Early IVUS-guided selection for non-invasive cardiac allograft vasculopathy (CAV) screening in heart transplant recipients

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REGION Rigshospitalet

UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

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Lærke Marie Nelson, MD

I will not discuss off label use and/or investigational use of drugs/devices.

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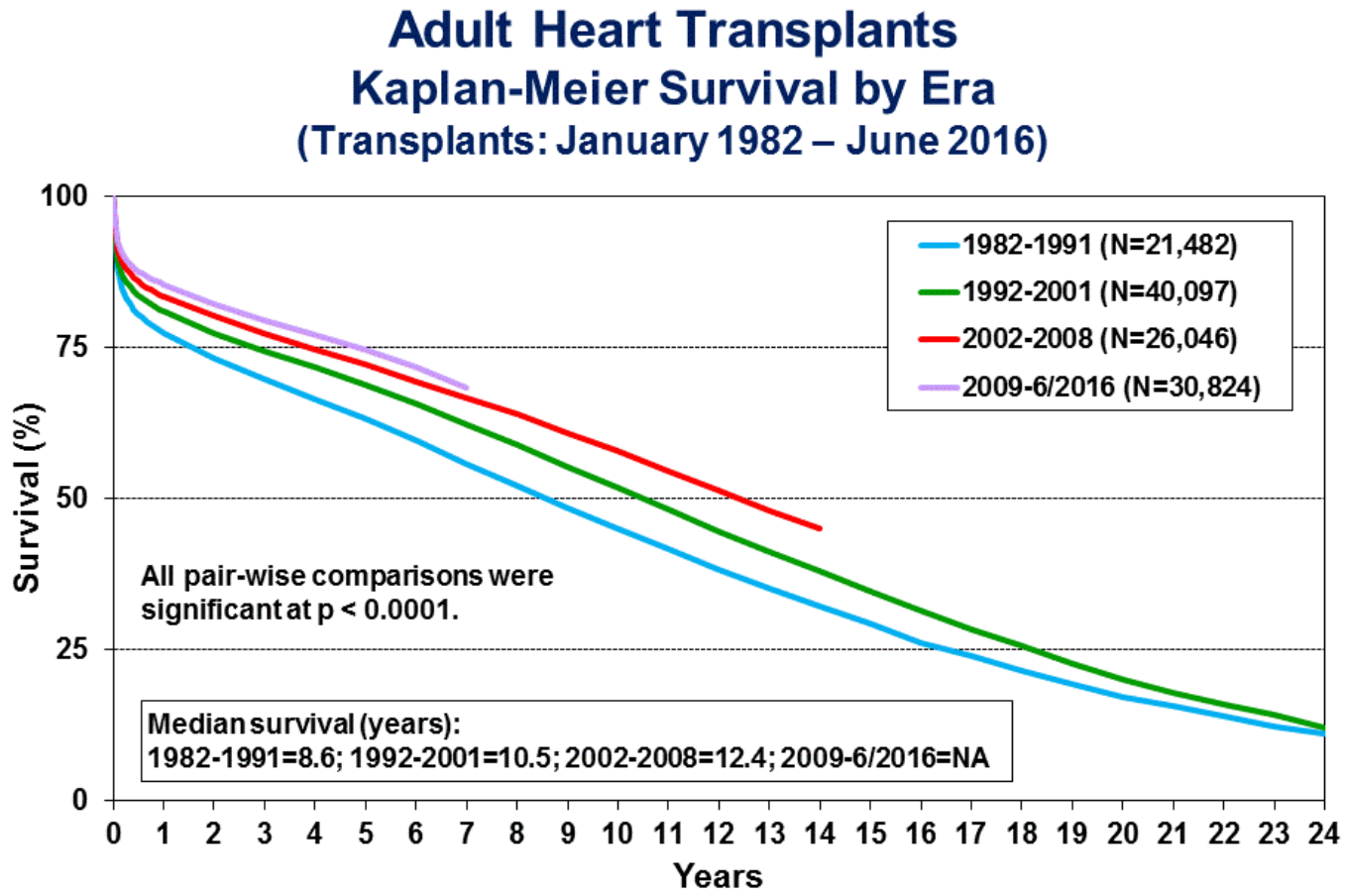
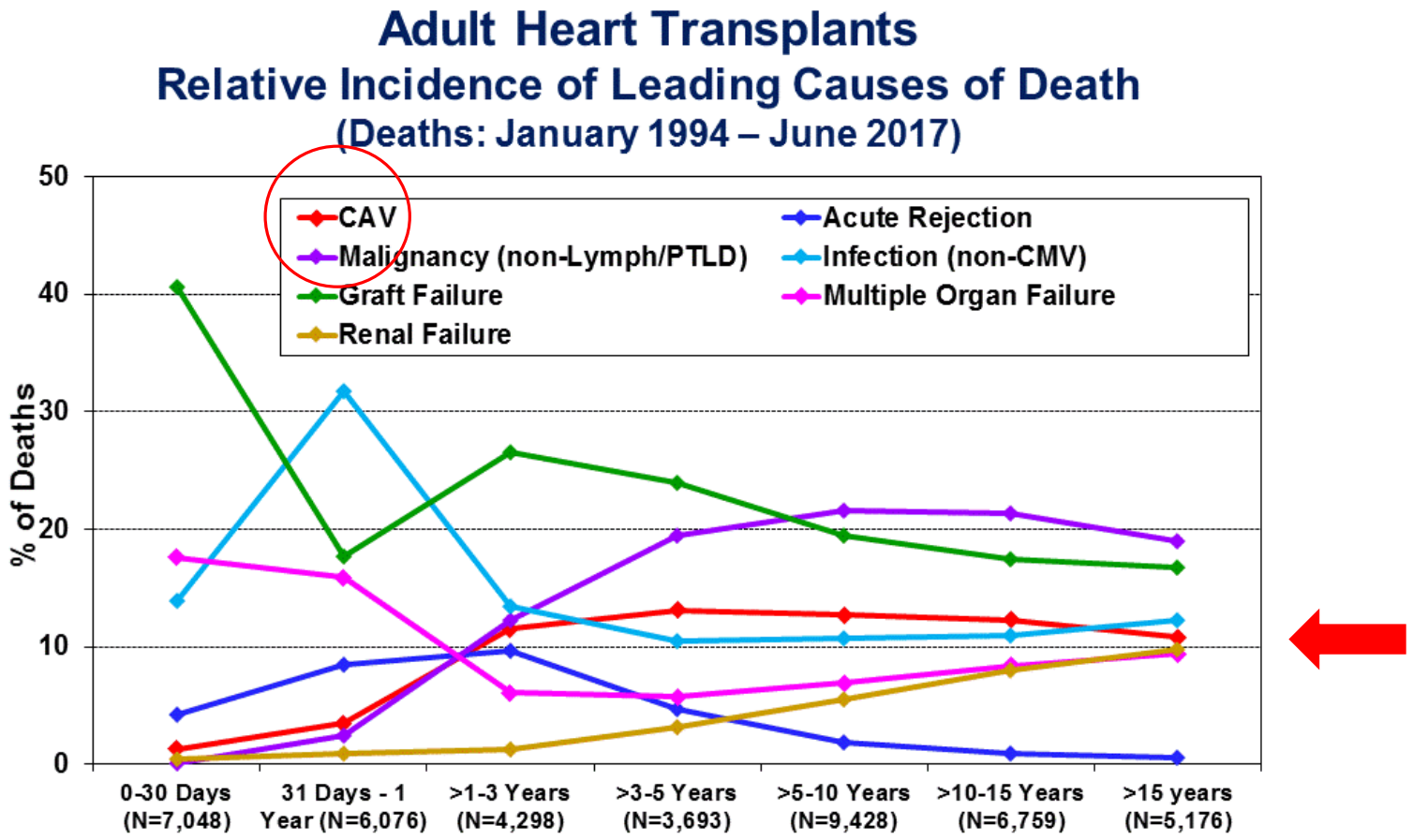
Background – Survival in Heart Transplantation (HTx)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2018
JHLT. 2018 Oct; 37(10): 1155-1206

