



Positive Family History of Aortic Dissection Dramatically Increases Dissection Risk in Family Members

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Clinical Scenario

A 45-year-old man comes for consultation

- Asymptomatic
- An enlarged ascending aorta: 4.5 cm
- His father had an aortic dissection 20 years ago

What is his risk of developing aortic dissection?

- Is it **higher**.
- But **how much** higher?
- What would you suggest? Surgical repair or wait?

Objectives

To examine the impact of a positive family history of aortic dissection (FHAD) on the risk of developing aortic dissection (AD) among 1st-degree family members, focusing on:

- age at which AD occurred
- years of exposure to FHAD in adulthood before AD occurred
- annual probability of developing a new AD per adult 1st-degree relative

Number of Events per Exposure Year in Adult First-Degree Relatives

No. of AoD events per exposure year in first degree relatives

$$= \frac{\text{Total No. of AoD events that occurred in the family}}{\sum[(\text{current age of relative or age at death or aortic surgery} - 18) + (\text{Patient age at AoD} - 18)]}$$

Explanation

- Adulthood starts at the age of 18
- Total No. of AoD events = No. of AoDs occurred in 1st-degree relatives
- Exposure years for patient = Age at dissection - 18
- Exposure years for alive relative = Current age - 18
- Exposure years for dead relative = Age at death - 18
- Exposure years for relatives with aortic surgery = Age at surgery - 18

Exposure Years per Adult First-Degree Relative per Event

Exposure years per first degree relative per event

$$= \frac{\sum[(\text{current age of relative or age at death or aortic surgery} - 18) + (\text{patient age at AoD} - 18)]}{\text{No. of AoD events in the family} \times \text{No. of first degree relatives}}$$

Explanation

- Adulthood starts at the age of 18
- Total No. of AoD events = No. of AoDs occurred in 1st-degree relatives
- No. of 1st-degree relatives = 2 parents + No. of siblings & children + 1
- Exposure years for patient = Age at dissection - 18
- Exposure years for alive relative = Current age - 18
- Exposure years for dead relative = Age at death - 18
- Exposure years for relatives with aortic surgery = Age at surgery - 18

Incidence Rates and Odds Ratios in Siblings and Children-Parent Settings

$$\text{Incidence rate of AoD in siblings} = \frac{\text{No. of siblings in whom AoD occurred}}{\text{Total No. of siblings in this study}}$$

