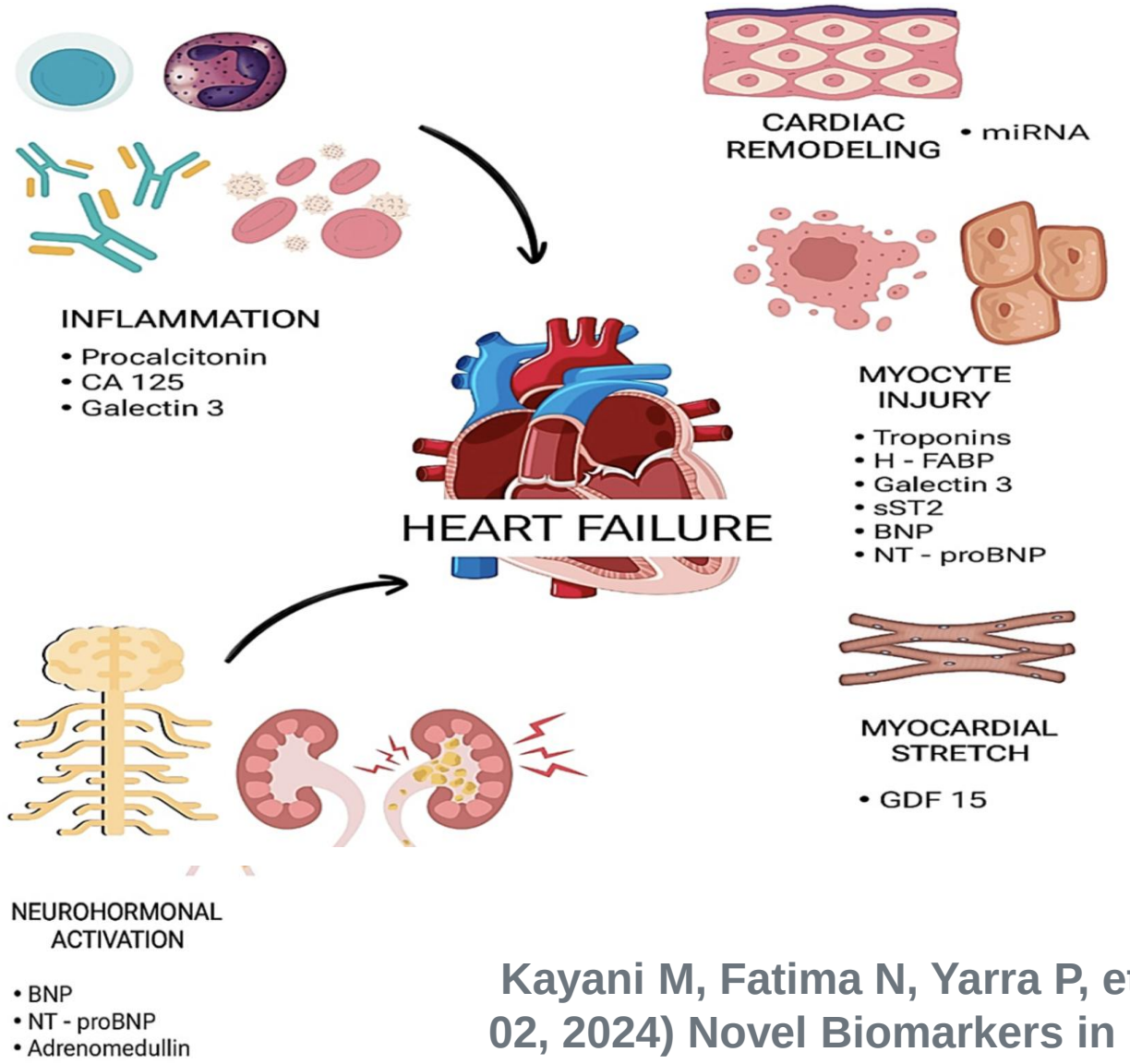
Biomarkery v diagnostice srdečního selhání – interpretace a možná úskalí

Jiří Veselý

kardiologická ambulance EDUMED

Biomarkery se vztahem k srdečnímu selhání



Kayani M, Fatima N, Yarra P, et al. (February 02, 2024) Novel Biomarkers in Early Detection of Heart Failure: A Narrative Review. Cureus 16(2):

Biomarkery se vztahem k srdečnímu selhání

Myocardial Insult

- Myocyte stretch
  - NT-proBNP, BNP, MR-proANP
- Myocardial Injury
  - Troponin T, troponin I, myosin light-chain I, heart-type fatty-acid protein, CKMB
- Oxidative stress
  - Myeloperoxidase, uric acid, oxidized low-density lipoproteins, urinary biopyrrins, urinary and plasma isoprostanes, plasma malodialdehyde

Neurohormonal Activation

- Renin angiotensin system
  - Renin, angiotensin II, aldosterone
- Sympathetic nervous system
  - Norepinephrine, Chromogranin A, MR-proADM
- Arginine vasopressin system
  - Arginine vasopressin, copeptin
- Endothelins
  - ET-1, big proET-1

Remodeling

- Inflammation
  - C-reactive protein, TNF-α, soluble TNF receptors, Fas, interleukins (I, 6 and 18), osteoprotegerin, adiponectin
- Hypertrophy/Fibrosis
  - Matrix metalloproteinases, collagen propeptides, galectin-3, soluble ST2
- Apoptosis
  - GDF-15
- Misc
  - MicroRNA, quiescin Q6, VEGFR-1

Comorbidities

- Renal biomarkers
  - Renal function
    - Creatinine, BUN, eGFR, cystatin C, β-trace protein
  - Renal injury markers
    - NGAL, KIM-1, NAG, liver-type fatty acid binding protein, IL-18
  - Hematologic biomarkers
    - Hemoglobin, RDW, iron deficiency (ferritin, transferrin sat)
  - Liver function tests
  - Albumin

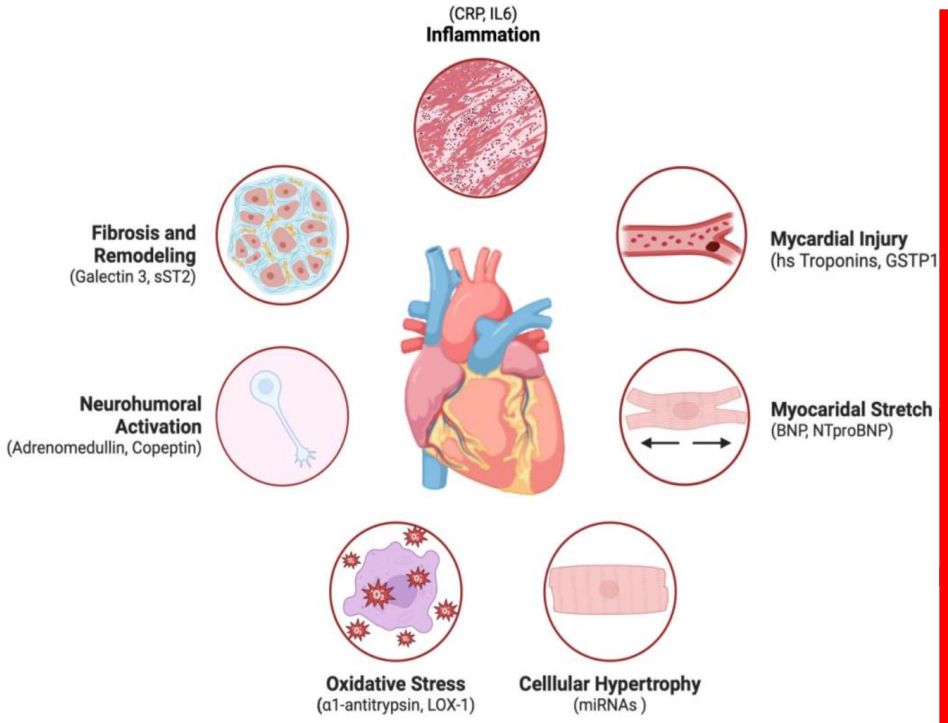
Diagnostický a prognostický potenciál biomarkerů u srdečního selhání

