona-Munoz C, et al. Cardiac manifestations in dermato-polymyositis. Clin Exp Rheumatol. 1996;14(4):373–9.
12. Hochberg MC, Feldman D, Stevens MB. Adult onset polymyositis/dermatomyositis: an analysis of clinical and laboratory features and survival in 76 patients with a review of the literature. Semin Arthritis Rheum. 1986;15(3):168–78.
13. Gupta R, Wayangankar SA, Targoff IN, Hennebry TA. Clinical cardiac involvement in idiopathic inflammatory myopathies: a systematic review. Int J Cardiol. 2011;148(3):261–70.
14. Bingham CO 3rd, Rizzo W, Kivitz A, Hassanali A, Upmanyu R, Klearman M. Humoral immune response to vaccines in patients with rheumatoid arthritis treated with tocilizumab: results of a randomised controlled trial (VISARA). Ann Rheum Dis. 2015;74(5):818–22.
15. Haupt HM, Hutchins GM. The heart and cardiac conduction system in polymyositis-dermatomyositis: a clinicopathologic study of 16 autopsied patients. Am J Cardiol. 1982;50(5):998–1006.
16. Denbow CE, Lie JT, Tancredi RG, Bunch TW. Cardiac involvement in polymyositis: a clinicopathologic study of 20 autopsied patients. Arthritis Rheum. 1979;22(10):1088–92.
17. Bae S, Khanlou N, Charles-Schoeman C. Cardiac transplantation in dermatomyositis: a case report and literature review. Hum Pathol Case Rep. 2017;8:55–8.
18. Stern R, Godbold JH, Chess Q, Kagen LJ. ECG abnormalities in polymyositis. Arch Intern Med. 1984;144(11):2185–9.
19. Kalluri M, Oddis CV. Pulmonary manifestations of the idiopathic inflammatory myopathies. Clin Chest Med. 2010;31(3):501–12.
20. Rai SK, Choi HK, Sayre EC, Avina-Zubieta JA. Risk of myocardial infarction and ischaemic stroke in adults with polymyositis and dermatomyositis: a general population-based study. Rheumatology (Oxford). 2016;55(3):461–9.
21. Riemekasten G, Opitz C, Audring H, Barthelmes H, Meyer R, Hiepe F, et al. Beware of the heart: the multiple picture of cardiac involvement in myositis. Rheumatology (Oxford). 1999;38(11):1153–7.
22. Zhang L, Wang GC, Ma L, Zu N. Cardiac involvement in adult polymyositis or dermatomyositis: a systematic review. Clin Cardiol. 2012;35(11):686–91.
23. Gottdiener JS, Sherber HS, Hawley RJ, Engel WK. Cardiac manifestations in polymyositis. Am J Cardiol. 1978;41(7):1141–9.
24. Lu Z, Wei Q, Ning Z, Qian-Zi Z, Xiao-Ming S, Guo-Chun W. Left ventricular diastolic dysfunction -- early cardiac impairment in patients with polymyositis/dermatomyositis: a tissue Doppler imaging study. J Rheumatol. 2013;40(9):1572–7.
25. Diederichsen LP, Simonsen JA, Diederichsen AC, Hvidsten S, Hougaard M, Junker P, et al. Cardiac abnormalities in adult patients with polymyositis or dermatomyositis as assessed by noninvasive modalities. Arthritis Care Res (Hoboken). 2016;68(7):1012–20.
26. Agrawal CS, Behari M, Shrivastava S, Ahuja GK, Bhandari S, Kothari SS. The heart in polymyositis-dermatomyositis. J Neurol. 1989;236(4):249–50.
27. Wang H, Liu HX, Wang YL, Yu XQ, Chen XX, Cai L. Left ventricular diastolic dysfunction in patients with dermatomyositis without clinically evident cardiovascular disease. J Rheumatol. 2014;41(3):495–500.
28. Silva CE, Ferreira LD, Peixoto LB, Monaco CG, Gil MA, Ortiz J. Study of the myocardial contraction and relaxation velocities through Doppler tissue imaging echocardiography: a new alternative in the assessment of the segmental ventricular function. Arq Bras Cardiol. 2002;78(2):200–11.
29. Peter A, Balogh A, Szilagyi S, Faludi R, Nagy-Vincze M, Edes I, et al. Echocardiographic abnormalities in new-onset polymyositis/dermatomyositis. J Rheumatol. 2015;42(2):272–81.

30. Danieli MG, Gelardi C, Guerra F, Cardinaletti P, Pedini V, Gabrielli A. Cardiac involvement in polymyositis and dermatomyositis. Autoimmun Rev. 2016;15(5):462–5.
31. Friedrich MG, Marcotte F. Cardiac magnetic resonance assessment of myocarditis. Circ Cardiovasc Imaging. 2013;6(5):833–9.
32. Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: final classification criteria. Ann Rheum Dis. 2010;69(5):798–806.
33. Rehwald WG, Fieno DS, Chen EL, Kim RJ, Judd RM. Myocardial magnetic resonance imaging contrast agent concentrations after reversible and irreversible ischemic injury. Circulation. 2002;105(2):224–9.
