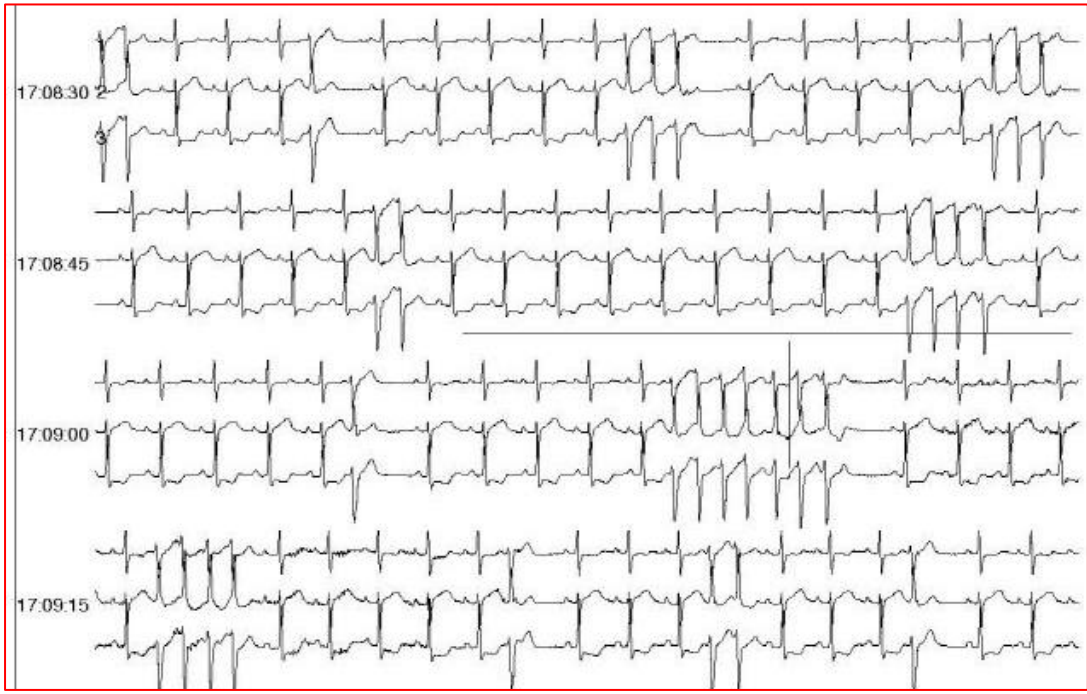
Amiodarone
Potent AAD vs Poison?

원광대학교병원

김 남 호

Case 1. 68세 남자

- 2003.5
  - ICMP : PCI on PDA & mLAD, EF 42%
- 2005.9
  - Hemodynamic stable Nonsustained VT
  - CAG
    - no changes
  - Medication
    - ASA+clopidogrel
    - Crestor 10 mg
    - Dilatrend 25 mg
    - Inhibace 2.5 mg
    - Aldacton 12.5 mg
    - Lasix 20 mg



NSVT에 대해 어떤 치료를 선택?

1. Beta-blocker
2. Class Ia agent
3. Class Ic agent
   - Flecainide
   - propafenone
4. Class III agent
   - Amiodarone
   - Sotalol
5. Radiofrequency catheter ablation
6. ICD
7. Observation – 현 상태의 치료 유지

NSVT에 대해 어떤 치료를 선택?

Clinical setting	Risk of sudden cardiac death	Arrhythmia specialist evaluation	Diagnostic evaluation	Diagnostics to be considered	Treatment	Treatment to be considered	Key references
ACS within 48 h	No increased risk	No	Coronary artery disease	Monitoring	Beta-blockers		Hohnloser et al.[70]
ACS after 48 h	Risk increased	Yes	Consider EPS if moderate LV dysfunction	Continued evaluation for repetitive arrhythmias	Beta-blockers	ICD	Zipes et al.[60]
Previous MI, EF 31 – 40	Increased risk	Yes	EPS		ICD withinducible VT/VF	ICD, see relevant guidelines	Zipes et al.[60]
Previous MI, EF ≤ 30	Increased risk	Yes	Non-driven by arrhythmia		ICD	Antiarrhythmic medical therapy or ablation with	Zipes et al.[60]
Chronic heart failure, EF ≤ 30							
Syncope with chronic CAD, EF –40	Increas					arrhytmic blation	Zipes et al.[60]
Non-ischaemic dilated CM	Uncert					nt guidelines	Zipes et al.[60]
HCM	Increas						Zipes et al.[60]
LQTS	Increas						Zipes et al.[60]
Short QT syndrome	Increas						
Brugada syndrome	Increased risk	Yes	Provocative testing	Genetic screening	With syncope or cardiac arrest: ICD	Quinidine	Aliot et al.[3]
ER syndrome	Increased risk	Yes					

CAD = coronary artery disease; CM = cardiomyopathy; EF = ejection fraction; EP = electrophysiology; EPS = electrophysiological study; ER = early repolarisation; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter defibrillator; LV = left ventricular; MI = myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

Concor 2.5 mg bid
Amiodarone 200 mg qD

NSVT with asymptomatic patient with LVEF > 40% : no specific treatment

EHRA/HRS/APHRS Expert Consensus. Heart Rhythm 2014;11:e166-96.

