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Úloha MRI v detekci vaskulopatie štěpu u pacientů po srdeční transplantaci

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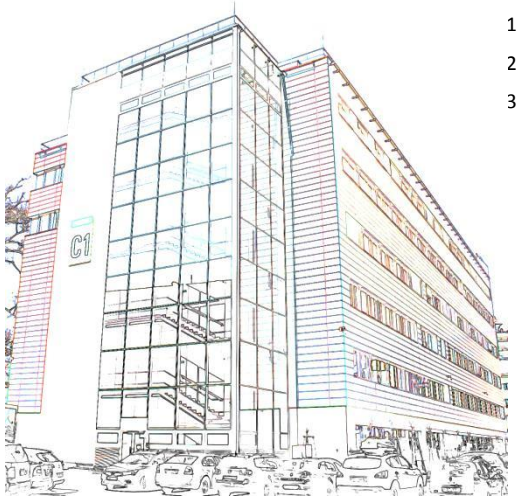

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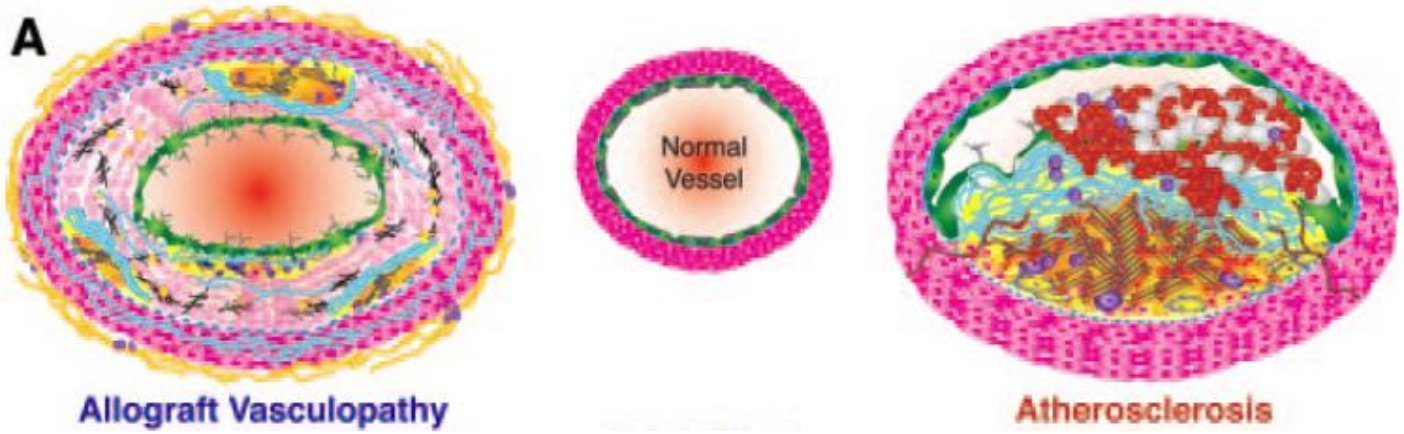
Vaskulopatie štěpu neboli Cardiac allograft vasculopathy (CAV)

- Koncentrická fibrózní hyperplazie intimy
- Imunologické a neimunologické faktory
- Rizikové faktory: hyperlipidémia, věk, mužské pohlaví, obezita, diabetes, příčina srdečního selhání (ICHS), ischemicko – reperfuzní poškození

Ramzy D., Can J Surg 2005
Olmetti F., J Heart Lung Transplant 2011
Chih et al, JAAC 2016



Allograft Vasculopathy	Atherosclerosis
(1) Epicardial and intramural arteries are involved	(1) Major epicardial muscular arteries are involved
(2) Veins can also be involved. The only vessels relatively unaffected are those with little or no muscular layer	(2) Largely affects the proximal epicardial coronary arteries. There is usually sparing of the intramyocardial vessels and arteries under muscular bridges
(3) Diffuse and very extensive vessel involvement	(3) Veins are never involved
(4) Affects the proximal and distal epicardial vessels, as well as their branches	(4) Three layers, intima, media and adventitia, are involved
(5) The media can be unaffected or almost completely replaced by fibrous tissue. As the intimal disease progresses in severity so does fibrosis of the media and adventitia.	
(6) A disease of the intima, media, and adventitia	
(1) Diffuse, concentric intimal thickening	(1) Focal, eccentric proliferative, and degenerative lesions of the intima of proximal coronary vessels
(2) Ranges from concentric, diffuse, intimal lesions to advanced fibrofatty plaques with degeneration	(2) Mostly fibrofatty plaques with ultimate necrotic coves and progressively thinned fibrous cap
(1) The initial lesions are SMC proliferation in the intima and accumulation of extracellular lipids	(1) Fatty streaks are seen initially
(2) Accelerated progression of intimal proliferation and luminal stenosis during the early phase of the disease, with foam cell development	(2) Slow progression of lesion development (decades)
(3) Surface endothelial erosion is not characterized in this setting but may be a rare finding	(3) Surface endothelial erosion is seen
(4) Fibrous cap thinning and plaque rupture is a rare finding until late in the disease	(4) Thin fibrous cap and plaque rupture are frequently seen in intermediate to advanced lesions

Rahmani et al. Circ. Res. 2006

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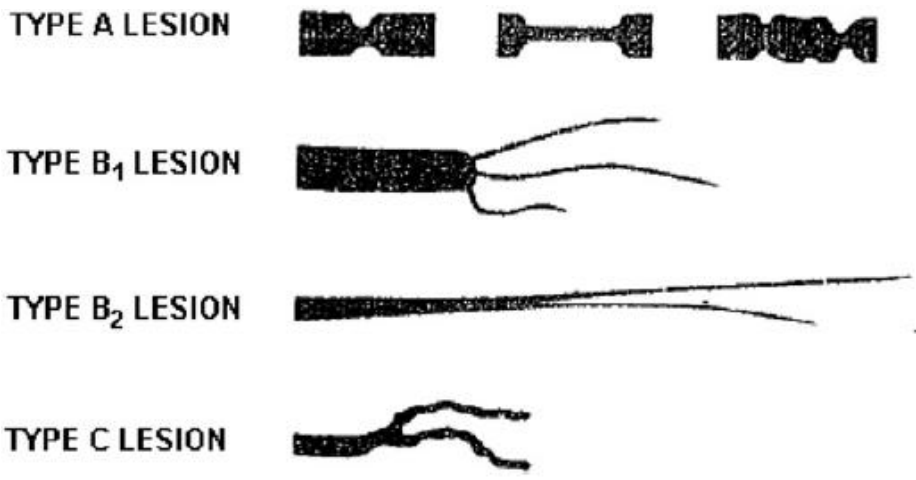
ISHLT klasifikace vaskulopatie

