

Table 8: Evidence Check

26 Sep 2023

Used the search terms “cardiomyopathy” and “systematic review” or “meta-analysis” in PubMed and PsycInfo (online databases) – searching from 2020 to 2023.

Reviewed the 2023 ESC Guidelines for the management of cardiomyopathies (www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Cardiomyopathy-Guidelines) and the 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease and searched the references using the same search terms and timeframe.

Question		
BASIC BIOLOGY		
<p>B1: What are the biological mechanisms that change heart muscle cells in cardiomyopathy? Could this understanding lead to new treatments?</p>	<p>Brazdil V, Kala P, Hudec M, Poloczek M, Kanovsky J, Stipal R, Jerabek P, Bocek O, Pail M, Brazdil M. The role of central autonomic nervous system dysfunction in Takotsubo syndrome: a systematic review. Clin Auton Res. 2022 Feb;32(1):9-17. doi: 10.1007/s10286-021-00844-z. Epub 2022 Jan 8. PMID: 34997877; PMCID: PMC8898237.</p> <p>Conclusion: In this review, we aim to summarize the state of the art in the field of the brain-heart axis, regional structural and functional brain abnormalities, and connectivity aberrancies in TTS.</p>	
CAUSE		
<p>C1: What triggers the start of cardiomyopathy (e.g. age, stress, pregnancy, other health conditions)? How do these triggers work and can they be blocked?</p>	<p>Arenas DJ, Beltran S, Zhou S, Goldberg LR. Cocaine, cardiomyopathy, and heart failure: a systematic review and meta-analysis. Sci Rep. 2020 Nov 13;10(1):19795. doi: 10.1038/s41598-020-76273-1. PMID: 33188223; PMCID: PMC7666138.</p> <p>Conclusion: There is in general a need for more primary data studies that investigate heart failure and/or cardiomyopathy in cocaine users for mechanisms independent of ischemia. There were, however, enough studies to combine by meta-analyses that showed that chronic cocaine use is associated with anatomical and functional changes more consistent with diastolic heart failure instead of the commonly taught dilated cardiomyopathy pathway. In patients without a history of ACS, chronic cocaine use was not associated with significantly reduced EF. The few studies on acute cocaine had conflicting results on whether single-dose intravascular cocaine results in acute heart failure.</p>	

Fazlollahi A, Zahmatyar M, Noori M, Nejadghaderi SA, Sullman MJM, Shekarriz-Foumani R, Kolahi AA, Singh K, Safiri S. Cardiac complications following mRNA COVID-19 vaccines: A systematic review of case reports and case series. *Rev Med Virol.* 2022 Jul;32(4):e2318. doi: 10.1002/rmv.2318. Epub 2021 Dec 17. PMID: 34921468.

Conclusion: Apart from inflammatory conditions, some rare cases of Takotsubo cardiomyopathy, myocardial infarction, myocardial infarction with non-obstructive coronary arteries, and isolated tachycardia were also reported following immunisation with mRNA COVID-19 vaccines. We acknowledge that only reviewing case reports and case series studies is one potential limitation of our study.

Khalid Ahmed S, Gamal Mohamed M, Abdulrahman Essa R, Abdelaziz Ahmed Rashad Dabou E, Omar Abdulqadir S, Muhammad Omar R. Global reports of takotsubo (stress) cardiomyopathy following COVID-19 vaccination: A systematic review and meta-analysis. *Int J Cardiol Heart Vasc.* 2022 Dec;43:101108. doi: 10.1016/j.ijcha.2022.101108. Epub 2022 Aug 17. PMID: 35992364; PMCID: PMC9381427.

In conclusion, takotsubo (stress) cardiomyopathy (TCM) complications associated with COVID-19 vaccination are rare but can be life-threatening. Chest pain should be considered an alarming symptom, especially in those who have received the first and second doses of the COVID-19 vaccine.

Omidi F, Hajikhani B, Kazemi SN, Tajbakhsh A, Riazi S, Mirsaeidi M, Ansari A, Ghanbari Boroujeni M, Khalili F, Hadadi S, Nasiri MJ. COVID-19 and Cardiomyopathy: A Systematic Review. *Front Cardiovasc Med.* 2021 Jun 17;8:695206. doi: 10.3389/fcvm.2021.695206. PMID: 34222385; PMCID: PMC8248804.

Conclusions: Cardiac injury and CMPs were common conditions in patients with COVID-19. Therefore, it is suggested that cardiac damage be considered in managing patients with COVID-19.

Motamed M, Liblik K, Miranda-Arboleda AF, Wamboldt R, Wang CN, Cingolani O, Rebman AW, Novak CB, Aucott JN, Farina JM, Baranchuk A. Disseminated Lyme disease and dilated cardiomyopathy: A systematic review. *Trends Cardiovasc Med.* 2022 Jun 3:S1050-1738(22)00077-9. doi: 10.1016/j.tcm.2022.05.010. Epub ahead of print. PMID: 35667636.

Conclusion: Although most studies (7/11) identified evidence associating Borrelia-infection with DCM, further research is required to isolate late disseminated Borrelia infection as a causative agent of DCM.

Pereañez JA, Granados J, Agudelo R. Tako-tsubo cardiomyopathy in clinical toxinology: A systematic review. *Toxicon*. 2022 Nov;219:106929. doi: 10.1016/j.toxicon.2022.09.015. Epub 2022 Sep 24. PMID: 36162498.

Conclusion: We hypothesized the possible mode of action of venoms, toxins or poisons to induce TTC, however other mechanisms may exist, but they have not been described yet. Therefore, further studies are needed. In some cases, venoms, toxins, or poisons might cause catecholamine discharge either directly or indirectly, therefore, this was suggested as the trigger of TTC. Finally, the appearance of TTC should be considered in clinical toxinology.

Mohamed AA, Basaran T, Othman MH, Andersen NH, Bonnema SJ. The association between Takotsubo cardiomyopathy and thyrotoxicosis: A systematic review. *Endocrine*. 2022 Dec;78(3):418-428. doi: 10.1007/s12020-022-03174-w. Epub 2022 Aug 26. PMID: 36018537.

Conclusion: Evidence-based on current case reports suggests an increased risk of Takotsubo Syndrome and subsequently increased risk of in-hospital complications in patients with thyrotoxicosis.

Lou X, Zhang Y, Guo J, Gao L, Ding Y, Zhuo X, Lei Q, Bian J, Lei R, Gong W, Zhang X, Jiao Q. What is the impact of ferroptosis on diabetic cardiomyopathy: a systematic review. *Heart Fail Rev*. 2023 Aug 9. doi: 10.1007/s10741-023-10336-z. Epub ahead of print. PMID: 37555989.

Conclusion: Iron overload increases the production of harmful reactive oxygen species in the Fenton reaction, which causes oxidative stress in the body and lipid peroxidation in the cell membrane, and eventually leads to ferroptosis. Diabetes is associated with increased intracellular oxidative stress, inflammation, autophagy, microRNA alterations, and advanced glycation end products (AGEs), which cause cardiac remodeling and cardiac diastolic contractile dysfunction, leading to the development of diabetic cardiomyopathy (DCM). While these factors are also closely associated with ferroptosis, more and more studies have shown that iron-mediated ferroptosis is an important causative factor in DCM. In order to gain fresh insights into the functions of ferroptosis in DCM, this review methodically summarizes the traits and mechanisms connected with ferroptosis and DCM.

Cherubin S, Peoples T, Gillard J, Lakhal-Littleton S, Kurinczuk JJ, Nair M. Systematic review and meta-analysis of prolactin and iron deficiency in peripartum cardiomyopathy. *Open Heart*. 2020 Oct;7(2):e001430. doi: 10.1136/openhrt-2020-001430. Erratum in: *Open Heart*. 2020 Nov;7(2): PMID: 33060142; PMCID: PMC7566429.

Conclusions: More robust molecular studies are needed to explore the association between prolactin and PPCM in human subjects and to determine the extent to which iron deficiency (with or without anaemia) contributes to the risk of PPCM.

Khatami A, Razizadeh MH, Ghadirali M, Yazdani S, Bahadory S, Soleimani A. Association of parvovirus B19 and myocarditis/dilated cardiomyopathy: A systematic review and meta-analysis. *Microb Pathog*. 2022 Jan;162:105207. doi: 10.1016/j.micpath.2021.105207. Epub 2021 Sep 24. PMID: 34563612.

Conclusion: Our findings have shown a significant association between Parvovirus B19 and myocarditis with a high prevalence. In the case of DCM, no significant association was found while the prevalence of the virus was relatively high.

Putra ICS, Irianto CB, Raffaello WM, Suciadi LP, Prameswari HS. Pre-pregnancy obesity and the risk of peripartum cardiomyopathy: A systematic review and meta-analysis. *Indian Heart J*. 2022 May-Jun;74(3):235-238. doi: 10.1016/j.ihj.2022.04.009. Epub 2022 Apr 28. PMID: 35490847; PMCID: PMC9243620.

Conclusion: Pre-pregnancy obesity was significantly associated with PPCM incidence compared to normal-weight subjects.

Lopera V, Pereañez JA, Amariles P. Drugs as Possible Triggers of Takotsubo Cardiomyopathy- Update 2022: Systematic Review. *Curr Vasc Pharmacol*. 2023 May 17. doi: 10.2174/1570161121666230517121037. Epub ahead of print. PMID: 37198980.

Conclusion: There are new case reports that link drugs with the development of TCM. The current list is principally made up of drugs that generate sympathetic overstimulation. However, some of the listed drugs do not have a clear link with sympathetic activation.

	<p>Alhuarrat MAD, Barzallo D, Seo J, Naser A, Alhuarrat MR, Minuti A, Kokkinidis DG, Schizas D. Meta-Analysis and Clinical Features of Perioperative Takotsubo Cardiomyopathy in Noncardiac Surgery. <i>Am J Cardiol.</i> 2023 Aug 15;201:78-85. doi: 10.1016/j.amjcard.2023.06.015. Epub 2023 Jun 21. PMID: 37352669.</p> <p>Conclusion: In conclusion, the risk factors, triggers, and outcomes of pTCM appear to differ from those of classic nonperioperative TCM presentations. Future studies will help shed light on this more frequently diagnosed condition complicating some noncardiac surgical cases.</p> <p>Y-Hassan S, Falhammar H. Clinical features, complications, and outcomes of exogenous and endogenous catecholamine-triggered Takotsubo syndrome: A systematic review and meta-analysis of 156 published cases. <i>Clin Cardiol.</i> 2020 May;43(5):459-467. doi: 10.1002/clc.23352. Epub 2020 Mar 3. PMID: 32125009; PMCID: PMC7244299.</p> <p>In conclusion, catecholamine-induced TS was characterized by a dramatic clinical presentation with extensive left ventricular dysfunction, and high complication rate.</p> <p>Ghasemi H, Kazemian S, Nejadghaderi SA, Shafie M. Takotsubo syndrome and COVID-19: A systematic review. <i>Health Sci Rep.</i> 2022 Dec 2;6(1):e972. doi: 10.1002/hsr2.972. PMID: 36479387; PMCID: PMC9718950.</p> <p>Conclusion: The TTS in patients with COVID-19 is almost rare, whereas it could lead to a great mortality and morbidity. An individual with COVID-19, especially an elderly woman, presented with dyspnea in addition to a rise in brain natriuretic peptide and troponin should be evaluated for TTS.</p>	
<p>C3: Which genetic variants are linked to cardiomyopathy, beyond the ones that are already identified?</p>		
<p>C4: What is the likelihood of developing cardiomyopathy for people with a relevant</p>	<p>Chandrashekar P, Alhuneafat L, Mannello M, Al-Rashdan L, Kim MM, Dungu J, Alexander K, Masri A. Prevalence and Outcomes of p.Val142Ile TTR Amyloidosis Cardiomyopathy: A Systematic Review. <i>Circ Genom Precis Med.</i> 2021 Oct;14(5):e003356. doi: 10.1161/CIRCGEN.121.003356. Epub 2021 Aug 31. PMID: 34461737; PMCID: PMC8530896.</p>	

<p>genetic variant?</p>	<p>Conclusions: The p.Val142Ile variant is the most common variant of the transthyretin gene with most carriers being of African descent. The true penetrance is unknown but the p.Val142Ile variant is associated with increased rates of incident heart failure and portends a lower overall survival. Increased awareness could lead to earlier diagnosis and improved heart failure outcomes among those of African descent, which is of increasing importance given the advent of novel therapeutics for this disease.</p> <p>Christian S, Cirino A, Hansen B, Harris S, Murad AM, Natoli JL, Malinowski J, Kelly MA. Diagnostic validity and clinical utility of genetic testing for hypertrophic cardiomyopathy: a systematic review and meta-analysis. <i>Open Heart</i>. 2022 Apr;9(1):e001815. doi: 10.1136/openhrt-2021-001815. PMID: 35387861; PMCID: PMC8987756.</p> <p>Conclusions: Overall, disease penetrance in adult cohorts was 62%, but differed significantly depending on if probands were included or excluded (73% vs 55%; p=0.003). This systematic review and meta-analysis is the first, to our knowledge, to collectively quantify historical understandings of detection rate, genotype-phenotype associations and disease penetrance for HCM, while providing the answers to important routine clinical questions and highlighting key areas for future study.</p> <p>Parker LE, Kramer RJ, Kaplan S, Landstrom AP. One gene, two modes of inheritance, four diseases: A systematic review of the cardiac manifestation of pathogenic variants in JPH2-encoded junctophilin-2. <i>Trends Cardiovasc Med</i>. 2023 Jan;33(1):1-10. doi: 10.1016/j.tcm.2021.11.006. Epub 2021 Dec 1. PMID: 34861382; PMCID: PMC9156715.</p> <p>Conclusions: In analyzing the 24 probands described in the studies, we found that autosomal recessive, loss-of-function variants are associated with severe, early onset DCM, while autosomal dominant missense variants are associated with a wider range of cardiac disease, including HCM, arrhythmia, SCD, and cardiac conduction disease.</p> <p>Fang HJ, Liu BP. Prevalence of TTN mutations in patients with dilated cardiomyopathy : A meta-analysis. <i>Herz</i>. 2020 Dec;45(Suppl 1):29-36. English. doi: 10.1007/s00059-019-4825-4. Epub 2019 Jun 17. PMID: 31209521.</p> <p>Conclusions: In conclusion, the present analysis suggests that TTN mutations are familial in DCM patients.</p>	
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	<p>More attention should be paid to TTN mutations in clinical examinations.</p> <p>Shen J, Qian X, Mei X, Yao J, Jiang H, Li K, Chen T, Jiang Y, Zhou Y. Effect of rs4646994 polymorphism of angiotensin-converting enzyme on the risk of nonischemic cardiomyopathy. <i>Biosci Rep.</i> 2021 Dec 22;41(12):BSR20211617. doi: 10.1042/BSR20211617. PMID: 34750628; PMCID: PMC8685642.</p> <p>Conclusion: ACE rs4646994 polymorphism increases the risk of DCM/HCM in Asians, but not in Caucasians. More case-control studies are needed to strengthen our conclusions and to assess the gene-gene and gene-environment interactions between ACE rs4646994 polymorphism and DCM/HCM.</p> <p>Shalata W, Abu-Salman A, Steckbeck R, Mathew Jacob B, Massalha I, Yakobson A. Cardiac Toxicity Associated with Immune Checkpoint Inhibitors: A Systematic Review. <i>Cancers (Basel).</i> 2021 Oct 18;13(20):5218. doi: 10.3390/cancers13205218. PMID: 34680365; PMCID: PMC8534225.</p> <p>Conclusion: Patients with this toxicity may present with myocarditis, pericarditis, Takotsubo cardiomyopathy, conduction disorders, and others within just a few weeks of starting immune checkpoint inhibitors. We present here a review of the current research on immune checkpoint inhibitors, their associated cardiotoxicities, the timing of presentation of these conditions, lab tests and histology for each condition, and finally the treatment of patients with cardiotoxicity. We observe a positive skew in the onset of presentation, which is significant for the treating physician.</p>
<p>C5: How can damage to the heart be prevented during cancer treatment, or treated afterwards?</p>	<p>Cozma A, Sporis ND, Lazar AL, Buruiana A, Ganea AM, Malinescu TV, Berechet BM, Fodor A, Sitar-Taut AV, Vlad VC, Negrean V, Orasan OH. Cardiac Toxicity Associated with Immune Checkpoint Inhibitors: A Systematic Review. <i>Int J Mol Sci.</i> 2022 Sep 19;23(18):10948. doi: 10.3390/ijms231810948. PMID: 36142866; PMCID: PMC9502843.</p> <p>Conclusion: A variety of cardiac-adverse effects are associated with ICI-based treatment, including pericarditis, arrhythmias, cardiomyopathy, and acute coronary syndrome, with myocarditis being the most studied due to its often-unexpected onset and severity. Considering the rising number of oncological patients treated with ICIs and the severity of their potential adverse effects, a good understanding and continuous investigation of cardiac irAEs is of the utmost importance. This systematic review aimed to revise recent publications (between 2016-2022) on ICI-induced cardiac toxicities and highlight the therapeutical approach and evolution in the selected cases.</p>

Shehram M, Khalid H, Shafique HM, Umer B, Zafar A, Ullah A, Zaidi SMJ, Basit J, Mehmoodi A, Malik J. Efficacy and safety of cardiac resynchronization therapy in chemotherapy-induced cardiomyopathy: A systematic review. *Ann Noninvasive Electrocardiol.* 2023 Sep;28(5):e13070. doi: 10.1111/anec.13070. Epub 2023 Jul 12. PMID: 37435629; PMCID: PMC10475884.

