

SAVE THE DATE

9.– 10. října 2026 | Hotel Passage, Brno

XXIX.
KONFERENCE
ČESKÉ ASOCIACE
SRDEČNÍHO SELHÁNÍ



ČESKÁ
KARDIOLOGICKÁ
SPOLEČNOST

DIGOXIN... starý, ale pořád dobrý...



J. Krejčí



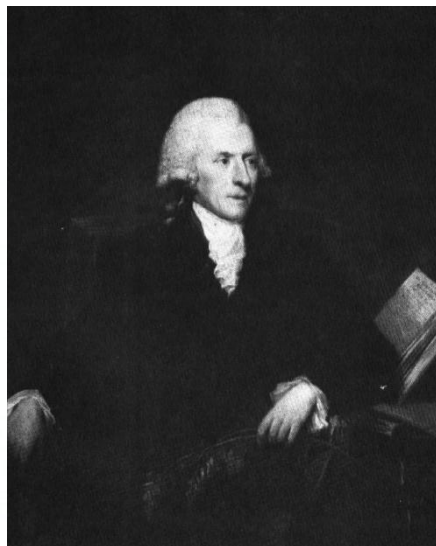
Deklarace konfliktu zájmů

	Nemám konflikt zájmů	Mám konflikt zájmů	Specifikace konfliktu (vyjmenujte subjekty, firmy či instituce, se kterými Vaše spolupráce může vést ke konfliktu zájmů)
Zaměstnanecký poměr	X		
Vlastník / akcionář	X		
Konzultant			
Přednášková činnost			Boehringer Ingelheim, Novartis, Pfizer, Bristol Myers Squibb, Bayer, AstraZeneca, Medison
Člen poradních sborů (advisory boards)			Pfizer, Bristol Myers Squibb, Bayer, AstraZeneca, Medison
Podpora výzkumu / granty	X		
Jiné honoráře (např. za klinické studie či registry)	X		



Historické okénko

AN
ACCOUNT OF THE FOXGLOVE,
AND
Some of its Medical Uses:
with
PRACTICAL REMARKS ON DROPSY,
AND OTHER DISEASES.
By
WILLIAM WITHERING, M. D.
Physician to the General Hospital at Birmingham.
nonumque prematur in annum.
Horace.
BIRMINGHAM: PRINTED BY M. SWINNEY;
FOR C.G.J. AND J. ROBINSON, PATERNOSTER ROW, LONDON.
MDCCLXXXV



*After all, in spite of opinion, prejudice, or error,
time will fix the real value upon this discovery.*
—Sir William Withering,
Birmingham, United Kingdom, July 1, 1785 (1)

Mother Hutton, also known as **Mrs. Hutton**, **old mother Hutton** and "**the old woman from Shropshire**", was a mythical English character, fabricated in 1928 for marketing purposes by a [pharmaceutical company](#), [Parke-Davis](#), that manufactured [digitalis](#), a drug used to treat [dropsy](#).

The story involved real-life physician [William Withering](#), who appeared to have learned of the value of the purple foxglove in the treatment of dropsy from 'Old Mother Hutton', the [Shropshire](#) herb-woman whom he met in [Stafford](#) or [Birmingham](#) and to whom he gave [gold sovereigns](#) for the information, as depicted hypothetically in the painting by [William Meade Prince](#) (1893–1951). However, he never mentioned a Mother Hutton in his works and a number of dates have since been found to be inconsistent.



Efekt digoxinu u srdečního selhání

The Use of Digoxin in Patients With Worsening Chronic Heart Failure

Reconsidering an Old Drug to Reduce Hospital Admissions

Andrew P. Ambrosy, MD,* Javed Butler, MD, MPH,† Ali Ahmed, MD,‡
Muthiah Vaduganathan, MD, MPH,§ Dirk J. van Veldhuisen, MD,||
Wilson S. Colucci, MD,¶ Mihai Gheorghiade, MD#

Stanford, California; Atlanta, Georgia; Birmingham, Alabama; Boston, Massachusetts;
Groningen, the Netherlands; and Chicago, Illinois

Table 2 Physiologic Effects of Digoxin Therapy

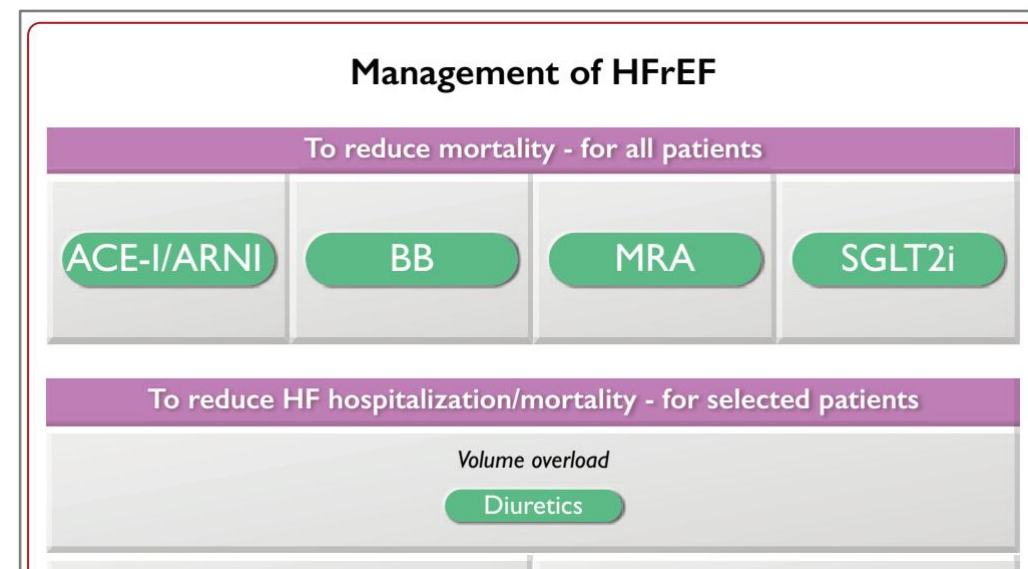
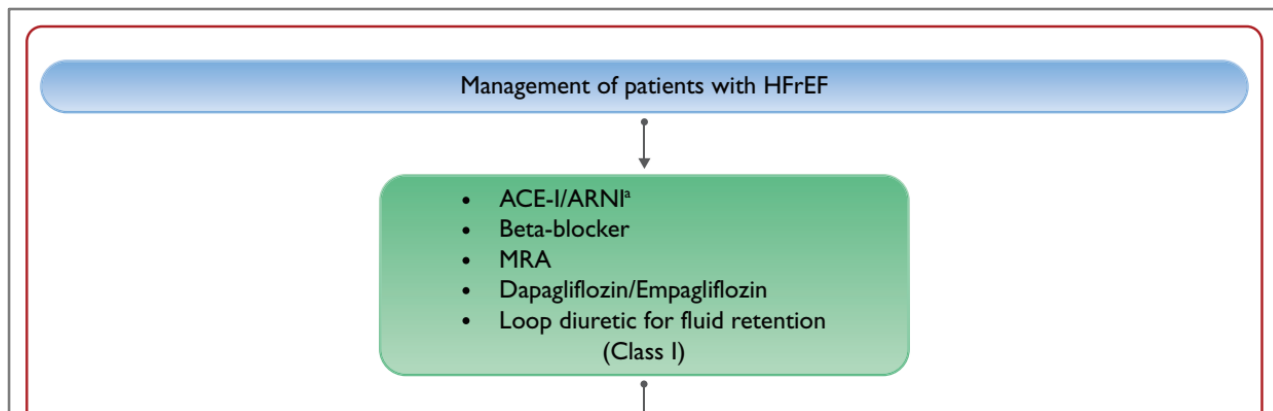
Hemodynamic	Neurohormonal	Electrophysiological
↑ LVEF	↑ Parasympathetic	SA node: slows sinus rate
↑ CO	↓ Sympathetic	AV node: prolongs conduction
↓ HR, ↔ BP	↓ RAAS	
↓ PCWP		

(J Am Coll Cardiol 2014;63:1823–32)



