Amylose cardiaque et arythmies

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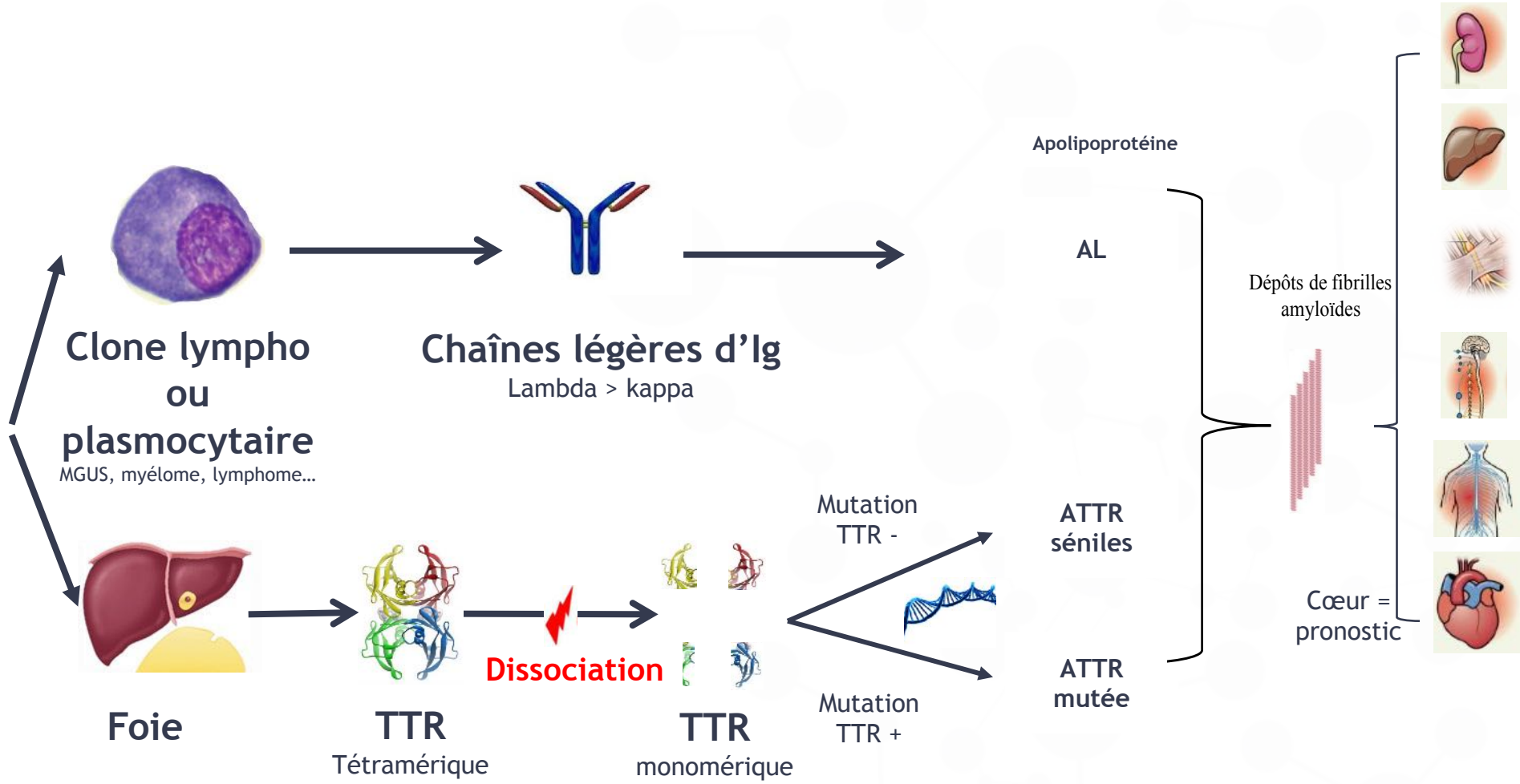
18/11/2023

Amylose(s) cardiaque(s)



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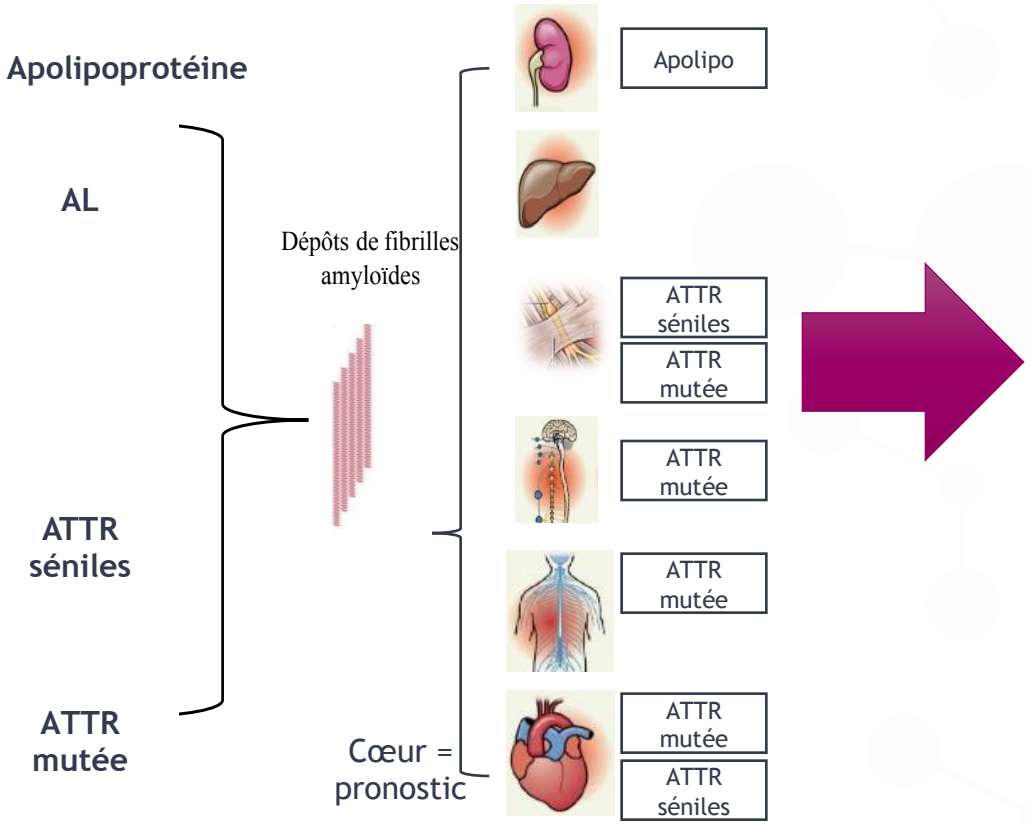

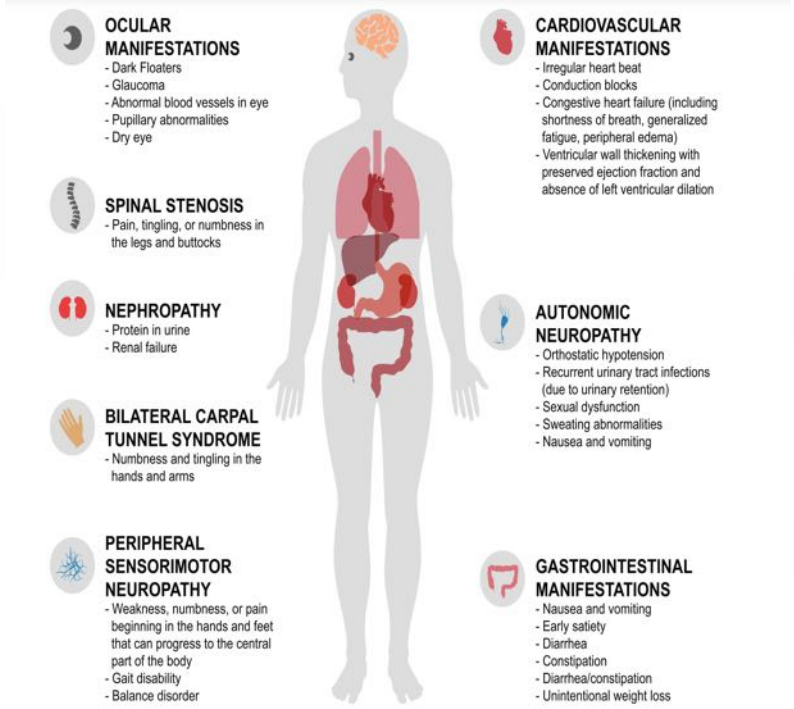

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Amylose cardiaque et arythmies

Quelles questions ?

