Neurological Complications of Cardiac Disease and Cardiac Surgery

Alejandro A. Rabinstein, MD

Professor of Neurology

Mayo Clinic

USA

Rabinstein.alejandro@mayo.edu

MAYO CLINIC

Disclosures

- None

Learning Objectives

- Understand the role of AF in the risk of ischemic stroke
- Recognize the main neurological complications of infective endocarditis
- Discuss the risk of cerebrovascular events and cognitive decline after cardiac revascularization
- Evaluate the risk of ICH in patients treated with LVAD or ECMO

Outline

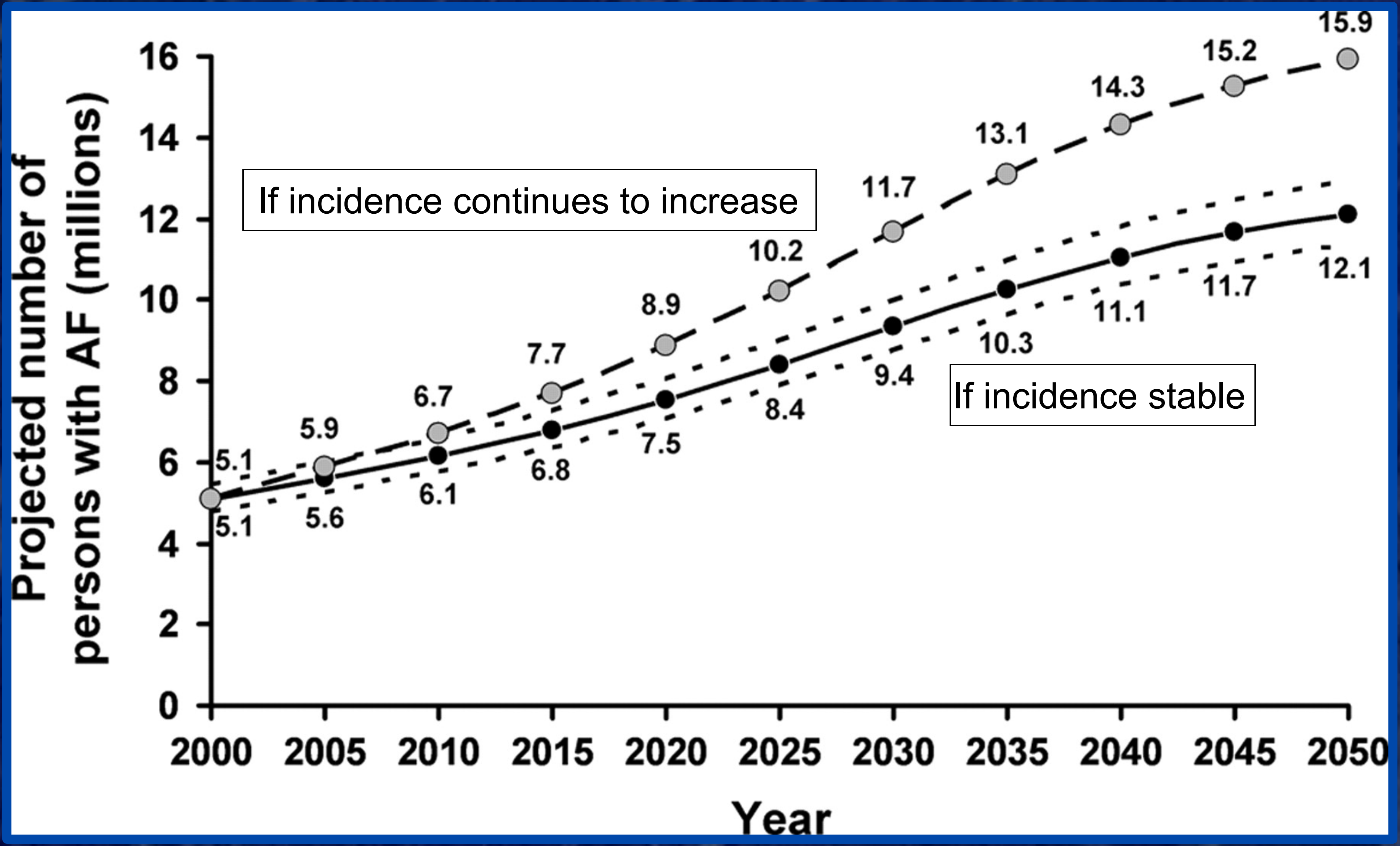
- Embolic stroke
- Infective Endocarditis
- Coronary revascularization
- LVAD
- ECMO
- *Cardiac Arrest*

Cardioembolic Stroke

- One of the most common mechanisms of ischemic stroke and probably the most common in the elderly
- Main risk factor: Atrial Fibrillation (or flutter, persistent or paroxysmal)
- Other risk factors:
  - Mechanical valves (mitral > aortic)
  - Infective or marantic endocarditis
  - Severe left ventricular dysfunction (mural thrombi, apical aneurysms)
  - Atrial myxoma

MAYO CLINIC

Up to 12 million by 2050 just in the US



➢ Heart Dis and Stroke Stats – AHA

Prolonged Cardiac Monitoring for Detection of Paroxysmal Atrial Fibrillation After Cerebral Ischemia

Alejandro A. Rabinstein, MD

Table 1. Main Characteristics of Available Methods for Prolonged Ambulatory Cardiac Rhythm Monitoring

