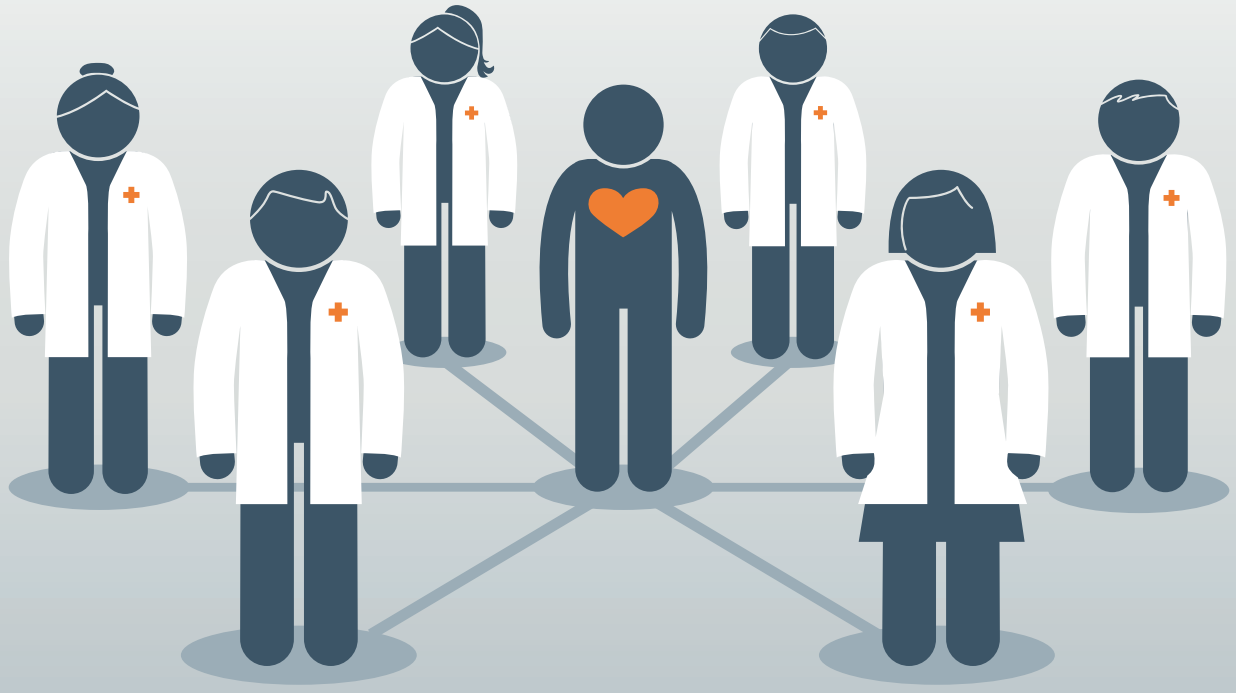
Hybrid AF™ Convergent Therapy Clinical Program Guide

for the Treatment of Long-Standing Persistent Atrial Fibrillation



This material is intended to provide and reinforce previous training addressing the closed-chest approach options and is intended for educational purposes only. Such information is not intended to be a substitute for professional medical advice, diagnosis or treatment. The material is not intended to direct clinical care in any specific circumstance. The judgment regarding a particular clinical procedure or treatment plan must be made by a qualified physician in light of the clinical data presented by the patient and the diagnostic and treatment options available.

AtriCure

Table of Contents

Overview

This resource aims to be a detailed and comprehensive guide for initiating a Hybrid AF Therapy program for the treatment of long-standing persistent atrial fibrillation. Included are clinical insight and best practice across the perioperative spectrum compiled from sites with extensive experience in the Hybrid AF Convergent Therapy. This guide should not be construed as medical advice or medical opinion related to any specific facts or circumstances. There are potential risks including (but not limited to) infection, cardiac tamponade, pulmonary vein stenosis, pericardial effusion, esophageal fistula, myocardial infarction, new arrhythmias, and thromboembolic complication. It is the responsibility of the individual clinician—and facility—to select the protocols, procedures, equipment and medications most appropriate for their patients' specific considerations.