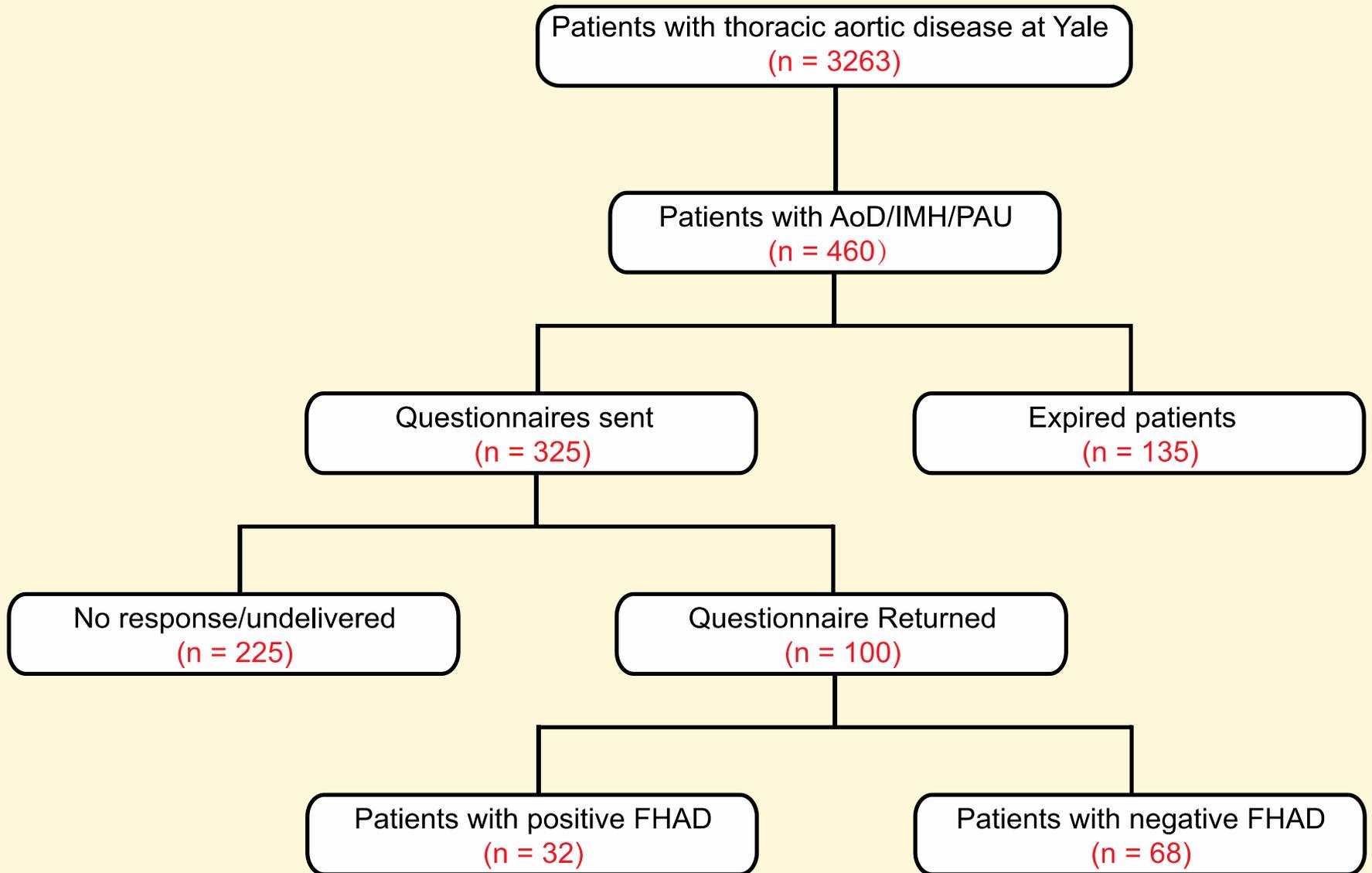
$$\text{OR of AoD in siblings} = \frac{\frac{\text{No. of siblings in whom AoD occurred}}{\text{Total No. of siblings in this study}}}{1 - \frac{\text{No. of siblings in whom AoD occurred}}{\text{Total No. of siblings in this study}}}$$

$$\text{Rate of dissected children per parent} = \frac{\text{No. of children in whom AoD occurred}}{\text{Total No. of parents in this study}}$$

OR of AoD in parent to children setting

$$= \frac{\frac{\text{No. of children in whom AoD occurred}}{\text{Total No. of parents in this study}}}{1 - \frac{\text{No. of children in whom AoD occurred}}{\text{Total No. of parents in this study}}}$$

