Atrial Fibrillation (AF) Management - Adult

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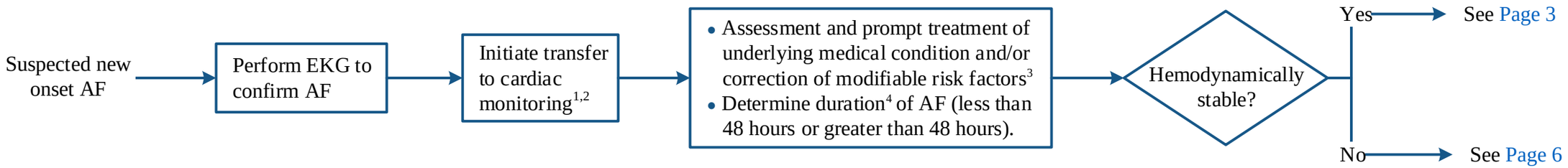
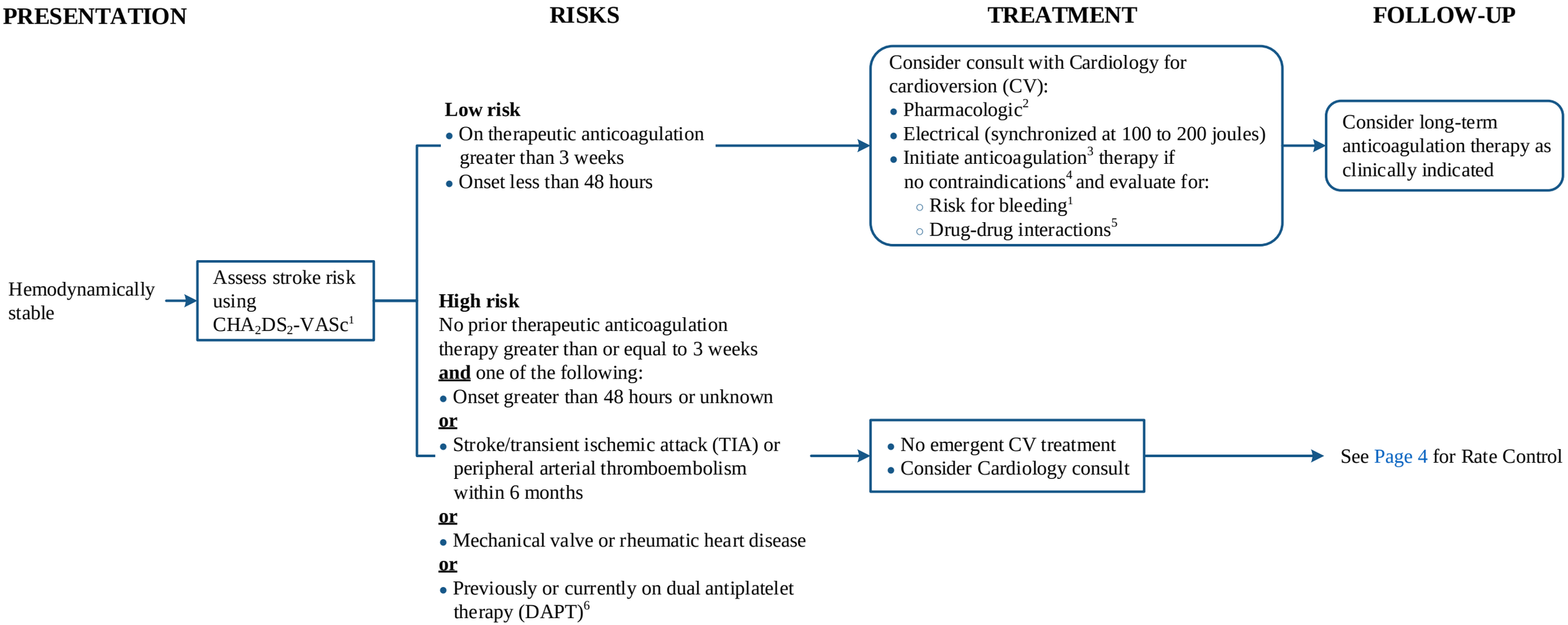
PATIENT PRESENTATION **ASSESSMENT**



[1] Refer to Adult Cardiac Monitoring Admission and Discharge Policy (#CLN0511)
[2] Transfer to cardiac monitoring may not be necessary for newly-diagnosed, rate controlled asymptomatic patients in the outpatient setting
[3] See Appendix A for Risk Factors for the Development of New Onset AF
[4] See Page 3 (RISKS) for treatment details based on duration

