Published in final edited form as:
Curr Heart Fail Rep. 2013 December ; 10(4): . doi:10.1007/s11897-013-0157-5.

Epidemiology and Natural History of Recovery of Left Ventricular Function in Recent Onset Dilated Cardiomyopathies

Michael M. Givertz, MD and **Douglas L. Mann, MD**

Abstract

Although the long term prognosis of patients with dilated cardiomyopathy (DCM) remains poor, approximately 25% of DCM patients with recent onset of heart failure (< 6 months) have a relatively benign clinical course with a spontaneously improvement in symptoms and partial, or in some cases complete, recovery of left ventricular (LV) function. Despite the longstanding recognition of the clinical phenomenon of LV recovery, relatively little attention has been paid to the etiology and natural history of this important group of DCM patients. Accordingly, in the present review we will focus on the epidemiology and natural history of recent onset DCM in patients who undergo spontaneous resolution of symptoms that is accompanied by recovery of LV function.

Keywords

Left ventricular recovery; reverse remodeling

Introduction

The term dilated cardiomyopathy (DCM) refers to a large group of heterogeneous myocardial disorders that are characterized by ventricular dilation and depressed myocardial contractility in the absence of abnormal loading conditions (e.g. valvular disease or hypertension). Although the overall prognosis in patients with symptomatic heart failure and DCM is relatively poor, with 25% mortality at 1 year and 50% mortality at 5 years [1], approximately 25% of DCM patients with recent onset of heart failure (< 6 months) have a relatively benign clinical course with spontaneously improvement in symptoms and partial, or in some cases complete, recovery of left ventricular (LV) function. Despite the longstanding recognition of this clinical phenomenon, relatively little attention has been paid to the etiology and natural history of this group of DCM patients. Accordingly, this review will focus on the epidemiology and natural history of recent onset DCM patients, in whom spontaneous resolution of symptoms and recovery of LV function occurs.

Epidemiology of LV Recovery

For some etiologies of DCM, recovery of left ventricular (LV) function and reverse LV remodeling occur once the inciting adverse event that precipitated the episode of heart failure is resolved or removed. Indeed, in some situations, recovery of LV function can

Address for Correspondence: Douglas L. Mann, MD Division of Cardiology Washington University School of Medicine 660 S. Euclid Ave, Campus Box 8086 St. Louis, MO 63110 Phone: (314) 362-8908 Fax: (314) 454-5550 dmann@dom.wustl.edu.

Conflict of Interest
Michael M. Givertz declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

occur in a relatively high proportion of individuals, even when the severity of the heart failure or LV dysfunction has been quire severe. In contrast to the well described clinical phenomenon of reverse LV remodeling and recovery of LV function that has been described with the pharmacologic and/or device treatment of patients with ischemic and non-ischemic heart failure, relatively little is known with regard to the phenomenon of the "spontaneous" recovery of LV function. As shown in the Figure there are three major etiologies of DCM that are associated with spontaneous recovery of LV function and reverse LV remodeling, including abnormal energetics, toxic insults and inflammation. Although clinically important, this review will not cover medical and/or device interventions that have been shown to lead to reverse remodeling in patients with chronic heart failure, since this has been reviewed in depth in several recent reviews [2,3].

Natural History of LV Recovery

The natural history of the recovery of LV function in patients with recent onset cardiomyopathy has been hard to establish with certainty for several reasons. First the great majority of the studies have been performed in single centers, with small numbers of patients, using different definitions of improvement in LV ejection fraction ranging from improvements in ejection fraction of 5% to 15% [4,5], although the great majority of studies have used 10%. Second, the definition for recovery of LV function has ranged from ejection fractions of greater than 40% to 50% [6]. For the purpose of this review, we will use the cut-off of 50% as a measure of complete LV recovery since this has been used by the majority of studies. However, the authors recognize that patients whose hearts have undergone reverse remodeling and have an EF > 50% may still have subclinical abnormalities in systolic and diastolic function [7]. Third, with the advent of modern medical therapy for heart failure, it is difficult to find studies in which patients are either untreated and/or in which treatment has been stopped following normalization of LV ejection fraction. Thus, it is often difficult to determine how much of the normalization of LV structure and function occurs because of the use of appropriate medical or device therapies, versus how much restoration of LV structure and function would have occurred in the absence of therapy. Moreover, institution of medical and/or device therapy makes it difficult to assess the durability of LV functional recovery. Nonetheless, by broadly reviewing the natural history of recovery of LV function in various clinical settings, we hope to highlight several unifying themes with regard to this phenomenon.

Abnormal Energetics

Tachyarrhythmias

Cardiac arrhythmias are common in patients with heart failure (HF) and often precipitate or exacerbate episodes of acute decompensation. In patients without structural heart disease, atrial and less commonly ventricular tachyarrhythmias may be the primary cause of a tachycardia-induced cardiomyopathy (TIC) [8]. Atrial fibrillation with rapid ventricular response and atrial tachycardia are the most common causes of TIC, but slow ventricular tachycardia and frequent ventricular ectopy have also been associated with reversible LV dysfunction. With TIC, effective antiarrhythmic therapy, cardioversion and/or radiofrequency ablation can result in improvement and often full recovery of LV function, especially if the tachycardia is transient [9]. However, LV dysfunction can rapidly recur in patients with recurrent tachycardia, and in patients with recovered LV function late sudden death has been reported [10]. The latter may be due to persistent hypertrophy and ultrastructural changes that have been documented in animal models of TIC [11]. In reported case series (see Table 1), more than 90% of patients with TIC had an improvement in EF > 10% with treatment and approximately 80% had full LV recovery. However, compared to

controls, patients with TIC had increased LV systolic and diastolic volumes [12], suggesting persistent negative remodeling.

Stress cardiomyopathy

Stress cardiomyopathy, also referred to as takotsubo cardiomyopathy or apical ballooning syndrome, is an acute cardiac syndrome characterized by transient apical and midventricular wall motion abnormality, electrocardiographic changes that mimic acute myocardial infarction, and modest cardiac enzyme release, in the absence obstructive coronary artery disease [13,14]. Women between the ages of 60 and 80, who suffer an acute emotional or physical stress, account for the majority of cases. Despite the dramatic presentation, almost all patients recover fully although recurrence rates as high as 5-10% have been reported [15,16]. In-hospital mortality is rare (1.1% in a systematic literature review). The predominant underlying mechanism appears to be acute sympathetic activation leading to “metabolic” myocardial stunning, which argues in favor of comprehensive adrenergic blockade and helps to explain the reversible nature of the LV and occasional RV injury [17]. Cardiac magnetic resonance imaging (MRI) reveals myocardial edema co-located with regional LV dysfunction, active inflammation and absence of significant fibrosis [18]. Large series (see Table 1) demonstrate that LV (and RV) wall motion abnormalities and systolic dysfunction uniformly normalize at or before hospital discharge. However, reverse remodeling may be delayed by up to 12 months in a small minority of patients.

