Scientific Research Publishing

Journal of Biosciences and Medicines, 2022, 10, 90-102
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Effects of Parasitic Diseases on the Cardiovascular System

Tao Zhang[1,2*], Jun Jiang[3*], Jianfa Liu[1*]

[1]Department of Parasitology, Ningbo University School of Medicine, Ningbo, China
[2]Department of Cardiology, Fenghua People's Hospital, Ningbo, China
[3]Department of Infectious Disease, School of Medicine, The Affiliated Hospital of Ningbo University, Ningbo, China
Email: *186001858@nbu.edu.cn, *liujianfa@nbu.edu.cn, *jjningbo2005@aliyun.com

How to cite this paper: Zhang, T., Jiang, J. and Liu, J.F. (2022) Effects of Parasitic Diseases on the Cardiovascular System. *Journal of Biosciences and Medicines*, **10**, 90-102.
https://doi.org/10.4236/jbm.2022.106008

Received: May 12, 2022
Accepted: June 14, 2022
Published: June 17, 2022

Abstract

The parasitic disease can significantly affect the cardiovascular system through various mechanisms; even though it is traditionally regarded as a disease characterized by parasitic sites' mechanical damage and some immune responses. Recent studies have shown that the role of parasitic factors in the cause of death due to cardiovascular events cannot be ignored. Considering the worldwide prevalence of parasitic diseases, exploring the effects of parasitic diseases on the cardiovascular system becomes increasingly essential. Here we summarize the latest understanding of common parasitic infections, explore the possible mechanisms of cardiovascular responses to parasitic infections, and propose feasible strategies for preventing and treating parasite-induced cardiac reactions.

Keywords

Parasite, Parasitic Diseases, Chagas Cardiomyopathy, Cardiovascular System

1. Introduction

Parasitic diseases account for the great burden of morbidity and mortality in extensive areas of the world, especially in developing countries. It is of significant note that their effects on the cardiovascular system cannot be ignored. In the tropical area, the cardiac complications of malaria incidence are between 17% and 26% [1] [2]. Due to the growing worldwide population movement and the increasing number of HIV infections and organ transplants, which produce many people with immunosuppression, parasite infection, and its cardiac manifestations, it may currently occur anywhere [3] [4]. Thus, clinicians must pay attention to the potential mechanisms of the various cardiac manifestations

caused by parasitic invading, such as cardiomyopathy, pericarditis, pericardial effusion, myocarditis, acute coronary syndrome, or space-occupying lesions. In addition to directly causing impairment of the myocardium and pericardium, parasitic damage to other systems can also cause cardiovascular responses. For example, pulmonary arterial hypertension, which may develop in schistosome infections, is associated with cardiac dysfunction tightly [5] [6] [7] [8]. Therefore, reviewing the possible mechanisms and coping strategies of parasitic diseases in the cardiovascular system is indispensable.

2. Overview of Common Parasitic Diseases

2.1. Malaria

Despite significant progress in combating malaria, it remains the world's deadliest parasitic disease. The disease is caused by the protozoan plasmodium, which infects a human host with a female Anopheles mosquito bite [9]. In the exo-erythrocytic cycle, sporophores multiply into merozoites, which enter the circulation and then mature to the schizont stage, bursting red blood cells [9]. Direct destruction of red blood cells by plasmodium and autoimmunity is the cause of anemia and splenomegaly [10]. Clinically, severe malaria is characterized by several common symptoms: severe anemia, cerebral malaria, and acute respiratory distress syndrome [10].

2.2. Schistosomiasis

Schistosomiasis is widespread worldwide and infects at least 250 million people [11]. Granuloma and fibrosis caused by egg deposition can lead to blockage or structural destruction of blood vessels, especially in the portal vein [12]. The eggs of Schistosoma aegypti are associated with bladder squamous carcinoma, and their deposit in the reproductive system can cause genital inflammation, bleeding, and HIV infection [12] [13]. The clinical manifestations of schistosomiasis occurring in the genitourinary system are frequent urination, painful urination and hematuria, and often proteinuria in cases of the severe immune response. There is a risk of acute schistosomiasis within a few weeks or months in people who are first exposed to schistosome antigens. Acute schistosomiasis has typical clinical manifestations of sudden onset of fever, muscle pain, headache, eosinophilia, malaise, and abdominal pain lasting 2 - 10 weeks [14].

2.3. Filariasis

Lymphatic filariasis and onchocerciasis are common parasitic diseases. Lymphatic filariasis mainly manifests as hydrocele testis and celiac disease, while onchocerciasis can cause skin disease and blindness [15]. In the 21st century, the prevalence of lymphatic filariasis has declined significantly worldwide, except in Africa and Southeast Asia [16]. However, the impact of epidemiological differences on the effectiveness of parasitic interventions has led to a severe challenge in the control of onchocerciasis. In addition, onchocerciasis may be associated with

nodding syndrome, but further studies are needed to prove this. It is worth noting that the possibility of parasitic filarial worms on pets entering the human body should also be a concern, as rare cases of parasitic filarial worms on pets resulting in ocular involvement and even microfilaraemia have been reported in the past [17] [18]. One of the cases showed that an immunocompetent 70-year-old woman living in rural France developed puffy left upper eyelid and conjunctivitis of the right eye. During a skin biopsy of one of the subcutaneous nodules, a 6 cm long immature worm was found and extracted, and cytologic testing of the blood showed 4 microfilariae per milliliter. She had had a dog for many years, but interestingly, to her knowledge, the dog had never had evidence of filarial disease [17].