Conclusion: CRT was associated with improvement in all patient parameters with CIC.

Kim J, Nishimura Y, Kewcharoen J, Yess J. Statin Use Can Attenuate the Decline in Left Ventricular Ejection Fraction and the Incidence of Cardiomyopathy in Cardiotoxic Chemotherapy Recipients: A Systematic Review and Meta-Analysis. *J Clin Med.* 2021 Aug 22;10(16):3731. doi: 10.3390/jcm10163731. PMID: 34442027; PMCID: PMC8397057.

Conclusion: Consequently, our study showed a significant reduction in the incidence of chemotherapy-induced cardiomyopathy and the degree of LVEF decline in patients in the statin group compared to those in the control group.

Keshavarzian E, Sadighpour T, Mortazavizadeh SM, Soltani M, Motevalipour AF, Khamas SS, Moazen M, Kogani M, Amin Hashemipour SM, Hosseinpour H, Valizadeh R. Prophylactic Agents for Preventing Cardiotoxicity Induced Following Anticancer Agents: A Systematic Review and Meta-Analysis of Clinical Trials. *Rev Recent Clin Trials.* 2023;18(2):112-122. doi: 10.2174/1574887118666230118102252. PMID: 36803186.

Conclusion: This meta-analysis showed that prophylactic treatment with cardio-protective drugs, including dexrazoxane, beta blocker, and ACEI drugs in patients undergoing chemotherapy with anthracycline, have a protective effect on LVEF and prevent EF drop.

Xu L, Long Y, Tang X, Zhang N. Cardioprotective Effects and Duration of Beta Blocker Therapy in Anthracycline-Treated Patients: A Systematic Review and Meta-analysis. *Cardiovasc Toxicol.* 2020 Feb;20(1):11-19. doi: 10.1007/s12012-019-09558-1. PMID: 31832905.

Conclusion: Prophylactic administration of beta blocker-based cardioprotective therapy may be beneficial to the myocardial preservation in anthracycline-treated patients. And long-term use of beta blocker appears to have a positive effect on ameliorating anthracycline-induced cardiomyopathy, especially in patients exposed to moderate accumulative doses of anthracycline.

	<p>Avila MS, Siqueira SRR, Waldeck L, Ayub-Ferreira SM, Takx R, Bittencourt MS, Bocchi EA. Renin-angiotensin System Antagonists and Beta-blockers in Prevention of Anthracycline Cardiotoxicity: a Systematic Review and Meta-analysis. <i>Arq Bras Cardiol.</i> 2023 May 26;120(5):e20220298. English, Portuguese. doi: 10.36660/abc.20220298. PMID: 37255127; PMCID: PMC10484562.</p> <p>Conclusion: The use of RAAS inhibitors and beta-blockers to prevent anthracycline-induced cardiotoxicity was associated with less pronounced reduction in LVEF, higher final LVEF, and lower incidence of heart failure. No changes in mortality were observed.</p> <p>Gao Y, Wang R, Jiang J, Hu Y, Li H, Wang Y. ACEI/ARB and beta-blocker therapies for preventing cardiotoxicity of antineoplastic agents in breast cancer: a systematic review and meta-analysis. <i>Heart Fail Rev.</i> 2023 Jul 7. doi: 10.1007/s10741-023-10328-z. Epub ahead of print. PMID: 37414918.</p> <p>Conclusion: In an exploratory subgroup analysis, the benefit of experimental agents on LVEF, whether anthracyclines or trastuzumab, was prominent in patients treated with ACEIs, ARBs, and BBs. Compared to placebo, ACEI/ARB and BB treatments in breast cancer patients protect against cardiotoxicity after trastuzumab and anthracycline-containing medication treatment, indicating a benefit for both.</p>	
<p>C8: How is cardiomyopathy linked to atrial fibrillation (an irregular and fast heartbeat)?</p>	<p>Ye TTS, Siah QZ, Tan BYQ, Ho JSY, Syn NLX, Teo YH, Teo YN, Yip JW, Yeo TC, Lin W, Wong RCC, Chai P, Chan B, Sharma VK, Yeo LLL, Sia CH. Ischaemic events in hypertrophic cardiomyopathy patients with and without atrial fibrillation: a systematic review and meta-analysis. <i>J Thromb Thrombolysis.</i> 2023 Jan;55(1):83-91. doi: 10.1007/s11239-022-02713-6. Epub 2022 Oct 3. PMID: 36192663.</p> <p>Conclusion: Concomitant atrial fibrillation in hypertrophic cardiomyopathy increases the risk of thromboembolic events including ischaemic stroke and transient ischaemic attack. The apical subgroup shows a similar risk of acute cerebrovascular events as the overall hypertrophic cardiomyopathy population.</p>	
<p>C9: Why are people with the same genetic variant affected differently? Why do some people with a genetic variant never</p>	<p>Christian S, Cirino A, Hansen B, Harris S, Murad AM, Natoli JL, Malinowski J, Kelly MA. Diagnostic validity and clinical utility of genetic testing for hypertrophic cardiomyopathy: a systematic review and meta-analysis. <i>Open Heart.</i> 2022 Apr;9(1):e001815. doi: 10.1136/openhrt-2021-001815. PMID: 35387861; PMCID: PMC8987756.</p>	

<p>develop cardiomyopathy? Could this understanding lead to new treatments?</p>	<p>Conclusions: The mean difference in age-of-onset in adults was significantly earlier for genotype-positive versus genotype-negative cohorts (8.3 years; $p < 0.0001$), MYH7 versus MYBPC3 cohorts (8.2 years; $p < 0.0001$) and individuals with multiple versus single variants (7.0 years; $p < 0.0002$). This systematic review and meta-analysis is the first, to our knowledge, to collectively quantify historical understandings of detection rate, genotype-phenotype associations and disease penetrance for HCM, while providing the answers to important routine clinical questions and highlighting key areas for future study.</p> <p>Grondin S, Wazirian AC, Jorda P, Terrone DG, Gagnon J, Robb L, Amyot J, Rivard L, Pagé S, Talajic M, Cadrin-Tourigny J, Tadros R. Missense variants in the spectrin repeat domain of DSP are associated with arrhythmogenic cardiomyopathy: A family report and systematic review. <i>Am J Med Genet A</i>. 2020 Oct;182(10):2359-2368. doi: 10.1002/ajmg.a.61799. Epub 2020 Aug 18. PMID: 32808748.</p> <p>Conclusion: Our findings highlight the predominance of cardiac arrhythmia and left ventricular involvement in desmoplakin cardiomyopathy and pinpoint to a potential mutation hotspot in DSP thereby facilitating missense variant interpretation in the diagnostic setting.</p>
<p>DIAGNOSIS</p>	
<p>D1: How can children and adults at risk of cardiomyopathy be identified earlier, before they have symptoms or know they have a genetic variant?</p>	
<p>D2: How can existing or new tests be used to diagnose cardiomyopathy most effectively?</p>	<p>Diaz-Arocutipa C, Saucedo-Chinchay J, Imazio M, Argulian E. Natriuretic peptides to differentiate constrictive pericarditis and restrictive cardiomyopathy: A systematic review and meta-analysis. <i>Clin Cardiol</i>. 2022 Mar;45(3):251-257. doi: 10.1002/clc.23772. Epub 2021 Dec 30. PMID: 34967020; PMCID: PMC8922532.</p> <p>Conclusion: Our review shows that BNP and NT-proBNP levels were significantly lower in patients with CP compared to RCM. The pooled AUC of BNP level showed a good diagnostic accuracy to differentiate both conditions.</p>

Bay K, Gustafsson F, Maiborg M, Bagger-Bahnsen A, Strand AM, Pilgaard T, Poulsen SH. Suspicion, screening, and diagnosis of wild-type transthyretin amyloid cardiomyopathy: a systematic literature review. *ESC Heart Fail.* 2022 Jun;9(3):1524-1541. doi: 10.1002/ehf2.13884. Epub 2022 Mar 27. PMID: 35343098; PMCID: PMC9065854.

Conclusion: The European Society of Cardiology recommends to screen patients with a wall thickness ≥ 12 mm and heart failure, aortic stenosis, or red flag symptoms, especially if they are >65 years. The underlying evidence was generally good for diagnosis, while significant gaps were identified for the relevance and mutual ranking of the different suspicion criteria and for systematic screening. Conclusively, patient entry was neglected in the reviewed literature. While multiple red flags were described, high-quality prospective studies designed to evaluate their suitability as suspicion criteria were lacking. An upcoming task lies in defining and evaluating at-risk populations for screening. All are steps needed to promote early detection and diagnosis of ATTRwt CM, a prerequisite for timely treatment.

Tingen HSA, Tubben A, van 't Oever JH, Pastoor EM, van Zon PPA, Nienhuis HLA, van der Meer P, Slart RHJA. Positron emission tomography in the diagnosis and follow-up of transthyretin amyloid cardiomyopathy patients: A systematic review. *Eur J Nucl Med Mol Imaging.* 2023 Aug 10. doi: 10.1007/s00259-023-06381-3. Epub ahead of print. Erratum in: *Eur J Nucl Med Mol Imaging.* 2023 Aug 22;; PMID: 37561144.

Conclusion: [^{11}C]PIB, Na[^{18}F]F and [^{18}F]FBP can be used to diagnose cardiac amyloidosis, although [^{18}F]FBP may not be suitable for the distinction of different types of amyloid cardiomyopathy. No studies on PET in the follow-up of ATTR amyloidosis patients were found. Future research should focus on the use of these PET tracers in the follow-up of ATTR amyloidosis patients.

Bakogiannis C, Mouselimis D, Tsarouchas A, Papatheodorou E, Vassilikos VP, Androulakis E. Hypertrophic cardiomyopathy or athlete's heart? A systematic review of novel cardiovascular magnetic resonance imaging parameters. *Eur J Sport Sci.* 2023 Jan;23(1):143-154. doi: 10.1080/17461391.2021.2001576. Epub 2021 Dec 2. PMID: 34720041.

Conclusion: Several novel CMR-derived parameters, most of which are currently under development,

show promising results in discerning between athlete's heart and HCM. Prospective studies examining the discriminatory capacity of all promising modalities side-by-side will yield definitive answers on their relative importance; diagnostic models can incorporate the best performing variables for optimal results.

Grondin S, Wazirian AC, Jorda P, Terrone DG, Gagnon J, Robb L, Amyot J, Rivard L, Pagé S, Talajic M, Cadrin-Tourigny J, Tadros R. Missense variants in the spectrin repeat domain of DSP are associated with arrhythmogenic cardiomyopathy: A family report and systematic review. *Am J Med Genet A*. 2020 Oct;182(10):2359-2368. doi: 10.1002/ajmg.a.61799. Epub 2020 Aug 18. PMID: 32808748.

Conclusion: Our findings highlight the predominance of cardiac arrhythmia and left ventricular involvement in desmoplakin cardiomyopathy and pinpoint to a potential mutation hotspot in DSP thereby facilitating missense variant interpretation in the diagnostic setting.

Wang J, Chen D, Dong F, Chi H. Diagnostic Sensitivity of Abdominal Fat Aspiration Biopsy for Cardiac Amyloidosis: A Systematic Review and Meta-Analysis. *Int J Surg Pathol*. 2023 Jun 6:10668969231177603. doi: 10.1177/10668969231177603. Epub ahead of print. PMID: 37282575.

Conclusion. Abdominal fat aspiration biopsy has high sensitivity and clinical value in the diagnosis of light chain amyloidosis cardiomyopathy, whereas there are limitations in the diagnosis of transthyretin amyloidosis cardiomyopathy.

Wu Z, Yu C. Diagnostic performance of CMR, SPECT, and PET imaging for the detection of cardiac amyloidosis: a meta-analysis. *BMC Cardiovasc Disord*. 2021 Oct 7;21(1):482. doi: 10.1186/s12872-021-02292-z. PMID: 34620092; PMCID: PMC8499558.

Conclusion: Our meta-analysis reveals that SEPCT scans present better diagnostic performance for the identification of CA as compared with other two modalities.

Pan JA, Kerwin MJ, Salerno M. Native T1 Mapping, Extracellular Volume Mapping, and Late Gadolinium Enhancement in Cardiac Amyloidosis: A Meta-Analysis. *JACC Cardiovasc Imaging*. 2020 Jun;13(6):1299-1310. doi: 10.1016/j.jcmg.2020.03.010. PMID: 32498919; PMCID: PMC7340140.

Conclusions: ECV demonstrates a higher diagnostic OR for assessing cardiac amyloid than LGE and a higher HR for adverse events compared with LGE and native T1. In addition, native T1 showed similar

	<p>sensitivity and specificity as ECV and LGE without requiring contrast material. Although limited by study heterogeneity, this meta-analysis suggests that ECV provides high diagnostic and prognostic utility for the assessment of cardiac amyloidosis.</p>	
<p>D4: How often should family members at risk of developing cardiomyopathy be screened and which are the best tests to use? When is it safe to stop screening?</p>	<p>Aziz A, Musiol SK, Moody WE, Pickup L, Cooper R, Lip GYH. Clinical prediction of genotypes in hypertrophic cardiomyopathy: A systematic review. Eur J Clin Invest. 2021 Aug;51(8):e13593. doi: 10.1111/eci.13593. Epub 2021 May 25. PMID: 33948946.</p> <p>Conclusion: Using clinical predictors to decide whom to test is a feasible alternative to investigating all comers. Nonetheless, currently there is not enough evidence to unequivocally recommend for or against this strategy. Further validation of current predictors and identification of new ones remain open research avenues.</p> <p>Sharma A, Bosman LP, Tichnell C, Nanavati J, Murray B, Nonyane BAS, Tandri H, Calkins H, James CA. Arrhythmogenic Right Ventricular Cardiomyopathy Prevalence and Arrhythmic Outcomes in At-Risk Family Members: A Systematic Review and Meta-Analysis. Circ Genom Precis Med. 2022 Jun;15(3):e003530. doi: 10.1161/CIRCGEN.121.003530. Epub 2022 May 17. PMID: 35579515.</p> <p>Conclusions: The prevalence of ARVC and VA in at-risk family members differs significantly based on family genotype. Although recent recommendations provide a guideline based only on age, we propose screening every 1 to 2 years for gene-positive family members and every 3 to 5 years for first-degree relatives of gene-elusive cases, as long as they are asymptomatic and not athletes.</p>	
<p>D5: Could genetic or routine tests (e.g. ECGs – recordings of electrical heart activity) be used to screen the general public for cardiomyopathy?</p>		
<p>D6: What are the best ways to communicate the genetic risk of cardiomyopathy to</p>		

affected families?		
HEALTH SERVICES		
H2: What are the best ways to provide holistic care for people with cardiomyopathy, so that all their health and support needs can be addressed at the same time?	<p>Carroll AJ, Goergen J, Wafford QE, Flaherty JD, Grady KL, Feingold KL. Psychiatric conditions in patients presenting with Takotsubo syndrome: A systematic review and synthesis of case studies. <i>Gen Hosp Psychiatry</i>. 2020 Jul-Aug;65:54-63. doi: 10.1016/j.genhosppsy.2020.05.010. Epub 2020 May 28. PMID: 32497926.</p> <p>Conclusions: Despite heterogeneous psychiatric presentations among TS patients, psychiatric treatment was rarely incorporated into the medical care or addressed at follow-up. This gap may be better attended to by integrating psychiatrists and psychologists into the multidisciplinary treatment team.</p>	
H4: What does ongoing monitoring and long-term care for people with cardiomyopathy need to include?		
H5: Are there better ways to measure the course of cardiomyopathy, to assess how the condition changes over time? Could these measurements help to target treatment and care to the people most in need?	<p>Serraino GF, Jiritano F, Costa D, Ielapi N, Napolitano D, Mastroberto P, Bracale UM, Andreucci M, Serra R. Metalloproteinases and Hypertrophic Cardiomyopathy: A Systematic Review. <i>Biomolecules</i>. 2023 Apr 11;13(4):665. doi: 10.3390/biom13040665. PMID: 37189412; PMCID: PMC10136246.</p> <p>Conclusion: MMPs-particularly MMP2-levels were found higher in HCM patients compared to healthy subjects. MMPs were used as biomarkers after surgical and percutaneous treatments. Understanding the molecular processes that control the cardiac ECM's collagen turnover allows for a non-invasive evaluation of HCM patients through the monitoring of MMPs and TIMPs.</p> <p>Scolari FL, Faganello LS, Garbin HI, Piva E Mattos B, Biolo A. A systematic review of microRNAs in patients with hypertrophic cardiomyopathy. <i>Int J Cardiol</i>. 2021 Mar 15;327:146-154. doi: 10.1016/j.ijcard.2020.11.004. Epub 2020 Nov 16. PMID: 33212095.</p> <p>Conclusion: Eighty-seven miRNAs were differentially expressed in HCM patients, the majority in up-regulation. Mir-21, mir-29a and mir-133 were the most reported. Correlation with left ventricular hypertrophy and fibrosis was evaluated in six studies for several miRNAs, nevertheless, mir-29a showed</p>	

more consistent findings and seems to be a promising biomarker.