Background – Causes of Death in HTx



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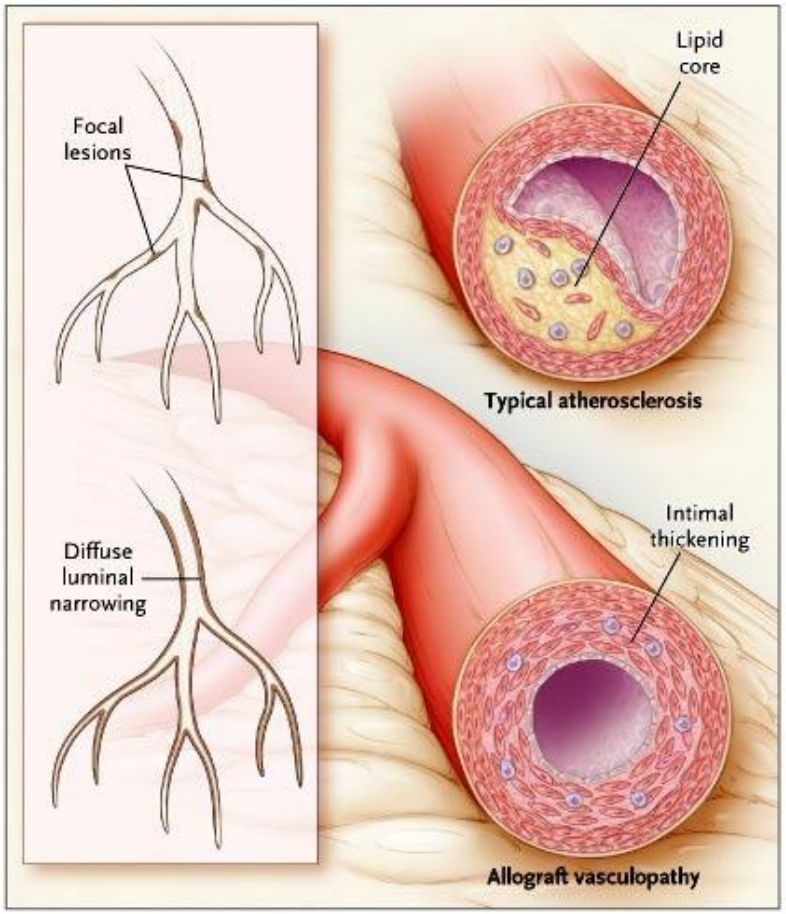
Background – Cardiac Allograft Vasculopathy (CAV)



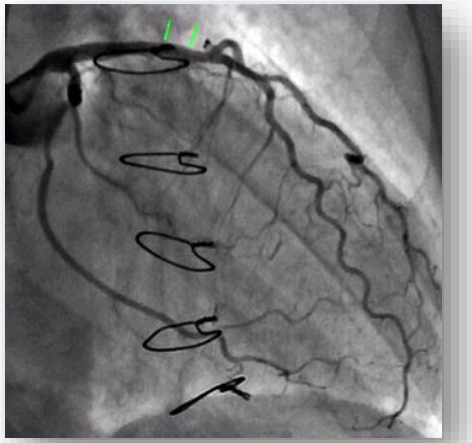
- Vascular disease confined to cardiac allograft
- Intimal thickening → luminal narrowing
- Diffuse, circumferential, longitudinal
- Causing graft failure and death
- Early diagnosis crucial (prevention/treatment)

  → Yearly surveillance

Avery RK. N Engl J Med. 2003 Aug 28;349(9):829-30.

