Myocarditis – in the spotlight as a result of the pandemic



The COVID-19 pandemic has brought myocarditis back into focus. The incidence of myocarditis before COVID-19 was reported to be between 1 and 10 cases/100,000 persons, and with COVID-19 between 150 and 4000 cases/100,000 persons. These data suggest an approximately 15-fold increased risk of developing myocarditis from SARS-CoV-2 infection compared with other causes. The reported incidence of myocarditis following COVID-19 vaccination varies widely depending on the type of vaccine and the number of doses administered. The highest incidence has been reported with an overall incidence of 10/100,000 (for Moderna mRNA vaccine).1

Therefore, and to identify new diagnostic developments and new therapeutic approaches, we have carried out a revision of the MIRA Myocarditis page. The scope of this revision was to include latest scientific evidence on morbidity and mortality.

Risk assessment approach

Myocarditis may present with a wide range of symptoms, ranging from mild dyspnea or chest pain that resolves without specific therapy to cardiogenic shock and death. Dilated cardiomyopathy with chronic heart failure is the major long-term sequela of myocarditis.

The prognosis depends on whether the myocarditis is a single episode, recurrent or even chronic. It also depends on the presence and severity of complications (including heart enlargement, heart failure and arrhythmias).

For risk assessment we should address the following questions:

- The first and most important question in myocarditis is if myocarditis is present, if it has turned into a chronic form or if it is in history.
- Postponement is recommended if myocarditis is present, as the prognosis is very difficult to assess while the disease is ongoing.
- Chronic myocarditis is defined as an ongoing inflammatory process with fibrosis and manifest with persistent cardiac dysfunction. Chronic myocarditis represents an intermediate stage between acute myocarditis and chronic inflammatory cardiomyopathy in patients with persisting myocardial inflammation. Since a large number of chronic myocarditis cases develop into end-stage cardiomyopathy, it is recommended to decline these cases.
- In the case of **myocarditis in history**, there a two features that are prognostically relevant (see step 2 and 3):

2. Was it a single episode of myocarditis or was it recurrent?

Recurrence of acute myocarditis is rare, with 1.1% of patients diagnosed with acute myocarditis reporting a history of previous myocarditis.² Recurrent myocarditis is usually associated with a significantly worse prognosis than a single episode – indeed, more than a third of recurrent myocarditis is associated with the latter diagnosis of an arrhythmogenic cardiomyopathy.³

3. Are or where there any complications of the myocarditis?

Patients presenting with complicated acute myocarditis are at increased risk for adverse cardiac events compared with patients without these risk factors.² The course of the myocarditis is complicated when there is heart enlargement (cardiomegaly), heart failure, pulmonary oedema or serious arrhythmias during the acute phase or afterwards.

New life ratings based on the latest evidence

For a long time, it was assumed that after myocarditis had been cured without complications, it would no longer be prognostically relevant in the long term. The prognosis for patients with apparently uncomplicated myocarditis was generally considered to be good, but data on long-term outcomes have been sparse. Now, however, there are new data that clearly cast doubt on this.

A recently published retrospective cohort study⁴ concluded that in patients admitted to hospital with a clinical suspicion of acute myocarditis, the excess mortality rate remains high for at least 10 years after the index hospitalisation.

Munich Re Myocarditis – in the spotlig

Myocarditis – in the spotlight as a result of the pandemic

Another study of even greater interest to insurers is a nation-wide Danish registry study,⁵ which included patients discharged alive with a first diagnosis of myocarditis and no previous heart disease. All-cause mortality was more than doubled (Hazard ration (HR) 2.10) in myocarditis patients compared with matched controls from the general population during a mean follow-up of 8.5 years. Even in patients who were free of events or heart failure medication one year after diagnosis, overall mortality remained increased (HR 1.62). (see Figure 1)



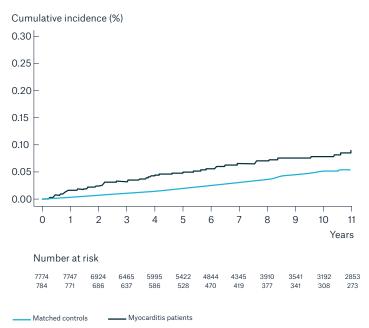


Figure 1: All-cause mortality among patients with myocarditis without events and HF medication in the first year post-discharge⁵

Based on this, we have increased the time periods and adjusted the rates for myocarditis with complications. By taking the latest medical evidence into account we were able to calculate up-to-date precise and risk adequate loadings, reflecting the newest prognostic criteria. Interestingly, resolved myocarditis that has led to hospitalisation is associated with a worse prognosis than previously thought. This new evidence is reflected in the latest clinical guidelines, which now recommend lifelong follow-up in these cases.

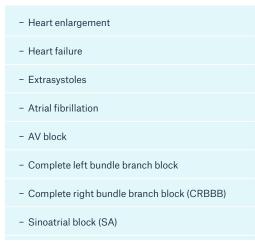
The rates for uncomplicated myocarditis remain unchanged, with a short postponement period and standard rates thereafter. This short postponement period appears to be entirely appropriate, as this is the period recommended for healing and complete resolution of uncomplicated myocarditis from a medical point of view, including international guidelines.

