IP Universitatea de Stat de Medicină și Farmacie “Nicolae Testemițanu”
IP IMSP Institutul Mamei și Copilului

Insuficiența cardiacă la copil

Ina Palii, dr. hab. med., prof. univ.
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Sef Clinica Pediatrie, Cardiologie IMSP IMşiC

Chișinău,2020

S–mul de IC constituie una din cauzele majore de morbiditate, invalidizare şi mortalitate la copii!!!

- **Proporții epidemice a IC - Prevalență de 3 cazuri la 1000 de populație anual;**
- **Prevalența IC în Europa - între 2 și 3 %, cauza a 5% din spitalizări!**
- **În SUA – 5 mln, Europa - 15 mln, Japonia – 2,4 mln!**
- **La copii în țările dezvoltate cauzată în special de MCC și CM primare;**
- **Incidența CM primare – 0,8 – 1,3 cazuri la 100000 copii 0 – 18 ani, 0 – 1 an de 10 ori mai frecvent (Andrews RE, Circulation, 2017); 40% din cazuri conduc la IC, 60% din copii necesită transplant cardiac!**
- **Incidența MCC – 8 la 1000 n-n vii, prevalență 0,8%, iar 1 din 3 copii (15 – 25 %) – dezvoltă IC! (Kantor PF et al. Heart failure in congenital heart disease. Can J Cardiol, 2013;29:759-67).**
- **Fiecare al 3-lea caz de IC la n-n fără maladie structurală de cord se soldează cu deces, iar în MCC - fiecare al 2-lea (în lipsa trat. adecvat!)**

1. Kantor P F și al. CCS Guidelines for HF in Children. Canadian journal of Cardiology nr. 29, 2013, 1535 – 1552;

2. Kirk R, Dipchand AI, Rosenthal DN, editors. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014.

3. Ponikowski P. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, 2016.

4. Heart Failure in Pediatric Patients with Congenital Heart Disease Circ Res. 2017 March 17; 120 (6): 978–994.

PRACTICE GUIDELINES

International Society for Heart and Lung Transplantation: Practice Guidelines for Management of Heart Failure in Children

David Rosenthal, MD, Chair, Maryanne R.K. Chrisant, MD, Erik Edens, MD, PhD, Lynn Mahony, MD, Charles Canter, MD, Steven Colan, MD, Anne Dubin, MD, Jacque Lamour, MD, Robert Ross, MD, Robert Shaddy, MD, Linda Addonizio, MD, Lee Beerman, MD, Stuart Berger, MD, Daniel Bernstein, MD, Elizabeth Blume, MD, Mark Boucek, MD, Paul Checchia, MD, Anne Dipchand, MD, Jonathan Drummond-Webb, MD, Jay Fricker, MD, Richard Friedman, MD, Sara Hallowell, RN, Robert Jaquiss, MD, Seema Mital, MD, Elfriede Pahl, MD, Bennett Pearce, MD, Larry Rhodes, Kathy Rotondo, MD, Paolo Rusconi, MD, Janet Scheel, MD, Tajinder Pal Singh, MD, and Jeffre

INTRODUCTION

The Need for Pediatric Guidelines

Heart failure (HF) in the United States is well recognized as a major public health problem, with over 900,000 hospital admissions annually in the United States, and greater than 250,000 deaths per year. The great majority of heart failure occurs in adults. In children, the scope of the problem is less well defined, but recent data from the Pediatric Cardiomyopathy Registry suggest an annual incidence of 1.13 cases of cardiomyopathy per 100,000 children.[1] While some of this represents asymptomatic disease, the burden of disease overall is nonetheless quite high. In the Pediatric Cardiomyopathy Registry, the majority of children with cardiomyopathy also had HF, with mortality rates of 13.6% at 2 years in dilated forms of cardiomyopathy.

The etiology of heart failure differs greatly between children and adults. Children in the Pediatric Cardiomyopathy Registry had a recognizable syndrome or genetic diagnosis in 27% of cases, with an additional 5% of cases due to myocarditis. Furthermore, a large percentage of children with end-stage HF (between 25% and 75%, depending upon the age group) have an underlying diagnosis of congenital heart disease.[2] In contrast to adult patients, ischemic heart disease is rare in children.

There is a large, and rapidly growing literature addressing HF treatment for adult patients, with a much smaller literature concerning HF therapy in children. little reason to believe that these gui applicable to children.[3] Accordingly, we have attempted to summarize the and synthesize management guidel with HF. The document that follows in a consensus fashion, with inp cardiologists at multiple sites throu States and Canada.

Levels of Evidence and Strength of Rec

Each recommendation in this docum regard to the level of supporting evi

- Level A recommendations are bas randomized clinical trials.
- Level B are based upon a single r multiple non-randomized trials.
- Level C are based primarily upon opinion.

The level of evidence upon which is based, differs from the strength of tion. A given recommendation ma randomized trials yet still be controv of therapy, which are based solely up sus, may be strongly recommended.

Recommendations in this docum format of guidelines previously publi ican College of Cardiology (ACC) an Association (AHA).

ISHLTG

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ISHLT GUIDELINES

The International Society of Heart and Lung Transplantation Guidelines for the management of pediatric heart failure: Executive summary

Richard Kirk, MA, FRCP, FRCPCH,[a] Anne I. Dipchand, MD, FRCPC,[b] David N. Rosenthal, MD,[c] Linda Addonizio, MD,[d] Michael Burch, MD,[e] Maryanne Chrisant, MD,[f] Anne Dubin, MD,[c] Melanie Everitt, MD,[g] Robert Gajarski, MD,[h] Luc Mertens, MD,[b] Shelley Miyamoto, MD,[i] David Morales, MD,[j] Elfriede Pahl, MD,[k] Robert Shaddy, MD,[l] Jeffrey Towbin, MD,[j] and Robert Weintraub, MD[m]

From the [a]Freeman Hospital, Newcastle upon Tyne, United Kingdom; [b]Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada; [c]Stanford University, Stanford, California; [d]Columbia University Medical Center, New York, New York; [e]Great Ormond Street Hospital, London, United Kingdom; [f]Joe DiMaggio Children's Hospital, Hollywood, Florida; [g]Primary Children's Medical Center, Salt Lake City, Utah; [h]C.S. Mott Children's Hospital, Ann Arbor, Michigan; [i]Children's Hospital, Denver, Colorado; [j]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [k]Ann & Robert H Lurie Children's Hospital, Chicago, Illinois; [l]Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; and the [m]Royal Melbourne Children's Hospital, Melbourne, Victoria, Australia.

These guidelines have been produced to bring together current recommendations on the evaluation and management of pediatric heart failure (HF) and update the previous guideline.[1]

The writing group was chosen from the membership of the International Society for Heart and Lung Transplantation (ISHLT), the Association of European Pediatric and Congenital Cardiology (AEPC), and the Pediatric and Congenital Electrophysiology Society (PACES) across health care disciplines to achieve representation of HF practice throughout the world. Overall, 90 contributors from 13 counties across 4 continents (Appendix 1) were assigned various aspects of HF according to their expertise. A comprehensive review of the available published evidence for HF management was undertaken. The strength and level of evidence was assessed according to standard practice.[2] The recommendations were achieved by consensus with the contributors; however, it is recognized that the evidence the recommendations is Level C due to th children. In some areas, there is such a lack no recommendations can be made: it i recognizing these deficiencies, research wi address them. External review was underta tional experts invited from adult advanc cardiology, and congenital cardiovascular sur The final guidelines were reviewed and ISHLT Board and Standards & Guide endorsed by the AEPC, and those guide electrophysiology, by the PACES Executi

The background information for thes complete references have been published series, Volume 8 by the ISHLT.[3] The abbr listed in Appendix 3.

Definition and documentation recommendation[4,5]

Chairs: Richard Kirk, Anne I. Dipchan Rosenthal

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Canadian Journal of Cardiology 29 (2013) 1535–1552

Society Guidelines

Presentation, Diagnosis, and Medical Management of Heart Failure in Children: Canadian Cardiovascular Society Guidelines

Paul F. Kantor, MBBCh,[a,b] Jane Lougheed, MD,[c] Adrian Dancea, MD,[d] Michael McGillion, PhD,[e] Nicole Barbosa, BSc,[a] Carol Chan, BSc, Phm,[a] Rejane Dillenburg, MD,[f] Joseph Atallah, MD, MDCM, SM,[b] Holger Buchholz, MD,[b] Catherine Chant-Gambacort, MN, NP,[f] Jennifer Conway, MD,[a,b] Letizia Gardin, MD,[c] Kristen George, BScN,[a] Steven Greenway, MD,[g] Derek G. Human, MBBS,[h] Aamir Jeewa, MD,[i] Jack F. Price, MD,[i] Robert D. Ross, MD,[j] S. Lucy Roche, MBChB,[a] Lindsay Ryerson, MD,[b] Reeni Soni, MD,[k] Judith Wilson, BScN,[a] and Kenny Wong, MD,[l] for The Children's Heart Failure Study Group

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[d]Montreal Children's Hospital, McGill University, Montreal, Québec, Canada
[e]The University of Toronto, School of Nursing, Toronto, Ontario, Canada
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[g]Alberta Children's Hospital, University of Calgary, Calgary, Alberta, Canada
[h]British Columbia's Children's Hospital, University of British Columbia, Vancouver, British Columbia, Canada
[i]Texas Children's Hospital, Baylor College of Medicine, Houston, Texas, USA
[j]Children's Hospital of Michigan, Wayne State University School of Medicine, Detroit, Michigan, USA
[k]Winnipeg Children's Hospital, University of Manitoba, Winnipeg, Manitoba, Canada
[l]Isaak Walton Killam Children's Hospital, Dalhousie University, Halifax, Nova Scotia, Canada

ABSTRACT

Pediatric heart failure (HF) is an important cause of morbidity and mortality in childhood. This article presents guidelines for the recognition, diagnosis, and early medical management of HF in infancy, childhood, and adolescence. The guidelines are intended to assist

RÉSUMÉ

L'insuffisance cardiaque (IC) chez l'enfant est une cause importante de morbidité et de mortalité durant l'enfance. Cet article présente les lignes directrices sur le dépistage, le diagnostic et la prise en charge médicale précoce de l'IC en bas âge, durant l'enfance et l'adolescence.

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The disclosure information of the authors and reviewers is available from the CCS on the following websites: www.ccs.ca and/or www.ccsguidelinesprograms.ca.

This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific Recommendations. These Recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgement in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these Recommendations will not necessarily produce successful outcomes in every case.

http://dx.doi.org/10.1016/j.cjca.2013.08.008

Alte studii analizate

- Steven E. Lipshultz; James D. Wilkinson**: Beta-adrenergic adaptation in idiopathic dilated cardiomyopathy: differences between children and adults în** *European Heart Journal (2014) 35, 10–12*
- Shelley D. Miyamoto, Brian L. Stauffer, Stephanie Nakano,et. al**: Beta-adrenergic adaptation in paediatric idiopathic dilated cardiomyopathy - în** *European Heart Journal (2014) 35, 33–41*
- Anna Bauer, Markus Khalil, Monika Lüdemann, Dietmar Schranz**: Creation of a restrictive atrial communication in heart failure with preserved and mid-range ejection fraction: effective palliation of left atrial hypertension and pulmonary congestion în** *Clinical Research in Cardiology https://doi.org/10.1007/s00392-018-1255-x, 2018.*
- Dietmar Schranz, Hakan Akintuerk and Norbert F Voelkel**: 'End-stage' heart failure therapy: potential lessons from congenital heart disease: from pulmonary artery banding and interatrial communication to parallel circulation în** *Heart 2017 103: 262-267 originally published online December 23, 2016.*
- Navaratnarajah M, Siedlecka U, Ibrahim M, van Doorn C, Soppa G, et al.**: Impact of Combined Clenbuterol and Metoprolol Therapy on Reverse Remodelling during Mechanical Unloading.** *PLoS ONE 9(9): e92909. (2014) doi:10.1371/journal.pone.0092909*
- Sabine Recla, MD, Blanka Steinbrenner, MD, and Dietmar Schranz, MD**: Medical therapy in dilated cardiomyopathy and pulmonary arterial banding in children în** *The Journal of Heart and Lung Transplantation, Vol 32, No 10, October 2013*
- Dietmar Schranz, Sabine Recla, Ivan Malcic, Gunter Kerst, Nathalie Mini, Hakan Akintuerk: **Pulmonary artery banding in dilative cardiomyopathy of young children: review and protocol based on the current knowledge în** *Translational Pediatrics, Vol 8, No 2 April 2019.*
- Dietmar Schranz, MD, Stefan Rupp, MD, Matthias Muller, MD, Dorle Schmidt, MD, Anna Bauer, CM: **Pulmonary artery banding in infants and young children with left ventricular dilated cardiomyopathy: A novel therapeutic strategy before heart transplantation în** *J Heart Lung Transplant 2013;32:475–481*

Alte studii analizate

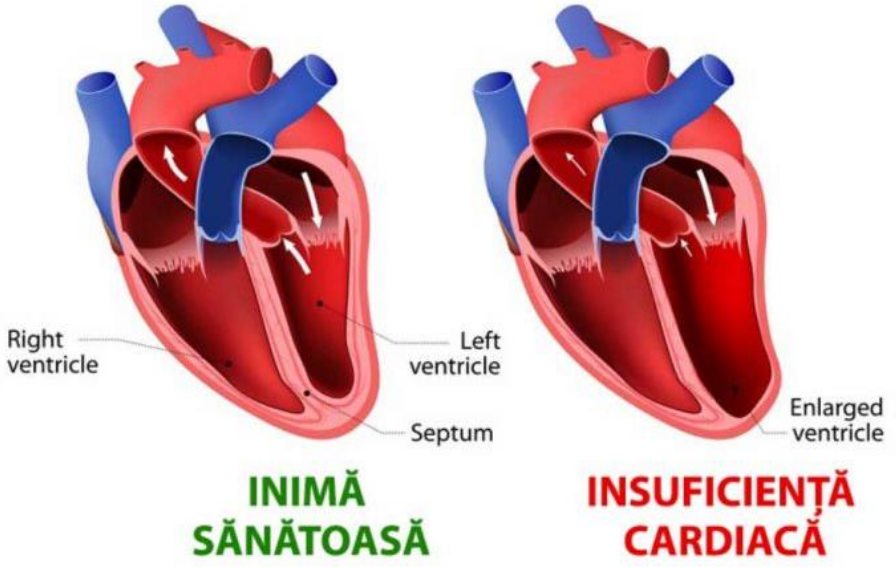
- Recla S, Schmidt D, Logeswaran T, Esmaeili A, Schranz D. **: Pediatric heart failure therapy: why β1- receptor blocker, tissue ACE-I and mineralocorticoid-receptor- blocker?** *Transl Pediatr 2019;8(2):127-132. doi: 10.21037/ tp.2019.04.08*

- Bauer A, Khalil M, Schmidt D, Recla S, Bauer J, Esmaili A, Penford G, Akintuerk H, Schranz D. **Transcatheter left atrial decompression in patients with dilated cardiomyopathy: bridging to cardiac transplantation or recovery.** *Cardiology in the Young (2019) page 1 of 8. doi: 10.1017/ S1047951118002433*

- Giovanni Fajardo a, Mingming Zhao a, Gerald Berry b, Lee-Jun Wong d, Daria Mochly-Rosen c, Daniel Bernstein **β2-adrenergic receptors mediate cardioprotection through crosstalk with mitochondrial cell death pathways** *Journal of Molecular and Cellular Cardiology 51 (2011) 781–789*

Definiție

Sindromul de Insuficiența cardiacă la copii (0 – 18 ani) este definit prin incapacitatea inimii de a asigura debitul cardiac sistemic sau pulmonar corespunzător necesităţilor tisulare sau asigura acest debit în condiţiile unor presiuni de umplere crescute.