Hyperthyroidism

In patients with hyperthyroidism, overt heart failure in the absence of underlying cardiac disease is uncommon [19]. While initial clinical studies highlighted the presence of increased cardiac output, low systemic vascular resistance, and hyperdynamic LV function causing high-output heart failure [20], subsequent case reports and small case series have also described a reversible dilated cardiomyopathy (see Table 1). Typically, these cases involve younger, otherwise healthy adults in whom the diagnosis of hyperthyroid-induced heart failure may be delayed due to non-specific symptoms of fatigue and dyspnea. Taken together, these cases demonstrate LV recovery in ~90% of patients and normalization of LV function in the majority, although selection bias is likely and persistent LV failure has been reported. Importantly, many of these cases are confounded by the presence of atrial tachycarrhythmias (due to the effects of thyroid hormone on atrial tissue and nodal conduction), raising the possibility of a tachycardia-induced cardiomyopathy. Underlying mechanisms are unclear, but the presence of activating auto-antibodies targeting beta-adrenergic and muscarinic receptors have been reported in patients with hyperthyroidism and atrial fibrillation [19]. Notably, circulating levels of catecholamines are usually low or normal in hyperthyroidism, and the effects of excess thyroid hormone act through downstream receptors and signaling G proteins. In fulminant cases of thyrotoxicosis with complete LV recovery, myocardial stunning similar to stress cardiomyopathy has been posited. Successful treatment of dilated cardiomyopathy secondary to hyperthyroidism generally requires anti-thyroid therapy (e.g.,propylthiouracil, radioactive iodine) to restore a euthryoid state. Beta-blockers should be used cautiously since they may lead to further reduction in myocardial contractility.

Toxins

Alcoholic cardiomyopathy

Alcohol has protective effects on coronary artery disease, but is a known cardiotoxin associated with arrhythmias, heart failure and LV dysfunction [21]. Alcoholic cardiomyopathy is a complication of longstanding alcohol abuse and related to a patient's total lifetime dose of ethanol. In one study, for example, the mean ethanol intake was 208 g

(12-15 standard drinks) per day for an average of 26 years. Frequent co-morbidities include atrial arrhythmias, hypertension, malnutrition and cirrhosis. In developed countries, alcohol may account for up to 25% of cases of dilated cardiomyopathy, and up to one-third of chronic alcoholics have asymptomatic LV dysfunction [22]. Genetic susceptibility has been postulated, and women have a lower threshold dose of ethanol for the development of cardiomyopathy [23]. During the course of cardiac remodeling, reduced EF is often preceded by LV dilation, an increase in LV mass, and diastolic dysfunction [24]. Abstinence can result in full recovery of LV function over a period of months to years, while "controlled" or moderate drinking has also been shown to promote reverse remodeling with improvement in EF and regression of hypertrophy (see Table 1). Patients who continue to drink heavily demonstrate either no change or further reduction in EF associated with excess cardiac mortality. A minority of patients who abstain from drinking also have no improvement in EF. Differences in racial, socio-economic and environmental factors, as well as other co-morbidities and treatment differences may contribute to variable remodeling outcomes

Trastuzumab-Related Cardiotoxicity

Trastuzumab is a monoclonal antibody that selectively targets the extracellular domain of human epidermal growth factor receptor 2 (HER2). For patients with early stage breast cancer that overexpresses HER2, trastuzumab significantly increases response rates and disease-free and overall survival. However, HER2 is also expressed in the adult heart and plays a fundamental role in cardiac protection via ErbB2-neuregulin 1 signaling. Cardiotoxicity has been reported in up to 7% of patients treated with trastuzumab alone, and is increased to 27% when trastuzumab is combined with an anthracycline. Other risk factors include lower baseline EF, older age, and hypertension. Cardiac troponin elevation prior to or during therapy is an independent predictor of toxicity [25]. Unlike anthracyline-induced cardiomyopathy, the cardiotoxicity of trastuzumab occurs rapidly and is potentially reversible [26]. In a prospective observational study of patients with trastuzumab-related cardiotoxicity, withdrawal of trastuzumab for 6 weeks resulted in an improvement in EF from 43% to 55%, with nearly 80% achieving EF > 50% (see Table 1). Following re-challenge, only 12% of patients had recurrent LV dysfunction [27]. In the Herceptin Adjuvant (HERA) trial, a significant drop in EF (≥ 10% below baseline and to < 50%) occurred in 118 of 1,678 patients (7%) with 67% achieving recovery of EF to ≥ 55% over 4-6 months. The absence of ultrastructural changes on endomyocardial biopsy, typically seen with anthracyclines, may explain the reversibility of trastuzumab cardiotoxicity. Negative troponin levels are also predictive of recovery supporting the theory that trastuzumab is associated with myocardial stunning, without necrosis. Clinical studies are underway to test the hypotheses that neurohormonal antagonists can prevent or attenuate traztusumab-related cardiotoxicity, hasten LV recovery, and/or allow ongoing chemotherapy.

Inflammation

Inflammation of the heart may lead to the development of symptomatic heart failure in ~ 10% of cases of initially unexplained cardiomyopathy [28,29]. There are three inflammatory etiologies that can lead to a dilated cardiomyopathy, including myocarditis, post-partum cardiomyopathy, and systemic inflammatory response syndrome (SIRS). The clinical diagnostic classification of recent onset dilated cardiomyopathy has been linked with inflammation in some cases, and will be discussed as well.

Recent Onset Cardiomyopathy

Recent onset heart failure with a dilated cardiomyopathy represent a heterogeneous grouping of diseases that includes myocarditis (4-67%), peripartum cardiomyopathy (10%), unknown toxins, and likely some undisclosed/unknown genetic abnormalities that present in adulthood . Recent onset cardiomyopathy is discussed herein as a separate entity insofar as there have been several longitudinal studies, including one multicenter study that examined the recovery of LV function. Recent onset DCM was defined as fewer than 6 months of cardiac symptoms with an LV EF of ≤ 40% at the time of presentation. Recovery of LV function was variously defined as an improvement of at least 5[4], 10 [30,31] or 15 [32] EF units from the baseline EF, and normalization of LV function was defined as attainment of an LV EF ≥ 50% at the time of follow-up. Several studies were conducted before the widespread use of evidence based medical therapies. As shown in Table 2, 26-70 % of patients with recent onset heart failure with a dilated cardiomypathy experience recovery of LV function. However, the percentage of patients with normalization of LV function was only 7-25%. Importantly, the percentage of patients with recovery of LV function by at least 10 EF units is greater in more recent studies in which evidence-based therapies for heart failure have been employed, consistent with the known effects of these agents on reverse remodeling. However, normalization of LV EF is the same in older and newer studies, and has not improved with implementation of evidence-based therapies. Interesting, in a recent report the use of serial B-type natriuretic peptide (BNP) levels and cardiac MRI provided a better prediction of recovery of LV function than conventional measures. Specifically, a BNP < 344 ng/l, as well as lower baseline late gadolinium enhancement and higher myocardial edema ratio improved the prediction of LV recovery of recent dilated cardiomyopathy [31]. Fibrosis or inflammation on biopsy was not an independent predictor of LV recovery.