Léčba HFrEF v Guidelines

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

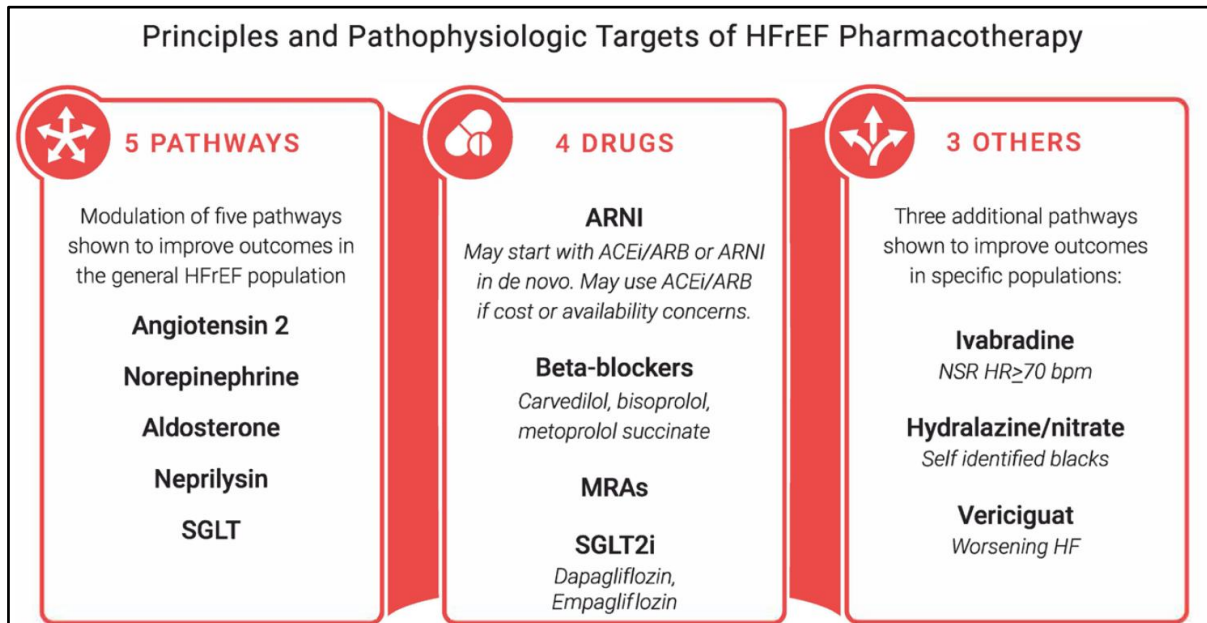


Eur Heart J. 2021;42(36):3599-3726.



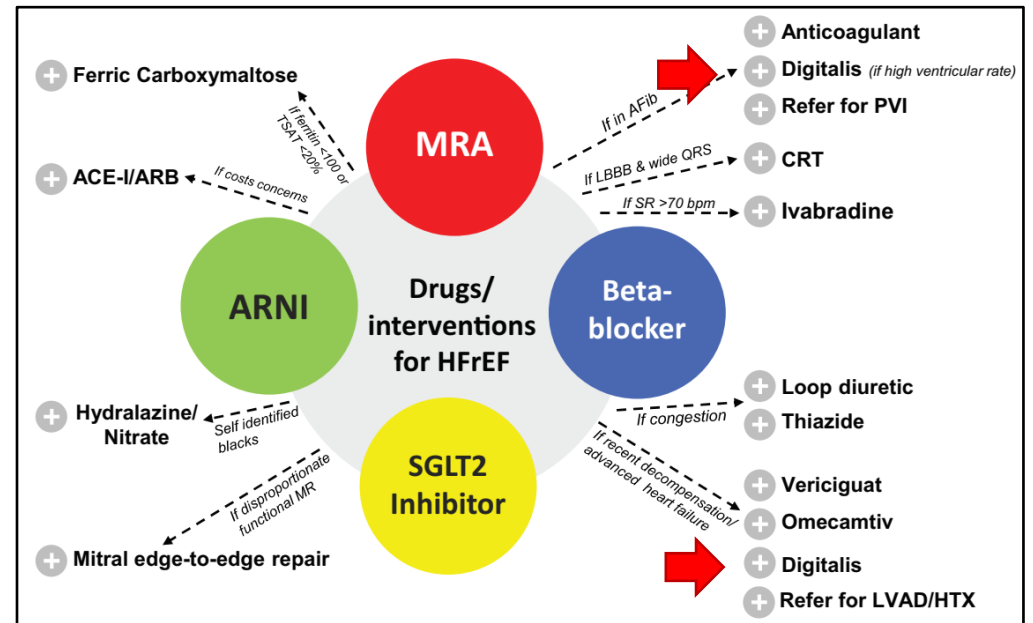
Léčba HFrEF v roce 2023

Victims of Success in Failure



Circulation. 2020;142:1129–1131.

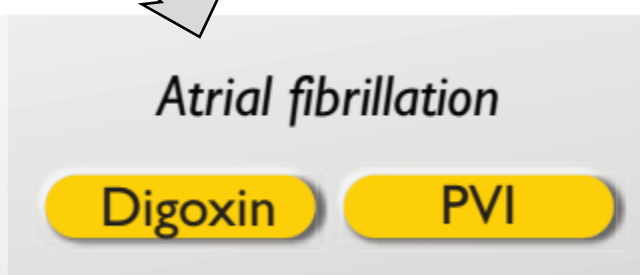
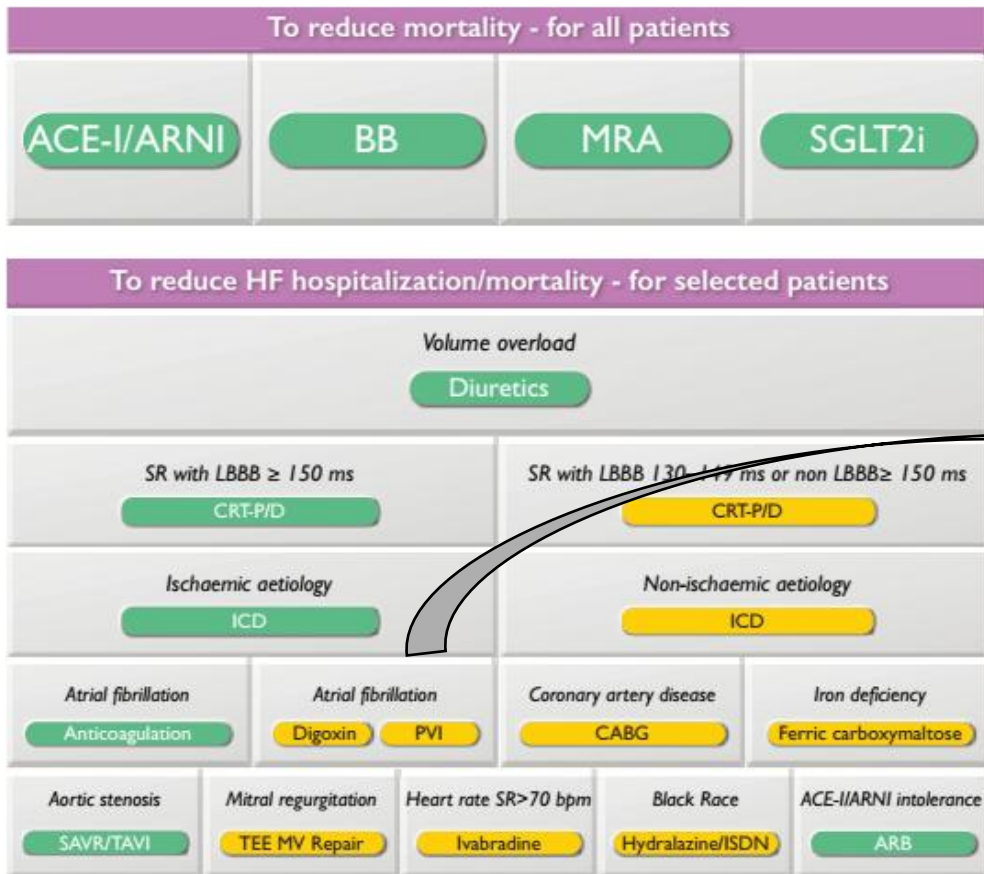
Heart failure drug treatment: the fantastic four



European Heart Journal (2021) 42, 681–683

Léčba HFrEF v Guidelines

Management of HFrEF



Eur Heart J. 2021;42(36):3599-3726.



Léčba HFrEF v Guidelines

Rate control

Beta-blockers should be considered for short- and long-term rate control in patients with HF and AF.⁵³⁵

IIa

B

Digoxin should be considered when the ventricular rate remains high, despite beta-blockers, or when beta-blockers are contraindicated or not tolerated.⁵³⁶

IIa

C

Digoxin

Digoxin may be considered in patients with symptomatic HFrEF in sinus rhythm despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA, to reduce the risk of hospitalization (both all-cause and HF hospitalizations).¹⁴⁴

IIb

B

Eur Heart J. 2021;42(36):3599-3726.



Léčba HFrEF v Guidelines

Rate control

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IIa

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Digoxin should be considered when the ventricular rate remains high, despite beta-blockers, or when beta-blockers are contraindicated or not tolerated.⁵³⁶

IIa

C

Není redukce počtu hospitalizací důležitým cílem léčby srdečního selhání?

Digoxin

Digoxin may be considered in patients with symptomatic HFrEF in sinus rhythm despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA, to reduce the risk of hospitalization (both all-cause and HF hospitalizations).¹⁴⁴

IIb

B

Eur Heart J. 2021;42(36):3599-3726.