- The EPi-Sense Guided Coagulation System is intended for the treatment of long-standing atrial fibrillation using radiofrequency (RF) energy via thoracoscopic, endoscopic, and pericardioscopic surgical techniques
- The EPi-Sense Guided Coagulation System may be used for temporary cardiac signal sensing and recording during surgery when connected to an external recording device
- The Hybrid AF Convergent Therapy includes sub-xiphoid access using a catheter, cannula, endoscope and radiofrequency (RF) generator to ablate the epicardial surface of cardiac tissue

Organizational Plan

It is strongly encouraged that a Core Team is formed at the onset of this process. This team should include key stakeholders across the different disciplines that will be involved. Often the first three members of this team are an Electrophysiologist (EP), a Cardiac Surgeon and an individual who functions as the Hybrid AF Therapy Coordinator/Navigator. From the onset this Coordinator may be full-time in this role or part-time as the program begins. In either event this Coordinator operates as the point person between departments—driving communication and gathering consensus as a program takes shape. Other members of the Core Team often include Administration, Nursing, Anesthesia, EP team, OR team and Finance.

In addition to the formation of the Core Team, informed patient selection, staff training, and clinical support promote a smooth launch. Pauses early in the program's development should be avoided since, in general, they make this period more challenging. The following text intends to help the Program establish a smart and flexible Organizational Plan that serves as a blueprint to this end.

Determine Core Team

- *Physicians, APP, Hybrid AF Therapy Coordinator/ Navigator, CVOR staff, Anesthesia, etc.*
- *When possible have the same CVOR staff, Anesthesia and Perfusion team members for all cases—especially during launch of the program*
- Ensure relevant scheduling coordinators are in frequent contact with one another regarding scheduled procedural days and/or cancellations
- Establish consensus within Core Team regarding patient flow
  - Schedule patient consults with both the EP and the Cardiac Surgeon prior to procedure
- Determine pre-operative testing protocol
  - CT or MRI to evaluate anatomy and pulmonary vein stenosis
  - TTE/TEE to evaluate mitral regurgitation, LA thrombus, and LVEF
  - Many facilities use the same screening process previously established for open heart surgery
  - Baseline 12-lead EKG or 24-hour Holter monitor
  - Basic pre-operative labs and anticoagulation status
- Establish consensus for time patients are expected to be in the procedure room
- Account to acquire necessary equipment and supplies in advance of launch
- Core Team to develop patient care plan and order sets (*Physicians should consider post-operative proton pump inhibitors (PPIs) to decrease the potential for post-operative esophageal irritations. Physicians should implement a comprehensive anti-coagulation protocol including pre-operative, intra-operative and post-operative anticoagulation management to prevent potential thromboemboli. Physicians should consider post-operative anti-inflammatory medication to decrease the potential for post-operative pericarditis and/or delayed post-procedure inflammatory pericardial effusions. Physicians should obtain post-procedural imaging (i.e. 1-3 weeks post-procedure) for detection of post-procedure inflammatory pericardial effusions.*)
  - Pre-operative care plans and order sets
  - Patient screening procedures/pre-admission testing (PAT)
  - Intra-operative patient care—plan and order sets
  - Post-operative patient care—plan and order sets
  - Determine where patient will be admitted post-op (PACU, ICU)
  - Gain consensus on discharge instructions

- Schedule team training to include case observation for relevant personnel (ideally not longer than one month prior to first procedure)
    - Surgeon case observation (recommended)
    - Surgeon cadaver lab (recommended: hands-on training)
    - EP case observation (optional)
    - Staff case observation (optional)
- Ideally schedule two patients on consecutive days to best facilitate proctoring as well as to optimize Surgeon and staff skill development
- Conduct comprehensive staff training; the clinical education processes by which a new program is started follows these steps prior to scheduling any clinical training
    - Cases are scheduled
    - Coordinate personnel for mock procedure (CVOR staff, Surgeon, Anesthesia, Perfusion) in advance of this training
    - Conduct mock procedure 1–2 weeks prior to first case
    - Ensure that all product and essential equipment are present (and in working order) prior to the mock procedure as they are integral to conducting this training
    - The mock procedure should occur in the procedure room and is scheduled for a minimum of 30–45 minutes (to include patient positioning, room setup, equipment setup, instrumentation, roles and responsibilities)
    - Non–CVOR staff training should occur no earlier than 1–2 weeks prior to the scheduled first case—ideally on the same day as the mock procedure. These unit in-services typically require 15–20 minutes and are conducted on a rotating basis (e.g., a 60-minute time block will allow for three 20-minute training rotations).
- Strongly consider developing protocols for risk mitigation of potential complications such as thromboembolic episodes, pericarditis or atrioesophageal fistula prior to the start of the program
- The first several cases may include a visiting Surgical Proctor (MD) and additional Clinical Education representation