Flow Diagram of Pedigrees Created



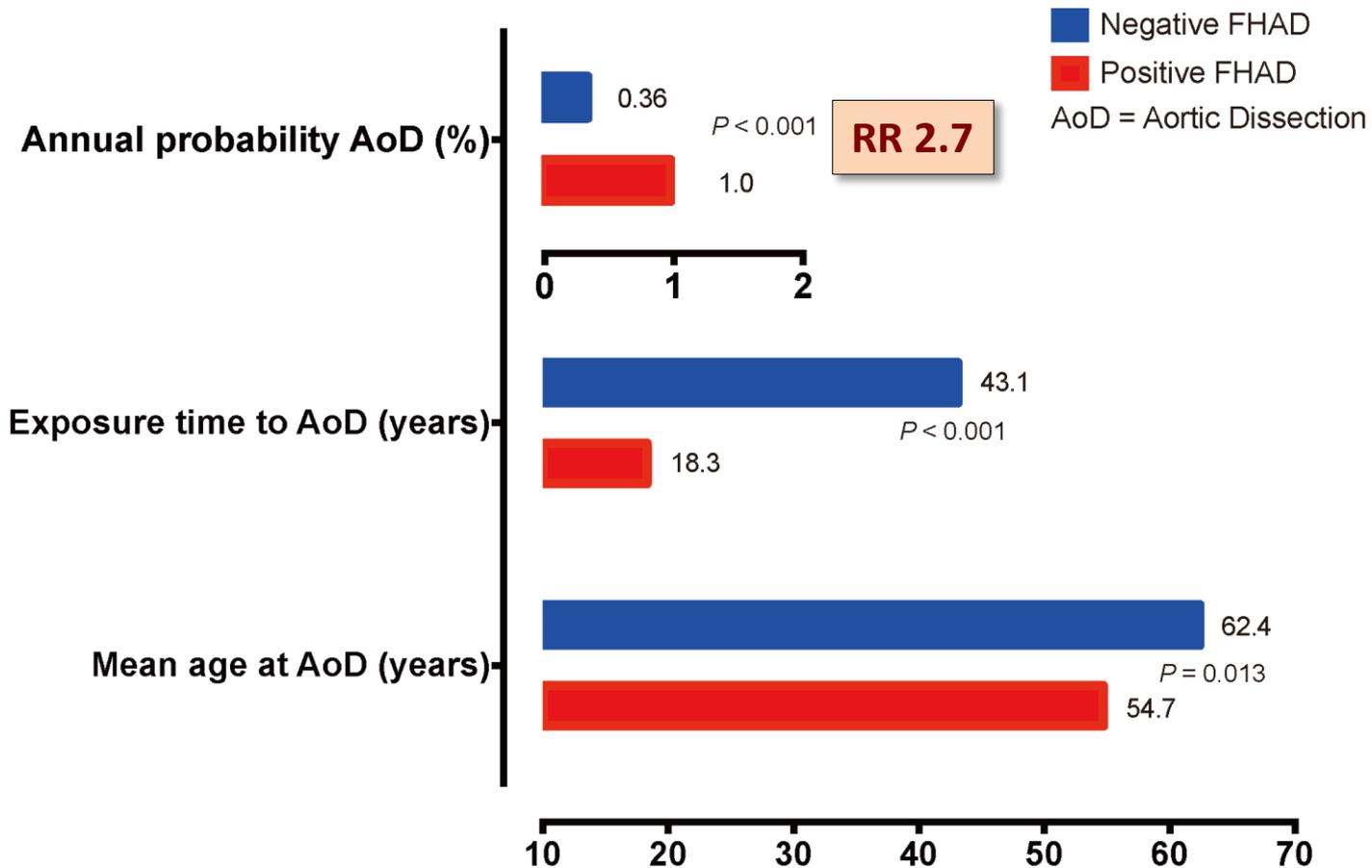
Risk of aortic dissection in patients with negative vs positive family history

Variables	Patients with negative FHAD (n = 68)	Patients with Positive FHAD (n = 32)	P value
Age at dissection (year)	62.4 ± 13.0	54.7 ± 16.8	0.013
Type of dissection (Stanford A/B)	24/8	46/22	0.454
Mean number of 1st-degree relatives	7.3 ± 2.2	7.5 ± 3.2	0.751
Mean number of siblings	3.4 ± 2.0	3.4 ± 1.7	0.957
Mean number of AD events	1.0 ± 0.0	2.3 ± 0.6	< 0.001
Total exposure years in adulthood	313.8 ± 108.5	322.7 ± 199.7	0.768
Number of ADs per year per adult relative (%)	0.359 ± 0.014	0.997 ± 0.057	< 0.001
Exposure years per relative before AD	43.1 ± 8.5	18.3 ± 6.7	< 0.001

Risk of aortic dissection in syndromic vs non-syndromic patients

Variables	Non-Syndromic patients (n = 84)	Syndromic patients (n = 16)	P value
Age at dissection (year)	63.2 ± 13.0	43.0 ± 10.7	< 0.001
Number of first-degree relatives	7.5 ± 2.7	6.7 ± 1.9	0.288
Number of AoD events	1.2 ± 0.4	2.6 ± 0.9	< 0.001
Total exposure years in adult life	332.8 ± 146.4	231.7 ± 86.7	0.009
Annual incidence of AoD per adult relative (%)	0.426 ± 0.283	1.282 ± 0.503	< 0.001
Exposure years per relative per event	39.0 ± 11.1	14.9 ± 10.0	< 0.001
Age at dissection (year)	63.2 ± 13.0	43.0 ± 10.7	< 0.001

Positive FHAD dramatically increases the risk of AoD in family members



Conclusions

- A positive family history of aortic dissection confers a significantly increased risk of developing a new dissection in unaffected family members, in whom dissection occurred at younger age and after shorter exposure years
- These findings are important to guide the strategy of screening, surveillance, and surgical management of other family members

Clinical Implications

- Positive family history of AD may trump all other parameters as a predictor of vulnerability
- In case of positive family history of aortic dissection, early operation should be strongly considered for any first-degree relative with a documented aortic aneurysm, perhaps regardless of the aortic size
- In this era of Whole Exome Sequencing, a positive family history of aortic dissection permits identification of such vulnerable family members via shared genetic variants