TABLE 1 ISHLT Recommended Nomenclature for CAV

Classification	Severity	Definition
CAV_0	Nonsignificant	No detectable angiographic lesion
CAV_1	Mild	Angiographic LM <50% or Primary vessel with maximum lesion <70% or Branch stenosis <70%
CAV_2	Moderate	Angiographic LM <50%, Single primary vessel ≥70% or Isolated branch stenosis in 2 systems ≥70%
CAV_3	Severe	Angiographic LM ≥50% or ≥2 primary vessel ≥70% or Isolated branch stenosis in all 3 systems ≥70% or CAV_1 or CAV_2 with allograft dysfunction (LVEF ≤45%) or evidence of significant restrictive physiology

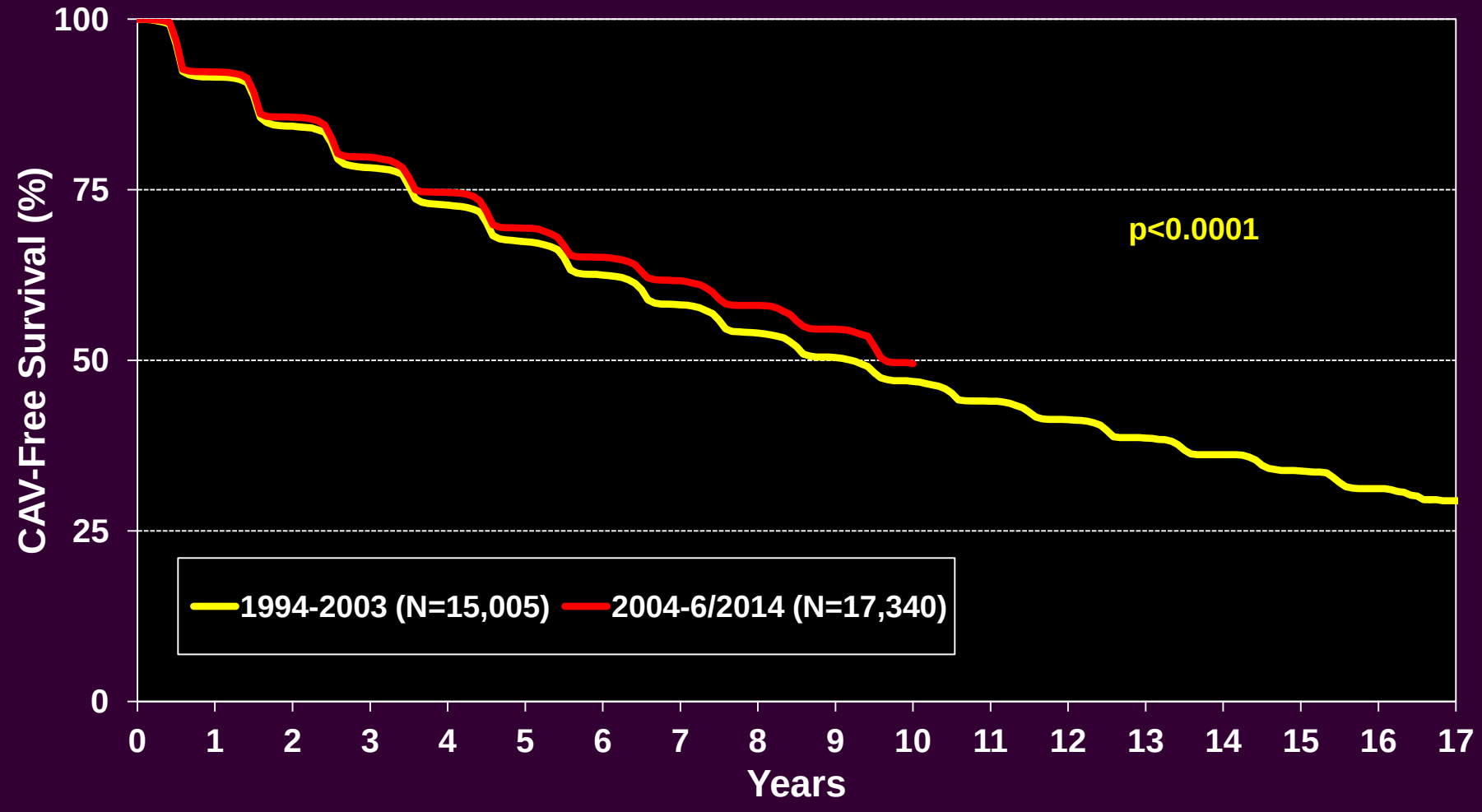


J Heart Lung Transplant 2010

Adult Heart Transplants

Cardiac Allograft Vasculopathy-Free Survival by Era

(Transplants: January 1994 – June 2014)



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2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Cause of Death (Deaths: January 1994 – June 2015)

Cause of Death	0-30 Days (N=6,238)	31 Days - 1 Year (N=5,370)	>1-3 Years (N=3,861)	>3-5 Years (N=3,347)	>5-10 Years (N=8,557)	>10-15 Years (N=5,997)	>15 Years (N=4,053)
Cardiac Allograft Vasculopathy	84 (1.3%)	187 (3.5%)	456 (11.8%)	448 (13.4%)	1,125 (13.1%)	768 (12.8%)	442 (10.9%)
Acute Rejection	272 (4.4%)	500 (9.3%)	393 (10.2%)	164 (4.9%)	167 (2.0%)	56 (0.9%)	25 (0.6%)
Lymphoma	2 (0.0%)	59 (1.1%)	92 (2.4%)	110 (3.3%)	298 (3.5%)	169 (2.8%)	95 (2.3%)
Malignancy, Other	3 (0.0%)	127 (2.4%)	466 (12.1%)	644 (19.2%)	1,821 (21.3%)	1,264 (21.1%)	769 (19.0%)
CMV	3 (0.0%)	55 (1.0%)	19 (0.5%)	6 (0.2%)	7 (0.1%)	4 (0.1%)	0
Infection, Non-CMV	835 (13.4%)	1,671 (31.1%)	500 (13.0%)	344 (10.3%)	909 (10.6%)	651 (10.9%)	489 (12.1%)
Graft Failure	2,510 (40.2%)	927 (17.3%)	1012 (26.2%)	781 (23.3%)	1,622 (19.0%)	1,043 (17.4%)	703 (17.3%)
Technical	456 (7.3%)	84 (1.6%)	28 (0.7%)	27 (0.8%)	92 (1.1%)	73 (1.2%)	49 (1.2%)
Other	272 (4.4%)	365 (6.8%)	304 (7.9%)	256 (7.6%)	670 (7.8%)	393 (6.6%)	305 (7.5%)
Multiple Organ Failure	1,110 (17.8%)	856 (15.9%)	229 (5.9%)	197 (5.9%)	592 (6.9%)	502 (8.4%)	383 (9.4%)
Renal Failure	29 (0.5%)	50 (0.9%)	53 (1.4%)	105 (3.1%)	470 (5.5%)	486 (8.1%)	394 (9.7%)
Pulmonary	181 (2.9%)	206 (3.8%)	158 (4.1%)	150 (4.5%)	381 (4.5%)	266 (4.4%)	180 (4.4%)
Cerebrovascular	481 (7.7%)	283 (5.3%)	151 (3.9%)	115 (3.4%)	403 (4.7%)	322 (5.4%)	219 (5.4%)
Total Deaths (N)	7,189	6,194	4,754	4,227	11,349	8,708	6,068