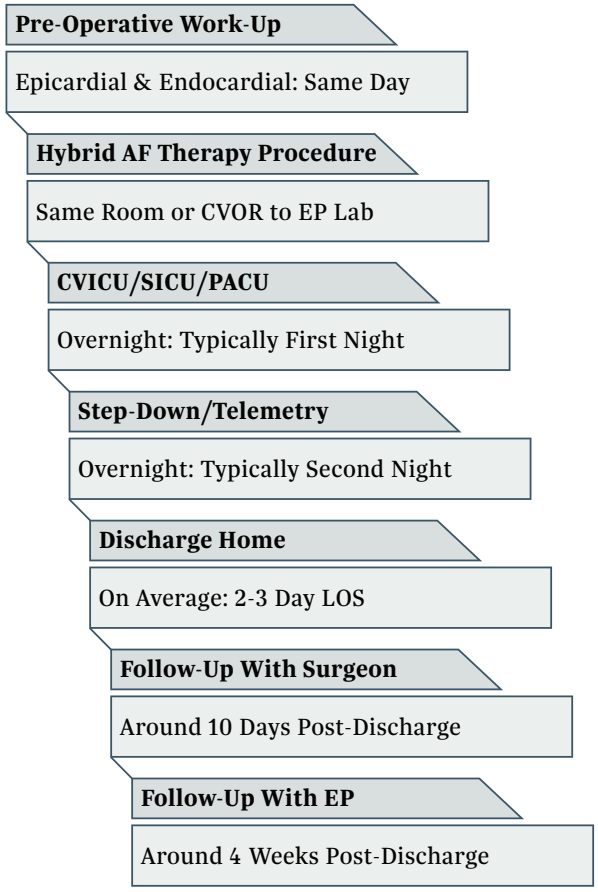
Procedural Logistics

Same Room vs. Separate Rooms

Coordination between Surgery and EP is critical in all variations of the Hybrid AF Therapy approach, but additional factors should be weighed when building a program wherein the epicardial and endocardial radiofrequency (RF) components are performed in the same procedure room. Often this room is a Hybrid OR/Hybrid Lab; however there is precedent in having the EP Lab serve for both components. When evaluating a candidate suite keep in mind the following considerations:

- If possible, schedule set days to perform the procedure. Agreeing with all disciplines on set day(s) of the week to perform the procedure ensures room and personnel availability (e.g., “TAVR days” / “Hybrid AF Therapy days”).
- Ensure the room is large enough for both epicardial and endocardial equipment. Appoint key personnel (RN) from Surgery and EP Lab to lead logistic, patient transport and equipment discussions.
- If equipment must be transported on a per case basis, ensure that such moves are practical
- If EP mapping and recording is not already installed, confirm the department is able/willing to transport
- Consider the proximity to desired recovery location or ICU
- Consider the room’s capabilities for general anesthesia
- Consider the location of pump standby and perfusion
- Confirm that the room possesses adequate mechanicals for suction, outlets and gas supply
- Verify that air flow and room sterility are adequate for surgical access
- Ensure that signage is adequate to limit traffic
- Verify that patient table is compatible with EP equipment (non-magnetic) and can accommodate reverse Trendelenburg

Figure 1. Patient Flow



Patient Selection

Thoughtful selection of the initial patients is important to the success of the program. The Core Team should have an established routine in place prior to attempting cases with a higher level of difficultly. The following guidelines will assist in determining which patients to select:

- Contraindications to the Hybrid AF Convergent Therapy
  - Patients with current thrombus of left atrial appendage
  - Patients with a history of Barrett's Esophagitis
  - Patients with an active infection or sepsis

