Research Open

Journal of Cardiology and Clinical Practice
Volume 4 Issue 2

Research Article

The Role of Interleukin-1β in the Pathogenesis and Treatment of Acute Pericarditis

Nightingale Syabbalo*

Professor of Physiology and Medicine, Nabanji Medical Centre, Zambia

Corresponding author: Nightingale Syabbalo, Professor of Physiology and Medicine, Nabanji Medical Centre, P. O. Box 30243, Lusaka, Zambia; **Tel:** +260 966 486117; **E-mail:** nightsyab@gmail.com

Received: August 21, 2021; **Accepted:** August 30, 2021; **Published:** September 07, 2021

Abstract

Acute pericarditis is characterized by severe inflammation of the fibrous and serous pericardial membranes covering the heart. It is caused by multifactorial conditions, such as systemic diseases, autoimmune inflammatory diseases, malignant tumours, bacterial and viral infections, including SARS-CoV-2. In Europe, most cases of acute pericarditis are idiopathic (80-90%), and may follow viral infections. In sub-Saharan Africa, the leading cause of effusive and constrictive pericarditis is tuberculous pericarditis, secondary to HIV/AIDS in about 70% of patients. Approximately, 30% of cases of acute pericarditis are recurrent despite the standard of care, and about 25-30% present as pericardial effusion which may lead to cardiac haemodynamic compromise (cardiac tamponade). Stepwise treatment of consists of aspirin, or any other non-steroidal anti-inflammatory drugs, colchicine, and corticosteroids. Interleukin-1 is a master proinflammatory cytokine existing in two isoforms, IL-1α and IL-1β, and the latter is the most studied, and is implicated in several autoinflammatory diseases, autoimmune diseases, metabolic syndromes, cardiovascular disease, including acute pericarditis. Anakinra is a recombinant, nonglycosylated human interleukin-1 receptor antagonist that competes and inhibits the effects of IL-1α and IL-1β, thus reducing their systemic inflammatory effects. Treatment with anakinra has been shown to be effective in the control of recurrent acute pericarditis in patients who are resistant to colchicine and corticosteroid-dependent. Additionally, treatment with anakinra results in more patients tapering or discontinuing corticosteroids, with no further recurrences of acute pericarditis. Furthermore, treatment with anakinra has been shown to prevent or reverse constrictive pericarditis. Rilonacept effectively acts as an "IL-1 trap" by binding to circulating IL-1α and IL- 1β molecules, inhibiting the downstream activation of IL-1β inflammatory cascade (Table 1).

Treatment with rilonacept has been shown to significantly relieve pain and other symptoms of pericarditis, and to rapidly resolve recurrent pericarditis. Additionally, rilonacept led to tapering or discontinuation of corticosteroids. Interleukin-1β antagonists should be initiated early in the course of acute pericarditis in order to avert the dreaded complications of acute pericarditis, such as recurrent pericarditis, tamponade, and constrictive pericarditis.

Keywords: *Acute pericarditis, Anakinra, Colchicine, Interleukin-1, Interleukin-1 inhibitors*

Introduction

Acute pericarditis is characterized by severe inflammation of the fibrous and serous pericardial membranes covering the heart [1,2]. It is caused by multifactorial conditions, such as systemic diseases, autoimmune inflammatory diseases, connective vascular diseases, neoplastic tumours, bacterial, fungal, and viral infections [3-6]. However, in Europe and North America, most cases of pericarditis are idiopathic (80-90%) [6], and may follow viral infection. In sub-Saharan Africa, the leading cause of chronic pericarditis is opportunistic tuberculous pericarditis (70%) [7,8], secondary to HIV/AIDS in about 70% of patients [8-11]. Recently, acute and recurrent pericarditis has been reported to be associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [12-17].

Approximately, 20-30% of cases of acute pericarditis are recurrent despite the standard of care (SoC) [1,3,18-22], and about 25-30% present as pericardial effusion which may lead to cardiac tamponade [3,4,12,23-25]. Cardiac tamponade is a life-threatening condition resulting in compression of the heart, reduced cardiac filling, haemodynamic compromise, and heart failure [25,26]. Constrictive pericarditis is another ominous complication of acute pericarditis [27,28]. It occurs in about 9% of patients with acute pericarditis, and may require pericardiectomy [29], which is lumbered by 5%-10% perioperative mortality [30].