Kantor et al.
CCS Guidelines for HF in Children

D. Presentation and Detection of HF in Children

Definition

HF in children (aged 0-18 years) can be defined broadly as the failure of the heart to supply blood to either systemic or pulmonary circulation at an appropriate rate of flow, or to receive venous return at an appropriate filling pressure, resulting in adverse effects on the heart, the circulation, and the patient. This definition is not different to that applied to adult patients. Symptoms of HF in children are superficially similar regardless of the underlying etiology, but physical signs might be more specific. Systemic manifestations are mediated by sympathetic and central neurologic pathways, activated in response to pulmonary congestion and/or decreased systemic perfusion.[9,10] Clinical features of HF unique to children are:

Kantor P F și al. CCS Guidelines for HF in Children, 2013

Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014.

Cauzele IC la copii - heterogene

(1. Bressieux-Degueldre, N. Sekarski. Insuffisance cardiaque chez l'enfant; reconnaotre et diagnostiquer, Vol. 26 No. 1, 2015;
2. Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham, 2014)

Anomalii structurale cardiace	Cord structural „normal“
MCC cu supraîncărcare de volum,șunt S-D •Comunicare interventriculară; •Canal arterial persistent; •Canal atrio-ventricular; •Trunchi arterial comun; •Fereastra Ao-P; •Comunicare interauriculară (foarte rar); **Insuficiențe valvulare** •Insuficiența valvulară aortică sau mitrală	**Cardiomiopatii primare** •CMD idiopatică; •Cardiomiopatia hipertrofică; •Cardiomiopatia restrictivă; •Cardiomiopatia aritmogenă de VD; •Cardiomiopatie de non-compactare.
MCC cu supraîncarcare de presiune •Stenoza supra/sub valvulară aortică ; •Sindromul cordului stg hipoplazic; •Coarctaţia de aortă;	**Cardiomiopatii secundare:** •Miocardite; •Boala Kawasaki; •Infarctul miocardic; •Aritmii (tahi/bradiaritmia); •Anemia, sepsisul; •Hipotiroidia; •Insuficiența renală; •Hipertensiunea arterială; •Boli metabolice (Pompe, mitocondriopatia); •Chimioterapia cu antracicline; •Distrofia musculară.

Cauzele IC la copii după vârstă

IC la fat:

TSV, bradicardie severa secundara BAV, anemia severă (hemoliză, transfuzia feto-maternă, anemia indusă de parvovirusul B19, anemia hipoplastică), regurgitare tricuspidă (b. Ebstein)/mitrala (CAVC) severă, miocardita;

IC la nou-născutul prematur:

Supraîncărcare de fluide, PDA, DSV, cord pulmonar (displazia bronhopulmonară), hipertensiune, miocardite, cardiomiopatie genetică/metabolică;

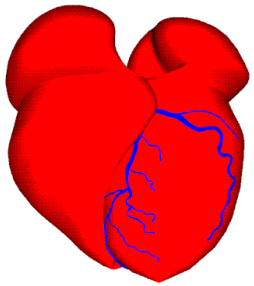
IC la nou – născut la termen:

IC în prima zi de viață:

Asfixie, hipoglicemie, hipocalcemie, sepsis, insuficienta tricuspida;

IC în prima săptămână de viață:

MCC cu circulatie pulmonară dependentă de canal,
MCC cu mixing mare (VU, TAC);
MCC cu debit sistemic dependent de canal,
CAP la prematur;
Malformațiile arterio-venoase (vena Galen, hepatică);
Cardiomiopatia genetică/metabolică;



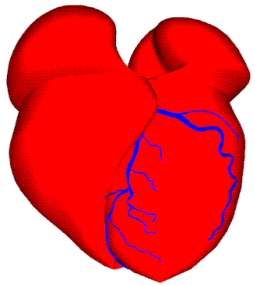
Cauzele IC la copii după vârstă

IC la sugar – copil mic:

- **Șuntul cardiac stânga-dreapta (Defectul de sept ventricular);**
- **Hemangiomul (malformațiile arterio-venoase);**
- **Anomaliile arterei coronare stângi;**
- **Cardiomiopatie genetică/metabolică;**
- **Hipertensiune acută (sindromul hemolitico-uremic);**
- **Maladia Kawasaki;**
- **Miocarditele;**
- **TSV;**
- **Canalul arterial persistent,**
- **ALCAPA;**

IC la copil- adolescent:

- **MCC + factor precipitant (regurgitare valvulara, endocardita, miocardita, anemie, sunt BT, etc)**
- **Stenoza aortica/pulmonara**
- **Boli cardiace dobandite**
- **Tirotoxicoza;**
- **Hemocromatoza-hemosideroza;**
- **Terapia cancerului (radiația, doxorubucina;**
- **Anemia Sickle;**
- **Endocarditele;**
- **Cordul pulmonar (Fibroza chistică);**
- **Miocardita.**



Criterii de definire, gradarea severităţii

Sistemul de clasificare NYHA/Ross (Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014)

Clasa funcţională	Interpretare
I	Asimptomatic
II	Tahipnee moderată sau diaforeză pe parcursul alăptării. Dispnee la efort la copilul mai mare
III	Tahipnee marcată sau diaforeză pe parcursul alăptării; alăptare prelungită sau întîrzierea creşterii datorate ICC. Dispnee intensă la efort la copilul mai mare
IV	Tahipnee, tiraj, dispnee, diaforeză în repaus

Table 1 Heart Failure Severity Classifications

Class	NYHA	Ross
I	No limitations of physical activity	No limitations or symptoms
II	May experience fatigue, palpitations, dyspnea, or angina during moderate exercise but not during rest	Mild tachypnea or diaphoresis with feeding
III	Symptoms with minimal exertion that interfere with normal daily activity	Infants with growth failure and marked tachypnea or diaphoresis with feedings, older children with marked dyspnea on exertion
IV	Unable to carry out any physical activity because they typically have symptoms of HF at rest that worsens with any exertion	Symptoms at rest such as tachypnea, retractions, grunting, or diaphoresis

Level of Evidence C

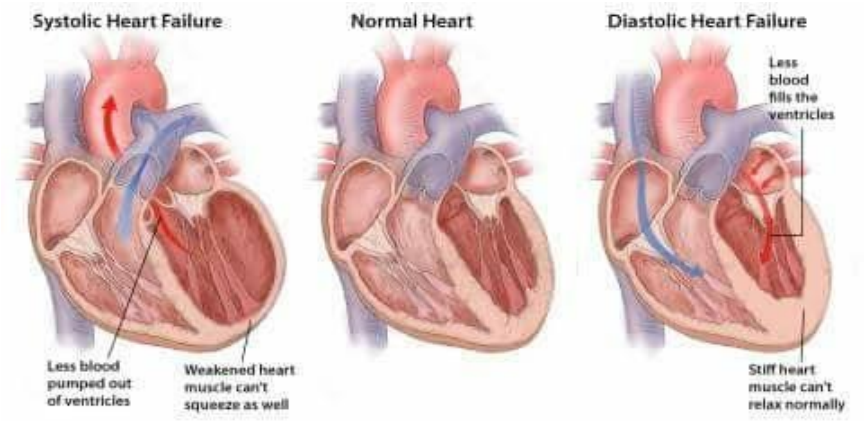
Stadiile IC la copil

(ACC/AHA, Sharon, Ghidul American, 2010)

Stadiile	Interpretare
A	Pt cu risc crescut către IC , dar cu funcţie cardiacă normală, fără probe de supraîncărcare de volum a cavităţilor. Ex: expunere anterioară la agenţi cardiotoxici, istoric familial de CMD, VU, TVM - L.
B	Pt cu morfologie şi funcţie cardiacă anormală, fără semne în trecut sau prezent de IC: IVAo cu VS dilatat, istoric de antracicline cu descreşterea funcţiei sistolice a VS
C	Pt cu maladie cardiacă structurală sau funcţională de bază şi simptome de IC în trecut sau prezent.
D	Pt cu IC în stadiul final ce necesită infuzie continuă cu agenţi inotropi, suport mecanic circulator, transplant cardiac sau îngrigire spitalicească.

Updatările ulterioare, 2014 - ultima clasificație a IC simplificată

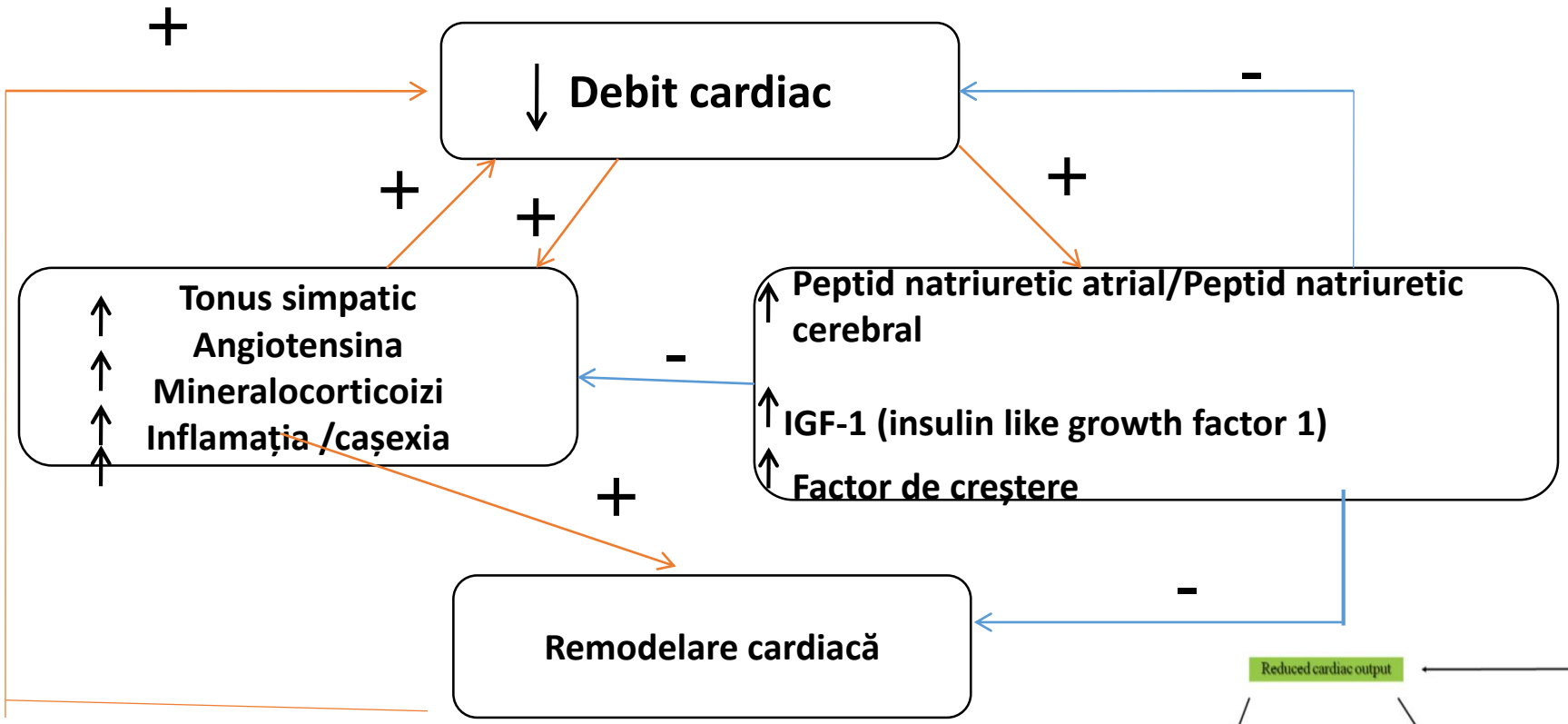
- **IC FE redusă – insuficiență cardiacă cu diminuarea fracției de ejecție (disfuncție sistolică);**
- **IC FE păstrată (disfuncție diastolică).**
- **IC acută decompensată**

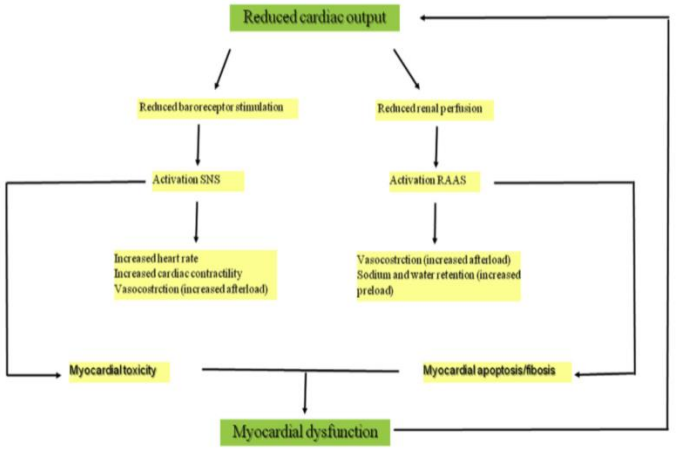


Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014.

