Ventricular arrhythmia in heart failure

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Outlines

- Mechanism & patho-physiology of VA in CHF
- Clinical presentations
- Treatment options with available evidence
- Current guideline

Chronic Heart Failure

- **Progressive disease with significant burden of hospitalization & mortality**

- **Basis of disease progression**

✓ **Activation of neuro-hormonal pathways**

✓ **Myocardial adverse remodeling & fibrosis**

✓ **Disruption of metabolism & energy homeostasis**

Ventricular Arrhythmia (VA) in Heart Failure

- Common (prevalence up to 33%) with increased mortality
- Clinical presentation varies from asymptomatic, syncope & SCD
- Positive correlation between VA & severity of HF
- Predictive value of VA to SCD is unclear

Mechanism of VA

- **Structural changes in advanced HF:**

✓ **replacement of fibrosis**

✓ **regional ventricular hypertrophy**

✓ **changes in myocyte mechanical & electrical function -**

promote the development & maintenance of VAs

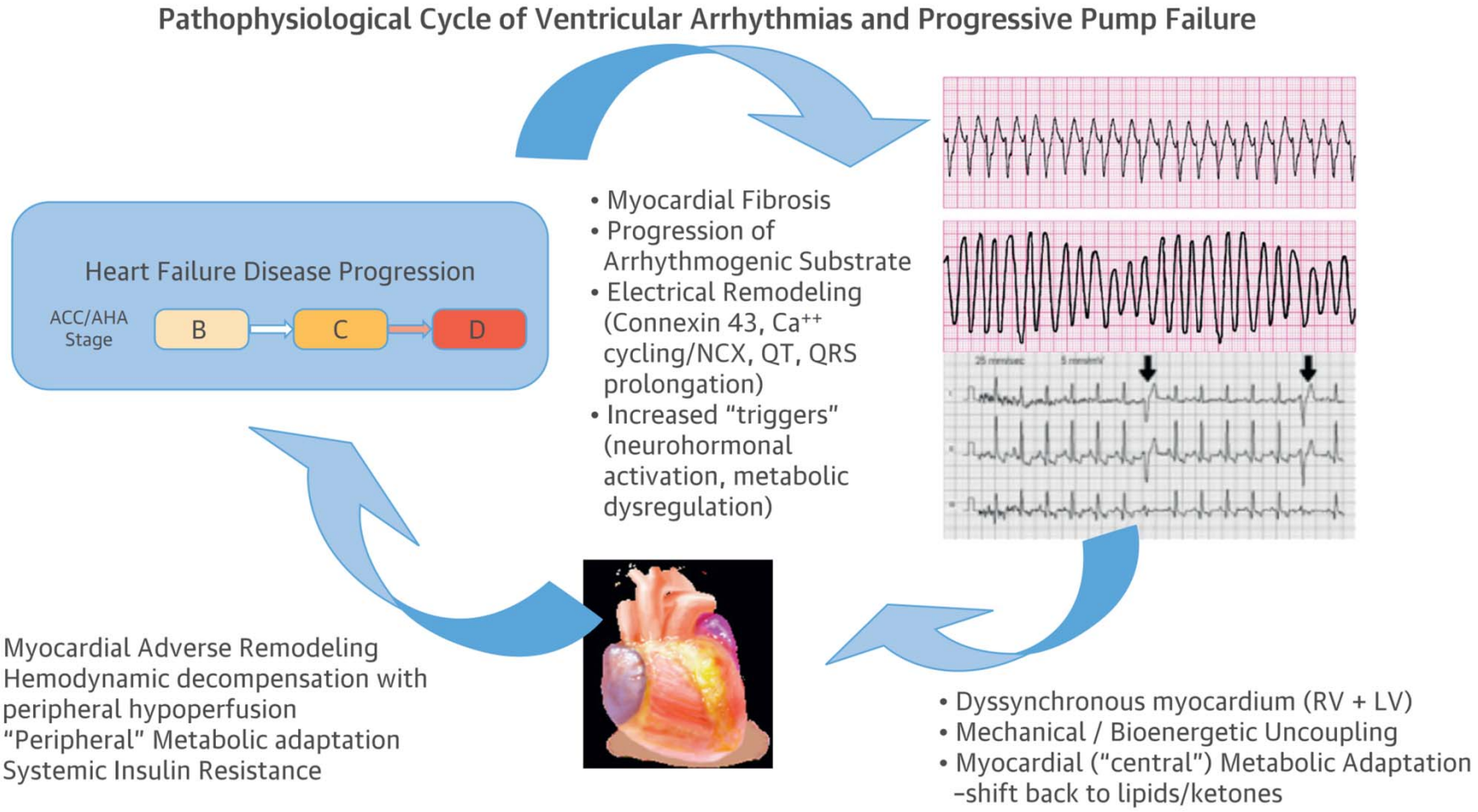
<u>"engine-out-of-fuel metabolic substrate"</u>