Atrial Fibrillation (AF) Management - Adult



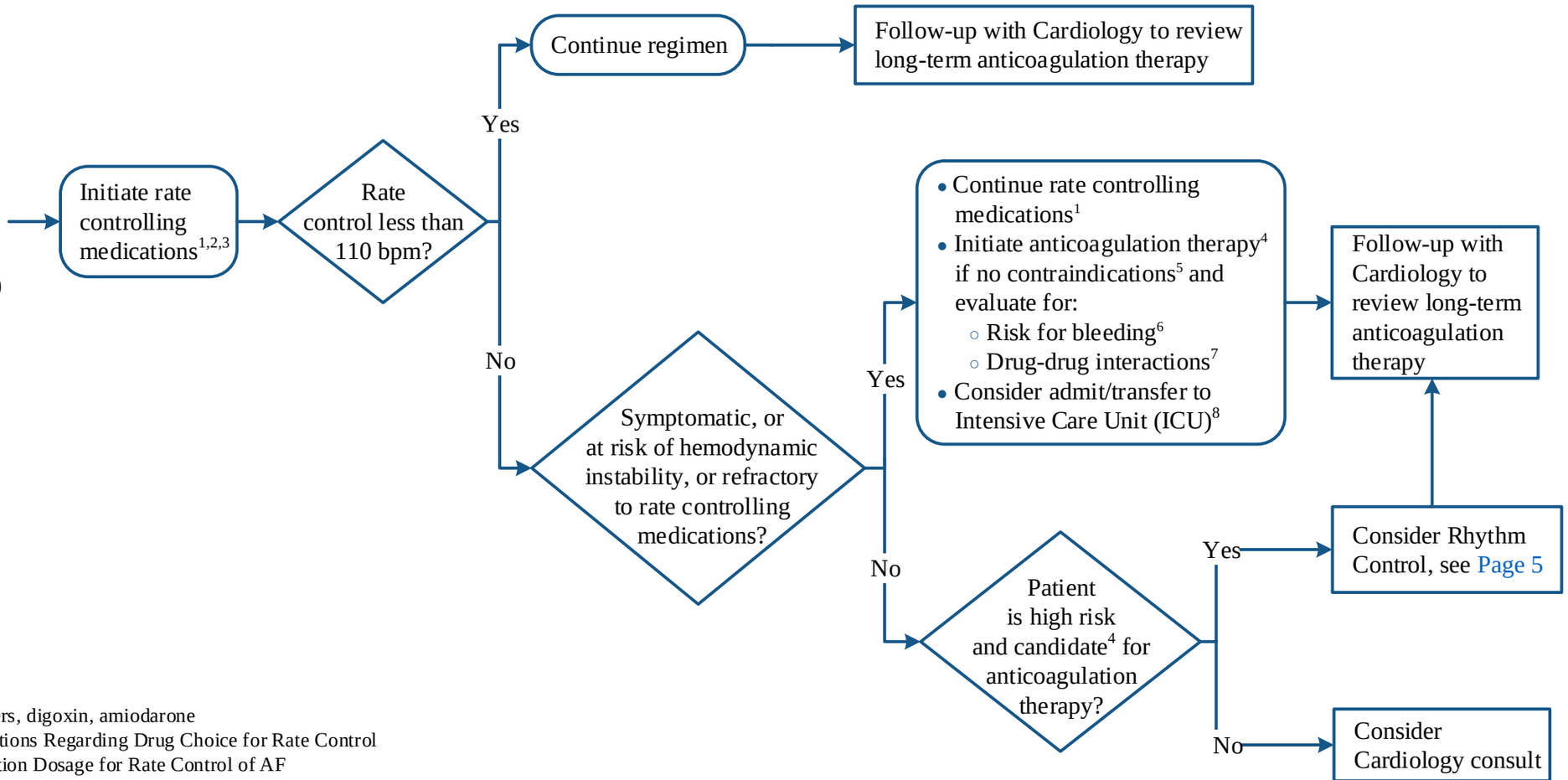
[1] See Appendix B for Risk Scores for Patients with AF (stroke and bleeding)
[2] See Appendix C for Chemical CV Exclusion Criteria
[3] See Appendix D for Anticoagulation Therapy Options for Cancer Patients
[4] See Appendix E for Contraindications to Anticoagulation Therapy
[5] Assessing for drug-drug interactions: Lexicomp® or Micromedex®, available at inside.mdanderson.org (for internal use only)
[6] Consider Benign Hematology consult

Atrial Fibrillation (AF) Management - Adult

Rate Control

Factors to consider for treatment include:

- Persistent AF
- Fewer symptoms
- Age greater than 65 years
- Hypertension
- No history of heart failure (HF)
- Patient preference
- Refractory to previous anti-arrhythmic drug therapy

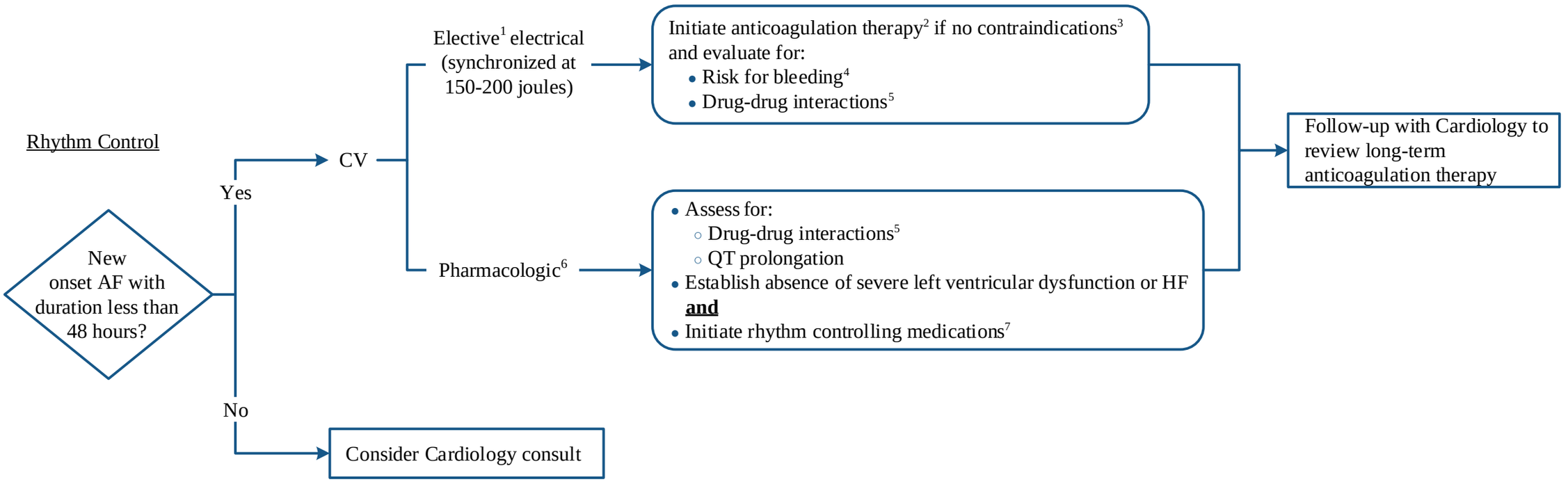


[1] Beta blockers, calcium channel blockers, digoxin, amiodarone
[2] See Appendix F for Special Considerations Regarding Drug Choice for Rate Control
[3] See Appendix G for Common Medication Dosage for Rate Control of AF
[4] See Appendix D for Anticoagulation Therapy Options for Cancer Patients
[5] See Appendix E for Contraindications to Anticoagulation Therapy
[6] See Appendix B for Risk Scores for Patients with AF (stroke and bleeding)
[7] Assessing for drug-drug interactions: Lexicomp® or Micromedex®, available at inside.mdanderson.org (for internal use only)
[8] Criteria for admit/transfer to ICU:
- Progressive hemodynamic instability
- Failure to respond to rate control agents

Department of Clinical Effectiveness V2
Approved by the Executive Committee of the Medical Staff on 10/30/2018