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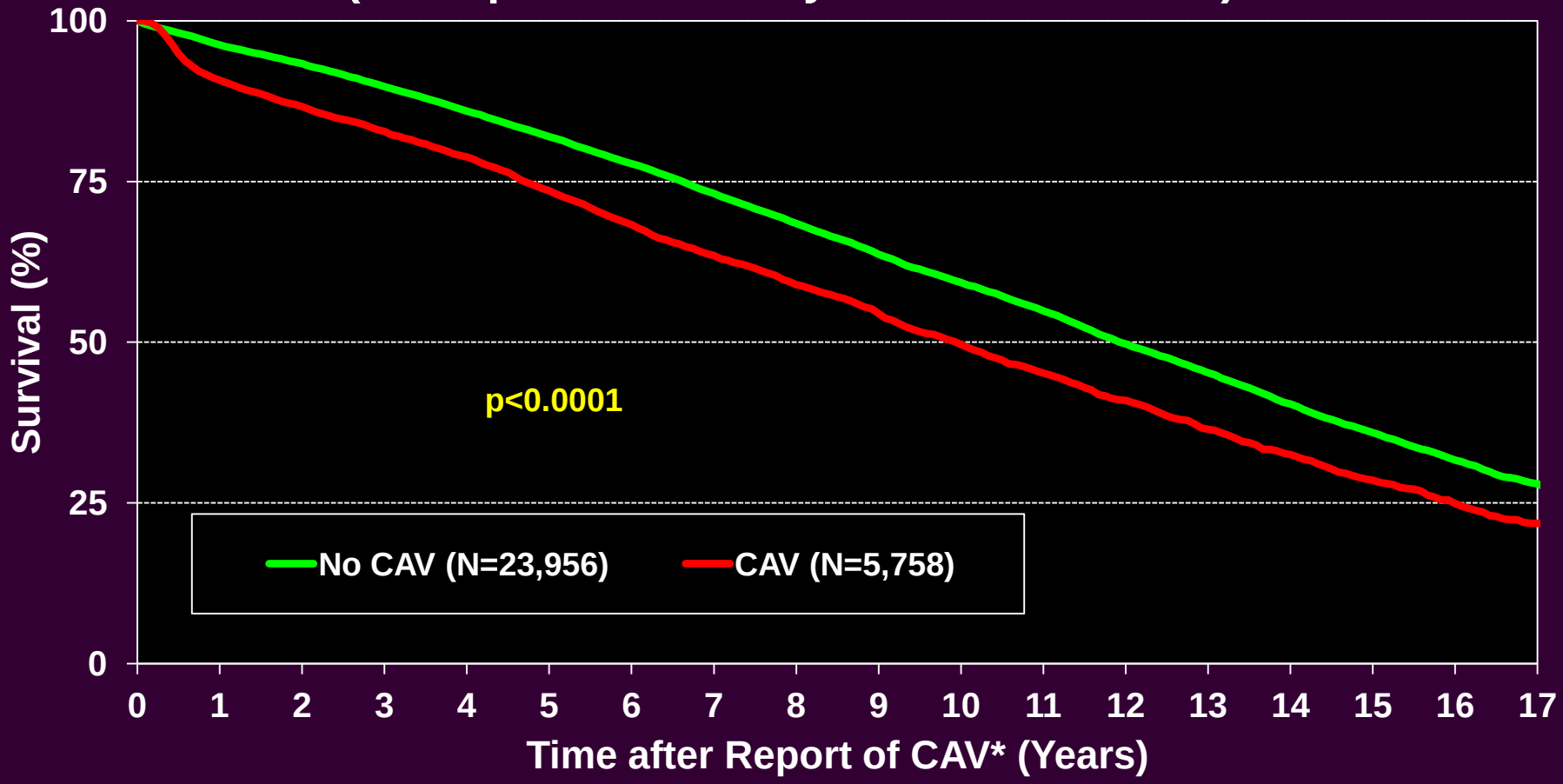
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Percentages represent % of deaths in the respective time period. Total number of deaths includes deaths with unknown causes.

Adult Heart Transplants

Survival After Report of CAV Within 3 Years of Transplant and Survival In Patients Without CAV*

(Transplants: January 1994 – June 2014)



*** Patient survival for those without CAV within 3 years after transplant was conditioned on survival to median time of CAV development (527 days). Median time to CAV development is based on patients who developed CAV within 3 years of transplant.**

