Acetylsalicylic acid use and development of cardiac allograft vasculopathy: A national prospective study using highly automated 3-D optical coherence tomography analysis

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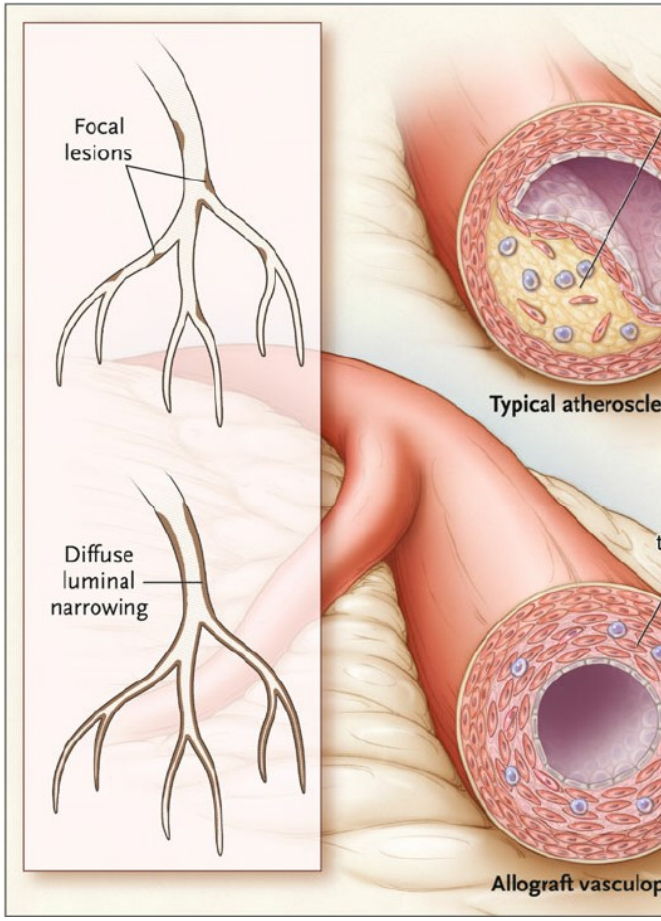
Background

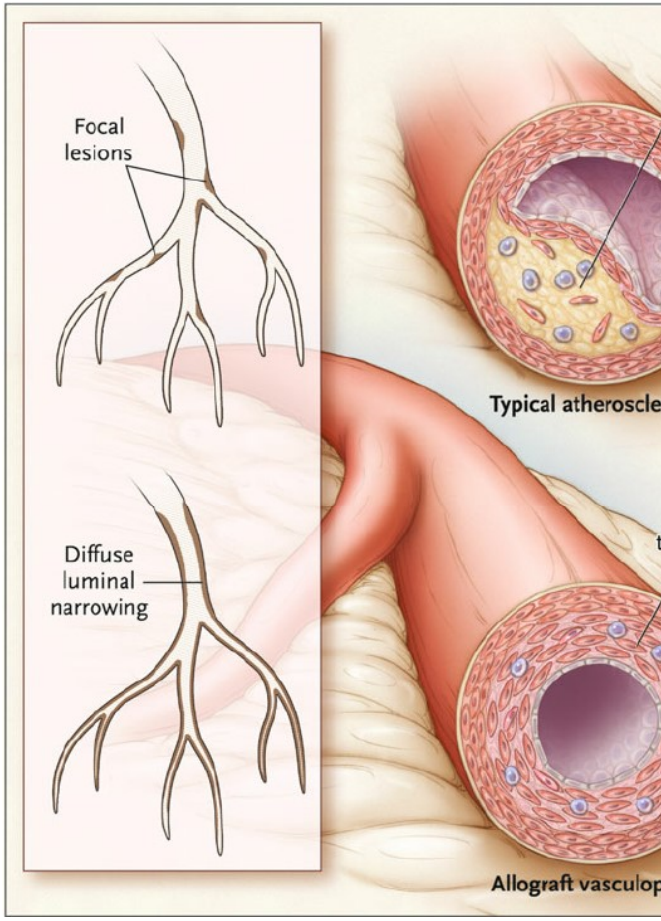
- Cardiac allograft vasculopathy (CAV) is a disease affecting the coronary arteries of cardiac allograft
- Leading cause of long-term graft dysfunction and loss
- Up to 50% patients at 10 years post-transplant



(2012). Endothelial Dysfunction and Cardiac Allograft Vasculopathy. Journal of cardiovascular translational research

Background

- Diffuse accelerated fibroproliferative process
  - endothelial dysfunction and injury leading to intimal hyperplasia
  - diffuse concentric stenoses
- Immune and non-immune risk factors
- Very limited prevention and therapy