Amiodarone 사용 환자의 추적 관찰

1. 모든 환자에서 정해진 일정에 따라 검사를 진행한다.
2. 환자가 증상이 있을 때 필요한 검사를 진행한다
3. 최소한 1년에 1번은 심전도, 혈액검사, 흉부사진을 실시한다.
4. 따로 검사를 시행하지 않는다.

왜 아미로다론인가?

- Class I
  - Heart rate dependent
- Class II
  - Bradycardia
  - AV conduction slowering
  - Anti-ischemic (HR decrease, Coronary flow improved)
- Class III
  - Refractory period increased : Excitability decrease
- Class IV
  - Bradycardia
  - AV conduction slowering

왜 아미로다론인가?

Amiodarone Trials Meta-analysis

	Studies	Patients (n)	Cordarone	Control
	EMIAT	1486	743	743
	CAMIAT	1202	606	596
	GEMICA	1073	542	531
	PAT	613	305	308
Post MI	SSSD	228	115	133
	GESICA	516	260	256
CHF	EPAMSA	127	66	61
	NICKLAS	101	49	52
	HAMER	34	19	15
	TOTAL	6553	-	-

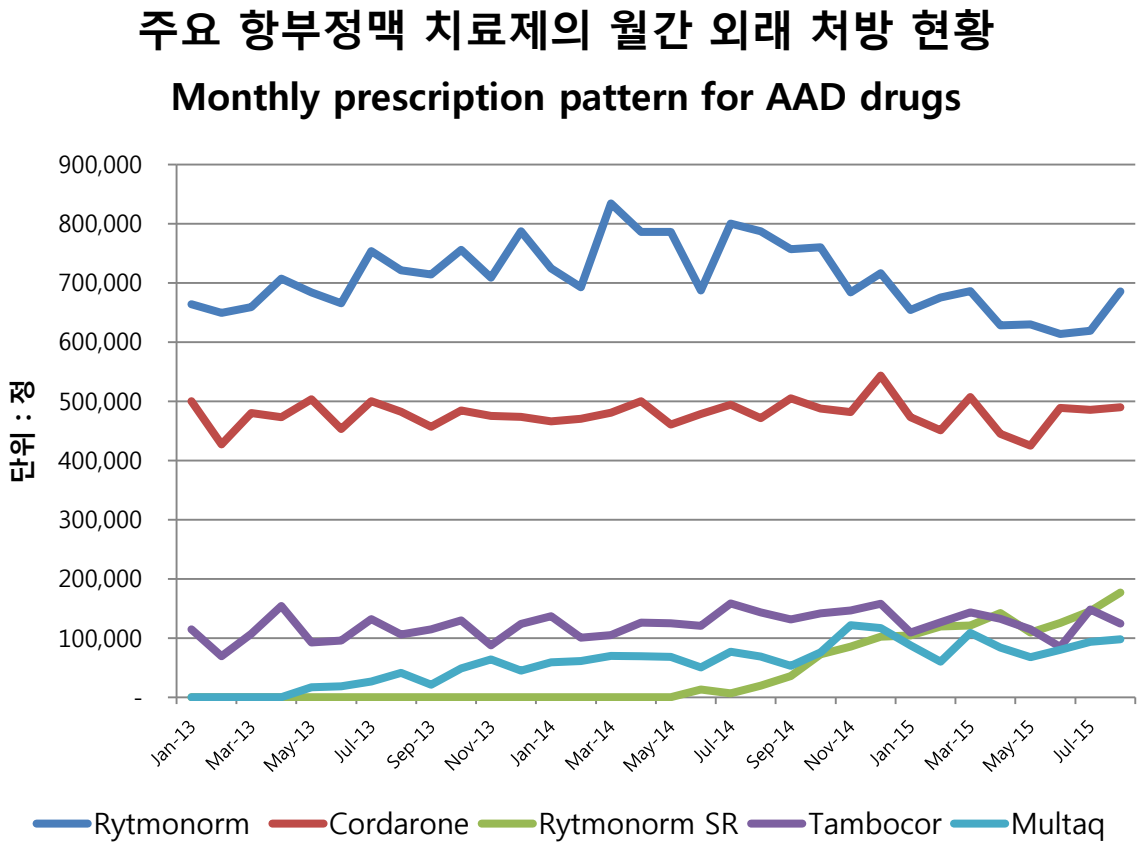
Cordarone reduce significatively the risk of

- **Total Mortality by *13 % (p=0.03)***
- **Mortality by arrhythmic/ sudden death by *29% (p=0.0003)***

No effect on nonarrhythmic death

1997 Lancet

국내에서 처방되는 주요 항부정맥제 현황



사노피아벤티스코리아 제공 자료

왜 아미오다론 사용 중 FU을 해야 하는가?

