Implantabilní oběhové srdeční podpory v léčbě srdečního selhání

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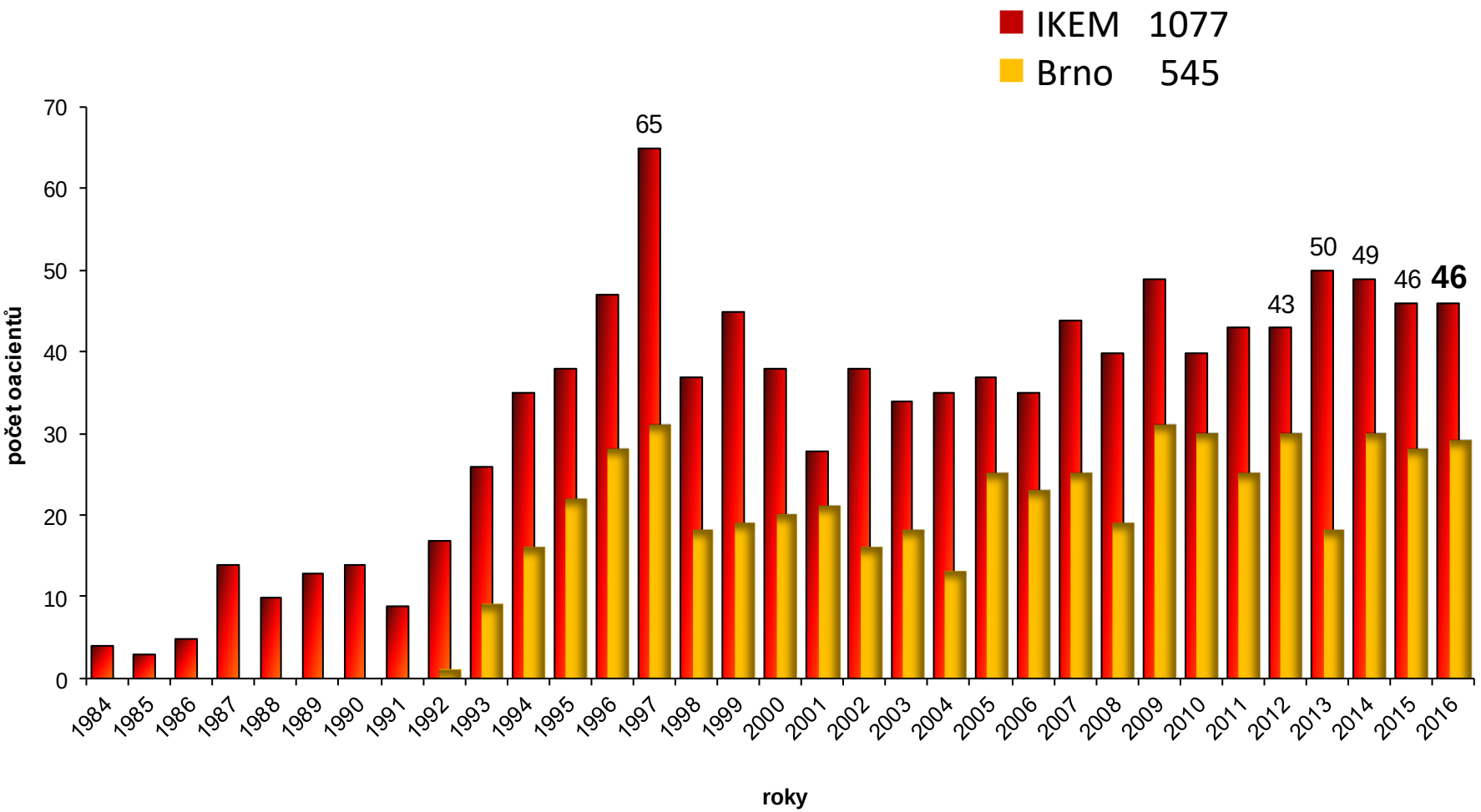
Úvod

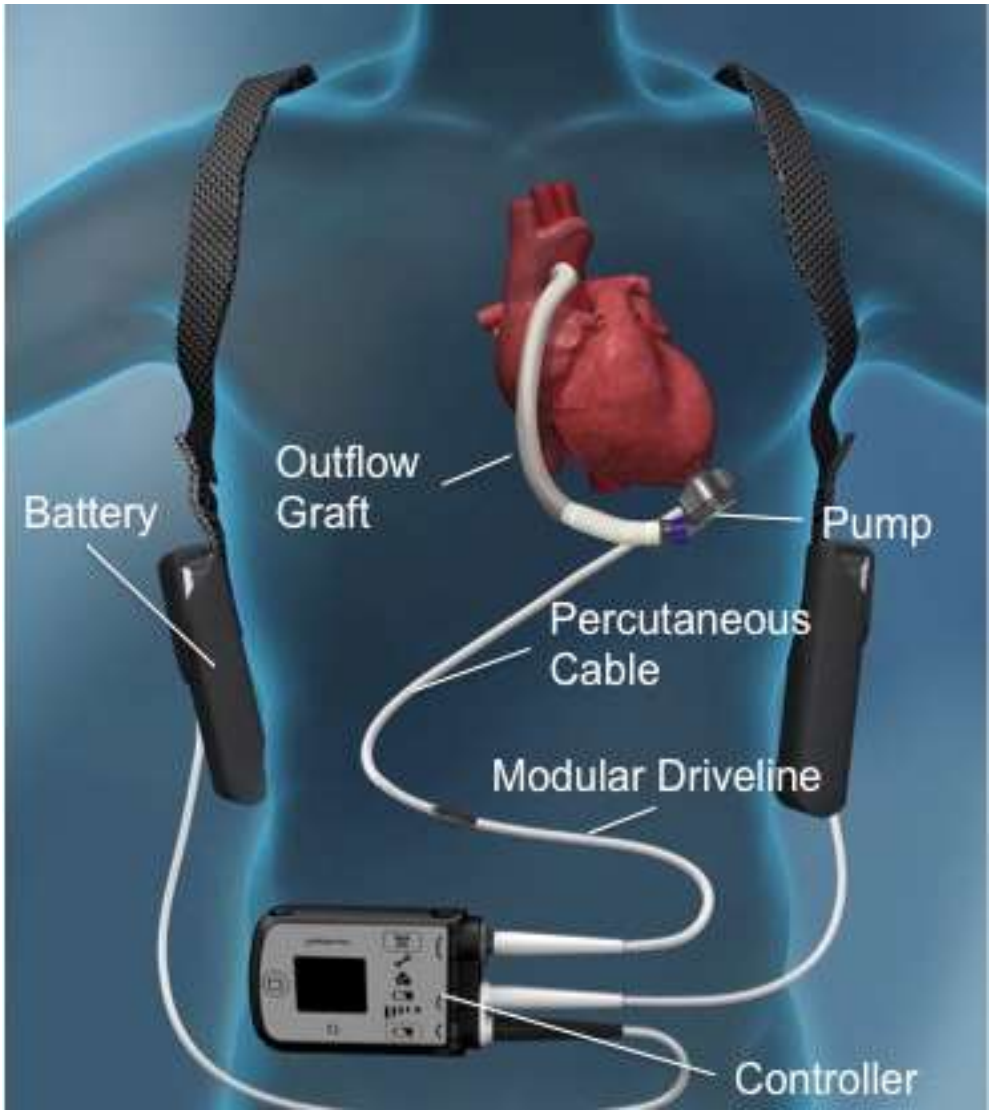
- Chronické srdeční selhání: 1–2% evropské populace[1]
- Faktory: demografické, životní styl, pokroky moderní komplexní kardiovaskulární léčby
- Vyčerpání možností konvenčních léčebných postupů
- → terminální srdeční selhání
- Transplantace srdce – prokazatelný přínos