Device	Location	Duration	Minimal Threshold	Limitations
Holter	Skin surface	Usually 1–2 d	Few seconds	Short duration
External loop recorder	Skin surface	≤30 d	Few seconds	Requires patient action
Ambulatory telemetry	Skin surface	≤30 d	Few seconds	Patient compliance Skin irritation Cost
Implantable loop recorder	Subcutaneous	≤3 y	2 min	Invasiveness (minimal) Does not detect PAF<2 min Cost
Dual-chamber pacemaker and defibrillator	Intracardiac	Many years	Seconds	Only indicated for life-threatening arrhythmias

Stroke 2014;45:1208-14

Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis

Luciano A Sposato, Lauren E Cipriano, Gustavo Saposnik, Estefanía Ruíz Vargas, Patricia M Riccio, Vladimir Hachinski

- Diagnostic yield by phases

ECG on admission	7.7%
In-hospital serial/continuous ECG	5.1%
Ambulatory Holter	10.7%
Prolonged ambulatory monitoring	16.9%

- Overall diagnostic yield 23.7%
- When including 20% of patients with known AF before the stroke/TIA → a total of 39% of stroke pts can be estimated to have AF

Lancet Neurol 2015;14:377-87

An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction

Zachi I Attia, Peter A Noseworthy*, Francisco Lopez-Jimenez, Samuel J Asirvatham, Abhishek J Deshmukh, Bernard J Gersh, Rickey E Carter, Xiaoxi Yao, Alejandro A Rabinstein, Brad J Erickson, Suraj Kapa, Paul A Friedman*

Summary

Background Atrial fibrillation is frequently asymptomatic and thus underdetected but is associated with stroke, heart failure, and death. Existing screening methods require prolonged monitoring and are limited by cost and low yield. We aimed to develop a rapid, inexpensive, point-of-care means of identifying patients with atrial fibrillation using machine learning.

Methods We developed an artificial intelligence (AI)-enabled electrocardiograph (ECG) using a convolutional neural network to detect the electrocardiographic signature of atrial fibrillation present during normal sinus rhythm using standard 10-second, 12-lead ECGs. We included all patients aged 18 years or older with at least one digital, normal sinus rhythm, standard 10-second, 12-lead ECG acquired in the supine position at the Mayo Clinic ECG laboratory between Dec 31, 1993, and July 21, 2017, with rhythm labels validated by trained personnel under cardiologist supervision. We classified patients with at least one ECG with a rhythm of atrial fibrillation or atrial flutter as positive for atrial fibrillation. We allocated ECGs to the training, internal validation, and testing datasets in a 7:1:2 ratio. We calculated the area under the curve (AUC) of the receiver operatoring characteristic curve for the internal validation dataset to select a probability threshold, which we applied to the testing dataset. We evaluated model performance on the testing dataset by calculating the AUC and the accuracy, sensitivity, specificity, and F1 score with two-sided 95% CIs.

Findings We included 180 922 patients with 649 931 normal sinus rhythm ECGs for analysis: 454 789 ECGs recorded from 126 526 patients in the training dataset, 64 340 ECGs from 18 116 patients in the internal validation dataset, and 130 802 ECGs from 36 280 patients in the testing dataset. 3051 (8·4%) patients in the testing dataset had verified atrial fibrillation before the normal sinus rhythm ECG tested by the model. A single AI-enabled ECG identified atrial fibrillation with an AUC of 0·87 (95% CI 0·86–0·88), sensitivity of 79·0% (77·5–80·4), specificity of 79·5% (79·0–79·9), F1 score of 39·2% (38·1–40·3), and overall accuracy of 79·4% (79·0–79·9). Including all ECGs acquired during the first month of each patient's window of interest (ie, the study start date or 31 days before the first recorded atrial fibrillation ECG) increased the AUC to 0·90 (0·90–0·91), sensitivity to 82·3% (80·9–83·6), specificity to 83·4% (83·0–83·8), F1 score to 45·4% (44·2–46·5), and overall accuracy to 83·3% (83·0–83·7).

Interpretation An AI-enabled ECG acquired during normal sinus rhythm permits identification at point of care of individuals with atrial fibrillation.

MAYO CLINIC

Lancet 2019; 394:861-867

AF and Stroke: How are they related?

AF → Diminished LAA contraction → LAA thrombus

Vascular Risk Factors → Atrial myopathy
Inflammation → Atrial myopathy
Atrial myopathy → AF (marker of disease burden)
Atrial myopathy → Mechanical dysfunction/ thrombus

Implications

- **AF should precede CVA**
- **Control of AF may prevent CVA**
- **LAA closure prevents CVA**

Implications

- **AF burden predicts risk**
- **No temporal association between AF and stroke**
- **Role of LAA depends on which tissue affected**

Stroke Prevention in AF

- **Chronic Anticoagulation**
  - DOACs have half the risk of ICH compared with warfarin
  - Aspirin does not really work
- **Left Atrial Appendage Occlusion**
  - Reserved for patients who cannot tolerate chronic anticoagulation

Infective Endocarditis

- Focal or diffuse neurological complications:
  - Cerebrovascular embolism
  - Intracranial Hemorrhage
  - Microbleeds
  - Encephalopathy
  - Seizures
  - Brain abscess/meningitis
  - Visual changes

Ischemic Stroke in IE

- Incidence 6-31%
- Presenting feature in 14% (75% of embolic strokes occur at presentation)
- Brain emboli in autopsy: 50-60%
- Risk greater with virulent organisms
- Recurrence very low after full course of antibiotics with good response