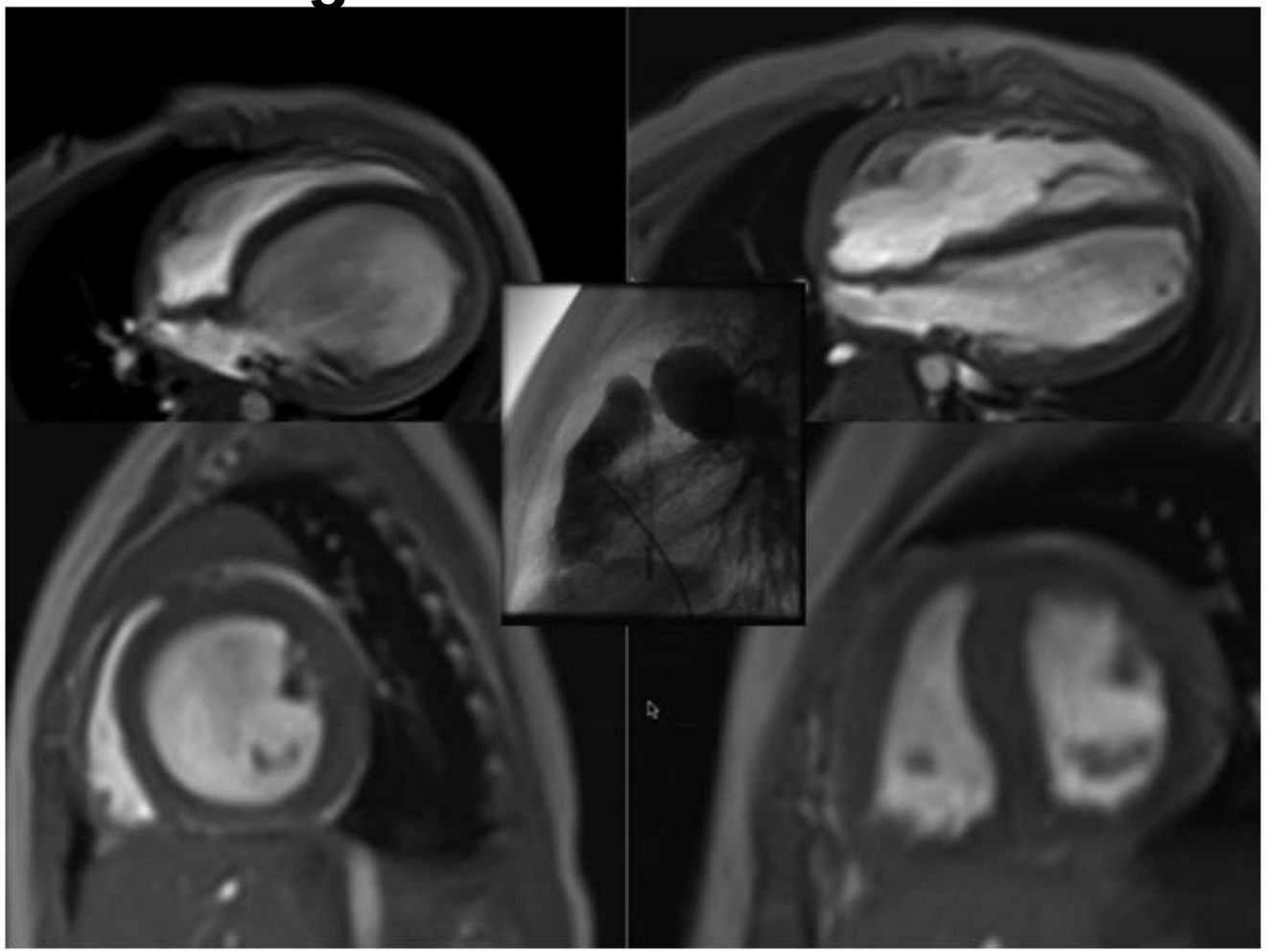
Fiziopatologie, diferita fata de adult – proliferarea cardiomiocitului este unica in IC pediatrica si reglarea slaba a β1 si β2 AR (la adulți – fără diferențe în reglarea expresiei β 2 AR)

(E. Madriago, M. Silberbach, Heart Failure in infants and children, Pediatrics in Review, Vol. 31, No.1, 2010)





Abilitate pentru regenerarea miocardului si o sansa pt proliferarea miocardului la copil - Regenerare în loc de HTX!



Giovanni Fajardo a, Mingming Zhao a, Gerald Berry b, Lee-Jun Wong d, Daria Mochly-Rosen c, Daniel Bernstein **β2-adrenergic receptors mediate cardioprotection through crosstalk with mitochondrial cell death pathways** *Journal of Molecular and Cellular Cardiology 51 (2011) 781–789*

Mecanisme compensatorii

Răspuns	Termen scurt	Termen lung
Retenţia de apă şi sodiu	Creştere presarcină	Hiperhidratare Edeme, anasarcă
Vasoconstricţie	Menţinerea presiunii de perfuzie organelor vitale	Creştere postsarcină Creşterea consumului energetic miocardic
Stimulare simpatică	Tahicardie Creşterea debitului cardiac	Risc de aritmii Creşterea consumului de oxigen miocardic
Modificări celulare	Creşterea calciului intracelular Hipertrofia miocitelor	Apoptoză Fibroză

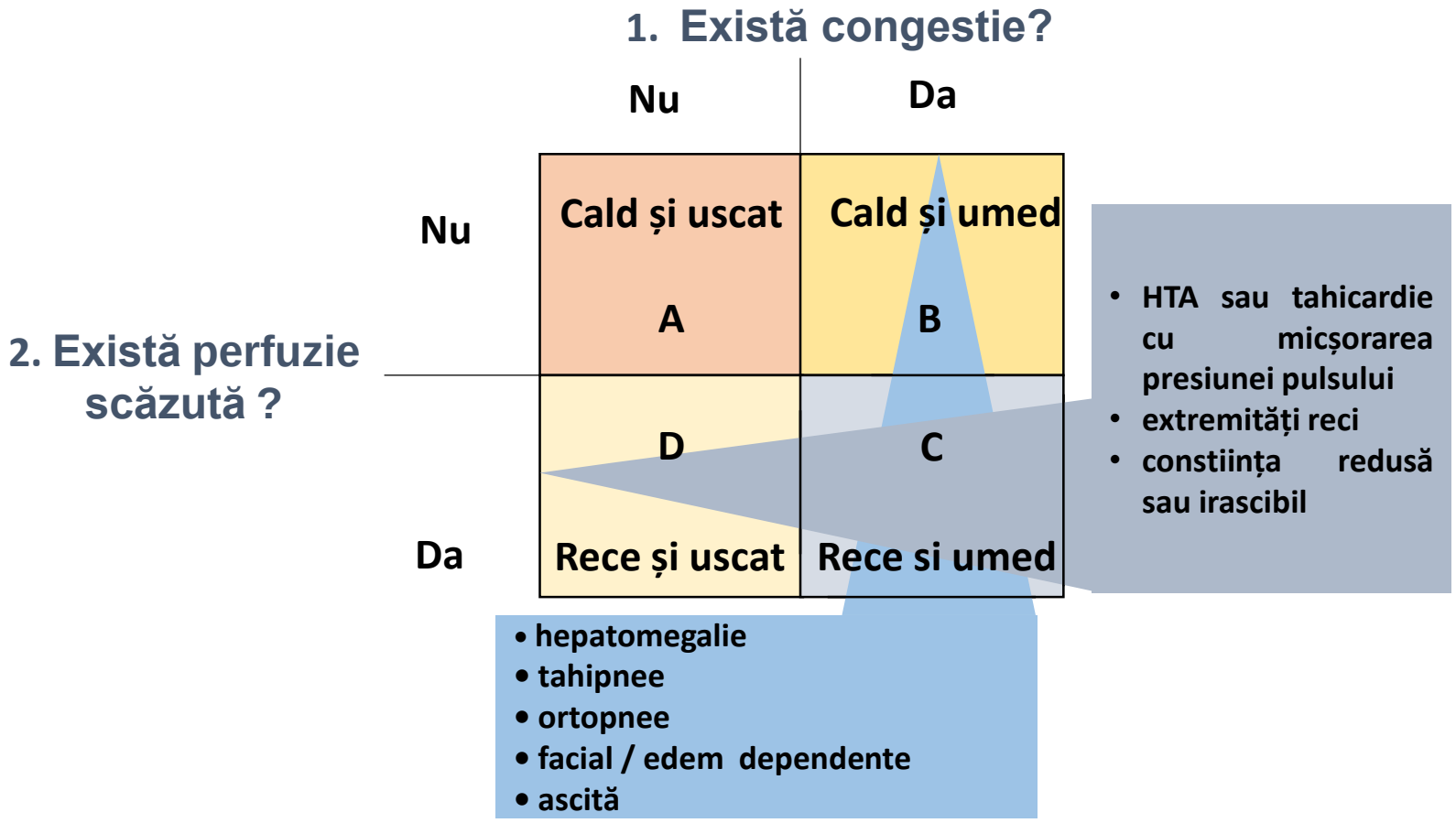
Simptomele caracteristice ale IC la copii

(Bressieux-Degueldre, Nicole Sekarski. Insuffisance cardiaque chez l'enfant; reconnaotre et diagnostiquer, Vol. 26 No. 1, 2015)

	Frecvent intîlnite	Mai puțin frecvente
Nou-născuții și sugarii	Tahipnee Dificultăți în alimentație (reflux, vome, inapetență) Diaforeză Paloare	Cianoza Palpitații Sincope Edem facial Edeme dependente Ascită
Copii mai mari și adolescenții	Fatigabilitate Intoleranță la efort Dispnee Ortopnee Durere abdominală Grețuri Vome	Palpitații Durere toracică Edeme dependente Ascită

Modelele de prezentare recunoscute în insuficiența cardiacă acută decompensată

2. Ponikowski P. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, 2016
3. Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014)



Metode obligatorii de diagnostic (1. Ghidul SEC IC acută și cronică, 2016, 2. Kantor P F și al. CCS Guidelines for HF in Children, 2013; 3. Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014))

Teste funcţionale şi intervenţionale

- ECG
- Rx-grafia torace + ICT
- Ecocardiografia
- Doppler-EcoCG
- RMN/CT (în situații speciale)
- Cateterizm cardiac (Nivelul dovezii C)
- se suspectează o rezistență pulmonară crescută și reversibilitatea HTP la pacienții cu MCC și IC.

Level of Evidence B

RECOMMENDATION

E2. Assessment of electrolytes (Na^+, K^+, Cl^-, Ca^{2+}), glucose, acid-base status, urea and creatinine, hepatic transaminases, thyroid hormone levels, and a complete blood count should be performed at initial presentation of HF and repeated as needed to assess ongoing clinical status (Strong Recommendation, Low-Quality Evidence).

Teste de laborator

- Hemograma (*anemia*)
- Nivelul de electroliţi (Na+, K+, Cl-, Ca2+)
- Glicemia
- Uree, creatinină
- NT-proBNP, BNP (C IIb)

Level of Evidence B

- ASAT, ALAT
- EAB
- CK, fr. MB, troponine
- INR, ind. protrombinic
- Proteina C- reactiva
- Urograma

Table 3 Laboratory test in heart failure.

Test	Rationale
Complete blood count	Useful to assess anemia, which may cause or aggravate heart failure. Leukocytosis may result from stress or signal an underlying infection.
Electrolytes	Hyponatremia reflects an expansion of extracellular fluid volume in the setting of a normal total body sodium. Hypokalemia and hypochloremia can be the result of prolonged administration of diuretics. Hyperkalemia can be the result of impaired renal perfusion and marked reductions in glomerular filtration rate or from intracellular potassium release due to impaired tissue perfusion.
Renal function tests	Elevated BUN and BUN/creatinine ratio are seen in decompensated heart failure.
Liver function tests	Congestive hepatomegaly is often associated with impaired hepatic function, which is characterized by elevation of AST, ALT, LDH, and other liver enzymes. Hyperbilirubinemia (both direct and indirect) is related to acute hepatic venous congestion and is common with severe right heart failure. Elevated ALP, and prolongation of the PTT time can be seen. In children with long-standing heart failure and poor nutritional status, hypoalbuminemia results from hepatic synthesis impairment.
Natriuretic peptides (NT-proBNP/BNP)	Natriuretic peptides levels correlate closely with the NYHA/Ross classification of heart failure and with ventricular filling pressures.
CPK-MB, troponin I and T	Useful if the clinical scenario is suggestive of an ischemic process or myocarditis
Lactate	Elevated lactate is seen in patients with decompensated heart failure as a result of decreased tissue perfusion and/or decreased metabolism due to secondary liver dysfunction and can be a useful serologic marker for monitoring response to therapeutic interventions.
Thyroid function tests	Both severe hyper or hypothyroidism can cause heart failure.
Arterial blood gas	Usually reveal mild hypoxemia in patients who have mild-to-moderate heart failure. Severe heart failure often leads to severe hypoxemia, or even hypoxia. Hypocapnia occurs in the early stages of pulmonary edema because of V/Q mismatch, progressing to hypercapnia and respiratory acidosis, related to decreased vital capacity and poor ventilation.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BNP = B-type natriuretic peptide; BUN = blood urea nitrogen; CPK-MB = creatine phosphokinase; LDH = lactic dehydrogenase; NT-proBNP = N-terminal proBNP; PTT = prothrombin time; V/Q = ventilation/perfusion.

Joseph W. Rossano, MD, and Robert E. Shaddy, Heart Failure in Children: Etiology and Treatment, 2014.

Biomarkerii în IC

Ponikowski P. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, 2016
Kantor P F și al. CCS Guidelines for HF in Children, 2013, 3. Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014)

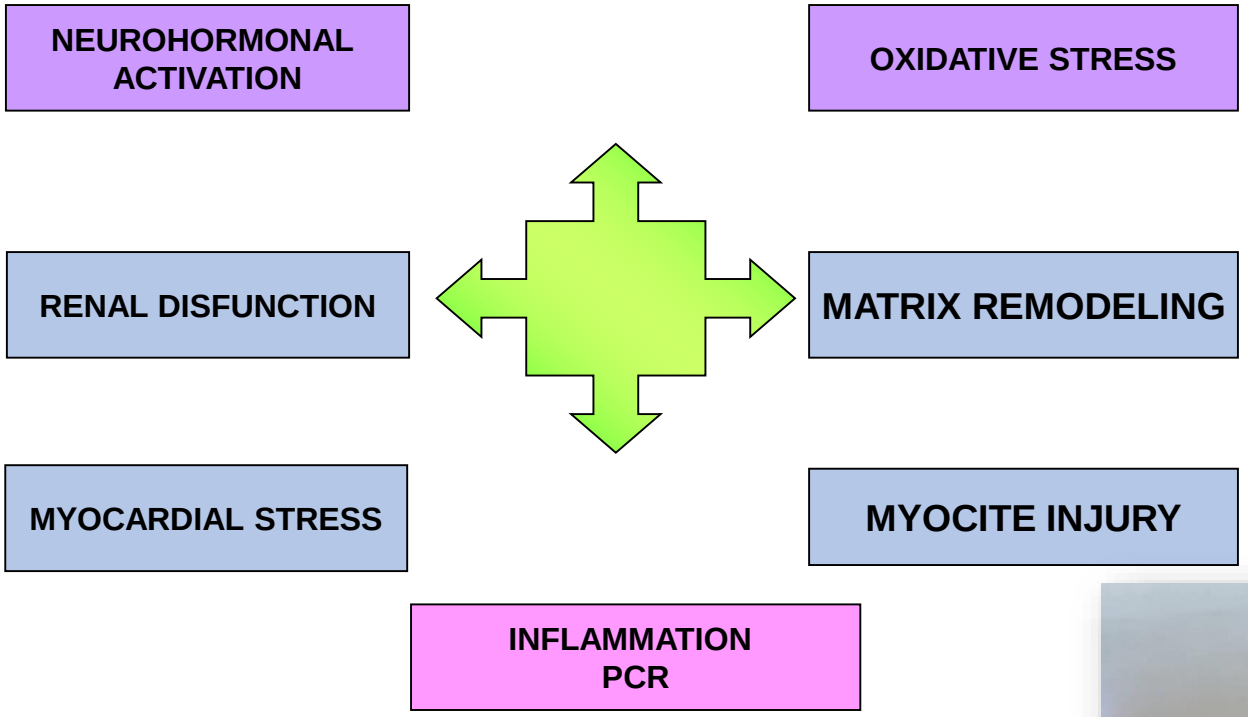
Pentru diagnosticul IC şi urmărirea evoluţiei:

- **BNP/NTpro BNP (marker adjuvant pentru stabilirea diagnosticului, răspunsul la tratament, evoluție și prognostic) crescut ≥ 100/300 pg/ml sugerează prognostic mai rezervat; > 400 pg/ml sugerează IC cronică. Utilitatea lui în pediatrie nu a fost încă confirmată ca la adulţi; (Cl IIb)** Level of Evidence B
- **Proteina C reactivă – marker de inflamaţie;**
- **TNF-alfa, interleukinele – markeri de inflamaţie, reduce relaxarea endotelială indusă de oxidul nitric;**
- **Troponina serică – crescută în condiţii care asociază ischemie miocardică (Kawasaki, infarct miocardic), CM, miocardită acută;**
- **Arginin vasopressina, Epinephrina, Norepinephrina;**
- **Enzime cardiace – CK-MB, LDH (opţional).**

RECOMMENDATION

E9. BNP or NT-proBNP levels are useful in distinguishing HF from respiratory or other noncardiac disease and should be used as a confirmatory test in the acute evaluation of pediatric HF (Strong Recommendation, Moderate-Quality Evidence).