Reaction	Incidence (%)	Diagnosis	Management
Pulmonary	2	Cough and/or dyspnea, especially with local or diffuse opacities on high-resolution CT scan and decrease in D_LCO from baseline	Usually discontinue drug; corticosteroids may be considered in more severe cases; occasionally, can continue drug if levels high and abnormalities resolve; rarely, continue amiodarone with corticosteroid if no other option
Gastrointestinal tract	30	Nausea, anorexia and constipation	Symptoms may decrease with decrease in dose
	15–30	AST or ALT level greater than 2 times normal	If hepatitis considered, exclude other causes
	<3	Hepatitis and cirrhosis	Consider discontinuation, biopsy, or both to determine whether cirrhosis is present
Thyroid	4–22	Hypothyroidism	L-Thyroxine
	2–12	Hyperthyroidism	Corticosteroids, propylthiouracil or methimazole; may need to discontinue drug;
	>90	Photophobia, visual blurring, and microdeposits	
Heart	5	Bradycardia and AV block	May need permanent cardiac pacing
	<1	Proarrhythmia	May need to discontinue the drug
Genitourinary	<1	Epididymitis and erectile dysfunction	Pain may resolve spontaneously

ALT = alanine aminotransferase; AST = aspartate aminotransferase; D_LCO = diffusion capacity of carbon monoxide

Adverse effects are common, with a prevalence as high as 15% in the first year of use and 50% during long-term use.

Goldschlager N, et al. Heart Rhythm 2007;4:1250-9

Amiodarone Pharmacokinetics

- Absorption : average 50 % (20~80%)
- Peak plasma level obtained in 3 to 7 hrs
- Therapeutic activity reached in one week
- Half-life between 20 to 100 days
- Extensively distributed and accumulated mainly in muscle and fat tissues

아미오다론 사용 중 Monitoring

	Baseline	Duration of Therapy			Only with symptoms
		3 mon	6 mon	12 mon	
ECG	0			0	
PFT(D_LCO)	0				0
Chest X-ray	0			0	
Thyroid	0		0	0	
LFT	0		0	0	
Opthalmic exam	Significant visual abnormalities				0

Practical guideline. Goldschlager N, et al. Heart Rhythm 2007;4:1250-9

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- 2005.9
  - Hemodynamic stable Nonsustained VT
  - Medication
    - Amiodarone 200 mg qD
    - Concor 2.5 mg bid
- 2007.11
  - TFT
    - FT4 : 2.35 ↑ (0.7-2.0 ng/dL)
    - TSH : 0.80 (0.2-5.0 uIU/mL)

이 환자에서 다음에 시행할 처치?

- Observation
- TFT FU with T3, Thyroglobulin Ab, microsomal Ab, TSH receptor Ab
- Consult to Endocrinogists
- Decrease the amiodarone
- Discontinue the amiodarone

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    - TSH : 0.80 (0.2-5.0 uIU/mL)
- 2008.3
  - TFT
    - FT4 : 2.55 ↑ (0.7-2.0 ng/dL)
    - TSH : 1.73 (0.2-5.0 uIU/mL)
    - Anti-thyroid Ab : negative

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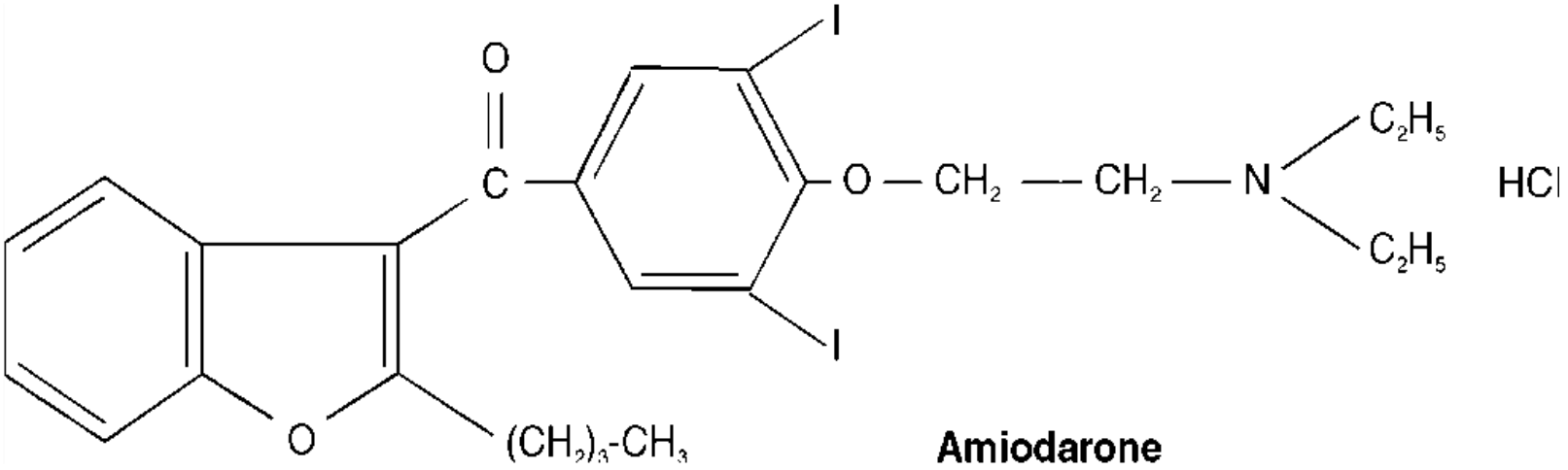
Amiodarone and Thyroid