Atrial Fibrillation (AF) Management - Adult

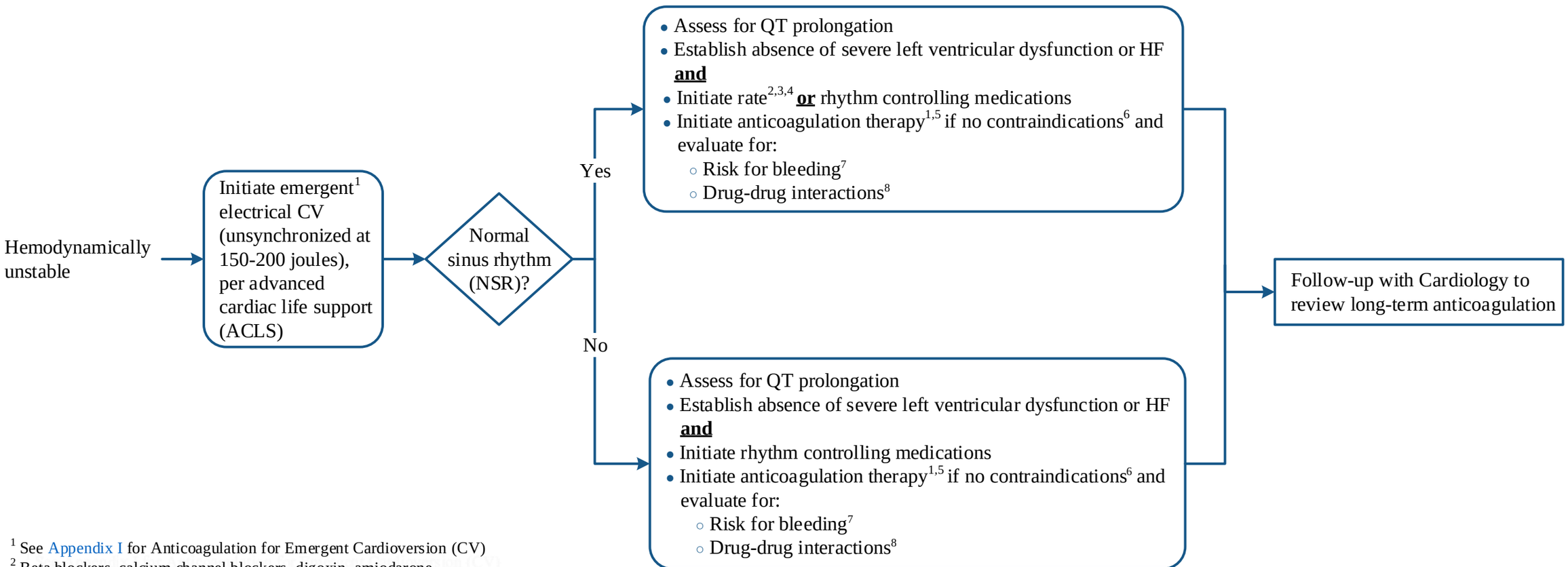
FOLLOW-UP



[1] See Appendix H for Anticoagulation Therapy for Elective Cardioversion (CV)
[2] See Appendix D for Anticoagulation Therapy Options for Cancer Patients
[3] See Appendix E for Contraindications to Anticoagulation Therapy
[4] See Appendix B for Risk Scores for Patients with AF (stroke and bleeding)
[5] Assessing for drug-drug interactions: Lexicomp® or Micromedex®, available at inside.mdanderson.org (for internal use only)
[6] See Appendix C for Chemical CV Exclusion Criteria
[7] Recommend consult to Cardiology before initiating rhythm controlling medications

Atrial Fibrillation (AF) Management - Adult

PRESENTATION **ASSESSMENT** **TREATMENT** **FOLLOW-UP**



[1] See Appendix I for Anticoagulation for Emergent Cardioversion (CV)
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[3] See Appendix F for Special Considerations Regarding Drug Choice for Rate Control
[4] See Appendix G for Common Medication Dosage for Rate Control of AF
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Atrial Fibrillation (AF) Management - Adult

APPENDIX A: Risk Factors for the Development of New-Onset AF

Patient Factors:

- Acid-base abnormalities
- Advanced age
- Anemia
- Electrolyte abnormalities
- Fluid overload
- Hypotension
- Hypoxemia
- Male sex
- Obesity
- Recent (within 24-48 hours) thoracic surgery (e.g., esophageal, lung, heart)

APPENDIX C: Chemical CV Exclusion Criteria

- Bundle branch block (BBB) (QRS greater than 120 ms)
- Preexisting 2nd/3rd degree atrioventricular block (AVB)
- Prolonged QT (QTc greater than 480) or Brugada
- Potassium less than 3 mEq/liter
- Patient already on an antiarrhythmic
- Pregnancy
- Severe hepatic or renal insufficiency with creatinine clearance (CrCl) less than 35 mL/minute

APPENDIX B: Risk Scores for Patients with AF (stroke and bleeding)[1]

Stroke or Systemic Embolism:

$CHADS_2$ VAS_c Score

	Condition	Points
C	Congestive Heart Failure	1
H	Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A	Age greater than or equal to 75 years	2
D	Diabetes mellitus	1
S_2	Prior stroke or TIA or thromboembolism	2
V	Vascular disease	1
A	Age 65-74	1
S_c	Sex category (1 point for female)	1

High risk: greater than or equal to 4

Bleeding:

HAS-BLED Score

	Condition	Points
H	Hypertension	1
A	Abnormal liver or renal function (1 point each)	1
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly (age greater than 65)	1
D	Drugs or alcohol (1 point each)	1

High risk: greater than or equal to 3

TIA = transient ischemic attack

[1] If patient has high risk of bleeding on full dose anticoagulation, consider aspirin 81 mg for anticoagulation

APPENDIX D: Anticoagulation Therapy Options for Cancer Patients

LMWH[1] Regimens for Treatment of Cancer Associated Thrombosis

DRUG	DOSE / ROUTE / FREQUENCY			MONITORING[2]	DOSE ADJUSTMENTS
Dalteparin (Fragmin®)* • Use dalteparin with caution in patients with platelets less than 50 K/microliter ***Preferred choice, FDA approved for cancer patients**	Round to nearest International Units (IU) dose, given subcutaneously daily			• Baseline CBC with platelets, aPTT, PT and serum creatinine • For surgical patients, platelets every 3 days between days 4 and 14 after beginning LMWH then as clinically indicated	• Consider reducing the daily dose by 50% when platelets are between 20 K/microliter - 50 K/microliter and to 5,000 IU when platelets are less than 20 K/microliter • If CrCl is less than 30 mL/minute: adjust dose to obtain anti-Xa level of 0.5-1.5 IU/mL (4-6 hours after fourth dose) • Obtain anti-Xa level in patients weighing greater than 150 kg or less than 50 kg, and adjust dose to obtain anti-Xa level of 1.5 IU/mL (4-6 hours after fourth dose)
	Actual Body Weight (kg)	Month 1 200 IU/kg	Months 2-6 150 IU/kg		
	Less than or equal to 56	10,000 IU	7,500 IU		
	57-68	12,500 IU	10,000 IU		
	69-82	15,000 IU	12,500 IU		
	83-98	18,000 IU	15,000 IU		
	Greater than or equal to 99	Limited data suggests dalteparin 200 IU/kg based on actual body weight (with no dose capping) in one or two divided doses. An alternative option is enoxaparin 1 mg/kg twice daily. Consider monitoring anti-Xa levels and adjust dose as needed.			
Enoxaparin (Lovenox®) • Use enoxaparin with caution in patients with platelets less than 100 K/microliter	1 mg/kg subcutaneously every 12 hours **or** 1.5 mg/kg* subcutaneously once daily in selected patients *Limited data suggest once per day dosing is inferior in cancer patients			Same as above	• If CrCl less than 30 mL/minute: use 1 mg/kg once daily • Obtain anti-Xa level in patients with weight greater than 150 kg or less than 50 kg ◦ For 1 mg/kg every 12 hour dosing regimen: adjust dose to obtain anti-Xa level of 0.6 – 1 IU/mL (4-6 hours after fourth dose) ◦ For 1.5 mg/kg once daily dosing regimen: adjust dose to obtain anti-Xa level of 1 - 1.5 IU/mL (4-6 hours after fourth dose)

[1] Notes:
- Low-Molecular Weight Heparins (LMWH) (preferred agents)
- If LMWHs are not accessible, consider switching to warfarin after 5 days of LMWH therapy. Heparin and warfarin therapy should overlap 5 days.
- Patients who tolerate anticoagulation should be continued on it indefinitely or until active cancer resolves
- Patient should be observed closely for bleeding and signs and symptoms of neurological impairment if therapy is administered during or immediately following diagnostic lumbar puncture, epidural anesthesia, or spinal anesthesia

[2] If lab results indicate heparin induced thrombocytopenia, follow management per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm

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APPENDIX D: Anticoagulation Therapy Options for Cancer Patients - continued

Unfractionated Heparin (UFH)

TREATMENT	MONITORING
• IV heparin infusion[1] (Refer to Adult Heparin Infusion Order Set for dosing) • **If fixed dose, unmonitored subcutaneous UFH is chosen** ◦ Initial dose: 333 units/kg subcutaneously times one dose, followed by 250 units/kg subcutaneously twice daily in addition to warfarin for at least 5 days until the INR is greater than 2 for 24 hours	Baseline CBC with platelets, aPTT/PT, serum creatinine

Warfarin[2] (Selected Vitamin K Antagonist) – For long-term management

TREATMENT	MONITORING
• Overlap warfarin (2.5 – 5 mg PO) with induction therapy (LMWH, Factor Xa Inhibitor, or subcutaneous UFH) beginning on Day 1 of therapy • Continue induction therapy subcutaneously until INR greater than or equal to 2 for two days, AND patient has received at least 4-5 days of induction therapy overlap	• INR Goal: 2-3 • Baseline CBC with platelet count, PT/INR, liver function tests • Follow-up for PT/INR within 3-5 days, then at least every month if not more frequently

