Sinkopa u bolesnika s dilatacijskom kardiomiopatijom: procjena aritmogenog rizika i suvremeni klinički pristup

Syncope in Dilated Cardiomyopathy: A Contemporary Review of Arrhythmic Risk and Clinical Management

Lucian Muresan[1]*, Gabriel Cismaru[2], Stefan Lucian Popa[3], Gabriel Gusetu[2], Mihai Puiu[2], Razvan Olimpiu Mada[4], Crina Muresan[1], Radu Rosu[2]

[1]Department of Cardiology, "Emile Muller" Hospital, Mulhouse, France
[2]Department of Cardiology, Clinical Rehabilitation Hospital, Cluj-Napoca, Romania
[3]2nd Medical Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania
[4]Department of Cardiology, "Niculae Stancioiu" Heart Institute, Cluj-Napoca, Romania

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SAŽETAK: Sinkopa u bolesnika s dilatacijskom kardiomiopatijom (DCM) klinički je važan događaj koji je povezan s ventrikulskim aritmijama, poremećajima provođenja, progresijom srčanog zatajivanja (HF) i povećanim rizikom od iznenadne srčane smrti. Međutim, mehanizmi nastanka sinkope, njezina prognostička važnost i optimalne strategije zbrinjavanja još uvijek nisu potpuno razjašnjeni. Proveli smo polusustavni narativni pregled literature pretraživanjem baza PubMed/MEDLINE, Scopus, Ovid i Cochrane Library od njihova osnutka do 1. ožujka 2026. Strategija pretraživanja obuhvaćala je kombinacije pojmova „sinkopa", „dilatacijska kardiomiopatija", „ventrikulska aritmija", „iznenadna srčana smrt" i „implantabilni kardioverterski defibrilator". U analizu su uključena izvorna istraživanja, sustavni pregledi, metaanalize i ključne smjernice stručnih društava. Učestalost sinkope u bolesnika s DCM-om kreće se od 3,3 % u općim kohortama do približno 14 % u populacijama s uznapredovalim HF-om. Prevladavaju kardiogeni uzroci, osobito ventrikulske tahiaritmije i poremećaji provođenja, premda se navode i neuralno posredovana sinkopa te ortostatska hipotenzija. Suvremena procjena rizika sve se više temelji na nalazima magnetne rezonancije srca (CMR) s kasnim nakupljanjem gadolinija i prisutnošću visokorizičnih genskih varijanti. Sinkopa u bolesnika s DCM-om povezana je sa znatno povećanom smrtnošću, osobito kada se sumnja na aritmijski mehanizam, a liječenje implantabilnim kardioverterskim defibrilatorom znatno poboljšava preživljenje u odgovarajuće odabranih bolesnika. Stoga sinkopu u bolesnika s DCM-om treba smatrati događajem koji je vrlo važan za stratifikaciju rizika te koji zahtijeva pravodobnu i sustavnu obradu. Integracija kliničke procjene, praćenja ritma srca, CMR-a, elektrofiziološkog ispitivanja i genske evaluacije može poboljšati prepoznavanje visokorizičnih bolesnika i omogućiti individualizirano liječenje.

SUMMARY: Syncope in patients with dilated cardiomyopathy (DCM) is a clinically important event associated with ventricular arrhythmias, conduction disease, progressive heart failure, and increased risk of sudden cardiac death. However, the mechanisms, prognostic implications, and optimal management strategies remain incompletely characterized. A semi-systematic narrative review was conducted using PubMed/MEDLINE, Scopus, Ovid, and the Cochrane Library from database inception through March 1, 2026. Search terms included combinations of "syncope," "dilated cardiomyopathy," "ventricular arrhythmia," "sudden cardiac death," and "implantable cardioverter-defibrillator." Original studies, systematic reviews, meta-analyses, and major society guidelines were included. The prevalence of syncope in DCM ranges from 3.3% in general DCM cohorts to approximately 14% in advanced heart failure populations. Cardiac causes predominate, particularly ventricular tachyarrhythmias and conduction disorders, although neurally mediated syncope and orthostatic hypotension also occur. Contemporary risk stratification increasingly incorporates cardiac magnetic resonance imaging with late gadolinium enhancement and high-risk genetic variants. Syncope in DCM is associated with significantly increased mortality, especially when arrhythmic mechanisms are suspected, and implantable cardioverter-defibrillator therapy substantially improves survival in appropriately selected patients. Syncope in DCM should therefore be regarded as a major risk-stratification event requiring prompt and systematic evaluation. Integration of clinical assessment, rhythm monitoring, cardiac magnetic resonance imaging, electrophysiological testing, and genetic evaluation may improve identification of high-risk patients and guide individualized management.

KLJUČNE RIJEČI: dilatacijska kardiomiopatija, magnetna rezonancija, iznenadna srčana smrt, sinkopa, ventrikulska tahikardija.

KEYWORDS: dilated cardiomyopathy, magnetic resonance imaging, sudden cardiac death, syncope, ventricular tachycardia.

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***ADDRESS FOR CORRESPONDENCE**: Lucian Muresan, Department of Cardiology, "Emile Muller" Hospital, 20 Avenue du Docteur René Laennec, 68100 Mulhouse, France. / Telephone: +33 389 64 64 64 / Fax: +33 389 64 27 35 / E-mail: lmure_san@yahoo.com

ORCID: Lucian Muresan, https://orcid.org/0000-0001-8314-4859 • Gabriel Cismaru, https://orcid.org/0000-0002-7352-9584 Stefan Lucian Popa, https://orcid.org/0000-0002-5508-2598 • Gabriel Gusetu, https://orcid.org/0000-0003-3796-6522 Razvan Olimpiu Mada, https://orcid.org/0000-0001-5574-3969 • Radu Rosu, https://orcid.org/0000-0001-8395-312X

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UVOD

Sinkopa, definirana kao prolazan gubitak svijesti uzrokovan globalnom cerebralnom hipoperfuzijom sa spontanim i potpunim oporavkom, česta je klinička slika koja čini dijagnostički izazov.[1,2] Iako refleksna sinkopa obično ima benignu prognozu, prisutnost strukturne bolesti srca bitno mijenja njezinu kliničku važnost.[3,4] Dilatacijska kardiomiopatija (DCM) visokorizična je bolest zbog popratne fibroze miokarda, remodeliranja klijetki, bolesti provodnog sustava i autonomne disfunkcije, a sinkopa u bolesnika s DCM-om povezana je s ventrikulskim aritmijama, iznenadnom srčanom smrću (SCD) i povećanom smrtnošću.[5-8]

Dvije strategije temeljene na implantabilnim uređajima odmah treba posebno naglasiti. Implantabilni elektrokardiografski snimači (ILR; prema engl. *implantable loop recorder*) omogućuju dugotrajno povezivanje simptoma s odgovarajućim ritmom srca u bolesnika s neobjašnjenom sinkopom; uređaji za kontinuirano praćenje ritma nove generacije omogućuju postavljanje dijagnoze u približno 42 % bolesnika te usmjeruju odluku o ugradnji kardiološkog uređaja u 15 % bolesnika,[9-11] a u bolesnika s kardiomiopatijama i graničnim aritmijskim rizikom dijagnoze postavljene s pomoću ILR-a dovode do ugradnje implantabilnog kardioverterskog defibrilatora (ICD) u 20 % bolesnika.[12] Postojeće europske smjernice preporučuju primjenu ILR-a u bolesnika s DCM-om, ejekcijskom frakcijom lijeve klijetke od 36 do 50 % te s neobjašnjenom sinkopom bez drugih čimbenika aritmijskog rizika.[12,13] Primjena resinkronizacije srca (CRT; prema engl. *cardiac resynchronization therapy*), s defibrilatorom ili bez njega, temeljna je terapijska opcija u bolesnika s DCM-om koji imaju smanjenu ejekcijsku frakciju lijeve klijetke i blok lijeve grane, jer poboljšava simptome i preživljenje te djeluje na mehanizme sinkope povezane i s poremećajima provođenja i s aritmijama;[14,15] istraživanja koja su trenutačno u tijeku, uključujući studiju *BRITISH*, uspoređuju strategiju ugradnje defibrilatora sa strategijom primjene ILR-a ili elektrostimulatora srca u sklopu CRT-a u bolesnika s neishemijskom kardiomiopatijom.[16] Ovaj pregledni rad prikazuje učestalost, mehanizme nastanka, prognostičku važnost i mogućnosti liječenja sinkope u bolesnika s DCM-om, s posebnim naglaskom na stratifikaciju aritmijskog rizika.