Digoxin a rehospitalizace

Digoxin Reduces 30-day All-cause Hospital Admission in Older Patients with Chronic Systolic Heart Failure

Robert C. Bourge, MD,^a Jerome L. Fleg, MD,^b Gregg C. Fonarow, MD,^c John G. F. Cleland, MD,^d John J. V. McMurray, MD,^e Dirk J. van Veldhuisen, MD, PhD,^f Mihai Gheorghiu, MD,^g Kanan Patel, MBBS, MPH,^a Inmaculada B. Aban, PhD,^a Richard M. Allman, MD,^{h,a} Connie White-Williams, RN, PhD,^a Michel White, MD,ⁱ Gerasimos S. Filippatos, MD, PhD,^j Stefan D. Anker, MD, PhD,^k Ali Ahmed, MD, MPH^{a,h}

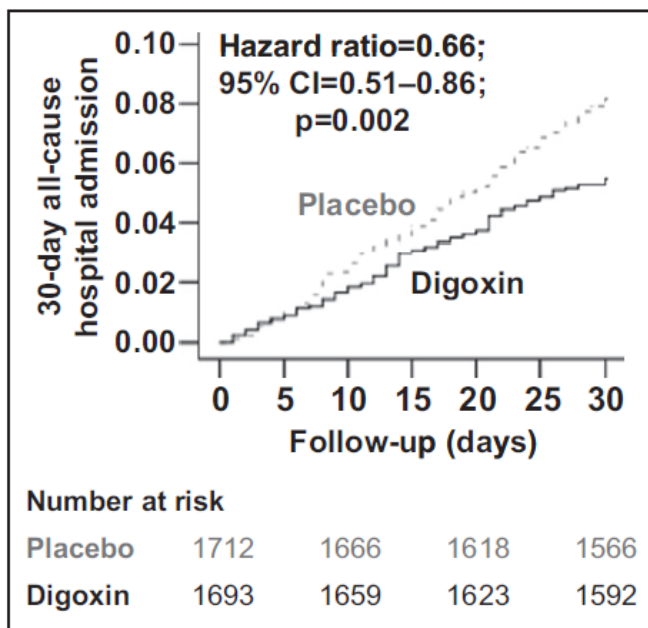
Table 3 Effect of Digoxin on Outcomes During 30 Days After Randomization in All 6800 Ambulatory Patients with Chronic Heart Failure and Reduced Ejection Fraction in the Main Digitalis Investigation Group Trial

Outcomes	% (events)		Absolute Risk Difference* (%)	Hazard Ratio† (95% CI)	P Value
	Placebo (n = 3403)	Digoxin (n = 3397)			
30-d all-cause hospitalization	7.9% (270)	5.5% (187)	-2.4	0.69 (0.57-0.83)	<.001
30-d cardiovascular hospitalization	6.1% (209)	3.6% (122)	-2.5	0.58 (0.46-0.72)	<.001
30-d heart failure hospitalization	4.1% (140)	1.6% (55)	-2.5	0.39 (0.29-0.53)	<.001
30-d all-cause mortality	1.1% (36)	0.7% (23)	-0.4	0.64 (0.38-1.08)	.093
30-d cardiovascular mortality	0.9% (32)	0.6% (21)	-0.3	0.66 (0.38-1.14)	.134
30-d heart failure mortality	0.4% (15)	0.1% (5)	-0.3	0.33 (0.12-0.92)	.033
30-d all-cause hospitalization or all-cause mortality	8.5% (288)	6.0% (204)	-2.5	0.70 (0.59-0.84)	<.001

CI = confidence interval.

*Absolute risk differences were calculated by subtracting percent events in patients receiving placebo from those receiving digoxin.

†HRs comparing patients receiving digoxin with those receiving placebo.



The American Journal of Medicine (2013) 126, 701-708



DIG trial



THE EFFECT OF DIGOXIN ON MORTALITY AND MORBIDITY IN PATIENTS WITH HEART FAILURE

THE DIGITALIS INVESTIGATION GROUP*

- **6800 nemocných, z nich 5812 mělo EF ≤ 45%**
- **léčba diuretikum, ACEI, nitráty**
- **bez betablokátorů, ARNI, SGL2i...**

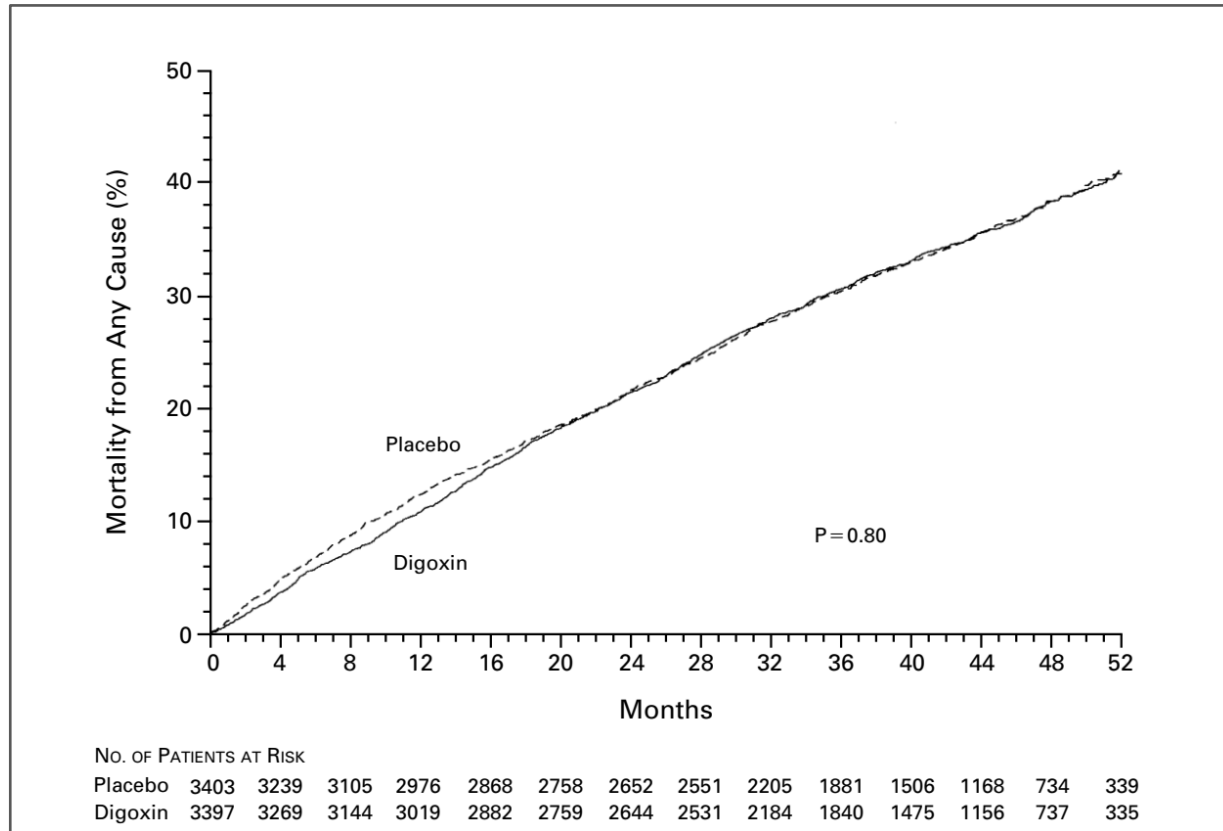
- **Primárním cílem byla celková mortalita.**

Concomitant medications		
Diuretics	81.2	82.2
ACE inhibitors	94.1	94.8
Nitrates	42.1	43.1
Other vasodilators§	0.9	1.5