IKEM

Transplantace srdce v ČR

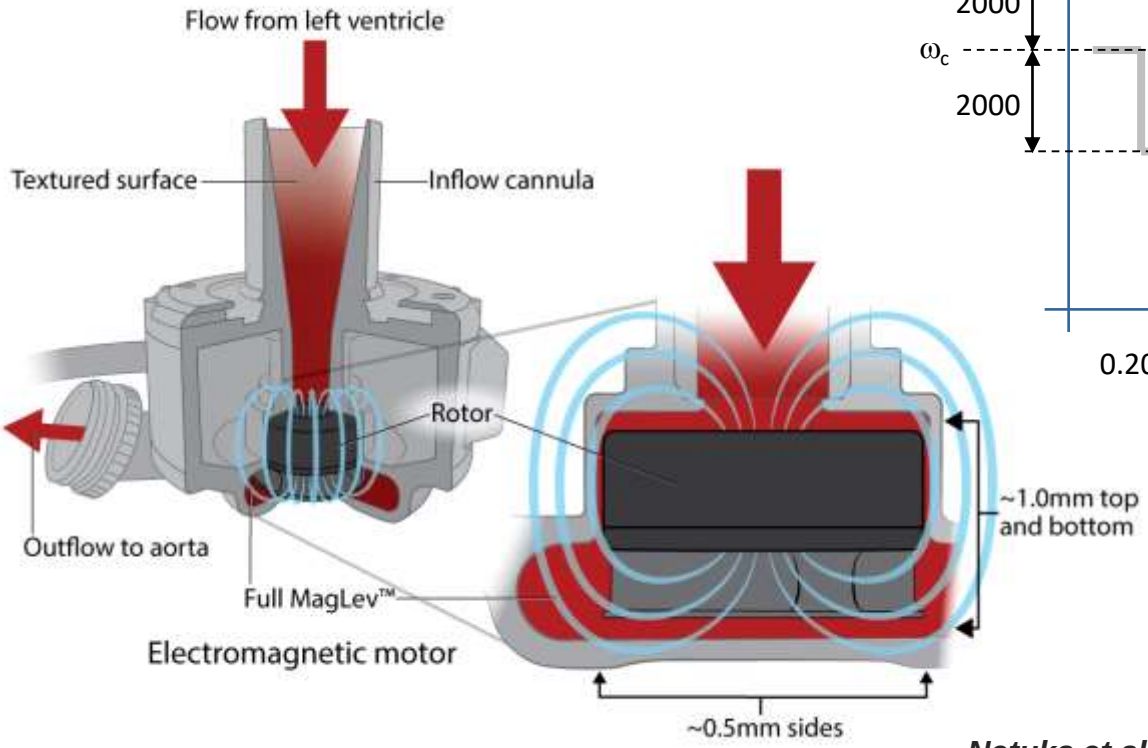


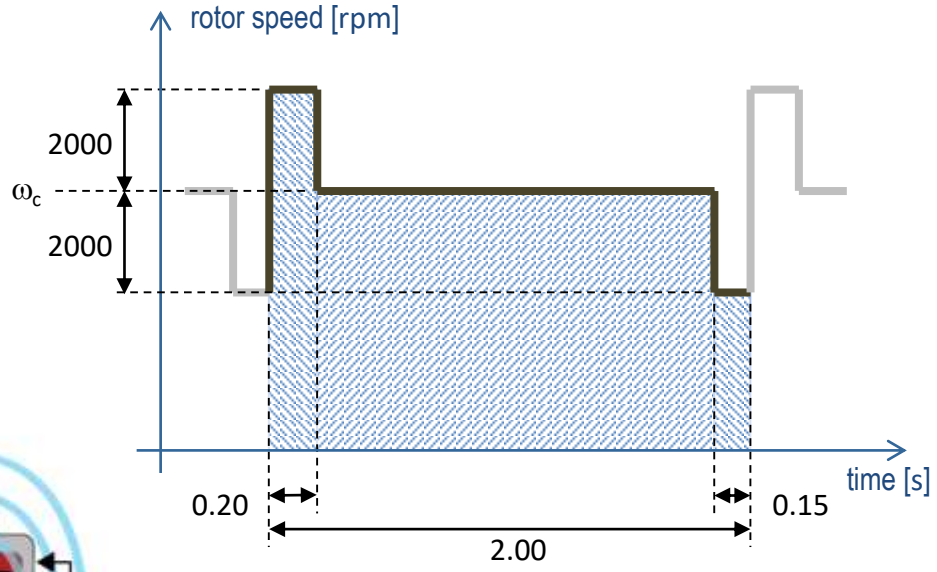
HeartMate 3


Outflow
Graft
Battery
Pump
Percutaneous
Cable
Modular Driveline
Controller

Magneticky levitující rotor

- Konzistentní šířka krevní cesty
- Umělá pulsatilita

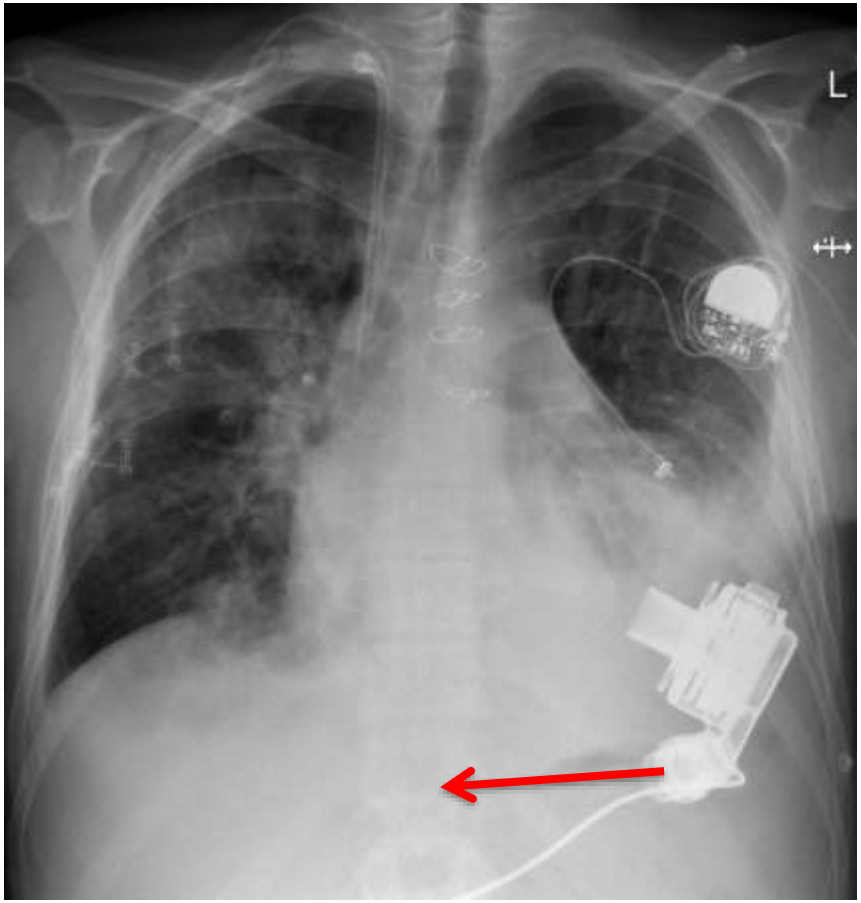


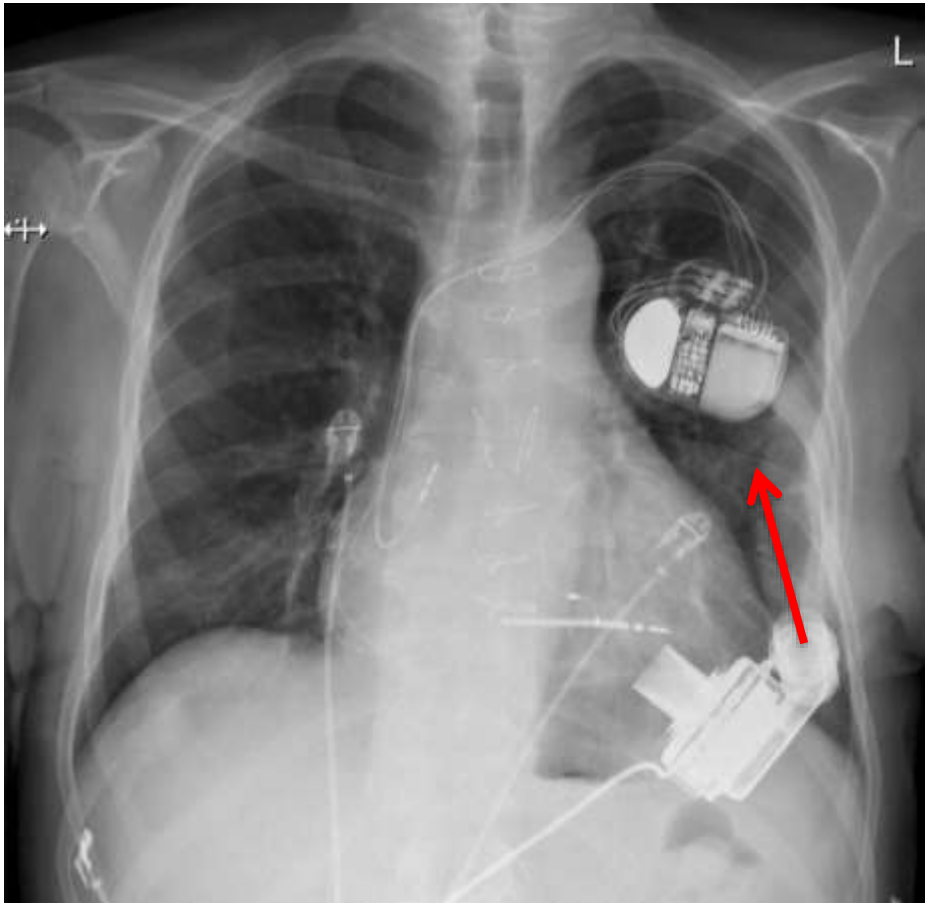


™Full MagLev is a trademark of Thoratec Corporation

Netuka et al. J Am Coll Cardiol. 2015 Dec 15;66(23):2579-89.

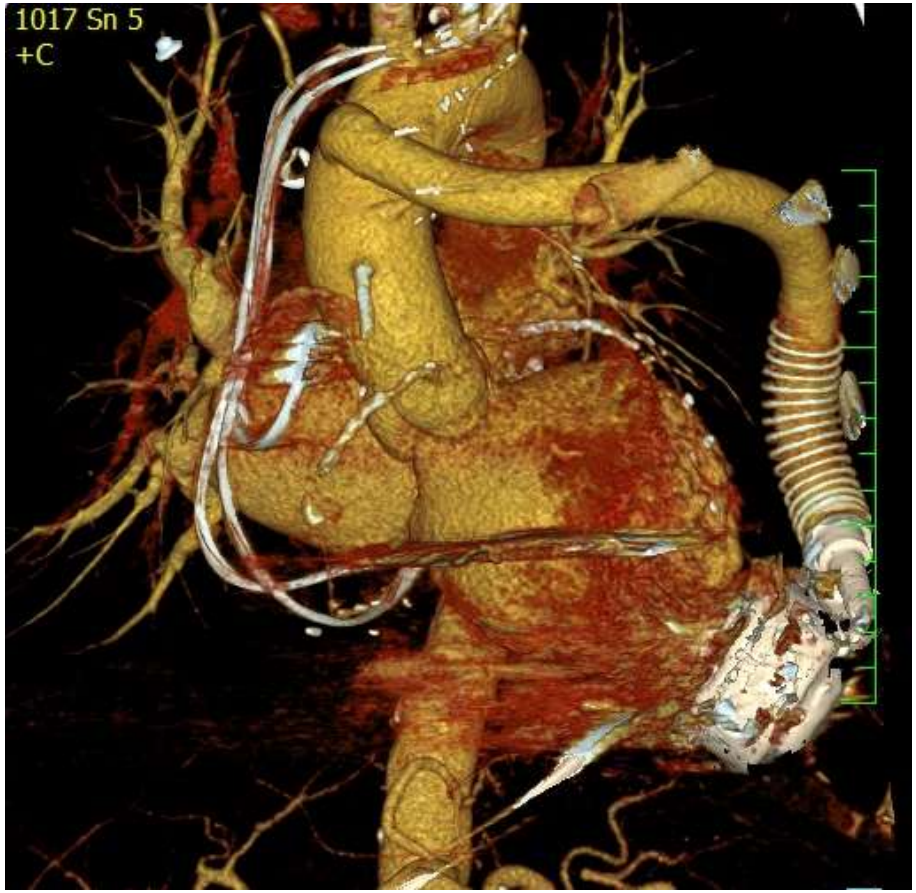
Miniinvazivní implantace

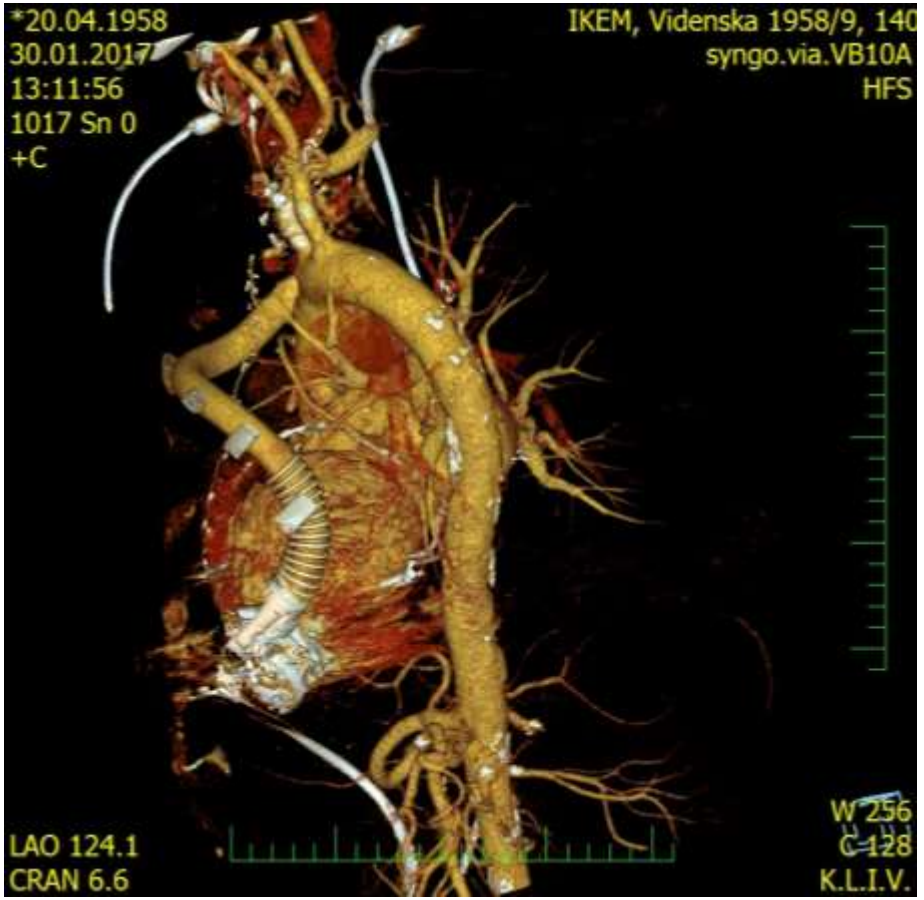




IKEM

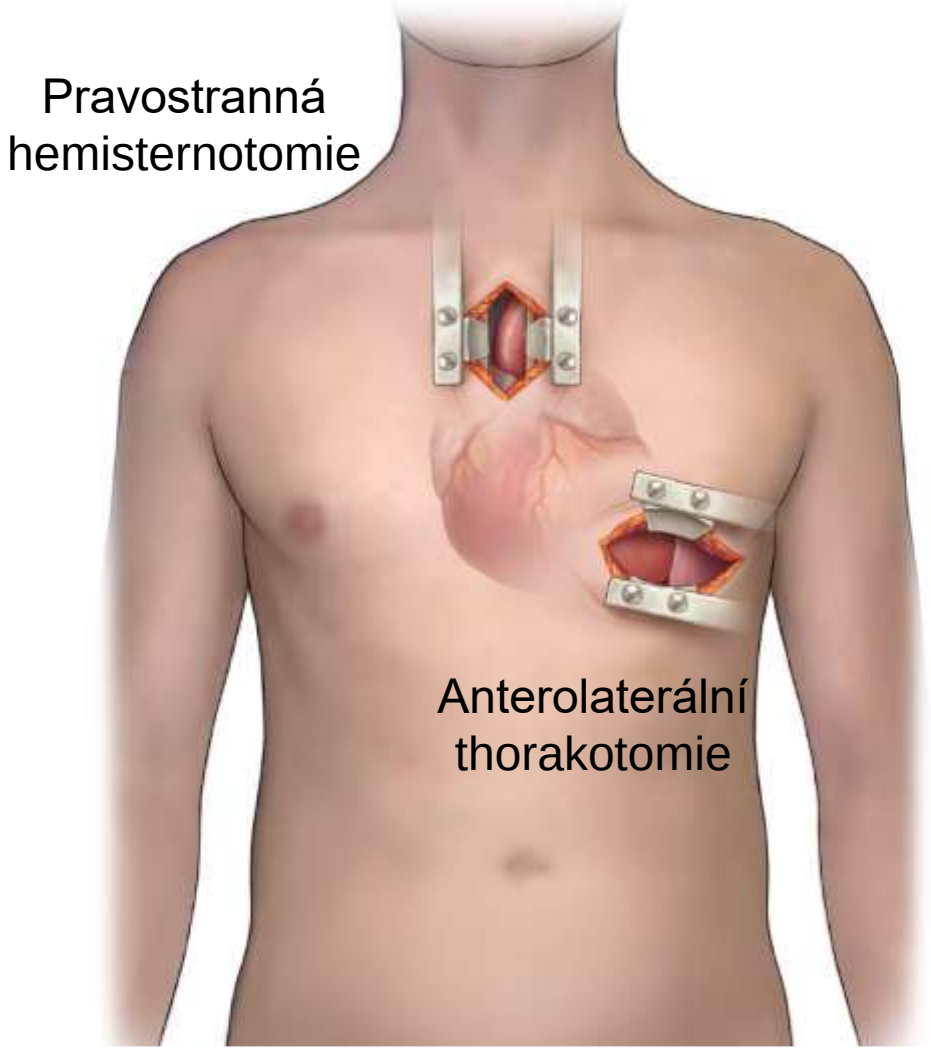
Implantace u komplexních reoperací





IKEM

Miniinvazivní implantace



ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Třída	Stupeň
I	B

Pacienti s výraznými symptomy srdečního selhání > 2 měsíce navzdory optimalizované medikamentózní terapii s >1 z následujících příznaků:

- **EF LK < 25%**
- **> 2 hospitalizace pro srdeční selhání během 1 roku bez jiné vyvolávající příčiny**
- **závislost na i.v. inotropní podpoře**
- **progresivní orgánové selhávání pro sníženou perfúzi a systolickým TK < 80-90 mmHg nebo SI <2,0 l/min/m^2)**
- **zhoršující se funkce pravé komory srdeční**

McMurray J. et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: Eur J Heart Fail. 2012;14(8):803-69.