METODE

Proveli smo polusustavno pretraživanje literature u bazama PubMed/MEDLINE, Scopus, Ovid i Cochrane Library, u razdoblju od njihova osnutka do 1. ožujka 2026. Pojmovi za pretraživanje bili su kombinacija izraza („syncope" OR „loss of consciousness" OR „fainting") s izrazom („dilated cardiomyopathy" OR „nonischemic cardiomyopathy" OR „non-ischemic cardiomyopathy" OR „idiopathic dilated cardiomyopathy" OR „DCM") te dodatni pojmovi „ventricular arrhythmia", „ventricular tachycardia", „sudden cardiac death", „implantable cardioverter-defibrillator", „ICD", „prognosis", „mortality", „conduction disorder" i „heart failure". Popisi u literaturi pronađenih članaka i relevantnih smjernica ručno su pregledani radi pronalaženja dodatnih istraživanja. Uključene su i novije publikacije preporučene tijekom recenzentskog postupka.

Kriteriji uključivanja obuhvaćali su izvorne znanstvene radove (prospektivna i retrospektivna kohortna istraživanja, studije slučajeva i kontrolne studije te klinička ispitivanja), sustavne preglede i metaanalize, smjernice za kliničku praksu vodećih kardioloških stručnih društava i narativne preglede s mehanističkim ili kliničkim spoznajama. Radovi su morali obrađivati etiologiju, učestalost, prognozu ili liječenje sinkope u odraslih bolesnika (≥18 godina) s DCM-om. Isključeni su prikazi slučajeva i serije slučajeva s manje od 10 bolesnika, istraživanja provedena isključivo u pedijatrijskoj populaciji, članci koji nisu objavljeni na engleskom jeziku, sažetci kongresnih

INTRODUCTION

Syncope, defined as transient loss of consciousness due to global cerebral hypoperfusion with spontaneous and complete recovery, is a common and diagnostically challenging presentation.[1,2] Although reflex syncope usually carries a benign prognosis, structural heart disease substantially alters its implications.[3,4] Dilated cardiomyopathy (DCM) is a high-risk substrate because of myocardial fibrosis, ventricular remodeling, conduction system disease, and autonomic dysfunction, and syncope in DCM is associated with ventricular arrhythmias, sudden cardiac death (SCD), and increased mortality.[5-8]

Two device-based strategies deserve particular emphasis from the outset. Implantable loop recorders (ILRs) provide long-term symptom–rhythm correlation in unexplained syncope; last-generation insertable cardiac monitors establish a diagnosis in approximately 42% of patients and guide cardiac device implantation in 15%,[9-11] and in patients with cardiomyopathies at borderline arrhythmic risk, ILR-guided diagnoses led to implantable cardioverter-defibrillator implantation in 20%.[12] Current European guidelines recommend an ILR in patients with DCM, a left ventricular ejection fraction of 36–50%, and unexplained syncope without other arrhythmic risk factors.[12,13] Cardiac resynchronization therapy (CRT), with or without a defibrillator, is a cornerstone of treatment in DCM with reduced left ventricular ejection fraction and left bundle branch block, because it improves symptoms and survival and addresses both conduction-related and arrhythmic mechanisms of syncope;[14,15] ongoing trials such as BRITISH are comparing a defibrillator strategy with an ILR/CRT-pacemaker strategy in non-ischemic cardiomyopathy.[16] This review summarizes the prevalence, mechanisms, prognostic implications, and management of syncope in DCM, with emphasis on arrhythmic risk stratification.

METHODS

A semi-systematic literature search of PubMed/MEDLINE, Scopus, Ovid, and the Cochrane Library was performed from database inception through March 1, 2026. Search terms combined ("syncope" OR "loss of consciousness" OR "fainting") with ("dilated cardiomyopathy" OR "nonischemic cardiomyopathy" OR "non-ischemic cardiomyopathy" OR "idiopathic dilated cardiomyopathy" OR "DCM"), and additionally with "ventricular arrhythmia," "ventricular tachycardia," "sudden cardiac death," "implantable cardioverter-defibrillator," "ICD," "prognosis," "mortality," "conduction disorder," and "heart failure." Reference lists of retrieved articles and relevant guidelines were manually screened for additional studies. Recent publications recommended during peer review were additionally included.

Eligible publications were original research articles (prospective and retrospective cohort studies, case-control studies, and clinical trials), systematic reviews and meta-analyses, clinical practice guidelines from major cardiovascular societies, and narrative reviews providing mechanistic or clinical insights, addressing the etiology, prevalence, prognosis, or management of syncope in adults (≥18 years) with DCM. Case reports and case series with fewer than 10 patients, exclusively pediatric studies, non-English articles, conference abstracts, and studies limited to hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, or other specific cardiomyopathies without DCM data were excluded.

priopćenja te istraživanja usmjerena na hipertrofičnu kardiomiopatiju, aritmogenu kardiomiopatiju desne klijetke ili druge specifične kardiomiopatije bez podataka o DCM-u.

Naslovi i sažetci pregledani su radi procjene relevantnosti, a cjeloviti tekstovi potencijalno prihvatljivih članaka podvrgnuti su daljnjoj procjeni. Zatim su izdvojeni podatci o ustroju istraživanja, obilježjima populacije, o prevalenciji sinkope, mehanizmima nastanka, čimbenicima rizika te o smrtnosti i liječenju. Zbog heterogenosti ustroja istraživanja i ishoda provedena je narativna sinteza, a ne formalna metaanaliza.

REZULTATI

REZULTATI PRETRAŽIVANJA LITERATURE

Literatura uključena u ovu sintezu izabrana je pretraživanjem baza podataka te ručnim pregledom popisa literature dobivenih rezultata, uz dodatak novijih publikacija preporučenih tijekom recenzentskog postupka, a obuhvaća izvorna kohortna istraživanja i klinička ispitivanja, sustavne preglede i meta-analize, kliničke smjernice i konsenzusne dokumente te narativne preglede.

PREVALENCIJA SINKOPE U DILATACIJSKOJ KARDIOMIOPATIJI

Prevalencija sinkope u bolesnika s DCM-om ovisi o obilježjima ispitivane populacije i o težini zatajivanja (HF). U retrospektivnoj analizi 897 bolesnika s DCM-om, sinkopa je zabilježena u 30 bolesnika (3,3 %).[6] U bolesnika s uznapredovalim HF-om funkcionalnog razreda III. – IV.. prema New York Heart Association (NYHA) klasifikaciji, učestalost raste na 12 – 14 %.[5,17] Middlekauff *i sur.* zabilježili su sinkopu u 12 % od 491 bolesnika upućena na procjenu za transplantaciju srca.[5] Sinkopa se nakon prve epizode ponavlja u približno 35 % bolesnika, a u 29 % bolesnika nastupa tjelesna ozljeda.[3,4] U općoj populaciji incidencija sinkope naglo raste nakon 70. godine života te nakon 80. godine doseže 19,5 slučajeva na 1000 osoba na godinu,[4] a izgledno je da je taj trend u bolesnika s DCM-om dodatno izražen zbog istodobnih komorbiditeta.

Mehanizmi nastanka sinkope

KARDIOLOŠKI UZROCI

Kardiološki mehanizmi odgovorni su za 50 – 60 % epizoda sinkope u bolesnika s DCM-om.[6,8]

Ventrikulske aritmije najčešći su utvrđeni uzrok sinkope i čine približno 33 % slučajeva.[6,18] Ventrikulska tahikardija (VT) i ventrikulska fibrilacija (VF) uzrokuju naglo smanjenje minutnoga volumena srca, a podloga DCM-a – fibroza, dilatacija srčanih šupljina i poremećeno provođenje – pogoduje nastanku ventrikulskih aritmija.[19,20] U skupini od 14 bolesnika s neishemijskim DCM-om i neobjašnjenom sinkopom kojima je ugrađen ICD, Knight *i sur.* zabilježili su odgovarajuću aktivaciju uređaja u 57 % bolesnika tijekom prosječnoga praćenja od 25 mjeseci.[7] Slično tomu, u skupini od 103 bolesnika s uznapredovalim neishemijskim HF-om i sinkopom, liječenje ICD-om poboljšalo je preživljenje u usporedbi s medikamentno liječenom kontrolnom skupinom.[8]

Poremećaji provođenja odgovorni su za približno 23 % slučajeva sinkope u bolesnika s DCM-om,[6,21] te uključuju potpun ili atrioventrikulski (AV) blok visokoga stupnja, disfunkciju sinusnoga čvora s pauzama te blok grane s povremenim napredovanjem u totalni blok. Fibrozni proces često zahvaća provodni sustav, što objašnjava visoku učestalost poremećaja provođenja u ovoj populaciji.[22]

Titles and abstracts were screened for relevance, and the full texts of potentially eligible articles were reviewed by the authors. Data were extracted on study design, population characteristics, syncope prevalence, mechanisms, risk factors, mortality, and treatment. Given the heterogeneity of study designs and outcomes, a narrative synthesis was performed rather than a formal meta-analysis.