34. Grun S, Schumm J, Greulich S, Wagner A, Schneider S, Bruder O, et al. Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. J Am Coll Cardiol. 2012;59(18):1604–15.
35. Kwong RY, Chan AK, Brown KA, Chan CW, Reynolds HG, Tsang S, et al. Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. Circulation. 2006;113(23):2733–43.
36. Hunold P, Schlosser T, Vogt FM, Eggebrecht H, Schmermund A, Bruder O, et al. Myocardial late enhancement in contrast-enhanced cardiac MRI: distinction between infarction scar and non-infarction-related disease. AJR Am J Roentgenol. 2005;184(5):1420–6.
37. Toong C, Puranik R, Adelstein S. Use of cardiac MR imaging to evaluate the presence of myocarditis in autoimmune myositis: three cases. Rheumatol Int. 2012;32(3):779–82.
38. Allanore Y, Vignaux O, Arnaud L, Puechal X, Pavy S, Duboc D, et al. Effects of corticosteroids and immunosuppressors on idiopathic inflammatory myopathy related myocarditis evaluated by magnetic resonance imaging. Ann Rheum Dis. 2006;65(2):249–52.
39. Mavrogeni S, Douskou M, Manoussakis MN. Contrast-enhanced CMR imaging reveals myocardial involvement in idiopathic inflammatory myopathy without cardiac manifestations. JACC Cardiovasc Imaging. 2011;4(12):1324–5.
40. Buchpiguel CA, Roizemblatt S, Pastor EH, Hironaka FH, Cossermelli W. Cardiac and skeletal muscle scintigraphy in dermato- and polymyositis: clinical implications. Eur J Nucl Med. 1996;23(2):199–203.
41. Duska F, Bradna P, Pospisil M, Kubicek J, Vizda J, Kafka P, et al. Pyrophosphate scintigraphy and other non-invasive methods in the detection of cardiac involvement in some systemic connective tissue diseases. Nuklearmedizin. 1987;26(1):28–32.
42. Buchpiguel CA, Roizenblatt S, Lucena-Fernandes MF, Soares Junior J, Meneguetti JC, Hironaka FH, et al. Radioisotopic assessment of peripheral and cardiac muscle involvement and dysfunction in polymyositis/dermatomyositis. J Rheumatol. 1991;18(9):1359–63.
43. Askari AD, Huettner TL. Cardiac abnormalities in polymyositis/dermatomyositis. Semin Arthritis Rheum. 1982;12(2):208–19.
44. Baraldi-Junkins C, Levin HR, Kasper EK, Rayburn BK, Herskowitz A, Baughman KL. Complications of endomyocardial biopsy in heart transplant patients. J Heart Lung Transplant. 1993;12(1 Pt 1):63–7.
45. Ohata S, Shimada T, Shimizu H, Murakami Y, Matsuno Y. Myocarditis associated with polymyositis diagnosed by gadolinium-DTPA enhanced magnetic resonance imaging. J Rheumatol. 2002;29(4):861–2.
46. Arenas J, Diaz V, Liras G, Gutierrez E, Santos I, Martinez A, et al. Activities of creatine kinase and its isoenzymes in serum in various skeletal muscle disorders. Clin Chem. 1988;34(12):2460–2.
47. Trask RV, Billadello JJ. Tissue-specific distribution and developmental regulation of M and B creatine kinase mRNAs. Biochim Biophys Acta. 1990;1049(2):182–8.
48. Tsung SH. Creatine kinase isoenzyme patterns in human tissue obtained at surgery. Clin Chem. 1976;22(2):173–5.
49. Kobayashi S, Tanaka M, Tamura N, Hashimoto H, Hirose S. Serum cardiac troponin T in polymyositis/dermatomyositis. Lancet. 1992;340(8821):726.
50. White GH, Tideman PA. Increased troponin T in a patient with dermatomyositis. Clin Chem. 2001;47(6):1130–1.
51. Bodor GS, Porterfield D, Voss EM, Smith S, Apple FS. Cardiac troponin-I is not expressed in fetal and healthy or diseased adult human skeletal muscle tissue. Clin Chem. 1995;41(12 Pt 1):1710–5.
52. Bodor GS, Survant L, Voss EM, Smith S, Porterfield D, Apple FS. Cardiac troponin T composition in normal and regenerating human skeletal muscle. Clin Chem. 1997;43(3):476–84.
53. Aggarwal R, Lebiedz-Odrobina D, Sinha A, Manadan A, Case JP. Serum cardiac troponin T, but not troponin I, is elevated in idiopathic inflammatory myopathies. J Rheumatol. 2009;36(12):2711–4.
54. Kiely PD, Bruckner FE, Nisbet JA, Daghir A. Serum skeletal troponin I in inflammatory muscle disease: relation to creatine kinase, CKMB and cardiac troponin I. Ann Rheum Dis. 2000;59(9):750–1.
55. Erlacher P, Lercher A, Falkensammer J, Nassonov EL, Samsonov MI, Shtutman VZ, et al. Cardiac troponin and beta-type myosin heavy chain concentrations in patients with polymyositis or dermatomyositis. Clin Chim Acta. 2001;306(1–2):27–33.