Biomarkers	HF Prognosis	Advantages	HF diagnosis
BNP	+	High negative predictive value [124]. Improves survival and hospital stay [139]. Easily accessible diagnostic methods [140]	+ At a threshold of 100 pg/mL [29], sensitivity of 90% and specificity of 76%
NT-proBNP			+ At a cutoff level of 300 pg/mL [30], sensitivity of 90% and specificity of 85%
Troponins	+	Risk stratification and powerful predictor of mortality at 3 months [141]. Easy to access [142]	+
Galectin-3	+	Predictive of long-term outcomes and mortality [68]	+ At a threshold of 16 ng/mL [67], sensitivity of 76.0% and specificity of 71.9%. At a threshold level of 8 ng/mL [66], sensitivity of 92% and specificity of 71%
Procalcitonin	+	High positive predictive value [79]. Assessment of severity	+ At a cutoff level of 0.09 ng/mL [79], sensitivity of 99.9% and specificity of 100%
CA-125	+	Treatment response. Independent predictor of mortality in 6 months of follow-up [88]. Easily available in clinical labs. Standardized measurement [85]	+ For diagnostic sensitivity [89]. Limited specificity
Adrenomedullin	+	74% accuracy in predicting 90-day survival with AHF [143]. Therapy guidance [99]. Independent predictor of hospitalization and mortality [96]	+ [96] Limited evidence supporting sensitivity and specificity
H-FABP	+	Independent predictor of all-cause deaths and CVS-related deaths [102]	+ [144] Limited evidence supporting sensitivity and specificity
miRNAs	+	Differentiates among individuals with no-HF, HFpEF, and HfrEF [110] Predictors for HF hospitalization and all-cause mortality [117]	+ Combined miRs 423-5p, 320a, 22, and 92b [109]. Sensitivity of 90% and specificity of 90%
GDF-15	+	Variations in levels over one year strongly predict mortality [124]	+ [145] Limited evidence supporting sensitivity and specificity
sST2	+	Risk stratification [127]. Predictive of all-cause deaths and CVS-related deaths [135]	+ [133] Limited evidence supporting sensitivity and specificity

BNP = brain natriuretic peptide;
NT-proBNP = N-terminal pro-B-type natriuretic peptide;
CA-125 = carbohydrate antigen 125;
AHF = acute heart failure;
H-FABP = heart-type fatty acid-binding protein;
CVS = cardiovascular;
GDF-15 = growth differentiation factor 15;
sST2 = soluble suppression of tumorigenicity

Kayani M, Fatima N, Yarra P, et al. (February 02, 2024) Novel Biomarkers in Early Detection of Heart Failure: A Narrative Review. Cureus 16(2): e53445. doi:10.7759/cureus.53445

Biomarkery u HF v aktuálních doporučených postupech



Biomarker	Advantages	Limitations	Guideline Recommendations
B-type Natriuretic Peptide (BNP) and N-terminal proBNP (NT-proBNP)	Sensitive indicators Reflect hemodynamic changes Prognostic value	Influenced by age, renal function, and obesity Variability in cut-off values	*Diagnosis*: ESC I A ACC/AHA IIa C *Prognosis*: ACC/AHA at admission I A and at discharge IIa B *Screening*: ACC/AHA IIa B
MR-proANP	Stable measure of ANP activity Additive diagnostic value over BNP or NT-proBNP	The role in clinical practice is still evolving	*Diagnosis*: ESC I A
Cardiac Troponins	Indicate myocardial injury High specificity	Elevation can be caused by other cardiac and non-cardiac conditions	*Diagnosis*: ESC I C *Prognosis*: ACC/AHA at admission I A
Galectin-3 Soluble ST2 (sST2)	Reflects fibrosis and inflammation Predictor of remodeling and progression	Elevated in other conditions like renal failure	*Prognosis*: ACC/AHA at admission IIb B

Licordari, R.; Correale, M.;Bonanno, S.; Beltrami, M.; Ciccarelli,M.; Micari, A.; Palazzuoli, A.; Dattilo, G. Beyond Natriuretic Peptides:Unveiling the Power o Emerging Biomarkers in Heart Failure.Biomolecules 2024, 14, 309. https://doi.org/10.3390/biom14030309

ESC European Society of Cardiology

European Journal of Heart Failure (2024) **26**, 1480–1492
doi:10.1002/ejhf.3336

RESEARCH ARTICLE

Biologically active adrenomedullin as a marker for residual congestion and early rehospitalization in patients hospitalized for acute heart failure: Data from STRONG-HF

**Geert H.D. Voordes[1], Beth Davison[2,3,4,5], Jan Biegus[6], Christopher Edwards[4], Kevin Damman[1], Jozine M. ter Maaten[1], Alexandre Mebazaa[2,3], Koji Takagi[4], Marianna Adamo[7], Andrew P. Ambrosy[8,9], Mattia Arrigo[10], Marianela Barros[4], Jelena Celutkiene[11], Kamilė Čerlinskaitė-Bajorė[11], Ovidiu Chioncel[12], Alain Cohen-Solal[13], Albertino Damasceno[14], Benjamin Deniau[2,3], Rafael Diaz[15], Gerasimos Filippatos[16], Etienne Gayat[2,3], Antoine Kimmoun[17], Carolyn S.P. Lam[18,19,20], Marco Metra[7], Maria Novosadova[4], Matteo Pagnesi[7], Peter Pang[21], Piotr Ponikowski[6], Hadiza Saidu[22], Karen Sliwa[23], Daniela Tomasoni[7], Gad Cotter[2,3,4,5], and Adriaan A. Voors[1]*

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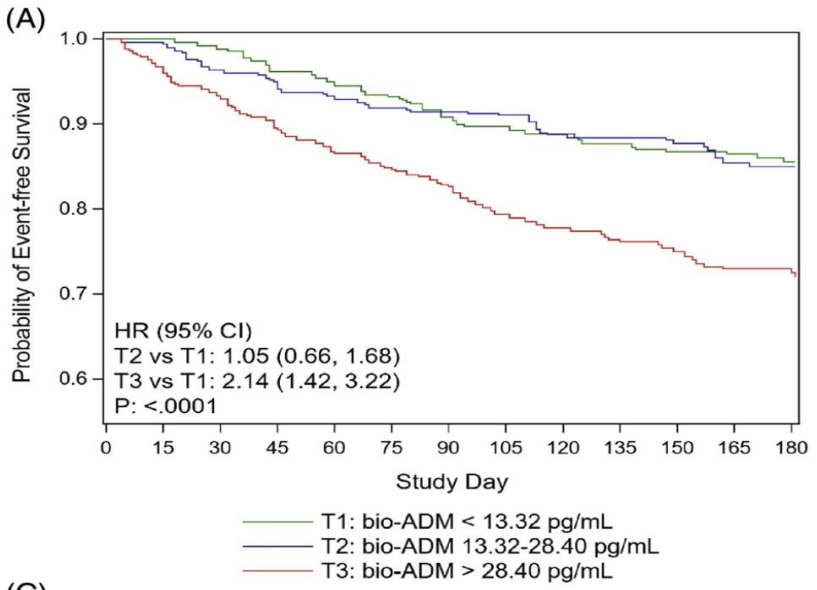
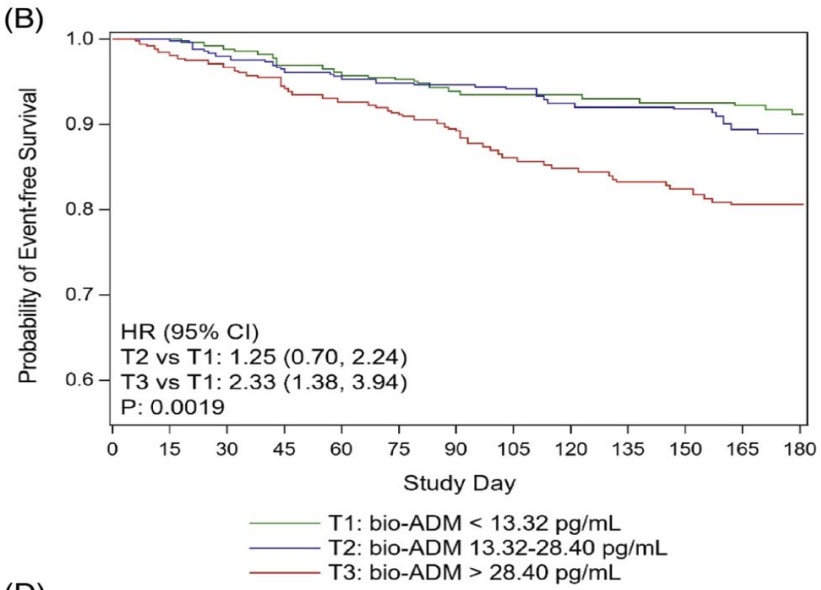
rehospitalizace pro HF nebo úmrtí