Pre-Admission Testing (PAT)

- EP and Surgeon to establish pre-admission testing protocol
  - CT or MRI to evaluate anatomy and pulmonary vein stenosis
  - TTE/TEE to evaluate mitral regurgitation, LA thrombus, and LVEF
  - Most facilities use the same screening process as for open-heart surgery
  - Baseline 12-lead EKG or 24-hour Holter monitor
  - Basic pre-op labs and anticoagulation status

Pre-Operative Orders

- Develop a specific set of Hybrid AF Therapy pre-op orders. These orders should include appropriate pre-op laboratory studies, imaging and other studies the Core Team deem necessary. CT scan and/or MRI often are performed prior to the procedure to identify details of the pulmonary vein anatomy.
- Consider if the patient has an ICD. If so, plan to reprogram (disable therapy) to accommodate the procedure
  - If patient has an implantable pacemaker, ensure that the Surgeon is comfortable with current settings (mode/rate)
- Determine, in advance, who will read the TEE (Anesthesia or Cardiology)
- Anticoagulation (suspension and resumption)
  - It is imperative that the Surgeon and EP align on an anticoagulation protocol (and then communicate this strategy to the rest of the Core Team) prior to launching the program
  - Many programs suspend Direct Oral Anticoagulants (DOAC) 24–48 hours prior to procedure (depending on the DOAC and its guidelines). Typically to resume on the evening of day zero.
  - Many programs will have patients remain on Coumadin (warfarin) with dosage adjusted to target an INR greater than 1.5 (preferably 1.8 to 2.4)

Procedure Day

- Team to determine what area patients should be admitted through (e.g., Same-Day Surgery or Cardiology Holding Area to name a few)
- Ensure circulators from CVOR and EP Lab are notified of patient's arrival so they may interview patient prior to procedure
- Nurses should verify the following:
  - Patient is NPO
  - Updated bloodwork and diagnostics are on file
  - Day and time patient stopped taking their anticoagulation therapy along with all other medications, vitamins and supplements
  - Patient has signed all pertinent consents (Epicardial, Endocardial, TEE, etc.)

Anesthesia Considerations

- Patients need to be paralyzed for surgery
- If patient is to be transported from OR to EP Lab, movement plan should be discussed
- TEE should be conducted immediately pre-operatively as to rule out thrombus in LA/LAA (and to evaluate cardiac structure, valves and ejection fraction)
- Communicate the findings of the TEE within the Core Team
  - Ejection fraction
  - LA size/volume
  - Presence/absence of thrombus
  - Presence/absence of structural abnormalities
- IV access should be discussed with Surgeon; in most cases a central line is not needed
  - If the Surgeon desires a central line, consult with EP to ensure that it will not interfere with the endocardial RF component
- Patient should have a radial arterial line and Foley catheter
- After TEE is complete, the probe is removed
- An esophageal temperature probe is placed (confirmed by fluoroscopy) prior to any ablation

- Temperature probe placement typically follows one of two techniques
    - **Option one**: placement occurs prior to patient sterile prep. Using fluoroscopy, the probe's thermistors are advanced 1.5 to 2 vertebral bodies below the carina (visually confirm heart silhouette as another landmark).
    - **Option two**: confirm with fluoroscopy (and sterile drape) once the cannula and catheter are positioned within the pericardial space
- Upon temperature probe placement, it is imperative to secure the probe to prevent accidental migration or dislodgement
- Most hemodynamic variation occurs when the cannula is positioned along the left side of the heart (near the left pulmonary veins)
    - The Surgeon should provide notice to Anesthesia when navigating in this area
    - Generally, manipulation on the left side of the left atrial posterior wall has a greater effect than on the right side of the left atrial posterior wall. A pharmacologic agent of choice (usually an alpha-adrenergic agonist) can be used to elevate the patient's blood pressure during this time. Otherwise, there should be limited hemodynamic variations during lesion creation.
- Carefully consider the selection of vasopressors. Agents which affect inotropic function of the heart should be avoided if possible. In a normally functioning heart these agents can cause the heart to become hyperdynamic, impeding the Surgeon's ability to safely create epicardial lesions.
- Anesthesia needs to be vigilant in maintaining fluid balance. Large volumes (>1 L) given early in the procedure may lead to right atrial distention. This distention may limit the surgeon's ability to access the anterior aspect of the right pulmonary veins. In addition, the patient may receive large volumes of fluid during the endocardial RF ablation; hence all parties should be aware of fluid balance throughout.
- Consider giving a dose of Lasix at the end of the procedure to minimize potential of fluid overload
- Patient is extubated (dependent upon the patient's pre-confirmed pulmonary status