Fondaparinux (Arixtra®) (Factor Xa Inhibitor) – Fondaparinux dose subcutaneously daily

ACTUAL BODY WEIGHT (kg)	FONDAPARINUX DOSE	MONITORING	
Less than 50 50 – 100 Greater than 100	5 mg 7.5 mg 10 mg	Baseline CBC with platelets, aPTT/PT, serum creatinine	• If CrCl is between 30 - 50 mL/minute: use with caution • If CrCl is less than 30 mL/minute: contraindicated • Use fondaparinux with caution in patients with platelets less than 100 K/microliter

[1] Indications for IV heparin infusion: post-operative patients, neurosurgery patients, presence of mechanical heart valves, and history of spinal block

[2] Use of warfarin in cancer patients has been shown to be less effective at preventing clot recurrence than LMWH

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APPENDIX D: Anticoagulation Therapy Options for Cancer Patients - continued

Direct Oral Anticoagulants (DOACs) (ATTENTION: Expert panels DO NOT RECOMMEND use of these drugs in patients with cancer. A multidisciplinary consultation is strongly recommended with Benign Hematology, Cardiology, and/or General Internal Medicine. Each case needs to be individually assessed prior to use of DOACs).

DOACs	**Rivaroxaban (Xarelto®)** Oral Factor Xa Inhibitor		**Dabigatran (Pradaxa®)** Direct Thrombin Inhibitor	
Non-valvular atrial fibrillation (NVAF) *Not for any heart valve*	CrCl greater than 50 mL/minute	20 mg once daily with food in evening	CrCl greater than 30 mL/minute	150 mg twice daily
			CrCl 15-30 mL/minute	75 mg twice daily
	CrCl 15-50 mL/minute	15 mg once daily with food in evening	CrCl less than 15 mL/minute **or** HD	No recommendations
			CrCl 30-50 mL/minute **and** dronaderone or ketoconazole	75 mg twice daily
	CrCl less than 15 mL/minute or ESRD	Avoid use	CrCl less than 30 mL/minute **and** Pgp-I	Avoid use
			Any P-glycoprotein inducer	Avoid use
Use in liver disease	CTP class B or C: NOT recommended		No recommendations by manufacturer	
Contraindications	Active bleed; spinal puncture, neuroaxial anesthesia			
Significant drug-drug interactions[1]	P-glycoprotein and CYP 3A4 interactions		P-glycoprotein interactions	
Monitoring parameters	• Routine monitoring of coagulation tests not required • Baseline CBC with differential, SCr, and hepatic function tests			

Pgp-I = P-glycoprotein inhibitor; CrCl = creatinine clearance (mL/minute); SCr = serum creatinine; ESRD = end stage renal disease; HD = hemodialysis; CTP = Child-Turcotte-Pugh score

Reasons to avoid use of DOACs in the cancer population:

- Limited number of patients with cancer studied in NOAC clinical trials
- Lack of standardized testing for monitoring
- Limited availability of reversal agents
- Complicated drug-drug interactions with chemotherapy agents

[1] Assessing for drug-drug interactions: Lexicomp® or Micromedex®, available at insidemdanderson.org (for internal use only)

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APPENDIX D: Anticoagulation Therapy Options for Cancer Patients - continued

Direct Oral Anticoagulants (DOAC) (ATTENTION: Expert panels DO NOT RECOMMEND use of these drugs in patients with cancer. A multidisciplinary consultation is strongly recommended with Benign Hematology, Cardiology, and/or General Internal Medicine. Each case needs to be individually assessed prior to use of DOACs).

DOACs	Edoxaban (Savaysa®)[1] Oral Factor Xa Inhibitor		Apixaban (Eliquis®)[1] Oral Factor Xa Inhibitor	
Non-valvular atrial fibrillation (NVAF) *Not for any heart valve*	CrCl greater than 95 mL/minute **MUST assess CrCl before initiating**	Avoid use	Age greater than or equal to 80 years Weight less than or equal to 60 kg SCr greater than or equal to 1.5 mg/dL	0-1 criterion: 5 mg twice daily 2-3 criteria: 2.5 mg twice daily
	CrCl greater than 50 mL/minute to 95 mL/minute	60 mg daily	ESRD on HD	5 mg twice daily If age greater than or equal to 80 years or body weight less than or equal to 60 kg then 2.5 mg twice daily
	CrCl 15-50 mL/minute	30 mg daily	Strong CYP 3A4 inhibitors (ketoconazole, itraconazole, ritonavir, clarithromycin) **and** P-gp inhibitors	Decrease current dose by 50% [If on 2.5 mg twice daily then **AVOID**]
	CrCl less than 15 mL/minute	Avoid use		
Use in liver disease	CTP class B or C: NOT recommended		CTP class C: NOT recommended	
Contraindications	Active bleed; spinal puncture, neuroaxial anesthesia			
Significant drug-drug interactions[2]	P-glycoprotein and CYP 3A4 interactions			
Monitoring parameters	• Routine monitoring of coagulation tests not required • Baseline CBC with differential, SCr, and hepatic function tests			