N Engl J Med 1997; 336:525-533



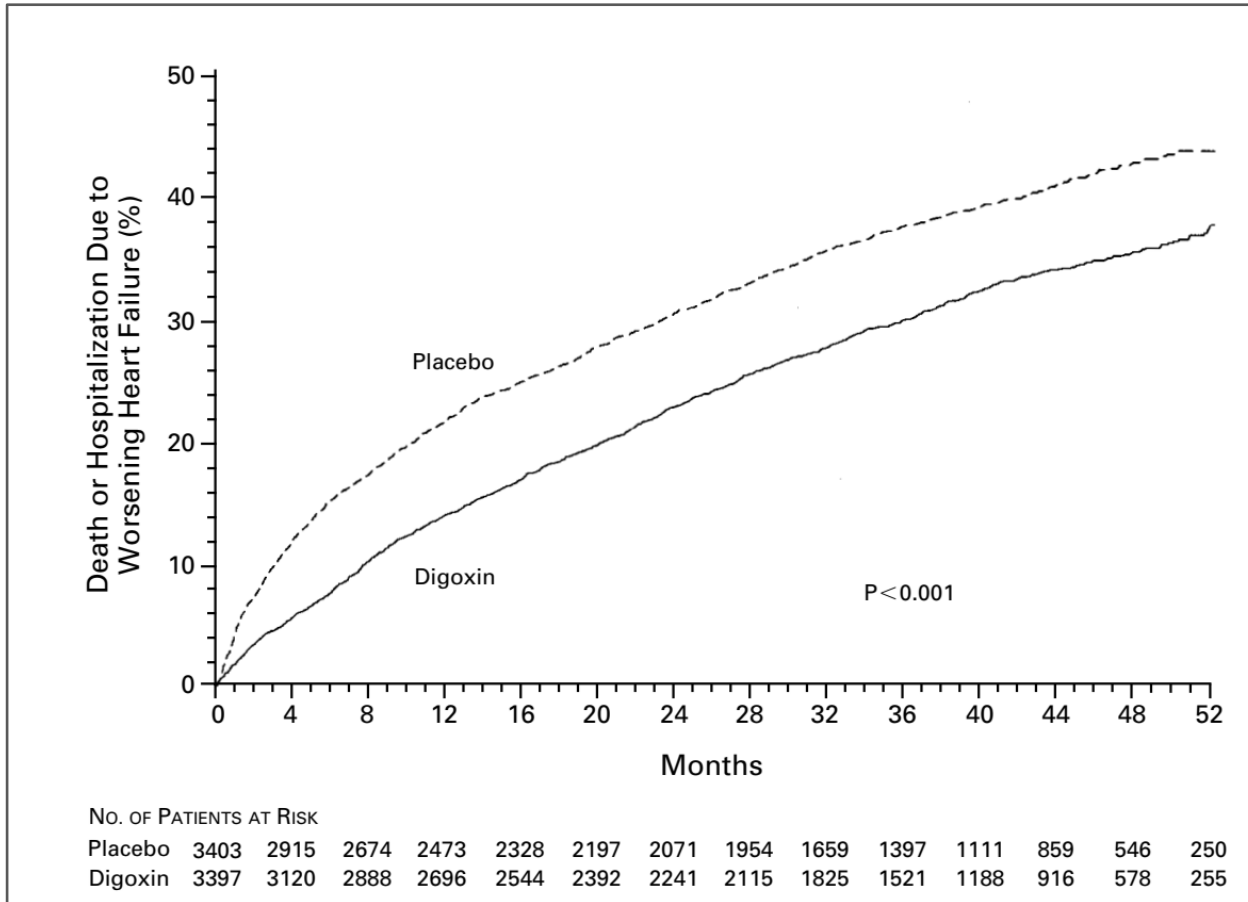
DIG trial



In conclusion, digoxin had no effect on overall mortality in patients receiving diuretics and angiotensin-converting-enzyme inhibitors, but it did reduce the overall number of hospitalizations and the combined outcome of death or hospitalization attributable to worsening heart failure. In clinical practice, digoxin therapy is likely to affect the frequency of hospitalization, but not survival.

N Engl J Med 1997; 336:525-533

DIG trial – ACM a HFH



(risk ratio, 0.75; 95 percent confidence interval, 0.69 to 0.82; $P < 0.001$)

In conclusion, digoxin had no effect on overall mortality in patients receiving diuretics and angiotensin-converting-enzyme inhibitors, but it did reduce the overall number of hospitalizations and the combined outcome of death or hospitalization attributable to worsening heart failure. In clinical practice, digoxin therapy is likely to affect the frequency of hospitalization, but not survival.

N Engl J Med 1997; 336:525-533

Jen pro srovnání...

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

Primary composite outcome — no. (%)				
Death from cardiovascular causes or first hospitalization for worsening heart failure	914 (21.8)	1117 (26.5)	0.80 (0.73–0.87)	<0.001

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

Efficacy outcomes						
Primary composite outcome — no. (%)†	386 (16.3)	11.6	502 (21.2)	15.6	0.74 (0.65 to 0.85)	<0.001
Hospitalization or an urgent visit for heart failure	237 (10.0)	7.1	326 (13.7)	10.1	0.70 (0.59 to 0.83)	NA
Hospitalization for heart failure	231 (9.7)	6.9	318 (13.4)	9.8	0.70 (0.59 to 0.83)	NA
Urgent heart-failure visit	10 (0.4)	0.3	23 (1.0)	0.7	0.43 (0.20 to 0.90)	NA
Cardiovascular death	227 (9.6)	6.5	273 (11.5)	7.9	0.82 (0.69 to 0.98)	NA

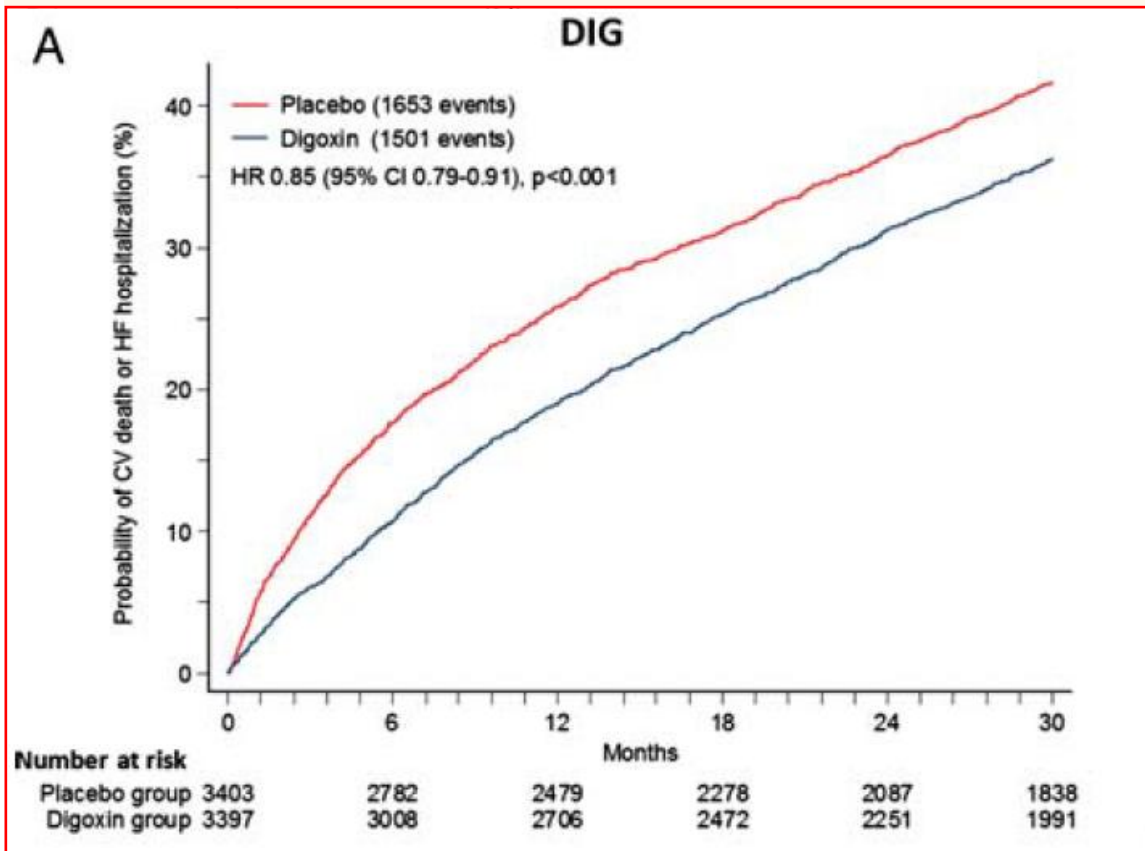
Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

Primary composite outcome — no. (%)	361 (19.4)	15.8	462 (24.7)	21.0	0.75 (0.65 to 0.86)	<0.001
Hospitalization for heart failure	246 (13.2)	10.7	342 (18.3)	15.5	0.69 (0.59 to 0.81)	
Cardiovascular death	187 (10.0)	7.6	202 (10.8)	8.1	0.92 (0.75 to 1.12)	



Jen pro srovnání...