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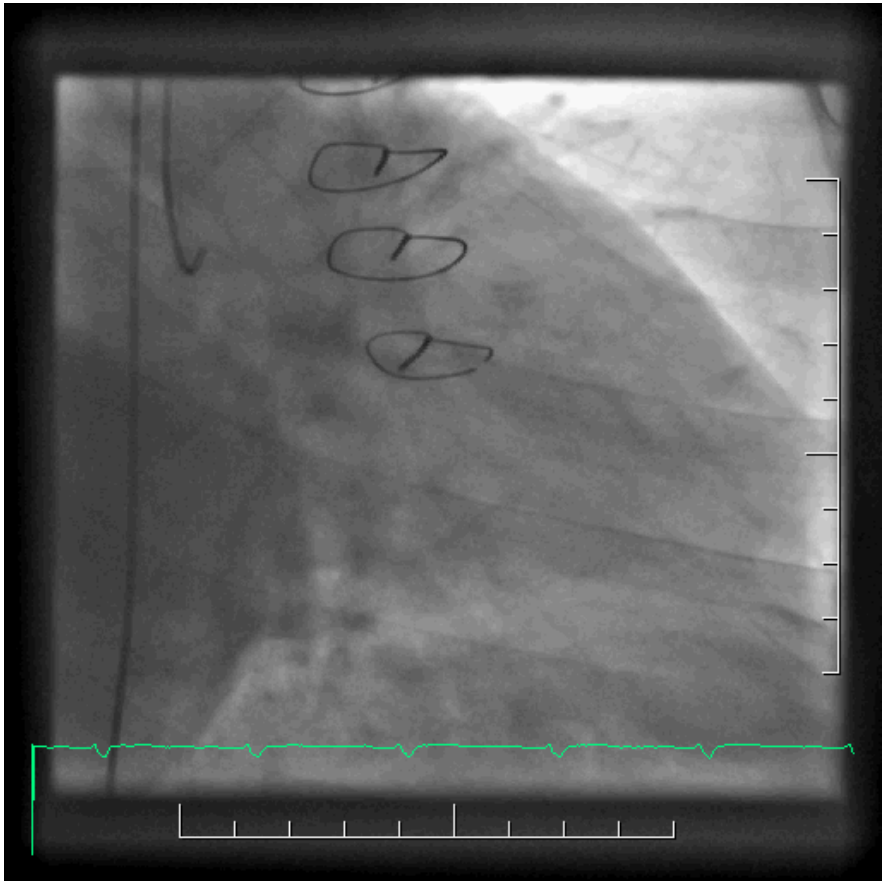
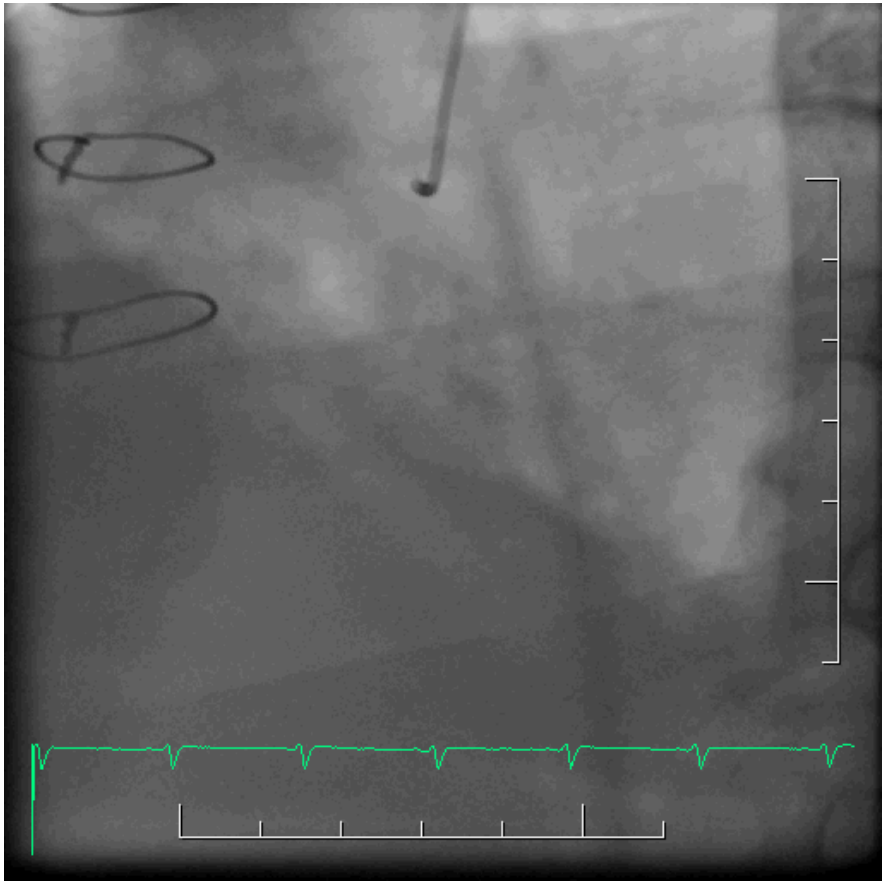
Koronarografie





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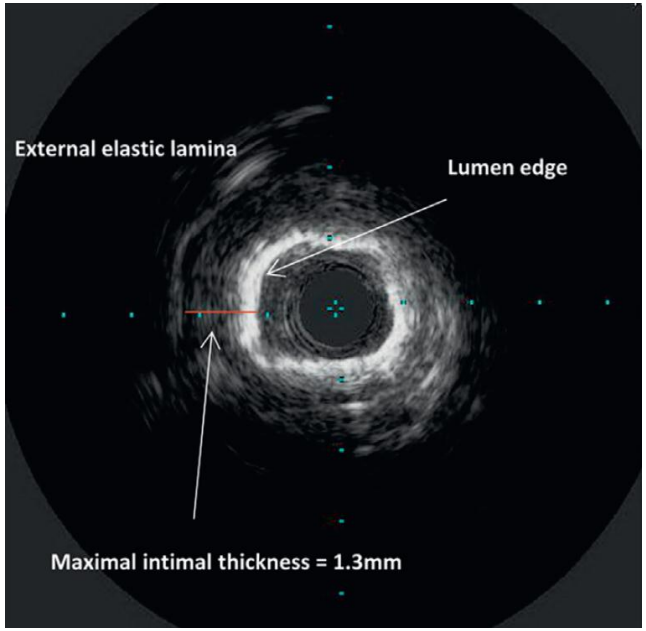
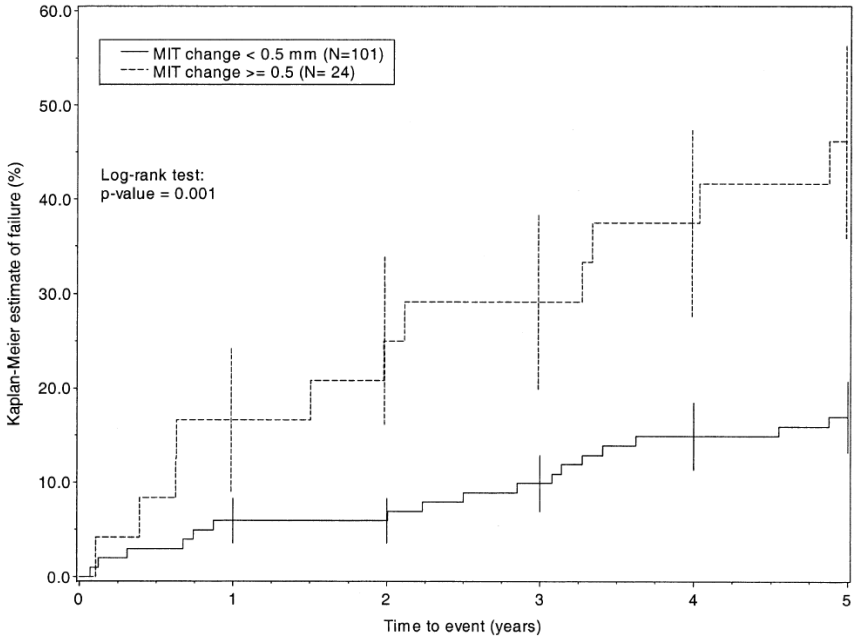
OCT/IVUS

- Progrese maximálního intimálního zesílení (MIT) ≥ 0,5 mm je prediktorem celkové mortality, nefatálních KV příhod a rozvoje angiograficky detekovatelné vaskulopatie.