Factors involved in the pathogenesis of tachy-arrhythmias in patients with heart failure

Structural and Hemodynamic Abnormalities	Myocardial scar Left ventricular hypertrophy Left ventricular stretch
Metabolic Abnormalities	Neurohormonal activation Electrolyte abnormalities
Electrophysiologic Changes	Prolongation of action potential Changes of calcium homeostasis Changes of potassium current
Others	Pharmacologic agents Myocardial ischemia

Masarone, D. et al.2017. management of arrhythmias in heart failure. *J. Cardiovasc. Dev. Dis*, 4, 3;

FIGURE 1 **Schema Illustrating the Pathophysiological Cycle of VAs in A-HF**



A-HF = advanced heart failure; ACC = American College of Cardiology; AHA = American Heart Association; LV = left ventricle; RV = right ventricle; VA = ventricular arrhythmia.

Mechanism of VA

- Pump failure as a substrate for VAs
- VAs as a basis of disease progression in HF

Clinical Presentation

- Asymptomatic in isolated PVC
- Palpitations, lightheadeness, pre-syncope or syncope & worsening of HF in complex VAs
- > 80% pts with HFrEF associated with frequent & complex VAs
- SCD in NSVT, sustained VT & VF

Treatment Options

- Pharmacological - Anti-arrhythmic Drug (AAD)
- Catheter Ablation
- Device therapy
- Autonomic modulation

Pharmacologic Management (AAD) - 1

- Clinical data on efficacy and safety of AAD for VAs suppression for A-HF are scant
- Overall evidence in patients with structural heart disease is disappointing, with limited options and inconclusive benefit.
- Negative inotropic & potential pro-arrhythmic effects of AAD are main concerns for worsening of HF & increased mortality

Summary of RCTs testing AAD vs Standard Medical Therapy for the prevention of VAs in patients with ICDs

	N Included		Age, yrs		ICM		Ejection Fraction		ICD Appropriate Therapy		Deaths	
First Author, Year (Ref. #)	AAD	CTRL	AAD	CTRL	AAD	CTRL	AAD	CTRL	AAD	CTRL	AAD	CTRL
Kühlkamp et al., 1999 (112)	46	47	59 ± 18	64 ± 17	31 (67)	28 (60)	35 ± 8	38 ± 19	15 (33)*	24 (51)*	4 (9)	3 (6)
Pacifico et al., 1999 (43)	151	151	63 ± 11	61 ± 11	110 (73)	100 (66)	37 ± 12	39 ± 14	33 (22)*	49 (32)*	4 (3)	7 (5)
Kettering et al., 2002 (113)	50	50	59 ± 12	60 ± 9	35 (70)	38 (76)	38 ± 15	38 ± 14	30 (60)	33 (66)	6 (12)	8 (16)
Dorian et al., 2004 (42)	419	214	63 ± 12	62 ± 12	266 (63)	141 (66)	35 ± 13	34 ± 14	247 (59)*	136 (64)*	13 (3)	7 (3)
Singer et al., 2004 (44)	135	37	66 ± 12	65 ± 11	109 (81)	30 (81)	30 ± 13	34 ± 14	NA	NA	2 (2)	3 (8)
Connolly et al., 2006 (41)												
Amiodarone	140	138	64 ± 11	63 ± 10	111 (79)	111 (80)	34 ± 12	34 ± 12	15 (11)*	45 (33)	6 (4)	2 (1)
Sotalol	134		66 ± 9		109 (81)		34 ± 12		38 (28)		4 (3)	
Kowey et al., 2011 (114)												
Celivarone	324	109	64 ± 10	65 ± 12	225 (69)	86 (79)	29 ± 8	29 ± 8	194 (59)	66 (61)	28 (9)	6 (6)
Amiodarone	53		67 ± 8		36 (68)		29 ± 8		20 (38)*		9 (17)	

Values are n, mean ± SD, or n (%). *$p < 0.05$ for comparison between AAD arm and CTRL arm.

AAD = antiarrhythmic drug; CTRL = control; ICD = implantable cardioverter-defibrillator; ICM = ischemic cardiomyopathy; NA = not available; VA = ventricular arrhythmia.

SANTANGELI, P., RAME, J. E., BIRATI, E. Y. & MARCHLINSKI, F. E. 2017. Management of Ventricular Arrhythmias in Patients With Advanced Heart Failure. *Journal of the American College of Cardiology,* 69**,** 1842-1860.