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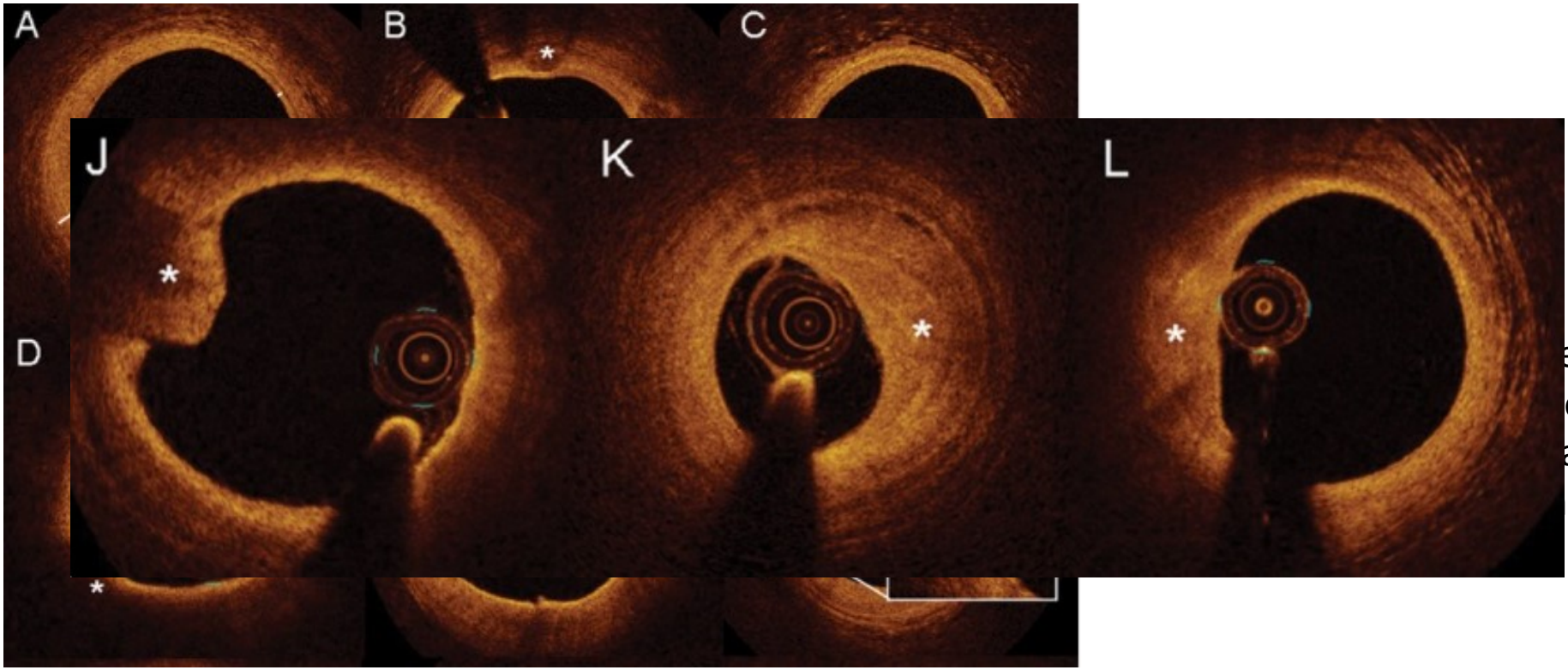
Background

- Changes typical for atherosclerosis –lipid pools, calcification, thin-cap fibroatheroma
- Layered fibrotic plaques – hypothesis of repeated thrombosis origin



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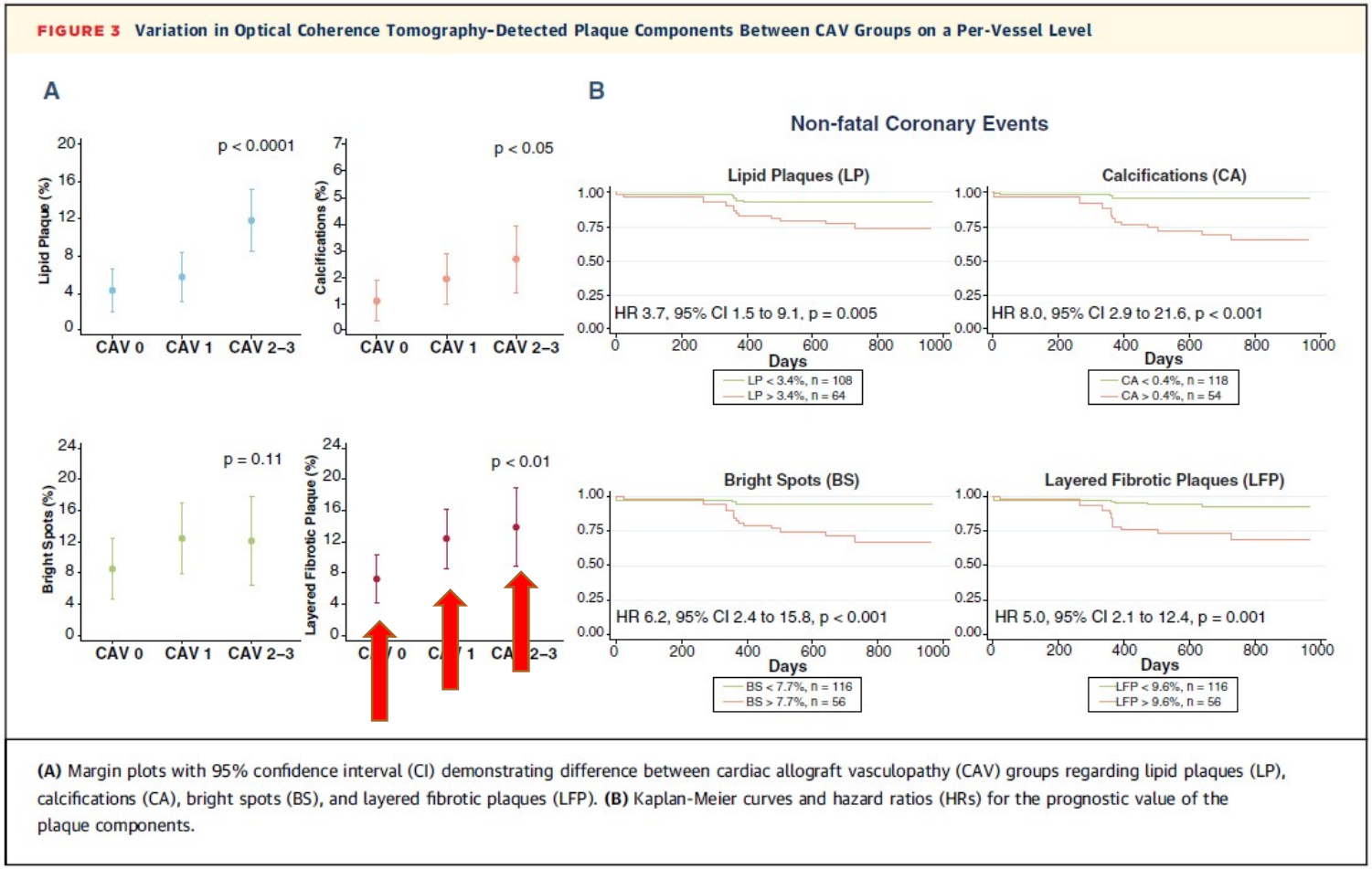
A, et al. Coronary atherosclerosis with vulnerable plaque and complicated lesions in transplant recipients: new insight into cardiac
t vasculopathy by optical coherence tomography. Eur Heart J. 2013

Background

- Layered fibrotic plaques –associated with CAV progression



(A) Margin plots with 95% confidence interval (CI) demonstrating difference between cardiac allograft vasculopathy (CAV) groups regarding lipid plaques (LP), calcifications (CA), bright spots (BS), and layered fibrotic plaques (LFP). **(B)** Kaplan-Meier curves and hazard ratios (HRs) for the prognostic value of the plaque components.

ensen et al. Layered Fibrotic Plaques Are the Predominant Component in Cardiac Allograft Vasculopathy: Systematic Findings and atification by OCT. JACC Cardiovasc Imaging. 2017

Study objective

Objective: Assess the impact of acetylsalicylic acid (ASA) on early development of cardiac allograft vasculopathy (CAV) using 3D optical coherence tomography (OCT).