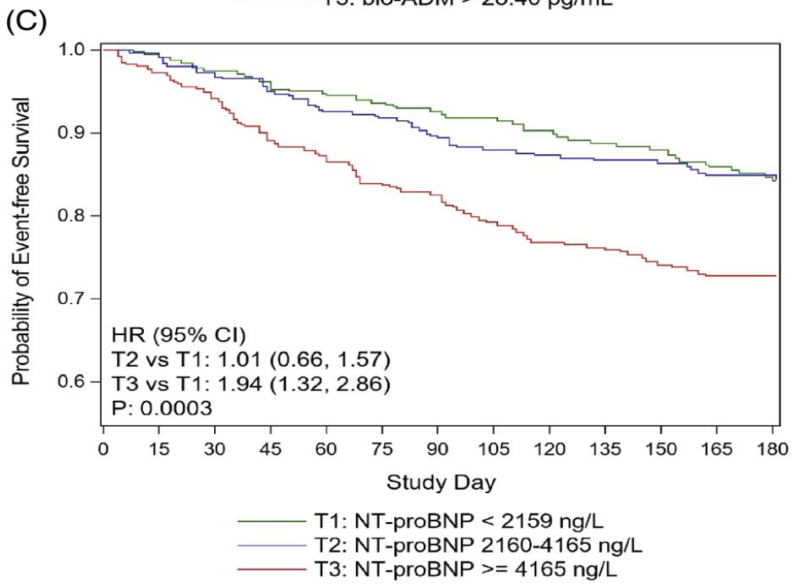
rehospitalizace pro HF

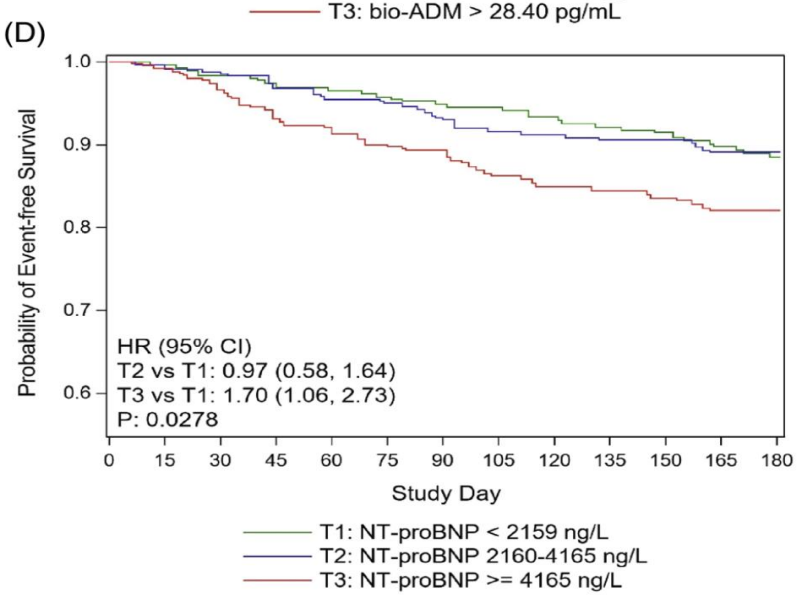
bio-ADM

NT-proBNP









Neverending story: hledání optimálních cut-off hodnot

		Cut-off Value	Sensitivity	Specificity	PPV	NPV
Acute Dyspnea	**To exclude acute HF**					
	BNP	<30-50 pg/mL	97%	62%	71%	96%
	NT-proBNP	<300 pg/mL	99%	68%	62%	99%
	To identify acute HF					
	Single cut-off point					
	BNP	<100 pg/mL	90%	76%	79%	89%
	NT-proBNP	<900 pg/mL	90%	85%	76%	94%
	Multiple cut-point					
	BNP	< 100 pg/mL to exclude	90%	73%	75%	90%
		100-400 pg/mL, "grey zone"	*	*	*	*
		> 400 pg/mL, to rule in	63%	91%	86%	74%
	NT-proBNP	<450 pg/mL for age <50 yr <900 pg/mL for age 50-75 yr < 1800 pg/mL for age > 75 yr	90%	84%	88%	66%
	BNP	20 pg/mL (asymptomatic)	*	*	*	96%
		or 40 pg/mL (symptomatic)	*	*	*	
Outpatient Screening	**NT-proBNP**	<125 pg/mL for age <75 yr	*	*	*	98%
		<450 pg/mL for age ≥75 yr	*	*	*	91%
		or				
		<50 pg/mL for age <50 yr	*	*	*	98%
		<75 pg/mL for age 50-75 yr	*	*	*	98%
		< 250 pg/mL for age > 75 yr	*	*	*	93%

Kim H-N, Januzzi JL, Jr. Natriuretic peptide testing in heart failure. *Circulation* 2011;123:2015-19.

ESC European Society of Cardiology

European Journal of Heart Failure (2021) **23**, 352–380
doi:10.1002/ejhf.2115

POSITION PAPER

Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure

Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association

Biykem Bozkurt* (Chair) (USA), Andrew J.S. Coats (Co-Chair) (UK and Australia), Hiroyuki Tsutsui (Co-Chair) (Japan), Ca Magdy Abdelhamid (Egypt), Stamatis Adamopoulos (Greece), Nancy Albert (USA), Stefan D. Anker (Germany), John Atherton (Australia), Michael Böhm (Germany), Javed Butler (USA), Mark H. Drazner (USA), G. Michael Felker (USA), Gerasimos Filippatos (Greece), Mona Fiuzat (USA), Gregg C. Fonarow (USA), Juan-Esteban Gomez-Mesa (Colombia), Paul Heidenreich (USA), Teruhiko Imamura (Japan), Ewa A. Jankowska (Poland), James Januzzi (USA), Prateeti Khazanie (USA), Koichiro Kinugawa (Japan), Carolyn S.P. Lam (Singapore), Yuya Matsue (Japan), Marco Metra (Italy), Tomohito Ohtani (Japan), Massimo Francesco Piepoli (Italy), Piotr Ponikowski (Poland), Giuseppe M.C. Rosano (Italy), Yasushi Sakata (Japan), Petar Seferović (Serbia), Randall C. Starling (USA), John R. Teerlink (USA), Orly Vardeny (USA), Kazuhiro Yamamoto (Japan), Clyde Yancy (USA), Jian Zhang (China), Shelley Zieroth (Canada)