Angiotensin–Neprilysin Inhibition versus Enalapril
in Heart Failure



(26.5) 0.80 (0.73–0.87) <0.001

**NNT pro redukcí hospitalizací
byl ve studii DIG nižší**

5.3) <0.001
0.0) NA
7) NA
4) NA
6) NA

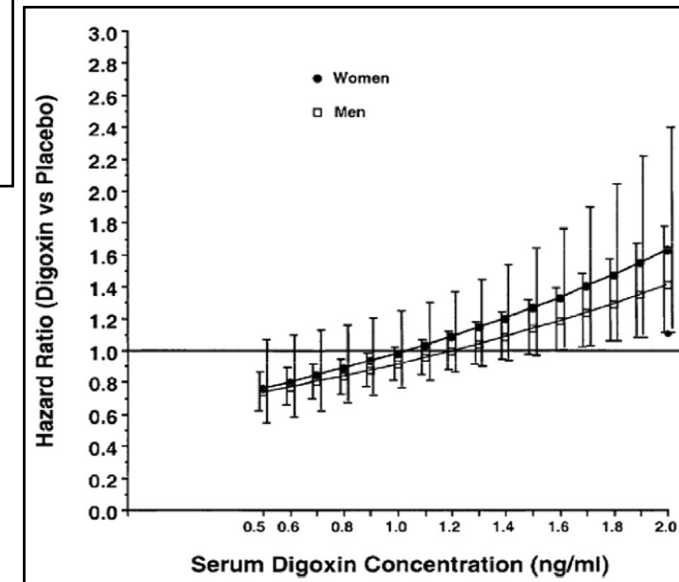
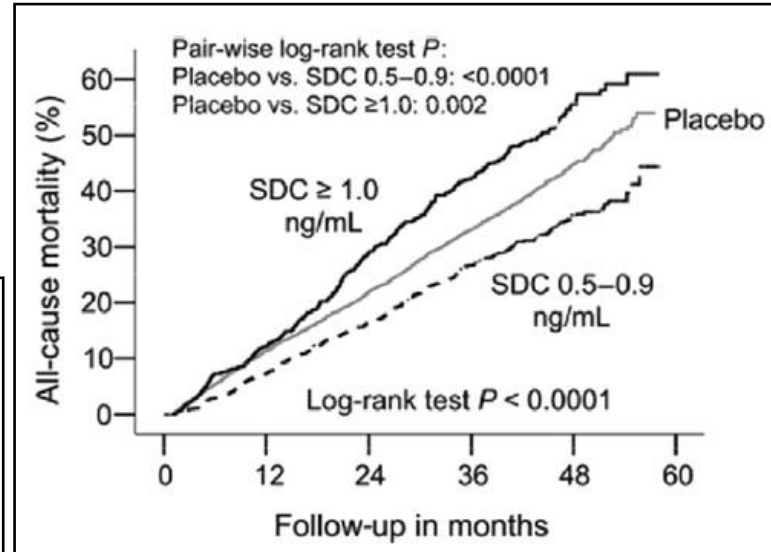
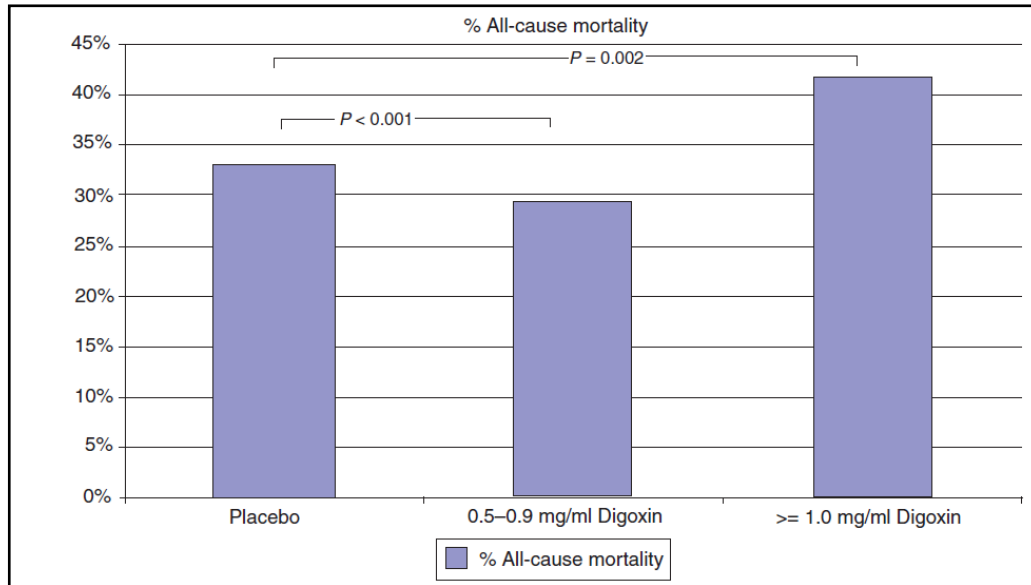
liflozin

9.4)	15.8	462 (24.7)	21.0	0.75 (0.65 to 0.86)	<0.001
3.2)	10.7	342 (18.3)	15.5	0.69 (0.59 to 0.81)	
0.0)	7.6	202 (10.8)	8.1	0.92 (0.75 to 1.12)	

DIG trial

Digoxin for patients with atrial fibrillation and heart failure: paradise lost or not?[†]

Dirk J. van Veldhuisen^{1*}, Isabelle C. Van Gelder¹, Ali Ahmed², and Mihai Gheorghiade³



European Heart Journal (2013) 34, 1468-1470

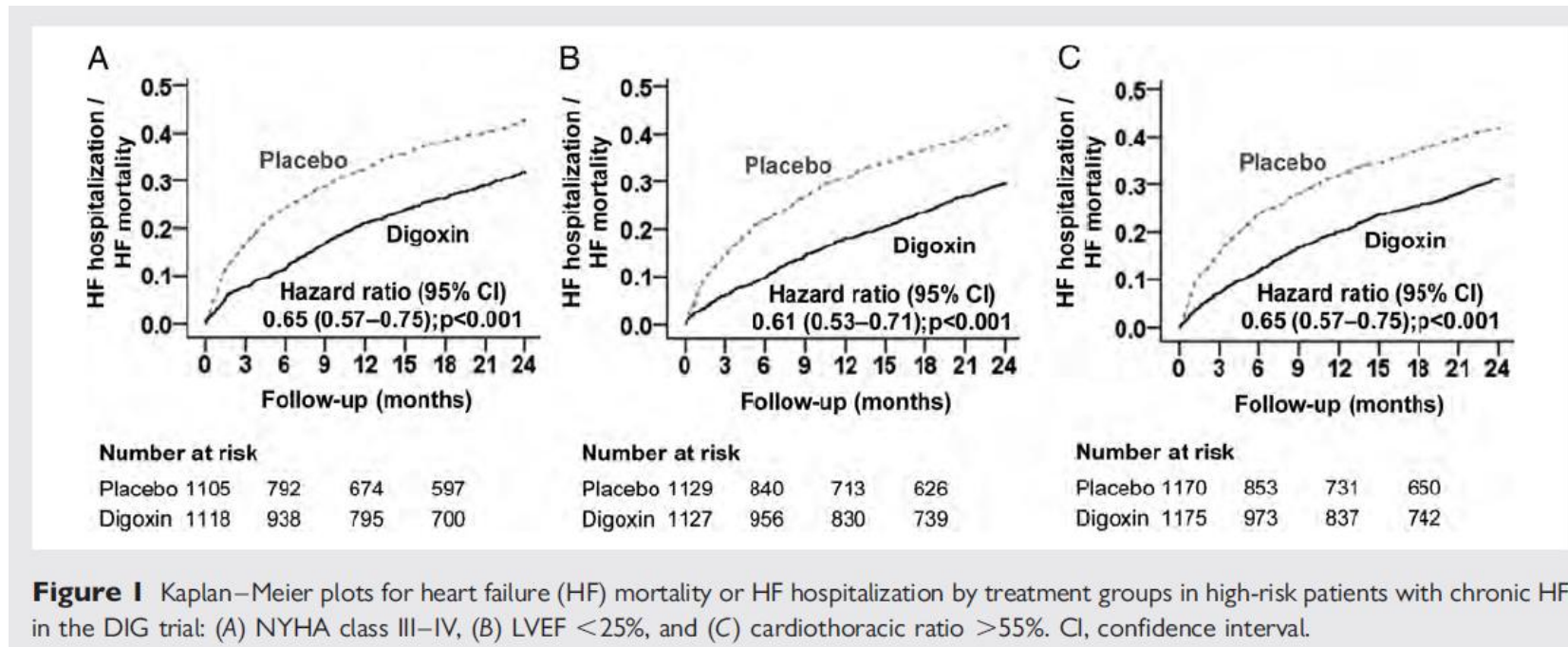


DIG trial

Effect of oral digoxin in high-risk heart failure patients: a pre-specified subgroup analysis of the DIG trial[†]

Mihai Gheorghiade¹, Kanan Patel², Gerasimos Filippatos³, Stefan D. Anker⁴, Dirk J. van Veldhuisen⁵, John G.F. Cleland⁶, Marco Metra⁷, Inmaculada B. Aban², Stephen J. Greene¹, Kirkwood F. Adams⁸, John J.V. McMurray⁹, and Ali Ahmed^{2,10*}