Chih et al, JAAC 2016



Kobashigawa, JACC 2005

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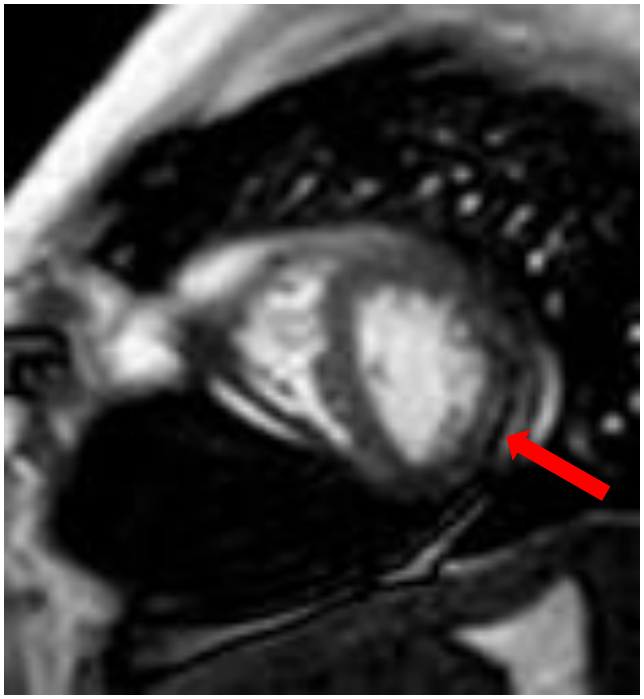
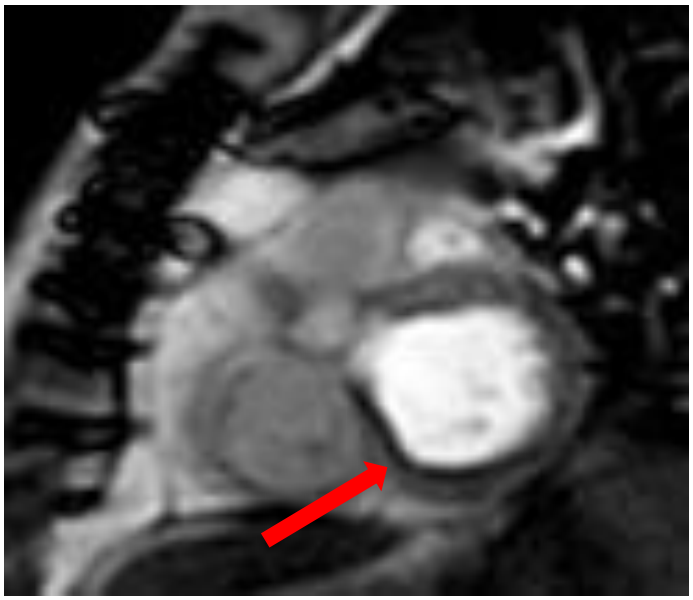
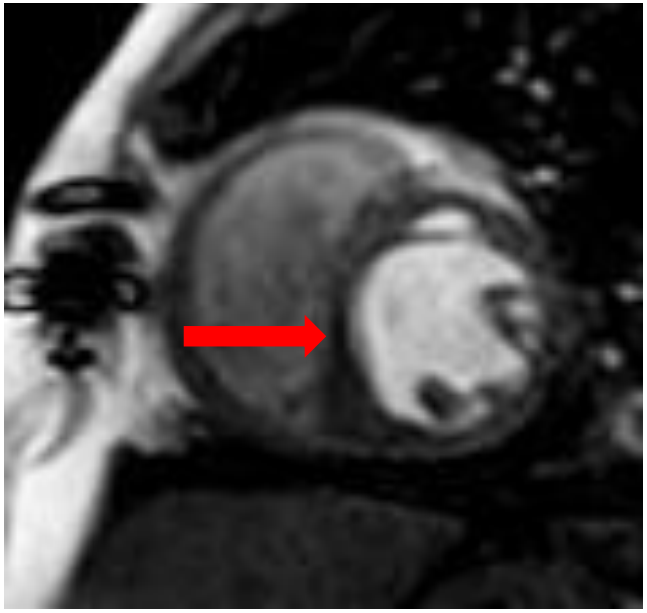
MRI perfuze

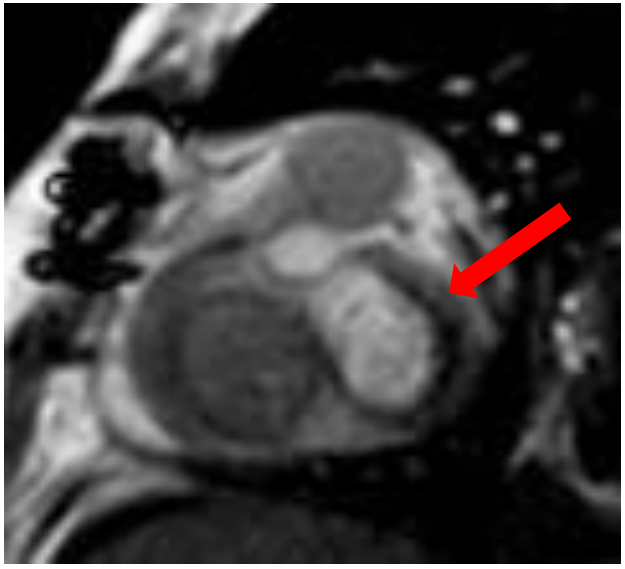
1. Zátěžové testování: Adenosin 140 µg/kg/min
2. Gadolinium
3. Vizuální hodnocení: first pass gadolinium enhancement
4. Klidové hodnocení s gadoliniem

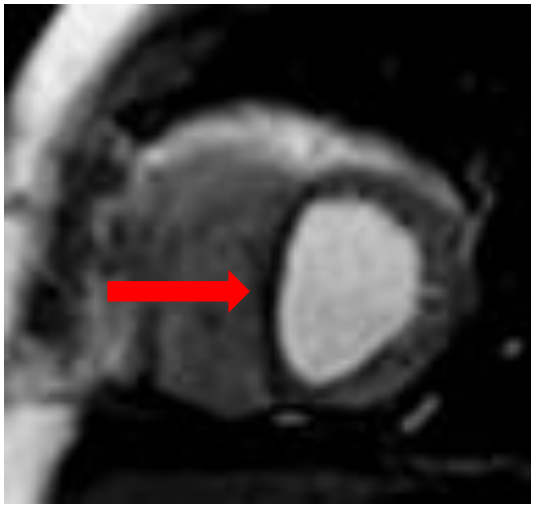
MRI











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MRI as rule-out method

$$MPR = \frac{\text{hyperemic myocardial blood flow (MBF)}}{\text{resting MBF}}$$