1. Quand anticoaguler ?

2. Que faire des TSV sur le plan antiarythmique ?

1. Quand anticoaguler ?
La fibrillation atriale est très prévalente dans l'AC

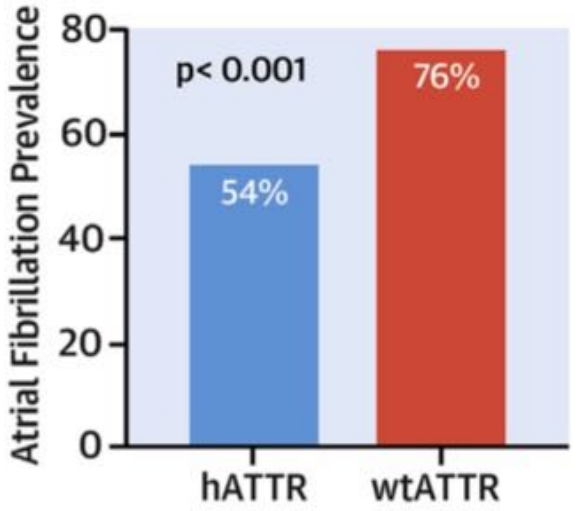
Atrial Fibrillation in Transthyretin Cardiac Amyloidosis

Predictors, Prevalence, and Efficacy of Rhythm Control Strategies

Eoin Donnellan, MD, Oussama M. Wazni, MD, Mazen Hanna, MD, Mohamed B. Elshazly, MD, Rishi Puri, MD, PhD, Walid Saliba, MD, Mohamed Kanj, MD, Sneha Vakamudi, MD, Divyang R. Patel, MD, Bryan Baranowski, MD, Daniel Cantillon, MD, Thomas Dresing, MD, Wael A. Jaber, MD

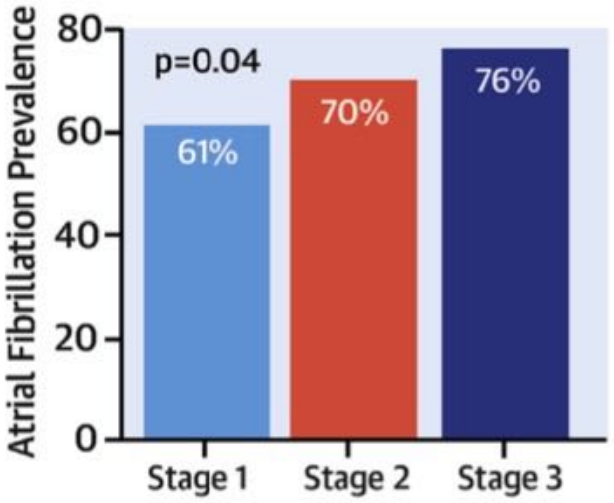
- 382 patients (111 ATTRv, 271 ATTRwt)
- 1 centre (Cleveland Clinic), 2004-2018
- Suivi médian = 35 mois
- Evaluation en fonction du NAC score

- **FA chez 265 patients (69%) dont 33% au diagnostic**
- **Temps médian entre dg d'ATTR et AFA : 15 mois**



NAC Score :

- ❑ Stade I : NT-proBNP ≤ 3000 ng/L et eGFR ≥ 45 ml/min
- ❑ Stade III : NT-proBNP >3000 ng/L et eGFR <45 ml/min
- ❑ Stade II : les autres



Donnellan et al., J Am Coll Cardiol EP 2020, Gillmore et al., Eur Heart J 2018

1. Quand anticoaguler ?
La fibrillation atriale n'est pas corrélée à la mortalité

- Pronostic incertain (patients très graves++)

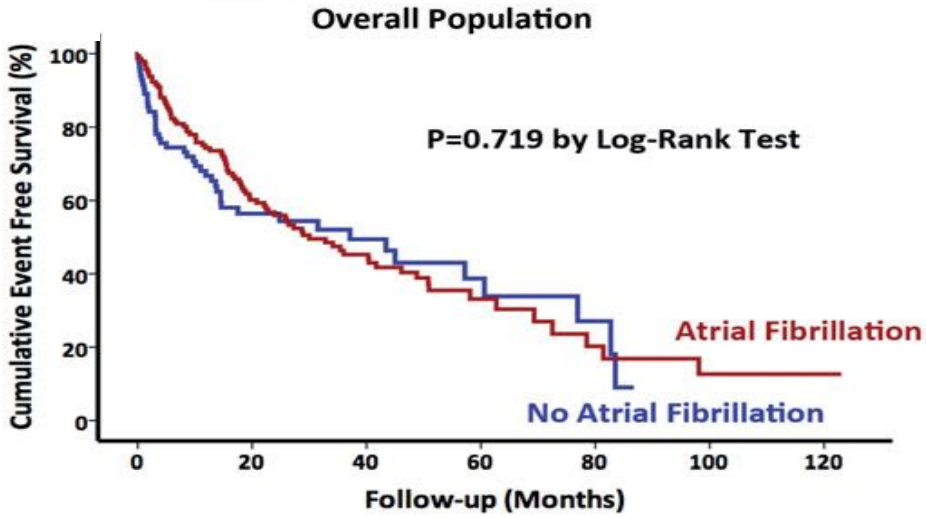
ARTICLE

Check for updates

Atrial fibrillation and subtype of atrial fibrillation in cardiac amyloidosis: clinical and echocardiographic features, impact on mortality

Kevin Sanchis[a,b], Eve Cariou[a,b,c], Magali Colombat[d], David Ribes[e,f], Antoine Huart[e,f], Pascal Cintas[g], Pauline Fournier[a,b], Anne Rollin[a], Didier Carrié[a,b,h], Michel Galinier[a,b,c], Philippe Maury[a,h,i], Alexandre Duparc[a] and Olivier Lairez[a,b,h,j], On behalf of the Toulouse Amyloidosis Research Network collaborators*

Results: One hundred and four (44%) patients had history of AF at the time of diagnosis: 62 (60%) permanent and 42 (40%) non-permanent. There were 30 (26%) and 74 (60%) patients with history of AF among patients with AL and ATTR (including 5 hereditary and 69 wild-type), respectively ($p<.0001$). During the follow-up, 48 new patients developed AF (29, 12 and 7 among patients with AL, wild-type ATTR and hereditary ATTR). After adjustment for age, survival was similar in patients with or without history of AF (HR 0.87 (95% CI, 0.60 to 1.27; $p=.467$). AF had no impact on cardiovascular mortality. Among the 152 patients with history of AF included in the whole study, there were 75 (49%) patients with permanent AF. After adjustment for age, survival was similar in patients with permanent and non-permanent AF: HR 1.29 (95% CI, 0.84 to 1.99; $p=.251$). The results were the same among patients with AL or wild-type amyloidosis. Subtype of AF had no impact on cardiovascular mortality.
Conclusions: AF is common in patients with CA. However, AF and clinical subtype of AF have no impact on all-cause mortality, whatever the type of amyloidosis.