In addition, the extent to which the individual complications are present is very relevant for estimating the risk. For exam-

ple, there are very different types of extrasystoles, which also have different prognostic relevance. For this reason, the following complications and sequalae should be rated on top of the myocarditis ratings:

Disability and Critical illness

When we look at critical illness products, we have to consider two main triggers - cardiac arrest and cardiomyopathy - in the context of or as a result of myocarditis, which could lead to a benefit issue.



Dilated cardiomyopathy (DCM) is a relevant sequelae that can develop on the basis of a previous myocarditis. Up to 20% of myocarditis patients may subsequently develop a chronic inflammatory dilated cardiomyopathy. At present, the reason why some patients recover without residual myocardial injury whereas others develop dilated cardiomyopathy is unclear. Patients with single-episode and uncomplicated acute myocarditis have benign short- and long-term outcomes.2 The presence of recurrent myocarditis, as well as complications such as heart enlargement or reduced left ventricular ejection fraction, is associated with a significantly increased risk of developing cardiomyopathy. Since it can take months to several years after an acute myocarditis to manifest cardiomyopathy, we recommend extending the safety period for postponing CI products with an in depth look on possible complications afterwards.

This raises the question of whether disability products should be treated with the same caution. The development of heart failure from myocarditis is a gradual process. While heart failure can be clearly diagnosed after a few years, disability does not yet occur. It is much later, if at all, that everyday life and the ability to work become impaired, and thus, potentially, leads to disability. This risk is covered by our loadings.

Myocarditis – in the spotlight as a result of the pandemic

Further considerations:

- The need for hospital treatment for myocarditis is associated with a worse prognosis (e.g. supportive care for heart failure, pulmonary oedema, pulmonary congestion, left bundle branch block or severe arrhythmia). For risk assessment, it would be helpful to ask whether someone was hospitalised or not. More specifically, there would have to be a distinction between whether someone was in hospital for treatment or whether it was a hospital stay for purely diagnostic purposes. As this information is not always available in day-to-day underwriting practice, it is advisable to ask about complications, as these are the reasons for hospitalisation and treatment.
- Given the high incidence of myocarditis in COVID-19, the question arises as to whether myocarditis caused by COVID-19 needs to be treated separately: COVID-19 myocarditis can be considered and treated as any other viral myocarditis. And compared with conventional myocarditis (including COVID-19 myocarditis), myocarditis following vaccination with SARS-CoV-2 mRNA vaccines was associated with better clinical outcomes.⁶

Our experts

Dr. Christiane Suchy Medical Consultant Medical Research and Development Tel.: +49 89 38 91-29 09 csuchy@munichre.com



Priv.-Doz. Dr. Mathias Orban Medical Consultant Medical Research and Development Tel.: +49 89 38 91-20 65 morban@munichre.com



Dr. Alban Senn Chief Medical Officer Medical Research and Development Tel.: +49 89 38 91-93 27 asenn@munichre.com



References

- 1 Fairweather D, Beetler DJ, Di Florio DN, Musigk N, Heidecker B, Cooper LT Jr. COVID-19, Myocarditis and Pericarditis. Circ Res. 2023 May 12;132(10):1302-1319.
- 2 Ammirati E, Cipriani M, Moro C. et al. Clinical presentation and outcome in a contemporary cohort of patients with acute myocarditis multicenter Lombardy registry. Circulation 2018;138:1088–99
- 3 Ollitrault P, Al Khoury M, Troadec Y, Calcagno Y, Champ-Rigot L, Ferchaud V, Pellissier A, Legallois D, Milliez P, Labombarda F. Recurrent acute myocarditis: An under-recognized clinical entity associated with the later diagnosis of a genetic arrhythmogenic cardiomyopathy. Front Cardiovasc Med. 2022 Oct 28:9:998883.
- 4 Kim MJ, Jung HO, Kim H, Bae Y, Lee SY, Jeon DS. 10-year survival outcome after clinically suspected acute myocarditis in adults: A nationwide study in the pre-COVID-19 era. PLoS One. 2023 Jan 31;18(1):e0281296
- 5 Ghanizada M, Kristensen SL, Bundgaard H, Rossing K, Sigvardt F, Madelaire C, Gislason GH, Schou M, Hansen ML, Gustafsson F. Long-term prognosis following hospitalization for acute myocarditis a matched nationwide cohort study. Scand Cardiovasc J. 2021 Oct;55(5):264-269.
- 6 Husby A et al. Clinical outcomes of myocarditis after SARS-CoV-2 mRNA vaccination in four Nordic countries: population based cohort study. BMJ Medicine 2023.

© 2023

Münchener Rückversicherungs-Gesellschaft Königinstrasse 107, 80802 München, Germany

Picture credits: Scanderbeg Sauer Photography

Münchener Rückversicherungs-Gesellschaft (Munich Reinsurance Company) is a reinsurance company organised under the laws of Germany. In some countries, including in the United States, Munich Reinsurance Company holds the status of an unauthorised reinsurer. Policies are underwritten by Munich Reinsurance Company or its affiliated insurance and reinsurance subsidiaries. Certain coverages are not available in all jurisdictions.

Any description in this document is for general information purposes only and does not constitute an offer to sell or a solicitation of an offer to buy any product.