Biomarkerii în IC



Conceptul regenerării miocardului - specific doar vîrstei pediatrice!!!

Ponikowski P. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, 2016
Kantor P F și al. CCS Guidelines for HF in Children, 2013, 3. Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014)

Modalități de evaluare imagistică

Table 2 Comparison of Imaging Modalities

Modality	Advantages	Limitations	Use in pediatric HF
Echocardiography	First-line technique for all patients in acute/chronic HF; anatomic + functional assessment possible	Limited by acoustic windows	First-line technique in the assessment of HF
M-mode	High temporal resolution	Only works if global remodeling/ dysfunction	Serial measurement of LV dimensions, wall thickness, and fractional shortening
	Normal pediatric values available	Not valid if paradoxical septal motion	
2-D echocardiography	Assessment of 2-D anatomy, identification of structural disease	Dependent on acoustic windows	Identification of structural disease as cause for HF
2-D EF	Good parameter for global performance	Geometrical assumptions	Recommended technique for assessment of LV performance
	Can be calculated in patients with regional dysfunction	Load dependency	
3-D EF	No geometric assumptions	Highly dependent on acoustic windows Lower temporal resolution	Emergent technique replacing 2-D EF
Blood Doppler techniques (MPI, dP/dt, S/D ratio)	Geometry-independent	Variability of measuring time intervals	Limited use in heart failure patients
	High temporal resolution	No spatial information Load dependency of different indices	
TDI	Geometry-independent	Angle-dependent	Assessment of longitudinal function, early detection of dysfunction, assessment of diastolic function
	High temporal resolution	Limited information on its use in children	Dyssynchrony detection
	Quantification of regional function	Load dependency	
Strain imaging	Geometry-independent	Software dependency and differences between vendors	Emergent technique
	Images myocardial mechanics	Load dependency Limited normal data	Dyssynchrony assessment
Cardiac MRI	Not limited by imaging windows, no radiation, good for imaging extracardiac structures, flow quantification, tissue characterization (fibrosis imaging)	Accessibility, requirement for general anesthesia, cost, not compatible with many devices (pacemaker, assist devices)	Limited use in HF patients; quantification of RV function, patients with limited acoustic windows, fibrosis detection
Steady-state free precession imaging	Clinical reference technique for quantification of LV and RV volumes + mass	Lower temporal resolution (ECG-gated)	Mainly calculation of volumes and EF
Phase contrast	Reference technique for quantifying flows	Lower temporal resolution than Doppler techniques	Calculation of CO, quantification of valve regurgitation
MR tagging	Allows quantifying myocardial mechanics	Difficult post-processing; lower frames rates compared with echocardiography	Limited clinical use in heart failure patients. Research tool
Late gadolinium enhancement	Identification of regional fibrosis	Limited spatial resolution, only detects regional fibrosis	Clinical use still uncertain; possible prognostic value in HCM, detection of EFE in DCM or obstructive lesions
Angiography	Detection of extracardiac abnormalities	Spatial resolution is less good than cardiac CT (coronary imaging)	Can be used to detect extracardiac abnormalities causing heart failure (arch, coronary anomalies)
Cardiac CT	Not limited by imaging windows; high resolution, allows studying spatial relationships between cardiovascular structures and the airway, anesthesia often not required	Exposure to radiation, limited functional information, no flow quantification, coronary imaging influenced by high heart rates	Mainly used for coronary artery imaging if uncertain about coronary artery origins on echocardiography; limited role in follow-up

Expansions for the abbreviations used in Table 2 are provided in Appendix 3.

Recomandări - EcoCG

Kantor P F și al. CCS Guidelines for HF in Children, 2013, 3. Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014) **)**

- **Ecocardiografie transtoracică– pentru diagnosticul cauzei:**
- **Tipul de MCC (cu atenție la a. coronare); Evaluarea aspectului miocardial pentru paternul fenotipic de CM;**
- **Parametrii funcției sistolice a VS - FE, FS; Dimensiunea sistolică și end diastolică a VS, scorul Z;**
- **Determinarea prezenței regurgitării mitrale; Evaluarea cantitativă și calitativă a fției VD și presiunii în VD; Evaluarea fției diastolice a VS; (Cl IIa)** Level of Evidence B Level of Evidence C
- **Excluderea trombilor intracardiaci.**
- **Pts cu DV necesita EcoCG screening, chiar și în absența simptomelor.**
- **Toți pts cu IC necesită periodic EcoCG follow-up pentru evaluarea raspunsului la tratamentul medical și a DV, sau în cazul modificărilor clinice.**

Class I

1. Measurement of LV dimensions and LV wall thickness is an essential part of every echocardiographic functional LV assessment in patients with HF. The recent American Society of Echocardiography pediatric recommendations propose the use 2-D imaging instead of M-mode, but this was not based on actual data proving its clinical superiority. Normal values are more readily available for M-mode measurements. **Level of Evidence B**
2. LV remodeling should be monitored during serial follow-up. This consists of measuring cavity dimensions, wall thickness, and where clinically relevant, LV mass. **Level of Evidence B**
3. For patients with HF, assessing LV function by calculating LVEF based on a well-standardized 2-D method (biplane Simpson's or area-length method) should be undertaken. **Level of Evidence B**

Class IIa

1. Fractional shortening can be used for sequential assessment of LV function, although caution is required in patients with abnormal or paradoxical septal motion. **Level of Evidence C**
2. No recommendations can be made about the use of automated 2-D methods or 3-D echocardiography. These are emerging techniques for EF calculation that still need further validation in pediatric HF. **Level of Evidence C**

Class IIb

1. LVEF is load-dependent. The use of methods correcting for afterload have been proposed that do not improve diagnostic accuracy and predictive value. **Level of Evidence C**

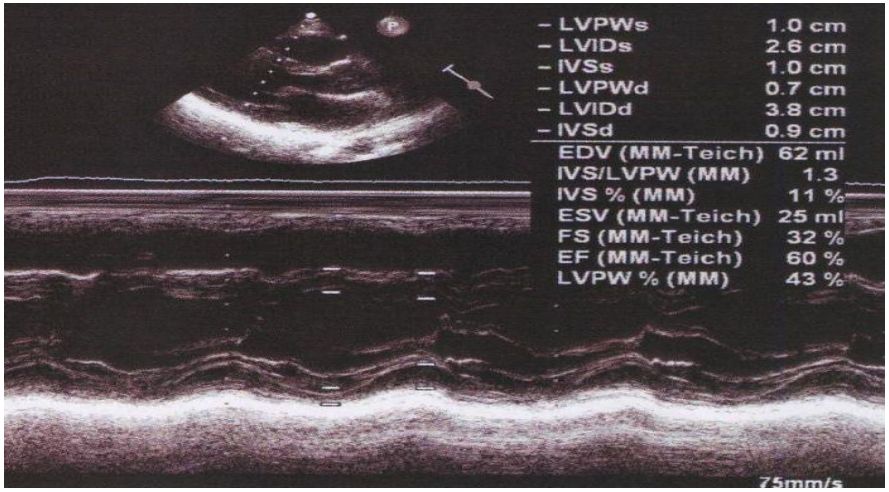
2. Although measured and reported, the value of blood pool Doppler parameters, such as dP/dt, myocardial performance index, and the ratio of systolic-to-diastolic duration, in the assessment of LV systolic function in pediatric patients with HF is probably limited. (Problems with reliability of measuring time intervals, loading, and heart rate dependency of the methods, and their uncertain prognostic value, all limit their clinical use.) **Level of Evidence C**
3. Although measured and reported, the role of tissue Doppler imaging (TDI) and strain imaging in pediatric patients with HF is still uncertain. Pulsed TDI at the annulus has the benefit of published normal ranges and may assist in the early detection of myocardial dysfunction. Apart from the potential additional predictive information, its use in the description of mechanical dyssynchrony and identification of candidates for CRT seems to be important but requires further investigation. **Level of Evidence C**

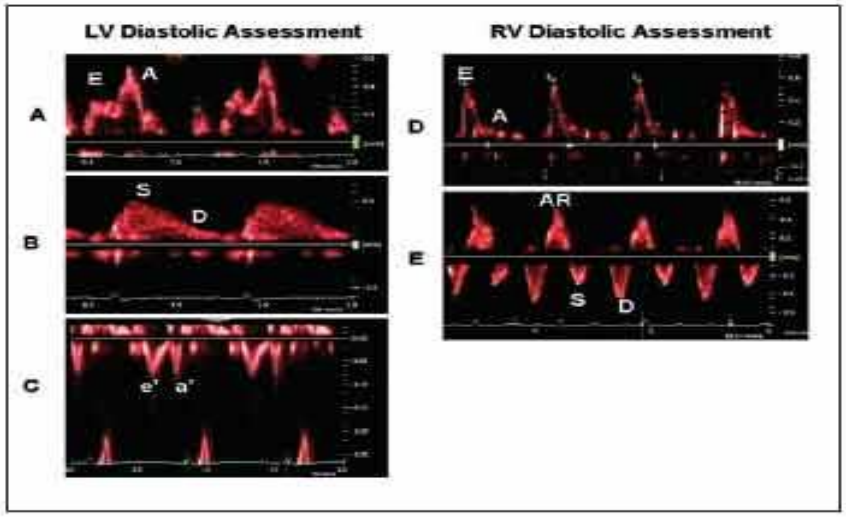
Echo diastolic function[31]

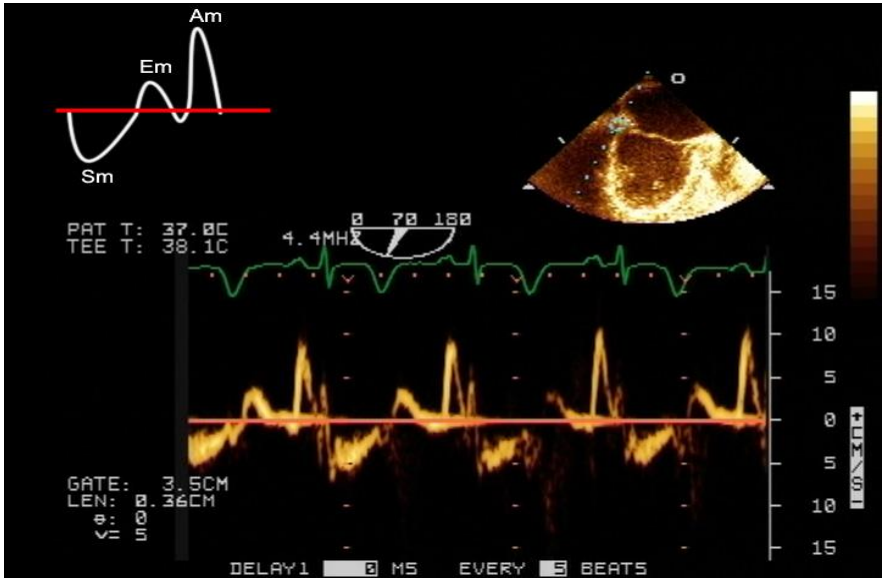
Class IIa

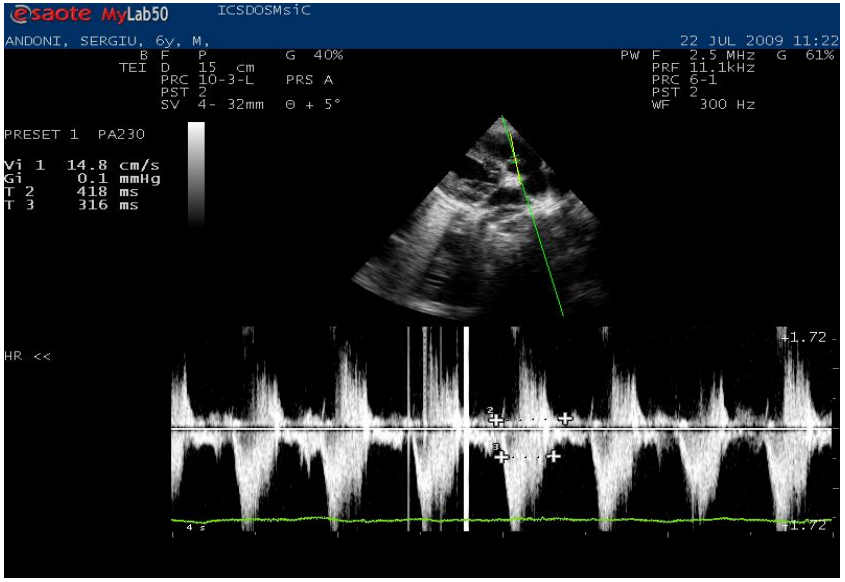
1. Diastolic function, including mitral inflow patterns, mitral annular TDI, and pulmonary venous Doppler flow patterns should be assessed by echocardiography in children with HF. The tracings should be interpreted to define the type of diastolic abnormality (relaxation abnormality, reduced compliance, restrictive filling) as well as to attempt to diagnose the presence of elevated filling pressure (Table 3 summarizes typical changes in progressive LV diastolic dysfunction). **Level of Evidence C**

Functia sistolica/diastolica VS/VD dimensiuni (indici), ind. derivaţi din Doppler, ind. stress-velociate, TDI, strain rate, ind. Tei VD/VS, dP/dt, propagare fluxului în Doppler color, 3D









Recomandări - RMN cardiac

(Kantor P F și al. CCS Guidelines for HF in Children, 2013, Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014)

- **RMN cardiac completează diagnosticul clinic al Miocarditelor și poate aduce informații suplimentare în cazul CMP, suspecție de rezistență pulmonară crescută, IC cu debut inexiplicabil, asociată cu dereglări hemodinamice, dereglări de ritm (CI IIb, Nivel de evidenta C).**

Cardiac MRI[32–34]

Class IIb

1. Cardiac MRI can be used to assess LV function in children. Use can be limited due to the requirement for general anesthesia in younger children, the presence of arrhythmia, and the availability and cost associated with cardiac MRI. **Level of Evidence C**
2. Balanced steady-state-free precession cine analysis has become the reference standard for volumetric and myocardial mass assessment of the LV. Where feasible, it should be used to assess children with HF. However, accuracy depends on standardization of analysis protocol and acquisition of adequate temporal and spatial resolution specific to the patient's heart rate and size. **Level of Evidence C**

RV systolic function[24]

Class IIa

1. For the quantitative assessment of RV function by 2-D echocardiography, it is reasonable to use fractional area of change from the apical 4-chamber view together with tricuspid annular planar systolic excursion. **Level of Evidence C**
2. TDI assessment of tricuspid annular motion is a useful technique for the assessment of RV longitudinal function and should be added in the quantitative assessment of RV function. **Level of Evidence C**

Class IIb

1. Due to methodologic variability and the load-dependency, the clinical use of RV myocardial performance index in the assessment of right HF is limited. **Level of Evidence C**
2. RV strain analysis of RV longitudinal deformation is an emerging technique and requires further validation before routine use for the assessment of RV function. **Level of Evidence C**

MRI RV function[35–37]

Class IIa

1. Assessment of RV size and EF by MRI is considered the clinical reference for the assessment of RV function in patients with RV failure. Restricted access, the need for general anesthesia or sedation in infants and young children, and costs remain important limitations. **Level of Evidence C**

RV diastolic function

Class IIb

1. Doppler echocardiography can be used for the assessment of RV diastolic function, although criteria for grading and assessment of filling pressures are still poorly validated. **Level of Evidence C**

RECOMMENDATION

E16. CMRI might assist in the clinical diagnosis of myocarditis, and might provide additional information in CMs by tissue and scar characterization. The prognostic value of CMRI findings is not yet known (Conditional Recommendation, Low-Quality Evidence).