- Lepší v detekci mikrovaskulárního a lehkého až středního epikardiálního postižení
- Optimální cutoff hodnota indexu myokardiální perfuzní rezervy (MPR) **≤ 1,68** předpovídá CAV se 100% senzitivitou a 63% specificitou.
- Negativní prediktivní hodnota 100%

Miller et al, JACC 2014
Chih et al, Am J Transplantation 2016

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Design

- U každého pacienta v 1. roce po OTS provádíme koronarografii s OCT (event. IVUS) a MR srdce se zátěžovou perfuzí.
- U všech pacientů s podezřením na vaskulopatii štěpu

- Úloha MRI v detekci vaskulopatie štěpu u pacientů po srdeční transplantaci

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Design

angiograficky nedetekovatelná (bez CAV + CAV 0)

X

angiograficky detekovatelná (CAV 1-3)

zcela bez vaskulopatie

X

CAV 0-3

- CAV 0 jsou pacienti s OCT resp. IVUS nálezem MIT ≥ 0,5mm

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n 40	CAV (n 26)	Without CAV (n 14)	p
věk	55,4	50,87	*ns*
věk při OTS	52,9	49,4	*ns*
muži	81%	71%	*ns*
ženy	19%	29%	*ns*
BMI	26,5	27,9	*ns*
EF LK (%)	69,3	68,8	*ns*
ICHS jako dg. OTS	2 (8 %)	4 (29 %)	*ns*
Doba od OTS (dny)	879	537	0,008
Hypertenze	61%	64%	*ns*
Hyperlipidémie	73%	78%	*ns*
Diabetes Mellitus	50%	42%	*ns*
TF (/min.)	82	82	*ns*
kouření	1	0	*ns*
CMV IgG	88%	71%	*ns*
CMV IgM	12%	28%	*ns*

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n 40	CAV (n 26)	Without CAV (n 14)	p
ACE-I/sartany	38%	28%	*ns*
Beta-blokátory	46%	43%	*ns*
Kalciové-blokátory	42%	57%	*ns*
Ivabradin	30%	21%	*ns*
ASA	65%	28%	0,045
Statiny	84%	78%	*ns*
Takrolimus	88%	93%	*ns*
Mykofenolát mofetil	80%	78%	*ns*
Everolimus/sirolimus	27%	14%	*ns*
Kortikoidy	58%	71%	*ns*

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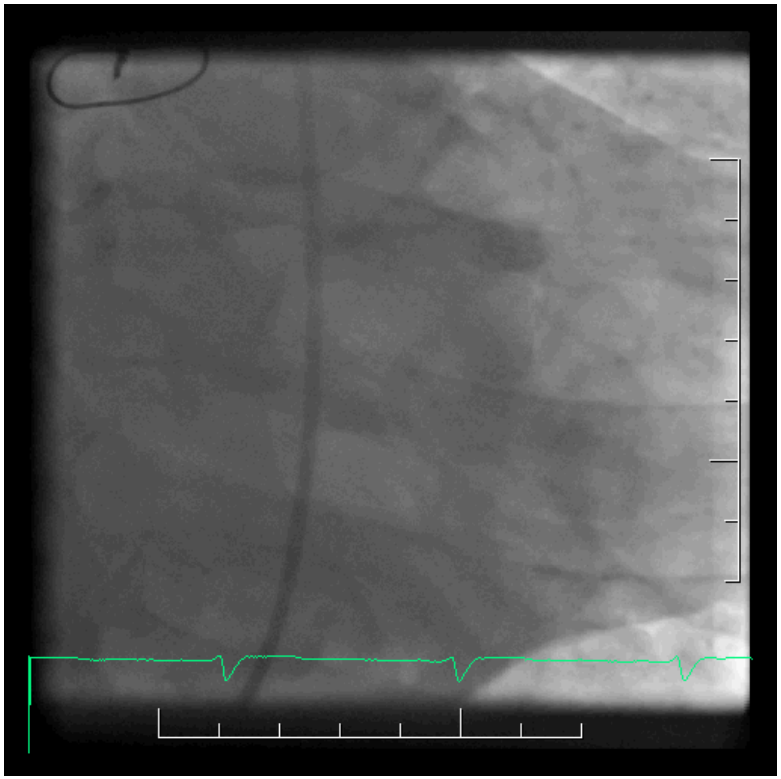
Výsledky

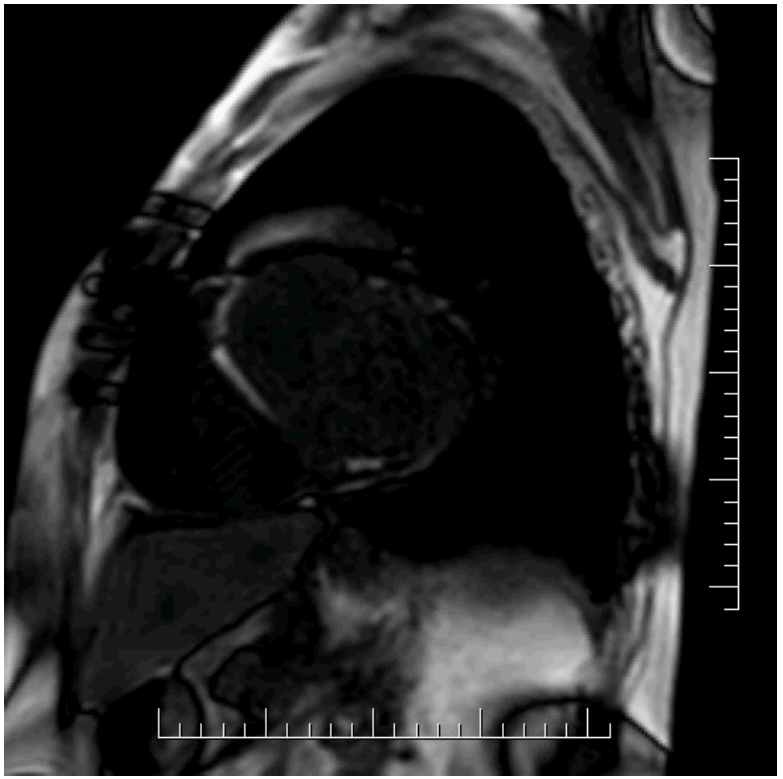
n 40	No CAV	CAV 0 {OCT +}	CAV 1	CAV 2	CAV 3
Koronarografie	14	23	0	1	2
MRI defekt v perfuzi	0	0	0	1	2