2.4. Trichinella Nematodes

Trichinella can infect humans through raw or semi-raw meat consumption containing Trichinella larvae cysts [19]. Trichinella is widely distributed, and the toxic metabolites released by the newborn larvae during the redevelopment into cysts can cause muscle pain, fever, edema, and increased eosinophilia. The most prominent symptom of trichinosis is generalized myalgia. However, it also shows different degrees of damage to the heart, lungs, and brain. For example, myocarditis complicated by heart failure is a common cause of death from trichinosis. Trichinella infection can also manifest psychiatric symptoms, most commonly headache (24.69%), confusion (14.2%), disorientation (11.73%), etc. [20].

2.5. Leishmaniasis

Leishmaniasis, caused by Leishmania protozoa infection, has been reported in more than 90 countries with an estimated population of 700,000 to 1 million infected, mostly in tropical and subtropical, and southern European regions [21]. The disease is transmitted by sandflies and presents clinically with skin and mucous membrane damage and visceral infections [22]. However, the treatment of leishmaniasis is currently unsatisfactory.

2.6. African Trypanosomiasis

African trypanosomiasis, whose causative agent is the tsetse flies, threatens 70 million people in 36 countries, mainly in Africa [23]. Despite a significant decrease in the number of reported disease cases in 2016, complete clearance of the pathogen remains extremely difficult [23]. The disease first presents as a generalized fever that progresses with the spread of the parasite, followed by neurological symptoms [24].

2.7. American Trypanosomiasis

American trypanosomiasis (Chagas disease) pathogen is Trypanosoma cruzi (T cruzi), mainly transmitted by triatomine. The acute phase of Chagas disease symptoms include fever, inflammation, lymphadenopathy, and occasionally se-

vere manifestations such as acute myocarditis, pericardial effusion, and meningoencephalitis; the chronic phase is characterized by cardiac involvement, followed by damage to the gastrointestinal tract [25].

3. Cardiovascular System Reactions Associated with Parasitic Diseases

Studies have shown that parasitic diseases contribute to cardiovascular disease or increase the incidence of certain diseases. However, data vary by individuals enrolled, sample size, and study methodology. Below are Chagas cardiomyopathy, myocarditis and pericarditis, acute coronary syndrome (ACS), arrhythmias, and cardiac dysfunction (Figure 1).

3.1. Chagas Cardiomyopathy

Chagas cardiomyopathy was defined in patients who tested serologically positive for Trypanosoma and had at least typical symptoms of heart disease such as electrocardiogram abnormalities. Chronic Chagas cardiomyopathy is characterized by early left anterior bundle branch block or right bundle branch block