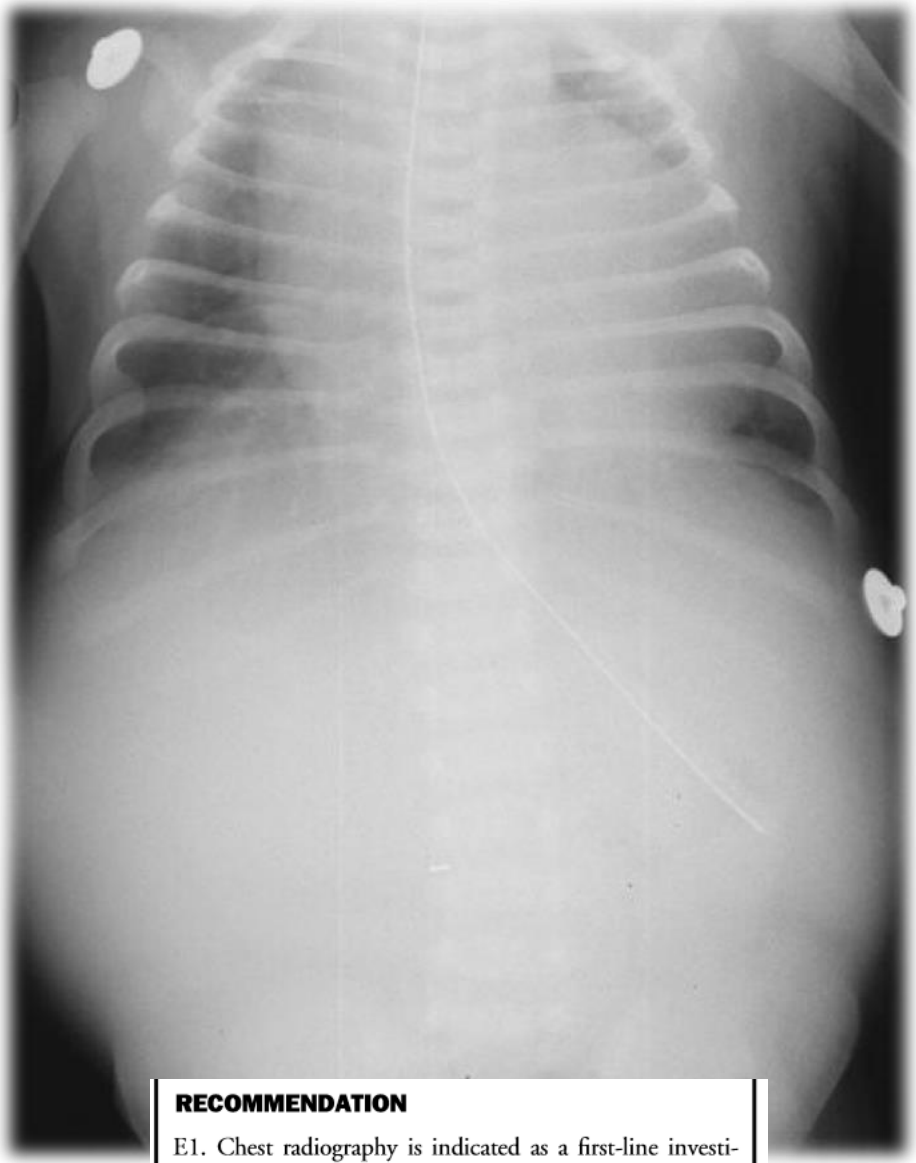
Recomandare - Rgr

Kantor P F și al. CCS Guidelines for HF in Children, 2013)

- **Radiografia toracică este indicată drept examinare de I linie la copiii cu suspecție la IC.**

(Recomandare strictă, Probe de Calitate - Moderate).

- **Totuși sensibilitatea și valoarea predictivă pozitivă a Rgr este joasă.**
- **La copiii cu CMD, cardiomegalia la Rgr toracică are valoare prognostică.**



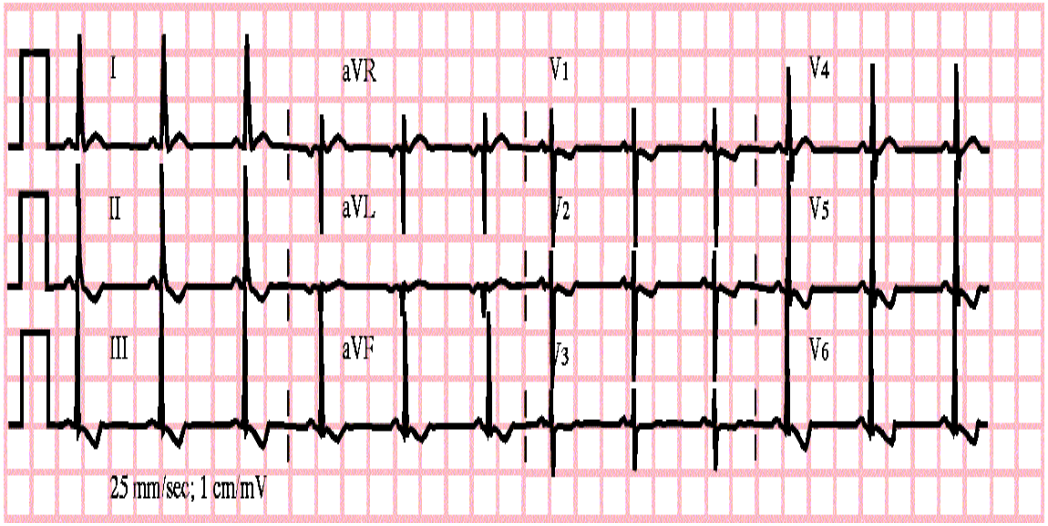
RECOMMENDATION

E1. Chest radiography is indicated as a first-line investigation in children with suspected HF (Strong Recommendation, Moderate-Quality Evidence).

Recomandări – ECG (Kantor P F și al. CCS Guidelines for HF in Children, 2013)

- **ECG standard 12 der este necesară a fi efectuată pts cu IC pentru a exclude semnele maladiei congenitale sau ischemice, tulburările de ritm, smul de pre-excitație.**

(Recomandare strictă, Probe de Calitate - Moderate).



RECOMMENDATION

E3. All patients should have 12-lead ECG performed at the time of presentation with HF, to exclude features of congenital or ischemic heart disease, arrhythmia and pre-excitation (Strong Recommendation, Moderate-Quality Evidence).

E4. Holter/ambulatory ECG monitoring is not indicated as a primary diagnostic test in HF, unless HCM, arrhythmogenic RV CM, or tachycardia-induced CM is the suspected cause (Conditional Recommendation, Low-Quality Evidence).

E5. Holter/ambulatory ECG monitoring might be indicated during chronic follow-up, particularly in higher arrhythmia risk groups, including patients with primary restrictive CM or HCM, with tachycardia-induced CM, or those who are taking anti-arrhythmic therapy (Conditional Recommendation, Low-Quality Evidence).

- **Holter ECG monitoring nu este indicat drept test diagnostic primar în IC, cu excepția – CMH, CM aritmogenă VD, după Fontan, swicth atrial, corecția TVM, urmărire cronică, la pts din gr. de risc – CMR, CMH etc.**

(Recomandare Condiționată, Probe de Calitate - Joasă).

Ambulatory monitoring[42–44]

Class I

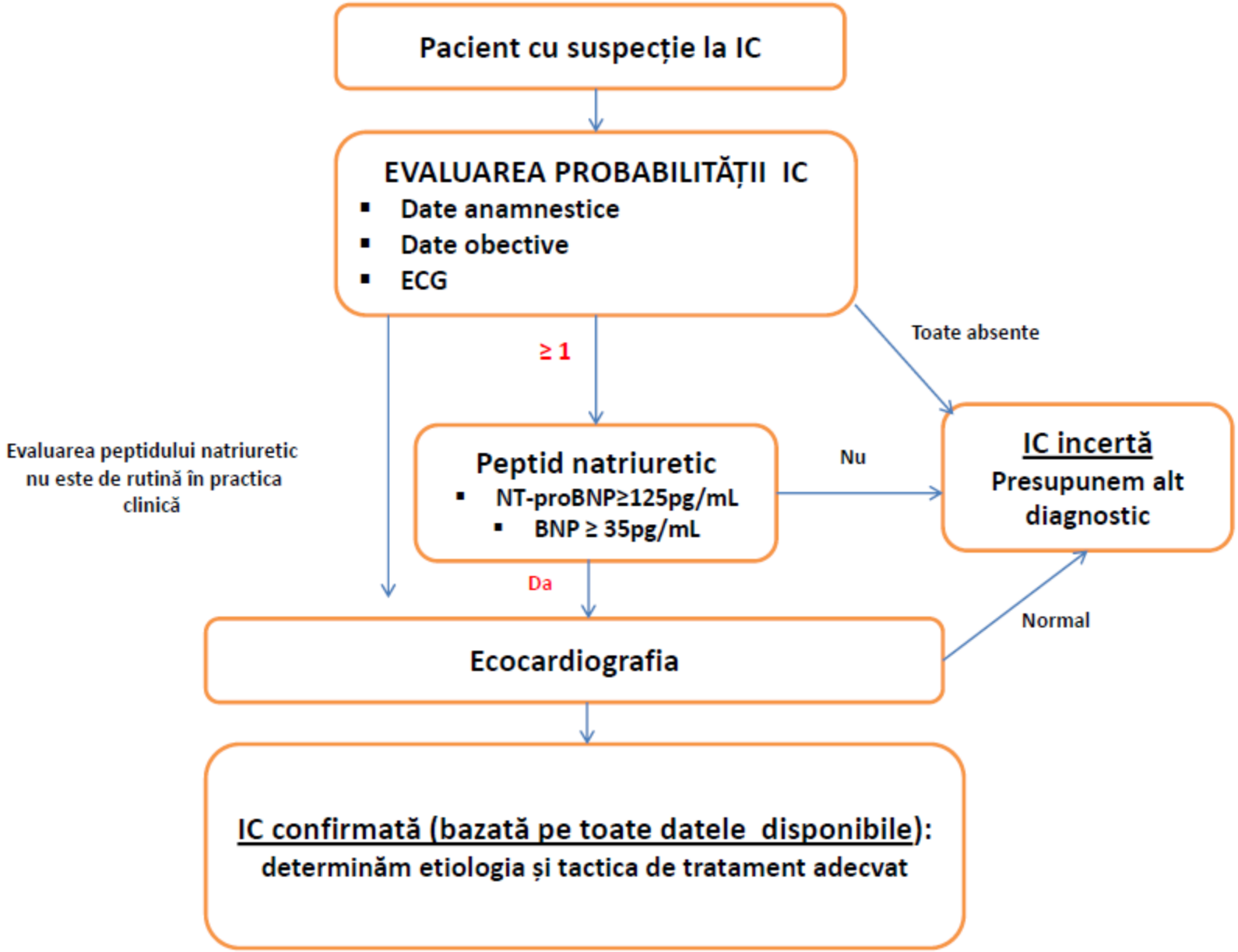
1. In a pediatric HF patient who presents with palpitations or syncope, some form of ambulatory monitoring should be considered to achieve a specific diagnosis and drive further management decisions. Less frequent symptoms may require use of longer-term event monitors. **Level of Evidence C**

Class IIa

1. In pediatric HF patients with a high risk of developing atrial or ventricular arrhythmias or heart block, regular ambulatory monitoring should be considered. This would include patients after a Fontan palliation, any form of atrial switch procedure, heterotaxy (isomeric) syndromes, congenitally corrected transposition of the great arteries, or cardiomyopathy (HCM, DCM, RCM, and LVNC). **Level of Evidence C**
2. In asymptomatic pediatric HF patients, there are no data to support the timing and frequency of regular ambulatory monitoring for arrhythmias; however, intermittent screening for asymptomatic arrhythmias should be considered. **Level of Evidence C**

Algoritmul de diagnostic al IC

(Ponikowski P. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.)