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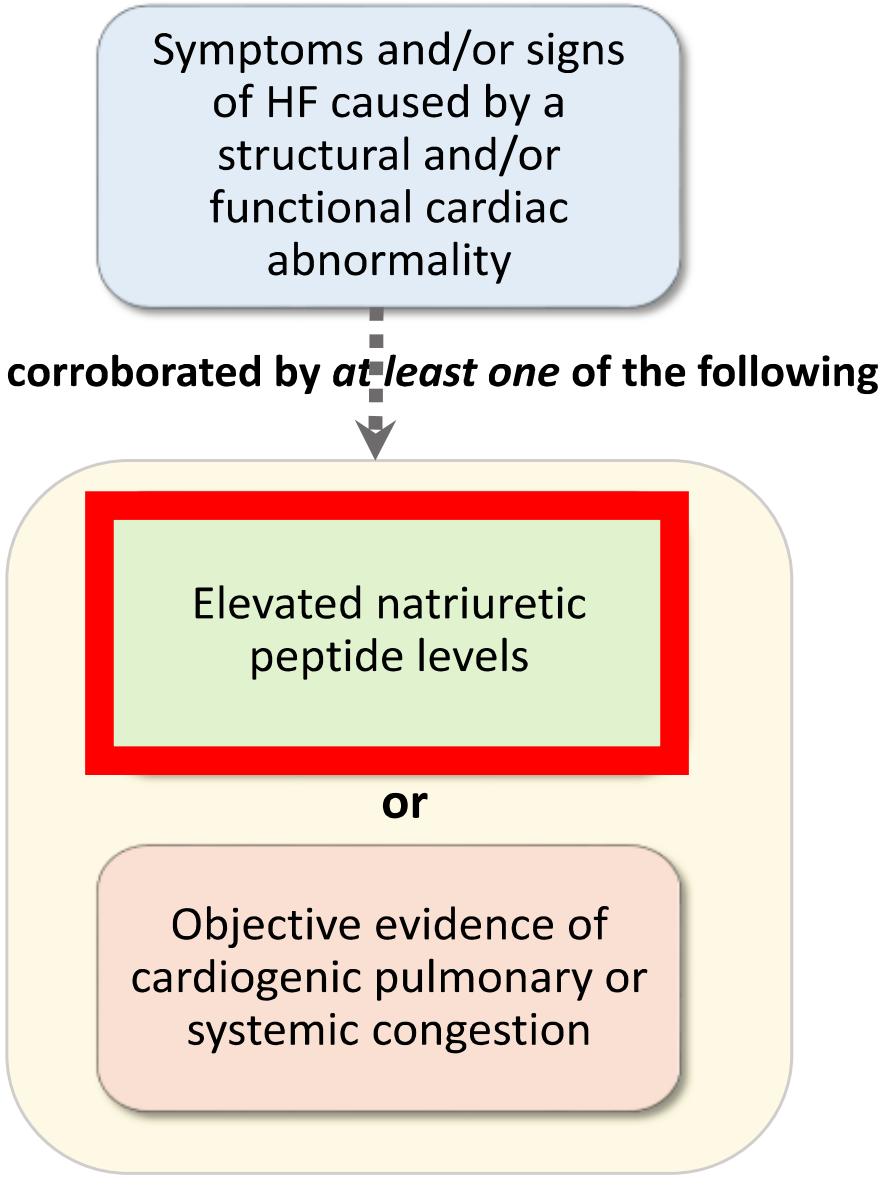

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Table 7 Natriuretic peptide levels supporting definition of heart failure

	Ambulatory	Hospitalized/ decompensated
BNP, pg/ml	≥35	≥ 100
NT-proBNP, pg/ml	≥ 125	≥ 300

Causes of elevated natriuretic peptide levels other than primary diagnosis of heart failure

Cardiovascular causes

- Acute coronary syndrome, myocardial infarction
- Pulmonary embolism
- Myocarditis
- Hypertrophic cardiomyopathy
- Valvular heart disease
- Congenital heart disease
- Atrial or ventricular arrhythmias
- Heart contusion, cardiac infiltration or malignancy
- Cardioversion, ICD shock
- Pericardial disease
- Invasive or surgical procedures involving the heart
- Pulmonary hypertension, right ventricular failure
- Infiltrative cardiomyopathies

Non-cardiovascular causes

- Advanced age
- Kidney disease
- Critical illnesses including sepsis syndrome, cytokine syndrome
- Ischaemic or haemorrhagic stroke
- Pulmonary disease (pneumonia, chronic obstructive pulmonary disease)
- Liver disease
- Severe anaemia
- Severe metabolic and hormone abnormalities (e.g. thyrotoxicosis, diabetic ketoacidosis, severe burns)

Causes of lower natriuretic peptide levels

- Obesity, or increased BMI
- Pericardial disease[a]

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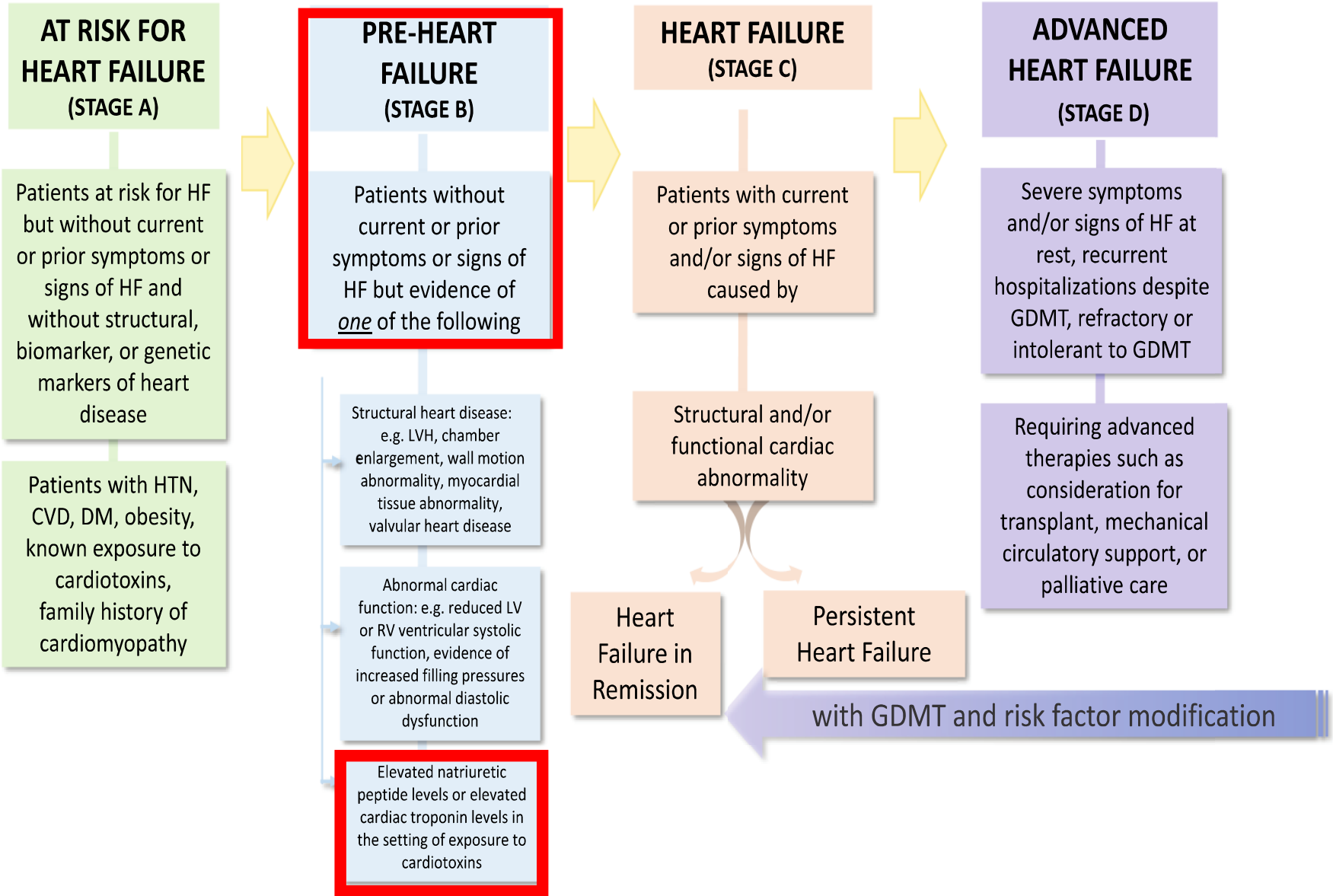
Stadia rozvoje srdečního selhání



Pre-Heart Failure, Heart Stress, and Subclinical Heart Failure: Bridging Heart Health and Heart Failure*