RESULTS

SEARCH RESULTS

Database searching, supplemented by manual screening of reference lists and by recent publications recommended during peer review, identified the literature included in this synthesis, comprising original cohort studies and clinical trials, systematic reviews and meta-analyses, clinical practice guidelines and consensus documents, and narrative reviews.

PREVALENCE OF SYNCOPE IN DILATED CARDIOMYOPATHY

The prevalence of syncope in DCM depends on the study population and heart failure (HF) severity. In a retrospective analysis of 897 patients with DCM, syncope occurred in 30 (3.3%).[6] Among patients with advanced HF (New York Heart Association [NYHA] class III–IV), prevalence rises to 12–14%;[5,17] Middlekauff *et al* reported syncope in 12% of 491 patients referred for transplant evaluation.[5] Syncope recurs in approximately 35% of patients after an initial episode, and 29% sustain physical injury.[3,4] In the general population, the incidence of syncope increases sharply after the age of 70 years, reaching 19.5 per 1,000 person-years after 80 years,[4] a pattern likely amplified in DCM by concurrent comorbidities.

Mechanisms of Syncope

CARDIAC CAUSES

Cardiac mechanisms account for 50–60% of syncopal episodes in DCM.[6,8]

Ventricular arrhythmias are the most common identified cause, accounting for approximately 33% of cases.[6,18] Ventricular tachycardia (VT) and ventricular fibrillation (VF) cause abrupt reductions in cardiac output, and the DCM substrate—fibrosis, chamber dilation, and abnormal conduction—predisposes to sustained ventricular arrhythmias.[19,20] Among 14 patients with nonischemic DCM and unexplained syncope who received an implantable cardioverter-defibrillator (ICD), Knight *et al* observed appropriate ICD therapy in 57% during a mean follow-up of 25 months.[7] Similarly, among 103 patients with nonischemic advanced HF and syncope, ICD therapy improved survival compared with historical medically treated controls.[8]

Conduction disorders account for approximately 23% of cardiac syncope in DCM[6,21] and include complete or high-grade atrioventricular (AV) block, sinus node dysfunction with prolonged pauses, and bundle branch block with intermittent progression to complete heart block. The fibrotic process frequently involves the conduction system, explaining the high incidence of conduction abnormalities in this population.[22]

Low cardiac output may precipitate syncope during exertion or increased demand, when the failing ventricle cannot

Smanjen minutni volumen srca može izazvati sinkopu tijekom tjelesnog napora ili povećanih metaboličkih potreba kada oslabjeli ventrikul ne može povećati minutni volumen; u uznapredovalom HF-u sinkopa se može pojaviti i bez zabilježene aritmije.[5]

Ostali kardiološki uzroci uključuju fibrilaciju atrija s brzim odgovorom klijetki ili dugim pauzama, plućnu emboliju i, rijetko, dinamičku opstrukciju izlaznoga trakta u određenim podtipovima DCM-a.[1,2]

NEKARDIOLOŠKI UZROCI

Nekardiološki mehanizmi utvrđeni su u znatnog dijela bolesnika s DCM-om i sinkopom.[6] **Neuralno posredovana (refleksna) sinkopa**, što uključuje vazovagalnu i situacijsku sinkopu te preosjetljivost karotidnog sinusa, čini približno 7 % oboljelih.[1,2,6,23] **Ortostatska hipotenzija** odgovorna je za daljnjih 7 % slučajeva[6,24] te nastaje zbog autonomne disfunkcije povezane s HF-om,[25] hipovolemije uzrokovane diureticima, primjene vazodilatacijskih lijekova (inhibitora angiotenzin-konvertirajućeg enzima [ACE], blokatora angiotenzinskih receptora [ARB] i nitrata), oslabljenog porasta frekvencije srca tijekom liječenja beta-blokatorima te dobno uvjetovanog oštećenja funkcije baroreceptora.[24]

Ekstremne temperature. Ekstremno visoke ili niske temperature okoliša mogu potaknuti ili pogoršati sinkopu i povezane simptome u bolesnika s DCM-om. Izloženost vrućini uzrokuje vazodilataciju kožnih krvnih žila, gubitak tekućine znojenjem te smanjenje središnjega venskog tlaka i udarnog volumena,[26] a oslabjela klijetka s ograničenom mogućnošću prilagodbe predopterećenju teško nadoknađuje te promjene. Učinci su izraženiji uz primjenu diuretika, inhibitora renin-angiotenzinskog sustava, inhibitora neprilizina i receptora angiotenzina, inhibitora kotransportera natrija i glukoze 2 (SGLT2) te beta-blokatora, koji ograničavaju kompenzaciju volumena ili frekvencije srca i povećavaju sklonost ortostatskoj hipotenziji.[24,27] U starijih osoba s kroničnim bolestima toplinski su valovi vezani su uz povećanje broja hospitalizacija povezanih s vrućinom, pri čemu rizik ovisi i o lijekovima koji se često primjenjuju.[27] Nasuprot tomu, izloženost hladnoći povećava simpatički tonus, naknadno opterećenje i potrebu miokarda za kisikom te može potaknuti ventrikulske aritmije i dekompenzaciju srca.[28] U multinacionalnoj analizi, koja je obuhvaćala ispitanike iz 27 zemalja, i ekstremna vrućina i ekstremna hladnoća bile su povezane s povećanom kardiovaskularnom smrtnošću, pri čemu je najveći relativni porast zabilježen za HF.[29] Međutim, izravni dokazi o povezanosti temperaturnih ekstrema sa sinkopom izričito za bolesnike s DCM-om i dalje su ograničeni, a navedene se povezanosti uglavnom temelje na izvođenju iz podataka za šire populacije bolesnika s HF-om i starijih osoba. Stoga bolesnicima s DCM-om treba dati individualizirane preporuke o izbjegavanju vrućine i unosu tekućine, a tijekom toplinskih valova potrebno je preispitati doze diuretika i vazodilatatora, uzimajući u obzir stupanj kongestije i bubrežnu funkciju.

NEOBJAŠNJENA SINKOPA

Unatoč sveobuhvatnoj dijagnostičkoj obradi, 30 – 37 % epizoda sinkope ostaje neobjašnjeno.[1,6] U bolesnika s DCM-om neobjašnjena sinkopa ima nepovoljno prognostičko značenje jer su često odgovorne prikrivene ventrikulske aritmije.[7,8,30] Brilakis *i sur.* proveli su istraživanje u 30 bolesnika s idiopatskim DCM-om i sinkopom te utvrdili da su bolesnici i dalje izloženi povećanom riziku i često imaju korist od ugradnje ICD-a, čak i kada je elektrofiziološko ispitivanje (EFI) negativno.[30] U registru *AVID* (engl. *Antiarrhythmics Versus Implantable Defibrillators*) bolesnici su s neobjašnjenom sinkopom i inducibilnim ventrikulskim tahiaritmijama imali ishode usporedive s ishodima bolesnika s dokumentiranom održivom VT.[31]

augment output; in advanced HF, syncope may occur even in the absence of documented arrhythmia.[5]

Other cardiac causes include atrial fibrillation with rapid ventricular response or long pauses, pulmonary embolism, and, rarely, dynamic outflow tract obstruction in specific DCM subtypes.[1,2]

NON-CARDIAC CAUSES

Non-cardiac mechanisms are identified in a substantial minority of patients with DCM and syncope.[6] **Neurally mediated (reflex) syncope**, including vasovagal syncope, situational syncope, and carotid sinus hypersensitivity, accounts for approximately 7% of cases.[1,2,6,23] **Orthostatic hypotension** accounts for another 7%[6,24] and results from HF-related autonomic dysfunction,[25] diuretic-induced volume depletion, vasodilator therapy (angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], and nitrates), a blunted heart rate response under beta-blockade, and age-related impairment of baroreceptor function.[24]