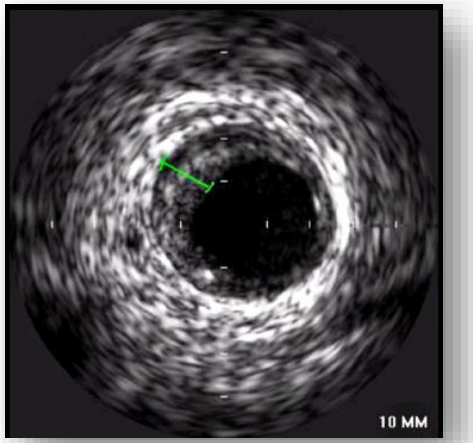
Background – CAV Diagnosis & Surveillance

Coronary angiography



- ISHLT diagnostic criteria[1]
- Risks (invasive, nephropathy)
- Underestimate CAV burden

Intravascular ultrasound (IVUS)



- Maximal intimal thickness (MIT)
- Subangiographic CAV (early)
- Not rutinely used

Dobutamine stress echocardiography (DSE)

- Non-invasive modality
- High sensitivity CAV
- Low risk patients / renal function↓

[1]Mehra MR et al. J Heart Lung Transplant 2010 Jul;29(7):717-27; Gustafsson F. UpToDate 2013.

Background – CAV Diagnosis & Surveillance

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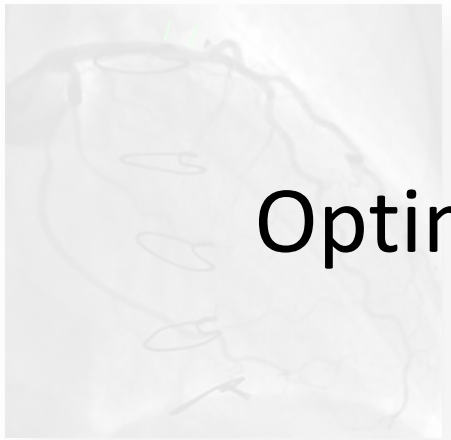

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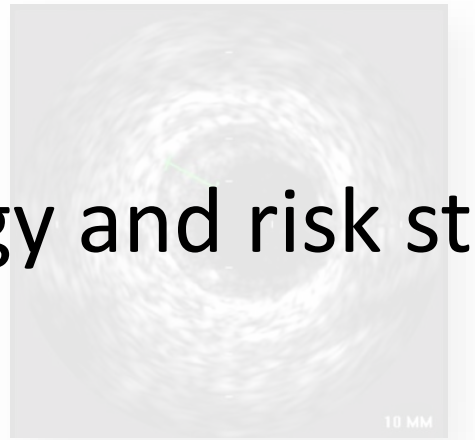

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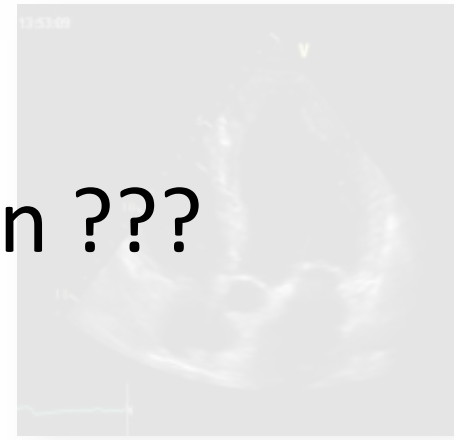


- Non-invasive modality
- High sensitivity CAV
- Low risk patients / renal function↓

Optimal strategy and risk stratification ???