Lewandowski P, Gołowski M, Baron M, Reichman-Warmusz E, Wojnicz R. A Systematic Review of miRNA and cfDNA as Potential Biomarkers for Liquid Biopsy in Myocarditis and Inflammatory Dilated Cardiomyopathy. *Biomolecules*. 2022 Oct 13;12(10):1476. doi: 10.3390/biom12101476. PMID: 36291684; PMCID: PMC9599237.

Conclusion: Serum levels of three miRNAs-miR-Chr8:96, miR-155, and miR-206-are the best candidates for myocardial inflammation liquid biopsy panel. Further studies are necessary to prove their role, specificity, and sensitivity.

Fong LCW, Lee NHC, Poon JW, Chin CWL, He B, Luo L, Chen C, Wan EYF, Pennell DJ, Mohiaddin R, Ng MY. Prognostic value of cardiac magnetic resonance derived global longitudinal strain analysis in patients with ischaemic and non-ischaemic dilated cardiomyopathy: a systematic review and meta-analysis. *Int J Cardiovasc Imaging*. 2022 Dec;38(12):2707-2721. doi: 10.1007/s10554-022-02679-9. Epub 2022 Aug 4. PMID: 36445666.

Conclusion: LVEF in IDCM and NDCM became an insignificant prognostic marker in multivariable analysis. CMR LV-GLS shows promise as an independent predictor of mortality in IDCM and NDCM patients. However, in patients with LVEF < 30% LV-GLS may have less prognostic value.

Kiaos A, Antonakaki D, Bazmpani MA, Karvounis C, Rimoldi O, Karamitsos TD. Prognostic value of cardiovascular magnetic resonance T1 mapping techniques in non-ischemic dilated cardiomyopathy: A systematic review and meta-analysis. *Int J Cardiol*. 2020 Aug 1;312:110-116. doi: 10.1016/j.ijcard.2020.04.052. Epub 2020 Apr 19. PMID: 32320782.

Conclusions: ECV and native T1 could potentially be used to improve risk stratification in DCM. Future studies should investigate the prognostic value of T1 mapping by separating mortality and morbidity as primary outcomes and evaluate its incremental value in addition to standard risk stratification criteria.

Dorobantu DM, Wadey CA, Amir NH, Stuart AG, Williams CA, Pieles GE. The Role of Speckle Tracking Echocardiography in the Evaluation of Common Inherited Cardiomyopathies in Children and Adolescents:

	<p>A Systematic Review. <i>Diagnostics</i> (Basel). 2021 Apr 1;11(4):635. doi: 10.3390/diagnostics11040635. PMID: 33915862; PMCID: PMC8066718.</p> <p>Conclusions: STE in childhood cardiomyopathies can detect early changes which may not be associated with changes in cardiac function detectable by non-STE methods. Longitudinal and circumferential strain should be introduced in the cardiomyopathy echocardiography protocol, reflecting current practice in adults.</p>	
<p>H6: What causes inequalities in accessing genetic tests, treatment and care amongst people affected by cardiomyopathy? How can this be improved?</p>		
<p>H7: Do people with cardiomyopathy experience better outcomes if they are treated at a specialist clinic rather than a general clinic?</p>		
<p>SELF MANAGEMENT</p>		
<p>M1: What is a safe and beneficial level of physical activity or exercise for people with cardiomyopathy?</p>	<p>Martínez-Solé J, Sabater-Molina M, Braza-Boïls A, Santos-Mateo JJ, Molina P, Martínez-Dolz L, Gimeno JR, Zorio E. Facts and Gaps in Exercise Influence on Arrhythmogenic Cardiomyopathy: New Insights From a Meta-Analysis Approach. <i>Front Cardiovasc Med</i>. 2021 Oct 18;8:702560. doi: 10.3389/fcvm.2021.702560. Erratum in: <i>Front Cardiovasc Med</i>. 2022 Feb 04;8:816280. PMID: 34733888; PMCID: PMC8558346.</p> <p>Conclusion: Hopefully, future research endeavors will provide solid evidence about the safest exercise dose for each patient from a personalized medicine perspective, taking into account a big batch of genetic, epigenetic, and epidemiological variables, for instance, in order to assist clinicians to provide a</p>	

	final tailored recommendation.	
M2: What are the best ways for people with cardiomyopathy to monitor their symptoms at home and to know when to seek medical help?		
M3: What lifestyle changes (e.g. diet) may help adults and children with a genetic risk to reduce their likelihood of developing cardiomyopathy?		
M4: What lifestyle changes (e.g. diet, avoiding alcohol) help people with cardiomyopathy to avoid getting worse, and/or reduce their risk of heart failure and sudden death?	<p>Tsartsalis D, Korela D, Karlsson LO, Foukarakis E, Svensson A, Anastasakis A, Venetsanos D, Aggeli C, Tsioufis C, Braunschweig F, Dragioti E, Charitakis E. Risk and Protective Factors for Sudden Cardiac Death: An Umbrella Review of Meta-Analyses. <i>Front Cardiovasc Med.</i> 2022 Jun 16;9:848021. doi: 10.3389/fcvm.2022.848021. PMID: 35783841; PMCID: PMC9246322.</p> <p>Conclusions: Lifestyle risk factors (physical activity, smoking), comorbidities like DM, and electrocardiographic features like ERP constitute modifiable risk factors of SCD. Alternatively, the use of MRA, beta-blockers, SGLT-2 inhibitors, and ICD in patients with HF are credible protective factors. Further investigation targeted in specific populations will be important for reducing the burden of SCD.</p>	
M5: What is a safe and beneficial level of exercise for adults and children with a genetic risk of cardiomyopathy?		
M6: What can be learnt about the treatment and		

management of cardiomyopathy from the people who improve faster than others?

PROGNOSIS

R1: What are the risks associated with pregnancy for people with cardiomyopathy? Can these risks be predicted and reduced? How is cardiomyopathy best treated during pregnancy?

Trongtorsak A, Kittipibul V, Mahabir S, Ibrahim M, Saint Croix GR, Hernandez GA, Chaparro S. Effects of bromocriptine in peripartum cardiomyopathy: a systematic review and meta-analysis. Heart Fail Rev. 2022 Mar;27(2):533-543. doi: 10.1007/s10741-021-10185-8. Epub 2021 Nov 1. PMID: 34725781.

Conclusion: In conclusion, the addition of bromocriptine to standard HF treatment in PPCM was associated with significantly higher survival and higher LVEF improvement. No association with lower composite adverse clinical outcomes or LVEF recovery was seen. The findings, although encouraging, warrant larger randomized-controlled studies.

Badianyama M, Das PK, Gaddameedi SR, Saukhla S, Nagammagari T, Bandari V, Mohammed L. A Systematic Review of the Utility of Bromocriptine in Acute Peripartum Cardiomyopathy. Cureus. 2021 Sep 24;13(9):e18248. doi: 10.7759/cureus.18248. PMID: 34603902; PMCID: PMC8475739.

Conclusion: Notably, bromocriptine combined with conventional HF treatment reduced mortality associated with PPCM, and no thromboembolism events were recorded in the 263 patients. PPCM is a severe condition affecting women globally. In this study, the combination of bromocriptine with conventional HF treatment enhanced the LVEF of women with acute PPCM and their clinical outcomes.

Kumar A, Ravi R, Sivakumar RK, Chidambaram V, Majella MG, Sinha S, Adamo L, Lau ES, Al'Aref SJ, Asnani A, Sharma G, Mehta JL. Prolactin Inhibition in Peripartum Cardiomyopathy: Systematic Review and Meta-analysis. Curr Probl Cardiol. 2023 Feb;48(2):101461. doi: 10.1016/j.cpcardiol.2022.101461. Epub 2022 Oct 17. PMID: 36261102; PMCID: PMC9805509.

Conclusion: Our analysis demonstrates that the addition of Bromocriptine to standard GDMT was associated with a significant improvement in LVEF% and greater odds of LV recovery, without significant reduction in all-cause mortality.

Eggleton EJ, McMurrugh KJ, Aiken CE. Maternal pregnancy outcomes in women with cardiomyopathy: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2022 Oct;227(4):582-592. doi: 10.1016/j.ajog.2022.05.039. Epub 2022 May 21. PMID: 35609641.

Conclusion: Pregnant women with cardiomyopathy have increased risks for adverse maternal outcomes, including maternal death, when compared with both women with no heart disease and women with noncardiomyopathy heart disease. Our results highlight the importance of preconception risk assessments to allow for informed decision-making before pregnancy. Pregnancies affected by cardiomyopathy are high risk and should be managed by expert, multidisciplinary obstetrical and cardiology teams.

Eggleton EJ, McMurrugh KJ, Aiken CE. Perinatal outcomes in pregnancies complicated by maternal cardiomyopathy: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2023 Mar;228(3):283-291. doi: 10.1016/j.ajog.2022.09.025. Epub 2022 Sep 20. PMID: 36150520.

Conclusion: There was an increased likelihood of adverse perinatal outcomes in pregnancies affected by maternal cardiomyopathy compared with both pregnancies affected by noncardiomyopathy cardiac disease and pregnancies without cardiac disease. Women with cardiomyopathy who plan to get pregnant should receive detailed counseling regarding these risks and have their pregnancies managed by experienced multidisciplinary teams that can provide close fetal monitoring and neonatology expertise.

Moolla M, Mathew A, John K, Yogasundaram H, Alhumaid W, Campbell S, Windram J. Outcomes of pregnancy in women with hypertrophic cardiomyopathy: A systematic review. *Int J Cardiol*. 2022 Jul 15;359:54-60. doi: 10.1016/j.ijcard.2022.04.034. Epub 2022 Apr 12. PMID: 35427704.

Conclusions: Women with HCM considering pregnancy can be reassured that the risk of maternal, fetal, or neonatal death is low. However, they are at risk of several non-fatal cardiac and pregnancy-related complications.

Topf A, Bacher N, Kopp K, Mirna M, Larbig R, Brandt MC, Kraus J, Hoppe UC, Motloch LJ, Lichtenauer M. Management of Implantable Cardioverter-Defibrillators during Pregnancy-A Systematic Review. *J Clin Med*. 2021 Apr 14;10(8):1675. doi: 10.3390/jcm10081675. PMID: 33919684; PMCID: PMC8069958.

Conclusions: Due to limited data on management of ICDs during pregnancy, further scientific

investigations are required. Consequently, careful risk assessment with individual risk evaluation and close follow ups with interdisciplinary treatment are recommended in pregnant ICD carriers.

Bardhi E, Faralli I, Deroma M, Galoppi P, Ventriglia F, Giancotti A, Perrone G, Brunelli R. Non-compaction cardiomyopathy in pregnancy: a case report of spongy myocardium in both mother and foetus and systematic review of literature. *J Matern Fetal Neonatal Med.* 2021 Sep;34(17):2910-2917. doi: 10.1080/14767058.2019.1671337. Epub 2019 Oct 1. PMID: 31570025.

Conclusions: LVNC is not a contraindication for pregnancy, but clearly increases the risk of preterm birth and the rate of cesarean section. On the other hand, pregnancy in a LVNC patient exposes her to increased risk of clinical deterioration. Further studies are needed to better characterize the management of pregnancies in women with cardiomyopathies.

Sanusi M, Momin ES, Mannan V, Kashyap T, Pervaiz MA, Akram A, Khan AA, Elshaikh AO. Using Echocardiography and Biomarkers to Determine Prognosis in Peripartum Cardiomyopathy: A Systematic Review. *Cureus.* 2022 Jun 20;14(6):e26130. doi: 10.7759/cureus.26130. PMID: 35875281; PMCID: PMC9299948.

Conclusion: Although no parameter proved consistent in all the studies, echocardiographic parameters, including strain profiles and biomarkers, proved significant in the prognostication of patients with PPCM in the various studies evaluated. Therefore, a holistic approach is still needed in the risk stratification of patients with PPCM. Future studies should evaluate these parameters as well as clinical characteristics in a larger cohort study with a long follow-up period of more than one year in order to potentially develop prognostic score criteria that can be used to accurately identify those patients at the highest risk of developing severe disease or death to allow for timely and targeted therapies to improve outcomes in these patients.

Esbrand FD, Zafar S, Panthangi V, Cyril Kurupp AR, Raju A, Luthra G, Shahbaz M, Almatooq H, Foucambert P, Balani P. Utility of N-terminal (NT)-Brain Natriuretic Peptide (proBNP) in the Diagnosis and Prognosis of Pregnancy Associated Cardiovascular Conditions: A Systematic Review. *Cureus.* 2022 Dec 22;14(12):e32848. doi: 10.7759/cureus.32848. PMID: 36699777; PMCID: PMC9870182.

	<p>Conclusion: NT-proBNP, when elevated in the pregnant patient, is a predictor of poor pregnancy outcomes, especially in patients with precursors. Testing for this peptide in pregnant women during the early stages of pregnancy could help determine the best course of action for a better outcome.</p> <p>Dodeja AK, Siegel F, Dodd K, Ma'ayeh M, Mehta LS, Fuchs MM, Rood KM, Mah ML, Bradley EA. Heart failure in pregnancy: what is the long-term impact of pregnancy on cardiac function? A tertiary care centre experience and systematic review. <i>Open Heart</i>. 2021 Aug;8(2):e001587. doi: 10.1136/openhrt-2021-001587. PMID: 34344721; PMCID: PMC8336161.</p> <p>Conclusions: In this contemporary cohort of women with CM, maternal MACE rates were lower than previously reported, and were less common in PPCM as compared with ICM and NICM. Heart function in women with MACE was negatively impacted immediately after delivery and in late postpartum follow-up, suggesting that pregnancy itself likely has influence on future left ventricular function in women with underlying CM.</p>	
<p>R2: What genetic and environmental factors influence the risk of getting worse, heart failure and/ or sudden death in people with cardiomyopathy?</p>	<p>Lu X, Li P, Teng C, Cai P, Jin L, Li C, Liu Q, Pan S, Dixon RAF, Wang B. Prognostic factors of Takotsubo cardiomyopathy: a systematic review. <i>ESC Heart Fail</i>. 2021 Oct;8(5):3663-3689. doi: 10.1002/ehf2.13531. Epub 2021 Aug 9. PMID: 34374223; PMCID: PMC8497208.</p> <p>Conclusion: We found that male sex, physical triggers, and certain comorbidities such as chronic kidney disease, malignant disease, higher body mass index, sepsis, chronic obstructive pulmonary disease, and anaemia were associated with poor TCM prognosis. In contrast, race, hyperlipidaemia, diabetes mellitus, and mood disorders were not clearly associated with TCM prognosis.</p> <p>Somma V, Ha FJ, Palmer S, Mohamed U, Agarwal S. Pacing-induced cardiomyopathy: A systematic review and meta-analysis of definition, prevalence, risk factors, and management. <i>Heart Rhythm</i>. 2023 Feb;20(2):282-290. doi: 10.1016/j.hrthm.2022.09.019. Epub 2022 Nov 7. PMID: 36356656.</p> <p>Conclusion: Pacing-induced cardiomyopathy is a potential complication of right ventricular pacing. In meta-analysis, risk factors included male sex, history of myocardial infarction, chronic kidney disease, atrial fibrillation, baseline left ventricular ejection fraction, native QRS duration, right ventricular pacing percentage, and paced QRS duration. More than 1 in 10 patients with chronic right ventricular pacing</p>	

developed PiCM. Key risk factors included baseline left ventricular ejection fraction, native QRS duration, RV pacing percentage, and paced QRS duration. The optimal management strategy has yet to be defined. Further research is needed to define and treat this understated complication.