- 구조적으로 유사
- **Iodine component of amiodarone**



Amiodarone

One 200 mg contain 75 mg of iodine = 6 mg of iodide

may reveal or provoked a thyroid disturbance (hypo or hyperthyroidism)

Amiodarone and Thyroid

- 첫 3개월 이내
  - TSH : 상승 (< 20 mIU/L)
  - FT4, total T4 : 상승
  - FT3, total T3 : 감소
- 3개월 이후(new equilibrium is reached)
  - TSH : 정상화
  - T4 : 높은 정상, 미세한 상승, 드물게는 저하

* 갑상선 기능에 대한 평가는 3개월 이후에...

Amiodarone-induced Thyrotoxicosis

- 진단
  - TSH 감소, FT4 상승
  - T3 : 상승 또는 높은 정상
  - 갑상선 기능 항진증 증상 : 체중 감소 등

	Type 1	Type 2
Underlying thyroid disease	Yes	No
Thyroid ultrasound	Diffuse or nodular goiter	Normal (hypoechoic) gland (small goiter)
CFDS	Increased vascularity	Absent hypervascularity
Thyroidal RAIU	Low/normal/increased	Low/absent
MIBI	Thyroid retention	Absent uptake
Thyroid antibody	Sometimes present	Usually absent
Pathogenesis	Iodine-induced hyperthyroidism	Destructive thyroiditis
Spontaneous remission	No	Possible
Preferred medical therapy	Thionamides (plus KClO4)	Glucocorticoids
Subsequent hypothyroidism	Unlikely	Possible
Subsequent therapy for the underlying thyroid disease	Likely	No

Bogazzi F, et al. J Clin Endocrinol Metab 2010;95:2529-35

이 환자에서 다음에 시행할 처치?

1. Observation
2. TFT FU with T3, Thyroglobulin Ab, microsomal Ab, TSH receptor Ab
3. Consult to Endocrinogists
4. Decrease the amiodarone
5. Discontinue the amiodarone

Concor 2.5 mg bid
Amiodarone 200 mg qD > Sotalol 80 mg bid

When to Consult an Endocrinologist

1. Any time hyperthyroidism is suspected (even if suppression of TSH is mild and subclinical disease is possible)
2. An acutely ill patient where interpretation of TFT's will be complicated by euthyroid sick syndrome
3. When considering treating subclinical hypothyroidism

Practical guideline. Goldschlager N, et al. Heart Rhythm 2007;4:1250-9

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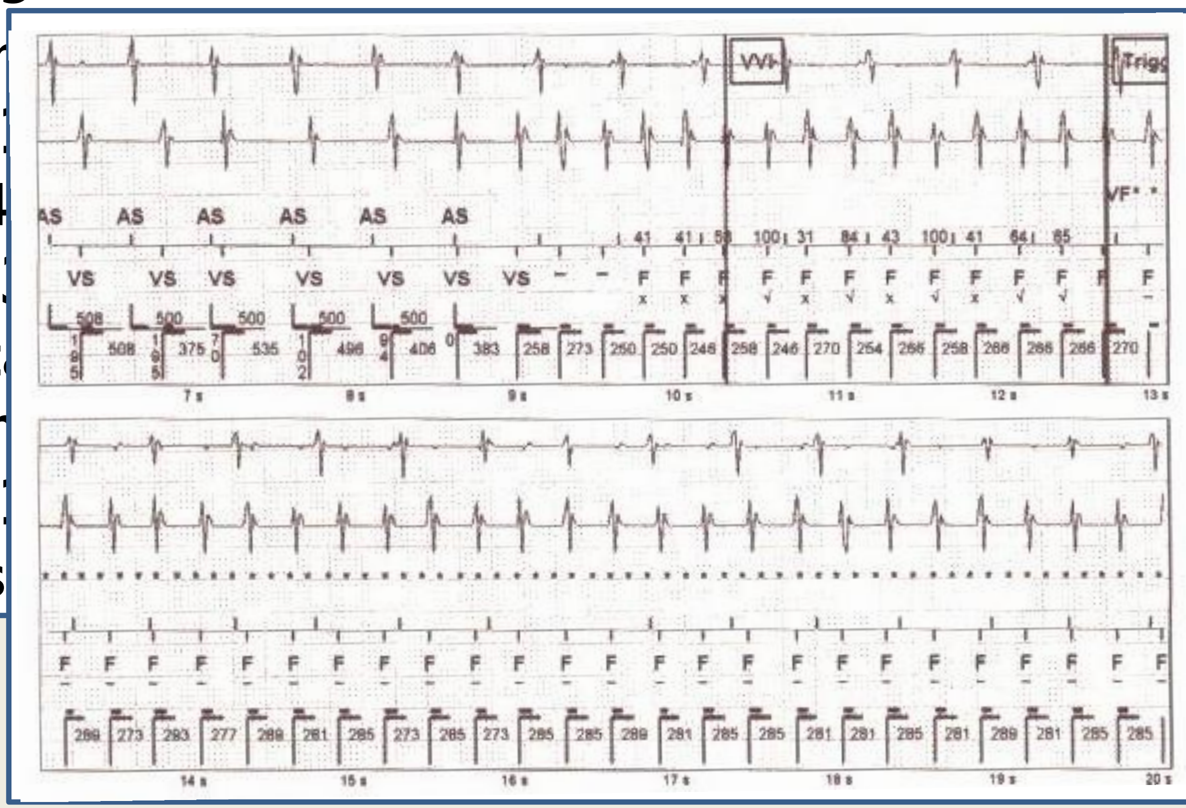
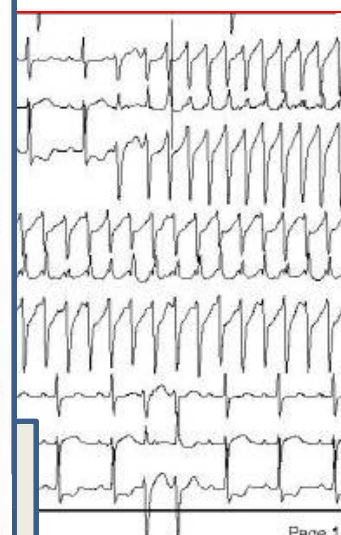
  - FT4…
- 2008.…
  - Sot…
  - Cor…
- 2010.…
  - Sus…
  - EF …