Treatment of pericarditis is challenging, recurrent pericarditis with effusion is frequent, despite treatment with the standard of care (SoC). The stepwise treatment acute pericarditis based on the 2015 European Society of Cardiology guidelines for the management of recurrent pericarditis [1], consists of aspirin, or any other non-steroidal anti-inflammatory drugs (NSAIDs), such as ibrufen, indomethacin, and naproxen; colchicine; and corticosteroids [6,18-22,31-33]. At the top of the ladder treatment, azathioprine, and intravenous immunoglobulins may be added if symptoms persist, or if patients develop complications, such as recurrent pericarditis, and effusive constrictive pericarditis. However, some of the patients become unresponsive to the SoC [34,35]. About 5% of the patients despite treatment with standard dosages of aspirin or NSAIDs, colchicine, and prednisone continue to complain of symptoms, or

Table 1: Causes of acute pericarditis and recurrent pericarditis.

Idiopathic
Viral infections Adenovirus, Coxsackie virus A and B, Echovirus, Epstein-Barr virus, Influenza, Mumps, HIV, SARS-CoV-2
Bacterial infection Mycobacterium tuberculosis, Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Legionella, Listeria, Meningococcus, Gonococcus, Salmonella, Syphilis
Fungal infections Aspergillosis, Blastomycosis, Coccidioidomycosis, Histoplasmosis, Candida
Parasitic infections Echinococcus granulomatosis, Entamoeba histolitica
Protozoal infection Toxoplasmosis gondii
Chest trauma
Irradiation
Cardiovascular disease Chronic heart failure Acute myocardial infarction Post-myocardial infarction (Dressler syndrome) Aortic dissection Cardiac surgery, post-pericardiotomy syndrome Cardiac procedures, catheterization, post-pacemaker insertion
Neoplastic diseases Primary: mesothelioma, angiosarcoma Metastatic: lung, breast, bone, lymphoma, leukaemia, melanoma
Collagen vascular diseases Rheumatoid arthritis, Systemic lupus erythromatosus, Scleroderma, Sjögren syndrome, Ankylosing spondylitis, Wegener granulomatosis, Behçet's syndrome, Dermatomyositis
Infiltrative diseases Sarcoidosis, Amyloidosis
Metabolic diseases Uraemia, Hypothyroidism (myxedema), Gout
Drugs Hydralazine, Minoxidil, Methysergide, Penicillin, Doxorubicin, Phenytoin, Procainamide, Sodium cromoglycate
Autoinflammatory diseases Familial Mediterranean fever, Cryopyrin-associated periodic syndrome
Chylopericardium

have recurrent pericarditis with effusion. This sub-group of patients is resistant to colchicine and azathioprine, and become corticosteroid-dependent [36-41]. They require innovative therapies, such as IL-1β inhibitors (anakinra, or rilonacept) which block the inflammatory cascade implicated in pathogenesis of acute pericarditis [42,43].

Interleukin-1 Family

The interleukin-I (IL-1) family is ranked at the top of the hierarchy of innate immune signaling, and is comprised of 11 soluble molecules and 10 receptors [44-46]. It is divided into three subgroups, depending on the IL-1 consensus sequence, and the signaling receptor chain. It include cytokines with agonistic activity, such as IL-1α, IL-1βb, IL-18, IL-33, IL-36a, IL-36b, and IL-36g; receptors antagonists, including IL-1Ra, IL-36Ra, and IL-38, and an anti-inflammatory cytokine IL-37 [44-47]. The IL-1 family signaling is via 10 receptors, coreceptors, decoy receptors, and inhibitory receptors with similar and different immunopathological effects [48,49]. Interleukin-1 receptors, and decoy receptors are potential targets for blockade, and have been exploited in the development of several biologics for the treatment of several diseases, including cardiovascular diseases, and cancer.

Interleukin-1 and its most related family members IL-18, and IL-33 play different roles in innate immunity and inflammation in response to microbial, and environmental insults. Interleukin-18 mediates mostly type 1 innate immunity, and inflammatory responses [50], whereas, IL-33 plays a central role in type 2 innate and adaptive immunity, and inflammation [51]. IL-33 is an 'alarmin' cytokines secreted by epithelial cells, in response to microbial infections, cell death, necrosis, mechanical stress, and trauma [52], and plays a central role in the pathogenesis of eosinophilic asthma [52-55], and chronic rhinosinusitis with nasal polyps [56-59]. IL-1β and IL-18 are the most studied family members [44,45], and IL-1β has emerged as the most promising therapeutic target for the treatment of several autoimmune, and inflammatory diseases, including cardiovascular diseases [60,61].

