Early Aspirin Use, Rejection, and Cardiac Allograft Vasculopathy after Heart Transplantation

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BACKGROUND

- Cardiac allograft vasculopathy (CAV) remains a major cause of graft loss, heart failure, and mortality after orthotopic heart transplant (OHT).
- CAV is mediated by endothelial inflammation and thrombosis.
- Aspirin has anti-inflammatory and antithrombotic actions, yet has rarely been studied post-OHT.
- We previously observed an association between early aspirin use post-OHT and lower rates of moderate-severe CAV (ISHLT ≥2).
- We hypothesize that the inverse association between aspirin use and CAV will be modified by the presence of rejection or CMV infection, two potent inflammatory processes common after OHT.

METHODS

- Retrospective cohort (N=120)
- Patients receiving OHT at a single institution from 2004-2010
- Early aspirin use defined as ≥6mo of aspirin in first 12mo post-OHT
- Cor angio and biopsies per institutional protocol unless clinically indicated otherwise
- Antibody mediated rejection (AMR) and acute cellular rejection (ACR) defined by biopsy

STATISTICAL ANALYSIS

- Primary end point: ISHLT ≥ 2 CAV
- KM Rates of the primary end point at 5 years based on aspirin use, rejection status, and CMV status
- Cox PH using inverse probability of treatment weighting (IPTW)

Table 1.

	Aspirin (n=59)	No aspirin (n=61)
Characteristics at the time of OHT		
Age, years	55	55
Men*, %	90	59
Caucasian, %	93	89
CAD*, %	42	21
VAD, %	59	57
Smoking*, %	73	53
LDL, mmol/L	2.6	2.5
Creat., umol/L	124	124
Characteristics up to 1 year post-OHT		
HTN, %	90	82
Diabetes, %	29	13
mToRi, %	5	5
CCB, %	75	74
ACEi/ARB, %	34	21
Statin, %	80	74
Vit.C/E, %	93	95
Events up to 5 years post-OHT		
ACR, %	61	56
AMR, %	19	26
CMV, %	19	30

*P<0.05

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Figure 1.

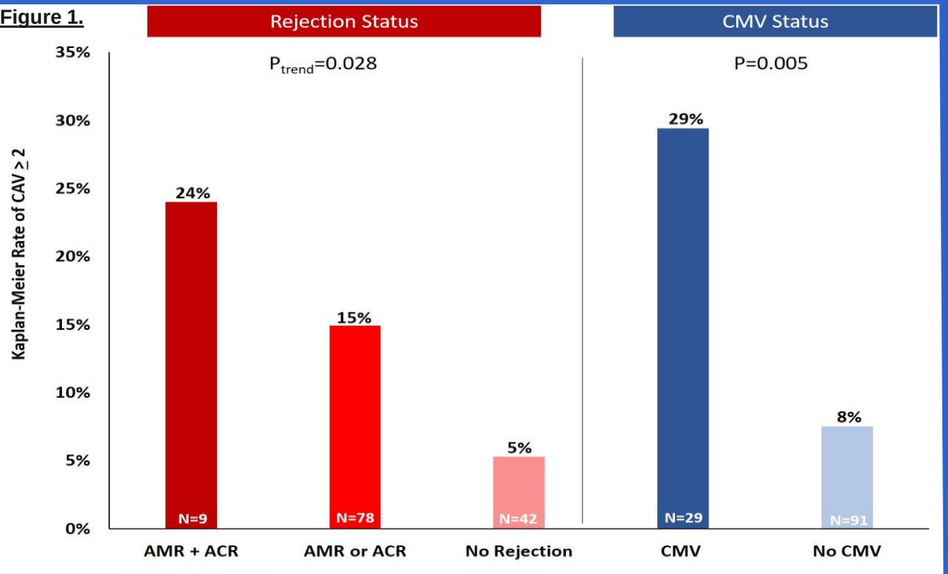


Figure 2.