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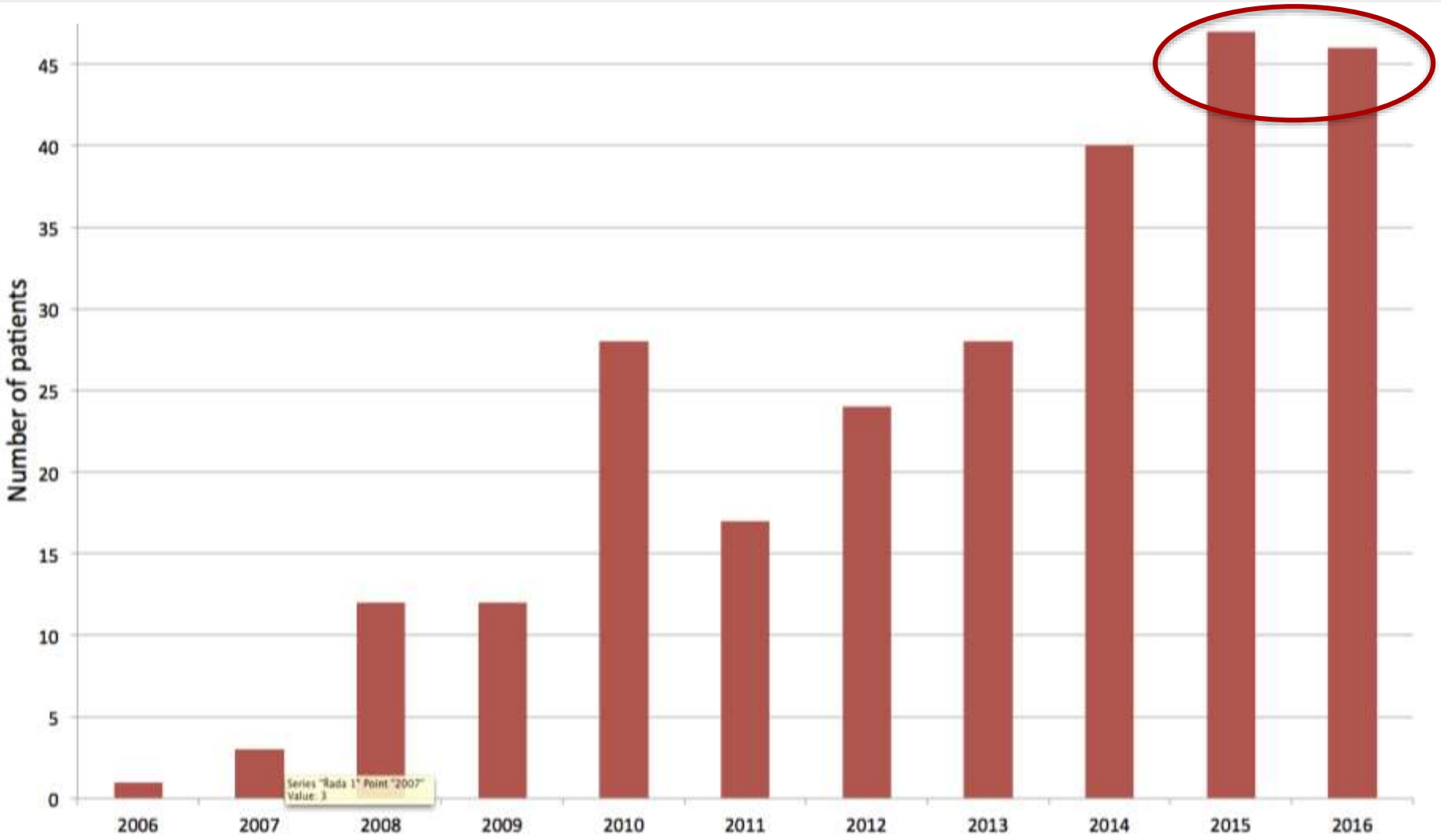
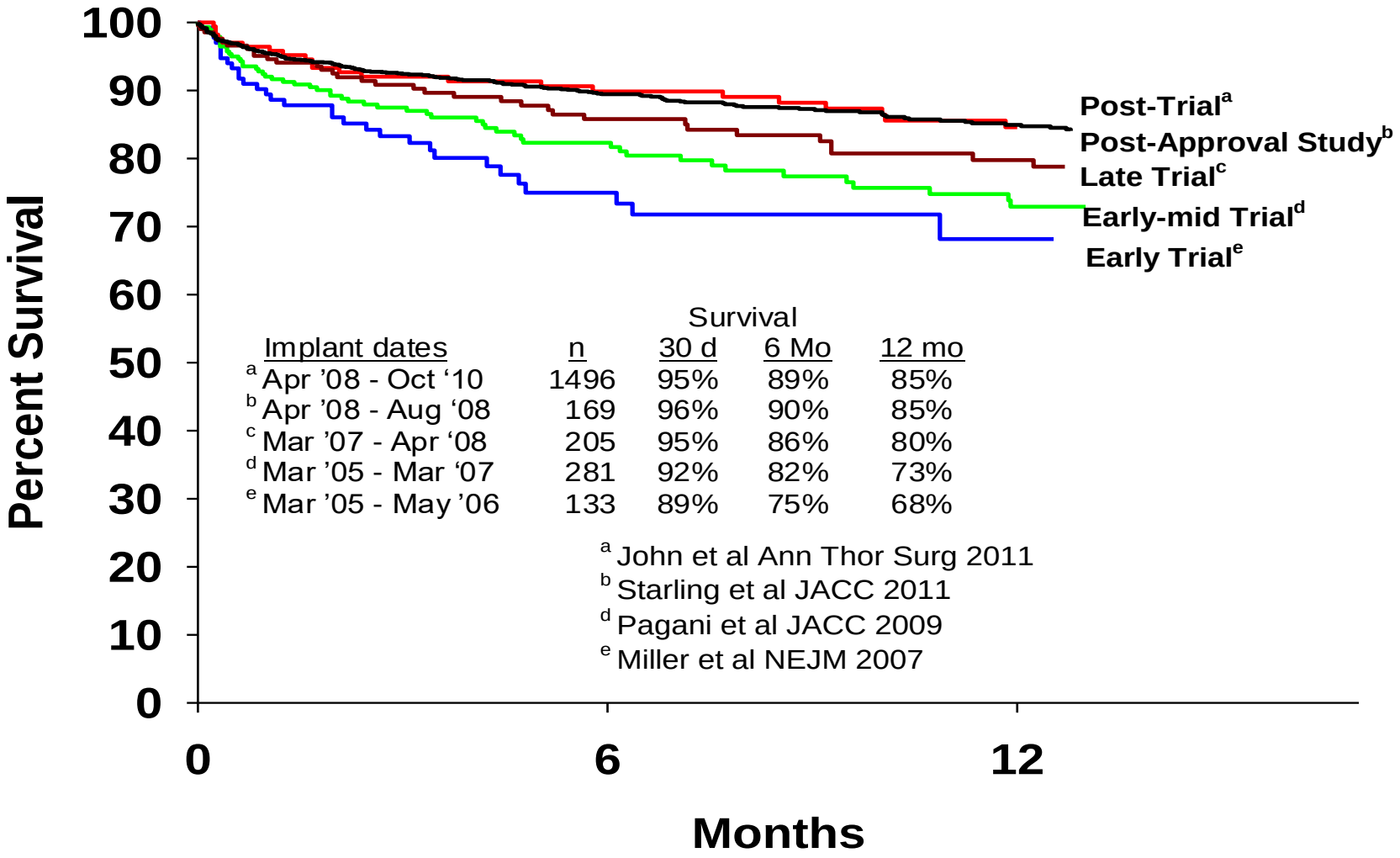
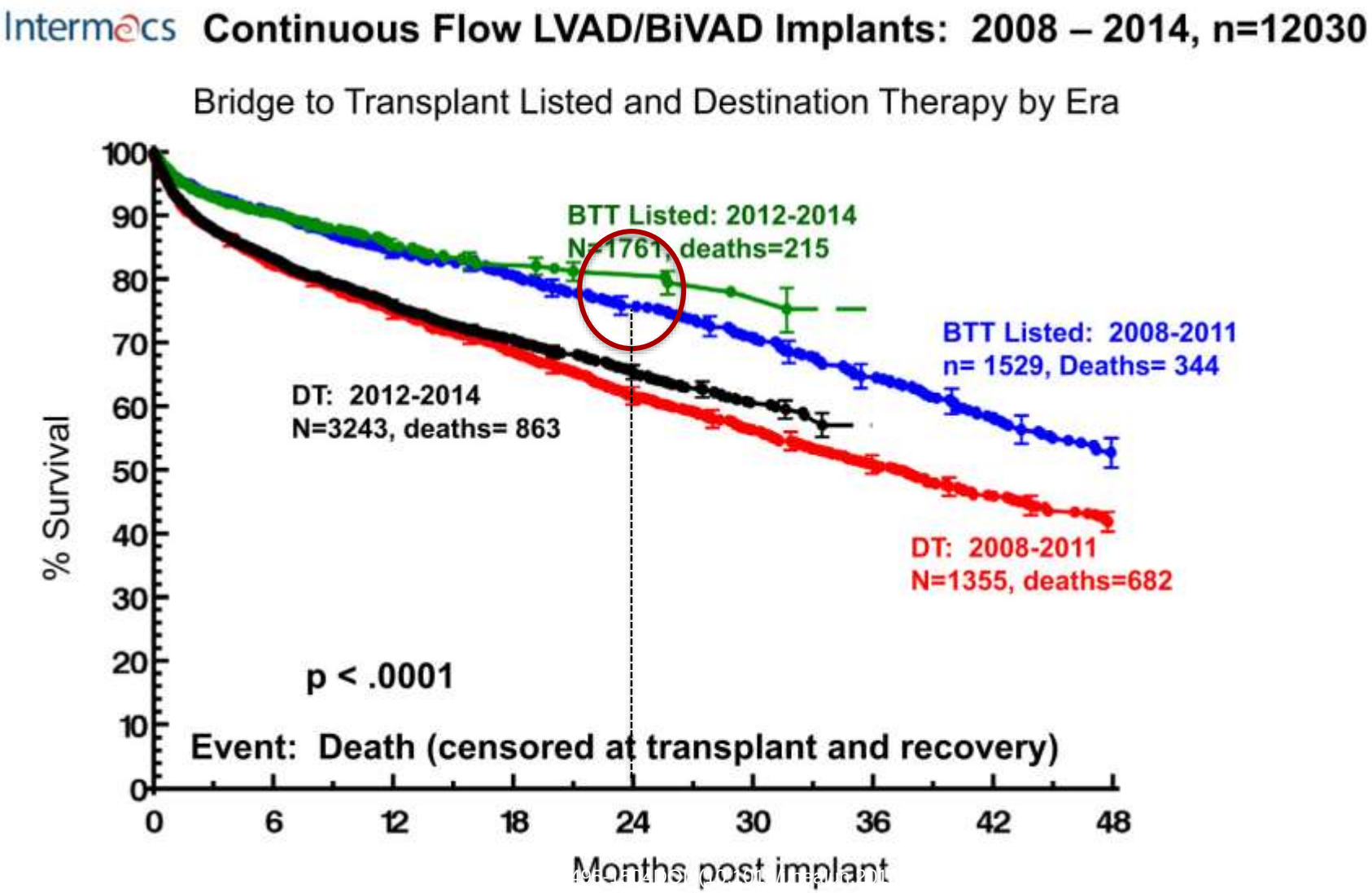
Dlouhodobé MSP v IKEM