Materials and Equipment for Epicardial Component of the Hybrid AF Convergent Therapy Procedure

Non–Sterile

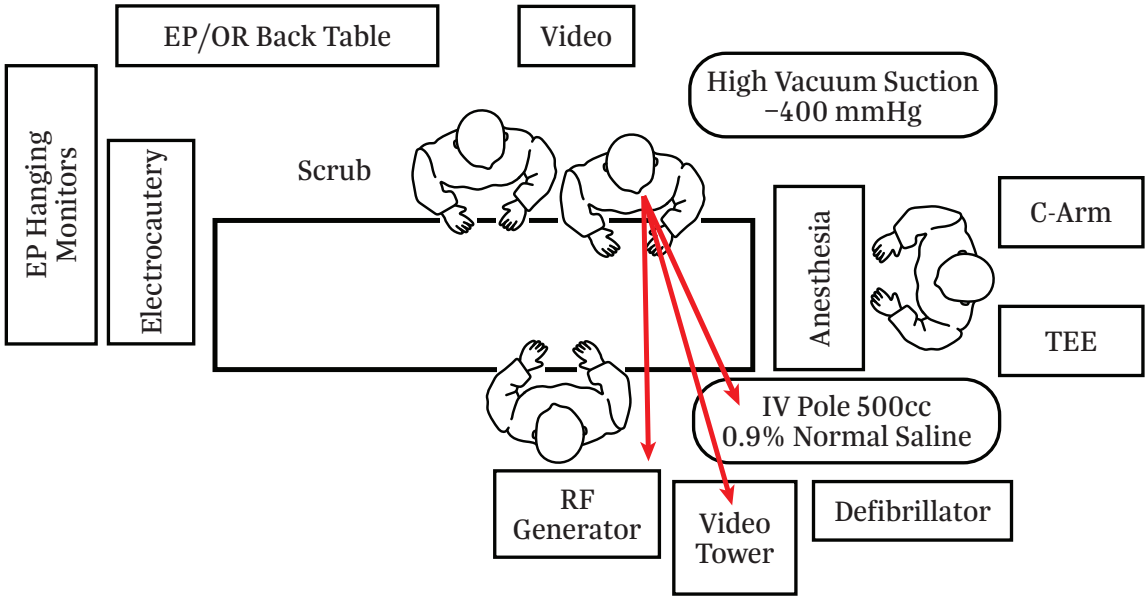
- ☐ RF Generator (power cable, footswitch)
- ☐ Laptop (power cable, data port cable)
- ☐ 1 Amp grounding pad
- ☐ Defibrillator pads
- ☐ TEE
- ☐ Arterial line
- ☐ CVP tray or 2 large bore IV sets
- ☐ Esophageal temperature probe
- ☐ Fluoroscopy capability
- ☐ Foley catheter
- ☐ Sequential Compression Device (SCD) (institution dependent)
- ☐ Warming blanket
- ☐ Standard grounding pad for Bovie
- ☐ Wall suction (–250 mmHg)
- ☐ High vacuum (–400 mmHg)
- ☐ Perfusion on standby

Sterile

- ☐ Pericardial window or open–heart surgical instrumentation
- ☐ EPi–Sense catheter
- ☐ Cannula
- ☐ RF connecting cable
- ☐ Drapes
- ☐ Dressings
- ☐ Sutures
- ☐ Standard surgical tray
- ☐ 5–mm 0–degree scope
- ☐ Vacuum tubing x2
- ☐ IV tubing or extension sets x2
- ☐ Asepto bulb syringe
- ☐ 19 or 24 Fr Blakemore drain
- ☐ Chest drainage system

Epicardial Component of the Hybrid AF Convergent Therapy Procedure Materials and Equipment *(continued)*