Findings of RCTs of AADs

- **Pooled analysis showed 34% reduction of recurrent VA episodes leading to appropriate ICD interventions with AAD compared with control medical Rx.**

- **That was not translated into a significant reduction in all cause mortality**

Pharmacologic Management (AAD) – 2 (HF PVCs)

- Correction of electrolyte abnormalities (particularly low K & Mg)
- Withdrawal of agents, might provoke arrhythmias
- Optimization of HF pharmacological Rx
- Tx of arrhythmias per se is generally not indicated

Pharmacologic Management (AAD) – 3
(NSVT in ischemic & non-ischemic CM)

- Tx with AAD is appropriate
- Optimization of beta blockers as a first line
- if fails, Amiodarone & Sotolol are indicated

Pharmacologic Management (AAD) – 4 (Sustained VT)

- The goal is to restore the stable rhythm rapidly
- For stable patients, pharmacological cardioversion with
  - ✓ IV Lidocaine (100-150 mg bolus, 2-4 mg/min)
  - ✓ IV Procainamide (10 mg /kg) for monomorphic VT (hypotension)
  - ✓ IV Amiodarone (150-300 mg in 5 min f/b 1050 mg/24 hr) (slow onset & the results of acute termination are variable)
- DC cardioversion is necessary for unstable haemodynamic
- For secondary prevention, Amiodarone or sotalol together with optimization of HF Rx : beta blockers
- Mexiletine considered in refractory cases (worsen the haemodynamic status)

Catheter Ablation

- **Recommended in patients with sustained monomorphic VT refractory to AAD, VT storm not due to a transient or reversible cause.**
- **Indicated in evidence of a consistent trigger for poly morphic VT/VF episodes with a reproducible premature ventricular depolarization**
- **The available evidence does not prove the mortality benefit in patients with structural heart d/s.**
- **Earlier adoption of CA with prevention of sustained VT episodes leading to appropriate ICD shocks.**

EHRA & HRS Consensus

- **Symptomatic monomorphic sustained VT despite AAD therapy or intolerance to AAD**
- **Frequent PVCs, non-sustained VT or VT causing myocardial dysfunction**
- **VT from bundle branch reentry or intrafasicular VT**
- **Recurrent sustained polymorphic VT or VF refractory to AAD with a suspected trigger of a single PVC morphology**

Ablation of PVC & non-sustained VT

- Common in patients with HF & structural heart d/s
- Difficult to distinguish whether PVCs are primary or secondary to CM
- Patients with frequent PVCs of single morphology (> 10% in 24 hr Holter) may be beneficial to improve LV function

Ablation of Ischemic Cardiomyopathy

- VT is usually reentry around myocardial scar but focal in 5-10%
- Inducible VT in 90%, the rate & morphology often differ from clinical VT
- Utilization of substrate-based (voltage & pace mapping) at sinus minimizes the unstable VT episodes and is better tolerated by patients
- Most VT can be ablated by endocardial approach
- Epicardial approach may be necessary for prior inferior MI
- Outcomes vary from 38-72% with procedure mortality 0.5-8%

Ablation of Non-ischemic Cardiomyopathy

- Sustained monomorphic VT is less common
- common to inducible multiple morphologies
- usually reentry, smaller area of scar and often located in the mid myocardium or epicardium layers
- increase the success of ablation with epicardial approach

Device Therapy
(Implantable Cardioverter Defibrillator - ICD)

- Arrhythmic, SCD is common in CHF with NYHA II & III, reduced LVEF
- MADIT-II demonstrated that patients with LVEF < 30% with structural heart d/s had rate of SCD 9.4% at 20 months
- ICD in patients with sustained VT increases survival compared with AAD.
- ICD should be considered in all patients with LV dysfunction and sustained VT