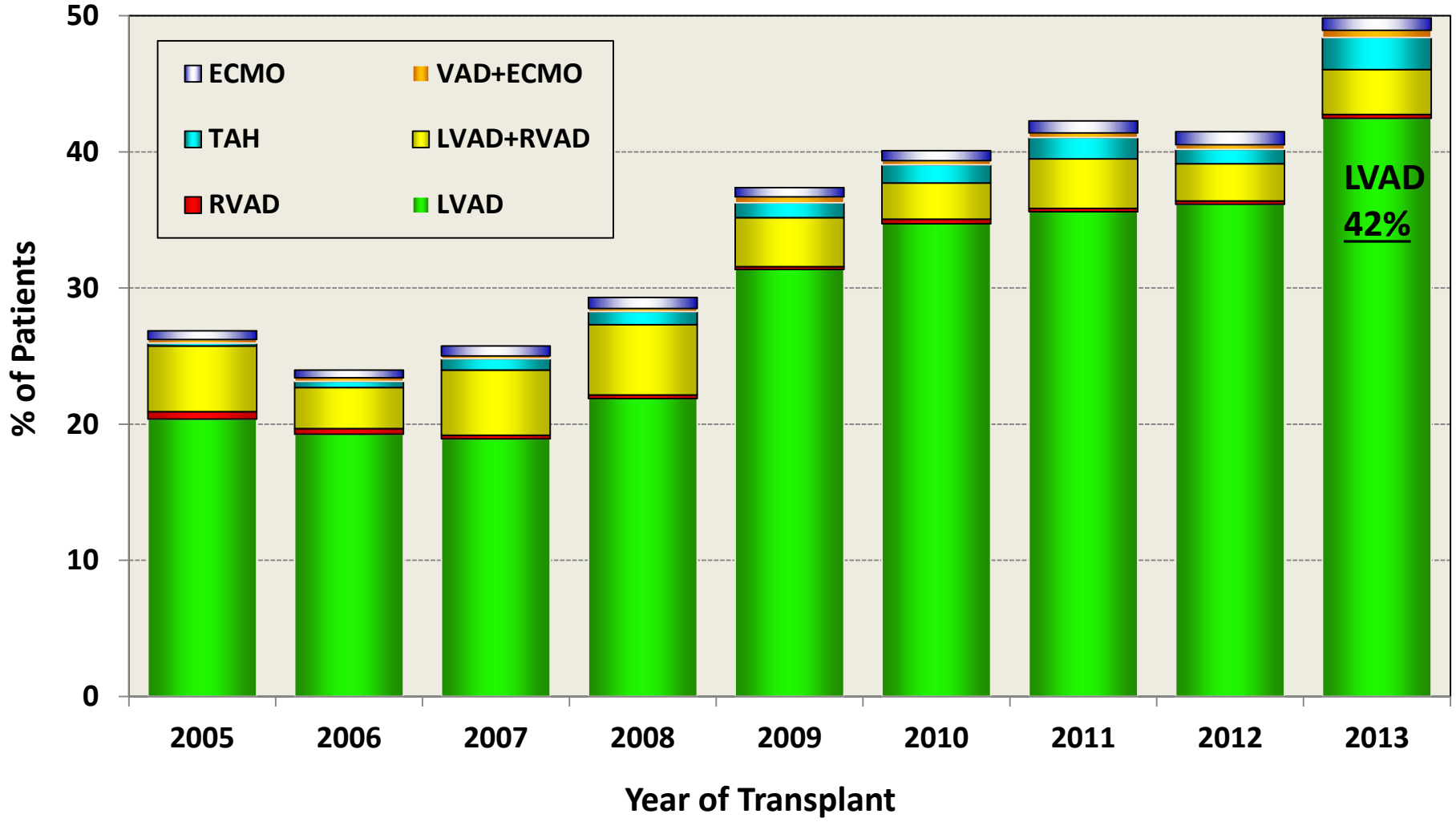
MSP - přemostění k transplantaci



Registr INTERMACS



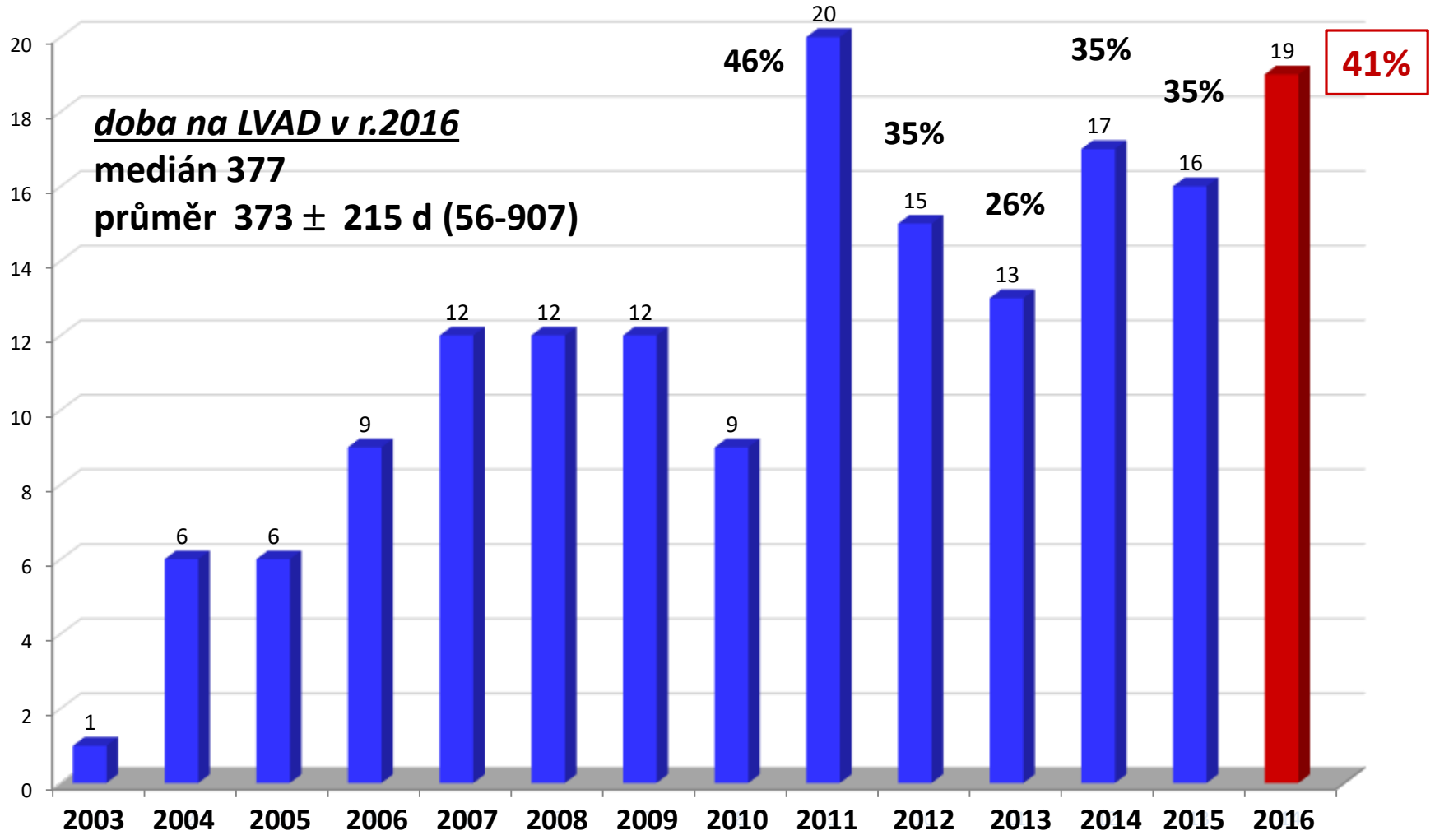
Mechanická podpora v přemostění k TxS



Registry ISHLT J Heart and Lung Transplant 2016; 35: 1158 - 1169

Mechanická srdeční podpora v přemostění k TxS

IKEM (2003 – 2016) n=167



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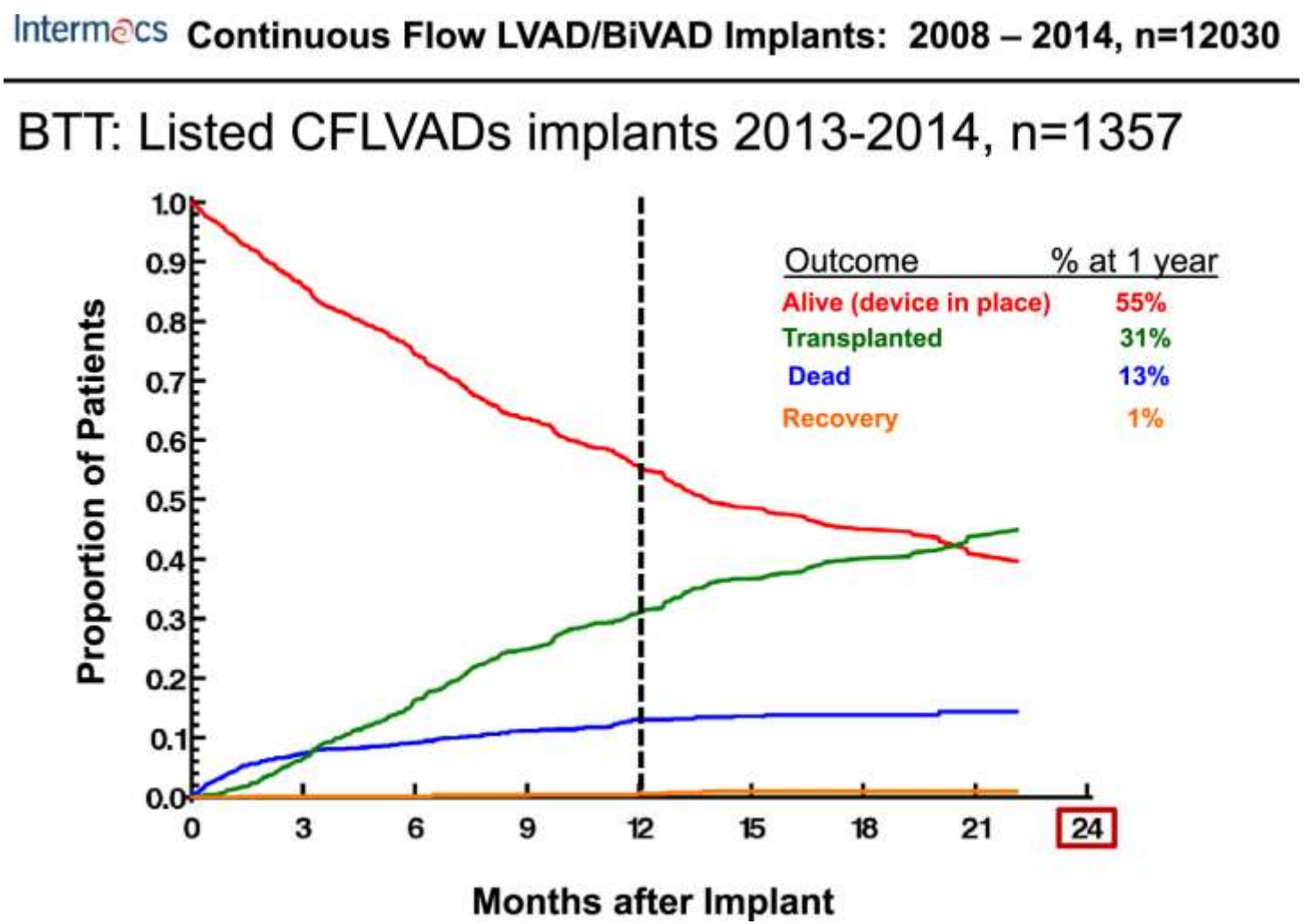
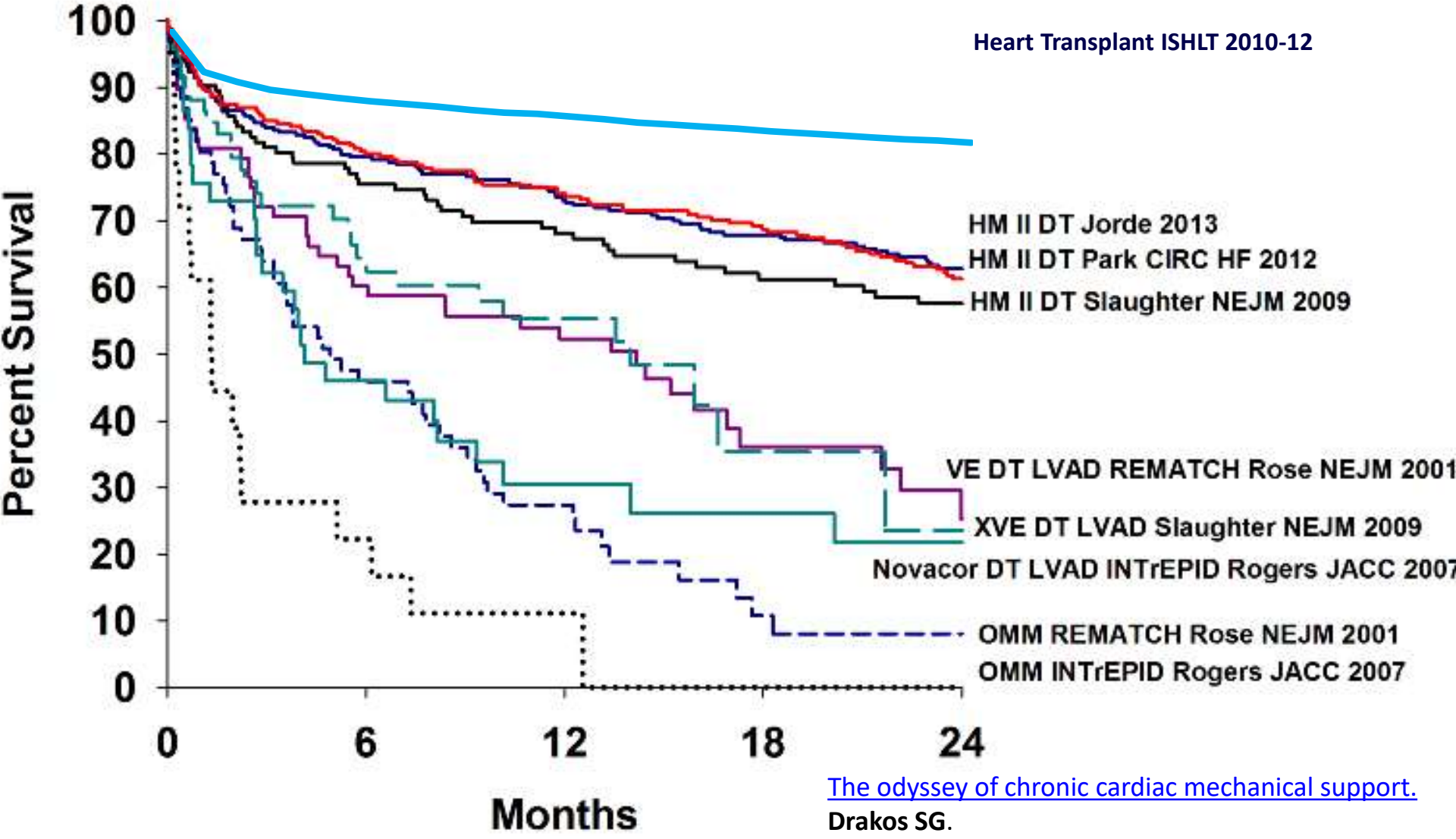


Destinační (permanentní) terapie

Indikace destinační terapie

- Věk pacienta (> 65 let)
- Diabetes mellitus s orgánovými komplikacemi
- Multietážová ateroskleroza
- Těžká obezita
- Excesivní imunosensitizace
- Interval vyléčené malignity < 5let

Pokroky permanentní terapie



The odyssey of chronic cardiac mechanical support.
Drakos SG.
J Am Coll Cardiol. 2014 May 6;63(17):1758-60.