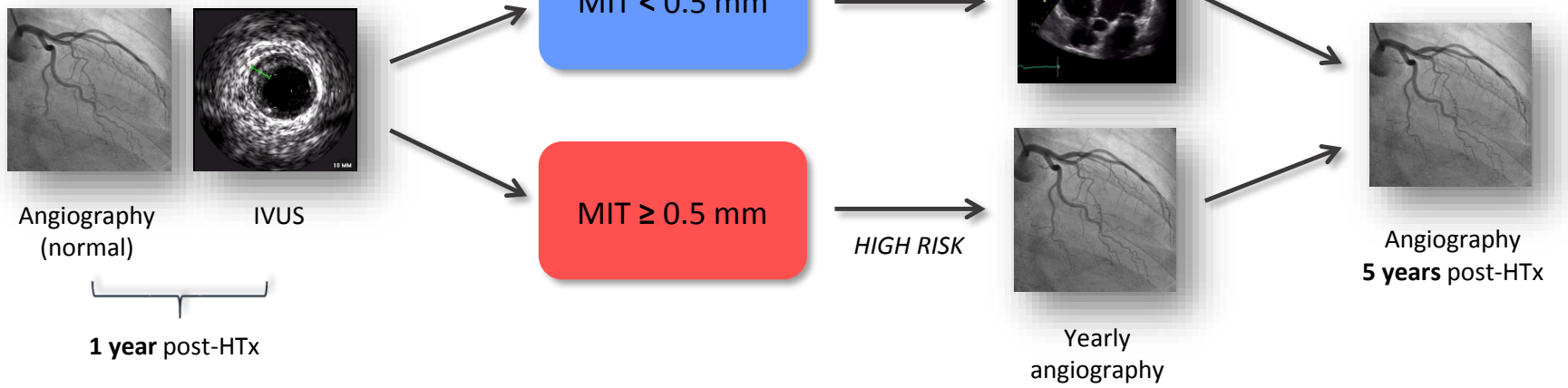
[1]Mehra MR et al. J Heart Lung Transplant 2010 Jul;29(7):717-27; Gustafsson F. UpToDate 2013.

Objective & Hypothesis

OBJECTIVE	Evaluate a strategy of early IVUS-guided selection to non-invasive screening for CAV in HTx recipients
HYPOTHESIS	Early IVUS-guided selection causes low risk of missing significant CAV as assessed by invasive coronary angiography at 5-year follow-up post-HTx

Methods - Algorithm

- Algorithm for early IVUS-guided selection to non-invasive CAV screening
- Employed at Rigshospitalet since 2009



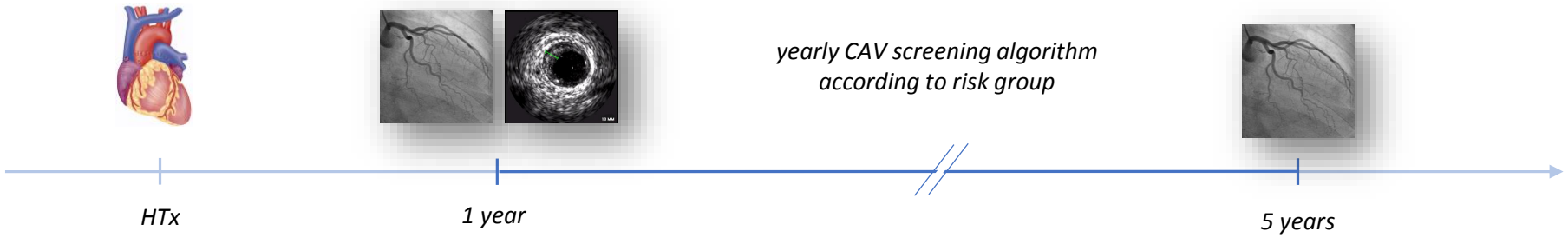
LOW RISK
Abnormal
non-invasive test
↓
Angiography

HIGH RISK
Contraindication
angiography
↓
Non-invasive test

IVUS=intravascular ultrasound, HTx=heart transplantation, MIT=maximal intimal thickness, DSE=dobutamine stress echocardiography

Methods – Design & Study Population

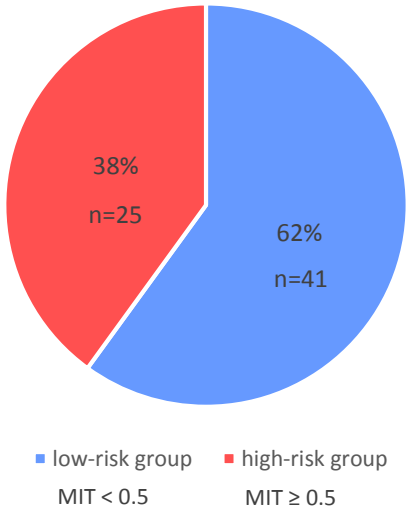
- Single center, retrospective study
- Consecutive adult HTx recipients at Rigshospitalet from 2008-2018 following the screening algorithm
- N = 66