Interleukin-1β

Interleukin-1 is a master pro-inflammatory cytokine which exists in two isoforms, including IL-1α, and IL-β, with proinflammatory and pyogenic properties [62,63]. It is produced principally in monocytes and macrophages, but also in neutrophils. IL-1β is a key up-regulator of inflammatory mediators, such as cyclo-oxygenase-2 (COX-2), and prostaglandins. Interleukin-1β, and the inflammatory mediators it induces for secretion are responsible for the inflammation, hyperaemia, hyperesthesia, and oedema characteristic of acute pericarditis [60,63-66]. IL-1β production and secretion is stimulated by NLRP3 inflammasome, pathogen-associated molecular patterns (PAMPs), damage-associated molecular patterns (DAMPs), and other inflammatory cytokines, such a TNFβ, IL-8, and in an autocrine

fashion by IL-1β [67]. NLRP3 (NACHT LRR and PYD domains-containing protein 3) plays a very important role in the production of IL-1β and IL-18 from their precursor immature forms [68,69]. Interleukin-1β is produced as a 269-AA precursor protein, and is processed by caspase-1 activated in the inflammasomes into its mature active form [70-73].

Interleukin-1β signaling is via two surface receptors, IL-1R1, and IL-1 type 2 receptor (IL-1R2), a decoy receptor. IL-1 binds to IL-1R1, which requires formation of a heterodimer with IL-1 type 3 receptor (IL-1R3) before binding [74]. Subsequently, MyD88 (myeloid differentiation factor 88) binding triggers a proinflammatory signaling via a cascade of phosphorylation resulting in activation of NF-kB (nuclear factor-kB) [74,75]. NF-kB translocates into the nucleus, henceforth, promoting transcription and translation of several proinflammatory genes, especially for the precursors of IL-1β, and IL-18, as well as components of the NLRP3 inflammasome [75]. Interleukin 1β and its receptors, coreceptor, and decoy receptor are favourable therapeutic targets in cardiovascular diseases [76-78], including acute and recurrent pericarditis [64-67].

Anakinra

Anakinra (Kineret; Swedish Orphan Biovitrum, Stockholm, Sweden) is a recombinant, nonglycosylated human interleukin-1 receptor 1 antagonists that competes and inhibits the effects of IL-1α and IL-1β, thus reducing their systemic inflammatory effects. It is approved for the treatment of several diseases, including rheumatoid arthritis, cryopyrin-associated periodic syndrome (CAPS), a multisystematic IL-1β-mediated disease due to a gain of function in NLRP3, and neonatal-onset multisystem inflammatory disease (NOMID). It is given as 100 mg subcutaneouly once daily. Anakinra when administered early has been shown to be very effective in in the treatment of colchicine resistant, and corticosteroid-dependent recurrent pericarditis [79,80]. Treatment with anakinra has been shown to be effective in the control of symptoms due to acute pericarditis, and in preventing recurrent pericarditis, and pericardial effusion [79-81], and reversing constrictive pericarditis [82]. Additionally, treatment with anakinra results in more patients tapering or discontinuing corticosteroids, with no further recurrences of acute pericarditis. Furthermore, treatment with anakinra has been shown to prevent or reverse constrictive pericarditis. Adverse events related to treatment with anakinra are listed in Table 2.

Table 2: Anakinra adverse effects.