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ORIGINAL INVESTIGATIONS

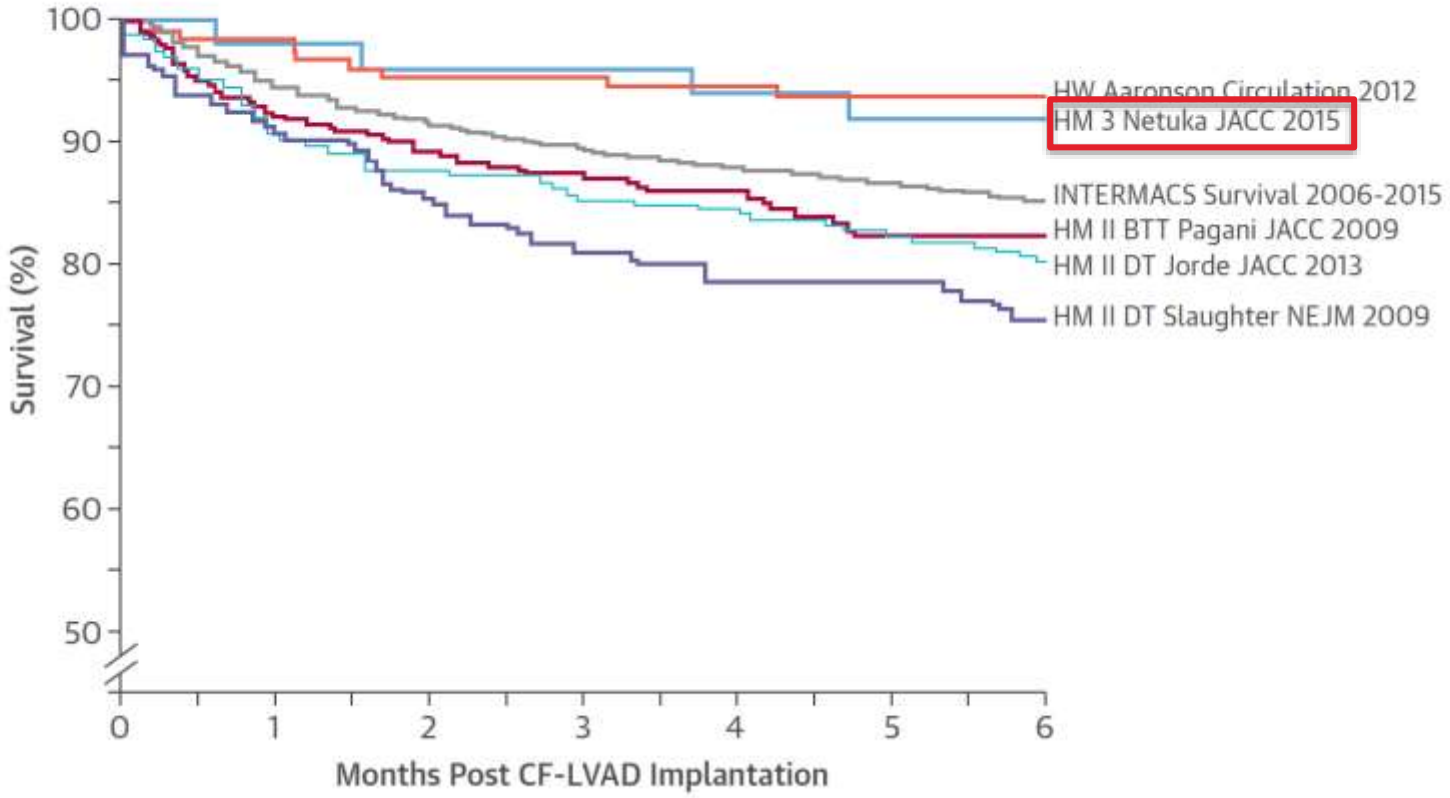
Fully Magnetically Levitated Left Ventricular Assist System for Treating Advanced HF

A Multicenter Study

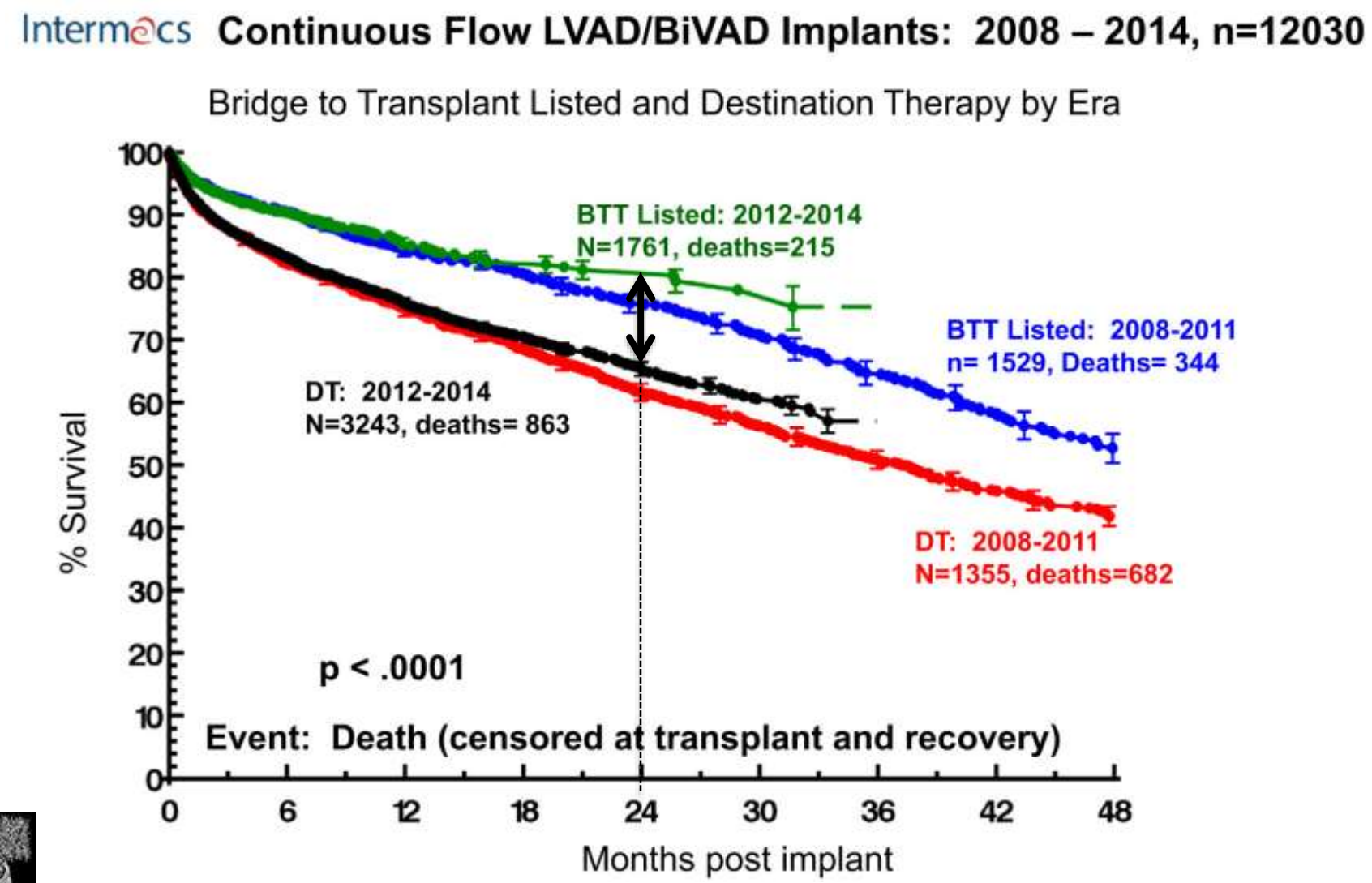
Ivan Netuka, MD, PhD,*† Poornima Sood, MD, MBA,‡ Yuriy Pya, MD,§ Daniel Zimpfer, MD,‖ Thomas Krabatsch, MD, PhD,¶ Jens Garbade, MD, PhD,# Vivek Rao, MD, PhD,** Michiel Morshuis, MD,†† Silvana Marasco, MBBS,‡‡ Friedhelm Beyersdorf, MD,§§ Laura Damme, RN, MPH,‡ Jan D. Schmitto, MD, PhD‖‖

Destinační terapie v IKEM

FIGURE 1 Progressive Improvement in Outcomes of Patients Supported With CF-LVADs for Advanced Heart Failure



Přežívání indikace přemostění k transplantaci a permanentní terapie



Nežádoucí příhody

Adverse Event	Post-approval (N=247)* 385.8 Patient Years		Trial (N=133) 211 Patient Years	
	Patients[1]	Event Rate[2]	Patients[1]	Event Rate[2]
Bleeding requiring PRBC	54%	0.84	81%	1.66
Bleeding: requiring re-exploration	13%	0.09	30%	0.23
Infection: Local non-device related	39%	0.59	49%	0.76
Sepsis	19%	0.18	41%	0.38
Device-related:	19%	0.22	35%	0.47
Cardiac arrhythmias: cardiover/ defib	37%	0.40	56%	0.69
Renal failure	18%	0.15	16%	0.10
Right heart failure*	18%	0.16	23%	0.16
RVAD	2.4%	0.02	3.8%	0.024
Stroke	11.7%	0.083	19%	0.13
Ischemic stroke	4.0%	0.031	8%	0.06
Hemorrhagic stroke	7.7%	0.052	11%	0.07
Hemolysis	6.5%	0.06	3.8%	0.024
Pump thrombosis	3.6%	0.027	3.8%	0.024
Pump replacement	4.0%	0.026	9.0%	0.057

Jorde et al. 2013

[1]Percent of patients
[2]Events per patient year
*Includes extended inotropic support

