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The Evolving Long-Term Outcome of Heart Transplantation in Amyloid Patients

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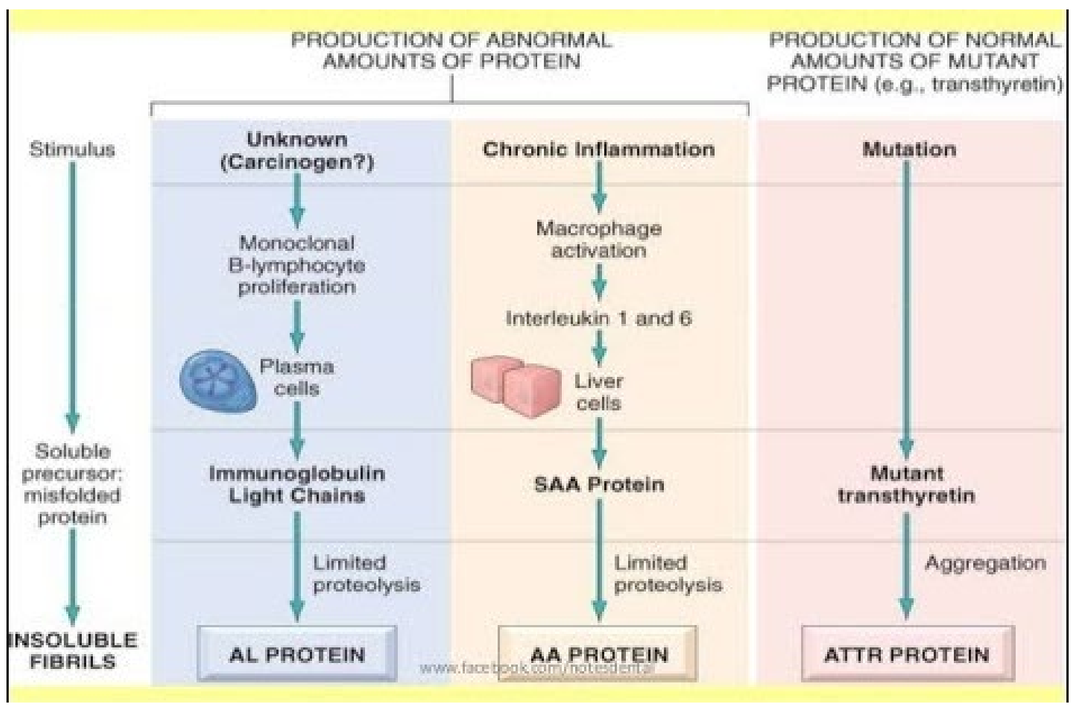
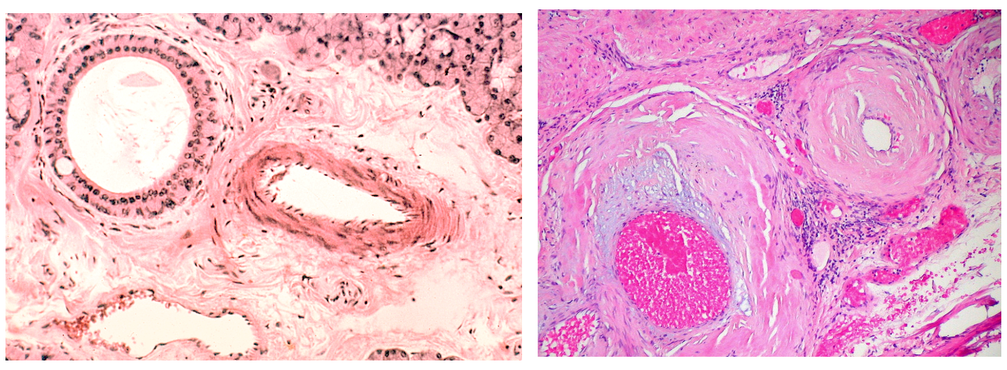
Background



Both amyloid light chain (AL) amyloidosis and transthyretin (TTR) amyloidosis <u>are now expanding indications for heart transplantation (HTx)</u>

In the <u>past</u>, **AL amyloid**, in particular, had been a <u>contraindication</u> to HTx given its <u>suboptimal control</u>, <u>systemic nature & progression to other organs, pre-malignant character, recurrence in allograft/transplanted organ, and the increased risk for mortality</u>.