Environmental temperature extremes. Ambient temperature extremes may precipitate or exacerbate syncope and related symptoms in DCM. Heat exposure induces cutaneous vasodilation, sweat-related volume loss, and a fall in central venous pressure and stroke volume,[26] which a failing ventricle with limited preload reserve compensates poorly; these effects are amplified by diuretics, renin–angiotensin system inhibitors, angiotensin receptor–neprilysin inhibitors, sodium–glucose cotransporter 2 inhibitors, and beta-blockers, which limit volume or heart-rate compensation and predispose to orthostatic hypotension.[24,27] In older adults with chronic conditions, heatwaves are associated with increased heat-related hospitalizations, with the risk modified by commonly used medications.[27] Cold exposure, conversely, increases sympathetic tone, afterload, and myocardial oxygen demand and may promote ventricular arrhythmias and HF decompensation.[28] In a multinational analysis of 27 countries, both extreme heat and extreme cold were associated with increased cardiovascular mortality, with the greatest relative excess for heart failure.[29] Direct evidence linking temperature extremes to syncope specifically in patients with DCM, however, remains limited, and these associations are largely extrapolated from broader heart failure and older-adult populations. Patients with DCM should therefore receive individualized advice on heat avoidance and fluid intake, and diuretic and vasodilator doses should be reviewed during heatwaves, taking into account congestion status and renal function.

UNEXPLAINED SYNCOPE

Despite comprehensive evaluation, 30–37% of syncopal episodes remain unexplained.[1,6] In DCM, unexplained syncope carries ominous implications, as occult ventricular arrhythmias are frequently responsible.[7,8,30] Brilakis *et al* evaluated 30 patients with idiopathic DCM and syncope and found that patients remained at elevated risk, and frequently benefited from ICD implantation, even when the electrophysiological study (EPS) was negative.[30] In the Antiarrhythmics Versus Implantable Defibrillators (AVID) registry, patients with unexplained syncope and inducible ventricular tachyarrhythmias had outcomes similar to those with documented sustained VT.[31]

GENETIC SUBSTRATES

Several pathogenic variants confer disproportionate arrhythmic risk, conduction disease, and syncope, sometimes before severe systolic dysfunction develops.[32] *LMNA*-related

GENSKA PODLOGA

Nekoliko je patogenih genskih varijanti povezano s nerazmjerno visokim aritmijskim rizikom, poremećajima provođenja i sinkopom, koji se mogu pojaviti i prije razvoja teške sistoličke disfunkcije.[32] Kardiomiopatija povezana s genom LMNA snažno je povezana s bolešću provodnog sustava, ventrikulskim tahiaritmijama i SCD-om.[33] Truncirajuće varijante gena FLNC izrazito su aritmogene te često povezane s fibrozom miokarda.[34,35] Varijante gena DSP, PLN, RBM20 i DES također mogu povećati aritmijski rizik, uz fenotipska obilježja koja se preklapaju s aritmogenom kardiomiopatijom.[36] Stoga neobjašnjena sinkopa u bolesnika s genski uvjetovanim DCM-om može upućivati na izraženu električnu nestabilnost, čak i bez teške disfunkcije klijetki.

Gensko testiranje treba razmotriti u bolesnika s DCM-om i neobjašnjenom sinkopom, osobito u prisutnosti sljedećih obilježja: (1) obiteljske anamneze DCM-a, SCD-a ili neobjašnjene smrti prije 50. godine života; (2) pri poremećajima provođenja koji su nerazmjerni stupnju ventrikulske disfunkcije; (3) pri početku bolesti prije 50. godine života; (4) zahvaćenosti skeletnih mišića ili povećane koncentracije kreatin-kinaze ili (5) pri nalazima magnetne rezonancije srca (CMR; prema engl. *cardiac magnetic resonance*) koji upućuju na specifičnu gensku etiologiju, primjerice prstenastu ili septalnu intramiokardnu fibrozu povezanu s varijantama gena LMNA. Ako se utvrde patogene ili vjerojatno patogene varijante visokorizičnih gena (LMNA, FLNC, PLN, DSP, RBM20), potrebno je primijeniti procjenu rizika prilagođenu genotipu, a ugradnja ICD-a može biti opravdana i pri višim vrijednostima LVEF-a nego u tradicionalnim preporukama, u skladu sa smjernicama Europskoga kardiološkog društva (ESC) iz 2023. godine.[22] Preporučuje se i kaskadno gensko testiranje srodnika prvoga stupnja.[22,37]

Rizični čimbenici za sinkopu u dilatacijskoj kardiomiopatiji

Nekoliko prediktora za koje se očekivala povezanost sa sinkopom, uključujući LVEF,[6,38] funkcionalni razred NYHA,[6] ishemijsku etiologiju nasuprot neishemijskoj,[38] fibrilaciju atrija i dislipidemiju,[6] nije pokazalo dosljednu povezanost sa sinkopom; Abdel-Hadi *i sur.* nisu utvrdili značajnu razliku u LVEF-u između bolesnika sa sinkopom i onih bez nje.[6] Izgledno je da to odražava multifaktorsku prirodu sinkope, u kojoj aritmogeni supstrat, autonomni tonus, učinci lijekova i komorbiditeti imaju važne uloge neovisno o funkciji srčane pumpe. Fibroza miokarda utvrđena CMR-om uz primjenu kasnog nakupljanja gadolinija (LGE; prema engl. *late gadolinium enhancement*) postala je važan prediktor ventrikulskih aritmija i SCD-a, s dodatnom prognostičkom vrijednošću povrh LVEF-a,[39,40] a varijante gena LMNA, FLNC, DSP i PLN označuju povećan aritmijski rizik, osobito kada su povezane s poremećajima provođenja, nepostojanom ventrikulskom tahikardijom (NSVT) ili neobjašnjenom sinkopom.[22]

Arterijska hipertenzija (61,5 % [8/13] nasuprot 23,5 % [4/17], P = 0,08) i šećerna bolest (46,2 % [6/13] nasuprot 5,9 % [1/17], P = 0,03) bile su češće u bolesnika s nekardijalnom nego u bolesnika s kardijalnom sinkopom,[6] što upućuje na moguću osobitu važnost autonomne neuropatije i ortostatskih mehanizama u dijabetičara.[6,25] Opći prediktori ponavljanja sinkope uključuju strukturnu bolest srca,[1,2] oštećenu bubrežnu funkciju,[41] AV-blok ili blok lijeve grane,[1] muški spol,[4] HF,[1,5] dob veću od 70 godina[3,4] te primjenu lijekova koji pogoduju nastanku ortostatske hipotenzije.[1,24]

Prognostička vrijednost

Sinkopa u bolesnika s DCM-om snažan je prediktor nepovoljnih ishoda, osobito SCD-a. Godišnja smrtnost iznosi 18 – 33 % kod kardijalne sinkope, a 0 – 12 % kod nekardijalne sinkope.[3,5] U skupini od 491 bolesnika s uznapredovalim HF-om sinkopa

cardiomyopathy is strongly associated with conduction system disease, ventricular tachyarrhythmias, and SCD;[33] truncating *FLNC* variants are highly arrhythmogenic and frequently associated with myocardial fibrosis;[34,35] and *DSP*, *PLN*, *RBM20*, and *DES* variants may also increase arrhythmic risk, with phenotypes overlapping arrhythmogenic cardiomyopathy.[36] Unexplained syncope in genetically mediated DCM may therefore reflect advanced electrical instability even without severe ventricular dysfunction.