Goyal A, Lahan S, Dalia T, Ranka S, Bhattad VB, Patel RR, Shah Z. Clinical comparison of V122I genotypic variant of transthyretin amyloid cardiomyopathy with wild-type and other hereditary variants: a systematic review. *Heart Fail Rev.* 2022 May;27(3):849-856. doi: 10.1007/s10741-021-10098-6. Epub 2021 Mar 25. PMID: 33768376.

Conclusion: The mean age of diagnosis among wild-type ATTR patients was 77 years, followed by 71.2 and 65 years in V122I and T60A group patients, respectively. V122I patients were mostly black, had a poor quality of life, and highest mortality risk compared with other subtypes. Merely, the presence of V122I mutation was identified as an independent predictor of mortality. V30M subtype correlated with the least severe cardiac disease and a median survival duration comparable with T60A subtype. V122I ATTR is an aggressive disease, prevalent in African-Americans, and is associated with a greater morbidity and mortality, which is partly attributed to its misdiagnosis and/or late diagnosis. Current advances in non-invasive studies to diagnose hATTR coupled with concurrent drug therapies have improved quality of life and provide a survival benefit to these patients.

Tsartsalis D, Korela D, Karlsson LO, Foukarakis E, Svensson A, Anastasakis A, Venetsanos D, Aggeli C, Tsioufis C, Braunschweig F, Dragioti E, Charitakis E. Risk and Protective Factors for Sudden Cardiac Death: An Umbrella Review of Meta-Analyses. *Front Cardiovasc Med.* 2022 Jun 16;9:848021. doi: 10.3389/fcvm.2022.848021. PMID: 35783841; PMCID: PMC9246322.

Conclusions: Lifestyle risk factors (physical activity, smoking), comorbidities like DM, and electrocardiographic features like ERP constitute modifiable risk factors of SCD. Alternatively, the use of MRA, beta-blockers, SGLT-2 inhibitors, and ICD in patients with HF are credible protective factors. Further investigation targeted in specific populations will be important for reducing the burden of SCD.

Ferradini V, Vacca D, Belmonte B, Mango R, Scola L, Novelli G, Balistreri CR, Sangiuolo F. Genetic and Epigenetic Factors of Takotsubo Syndrome: A Systematic Review. *Int J Mol Sci.* 2021 Sep 13;22(18):9875.

	<p>doi: 10.3390/ijms22189875. PMID: 34576040; PMCID: PMC8471495. Conclusions: Consequently, we concluded that further work is needed to address the gaps discussed, and clear evidence may arrive by using multi-omics investigations.</p> <p>Campos FAD, Ritt LEF, Costa JPS, Cruz CM, Feitosa-Filho GS, Oliveira QB, Darzé ES. Factors Associated with Recurrence in Takotsubo Syndrome: A Systematic Review. Arq Bras Cardiol. 2020 Mar;114(3):477-483. English, Portuguese. doi: 10.36660/abc.20180377. PMID: 32049155; PMCID: PMC7792734. Conclusions: Female gender, time from the first episode of the syndrome, low BMI and midventricular obstruction were reported as potential predictors of TTS recurrence.</p> <p>Guo S, Xie B, Tse G, Roeber L, Xia Y, Li G, Wang Y, Liu T. Malignancy predicts outcome of Takotsubo syndrome: a systematic review and meta-analysis. Heart Fail Rev. 2020 May;25(3):513-522. doi: 10.1007/s10741-020-09917-z. PMID: 31956929. Conclusions: Our meta-analysis suggested that malignancy plays a significant role in predicting the mortality of Takotsubo syndrome patients whether in the short term or long term.</p>	
<p>R3: What happens to people with cardiomyopathy as they get older? How does the condition change over time?</p>	<p>Maron BJ, Desai MY, Nishimura RA, Spirito P, Rakowski H, Towbin JA, Dearani JA, Rowin EJ, Maron MS, Sherrid MV. Management of Hypertrophic Cardiomyopathy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2022 Feb 1;79(4):390-414. doi: 10.1016/j.jacc.2021.11.021. PMID: 35086661. Conclusion: HCM patients with disease-related complications benefit from: matured risk stratification in which major markers reliably select patients for prophylactic defibrillators and prevention of arrhythmic sudden death; low risk to high benefit surgical myectomy (with percutaneous alcohol ablation a selective alternative) that reverses progressive heart failure caused by outflow obstruction; anticoagulation prophylaxis that prevents atrial fibrillation-related embolic stroke and ablation techniques that decrease the frequency of paroxysmal episodes; and occasionally, heart transplant for end-stage nonobstructive patients. Those innovations have substantially improved outcomes by significantly reducing morbidity and HCM-related mortality to 0.5%/y. Notably, a substantial proportion of HCM patients (largely those identified without outflow obstruction) experience a stable/benign course without major interventions.</p>	

<p>R4: How does cardiomyopathy affect life expectancy?</p>	<p>Maron BJ, Desai MY, Nishimura RA, Spirito P, Rakowski H, Towbin JA, Dearani JA, Rowin EJ, Maron MS, Sherrid MV. Management of Hypertrophic Cardiomyopathy: JACC State-of-the-Art Review. <i>J Am Coll Cardiol</i>. 2022 Feb 1;79(4):390-414. doi: 10.1016/j.jacc.2021.11.021. PMID: 35086661.</p> <p>Conclusion: HCM patients with disease-related complications benefit from: matured risk stratification in which major markers reliably select patients for prophylactic defibrillators and prevention of arrhythmic sudden death; low risk to high benefit surgical myectomy (with percutaneous alcohol ablation a selective alternative) that reverses progressive heart failure caused by outflow obstruction; anticoagulation prophylaxis that prevents atrial fibrillation-related embolic stroke and ablation techniques that decrease the frequency of paroxysmal episodes; and occasionally, heart transplant for end-stage nonobstructive patients. Those innovations have substantially improved outcomes by significantly reducing morbidity and HCM-related mortality to 0.5%/y.</p>
<p>R5: Are there groups of people at greater risk of developing cardiomyopathy or at greater risk of becoming seriously ill (e.g. men, menopausal women, some ethnic groups)?</p>	<p>Lu X, Li P, Teng C, Cai P, Jin L, Li C, Liu Q, Pan S, Dixon RAF, Wang B. Prognostic factors of Takotsubo cardiomyopathy: a systematic review. <i>ESC Heart Fail</i>. 2021 Oct;8(5):3663-3689. doi: 10.1002/ehf2.13531. Epub 2021 Aug 9. PMID: 34374223; PMCID: PMC8497208.</p> <p>Conclusion: We found that male sex, physical triggers, and certain comorbidities such as chronic kidney disease, malignant disease, higher body mass index, sepsis, chronic obstructive pulmonary disease, and anaemia were associated with poor TCM prognosis. In contrast, race, hyperlipidaemia, diabetes mellitus, and mood disorders were not clearly associated with TCM prognosis.</p> <p>Kroi F, Fischer N, Gezin A, Hashim M, Rozenbaum MH. Estimating the Gender Distribution of Patients with Wild-Type Transthyretin Amyloid Cardiomyopathy: A Systematic Review and Meta-Analysis. <i>Cardiol Ther</i>. 2021 Jun;10(1):41-55. doi: 10.1007/s40119-020-00205-3. Epub 2020 Dec 14. PMID: 33315233; PMCID: PMC8126539.</p> <p>Conclusions: Studies conducted to date suggest ATTRwt disproportionately affects males. The proportion of males was significantly impacted by the age at diagnosis and method diagnosis, which may suggest important gender-based differences in the clinical manifestation and diagnostic challenges of ATTRwt in females that warrant future research.</p>

Abbas J, Zulqarnain M, Waqar F, Waqar Z, Malik J, Satti DI, Zaidi SMJ. Incidence and predictors of pacemaker-induced cardiomyopathy with right ventricular pacing: a systematic review. *Expert Rev Cardiovasc Ther.* 2022 Apr;20(4):267-273. doi: 10.1080/14779072.2022.2062323. Epub 2022 Apr 6. PMID: 35365062.

Conclusions: RV pacing was associated with a considerable risk of PICM, with biological factors, such as male gender, old age, increased QRS duration, and chronic RV pacing burden playing an important role in the development of disease.

Zhao H, Tan Z, Liu M, Yu P, Ma J, Li X, Wang J, Zhao Y, Zhu W, Liu X. Is There a Sex Difference in the Prognosis of Hypertrophic Cardiomyopathy? A Systematic Review and Meta-Analysis. *J Am Heart Assoc.* 2023 Jun 6;12(11):e026270. doi: 10.1161/JAHA.122.026270. Epub 2023 May 26. PMID: 37232242; PMCID: PMC10381980.

Conclusions: Based on current evidence, our results show significant sex-specific differences in the prognosis of HCM. Future guidelines may emphasize the use of a sex-specific risk assessment for the diagnosis and management of HCM. (women at higher risk of adverse events).

Ukah UV, Li X, Wei SQ, Healy-Profítos J, Dayan N, Auger N. Black-White disparity in severe cardiovascular maternal morbidity: A systematic review and meta-analysis. *Am Heart J.* 2022 Dec;254:35-47. doi: 10.1016/j.ahj.2022.07.009. Epub 2022 Aug 6. PMID: 35944667.

Conclusions: Black women have a considerably higher risk of severe cardiovascular maternal morbidity than White women, including acute myocardial infarction, peripartum cardiomyopathy, and stroke. Reducing inequality in adverse cardiovascular outcomes of pregnancy between Black and White women should be prioritized.

Abuelazm M, Saleh O, Hassan AR, Ahmad S, Albarakat MM, Abdalshafy H, Katamesh BE, Abdelazeem B, Paul TK. Sex Difference in Clinical and Management Outcomes in Patients With Takotsubo Syndrome: A Systematic Review and Meta-Analysis. *Curr Probl Cardiol.* 2023 Apr;48(4):101545. doi: 10.1016/j.cpcardiol.2022.101545. Epub 2022 Dec 21. PMID: 36563919.

Conclusions: Despite women having a higher incidence of TTS, men have higher morbidity and mortality

rates. Hence, further studies are necessary to identify the pathophysiological factors of this sex difference in clinical outcomes, including hormonal and psychological variables.

Long C, Liu X, Xiong Q, Su Y, Hong K. Sex Differences in Dilated Cardiomyopathy Prognosis. *Int Heart J.* 2022;63(1):36-42. doi: 10.1536/ihj.20-448. PMID: 35095074.

Conclusions: The evidence from the published studies suggested that compared with females, males with DCM had an increased risk of all-cause mortality, cardiovascular mortality, and SCD.

Bruno M, Castaño A, Burton A, Grodin JL. Transthyretin amyloid cardiomyopathy in women: frequency, characteristics, and diagnostic challenges. *Heart Fail Rev.* 2021 Jan;26(1):35-45. doi: 10.1007/s10741-020-10010-8. PMID: 32794090; PMCID: PMC7769788.

Conclusions: Data available on disease characteristics were limited and very heterogeneous, but trends suggested some cardiac structural/functional differences, i.e., lower interventricular septal and posterior wall thickness and left ventricular (LV) end diastolic diameter, and higher LV ejection fractions, in women versus men across ATTR-CM subtypes. Because LV wall thickness > 12 mm is generally the suggested threshold for ATTR-CM diagnosis in both sexes, smaller cardiac anatomy in women with the disease may lead to underdiagnosis. Additional research and studies are needed to elucidate potential disparities between sexes in ATTR-CM frequency, clinical characteristics, and underlying biological mechanisms.

Shen J, Qian X, Mei X, Yao J, Jiang H, Li K, Chen T, Jiang Y, Zhou Y. Effect of rs4646994 polymorphism of angiotensin-converting enzyme on the risk of nonischemic cardiomyopathy. *Biosci Rep.* 2021 Dec 22;41(12):BSR20211617. doi: 10.1042/BSR20211617. PMID: 34750628; PMCID: PMC8685642.

Conclusion: ACE rs4646994 polymorphism increases the risk of DCM/HCM in Asians, but not in Caucasians. More case-control studies are needed to strengthen our conclusions and to assess the gene-gene and gene-environment interactions between ACE rs4646994 polymorphism and DCM/HCM.

Trongtorsak A, Polpichai N, Thangjui S, Kewcharoen J, Yodsuwan R, Devkota A, Friedman HJ, Estrada AQ. Gender-Related Differences in Hypertrophic Cardiomyopathy: A Systematic Review and Meta-Analysis. *Pulse (Basel).* 2021 Aug 2;9(1-2):38-46. doi: 10.1159/000517618. PMID: 34722354; PMCID: PMC8527921.

	<p>Conclusions: Female gender was associated with a worse prognosis in HCM. These findings suggest the need for improved care in women including early identification of disease and more possible aggressive management. Moreover, gender-based strategy may benefit in HCM patients.</p>	
<p>R6: Are people with cardiomyopathy at greater risk of other health conditions? How does having cardiomyopathy affect their treatment for other conditions (e.g. cancer, diabetes)?</p>	<p>Gruhl SL, Su J, Chua WC, Tay KV. Takotsubo cardiomyopathy in post-traumatic brain injury: A systematic review of diagnosis and management. Clin Neurol Neurosurg. 2022 Feb;213:107119. doi: 10.1016/j.clineuro.2021.107119. Epub 2022 Jan 4. PMID: 34998160.</p> <p>Discussion: Our analysis was limited by the fact that not all papers analysed had reported the parameters we required. However, based on our review, we conclude that most patients with TC demonstrate a resolution of cardiac function independent of cardiac interventions from as fast as a few hours to as long as 6-12 weeks. Therefore, despite high cardiac risks, if neurosurgical intervention is needed, it should be offered to improve the chance of survival as transient cardiomyopathy can be supported with inotropes. We have developed a new algorithm for management of cases of concurrent TBI and TC.</p> <p>Guo J, Wang D, Jia J, Zhang J, Peng F, Lu J, Zhao X, Liu Y. Atrial cardiomyopathy and incident ischemic stroke risk: a systematic review and meta-analysis. J Neurol. 2023 Jul;270(7):3391-3401. doi: 10.1007/s00415-023-11693-3. Epub 2023 Apr 4. PMID: 37014420; PMCID: PMC10267254.</p> <p>Conclusion: Atrial cardiomyopathy markers, including electrocardiographic markers, serum markers, LA structural and functional markers, can be used to stratify the risk of incident ischemic stroke.</p> <p>Lin W, Tay SH, Mak A. Takotsubo syndrome and rheumatic diseases-a critical systematic review. Rheumatology (Oxford). 2021 Jan 5;60(1):11-22. doi: 10.1093/rheumatology/keaa504. PMID: 33063091.</p> <p>Conclusion: Potential impact of disease manifestations and treatment of rheumatological conditions on TTS are critically discussed.</p>	
<p>R8: Are there tests which can predict the risk of getting worse, heart failure and/or sudden death in people with</p>	<p>Yang Y, Wu D, Wang H, Wang Y. Prognostic value of global longitudinal strain in hypertrophic cardiomyopathy: A systematic review and meta-analysis. Clin Cardiol. 2022 Dec;45(12):1184-1191. doi: 10.1002/clc.23928. Epub 2022 Sep 30. PMID: 36177652; PMCID: PMC9748764.</p> <p>Conclusion: The meta-analysis suggested that impaired LVGLS was associated with poor prognosis in</p>	

cardiomyopathy? How do people with different levels of risk need to be treated differently?

HCM patients.

Bazoukis G, Tyrovolas K, Letsas KP, Vlachos K, Radford D, Chung CT, Liu T, Efremidis M, Tse G, Baranchuk A. Predictors of fatal arrhythmic events in patients with non-compaction cardiomyopathy: a systematic review. *Heart Fail Rev.* 2022 Nov;27(6):2067-2076. doi: 10.1007/s10741-022-10257-3. Epub 2022 Jul 1. PMID: 35776368.

Conclusion: Risk stratification of LVNC patients with no prior history of a fatal arrhythmic event remains challenging. Symptoms assessment, electrocardiogram, Holter monitoring, and cardiac imaging should be performed on every patient, while an electrophysiological study should be performed for moderate-risk patients. Large cohort studies are needed for the construction of score models for arrhythmic risk stratification purposes.