<u>Advanced ACM carries a poor prognosis!</u>
Standard heart failure therapies have limited utility & can be harmful: including Beta-blockers, ACEIs, ARBs, Digoxin

Left Ventricular Assist Devices (LVADs) have had only isolated successes
- Use of these is often limited by RV dysfunction -> restrictive CM

Modern treatments including <u>proteasome inhibitors</u> *(*reversible*, such as Bortezomib, or* irreversible*)* combined <u>with traditional chemotherapy drugs</u> *(such as melphalan or dexamethasone)* have allowed amyloid patients to increasingly receive heart transplants
- Normalization of free-light chains
- Rapid hematological improvement
- Used for amyloidosis relapse post-HTx

Purpose

In past research, the 2-year survival rate of patients with cardiac amyloidosis is less than 20% without HTx compared to a survival rate of 60% after HTx

We sought to assess long-term post-transplant outcome in amyloid patients in the current era, using our patient population that underwent HTx for cardiac amyloidosis at our single center.

Methods

- **Between 2010 and 2015**, we assessed 45 Heart Transplant Pts:
  - All Amyloid (n=27) -> broken up into AL (n=5), TTR wt senile (n=10), TTR mutant (n=12)
  - Non-Amyloid Restrictive Control (n=18)

- **<u>Endpoints included:</u>**
  - Subsequent 3-year survival
  - Subsequent 3-year freedom from CAV (as defined by stenosis ≥ 30% by angiography)
  - Subsequent 3-year freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke).
  - Subsequent 3-year freedom from any-treated rejection, acute cellular rejection, and antibody-mediated rejection

Demographics & Outcomes

Demographics	All Amyloid (n=27)	Non-Amyloid Restrictive Control (n=18)	P-Value
Mean Recipient Age, Years ± SD	66.6 ± 7.6	47.8 ± 14.3	<0.001
Mean Donor Age, Years ± SD	35.3 ± 11.7	34.2 ± 10.2	0.768
Body Mass Index, Mean ± SD	25.0 ± 3.9	24.7 ± 3.9	0.818
Female (%)	11.1%	61.1%	<0.001
Previous Pregnancy in Females (%)	66.7%	45.5%	0.514
Ischemic Time, Mean Mins ± SD	144.1 ± 47.5	157.1 ± 59.2	0.420
Diabetes Mellitus (%)	22.2%	5.6%	0.130
Status 1 at Transplant (%)	74.1%	77.8%	0.777
Cytomegalovirus Mismatch (%)	22.2%	22.2%	1.000
Treated Hypertension (%)	43.5%	26.7%	0.293
Insertion of Mechanical Circulatory Support Device (%)	14.8%	5.6%	0.332
Prior Blood Transfusion (%)	30.4%	14.3%	0.266
Pre-Transplant PRA ≥ 10% (%)	25.9%	27.8%	0.890
Pre-Transplant Creatinine, Mean ± SD	1.5 ± 0.7	1.4 ± 1.0	0.629

Endpoints	All Amyloid (n=27)	Non-Amyloid Restrictive Control (n=18)	Log-Rank P-Value
3-Year Survival	88.9%	94.4%	0.883
3-Year Freedom from CAV	81.5%	88.9%	0.828
3-Freedom from NF-MACE	85.2%	100.0%	0.112
3-Freedom from Any-Treated Rejection	96.3%	94.4%	0.436
3-Year Freedom from Acute Cellular Rejection	96.3%	100.0%	0.535
3-Year Freedom from Antibody-Mediated Rejection	100.0%	94.4%	0.075

Endpoints	AL (n=5)	TTR wt senile (n=10)	TTR mutant (n=12)	Non-Amyloid Restrictive Control (n=18)	Log-Rank P-Value
3-Year Survival	100.0%	90.0%	83.3%	94.4%	0.790
3-Year Freedom from CAV	80.0%	80.0%	83.3%	88.9%	0.990
3-Freedom from NF-MACE	100.0%	90.0%	75.0%	100.0%	0.112
3-Freedom from Any-Treated Rejection	100.0%	100.0%	91.7%	94.4%	0.619
3-Year Freedom from Acute Cellular Rejection	100.0%	100.0%	91.7%	100.0%	0.518
3-Year Freedom from Antibody-Mediated Rejection	100.0%	100.0%	100.0%	94.4%	0.367

Results Summary

There was no significant difference between the All amyloid and restrictive non-amyloid patients with respect to 3-year survival and 3-year freedom from CAV, NF-MACE, and rejection.

Furthermore, there was no significant difference between the AL amyloid, TTR-wt, TTR-m, and restrictive non-amyloid patients with respect to 3-year survival and 3-year freedom from CAV, NF-MACE, and rejection.

Endomyocardial biopsies post-transplant did not show amyloid.

Conclusion

- In the current era, both AL & TTR amyloid patients have <u>acceptable</u> mid-term outcome after HTx.
- <u>Larger numbers & longer follow-ups</u> are needed to confirm findings.
- Need to consider <u>sociological & economical components</u> to analyze the capability of patients to undergo & afford such extensive Tx.

- **RNA TAFAMIDIS THERAPY, Doxycycline, Green Tea for now!**