Genetic testing should be considered in patients with DCM and unexplained syncope, particularly in the presence of (1) a family history of DCM, SCD, or unexplained death before 50 years of age; (2) conduction disease disproportionate to the degree of ventricular dysfunction; (3) disease onset before 50 years of age; (4) skeletal muscle involvement or elevated creatine kinase; or (5) cardiac magnetic resonance (CMR) findings suggestive of a specific genetic etiology (e.g., ring-like or septal mid-wall fibrosis associated with *LMNA* variants). When pathogenic or likely pathogenic variants in high-risk genes (*LMNA, FLNC, PLN, DSP, RBM20*) are identified, genotype-specific risk stratification applies, and ICD implantation may be warranted at higher left ventricular ejection fraction (LVEF) thresholds than traditionally recommended, consistent with the 2023 European Society of Cardiology (ESC) guidelines.[22] Cascade genetic screening of first-degree relatives is also recommended.[22,37]

Risk Factors for Syncope in Dilated Cardiomyopathy

Several expected predictors, including LVEF,[6,38] NYHA class,[6] ischemic versus non-ischemic etiology,[38] atrial fibrillation, and dyslipidemia,[6] have not shown consistent associations with syncope; Abdel-Hadi *et al* found no significant difference in LVEF between patients with and without syncope.[6] This likely reflects the multifactorial nature of syncope, in which arrhythmogenic substrate, autonomic tone, medication effects, and comorbidities play roles beyond pump function. Myocardial fibrosis detected by late gadolinium enhancement (LGE) on CMR has emerged as a major predictor of ventricular arrhythmias and SCD, with incremental prognostic value beyond LVEF,[39,40] and *LMNA, FLNC, DSP,* and *PLN* variants mark heightened arrhythmic risk, particularly when associated with conduction disease, nonsustained VT (NSVT), or unexplained syncope.[22]

Arterial hypertension (61.5% [8/13] vs 23.5% [4/17], *P* = .08) and diabetes mellitus (46.2% [6/13] vs 5.9% [1/17], *P* = .03) were more frequent in patients with non-cardiac than with cardiac syncope,[6] suggesting that autonomic neuropathy and orthostatic mechanisms may be particularly important in diabetic patients.[6,25] General predictors of recurrent syncope include structural heart disease,[1,2] impaired renal function,[41] AV block or left bundle branch block,[1] male sex,[4] HF,[1,5] age >70 years,[3,4] and medications predisposing to orthostatic hypotension.[1,24]

Prognostic Impact

Syncope in DCM is a powerful predictor of adverse outcomes, particularly SCD. Annual mortality is 18–33% for cardiac syncope and 0–12% for non-cardiac syncope.[3,5] In 491 patients with advanced HF, syncope predicted sudden death regardless of whether an arrhythmic mechanism was identified,

je predviđala iznenadnu smrt neovisno o tome je li utvrđen aritmijski mehanizam, što upućuje na to da sve epizode sinkope u spomenutoj populaciji zahtijevaju ozbiljnu pozornost.[5] U skupini od 104 bolesnika s DCM-om sinkopa je bila neovisan prediktor SCD-a (relativan rizik 4,7; P < 0,01).[42] Liječenje ICD-om u bolesnika s DCM-om i sinkopom bilo je povezano s dvogodišnjim preživljenjem od 85 %, u usporedbi s 44 % uz medikamentno liječenje.[8] Grimm *i sur.*, proučavajući 343 bolesnika s idiopatskim DCM-om, utvrdili su da NSVT zabilježena u holter EKG-u i LVEF < 30% predviđa aritmijske događaje, dok je sinkopa bila dodatan neovisni prognostički čimbenik.[38]

Nekoliko opservacijskih studija ukazalo je na produljenje preživljenja povezano s primjenom ICD-a kod odabranih bolesnika s DCM-om i sinkopom.[7,8,13,43,44] U ispitivanju *SCD-HeFT* (engl. *Sudden Cardiac Death in Heart Failure Trial*) primjena ICD-a smanjila je smrtnost za 23 % u bolesnika s HF-om funkcionalnog razreda II. – III., prema NYHA-i i LVEF-om ≤35 %.[45] Stoga sinkopu u bolesnika s DCM-om ne treba tumačiti samo kao prolazni simptom nego i kao mogući pokazatelj električne nestabilnosti i progresije bolesti.

Zbrinjavanje

POČETNA PROCJENA I STRATIFIKACIJA RIZIKA

Početna procjena obuhvaća detaljnu anamnezu, fizikalni pregled s mjerenjem arterijskoga tlaka u ortostazi, 12-kanalni elektrokardiogram (EKG), ehokardiografiju i ciljane laboratorijske pretrage;[1,2] samom se anamnezom dijagnoza može postaviti u do 50 % oboljelih.[46] Obilježja visokog rizika koja zahtijevaju hospitalizaciju uključuju sinkopu tijekom tjelesnog napora ili u ležećem položaju, pridruženu bol u prsima ili dispneju, palpitacije prije sinkope, obiteljsku anamnezu iznenadne smrti prije 50. godine života, LVEF <35%, nove ili znatne promjene na EKG-u (bifascikularni blok, korigirani QT-interval [QTc] >500 ms), značajnu ozljedu srca te otprije poznatu strukturnu bolest srca, uključujući DCM.[1,2] Alati *San Francisco Syncope Rule*, bodovni sustav OESIL (*Osservatorio Epidemiologico sulla Sincope nel Lazio*) i sustav *EGSYS* (*Evaluation of Guidelines in Syncope Study*) validirani su za stratifikaciju rizika, iako je njihovu učinkovitost u bolesnika s DCM-om potrebno dodatno istražiti.[1,47]

NAPREDNA DIJAGNOSTIČKA OBRADA

Praćenje ritma srca. Bolnički telemetrijski nadzor indiciran je u bolesnika s visokim rizikom.[1,2] Nakon otpusta mogućnosti daljnjega praćenja uključuju praćenje holter EKG-om tijekom 24 – 72 sata kada se sinkopa pojavljuje često,[2] vanjske snimače tijekom 2 – 4 tjedna kod rjeđih simptoma te implantabilne elektrokardiografske snimače kod rijetkih, neobjašnjenih i ponavljajućih epizoda sinkope, pri čemu je dijagnostički prinos potonjih 35-43 % tijekom jedne do dvije godine.[9,10] Uređaji za kontinuirano praćenje ritma srca nove generacije ostvaruju usporediv dijagnostički prinos (42 %) uz manji klinički radni angažman,[11] a u bolesnika s kardiomiopatijom i graničnim aritmijskim rizikom barem je jedna dijagnoza postavljena s pomoć ILR-a zabilježena u 44 % bolesnika tijekom prosječnoga praćenja od 19 mjeseci, najčešće novonastala fibrilacija atrija.[12] U bolesnika s DCM-om je ILR osobito koristan kada je LVEF samo blago ili umjereno smanjena, a aritmijsko je podrijetlo sinkope nejasno.[12,13]

Elektrofiziološko ispitivanje. Programirana ventrikulska stimulacija može utvrditi inducibilnu VT,[30,48,49] no njezina se prediktivna vrijednost razlikuje ovisno o etiologiji: osjetljivost za predviđanje naknadnih aritmijskih događaja iznosi približno 50 – 80 % u ishemijskoj kardiomiopatiji,[48] ali samo 20 – 30 % kod neishemijskog DCM-a, pa stoga negativan nalaz ne može pouzdano isključiti aritmijski rizik.[30,49] Indikacije za EFI u bolesnika sa sinkopom i strukturnom bolešću srca, uključujući DCM, skupljene su i sažete u posebnim preporukama na tu temu.[50]

suggesting that all syncope in this population deserves serious attention.[5] In 104 patients with DCM, syncope was an independent predictor of SCD (relative risk 4.7, $P < .01$).[42] ICD therapy in patients with DCM and syncope was associated with a 2-year survival of 85%, compared with 44% under medical therapy.[8] Grimm *et al*, studying 343 patients with idiopathic DCM, found that NSVT on Holter monitoring and LVEF <30% predicted arrhythmic events, with syncope adding independent prognostic information.[38]

Several observational studies suggest a survival benefit associated with ICD therapy in selected patients with DCM and syncope.[7,8,13,43,44] In the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), ICD therapy reduced mortality by 23% in patients with NYHA class II–III HF and LVEF ≤35%.[45] Syncope in DCM should therefore be interpreted not merely as a transient symptom but as a potential marker of electrical instability and disease progression.