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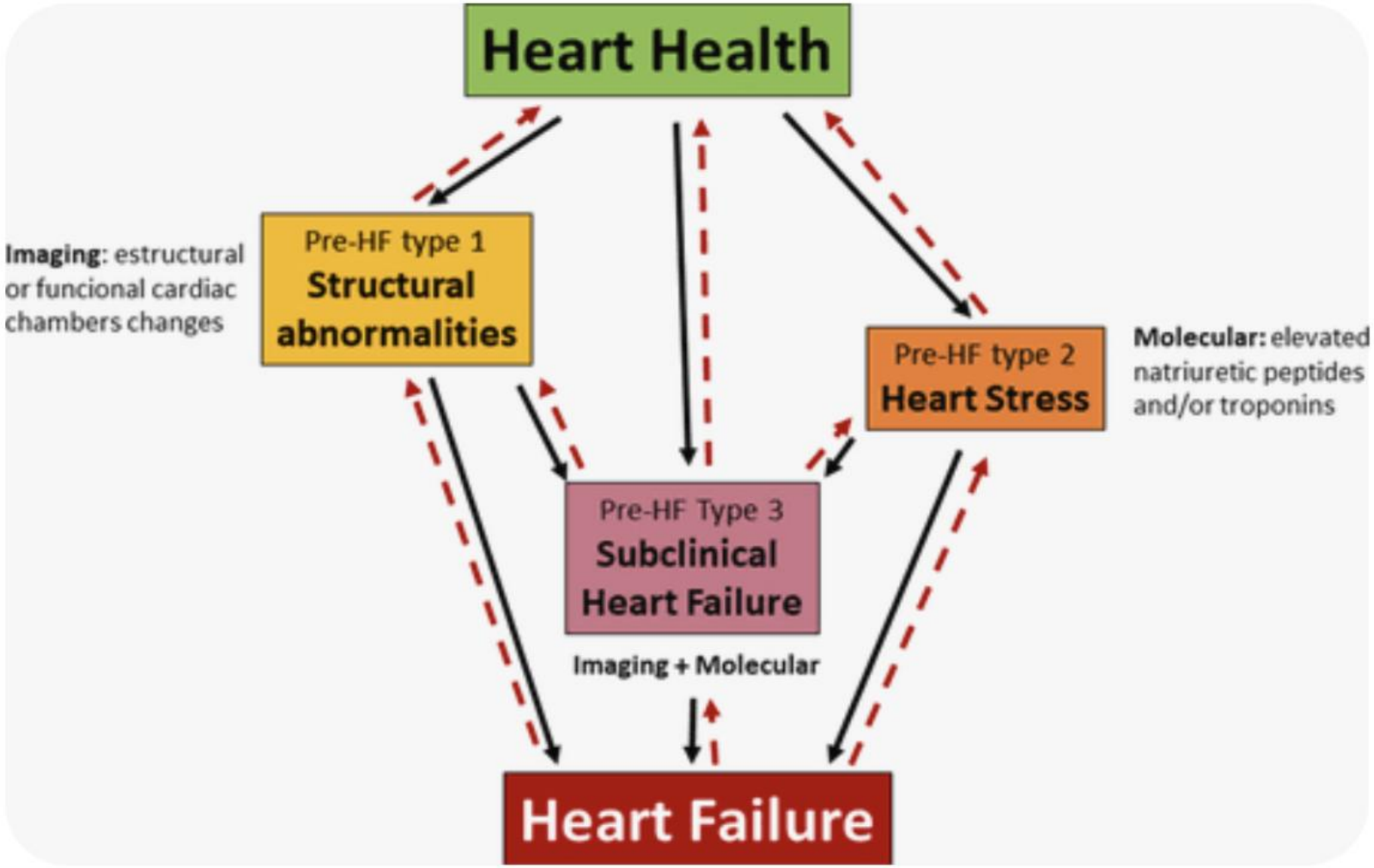
Leading Edge Commentary

Antoni Bayes-Genis and Biykem Bozkurt

J Am Coll Cardiol HF. 2024 Jun, 12 (6) 1115–1118

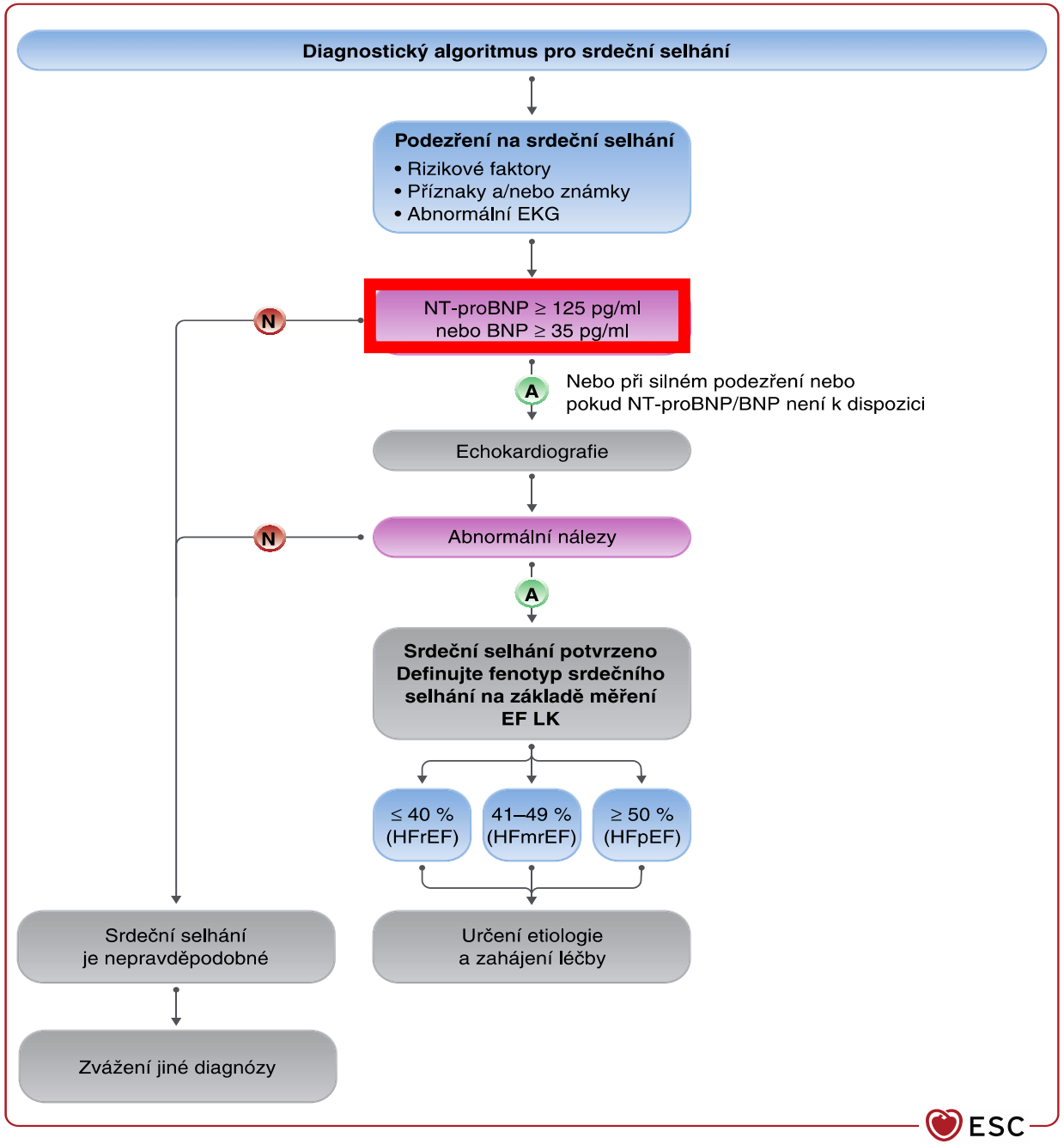
Topic(s): Health Promotion & Preventive Cardiology, Heart Failure & Cardiomyopathies



Souhrn Doporučených postupů Evropské kardiologické společnosti pro diagnostiku a léčbu srdečního selhání z roku 2021

(Summary of 2021 ESC Guidelines for the diagnosis and treatment of heart failure)

Filip Málek[a], Jiří Veselý[b], Radek Pudil[c], Jindřich Špinar[d], Ivan Málek[e], Lenka Špinarová[d], Petr Ošťádal[a], Jan Bělohlávek[f], Jiří Vítovec[d], Jan Krejčí[d], Jaromír Hradec[g]



Produkce = produkční masa x jednotková produkce

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ISSN: 1097-6647 print / 1532-429X online
DOI: 10.1080/10976640500295516

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VENTRICULAR FUNCTION

Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging

LUCY E. HUDSMITH, M.A., M.R.C.P.,*,† STEFFEN E. PETERSEN, M.D.,† JANE M. FRANCIS, D.C.R.R., D.N.M., MATTHEW D. ROBSON, PH.D., and STEFAN NEUBAUER, M.D., F.R.C.P.