Pgp-I = P-glycoprotein inhibitor; CrCl = creatinine clearance (mL/minute); SCr = serum creatinine; ESRD = end stage renal disease; HD = hemodialysis; CTP = Child-Turcotte-Pugh score

Reasons to avoid use of DOACs in the cancer population:

- Limited number of patients with cancer studied in DOAC clinical trials
- Lack of standardized testing for monitoring
- Limited availability of reversal agents
- Complicated drug-drug interactions with chemotherapy agents

[1] Edoxaban and apixaban are currently not on the MD Anderson formulary

[2] Assessing for drug-drug interactions: Lexicomp® or Micromedex®, available at insidemdanderson.org (for internal use only)

APPENDIX E: Contraindications to Anticoagulation Therapy

Absolute contraindications:

- Cerebral hemorrhage, hemorrhage in the eye or vital organs, or a drop in hemoglobin of 2 grams/dL in 24 hours
- Neurosurgery[1], ocular surgery (excluding cataract), or intracranial bleeding within past 10 days

Relative contraindications:

- Brain metastases with higher risk of bleeding (renal, choriocarcinoma, melanoma, thyroid cancer)
- Spinal procedure and/or epidural placement
- Major trauma or head trauma
- Major abdominal surgery within 48 hours
- Severe hypertension (systolic BP greater then 200 mmHg, diastolic BP greater than 120 mmHg)
- Endocarditis/pericarditis
- Gastrointestinal or genitourinary bleeding within past 14 days
- Preexisting coagulopathy
- Thrombocytopenia less than 50 K/microliter
- Hypersensitivity to heparin, LMWH, or HIT
- Patient on active protocol that prohibits use of anticoagulation
- Bleeding diathesis

APPENDIX F: Special Considerations Regarding Drug Choice[2] for Rate Control

Clinical Condition	Drug of Choice[2]	Caution
Reactive airway disease (asthma, chronic obstructive pulmonary disease)	Calcium channel blockers	$Beta_1$ selective beta blockers may be used with caution
Hypertension and HF with normal left ventricular systolic function	Beta blockers or calcium channel blockers	
Left ventricular systolic dysfunction with or without HF	Beta blockers or digoxin	Beta blockers should be used with caution as not to decompensate. Calcium channel blockers are contraindicated.
No other cardiovascular disease	Beta blockers or calcium channel blockers	

[1] IV heparin administration acceptable
[2] Obtain EKG for baseline pre-excitation

APPENDIX G: Common Medication Dosage for Rate Control of AF[1,2]

	Intravenous Administration	Usual Oral Maintenance Dose
Beta Blockers		
Metoprolol tartrate	2.5-5 mg IV bolus over 2 minutes; up to 3 doses	25-100 mg twice daily
Metoprolol XL (succinate)	N/A	50-400 mg once daily
Atenolol	N/A	25-100 mg once daily
Esmolol	500 mcg/kg IV bolus over 1 minute, then 50-300 mcg/kg/minute IV	N/A
Propranolol	1 mg IV over 1 minute, up to 3 doses at 2-minute intervals	10-40 mg three to four times a day
Nadolol	N/A	10-240 mg four times a day
Carvedilol	N/A	3.125-25 mg twice daily
Bisoprolol	N/A	2.5-10 mg once daily
Nondihydropyridine Calcium Channel Blockers		
Verapamil	0.075-0.15 mg/kg IV bolus over 2 minutes; may give an additional 10 mg after 30 minutes if no response, then 0.005 mg/kg/minute infusion	180-480 mg once daily (extended release)
Diltiazem	0.25 mg/kg IV bolus over 2 minutes, then 5-15 mg/hour	120-360 mg once daily (extended release)
Digitalis Glycosides		
Digoxin	0.25 mg IV with repeat dosing to a maximum of 1.5 mg over 24 hours	0.125-0.25 mg once daily