Myocarditis

Although the term myocarditis refers to *any* inflammation of the myocardium, and can be observed following any form or injury to the heart (e.g. acute ischemic injury or mechanical trauma), the colloquial use of the term myocarditis has generally been used to describe inflammation of the heart muscle as a result of exposure to either external antigens (such as viruses, bacteria, parasites, toxins, or drugs) or internal triggers, such as autoimmune activation against self antigens. Although viral infection remains the most commonly identified cause for myocarditis, drug hypersensitivity and toxic drug reactions, and other infections, can also lead to myocarditis. One of the difficulties in defining the natural history of recovery of LV function in viral myocarditis is that histological evidence of myocarditis is often lacking and/or equivocal, and the definitions used vary from study to study. Nonetheless, for documented viral myocarditis the prognosis varies, with spontaneous complete resolution of symptoms and recovery of LV function in 40-100% of patients, and complete recovery of LV function in 40- 80% of patients (see Table 2). In the Myocarditis Treatment Trial improvements in LV ejection fraction > 10% occurred in all of the treatment (azathioprine and cyclosporine or azathioprine and prednisone) and control groups by week 28 of the study, and were maintained through 52 weeks [33]. There was, however, no difference in the LV ejection fraction in the treatment and control groups at any time. It is important to recognize that the improvements in LV function in these patients pre-dated the widespread use of neurohormonal antagonists, and thus represent the actual natural history of LV recovery in this disease entity. Improvements in LV function by > 15-20 ejection fraction units have also been reported in multiple case series that have used immunosuppression, immunoadsorption and/or anti-viral therapy (reviewed in reference [29]). These studies were not included in this review because of the small numbers of patients, lack of concurrent control groups, and heterogeneity of therapies used.

Interestingly, and seemingly paradoxically, the best outcomes of patients with documented viral myocarditis are most often seen in fulminant myocarditis [34].

Peripartum cardiomyopathy

Peripartum cardiomyopathy is a disease of unknown etiology in which LV dysfunction occurs during the last trimester of pregnancy or during early puerperium. Although the etiology remains unknown, most theories have focused on hemodynamic and immunologic causes [35], hence this entity will be discussed here. The prognosis of peripartum cardiomyopathy is related to the recovery of ventricular function. Significant improvement in LV function is seen in 60% to 100% of patients in the first 6 months after presentation (see Table 2), whereas full restoration of function is only seen in 20- 50% of patients. Of note, some series have reported improvements in LV function over 24 months, which may reflect, at least in part, institution of evidence-based therapies for heart failure [36]. The IMAC2 study included a small subset (n= 37) of patients with PPCM. Of interest, the mean EF at baseline (27 ± 7) and at 6 months (45 ± 14) was significantly greater in the PPCM group, and the percentage of patients with normalization of LV EF (48%) was significantly better in the PPCM group. Interpreting recovery of LV function in peripartum cardiomyopathy is complicated by the observation that recovery of LV function is greater in white than black patients [37], as well as the observation that many women with peripartum cardiomyopathy may have a viral etiology or a genetic cardiomyopathy that is unmasked by pregnancy.

In patients presenting with peripartum cardiomyopathy, inotropic contractile reserve during dobutamine stress echocardiography correlates with the subsequent recovery of LV function and a good prognosis [38]. However, for those patients who do not recover to normal or near-normal function, the prognosis is similar to other forms of DCM, with a 50% mortality rate at 6 years [39]. Predictors of lack of recovery of LV function in peripartum cardiomyopathy include: troponin T levels > 0.04 ng/ml, fractional shortening < 20%, or an LV end-diastolic dimension > 6 cm at the time of diagnosis. Although recovery of LV function is generally associated with good outcomes during subsequent pregnancies in women with a history of peripartum cardiomyopathy, these pregnancies can result in clinical deterioration, including death, even in patients who have normalized their LV function [40]. Retrospective studies estimate the risk of recurrent cardiomyopathy at ~ 20% in women with normal LV function, compared to 40-50% in those with impaired LV function [40]. In one series, ~70% of patients who recovered their LV function were taken off of their ACE inhibitors and beta-blockers, with no regression of LV function. However, it bears emphasis that patients who have full recovery of LV function have diminished contractile reserve during dobutamine stress echocardiography [41], suggesting that complete normalization of LV structure and function does not necessarily indicate that heart failure will not supervene with a subsequent hemodynamic stress.

Systemic Inflammatory Response Syndrome (SIRS)

The mechanisms for the development of LV dysfunction during sepsis and septic shock have been the focus of numerous studies. Although the current literature suggests that the majority of patients with septic shock develop a hyperdynamic circulatory state after fluid resuscitation, myocardial depression, biventricular dilation and depressed LV function have been demonstrated in ~ 30% of patients who present in the early stages of sepsis [42]. Remarkably, the patients with the most profound LV dilation and depression of LV function appear to have the best overall prognosis, perhaps because the increase in LV volumes enables the patients to maintain a normal stroke volume and cardiac index, despite a decrease in LV contractility. The extant literature suggests that the LV dysfunction that occurs in sepsis is largely reversible within 7- 10 days in those patients who survive [43].

Although exact numbers are not reported in the literature, recovery of LV function by 10 EF units from baseline occurs in ~100 % of survivors, whereas a return in EF to ≥ 50% occurs in ~60 % of patients who present with LV depression who survive sepsis. However, it should be emphasized that interpreting changes in LV function in the setting is not straightforward, given the use of positive pressure ventilation, inotropes, pressors and volume expansion, and the endogenous release of catecholamines, any or all of which can have an impact on the assessment of LV ejection.

Conclusion

In this review we have summarized the literature regarding recovery and normalization of LV function in patients with recent onset dilated cardiomyopathy. Given the differences in definitions and background therapies, and the heterogeneity of patient populations studied, it not possible to make definitive statements with respect to the natural history of the recovery of LV structure and function in this patient population. This statement notwithstanding, there are several observations and potential inferences that can be drawn from this review. First, as shown in the figure recovery of LV function appears to occur in all forms of recent onset dilated cardiomyopathy, ranging from 20-100% of patients. The greatest degree of recovery and/or normalization of LV function was observed in cardiomyopathies associated with abnormal energetics, whereas the cardiomyopathies associated with the least degree of recovery and/or normalization of LV function occurred with myocarditis and post-partum cardiomyopathy. Importantly, the percentage of patients with recovery of LV function is greater in more recent clinical studies than in older case series, suggesting the implementation of evidence-based therapies for heart failure has impacted the natural history of the disease.