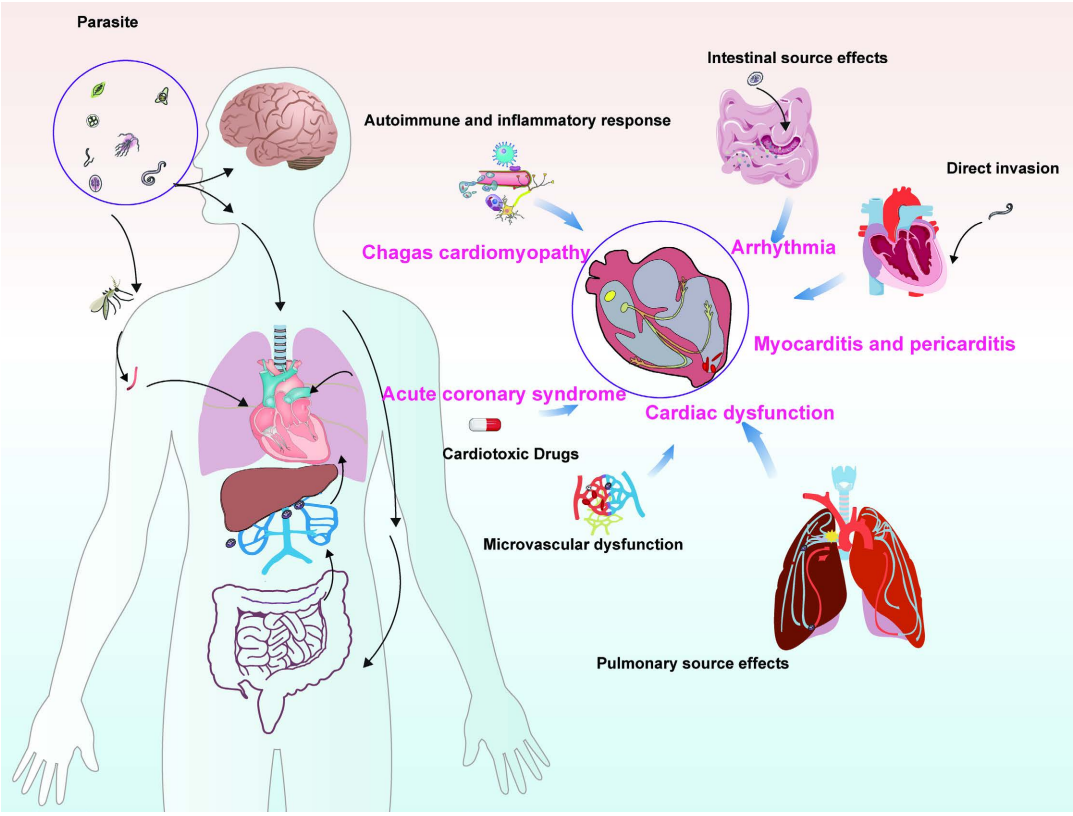

Figure 1. Flow chart showing the cardiovascular system reactions associated with parasitic diseases and pathophysiological mechanisms of them. The parasitic disease increases the risk of cardiovascular disease, such as Chagas cardiomyopathy, myocarditis pericarditis, acute coronary syndrome, arrhythmias, and cardiac dysfunction. And comprehensive clinical studies of parasitic diseases have concluded that direct infestation, pulmonary effects, microvascular dysfunction, autoimmune and inflammatory responses, cardiotoxic drugs, and intestinal source effect are several mechanisms underlying the increased risk of cardiovascular disease.

[26]. It progresses to severe ventricular arrhythmias, which can lead to heart failure [26]. Some patients have a poor prognosis and are at higher risk of fatal arrhythmias and heart failure, so there is a need to evaluate this disease's prognosis effectively. Experts recommended risk stratification for all patients with chronic Chagas. The study found impaired left ventricular function and the New York Heart Association (NYHA) cardiac function rating of Grade 3 or 4 were the manifestations of poor prognosis Chagas cardiomyopathy [27].

The distinctive myocardial fibrosis exhibited pathologically in Chagas cardiomyopathy is a feature that distinguishes it from other cardiomyopathies [28]. However, the disease still presents some complicated problems, as below. Current conventional serologic testing is challenging to be effective in patients with low parasitemia levels, antiparasitic therapy is not indicated for patients in the nonacute phase, and patients cannot tolerate angiotensin-converting enzyme inhibitors and β-blockers [25]. The lack of early replacement markers prevents effective follow-up of chronic Chagas disease. And the difficulty of effectively implementing implantable cardioverter-defibrillators and cardiac transplantation therapy.

3.2. Myocarditis and Pericarditis

Studies have shown that 21.4% of patients with trichinosis died with a histological diagnosis of myocarditis [29]. In addition, in a review of 19 autopsy cases of acute Chagas disease, myocarditis was the main cardiac damage [30]. However, clinical symptoms of the acute phase of Chagas disease are not obvious, so the cardiac manifestations of the acute phase of T cruzi infection should be treated with caution and emphasis.

Notably, cardiac involvement was detected in 8 (13%) of 62 patients with trichinosis infection, of which 6 (10%) had pericardial effusion by echocardiography (ECG) [31]. This result indicates that pericarditis is a widespread manifestation of trichinosis cardiac involvement. In addition, toxoplasmosis, cysticercosis, and amoebiasis also occasionally cause pericarditis [3]. The above observations suggest that parasitic infections strongly correlate with the development of myocarditis and pericarditis. However, they are not the main contributors to these symptoms.

3.3. Acute Coronary Syndrome

Of the 33 case reports of malaria with cardiovascular complications, 4 were diagnosed with ACS [32]. In addition, in a study of 10 patients with trichinosis, 2 of them had cardiac complications in the form of ST-segment elevation myocardial infarction [33]. Notably, patients with the parasitic disease with ACS may not have significant coronary artery obstruction. More researches still need to confirm whether it could be a neglected pathogenetic factor. In addition, compression of internal cardiac structures by the encapsulated cyst, or immediate opening of the encapsulated cyst located in the heart chambers may exhibit symptoms similar to ACS.

Localization of encapsulated cysts in the heart is rare, occurring in less than 2% of cases [34]. However, the current method of eradicating these worm cysts is primarily surgical. The damage that surgery can cause to patients cannot be ignored. Eosinophilic myocarditis may lead to ACS too. It is also worth considering when parasitic diseases are found to coexist with ACS [35]. However, parasite-induced ACS is difficult to identify in some cases, such as noncardiogenic pulmonary edema due to severe malaria, which may interfere with the diagnosis of ACS by inducing acute heart failure or acute myocardial infarction. Accordingly, the clinical management of some cardiovascular symptoms associated with parasitemia should be carefully managed. And the mechanisms behind them deserve further exploration.