Injection-site reaction, redness and swelling
Arthralgia
Myalgia
Mild fever
Hives
Tiredness or weakness
Headache
Stomachache
Nausea, vomiting
Diarrhoea
Swelling of face, lips, tongue, and eyelids
Unusual bruising or bleeding
Infections, nasopharyngitis, sore throat
Neutropenia
Hypereosinophilia
Thrombocytopenia
Elevation of transaminases
Optic neuritis (rare)
Diverticulitis perforation (rare)

Rilonacept

Rilonacept (Arcalyst; Regeneron Phamaceuticals, Tarrytown, NY) is a dimeric fusion protein that consists of ligand binding domains of the extracellular portions of the IL-1 receptor component (IL-R1), and the IL-1 receptor accessory protein that is linked to the Fc portion of human IgG1. Rilonacept effectively act as an "IL-1 trap" by binding to circulating IL-1α and IL- 1β molecules, effectively blocking the engagement of IL-1β to pro-inflammatory cell surface receptors, and inhibiting the downstream activation of IL-1β inflammatory cascade. It is approved for the treatment of CAPS, and is administered as a loading dose of 320 mg subcutaneously once, then followed by 160 mg every 2 weeks. Treatment with rilonacept has been shown to significantly relieve pain and other symptoms of pericarditis, and to rapidly resolve recurrent pericarditis [83]. Additionally, rilonacept led to tapering or discontinuation of corticosteroids [83]. Notably, rilonacept has been demonstrated to reverse constrictive pericarditis [83]. Adverse effects of rilonacept include injection-site reaction, and neutropnea with danger of susceptibility to infections. Rilonacept was approved by the US Food and Drug Administration (FDA) in March 2021 for the treatment of pericarditis, in patients aged 12 years and older.

Interleukin-1 Antagonists And Covid-19

Interleukin-1 blockade causes neutropnenia and susceptibility to infection. However, it seems that anakinra and rilonacept do not influence the epidemiology, and clinical outcome of SARS-CoV-2. Moreover, several studies have reported that anakinra is associated with reduced mortality and need for mechanical ventilation, and has a good safety profile in patients with SARS-CoV-2 [84-90].

Conclusion

Acute pericarditis is characterized by severe inflammation of the fibrous and serous pericardial membranes covering the heart. The stepwise treatment of acute pericarditis consists of aspirin or NSAIDs, colchicine, and prednisone. About 5% of the patients with acute pericarditis develop resistance to colchicine, and are corticosteroid-dependent. Interleukin-1β antagonists, such as anakinra and rilonacept should be initiated early in the course of acute pericarditis in order to avert the troublesome complications of acute pericarditis, such as recurrent pericarditis, cardiac tamponade, and constrictive pericarditis.