Sanchis et al. Amyloid. 2019 Sep;26(3):128-138.

1. Quand anticoaguler ?

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Réseau Amylose

Arterial thrombo-embolic events in cardiac amyloidosis: a look beyond atrial fibrillation

Francesco Cappelli[a,b], Giacomo Tini[c,d], Domitilla Russo[e], Michele Emdin[f,g], Annamaria Del Franco[f,g], Giuseppe Vergaro[f,g], Gianluca Di Bella[h], Anna Mazzeo[h], Marco Canepa[c,d], Massimo Volpe[e,i], Federico Perfetto[a], Camillo Autore[e], Carlo Di Mario[b], Claudio Rapezzi[j,k] and Maria Beatrice Musumeci[e]

- 406 patients (134 AL, 73 ATTRv, 199 ATTRwt)
- 5 centres en Italie
- Suivi médian = 19 mois
- **AEs = évt thrombo embolique artériel**

Messages :

- **31 AEs (7,6%) dont 10 au diagnostic / 21 pdt suivi**
  - **29 évt cérébraux (8 AIT and 21 AVC) et 2 évt périphériques (1 mésentérique et 1 fémorale)**
  - **32% des patients étaient en RS (et sans histoire de FA)**
  - **23% avec CHADS-VASc 1-2**
- **7.6% des patients anticoagulés ont fait un AEs**
- **9 AL (6.7%), 6 ATTRv (8.2%), 16 ATTRwt (8.0%).**

Cappelli et al, Amyloid 2020

Table 1. Characteristics of cardiac amyloidosis patients with versus without arterial thrombo-embolic events.

	No AEs $n=375$	AEs at first presentation $n=10$	AEs during follow up $n=21$	p^a
Age at diagnosis	72.5 ± 11.2	74 ± 5.0	73.7 ± 8.9	.80
Age ≥75 years	217 (57.9)	5 (50.0)	13 (61.9)	.84
Males	298 (79.5)	7 (70.0)	18 (85.7)	.83
Type of CA				.71
AL	125 (33.3)	3 (30.0)	6 (28.0)	
ATTRm	67 (17.9)	2 (20.0)	4 (19.0)	
ATTRwt	183 (48.8)	5 (50.0)	11 (52.4)	
Previous arterial thrombo-embolic event	13 (3.5)	0 (0)	1 (4.8)	.79
BMI	24.9 ± 3.9	23.0 ± 2.0	25.1 ± 3.0	.30
NYHA functional class III–IV at first evaluation	116 (30.9)	2 (20.0)	6 (28.6)	.46
Any atrial fibrillation at first evaluation	125 (33.3)	7 (70.0)	6 (28.6)	.05
LV ejection fraction (%)	53.5 ± 9.0	49.0 ± 8.0	50.7 ± 12.2	.19
≤50%	146 (38.9)	5 (50.0)	11 (52.4)	.39
IVS (mm)	16.7 ± 3.5	15.8 ± 3.0	17.0 ± 3.0	.66
Left atrial dimension (mm)	45.1 ± 6.4	47.0 ± 6.0	46.9 ± 4.7	.42
Restrictive pattern	138 (36.8)	4 (40.0)	8 (38.1)	.47
BNP (ng/ml)	475 (176–1100)	335 (245–335)	395 (236–522)	.32
NT-proBNP (ng/ml)	3125 (1271–6607)	4527 (2633–9049)	2483 (684–3892)	.23
Troponin I (ng/ml)	0.07 (0.04–0.15)	0.08 (0.02–0.17)	0.07 (0.03–0.08)	.33
CKD	170 (45.3)	6 (60.0)	13 (61.9)	.13
CHA_2DS_2-VASc score				<.0001
0	8 (2.0)	0 (0)	0 (0)	
1–2	131 (34.9)	0 (0)	5 (23.8)	
≥3	236 (62.8)	10 (100.0)	16 (76.2)	
NYHA functional class III–IV at follow-up[b]	192 (51.2)	4 (40.0)	14 (66.7)	.29
Any atrial fibrillation at follow-up[b]	178 (47.7)	7 (70.0)	14 (66.7)	.03
LV ejection fraction ≤50% at follow-up[b]	164 (43.7)	7 (70.0)	15 (71.4)	.03
Anticoagulation therapy[b,c]	171 (45.6)	2 (20.0)	12 (57.1)	.17
Death	111 (29.6)	2 (20.0)	8 (38.1)	.94

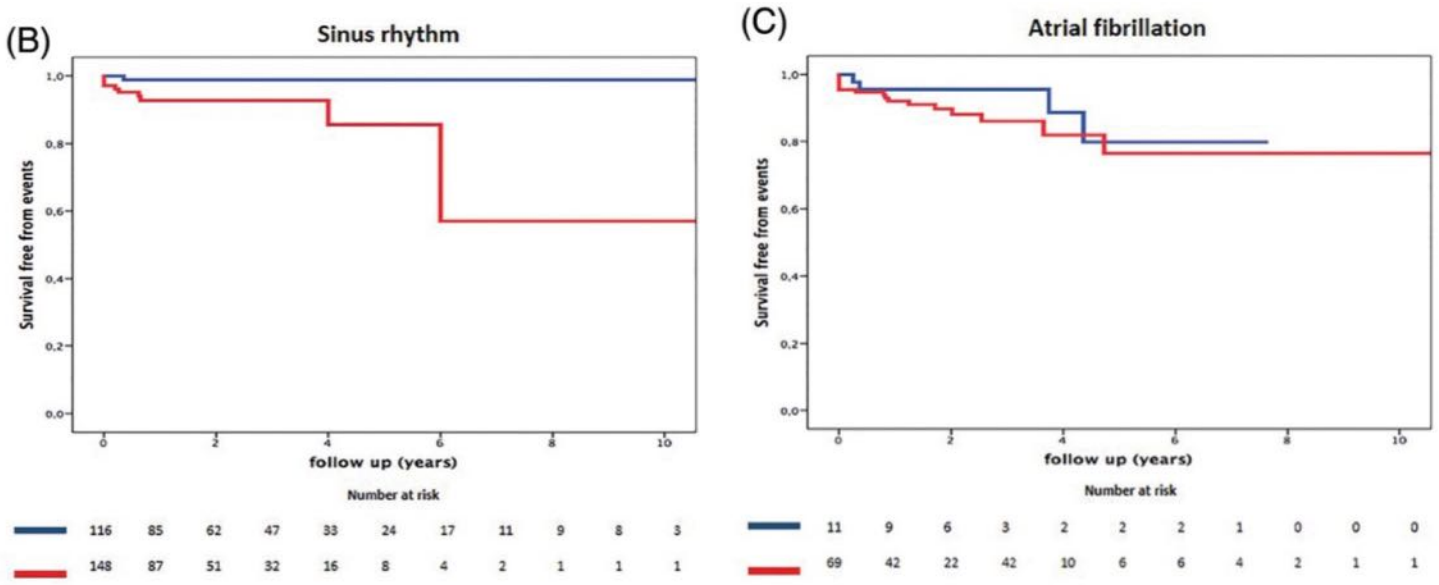
1. Quand anticoaguler ? Plus récemment

Arterial thrombo-embolic events in cardiac amyloidosis: a look beyond atrial fibrillation

Francesco Cappelli[a,b], Giacomo Tini[c,d], Domitilla Russo[e], Michele Emdin[f,g], Annamaria Del Franco[f,g], Giuseppe Vergaro[f,g], Gianluca Di Bella[h], Anna Mazzeo[h], Marco Canepa[c,d], Massimo Volpe[e,i], Federico Perfetto[a], Camillo Autore[e], Carlo Di Mario[b], Claudio Rapezzi[j,k] and Maria Beatrice Musumeci[e]

Table 2. Relationship between clinical, morphologic and functional features at initial evaluation and occurrence of arterial thrombo-embolic events in patients with cardiac amyloidosis.