*Note follow up still in progress

Technologické trendy a novinky

Antikoagulace
Krvácení

⟷

Trombóza
čerpadla

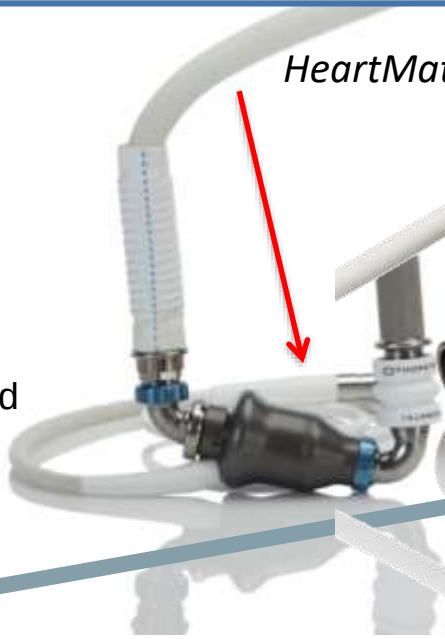
Pulsatile Technology

HeartMate XVE

FDA Approved
BTT 1998
DT 2002

Continuous Flow Technology: Axial Design

HeartMate II



Rotor with bearings

Continuous Flow Technology: Centrifugal Design

HeartMate 3

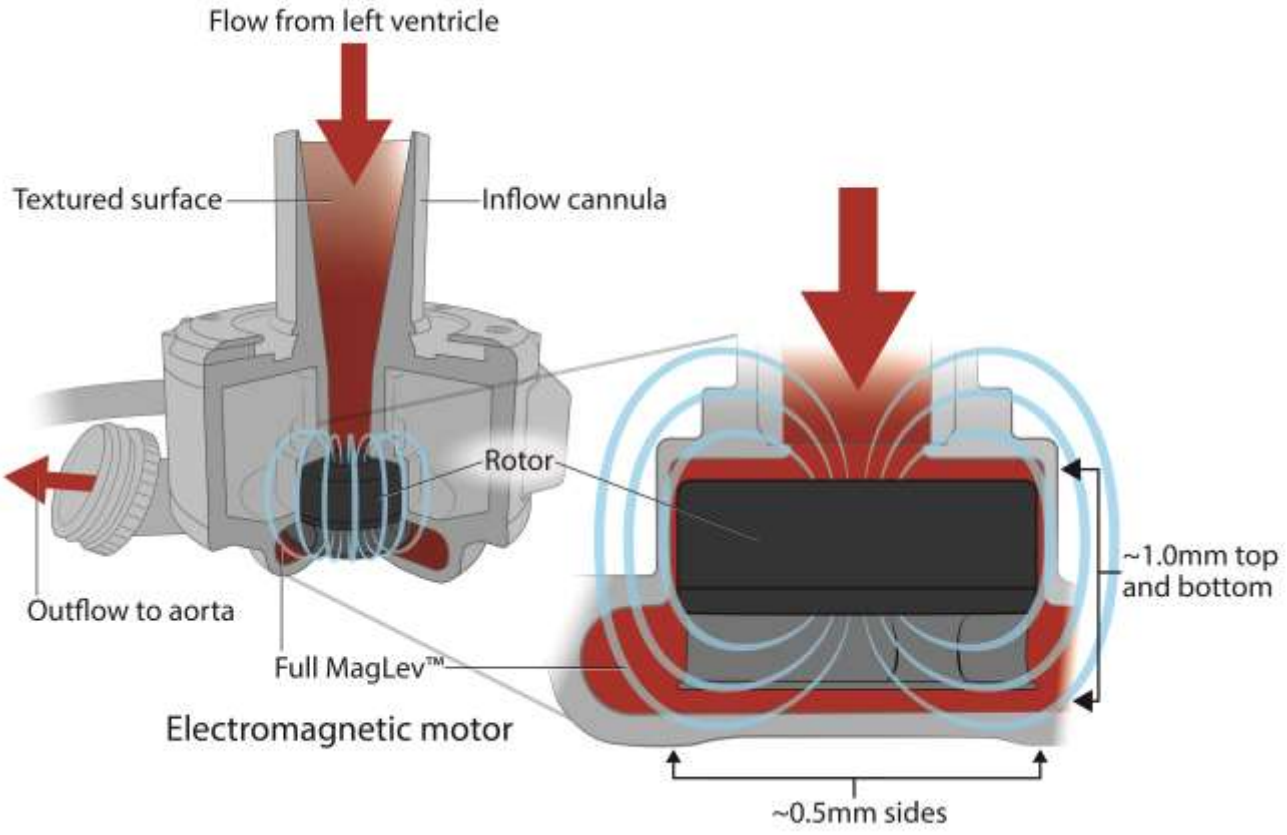
FD
B

Heartware HVAD

aringless rotor with
agnetic Levitation

Pusher plate &
Inflow and outflow valve

Magnetická levitace rotoru
HeartMate 3



Destinační terapie v IKEM

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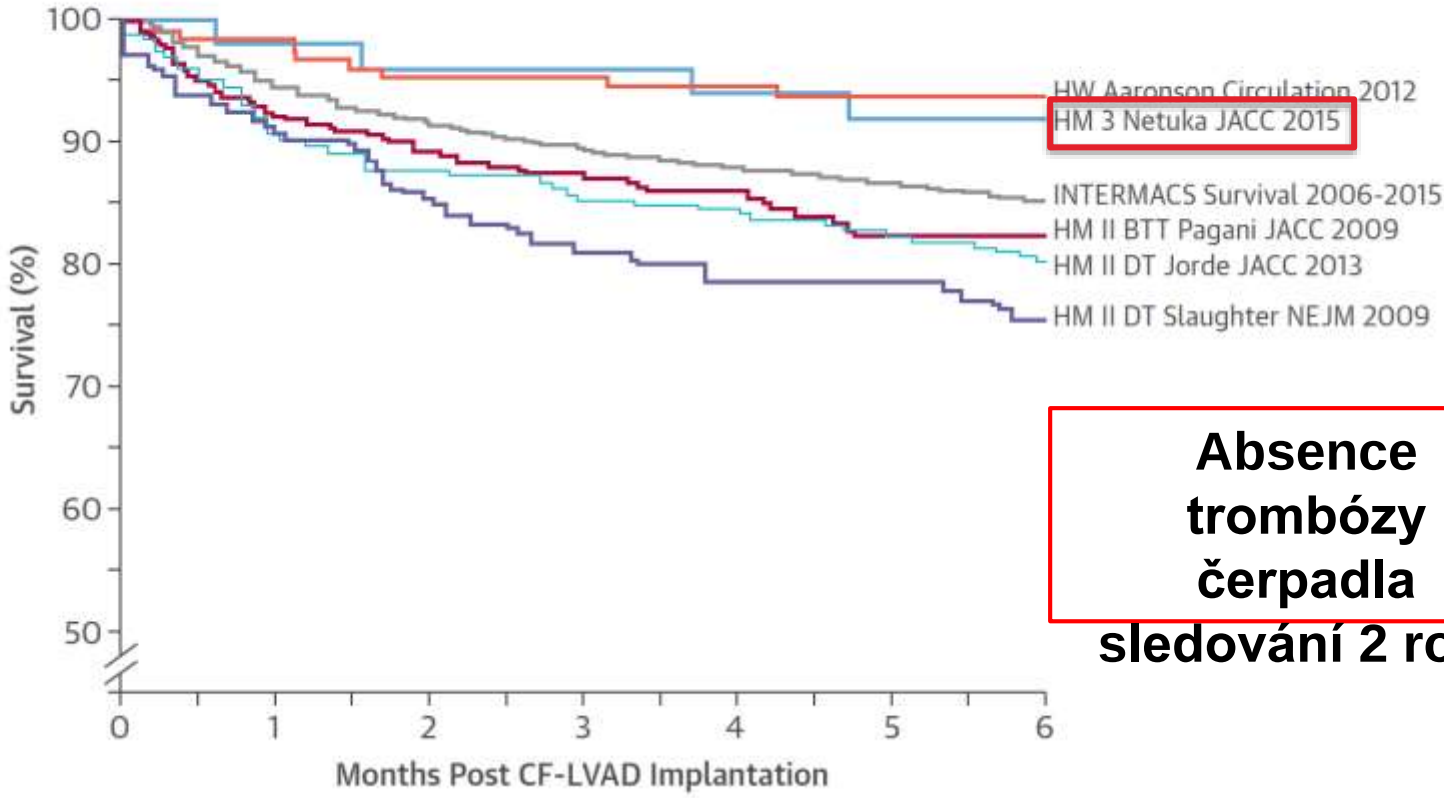


Absence trombózy čerpadla

sledování 2 roky

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

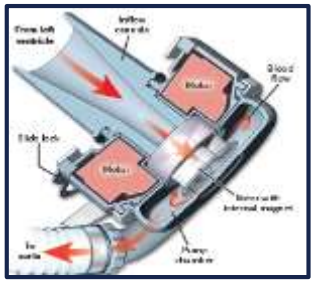
A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure

Mandeep R. Mehra, M.D., Yoshifumi Naka, M.D., Nir Uriel, M.D., Daniel J. Goldstein, M.D., Joseph C. Cleveland, Jr., M.D., Paolo C. Colombo, M.D., Mary N. Walsh, M.D., Carmelo A. Milano, M.D., Chetan B. Patel, M.D., Ulrich P. Jorde, M.D., Francis D. Pagani, M.D., Keith D. Aaronson, M.D., David A. Dean, M.D., Kelly McCants, M.D., Akinobu Itoh, M.D., Gregory A. Ewald, M.D., Douglas Horstmanshof, M.D., James W. Long, M.D., and Christopher Salerno, M.D., for the MOMENTUM 3 Investigators*

Mehra MR, Naka Y, et al. Published Nov 16, 2016 at NEJM.org

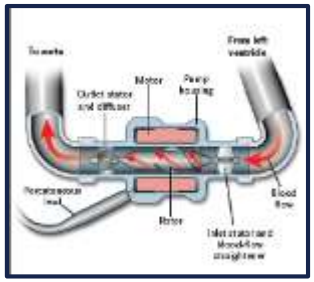
Study Design

HeartMate 3



Patient meets MOMENTUM 3 eligibility criteria?

Randomization 1:1



HeartMate II

Short Term (ST) Cohort
N=294
6-month follow-up

Long Term (LT) Cohort
N=366
24-month follow-up

Full Study Cohort
N=1028
24-month follow-up for powered secondary endpoint

Intent-to-Treat (ITT) Population
N=294

HeartMate 3
N=152

HeartMate II
N=142

Treatment failures
(not treated with study device)
N=1

Death: 1

Treatment failures
(not treated with study device)
N=4

No LVAD implant: 1
Withdrawal of consent: 1
Transplant: 1
Implanted with non-study LVAD: 1

As Treated Population
N=289

Implanted with HeartMate 3
N=151

Implanted with HeartMate II
N=138

Primární cíl studie

- Přežití v 6 měsících bez závažné mozkové příhody (modifikované Rankin skóre >3) nebo nutnosti reoperace k výměně čerpadla pro trombózu

Předimplantační charakteristiky I

Characteristic	HeartMate 3 (n=152)	HeartMate II (n=142)
Age - years		
Mean	60 ± 12	59 ± 12
Median (range)	64 (19 - 81)	61 (24 - 78)
Male sex - no. (%)	121 (80)	114 (80)
Race – no. (%)		
White	104 (68)	107 (75)
Black or African American	37 (24)	24 (17)
Other*	11 (8)	11 (8)
Body surface area - m^2	2.1 ± 0.3	2.1 ± 0.3
Ischemic cause of heart failure - no. (%)	68 (45)	72 (51)
History of stroke - no. (%)	12 (8)	14 (10)
Concomitant medication or intervention - no (%)		
Intravenous inotropic agents	132 (87)	121 (85)
Diuretics**	134 (88)	136 (96)
ACE inhibitor	37 (24)	38 (27)
Angiotensin II -receptor antagonist	10 (7)	18 (13)
Beta blocker	91 (60)	79 (56)
CRT/CRT-D	59 (39)	51 (36)
ICD/CRT-D	101 (66)	100 (70)
IABP	18 (12)	21 (15)

*Other: includes Asian, Native Hawaiian or Pacific Islanders and patient who refused to provide race
**Diuretic use was statistically significant (P=0.02)