Although the biological mechanisms that underlie recovery of LV function are not known, and were not the intended focus of this review, the observation that LV function recovery occurs in all forms of recent onset dilated cardiomyopathy suggests that LV recovery is a fundamentally conserved response of the heart following the resolution of cardiac injury. The role that local factors or stem cells play in this process have yet to be determined. Second, as shown in the Figure normalization of LV structure and function occurs far less frequently than does recovery LV function, suggesting that end organ changes may prevent normalization of LV structure and function in recent onset dilated cardiomyopathy. Indeed the dilated cardiomyopathies that are associated with the greatest discrepancy between recovery of LV function and normalization of LV function are also associated with the most end organ damage (e.g. myocarditis and post partum cardiomyopathy), whereas the dilated cardiomyopathies that are associated with a similar degree of LV functional recovery and normalization of LV function are associated with energetic deficits, which would be expected to be fully reversible (e.g. tachycardia induced cardiomyopathy). A second line of evidence that supports this point of view is that normalization of LV function occurs more often in patients with a shorter course of disease, who have less LV remodeling, less necrotic cell death and less fibrosis detected by cardiac MRI imaging.

In terms of clinical predictors of LV recovery, the aggregate data suggest that neither baseline ejection fraction nor hemodynamic status are good predictors of LV recovery and/or normalization of LV function. Indeed, stress cardiomyopathy and fulminant myocarditis (as described above) are dramatic examples of clinical scenarios wherein normalization of LV structure and function occur despite profound depression of LV function. There also appear to be differences in recovery of LV function in women and men, as well as white and black patients [44], with greater recovery of LV function and event free survival in women and whites. Whether outcomes by gender and race reflect a differential genomic response to tissue injury, or other socioeconomic variables, will require further analysis. It is likely that

broader application of cardiac MRI and novel biomarkers will allow for increased prediction of LV recovery, as has been reported in some patients with recent onset of dilated cardiomyopathy [31]. It bears emphasis that while recovery and/or normalization of LV function generally portend a good prognosis in most studies, contractile reserve and diastolic function can be abnormal in hearts with normalized LV function [41] and symptomatic heart failure can reoccur in up to 20% of patients who have normalization of LV function. Moreover, sudden cardiac death has been reported in some patients despite normalization of LV function [36]. While the extant literature does not allow the authors to comment on the importance (or lack thereof) of continuing medical therapy after normalization of LV function has occurred, the untoward outcomes of some patients after normalization of LV function would at least argue for long-term follow-up of these patients. Clinical studies to test the efficacy and safety of longer vs. shorter term therapy in this patient population are needed.

Acknowledgments

Douglas L. Mann is supported by research grants from the National Institutes of Health (NIH) (RO1 HL89543 and RO1 111094).

References

1. Dec GW, Fuster V. Medical Progress: Idiopathic dilated cardiomyopathy. N Engl J Med. 1994; 331:1564. [PubMed: 7969328]
2. Hellawell JL, Margulies KB. Myocardial Reverse Remodeling. Cardiovasc Ther. 2012; 20:172–181. [PubMed: 21108773]
3•. Mann DL, Barger PM, Burkhoff D. Myocardial recovery: myth, magic or molecular target? J Amer Coll Cardiol. 2012; 60:2465–2472. [PubMed: 23158527] [Recent article that addresses the biology of LV recovery and reverse remodeling and that introduces the concept that end organ damage prevents restoration of LV function.]
4. Dec GW Jr. Palacios IF, Fallon JT, Aretz HT, Mills J, Lee DC, Johnson RA. Active myocarditis in the spectrum of acute dilated cardiomyopathies. N Engl J Med. 1985; 312:885–890. [PubMed: 3974674]
5. Amos AM, Jaber WA, Russell SD. Improved outcomes in peripartum cardiomyopathy with contemporary. Am Heart J. 2006; 152:509–513. [PubMed: 16923422]
6. Duran N, Gunes H, Duran I, Biteker M, Ozkan M. Predictors of prognosis in patients with peripartum cardiomyopathy. Int J Gynaecol Obstet. 2008; 101:137–140. [PubMed: 18280479]
7. Okada M, Tanaka H, Matsumoto K, Ryo K, Kawai H, Hirata K. Subclinical myocardial dysfunction in patients with reverse-remodeled dilated cardiomyopathy. J Am Soc Echocardiogr. 2012; 25:726–732. [PubMed: 22537395]
8. Gopinathannair R, Sullivan R, Olshansky B. Tachycardia-mediated cardiomyopathy: recognition and management. Curr Heart Fail Rep. 2009; 6:257–264. [PubMed: 19948094]
9. Shinbane JS, Wood MA, Jensen DN, Ellenbogen KA, Fitzpatrick AP, Scheinman MM. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies. J Am Coll Cardiol. 1997; 29:709–715. [PubMed: 9091514]
10. Nerheim P, Birger-Botkin S, Piracha L, Olshansky B. Heart failure and sudden death in patients with tachycardia-induced cardiomyopathy and recurrent tachycardia. Circulation. 2004; 110:247–252. [PubMed: 15226218]
11. Khasnis A, Jongnarangsin K, Abela G, Veerareddy S, Reddy V, Thakur R. Tachycardia-induced cardiomyopathy: a review of literature. Pacing Clin Electrophysiol. 2005; 28:710–721. [PubMed: 16008809]
12. Dandamudi G, Rampurwala AY, Mahenthiran J, Miller JM, Das MK. Persistent left ventricular dilatation in tachycardia-induced cardiomyopathy patients after appropriate treatment and normalization of ejection fraction. Heart Rhythm. 2008; 5:1111–1114. [PubMed: 18675220]

13. Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. Eur Heart J. 2006; 27:1523–1529. [PubMed: 16720686]

14. Bybee KA, Prasad A. Stress-related cardiomyopathy syndromes. Circulation. 2008; 118:397–409. [PubMed: 18645066]

15. Sharkey SW, Windenburg DC, Lesser JR, Maron MS, Hauser RG, Lesser JN, Haas TS, Hodges JS, Maron BJ. Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. J Am Coll Cardiol. 2010; 55:333–341. [PubMed: 20117439]

16. Elesber AA, Prasad A, Lennon RJ, Wright RS, Lerman A, Rihal CS. Four-year recurrence rate and prognosis of the apical ballooning syndrome. J Am Coll Cardiol. 2007; 50:448–452. [PubMed: 17662398]

17. Booysen HL, Norton GR, Opie LH, Woodiwiss AJ. Reverse chamber remodelling following adrenergic-induced advanced cardiac dilatation and pump dysfunction. Basic Res Cardiol. 2012; 107:238. [PubMed: 22189564]

18. Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P, Carbone I, Muellerleile K, Aldrovandi A, Francone M, Desch S, Gutberlet M, Strohm O, Schuler G, Schulz-Menger J, Thiele H, Friedrich MG. Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. JAMA. 2011; 306:277–286. [PubMed: 21771988]

19. Siu CW, Yeung CY, Lau CP, Kung AW, Tse HF. Incidence, clinical characteristics and outcome of congestive heart failure as the initial presentation in patients with primary hyperthyroidism. Heart. 2007; 93:483–487. [PubMed: 17005710]