Tratamentul IC la copii

- **Studii bazate pe dovezi? Puține, practic absente!**
- **Studii empirice? Prăbușite!**
- **Dar ce cunoaștem despre cunoștințe în patofiziologie și farmacologie?**

Scopul tratamentului în IC:

- **Prevenirea IC și tratamentul chirurgical oportun la copiii cu MCC;**
- **Prevenirea progresiei IC;**
- **Menținerea și ameliorarea calității vieții;**
- **Prevenirea invalidității;**
- **Micșorarea numărului de spitalizări repetate;**
- **Majorarea duratei de viață;**
- **Micșorarea mortalității.**

Măsuri generale de tratament

- **Repaus la pat, rareori necesar chiar ca repaos strict;**
- **Poziția de decubit cu trunchiul ridicat la 30 grade;**
- **Sedarea copilului anxios, oxigenoterapie (40-50%);**
- **Aportul caloric – peste 150-160 kcal/kg/zi la sugar;**
- **Îmbogățirea laptelui cu glucide (12-15%) și lipide (5-6%) pentru obținerea unei valori calorice de 120kcal/100ml;**
- **Volumele alimentare mai mici și frecvente sunt mai bine tolerate de către sugari;**
- **Supliment de proteine, vitamine și minerale (fier, calciu);**
- **Corectarea unor deficite nutriționale specifice: (L-carnitina, seleniu).**

Tratamentul medicamentos la pts cu IC acută decompensata

- **Furosemidul** initial 0,5-2mg/kg/doză i/v și 1-4mg/kg/24h p/o administrată în 1-4 prize/zi (în terapia cronică), cu monitorizarea riguroasă a electroliților (reduc simptomele, episoadele de acutizare a IC, imbunătățesc toleranța la efort, influiențează pozitiv supraviețuirea).
- **Torasemidul** 5 mg la copii >12 ani.
- Monitorizare a TA, nivelului de electroliți, funcției renale!
- La pts cu răspuns limitat la diureticele de ansă pot fi asociate diureticele Tiazide (Metozalone).
- Antagoniștii Vasopressinei (Tolvaptan, Conivaptan, și al.) reduc simptomele, nu influiențează supraviețuirea, dar puține dovezi despre eficacitatea lor în IC pediatrică.
- **Nou!** Utilizarea cronică a diureticelor este evitată în măsura posibilităților! Deficitul de volum intravascular stimulează axa neurohumorală!

- Ieri? Nu azi!

RECOMMENDATION

F1. A loop diuretic, such as furosemide, is recommended for patients with HF and signs and symptoms of congestion. An initial starting dose of 0.5-1 mg/kg intravenously or orally every 6-12 hours, is safe and effective (Strong Recommendation, Moderate-Quality Evidence).

Tratamentul medicamentos la pts cu IC acută decompensată

Terapia inotropă (puține dovezi) – Catecolaminele și Inhibitorii FDE – 3.

IDEAL - creşterea contractilităţii fără creşterea consumului de oxigen miocardic; nu modifică RVS, RVP

- **Milrinona i.v.: iniţial 50 mcg /kg/doză; ulterior 0,5 mcg/kg/min;**
- **Dobutamina i.v.: doza 2-20 mcg/kg/min în perfuzie endovenoasă; și doze mici de Epinephrină i.v.: iniţial 0,01 mcg /kg/min (pînă la 1 mcg /kg/min);**
- **Sunt indicate la copiii cu IC și DC scăzut (perfuzie joasă, extremități reci, oligurie), inclusiv la copiii cu disfuncție miocardică după bypassul cardiopulmonar.**
- **Milrinona la copii previne sindromul DC diminuat după chirurgia cardiacă. Atenție la pts hipotensivi!**

RECOMMENDATION

F2. Children presenting with HF because of reduced cardiac output with end-organ dysfunction are likely to benefit from inotropic therapy as a rescue strategy. In this setting, milrinone, dobutamine, and low dose epinephrine have all shown efficacy in children (Strong Recommendation, Low-Quality Evidence).

Table 7 Summary of drug therapy recommendations for acute heart failure

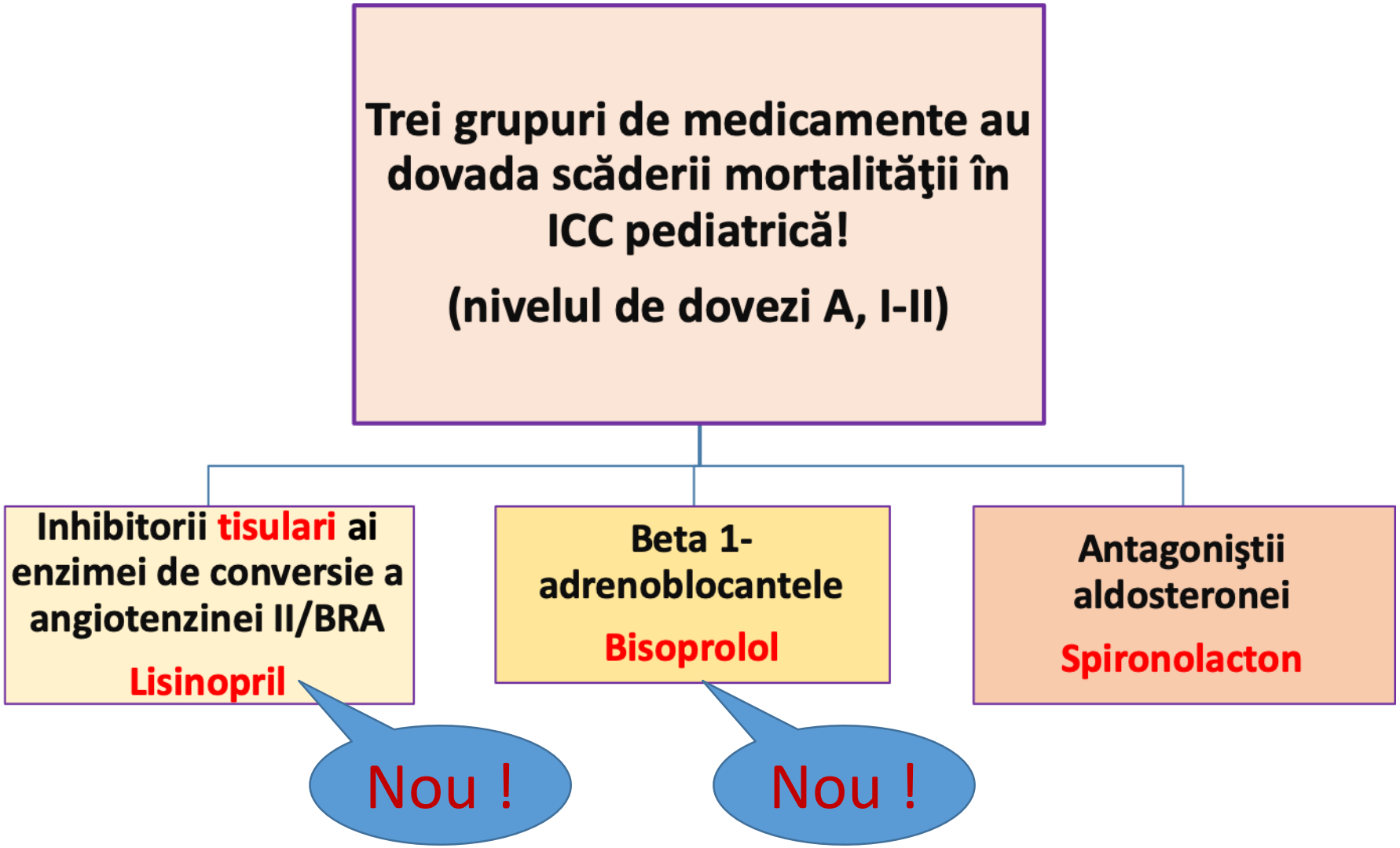
Drug/class	Recommendation
Diuretics	Initial and ongoing assessment of fluid status should be performed in all patients admitted with acute heart failure (2014: Class I, LOE C)
	First-line therapy for evidence of fluid overload (2014: Class I, LOE C)
	Careful monitoring for side effects, including renal function, electrolytes, and hypotension, should be performed (2014: Class I, LOE C)
Vasodilators	May be used with acute heart failure in absence of hypotension. May be used in combination with diuretics for symptomatic relief of pulmonary edema (2014: Class I, LOE C)
Inotropes	May be temporarily utilized in patients presenting with cardiogenic shock with poor systemic and end-organ perfusion (2014: Class I, LOE C)
	May be temporarily utilized in patients presenting with hypotension with evidence of low cardiac output and compromised end-organ perfusion (2014: Class IIa, LOE C)
	Choice of agent(s) depends on clinical presentation. Milrinone and/or dobutamine can be used as first-line rescue therapy with epinephrine playing a role in refractory hypotension and poor end-organ perfusion (2014: Class IIa, LOE C)
	Potentially harmful in absence of clinical evidence of hypotension, impaired perfusion, low cardiac output, and/or decreased end-organ perfusion (2014: Class III, LOE B)
Levosimendan	Consider if unresponsive to traditional inotropic therapy (2014: Class IIb, LOE C)
Corticosteroids	Consider after evaluation to treat adrenal insufficiency (2014: Class IIb, LOE C)
Anticoagulation	Consider prophylactic anticoagulation, especially in acute care setting and in presence of indwelling intravascular lines (2014: Class IIa, LOE C)
Thyroid replacement	Evaluation of a critically ill patient's systemic thyroid homeostasis is reasonable, and thyroid hormone replacement may be considered if hypothyroidism present (2014: Class IIa, LOE C)
	No indication for routine use of thyroid hormone to treat acute heart failure in absence of documented abnormal thyroid function (2014: Class IIb, LOE C)
	Consider thyroid hormone use in the acutely unwell post-cardiac surgery patient (2014: Class IIb, LOE B)
Immunomodulation	No evidence to support routine use of corticosteroids or IVIG in children with myocarditis (2014: Class IIb, LOE C)

IVIG intravenous immune globulin, *LOE* level of evidence

Alexander D. Hussey1 • Robert G. Weintraub1,2, Drug Treatment of Heart Failure in Children: Focus on Recent Recommendations from the ISHLT Guidelines for the Management of Pediatric Heart. Failure Pediatr Drugs DOI 10.1007/s40272-016-0166-4.

Tratamentul farmacologic IC cronică cu FE redusă (IC sistolică) la copii

Recla S, Schmidt D, Logeswaran T, Esmaeili A, Schranz D. Pediatric heart failure therapy: why β1- receptor blocker, tissue ACE-I and mineralocorticoid-receptor- blocker? *Transl Pediatr 2019;8(2):127-132. doi: 10.21037/ tp.2019.04.08*



IECA –Captopril, Enalapril, Ramipril, Perindoprilul, BRA - Losartan

Momma K. ACE inhibitors in pediatric patients with heart failure. *Paediatr Drugs*. 2006;8:55– 69; Kirk R, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014;

- **Tratament de prima linie la toţi pts cu IC cronică, simptomatică (CI, HF Stage C).**
- **ICC asimptomatică şi disfuncţie VS (CIIa, Stage B) (Nivel de evidență B).**
- **În ICC din Distrofia musculară Duchenne, baieți (Nivel de evidență B).**
- **Eficienţa IECA şi în disfuncţia VD, prin majorarea FE VD cu reducerea vol. diastolic final şi a presiunii de umplere la pts cu IC biventriculară (Haddad, Francois, 2008)**
- **Nu sunt indicate ICC cu FE p! (Cl IIb, Nivel de evidență C).**

Dovezi noi

- **Lisinopril (ACE - tisular) și nu Captopril (ACE 1 - seric)!**

Table 2 Medical therapy (cardiac anti-congestive/anti-remodeling therapy)

Drugs	Dosages	Comment
Bisoprolol (B)	0.05–0.1–0.2 (0.3) mg/kg/d	Adaption to SAP/HR (avoid diuretics)
Lisinopril (L)	0.05–0.1–0.2 (0.3) mg/kg/d	Adaption to SAP/fluid status!
Spironolactone (S)	1–[2] mg/kg/ED	Anti-remodeling dosage!
Digoxin	Saturation dosage 0.01 mg/kg/8 h	HR-control together with (B)
	Daily dosage: 0.008 mg/kg/d (blood level: 0.5–0.8 nmol/L)	
Furosemide	0.5 mg/kg ED if necessary	Not for chronic therapy
Hydrochlorothiazide	1–[2] mg/kg ED	If possible, avoid diuretics (D)

HR, heart rate.

Table 3 Supplemental therapy (cardiac anti-congestive/anti-remodeling therapy)

Drugs	Dosage	Goals
Co-Enzyme Q	10–15 mg/kg/d	All DCM-patients
Riboflavin	3–20/mg/d	Mitochondriopathy
Carnitin	25–100 mg/kg/d	If deficient
Nicotinamid	50 mg/kg/d	Mitochondriopathy
Erythropoietin	150 U/kg/3×/wk	Goal: Hb 12–14 g/dL

DCM, dilated cardiomyopathy.

B-blocante – experienţa utilizării în ICC pediatrică este modestă, rezultatele sunt controversate şi necesită cercetări suplimentare

(Kantor P F și al. CCS Guidelines for HF in Children, 2013;
Frobel AK. Alabed S, Sabouni A, Al Dakhoul S, et al. Beta-blockers for congestive heart failure in children. Cochrane Database Syst Rev 2016)

- Eficacitatea Metoprololului, Carvedilolului, Bisoprololului la pts simptomatici cu disfuncţia sistolică de VS sistemic, în CMD (CIIa, Nivel de evidență B).

Kirk R, Dipchand AI, Rosenthal DN. ISHLT Guidelines for the Management of Pediatric Heart Failure. Birmingham: University of Alabama at Birmingham; 2014)

- La pts asimptomatici cu disfuncţia sistolică de VS sistemic, în CMD (CIIa, Nivel de evidență B).
- Studiul CHF-PRO-INFANT, BB în ICC secundară MCC reduce semnif. eliberarea reninei prin prevenţia schimbărilor mediate de către SNS (Buchhorn R, 2011, Ghidul AHA, 2009)

Doze:

- Metoprololul succinat: 1-2 mg/kg zi,
- Bisoprololul: 0,04 – 0,1 mg/kg zi,
- Carvedilolul în disfuncţie sistolică de VS:

iniţial 0,1 mg/kg zi (maxim 6,25 mg) 2 ori/zi

întreţinere 0,5-1 mg/kg zi

Dovezi noi!

- **β-blocantele Bisoprolol (β 1) și nu Carvedilol (β 1 + β 2 + alpha 1)**

Antagoniștii aldosteronei. Spironolactona

- **Recomandate a fi administrate la copiii cu disfucție sistemică de VS şi funcție renală normală, monitoringul f-ției renale și K seric!** (Kantor P F și al. CCS Guidelines for HF in Children, 2013,) **(CI, Nivel de evidență C)**
- **Indicate în retenţie hidrosalină,**
- **Reduc hipervolemia pulmonară, îmbunătăţind statusul respirator,**
- **Efecte de prevenţie a remodelării cardiace,**
- **Efect antifibrotic etc.**
- **Doze: Spironolactonă per os: - 1-3 mg/kg/zi în 2-3 prize**

- **Precauţie la utilizarea diureticelor osmotice** (Am J Kidney Dis 2008; 51: 491-503)

Edelmann F, et al. Effect of spironolactone on diastolic function and exe failure with preserved ejection fraction: the Aldo-DHF randomized controll

RECOMMENDATION

F6. Aldosterone antagonist therapy is reasonable in children with chronic systolic HF, provided renal function is normal or only mildly impaired. Close monitoring of renal function and serum potassium is required when coadministering aldosterone antagonist therapy with ACEi therapy (Conditional Recommendation, Low-Quality Evidence).