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Case 1. 68세 남자

- 2015.10 - 5년후 Hyperpigmentation

향후 어떤 처치를?

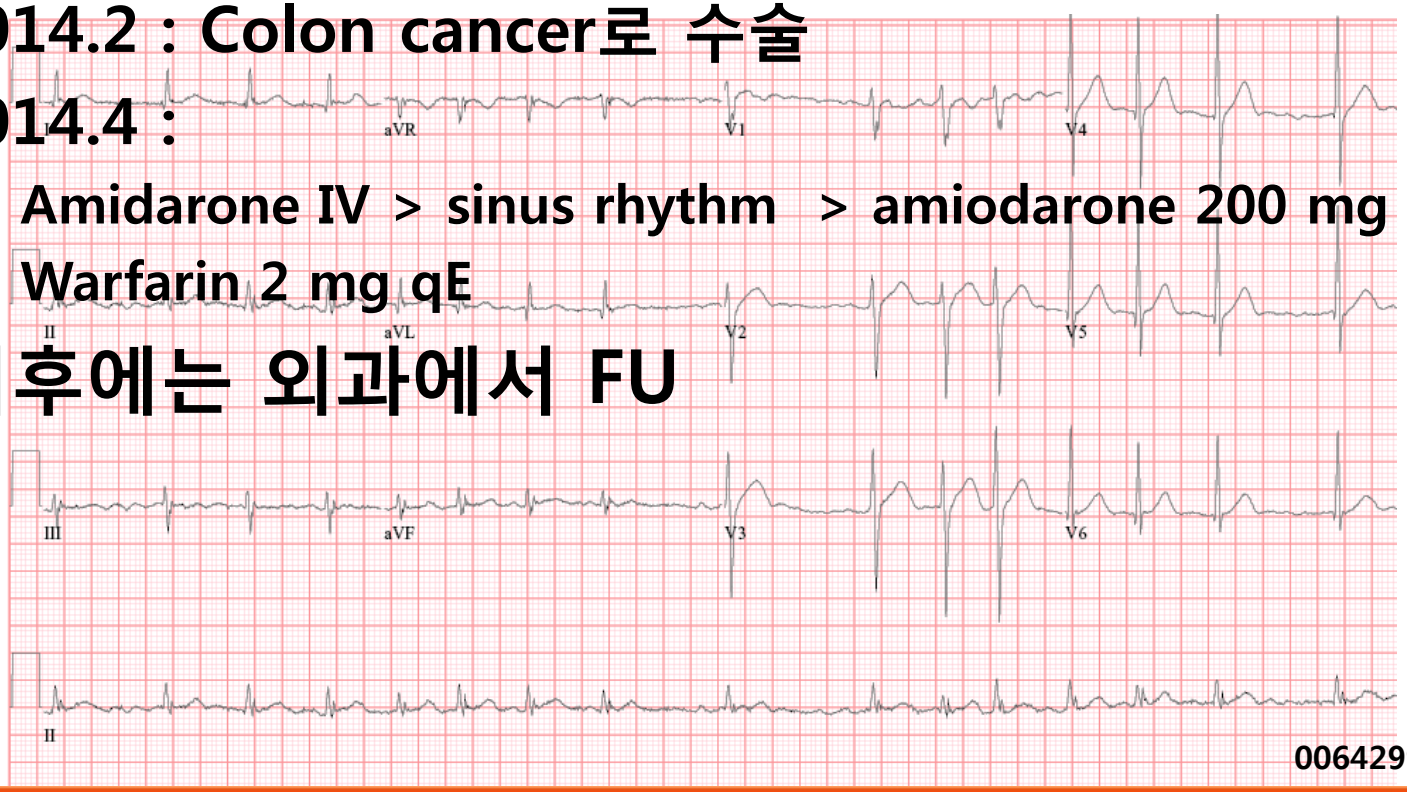
1. 지켜본다.
2. Amiodarone 용량을 줄이거나 끊는다.
3. RFCA

Case 1. 요약

- Amiodarone은 허혈성 심질환 및 심부전을 동반한 환자에서 발생한 심실 빈맥에 효과적인 약제이다.
- Amiodarone은 갑상선 이상을 포함한 다양한 부작용이 유발될 수 있다.
- Amiodarone을 사용하면 갑상선 이상이 없더라도 미세한 FT4의 상승 소견이 관찰될 수 있다.
- 약제를 줄이거나 끊는 것은 환자의 상태에 따라 판단하여야 한다.