20. Poletto R, Janczak AM, Marchant-Forde RM, Marchant-Forde JN, Matthews DL, Dowell CA, Hogan DF, Freeman LJ, Lay DC Jr. Identification of low and high frequency ranges for heart rate variability and blood pressure variability analyses using pharmacological autonomic blockade with atropine and propranolol in swine. Physiol Behav. 2011; 103:188–196. [PubMed: 21281655]

21. Laonigro I, Correale M, Di BM, Altomare E. Alcohol abuse and heart failure. Eur J Heart Fail. 2009; 11:453–462. [PubMed: 19336433]

22. Urbano-Marquez A, Estruch R, Navarro-Lopez F, Grau JM, Mont L, Rubin E. The effects of alcoholism on skeletal and cardiac muscle. N Engl J Med. 1989; 320:409–415. [PubMed: 2913506]

23. Urbano-Marquez A, Estruch R, Fernandez-Sola J, Nicolas JM, Pare JC, Rubin E. The greater risk of alcoholic cardiomyopathy and myopathy in women compared with men. JAMA. 1995; 274:149–154. [PubMed: 7596003]

24. Lazarevic AM, Nakatani S, Neskovic AN, Marinkovic J, Yasumura Y, Stojicic D, Miyatake K, Bojic M, Popovic AD. Early changes in left ventricular function in chronic asymptomatic alcoholics: relation to the duration of heavy drinking. J Am Coll Cardiol. 2000; 35:1599–1606. [PubMed: 10807466]

25•. Cardinale D, Colombo A, Torrisi R, Sandri MT, Civelli M, Salvatici M, Lamantia G, Colombo N, Cortinovis S, Dessanai MA, Nole F, Veglia F, Cipolla CM. Trastuzumab-induced cardiotoxicity: clinical and prognostic implications of troponin I evaluation. J Clin Oncol. 2010; 28:3910–3916. [PubMed: 20679614] [A recent article that addresses LV recovery in patients who are receiving chemotherapy. This study shows that that patients who have elevated levels of troponin after trastuzumab are less likely to recover LV function than patients who do not have elevated troponin levels.]

26. Telli ML, Hunt SA, Carlson RW, Guardino AE. Trastuzumab-related cardiotoxicity: calling into question the concept of reversibility. J Clin Oncol. 2007; 25:3525–3533. [PubMed: 17687157]

27. Ewer MS, Vooletich MT, Durand JB, Woods ML, Davis JR, Valero V, Lenihan DJ. Reversibility of trastuzumab-related cardiotoxicity: new insights based on clinical course and response to medical treatment. J Clin Oncol. 2005; 23:7820–7826. [PubMed: 16258084]

28. Richardson P, McKenna W, Bristow M, Maisch B, Mautner B, O'Connell J, Olsen E, Thiene G, Goodwin J, Gyarfas I, Martin I, Nordet P. Report of the 1995 world health organization/ international society and federation of cardiology task force on the definition and classification of cardiomyopathies. Circulation. 199693:841–842.

29. Kindermann I, Barth C, Mahfoud F, Ukena C, Lenski M, Yilmaz A, Klingel K, Kandolf R, Sechtem U, Cooper LT, Bohm M. Update on myocarditis. J Am Coll Cardiol. 2012; 59:779–792. [PubMed: 22361396]
30. McNamara DM, Holubkov R, Starling RC, Dec GW, Loh E, Torre-Amione G, Gass A, Janosko K, Tokarczyk T, Kessler P, Mann DL, Feldman AM. Controlled trial of intravenous immune globulin in recent-onset dilated cardiomyopathy. Circulation. 2001; 103:2254–2259. [PubMed: 11342473]
31••. Kubanek M, Sramko M, Maluskova J, Kautznerova D, Weichet J, Lupinek P, Vrbska J, Malek I, Kautzner J. Novel predictors of left ventricular reverse remodeling in individuals with recent-onset dilated cardiomyopathy. J Am Coll Cardiol. 2013; 61:54–63. [PubMed: 23287372] [Carefully done study that examines longitudinal assessment of LV function in patients with recent onset dilated cardiomyopathy. This study also examined the utility of cardiac MRI and biomarkers for predicting LV recovery in a subset of patients.]
32. Steimle AE, Stevenson LW, Fonarow GC, Hamilton MA, Moriguchi JD. Prediction of improvement in recent onset cardiomyopathy after referral for heart transplantation. J Am Coll Cardiol. 1994; 23:553–559. [PubMed: 8113533]
33. Mason JW, O'Connell JB, Herskowitz A, Rose NR, McManus BM, Billingham ME, Moon TE. A clinical trial of immunosuppressive therapy for myocarditis. The Myocarditis Treatment Trial Investigators. N Engl J Med. 1995; 333:269–275. [PubMed: 7596370]
34. McCarthy RE III, Boehmer JP, Hruban RH, Hutchins GM, Kasper EK, Hare JM, Baughman KL. Long-term outcome of fulminant myocarditis as compared with acute (nonfulminant) myocarditis. N Engl J Med. 2000; 342:690–695. [PubMed: 10706898]
35. Abboud J, Murad Y, Chen-Scarabelli C, Saravolatz L, Scarabelli TM. Peripartum cardiomyopathy: a comprehensive review. Int J Cardiol. 2007; 118:295–303. [PubMed: 17208320]
36. Sliwa K, Forster O, Tibazarwa K, Libhaber E, Becker A, Yip A, Hilfiker-Kleiner D. Long-term outcome of peripartum cardiomyopathy in a population with high seropositivity for human immunodeficiency virus. Int J Cardiol. 2011; 147:202–208. [PubMed: 19751951]
37. Cooper LT, Mather PJ, Alexis JD, Pauly DF, Torre-Amione G, Wittstein IS, Dec GW, Zucker M, Narula J, Kip K, McNamara DM. Myocardial recovery in peripartum cardiomyopathy: prospective comparison with recent onset cardiomyopathy in men and nonperipartum women. J Card Fail. 2012; 18:28–33. [PubMed: 22196838]
38. Chapa JB, Heiberger HB, Weinert L, Decara J, Lang RM, Hibbard JU. Prognostic value of echocardiography in peripartum cardiomyopathy. Obstet Gynecol. 2005; 105:1303–1308. [PubMed: 15932821]
39. O'Connell JB, Costanzo-Nordin MR, Subramanian R, Robinson JA, Wallis DE, Scanlon PJ, Gunnar RM. Peripartum cardiomyopathy: clinical, hemodynamic, histologic and prognostic characteristics. J Am Coll Cardiol. 1986; 8:52–56. [PubMed: 3711532]
40. Elkayam U, Tummala PP, Rao K, Akhter MW, Karaalp IS, Wani OR, Hameed A, Gviazda I, Shotan A. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. N Engl J Med. 2001; 344:1567–1571. [PubMed: 11372007]
41. Lampert MB, Weinert L, Hibbard J, Korcarz C, Lindheimer M, Lang RM. Contractile reserve in patients with peripartum cardiomyopathy and recovered left ventricular function. Am J Obstet Gynecol. 1997; 176:189–195. [PubMed: 9024112]
42. Jardin F, Brun-Ney D, Auvert B, Beauchet A, Bourdarias JP. Sepsis-related cardiogenic shock. Crit Care Med. 1990; 18:1055–1060. [PubMed: 2209030]
43. Parker MM, Shelhamer JH, Bacharach SL, Green MV, Natanson C, Frederick TM, Damske BA, Parrillo JE. Profound but reversible myocardial depression in patients with septic shock. Ann Intern Med. 1984; 100:483–490. [PubMed: 6703540]
44. McNamara DM, Starling RC, Cooper LT, Boehmer JP, Mather PJ, Janosko KM, Gorcsan J III, Kip KE, Dec GW. Clinical and Demographic Predictors of Outcomes in Recent Onset Dilated Cardiomyopathy Results of the IMAC (Intervention in Myocarditis and Acute Cardiomyopathy)-2 Study. J Am Coll Cardiol. 2011; 58:1112–1118. [PubMed: 21884947]
45. Donghua Z, Jian P, Zhongbo X, Feifei Z, Xinhui P, Hao Y, Fuqiang L, Yan L, Yong X, Xinfu H, Surong M, Muli W, Dingli X. Reversal of cardiomyopathy in patients with congestive heart failure secondary to tachycardia. J Interv Card Electrophysiol. 2013; 36:27–32. [PubMed: 23090777]