Intracranial Hemorrhage in IE

- ICH, SAH, hemorrhagic conversion
- Septic arteritis → mycotic aneurysms
- Risk factors: Anticoagulation
  Staph aureus
  IVDA
  Large infarcts
  Delay in starting ATB

Prevention and Treatment

- **Prompt antibiotics**
- **Valve surgery when indicated**
- **Avoid anticoagulants**
- ***Treat mycotic aneurysms***

Variable Significance of Brain MRI Findings in Infective Endocarditis and Its Effect on Surgical Decisions

Tia Chakraborty, MD; Eugene Scharf, MD; Daniel DeSimone, MD; Abdelghani El Rafei, MD; Waleed Brinjikji, MD; Larry M. Baddour, MD; Walter Wilson, MD; James M. Steckelberg, MD; Jennifer E. Fugate, DO; Eelco F.M. Wijdicks, MD, PhD; and Alejandro A. Rabinstein, MD

Abstract

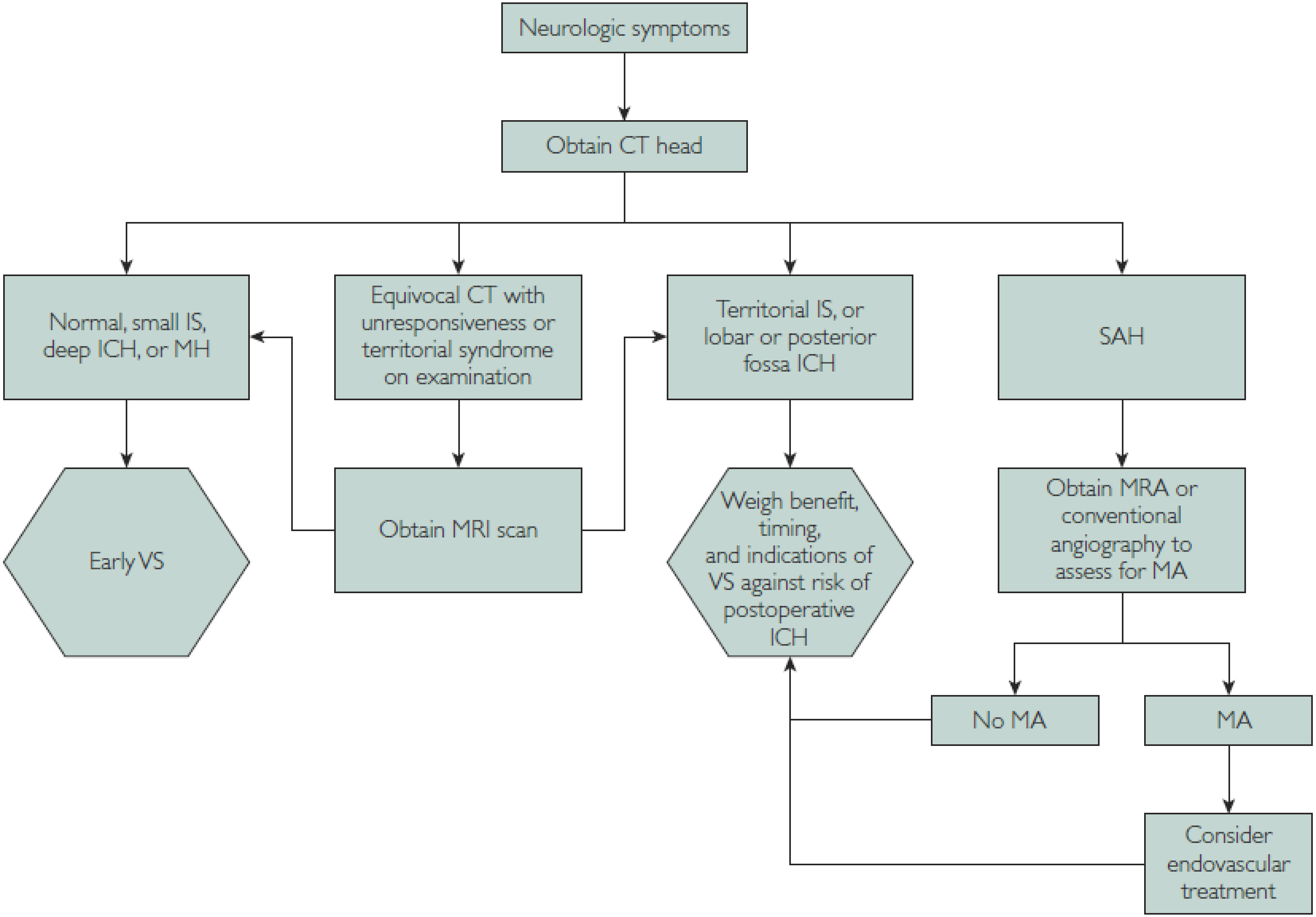
Objective: To determine how brain magnetic resonance imaging (MRI) findings impact clinical outcomes in patients with infective endocarditis (IE) and to propose a management algorithm for patients with neurologic symptoms who are candidates for valve surgery (VS).

Patients and Methods: Data from our center were retrospectively reviewed for patients hospitalized with IE between January 1, 2007, and December 31, 2014. Outcomes were postoperative intracerebral hemorrhage (ICH), 6-month mortality, and functional outcome at last follow-up as described by the modified Rankin Scale (mRS) score. Good outcome was defined as an mRS score of 2 or less.