References

1. Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J, et al. (2015) 2015 ESC guidelines for the diagnosis and management of pericardial diseases. *Eur Heart J* 36: 2921-2964. [crossref]
2. Tombetti E, Mulè A, Tamanini S, Matteuci L, Negro E, et al. (2020) Novel pharmacotherapies for recurrent pericarditis; Current options in 2020. *Curr Cardiol Rep* 22: 59. [crossref]
3. Schwier NC, Hale GH, Davies ML (2017) Treatment of adults with idiopathic recurrent pericarditis: novel use of immunotherapy. *Pharmacotherapy* 37: 305-318. [crossref]
4. Brucato A, Imazio M, Cremer PC, Adler Y, Maisch B, et al. (2018) Recurrent pericarditis: still idiopathic? The pros and cons of a well-honoured term. *Intern Emerg Med* 13: 839-844. [crossref]
5. Chang SA (2017) Tuberculous and infectious pericarditis. *Cardiol Clin* 35: 615-622. [crossref]
6. Andreis A, Imazio M, Casula M, Avondo S, Brucato A (2021) Recurrent pericarditis: an update on diagnosis and treatment. *Intern Emerg Med* 1-8. [crossref]
7. Imazio M, Gaita F, LeWinter M (2015) Evaluation and treatment of pericarditis: a systemic review. *JAMA* 314: 1498-1506. [crossref]
8. Mayosi BM, Wiysonge CS, Ntsekhe M, Volmink JA, Gumedze P, et al. (2006) Clinical characteristics and initial management of patients with tuberculous pericarditis in the HIV era: the investigation and management of pericarditis in Africa (IMP Africa) registry. *BMC Infect Dis* 6:2. [crossref]
9. Ntsekhe M, Mayosi BM (2009) Cardiac manifestation of HIV infection: An African perspective. *Nat Clin Pract Cardiovasc Med* 6: 120-127. [crossref]
10. Abubaker U, Adeoye PO, Adebo OA, Adegboye VO, Kesieme EB, et al. (2011) Pattern of pericardial diseases in HIV-positive patients at University College Hospital, Ibadan, Nigeria. *HIV Medicine* 12: 2.
11. Noubiap JJ, Agbor VN, Ndoadoumgue AL, Nkeck JN, Kamguia A, et al. (2018) Epidemiology of pericardial disease in Africa: a systemic scoping review. *BMJ Heart* 105.
12. Blagojevic NR, Bosnjakovic D, Vukomanovic V, Arsenovic S, Lazic JS, et al. (2020) Acute pericarditis and severe acute respiratory syndrome coronavirus 2: Case report. *Int J Infect Dis* 101: 180-182. [crossref]
13. Farina A, Uccello G, Spreafico M, Bassanelli G, Savonitto S (2020) SARS-CoV-2 dtected in the pericardial fluid of a patient with cardiac tamponade. *Eur J Intern Med* 76: 100-1001. [crossref]
14. Fox K, Prokup JA, Butson K, et al. (2020) Acute effusive pericarditis: A late complication of COVID-19. *Cureus* 12: e9074. [crossref]
15. Kumar R, Kumar J, Daly C, Edroos SA (2020) Acute pericarditis as a primary presentation of COVID-19. *BMJ* 13.
16. Tung-Chen Y (2020) Acute pericarditis due to COVID-19 infection: An undiagnosed disease? *Med Clin (Engl Ed)* 155: 44-45. [crossref]
17. Fajay R, Belkhayat C, Bouchlarhem A, El Aidouni G, Bkiyar H, et al. (2021) Acute pericarditis revealing COVID-19 infection. Case report. *Annal Med Surg* 62: 225-227. [crossref]
18. Imazio M, Brucato A, Cemin R, Ferrua S, Maggiolini S, et al. (2013) A randomized trial of colchicine for acute pericarditis. *N Engl J Med* 369: 1522-1528. [crossref]
19. Imazio M, Brucato A, Cemin R, Ferrua S, Belli R (2011) CORP (Colchicine for Recurent Pericarditis) Investigators. Colchicine for recurrent pericarditis (CORP): a randomized trial. *Ann Intern Med* 155: 409-414. [crossref]
20. Imazio M (2014) Treatment of recurrent pericarditis. *Revista Espanola de Cardiologia* 67: 345-348.
21. Tombetti E, Giani T, Brucato A, Cimaz R (2019) Recurrent pericarditis in children and adolescents. *Front Pediatr* 7: 419. [crossref]
22. Chiabrando JG, Bonaventura A, Vecchie A, Wohlford GF, Mauro AG, et al. (2020) Management of acute and recurrent pericarditis: JACC state-of-the-art review. *J Am Coll Cardiol* 75: 76-92. [crossref]
23. Sagristà-Sauleda J, Mercé AS, Soler-Soler J (2011) Diagnosis and management of pericardial effusion. *World J Cardiol* 3: 135-143. [crossref]
24. Imazio M, Mayosi BM, Brucato A, Markel G, Trinchero R, et al. (2010) Triage and management of pericardial effusion. *I Cardiovasc Med* 11: 928-935. [crossref]
25. Imazio M, Adler Y (2013) Management of pericardial effusion. *Eur Heart J* 34: 1186-1197.
26. Ristic AD, Imazio M, Alder Y, Anastasakis A, Badano LP, et al. (2014) Triage strategy for urgent management of cardiac tamponade: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 35: 2279-2284. [crossref]
27. Matshela MR (2017) Constrictive pericarditis: prevention and treatment. *E-J Cardiol* 15:24.
28. Maisch B (2018) Management of pericarditis and pericardial effusion, constrictive and effusive-constrictive pericarditis. *Herz* 43: 663-678. [crossref]
29. Yadav NJ, Siddique MS (2021) Constrictive pericarditis. *StatPearls*. [crossref]
30. Khandaker MH, Sahaff HV, Greason KL, Anavekar NS, Espinosa RE, et al. (2012) Pericardiectomy vs medical management in patients with relapsing pericarditis. *Mayo Clin Proc* 87: 1062-1070. [crossref]
31. Dauphin C, Merlin E, Chalard A, Trésorier R, Lusson J, et al. (2016) Recurrent pericarditis: current challenges and future prospects. *Res Reports Clin Cardiol* 7: 99-108.
32. Imazio M, Bobbio M, Cecchi E, Demarie D, Pomari F, et al. (2005) Colchicine as first-choice therapy for recurrent pericarditis: results of the CORE (Colchicine for Recurrent pericarditis) trial. *Arch Intern Med* 165: 1987-1991. [crossref]
33. Imazio M, Belli R, Brucato A, Cemin R, Ferrua S, et al. (2014) Efficacy and safety of colchicine for the treatment of multiple recurrences of pericarditis (CORP-2): a multicentre, double-blind, placebo-controlled, randomised trial. *Lancet* 383: 2232-2237. [crossref]
34. Soler-Soler J, Sagristà-Sauleda J, Permanyer-Miralda G (2004) Relapsing pericarditis. *Heart* 90: 1364-1368. [crossref]
35. Imazio M, Trinchero R, Shabetai R (2007) Pathogenesis, management, and prevention of recurrent pericarditis. *J Cardiovasc Med (Hagerstown)* 8: 404-410. [crossref]
36. Spodick DH (2003) Acute pericarditis: current concepts and practice. *JAMA* 289: 1150-1153. [crossref]
37. Little WC, Freeman GL (2006) Pericardial disease. *Circulation* 113: 1622-1632. [crossref]
38. Imazio M, Brucato A, Trinchero R, Adler Y (2009) Diagnosis and management of pericardial disease. *Nat Rev Cardiol* 6: 743-751. [crossref]
39. Imazio M, Spodick DH, Brucato A, Trinchero R, Adler Y (2010) Controversial issues in the management of pericardial disease. *Circulation* 121: 916-928. [crossref]
40. Cremer PC, Kumar A, Kontzias A, Tan CD, Rodriguez ER, et al. (2016) Complicated pericarditis: understanding risk factors and pathophysiology to inform imaging and treatment. J Am Coll Cardiol 68: 2311-2328. [crossref]
41. Lazaros G, Antonopoulos AS, Antonatou K, Skendros P, Ritis K, et al. (2020) Hydroxychloroquine for colchicine-resistant glucocorticoid-dependent idiopathic recurrent pericarditis: a pilot observational study. *In J Cardiol* 311: 77-82. [crossref]
42. Lazaros G, Anthonatou K, Vassilopoulos D (2017) The therapeutic role of interleukin-1 inhibition in idiopathic recurrent pericarditis: current evidence and future challenges. *Front Med (Lausanne)* 4: 78. [crossref]
43. Brucato A, Emmi G, Cantarini L, Di Lenarda A, Gattorno M, et al. (2018) Management of idiopathic recurrent pericarditis in adults and in children: a role for IL-1 receptor antagonism. *Emerg Med* 13: 475-489. [crossref]
44. Dinarello CA (2009) Immunological and inflammatory functions of the interleukin-1 family. *Annu Rev Immunol* 27: 519-550. [crossref]
45. Dinarello CA (2017) Overview of the IL-1 family in innate inflammation and acquired immunity. *Immunol Rev* 281: 8-27. [crossref]
46. Dinarello CA (2019) The IL-1 family of cytokines and receptors in rheumatic diseases. *Nat Rev Rheumatol* 15: 612-632. [crossref]
47. Martovani A, Dinarello CA, Molgora M, Garlanda C (2019) Interleukin-1 and related cytokines in the regulation of inflammation and immunity. *Immunity Rev*. [crossref]
48. Dinerallo C, Arend W, Sims J, Smith D, Blumberg H, et al. (2010) IL-1 family nomenclature. *Nat Immunol* 11: 973. [crossref]