56. Reid JM, Murdoch R. Polymyositis and complete heart block. Br Heart J. 1979;41(5):628–9.
57. Drucker NA, Colan SD, Lewis AB, Beiser AS, Wessel DL, Takahashi M, et al. Gamma-globulin treatment of acute myocarditis in the pediatric population. Circulation. 1994;89(1):252–7.
58. Danieli MG, Gelardi C, Pedini V, Moretti R, Gabrielli A, Logullo F. Subcutaneous IgG in immune-mediate

diseases: proposed mechanisms of action and literature review. Autoimmun Rev. 2014;13(12):1182–8.
59. Kindermann I, Barth C, Mahfoud F, Ukena C, Lenski M, Yilmaz A, et al. Update on myocarditis. J Am Coll Cardiol. 2012;59(9):779–92.
60. Kehoe RF, Bauernfeind R, Tommaso C, Wyndham C, Rosen KM. Cardiac conduction defects in polymyositis: electrophysiologic studies in four patients. Ann Intern Med. 1981;94(1):41–3.
61. Dickstein K, Vardas PE, Auricchio A, Daubert JC, Linde C. McMurray J, et al. 2010 focused update of ESC guidelines on device therapy in heart failure: an update of the 2008 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy. Developed with the special contribution of the Heart Failure Association and the European Heart Rhythm Association. Eur J Heart Fail. 2010;12(11):1143–53.
62. Limaye VS, Lester S, Blumbergs P, Roberts-Thomson PJ. Idiopathic inflammatory myositis is associated with a high incidence of hypertension and diabetes mellitus. Int J Rheum Dis. 2010;13(2):132–7.
63. Wang H, Tang J, Chen X, Li F, Luo J. Lipid profiles in untreated patients with dermatomyositis. J Eur Acad Dermatol Venereol. 2013;27(2):175–9.
64. de Moraes MT, de Souza FH, de Barros TB, Shinjo SK. Analysis of metabolic syndrome in adult dermatomyositis with a focus on cardiovascular disease. Arthritis Care Res (Hoboken). 2013;65(5):793–9.
65. Diederichsen LP, Diederichsen AC, Simonsen JA, Junker P, Sondergaard K, Lundberg IE, et al. Traditional cardiovascular risk factors and coronary artery calcification in adults with polymyositis and dermatomyositis: a Danish multicenter study. Arthritis Care Res (Hoboken). 2015;67(6):848–54.
66. Tisseverasinghe A, Bernatsky S, Pineau CA. Arterial events in persons with dermatomyositis and polymyositis. J Rheumatol. 2009;36(9):1943–6.
67. Volkmann ER, Grossman JM, Sahakian LJ, Skaggs BJ, FitzGerald J, Ragavendra N, et al. Low physical activity is associated with proinflammatory high-density lipoprotein and increased subclinical atherosclerosis in women with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2010;62(2):258–65.
68. Metsios GS, Stavropoulos-Kalinoglou A, Panoulas VF, Wilson M, Nevill AM, Koutedakis Y, et al. Association of physical inactivity with increased cardiovascular risk in patients with rheumatoid arthritis. Eur J Cardiovasc Prev Rehabil. 2009;16(2):188–94.
69. Alexanderson H, Munters LA, Dastmalchi M, Loell I, Heimburger M, Opava CH, et al. Resistive home exercise in patients with recent-onset polymyositis and dermatomyositis -- a randomized controlled single-blinded study with a 2-year followup. J Rheumatol. 2014;41(6):1124–32.
70. Munters LA, Loell I, Ossipova E, Raouf J, Dastmalchi M, Lindroos E, et al. Endurance exercise improves molecular pathways of aerobic metabolism in patients with myositis. Arthritis Rheumatol. 2016;68(7):1738–50.
71. Christopher-Stine L, Casciola-Rosen LA, Hong G, Chung T, Corse AM, Mammen AL. A novel autoantibody recognizing 200-kd and 100-kd proteins is associated with an immune-mediated necrotizing myopathy. Arthritis Rheum. 2010;62(9):2757–66.
72. Charles-Schoeman C, Amjadi SS, Paulus HE, International Myositis A, Clinical Studies G. Treatment of dyslipidemia in idiopathic inflammatory myositis: results of the International Myositis Assessment and Clinical Studies Group survey. Clin Rheumatol. 2012;31(8):1163–8.
73. Afzal A, Higgins RS, Philbin EF. Heart transplant for dilated cardiomyopathy associated with polymyositis. Heart. 1999;82(4):e4.
74. Ruperto N, Ozen S, Pistorio A, Dolezalova P, Brogan P, Cabral DA, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part I: overall methodology and clinical characterisation. Ann Rheum Dis. 2010;69(5):790–7.
75. Benbassat J, Gefel D, Larholt K, Sukenik S, Morgenstern V, Zlotnick A. Prognostic factors in polymyositis/dermatomyositis. A computer-assisted analysis of ninety-two cases. Arthritis Rheum. 1985;28(3):249–55.