The University of Oxford Centre for Clinical Magnetic Resonance Research, Department of Cardiovascular Medicine, University of Oxford, The John Radcliffe Hospital, Oxford, UK

	Mean ± SD (n = 108)
LV ejection fraction (%)	69 ± 6
LV mass (g)	112 ± 27
LV mass index (g/m^2)	59.2 ± 11
LV end-diastolic volume (mL)	150 ± 31
LV end-diastolic volume index (mL/m^2)	80 ± 13
LV end-systolic volume (mL)	47 ± 15
LV end-systolic volume index (mL/m^2)	25 ± 7
LV stroke volume (mL)	104 ± 21
LV stroke volume index (mL/m^2)	55 ± 8
RV ejection fraction (%)	61 ± 6
RV mass (g)	38 ± 8
RV mass index (g/m^2)	20.3 ± 3.6
RV end-diastolic volume (mL)	173 ± 39
RV end-diastolic volume index (mL/m^2)	91 ± 16
RV end-systolic volume (mL)	69 ± 22
RV end-systolic volume index (mL/m^2)	36 ± 10
RV stroke volume (mL)	104 ± 21
RV stroke volume index (mL/m^2)	55 ± 9

ELSEVIER

Cardiovascular Pathology
Volume 49, November–December 2020, 107265

Original Article

Left atrial mass: relationship between gross anatomy and quantitative echocardiography

Laura Flink [a b], Purvi Parwani [b], Philip C. Ursell [c], Dwight Bibby [b], Qizhi Fang [b], Nelson B. Schiller [a b]

In this study, we defined normal LA mass on anatomic specimens as 25.5 ± 6.3 g

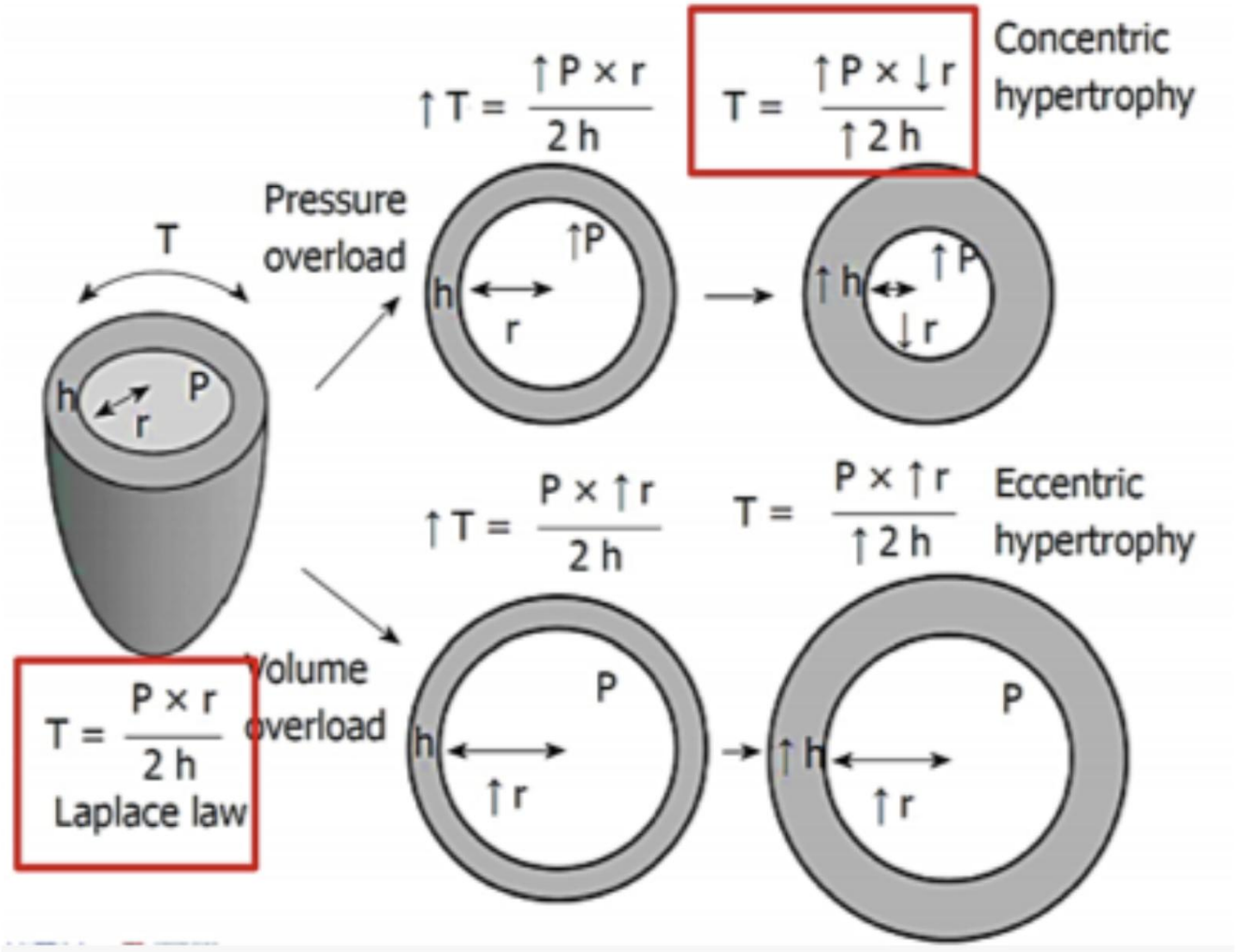
LV 112 g

RV 38 g

LA 25 g

Produkce je závislá na napětí ve stěně

Laplaceův zákon – napětí stěny roztaženého dutého tělesa je přímo úměrné součinu tlaku uvnitř telesa a poloměru křivosti tělesa a nepřímo úměrné tloušťce stěny. Pro kulovou vrstvu má tvar $T = Pr/2h$, kde T je napětí stěny, P je tlak uvnitř dutiny, r je poloměr dutiny a h je tloušťka stěny.



ESC European Society of Cardiology

European Journal of Heart Failure (2023) **25**, 1891–1898
doi:10.1002/ejhf.3036

POSITION PAPER

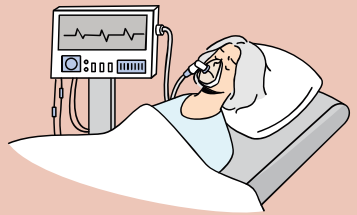
Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: A clinical consensus statement from the Heart Failure Association of the ESC

Antoni Bayes-Genis[1]*, Kieran F. Docherty[2], Mark C. Petrie[2], James L. Januzzi[3], Christian Mueller[4], Lisa Anderson[5], Biykem Bozkurt[6], Javed Butler[7], Ovidiu Chioncel[8], John G.F. Cleland[9], Ruxandra Christodorescu[10], Stefano Del Prato[11], Finn Gustafsson[12], Carolyn S.P. Lam[13], Brenda Moura[14,15], Rodica Pop-Busui[16], Petar Seferovic[17,18], Maurizio Volterrani[19,20], Muthiah Vaduganathan[21], Marco Metra[22], and Giuseppe Rosano[23]

Suspicion of Heart Failure in the

Emergency Department

(History, physical exam, CXR, ECG)



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"wet" NT-proBNP

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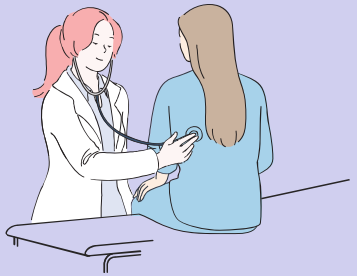
Suspected *de novo* Heart Failure as an

Outpatient

(History, physical exam, ECG)



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NT-proBNP

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Screening for

Heart Stress

in Asymptomatic patients with T2D

(or other risk factors for CVD)

NT-proBNP

ESC European Society of Cardiology

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POSITION PAPER

Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: A clinical consensus statement from the Heart Failure Association of the ESC

Antoni Bayes-Genis[1]*, Kieran F. Docherty[2], Mark C. Petrie[2], James L. Januzzi[3], Christian Mueller[4], Lisa Anderson[5], Biykem Bozkurt[6], Javed Butler[7], Ovidiu Chioncel[8], John G.F. Cleland[9], Ruxandra Christodorescu[10], Stefano Del Prato[11], Finn Gustafsson[12], Carolyn S.P. Lam[13], Brenda Moura[14,15], Rodica Pop-Busui[16], Petar Seferovic[17,18], Maurizio Volterrani[19,20], Muthiah Vaduganathan[21], Marco Metra[22], and Giuseppe Rosano[23]