Indication of ICD Implantation in HF patients. COR : Class of Recommendation

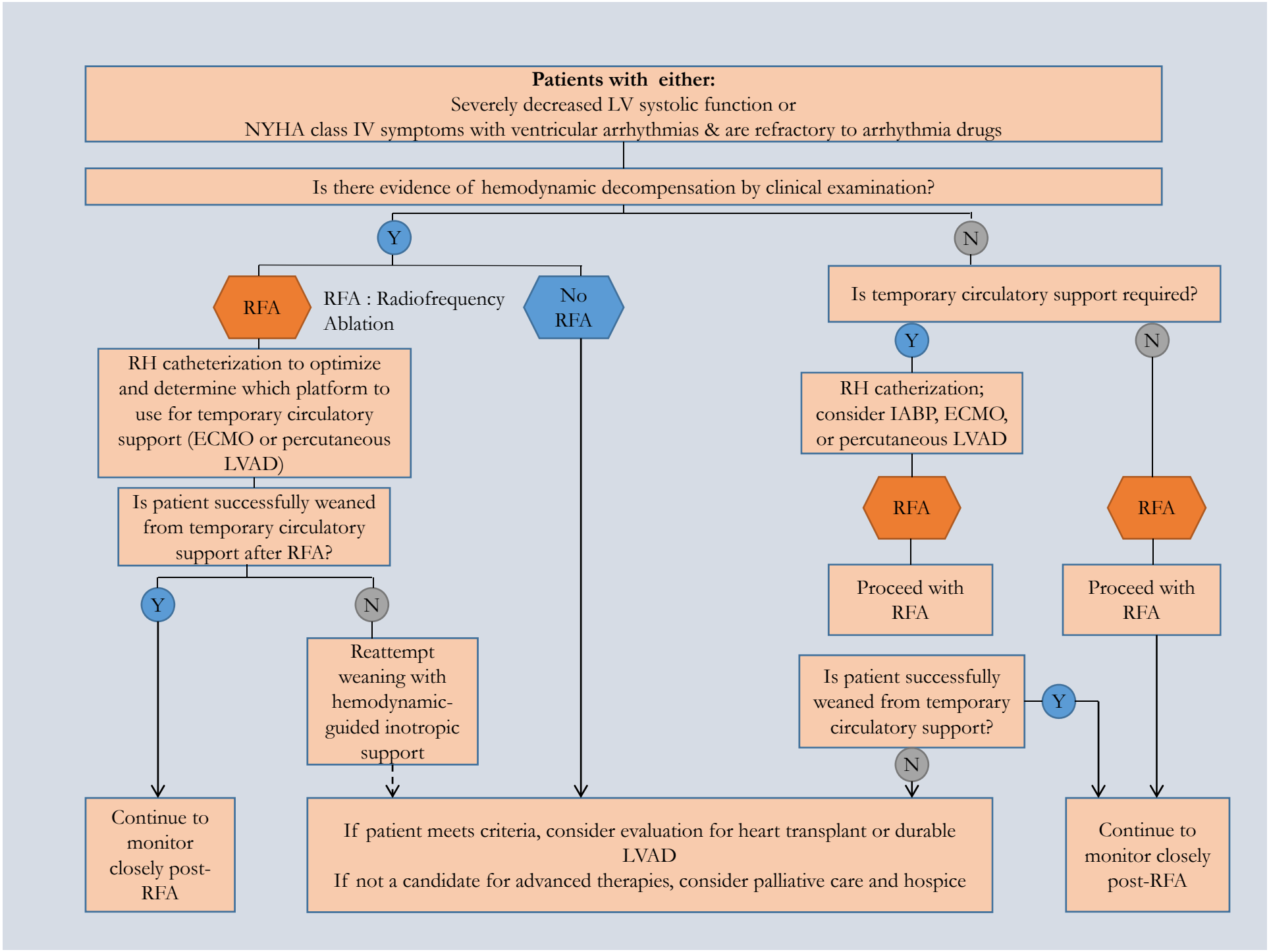
2012 ACC/AHA/HRS Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities	COR-LOE
Ischemic DCM (at least 40 days post-MI), LVEF less than or equal to 35%, NYHA functional Classes II or III	**I-A**
Non-ischemic DCM, LVEF less than or equal to 35%, NYHA functional Classes II or III	**I-B**
Ischemic DCM (at least 40 days post-MI) LVEF less than or equal to 35%, NYHA functional Class I	**I-A**
2013 ACCF/AHA Guideline for the Management of Heart Failure	
HFrEF (irrespective of etiology, but in case of ischemic etiology at least 40 days post-MI), LVEF less or equal to 35%, NYHA Classes II or III	**I-A**
HFrEF (irrespective of etiology, but in case of ischemic etiology at least 40 days post-MI), LVEF less or equal to 30%, NYHA Class I	**I-B**
2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death	
Ischemic HFrEF (at least 6 weeks after myocardial infarction), LVEF less or equal to 35%, NYHA Classes II or III	**I-A**
Non ischemic HFrEF, LVEF less or equal to 35%, NYHA Classes II or III	**I-B**
Patients who are listed for heart transplant	**IIa-C**
2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure	
Ischemic HFrEF, LVEF less or equal to 35%, NYHA Classes II or III	**I-A**
Non-ischemic HFrEF, LVEF less or equal to 35%, NYHA Classes II or III	**I-B**

Autonomic Modulation

- A significant autonomic imbalance by sympathetic- up regulation & parasympathetic withdrawal in HF
- Autonomic Modulation is a promising therapeutic strategy
- Neuraxial modulation with thoracic epidural anesthesia or surgical cardiac sympathetic denervation can reduce VT burden demonstrated by 2 small pilot studies
- The value of the AM in Mx of VAs warrants further investigation

Treatment options for A-HF with refractory VAs

- Heart transplantation & durable mechanical assist device (LVAD, biventricular assist device or total artificial heart) for severely reduced LVEF (< 25 %) associated with high burden or incessant drug refractory VAs