3.4. Arrhythmia

The presence of parasitic infections is likely to increase the incidence or exacerbate the onset of arrhythmias. However, the clinical manifestations of arrhythmias vary widely among different types of parasitic infections. In a prospective study of severe malaria, ECG showed sinus bradycardia in 7% of cases, sinus tachycardia in 3.7%, and atrial tachycardia in 3.7% of patients [1]. Although the fever and hypoxemia caused by the parasite can be a reasonable background for tachycardia, the decrease in blood volume and cardiac reserve caused by its direct damage to the heart is also a significant cause of death. Therefore, it is of value to estimate the proportion of influence of plasmodium infection in patients with severe cardiovascular disease and malaria comorbidities.

In a systematic review of 49 population-based studies, patients with Chagas had a higher incidence of overall ECG abnormalities compared to those without Chagas (OR = 2.78; 95% CIs = 2.37 - 3.26), including complete right bundle branch block (OR = 4.60; 95% CIs = 2.97 - 7.11), left anterior bundle block (OR = 1.60; 95% CIs = 1.21 - 2.13), atrial fibrillation OR flutter (OR = 2.11; 95% CIs = 1.40 - 3.19) and premature ventricular contraction (OR = 1.62; 95% CIs = 1.14 - 2.30) [36]. Given the high incidence of lethal arrhythmias, managing arrhythmias in patients with Chagas cardiomyopathy is currently a major challenge and requires the consideration of more effective and innovative therapies and the exploration of the causes of arrhythmias induced during parasitic infections [37].

Notably, drugs used to treat parasitic diseases can also cause alterations in cardiac electrophysiology, such as pentavalent antimony and amphotericin B, which have significant cardiotoxicity. The cardiotoxicity of pentavalent antimony is particularly manifested by dose-dependent ECG changes, while its most common ECG changes include T-wave inversion and QT interval prolongation; other arrhythmias, such as premature atrial and ventricular beats and tip-twisting ventricular tachycardia, also occur with heavy dosing, and these abnormal ECG manifestations are reversed upon discontinuation of the drug [38]. And amphotericin B also often causes electrocardiographic changes by causing hypokalemia. The antimalarial drug quinine also causes prolongation of the QT interval [39], but this needs to be considered as a short-term change in rhythm after malaria subsides.

3.5. Cardiac Dysfunction

In studies of malaria, smaller baseline indices of left ventricular diastolic internal diameter and left ventricular systolic internal diameter were found to have a poor prognosis [40]. In addition, chronic infection with parasites often leads to cardiomyopathy. Patients with advanced Chagas cardiomyopathy often exhibit systolic and diastolic dysfunction, among which a significant reduction in left ventricular systolic function is strongly associated with lethality [26]. African trypanosomiasis also causes dilated cardiomyopathy-like manifestations in the heart. A study in Cameroon showed that antibodies to African trypanosomes were observed in 27% of patients with dilated cardiomyopathy [41]. Tropical endocardial myocardial fibrosis is now the most common cause of restrictive cardiomyopathy, often caused by filariasis, which is similar to eosinophilic myocarditis caused by parasites [42]. Extensive endocardial fibrosis typical of one or both ventricles is characteristic of the disease and is an important cause of heart failure and fatal arrhythmias in this disease [42].

In summary, parasitic cardiac complications can lead to decreased cardiac function and poor prognosis in patients, and these severe effects are not uncommon.

4. Possible Mechanisms Underlying the Increased Risk of Cardiovascular Disease

Parasites can affect the cardiovascular system through various mechanisms, including direct infestation, pulmonary effects, microvascular dysfunction, autoimmune and inflammatory responses, and intestinal source effects (**Figure 1**).

4.1. Direct Invasion

Parasites can directly invade and multiply in the myocardium, which in turn causes myocardial damage, necrosis, and apoptosis. T cruzi can invade numerous intracardiac cells including cardiomyocytes, endothelial cells, neuronal cells, fibroblasts, and other cells, and multiply within the cells to form cysts [28]. In a review of deaths from malaria with cardiovascular complications, histopathological studies in all cases found evidence of plasmodium parasitized red blood cells in the myocardium [32]. In a study of biomarkers of myocardial injury in the serum of 20 hypertensive patients, 20 patients with Chagas disease combined with hypertension, 20 patients with Chagas disease, and 20 normative volunteers, serum from patients with Chagas cardiomyopathy, with or without hypertension, showed more significant elevations of high-sensitive cardiac troponin T (high-sensitive cardiac troponin T (hs-cTnT) and B-type natriuretic peptide (BNP) (hs-cTnT ($p < 0.001$) and BNP ($p = 0.001$)) [43].

4.2. Pulmonary Source Effects

The main effects of parasites on the respiratory system include pneumonia or pulmonary embolism caused by parasites and parasite products. Hypoxia and carbon dioxide retention mediated by these respiratory pathologies can lead to

increased pressure in the pulmonary circulation and subsequently to pulmonary arterial hypertension (PAH). Schistosomiasis is one of the most common causes of PAH, leading to chronic pulmonary heart disease. Potential mechanisms of this PAH include systemic and localized pulmonary inflammation, involvement of other organs, especially portal hypertension associated with the liver and spleen, and direct pre-capillary occlusion caused by embolism of parasitic eggs [6]. In PAH, which is caused by worm eggs, the helper T cell-mediated type 2 cellular immune response, interleukin (IL)-4 and IL-13 with other immune mediators induce the release of transforming growth factor-β as a vital mechanism of pulmonary vascular remodeling [42]. And vasoconstrictors can escape hepatic metabolism and eventually cause ventilation/perfusion imbalance [44].