Management

INITIAL EVALUATION AND RISK STRATIFICATION

Initial evaluation includes detailed history taking, physical examination with orthostatic blood pressure measurement, 12-lead electrocardiogram (ECG), echocardiography, and targeted laboratory testing;[1,2] history alone establishes the diagnosis in up to 50% of cases.[46] High-risk features warranting hospitalization include syncope during exertion or while supine, associated chest pain or dyspnea, preceding palpitations, family history of sudden death before 50 years of age, LVEF <35%, new or significant ECG abnormalities (bifascicular block, corrected QT interval [QTc] >500 ms), significant injury, and known structural heart disease, including DCM.[1,2] The San Francisco Syncope Rule, the Osservatorio Epidemiologico sulla Sincope nel Lazio (OESIL) score, and the Evaluation of Guidelines in Syncope Study (EGSYS) score have been validated for risk stratification, although their performance in DCM requires further study.[1,47]

ADVANCED EVALUATION

Rhythm monitoring. In-hospital telemetry is indicated for high-risk patients.[1,2] After discharge, options include Holter monitoring (24–72 hours) when syncope is frequent,[2] external event recorders (2–4 weeks) for less frequent symptoms, and implantable loop recorders for infrequent, unexplained, recurrent syncope, with a diagnostic yield of 35–43% over 1–2 years.[9,10] Last-generation insertable cardiac monitors offer a comparable diagnostic yield (42%) with a lower clinical workload,[11] and in cardiomyopathy patients at borderline arrhythmic risk at least one ILR-guided diagnosis was made in 44% during a mean follow-up of 19 months, most frequently de novo atrial fibrillation.[12] In DCM, an ILR is particularly useful when LVEF is only mildly or moderately reduced and the arrhythmic origin of syncope remains uncertain.[12,13]

Electrophysiological study. Programmed ventricular stimulation can identify inducible VT,[30,48,49] but its predictive value differs by etiology: sensitivity for subsequent arrhythmic events is approximately 50–80% in ischemic cardiomyopathy[48] but only 20–30% in non-ischemic DCM, so a negative study does not reliably exclude arrhythmic risk.[30,49] Indications for EPS in patients with syncope and structural heart disease, including DCM, have been summarized in dedicated recommendations.[50]

Magnetna rezonancija srca. Osim procjene veličine i funkcije klijetki, CMR omogućuje karakterizaciju tkiva primjenom LGE-a, čime se utvrđuju fibroza miokarda i aritmogeni supstrat.[39] LGE je neovisan prediktor ventrikulskih aritmija, SCD-a, odgovarajućih terapijskih intervencija primjenom ICD-a i ukupne smrtnosti u bolesnika s DCM-om,[40] a prognostička vrijednost LGE-a nadilazi prognostičku vrijednost izrazito smanjene LVEF.[51,52]

***Til-table* test i masaža karotidnog sinusa.** Test nagibnoga stola indiciran je kada se sumnja na refleksnu sinkopu. Specifičnost testa iznosi približno 90 %, dok je osjetljivost u rasponu od 30 do 70 %, ovisno o protokolu.[1,2,53] Masaža karotidnog sinusa preporučuje se u bolesnika s neobjašnjenom sinkopom starijih od 40 godina. Preosjetljivost karotidnog sinusa dijagnosticira se ako masaža izazove asistoliju dulju od 3 sekunde ili smanjenje sistoličkog tlaka za više od 50 mmHg.[1,2]

TERAPIJSKE INTERVENCIJE

Liječenje primjenom uređaja. Ugradnja ICD-a indicirana je u bolesnika s DCM-om i sinkopom kada je LVEF ≤35 % nakon najmanje tri mjeseca medikamentnog liječenja prema smjernicama (indikacija klase I. za primarnu prevenciju), kod dokumentirane ili inducibilne održive VT/VF (indikacija klase I. za sekundarnu prevenciju) ili kod neobjašnjene sinkope uz visok stupanj sumnje na aritmijsku etiologiju.[44,45,54] U ispitivanju DEFINITE (engl. *Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation*) liječenje ICD-om rezultiralo je trendom smanjenja ukupne smrtnosti (omjer hazarda 0,65; P = 0,08) te je znatno smanjilo SCD.[55] Ugradnja elektrostimulatora srca indicirana je kod dokumentiranih bradiaritmija ili bolesti provodnog sustava,[24,56] a, kada postoje indikacije i za CRT i za ICD, prednost se daje terapiji resinhkonizacijom srca s defibrilatorom (CRT-D).[14,54] CRT se preporučuje simptomatskim bolesnicima s LVEF-om ≤35 % i blokom lijeve grane uz trajanje QRS kompleksa ≥150 ms unatoč optimalnome medikamentnom liječenju, a treba je razmotriti i pri trajanju QRS-a od 130 do 149 ms.[15] Odabir između CRT-D-a i CRT-a s elektrostimulatorom srca (CRT-P; prema engl. *CRT with a pacemaker*) može se dodatno usmjeriti karakterizacijom tkiva CMR-om, te testiranjem genotipa i elektrofiziološkim ispitivanjem.[16]

Medikamentno liječenje. Medikamentno liječenje HF-a prema smjernicama, koje uključuje ACE inhibitore, ARB-e ili inhibitore neprilizina i receptora angiotenzina (ARNI), beta-blokatore, antagoniste mineralokortikoidnih receptora i inhibitore koprijenosnika natrija i glukoze 2 (SGLT2), potrebno je optimirati.[54,57] Amiodaron ili sotalol mogu se primijeniti u odabranih bolesnika radi suzbijanja VT-a, najčešće kao dodatak liječenju ICD-om.[44,58] Terapiju lijekovima potrebno je prilagoditi kada se utvrdi ortostatska hipotenzija, a, kada hipovolemija pridonosi bolesti, potrebno je nadoknaditi volumen.[24]

Kateterska ablacija. Ablacija se, u pravilu, razmatra kod ponavljajuće monomorfne VT koja je prisutna unatoč liječenju ICD-om.[44,59,60] Uspješnost postupka niža je u neishemijskom DCM-u (približno 50 – 70 %) nego u ishemijskoj kardiomiopatiji (približno 70 – 80 %) zbog difuznog supstrata, koji je često smješten epikardijalno ili intramiokardno, zbog čega je često potreban epikardijalni pristup.[59,60]

Liječenje nekardijalnih uzroka. Zbrinjavanje vazovagalne sinkope provodi se edukacijom bolesnika, izbjegavanjem „okidača" bolesti, fizički kontramanevrima i dostatnom hidratacijom,[1,23] a ortostatska hipotenzija liječi se prilagođavanjem lijekova, kompresijskim čarapama te povećanim unosom soli i tekućine.[24] Ugradnja elektrostimulatora srca preporučuje se kod ponavljajuće kardioinhibitorne preosjetljivosti karotidnog sinusa ili vazovagalne sinkope s dokumentiranom asistolijom.[1,56]

Glavna su obilježja sinkope u dilatacijskoj kardiomiopatiji sažeta u **Tablici 1**, ključni praktični aspekti dijagnostičke obrade

Cardiac magnetic resonance. Beyond assessment of ventricular size and function, CMR enables tissue characterization through LGE, which reflects myocardial fibrosis and arrhythmogenic substrate.[39] LGE independently predicts ventricular arrhythmias, SCD, appropriate ICD therapies, and all-cause mortality in DCM,[40] and its prognostic value extends beyond severely reduced LVEF.[51,52]

Tilt-table testing and carotid sinus massage. Tilt testing is indicated when reflex syncope is suspected and has approximately 90% specificity but variable sensitivity (30–70%), depending on the protocol.[1,2,53] Carotid sinus massage is recommended in patients >40 years of age with unexplained syncope; carotid sinus hypersensitivity is diagnosed when massage produces asystole >3 seconds or a systolic blood pressure decrease >50 mmHg.[1,2]

THERAPEUTIC INTERVENTIONS

Device therapy. ICD implantation is indicated in patients with DCM and syncope with LVEF ≤35% after at least 3 months of guideline-directed medical therapy (GDMT) (class I, primary prevention), documented or inducible sustained VT/VF (class I, secondary prevention), or unexplained syncope with high suspicion of arrhythmic etiology.[44,45,54] In the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial, ICD therapy showed a trend toward reduced mortality (hazard ratio 0.65, *P* = .08) and significantly reduced sudden death.[55] Pacemaker implantation is indicated for documented bradyarrhythmias or conduction system disease,[21,56] and cardiac resynchronization therapy with a defibrillator (CRT-D) is preferred when indications for both CRT and an ICD exist.[14,54] CRT is recommended in symptomatic patients with LVEF ≤35% and left bundle branch block with QRS duration ≥150 ms despite optimal medical therapy, and should be considered at QRS durations of 130–149 ms;[15] the choice between CRT-D and CRT with a pacemaker (CRT-P) may be refined by CMR tissue characterization, genotype, and electrophysiological testing.[16]

Medical therapy. GDMT for HF, including ACE inhibitors, ARBs, or angiotensin receptor–neprilysin inhibitors (ARNIs), beta-blockers, mineralocorticoid receptor antagonists, and sodium–glucose cotransporter 2 (SGLT2) inhibitors, should be optimized.[54,57] Amiodarone or sotalol may be used for VT suppression in selected cases, typically as an adjunct to ICD therapy.[44,58] Medications should be adjusted when orthostatic hypotension is identified, and volume should be repleted when hypovolemia contributes.[24]

Catheter ablation. Ablation is generally considered for recurrent monomorphic VT despite ICD therapy.[44,59,60] Success rates are lower in non-ischemic DCM (approximately 50–70%) than in ischemic cardiomyopathy (approximately 70–80%) because of diffuse, often epicardial or mid-myocardial substrate, and epicardial access is frequently required.[59,60]

Treatment of non-cardiac causes. Vasovagal syncope is managed with education, trigger avoidance, counter-pressure maneuvers, and adequate hydration;[1,23] orthostatic hypotension with medication adjustment, compression stockings, and increased salt and fluid intake.[24] Pacemaker implantation is recommended for recurrent cardioinhibitory carotid sinus hypersensitivity or vasovagal syncope with documented asystole.[1,56]

The main characteristics of syncope in DCM are summarized in **Table 1,** key practical considerations for its evalua-

TABLE 1. Summary of syncope characteristics in dilated cardiomyopathy.