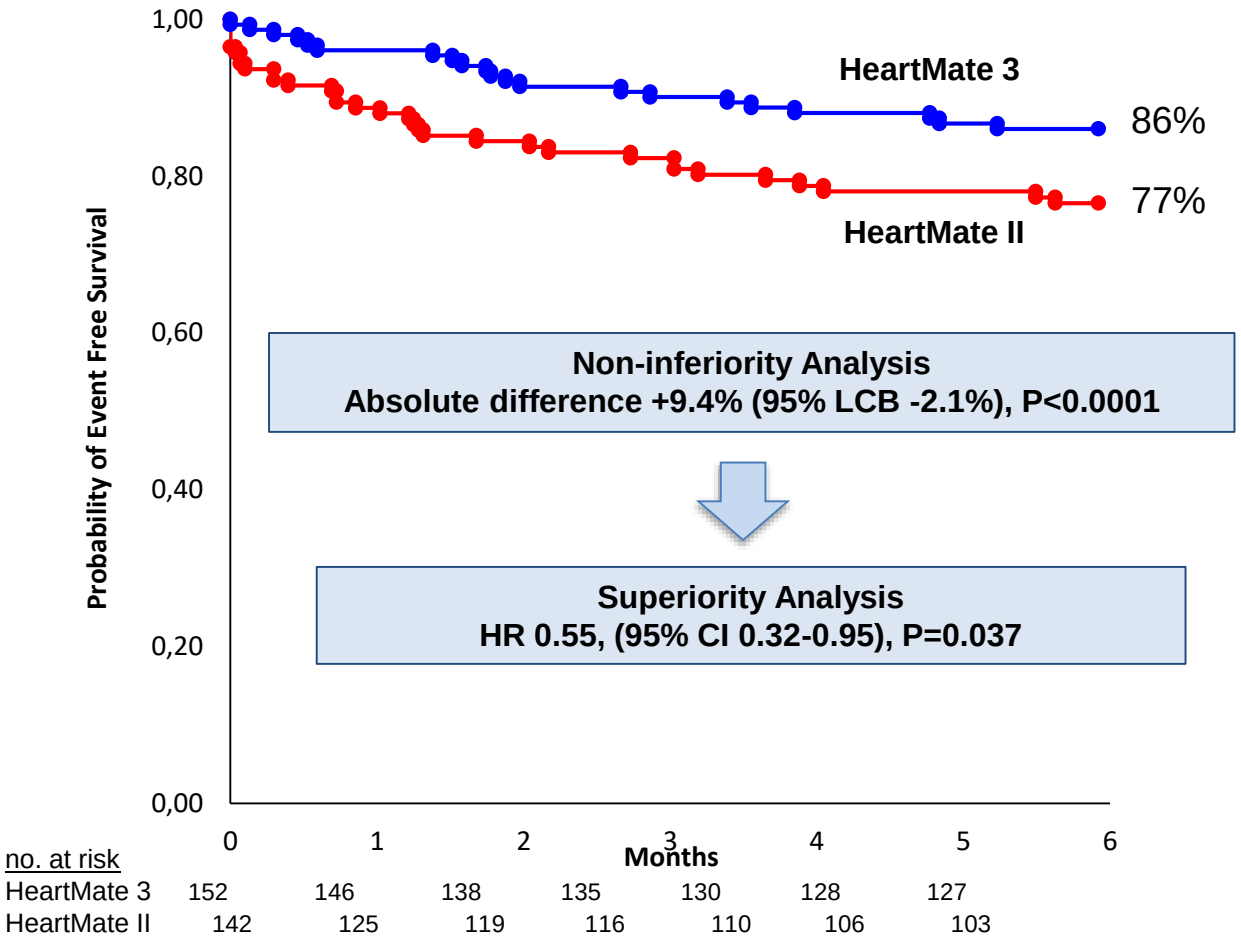
Předimplantační charakteristiky II

Characteristic	HeartMate 3 (n=152)	HeartMate II (n=142)
Left ventricular ejection fraction - %	17.1 ± 5.0	17.3 ± 4.9
Arterial blood pressure - mmHg		
Systolic*	110 ± 16	106 ± 12
Diastolic	67 ± 10	66 ± 10
Mean arterial pressure* - mmHg	81 ± 10	79 ± 9
PCWP - mmHg	23 ± 9	22 ± 9
Cardiac index - liters/min/m^2 of body surface area	1.9 ± 0.5	2.0 ± 0.7
PVR - Wood Units	3.3 ± 1.7	3.0 ± 1.6
Right atrial pressure - mmHg	10 ± 6	11 ± 7
Serum sodium - mmol/liter	135.6 ± 3.9	134.9 ± 4.2
Serum creatinine - mg/ml	1.4 ± 0.4	1.4 ± 0.4
INTERMACS Profile** – no (%)		
1	1 (1)	4 (3)
2	50 (33)	44 (31)
3	76 (50)	69 (49)
4	22 (14)	23 (16)
5-7†	2 (1)	2 (1)
Intended Use of device at implant – no (%)		
Bridge to Transplant (BTT)	41 (27)	37 (26)
Bridge to Candidacy	27 (18)	27 (18)
Destination Therapy (DT)	84 (55)	78 (55)

* Systolic blood pressure (P= 0.01) and Mean arterial pressure (P=0.04) were statistically significantly;
** one subject in HM3 group expired prior to INTERMACS Assessment;
† There were no subjects with INTERMACS 6 and 7 in either groups; PCWP denotes pulmonary capillary wedge pressure and PVR pulmonary vascular resistance

Primární cíl studie

Survival at 6 months free of disabling stroke or reoperation to replace or remove the pump



LCB, lower confidence boundary, HR, hazard ratio, and CI, confidence interval

Klíčové nežádoucí příhody

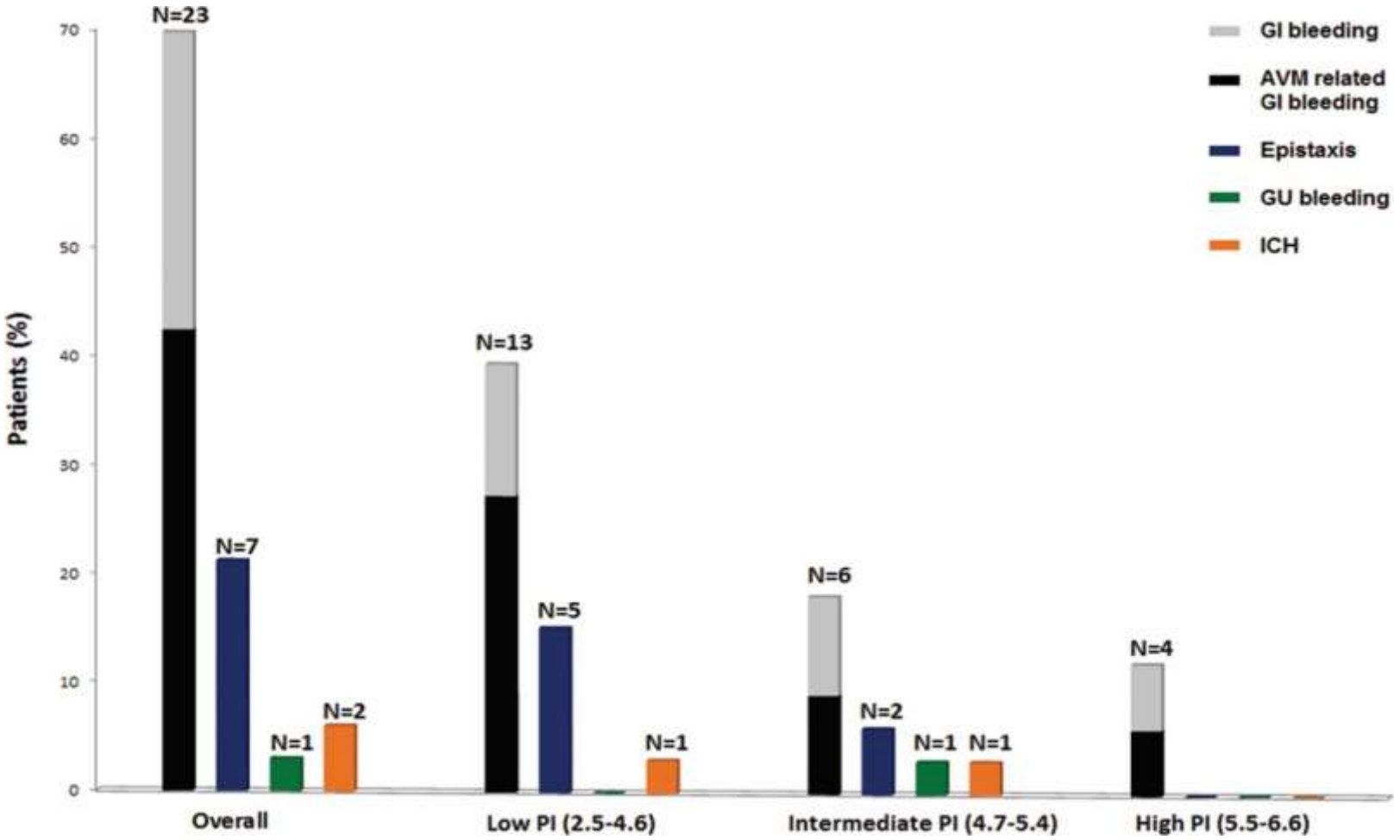
	HeartMate 3 (n=151)		HeartMate II (n=138)				
	n (%)	no. of Events	n (%)	no. of Events	RR	95% CI for RR	P Value
Suspected or Confirmed Pump Thrombosis	**0 (0)**	**0**	**14 (10)**	**18**	**N/A**	**N/A**	**< 0.0001**
All Stroke	12 (7)	12	15 (10)	17	0.73	0.35-1.51	0.39
Hemorrhagic Stroke	4 (2)	4	8 (5)	8	0.46	0.14-1.48	0.18
Ischemic Stroke	8 (5)	8	9 (6)	9	0.81	0.32-2.05	0.66
Disabling Stroke	9(6)	9	5(3)	5	1.65	0.57-4.79	0.36
Other Neurologic Events*	9 (6)	9	8 (5)	8	1.03	0.41-2.59	0.95
Bleeding	50 (33)	100	54 (39)	98	0.85	0.62-1.15	0.29
Bleeding Requiring Surgery	15 (9)	15	19 (13)	21	0.72	0.38-1.36	0.31
Gastrointestinal Bleeding	**24 (15)**	**47**	**21 (15)**	**36**	**1.04**	**0.61-1.79**	**0.87**

Úplná absence trombózy u HeartMate 3
Shodný výskyt krvácivých komplikací

RR, denotes Relative Risk and CI, confidence interval
*Includes transient ischemic attacks and neurologic events other than stroke

Pulsatility and the Risk of Nonsurgical Bleeding in Patients Supported With the Continuous-Flow Left Ventricular Assist Device HeartMate II

Omar Wever-Pinzon, MD; Craig H. Selzman, MD; Stavros G. Drakos, MD, PhD; Abdulfattah Saidi, MD; Gregory J. Stoddard, MPH; Edward M. Gilbert, MD; Mohamed Labedi, MD; Bruce B. Reid, MD; Erin S. Davis, RN, BSN; Abdallah G. Kfoury, MD; Dean Y. Li, MD, PhD; Josef Stehlik, MD, MPH; Feras Bader, MD, MS



Wever-Pinzon et al. Circ Heart Fail. 2013 May;6(3):517-26.