Xia K, Sun D, Wang R, Zhang Y. Factors associated with the risk of cardiac death in children with hypertrophic cardiomyopathy: a systematic review and meta-analysis. *Heart Lung.* 2022 Mar-Apr;52:26-36. doi: 10.1016/j.hrtlng.2021.11.006. Epub 2021 Nov 24. PMID: 34837725.

Conclusion: The results indicated that children with previous adverse cardiac events during childhood and with a history of syncope had an increased risk of sudden CD or CD. Non-sustained ventricular tachycardia (VT) in HCM children was associated with sudden CD or CD. Children with left ventricular hypertrophy (LVH) were at higher risk of sudden CD or CD. And left ventricular outflow tract (LVOT) obstruction was a potential risk factor for sudden CD in children with HCM (all $P < 0.05$). Optimal care and appropriate monitoring is necessary for HCM children with higher risk of sudden CD or CD.

Ye TTS, Siah QZ, Tan BYQ, Ho JSY, Syn NLX, Teo YH, Teo YN, Yip JW, Yeo TC, Lin W, Wong RCC, Chai P, Chan B, Sharma VK, Yeo LLL, Sia CH. Ischaemic events in hypertrophic cardiomyopathy patients with and without atrial fibrillation: a systematic review and meta-analysis. *J Thromb Thrombolysis.* 2023 Jan;55(1):83-91. doi: 10.1007/s11239-022-02713-6. Epub 2022 Oct 3. PMID: 36192663.

Conclusion: Concomitant atrial fibrillation in hypertrophic cardiomyopathy increases the risk of thromboembolic events including ischaemic stroke and transient ischaemic attack. The apical subgroup shows a similar risk of acute cerebrovascular events as the overall hypertrophic cardiomyopathy

population.

Chiang LL, Tsang SL, Lee JX, Gong M, Liu T, Tse G, Chang D, Lakhani I, Li KHC. Takotsubo cardiomyopathy with low ventricular ejection fraction and apical ballooning predicts mortality: a systematic review and meta-analysis. *Heart Fail Rev.* 2021 Mar;26(2):309-318. doi: 10.1007/s10741-020-10018-0. Epub 2020 Sep 7. PMID: 32895749.

Conclusion: LVEF and apical ballooning are both potential prognostic markers for mortality.

Rodrigues T, Raposo SC, Brito D, Lopes LR. Prognostic relevance of exercise testing in hypertrophic cardiomyopathy. A systematic review. *Int J Cardiol.* 2021 Sep 15;339:83-92. doi: 10.1016/j.ijcard.2021.06.051. Epub 2021 Jun 30. PMID: 34214502; PMCID: PMC8425182.

Conclusion: Although most studies concluded that exercise test results are useful to determine prognosis in HCM, further investigation is needed regarding whether it adds independent value to the current risk stratification strategies.

Alphonse P, Virk S, Collins J, Campbell T, Thomas SP, Semsarian C, Kumar S. Prognostic impact of atrial fibrillation in hypertrophic cardiomyopathy: a systematic review. *Clin Res Cardiol.* 2021 Apr;110(4):544-554. doi: 10.1007/s00392-020-01730-w. Epub 2020 Sep 3. PMID: 32880676.

Conclusions: AF is highly prevalent in patients with HCM. The presence of AF is associated with major adverse clinical outcomes. These findings suggest that both, aggressive screening and treatment of AF, are likely to have major prognostic impact on outcomes in HCM. Incidence, prevalence and prognostic impact of AF in HCM. In this systematic review, AF incidence was 2.5 cases per-person years, prevalence was 22.3%. AF in HCM was associated with a seven-fold increased risk of thromboembolism, 2.8-fold increased risk of heart failure, 1.7-fold increased risk of sudden death and 2.5-fold increased risk of all-cause mortality.

Jansen M, Algül S, Bosman LP, Michels M, van der Velden J, de Boer RA, van Tintelen JP, Asselbergs FW, Baas AF. Blood-based biomarkers for the prediction of hypertrophic cardiomyopathy prognosis: a systematic review and meta-analysis. *ESC Heart Fail.* 2022 Oct;9(5):3418-3434. doi: 10.1002/ehf2.14073.

Epub 2022 Jul 17. PMID: 35842920; PMCID: PMC9715795.

Conclusions: Several blood-based biomarkers were identified as predictors of HCM outcomes. Additional studies are required to validate their prognostic utility within current risk stratification models.

Hosseinpour A, Hosseinpour H, Kheshti F, Abdollahifard S, Attar A. Prognostic value of various markers in recovery from peripartum cardiomyopathy: a systematic review and meta-analysis. *ESC Heart Fail.* 2022 Oct;9(5):3483-3495. doi: 10.1002/ehf2.14085. Epub 2022 Jul 26. PMID: 35883253; PMCID: PMC9715862.

Conclusions: Patients with PPCM who have a higher baseline LVEF, lower left ventricular diameters, and higher blood pressure levels have a greater chance to recover from PPCM.

Golukhova EZ, Alexandrova SA, Bulaeva NI, Mrikaev DV, Gromova OI, Berdibekov BS. Prognostic value of myocardial strain by magnetic resonance imaging in nonischemic dilated cardiomyopathy: a systematic review and meta-analysis. *Kardiologiia.* 2022 Oct 30;62(10):35-41. Russian, English. doi: 10.18087/cardio.2022.10.n2034. PMID: 36384407.

Conclusion: The LV GLS, GCS, and GRS variables by MR feature-tracking data are powerful predictors for the development of major adverse cardiovascular events. Evaluation of myocardial strain can be used as an effective instrument for risk stratification in patients with non-ischemic dilated cardiomyopathy.

Sammani A, Kayvanpour E, Bosman LP, Sedaghat-Hamedani F, Proctor T, Gi WT, Broezel A, Jensen K, Katus HA, Te Riele ASJM, Meder B, Asselbergs FW. Predicting sustained ventricular arrhythmias in dilated cardiomyopathy: a meta-analysis and systematic review. *ESC Heart Fail.* 2020 Aug;7(4):1430-1441. doi: 10.1002/ehf2.12689. Epub 2020 Apr 14. PMID: 32285648; PMCID: PMC7373946.

Conclusions: In patients with DCM, the annual event rate of sustained ventricular arrhythmias is approximately 4.5%. This risk is considerably higher in younger patients with hypertension, prior (non-)sustained ventricular arrhythmia, decreased left ventricular ejection fraction, left ventricular dilatation, late gadolinium enhancement, and genetic mutations (PLN, LMNA, and FLNC). These results may help determine appropriate candidates for implantable cardioverter-defibrillator implantation.

Matteo S, Anna C, Federico S, Daniele M, Gioele F, Beatrice DP, Rita P, Elisabetta T, Giulia P, Claudio R,

Gianluca C. Stroke volume and myocardial contraction fraction in transthyretin amyloidosis cardiomyopathy: A systematic review. *Front Cardiovasc Med.* 2023 Jan 27;10:1085824. doi: 10.3389/fcvm.2023.1085824. PMID: 36776259; PMCID: PMC9911429.

Conclusion: Stroke volume and MCF are very informative parameters that should be routinely assessed during the standard echocardiographic examination of all patients with TTR-CA. They carry a prognostic role while being associated with patients' symptoms.

Korabathina R, Porcadas J, Kip KE, Korabathina PR, Rosenthal AD, Wassmer P. Left Ventricular Ballooning Patterns in Recurrent Takotsubo Cardiomyopathy: A Systematic Review and Meta-analysis of Reported Cases. *Tex Heart Inst J.* 2021 Nov 1;48(5):e207223. doi: 10.14503/THIJ-20-7223. PMID: 34902024; PMCID: PMC8788638.

Conclusions: Our results suggest that left ventricular ballooning patterns influence clinical outcomes, and that outcomes are more favorable in patients with recurrent TTC who have atypical left ventricular ballooning patterns.

Papanastasiou CA, Zegkos T, Karamitsos TD, Rowin EJ, Maron MS, Parcharidou D, Kokkinidis DG, Karvounis H, Rimoldi O, Maron BJ, Efthimiadis GK. Prognostic role of left ventricular apical aneurysm in hypertrophic cardiomyopathy: A systematic review and meta-analysis. *Int J Cardiol.* 2021 Jun 1;332:127-132. doi: 10.1016/j.ijcard.2021.03.056. Epub 2021 Mar 29. PMID: 33794232.

Conclusions: These data demonstrate that LV apical aneurysm in HCM patients is associated with an increased risk for SCD events and thromboembolism. This finding might encourage the inclusion of LV apical aneurysm into the HCM SCD risk stratification algorithm as a novel risk marker that supports consideration for primary prevention implantable cardioverter defibrillator and anticoagulation for stroke prophylaxis.

Cantone A, Serenelli M, Sanguettoli F, Maio D, Fabbri G, Dal Passo B, Agostoni P, Grazi G, Campo G, Rapezzi C. Cardiopulmonary exercise testing predicts prognosis in amyloid cardiomyopathy: a systematic review and meta-analysis. *ESC Heart Fail.* 2023 Aug;10(4):2740-2744. doi: 10.1002/ehf2.14406. Epub 2023 Jun 1. PMID: 37264762; PMCID: PMC10375073.

Conclusions: CPET is a valuable tool for prognostic stratification in CA, identifying patients at increased risk of death. Large prospective clinical trials are needed to confirm this exploratory finding.

Kamp NJ, Chery G, Kosinski AS, Desai MY, Wazni O, Schmidler GS, Patel M, Lopes RD, Morin DP, Al-Khatib SM. Risk stratification using late gadolinium enhancement on cardiac magnetic resonance imaging in patients with hypertrophic cardiomyopathy: A systematic review and meta-analysis. *Prog Cardiovasc Dis.* 2021 May-Jun;66:10-16. doi: 10.1016/j.pcad.2020.11.001. Epub 2020 Nov 7. PMID: 33171204.

Conclusion In patients with HCM, LGE on c-MRI is a strong predictor of arrhythmic outcomes including SCD, aborted SCD, and appropriate ICD therapy. These data support the routine use of LGE on c-MRI as a marker of SCD risk in this population.

de Lavallaz JDF, Mézier J, Mertz L, Mannhart D, Serban T, Knecht S, Abid QU, Nguyen TT, Kühne M, Sticherling C, Huang H, Gold MR, Badertscher P. Risk factors for the development of premature ventricular complex-induced cardiomyopathy: a systematic review and meta-analysis. *J Interv Card Electrophysiol.* 2023 Aug;66(5):1145-1163. doi: 10.1007/s10840-022-01421-8. Epub 2022 Nov 21. PMID: 36414810; PMCID: PMC10333144.

Conclusions: In this meta-analysis, the most consistent risk factors for PVC-CM were age, non-sustained VT, LV, epicardial origin, interpolation, and PVC burden, whereas the presence of symptoms significantly reduced the risk. These findings help tailor stringent follow-up of patients presenting with frequent PVCs and normal LV function.

Chery G, Kamp N, Kosinski AS, Schmidler GS, Lopes RD, Patel M, Al-Khatib SM. Prognostic value of myocardial fibrosis on cardiac magnetic resonance imaging in patients with ischemic cardiomyopathy: A systematic review. *Am Heart J.* 2020 Nov;229:52-60. doi: 10.1016/j.ahj.2020.08.004. Epub 2020 Aug 11. PMID: 32916608; PMCID: PMC7417269.

Conclusions: LGE has high prognostic value in predicting adverse outcomes in patients with ICM and may provide helpful information for clinical decision making related to SCD prevention. Our findings illustrate how LGE may improve current risk stratification, prognostication, and selection of patients with ICM for ICD therapy.

Golukhova EZ, Bulaeva NI, Alexandrova SA, Mrikaev DV, Gromova OI, Ruzina EV, Berdibekov BS. The extent of late gadolinium enhancement predicts mortality, sudden death and major adverse cardiovascular events in patients with nonischemic cardiomyopathy: a systematic review and meta-analysis. *Clin Radiol*. 2023 Apr;78(4):e342-e349. doi: 10.1016/j.crad.2022.12.015. Epub 2023 Jan 13. PMID: 36707397.

Conclusions: Extent of LGE in CMR predicts all-cause mortality, arrhythmic events, and MACE. Collectively, these findings emphasise that extent of LGE by CMR may have value for optimising current predictive models for clinical events or mortality in patients with NICM.

Anagnostopoulos I, Kousta M, Kossyvakis C, Lakka E, Paraskevaidis NT, Schizas N, Alexopoulos N, Deftereos S, Giannopoulos G. The prognostic role of late gadolinium enhancement on cardiac magnetic resonance in patients with nonischemic cardiomyopathy and reduced ejection fraction, implanted with cardioverter defibrillators for primary prevention. A systematic review and meta-analysis. *J Interv Card Electrophysiol*. 2022 Apr;63(3):523-530. doi: 10.1007/s10840-021-01027-6. Epub 2021 Jul 3. PMID: 34218421.

Conclusion: LGE is a highly sensitive predictor of ADT and cardiac death in NICM patients implanted with a defibrillator for primary prevention. However, due to moderate specificity, derivation of a cutoff with adequate predictive values and probably a multifactorial approach are needed to improve discrimination of patients who will not benefit from ICDs.

Theerasuwipakorn N, Chokesuwattanaskul R, Phannajit J, Marsukjai A, Thapanasuta M, Klem I, Chattranukulchai P. Impact of late gadolinium-enhanced cardiac MRI on arrhythmic and mortality outcomes in nonischemic dilated cardiomyopathy: updated systematic review and meta-analysis. *Sci Rep*. 2023 Aug 23;13(1):13775. doi: 10.1038/s41598-023-41087-4. PMID: 37612359; PMCID: PMC10447440.

Conclusion: Real-world evidence suggests that the presence of LGE on CMR was a strong predictor of adverse long-term outcomes in patients with NIDCM. Scar assessment should be incorporated as a primary determinant in the patient selection criteria for primary prophylactic implantable cardioverter-defibrillator placement.

Georgiopoulos G, Figliozzi S, Pateras K, Nicoli F, Bampatsias D, Beltrami M, Finocchiaro G, Chiribiri A, Masci PG, Olivotto I. Comparison of Demographic, Clinical, Biochemical, and Imaging Findings in Hypertrophic Cardiomyopathy Prognosis: A Network Meta-Analysis. *JACC Heart Fail.* 2023 Jan;11(1):30-41. doi: 10.1016/j.jchf.2022.08.022. Epub 2022 Dec 7. PMID: 36599547.

Conclusions: This network meta-analysis supports the development of multiparametric risk prediction algorithms, including advanced imaging markers additively to conventional risk factors, for refined risk stratification in HCM.

Aung N, Doimo S, Ricci F, Sanghvi MM, Pedrosa C, Woodbridge SP, Al-Balah A, Zemrak F, Khanji MY, Munroe PB, Naci H, Petersen SE. Prognostic Significance of Left Ventricular Noncompaction: Systematic Review and Meta-Analysis of Observational Studies. *Circ Cardiovasc Imaging.* 2020 Jan;13(1):e009712. doi: 10.1161/CIRCIMAGING.119.009712. Epub 2020 Jan 21. PMID: 31959004; PMCID: PMC7012350.

Conclusions: Patients with LVNC carry a similar cardiovascular risk when compared with dilated cardiomyopathy patients. Left ventricular ejection fraction-a conventional indicator of heart failure severity, not the extent of trabeculation-appears to be an important determinant of adverse outcomes in LVNC patients.

Milaras N, Dourvas P, Doundoulakis I, Sotiriou Z, Nevras V, Xintarakou A, Laina A, Soulaïdopoulos S, Zachos P, Kordalis A, Arsenos P, Archontakis S, Antoniou CK, Tsiachris D, Dilaveris P, Tsioufis K, Sideris S, Gatzoulis K. Noninvasive electrocardiographic risk factors for sudden cardiac death in dilated cardiomyopathy: is ambulatory electrocardiography still relevant? *Heart Fail Rev.* 2023 Jul;28(4):865-878. doi: 10.1007/s10741-023-10300-x. Epub 2023 Mar 6. PMID: 36872393; PMCID: PMC10289982.

Conclusions: Although ambulatory electrocardiographic monitoring is frequently used in clinical practice in DCM patients, no single risk marker can be used for the selection of patients at high-risk for malignant ventricular arrhythmic events and sudden cardiac death who could benefit from the implantation of a defibrillator. More studies are needed in order to establish a risk score or a combination of risk factors with the purpose of selecting high-risk patients for ICD implantation in the context of primary prevention.

Pan JA, Kerwin MJ, Salerno M. Native T1 Mapping, Extracellular Volume Mapping, and Late Gadolinium

Enhancement in Cardiac Amyloidosis: A Meta-Analysis. *JACC Cardiovasc Imaging*. 2020 Jun;13(6):1299-1310. doi: 10.1016/j.jcmg.2020.03.010. PMID: 32498919; PMCID: PMC7340140.