	Univariate		
	Hazard ratio	95% CI	*p*
Female sex	0.53	0.16–1.82	.31
Transthyretin cardiac amyloidosis	0.50	0.13 – 1.92	.31
Age ≥75 years	1.34	0.55–3.24	.52
Chronic kidney disease	1.94	0.77–4.87	.16
Atrial fibrillation at first evaluation	1.65	0.80–3.39	.17
CHA_2DS_2-VASc score ≥3	2.84	1.02–7.92	.05
Left ventricular ejection fraction ≤50% at first evaluation	1.95	0.83–4.60	.13
Anticoagulation therapy	1.23	0.52–2.92	.64



Facteurs prédictifs d'évènements thrombo emboliques

Patient en FA :

- ❖ CHADS-VASc non prédictif d'AEs

Patients en RS :

- ❖ CHADS-VASC ≥ 3 prédictif d'AEs

Cappelli et al, Amyloid 2020

1. Quand anticoaguler ?
Que nous disent les recommandations ?

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Réseau Amylose

Table 7 Proposed follow-up scheme in cardiac amyloidosis

	AL	ATTR
Patients with cardiac amyloidosis	*Every month* (during initial haematological treatment): • Complete blood count, basic biochemistry, NT-proBNP, and troponin • Serum free light chain quantification • Clinical evaluation by Haematology • Evaluation by Cardiology if clinically indicated *Every 3–4 months* (after completing initial haematological treatment): • Complete blood count, basic biochemistry, NT-proBNP, and troponin • Serum free light chain quantification • Clinical evaluation by Haematology *Every 6 months:* • ECG • Echocardiography/CMR • Evaluation by Cardiology *Every 12 months:* • 24-h Holter ECG	*Every 6 months:* • ECG • Blood tests including NT-proBNP and troponin • Neurological evaluation (if ATTRv) • 6MWD (optional) • KCCQ (optional) *Every 12 months:* • Echocardiography/CMR • 24-h Holter ECG • Ophthalmological evaluation (if ATTRv)

Table 8 Areas of investigation and uncertainty in cardiac amyloidosis

Pathophysiology

Amyloidogenesis
- Mechanism for tissue tropism
- Role of enzymatic cleavage
- Role of mechanical stress at tissue level

Determinants of phenotypic heterogeneity
- Gender
- Modifier genes
- Epigenetics
- Fibre composition

Diagnosis

Populations to screen for cardiac amyloidosis and optimal screening method

Expanded genetic testing in the overall population

Identification of a plasmatic biomarkers of unfolded TTR

Artificial intelligence tools to facilitate diagnosis (imaging, ECG, etc.)

Identification of the target of bone tracers within amyloid deposits

Validation of PET tracers for diagnosis of cardiac amyloidosis, differential diagnosis of ATTR vs. AL, and evaluation of amyloid burden

Natural history

Disease trajectories among carriers of different mutations

Definition and measurement of disease progression
- Ventricular thickness, mass, function
- Exercise capacity
- Biomarkers including monitoring of pre-albumin.
- TTR stability, kinetics, ligands as monitors of disease progression

Treatment of complications

Initiation of anticoagulation in patients without atrial fibrillation

Efficacy of heart failure drugs in patients with different degrees of heart failure

Efficacy of beta-blockers. Identification of patients who could benefit

Role of invasive heart failure monitoring devices

Identification of patients that benefit from prophylactic pacemaker

Identification of subgroups that can benefit from ICD and CRT

Continued

Garcia Pavia et al. European Heart Journal (2021) 42, 1554–1568

1. Quand anticoaguler ?
Que nous disent les recommandations ?

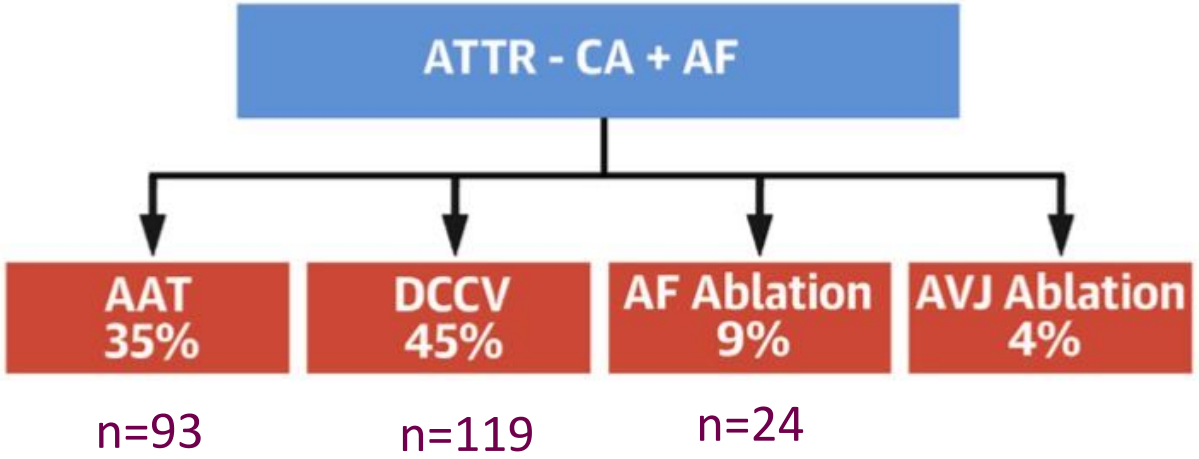
Le risque élevé continu d'événements thromboemboliques chez les patients atteints d'une amylose cardiaque justifie de discuter pour chaque patient des bénéfices (prévention de la thrombose) et des risques hémorragiques (atteinte cutanée importante ou gastrique) d'une anticoagulation à dose efficace. Il est nécessaire de demander un avis au centre expert le plus proche.

	Risques Thrombotiques	Risques Hémorragiquse
AL	-Profil transmitral restrictif -Onde E unique avec onde A absente sur le flux transmitral -Hyperexcitabilité atriale ou fibrillation atriale -Dysfonction VG	-Lésions cutanées ou muqueuses importantes -Déficit en facteur X
ATTRwt		
ATTRv		-Lésions digestives avec antécédents de saignement. -Mutation ATTR Val30Met p.(Val50Met) avec antécédent de greffe hépatique

Tableau 7 : Anomalies associées au risque thrombotique ouhémorragique dans les amyloses cardiaques

2. Que faire des TSV ? Cardioversion ?

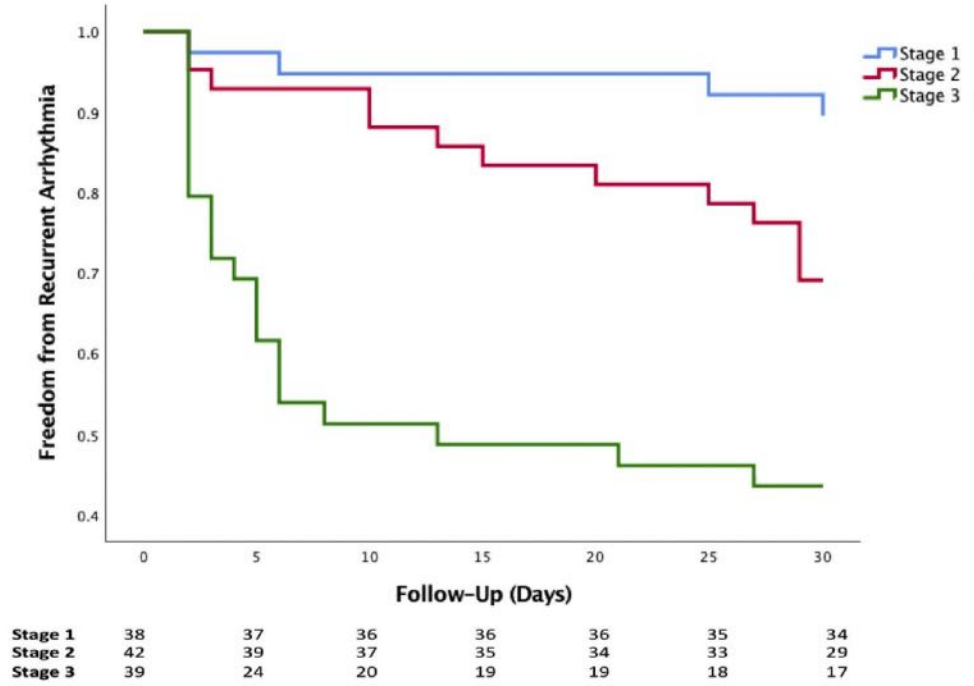
- Difficultés de maintien en RS
- **Cardioversion (taux de succès environ 50% à 30 jours)**