46. Medi C, Kalman JM, Haqqani H, Vohra JK, Morton JB, Sparks PB, Kistler PM. Tachycardia-mediated cardiomyopathy secondary to focal atrial tachycardia: long-term outcome after catheter ablation. J Am Coll Cardiol. 2009; 53:1791–1797. [PubMed: 19422986]
47. Parodi G, Bellandi B, Del PS, Barchielli A, Zampini L, Velluzzi S, Carrabba N, Gensini GF, Antoniucci D. Natural history of tako-tsubo cardiomyopathy. Chest. 2011; 139:887–892. [PubMed: 20884730]
48. Looi JL, Wong CW, Khan A, Webster M, Kerr AJ. Clinical characteristics and outcome of apical ballooning syndrome in Auckland, New Zealand. Heart Lung Circ. 2012; 21:143–149. [PubMed: 22237138]
49. Samardhi H, Raffel OC, Savage M, Sirisena T, Bett N, Pincus M, Small A, Walters DL. Takotsubo cardiomyopathy: an Australian single centre experience with medium term follow up. Intern Med J. 2012; 42:35–42. [PubMed: 21395961]
50. Umpierrez GE, Challapalli S, Patterson C. Congestive heart failure due to reversible cardiomyopathy in patients with hyperthyroidism. Am J Med Sci. 1995; 310:99–102. [PubMed: 7668312]
51. Riaz K, Forker AD, Isley WL, Hamburg MS, McCullough PA. Hyperthyroidism: a “curable” cause of congestive heart failure--three case reports and a review of the literature. Congest Heart Fail. 2003; 9:40–46. [PubMed: 12556677]
52. Nicolas JM, Fernandez-Sola J, Estruch R, Pare JC, Sacanella E, Urbano-Marquez A, Rubin E. The effect of controlled drinking in alcoholic cardiomyopathy. Ann Intern Med. 2002; 136:192–200. [PubMed: 11827495]
53. Gavazzi A, De MR, Parolini M, Porcu M. Alcohol abuse and dilated cardiomyopathy in men. Am J Cardiol. 2000; 85:1114–1118. [PubMed: 10781762]
54. La Vecchia LL, Bedogni F, Bozzola L, Bevilacqua P, Ometto R, Vincenzi M. Prediction of recovery after abstinence in alcoholic cardiomyopathy: role of hemodynamic and morphometric parameters. Clin Cardiol. 1996; 19:45–50. [PubMed: 8903537]
55. Suter TM, Procter M, van Veldhuisen DJ, Muscholl M, Bergh J, Carlomagno C, Perren T, Passalacqua R, Bighin C, Klijn JG, Ageev FT, Hitre E, Groetz J, Iwata H, Knap M, Gnant M, Muehlbauer S, Spence A, Gelber RD, Piccart-Gebhart MJ. Trastuzumab-associated cardiac adverse effects in the herceptin adjuvant trial. J Clin Oncol. 2007; 25:3859–3865. [PubMed: 17646669]
56. Romond EH, Jeong JH, Rastogi P, Swain SM, Geyer CE Jr. Ewer MS, Rathi V, Fehrenbacher L, Brufsky A, Azar CA, Flynn PJ, Zapas JL, Polikoff J, Gross HM, Biggs DD, Atkins JN, Tan-Chiu E, Zheng P, Yothers G, Mamounas EP, Wolmark N. Seven-year follow-up assessment of cardiac function in NSABP B-31, a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel (ACP) with ACP plus trastuzumab as adjuvant therapy for patients with node-positive, human epidermal growth factor receptor 2-positive breast cancer. J Clin Oncol. 2012; 30:3792–3799. [PubMed: 22987084]
57. Farolfi A, Melegari E, Aquilina M, Scarpi E, Ibrahim T, Maltoni R, Sarti S, Cecconetto L, Pietri E, Ferrario C, Fedeli A, Faedi M, Nanni O, Frassineti GL, Amadori D, Rocca A. Trastuzumab-induced cardiotoxicity in early breast cancer patients: a retrospective study of possible risk and protective factors. Heart. 2013; 99:634–639. [PubMed: 23349345]
58. Demakis JG, Rahimtoola SH, Sutton GC, Meadows WR, Szanto PB, Tobin JR, Gunnar RM. Natural course of peripartum cardiomyopathy. Circulation. 1971; 44:1053–1061. [PubMed: 4256828]
59. Horgan SJ, Margey R, Brennan DJ, O'Herlihy C, Mahon NG. Natural history, management, and outcomes of peripartum cardiomyopathy: an Irish single-center cohort study. J Matern Fetal Neonatal Med. 2013; 26:161–165. [PubMed: 22978474]
60. Hu CL, Li YB, Zou YG, Zhang JM, Chen JB, Liu J, Tang YH, Tang QZ, Huang CX. Troponin T measurement can predict persistent left ventricular dysfunction in peripartum cardiomyopathy. Heart. 2007; 93:488–490. [PubMed: 17065185]
61. Fett JD, Sannon H, Thelisma E, Sprunger T, Suresh V. Recovery from severe heart failure following peripartum cardiomyopathy. Int J Gynaecol Obstet. 2009; 104:125–127. [PubMed: 19036370]

62. Sliwa K, Skudicky D, Bergemann A, Candy G, Puren A, Sareli P. Peripartum cardiomyopathy: analysis of clinical outcome, left ventricular function, plasma levels of cytokines and Fas/APO-1. J Am Coll Cardiol. 2000; 35:701–705. [PubMed: 10716473]