Conclusions: ECV demonstrates a higher diagnostic OR for assessing cardiac amyloid than LGE and a higher HR for adverse events compared with LGE and native T1. In addition, native T1 showed similar sensitivity and specificity as ECV and LGE without requiring contrast material. Although limited by study heterogeneity, this meta-analysis suggests that ECV provides high diagnostic and prognostic utility for the assessment of cardiac amyloidosis.

Yue T, Chen BH, Wu LM, Xu JR, Pu J. Prognostic Value of Late Gadolinium Enhancement in Predicting Life-Threatening Arrhythmias in Heart Failure Patients With Implantable Cardioverter-Defibrillators: A Systematic Review and Meta-Analysis. *J Magn Reson Imaging*. 2020 May;51(5):1422-1439. doi: 10.1002/jmri.26982. Epub 2019 Nov 11. PMID: 31710415.

Data conclusion: The presence of MR-LGE may worsen the prognosis for adverse cardiovascular events in both ICM and NIMC patients who benefit more from ICDs.

Harapoz M, Zada M, Matthews J, Kumar S, Thomas L. Echocardiographic predictors of ventricular arrhythmias in patients with non-ischemic cardiomyopathy. *Int J Cardiol Heart Vasc*. 2022 Feb 4;39:100962. doi: 10.1016/j.ijcha.2022.100962. PMID: 35169613; PMCID: PMC8829059.

Conclusion: LV GLS impairment demonstrates value for predicting VA endpoints in NICM patients. Inclusion of LV GLS may be appropriate in the surveillance, screening, and clinical management of NICM patients.

Bayonas-Ruiz A, Muñoz-Franco FM, Ferrer V, Pérez-Caballero C, Sabater-Molina M, Tomé-Esteban MT, Bonacasa B. Cardiopulmonary Exercise Test in Patients with Hypertrophic Cardiomyopathy: A Systematic Review and Meta-Analysis. *J Clin Med*. 2021 May 25;10(11):2312. doi: 10.3390/jcm10112312. PMID: 34070695; PMCID: PMC8198116.

Conclusions: CPET is a valuable tool and can safely perform for assessment of physical functional capacity in patients with HCM. VO₂max is the most common performance measurement evaluated in functional studies, showing higher values in those based on cycle-ergometer compared to treadmill. Subgroup analysis shows that exercise intolerance seems to be more related to age, medication and comorbidities

	<p>than HCM phenotype itself. Lower VO2max is consistently seen in HCM patients at major cardiovascular risk.</p> <p>Al-Sadawi M, Aslam F, Tao M, Fan R, Singh A, Rashba E. Association of late gadolinium enhancement in cardiac magnetic resonance with mortality, ventricular arrhythmias, and heart failure in patients with nonischemic cardiomyopathy: A systematic review and meta-analysis. Heart Rhythm O2. 2023 Jan 13;4(4):241-250. doi: 10.1016/j.hroo.2023.01.001. PMID: 37124560; PMCID: PMC10134398.</p> <p>Conclusion: LGE in NICM patients is associated with increased mortality, VA and SCD, and HF hospitalization and heart transplantation referral during long-term follow up. Given these competing risks of mortality and HF progression, prospective randomized controlled trials are required to determine if LGE is useful for guiding prophylactic implantable cardioverter-defibrillator placement in NICM patients.</p>	
<p>R9: Why do the symptoms of cardiomyopathy vary so much from day to day and what are the best ways to manage this variation?</p>		
<p>SUPPORT</p>		
<p>S1: What training and information would help partners and family members to provide the best possible care for people with cardiomyopathy?</p>		
<p>S2: How are the lives of children and young people affected by their cardiomyopathy? What</p>		

are the best ways to support them in their social lives, education and conversations with health professionals?		
S3: What are the best ways to support the partners and family members of people with cardiomyopathy to ensure their own needs are met?		
S4: What are the best ways to support partners and family members affected by a sudden death from cardiomyopathy?		
TREATMENT		
T1: What are the best ways to treat and manage dizziness in people with cardiomyopathy?		
T2: What are the best ways to treat and manage breathlessness in people with cardiomyopathy?		
T3: Can stem cells be used to repair or restore damaged heart muscle in people with cardiomyopathy?	<p>Hoeeg C, Frljak S, Qayyum AA, Vrtovec B, Kastrup J, Ekblond A, Follin B. Efficacy and Mode of Action of Mesenchymal Stem Cells in Non-Ischemic Dilated Cardiomyopathy: A Systematic Review. <i>Biomedicines</i>. 2020 Dec 5;8(12):570. doi: 10.3390/biomedicines8120570. PMID: 33291410; PMCID: PMC7762005.</p> <p>Conclusion: Consequently, MSC treatment can improve cardiac function in NIDCM patients. The MoA underlying this effect involves anti-fibrosis, angiogenesis, immunomodulation, and anti-apoptosis, though</p>	

these processes seem to be interdependent. These encouraging results calls for larger confirmatory clinical studies, as well as preclinical studies utilizing unbiased investigation of the potential MoA.

Tripathi A, Khan MS, Khan AR, Vaughn VM, Bolli R. Cell therapy for nonischemic dilated cardiomyopathy: A systematic review and meta-analysis of randomized controlled trials. *Stem Cells Transl Med.* 2021 Oct;10(10):1394-1405. doi: 10.1002/sctm.21-0094. Epub 2021 Aug 4. PMID: 34346555; PMCID: PMC8459637.

Conclusion: This meta-analysis suggests that cell therapy may improve LV systolic function and may be associated with improvement in LVEDD and functional capacity compared with maximal medical therapy. Cell therapy was safe, with no significant difference in MACEs between treatment and control groups. However, given the limitations of current studies, larger well-designed RCTs are needed to evaluate the efficacy of cell therapy in patients with NICM.

Wang H, Roche CD, Gentile C. Omentum support for cardiac regeneration in ischaemic cardiomyopathy models: a systematic scoping review. *Eur J Cardiothorac Surg.* 2020 Dec 1;58(6):1118-1129. doi: 10.1093/ejcts/ezaa205. PMID: 32808023; PMCID: PMC7697859.

Conclusions: The omentum is a promising support for myocardial regenerative bioengineering in vivo. Future studies would benefit from more homogenous methodologies and reporting of outcomes to allow for direct comparison.

Liu B, Zhang J, Zhou Z, Feng B, He J, Yan W, Zhou X, Amponsah AE, Guo R, Du X, Liu X, Cui H, O'Brien T, Ma J. Preclinical Evidence for the Effectiveness of Mesenchymal Stromal Cells for Diabetic Cardiomyopathy: A Systematic Review and Meta-Analysis. *Curr Stem Cell Res Ther.* 2023 May 10. doi: 10.2174/1574888X18666230510111302. Epub ahead of print. PMID: 37165495.

Conclusion: Our results suggest a therapeutic role for MSCs in the treatment of DCM, and these results provide support for the use of MSCs in clinical trials of patients with DCM.

Xia L, Zeng L, Pan J, Ding Y. Effects of stem cells on non-ischemic cardiomyopathy: a systematic review and meta-analysis of randomized controlled trials. *Cytotherapy.* 2020 Dec;22(12):699-711. doi: 10.1016/j.jcyt.2020.06.006. Epub 2020 Sep 4. PMID: 32893120.

Conclusions: This meta-analysis demonstrates that stem cell therapy may improve survival, exercise capacity and cardiac ejection fraction in NICM, which suggests that stem cells are a promising option for NICM treatment.

Gorjipour F, Hosseini Gohari L, Hajimiresmaiel SJ, Janani L, Moradi Y, Pazoki-Toroudi H. Amniotic Membrane-Derived Mesenchymal Stem Cells for Heart Failure: A Systematic Review and Meta-Analysis of the Published Preclinical Studies. *Med J Islam Repub Iran.* 2021 Dec 30;35:187. doi: 10.47176/mjiri.35.187. PMID: 36042827; PMCID: PMC9391776.

Conclusion: Present low and medium quality evidence from preclinical studies confirm the efficacy of the AMSCs in the preclinical models of acute MI and HF following ischemia due to coronary artery stenosis and permanent/temporary coronary artery occlusion. High-quality preclinical studies are indicated to bridge the gaps in translation of the current findings of AMSCs research for the treatment of patients with acute and chronic myocardial ischemia and heart failure.

Diaz-Navarro R, Urrútia G, Cleland JG, Poloni D, Villagran F, Acosta-Dighero R, Bangdiwala SI, Rada G, Madrid E. Stem cell therapy for dilated cardiomyopathy. *Cochrane Database Syst Rev.* 2021 Jul 21;7(7):CD013433. doi: 10.1002/14651858.CD013433.pub2. PMID: 34286511; PMCID: PMC8406792.

Authors' conclusions: We are uncertain whether SCT in people with DCM reduces the risk of all-cause mortality and procedural complications, improves HRQoL, and performance status (exercise capacity). SCT may improve functional class (NYHA), compared to usual care (no cells). Similarly, when compared to G-CSF, we are also uncertain whether SCT in people with DCM reduces the risk of all-cause mortality although some studies within this comparison observed a favourable effect that should be interpreted with caution. SCT may not improve HRQoL but may improve to some extent performance status (exercise capacity). Very low-quality evidence reflects uncertainty regarding procedural complications. These suggested beneficial effects of SCT, although uncertain due to the very low certainty of the evidence, are accompanied by favourable effects on some physiological measures of cardiac function. Presently, the most effective mode of administration of SCT and the population that could benefit the most is unclear. Therefore, it seems reasonable that use of SCT in people with DCM is limited to clinical research settings. Results of ongoing studies are likely to modify these conclusions.

<p>T4: Are there treatments which can prevent cardiomyopathy developing in people at risk? Are there treatments to stop it getting worse in people with symptoms?</p>		
<p>T5: Should treatment for cardiomyopathy be tailored to the individual, e.g. based on their specific gene variant, age or gender?</p>	<p>Bariani R, Rigato I, Cason M, Marinas MB, Celeghin R, Pilichou K, Bauce B. Genetic Background and Clinical Features in Arrhythmogenic Left Ventricular Cardiomyopathy: A Systematic Review. J Clin Med. 2022 Jul 25;11(15):4313. doi: 10.3390/jcm11154313. PMID: 35893404; PMCID: PMC9332695.</p> <p>Conclusion: Overall, ECG abnormalities were reported in 58% of patients. Major ventricular arrhythmias were recorded in 26% of cases; an ICD was implanted in 29% of patients. A total of 6% of patients showed heart failure symptoms, and 15% had myocarditis-like episodes. DSP is confirmed to be the most represented disease-gene in ALVC patients. An analysis of reported clinical features of ALVC patients show an important degree of electrical instability, which frequently required an ICD implant. Moreover, myocarditis-like episodes are common.</p> <p>Bariani R, Rigato I, Cipriani A, Bueno Marinas M, Celeghin R, Basso C, Corrado D, Pilichou K, Bauce B. Myocarditis-like Episodes in Patients with Arrhythmogenic Cardiomyopathy: A Systematic Review on the So-Called Hot-Phase of the Disease. Biomolecules. 2022 Sep 19;12(9):1324. doi: 10.3390/biom12091324. PMID: 36139162; PMCID: PMC9496041.</p> <p>In conclusion, ACM patients showing hot-phase episodes are usually young, and <i>DSP</i> is the most common disease gene, accounting for 69% of cases. Currently, the role of "hot-phase" episodes in disease progression and arrhythmic risk stratification remains to be clarified.</p> <p>Peters S, Thompson BA, Perrin M, James P, Zentner D, Kalman JM, Vandenberg JI, Fatkin D. Arrhythmic Phenotypes Are a Defining Feature of Dilated Cardiomyopathy-Associated SCN5A Variants: A Systematic Review. Circ Genom Precis Med. 2022 Feb;15(1):e003432. doi: 10.1161/CIRCGEN.121.003432. Epub 2021 Dec 24. PMID: 34949099.</p> <p>Conclusions: SCN5A variants can present with a diverse spectrum of primary arrhythmic features. A</p>	

	<p>majority of DCM-associated variants cause a multifocal VPB-predominant cardiomyopathy that is reversible with sodium channel blocking drug therapy. Early recognition of the distinctive phenotype and prompt genetic testing to identify variant carriers are needed. Our findings have implications for interpretation and management of SCN5A variants found in DCM patients with and without arrhythmias.</p> <p>Goyal A, Lahan S, Dalia T, Ranka S, Bhattad VB, Patel RR, Shah Z. Clinical comparison of V122I genotypic variant of transthyretin amyloid cardiomyopathy with wild-type and other hereditary variants: a systematic review. Heart Fail Rev. 2022 May;27(3):849-856. doi: 10.1007/s10741-021-10098-6. Epub 2021 Mar 25. PMID: 33768376.</p> <p>Conclusion: The mean age of diagnosis among wild-type ATTR patients was 77 years, followed by 71.2 and 65 years in V122I and T60A group patients, respectively. V122I patients were mostly black, had a poor quality of life, and highest mortality risk compared with other subtypes. Merely, the presence of V122I mutation was identified as an independent predictor of mortality. V30M subtype correlated with the least severe cardiac disease and a median survival duration comparable with T60A subtype. V122I ATTR is an aggressive disease, prevalent in African-Americans, and is associated with a greater morbidity and mortality, which is partly attributed to its misdiagnosis and/or late diagnosis. Current advances in non-invasive studies to diagnose hATTR coupled with concurrent drug therapies have improved quality of life and provide a survival benefit to these patients.</p>	
<p>T6: Can gene therapy be used to prevent cardiomyopathy developing in people at risk or to treat people with symptoms?</p>		
<p>T7: What are the long-term side-effects of treatment for cardiomyopathy? Can drugs with fewer side-</p>		

effects be developed?		
T8: What causes fatigue in people with cardiomyopathy and how is it best treated and managed?		
T9: What are the best ways to treat and manage chest, joint and muscle pain in people with cardiomyopathy?		
T10: Could a mechanical heart or a pig heart be used as an alternative to human heart transplants for people with cardiomyopathy?		
T11: Would treatment through changes in diet and supplements (e.g. to reduce inflammation) benefit people with cardiomyopathy?		
T12: Can existing surgical and non-surgical procedures (e.g. ablation) be improved, or new ones developed to improve outcomes for people with cardiomyopathy?	<p>Seco M, Lau JC, Medi C, Bannon PG. Atrial fibrillation management during septal myectomy for hypertrophic cardiomyopathy: A systematic review. <i>Asian Cardiovasc Thorac Ann.</i> 2022 Jan;30(1):98-107. doi: 10.1177/02184923211042136. Epub 2021 Sep 6. PMID: 34486381.</p> <p>Conclusion: In patients with atrial fibrillation undergoing septal myectomy, the addition of ablation surgery adds low overall risk to the procedure, and likely reduces the risk of recurrent atrial fibrillation in the long term. Future randomised studies comparing septal myectomy with or without concomitant AF ablation are needed.</p>	

Kanagaratnam A, Virk SA, Pham T, Anderson RD, Turnbull S, Campbell T, Bennett R, Thomas SP, Lee G, Kumar S. Catheter Ablation for Ventricular Tachycardia in Ischaemic Versus Non-Ischaemic Cardiomyopathy: A Systematic Review and Meta-Analysis. *Heart Lung Circ.* 2022 Aug;31(8):1064-1074. doi: 10.1016/j.hlc.2022.02.014. Epub 2022 May 25. PMID: 35643798.

Conclusions: NICM and ICM patients undergoing VT ablation are fundamentally different in their clinical characteristics, ablation approaches, acute procedural outcomes and likelihood of VA recurrence. VT ablation in NICM has a lower likelihood of procedural success with increased risk of VA recurrence, consistent with known challenging arrhythmia substrate.

Jiang T, Huang B, Huo S, Mageta LM, Guo J, Lv J, Lin L. Endocardial Radiofrequency Ablation vs. Septal Myectomy in Patients With Hypertrophic Obstructive Cardiomyopathy: A Systematic Review and Meta-Analysis. *Front Surg.* 2022 Apr 26;9:859205. doi: 10.3389/fsurg.2022.859205. PMID: 35558385; PMCID: PMC9086505.

Conclusions: This systematic review suggests that SM is superior to ERASH in the treatment of HOCM. But for the patients who are at risk for open cardiac surgeries or prefer a less invasive approach, ERASH might be an optional approach.