Case 2. 78세 남자

- 주소 : 호흡곤란(NYHA 3-4)
- 병력 :
  - 2014.2 : Colon cancer로 수술
  - 2014.4 :
    - Amidarone IV > sinus rhythm > amiodarone 200 mg qD
    - Warfarin 2 mg qE
  - 이후에는 외과에서 FU



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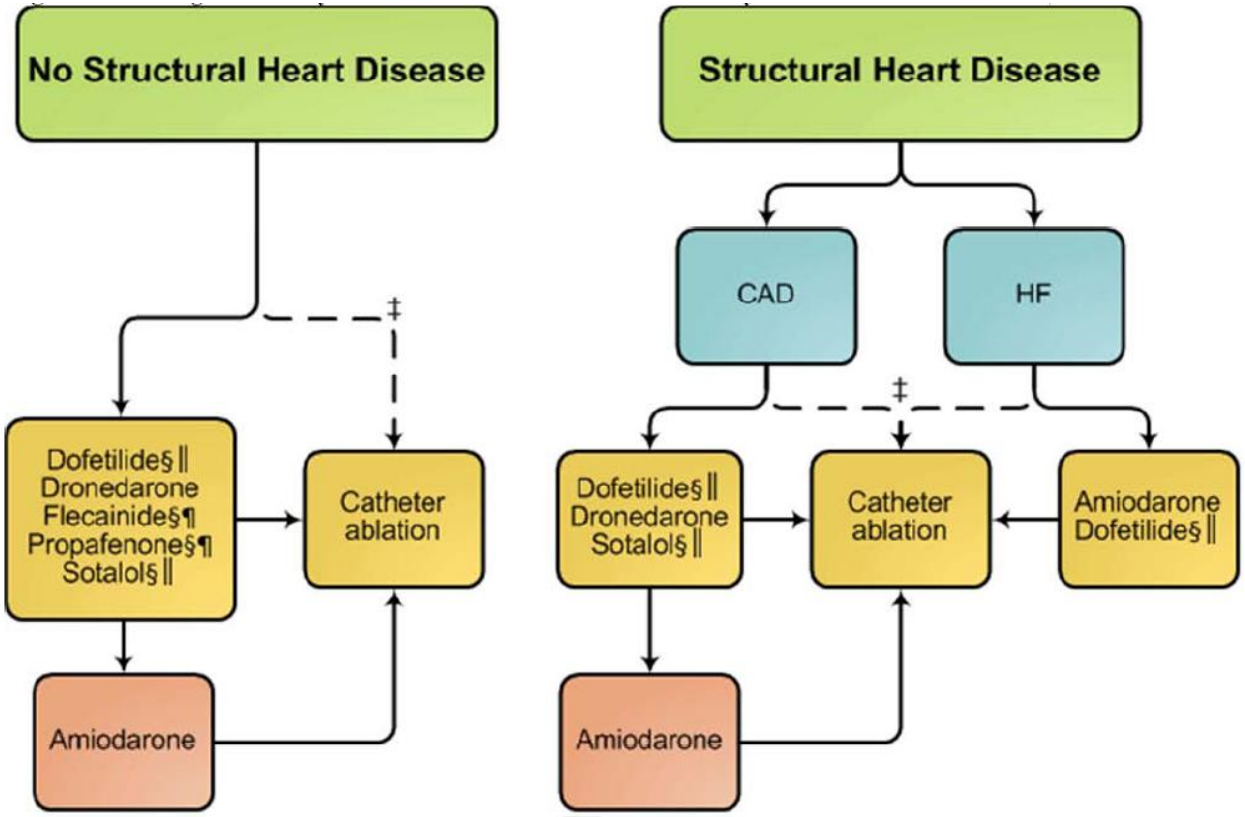
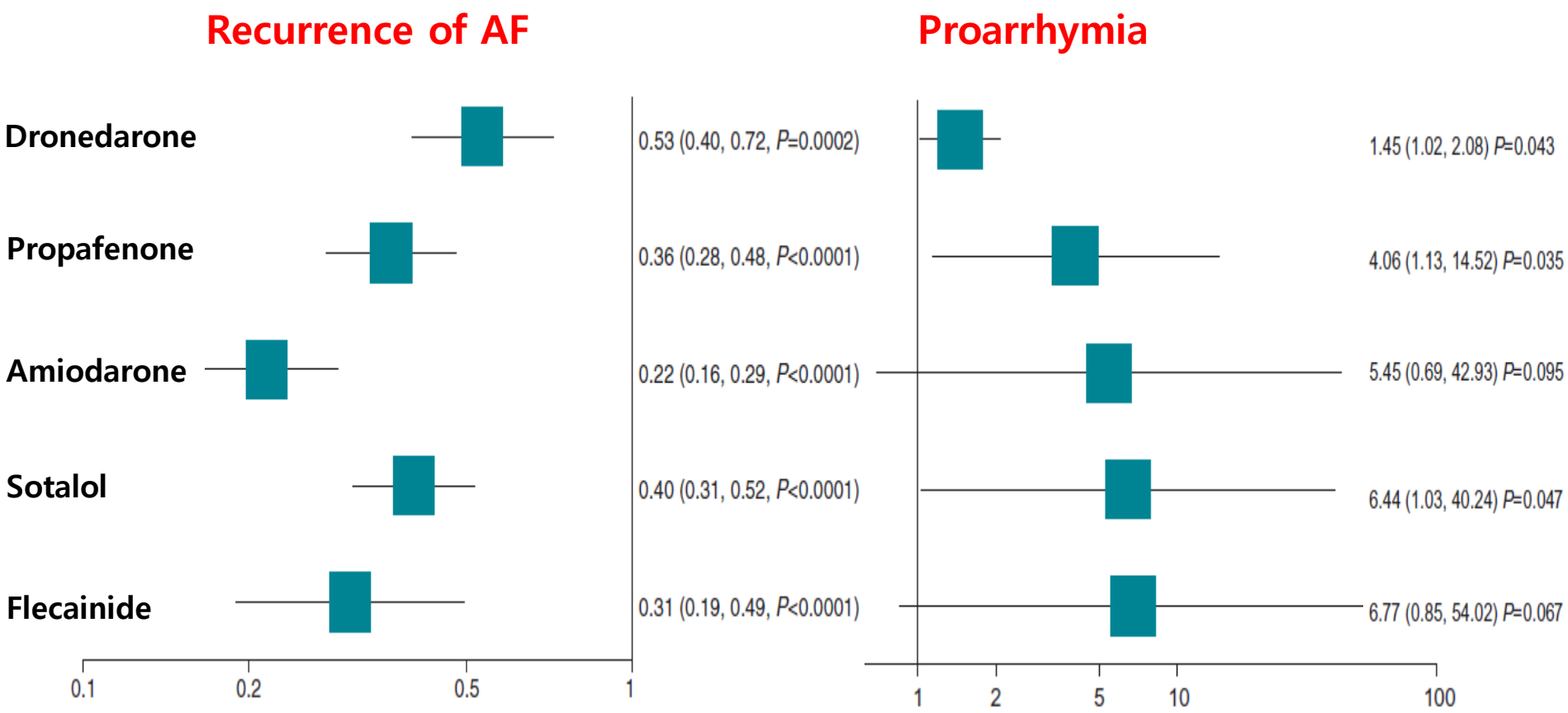
Rhythm Control in Patients with PAF and PeAF