Importance: CAV is the leading cause of long-term graft dysfunction and loss post-HTx. Role of ASA in the prevention of CAV is not understood.

Aspirin	
2010 Prior Guideline Recommendation	2023 Guideline Update Recommendation
New recommendation	It is reasonable to consider routine use of aspirin early after heart transplant for prevention of CAV. **Class IIb, Level of Evidence: C**

Patient population

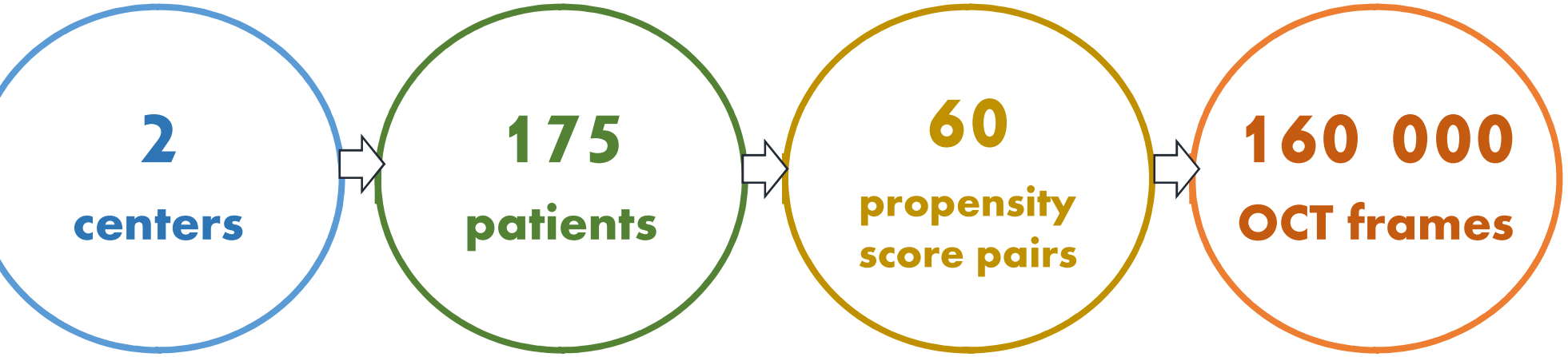
Study included 175 heart transplant (HTx) patients from two centers in the Czech Republic – IKEM, Prague and CKTCH, Brno.

Inclusion criteria: Patients ≥18 years old who survived the first 12 months post-HTx and consented to participate.

Exclusion criteria: ASA initiation after 4 weeks post-HTx or use of other antiplatelet or anticoagulant therapies.

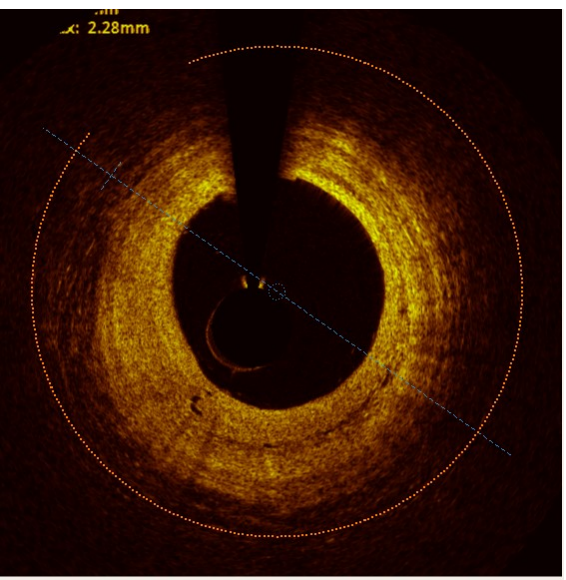
Statistical analysis

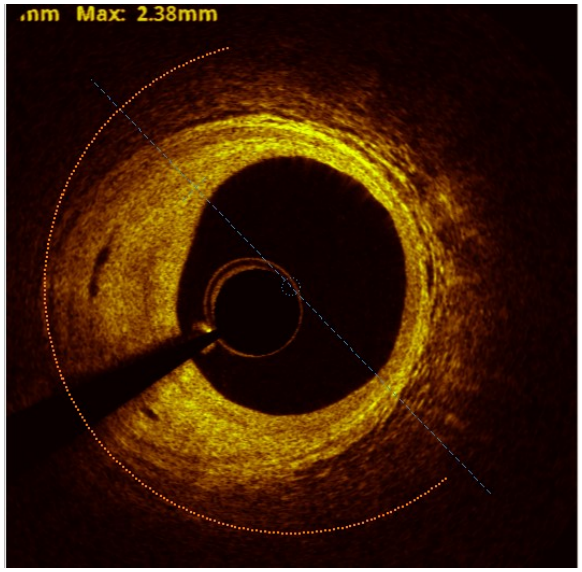
- Prospective study with nationwide data collection and analysis from two centers.
- Two patients cohorts – ASA started within 30 days after HTx vs. no ASA
- Propensity score matching 60 pairs for 9 clinical risk factors