Après AAT (medt) : 31% maintiennent le RS (53% stade 1 vs 17% stade 3)
Après DCCV (CEE) :

- Efficacité immédiate : 95% (97% stade 1; 95% stade 2; 92% stade 3 ; p 0.58).
- A 30 jours : 61% en RS (90% stade 1 ; 60% stade 2 ; 33% stade 3)
- A 1 an : 41% en RS (74% stade 1 ; 33% stade 2 ; 18% stade 3)

Après ablation de FA : Après un suivi médian de 40 mois : récidive chez 58% (36% stade 1 ou 2 ; 90% stade 3 (p 0.005)



30-day maintenance of NSR following DCCV

Donnellan et al. JACC Clin Electrophysiol. 2020 Sep;6(9):1118-1127.

2. Que faire des TSV ? Cardioversion ?

Meilleur pronostic en cas de maintien du RS après cardioversion

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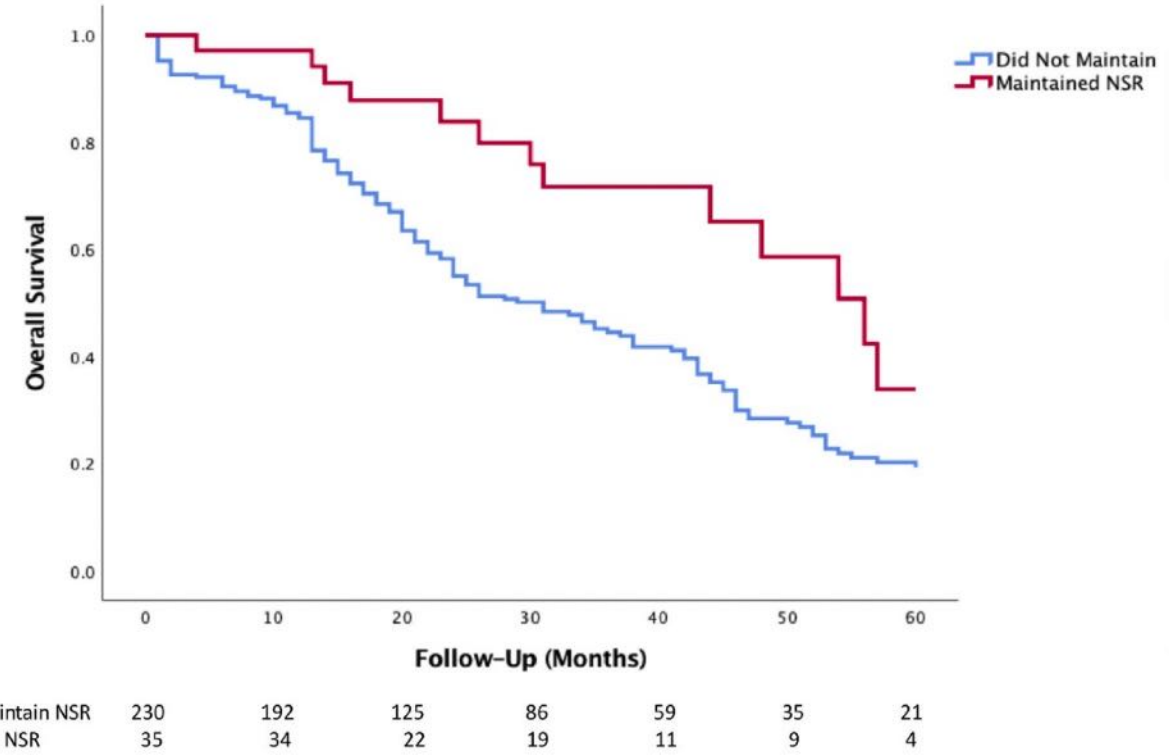


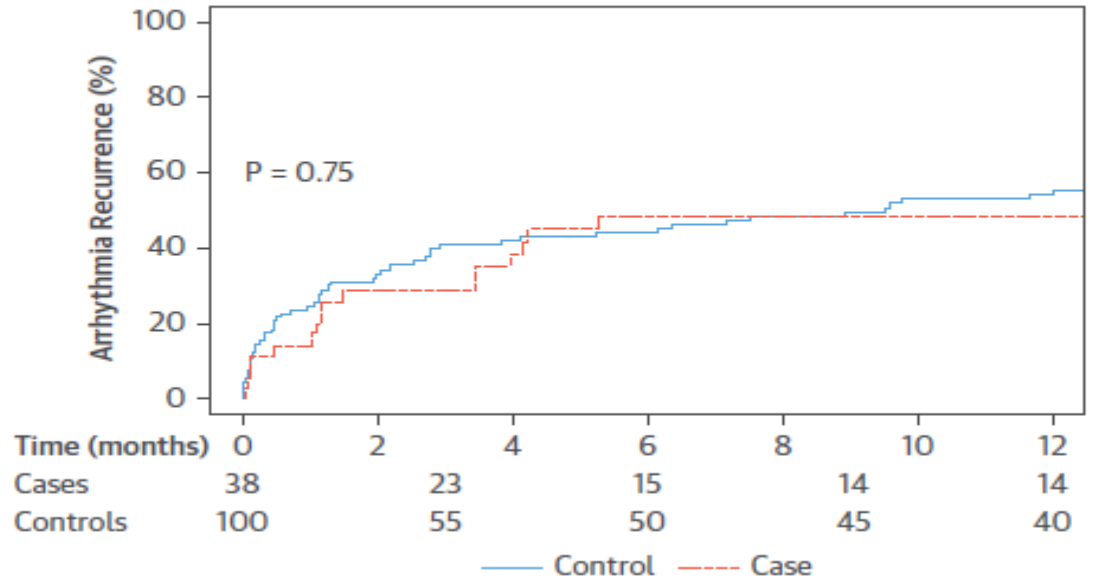
Donnellan et al. JACC Clin Electrophysiol. 2020 Sep;6(9):1118-1127.

2. Que faire des TSV ? Cardioversion ? Oui, mais …

Direct Current Cardioversion of Atrial Arrhythmias in Adults With Cardiac Amyloidosis

Edward A. El-Am, MD,[a] Angela Dispenzieri, MD,[b] Rowlens M. Melduni, MD, MPH,[a] Naser M. Ammash, MD,[a] Roger D. White, MD,[c] David O. Hodge, MS,[d] Peter A. Noseworthy, MD,[a] Grace Lin, MD,[a] Sorin V. Pislaru, MD, PhD,[a] Alexander C. Egbe, MBBS, MPH,[a] Martha Grogan, MD,[a] Vuyisile T. Nkomo, MD, MPH[a]

FIGURE 1 Rate of Atrial Arrhythmia Recurrence Following Successful DCCV in Patients With CA Compared With Control Patients



58 AC comparé à une population sans amylose
28% d'annulation de cardioversion chez les AC vs. 7%; p < 0.001 pour cause de thrombus malgré anticoagulation efficace ou FA < 48h

Succès cardioversion identique (90% vs. 94%; p = 0.4)

Plus de **complications** chez les AC : arythmie vetriculaire et **bradycardie nécessitant PM**

➔ Taux élevé de thrombus intra-OG ➔ ETO systématique avant CEE

TABLE 3 TEE Data of CA Compared With Control Patients

	Cardiac Amyloidosis (n = 46)	Control Group (n = 79)	p Value
Spontaneous echocardiogram contrast	31 (67)	34 (43)	0.01
Thrombus identified on echocardiogram	13 (28)	2 (2.5)	<0.001
Echo LAA emptying velocity, cm/s	20.6 ± 14.1 (n = 38)	33.9 ± 18.4 (n = 65)	<0.001

Values are n (%) or mean ± SD.
LAA = left atrial appendage; other abbreviations as in Table 1.