Kharbanda RK, Ramdat Misier NL, Van den Eynde J, El Mathari S, Tomšič A, Palmen M, Klautz RJM. Outcomes of concomitant surgical ablation in patients undergoing surgical myectomy for hypertrophic obstructive cardiomyopathy: A systematic review and meta-analysis. *Int J Cardiol.* 2023 Sep 15;387:131099. doi: 10.1016/j.ijcard.2023.05.049. Epub 2023 May 30. PMID: 37263356.

Conclusion: This meta-analysis supports concomitant surgical AF ablation at the time of surgical myectomy in HOCM patients, as it seems to be safe and effective in terminating AF.

Mihos CG, Escolar E, Fernandez R, Nappi F. A systematic review and pooled analysis of septal myectomy and edge-to-edge mitral valve repair in obstructive hypertrophic cardiomyopathy. *Rev Cardiovasc Med.* 2021 Dec 22;22(4):1471-1477. doi: 10.31083/j.rcm2204151. PMID: 34957786.

Conclusion: In conclusion, combined septal myectomy and edge-to-edge MV repair is a safe and effective treatment strategy in carefully selected patients requiring surgical HCM management.

Romero J, Patel K, Briceno D, Alviz I, Gabr M, Diaz JC, Trivedi C, Mohanty S, Della Rocca D, Al-Ahmad A, Yang R, Rios S, Cerna L, Du X, Tarantino N, Zhang XD, Lakkireddy D, Natale A, Di Biase L. Endo-epicardial ablation vs endocardial ablation for the management of ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy: A systematic review and meta-analysis. *J Cardiovasc Electrophysiol*. 2020 Aug;31(8):2022-2031. doi: 10.1111/jce.14593. Epub 2020 Jun 18. PMID: 32478430.

Conclusions: Our findings suggest that in patients with ARVC, endo-epicardial VT ablation is associated with a significant reduction in VA recurrence as opposed to endocardial ablation alone, without a significant difference in all-cause mortality or acute procedural complications.

Yokoyama Y, Shimoda T, Shimada YJ, Shimamura J, Akita K, Yasuda R, Takayama H, Kuno T. Alcohol septal ablation versus surgical septal myectomy of obstructive hypertrophic cardiomyopathy: systematic review and meta-analysis. *Eur J Cardiothorac Surg*. 2023 Mar 1;63(3):ezad043. doi: 10.1093/ejcts/ezad043. PMID: 36782361.

Conclusions: Although both septal reduction therapies were associated with similar all-cause mortality, ASA was associated with a higher rate of reoperation and less reduction of LVOT pressure gradient. Furthermore, all-cause mortality with follow-up ≥ 5 years showed favourable outcomes with septal myectomy, although the result is only hypothesis-generating given a subgroup analysis.

Shah K, Turagam M, Patel B, Natale A, Lakkireddy D, Garg J. Prophylactic Catheter Ablation of Ventricular Tachycardia in Ischemic Cardiomyopathy: a systematic review and meta-analysis of randomized controlled trials Electrophysiology Collaborative Consortium for Metaanalysis - ELECTRAM Investigators. *J Atr Fibrillation*. 2020 Aug 31;13(2):2371. doi: 10.4022/jafib.2371. PMID: 34950297; PMCID: PMC8691309.

Conclusions: Prophylactic catheter ablation in ischemic cardiomyopathy patients was associated with a lower risk of ICD therapies, including ICD shocks and VT storm with no difference in cardiac and all-cause mortality.

Shen LS, Liu LM, Zheng LH, Hu F, Hu ZC, Liu SY, Guo JR, Bhagat KK, Yao Y. Ablation strategies for arrhythmogenic right ventricular cardiomyopathy: a systematic review and meta-analysis. *J Geriatr Cardiol*. 2020 Nov 28;17(11):694-703. doi: 10.11909/j.issn.1671-5411.2020.11.001. PMID: 33343648; PMCID:

	<p>PMC7729178.</p> <p>Conclusion: Catheter ablation for VT in ARVC is feasible and effective. Epicardial ablation is associated with better long-term VT freedom, but with more major complications and unremarkable survival or acute efficacy benefit.</p> <p>Bytyci I, Nistri S, Morner S, Henein MY. Alcohol septal ablation versus septal myectomy treatment of obstructive hypertrophic cardiomyopathy: a systematic review and meta-analysis. J Clin Med 2020;9:3062. https://doi.org/10.3390/jcm9103062</p> <p>Conclusion: Thus, ASA and SM treatment of HOCM carry a similar risk of mortality. Peri-procedural complications are less in alcohol ablation but re-intervention and pacemaker implantations are more common. These results might impact the procedure choice in individual patients, for the best clinical outcome.</p>	
<p>T13: What are the best approaches to cardiac rehabilitation for people with cardiomyopathy?</p>	<p>Bjarnason-Wehrens B, Nebel R, Jensen K, Hackbusch M, Grilli M, Gielen S, Schwaab B, Rauch B; German Society of Cardiovascular Prevention and Rehabilitation (DGPR). Exercise-based cardiac rehabilitation in patients with reduced left ventricular ejection fraction: The Cardiac Rehabilitation Outcome Study in Heart Failure (CROS-HF): A systematic review and meta-analysis. Eur J Prev Cardiol. 2020 Jun;27(9):929-952. doi: 10.1177/2047487319854140. Epub 2019 Jun 8. PMID: 31177833; PMCID: PMC7272131.</p> <p>Conclusion: No association between exercise-based cardiac rehabilitation and mortality or hospitalisation could be observed in HFrEF patients but exercise-based cardiac rehabilitation is likely to improve exercise capacity and quality of life.</p>	
<p>T14: How does cardiomyopathy affect people's sex lives and what treatments (e.g. Viagra and contraception) are safe and effective?</p>		
<p>T15: Can drug treatment reverse changes to the</p>		

<p>heart to a point where people with cardiomyopathy can safely stop their medication?</p>		
<p>T16: What are the best ways to treat heart failure in people with cardiomyopathy?</p>	<p>Botello-Flores YA, Yocupicio-Monroy M, Balderrábano-Saucedo N, Contreras-Ramos A. A systematic review on the role of MSC-derived exosomal miRNAs in the treatment of heart failure. <i>Mol Biol Rep.</i> 2022 Sep;49(9):8953-8973. doi: 10.1007/s11033-022-07385-2. Epub 2022 Apr 1. Erratum in: <i>Mol Biol Rep.</i> 2022 May 2;: PMID: 35359236.</p> <p>Conclusions: The results from this systematic review support the initial hypothesis and encourage us to test it in future experimental research works but more importantly, we seek to encourage other researchers in the field to propose other hypotheses aimed at the possible use of exo-miRNAs in HF secondary to cardiac disease.</p> <p>Kalou Y, Al-Khani AM, Haider KH. Bone Marrow Mesenchymal Stem Cells for Heart Failure Treatment: A Systematic Review and Meta-Analysis. <i>Heart Lung Circ.</i> 2023 Jul;32(7):870-880. doi: 10.1016/j.hlc.2023.01.012. Epub 2023 Mar 3. PMID: 36872163.</p> <p>Conclusion: BM-MSCs treatment is an effective intervention for managing patients with heart failure, but it requires larger and more robust clinical trials to support its routine use in clinics.</p> <p>Edwards JJ, O'Driscoll JM. Exercise Training in Heart failure with Preserved and Reduced Ejection Fraction: A Systematic Review and Meta-Analysis. <i>Sports Med Open.</i> 2022 Jun 8;8(1):76. doi: 10.1186/s40798-022-00464-5. PMID: 35674912; PMCID: PMC9177931.</p> <p>Conclusion: ET significantly improves exercise capacity and quality of life in both HFpEF and HFrEF patients. In HFpEF patients, ET significantly improved an important index of diastolic function, with significant improvements in LVEF and NTproBNP/BNP seen in HFrEF patients only. Such benefits did not translate into significantly reduced hospitalisation or mortality after short-term follow-up.</p> <p>Pan D, Xu L, Chen P, Jiang H, Shi D, Guo M. Empagliflozin in Patients With Heart Failure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. <i>Front Cardiovasc Med.</i> 2021 Jun 22;8:683281.</p>	

doi: 10.3389/fcvm.2021.683281. PMID: 34239906; PMCID: PMC8257947.

Conclusion: The findings suggest that empagliflozin was effective in reducing a composite of cardiovascular death or hospitalization for worsening heart failure. Further well-designed RCTs are needed to evaluate the long-term effect of empagliflozin in patients with HF.

McGee MJ, Ray M, Briennes SC, Sritharan S, Boyle AJ, Jackson N, Leitch JW, Sverdlov AL. Remote monitoring in patients with heart failure with cardiac implantable electronic devices: a systematic review and meta-analysis. *Open Heart*. 2022 Nov;9(2):e002096. doi: 10.1136/openhrt-2022-002096. PMID: 36442906; PMCID: PMC9710367.

Conclusion: RM for patients with CIEDs and HF was not uniformly performed. As currently implemented, RM does not provide a benefit on overall mortality or the key metric of HF readmission. It does provide a reduction in healthcare costs and healthcare presentations.

Yang D, Zhang Y, Yan J, Liu M, An F. SGLT-2 inhibitors on prognosis and health-related quality of life in patients with heart failure and preserved ejection fraction: A systematic review and meta-analysis. *Front Cardiovasc Med*. 2022 Sep 8;9:942125. doi: 10.3389/fcvm.2022.942125. PMID: 36158789; PMCID: PMC9492916.

Conclusion: Treating HFpEF patients with SGLT-2 inhibitors is associated with reducing the composite outcome of CV death and HFrEF and improving health-related quality of life. Further studies with more evidence are in need to confirm this conclusion.

Siranart N, Chokesuwattanaskul R, Prasitlumkum N, Huntrakul A, Phanthong T, Sowalertrat W, Navaravong L, Cheungpasitporn W, Jongnarangsin K. Reverse of left ventricular remodeling in heart failure patients with left bundle branch area pacing: Systematic review and meta-analysis. *Pacing Clin Electrophysiol*. 2023 Jun;46(6):459-466. doi: 10.1111/pace.14661. Epub 2023 Jan 30. PMID: 36633357.

Conclusions: LBBAP was associated with improvements in both cardiac function and electrical synchrony. The benefits of LBBAP in individuals with HFrEF and dyssynchrony should be further validated by randomized studies.

He Z, Yang L, Nie Y, Wang Y, Wang Y, Niu X, Bai M, Yao Y, Zhang Z. Effects of SGLT-2 inhibitors on health-related quality of life and exercise capacity in heart failure patients with reduced ejection fraction: A systematic review and meta-analysis. *Int J Cardiol.* 2021 Dec 15;345:83-88. doi: 10.1016/j.ijcard.2021.10.008. Epub 2021 Oct 13. PMID: 34653575.

Conclusions: Our meta-analysis demonstrates that SGLT-2 inhibitors significantly improve HRQoL, and supports the concept that SGLT-2 inhibitors do not significantly improve exercise capacity in patients with HFrEF. Studies with larger sample sizes and longer follow-up duration are needed to determine whether the treatment with SGLT-2 inhibitors may improve exercise ability.

Moghaddam N, Malhi N, Toma M. Impact of oral soluble guanylate cyclase stimulators in heart failure: A systematic review and Meta-analysis of randomized controlled trials. *Am Heart J.* 2021 Nov;241:74-82. doi: 10.1016/j.ahj.2021.07.003. Epub 2021 Jul 18. PMID: 34283990.

Conclusion: Oral sGC stimulators are well tolerated in HF and reduce the incidence of HF hospitalization but not cardiovascular death among patients with HFrEF. However, there are no apparent benefits in HFpEF.

Karakasis P, Pamporis K, Stachteas P, Patoulis D, Bougioukas KI, Fragakis N. Efficacy and safety of sodium-glucose cotransporter-2 inhibitors in heart failure with mildly reduced or preserved ejection fraction: an overview of 36 systematic reviews. *Heart Fail Rev.* 2023 Sep;28(5):1033-1051. doi: 10.1007/s10741-023-10324-3. Epub 2023 Jun 7. PMID: 37284930.

Conclusion: The use of SGLT2i in HFpEF is both efficient and safe. Further research is required to clarify the impact of SGLT2i on different subphenotypes of HFpEF and the cardiorespiratory capacity of these patients.

Yang HR, Xu XD, Shaikh AS, Zhou BT. Efficacy and Safety of Sacubitril/Valsartan Compared With ACEI/ARB on Health-Related Quality of Life in Heart Failure Patients: A Meta-Analysis. *Ann Pharmacother.* 2023 Aug;57(8):907-917. doi: 10.1177/10600280221140575. Epub 2022 Dec 8. PMID: 36475871.

Conclusions: Sacubitril/valsartan may have the potential to improve HRQoL in heart failure patients with reduced ejection fraction compared with ACEI/ARB. Hypotension is the most common adverse event with

sacubitril/valsartan compared with ACEI/ARB. The results of this study may contribute to the rational use of sacubitril/valsartan.

Tegegne TK, Rawstorn JC, Nourse RA, Kibret KT, Ahmed KY, Maddison R. Effects of exercise-based cardiac rehabilitation delivery modes on exercise capacity and health-related quality of life in heart failure: a systematic review and network meta-analysis. *Open Heart*. 2022 Jun;9(1):e001949. doi: 10.1136/openhrt-2021-001949. PMID: 35680170; PMCID: PMC9185675.

Conclusion: ExCR programmes have broader benefits for people with HF and since different delivery modes were comparably effective for improving exercise capacity and HRQoL, the selection of delivery modes should be tailored to individuals' preferences.

Li M, Yi T, Fan F, Qiu L, Wang Z, Weng H, Ma W, Zhang Y, Huo Y. Effect of sodium-glucose cotransporter-2 inhibitors on blood pressure in patients with heart failure: a systematic review and meta-analysis. *Cardiovasc Diabetol*. 2022 Jul 25;21(1):139. doi: 10.1186/s12933-022-01574-w. PMID: 35879763; PMCID: PMC9317067.

Conclusions: SGLT2i decreased systolic blood pressure in patients with HF but had no effect on diastolic blood pressure. These inhibitors may have numerous potentially beneficial clinical effects in patients with HF.

Maagaard M, Nielsen EE, Sethi NJ, Liang N, Yang SH, Gluud C, Jakobsen JC. Ivabradine added to usual care in patients with heart failure: a systematic review with meta-analysis and trial sequential analysis. *BMJ Evid Based Med*. 2022 Aug;27(4):224-234. doi: 10.1136/bmjebm-2021-111724. Epub 2021 Nov 17. PMID: 34789473; PMCID: PMC9340018.

Conclusion and relevance: High certainty evidence shows that ivabradine does not seem to affect the risks of all-cause mortality and cardiovascular mortality. The effects on quality of life were small and possibly without relevance to patients on the KCCQ and were very uncertain for the MLWHFQ. The effects on serious adverse events, myocardial infarction and hospitalisation are uncertain. Ivabradine seems to increase the risk of atrial fibrillation, bradycardia and non-serious adverse events.

Chambergo-Michilot D, Tauma-Arrué A, Loli-Guevara S. Effects and safety of SGLT2 inhibitors compared to placebo in patients with heart failure: A systematic review and meta-analysis. *Int J Cardiol Heart Vasc*. 2020 Dec 11;32:100690. doi: 10.1016/j.ijcha.2020.100690. PMID: 33335975; PMCID: PMC7734238.

Conclusions: SGLT2i showed to improve critical outcomes in HF patients, and it is apparently safe.

Treewaree S, Kulthamrongsri N, Owattanapanich W, Krittayaphong R. Is it time for class I recommendation for sodium-glucose cotransporter-2 inhibitors in heart failure with mildly reduced or preserved ejection fraction?: An updated systematic review and meta-analysis. *Front Cardiovasc Med*. 2023 Feb 7;10:1046194. doi: 10.3389/fcvm.2023.1046194. PMID: 36824458; PMCID: PMC9941559.

Conclusion: This study demonstrates the benefits of SGLT2 inhibitors for improving cardiovascular outcomes and QoL in HFmrEF or HFpEF patients.

Jain A, Meyur S, Wadhwa L, Singh K, Sharma R, Panchal I, Varrassi G. Effects of Angiotensin Receptor-Nepriylsin Inhibitors Versus Enalapril or Valsartan on Patients With Heart Failure: A Systematic Review and Meta-Analysis. *Cureus*. 2023 Jul 8;15(7):e41566. doi: 10.7759/cureus.41566. PMID: 37554618; PMCID: PMC10405977.

Conclusion: The research findings suggest that sacubitril/valsartan (LCZ696) reduces hospitalizations due to heart failure and improves KCCQ clinical scores. This treatment also reduces the decline in renal function and side effects associated with enalapril or valsartan. Nonetheless, further high-quality randomized controlled trials with large sample sizes are needed to assess other impacts of this therapy on heart failure patients. Overall, the use of LCZ696 represents a promising new approach to the treatment of heart failure.