Through the above mechanisms, hypoxemia may have developed before schistosomiasis caused PAH. It can cause an imbalance in the oxidative and antioxidant systems of cardiomyocytes, causing the accumulation of reactive oxygen species (ROS), which can damage the phospholipid layer of the cell membrane or affect the intracellular calcium ion (Ca^{2+}) transport leading to pathophysiological changes of Ca^{2+} overload in cardiomyocytes [45]; in addition, elevated ROS can activate a variety of inflammatory factors, causing myocardial inflammation and fibrosis [46].

4.3. Microvascular Dysfunction

Parasites secreted procoagulant substances are an important cause of thromboembolic events in patients. Cardiac remodeling and arrhythmia in severe Chagas cardiomyopathy often lead to hemodynamic changes, presenting as intracardiac aneurysms and mural thrombus [26] [37]. Not only can parasitic cysts in the pericardium or inside the heart cause infarction or infarct-like symptoms, but sepsis due to infection is often associated with microthrombosis and is closely related to complement activation and inflammatory factors after infection. And parasitic infection is a common cause of endocardial elastosis associated with intractable endocardial thrombosis [47]. Embolism can also occur in the brain, as in the case of small and medium-sized intracranial arteries obstructed by the cysts of the tapeworm, resulting in focal neurological symptoms such as hearing loss, extraocular muscle paralysis, and facial nerve palsy [48].

4.4. Autoimmune and Inflammatory Responses

Parasitic infections cause immunosuppression and chronic autoimmune reactions. Autoimmune-induced inflammation may be a significant cause of cardiac involvement due to parasites. The possible mechanisms causing autoimmunity include polyclonal activation, molecular self-mimicry of parasite antigens, or hidden epitopes shared by host and parasite.

Inflammation plays a crucial role in parasite-mediated cardiovascular injury and thus cardiovascular disease. Parasitic infection causes severe inflammation at the heart site by activating the innate immune response, inducing systemic in-

flammatory response syndrome (SIRS) and cytokine storm [49] [50]. On the one hand, acute myocarditis is the most common cause of death in the acute phase of parasitic infections such as T cruzi [30]. On the other hand, necrotic cardiomyocytes due to inflammation can further drive inflammatory factors into the heart, causing the heart to respond to injury and mediating myocardial remodeling, and disturbances in the function of the myocardium to inhibit inflammation are an essential cause of poor myocardial remodeling [51]. In addition, autonomic dysfunction will also lead to a greater susceptibility to adverse cardiac events due to inflammatory responses and oxidative stress, and elevated levels of catecholamines in patients with parasitemia, the latter of which can mediate myocardial toxicity [52] [53].

4.5. Intestinal Source Effects

Parasites can mediate intestinal microecology and nutrient absorption disturbances through damage to the digestive tract, thereby exacerbating cardiovascular damage. Digestive symptoms such as diarrhea, nausea, and vomiting are common clinical manifestations of parasitic infections. First, the systemic or intestinal inflammation caused by the parasite can alter the microbial spectrum of the intestine [54]. Second, the physiological function of the myocardium is highly susceptible to metabolic disorders such as disordered water and electrolytes. Third, the intestinal barrier weakened by parasitic infection makes it highly likely that metabolites of harmful intestinal bacteria such as lipopolysaccharides will enter the circulation and increase the burden on the heart. In addition, the adverse effects of parasites on intestinal absorption mean that enhancing patient absorption of some of the nutrients previously studied for cardiovascular benefit may be worth considering [55].

5. Conclusion

Parasitic infections can affect the cardiovascular system, triggering various clinical cardiac symptoms and cardiac dysfunctions. Considering that the elderly population and low-immunity population are vulnerable to parasitic infections, particular attention should be paid to managing these patients with progression of the underlying cardiovascular pathology or recurrence of cardiovascular disease. Therefore, in areas where parasitic diseases are endemic, it is important to pay attention to Chagas cardiomyopathy and other parasitic cardiomyopathies; it is also important to evaluate cardiovascular diseases, including ACS and arrhythmias myocarditis and heart failure during the infection period. Common clinical evaluation tools for these parasite-associated cardiovascular diseases include a clear history of infection, screening 24-hour ambulatory ECG, B-type natriuretic peptide, serum myocardial damage markers with echocardiography, and even myocardial endomyocardial biopsy for clarification if necessary. Nevertheless, these assessment tools and their data for patient mortality risk stratification are still challenging to achieve full access in the backward areas of en-

demic countries. This phenomenon demands the control of infectious diseases caused by parasites. Apart from infection control, individualized prevention of cardiovascular outcomes due to various parasites is needed to achieve better clinical benefits, such as focusing on the progression of inflammation during treatment and avoiding arrhythmogenic anti-infectives such as quinine and amphotericin B.