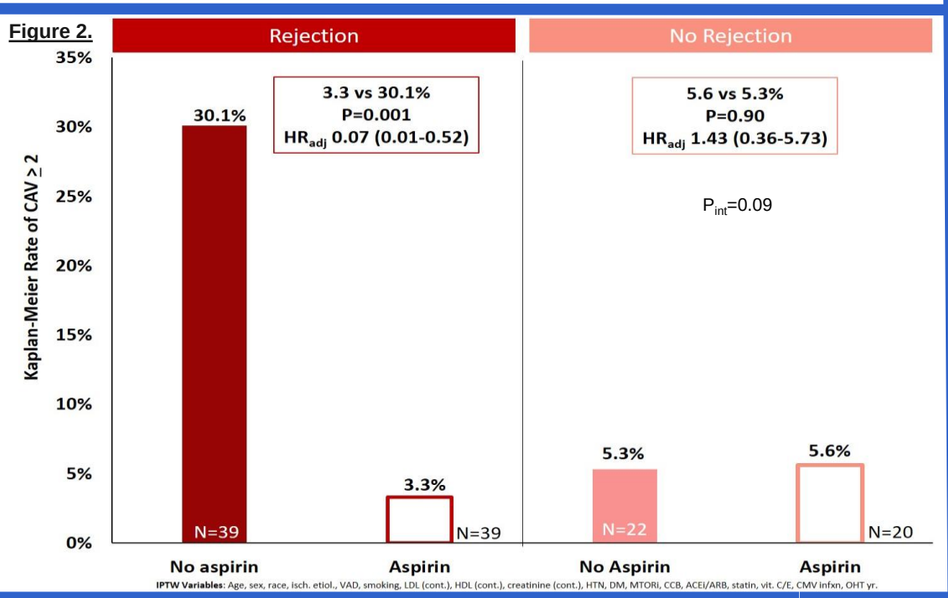
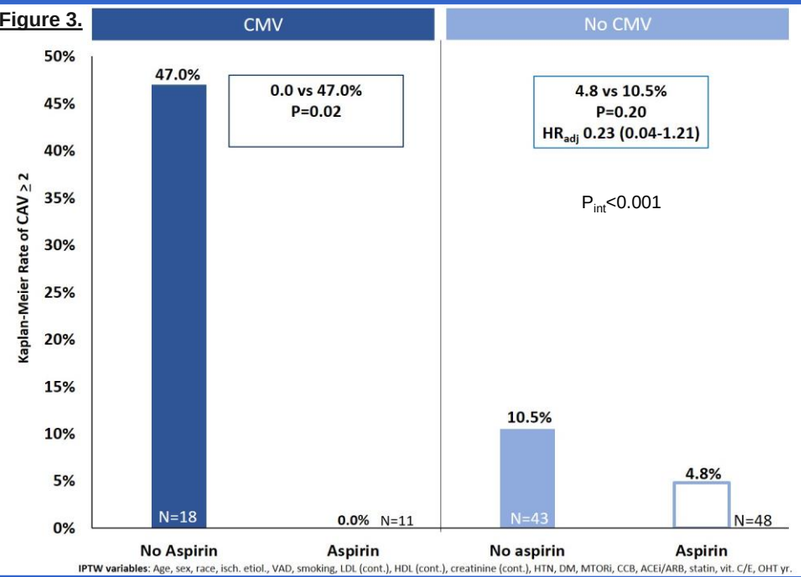


Figure 3.



LIMITATIONS

- Retrospective, non-randomized
- Small sample size
- Single center
- Lack of granularity concerning timing of aspirin use vs timing of rejection, CMV, and CAV
- No correction for multiple testing

CONCLUSIONS

- CAV, which is mediated by endothelial inflammation and platelet activation, remains a major cause of morbidity and mortality after OHT.
- As an anti-inflammatory and antithrombotic agent, aspirin might be expected to impact the risk of CAV, though data are lacking.
- The prevalence of aspirin use after transplant is not known; approximately half of patients receiving OHT were treated with aspirin in this single center cohort.
- Among patients who experienced rejection or CMV infection, there was a strong association between aspirin use and lower rates of moderate or severe CAV.
- These observations suggest the possibility of a biologically plausible role for aspirin and support the need for a randomized evaluation of aspirin's efficacy and safety following heart transplantation.