Results: A total of 361 patients with IE were identified, including 127 patients (35%) who had MRI. One hundred twenty-six of 361 patients (35%) had neurologic symptoms, which prompted MRI in 79 of 127 patients (62%); 74 of 79 (94%) had acute or subacute MRI abnormalities. One patient with subarachnoid and multifocal ICH on MRI developed postoperative ICH. Patients with VS despite MRI abnormalities had lower 6-month mortality (odds ratio [OR], 0.17; 95% CI, 0.06-0.48; $P<.001$) and better functional outcome (OR, 4.43; 95% CI, 1.51-13.00; $P=.005$). Irrespective of VS, lobar or posterior fossa ICH on MRI was associated with 6-month mortality (OR, 3.58; 95% CI, 1.22-10.50; $P=.02$) and territorial ischemic stroke was inversely associated with good mRS (OR, 0.29; 95% CI, 0.13-0.66; $P=.002$). In neurologically asymptomatic patients who had VS, MRI findings did not impact 6-month mortality or functional outcomes.

Conclusion: Magnetic resonance imaging detects a large number of abnormalities in patients with IE. Preoperative lobar hematoma and large territorial stroke determine outcome irrespective of VS. When indicated, VS increases the odds of a good outcome despite MRI abnormalities.

 ■ Mayo Clin Proc. 2019;94(6):1024-1032


Neurologic symptoms
Obtain CT head
Normal, small IS, deep ICH, or MH
Equivocal CT with unresponsiveness or territorial syndrome on examination
Territorial IS, or lobar or posterior fossa ICH
SAH
Early VS
Obtain MRI scan
Weigh benefit, timing, and indications of VS against risk of postoperative ICH
Obtain MRA or conventional angiography to assess for MA
No MA
MA
Consider endovascular treatment

Coronary Revascularization

- Stroke is an uncommon but severe complication of coronary revascularization
- Main risk factors are older age and previous stroke
- Risk is lower with PCI (0.2% to 0.4%) than with CABG (1% to 3%)
- Silent infarctions much more common
- Most strokes are thromboembolic

The Safety and Efficacy of Thrombolysis for Strokes After Cardiac Catheterization

Pooja Khatri, MD,* Robert A. Taylor, MD,† Vanessa Palumbo, MD,‡ Venkatakrishna Rajajee, MD,§ Jeffrey M. Katz, MD,‖ Julio A. Chalela, MD,¶ Ann Geers, RN,* Joseph Haymore, MS, ACNP,# Daniel M. Kolansky, MD,** Scott E. Kasner, MD,†† for the Treatment of Acute Stroke after Cardiac Catheterization (TASCC) Study Group

Cincinnati, Ohio; Minneapolis, Minnesota; Florence, Italy; Chennai, India; Bronx, New York; Charleston, South Carolina; Washington, DC; and Philadelphia, Pennsylvania

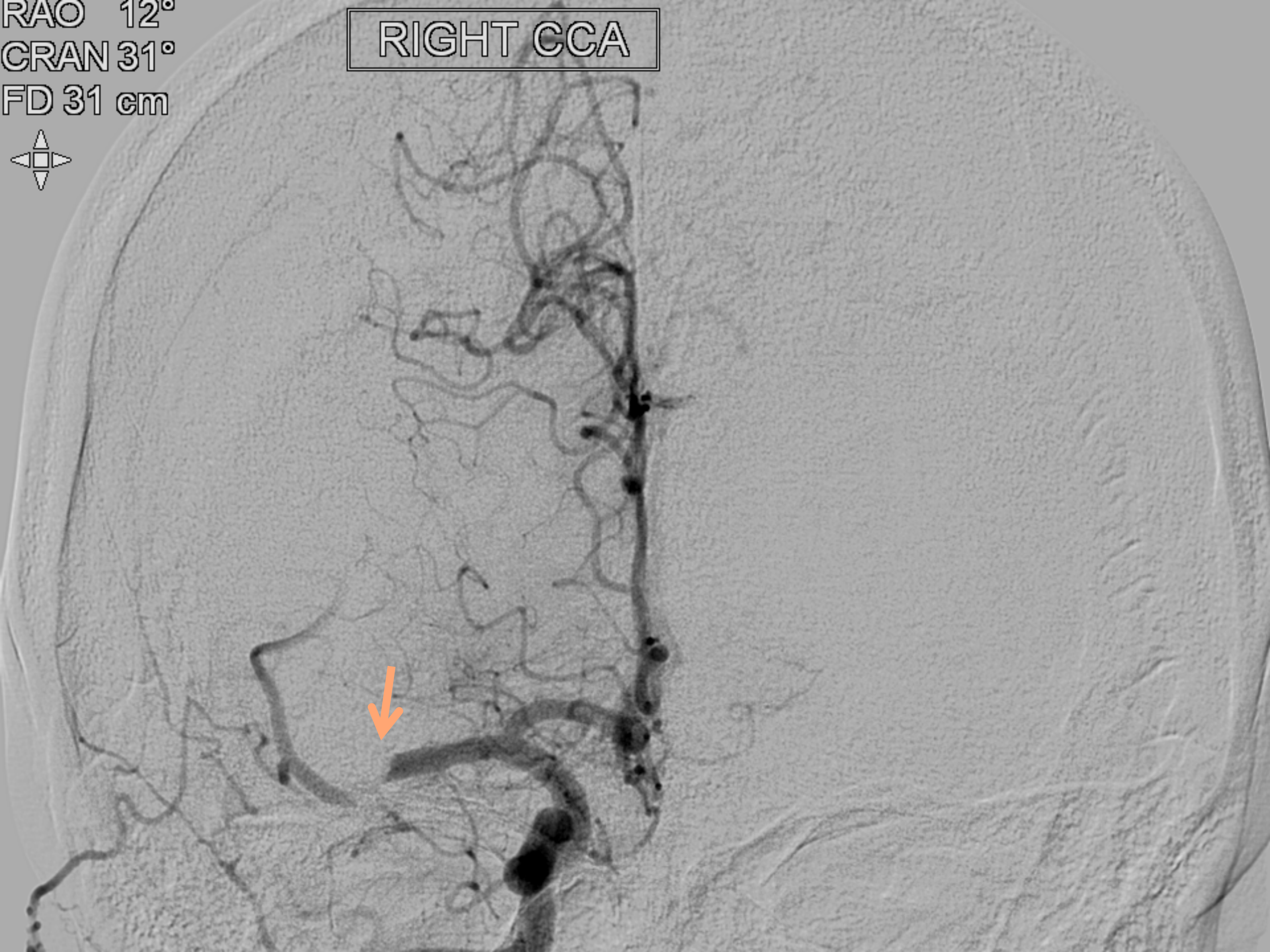
Objectives The purpose of this study was to systematically compare clinical outcomes of patients treated with thrombolysis with those without treatment in a multi-year, multicenter cohort of strokes after cardiac catheterization.