63. Sliwa K, Forster O, Libhaber E, Fett JD, Sundstrom JB, Hilfiker-Kleiner D, Ansari AA. Peripartum cardiomyopathy: inflammatory markers as predictors of outcome in 100 prospectively studied patients. Eur Heart J. 2006; 27:441–446. [PubMed: 16143707]

64. Blauwet LA, Libhaber E, Forster O, Tibazarwa K, Mebazaa A, Hilfiker-Kleiner D, Sliwa K. Predictors of outcome in 176 South African patients with peripartum cardiomyopathy. Heart. 2013; 99:308–313. [PubMed: 23118348]

65. Modi KA, Illum S, Jariatul K, Caldito G, Reddy PC. Poor outcome of indigent patients with peripartum cardiomyopathy in the United States. Am J Obstet Gynecol. 2009; 201:171–175. [PubMed: 19564021]

66. Chau EM, Chow WH, Chiu CS, Wang E. Treatment and outcome of biopsy-proven fulminant myocarditis in adults. Int J Cardiol. 2006; 110:405–406. [PubMed: 16297469]

67. Horwich TB, Patel J, MacLellan WR, Fonarow GC. Cardiac troponin I is associated with impaired hemodynamics, progressive left ventricular dysfunction, and increased mortality rates in advanced heart failure. Circulation. 2003; 108:833–838. [PubMed: 12912820]

68. Goland S, Czer LS, Siegel RJ, Tabak S, Jordan S, Luthringer D, Mirocha J, Coleman B, Kass RM, Trento A. Intravenous immunoglobulin treatment for acute fulminant inflammatory cardiomyopathy: series of six patients and review of literature. Can J Cardiol. 2008; 24:571–574. [PubMed: 18612500]

69. Preeta R, Nair RR. Stimulation of cardiac fibroblast proliferation by cerium: a superoxide anion-mediated response. J Mol Cell Cardiol. 1999; 31:1573–1580. [PubMed: 10423354]

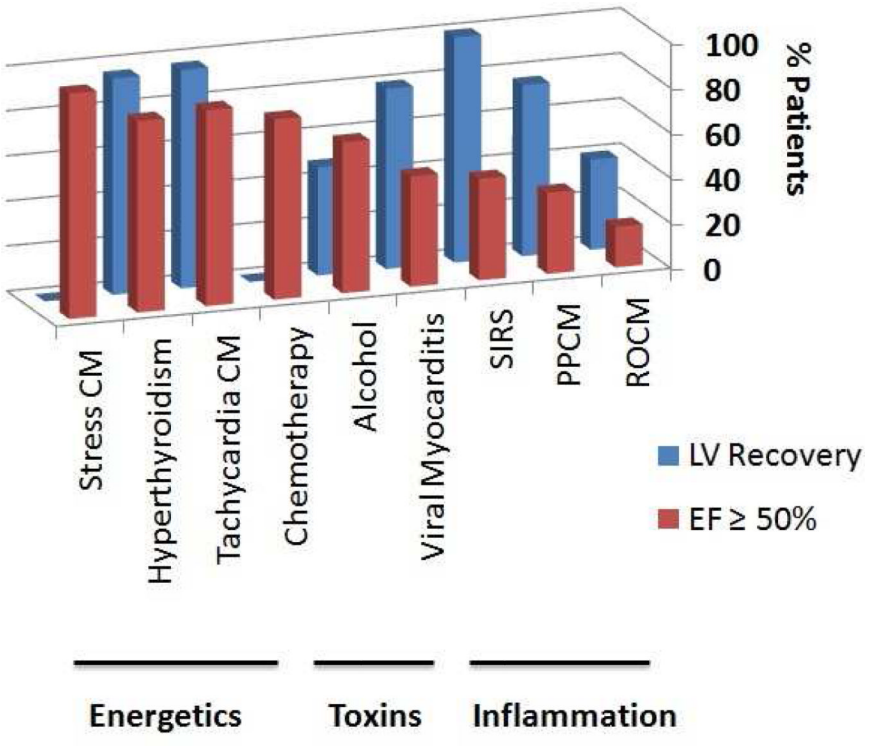

Figure.

Recovery and normalization LV function in clinical settings. Recovery of LV function, defined as an improvement in LF ejection fraction from 5 – 15% occurs in all forms of dilated cardiomyopathy reviewed. Recovery of LV function was greater for energetic defects > toxins > inflammatory etiologies. Note that data on recovery of LV function were not available in the literature for stress cardiomyopathy (CM) and chemotherapy (and hence are shown as zero). Normalization of LV function, defined as an EF ≥ 50%, occured in all forms of cardiomyopathy that were reviewed. Normalization of LV function paralleled recovery of LV function and was greater for energetic defects > toxins > inflammatory etiologies. As shown in normalization of LV structure function occurs far less frequently than does recovery LV function. (The data for this figure were obtained by averaging the data from tables 1 and 2) (Key: CM = cardiomyopathy; PPCM = post-partum cardiomyopathy; ROCM = recent onset cardiomyopathy; SIRS = systemic inflammatory response syndrome)

Table 1

Abnormal Energetics and Toxins in Left Ventricular Recovery

	Disease	N (age)	Follow-up	Baseline EF	Follow-up EF	↑ EF > 10%	EF > 50%	Meds
Nerheim [10]	TIC	24 (46)	6 m	26 ± 9	52 ± 5	100%	79%	B,C,D,AA RFA
Dandamudi [12]	TIC	24 (64)	14 m	31 ± 8	55 ± 6	92%	83%	AA RFA
Donghua [45]	TIC	17 (36)	3 m	37 ± 8	60 ± 10	94%	88%	RFA
Medi [46]	TIC	30 (39)	3 m	35 ± 11	59 ± 3	100%	97%	AA RFA
Sharkey [15]	SC	136 (68)	2-3 m	32 ± 11	59 ± 7		96%	
Parodi [47]	SC	116 (73)	8 d	36 ± 9			99%	A,B,C
Looi [48]	SC	100 (65)	43 d	Normal -21% Mild 26% Moderate 38% Severe 15%	NS	NS	68%	A,B,C
Sarmardhi [49]	SC	52 (64)	3 m	47 (20-70)	63 (44-76)	NS	100% *	A,B
Eitel [18]	SC	256 (69)	3 m	48 ± 11	68 ± 6		100%	A,B
Umpierrez [50]	HT	7 (47)	6-12 m	28 ± 2	55 ± 5	100%	71%	A,B,D,ATT
Riaz [51]	HT	3 (41)	1w-6 m	21 ± 3	47 ± 9	100%	67%	A,D,ATT
Siu [19]	HT	16 (58) **	3 m	29 ± 2	55 ± 4	88%	63%	A,B, D,ATT
Nicolas [52]	AC	55 (48)	1 y	39 ± 11	Abstinent: 53 ± 7 Moderate *: 50 ± 10 Heavy **: 40 ± 11	NS	Abstinent - 82% Moderate * - 47% Heavy ** - 22%	A,D
Gavazzi [53]	AC	79 (45)	3 y	28 ± 9	Abstinent: 36 ± 11 Continued: 32 ± 9	NS	NS	A,B,AA
La Vecchia [54]	AC	19 (52)		29 ± 10	Abstinent - 54 ± 10	48%	Abstinent - 67%	A,D,AA
Ewer [27]	TRC	38 (52)	1.5 m	43 ± 16	55 ± 11	NS	79%	A,B
Suter [55]	TRC	61 (49)	4-6 m	NS	NS	NS	Severe HF and LVD - 60% † Symptomatic HF and LVD - 67% † Asymptomatic LVD - 69% †	NS
Romond [56]	TRC	106 (?NS)	> 6 m	NS	NS	NS	HF and LVD - 57% Asymptomatic LVD - 78%	NS