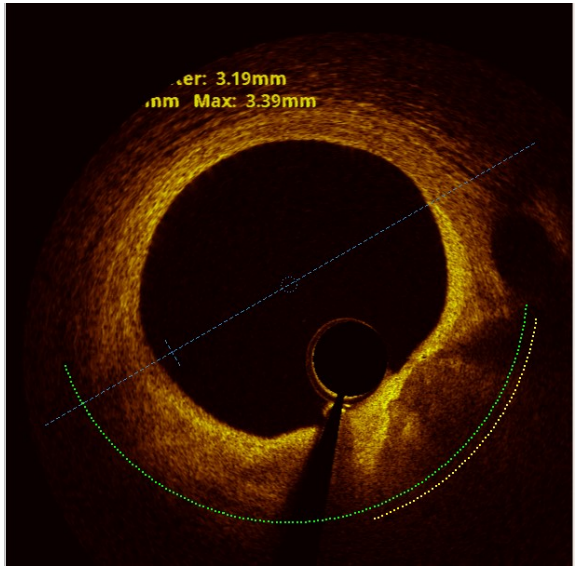


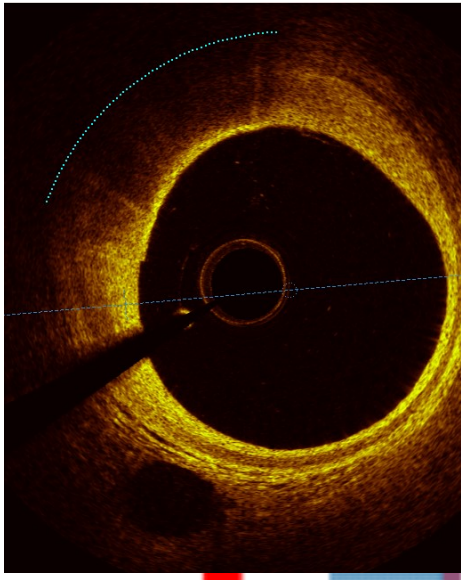
OCT analysis

- OCT imaging performed at 1 month and 12 months post-HTx
- 54mm segment of the coronary artery, ≈435 frames/pullback, over 160 000 frames analyzed
- OCT analyzed in two ways:



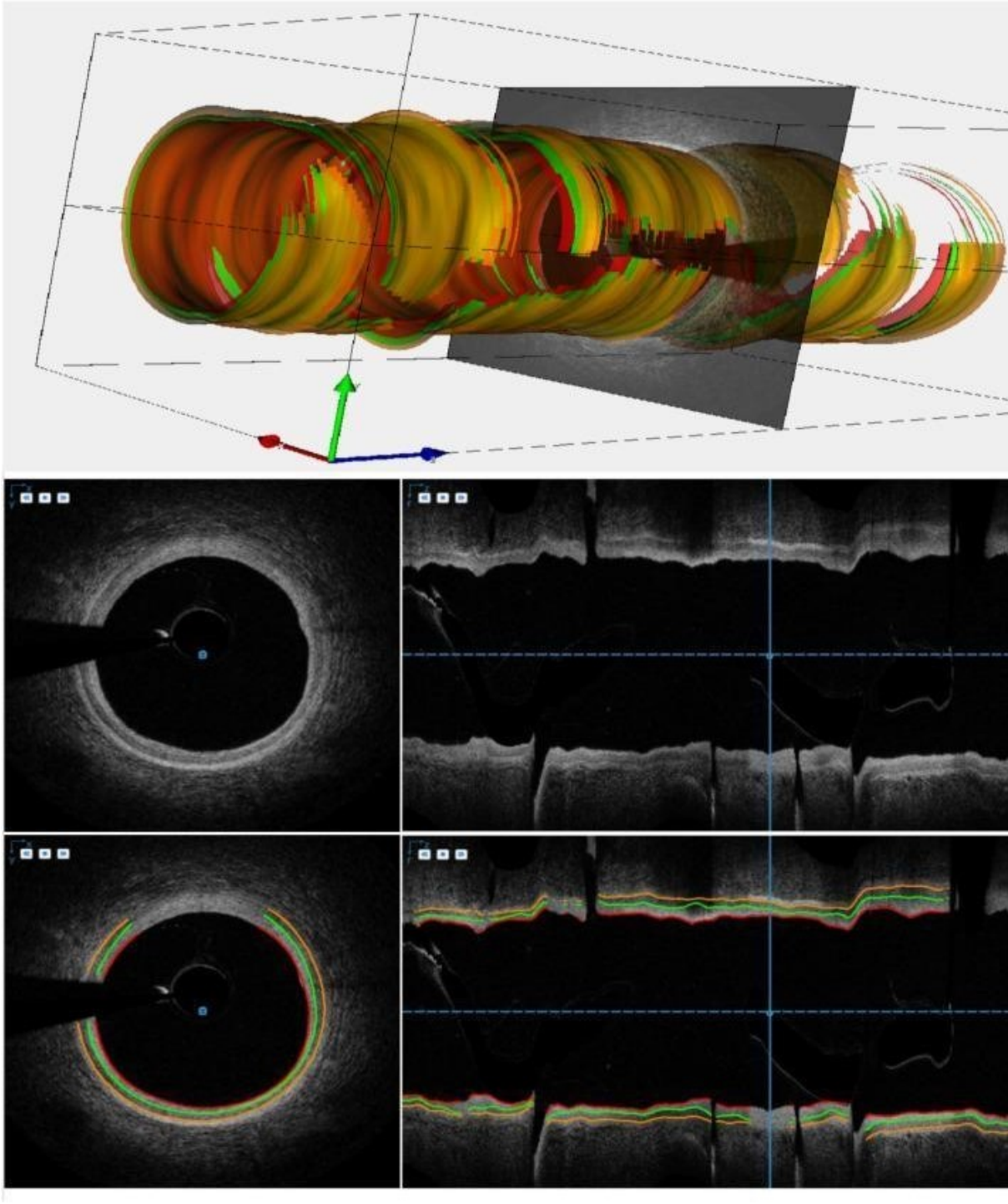






uantitative OCT analysis

- Highly automated 3D software developed at Iowa Institute for Biomedical Imaging
- Tracing of lumen area, intima and media layers of the artery