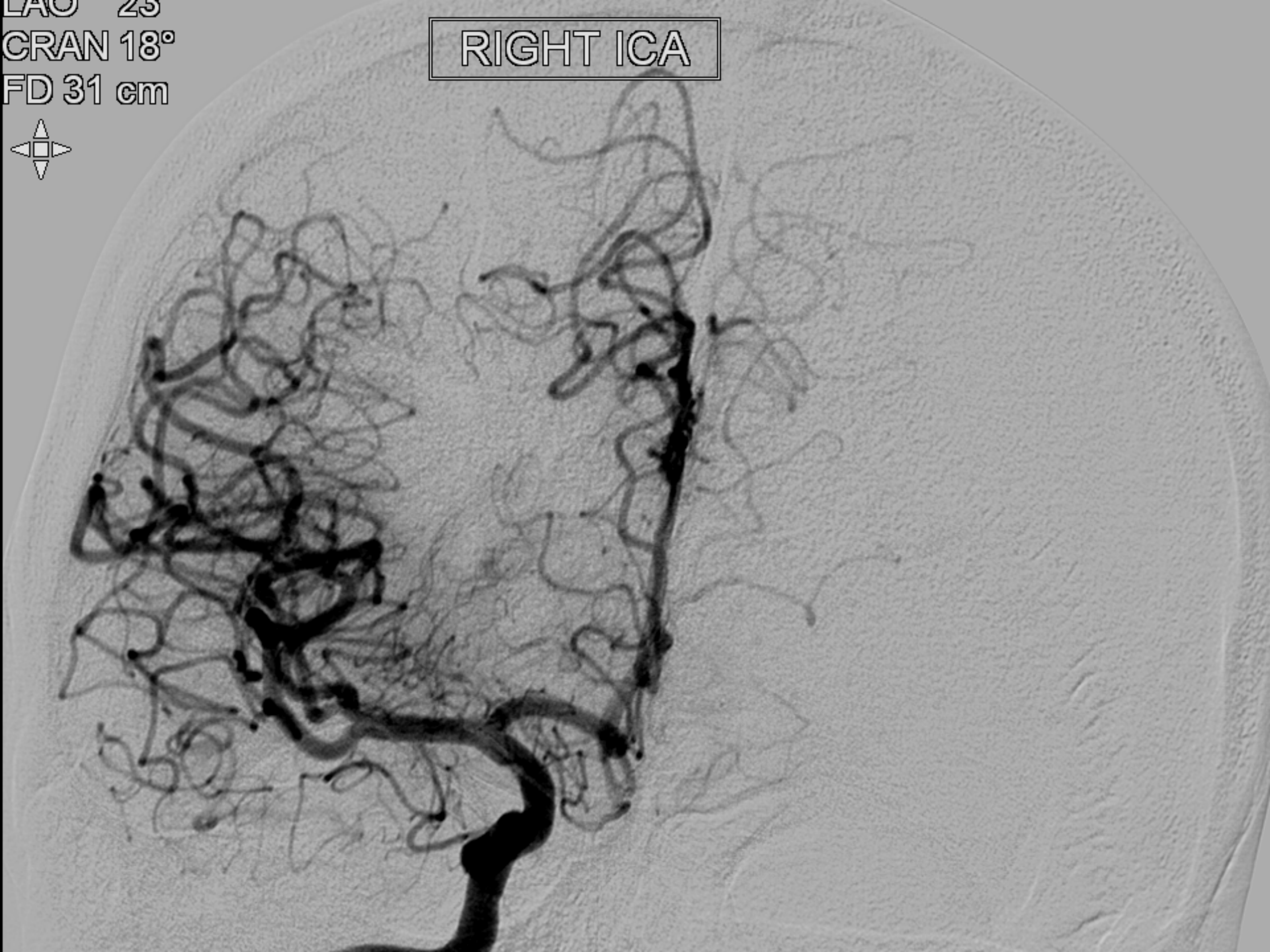
Background Ischemic strokes after cardiac catheterization procedures, although uncommon, lead to the morbidity and mortality of thousands of patients each year. Despite the availability of Food and Drug Administration–approved thrombolytic therapy for acute ischemic stroke since 1996, thrombolysis remains unestablished in the setting of cardiac catheterization, owing to unique concerns regarding safety and efficacy.