Patients with either:
Severely decreased LV systolic function or
NYHA class IV symptoms with ventricular arrhythmias & are refractory to arrhythmia drugs
Is there evidence of hemodynamic decompensation by clinical examination?
Y
N
RFA
RFA : Radiofrequency Ablation
No RFA
RH catheterization to optimize and determine which platform to use for temporary circulatory support (ECMO or percutaneous LVAD)
Is patient successfully weaned from temporary circulatory support after RFA?
Y
N
Reattempt weaning with hemodynamic-guided inotropic support
Continue to monitor closely post-RFA
Is temporary circulatory support required?
Y
N
RH catherization; consider IABP, ECMO, or percutaneous LVAD
RFA
Proceed with RFA
RFA
Proceed with RFA
Is patient successfully weaned from temporary circulatory support?
Y
N
If patient meets criteria, consider evaluation for heart transplant or durable LVAD
If not a candidate for advanced therapies, consider palliative care and hospice
Continue to monitor closely post-RFA


GUIDELINES

Recommendations for the management of ventricular tachyarrhythmias in heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
Potential aggravating/precipitating factors (e.g. low serum potassium/ magnesium, ongoing ischaemia) should be sought and corrected in patients with ventricular arrhythmias.	IIa	C	
Treatment with beta-blocker, MRA and sacubitril/valsartan reduces the risk of sudden death and is recommended for patients with HFrEF and ventricular arrhythmias (as for other patients)(see Section 7).	I	A	162, 170–175
Implantation of an ICD or CRT-D device is recommended for selected patients with HFrEF (see Section 8).	I	A	223–226, 388
Several strategies should be considered to reduce recurrent symptomatic arrhythmias in patients with an ICD (or in those who are not eligible for ICD), including attention to risk factors and optimal pharmacological treatment of HF, amiodarone, catheter ablation and CRT.	IIa	C	
Routine use of antiarrhythmic agents is not recommended in patients with HF and asymptomatic ventricular arrhythmias because of safety concerns (worsening HF, proarrhythmia, and death).	III	A	247, 248, 364, 365

Ponikowski et al., 2016 ESCGuidelines for the diagnosis and treatment of acute and chronic heart failure: *Eur Heart J,* 37**,** 2129-200.

Catheter Ablation for VAs in HF

Recommendations	Class[a]	Level[b]
Urgent catheter ablation in specialized or experienced centres is recommended in patients presenting with incessant VT or electrical storm resulting in ICD shocks.	I	B
Amiodarone or catheter ablation is recommended in patients with recurrent ICD shocks due to sustained VT.	I	B
ICD implantation is recommended in patients undergoing catheter ablation whenever they satisfy eligibility criteria for ICD.	I	C