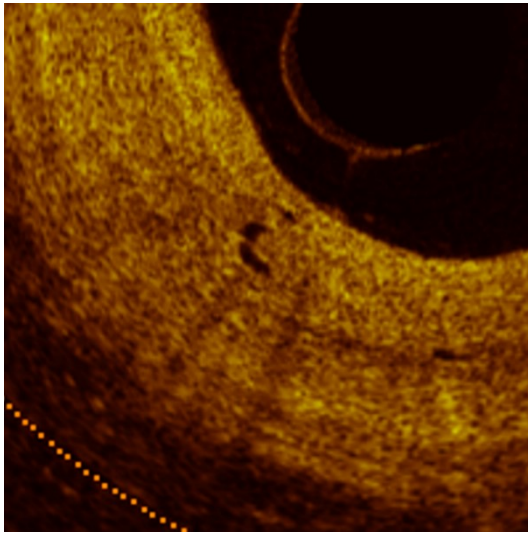


Qualitative OCT analysis

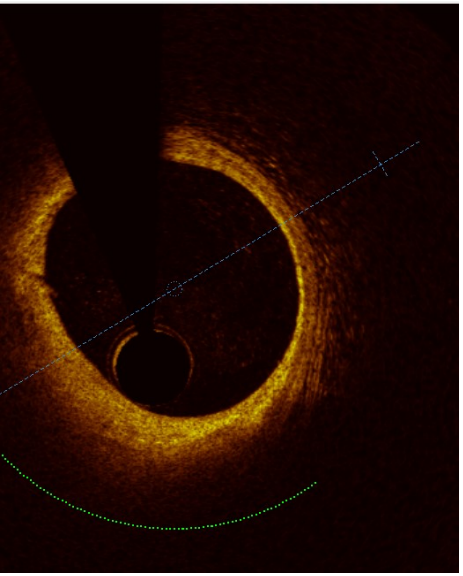
Each frame manually analyzed for the presence of 5 pathologies