Methods Consecutive cases of ischemic stroke after cardiac catheterization were abstracted retrospectively and reviewed by clinicians at 7 major North American academic centers with acute stroke teams. Safety and efficacy outcome measures were pre-defined.

Results A total of 66 cases of ischemic strokes after cardiac catheterization were identified over 3 to 4 years; 12 (18%) were treated with thrombolysis, consisting of 7 intravenous and 5 intra-arterial recombinant tissue plasminogen activator cases. Improvement in stroke symptoms, as measured by the primary efficacy measure of median change in National Institutes of Health Stroke Scale score from baseline to 24 h, was greater in treated versus nontreated cases ($p < 0.001$). Additional secondary measures of efficacy also showed better outcomes in the treated group. There were no significant differences in bleeding events, defined as symptomatic intracerebral hemorrhage, hemopericardium, or other systemic bleeding resulting in hemodynamic instability or blood tranfusions. Mortality rates were also similar.

Conclusions Thrombolysis might improve early outcomes after post-catheterization strokes and seems safe in this context. Emergent cerebral revascularization should be a routine consideration. (J Am Coll Cardiol 2008;51:906–11)

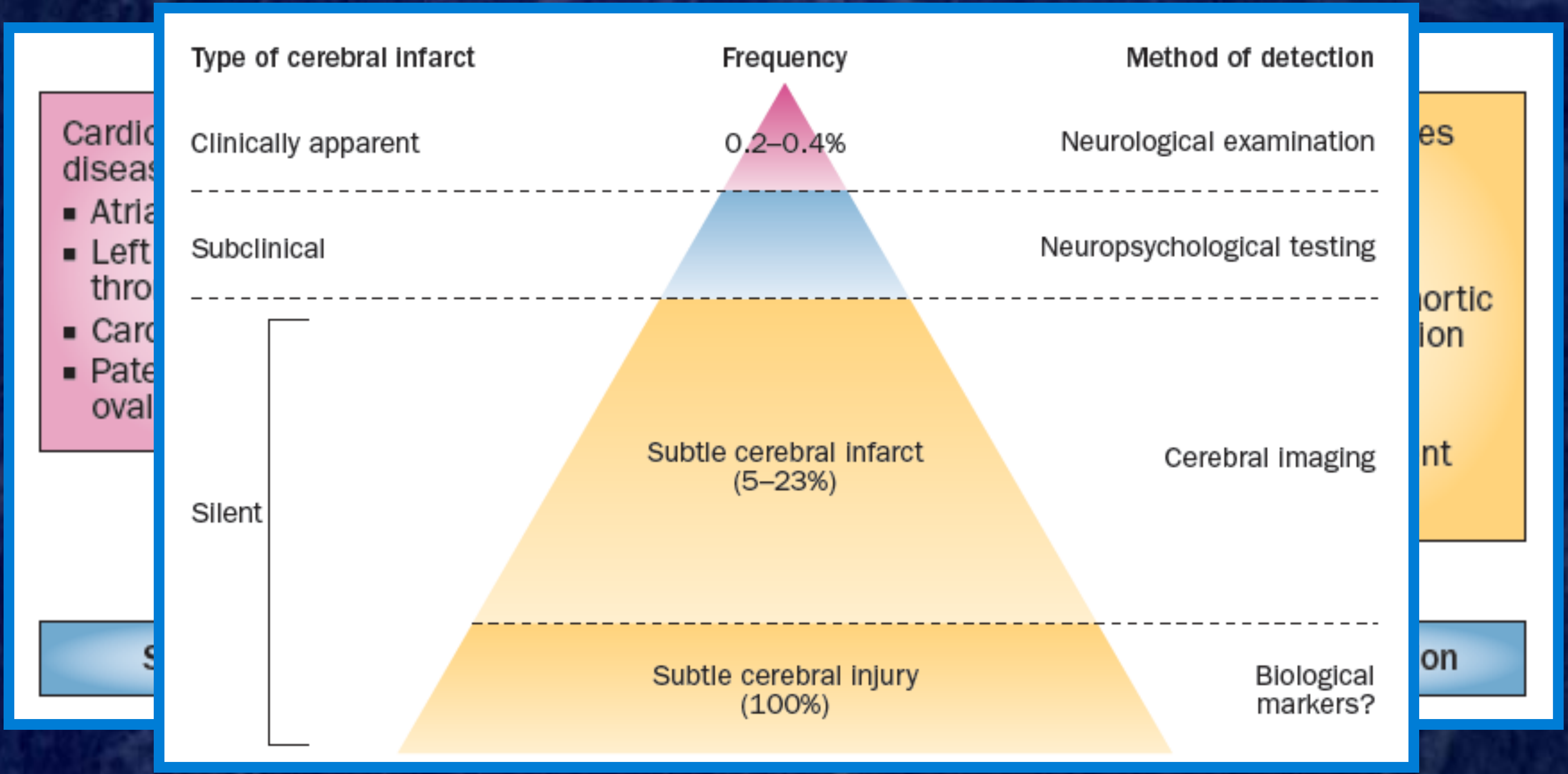

RAO 12°
CRAN 31°
FD 31 cm
RIGHT CCA


LAO 23
CRAN 18°
FD 31 cm
RIGHT ICA

Challenges of managing post-CABG stroke

- Delayed recognition
- High, if not prohibitive risk of IV lysis
- Patients may be less stable to undergo endovascular intervention
- Stroke is not always caused by thromboembolism