- EF < 25%
- NYHA III-IV
- CT-ratio > 55%

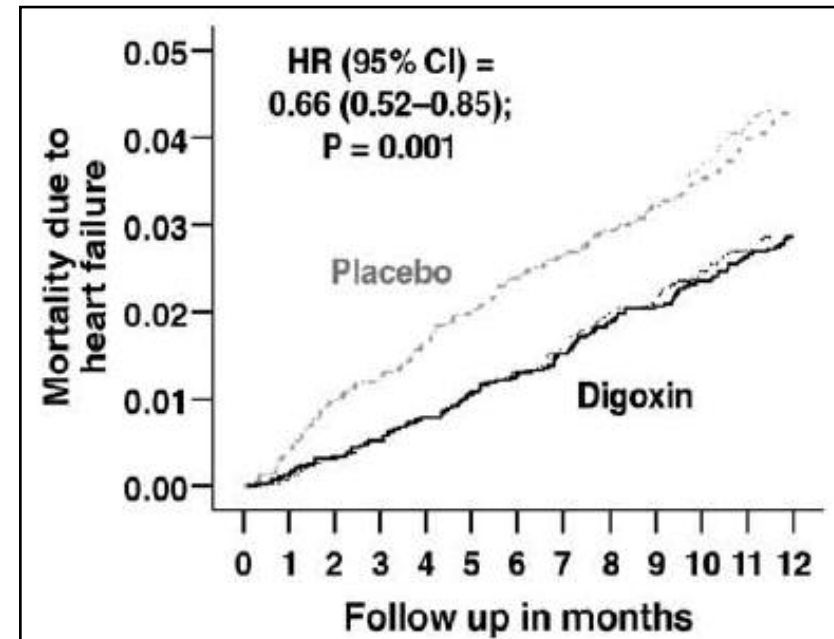
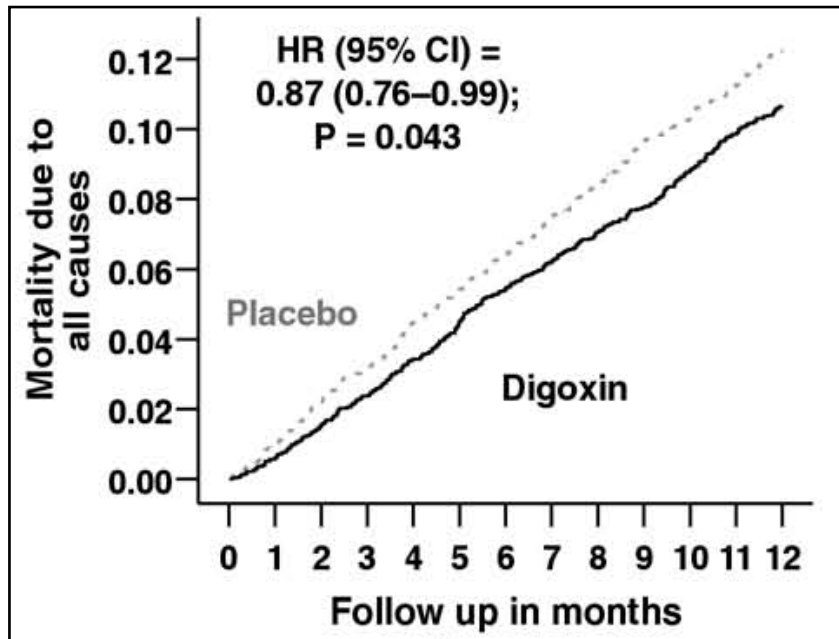


DIG trial

Effectiveness of Digoxin in Reducing One-Year Mortality in Chronic Heart Failure in the Digitalis Investigation Group Trial

Ali Ahmed, MD, MPH^{a,b,*}, Finn Waagstein, MD^c, Bertram Pitt, MD^d, Michel White, MD^e,
Faiez Zannad, MD, PhD^f, James B. Young, MD^g, and Shahbudin H. Rahimtoola, MD^h

- Pokud zkrátíme follow-up na 1 rok...
- Řada nemocných v placebové větvi začala užívat digoxin
- Dlouhodobá expozice a progresse onemocnění vedly k vzestupu hladin DIG a tím k vyššímu riziku NÚ



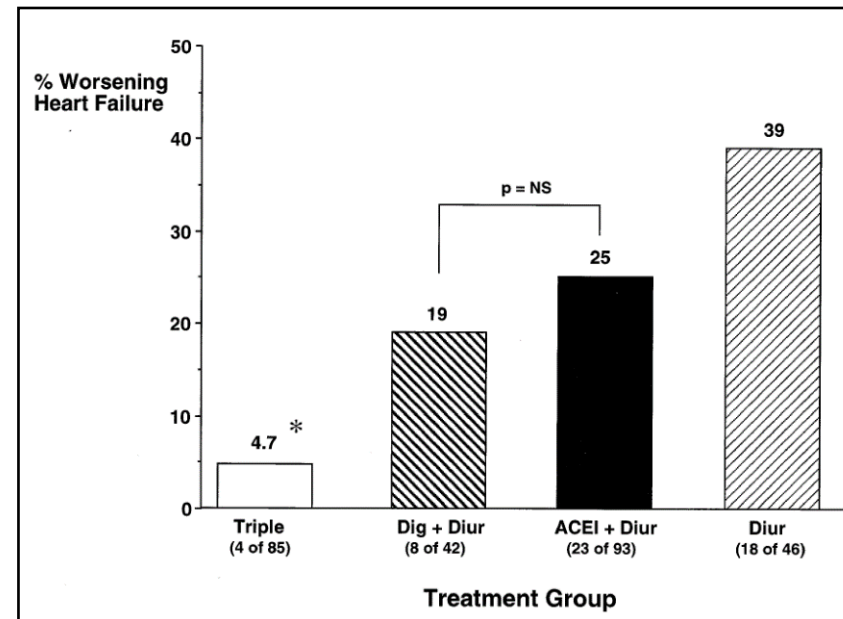
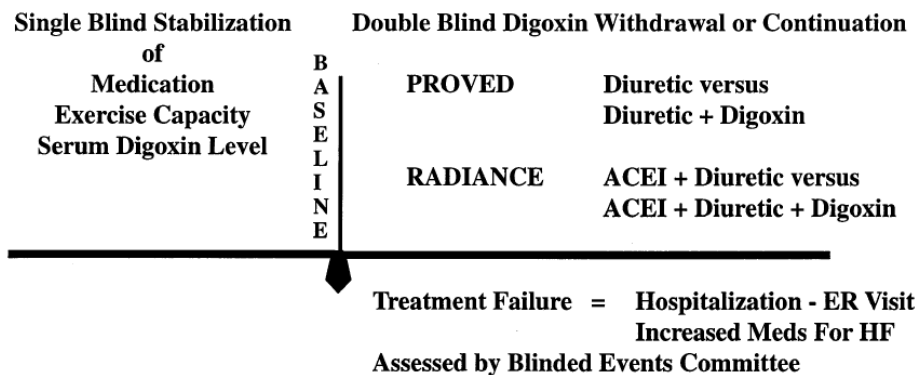
Am J Cardiol 2009;103:82–87



Vysazení digoxinu u stabilních nemocných

Superiority of “Triple” Drug Therapy in Heart Failure: Insights from the PROVED and RADIANCE Trials

JAMES B. YOUNG, MD, FACC,* MIHAI GHEORGHIADÉ, MD, FACC,†
BARRY F. URETSKY, MD, FACC,‡ J. HERBERT PATTERSON, PHARM.D.§
KIRKWOOD F. ADAMS, JR., MD, FACC||



Závěry: vysazení digoxinu u původně stabilních jedinců s HFrEF je spojeno s vyšším rizikem progresu srdečního selhání, sníženou tolerancí námahy, poklesem LVEF a vzestupem tepové frekvence

Vysazení léčby srdečního selhání

Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial

Brian P Halliday, Rebecca Wassall, Amrit S Lota, Zohya Khaliq, John Gregson, Simon Newsome, Robert Jackson, Tsveta Rahneva, Rick Wage, Gillian Smith, Lucia Venneri, Upasana Tayal, Dominique Auger, William Midwinter, Nicola Whiffin, Ronak Rajani, Jason N Dzung, Antonis Pantazis, Stuart A Cook, James S Ware, A John Baksi, Dudley J Pennell, Stuart D Rosen, Martin R Cowie, John GF Cleland, Sanjay K Prasad

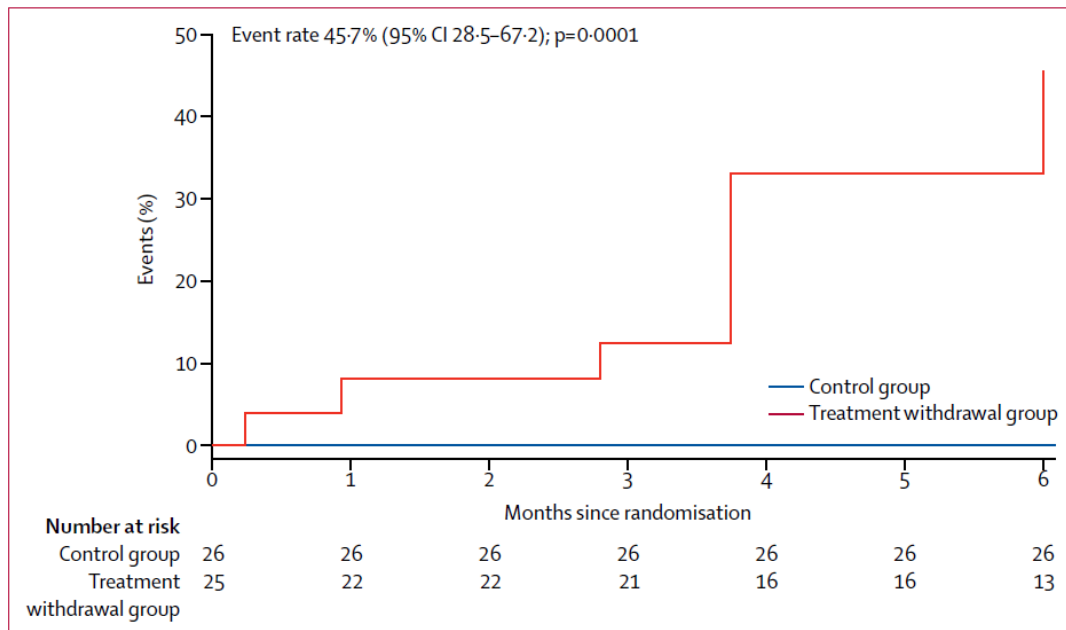


Figure 3: Kaplan-Meier curve of time to primary endpoint in randomised phase, according to treatment group