El-Am et al. J Am Coll Cardiol. 2019 Feb 12;73(5):589-597.

2. Que faire des TSV ?
Eliminer thrombus intracardiaque +++

RÉSEAU AMYLOSE MONDOR
CRMR - AMYLOSES CARDIAQUES
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Filière CARDIOGEN

Electrical cardioversion of atrial arrhythmias with cardiac amyloidosis in the era of direct oral anticogulants

Olivier Touboul[1], Vincent Algalarrondo[2], Silvia Oghina[1], Nathalie Elbaz[1], Segolene Rouffiac[1], David Hamon[1], Fabrice Extramiana[2], Estelle Gandjbakhch[3], Thomas D'Humieres[4], Eloi Marijon[5], Tarvinder S. Dhanjal[6], Emmanuel Teiger[1], Thibaud Damy[1] and Nicolas Lellouche[1]*

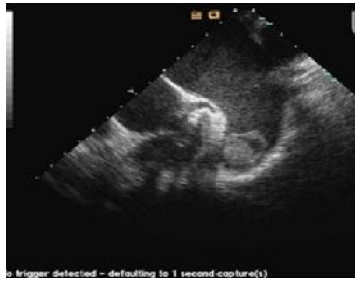
[1]Department of Cardiology, AP-HP, University Hospital Henri Mondor, 51, Avenue du Maréchal de Lattre de Tassigny, 94000, Creteil, France; [2]Department of Cardiology, AP-HP, University Hospital Bichat, Paris, France; [3]Department of Cardiology, AP-HP, University Hospital Pitié-Salpétrière, Paris, France; [4]Department of Physiology, AP-HP, University Hospital Henri Mondor, Creteil, France; [5]Department of Cardiology, AP-HP, University Hopital Européen Georges Pompidou, Paris, France; and [6]Department of Cardiac Electrophysiology, University of Warwick, Gibbet Hill, Coventry, UK

66 patients
Tous anticoagulés sauf 1 (AOD dans 74% des cas)
Imagerie à la recherche de thrombus systématique (ETO ou scanner)

14% des cardioversions annulées pour cause de thrombus

Résolution complète du thrombus dans seulement 17% des cas.
Deux facteurs prédictifs de thrombus : créatinine, AAP The two

88% de succès. Récidive (sous Cordarone) dans 51% des cas après un suivi médian de 30 ± 27 mois



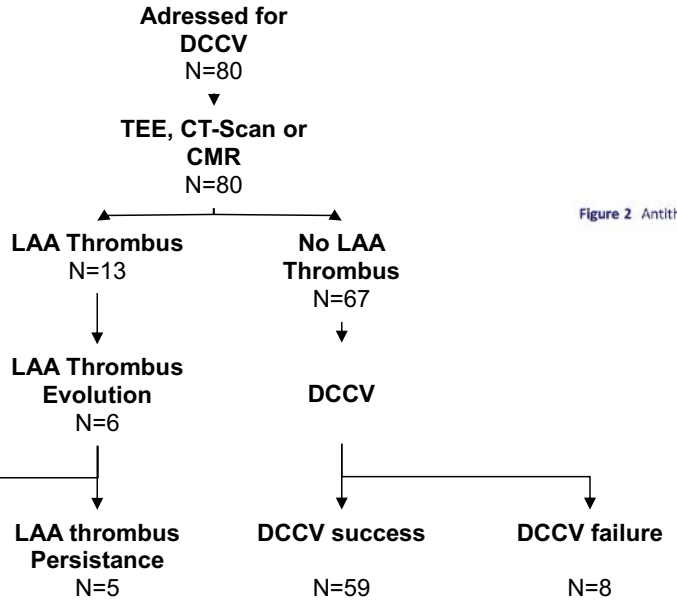
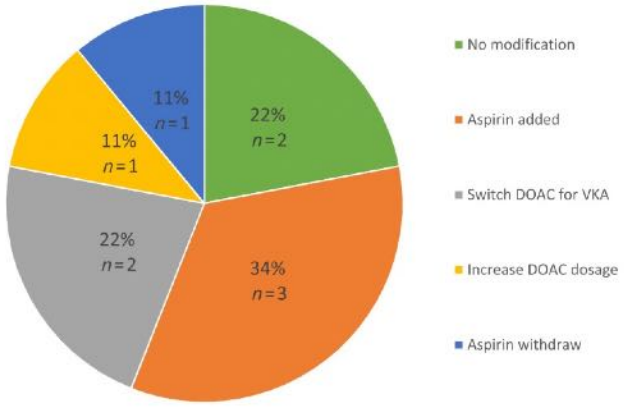
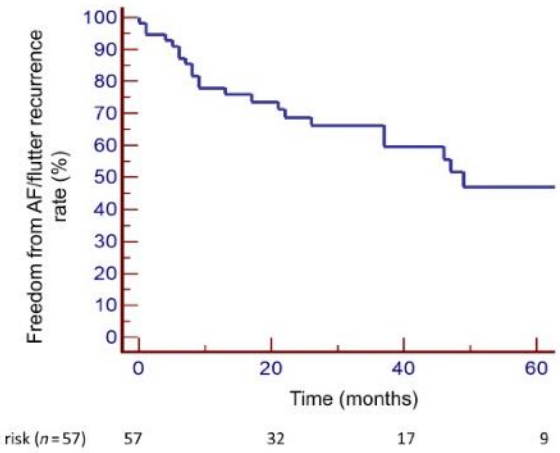


Figure 2 Antithrombotic strategy following left atrial thrombus diagnosis (n = 13). DOAC, direct oral anticoagulant; VKA, vitamin K antagonist.

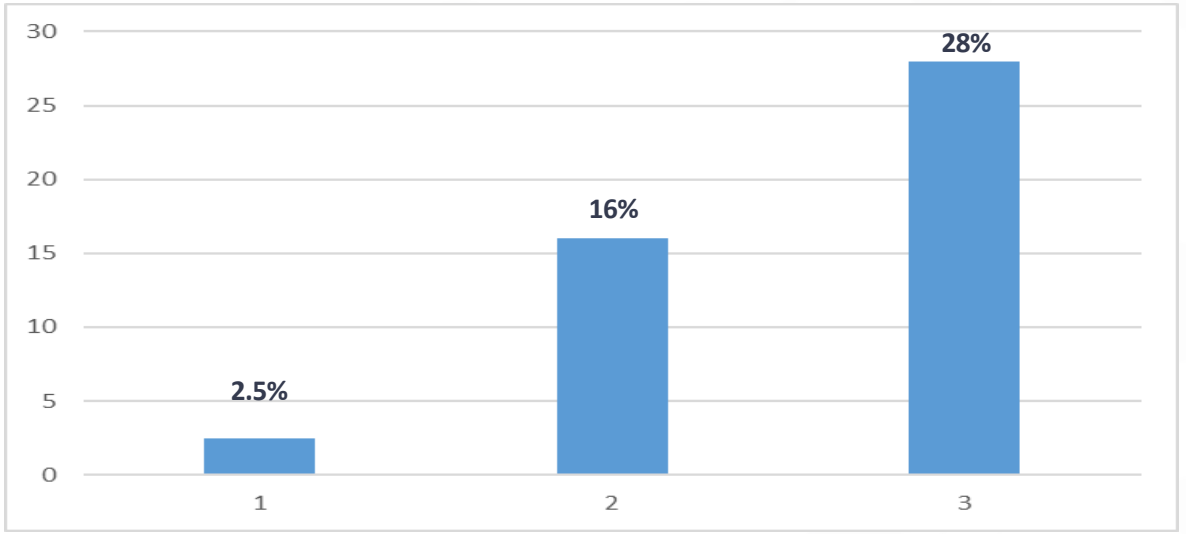




Touboul et al. ESC Heart Fail. 2022 Jul 28.