Silent cerebral infarctions



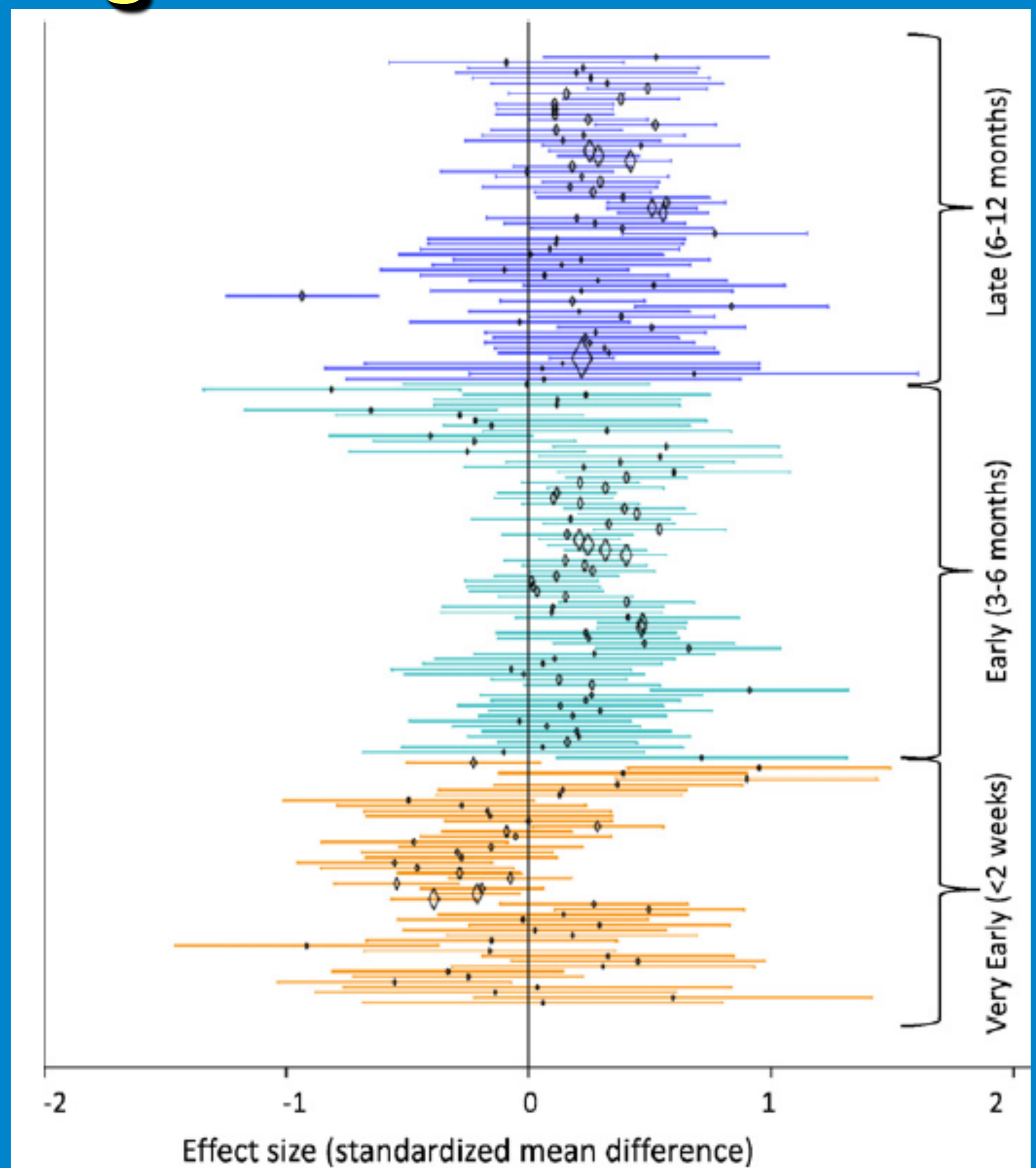
Nat Rev Cardiol 2013;10:696-706

Cognitive decline after CABG

- A recent meta-analysis concluded that there is little if any evidence of persistent cognitive decline after CABG
- However, there is still insufficient information on whether some patients may be at higher risk
- No interventions (off-pump, hypothermia, minimal vs conventional extracorporeal bypass) proved beneficial in reducing the risk of persistent cognitive decline

Ann Intern Med 2015;163:107-17

Cognition after CABG: goes but comes back



Neurosci Behav Rev 2012

MAYO CLINIC

LVAD

- Intracranial hemorrhage
  (intracerebral > subarachnoid >subdural)
- Ischemic infarction
- Seizures
- Cerebral hypoperfusion
- Cognitive impairment

Table 1. Summary of risk factors for neurologic complications in patients with CF-LVAD.

Preoperative risk factors	Intraoperative risk factors	Postoperative risk factors
Female gender	Surgical closure of the aortic valve	No aspirin 7 days prior to event
Diabetes mellitus	Cross-clamping the aorta with cardioplegic arrest	INR <2 or INR >3
Prior stroke	Inflow and outflow graft angles	Driveline/pump infection
Hypertension (SBP >140 or DBP >90)	Pulsatile flow device >Continuous flow device	Hypertension (MAP >90 mmHg)
Tobacco use	HeartWare >HeartMate II >HeartMate 3	Bacteremia
Malnutrition	Concurrent valve repair or CABG	UTI
Hyponatremia	Cardiopulmonary bypass time	Pump thrombosis
Atrial fibrillation		Venous thromboembolism
		Hypoalbuminemia
		Pump speed <9000 RPM

Expert Rev Cardiovasc Ther. 2018;16:909-917

Table 2. Current devices and stroke rate estimates.