Figure 2. Hybrid AF Convergent Therapy Room Setup

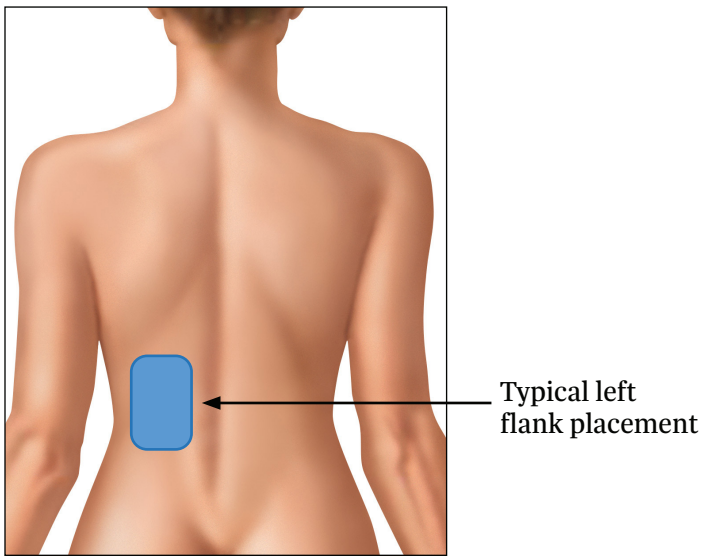


Endocardial RF materials and equipment will be determined by the Electrophysiologist and their team (institution dependent).

Patient Positioning and Prep

- Patient will be in supine position, arms tucked with no shoulder roll. If sleds must be used, try to avoid use on the right side as it may interfere with the Surgeon.
- General anesthesia
- Standard grounding pad for Bovie—usually placed on thigh or buttock
- Grounding pad (1 Amp) for RF generator—placed left flank (see Figure 3)
- EP patches for mapping—placed by EP staff prior to beginning of procedure (if being done same room/ same day)
- Defibrillator pads placed and connected to AED
- TEE performed to rule out thrombus (LAA)
- Central line usually placed after TEE
- Arterial line
- Foley catheter
- Warming blanket
- SCD (institution dependent)
- Esophageal temperature probe placed by Anesthesia and verified under fluoroscopy (C-Arm needed if done in cardiac OR)
- Prep chin to mid-thigh

Figure 3. 1 Amp Ground Pad Placement



EPi-Sense Catheter and Cannula Setup

EPi-Sense

- Attach one end of the sterile vacuum tubing to the graduated fitting where indicated on device handle by the vacuum symbol ("VAC") and the other end to the vacuum trap. Use the stopcock to apply and release the vacuum to the distal assembly.
- Ensure that the vacuum unit pressure is set to –400 mmHg (do not exceed –550 mmHg)
- Place unpressurized saline IV bag at patient height or above
- Connect perfusion tubing to female Luer connection where indicated on device handle by the perfusion "droplet" symbol
- Verify that IV line is fully open
- Insert IV tubing set into 0.9% normal saline bag (room temperature)
- Turn on vacuum pressure and prime device by engaging the suction with a sterile surface (gloved hand). Ensure that perfusion flow is functioning by observing drops in IV tubing drip chamber. Make sure the device is primed by observing perfusion at distal end of coagulation device before starting operation of device. Ensure that IV line is fully open.
- Connect RF cable to generator

Cannula

- Attach stopcock (supplied with the 30-cm cannula)
- Connect suction tubing to graduated fitted connector
- On stopcock, attach sterile IV tubing and connect to 1 LITER NS or STERILE WATER (room temperature, pressurized); alternatively, Asepto syringe may be used instead of IV tubing/pressurized 1 liter bag of fluid for cannula irrigation