49. Garlanda C, Dinarello CA, Mantovani A (2013) The interleukin-1 family: back to the future. *Immunity* 39: 1003-1018. [crossref]

50. Kaplanski G (2018) Interleukin-18: Biological properties and roles in disease pathogenesis. *Immunol Rev* 281: 138-153. [crossref]

51. Schmitz J, Owyang A, Oldham E, Song Y, Murphy E, et al. (2005) IL-33, an interleukin-1-like cytokine that signals via IL-1 receptor related protein ST2 and induces T helper type 2-associated cytokines. *Immunity* 23: 479-490. [crossref]

52. Borish L, Steinke JW (2011) Interleukin-33 in asthma: How big of a role does it play? *Curr Allergy Asthma Rep* 11: 7-11. [crossref]

53. Wang Y, Wang L, Hua S (2017) Interleukin-33 in children with asthma: A systemic review and meta-analysis. *Allergol Immunopathol (Madr)* 45: 387-392. [crossref]

54. Ding W, Zou G-L, Zhang W, Lai X-N, Chen H-W, et al. (2018) Interleukin-33 its emerging role in allergic diseases. *Molecules* 23: 1665. [crossref]

55. Syabbalo N (2021) The role of alarmin cytokines in the pathogenesis of severe uncontrolled asthma. *Ann Clin Med Res* 2: 1022.