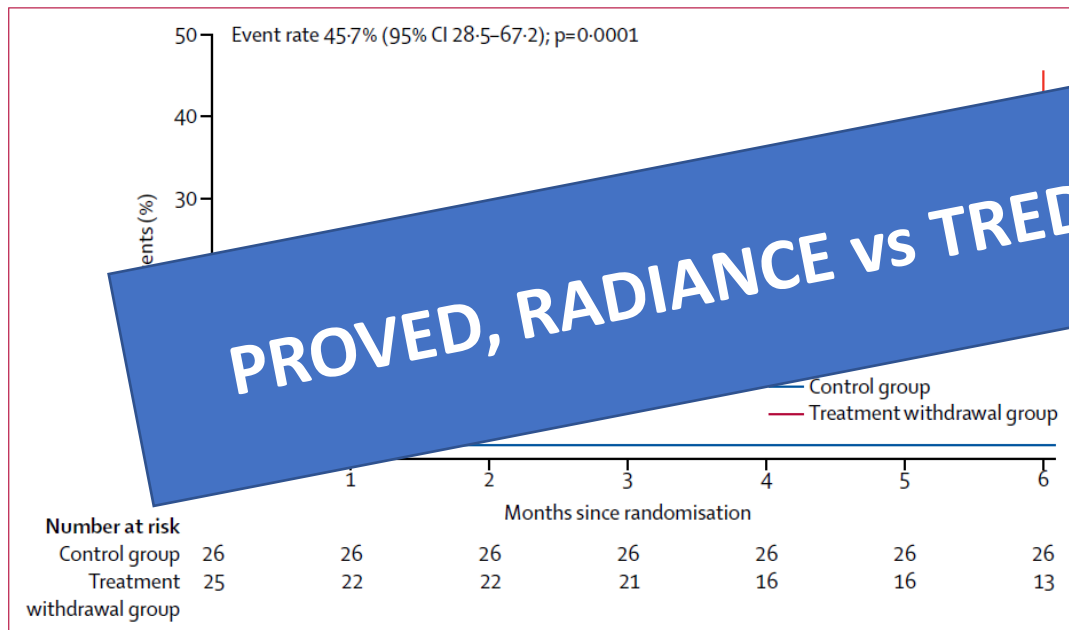
- během prvních 6 měsíců 11 z 25 pts randomizovaných k ukončení léčby dosáhlo endpointu, zatímco ten se neobjevil u žádného z pokračujících v léčbě (Kaplan-Meier event rate 45.7%; p=0,0001)
- po 6 měsících 25 z 26 původně pokračujících ukončilo léčbu, u 9 z nich se objevil endpoint (Kaplan-Meier event rate 36.0%)

Lancet 2019; 393: 61–73

Vysazení léčby srdečního selhání

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PROVED, RADIANCE VS TRED-HF - jde o podobnost čistě náhodnou?

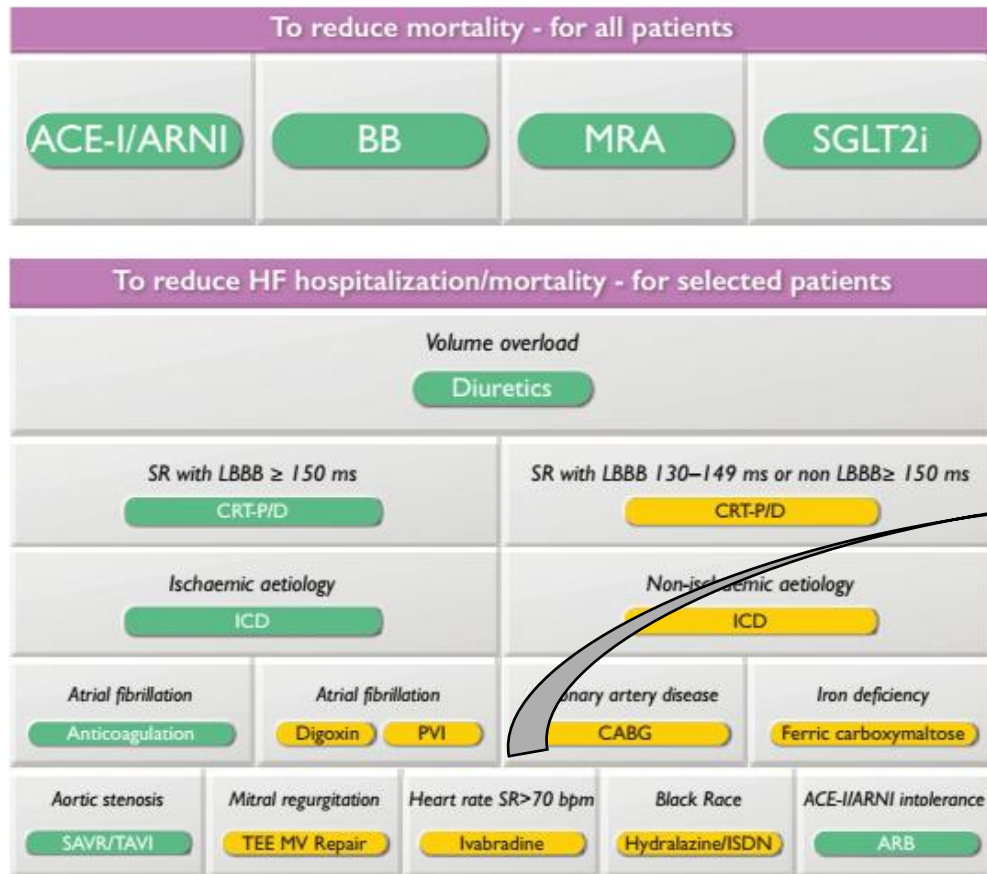
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Figure 3: Kaplan-Meier curve of time to primary endpoint in randomised phase, according to treatment group

Lancet 2019; 393: 61-73

Léčba HFrEF v Guidelines

Management of HFrEF



Heart rate SR > 70 bpm

Ivabradine

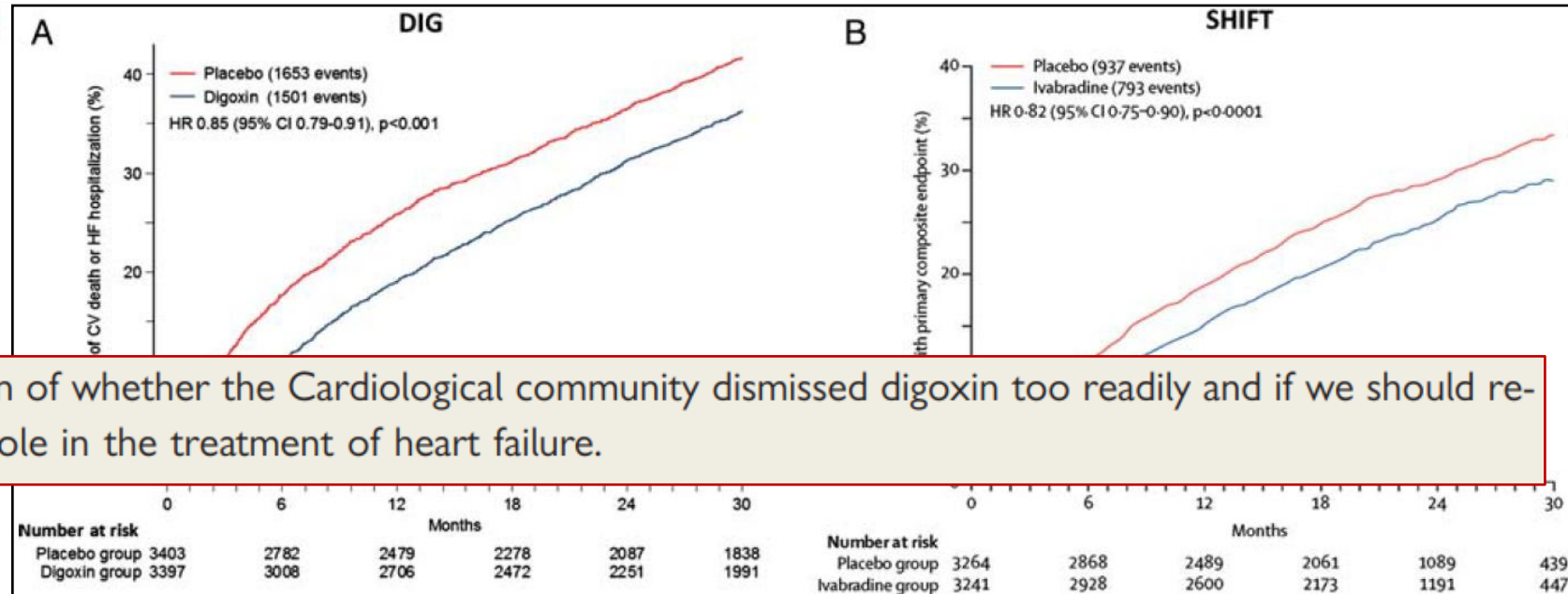
Eur Heart J. 2021;42(36):3599-3726.