Parameter	Findings	References
Prevalence	3.3% (general DCM); 12–14% (advanced HF)	5,6,17
Cardiac causes (total)	50–60%	6,8
Ventricular arrhythmias	≈33%	6,18
Conduction disorders	≈23%	6,21
Low cardiac output	Variable	5
Non-cardiac causes	≈14%	6
Unexplained syncope	30–37%	1,6
Recurrence rate	35%	3,4
Physical injury rate	29%	3,4
Annual mortality (cardiac syncope)	18–33%	3,5
Annual mortality (non-cardiac syncope)	0–12%	3
Appropriate ICD therapy	40–60%	7,8,30

DCM: Dilated cardiomyopathy; HF: Heart failure; ICD: Implantable cardioverter-defibrillator

TABLE 2. Clinical pearls in the evaluation of syncope in dilated cardiomyopathy

Clinical finding	Potential implication
Syncope during exertion or while supine	Increased suspicion of arrhythmic syncope
Syncope associated with palpitations	Possible ventricular tachyarrhythmia
Syncope and LGE on CMR	Increased risk of ventricular arrhythmias and sudden cardiac death
Syncope and *LMNA* or *FLNC* variant	High-risk arrhythmogenic phenotype
Negative EPS in non-ischemic DCM	Does not exclude malignant arrhythmias
Orthostatic symptoms and diabetes mellitus	Evaluate for autonomic dysfunction
Recurrent unexplained syncope	Consider prolonged monitoring or ICD implantation
Syncope with conduction abnormalities	Evaluate for progressive conduction system disease
Syncope despite mildly reduced EF	Consider fibrosis or genetic arrhythmic substrate
Syncope in advanced HF	Increased mortality regardless of mechanism
Syncope during heatwaves or heat exposure	Review hydration and diuretic/vasodilator dosing; consider orthostatic mechanism

CMR: Cardiac magnetic resonance; DCM: Dilated cardiomyopathy; EF: Ejection fraction; EPS: Electrophysiological study; *FLNC*: Filamin C gene; HF: Heart failure; ICD: Implantable cardioverter-defibrillator; LGE: Late gadolinium enhancement; *LMNA*: Lamin A/C gene

prikazani su u **Tablici 2**, a dijagnostički i terapijski algoritam prikazan je na **Slici 1**.

DISKUSIJA

Ovaj pregledni rad pokazuje da se sinkopa pojavljuje u 3 – 14% bolesnika s DCM-om i ima bitnu prognostičku važnost, pri čemu je većina slučajeva posljedica kardijalnih uzroka, ponajprije ventrikulskih aritmija i poremećaja provođenja.[5,6,8] Razlika u godišnjoj smrtnosti kod kardijalne i nekardijalne sinkope može biti i do 20 puta veća.[3,5] Čak i „neobjašnjena" sinkopa često odražava prikrivenu aritmiju, što potvrđuju visoke stope uspješnih terapijskih intervencija ICD-om tijekom praćenja,[7,8,30] pa je stoga izgledno da zabilježeni udio ventrikulskih aritmija od 33 % podcjenjuje njihovu stvarnu ulogu. Nasuprot tomu, tradicionalni pokazatelji težine HF-a, poput LVEF-a i funkcio-

tion in **Table 2**, and a diagnostic and management algorithm is presented in **Figure 1**.

DISCUSSION

This review shows that syncope affects 3–14% of patients with DCM and carries substantial prognostic weight, with cardiac causes, predominantly ventricular arrhythmias and conduction disorders, responsible for most cases.[5,6,8] Annual mortality differs by as much as 20-fold between cardiac and non-cardiac syncope.[3,5] Even "unexplained" syncope frequently reflects occult arrhythmia, as shown by high rates of appropriate ICD therapy during follow-up,[7,8,30] so the reported 33% contribution of ventricular arrhythmias probably underestimates their true role. Conversely, traditional markers of HF severity such as LVEF and NYHA class do not reliably identify which patients

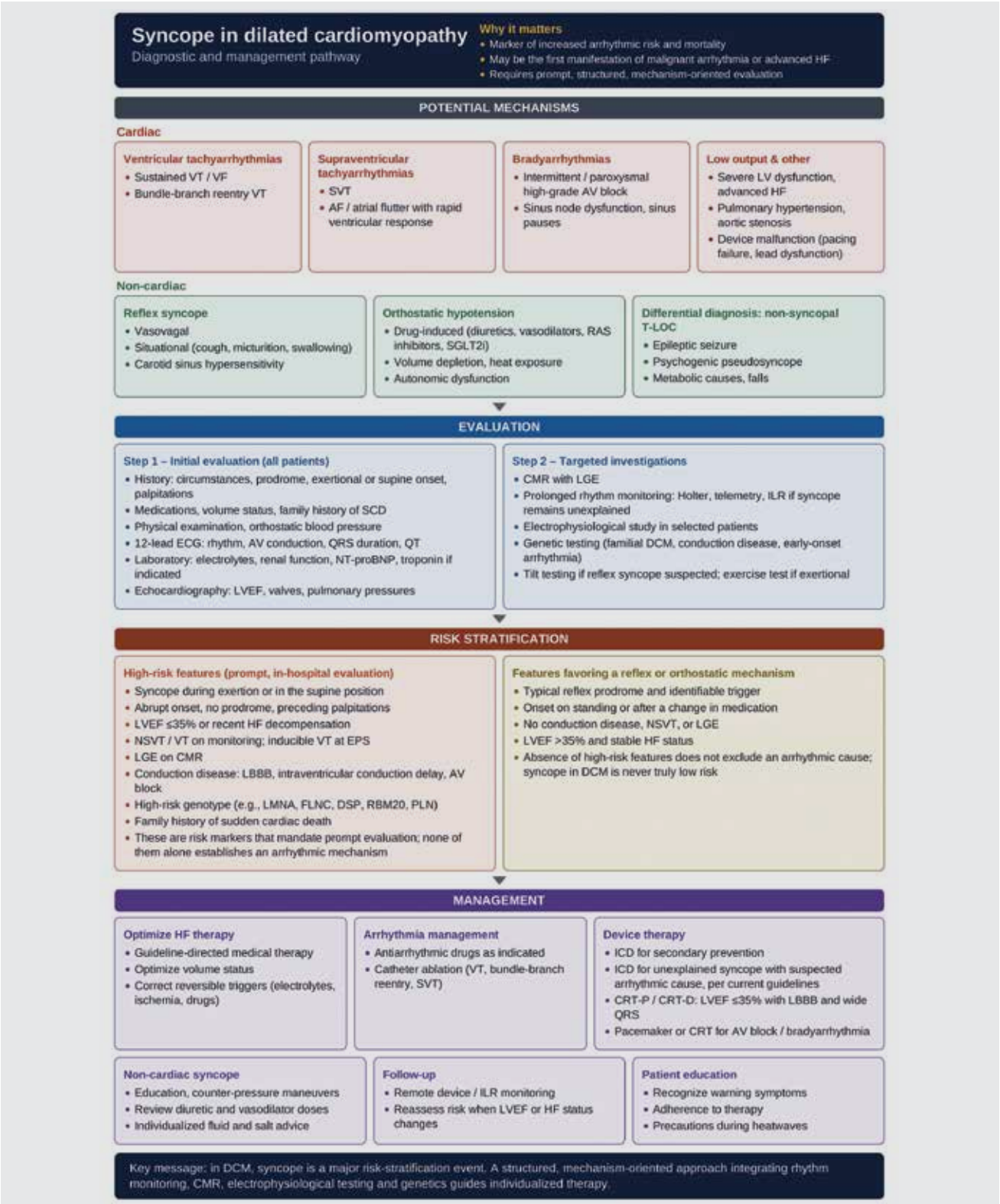


FIGURE 1. Diagnostic and management pathway for syncope in dilated cardiomyopathy, summarizing cardiac and non-cardiac mechanisms, stepwise evaluation, risk stratification, and management.