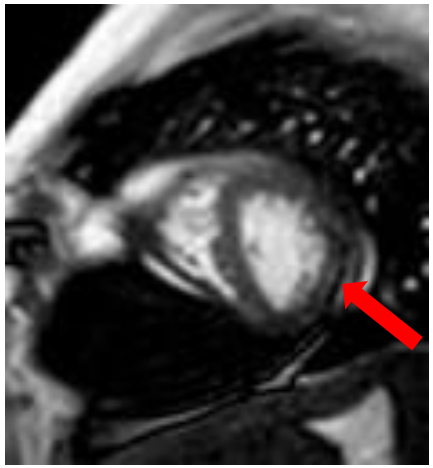
	No CAV	CAV 0-3
Koronarografie	14	26
MRI defekt v perfuzi	0	3
		p 0,53

	No CAV and CAV 0	CAV 1-3
Koronarografie	37	3
MRI defekt v perfuzi	0	3
		p 0,0001

Z. L.







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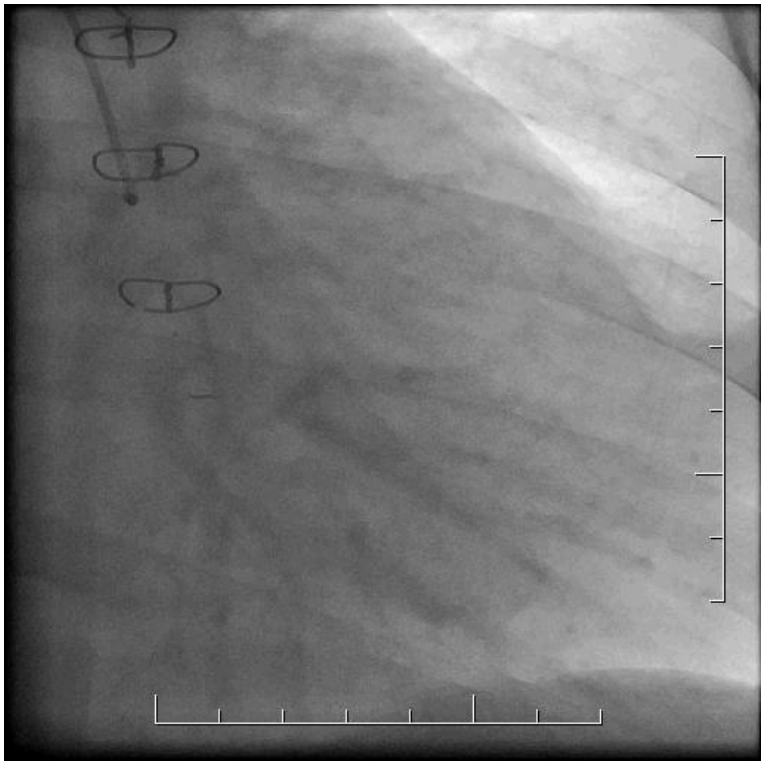