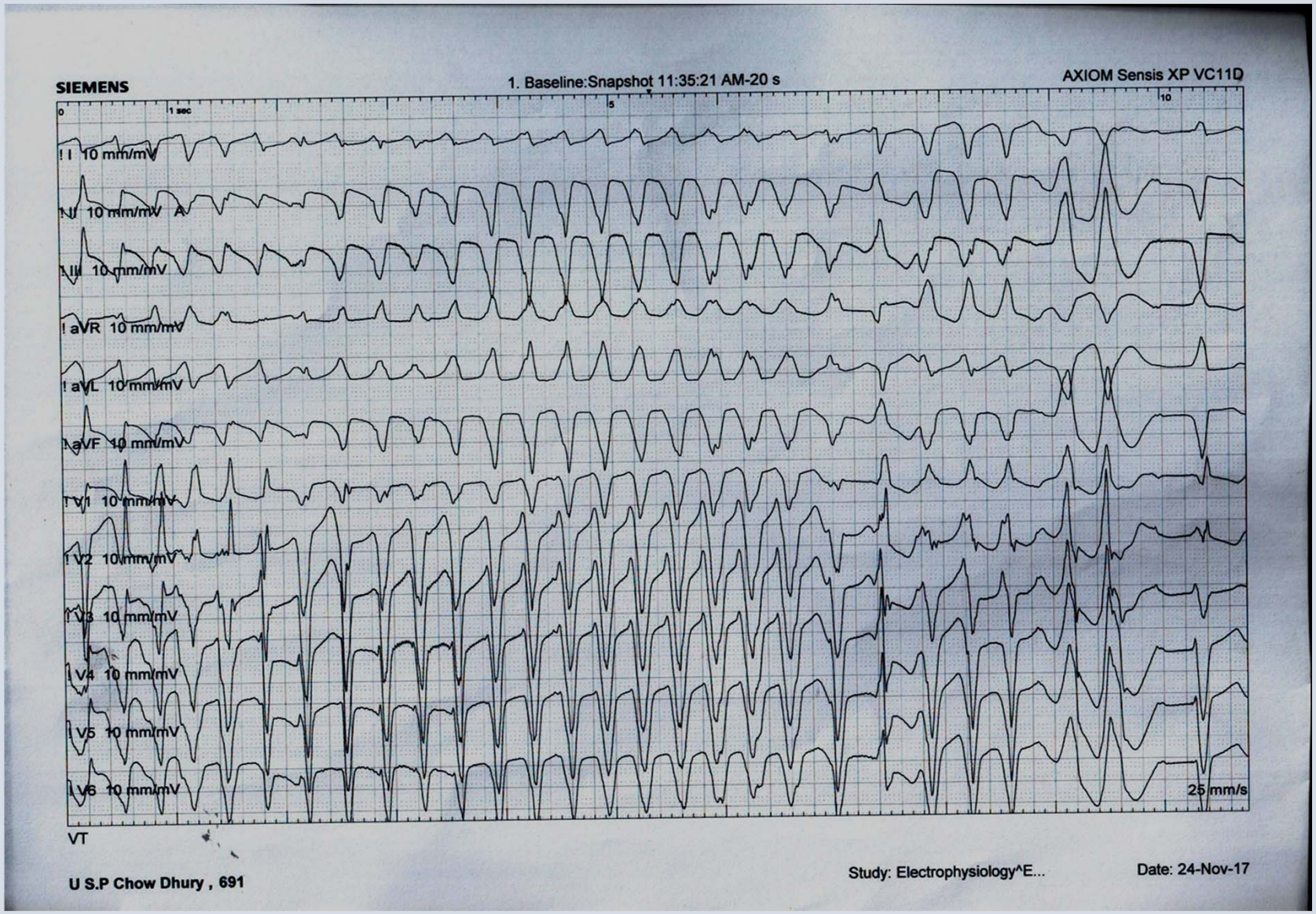
Case Scenario

- 75 year old man, recurrent episodes of VT
- Underlying dilated cardiomyopathy (LVEF 34 %, LVIDd 6.3 cm, Global hypokinesia of LV)
- CAG was reported as minor coronary artery disease (mid LAD 40 %)
- ICD was implanted in 10/2016
- Frequent appropriate ICD shocks were recorded
- ICD battery was run out and 2nd device was replaced.

Medications

- Amiodarone 200 mg BD
- Spironolactone 25 mg OD
- Frusemide 60 mg BD
- Atorvastatin 10 mg HS
- Aspirin 75 mg OD
- Metoprolol XL 12.5 mg OD