Conflicts of Interest

The authors disclose no conflicts.

References

[1] Ray, H.N., *et al.* (2017) Cardiovascular Involvement in Severe Malaria: A Prospective Study in Ranchi, Jharkhand. *Journal of Vector Borne Diseases*, **54**, 177-182.

[2] Nayak, K.C., Meena, S.L., Gupta, B.K., Kumar, S. and Pareek, V. (2013) Cardiovascular Involvement in Severe Vivax and Falciparum Malaria. *Journal of Vector Borne Diseases*, **50**, 285-291.

[3] Hidron, A., *et al.* (2010) Cardiac Involvement with Parasitic Infections. *Clinical Microbiology Reviews*, **23**, 324-349. https://doi.org/10.1128/CMR.00054-09

[4] Franco-Paredes, C., *et al.* (2007) Cardiac Manifestations of Parasitic Infections Part 1: Overview and Immunopathogenesis. *Clinical Cardiology*, **30**, 195-199. https://doi.org/10.1002/clc.12

[5] Graham, B.B. and Kumar, R. (2014) Schistosomiasis and the Pulmonary Vasculature (2013 Grover Conference Series). *Pulmonary Circulation*, **4**, 353-362. https://doi.org/10.1086/675983

[6] Knafl, D., Gerges, C., King, C.H., Humbert, M. and Bustinduy, A.L. (2020) Schistosomiasis-Associated Pulmonary Arterial Hypertension: A Systematic Review. *European Respiratory Review*: *An Official Journal of the European Respiratory Society*, **29**, Article ID: 190089. https://doi.org/10.1183/16000617.0089-2019

[7] Rahaghi, F.N., *et al.* (2021) Arterial Vascular Volume Changes with Haemodynamics in Schistosomiasis-Associated Pulmonary Arterial Hypertension. *European Respiratory Journal*, **57**, Article ID: 2003914. https://doi.org/10.1183/13993003.03914-2020

[8] Şen, N. (2017) Schistosomiasis and Pulmonary Hypertension. *Tuberkuloz ve Toraks*, **65**, 237-244. https://doi.org/10.5578/tt.53798

[9] Ménard, R., *et al.* (2013) Looking under the Skin: The First Steps in Malarial Infection and Immunity. *Nature Reviews Microbiology*, **11**, 701-712. https://doi.org/10.1038/nrmicro3111

[10] Moxon, C.A., Gibbins, M.P., McGuinness, D., Milner, D.A. and Marti, M. (2020) New Insights into Malaria Pathogenesis. *Annual Review of Pathology*, **15**, 315-343. https://doi.org/10.1146/annurev-pathmechdis-012419-032640

[11] Molehin, A.J. (2020) Schistosomiasis Vaccine Development: Update on Human Clinical Trials. *Journal of Biomedical Science*, **27**, 28. https://doi.org/10.1186/s12929-020-0621-y

[12] Colley, D.G., Bustinduy, A.L., Secor, W.E. and King, C.H. (2014) Human Schistosomiasis. *The Lancet*, **383**, 2253-2264. https://doi.org/10.1016/S0140-6736(13)61949-2

[13] McManus, D.P., *et al.* (2018) Schistosomiasis. *Nature Reviews Disease Primers*, **4**, 13. https://doi.org/10.1038/s41572-018-0013-8

[14] Ross, A.G., Vickers, D., Olds, G.R., Shah, S.M. and McManus, D.P. (2007) Katayama Syndrome. *The Lancet Infectious Diseases*, **7**, 218-224. https://doi.org/10.1016/S1473-3099(07)70053-1

[15] Taylor, M.J., Hoerauf, A. and Bockarie, M. (2010) Lymphatic Filariasis and Onchocerciasis. *The Lancet*, **376**, 1175-1185. https://doi.org/10.1016/S0140-6736(10)60586-7

[16] (2020) The Global Distribution of Lymphatic Filariasis, 2000-18: A Geospatial Analysis. *The Lancet Global Health*, **8**, e1186-e1194.

[17] Blaizot, R., Receveur, M.C., Millet, P., Otranto, D. and Malvy, D.J.M. (2018) Systemic Infection with *Dirofilaria repens* in Southwestern France. *Annals of Internal Medicine*, **168**, 228-229. https://doi.org/10.7326/L17-0426

[18] Khoramnia, R. and Wegner, A. (2010) Images in clinical medicine: Subconjunctival *Dirofilaria repens*. *The New England Journal of Medicine*, **363**, e37. https://doi.org/10.1056/NEJMicm1003006

[19] Rostami, A., Gamble, H.R., Dupouy-Camet, J., Khazan, H. and Bruschi, F. (2017) Meat Sources of Infection for Outbreaks of Human Trichinellosis. *Food Microbiology*, **64**, 65-71. https://doi.org/10.1016/j.fm.2016.12.012