Úprava cut-point NT-proBNP dle eGFR

eGFR 45 - 60 ml/min/1,73m^2 → zvýšení o 15%

eGFR 30 - 45 ml/min/1,73m^2 → zvýšení o 25%

eGFR pod 30 ml/min/1,73m^2 → zvýšení o 35%

ESC European Society of Cardiology

European Journal of Heart Failure (2023) **25**, 1891–1898
doi:10.1002/ejhf.3036

POSITION PAPER

Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: A clinical consensus statement from the Heart Failure Association of the ESC

Antoni Bayes-Genis[1]*, Kieran F. Docherty[2], Mark C. Petrie[2], James L. Januzzi[3], Christian Mueller[4], Lisa Anderson[5], Biykem Bozkurt[6], Javed Butler[7], Ovidiu Chioncel[8], John G.F. Cleland[9], Ruxandra Christodorescu[10], Stefano Del Prato[11], Finn Gustafsson[12], Carolyn S.P. Lam[13], Brenda Moura[14,15], Rodica Pop-Busui[16], Petar Seferovic[17,18], Maurizio Volterrani[19,20], Muthiah Vaduganathan[21], Marco Metra[22], and Giuseppe Rosano[23]

Úprava cut-point NT-proBNP dle BMI

BMI 30 - 35 kg/m^2 → snížení o 25%

BMI 35 - 40 kg/m^2 → snížení o 30%

BMI nad 40 kg/m^2 → snížení o 40%

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Úprava cut-point NT-proBNP při fibrilaci síní

komorová odpověď ≤90/min → **zvýšení o 50%**

komorová odpověď >90bpm → **zvýšení o 100%**

JACC: HEART FAILURE VOL. 11, NO. 11, 2023
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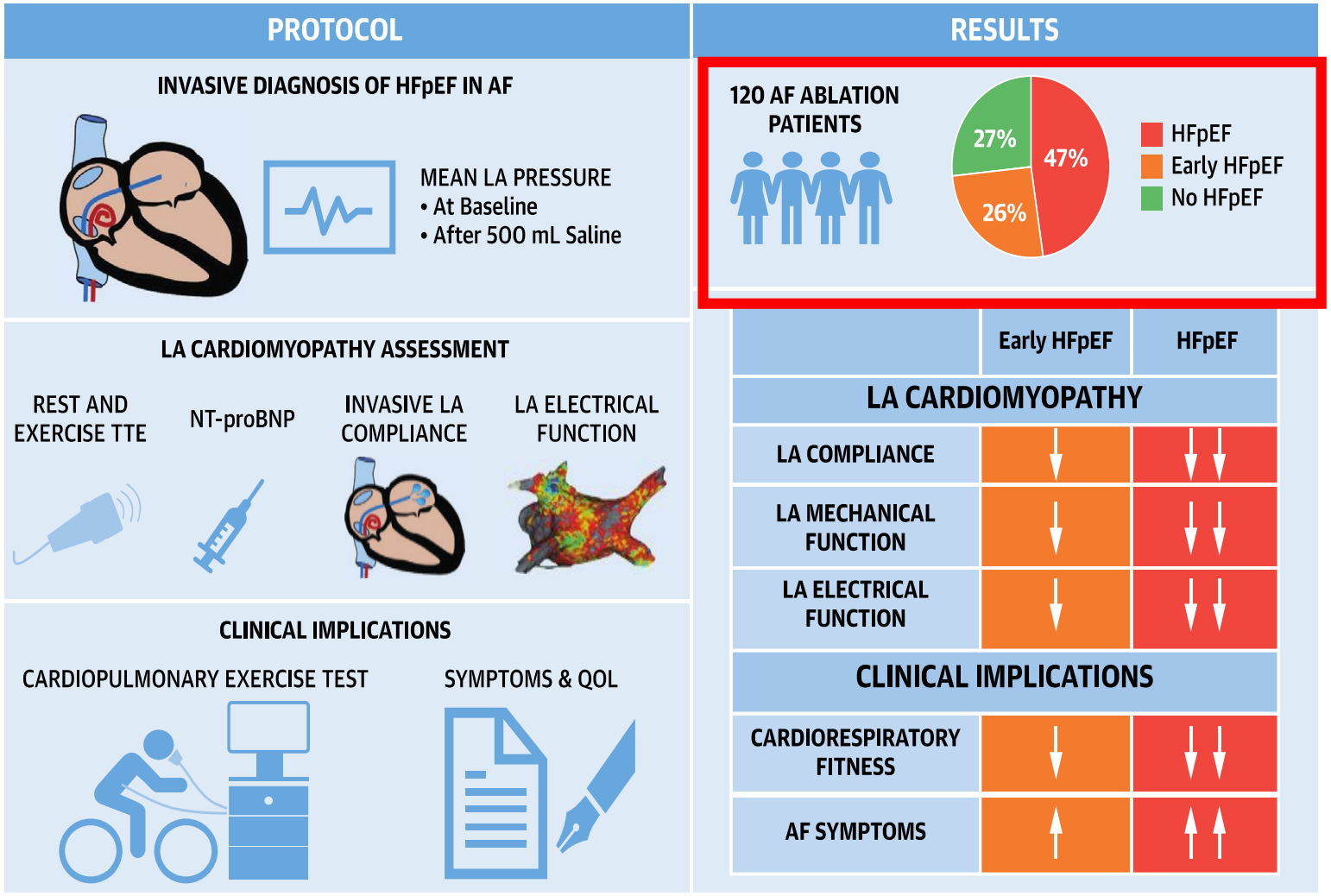
Identification of Subclinical Heart Failure With Preserved Ejection Fraction in Patients With Symptomatic Atrial Fibrillation

Jonathan P. Ariyaratnam, MB, BCHIR,[a] Adrian D. Elliott, PHD,[a,*] Ricardo S. Mishima, MD, PHD,[a] Kadhim Kadhim, MBCHB, PHD,[a] Olivia McNamee, RN,[a] Pawel Kuklik, PHD,[b] Mehrdad Emami, MD,[a] Varun Malik, MBBS, PHD,[a] John L. Fitzgerald, MBBS,[a] Celine Gallagher, PHD,[a] Dennis H. Lau, MBBS, PHD,[a] Prashanthan Sanders, MBBS, PHD[a,*]

