

## Management strategies for atrial fibrillation and flutter in patients with transthyretin cardiac amyloidosis

Z. Dale, P. Chandrashekar, L. Al-Rashdan, M. Kim, A. Masri, B. Nazer

Oregon Health and Science University, Knight Cardiovascular Institute, Portland, United States of America

**Funding Acknowledgement:** Type of funding sources: None.

**Background:** Atrial fibrillation (AF) and flutter (AFL) are common in transthyretin cardiac amyloidosis (ATTR-CM). Ventricular rate control drugs in ATTR-CM are poorly tolerated but data addressing tolerability and efficacy of rhythm control strategies is limited.

**Purpose:** We report characteristics and outcomes of AF/AFL in a cohort with ATTR-CM.

**Methods:** A single center observational study of patients seen at our Amyloidosis Center with wild-type or hereditary ATTR-CM diagnosed between 2005–2019. Treatment was prescribed as per treating cardiologists.

**Results:** Eighty-four patients with ATTR-CM (average age 74±10 years, 94% male) had mean follow-up of 27.6±22.8 months. AF/AFL occurred in 61 patients (73%). Clinically significant rapid ventricular response (RVR) was common as well attempted rate control with AV node blockers (Table 1). However, discontinuation was frequent (80%), often for adverse effects of hypotension (33%), bradycardia (15%), or presyncope/syncope (10%). Rhythm control was initiated in 64%, most often with cardioversion (DCCV) or ablation (Table 2). Post-DCCV recurrence was common (91%) and time to recurrence did not differ with use of anti-arrhythmic drugs (AAD; 5.8 months (IQR 1.9–12.5) vs without AAD 6.2 months (IQR 1.9–12.5) p=0.83). TEE was performed for 33% of DCCV with thrombus seen in 11% of cases

– all patients who were not anticoagulated at the time. TEE was otherwise deferred due to known AF/AFL duration <48 hours (13%) or adequate anticoagulation (54%). Ablation was performed in 23% of patients with AFL (all for typical AFL) with 2 patients (14%) having recurrence after mean of 60.9 months. Pulmonary vein isolation for AF was performed in 12% (86% for persistent AF) with 86% recurrence after median of 6.2 months (IQR 5.6–12.3). Most patients (62%) with rhythm control had subjective improvement (≥1 NYHA class or resolved palpitations). Among AAD, amiodarone was most well tolerated with only 8% of patient discontinuing due to side effects. DCCV and ablation resulted in no direct complications although one patient had a perforation of a previously unknown Zenker diverticulum during TEE pre-DCCV.

**Conclusions:** In our ATTR-CM cohort, AF/AFL was common. Rate control was poorly tolerated and often abandoned. While rhythm control of AF/AFL had a favorable safety profile and successful conversion to sinus rhythm led to symptomatic improvement in a majority of cases, durable success with rhythm control was limited, often requiring multiple therapies. DCCV is only modestly successful and not significant improved with AAD. Ablation was successful in cases of cavo-tricuspid isthmus dependent AFL but had limited success in AF.

**Table 1.** Rate Control of AF/AFL in ATTR-CM

Rate control attempted, n (% of total with AF/AFL)	35 (57.4)
Patients with RVR, n (% of total with AF/AFL)	28 (45.9)
Patients with clinically significant RVR, n (% of total with AF/AFL)	25 (41.0)
<b>Beta Blocker</b>	
Number treated, n (% of total with AF/AFL)	34 (55.7)
Number stopped, n (% of subset)	28 (82.4)
Hypotension, n (% of subset)	12 (35.3%)
Bradycardia, n (% of subset)	5 (14.7)
Orthostasis/presyncope/syncope, n (% of subset)	5 (14.7)
Fatigue, n (% of subset)	3 (8.8)
<b>Calcium Channel Blocker</b>	
Number treated, n (% of total with AF/AFL)	6 (9.8)
Number stopped, n (% of subset)	6 (100.0)
Hypotension, n (% of subset)	1 (16.7)
Bradycardia, n (% of subset)	1 (16.7)
Orthostasis/presyncope/syncope, n (% of subset)	1 (16.7)
Constipation, n (% of subset)	1 (16.7)
<b>Digoxin</b>	
Number treated, n (% of total with AF/AFL)	6 (9.8)
Number stopped, n (% of subset)	6 (100.0)
Bradycardia, n (% of subset)	1 (16.7)
Fatigue, n (% of subset)	1 (16.7)
Breakthrough RVR on rate control agent, n (% of subset with RVR)	12 (42.9)
AV node ablation, n (% of subset with RVR)	4 (14.3)

**Table 2.** Rhythm Control of AF/AFL in ATTR-CM

	AF	AFL
<b>DCCV</b>		
Patients with DCCV attempt, n	21	6
DCCV attempts, n	47	8
Patients with recurrence after DCCV, n	19	2
<b>DCCV attempted on AAD, n (% of total)</b>		
Amiodarone, n (% of subset)	28 (59.6)	5 (62.5)
Dofetilide, n (% of subset)	20 (71.4)	5 (100.0)
Sotalol, n (% of subset)	4 (14.3)	0 (0.0)
Propafenone, n (% of subset)	2 (7.1)	0 (0.0)
Dronedarone, n (% of subset)	1 (3.6)	0 (0.0)
Dronedarone, n (% of subset)	1 (3.6)	0 (0.0)
Median time in sinus rhythm, months (IQR)	7.8 (1.5-12.5)	10.9 (5.4-21.3)
Median time in sinus rhythm with amiodarone, months (IQR)	11.5 (7.5-20.9)	6.3 (5.8-15.5)
<b>ABLATION</b>		
Patients with AFL ablation, n (% of total AF/AFL population)	14 (23.0)	
Number of AFL ablation, n	15	
Cavo-tricuspid isthmus ablation, n (% of subset)	15 (100.0)	
Recurrence of AFL ablation, n (% of subset)	2 (14.3)	
Median time to recurrence, months	60.9	
Patients with AF ablation*, n (% of total AF/AFL population)	7 (11.4)	
Ablation with amiodarone, n (% of subset)	0 (0.0)	
Ablation with sotalol, n (% of subset)	1 (14.3)	
Ablation with dofetilide, n (% of subset)	1 (14.3)	
Recurrence after AF ablation, n (% of subset)	6 (85.7)	
Median time to recurrence, months (IQR)	6.2 (5.6-12.3)	