[20] Rosca, E.C., Tudor, R., Cornea, A. and Simu, M. (2021) Central Nervous System Involvement in Trichinellosis: A Systematic Review. *Diagnostics* (*Basel*), **11**, 945. https://doi.org/10.3390/diagnostics11060945

[21] Basmaciyan, L. and Casanova, M. (2019) Cell Death in Leishmania. *Parasite*, **26**, 71. https://doi.org/10.1051/parasite/2019071

[22] Conceição-Silva, F. and Morgado, F.N. (2019) Leishmania Spp-Host Interaction: There Is Always an Onset, but Is There an End? *Frontiers in Cellular and Infection Microbiology*, **9**, 330. https://doi.org/10.3389/fcimb.2019.00330

[23] Kennedy, P.G.E. (2019) Update on Human African Trypanosomiasis (Sleeping Sickness). *Journal of Neurology*, **266**, 2334-2337. https://doi.org/10.1007/s00415-019-09425-7

[24] Kennedy, P.G. (2008) The Continuing Problem of Human African Trypanosomiasis (Sleeping Sickness). *Annals of Neurology*, **64**, 116-126. https://doi.org/10.1002/ana.21429

[25] Pérez-Molina, J.A. and Molina, I. (2018) Chagas Disease. *The Lancet*, **391**, 82-94. https://doi.org/10.1016/S0140-6736(17)31612-4

[26] Nunes, M.C.P., *et al.* (2018) Chagas Cardiomyopathy: An Update of Current Clinical Knowledge and Management: A Scientific Statement from the American Heart Association. *Circulation*, **138**, e169-e209. https://doi.org/10.1161/CIR.0000000000000599

[27] Rassi, A., Rassi, A. and Rassi, S.G. (2007) Predictors of Mortality in Chronic Chagas Disease: A Systematic Review of Observational Studies. *Circulation*, **115**, 1101-1108. https://doi.org/10.1161/CIRCULATIONAHA.106.627265

[28] Bonney, K.M., Luthringer, D.J., Kim, S.A., Garg, N.J. and Engman, D.M. (2019) Pathology and Pathogenesis of Chagas Heart Disease. *Annual Review of Pathology*, **14**, 421-447. https://doi.org/10.1146/annurev-pathol-020117-043711

[29] Neghina, R., Neghina, A.M., Marincu, I. and Iacobiciu, I. (2010) Cardiac Involvement in Patients with Trichinosis Hospitalized in Western Romania. *Foodborne Pathogens and Disease*, **7**, 1235-1238. https://doi.org/10.1089/fpd.2010.0573

[30] Dias, E., Laranja, F.S., Miranda, A. and Nobrega, G. (1956) Chagas' Disease; a Clinical, Epidemiologic, and Pathologic Study. *Circulation*, **14**, 1035-1060. https://doi.org/10.1161/01.CIR.14.6.1035

[31] Lazarević, A.M., *et al.* (1999) Low Incidence of Cardiac Abnormalities in Treated Trichinosis: A Prospective Study of 62 Patients from a Single-Source Outbreak. *The American Journal of Medicine*, **107**, 18-23. https://doi.org/10.1016/S0002-9343(99)00161-8

[32] Holm, A.E., *et al.* (2021) Prevalence of Cardiovascular Complications in Malaria: A Systematic Review and Meta-Analysis. *The American Journal of Tropical Medicine and Hygiene*, **104**, 1643-1650. https://doi.org/10.4269/ajtmh.20-1414

[33] Dalcin, D., *et al.* (2017) Trichinella Nativa Outbreak with Rare Thrombotic Complications Associated with Meat from a Black Bear Hunted in Northern Ontario. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, **64**, 1367-1373. https://doi.org/10.1093/cid/cix165

[34] Tekin, A.F., *et al.* (2018) Left Ventricular Hydatid Cyst Mimicking Acute Coronary Syndrome. *Radiology Case Reports*, **13**, 697-701. https://doi.org/10.1016/j.radcr.2018.03.019

[35] Şimşek, E., Özerkan Çakan, F. and Akın, M. (2017) Eosinophilic Myocarditis Presenting as Acute Coronary Syndrome. *Turk Kardiyoloji Dernegi arsivi: Turk Kardiyoloji Derneginin yayin organidir*, **45**, 358-361. https://doi.org/10.5543/tkda.2016.49392

[36] Rojas, L.Z., *et al.* (2018) Electrocardiographic Abnormalities in Chagas Disease in the General Population: A Systematic Review and Meta-Analysis. *PLoS Neglected Tropical Diseases*, **12**, e0006567. https://doi.org/10.1371/journal.pntd.0006567

[37] Romero, J., *et al.* (2021) Advanced Therapies for Ventricular Arrhythmias in Patients with Chagasic Cardiomyopathy: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*, **77**, 1225-1242. https://doi.org/10.1016/j.jacc.2020.12.056

[38] Oliveira, L.F., *et al.* (2011) Systematic Review of the Adverse Effects of Cutaneous Leishmaniasis Treatment in the New World. *Acta Tropica*, **118**, 87-96. https://doi.org/10.1016/j.actatropica.2011.02.007