Procedure Overview for OR Staff

- Surgeon makes small (3–4 cm) incision over xiphoid (+/– remove xiphoid)
- Surgeon establishes sub-xiphoid pericardial window
- Place AtriCure cannula behind the heart within pericardial window
- Introduce a scope through the cannula to identify landmarks on poster left atrium (0-degree 5 mm)
- Surgeon introduces EPi-Sense catheter through cannula (catheter has been prepped and primed)
- Irrigate (1L NS pressurized connected to cannula or with Asepto)
- Surgeon ablates posterior left atrium
- Once the epicardial ablation is completed, advance a drain—usually a 19 or 24 Fr Blakemore—through the cannula under direct vision, after which the cannula will be slowly removed. After this step is complete the Surgeon will pass the drain through the sub-xiphoid incision or lateral slit site and secure the drain to the skin (usually the left side).
- Endocardial RF ablation will follow (in either the same room or the EP Lab)
- Patient is extubated dependent on the patient's pre-confirmed pulmonary status

Post-Op Orders

Typical patient flow within the hospital length of stay (LOS) is an overnight stay in a critical-care unit, stepdown or telemetry the second day, and discharge home on the third day

- Usually the patient is best served with an independent set of orders for Hybrid AF Therapy
  - CABG orders are usually too in depth and invasive for most of these patients
  - Typically the patient will not require vent, inotropic or pressor support
  - EP orders usually fail to adequately address surgical aspects of case
- Respiratory concerns
  - Should start receiving instruction on Incentive Spirometry pre-operatively (and should begin immediately upon arrival to post-op unit)
- Wound care
  - Sub-xiphoid incision will have dressing; keep dry and follow nursing standard of care
  - Groin care: bruising is common and can sometimes be extensive; monitor closely
- DVT prophylaxis
  - No contraindication to using mechanical DVT prevention, unless the EP objects (venous sticks in the groins)
- Pain
  - Typically, pain is greatest in the first 24 hours, then quickly abates
  - PCA (morphine or Dilaudid) may be used but is not routinely necessary
- Steroids are thought to help reduce pericarditis, post-op pain, pericardial effusion
  - Administration of steroids
    - Solu-Medrol 125 mg IV pre-incision, then 40 mg IV every 6 hours for 36–48 hours
    - Solu-Cortef (hydrocortisone) 2 mg/kg IV every 6 hours for 3–6 doses
    - Oral prednisone starting night of surgery (dose is usually 1 mg/kg daily for 1–3 days post-procedure)
- Anti-inflammatory
  - Colchicine as tolerated (i.e., 0.3 mg BID initially either prophylactic a few days prior to procedure and, if tolerated, increase to 0.6 mg BID thru discharge and continue for 2–3 weeks)
- NSAIDs
  - Toradol is most commonly used in the immediate post-op period

- Thought must be given to Toradol contraindications
  - Renal function
  - Age
  - Allergy
  - Indocin is also very effective when patient is taking PO meds without dyspepsia or ileus
- Should be very careful to account for any history of GI bleed
  - Ibuprofen can also be used especially in outpatient setting
- GI prophylaxis
  - Most institutions use PPI or H2 blocker for prevention of stress gastritis (i.e., Protonix 40 mg 24 hours x 1 dose)
- Fluid balance
  - Monitor patient's fluid balance during the procedure time
  - May need diuretics due to fluid load
- Ambulation
  - Early ambulation helps prevent ileus
  - Goal: patient out of bed night of surgery and mobilized by post-op day one
  - Mobilization should be explicitly ordered by nursing staff (or PT)
  - Nursing staff (especially ICU) need to be aware of an expected two- or three-day hospital LOS
- Pericardial drain management
  - Drain output is typically serosanguineous (pinkish in tint or dark pink). The surgical team should be called when output is bright, frank blood.
  - Most facilities remove the drain the day after the procedure—provided there is no drop in Hgb—and hemodynamics are stable
  - Follow existing standard-of-care protocol for removal of drain (less than 100cc in 8-hour shift is not uncommon)
- Antiarrhythmic and anticoagulation management
  - It is not uncommon for patients to experience intermittent recurrence of arrhythmia(s) during the blanking period. This expectation should be communicated with the patient and referring physician prior to procedure.
  - Pre-operative antiarrhythmic drugs should be resumed post-procedure (and continued for at least 2–3 months) to maximize sinus rhythm while any edema abates
  - Bridging with heparin is suggested if the patient will be maintained on Coumadin
  - Restarting of DOACs should be coordinated by HCPs: typically, 6 hours post-procedure
  - Anticoagulation should be initiated regardless of patient's CHA2DS2-VASc Score