Digoxin vs ivabradin

Should we SHIFT our thinking about digoxin? Observations on ivabradine and heart rate reduction in heart failure

Davide Castagno¹, Mark C. Petrie², Brian Claggett³, and John McMurray^{4*}



Conclusions

This raises the question of whether the Cardiological community dismissed digoxin too readily and if we should re-appraise its potential role in the treatment of heart failure.

Methods and results

In this short commentary, we retrospectively analyse the Digitalis Investigation Group (DIG) Trial looking at the primary composite endpoint used in SHIFT (i.e. cardiovascular death or hospital admission for worsening heart failure) and compare the effect of digoxin on this endpoint with that of ivabradine. A remarkably similar risk reduction in the composite outcome and in its components appears evident among patients receiving the active treatment in both studies (although ivabradine was added to a beta-blocker, whereas digoxin was not).

Conclusions

This raises the question of whether the Cardiological community dismissed digoxin too readily and if we should re-appraise its potential role in the treatment of heart failure.

European Heart Journal (2012) **33**, 1137–1141

Digoxin je stále vzrušující téma...

Digoxin for patients with atrial fibrillation and heart failure: paradise lost or not?[†]

Dirk J. van Veldhuisen^{1*}, Isabelle C. Van Gelder¹, Ali Ahmed²,
and Mihai Gheorghiade³

while in DIG no beta-blockers were used. Therefore, digoxin in patients with HF may still have a place, not as an inotropic drug, because for these drugs paradise is 'lost',²⁰ but as a neurohormonal modulator, when given in low doses. Indeed, low-dose digoxin may still be useful, but trials examining this question are urgently needed.

European Heart Journal (2013) **34**, 1468–1470



Srdeční selhání a digoxin

The Use of Digoxin in Patients With Worsening Chronic Heart Failure

Reconsidering an Old Drug to Reduce Hospital Admissions

Andrew P. Ambrosy, MD,* Javed Butler, MD, MPH,† Ali Ahmed, MD,‡
Muthiah Vaduganathan, MD, MPH,§ Dirk J. van Veldhuisen, MD,||
Wilson S. Colucci, MD,¶ Mihai Gheorghiadu, MD#

Stanford, California; Atlanta, Georgia; Birmingham, Alabama; Boston, Massachusetts;
Groningen, the Netherlands; and Chicago, Illinois

Table 2 Physiologic Effects of Digoxin Therapy

Hemodynamic	Neurohormonal	Electrophysiological
↑ LVEF	↑ Parasympathetic	SA node: slows sinus rate
↑ CO	↓ Sympathetic	AV node: prolongs conduction
↓ HR, ↔ BP	↓ RAAS	
↓ PCWP		

(J Am Coll Cardiol 2014;63:1823–32)



Drobné pochyby...

Digoxin: beneficial or harmful?

Gianluigi Savarese* and Lars H. Lund

Division of Cardiology, Department of Medicine, Karolinska Institutet, Stockholm, Sweden

ers. Thus, although alarming, the evidence of increased mortality associated with digitalis in observational and post-hoc studies cannot be used to decide whether digitalis may still have a place in HF or AF, but points out the urgency of randomized clinical trials to address this question.

např. v post-hoc analýze studie AFFIRM (kde byl digoxin spojen s vyšším relativním rizikem mortality) bylo doporučeno udržovat SDC $\geq 1,0$ ng/ml

European Heart Journal - Cardiovascular Pharmacotherapy (2017) 3, 127–128



Why is the use of digitalis withering? Another reason that we need medical heart failure specialists

Milton Packer*

Digitalis should always be prescribed under specialist supervision.

- **Zásadní je zohlednění komorbidit a lékových interakcí spojených se zvýšením SDC (bezpečné rozmezí je 0,5-0,9 ng/ml), resp. precipitujících faktorů zvýšeného rizika arytmií (např. hypokalemie)**

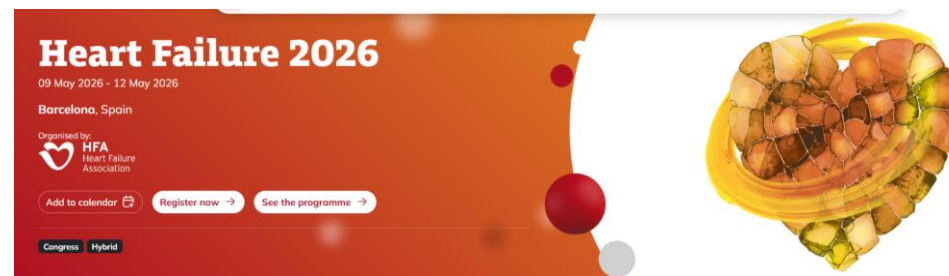
European Journal of Heart Failure (2017)
doi:10.1002/ejhf.1043



Efficacy and safety of low-dose digoxin in patients with heart failure. Rationale and design of the **DECISION** trial

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...uvidíme odpoledne...



Prezentace hlavních výsledků studie **DECISION** (Digoxin Evaluation in Chronic heart failure), která zkoumá účinnost nízkých dávek digoxinu u pacientů se srdečním selháním, je naplánována na kongres **Heart Failure 2026**. [TCTMD.com](https://www.tctmd.com)

Podrobnosti k prezentaci:

- **Datum a místo:** Studie bude prezentována v rámci bloku „Hottest Trials (2)“ v **neděli 10. května 2026** v Barceloně (v čase 13:15–13:24).
- **Přednášející:** Hlavní výsledky představí **Dirk van Veldhuisen** z University Medical Centre Groningen.
- **Související data:** Součástí stejného bloku bude také meta-analýza studií DECISION, [DIGIT-HF](#) a historické studie DIG, kterou přednese Kevin Damman. [ESC 365](#)

Studie DECISION se zaměřuje na to, zda nízká hladina digoxinu v krvi (0,5–0,9 ng/ml) může u moderně léčených pacientů se srdečním selháním (HFrEF i HFmrEF) snížit riziko úmrtí nebo hospitalizací. [Wiley Online Library +1](#)

Závěry

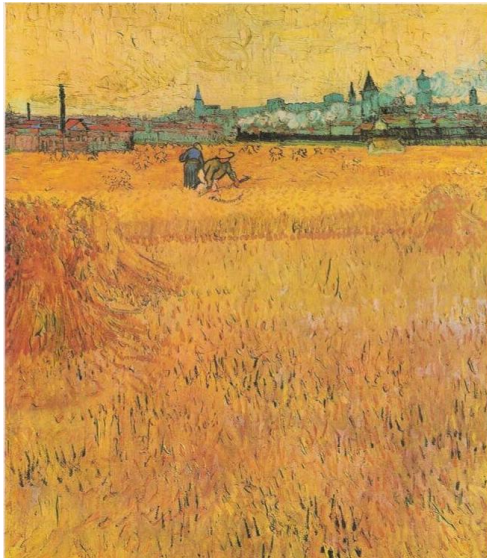
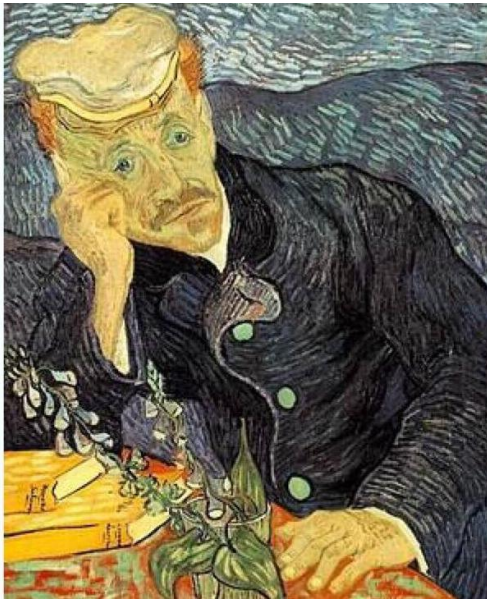
- Digoxin je velmi starý a obyčejný lék, jehož používání není vzhledem k jeho úzkému terapeutickému oknu úplně jednoduché.
- Nicméně pokud je využíván s rozvahou a poučeně, může i v nynější době přinést řadě nemocných významné benefity, zejména v situacích, kdy převládnou důvody pro redukci symptomů nad snahou o zlepšení prognózy.
- Základním handicapem pro posouzení jeho významu je skutečnost, že dosud neměl data z prospektivních klinických studií v éře současné farmakologické i nefarmakologické léčby...



Závěry

- Retrospektivní hodnocení mohou trpět skutečností, že k digoxinu často sáhneme až v bezvýchodných stavech, kdy nám už nezbývají jiné terapeutické možnosti.
- Právě dnes by měla být na kongresu HFA prezentována data ze studie DECISION, která nám mohou pomoci zhodnotit roli digoxinu v moderní éře léčby srdečního selhání.
- Digoxin není lékem pro všechny nemocné se srdečním selháním, ale nevylijme s vaničkou i dítě...





Děkuji za pozornost!