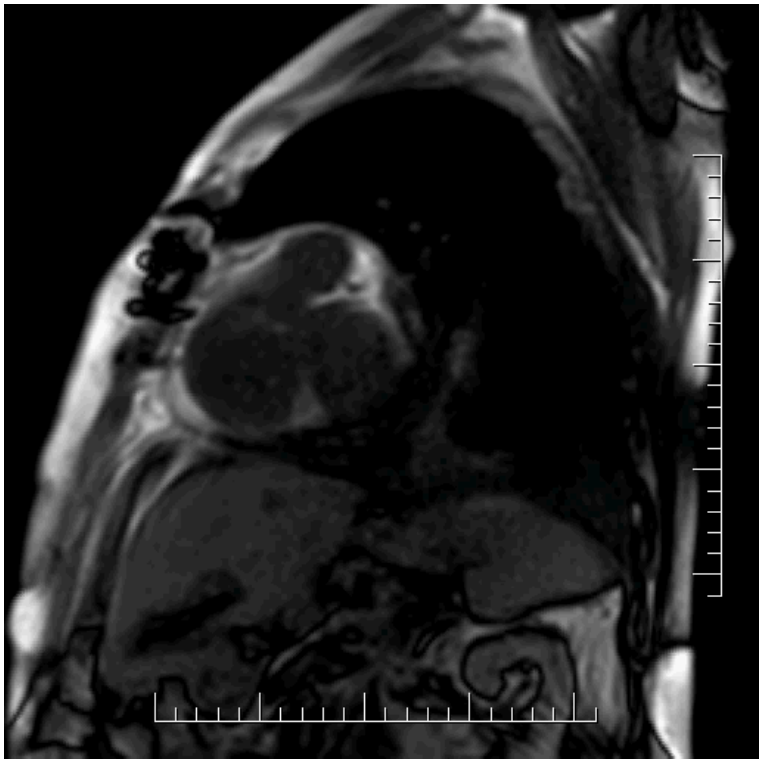

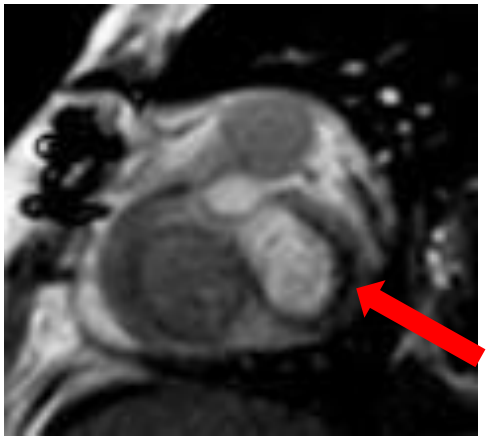

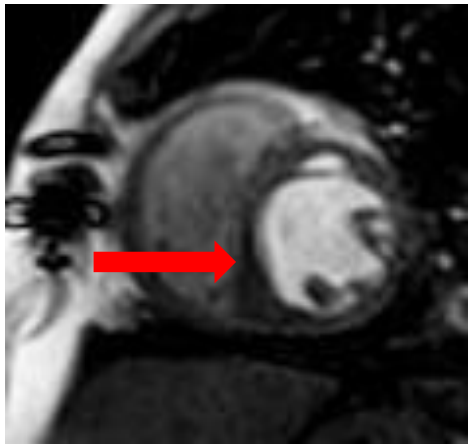

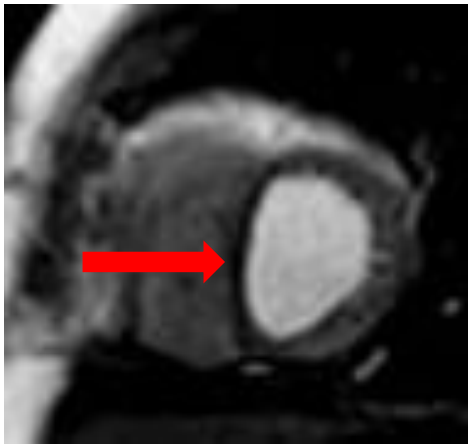

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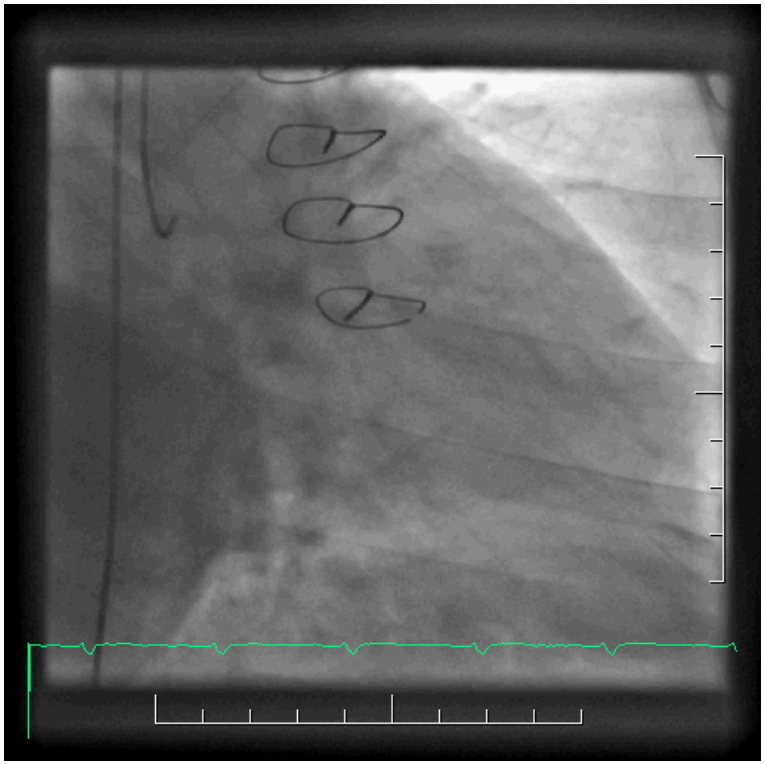

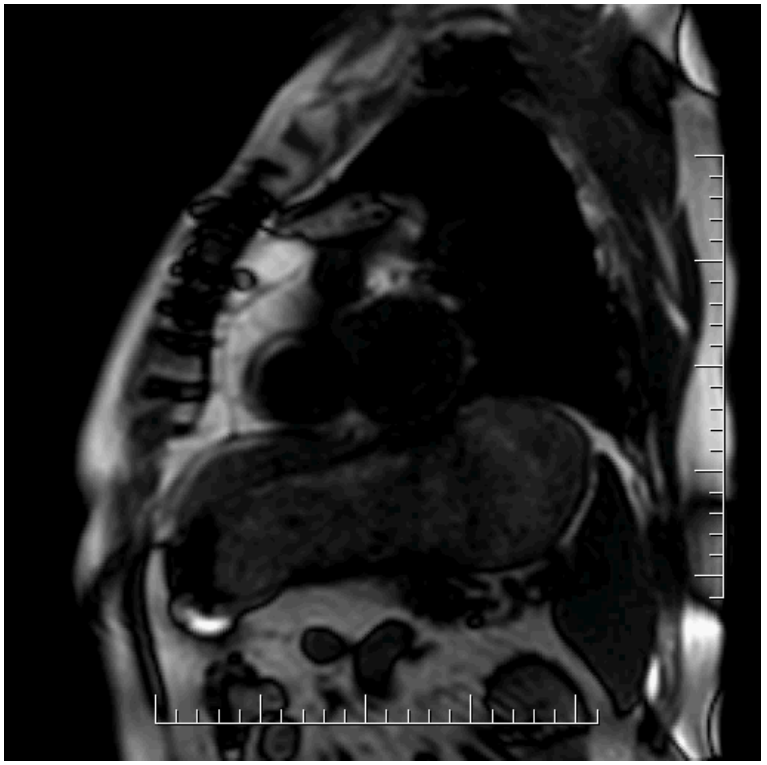

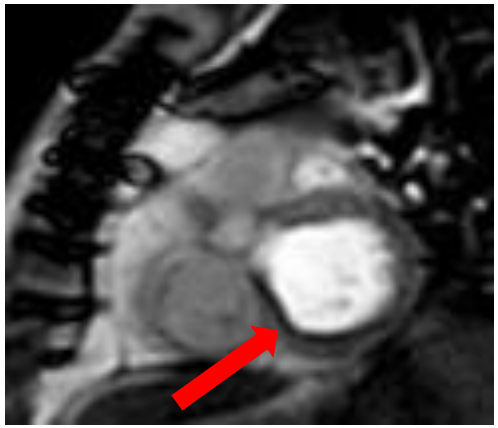

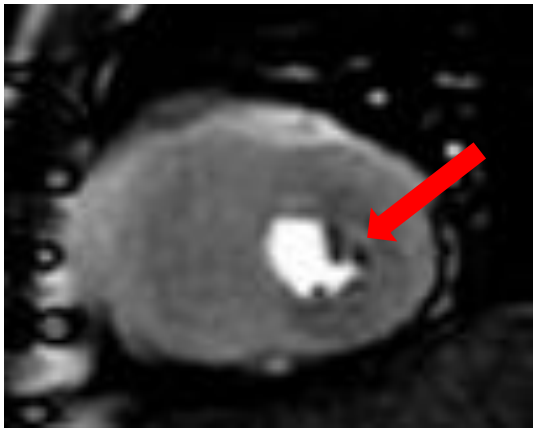

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Výsledky

- Perfuzní defekty pomocí MRI srdce jsme zjistili u 3 z 26 pacientů s vaskulopatií v jakémkoliv stádiu *p 0,53*

- Všichni 3 pacienti s angiograficky detekovatelnou vaskulopatií CAV 1-3 měli zároveň poruchu perfuze na MRI (100% match) *p 0,0001*

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Diskuze

- MRI má velký potenciál v diagnostice vaskulopatie
- Detekce skorých stádií vaskulopatie vyžaduje další výzkum
- MPRi kvantifikace je technicky i časově náročna
- Komerčně a široce dostupný software je pořád ve vývoji a není běžně dostupný
- Nicméně i tak pracujeme na začlenění MPR indexu do standardních protokolů

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Děkuji za pozornost!

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