Discharge Instructions

Follow-up considerations (as established by HCPs in advance)

- Medications:
  - Pain management
  - Anticoagulation therapy
  - Antiarrhythmics
  - Gastric acid suppression (PPI or H2 Blocker for 1 month)
- Post-op restrictions as per standard nursing protocol
- Driving need not be restricted (except when prescribed narcotics)
- Patient instruction to include Hybrid AF Therapy Patient Card
- Patient should immediately contact their HCP in the event of any fevers, nausea, diarrhea, abdominal or chest fullness, difficulty swallowing and/or increase in pain
- As mentioned above, after an ablation many patients experience heart rate and rhythm changes which are not atypical and can occur for several months

Follow-Up, Monitoring and Data Collection

It is important to establish a uniform follow-up visit schedule such that outcomes data can be gathered/analyzed at consistent intervals. As such, the Core Team should:

- Agree on the definition of procedural success and failure
- Agree on monitoring method (e.g., EKG, 48- or 72-hour Holter, Reveal, event monitor)
- Define a process that outlines how data will be maintained and shared
- Agree who will be responsible to collect data

In summary, the Clinical Program Guide seeks to provide a road map for planning and implementing a successful program. This resource should be considered alongside the Physician Training Guide, CVOR Staff Training Guide, product IFU(s) and other supplemental resources as a program develops.

NOTES

EPi-Sense® Guided Coagulation System

U.S. Indications: *The EPi-Sense Guided Coagulation System is intended for the treatment of symptomatic long-standing persistent atrial fibrillation (continuous atrial fibrillation greater than 12 months duration) when augmented in a hybrid procedure with an endocardial catheter listed in the instructions for use, in patients (1) who are refractory or intolerant to at least one Class I and/or III antiarrhythmic drug (AAD); and (2) in whom the expected benefit from rhythm control outweighs the potential known risks associated with a hybrid procedure such as delayed post-procedure inflammatory pericardial effusions.* ***Contraindications*** *include patients with Barrett's Esophagitis, left atrial thrombus, a systemic infection, active endocarditis, or a localized infection at the surgical site at the time of surgery.* ***Adverse Events:*** *Reported adverse events associated with epicardial ablation procedure may include, but are not limited to, the following: pericardial effusion/cardiac tamponade, pericarditis, excessive bleeding, phrenic nerve injury, stroke/TIA/neurologic complication. Please review the Instructions for Use for a complete listing of contraindications, warnings, precautions and potential adverse events located at the following AtriCure web address: https://www.AtriCure.com/EPi-Sense-Coagulation-Device.* ***Warnings:*** *Physicians should consider post-operative anti-inflammatory medication to decrease the potential for post-operative pericarditis. and/or delayed post-procedure inflammatory pericardial effusions. Physicians should consider post-procedural imaging (i.e. 1-3 weeks post-procedure) for detection of post-procedure inflammatory pericardial effusions.* ***Precautions:*** *Precautionary measures should be taken prior to considering treatment of patients: (1) Deemed to be high risk and who may not tolerate a potential delayed post-procedure inflammatory pericardial effusion. (2) Who may not be compliant with needed follow-ups to identify potential safety risks. To ensure patients undergoing treatment with the EPi-Sense device are well informed, the benefits, potential risks and procedural outcomes associated with the EPi-Sense Hybrid Convergent procedure should be discussed with the patient. Physicians should document accordingly in the medical record. Qualified operators are physicians authorized by their institution to perform surgical sub-xyphoid pericardial access. The coagulation devices should be used by physicians trained in the techniques of minimally invasive endoscopic surgical procedures and in the specific approach to be used. Operators should undergo training on the use of EPi-Sense device before performing the procedure. Safety and effectiveness of concomitant left atrial appendage closure was not evaluated in the CONVERGE study. Follow-up should be conducted at approximately 30 days post-procedure to monitor for signs of delayed onset pericarditis or pericardial effusion.* ***Rx Only.***

ATRICURE, INC.
7555 Innovation Way
Mason, OH 45040 USA
+1 (866) 349-2342
www.AtriCure.com

PE-US-1093D-0122-G

AtriCure