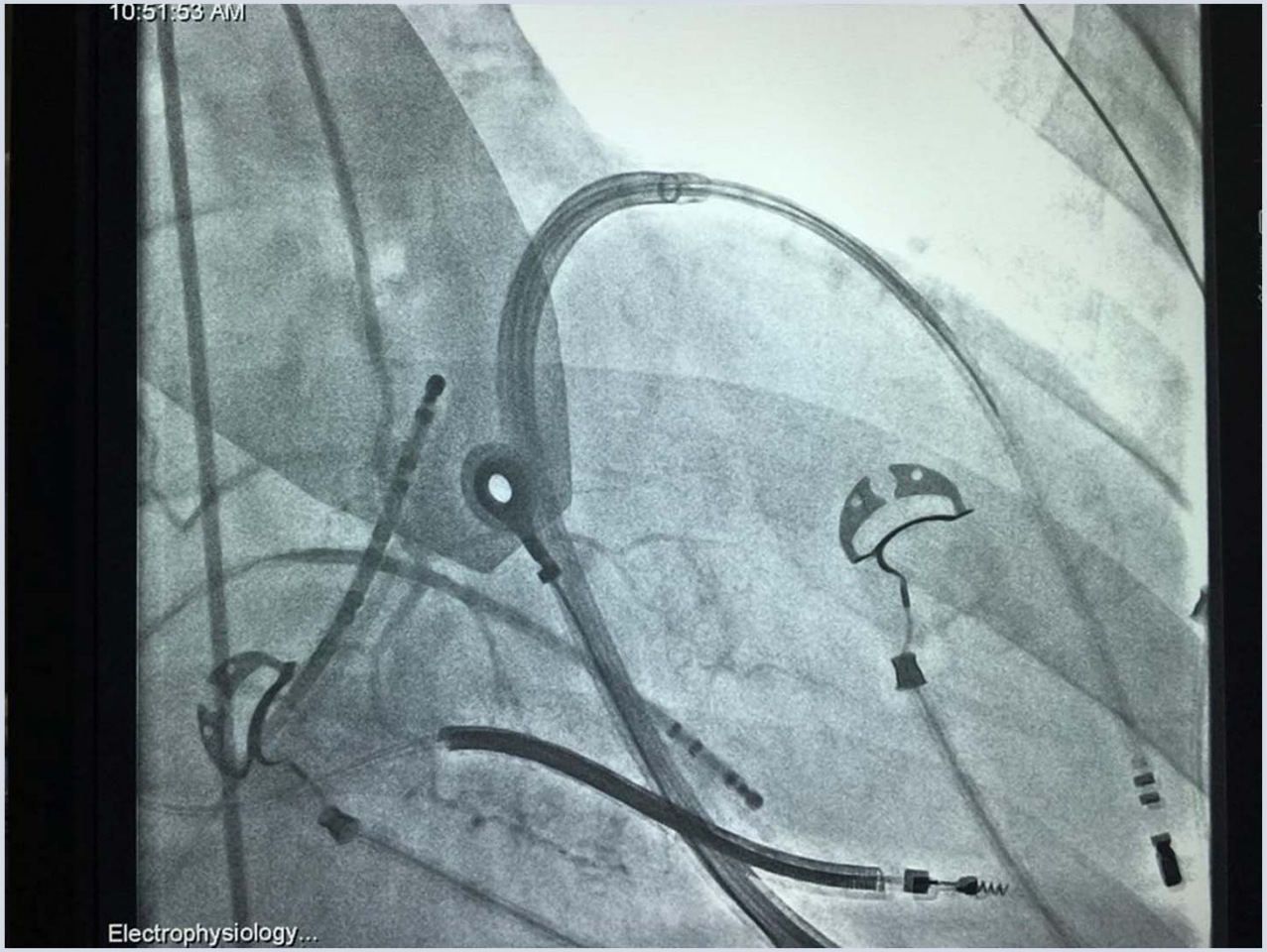
Ventricular Tachycardia



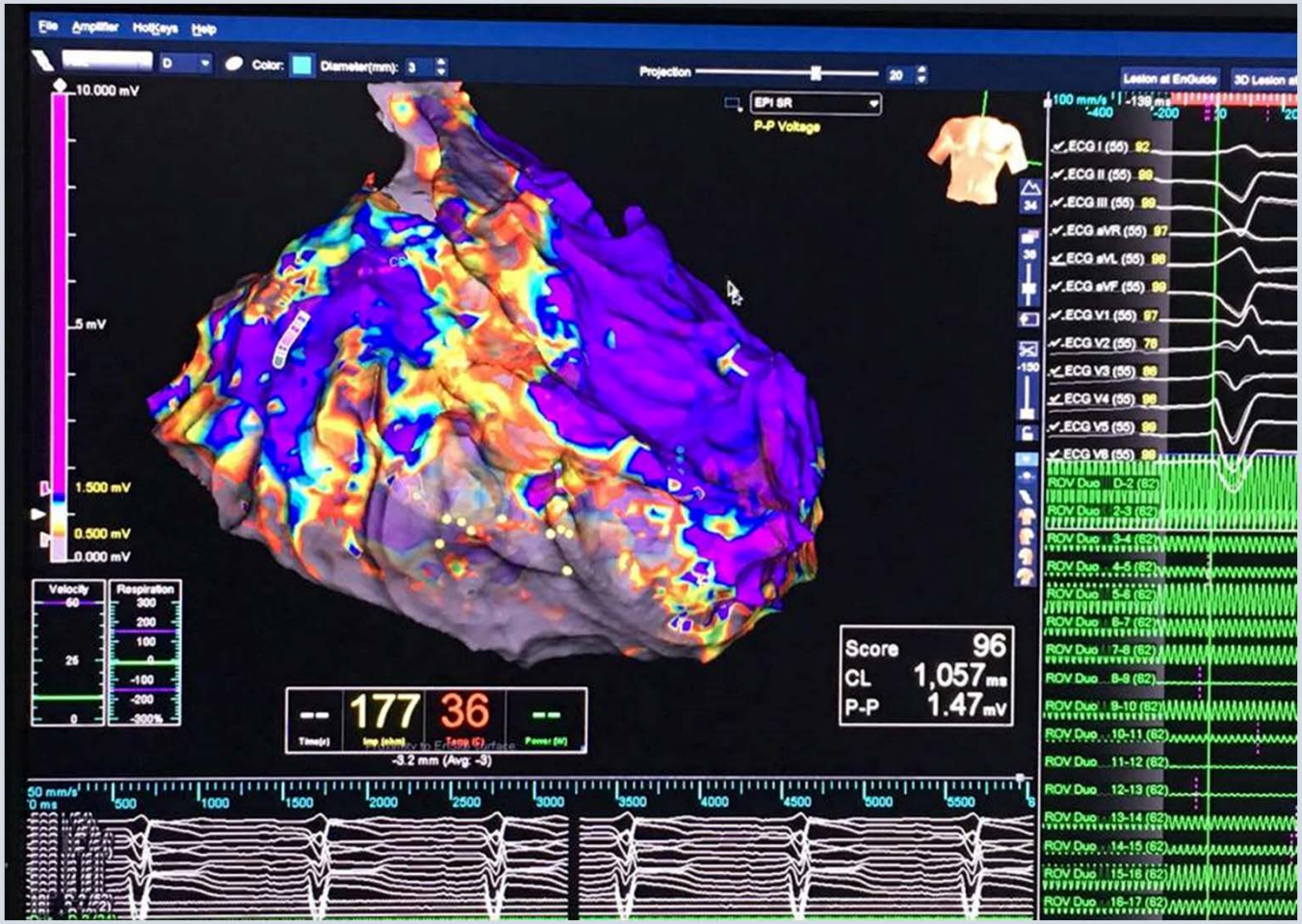
VT ablation

- Under general anaesthesia
- 3 D mapping system (Ensite Precision)
- Epicardial voltage mapping
- Substrate modification of epicardial scar involving basal to apical area