[1] Refer to Adult Cardiac Medication Monitoring Guidelines Policy (#CLN0500)
[2] Not to be used if evidence of pre-excitation on EKG

APPENDIX H: Anticoagulation Therapy for Elective Cardioversion (CV)

Duration of AF	Thromboembolism Risk	Anticoagulation Before CV	Anticoagulation After CV
Less than 48 hours	Low	Optional	Minimum of 4 weeks
Less than 48 hours	High	Periprocedural	Long term
Greater than 48 hours	Low	Minimum of 3 weeks[1]	Minimum of 4 weeks
Greater than 48 hours	High	Minimum of 3 weeks[1]	Long term

[1] Alternatively, anticoagulation can be initiated and once therapeutic, a transesophageal echocardiogram should be performed, especially for patients with $CHADS_2$-VAS_c score of 2 or more. If no thrombi are present, then CV can be performed.

APPENDIX I: Anticoagulation for Emergent Cardioversion (CV)

Duration of AF	Thromboembolism Risk	Anticoagulation Before CV	Anticoagulation After CV
Less than 48 hours	Low	Initiate immediately[1]	Optional
Less than 48 hours	High	Initiate immediately[1]	Long term
Greater than 48 hours	Low	Initiate immediately[1]	Minimum of 4 weeks
Greater than 48 hours	High	Initiate immediately[1]	Long term

[1] Usually with heparin. Emergent CV should not be delayed while waiting for anticoagulation.

APPENDIX J: Child-Turcotte-Pugh (CTP) Scoring System

Chemical and Biochemical Parameters	Points for Increasing Abnormality		
	1	2	3
Hepatic encephalopathy	None	Grade 1 or 2, or suppressed with medication	Grade 3 or 4, or refractory to medication
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Serum albumin	Greater than 3.5 g/dL	2.8 – 3.5 g/dL	Less than 2.8 g/dL
Total bilirubin For primary biliary cirrhosis	Less than 2 mg/dL 1 – 4 mg/dL	2 – 3 mg/dL 4 – 10 mg/dL	Greater than 3 md/dL Greater than 10 mg/dL
Prothrombin time prolonged or INR	less than 4 seconds Less than 1.7	4 – 6 seconds 1.7 – 2.3	Greater than 6 seconds Greater than 2.3

*CTP score is obtained by adding the score for each parameter.
CTP class:
Class A = 5 to 6 points
Class B = 7 to 9 points
Class C = 10 to 15 points

SUGGESTED READINGS

Elmouchi, D. A., VanOosterhout, S., Muthusamy, P., Khan, M., Puetz, C., Davis, A. T., & Brown, M. D. (2014). Impact of an emergency department–initiated clinical protocol for the evaluation and treatment of atrial fibrillation. *Critical Pathways in Cardiology*, 13(2), 43-48.

January, C. T., Wann, L. S., Alpert, J. S., Calkins, H., Cigarroa, J. E., Cleveland Jr, J. C., ... Murray, K. T. (2014). ACC/AHA Task Force Members 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation*, 130(23), 2071-2104.

Moukabary, T., & Gonzalez, M. D. (2015). Management of atrial fibrillation. *Medical Clinics*, 99(4), 781-794.

Pugh, R., Murray-Lyon, I. M., Dawson, J. L., Pietroni, M. C., & Williams, R. (1973). Transection of the oesophagus for bleeding oesophageal varices. *British Journal of Surgery*, *60*(8), 646-649. http://www.ncbi.nlm.nih.gov/pubmed/?term=4541913 or http://www.mdcalc.com/child-pugh-score-for-cirrhosis-mortality

Sibley, S., & Muscedere, J. (2015). New-onset atrial fibrillation in critically ill patients. *Canadian Respiratory Journal*, 22(3), 179-182.

Steinberg, B. A., Beckley, P. D., Deering, T. F., Clark, C. L., Amin, A. N., Bauer, K. A., ... Bhatt, D. L. (2013). Evaluation and management of the atrial fibrillation patient: a report from the Society of Cardiovascular Patient Care. *Critical Pathways in Cardiology*, 12(3), 107-115.

Verma, A., Cairns, J. A., Mitchell, L. B., Macle, L., Stiell, I. G., Gladstone, D., ... Healey, J. F. (2014). 2014 focused update of the Canadian Cardiovascular Society Guidelines for the management of atrial fibrillation. *Canadian Journal of Cardiology*, 30(10), 1114-1130.

Woosley, R. L., Heise, C. W., & Romero, K. A. Qtdrugs list. https://www.CredibleMeds.org. Accessed August 17, 2018.

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