extent delineated with circumferential angulation

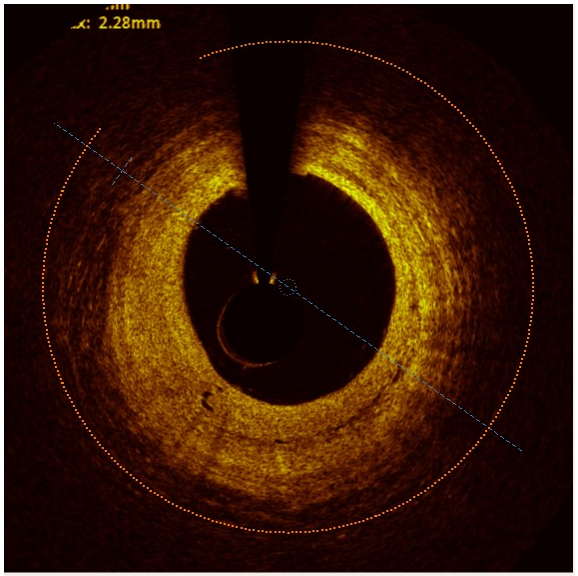
NEOVASCULARIZATION



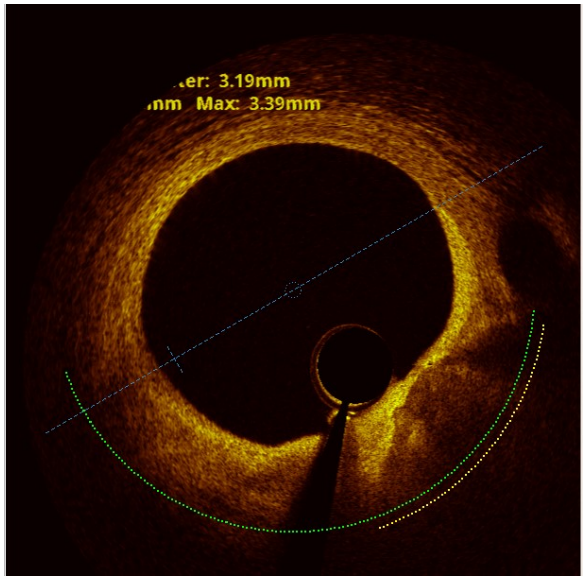
LIPID PLAQUE



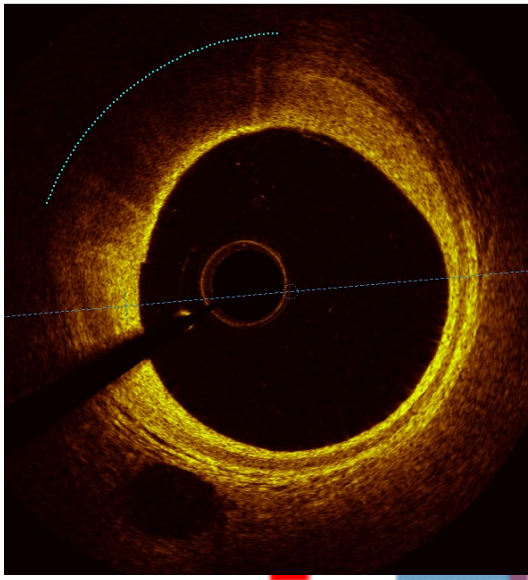
LAYERED FIBROTIC PLAQUE



CALCIFICATION



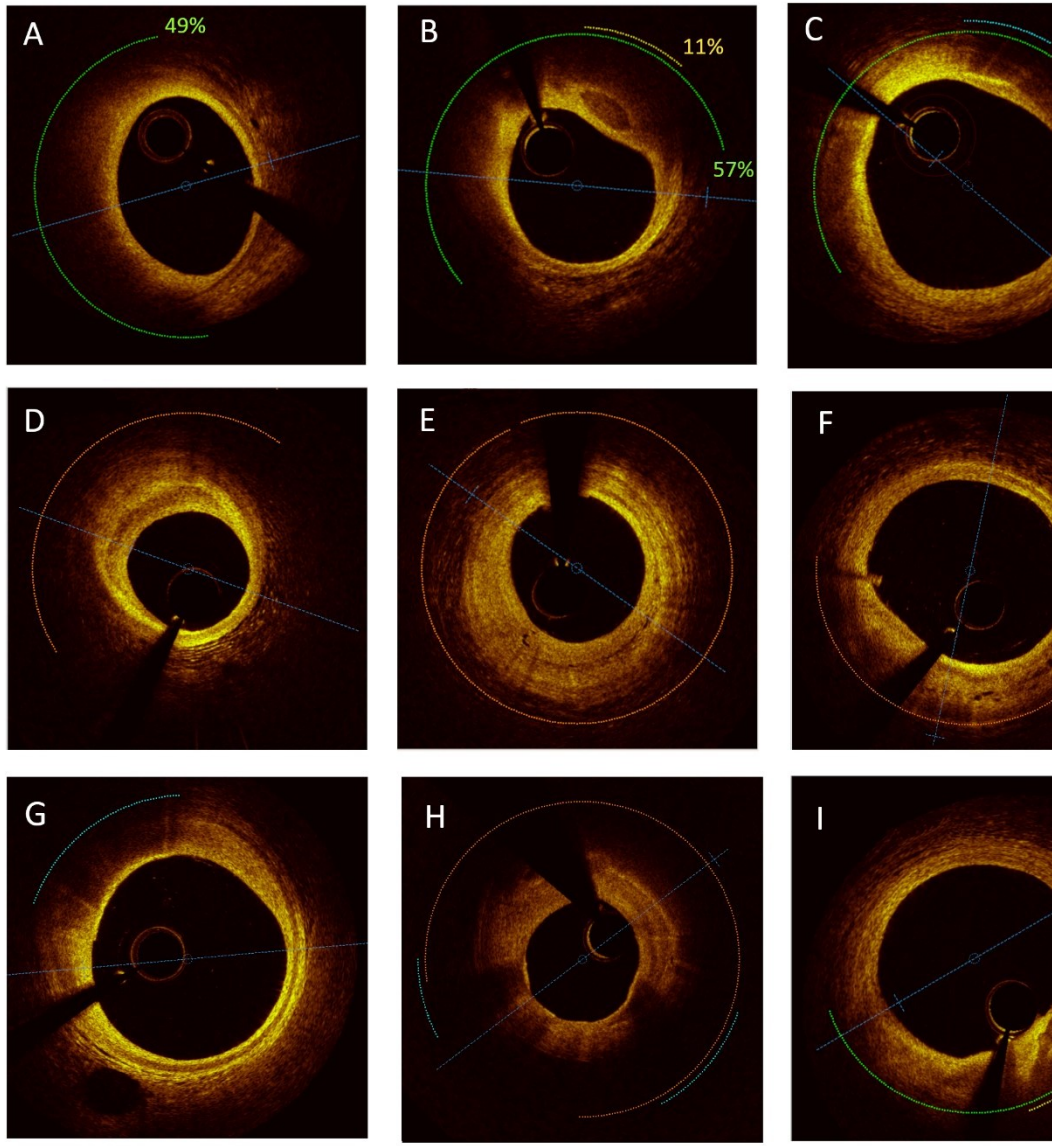
MACROPHAGES



Risk score assessment

1 point for the presence of each observed pathology in every frame

Sum of all points divided by the number of frames in each pull-back.



Risk score assessment

1 point for the presence of each observed pathology in every frame

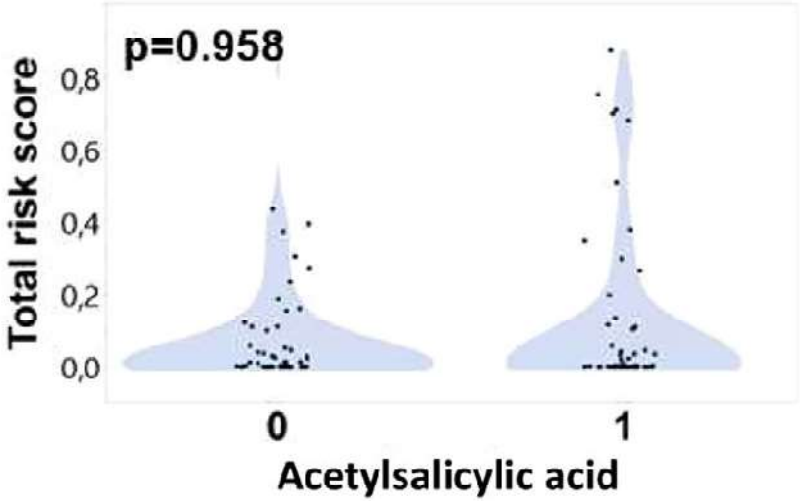
Sum of all points divided by the number of frames in each pull-back.

Results

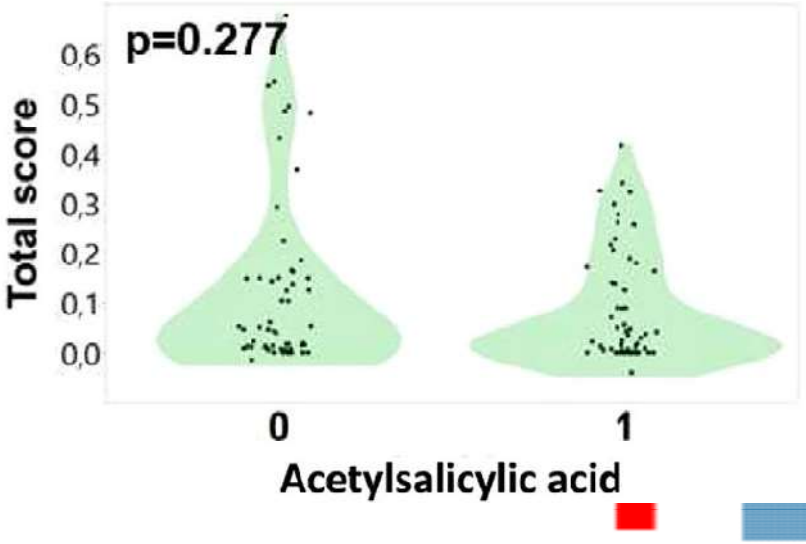
Dramatic increase during the 1st year

ASA use had no beneficial effect (p=0.277)

BASELINE 1 MONTH



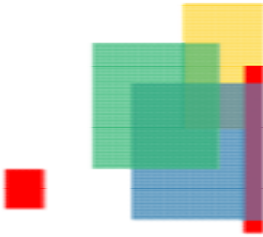
FOLLOW-UP 12 MONTH



Results – quantitative analysis

During the first year after HTx, both intimal ($p < .001$) and medial thickness ($p = .012$) progressed, with ASA use having no effect on its progression.