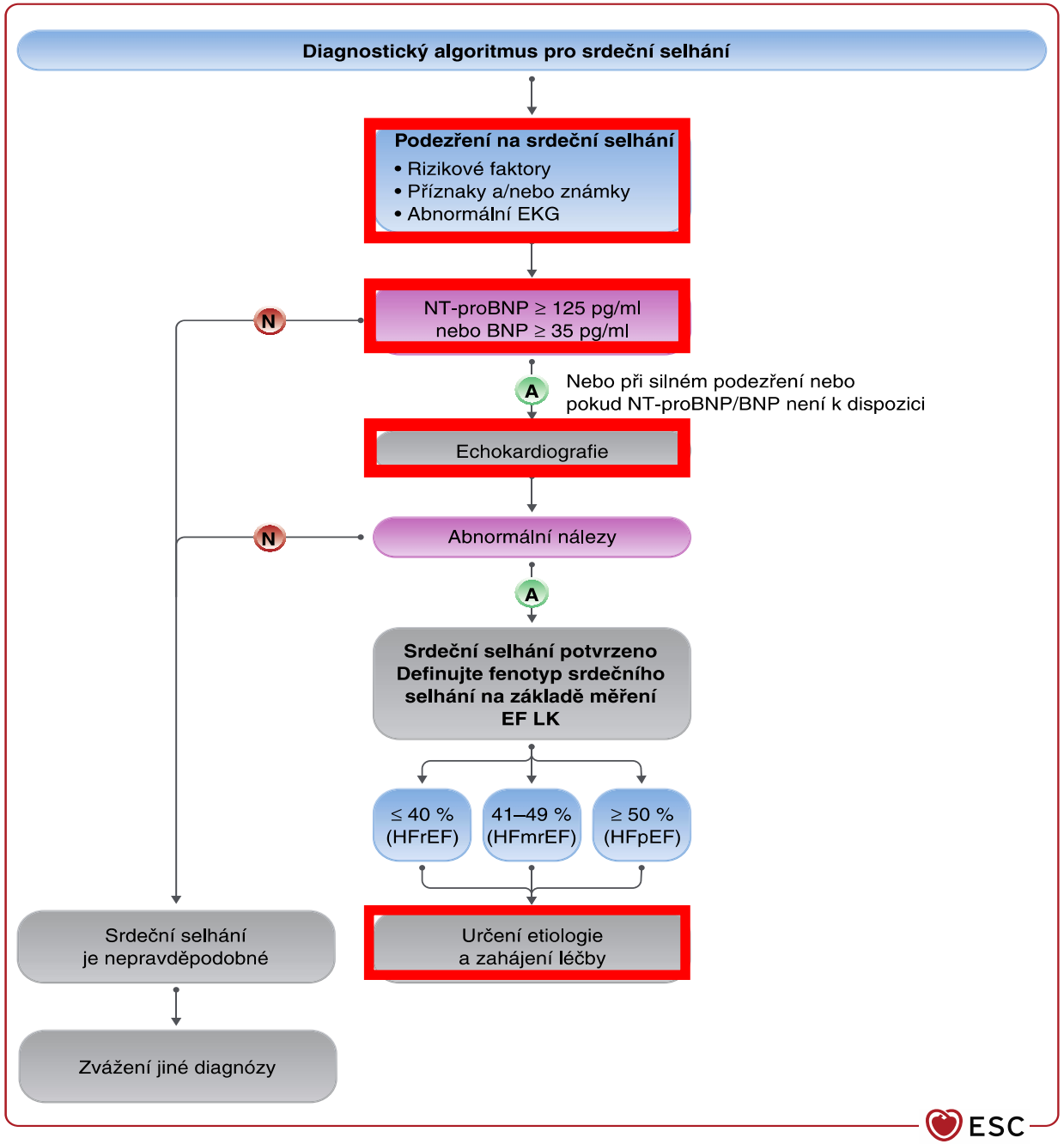


Ariyaratnam JP, et al. J Am Coll Cardiol HF. 2023;11(11):1626-1638.

Souhrn Doporučených postupů Evropské kardiologické společnosti pro diagnostiku a léčbu srdečního selhání z roku 2021

(Summary of 2021 ESC Guidelines for the diagnosis and treatment of heart failure)

Filip Málek[a], Jiří Veselý[b], Radek Pudil[c], Jindřich Špinar[d], Ivan Málek[e], Lenka Špinarová[d], Petr Ošťádal[a], Jan Bělohlávek[f], Jiří Vítovec[d], Jan Krejčí[d], Jaromír Hradec[g]



Stanovení natriumuretických peptidů

Evropská unie
Evropský sociální fond
Operační program Zaměstnanost

MINISTERSTVO ZDRAVOTNICTVÍ
ČESKÉ REPUBLIKY

Seznam zdravotních výkonů

Registrační list - 81731

STANOVENÍ NATRIURETICKÝCH PEPTIDŮ V SÉRU A V PLAZMĚ

Obsah registračního listu

Tisk

Číslo výkonu	81731
Název	STANOVENÍ NATRIURETICKÝCH PEPTIDŮ V SÉRU A V PLAZMĚ
Nepočítat režii	
Poznámka	

Autorská odbornost

Kód	Název	Pořadí	Sazba režie
801	klinická biochemie	8010	4,47

Další odbornost

Kód	Název	Sazba režie
815	laboratoř nukleární medicíny	4,47

Kategorie	P - hrazen plně
Omezení místem	S - pouze na specializovaném pracovišti
Omezení frekvencí	1/1 den, 12/1 rok

Evropská unie
Evropský sociální fond
Operační program Zaměstnanost

MINISTERSTVO ZDRAVOTNICTVÍ
ČESKÉ REPUBLIKY

Seznam zdravotních výkonů

Registrační list - 01148

STANOVENÍ PRO BNP V ORDINACI

Obsah registračního listu

Tisk

Číslo výkonu	01148
Název	STANOVENÍ PRO BNP V ORDINACI
Nepočítat režii	
Poznámka	

Autorská odbornost

Kód	Název	Pořadí	Sazba režie
001	všeobecné praktické lékařství	1020	4,47

Další odbornost

Kód	Název	Sazba režie
103	diabetologie	4,47
102	angiologie	4,47
205	pneumologie a ftizeologie	4,47
101	vnitřní lékařství - interna	4,47
002	praktické lékařství pro děti a dorost a pediatrie	4,47
107	kardiologie	4,47

Kategorie	P - hrazen plně
Omezení místem	A - pouze ambulantně
Omezení frekvencí	1/1 den

Reference: https://szv.mzcr.cz (16.3.2025)

ESC European Society of Cardiology

European Journal of Heart Failure (2025)
doi:10.1002/ejhf.3646

POSITION PAPER

The use of left ventricular ejection fraction in the diagnosis and management of heart failure. A clinical consensus statement of the Heart Failure Association (HFA) of the ESC, the Heart Failure Society of America (HFSA), and the Japanese Heart Failure Society (JHFS)

Giuseppe M.C. Rosano[1,2]*, John R. Teerlink[3], Koichiro Kinugawa[4], Antoni Bayes-Genis[5], Ovidiu Chioncel[6], James Fang[7], Barry Greenberg[8], Nasrien E. Ibrahim[9], Teruhiko Imamura[4], Takayuki Inomata[10], Koichiro Kuwahara[11], Brenda Moura[12], Anekwe Onwuanyi[13], Naoki Sato[14], Gianluigi Savarese[15], Yasuhiko Sakata[16], Nancy Sweitzer[17], Jane Wilcox[18], Kazuhiro Yamamoto[19], Marco Metra[20], and Andrew J.S. Coats[21]

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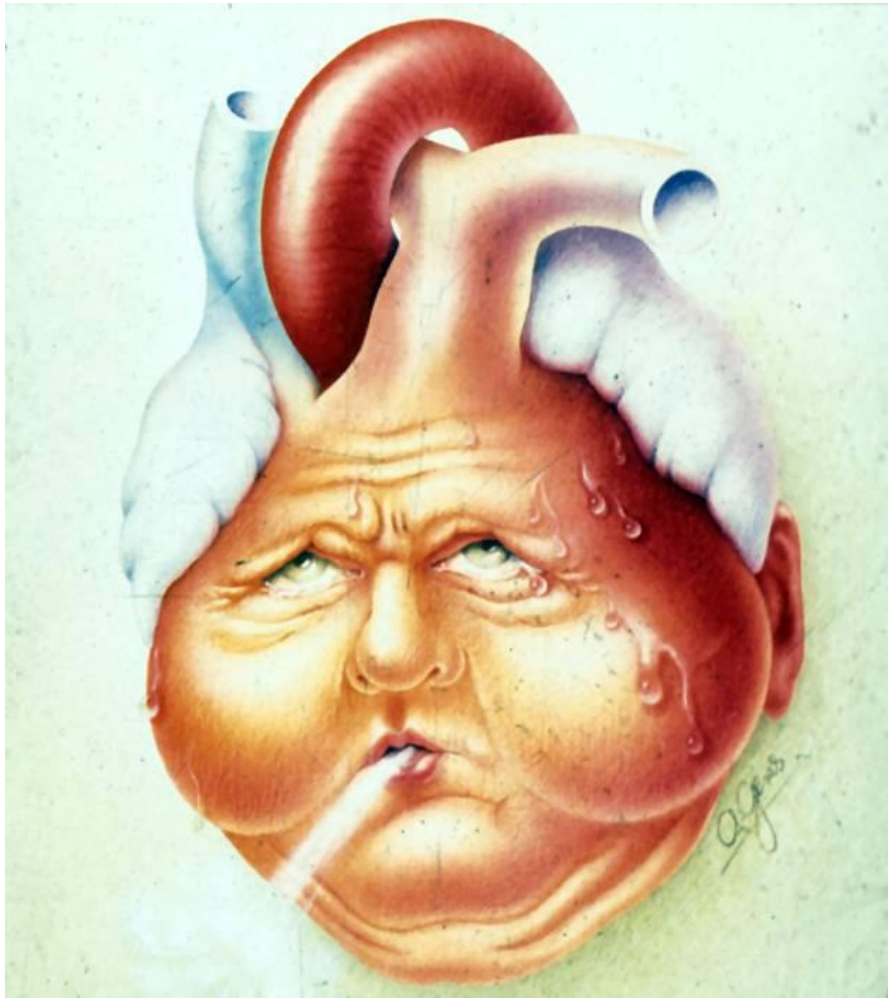
Biomarkery v diagnostice srdečního selhání

Ne vždy snadná interpretace

Nezpochybnitelný přínos

Děkuji za pozornost