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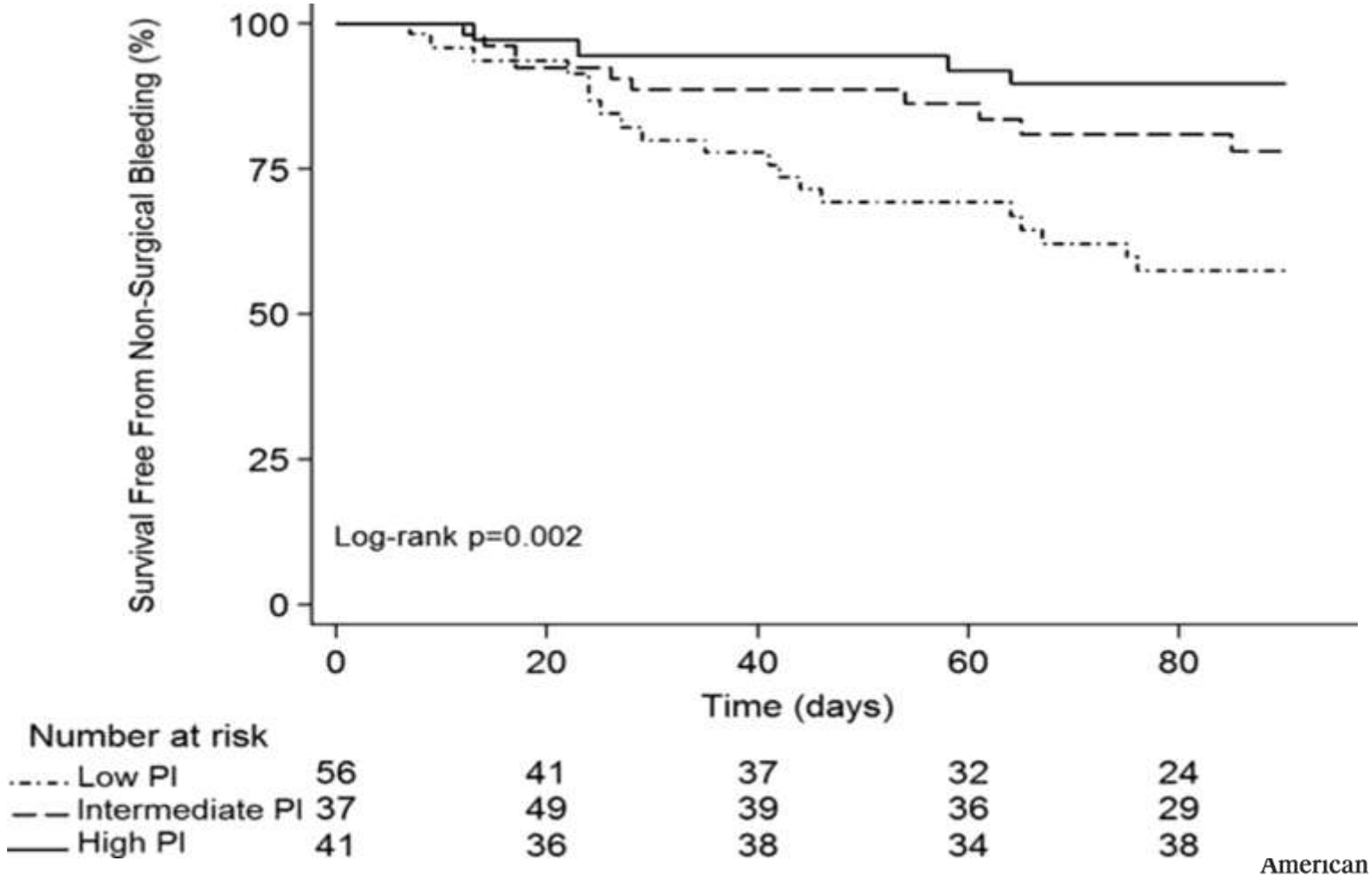
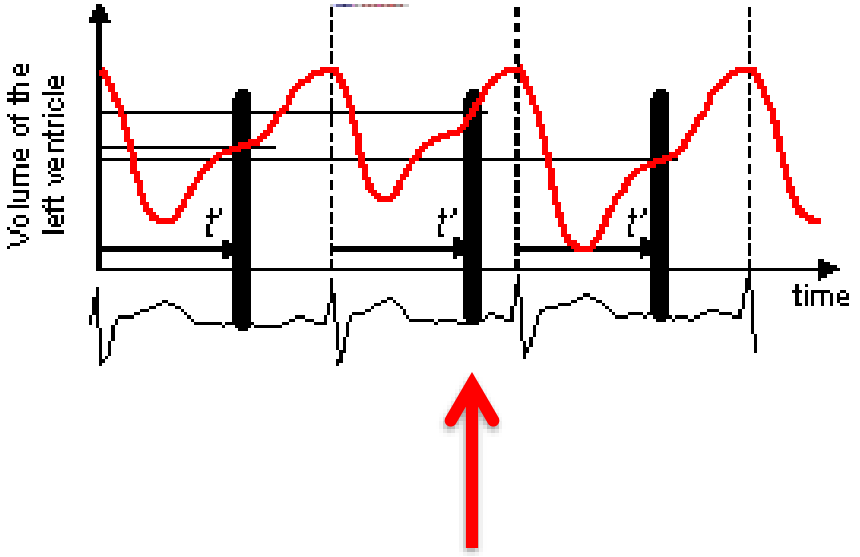
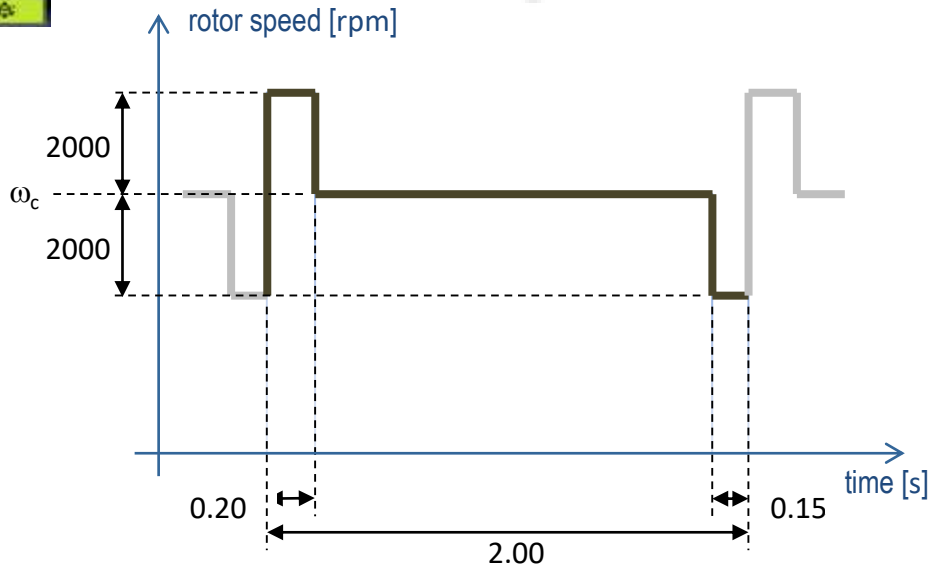
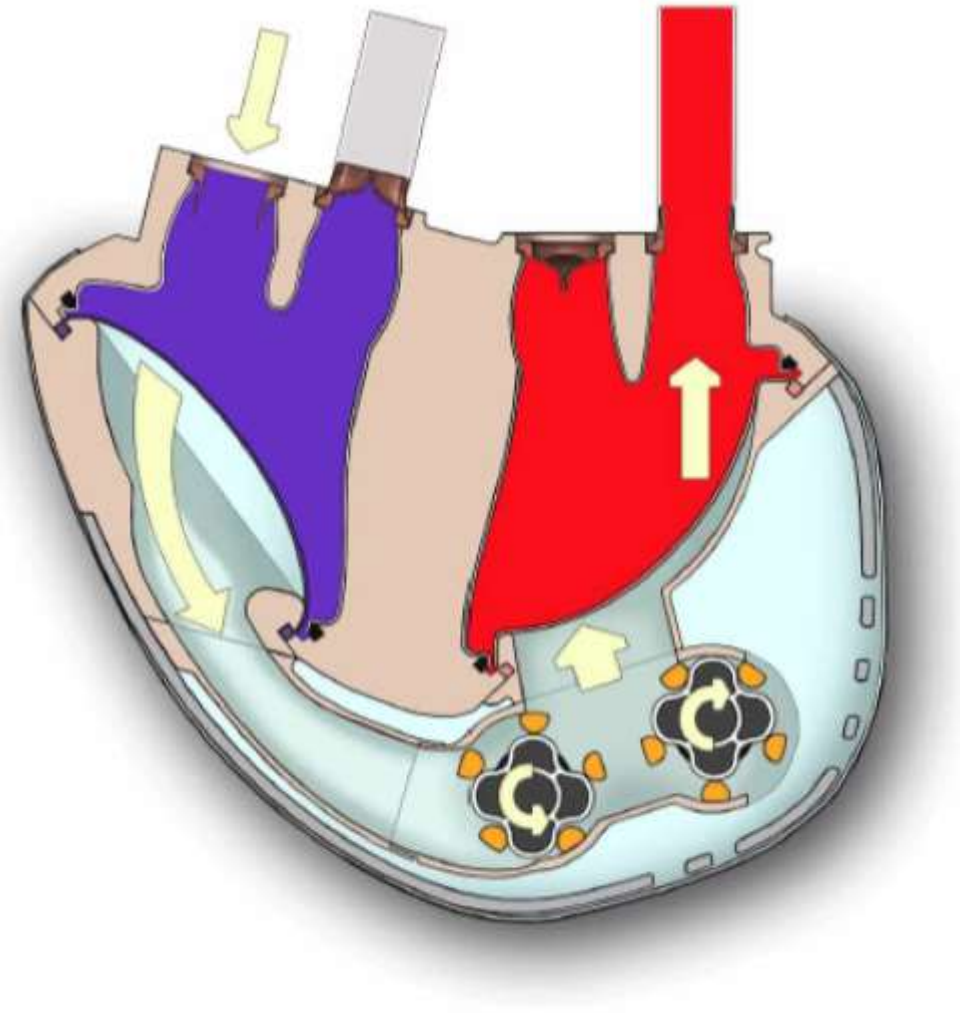


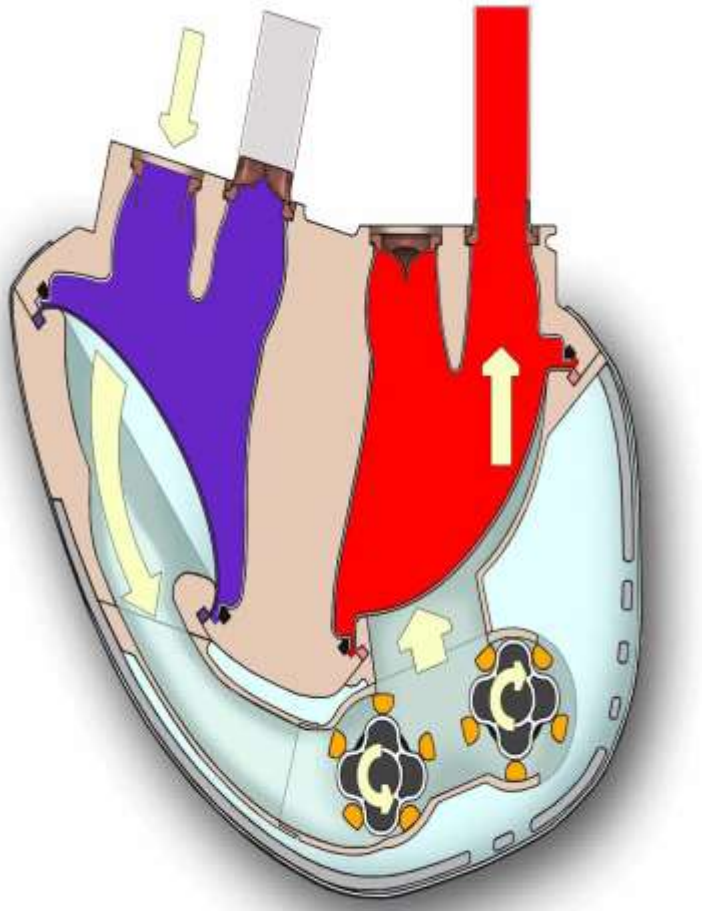
Limitace pulsatility rotačních čerpadel

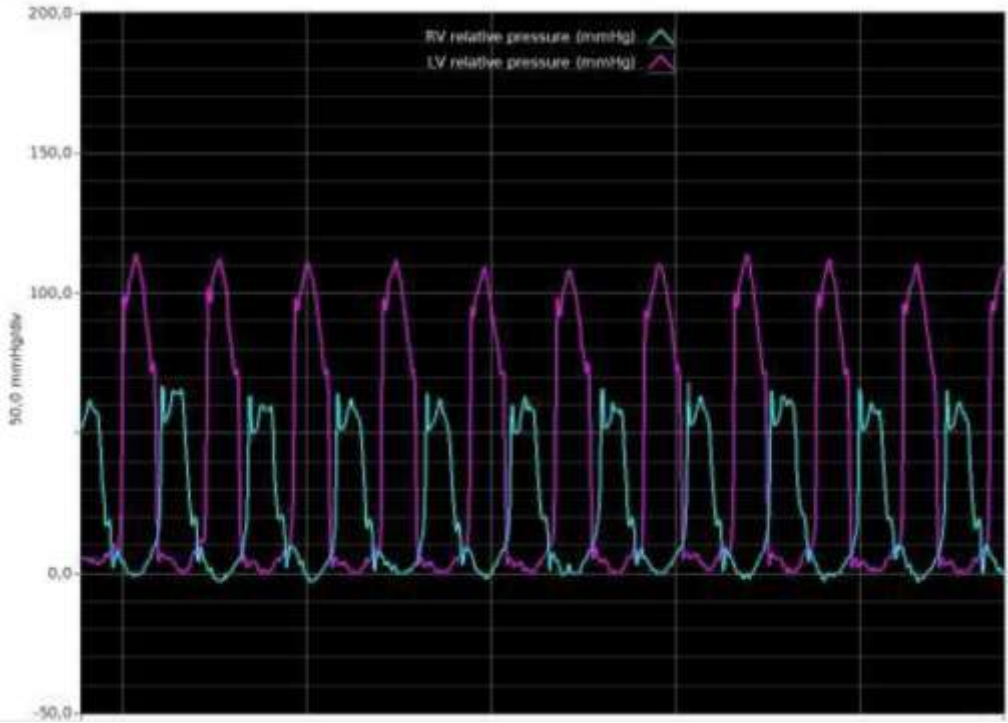


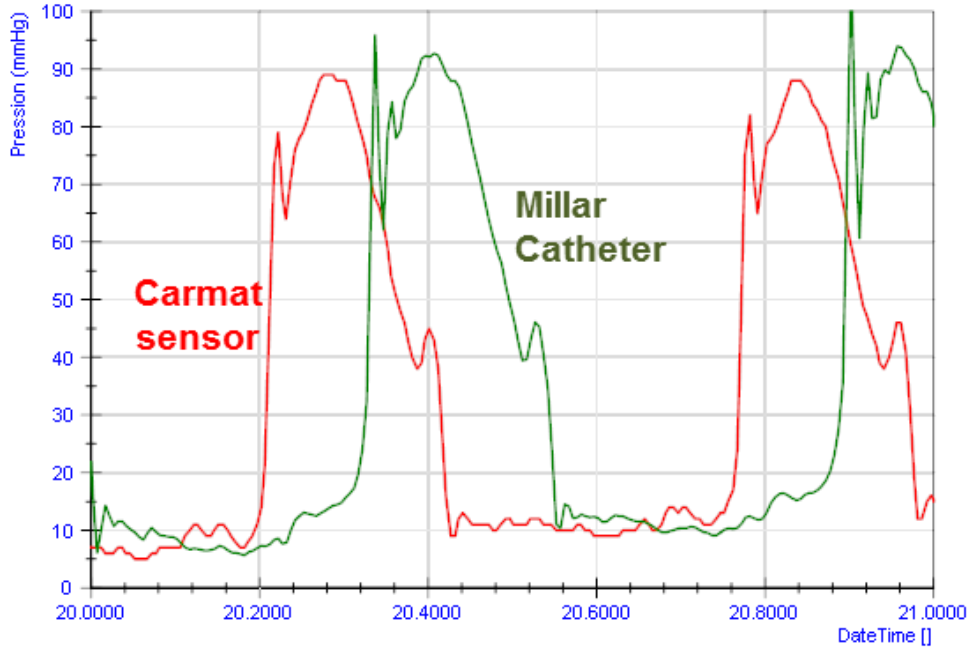


Pulsatilní biokompatibilní TAH






RV relative pressure (mmHg)
LV relative pressure (mmHg)
200,0
150,0
100,0
50,0 mmHg/div
0,0
-50,0


Pression (mmHg)
100
90
80
70
60
50
40
30
20
10
0
Carmat sensor
Millar Catheter
20.0000
20.2000
20.4000
20.6000
20.8000
21.0000
DateTime []

Závěry

- Integrální součást programu transplantace srdce
- Efektivní alternativa pro nemocné za hranicí indikace k transplantaci i v České republice
- Technologické inovace snižují výskyt klíčových komplikací – revize paradigmatu pulsatility?
- Nová alternativa destinace i pro pokročilé biventrikulární selhání
- Komplexní a včasná indikace

IKEM