56. Schleimer RP (2017) Immunopathogenesis of chronic rhinosinusitis and nasal polposis. *Annu Rev Pathol* 12: 331-357.

57. Kim DK, Jin HR, Eun KM, et al. (2017) The role of interleukin 33 in chronic rhinosinusitis. *Thorax* 72: 635-645. [crossref]

58. Sehmi R (2017) Role of interleukin 33 in chronic rhinosinusitis. *Thorax* 72.

59. Zhang L, Jiang L-L, Cao Z-W (2017) Interleukin-33 promotes the inflammatory reaction in chronic rhinosinusitis with nasal polyps by NF-kB signaling. *Eur Rev Med Pharmacol Sci* 21: 4501-4508. [crossref]

60. Dinarello CA (2011) Interleukin-1 in the pathogenesis and treatment of inflammatory diseases. *Blood* 117: 3720-3732. [crossref]

61. Dinarello CA (2009) Interleukin-1 beta and the autoinflammatory disease. *N Engl J Med* 360: 2467-2470. [crossref]

62. Abbate R, Trankle CT, Buckley LF, Lipinski MJ, Appleton D, et al. (2020) Interleukin-1 blockade inhibits the acute inflammatory response in patients with ST-segment-elevation myocardial infarction. *J Am Heart Assoc* 9: e014941. [crossref]

63. Dinarello CA, Anna S, van der Meer J (2012) Treating inflammation by blocking interleukin-1 in a broad spectrum of diseases. *Nat Rev Drug Discov* 11: 633-652. [crossref]

64. Brucato A, Emmi G, Cantarini L, et al. (2018) Management of idiopathic recurrent pericarditis in adults and children: a role for IL-1 receptor antagonism. *Int Emerg Med* 13: 475-489. [crossref]

65. Buckley LF, Viscusi MM, Van tassel BW, Abbate A (2018) Interleukin-1 blockade for the treatment of pericarditis. *Eur Heart J Cardiovasc Pharmacother* 4: 46-53. [crossref]

66. Emmi G, Urban ML, Imazio M, et al. (2018) Use of interleukin-1 blockers in pericardial and cardiovascular disease. *Curr Cardiol Rep* 20: 61. [crossref]

67. Picco P, Brisca G, Traverso F, Loy A, Gattorno M, et al. (2009) Successful treatment idiopathic recurrent pericarditis in children with interleukin-1 receptor antagonist (anakinra): an unrecognized autoinflammatory disease? *Arthritis Rheum* 60: 264-268. [crossref]

68. Hoffman HM, Gregory SG, Mueller JL, Tresiettas M, Broide DH, et al. (2003) Fine structure mapping of CIAS1: identification of an ancenstral haplotype and a common FCAS mutation, L353P. *Human Genet* 112: 209-216. [crossref]

69. Karasawa T, Takahashi M (2017) Role of NLRP3 inflammasomes in atherosclerosis. *J Atherosclerosis Thrombosis* 24: 443-451. [crossref]

70. March CJ, Mosley B, Larsen A, Cerretti DP, Braedt G, et al. (1985) Cloning, sequence and processing of two distinct human interleukin-1 complementary DNAs. *Nature* 15: 641-647. [crossref]

71. Martinon F, Burns K, Tschopp J (2003) The inflammasome: a molecular platform triggering activation of inflammatory caspases and processing of proIL-β. *Mol Cell* 10: 417-426. [crossref]

72. Agostini L, Martinon F, Burns K, McDermott MF, Hawkins PN, et al. (2004) NALP3 forms an IL-1beta-processing inflammasome with increased activity in muckle-wells autoinflammatory disorder. *Immunity* 20: 319-325. [crossref]

73. Amin J, Boche D, Rakic S (2017) What do we know about the inflammasome in human? *Brain Pathol* 27: 192-194. [crossref]