ntitative OCT measurements 1 M/12 M						
out ASA ($N = 61$)			With ASA ($N = 114$)		*p*-value	
	1 M/12 M	M12 – M1	1 M/12 M	M12 – M1	1 M/12 M	M12
n intimal thickness (μm)	106.4 ± 36.7/138 ± 67.9	31.6 ± 48	109.4 ± 47.3/134.7 ± 63.2	25.3 ± 37.5	.668/.745	.335
n medial thickness (μm)	86.0 ± 23.5/89.8 ± 25.0	3.9 ± 11.1	84.8 ± 23.9/86.1 ± 23.0	1.4 ± 12.0	.746/.328	.183



Results – Lipid plaques

- **ASA use was associated with significantly lower progression of lipid plaques over the first year post-HTx (p=0.013).**
- **Propensity-matched analysis (120 patients) confirmed ASA use reduced lipid plaque burden (p=0.002).**

OCT baseline	Without ASA ($n = 60$)	With ASA ($n = 60$)	*p*-value
Qualitative OCT measurements—*overall coronary artery change per one OCT frame over follow-up period*			
Lipid plaque	.00 [.00–.99]	.00 [.00–1.23]	.753
Layered fibrotic plaque	.00 [.00–.00]	.00 [.00–.00]	.139
Calcification	.00 [.00–.00]	.00 [.00–.00]	.534
Macrophages	.00 [.00–.06]	.00 [.00–.06]	.670
Total risk score	.004 [.00–.05]	.001 [.00–.08]	.958
OCT change during follow-up			
Lipid plaque	.20 [.00–2.85]	.00 [.00–.39]	.002
Layered fibrotic plaque	.00 [.00–1.09]	.00 [.00–2.09]	.224
Calcification	.00 [.00–.00]	.00 [.00–.00]	.231
Macrophages	.00 [.00–.25]	.00 [.00–.09]	.197
Total risk score	.04 [.01–.15]	.03 [.00–.15]	.277

Data are presented as mean ± standard deviation, and median with interquartile ranges [IQRs].
Abbreviations: ASA, acetylsalicylic acid; M, month; OCT, optical coherence tomography.

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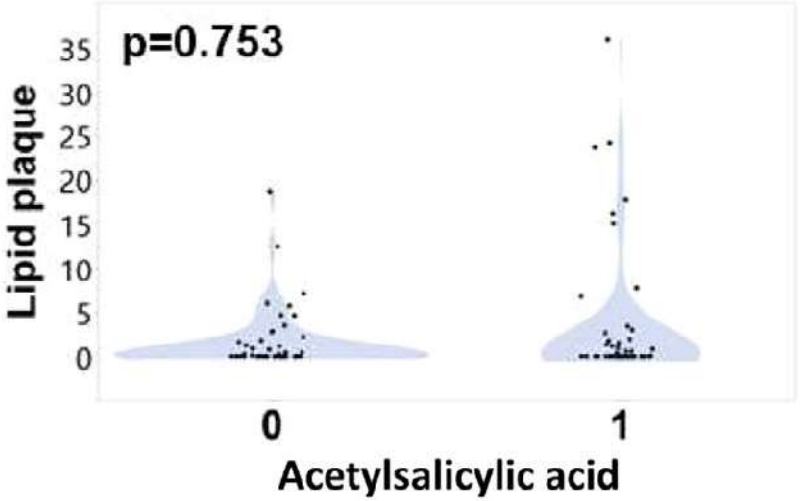
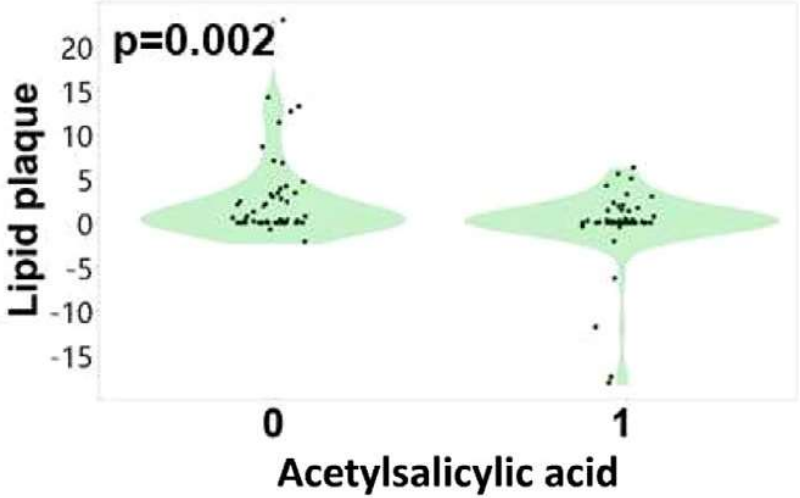


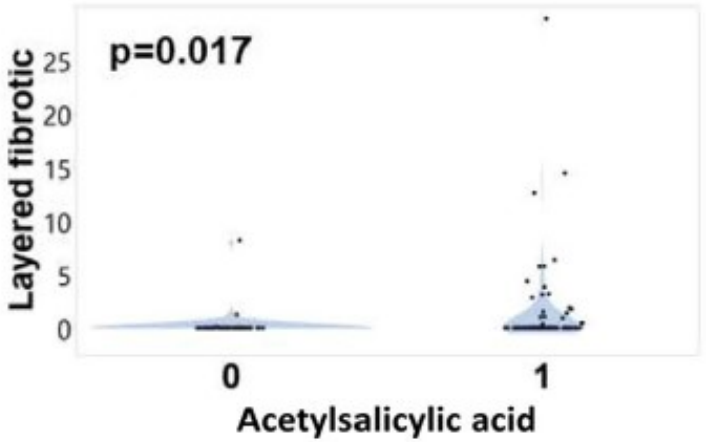
FOLLOW-UP 12 MONTH



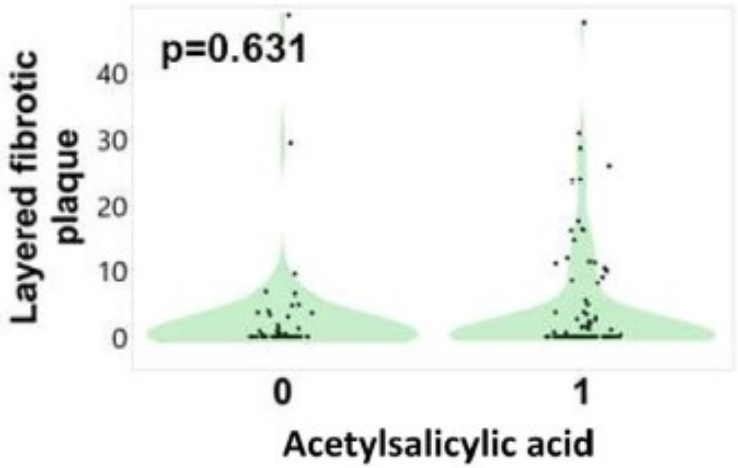
Results – LFP

- There was a significant progression in LFPs burden over the follow-up period
- ASA use had no effect on its developement (p = .224)