Eligibility	Isolated HTx Age ≥ 18	Normal angiogram IVUS performed (MIT)
Follow-up		1 year post-HTx → 5 years post-HTx
Primary endpoint		Angiographic CAV (by ISHLT criteria) + all-cause mortality at 5-year follow-up after HTx (combined endpoint)

Results - Baseline

Table 1. Baseline characteristics (n=66)

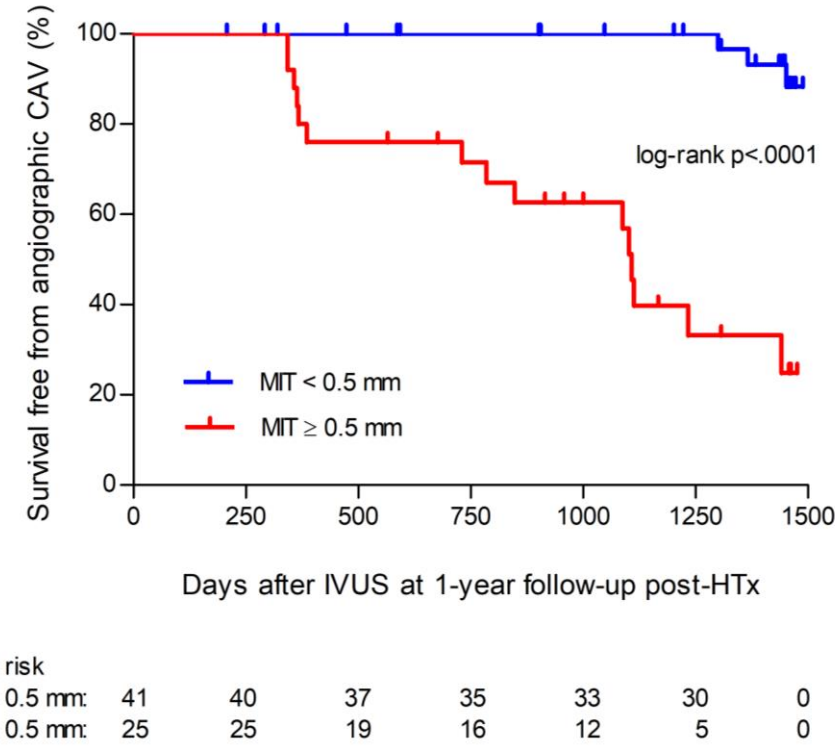


	All (n=66)	MIT < 0.5 (n=41)	MIT ≥ 0.5 (n=25)	p-value
Recipient characteristics				
Recipient age (years)	51 (33-60)	52 (33-59)	49 (42-63)	0.39
Male sex (n, %)	41 (62%)	25 (61%)	16 (64%)	0.81
LVAD (n, %)	26 (39%)	18 (44%)	8 (32%)	0.34
BMI (kg/m^2)	25 (22-27)	24 (23-27)	25 (22-30)	0.26
Diabetes (%)	9 (9%)	5 (12%)	1 (4%)	0.27
HTx primary indication				
Idiopatic DCM (n, %)	36 (54%)	23 (56%)	13 (52%)	
Ischemic (n, %)	15 (23%)	7 (17%)	8 (32%)	0.31
Other* (n, %)	15 (23%)	11 (27%)	4 (16%)	
Donor characteristics				
Donor age (years)	41 (32-47)	34 (26-42)	45 (41-49)	0.0001
Donor male sex (n, %)	37 (56%)	22 (54%)	15 (60%)	0.62
Ischemic time (min)	240 (161-300)	275 (183-300)	222 (140-300)	0.50

Data are reported as median (IQR) or absolute number (percentage) as appropriate. Groups are compared with qui-square, Fishers exact or Mann-Whitney U test as appropriate. MIT=maximal intimal thickness, LVAD= left ventricular assist device, BMI=body mass index, HTx=heart transplantation, DCM=dilated cardiomyopathy. *HCM, RCM, ARVC, non-compaction, valvular, chemotherapy induced, and congenital.