AF: Atrial fibrillation; AV: Atrioventricular; CMR: Cardiac magnetic resonance; CRT-D: Cardiac resynchronization therapy with defibrillator; CRT-P: Cardiac resynchronization therapy pacemaker; DCM: Dilated cardiomyopathy; ECG: Electrocardiogram; EPS: Electrophysiological study; HF: Heart failure; ICD: Implantable cardioverter-defibrillator; ILR: Implantable loop recorder; LBBB: Left bundle branch block; LGE: Late gadolinium enhancement; LV: Left ventricular; LVEF: Left ventricular ejection fraction; NSVT: Non-sustained ventricular tachycardia; NT-proBNP: N-terminal pro-B-type natriuretic peptide; RAS: Renin–angiotensin system; SCD: Sudden cardiac death; SGLT2i: Sodium–glucose cotransporter 2 inhibitors; SVT: Supraventricular tachycardia; T-LOC: Transient loss of consciousness; VF: Ventricular fibrillation; VT: Ventricular tachycardia.

nalnog razreda NYHA, ne omogućuju pouzdano prepoznavanje bolesnika u kojih će se pojaviti sinkopa,[6,38] što potkrepljuje primjenu modela procjene usmjerenog na aritmogeni supstrat koji uključuje fibrozu miokarda, aritmijsko opterećenje, poremećaje provođenja, autonomnu disfunkciju i testiranje genotipa.

Premda 40 – 60 % bolesnika s DCM-om i neobjašnjenom sinkopom tijekom praćenja prima odgovarajuću terapiju ICD-om,[7,8,30,43] dansko istraživanje *DANISH* (engl. *Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on Mortality*) pokazalo je da profilaktička ugradnja ICD-a nije znatno smanjila ukupnu smrtnost u bolesnika s neishemijskim HF-om, iako je znatno smanjila SCD.[61] Stoga odluke o liječenju trebaju uzimati u obzir anamnezu sinkope, opseg fibroze, gensku podlogu i aritmijske pokazatelje, a ne samo LVEF.[16] Zajedničko donošenje odluka s bolesnikom ostaje ključno jer liječenje ICD-om može biti povezano s tjeskobom, psihološkim opterećenjem i promjenama kvalitete života.[62] Suvremene terapije, poput ARNI-ja i inhibitora SGLT2, mogu istodobno smanjivati aritmogeni supstrat i povećavati rizik od ortostatske hipotenzije, pa njihov utjecaj na sinkopu treba sustavno istražiti.[63]

Ishemijska i neishemijska DCM razlikuju se u aritmijskom supstratu, dijagnostičkom prinosu i terapijskim ishodima (**Tablica 3**). Ishemijsku kardiomiopatiju obilježavaju kružni mehanizmi ponovnog ulaska impulsa unutar gustoga subendokardijalnog ožiljka, dok neishemijsku DCM obilježavaju difuzna intramiokardna ili epikardijalna fibroza,[20] niža osjetljivost programirane stimulacije,[49] manja uspješnost ablacije,[59,60] te nerazmjerno visok aritmijski rizik u nekim genskim oblicima.[22]

will experience syncope,[6,38] supporting a substrate-oriented model that integrates myocardial fibrosis, arrhythmic burden, conduction disease, autonomic dysfunction, and genotype.

Although 40–60% of patients with DCM and unexplained syncope receive appropriate ICD therapy during follow-up,[7,8,30,43] the Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on Mortality (DANISH) showed that prophylactic ICD implantation did not significantly reduce all-cause mortality in non-ischemic HF, although SCD was significantly reduced.[61] Decisions should therefore integrate syncope history, fibrosis burden, genetic substrate, and arrhythmic markers rather than LVEF alone.[16] Shared decision-making remains essential, as ICD therapy may be associated with anxiety, psychological distress, and altered quality of life.[62] Contemporary therapies such as ARNIs and SGLT2 inhibitors may both reduce arrhythmogenic substrate and increase orthostatic risk, and their effect on syncope warrants systematic investigation.[63]

Ischemic and non-ischemic DCM differ in arrhythmic substrate, diagnostic yield, and therapeutic outcomes (**Table 3**). Ischemic cardiomyopathy features re-entry circuits within dense subendocardial scar, whereas non-ischemic DCM is characterized by diffuse mid-myocardial or epicardial fibrosis,[20] lower sensitivity of programmed stimulation,[49] lower ablation success,[59,60] and, in some genetic forms, disproportionate arrhythmic risk.[22]

TABLE 3. Key differences between ischemic and non-ischemic dilated cardiomyopathy.

Feature	Ischemic DCM	Non-ischemic DCM
Substrate	Discrete scar	Diffuse fibrosis
LGE pattern	Subendocardial/transmural	Mid-wall, patchy
EPS sensitivity	Higher (50–80%)	Lower (20–30%)
Ablation success	Higher (70–80%)	Lower (50–70%)
Epicardial substrate	Less common	More common

DCM: Dilated cardiomyopathy; EPS: Electrophysiological study; LGE: Late gadolinium enhancement

Buduća bi istraživanja trebala razviti specifične bodovne sustave za procjenu rizika od sinkope u DCM-u koji bi integrirali kliničke, slikovne, genske i elektrofiziološke pokazatelje; validirati nosive uređaje za praćenje i algoritme potpomognute umjetnom inteligencijom u raznolikim populacijama bolesnika s DCM-om; razjasniti ulogu kateterske ablacije prospektivnim istraživanjima te uspostaviti suradničke registre radi poboljšanja zbrinjavanja prilagođena genotipu.

Ovaj pregledni rad ima nekoliko ograničenja. Literatura koja se izričito bavi sinkopom u DCM-u oskudna je, pa je često potrebno ekstrapolirati podatke iz širih populacija; istraživanja su heterogena, često uključuju mali broj bolesnika te su provedena u pojedinačnim specijaliziranim centrima; usto, velik dio dostupnih dokaza prethodi uvođenju suvremenih terapija HF-a.

ZAKLJUČAK

Sinkopu u bolesnika s DCM-om treba smatrati važnim kliničkim znakom upozorenja. Premda su mogući i nekardijalni

Future research should develop DCM-specific syncope risk scores integrating clinical, imaging, genetic, and electrophysiological markers; validate wearable monitoring and artificial intelligence–assisted algorithms in diverse DCM populations; clarify the role of catheter ablation through prospective trials; and establish collaborative registries to refine genotype-guided management.

This review has several limitations. The literature on syncope specifically in DCM is sparse and often requires extrapolation from broader populations; studies are heterogeneous, frequently small, and derived from single specialized centers; and much of the evidence predates contemporary HF therapies.

CONCLUSION

Syncope in DCM should be regarded as a major clinical warning sign. Although non-cardiac mechanisms remain possi-

mehanizmi, prisutnost strukturne bolesti miokarda znatno povećava vjerojatnost malignih ventrikulskih aritmija, poremećaja provođenja i SCD-a. Suvremena dijagnostička obrada ne temelji se samo na procjeni LVEF-a te uključuje produljeno praćenje ritma srca, CMR s karakterizacijom fibroze i genško testiranje radi prepoznavanja visokorizičnih fenotipova. Strukturiran pristup usmjeren na mehanizam nastanka sinkope, uz rano prepoznavanje visokorizičnih obilježja i pravodobnu individualiziranu terapiju, uključujući ugradnju ICD-a i optimizaciju liječenja HF-a, što može poboljšati ishode u ovoj, ranjivoj populaciji.

ble, structural myocardial disease substantially increases the likelihood of malignant ventricular arrhythmias, conduction abnormalities, and SCD. Contemporary evaluation extends beyond LVEF, integrating prolonged rhythm monitoring, CMR with fibrosis characterization, and genetic testing to identify high-risk phenotypes. A structured, mechanism-oriented approach, with early recognition of high-risk features and timely individualized therapy, including ICD implantation and HF optimization, may improve outcomes in this vulnerable population.

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