BASELINE 1 MONTH



FOLLOW-UP 12 MONTH



Results

- Calcifications: No significant impact of ASA (p=0.231).
- Macrophage Infiltration: No significant impact of ASA (p=0.197).
- Total risk score combining plaque types showed no benefit with ASA.

OCT baseline	Without ASA (*n* = 60)	With ASA (*n* = 60)	*p*-value
Qualitative OCT measurements—*overall coronary artery change per one OCT frame over follow-up period*			
Lipid plaque	.00 [.00–.99]	.00 [.00–1.23]	.753
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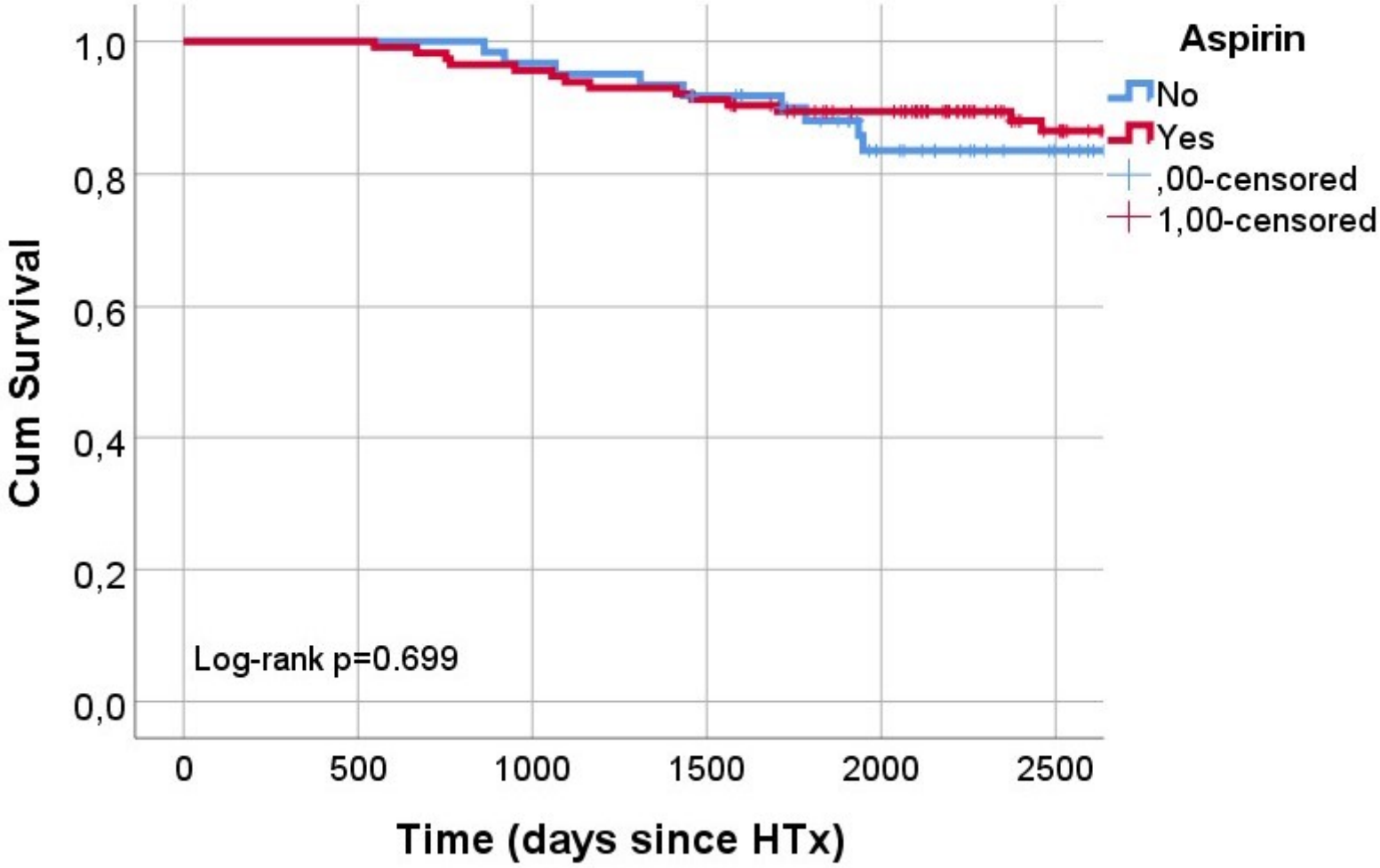
Data are presented as mean ± standard deviation, and median with interquartile ranges [IQRs].
Abbreviations: ASA, acetylsalicylic acid; M, month; OCT, optical coherence tomography.

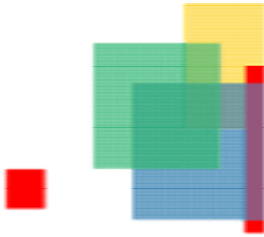
Survival

- ASA use was not associated with a significant difference in survival (p=0.699)
- Follow-up 9-13 years



Conclusions

1. **Early initiation of ASA was associated with a significantly lower increase in the extent of lipid plaque progression**
2. We observed significant intimal and medial thickness progression with no impact of ASA use
3. Layered fibrotic plaques burden significantly increased over the first year post-HTx, with ASA use having no effect on its developement.
4. No significant effect of ASA on survival or progression of layered fibrotic plaques, calcification, or macrophages.
5. Future research, including randomized trials, is needed to understand ASA's potential role in CAV prevention.



Thank you for your attention!