Li R, Dai G, Guan H, Gao W, Ren L, Wang X, Qu H. Scientific evidence of sodium-glucose cotransporter-2 inhibitors for heart failure with preserved ejection fraction: an umbrella review of systematic reviews and meta-analyses. *Front Cardiovasc Med*. 2023 May 12;10:1143658. doi: 10.3389/fcvm.2023.1143658. PMID: 37252111; PMCID: PMC10213331.

Conclusions: SGLT-2 is a potential treatment for HFpEF with favourable safety. Given the dubious methodological quality, reporting quality, evidence quality, and high risk of bias for certain included

	<p>SRs/MAs, this conclusion must be drawn with caution.</p> <p>Chen Z, Zhao K, Xiao C, He Z, Liu S, Wu X, Shi S, Guo Y. Phosphodiesterase inhibitor for heart failure with preserved ejection fraction: A systematic review and meta-analysis. Saudi Pharm J. 2022 Aug;30(8):1079-1087. doi: 10.1016/j.jsps.2022.05.012. Epub 2022 Jun 1. PMID: 36164567; PMCID: PMC9508622.</p> <p>Conclusions: PDE inhibitors did not effectively improve LV function, PAP, exercise capacity, and QOL in patients with HFpEF. However, they improved RV function with significant difference, suggesting that PDE inhibitors might be a promising option for HFpEF patients with RV dysfunction.</p> <p>Qin J, Wang W, Wei P, Huang P, Lin R, Yue J. Effects of sacubitril-valsartan on heart failure patients with mid-range ejection fractions: A systematic review and meta-analysis. Front Pharmacol. 2022 Oct 24;13:982372. doi: 10.3389/fphar.2022.982372. PMID: 36353496; PMCID: PMC9638065.</p> <p>Conclusion: This meta-analysis suggests ARNI may be an effective strategy with which to improve the left ventricular function, and quality of life, and reduce the readmission rate in HFmrEF patients. However, long-term clinical studies with large samples are still needed to further explore the efficacy and safety of ARNI compared with ACEI or ARB in the HFmrEF population.</p> <p>Molina-Linde JM, Cordero-Pereda D, Baños-Álvarez E, Rosario-Lozano MP, Blasco-Amaro JA. Efficacy and safety of baroreflex activation therapy for heart failure with reduced ejection fraction: systematic review. ESC Heart Fail. 2023 Jul 31. doi: 10.1002/ehf2.14473. Epub ahead of print. PMID: 37522644.</p> <p>Conclusion: The results show that BAT is safe and improves functional class, quality of life and congestion in selected patients with HFrEF. Further studies and long-term follow-up are needed to assess efficacy in reducing cardiovascular events and mortality.</p>	
<p>T17: What is the optimum blood pressure and heart rate for people with cardiomyopathy?</p>		
<p>T18: Which people with cardiomyopathy benefit</p>	<p>He W, Xue C, Zheng J, Shuai Z. The mortality for the implantable cardiac defibrillator in nonischemic cardiomyopathy: An updated systematic review and meta-analysis. Clin Cardiol. 2022 Dec;45(12):1163-</p>	

most from an ICD (implantable cardioverter defibrillator)?

1170. doi: 10.1002/clc.23907. Epub 2022 Sep 3. PMID: 36056632; PMCID: PMC9748743.

Conclusion: In the current meta-analysis, the ICD treatment might show a lower relative risk and hazard ratio of all-cause mortality and sudden cardiac death when compared with medicine treatment. However, no significant differences were observed in cardiovascular mortality between ICD and medicine treatment.

Tukker M, Schinkel AFL, Dereci A, Caliskan K. Clinical outcomes of implantable cardioverter-defibrillator therapy in noncompaction cardiomyopathy: a systematic review and meta-analysis. *Heart Fail Rev.* 2023 Jan;28(1):241-248. doi: 10.1007/s10741-022-10250-w. Epub 2022 Jun 10. PMID: 35689132; PMCID: PMC9902401.

Conclusion: Patients with NCCM who are at increased risk of SCD may significantly benefit from ICD therapy, with a high appropriate ICD therapy rate of 11.95 per 100 person-years and a low cardiac mortality rate of 2.37 per 100 person-years. Inappropriate therapy rate of 4.8 per 100 person-years and ICD-related complications were not infrequent and may lead to patient morbidity.

Sammani A, Kayvanpour E, Bosman LP, Sedaghat-Hamedani F, Proctor T, Gi WT, Broezel A, Jensen K, Katus HA, Te Riele ASJM, Meder B, Asselbergs FW. Predicting sustained ventricular arrhythmias in dilated cardiomyopathy: a meta-analysis and systematic review. *ESC Heart Fail.* 2020 Aug;7(4):1430-1441. doi: 10.1002/ehf2.12689. Epub 2020 Apr 14. PMID: 32285648; PMCID: PMC7373946.

Conclusions: In patients with DCM, the annual event rate of sustained ventricular arrhythmias is approximately 4.5%. This risk is considerably higher in younger patients with hypertension, prior (non-)sustained ventricular arrhythmia, decreased left ventricular ejection fraction, left ventricular dilatation, late gadolinium enhancement, and genetic mutations (PLN, LMNA, and FLNC). These results may help determine appropriate candidates for implantable cardioverter-defibrillator implantation.

Wasiak M, Tajstra M, Kosior D, Gąsior M. An implantable cardioverter-defibrillator for primary prevention in non-ischemic cardiomyopathy: A systematic review and meta-analysis. *Cardiol J.* 2023;30(1):117-124. doi: 10.5603/CJ.a2021.0041. Epub 2021 Apr 12. PMID: 33843044; PMCID: PMC9987540.

Conclusions: In comparison with optimal medical treatment, ICD implantation in patients with heart failure improves the long-term prognosis in terms of sudden cardiac death, with a strong tendency

towards all-cause mortality reduction.

Papanastasiou CA, Zegkos T, Karamitsos TD, Rowin EJ, Maron MS, Parcharidou D, Kokkinidis DG, Karvounis H, Rimoldi O, Maron BJ, Efthimiadis GK. Prognostic role of left ventricular apical aneurysm in hypertrophic cardiomyopathy: A systematic review and meta-analysis. *Int J Cardiol.* 2021 Jun 1;332:127-132. doi: 10.1016/j.ijcard.2021.03.056. Epub 2021 Mar 29. PMID: 33794232.

Conclusions: These data demonstrate that LV apical aneurysm in HCM patients is associated with an increased risk for SCD events and thromboembolism. This finding might encourage the inclusion of LV apical aneurysm into the HCM SCD risk stratification algorithm as a novel risk marker that supports consideration for primary prevention implantable cardioverter defibrillator and anticoagulation for stroke prophylaxis.

Kamp NJ, Chery G, Kosinski AS, Desai MY, Wazni O, Schmidler GS, Patel M, Lopes RD, Morin DP, Al-Khatib SM. Risk stratification using late gadolinium enhancement on cardiac magnetic resonance imaging in patients with hypertrophic cardiomyopathy: A systematic review and meta-analysis. *Prog Cardiovasc Dis.* 2021 May-Jun;66:10-16. doi: 10.1016/j.pcad.2020.11.001. Epub 2020 Nov 7. PMID: 33171204.

Conclusion: In patients with HCM, LGE on c-MRI is a strong predictor of arrhythmic outcomes including SCD, aborted SCD, and appropriate ICD therapy. These data support the routine use of LGE on c-MRI as a marker of SCD risk in this population.

Chery G, Kamp N, Kosinski AS, Schmidler GS, Lopes RD, Patel M, Al-Khatib SM. Prognostic value of myocardial fibrosis on cardiac magnetic resonance imaging in patients with ischemic cardiomyopathy: A systematic review. *Am Heart J.* 2020 Nov;229:52-60. doi: 10.1016/j.ahj.2020.08.004. Epub 2020 Aug 11. PMID: 32916608; PMCID: PMC7417269.

Conclusions: LGE has high prognostic value in predicting adverse outcomes in patients with ICM and may provide helpful information for clinical decision making related to SCD prevention. Our findings illustrate how LGE may improve current risk stratification, prognostication, and selection of patients with ICM for ICD therapy.

Anagnostopoulos I, Kousta M, Kossyvakis C, Lakka E, Paraskevaidis NT, Schizas N, Alexopoulos N, Deftereos S, Giannopoulos G. The prognostic role of late gadolinium enhancement on cardiac magnetic resonance in patients with nonischemic cardiomyopathy and reduced ejection fraction, implanted with cardioverter defibrillators for primary prevention. A systematic review and meta-analysis. *J Interv Card Electrophysiol.* 2022 Apr;63(3):523-530. doi: 10.1007/s10840-021-01027-6. Epub 2021 Jul 3. PMID: 34218421.

Conclusion: LGE is a highly sensitive predictor of ADT and cardiac death in NICM patients implanted with a defibrillator for primary prevention. However, due to moderate specificity, derivation of a cutoff with adequate predictive values and probably a multifactorial approach are needed to improve discrimination of patients who will not benefit from ICDs.

Theerasuwipakorn N, Chokesuwattanaskul R, Phannajit J, Marsukjai A, Thapanasuta M, Klem I, Chattranukulchai P. Impact of late gadolinium-enhanced cardiac MRI on arrhythmic and mortality outcomes in nonischemic dilated cardiomyopathy: updated systematic review and meta-analysis. *Sci Rep.* 2023 Aug 23;13(1):13775. doi: 10.1038/s41598-023-41087-4. PMID: 37612359; PMCID: PMC10447440.

Conclusion: Real-world evidence suggests that the presence of LGE on CMR was a strong predictor of adverse long-term outcomes in patients with NIDCM. Scar assessment should be incorporated as a primary determinant in the patient selection criteria for primary prophylactic implantable cardioverter-defibrillator placement.

Milaras N, Dourvas P, Doundoulakis I, Sotiriou Z, Nevras V, Xintarakou A, Laina A, Soulaïdopoulos S, Zachos P, Kordalis A, Arsenos P, Archontakis S, Antoniou CK, Tsiachris D, Dilaveris P, Tsioufis K, Sideris S, Gatzoulis K. Noninvasive electrocardiographic risk factors for sudden cardiac death in dilated cardiomyopathy: is ambulatory electrocardiography still relevant? *Heart Fail Rev.* 2023 Jul;28(4):865-878. doi: 10.1007/s10741-023-10300-x. Epub 2023 Mar 6. PMID: 36872393; PMCID: PMC10289982.

Conclusions: Although ambulatory electrocardiographic monitoring is frequently used in clinical practice in DCM patients, no single risk marker can be used for the selection of patients at high-risk for malignant ventricular arrhythmic events and sudden cardiac death who could benefit from the implantation of a defibrillator. More studies are needed in order to establish a risk score or a combination of risk factors

with the purpose of selecting high-risk patients for ICD implantation in the context of primary prevention.

Theuns DA, Verstraelen TE, van der Lingen ACJ, Delnoy PP, Allaart CP, van Erven L, Maass AH, Vernoooy K, Wilde AAM, Boersma E, Meeder JG. Implantable defibrillator therapy and mortality in patients with non-ischaemic dilated cardiomyopathy : An updated meta-analysis and effect on Dutch clinical practice by the Task Force of the Dutch Society of Cardiology. *Neth Heart J*. 2023 Mar;31(3):89-99. doi: 10.1007/s12471-022-01718-3. Epub 2022 Sep 6. PMID: 36066840; PMCID: PMC9950314.

Conclusion: ICD use significantly improved survival among patients with NICMP who are not eligible for CRT. Considering CRT, the addition of defibrillator therapy was not significantly associated with mortality benefit compared with CRT pacemaker.

Al-Sadawi M, Aslam F, Tao M, Fan R, Singh A, Rashba E. Association of late gadolinium enhancement in cardiac magnetic resonance with mortality, ventricular arrhythmias, and heart failure in patients with nonischemic cardiomyopathy: A systematic review and meta-analysis. *Heart Rhythm O2*. 2023 Jan 13;4(4):241-250. doi: 10.1016/j.hroo.2023.01.001. PMID: 37124560; PMCID: PMC10134398.

Conclusion: LGE in NICM patients is associated with increased mortality, VA and SCD, and HF hospitalization and heart transplantation referral during long-term follow up. Given these competing risks of mortality and HF progression, prospective randomized controlled trials are required to determine if LGE is useful for guiding prophylactic implantable cardioverter-defibrillator placement in NICM patients.

Khanra D, Manivannan S, Mukherjee A, Deshpande S, Gupta A, Rashid W, Abdalla A, Patel P, Padmanabhan D, Basu-Ray I. Incidence and Predictors of Implantable Cardioverter-defibrillator Therapies After Generator Replacement-A Pooled Analysis of 31,640 Patients' Data. *J Innov Card Rhythm Manag*. 2022 Dec 15;13(12):5278-5293. doi: 10.19102/icrm.2022.13121. PMID: 37293556; PMCID: PMC10246925.

Conclusion: The incidences of inappropriate shocks and other procedural complications were 2 and 2 per 100 patient-years, respectively, which corresponded to 6% and 4% of the entire cohort. Patients undergoing ICD GR continue to require therapy in a significant proportion of cases without any correlation with an improvement in LVEF. Further prospective studies are necessary to risk-stratify ICD patients undergoing GR.

<p>T19: Should people with cardiomyopathy but no symptoms be given treatment?</p>		
<p>T20: How can the devices used to treat cardiomyopathy (e.g. pacemakers) be improved?</p>	<p>Austin MA, Maynes EJ, Gadda MN, O'Malley TJ, Morris RJ, Shah MK, Pirlamarla PR, Alvarez RJ, Entwistle JW, Massey HT, Tchantchaleishvili V. Continuous-flow LVAD exchange to a different pump model: Systematic review and meta-analysis of the outcomes. <i>Artif Organs</i>. 2021 Jul;45(7):696-705. doi: 10.1111/aor.13893. Epub 2021 Feb 12. PMID: 33350485.</p> <p>Conclusions: Following device exchange from a different CF-LVAD model, HM3 is associated with lower stroke and higher survival when compared to HW.</p>	
<p>T21: What impact does hormone therapy have on people with cardiomyopathy e.g. for transgender people and menopausal women?</p>		
<p>PSYCHOLOGICAL & SOCIAL</p>		
<p>Y2: What are the emotional and psychological impacts of living with cardiomyopathy? How are these best treated and managed?</p>	<p>Pike A, Dobbin-Williams K, Swab M. Experiences of adults living with an implantable cardioverter defibrillator for cardiovascular disease: a systematic review of qualitative evidence. <i>JBI Evid Synth</i>. 2020 Nov;18(11):2231-2301. doi: 10.11124/JBISRIR-D-19-00239. PMID: 32813405.</p> <p>Conclusions: Evidence suggests that while implantable cardioverter defibrillator recipients do experience psychosocial distress, they gradually positively embrace the device as part of their everyday norm. Recommendations for practice and education point to the further development of best practice guidelines for implantable cardioverter defibrillator management, continuing education programs for health care providers, and strategies to support implantable cardioverter defibrillator recipients and their families to cope with the device. Research that examines onset, level, and duration of implantable cardioverter defibrillator psychosocial distress is needed to target specific interventions reflective of this population's needs. While findings suggest the experiences of women living with an implantable cardioverter</p>	

	defibrillator are similar to men, the low number of women in included studies limits the strength of this conclusion.	
Y3: How does cardiomyopathy affect quality of life for people living with the condition and their families (including financial impacts)? How can this be improved?	<p>Wiethoff I, Goversen B, Michels M, van der Velden J, Hiligsmann M, Kugener T, Evers SMAA. A systematic literature review of economic evaluations and cost-of-illness studies of inherited cardiomyopathies. <i>Neth Heart J</i>. 2023 Jun;31(6):226-237. doi: 10.1007/s12471-023-01776-1. Epub 2023 May 12. PMID: 37171710; PMCID: PMC10188671.</p> <p>Conclusion: Overall, knowledge of the societal and economic burden of inherited cardiomyopathies is limited. Future research needs to include quality-adjusted life years and a broader range of costs to provide an information base for optimising care for affected patients.</p>	
Y4: What psychological and practical support do people and their families need at the time they are first diagnosed with cardiomyopathy?		
Y6: How does living with the risk of cardiomyopathy affect the wellbeing of families? What emotional and practical support would be helpful?		
Y7: How does living with cardiomyopathy affect relationships with partners and family members? What emotional support would be helpful?		

Y8: How helpful is peer support for people with cardiomyopathy?		
Y9: How can people with cardiomyopathy best be supported in a return to good health after treatment?		