Device	Stroke rate		
	6 Months	12 months	24 Months
HeartWare (C)	13.3%	16.9%	31.1%
HeartMate II (A)	10.1%	14.6%	15–19.2%
HeartMate 3 (C)	5.4–7.9%	9.4%	10.1%

C: centrifugal-flow device; A: axial-flow device.

Expert Rev Cardiovasc Ther. 2018;16:909-917

CV events with LVAD

- Mortality rate much higher after ICH than after ischemic stroke
- Highest with early ICH
- Major drop in chances of getting heart transplant
- Optimal timing of reinitiation of anticoagulation after large infarction or ICH remains unclear

ECMO

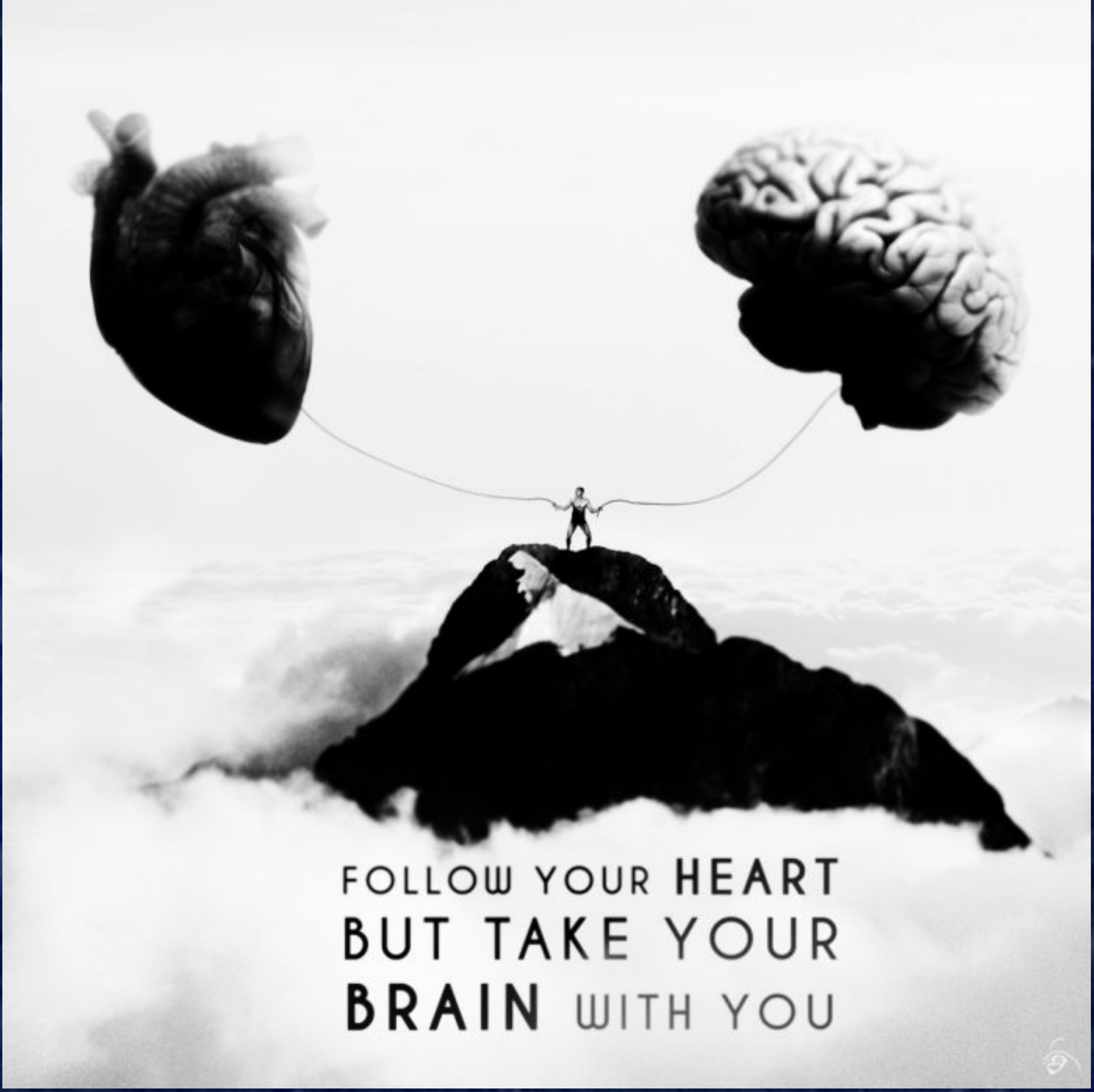
- Intracranial hemorrhage
- Ischemic infarction
- Seizures
- Cerebral hypoperfusion
- Encephalopathy
- Cognitive impairment
- Brain death

ECMO

- Rates of neurological complication are highly variable (15-50%) depending on definitions, age of patients, type of ECMO and indications
- Ischemic stroke or ICH: 5-10% (risk greatest in the first week)
- Brain complications are leading causes of mortality (especially ICH has 74% mortality rate)
- Possible risk factors for ICH: VA ECMO, greater fluctuations in CO2 upon connection, low platelet count, sepsis, hemolysis, renal failure

Key Messages

- AF and atrial cardiopathy are a major and growing risk factor for stroke
- Infective endocarditis primarily causes a septic arteritis
- PCI and CABG still have a 0.2-3% risk of clinical stroke and risk of higher in older patients with previous stroke
- ICH is a major cause of death in patients treated with LVAD or ECMO


FOLLOW YOUR HEART
BUT TAKE YOUR
BRAIN WITH YOU


Thank You