74. Abbate A, Toldo S, Marchetti C, Kron J, Van Tassell BW, et al. (2020) Interleukin-1 and the inflammasome as a therapeutic target in cardiovascular disease. *Circ Res* 126: 9. [crossref]

75. Brikos C, Wait R, Begum S, O'Neill LA, Saklatvala J (2007) Mass spectrometric analysis of the endogenous type 1 interleukin-1 (IL-1) receptor signaling complex formed after IL-1 binding identifies IL-1RAcP, MyD88, and IRAK-4 as the stable components. *Mol Cell Proteomics* 6: 1551-1559. [crossref]

76. Toldo S, Abbate A (2018) The NLRP3 inflammasome in acute myocardial infarction. *Nat Rev Cardiol* 15: 203-214. [crossref]

77. Toldo S, Mauro AG, Cutter Z, Abbate A (2018) Inflammasome, pyroptosis, and cytokines in myocardial ischaemia-reperfusion injury. *Am J Physiol Circ Physiol* 315: H1553-H1568. [crossref]

78. Zhou W, Chen C, Chen Z, Liu L, Jiang J, et al. (2018) NLRP3: A novel mediator in cardiovascular disease. *J Immunol Res* 2018: 5702103. [crossref]

79. Basker S, Klein AL, Zeft A (2016) The role of IL-1 receptor antagonist (anakinra) in idiopathic recurrent pericarditis: A narrative review. *Cardiol Res Pract* 7840724. [crossref]

80. Chiabrando JG, Bonaventura A, Vecchié A, et al. (2020) Management of acute and recurrent pericarditis. JACC state-of-art review. *J Am Coll Cardiol* 75: 76-92. [crossref]

81. Brucato A, Emmi G, Cantarini L, Di Lenarda A (2018) Management of idiopathic recurrent pericarditis in adults and children: a role of IL-1 receptor antagonism. *Int Emerg Med* 13. [crossref]

82. Lazaros G, Tousoulis D (2020) Interleukin-1 inhibition with anakinra: a valuable ally to reverse constrictive pericarditis? *Heart* 106: 1540-1542.

83. Klein AL, Imazio M, Cremer P, Brucato A, Abbate A, et al. (2021) Phase 3 trial of interleukin-trap rilonacept in recurrent pericarditis. *N Engl J Med* 384: 31-41. [crossref]

84. Pontali E, Volpi S, Antonucci G, Castellaneta M, Buzzi D, et al. (2020) Safety and efficacy of early high-dose IV anakinra in severe COVID-19 lung disease. *J Allergy Clin Immunol* 146: 213-215. [crossref]

85. Aouba A, Baldolli A, Geffray L, Verdon R, Bergot E, et al. (2020) Targeting the inflammatory cascade with anakinra in moderate to severe COVID-19 pneumonia: case series. *Ann Rheum Dis* 2020. [crossref]

86. Dimopoulos G, de Mast Q, Markou N, Theodorakopoulou M, Komnos A, et al. (2020) Favorable anakinra responses in severe Covid-19 patients with secondary hemophagocytic lymphohistiocytosis. *Cell Host Microbe* 2020. [crossref]

87. Navarro-Millán I, Sattui S, Lakhanpal A, Zisa D, Siegel C, et al. (2020) Use of anakinra to prevent mechanical ventilation in severe COVID-19: a case series. *Arthritis Rheumatol.* [crossref]

88. Huet T, Beaussier H, Voisin O, Jouveshomme S, Dauriat G, et al. (2020) Anakinra for severe forms of COVID-19: a cohort study. *Lancet Rheumatol* 2020.

89. Kooistra EJ, Waalders NJB, Grondman I, Jassen NAF, de Nooijer AH, et al. (2020) Anakinra treatment in critically ill COVID-19 patients: a prospective cohort study. *Critical Care* 24: 688. [crossref]

90. Pasin L, Cavalli G, Navalesi P, Sella N, Landoni G, et al. (2021) Anakinra for patients with COVID-19: a meta-analysis of non-randomized cohort studies. *Eur J Intern Med* 86: 34-40. [crossref]

Citation:

Syabbalo N (2021) The Role of Interleukin-1β in the Pathogenesis and Treatment of Acute Pericarditis. *J Cardiol Clin Pract* Volume 4(2): 1-5.