	Disease	N (age)	Follow-up	Baseline EF	Follow-up EF	↑ EF > 10%	EF > 50%	Meds
Farolfi [57]	TRC	78 (54)	1-3 m	NS	NS	NS	83%††	NS
Cardinale [25]	TRC	42 (52)	12 m	44 ± 6	NS	NS	60%	A,B

Key: AC = alcoholic cardiomyopathy; A = ACE inhibitor/ARB; AA = anti-arrhythmic; ATT = anti-thyroid therapy; B = beta-blocker; C = calcium blocker; D = digoxin; HF = heart failure; HT = hyperthyoidism; LVD = left ventricular dysfunction; NS = not specfied; RFA = radiofrequency ablation; RAI = radioactive iodine; SC = stress cardiomyopathy; TIC = tachycardia-induced cardiomyopathy; TRC = trastuzumab-related cardiotoxicity.

*1-4 standard drinks daily

**>4 standard drinks daily

†LVEF ≥55%

††Absolute EF increase ≥10% EF >50% or resolution of symptoms

*N = 10 patients with baseline and follow-up MRI

**represents 2.6% of 618 patients with hyperthyroidism

Table 2

Inflammation and Left Ventricular Recovery

	Disease	n/(age)	Follow-up	Baseline EF	Follow-up EF	↑ EF > 5-15%	EF > 50%	Meds
Demakis [58]	PPCM	27	6 m	N/A	N/A	(52%*)	N/A	D
Horgan [59]	PPCM	12/35(28-41)	6 m	27 ± 8	47 ± 13	90%	50 %	A,B, H/N
O'Connell [39]	PPCM	14/28±5.7	6m	23 ± 12 [S] 11 ± 2 [NS]	NS	100%	NS	Bedrest
Amos [5]	PPCM	55/29±6	12 m	20.5	41 ±14	62%	45%	A,B
Duran [6]	PPCM	33/32 ± 7	48 m	27 ± 6	24.5 ± 4.3 [A 34.5 ± 3.5 [B]	NS	NS	A,B
Hu [60]	PPCM	106/28±6.5	6 m	27 ± 6	45 ± 13	NS	52%	A,B
Elkayam [40]	PPCM	92/29 ±6	27 m	32 ± 11	49 ± 12	NS	NS	unknown
Cooper (IMAC2) [37]	PPCM	39/30 ± 7	6m	27 ± 7	45 ± 14	NS	48 %	A,B, S
Fett [61]	PPCM	116/32 (17-50)	35 m	23 (15-35) [A] 28 (15-40) [B]	NS NS	NS	28%	A (±B)
Sliwa [62]	PPCM	29/29 ± 7	6 m	27 ± 10	43 ± 16	59 %	23 %	A,B
Sliwa [63]	PPCM	100/32 ± 7	6 m	26 ± 8 [S] 22 ±6 [NS]	43 ± 14 [S]	NS	23 %	A,B
Sliwa [36]	PPCM	80/30 ± 7 [all] 53/30 ± 7 [HIV−] 27/32 ± 8 [HIV+]	24 m	30 ± 9 [all] 30 ± 9 [HIV−] 30 ± 8 [HIV+]	50 ± 14 [all] 50 ± 15 [HIV−] 50 ± 14 [HIV+]	NS	NS	A,B
Blauwet [64]	PPCM	176/30.7±6.0	6 m	27 ± 8 [S]	43 ± 12	NS	21%††	A (±B)
Modi [65]	PPCM	44/25 ± 7	9 m	21.1 (15-30) [A] 28.6 (15-42) [B]	36.15 (20-50) 34.4 (10-64)	NS	35%	A,B
Myocarditis Treatment Trial [33]	VCM	111/42 ± 14	28,52w	0.25 ± 0.01	0.34 ± 0.02	100%	0 %	I
Chau [66]	VCM	8(NS)	2-3w	NS	NS	NS	88%	MCS
Bossone [67]	VCM	6 (32±11) [A] 9 (45±14) [B]		26.4± 12.9 39.5± 9.0	34.4±14.3 61.5±8.8	~ 40%	40%	D,A
Goland [68]	VCM	6/44 ± 12	13.2m	21.7 ± 7.5	53 ± 6	100%	67%	IVIG
Dec [4]	ROCM	27 (42 ±3)	18 m	22 ±0.08	31 ± 0.01%	26%	13%	I
Steimle [32]	ROCM	49	8 m	0.22 ± 0.08	0.49 ± 0.09	27%	8%	D,A,H
Kubanek [31]	ROCM**	44 (43 ± 11)	3,6,12 m	24 ± 8 22 ± 6	26 ± 6 42 ± 6	20 %	7%	A,B, S

Curr Heart Fail Rep. Author manuscript; available in PMC 2014 December 01.

	Disease	n/(age)	Follow-up	Baseline EF	Follow-up EF	↑ EF > 5-15%	EF > 50%	Meds
IMAC1 [69]	ROCM	62 (43 ±12)	12 m	25± 0.08	0.42±0.14	56%	36%	A,B,IVIG
IMAC2 [44]	ROCM	373 (45±14)	6 m	24 ± 0.8	40 ± 12	70 %	25%	A,B, S
Parker [43]	SIRS	43.6 (9-45)	7-10 d	40 ± 0.04 [all] 0.55 ± 0.03[NS] 0.32 ± 0.04 [S]	55 ± 0.05 [all] ~ 63 ± 0.05 [NS] 55 ±0.05 [S]	NS	~ 45% [all] 30% [NS] 60 % [S]	P,F
Jardin [42]	SIRS	21† (51 ±17)	3 d	21 ±8	59 ±9	100%	NS	P,F

Key: PPCM = post-partum cardiomyopathy; H/N = hydralzine and isosorbide; I = immunosuppression; ROCM = recent onset cardiomyopathy; SIRS = systemic inflammatory response syndrome; VCM = viral cardiomyopathy; P = pressors, F = fluids, NS = non-survivor, S = survivor [A] – non-recover [B] recover

*resolution of cardiomegaly on CXR

†This is 6 patients with LV dysfunction

††Used EF of > 55% for LV recovery