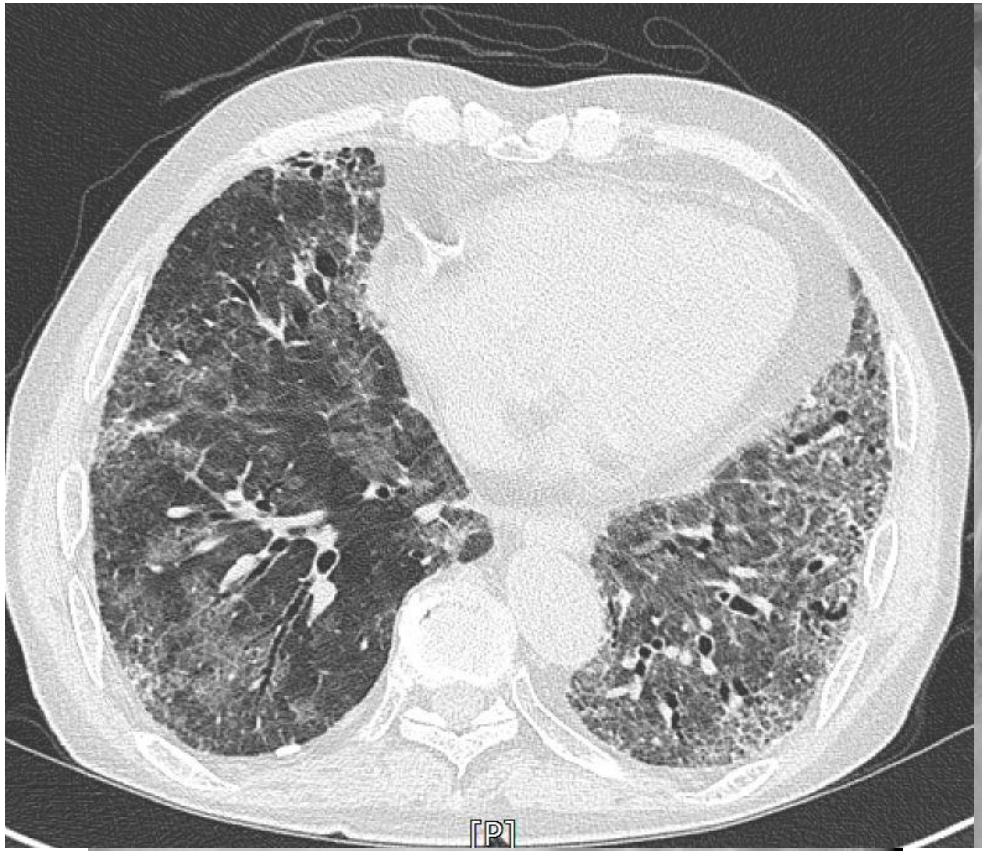
*Catheter ablation is only recommended as first-line therapy for patients with paroxysmal AF (Class IIa recommendation).
†Drugs are listed alphabetically.
‡Depending on patient preference when performed in experienced centers.
§Not recommended with severe LVH (wall thickness >1.5 cm).
‖Should be used with caution in patients at risk for torsades de pointes ventricular tachycardia.
¶Should be combined with AV nodal blocking agents.
AF indicates atrial fibrillation; CAD, coronary artery disease; HF, heart failure; and LVH, left ventricular hypertrophy.