Results – Outcome

Figure 1. Survival free from angiographic CAV according to MIT risk group



18 patients met the combined endpoint:

- 4 patients died from any cause

  2 deaths (low-risk group)

  2 deaths (high-risk group)

- Angiographic CAV detected in 14 patients

  1 CAV (low-risk group)

  13 CAV (high-risk group)

CAV=cardiac allograft vasculopathy, MIT=maximal intimal thickness, IVUS=intravascular ultrasound, HTx=heart transplantation. Median (IQR) follow-up was 1307 days (848-1456).

Results – Outcome

Table 2. Cardiac allograft vasculopathy in the subgroup completing invasive coronary angiography at 5 years follow-up post-HTx (n=27)

	All (n=27)	MIT < 0.5 (n=15)	MIT ≥ 0.5 (n=12)	p-value
Any degree of CAV* (n, %)	11 (41%)	1 (7%)	10 (83%)	<.0001
ISHLT CAV1 (n, %)	9 (33%)	-	9 (75%)	
ISHLT CAV2 (n, %)	-	-	-	0.18
ISHLT CAV3 (n, %)	2 (8%)	1 (7%)	1 (8%)	

Data are reported as absolute number (percentage). Groups are compared with qui-square or Fishers exact test as appropriate.
CAV=cardiac allograft vasculopathy, MIT=maximal intimal thickness, ISHLT= international society for heart and lung transplantation.
*According to the 2010 ISHLT criteria.

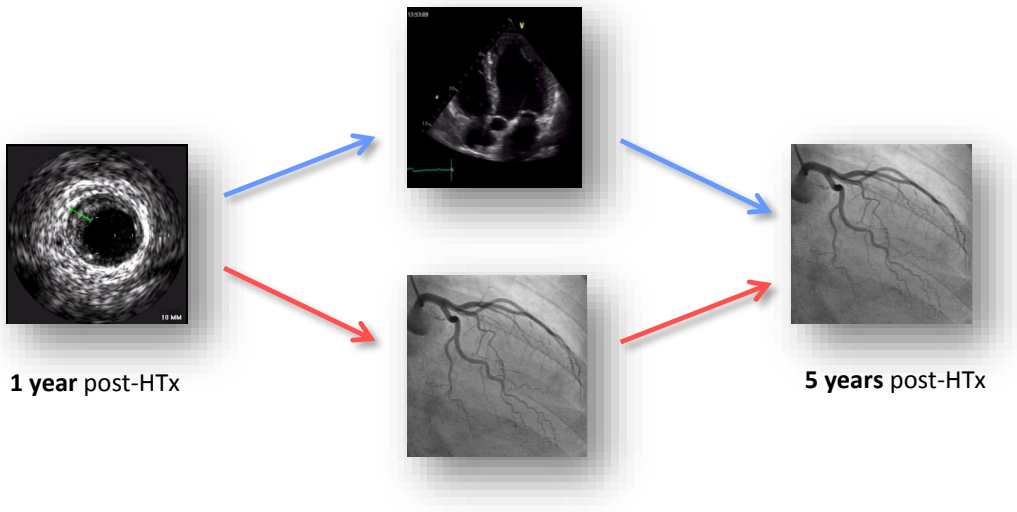
- Angiographic CAV was rare in low-risk patients
- No re-HTx
- No revascularization

Limitations

- Single center retrospective evaluation
- Small study population
- Incomplete adherence to algorithm
- No re-evaluation of coronary angiograms

Conclusions & Perspectives

- Early IVUS-guided selection to non-invasive CAV screening in selected patients appears to be safe
- Holds promise as a novel strategy for early risk stratification and CAV surveillance after HTx



1 year post-HTx

5 years post-HTx

- Reduce burden of invasive procedures in *low risk* patients
- Intensify preventive interventions in *high risk* patients

Acknowledgements

Co-authors
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- Echo lab Section 2142 (DSE)

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Thank you for your attention!