2. Que faire des TSV ?
Eliminer thrombus intracardiaque +++

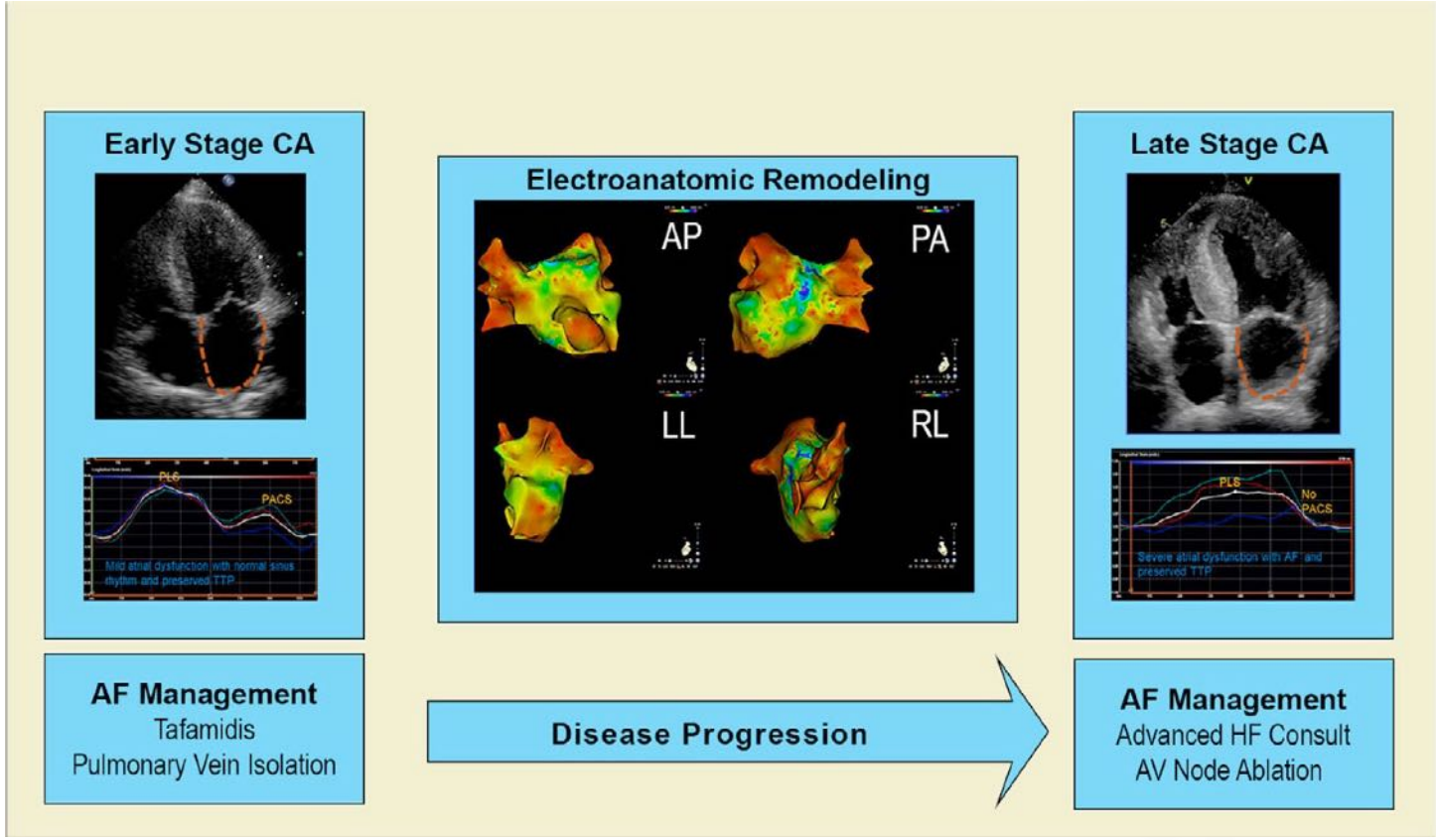
- Moins de thrombi sous AOD ?



Taux de thrombus auriculaire gauche chez les patients en FA :
1 : sans AC sous OAD ; 2 : dans notre étude avec des AC majoritairement sous AOD (75 %) ; 3 : chez les AC sous AVK

2. Que faire des TSV ?
Ablation de FA

Résultats moins bons que pour les autres patients (petites séries)
Oreillettes très pathologiques



2. Que faire des TSV ?
Ablation de FA – Série Française

Background:

Atrial arrhythmias (AA) commonly affect patients with cardiac amyloidosis (CA) and are a relevant cause of heart failure (HF) in CA. This study sought to investigate the long-term impact of catheter ablation in patients with CA and AA.

Methods:

Thirty-one patients with CA and AA undergoing catheter ablation were retrospectively included (ATTR CA 61 % and AL CA 39 %). AA were atrial fibrillation (AFib) in 22 (paroxysmal in 10 and persistent in 12), atrial common flutter (AF) in 17 and atrial tachycardia (AT) in 11.

Results:

Recurrences of any AA were observed in 14 patients (45 %) at a median of 4 months (AFib 8, AT 6, AF 0). After cardioversions, medical therapy or new ablation procedures, 10 patients remained in permanent AA (32%). Over a mean follow-up of 27±28 months, all-cause mortality was 39% (12 patients, 3 with intractable HF and 5 due to late complications of amyloidosis).

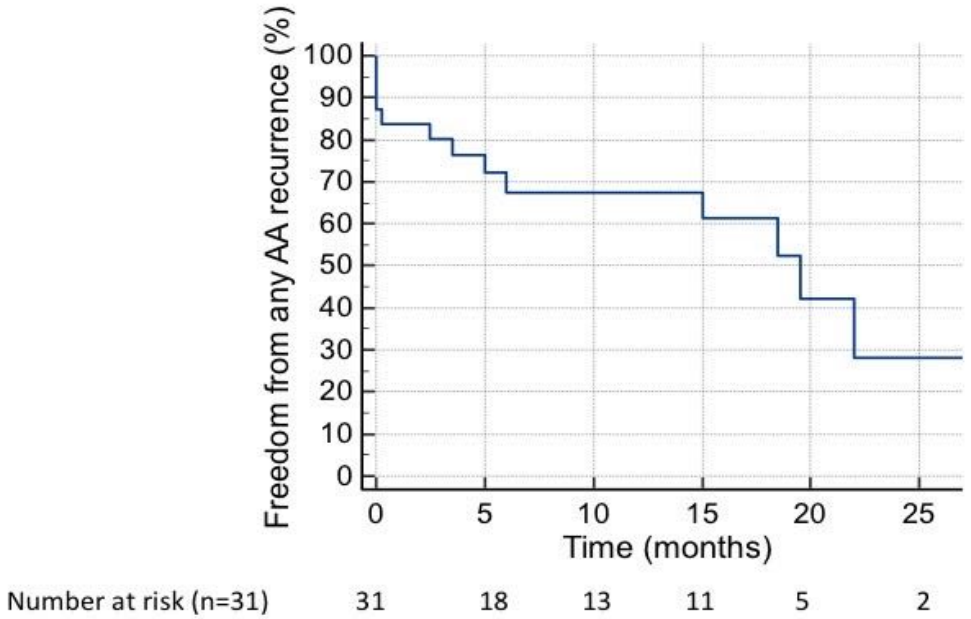
Post- ablation analyses (while in sinus rhythm) demonstrated significant reductions in serum creatinine and BNP levels as well as NYHA class. Only two patients required hospitalisation for HF while remaining in sinus rhythm compared to five with relapse of AA (p=0.1). All three patients with intractable heart failure leading to death had recurrent AA compared to 11 out of the 28 surviving patients or patients not deceased from heart failure (p=0.04). When comparing surviving and deceased patients from any cause, recurrence of AA was not associated with survival.