[39] Wroblewski, H.A., Kovacs, R.J., Kingery, J.R., Overholser, B.R. and Tisdale, J.E. (2012) High Risk of QT Interval Prolongation and Torsades de Pointes Associated with Intravenous Quinidine Used for Treatment of Resistant Malaria or Babesiosis. *Antimicrobial Agents and Chemotherapy*, **56**, 4495-4499. https://doi.org/10.1128/AAC.06396-11

[40] Kingston, H.W.F., *et al.* (2020) Reduced Cardiac Index Reserve and Hypovolemia in Severe Falciparum Malaria. *The Journal of Infectious Diseases*, **221**, 1518-1527. https://doi.org/10.1093/infdis/jiz568

[41] Blum, A., *et al.* (2020) Sleeping Hearts: 12 Years after a Follow up Study on Cardiac Findings Due to Sleeping Sickness. *One Health* (*Amsterdam, Netherlands*), **11**, Article ID: 100182. https://doi.org/10.1016/j.onehlt.2020.100182

[42] Nunes, M.C., Guimarães Júnior, M.H., Diamantino, A.C., Gelape, C.L. and Ferrari, T.C. (2017) Cardiac Manifestations of Parasitic Diseases. *Heart* (*British Cardiac Society*), **103**, 651-658. https://doi.org/10.1136/heartjnl-2016-309870

[43] de Oliveira Vieira, A., Nascentes, G.A.N., de Morais Oliveira, A.C., Correia, D. and Cabrine-Santos, M. (2021) Biomarkers Assessment in Patients with Chagas Disease and Systemic Arterial Hypertension. *Parasitology Research*, **120**, 1429-1435. https://doi.org/10.1007/s00436-020-06954-3

[44] Safdar, Z., Bartolome, S. and Sussman, N. (2012) Portopulmonary Hypertension: An Update. *Liver Transplantation: Official Publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society*, **18**, 881-891. https://doi.org/10.1002/lt.23485

[45] Krylatov, A.V., *et al.* (2018) Reactive Oxygen Species as Intracellular Signaling Molecules in the Cardiovascular System. *Current Cardiology Reviews*, **14**, 290-300. https://doi.org/10.2174/1573403X14666180702152436

[46] Tsutsui, H., Kinugawa, S. and Matsushima, S. (2011) Oxidative Stress and Heart Failure. *American Journal of Physiology. Heart and Circulatory Physiology*, **301**, H2181-H2190. https://doi.org/10.1152/ajpheart.00554.2011

[47] Ozdemir, D., Cortopassi, I.O. and McNamara, R.L. (2019) An Illustrative Case of Endocardial Fibroelastosis and Recalcitrant Intracardiac Thrombosis: A Case Report. *Thrombosis Journal*, **17**, 8. https://doi.org/10.1186/s12959-019-0199-3

[48] Garcia, H.H., Nash, T.E. and Del Brutto, O.H. (2014) Clinical Symptoms, Diagnosis, and Treatment of Neurocysticercosis. *The Lancet Neurology*, **13**, 1202-1215. https://doi.org/10.1016/S1474-4422(14)70094-8

[49] Hübner, M.P., Layland, L.E. and Hoerauf, A. (2013) Helminths and Their Implication in Sepsis—A New Branch of Their Immunomodulatory Behaviour? *Pathogens and Disease*, **69**, 127-141. https://doi.org/10.1111/2049-632X.12080

[50] Gutman, J.R., *et al.* (2020) Malaria and Parasitic Neglected Tropical Diseases: Potential Syndemics with COVID-19? *The American Journal of Tropical Medicine and Hygiene*, **103**, 572-577. https://doi.org/10.4269/ajtmh.20-0516

[51] Prabhu, S.D. and Frangogiannis, N.G. (2016) The Biological Basis for Cardiac Repair after Myocardial Infarction: From Inflammation to Fibrosis. *Circulation Research*, **119**, 91-112. https://doi.org/10.1161/CIRCRESAHA.116.303577

[52] Cygankiewicz, I. and Zareba, W. (2013) Heart Rate Variability. *Handbook of Clinical Neurology*, **117**, 379-393. https://doi.org/10.1016/B978-0-444-53491-0.00031-6

[53] Liaudet, L., Calderari, B. and Pacher, P. (2014) Pathophysiological Mechanisms of Catecholamine and Cocaine-Mediated Cardiotoxicity. *Heart Failure Reviews*, **19**, 815-824. https://doi.org/10.1007/s10741-014-9418-y

[54] Partida-Rodríguez, O., *et al.* (2017) Human Intestinal Microbiota: Interaction between Parasites and the Host Immune Response. *Archives of Medical Research*, **48**, 690-700. https://doi.org/10.1016/j.arcmed.2017.11.015

[55] Sarandria, D. and Sarandria, N. (2022) Omega 3 Fatty Acids, Inflammation, and Cardiovascular Diseases Prevention—An Essay. *World Journal of Cardiovascular Diseases*, **12**, 152-159. https://doi.org/10.4236/wjcd.2022.123016