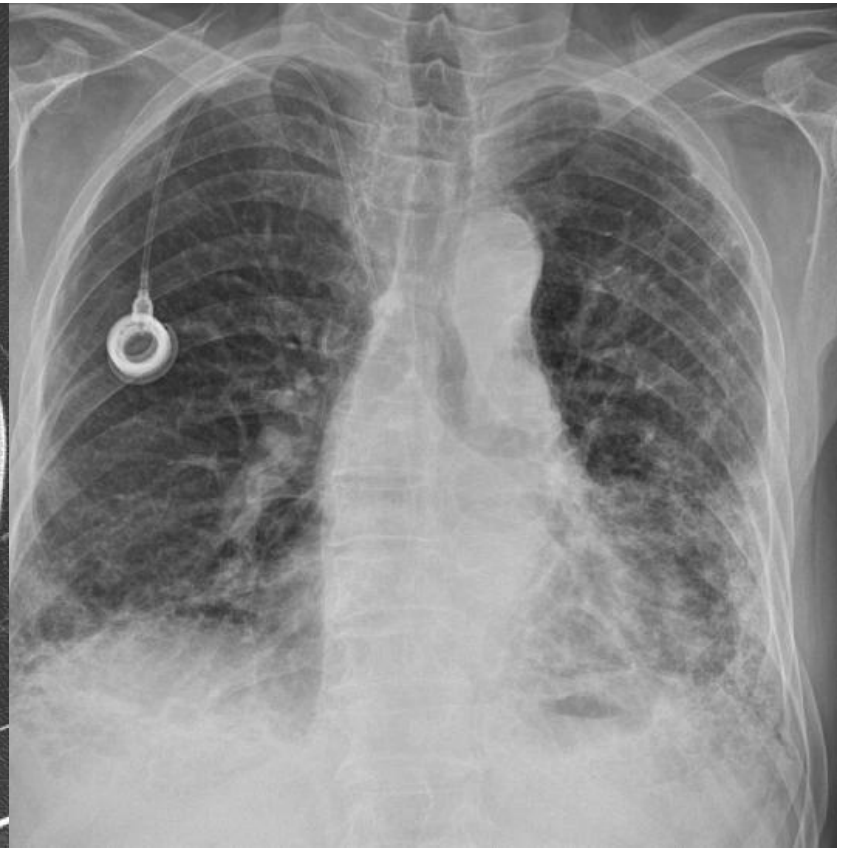
항부정맥제의 비교



Freemantle N, et al. 2011 Europace

Case 2. 78세 남자





2014.04.11

2014.09.01

cordarone 200 mg qD > rytmonorm 225 mg, verapamil 40 mg bid

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Pulmonary Toxicity

- Different type of pulmonary toxicity
  - Interstitial pneumonitis : m.c
  - Organizing pneumonia
  - Acute respiratory distress syndrome
  - Solitary pulmonary mass
- Pathogenesis
  - Cytotoxicity : direct toxic reaction
  - Hypersensitivity
- Risk factors
  - Cumulative dose
  - Daily dose
  - Preexisting lung disease

모든 약은
독이 될 수도 있다

빈대 잡으려다
초가 삼칸 다 태운다

조정관 교수 슬라이드

Case 2. 요약

- Amiodarone은 심방세동 환자에서 정상 동율동 유지를 위한 가장 효과적인 약물이나 부작용이 많은 약제이므로 사용시 주의하여야 한다.
- 특히 폐 독성은 치명적인 경과를 갖을 수 있다.

감사합니다.


Cordarone (Amiodarone)
"Don Cordarone... The Enforcer"
They use me to protect you from recurrent life threatening ventricular fibrillation and ventricular tachycardia by decreasing the cardiac conduction and automaticity.
©2007 Nursing Education Consultants, Inc.
www.fb.com/onlyfornurses
Be careful with this drug... It's effects can last a long time! Monitor for progressive pulmonary problems- dyspnea, decreased breath sounds, cough with rales.
Yeah, watch for side effects of bradycardia, AV block, hypotension and visual problems.