Bisoprolol și Lisinopril sunt utilizate avind o înaltă specificitate și acțiunea de lunga durată a b-1 blocker și ACE-I tisular respectiv. Aceasta recomandare este bazată pe specificitate și eficacitate la copiii, cunoștințele fiziologice ale receptorilor și rezultatele negative a câteva studii pediatrice în IC – (studii bazate pe dovezi)

Table 3 Summary of drug therapy recommendations for HFrEF

Drug/class	Recommendation
Diuretics	Should be used to treat fluid retention associated with ventricular dysfunction to achieve euvolemia (2014: Class I, LOE C; 2004: Class I, LOE C)
ACE-I	Recommended (unless specific contraindication) for the treatment of symptomatic LV dysfunction. Start at low doses, and up-titrate to a maximum tolerated safe dose (2014: Class I, LOE B; 2004: Class I, LOE B)
	Recommended (unless specific contraindication) for the treatment of asymptomatic LV dysfunction (2014: Class IIa, LOE B; Class I, LOE B)
	Consider for individuals with DMD unless specific contraindication, although the optimal age of institution of therapy is unclear (2014: Class IIa, LOE B)
	Should not be routinely instituted for all patients with single ventricle morphology, but could be considered in specific cases, e.g. valve regurgitation or ventricular dysfunction (2014: Class IIb, LOE B)
β-Blockers	Consider in symptomatic children with systemic LV systolic dysfunction, particularly if the systemic ventricle has a left ventricular morphology. Start as low dose and slowly up-titrate (2014: Class IIa, LOE B)
	Consider in asymptomatic children with systemic LV systolic dysfunction. Start as low dose and slowly up-titrate (2014: Class IIa, LOE B)
Aldosterone receptor antagonists	Consider in systemic ventricular systolic dysfunction (2014: Class I, LOE C)
ARBs	Generally reserved for systemic ventricular systolic dysfunction that would benefit from RAAS blockade but are intolerant of ACE-I. (2014: Class IIa, LOE A; 2004: Class IIa, LOE C)
Digoxin	Not recommended with asymptomatic LV dysfunction because no survival benefit seen in adults (2014: Class I, LOE C; 2004: Class IIb, LOE C)
	Used for symptom relief. Consider doses targeting lower serum digoxin concentrations (e.g., 0.5–0.9 ng/mL). Dose reductions in patients on carvedilol and amiodarone or those who have or are at risk for renal dysfunction (2014: Class IIa, LOE C; 2004: Class I, LOE B)
Hydralazine and Isosorbide dinitrate	Not recommended (2014: Class III, LOE C)
Antiarrhythmics	May be needed in select cases where dysrhythmias persist after normalization of electrolyte disturbances or metabolic issues (i.e., hyperthyroidism) and the dysrhythmias are poorly tolerated (2014: Class IIb, LOE C)
	Should not be used routinely (2014: Class III, LOE C)
Statins	Not indicated (2014: Class III, LOE C)

Alexander D. Hussey1 • Robert G. Weintraub1,2, Drug Treatment of Heart Failure in Children: Focus on Recent Recommendations from the ISHLT Guidelines for the Management of Pediatric Heart. Failure Pediatr Drugs DOI 10.1007/s40272-016-0166-4.

Statins	Not indicated (2014: Class III, LOE C)
Renin inhibitors	Not recommended (2014: Class III, LOE C)
Anticoagulants	Patients with intracardiac thrombus should receive anticoagulation with heparin or warfarin (2014: Class I, LOE B)
	Consider anticoagulation with heparin or warfarin if history of prior thrombus or thromboembolic event with EF <25 % (FS <15 %) (2014: Class IIa, LOE C)
	Recommend anticoagulation with unfractionated heparin, LMW heparin or warfarin if persistent or uncontrolled paroxysmal atrial fibrillation or flutter (2014: Class IIa, LOE C)
	Not recommended if no history of thrombus or thromboembolic event, as insufficient evidence (2014: Class III, LOE C)
Nesiritide	Not recommended for routine use but may be considered in select situations to lower CVP when other interventions have been unsuccessful (2014: Class IIb, LOE C)
Pulse or chronic inotropic support	Consider for symptomatic relief in palliative setting (2014: Class IIa, LOE C)
	Not recommended for use other than as a bridge to transplant (2014: Class III, LOE C)
Vasopressin receptor antagonists	Not recommended for routine use (2014: Class III, LOE C)

ACE-I angiotensin-converting enzyme inhibitors, *ARBs* angiotensin II receptor blockers, *CVP* central venous pressure, *DMD* Duchenne muscular dystrophy, *EF* ejection fraction, *FS* fractional shortening, *HFrEF* chronic heart failure with reduced ejection fraction, *LMW* low molecular weight, *LOE* level of evidence, *LV* left ventricle, *RAAS* renin–angiotensin–aldosterone system

Alexander D. Hussey1 • Robert G. Weintraub1,2, Drug Treatment of Heart Failure in Children: Focus on Recent Recommendations from the ISHLT Guidelines for the Management of Pediatric Heart. Failure Pediatr Drugs DOI 10.1007/s40272-016-0166-4.

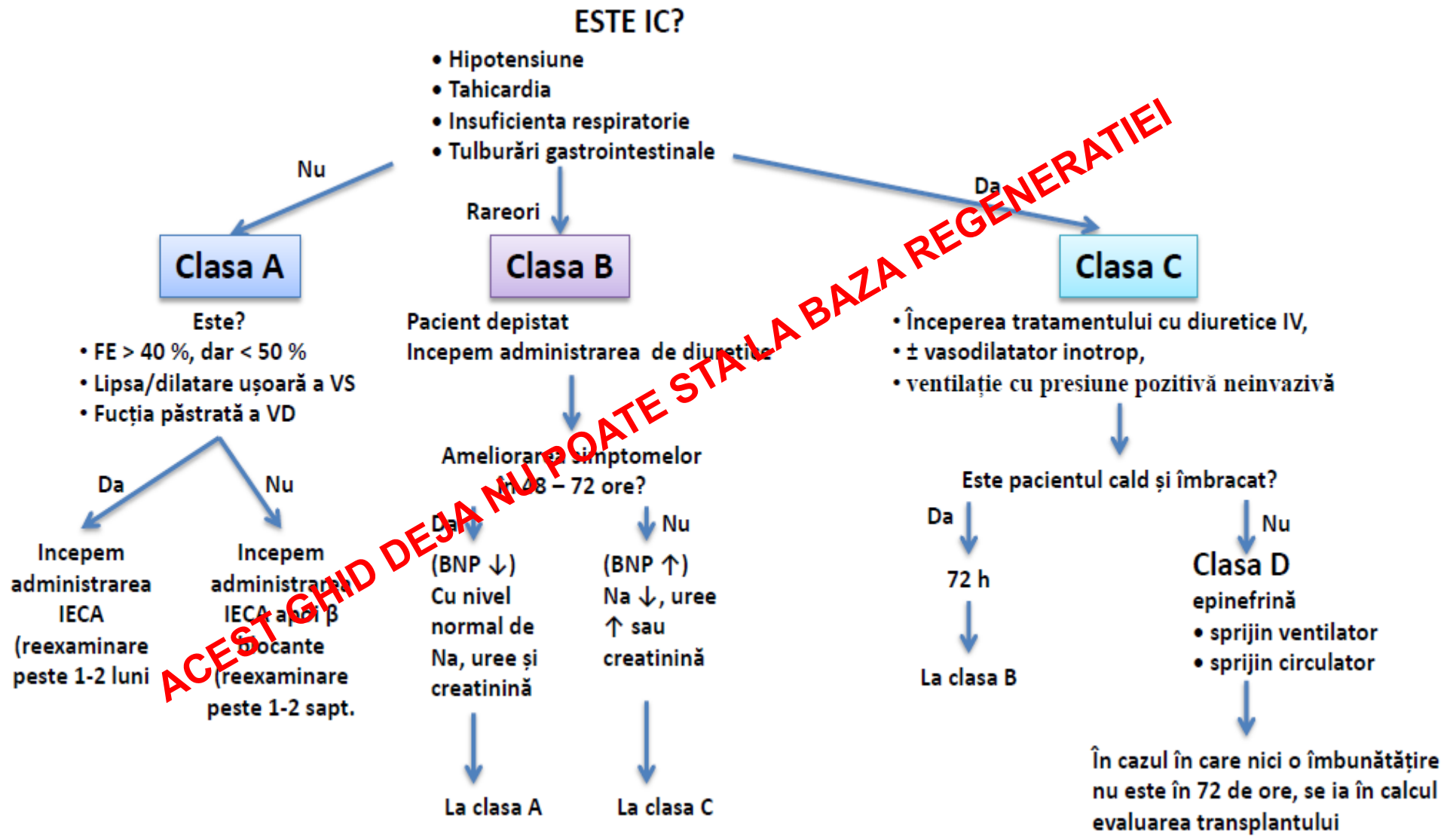
Table 4 Summary of drug therapy recommendations for HFpEF

Drug/class	Recommendation
Diuretics	Recommended to establish a clinically euvolemic state (2014: Class I, LOE C; 2004: Class I, LOE C)
	Close monitoring of renal function and BP during initiation and up-titration of diuretic therapy (2014: Class I, LOE C; 2004: Class I, LOE C)
	Treatment of systemic hypertension is recommended although no preferred particular class of medication, diuretics may be considered (2014: Class IIa, LOE C)
ACE-I and ARBs	Not recommended unless additional indication (e.g., hypertension), with careful monitoring of hemodynamics and renal function (2014: Class IIb, LOE C; 2004: Class IIb, LOE C)
Calcium channel antagonists	Not recommended unless additional indication (2014: Class III, LOE C)
Aldosterone receptor antagonists	Not recommended (2014: Class IIb, LOE C)
Aldosterone receptor antagonists	Not recommended (2014: Class IIb, LOE C)
Phosphodiesterase inhibitors	Not recommended unless additional indication (e.g., pulmonary hypertension) (2014: Class IIb, LOE C)
Digoxin	Not recommended unless additional indication (e.g., arrhythmia requiring atrial rate control) (2014: Class III, LOE C)
Inotropic support	Intravenous beta agonists (dopamine, dobutamine and epinephrine) not indicated (2014: Class III, LOE C)
Pulmonary vasodilators	Use of prostaglandins and endothelin receptor antagonists to treat secondary pulmonary hypertension is not recommended (2014: Class III, LOE C)

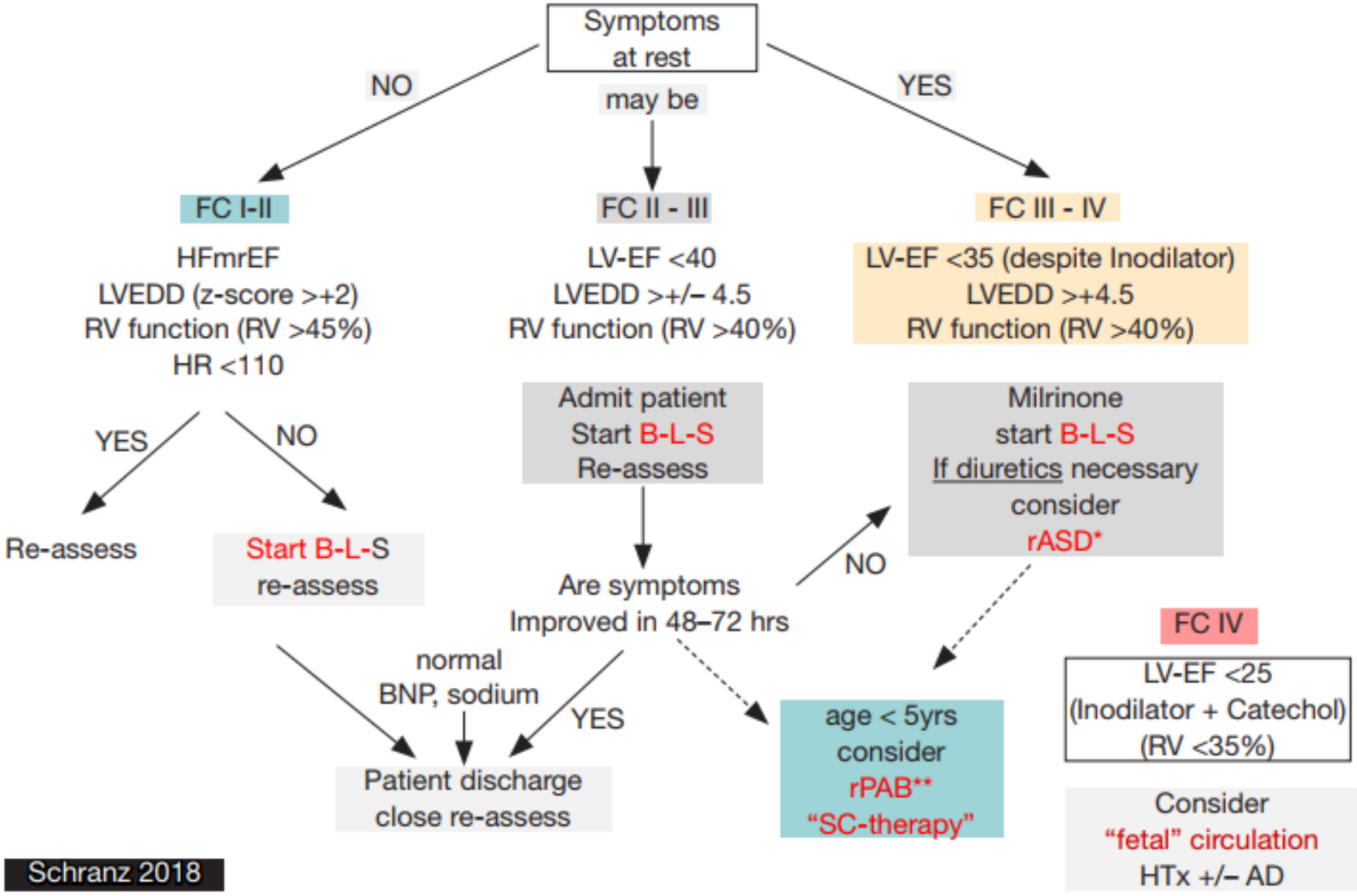
ACE-I angiotensin-converting enzyme inhibitors, *ARBs* angiotensin II receptor blockers, *BP* blood pressure, *HFpEF* chronic heart failure with preserved ejection fraction, *LOE* level of evidence

Alexander D. Hussey1 • Robert G. Weintraub1,2, Drug Treatment of Heart Failure in Children: Focus on Recent Recommendations from the ISHLT Guidelines for the Management of Pediatric Heart. Failure Pediatr Drugs DOI 10.1007/s40272-016-0166-4.