Conclusion:

This study demonstrates moderate long-term efficacy of catheter ablation of AA in CA in maintenance of sinus rhythm. However, enhancements in clinical and biological status and positive trends in cardiovascular mortality are observed if sinus rhythm can be preserved.

➔ Intérêt d'une intervention thérapeutique rythmologique précoce au cours de la FA++

2. Que faire des TSV ?
Ablation de FA - Série Française



	Before ablation	After ablation	p value
Creatinine (µm/l)	141 ± 68	123 ± 51	0.003
NT-proBNP (pg/mL)	4001 ± 3292	3189 ± 2843	0.01
Weight (kg)	79 ± 13	78 ± 13	0.16
NYHA class	2.7 ± 0.7	2 ± 0.6	0.0009
Left atrial volume (ml/m²)	97 ± 25	92 ± 30	0.6
Systolic pulmonary arterial pressure (mm Hg)	44 ± 13	36 ± 9	0.26

2. Que faire des TSV ?
Gestion des antiarythmiques

- Les béta-bloquants, les AA de classe I et la digoxine sont contre-indiqués (mauvaise tolérance)

- Seule l'amiodarone peut être utilisée

2. Que faire des TSV ?
FAG

Fermeture de l'auricule gauche

avec thrombus intra auriculaire

(ici protection carotidienne ou

non)

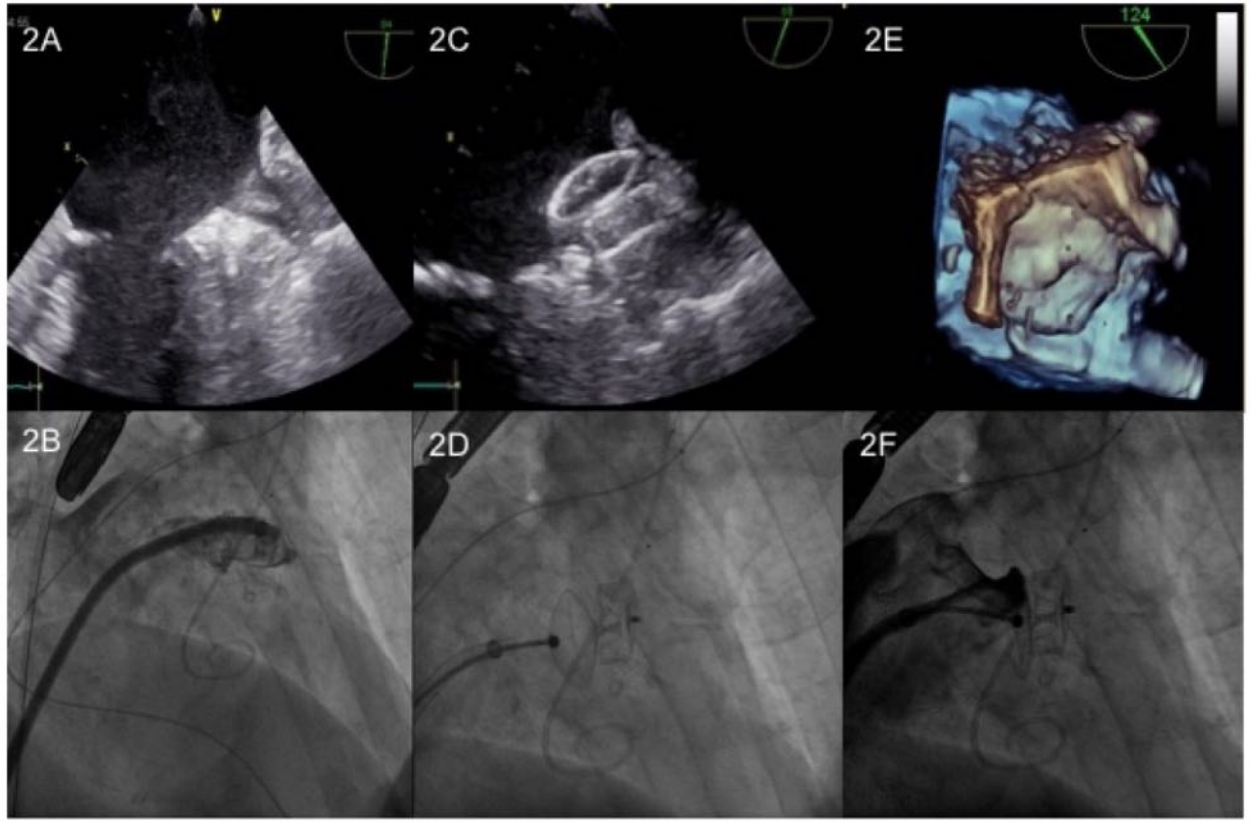


FIGURE 2. [A] Transesophageal echocardiography [TEE] showing thrombus in the left atrial appendage [LAA]. [B] Angiography of the LAA. Amplatzer Amulet device was deployed and its stability was confirmed by Minnesota maneuver at [C] TEE and [D] fluoroscopy. [E] Three-dimensional TEE showing the Amplatzer Amulet device in place. [F] No leaks were documented at final angiography.

Bordignon S, et al. J Cardiovasc Electrophysiol. 2019 Dec;30(12):2858-2863.

Quand / qui anticoaguler ? Que faire de la TSV ? Dans notre pratique

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Centre de Référence des Cardiomyopathies et des Troubles du Rythme Héréditaires ou Rares
Filière CARDIOGEN

- Traquer la FA +++
  - Holter ECG / 6 mois
  - Discuter Reveal si palpitations
  - Anticoagulation de la FA quel que soit le score CHA2DS2-VASc
- Anticoaguler si absence de systole atriale en ETT (onde A)
- Discuter anticoagulation en rythme sinusal au cas par cas (CHA2DS2-VASc élevé, profil mitral restrictif, dysfonction VG)

- Toujours vérifier l'absence du thrombus avant la cardioversion (ETO/scanner/IRM)

Quand / qui anticoaguler ? Que faire de la TSV ? Dans notre pratique

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- Fréquence cardiaque ou contrôle du rythme ? Dépend des malades :
  - Certains patients ne tolèrent pas la FA (majorité) : cardioversion sous amiodarone++ si possible ➔ meilleur pronostic en rythme sinusal / meilleurs résultats si stade NAC bas
  - Certains patients sont mieux en FA (avec une FC généralement plus élevée) : ne pas les ralentir, tolérer une FC élevée
- 1 AA possible : Amiodarone / absence de données sur les autres AA
- Ablation de flutter possible avec bons résultats / ablation FA plus compliquée mais à discuter, surtout chez les score NAC bas
- Attention au choc cardiogénique après cardioversion / ablation (euvolémie, cadence ventriculaire élevée)

AP-HP.
Hôpitaux universitaires
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Réseau Amylose

MERCI DE VOTRE ATTENTION!!!

GROUPE HOSPITALIER
HENRI MONDOR