Epicardial Mapping

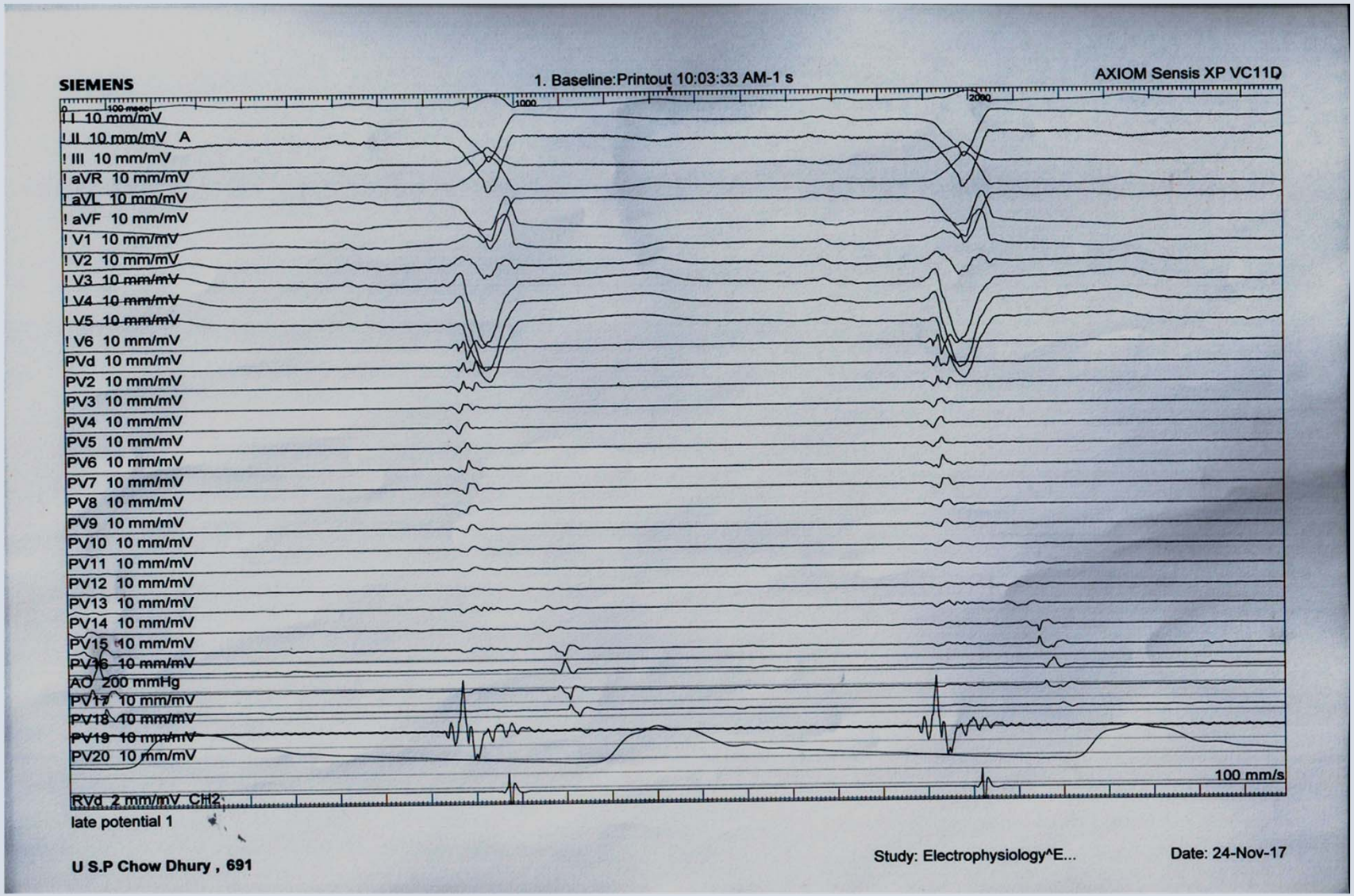


Epicardial voltage map



Site of successful ablation with epicardial approach

Late potentials at scar area



Summary

- VAs are common in A-CHF
- Clinical studies evaluating different therapies to prevent VAs were very limited
- Optimization of CHF Rx & ICD recommendations are crucial
- Among AADs, only Amiodarone reduces VAs, although its use may be associated with increased mortality
- Catheter ablation with substrate modification is effective to achieve VA suppression in A-HF
- Temporary mechanical hemodynamic support may be beneficial in high risk cases
- Heart transplantation & durable mechanical circulatory support may be advanced therapies for pump failure or refractory VAs

THANK YOU