Algoritmul terapeutic al Ghidului canadian, 2013 actualmente nu poate servi drept baza regenerării. (Kantor P F și al. CCS Guidelines for HF in Children, 2013)



Algorithm for pediatric (age!) heart failure therapy (DCM, HFrEF)

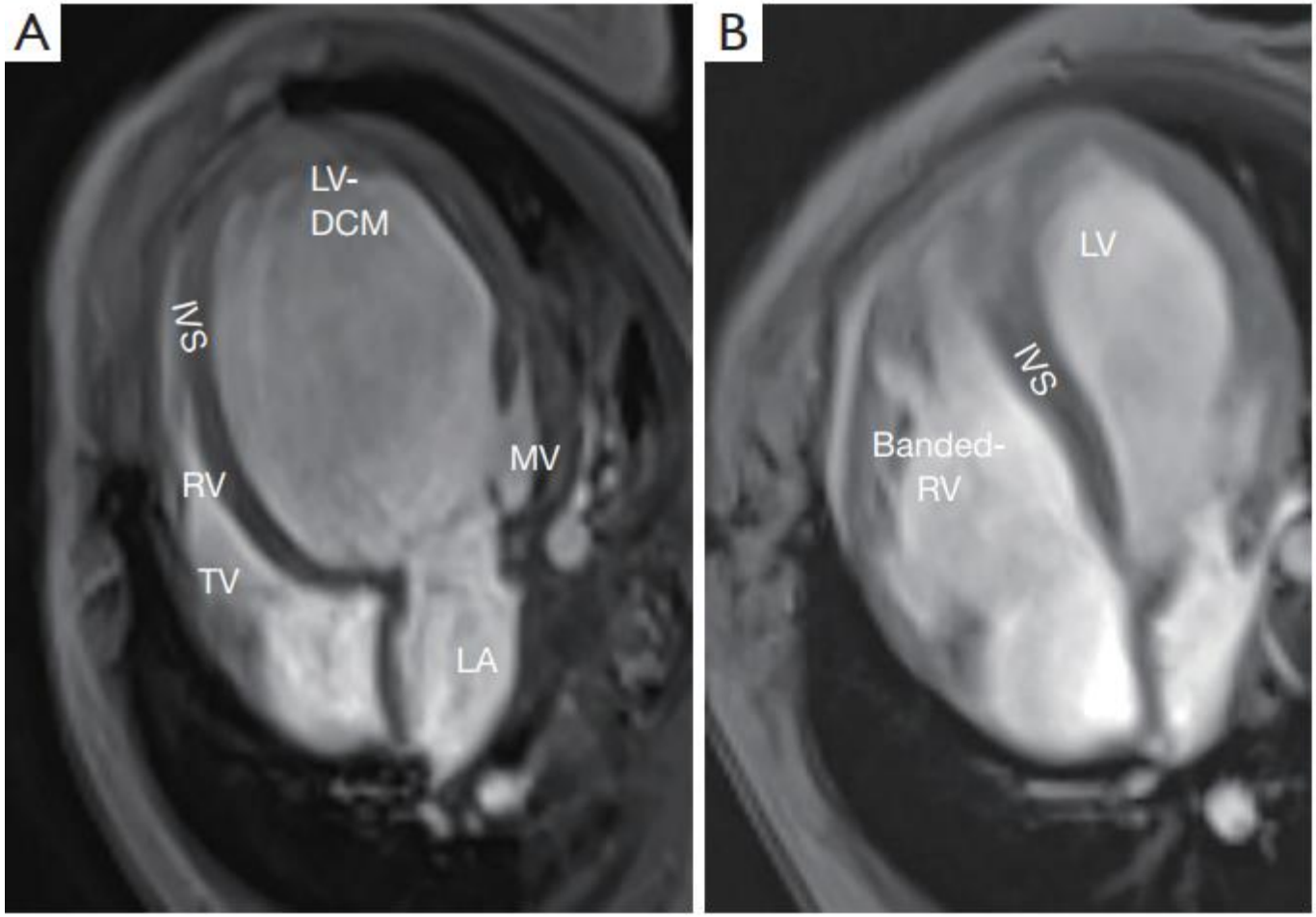


Schranz 2018

O nouă abordare …

Schranz et al. Pulmonary artery banding

PAB-effects on right (RV) and left (LV) ventricle



RV

- Increased RV contractility
- Leftward-shifting of IVS
- Improved RV diastolic inflow
- RV hypertrophy
- RV matrix remodeling

LV

- Reduced LV preload
- Reduced LV-volume
- Re-synchrony
- Increased LV contractility
- LV Co-hypertrophy
- Normalized MVR

Anticoagulante

2.1.11 Anticoagulants

Poor LV systolic function (fractional shortening [FS] <15 % or EF <25 %) appears to be the most significant risk factor for thromboembolism in pediatric DCM with a reported cardiac thrombosis incidence of 6–53 % and pulmonary or systemic embolism incidence of 1–16 %.

Warfarin use is weighed up against the need for frequent blood tests and potential risk of major hemorrhage (including intracranial bleeding) in a toddler or active child.

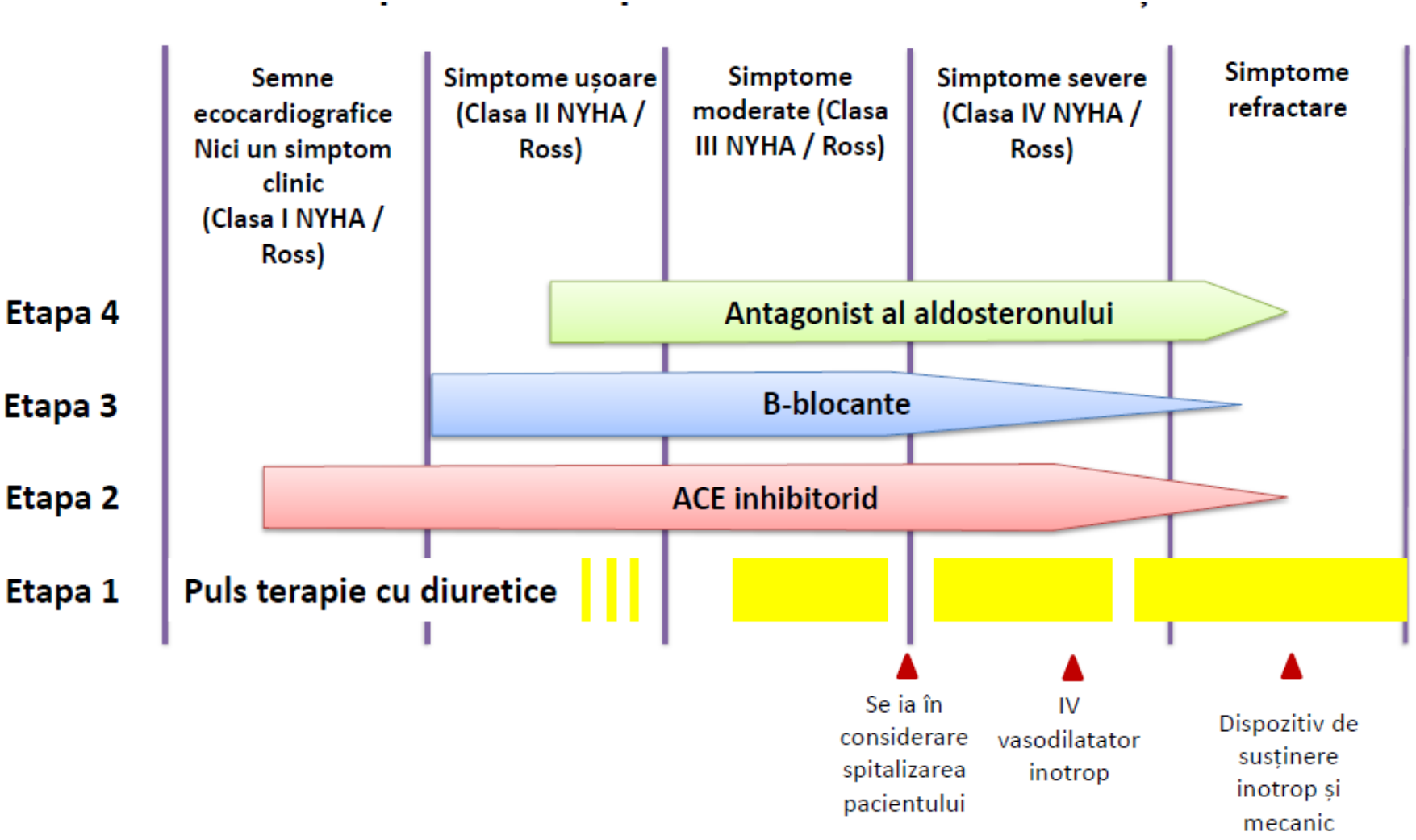
Low Molecular Weight (LMW) Heparins (*i.e., enoxaparin*) is more easily monitored; however, the need for subcutaneous administration makes long-term use less appealing.

Aspirin is commonly used as it is easy to administer and is presumed to have a less likely risk of major hemorrhage, but has unproven efficacy in thrombosis prevention with systolic dysfunction.

On review of the current pediatric literature, the current ISHLT guidelines suggest the use of warfarin (target international normalized ratio [INR] 2–3) or LMW heparin (target anti-Xa 0.5–1) in the setting of DCM and EF <25 %, restrictive cardiomyopathy, LV non-compaction cardiomyopathy with poor EF, history of thromboembolism, and presence of intracardiac thrombus. Use of prophylactic aspirin for those with EF 25–30 % is recommended.

Introducerea etapizată a terapiei medicale în insuficiența cardiacă

(Kantor P F și al. CCS Guidelines for HF in Children, 2013)



Noile clase de medicamente în curs de investigare din trialurile clinice curente

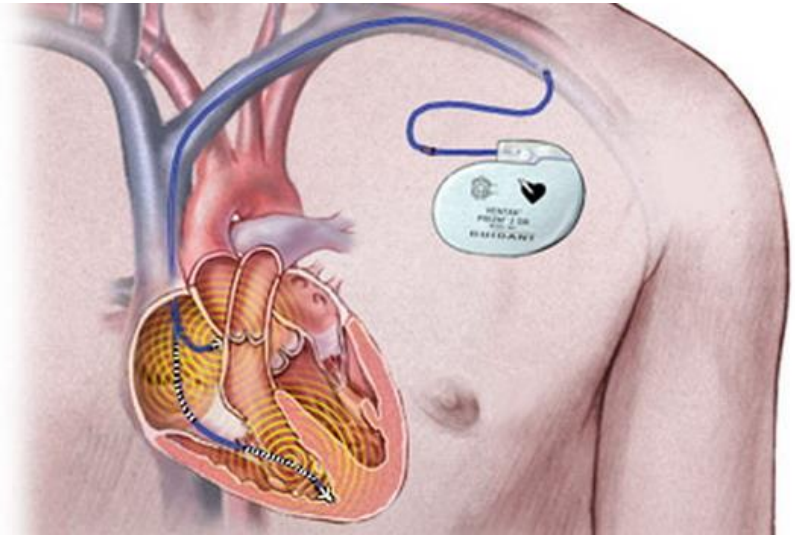
- **Serelexina (formă recombinantă de relaxină-2 umană)- utilizată în tratamentul IC acute, are ca rezultat reducerea deceselor;**
- **Ivabradina (inhibitor selectiv al impulsului electric If din nodul sinusal) –administrată la pac. cu IC cronică și ritm cardiac crescut, nu afectează contractilitatea;**
- **BRA+inhibitor al neprilysinei**
- **Peptidele natriuretice tip B**
- **Antagoniştii vasopresinei (conivaptan);**
- **Antagoniştii receptorilor endotelinei (Darusentan, sitaxentan, bosentan, tezosentan);**
- **Inhibitorii FDE-5 (Sildenafil);**
- **Levosimendanul (Calcium sensitizing agents);**
- **Antagoniştii aldosteronei (eplerenone);**
- **Inhibitorii TNF-alfa (Etanercept (Enbrel));**

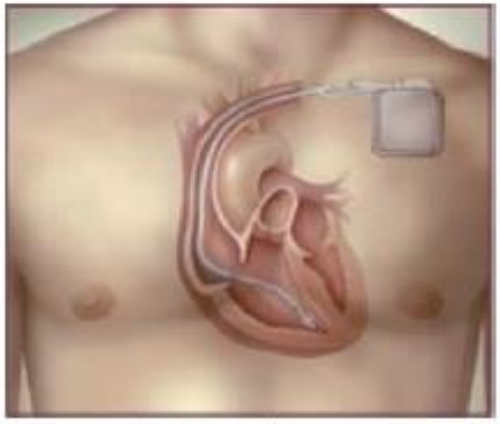
AVÎND CA SUPORT MODELUL NEUROHORMONAL AL IC.

- **Pharmacogenetica (studierea polimorfismului genelor pt ACE, pt receptorii alfa și beta adrenergici, receptorii endotelinei);**
- **Terapia cu celule Stem.**

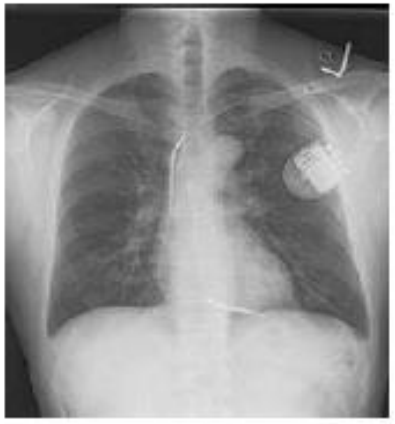
Noi abordări electrofiziologice

Aritmiile sunt o cauză principală a decesului subit la pacienții cu cardiomiopatie severă și IC (atât dilatativă cât și hipertrofică). Deși antiaritmicele pot reduce uneori acest risc, pentru pacienții cu un risc deosebit de mare (maldii asociate cu un risc ridicat de aritmie ventriculară, pac. care au în anamneză un episod de "moarte subită ratată", un defibrilator cardioverter implantabil poate fi salvator.





Dispozitivul ICD arată ca un pacemaker



Imagine RX torace

CONCLUZII

- **Cauzele IC la copil sunt multiple (MCC cu supaîncărcare de volum, presiune, Insuficiențele valvulare, CM primare și secundare), iar MCC și CMp constituie cele mai frecvente cauze de IC la copil!**
- **Principalii biomarcheri recunoscuți a fi implicați în fiziopatologia IC cu rol diagnostic, evolutiv și prognostic sunt: neurohormonali, ai inflamatiei (PCR, TNF-alfa, IL), BNP/NT-proBNP, stresului oxidativ etc. Noul concept al regenerarii!**
- **Arsenalul farmacoterapeutic curent pentru IC pediatrică este limitat în lipsa dovezilor medicale puternice.**
- **Considerind ca lipsesc studiile pediatrice bazate pe evidente, indicatia pe durata a β1 AB receptori specifici in combinatie cu IECA tisulare si antagonistii mineralocorticoizi pot fi explicate in contextul farmacologic si receptorilor specifici in IC la sugar si copil (Sabine Recla, 2019). Bisoprolol, Lisinopril si spironolactone sunt utilizate in trat. IC la pts cu sunt S – D, in CMD, smul HLHS, procedura Hybrid.**
- **Promitator este caracterul paleativ de a crea o comunicatie atriala restrictive pentru a imbunatati efectiv simptomele a IC, permitind deasemenea in viitor bazele strategiilor regenerative (Anna Bauer, 2019).**
- **Bandingul de AP in CMD!**
- **Considerind cresterea, capacitatea proliferative si …**

Vă mulţumesc pentru atenţie!